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(54) PIPERAZINE-SUBSTITUTED BENZOTHIOPHENE DERIVATIVES AS ANTIPSYCHOTIC AGENTS

PIPERAZIN-SUBSTITUIERTE BENZOTHIOPHENDERIVATE ALS ANTIPSYCHOTISCHE WIRKSTOFFE

DÉRIVÉS DE BENZOTHIOPHÈNE SUBSTITUÉ PAR PIPÉRAZINE EN TANT QU'AGENTS ANTIPSYCHOTIQUES

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(56) References cited:
WO-A1-2006/112464

EP 2 753 617 B9

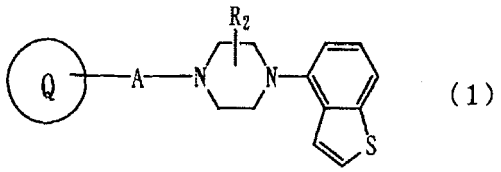
Description

TECHNICAL FIELD OF THE INVENTION

[0001] The present invention relates to a novel heterocyclic compound and use thereof.

BACKGROUND OF THE INVENTION

[0002] As a compound having a broad treatment spectrum for central neurological diseases such as schizophrenia and the like, for example, a compound represented by the following formula (1) (hereinafter compound (1)) has been reported (patent document 1).



(1)

wherein each symbol is as defined in patent document 1.

[0003] The above-mentioned compound (1) is an antipsychotic agent having a broader treatment spectrum as compared to conventional typical antipsychotic agents and atypical antipsychotic agents, causing less side effects, and superior in tolerability and safety. However, this compound is associated with problems in that its application to oil injections is limited and the like, since it is poorly soluble in oil such as sesame oil and benzyl benzoate. Oil injections are useful as compared to aqueous suspensions from the aspects of imparted blood concentration sustainability (control of diffusion in administration site by oily base), shortened liquid preparation time when in use (unnecessitated mixing and shaking), secured sterilization by filtration (oily base filtration), avoidance of physical stimulation at administration site (oily base stability), improved accuracy of filling into injection container (container filled with oily base) and the like.

Document List

patent document

[0004] patent document 1: WO2006/112464

SUMMARY OF THE INVENTION

Problems to be Solved by the Invention

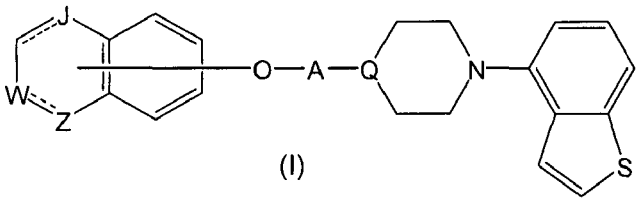
[0005] The problem of the present invention is to provide a superior, novel heterocyclic compound with improved solubility in oil such as sesame oil and benzyl benzoate and use thereof.

Means of Solving the Problems

[0006] The present inventors have conducted various studies in an attempt to solve the aforementioned problems and found that the liposolubility of compound (1) can be markedly improved by introducing a substituent into a particular position on ring Q. The present invention has been completed based on such finding.

[0007] The present invention preferably provides a heterocyclic compound or a salt thereof shown in the following Items 1 - 4, a pharmaceutical composition shown in the Item 5, a prophylactic and/or therapeutic agent shown in the Items 6 and 7, use shown in the Items 8, 9 and 10, and a production method shown in the Item 11.

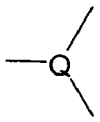
Item 1. A heterocyclic compound represented by the formula (I)



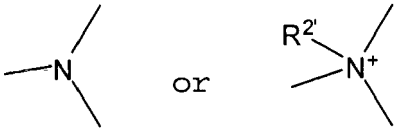
(I)

wherein

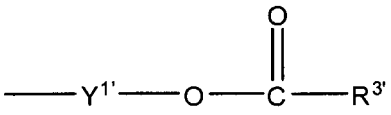
A is a C1-6 alkylene group;



in the monocyclic heterocycle containing Q is



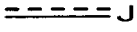
wherein
$R^{2'}$ is the following group



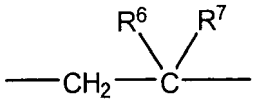
wherein

$Y^{1'}$ is a C1-6 alkylene group,
$R^{3'}$ is

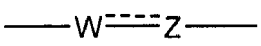
(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group optionally substituted by a C1-6 alkyl group,
(3) a phenyl group,
(4) a phenyl C1-6 alkyl group
(5) a C1-6 alkoxy group,
(6) a C3-20 cycloalkyloxy group,
(7) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a phenyl C1-6 alkyl group, or
(8) a piperidyl group optionally having a piperidyl group;



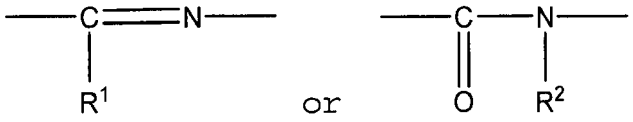
at the 3-position and the 4-position of the bicyclic heterocycle skeleton containing Z and W is -CH=CH- or



wherein R^6 and R^7 are the same or different and each is a hydrogen or a C1-6 alkyl group;



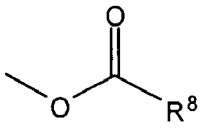
is



wherein
R^1 is

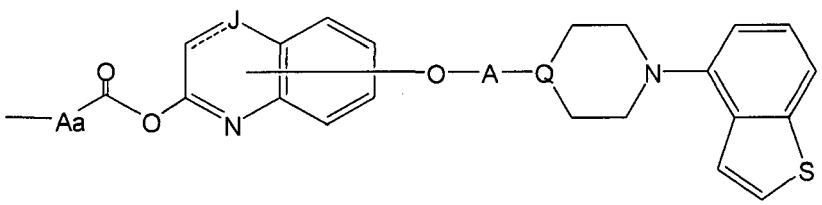
a C1-6 alkoxy C1-6 alkoxy group,
a phosphonooxy C1-6 alkoxy group,
a phenyl C1-6 alkoxy C1-6 alkoxy group, a phosphonooxy group optionally having 1 or 2 C1-6 alkyl groups,

the following group

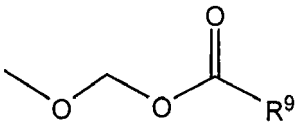


wherein
R^8 is

(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a phenyl group,
(5) a phenyl C1-6 alkyl group,
(6) a C2-30 alkenyl group,
(7) a C1-6 alkoxy group,
(8) a C3-20 cycloalkyloxy group,
(9) a C1-6 alkoxy C1-6 alkoxy group,
(10) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group,
(11) a piperidyl group optionally having a piperidyl group,
(12) a piperazinyl group optionally having a C1-6 alkyl group, or
(13) the following group



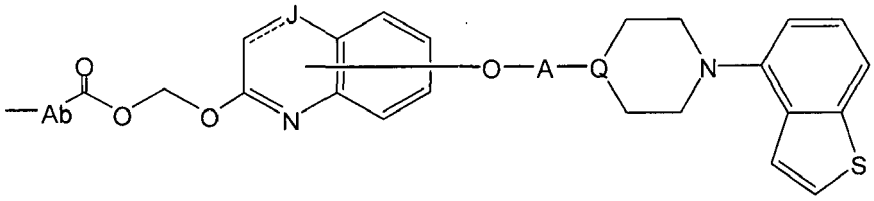
wherein Aa is a C1-30 alkylene group, and other symbols are as defined above, or
the following group



wherein

R^9 is

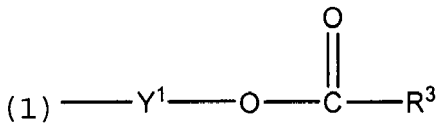
(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a phenyl group,
(5) a phenyl C1-6 alkyl group,
(6) a C2-30 alkenyl group,
(7) a C1-6 alkoxy group,
(8) a C3-20 cycloalkyloxy group,
(9) a C1-6 alkoxy C1-6 alkoxy group,
(10) a phenyloxy group,
(11) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group,
(12) a piperidyl group optionally having a piperidyl group,
(13) a piperazinyl group optionally having a C1-6 alkyl group, or
(14) the following group

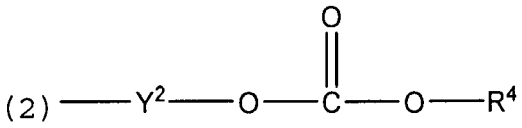


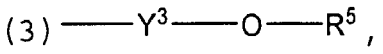
wherein Ab is a C1-30 alkylene group, and other symbols are as defined above;

R^2 is a hydrogen or

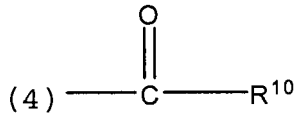
the following group







or



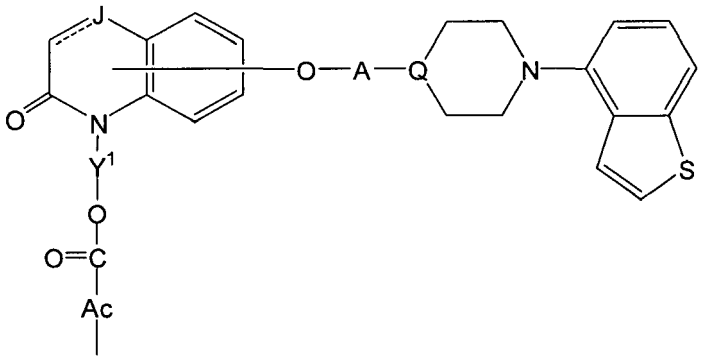
wherein

Y^1 is a C1-6 alkylene group optionally substituted by

(1) a C1-6 alkoxycarbonyl group or
(2) a C1-6 alkyl group,

Y^2 is a C1-6 alkylene group,
Y^3 is a single bond or a C1-6 alkylene group optionally substituted by a C1-6 alkyl group,
R^3 is

(1) a C1-30 alkyl group,
(2) a halogen-substituted C1-6 alkyl group,
(3) a C2-30 alkenyl group,
(4) an amino C1-6 alkyl group,
(5) a C3-20 cycloalkyl group,
(6) a phenyl group,
(7) a phenyl C1-6 alkyl group,
(8) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group and a piperidyl group,
(9) a halogen-substituted piperidyl group,
(10) a morpholinyl group,
(11) a pyrrolidinyl group,
(12) a tetrahydropyranyl group,
(13) a furyl group,
(14) a thienyl group,
(15) a pyridyl group,
(16) a pyrimidinyl group,
(17) a pyridazinyl group,
(18) a benzofuryl group,
(19) a quinolyl group,
(20) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(21) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(22) a C1-6 alkoxy C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(23) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group, a C3-20 cycloalkyl group, a C3-20 cycloalkyl C1-6 alkyl group, a C2-6 alkenyl group, a halogen-substituted C1-6 alkyl group, a C1-6 alkoxy group, a C1-6 alkoxy C1-6 alkyl group, a C1-6 alkoxycarbonyl C1-6 alkyl group, a phenyl C1-6 alkyl group, a phenyl C1-6 alkoxy group, a furyl C1-6 alkyl group, a pyridyl C1-6 alkyl group, a hydroxy-substituted C1-6 alkyl group,
(24) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group,
(25) a piperazinyl group optionally having a C1-6 alkyl group, or
(26) the following group



wherein Ac is a C1-30 alkylene group, and other symbols are as defined above,

R^4 is

(1) a C1-30 alkyl group,
(2) a phenyl group,
(3) a phenyl C1-6 alkyl group,
(4) a halogen-substituted C1-6 alkyl group, or
(5) a C3-20 cycloalkyl group,

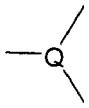
R^5 is

(1) a hydrogen,
(2) a C1-6 alkyl group,
(3) a halogen-substituted C1-6 alkyl group,
(4) a phenyl C1-6 alkyl group,
(5) a phenyl C1-6 alkoxy C1-6 alkyl group,
(6) a tri-C1-6 alkylsilyl group,
(7) a tetrahydropyranyl group, or
(8) a phosphono group,

R^{10} is

(2) a C2-30 alkenyl group,
(4) a phenyl C1-6 alkyl group,
(5) a hydroxy-substituted C1-6 alkyl group,
(6) a C3-20 cycloalkyl group,
(7) an amino C1-6 alkyl group optionally having 1 or 2 substituents selected from the group consisting of an amino C1-6 alkylcarbonyl group and a C1-6 alkylcarbonyl group,
(8) a pyrrolidinyl group optionally having an amino C1-6 alkylcarbonyl group,
(9) an alkoxy group,
(10) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(11) a C1-6 alkoxy C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(12) a phenyl C1-6 alkoxy group,
(13) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group, a hydroxy-substituted C1-6 alkyl group and a phenyl C1-6 alkyl group,
(14) a morpholino group,
(15) a piperazinyl group optionally having a C1-6 alkyl group,
(16) a piperidyl group optionally having a piperidyl group, or
(17) a C3-20 cycloalkyloxy group;

provided when



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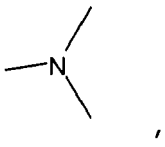
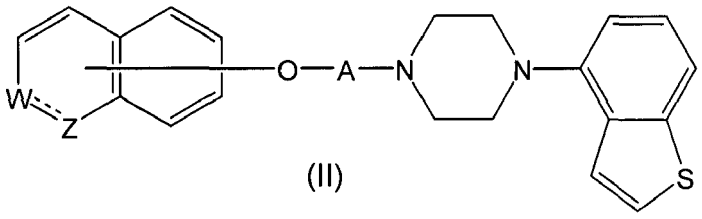


then

R^2 is not a hydrogen,

or a salt thereof.

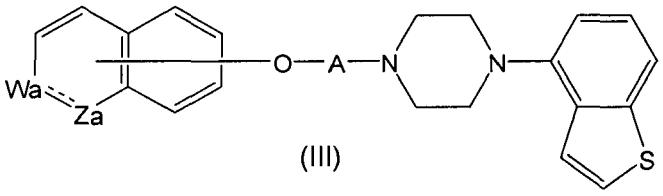
Item 2. The heterocyclic compound according to Item 1, which is represented by the formula (II)



(II)

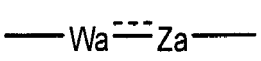
wherein each symbol is as defined in Item 1, or a salt thereof.

Item 3. The heterocyclic compound according to Item 1, which is represented by the formula (III)

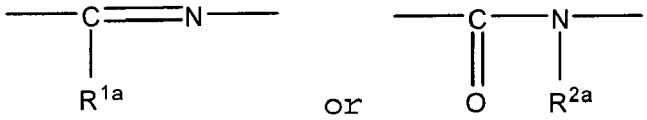


(III)

wherein

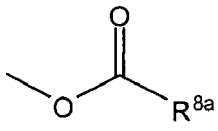


is



wherein

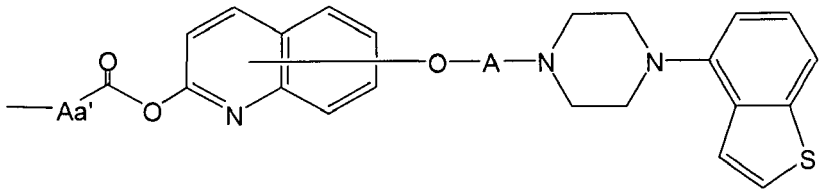
R^{1a} is the following group



wherein

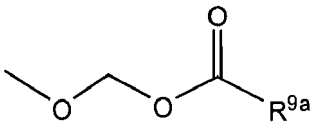
R^{8a} is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a C1-6 alkoxy group,
(4) a C3-20 cycloalkyloxy group,
(5) a C1-6 alkoxy C1-6 alkoxy group,
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group, or
(7) the following group



wherein Aa' is a C1-30 alkylene group, and other symbol is as defined in Item 1, or

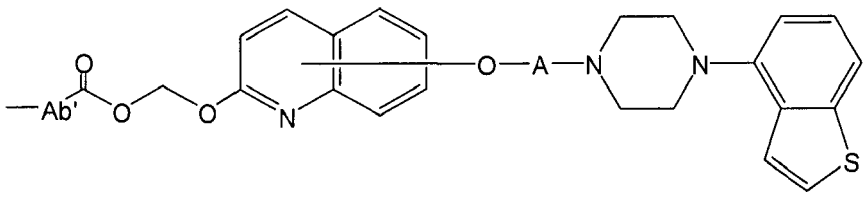
the following group



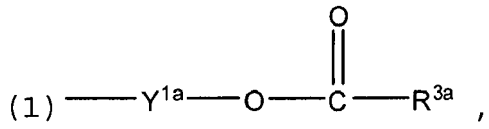
wherein

R^{9a} is

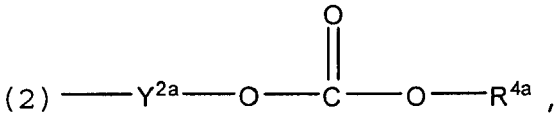
(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a C1-6 alkoxy group,
(5) a C3-20 cycloalkyloxy group,
(6) a C1-6 alkoxy C1-6 alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group,
(9) a piperidyl group optionally having a piperidyl group,
(10) a piperazinyl group optionally having a C1-6 alkyl group, or
(11) the following group



wherein Ab' is a C1-30 alkylene group, and other symbol is as defined in Item 1;
R^{2a} is
the following group



or

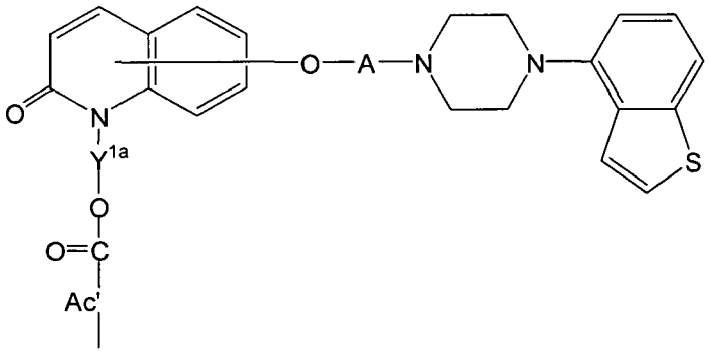


wherein

Y^{1a} is a C1-6 alkylene group,
Y^{2a} is a C1-6 alkylene group,

R^{3a} is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group,
(4) a tetrahydropyranyl group,
(5) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(6) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group
(7) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group, or
(8) the following group



wherein Ac' is a C1-30 alkylene group, Y^{1a} is a C1-6 alkylene group and other symbols are as defined in Item 1,
R^{4a} is

(1) a C1-30 alkyl group, or
(2) a C3-20 cycloalkyl group; and

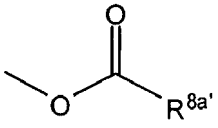
A is a C1-6 alkylene group,

or a salt thereof.

Item 4. The heterocyclic compound according to Item 2, wherein

R^1 is

the following group

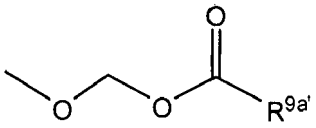


wherein

$R^{8a'}$ is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a C1-6 alkoxy group,
(4) a C3-20 cycloalkyloxy group,
(5) a C1-6 alkoxy C1-6 alkoxy group, or
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group, or

the following group



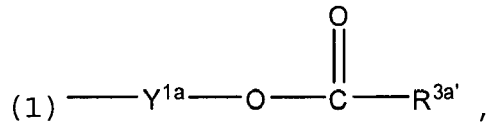
wherein

$R^{9a'}$ is

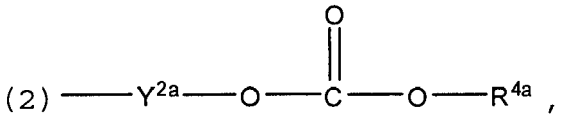
(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a C1-6 alkoxy group,
(5) a C3-20 cycloalkyloxy group,
(6) a C1-6 alkoxy C1-6 alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group,
(9) a piperidyl group optionally having a piperidyl group, or
(10) a piperazinyl group optionally having a C1-6 alkyl group;

R^2 is

the following group



or



wherein

Y^{1a} is a C1-6 alkylene group,
Y^{2a} is a C1-6 alkylene group,

$R^{3a'}$ is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group,
(4) a tetrahydropyranyl group,
(5) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(6) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group
(7) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group,

R^{4a} is

(1) a C1-30 alkyl group, or
(2) a C3-20 cycloalkyl group;

or a salt thereof.

Item 5. A pharmaceutical composition comprising the heterocyclic compound according to Item 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent and/or a carrier. Item 6. A prophylactic and/or therapeutic agent for a central neurological disease, comprising the heterocyclic compound according to Item 1 or a pharmaceutically acceptable salt thereof as an active ingredient.

Item 7. The agent according to Item 6, wherein the central neurological disease is selected from the group consisting of schizophrenia, treatment-resistant, refractory or chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, adjustment disorder, substance-related disorder, anhedonia, delirium, Alzheimer's disease, Parkinson disease, cognitive impairment, cognitive impairment associated with neurodegenerative diseases, cognitive impairment caused by neurodegenerative diseases, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autistic disorder, Tourette's disorder, tic disorder, attention deficit hyperactivity disorder, conduct disorder and Down's syndrome.

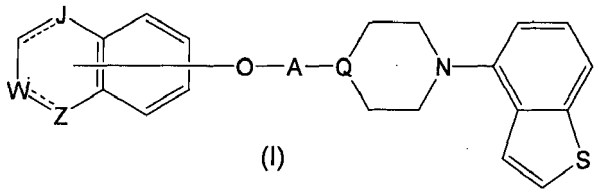
Item 8. Heterocyclic compound according to Item 1 or a pharmaceutically acceptable salt thereof for use as a medicament.

Item 9. Heterocyclic compound according to Item I for use in a method of preventing and/or treating a central neurological diseases.

Item 10. The method according to Item 9, wherein the central neurological disease is selected from the group consisting of schizophrenia, treatment-resistant, refractory or chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, ad-

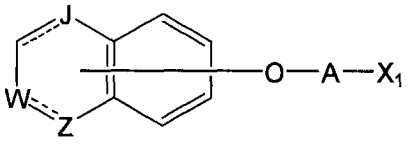
justment disorder, substance-related disorder, anhedonia, delirium, Alzheimer's disease, Parkinson disease, cognitive impairment, cognitive impairment associated with neurodegenerative diseases, cognitive impairment caused by neurodegenerative diseases, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autistic disorder, Tourette's disorder, tic disorder, attention deficit hyperactivity disorder, conduct disorder and Down's syndrome.

Item 11. A method of producing a heterocyclic compound represented by the formula (I)

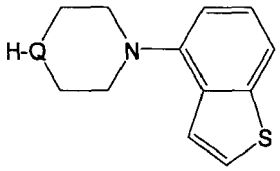


(I)

wherein each symbol is as defined in Item 1,
or a salt thereof, comprising reacting a compound represented by the formula



wherein X_1 is a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined in Item 1, or a salt thereof, with a compound represented by



wherein Q is as defined in Item 1, or a salt thereof.

Brief description of drawings

[0008] Fig.1 is a graph showing the transition of blood concentration of test preparations 1, 2 and 3 after administration.

Description of Embodiments

[0009] Each group shown in the aforementioned formula (I) is specifically as follows.

[0010] Lower means, unless otherwise specified, a group having 1 to 6 (preferably 1 - 4) carbon atoms.

[0011] As the halogen atom, a fluorine atom, a chlorine atom, a bromine atom and an iodine atom can be mentioned.

[0012] As the alkyl group, a straight chain or branched chain alkyl group having a carbon number of 1 - 30 (preferably 1 - 20) can be mentioned. More specific examples thereof include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, n-pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, isopentyl, 1-ethylpropyl, neopentyl, n-hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, isohexyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 2-ethylbutyl, n-heptyl, 1-methylhexyl, 2-methylhexyl, 3-methylhexyl, 4-methylhexyl, 5-methylhexyl, 1-propylbutyl, 1,1-dimethylpentyl, 4,4-dimethylpentyl, 1-pentylhexyl, n-octyl, 1-methylheptyl, 2-methylheptyl, 3-methylheptyl, 4-methylheptyl, 5-methylheptyl, 6-methylheptyl, 1,1-dimethylheptyl, 1-propylpentyl, 2-ethylhexyl, 5,5-dimethylhexyl, n-nonyl, 3-methyloctyl, 4-methyloctyl, 5-methyloctyl, 6-methyloctyl, 1-propylhexyl, 2-ethylheptyl, 6,6-dimethylheptyl, n-decyl, 1-methylnonyl, 3-methylnonyl, 8-methylnonyl, 3-ethyloctyl, 3,7-dimethyloctyl, 7,7-dimethyloctyl, n-undecyl, 1,1-dimethylundecyl, 4,8-dimethylnonyl, dodecyl, tridecyl, tetradecyl, pentadecyl, 3,7,11-trimethyldodecyl, hexadecyl, 4,8,12-trimethyltridecyl, 1-methylpentadecyl, 14-methylpentadecyl, 13,13-dimethyltetradecyl, heptadecyl, 15-methylhexadecyl, octadecyl, 1-methylheptadecyl, nonadecyl, icosyl, 3,7,11,15-tetramethylhexade-

cyl, henicosyl, docosyl, tricosyl, tetracosyl, pentacosyl, hexacosyl, heptacosyl, octacosyl, nonacosyl, triacontyl group and the like.

[0013] As the lower alkyl group, a linear or branched chain alkyl group having a carbon number of 1 - 6 can be mentioned. More specific examples thereof include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, n-pentyl, 1-methylbutyl, 2-methylbutyl, isopentyl, 1-ethylpropyl, neopentyl, n-hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, isohexyl, 1,1-dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 2-ethylbutyl, 1,2,2-trimethylpropyl, 3,3-dimethylbutyl group and the like.

[0014] As the alkenyl group, a straight chain or branched chain alkenyl group having 1 - 10 double bonds and a carbon number of 2 - 30 can be mentioned, including both a trans form and a cis form. More specific examples thereof include ethenyl(vinyl), 1-propenyl, 2-propenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 2-methyl-2-propenyl, 2-propenyl, 2-butenyl, 1-butenyl, 3-butenyl, 2-pentenyl, 1-pentenyl, 3-pentenyl, 4-pentenyl, 1,3-butadienyl, 1,3-pentadienyl, 2-pentene-4-ynyl, 2-hexenyl, 1-hexenyl, 5-hexenyl, 3-hexenyl, 4-hexenyl, 3,3-dimethyl-1-propenyl, 2-ethyl-1-propenyl, 1,3,5-hexatrienyl, 1,3-hexadienyl, 1,4-hexadienyl, heptenyl, octenyl, nonenyl, decenyl, undecenyl, dodecenyl, tridecenyl, tetradecenyl, pentadecenyl, hexadecenyl, heptadecenyl, octadecenyl, nonadecenyl, icocenyl group and the like.

[0015] As the lower alkenyl group, a straight chain or branched chain alkenyl group having 1 - 3 double bonds and a carbon number of 2 - 6 can be mentioned, including both a trans form and a cis form. More specific examples thereof include vinyl, 1-propenyl, 2-propenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 2-methyl-2-propenyl, 2-propenyl, 2-butenyl, 1-butenyl, 3-butenyl, 2-pentenyl, 1-pentenyl, 3-pentenyl, 4-pentenyl, 1,3-butadienyl, 1,3-pentadienyl, 2-pentene-4-ynyl, 2-hexenyl, 1-hexenyl, 5-hexenyl, 3-hexenyl, 4-hexenyl, 3,3-dimethyl-1-propenyl, 2-ethyl-1-propenyl, 1,3,5-hexatrienyl, 1,3-hexadienyl, 1,4-hexadienyl group and the like.

[0016] As the cycloalkyl group, cyclo C3-C20 alkyl group having 3 - 20 carbon atoms can be mentioned. More specific examples thereof include monocycloalkyl such as cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group, cyclodecyl group, cyclododecyl group and the like, bicycloalkyl, tricycloalkyl, polycycloalkyl and the like. As the bicycloalkyl, norbornyl, pinanyl, bicyclo[2,2,2]octyl group and the like can be mentioned, and as the tricycloalkyl and polycycloalkyl, adamantyl group and the like can be mentioned.

[0017] As the cycloalkyloxy group, a cyclo C3-C20 alkyl having 3 - 20 carbon atoms - oxy group can be mentioned. More specific examples thereof include monocycloalkyloxy such as cyclopropyloxy group, cyclobutyloxy group, cyclopentyloxy group, cyclohexyloxy group, cycloheptyloxy group, cyclooctyloxy group, cyclodecyloxy group, cyclododecyloxy group and the like, bicycloalkyloxy, tricycloalkyloxy, polycycloalkyloxy and the like. As the cycloalkyloxy, norbornyloxy, pinanyloxy, bicyclo[2,2,2]octyloxy group and the like can be mentioned, and as the tricycloalkyloxy and polycycloalkyloxy, adamantyloxy group and the like can be mentioned.

[0018] As the lower alkoxy group, a straight chain or branched chain alkoxy group having a carbon number of 1 - 6 can be mentioned. More specific examples thereof include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, tert-butoxy, sec-butoxy, n-pentyloxy, isopentyloxy, neopentyloxy, n-hexyloxy, isohexyloxy, 3-methylpentyloxy group and the like.

[0019] As the halogen-substituted lower alkyl group, the aforementioned lower alkyl group, which is substituted by 1 - 7, more preferably 1 - 3, halogen atoms can be mentioned. More specific examples thereof include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, bromomethyl, dibromomethyl, dichlorofluoromethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 2-fluoroethyl, 2-chloroethyl, 3,3,3-trifluoropropyl, heptafluoropropyl, 2,2,3,3,3-pentafluoropropyl, heptafluoroisopropyl, 3-chloropropyl, 2-chloropropyl, 3-bromopropyl, 4,4,4-trifluorobutyl, 4,4,4,3,3-pentafluorobutyl, 4-chlorobutyl, 4-bromobutyl, 2-chlorobutyl, 5,5,5-trifluoropentyl, 5-chloropentyl, 6,6,6-trifluorohexyl, 6-chlorohexyl, perfluorohexyl group and the like.

[0020] As the hydroxy-substituted lower alkyl group, the aforementioned lower alkyl group, which is substituted by 1 - 7, more preferably 1 - 3, hydroxy groups can be mentioned. More specific examples thereof include hydroxymethyl, 2-hydroxyethyl, 1,1-dimethyl-2-hydroxyethyl, 3-hydroxypropyl, 4-hydroxybutyl, 2-hydroxybutyl, 5-hydroxypentyl, 1-hydroxypentyl, 6-hydroxyhexyl and the like.

[0021] As the cycloalkyl lower alkyl group, the aforementioned lower alkyl group (preferably a straight chain or branched chain alkyl group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, cycloalkyl group mentioned above can be mentioned. It may be substituted with a lower alkyl group on the cycloalkyl group. Specific examples of the cycloalkyl lower alkyl group include cyclopropylmethyl, cyclohexylmethyl, 2-cyclopropylethyl, 1-cyclobutylethyl, cyclopentylmethyl, 3-cyclopentylpropyl, 4-cyclohexylbutyl, 5-cycloheptylpentyl, 6-cyclooctylhexyl, 1,1-dimethyl-2-cyclohexylethyl, 2-methyl-3-cyclopropylpropyl group and the like.

[0022] As the amino lower alkyl group, the aforementioned lower alkyl group (preferably a straight chain or branched chain alkyl group having a carbon number of 1 - 6), which has 1 - 5, preferably 1 - 3, amino group can be mentioned. Specific examples of the amino lower alkyl group include aminomethyl, diaminomethyl, triaminomethyl, 1-aminoethyl, 2-aminoethyl, 1-aminopropyl, 2-aminopropyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1-amino-2-methylethyl, 1-aminobutyl, 1-amino-2-methylpropyl, 1-amino-2,2-dimethylethyl, 1-amino-2-methylbutyl, 1-amino-3-methylbutyl, 1-aminohexyl, 1-amino-2-methylpentyl group and the like.

[0023] As the phenyl lower alkyl group, the aforementioned lower alkyl group, which has 1 - 3, preferably 1, phenyl group can be mentioned. It may be substituted with a lower alkyl group on the phenyl group. Specific examples of the phenyl lower alkyl group include benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 4-phenylbutyl, 1,1-dimethyl-2-phenylethyl, 5-phenylpentyl, 6-phenylhexyl, 2-methyl-3-phenylpropyl, diphenylmethyl, 2,2-diphenylethyl group and the like.

[0024] As the furyl lower alkyl group, the aforementioned lower alkyl group, which has 1 - 3, preferably 1, furyl group can be mentioned. It may be substituted with a lower alkyl group on the furyl group. Specific examples of the furyl lower alkyl group include (2-furyl)methyl, 2-(3-furyl)ethyl, 1-(2-furyl)ethyl, 3-(3-furyl)propyl, 4-(2-furyl)butyl, 5-(3-furyl)pentyl, 6-(2-furyl)hexyl, 1,1-dimethyl-2-(3-furyl)ethyl, 2-methyl-3-(2-furyl)propyl group and the like.

[0025] As the pyridyl lower alkyl group, the aforementioned lower alkyl group, which has 1 - 3, preferably 1, pyridyl group can be mentioned. It may be substituted with a lower alkyl group on the pyridyl group. Specific examples of the pyridyl lower alkyl group include (4-pyridyl)methyl, 1-(3-pyridyl)ethyl, 2-(2-pyridyl)ethyl, 3-(2-pyridyl)propyl, 4-(3-pyridyl)butyl, 5-(4-pyridyl)pentyl, 6-(2-pyridyl)hexyl, 1,1-dimethyl-2-(3-pyridyl)ethyl, 2-methyl-3-(4-pyridyl)propyl group and the like.

[0026] As the lower alkoxy lower alkyl group, the aforementioned lower alkyl group (preferably a straight chain or branched chain alkyl group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, lower alkoxy group (preferably a straight chain or branched chain alkoxy group having a carbon number of 1 - 6) mentioned above can be mentioned. Specific examples of the lower alkoxy lower alkyl group include methoxymethyl, ethoxymethyl, propoxymethyl, hexyloxymethyl, methoxyethyl, ethoxyethyl, propoxyethyl, isopropoxymethyl, butoxy methyl, tert-butoxy methyl, pentyloxymethyl, hexyloxymethyl group and the like.

[0027] As the lower alkoxycarbonyl group, a straight chain or branched chain alkoxycarbonyl group having a carbon number of 1 - 6, wherein the lower alkoxy moiety is the aforementioned lower alkoxy group can be mentioned. More specific examples thereof include methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl, sec-butoxycarbonyl, n-pentyloxycarbonyl, neopentyloxy, n-hexyloxycarbonyl, isohexyloxycarbonyl, 3-methylpentyloxycarbonyl group and the like.

[0028] As the lower alkylcarbonyl group, a straight chain or branched chain alkylcarbonyl group having a carbon number of 1 - 6, wherein the lower alkyl moiety is the aforementioned lower alkyl group can be mentioned. More specific examples thereof include acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl and the like.

[0029] As the amino lower alkylcarbonyl group, the aforementioned lower alkylcarbonyl group having 1 - 5, preferably 1 or 2, amino groups, can be mentioned. More specific examples thereof include aminomethylcarbonyl, 2-aminoethylcarbonyl, 1-aminoethylcarbonyl, 3-aminopropylcarbonyl, 4-aminobutylcarbonyl, 5-aminopentylcarbonyl, 6-aminohexylcarbonyl, 1,1-dimethyl-2-aminoethylcarbonyl, 2-methyl-3-aminopropylcarbonyl group and the like.

[0030] As the lower alkoxycarbonyl lower alkyl group, the aforementioned lower alkyl group (preferably straight chain or branched chain alkyl group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, lower alkoxycarbonyl group (e.g., methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl, sec-butoxycarbonyl, n-pentyloxycarbonyl, neopentyloxy, n-hexyloxycarbonyl, isohexyloxycarbonyl, 3-methylpentyloxycarbonyl group etc.) can be mentioned. Specific examples of the lower alkoxycarbonyl lower alkyl group include methoxycarbonylmethyl group, ethoxycarbonylmethyl group, propoxycarbonylmethyl group, isopropoxycarbonylmethyl group, butoxycarbonylmethyl group, isobutoxycarbonylmethyl group, sec-butoxycarbonylmethyl group, tert-butoxycarbonylmethyl group, 2-methoxycarbonylethyl group, 2-ethoxycarbonylethyl group, 2-propoxycarbonylethyl group, 3-methoxycarbonylpropyl group, 3-ethoxycarbonylpropyl group, 4-methoxycarbonylbutyl group, 4-ethoxycarbonylbutyl group and the like.

[0031] As the lower alkoxy lower alkoxy group, the aforementioned lower alkoxy group (preferably straight chain or branched chain alkoxy group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, lower alkoxy group (preferably straight chain or branched chain alkoxy group having a carbon number of 1 - 6) mentioned above can be mentioned. Specific examples of the lower alkoxy lower alkoxy group include methoxymethoxy, ethoxymethoxy, propoxymethoxy, hexyloxymethoxy, methoxyethoxy, ethoxyethoxy, propoxyethoxy, isopropoxymethoxy, butoxymethoxy, tert-butoxymethoxy, pentyloxymethoxy, hexyloxymethoxy group and the like.

[0032] As the phenyl lower alkoxy lower alkoxy group, the aforementioned lower alkoxy lower alkoxy group having 1 - 3, preferably 1, phenyl group can be mentioned. Specific examples of the phenyl lower alkoxy lower alkoxy group include benzyloxymethoxy, 2-phenylethoxymethoxy, 1-phenylethoxymethoxymethoxy, 3-phenylpropoxymethoxy, 4-phenylbutoxymethoxy, 1,1-dimethyl-2-phenylethoxymethoxy, 5-phenylpentyloxymethoxy, 6-phenylhexyloxymethoxy, 2-benzyloxyethoxy, 3-benzyloxypropoxy, 4-benzyloxybutoxy, 1,1-dimethyl-2-benzyloxyethoxy, 5-benzyloxypentoxy, 6-benzyloxyhexyloxy, 2-methyl-3-benzyloxypropoxy group and the like.

[0033] As the lower alkoxy lower alkoxy lower alkyl group, the aforementioned lower alkyl group (preferably straight chain or branched chain alkyl group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, lower alkoxy lower alkoxy group mentioned above can be mentioned. Specific examples of the lower alkoxy lower alkoxy lower alkyl group include methoxymethoxymethyl, 3-(3-methoxypropoxy)propyl, ethoxymethoxymethyl, 3-(3-ethoxypropoxy)propyl, 4-(4-

ethoxybutoxy)butyl, 5-(5-isopropoxypentyloxy)pentyl, 6-(6-propoxyhexyloxy)hexyl, 1,1-dimethyl-2-(2-butoxyethoxy)ethyl, 2-methyl-3-(3-tert-butoxypropoxy)propyl, 2-(2-pentyloxyethoxy)ethyl, hexyloxymethoxymethyl group and the like.

[0034] As the lower alkoxy lower alkoxy lower alkoxy lower alkyl group, the aforementioned lower alkoxy lower alkyl group having 1 - 3, preferably 1, lower alkoxy lower alkoxy group mentioned above can be mentioned. Specific examples of the lower alkoxy lower alkoxy lower alkoxy lower alkyl group include methoxyethoxyethoxyethyl, ethoxyethoxyethoxyethyl group and the like.

[0035] As the phenyl lower alkoxy group, the aforementioned lower alkoxy group having 1 - 3, preferably 1, phenyl group can be mentioned. Specific examples of the phenyl lower alkoxy group include benzyloxy, 2-phenylethoxy, 1-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 1,1-dimethyl-2-phenylethoxy, 5-phenylpentyloxy, 6-phenylhexyloxy, 2-benzyloxy, 3-benzyloxy, 4-benzyloxy, 1,1-dimethyl-2-benzyloxy, 5-benzyloxy, 6-benzyloxy, 2-methyl-3-benzyloxy group and the like.

[0036] As the phosphono lower alkoxy group, the aforementioned lower alkoxy group (preferably straight chain or branched chain alkoxy group having a carbon number of 1 - 6), which has 1 - 3, preferably 1, phosphono group can be mentioned. Specific examples of the phosphono lower alkoxy group include phosphonomethoxy, phosphonoethoxy, phosphonopropoxy, phosphonobutoxy, phosphonopentyloxy, phosphonohexyloxy group and the like.

[0037] As the piperidyl group optionally having a lower alkyl group, a piperidyl group optionally having 1 - 3, preferably 1, lower alkyl group mentioned above can be mentioned. Specific examples of the piperidyl group optionally having a lower alkyl group include piperidyl, 2-methylpiperidyl, 3-methylpiperidyl, 2-ethylpiperidyl, 3-ethylpiperidyl group and the like.

[0038] As the halogen-substituted piperidyl group, a piperidyl group substituted by 1 - 7, more preferably 1 - 3, halogen atoms can be mentioned. More specific examples thereof include fluoropiperidyl, difluoropiperidyl, chloropiperidyl, dichloropiperidyl, bromopiperidyl, dibromopiperidyl group and the like.

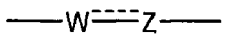
[0039] The tri-lower alkylsilyl group is a silyl group substituted by 3 lower alkyl groups mentioned above. Specific examples thereof include trimethylsilyl, ethyldimethylsilyl, n-propyldimethylsilyl, tert-butyldimethylsilyl, triethylsilyl, methyldiethylsilyl, dimethylethylsilyl, triisopropylsilyl group and the like.

[0040] As the lower alkylene group, a straight chain or branched chain alkylene group having a carbon number of 1 - 6 can be mentioned. More specific examples thereof include methylene, ethylene, trimethylene, 2-methyltrimethylene, 3-methyltetramethylene, 2,2-dimethyltrimethylene, 1-methyltrimethylene, methylmethylene, ethylmethylene, tetramethylene, pentamethylene, hexamethylene group and the like.

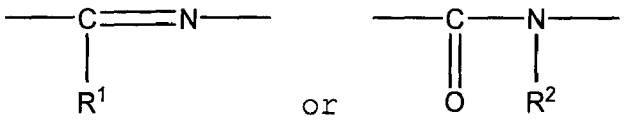
[0041] As the alkylene group, a straight chain or branched chain alkylene group having a carbon number of 1 - 30 can be mentioned. More specific examples thereof include methylene, ethylene, trimethylene, tetramethylene, hexamethylene, heptamethylene, octamethylene, decamethylene, undecamethylene, dodecamethylene, tridecamethylene, tetradecamethylene, hexadecamethylene, octadecamethylene, tricosamethylene, hexacosamethylene, triacontamethylene, 1-methylethylene, 2-ethyltrimethylene, 1-methylheptamethylene, 2-methylheptamethylene, 1-butylhexamethylene, 2-methyl-5-ethylheptamethylene, 2,3,6-trimethylheptamethylene, 6-ethyldecamethylene, 7-methyltetradecamethylene, 7-ethylhexadecamethylene, 7,12-dimethyloctadecamethylene, 8,11-dimethyloctadecamethylene, 7,10-dimethyl-7-ethylhexadecamethylene, 1-octadecylethylene, 9,10-dioctyloctadecamethylene, 8,9-dinonylhexadecamethylene, ethenylene, 1-octadecenylethylene, 7,11-octadecadienylene, 7-ethenyl-9-hexadecamethylene, 7,12-dimethyl-7,11-octadecadienylene, 8,11-dimethyl-7,11-octadecadienylene, 9,10-dioctyl-7,11-octadecadienylene, 8,9-dinonyl-6,10-hexadecadienylene group and the like.

[0042] When the heterocyclic compound represented by the formula (I) is a cation, it is preferably present as a salt together with anion. The anion includes a halogen ion (e.g., C1-, I-) and the like.

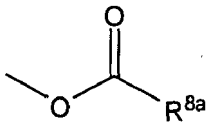
[0043] In the formula (I),



is



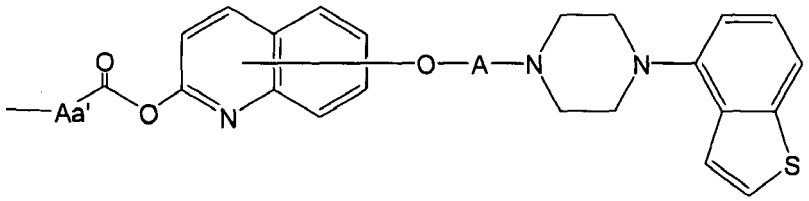
R^1 is preferably the following group



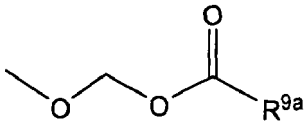
wherein

R^{8a} is

(1) an alkyl group,
(2) a cycloalkyl group,
(3) a lower alkoxy group,
(4) a cycloalkyloxy group,
(5) a lower alkoxy lower alkoxy group,
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of an alkyl group and a hydroxy-substituted lower alkyl group, or
(7) the following group

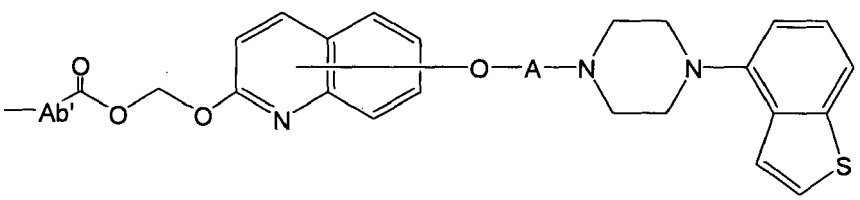


wherein Aa' is an alkylene group and A is a lower alkylene group, or
the following group

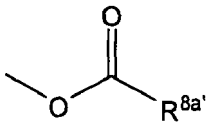


wherein
R^{9a} is

(1) an alkyl group,
(2) a hydroxy-substituted lower alkyl group,
(3) a cycloalkyl group,
(4) a lower alkoxy group,
(5) a cycloalkyloxy group,
(6) a lower alkoxy lower alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of an alkyl group,
(9) a piperidyl group optionally having a piperidyl group,
(10) a piperazinyl group optionally having a lower alkyl group, or
(11) the following group



wherein Ab' is an alkylene group and A is a lower alkylene group,
more preferably,
the following group

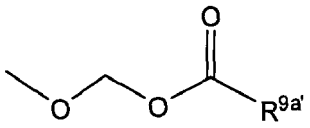


wherein

$R^{8a'}$ is

(1) an alkyl group,
(2) a cycloalkyl group,
(3) a lower alkoxy group,
(4) a cycloalkyloxy group,
(5) a lower alkoxy lower alkoxy group, or
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of an alkyl group and a hydroxy-substituted lower alkyl group, or

the following group

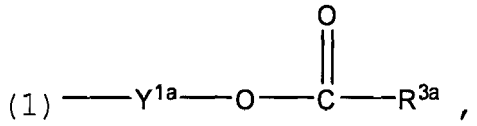


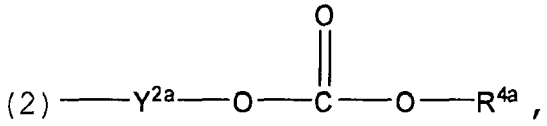
wherein

$R^{9a'}$ is

(1) an alkyl group,
(2) a hydroxy-substituted lower alkyl group,
(3) a cycloalkyl group,
(4) a lower alkoxy group,
(5) a cycloalkyloxy group,
(6) a lower alkoxy lower alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of an alkyl group,
(9) a piperidyl group optionally having a piperidyl group, or
(10) a piperazinyl group optionally having a lower alkyl group. As R^2,

the following group



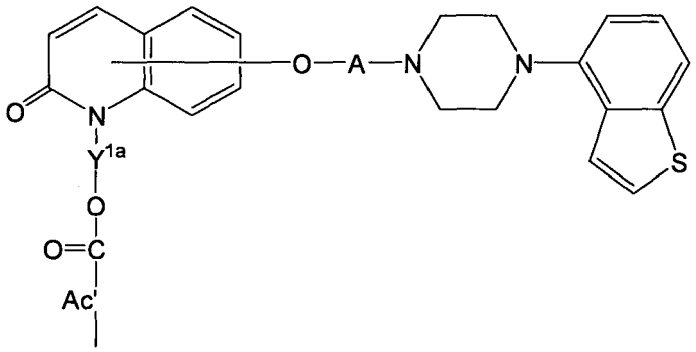


wherein

Y^{1a} is a lower alkylene group,
Y^{2a} is a lower alkylene group,

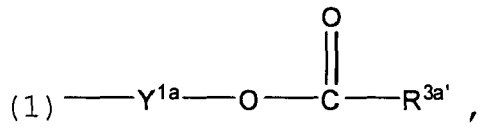
R^{3a} is

(1) an alkyl group,
(2) a cycloalkyl group,
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a lower alkyl group,
(4) a tetrahydropyranyl group,
(5) a lower alkoxycarbonyl lower alkyl group,
(6) a lower alkoxy lower alkoxy lower alkyl group,
(7) an amino lower alkyl group optionally having a lower alkylcarbonyl group, or
(8) the following group



wherein Ac' is an alkylene group, Y^{1a} is a lower alkylene group and A is a lower alkylene group,
R^{4a} is

(1) an alkyl group, or
(2) a cycloalkyl group is preferable, more preferably, R^2 is the following group



,

wherein

Y^{1a} is a lower alkylene group,
Y^{2a} is a lower alkylene group,

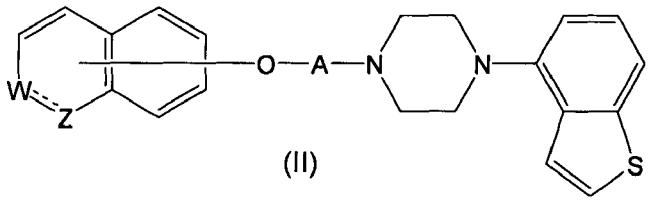
$R^{3a'}$ is

(1) an alkyl group,
(2) a cycloalkyl group,
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a lower alkyl group,
(4) a tetrahydropyranyl group,
(5) a lower alkoxycarbonyl lower alkyl group,
(6) a lower alkoxy lower alkoxy lower alkyl group, or
(7) an amino lower alkyl group optionally having a lower alkylcarbonyl group,

R^{4a} is

(1) an alkyl group, or
(2) a cycloalkyl group.

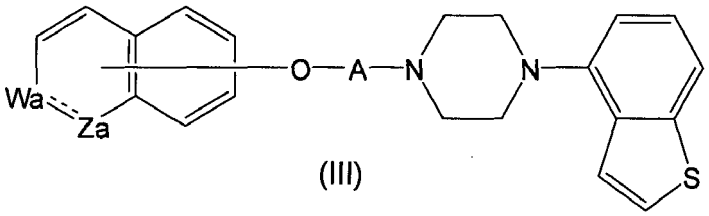
[0044] The heterocyclic compound represented by the formula (I) is preferably a heterocyclic compound represented by the following formula (II)



(II)

wherein each symbol is as defined in the present specification.

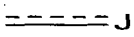
[0045] More preferably, it is a heterocyclic compound represented by the following formula (III)



(III)

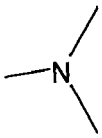
wherein each symbol is as defined In the present specification.

[0046] That is, in the formula (I)



shown at the 3-position and the 4-position of the bicyclic heterocycle skeleton containing Z and W is preferably -CH=CH-, and

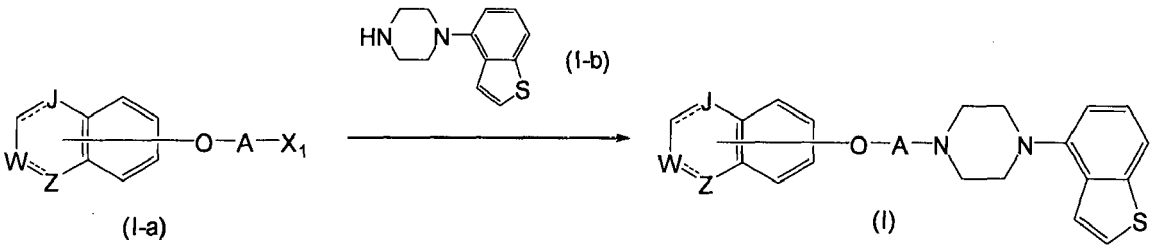
in the monocyclic heterocycle containing Q is preferably



[0047] A heterocyclic compound represented by the above-mentioned formula (I) (hereinafter sometimes to be referred to as compound (I)) can be produced by various methods. For example, it can be produced by a method shown by the following reaction scheme.

[Reaction scheme - 1]

[0048]



wherein each symbol is as defined above.

[0049] In the formula (I-a), the halogen atom for X_1 is as defined above.

[0050] Examples of the group that causes a substitution reaction similar to that by a halogen atom include a lower alkanesulfonyloxy group, an arylsulfonyloxy group, an aralkylsulfonyloxy group and the like.

[0051] Specific examples of the lower alkanesulfonyloxy group for X_1 include a straight chain or branched chain alkanesulfonyloxy group having a carbon number of 1 - 6 such as methanesulfonyloxy, ethanesulfonyloxy, n-propanesulfonyloxy, isopropanesulfonyloxy, n-butanesulfonyloxy, tert-butanesulfonyloxy, n-pentanesulfonyloxy, n-hexanesulfonyloxy group and the like.

[0052] Examples of the arylsulfonyloxy group for X_1 include phenylsulfonyloxy, naphthylsulfonyloxy group and the like, which optionally have, as a substituent on the phenyl ring, 1 - 3 groups selected from the group consisting of a straight chain or branched chain alkyl group having a carbon number of 1 - 6, a straight chain or branched chain alkoxy group having a carbon number of 1 - 6, a nitro group and a halogen atom. Specific examples of the above-mentioned phenylsulfonyloxy group optionally having substituent(s) include phenylsulfonyloxy, 4-methylphenylsulfonyloxy, 2-methylphenylsulfonyloxy, 4-nitrophenylsulfonyloxy, 4-methoxyphenylsulfonyloxy, 2-nitrophenylsulfonyloxy, 3-chlorophenylsulfonyloxy group and the like. Specific examples of the naphthylsulfonyloxy group include α-naphthylsulfonyloxy, β-naphthylsulfonyloxy group and the like.

[0053] Examples of the aralkylsulfonyloxy group for X_1 include a straight chain or branched chain alkanesulfonyloxy group having a carbon number of 1 - 6 and substituted by a phenyl group, which optionally have, as a substituent on the phenyl ring, 1 - 3 groups selected from the group consisting of a straight chain or branched chain alkyl group having a carbon number of 1 - 6, a straight chain or branched chain alkoxy group having a carbon number of 1 - 6, a nitro group and a halogen atom, a straight chain or branched chain alkanesulfonyloxy group having a carbon number of 1 - 6 and substituted by a naphthyl group and the like. Specific examples of the above-mentioned alkanesulfonyloxy group substituted by a phenyl group include benzylsulfonyloxy, 2-phenylethylsulfonyloxy, 4-phenylbutylsulfonyloxy, 4-methylbenzylsulfonyloxy, 2-methylbenzylsulfonyloxy, 4-nitrobenzylsulfonyloxy, 4-methoxybenzylsulfonyloxy, 3-chlorobenzylsulfonyloxy group and the like. Specific examples of the above-mentioned alkanesulfonyloxy group substituted by a naphthyl group include α-naphthylmethylsulfonyloxy, β-naphthylmethylsulfonyloxy group and the like.

[0054] The reaction of a compound represented by the formula (I-a) and a compound represented by the formula (I-b) is performed without solvent or in an inert solvent, in the presence or absence of a basic compound.

[0055] Examples of the inert solvent include water; ethers such as dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethylether, ethylene glycol dimethylether and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; lower alcohols such as methanol, ethanol, isopropanol and the like; ketones such as acetone, methylethyl ketone and the like; polar solvents such as N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), hexamethylphosphoric acid triamide, acetonitrile and the like.

[0056] As the basic compound, known ones can be widely used and, for example, alkali metal hydroxide such as sodium hydroxide, potassium hydroxide, cesium hydroxide, lithium hydroxide and the like; alkali metal carbonate such as sodium carbonate, potassium carbonate, cesium carbonate, lithium carbonate and the like; alkali metal hydrogen carbonate such as lithium hydrogen carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate and the like; alkali metal such as sodium, potassium and the like; inorganic base such as sodium amide, sodium hydride, potassium hydride and the like, and alkali metal alcoholates such as sodium methoxide, sodium ethoxide, potassium methoxide, potassium ethoxide and the like; organic base such as triethylamine, tripropylamine, pyridine, quinoline, piperidine, imidazole, N-ethyldiisopropylamine, dimethylaminopyridine, trimethylamine, dimethylaniline, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]nonene-5(DBN), 1,8-diazabicyclo[5.4.0]undecene-7(DBU), 1,4-diazabicyclo[2.2.2]octane(DABCO) and the like.

[0057] One kind alone from these basic compounds is used, or two or more kinds thereof are mixed and used.

[0058] The amount of the basic compound to be used is generally 0.5 - 10-fold mol, preferably 0.5 - 6-fold mol, relative

to the compound of the formula (I-a).

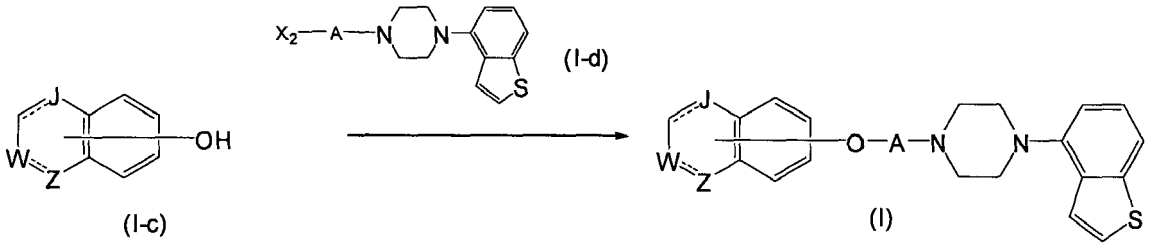
[0059] The above-mentioned reaction can be performed by adding, as necessary, an alkali metal iodide such as potassium iodide, sodium iodide and the like as a reaction promoter.

[0060] The proportion of the compound of the formula (I-a) and the compound of the formula (I-b) to be used in the above-mentioned reaction scheme - 1 is generally at least 0.5-fold mol, preferably about 0.5- to 5-fold mol, of the latter relative to the former.

[0061] The above-mentioned reaction is performed generally at room temperature - 200°C, preferably room temperature - 150°C, and completes in about 1 - 30 hr.

[Reaction scheme - 2]

[0062]



wherein X_2 is a hydroxyl group, a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined above.

[0063] The halogen atom or group that causes a substitution reaction similar to that by a halogen atom for X_2 is as defined above.

[0064] The reaction of a compound represented by the formula (I-c) and a compound represented by the formula (I-d) is performed under the reaction conditions similar to those of the reaction of a compound represented by the formula (I-a) and a compound represented by the formula (I-b) in the aforementioned reaction scheme - 1.

[0065] When compound (I-d) wherein X_2 is a hydroxyl group is used, the reaction of compound (I-c) and compound (I-d) can also be performed in a suitable solvent, in the presence of a condensing agent.

[0066] Specific examples of the solvent to be used here include water; halogenated hydrocarbons such as chloroform, dichloromethane, dichloroethane, carbon tetrachloride and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as diethyl ether, diisopropyl ether, tetrahydrofuran, dimethoxyethane and the like; esters such as methyl acetate, ethyl acetate, isopropyl acetate and the like; alcohols such as methanol, ethanol, isopropanol, propanol, butanol, 3-methoxy-1-butanol, ethylcellosolve, methylcellosolve and the like; aprotic polar solvent such as acetonitrile, pyridine, acetone, DMF, DMSO, hexamethylphosphoric acid triamide and the like, and a mixed solvent thereof and the like.

[0067] As the condensing agent, a mixture of azocarboxylate such as diethylazodicarboxylate and the like and phosphorus compound such as triphenylphosphine and the like, and the like can be mentioned.

[0068] The amount of the condensing agent to be used is generally at least an equimolar amount, preferably equimole to 2-fold molar amount, relative to compound (I-c).

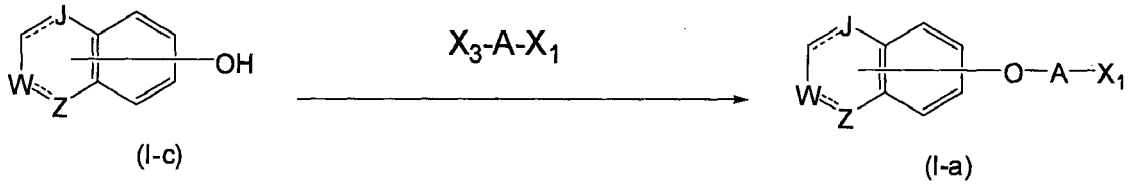
[0069] The amount of compound (I-d) to be used is generally at least an equimolar amount, preferably equimole to 2-fold molar amount, relative to compound (I-c).

[0070] This reaction preferably proceeds generally at 0 - 200°C, preferably about 0 - 150°C, and generally completes in about 1 - 10 hr.

[0071] The compound of the formula (I-a) to be used as a starting material is produced, for example, by of the method shown in the following reaction scheme - 3, and the compound represented by the formula (I-d) is produced, for example, by of the method shown in the following reaction scheme - 4.

[Reaction scheme - 3]

[0072]



(I-c) (I-a)

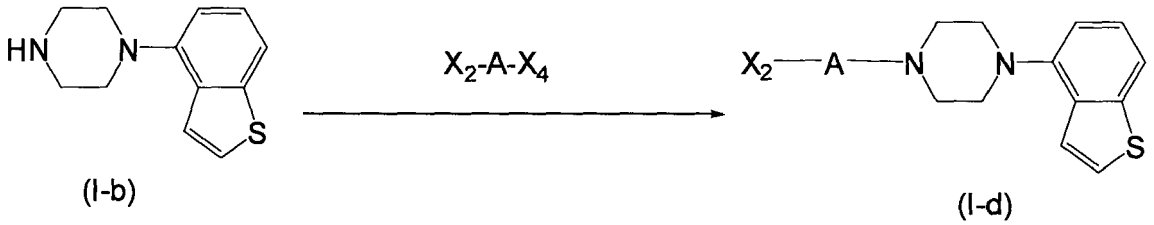
wherein X_3 is a hydroxyl group, a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined above.

[0073] The halogen atom or group that causes a substitution reaction similar to that by a halogen atom for X_3 is as defined above.

[0074] The reaction of a compound represented by the formula (I-c) and a compound represented by X_3-A-X_1 is performed under the reaction conditions similar to those of the reaction of a compound represented by the formula (I-c) and a compound represented by the formula (I-d) in the aforementioned reaction scheme - 2.

[Reaction scheme - 4]

[0075]



(I-b) (I-d)

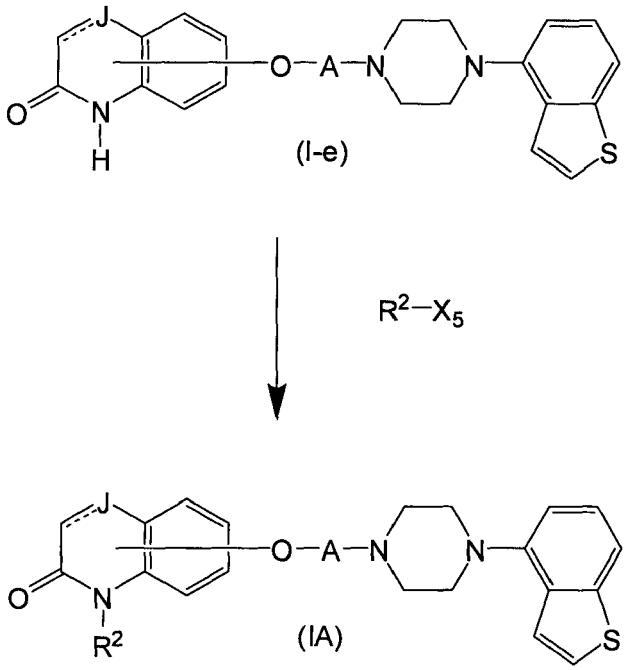
wherein X_4 is a hydroxyl group, a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined above.

[0076] The halogen atom or group that causes a substitution reaction similar to that by a halogen atom for X_4 is as defined above.

[0077] The reaction of a compound represented by the formula (I-b) and a compound represented by X_2-A-X_4 is performed under the reaction conditions similar to those of the reaction of a compound represented by the formula (I-a) and a compound represented by the formula (I-b) in the aforementioned reaction scheme - 1. Both the compound of the formula (I-b) and a compound represented by X_2-A-X_4 are easily-available known compounds.

[Reaction scheme - 5]

[0078]

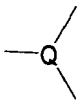


wherein X_5 is a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined above.

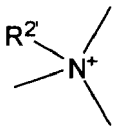
[0079] The halogen atom or group that causes a substitution reaction similar to that by a halogen atom for X_5 is as defined above.

[0080] The reaction of a compound represented by the formula (I-e) and a compound represented by R^2-X_5 is performed under the reaction conditions similar to those of the reaction of a compound represented by the formula (I-a) and a compound represented by the formula (I-b) in the aforementioned reaction scheme - 1.

[0081] When

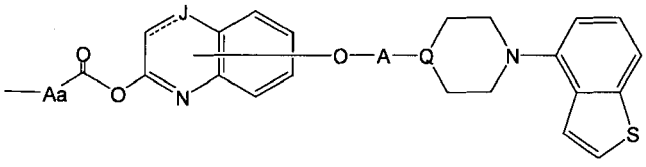


in the monocyclic heterocycle containing Q is

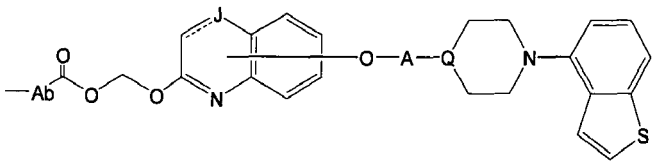


wherein $R^{2'}$ is as defined above,
the compound can be synthesized in the same manner as in the below-mentioned Example 383.

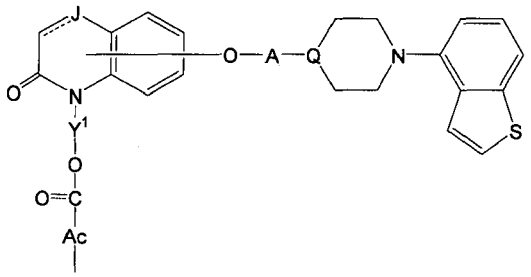
[0082] A compound wherein R^8 is



wherein each symbol is as defined above, a compound wherein R^9 is



wherein each symbol is as defined above, and a compound wherein R^3 is



wherein each symbol is as defined above, can be synthesized by a combination of the methods described in the below-mentioned Example 14 and Example 22.

[0083] A compound (I) having a hydroxyl group on the bicyclic heterocycle skeleton containing Z and W is produced by treating a compound (I) having a methoxy group on the skeleton in a suitable solvent or without solvent, in the presence of an acid.

[0084] Examples of the solvent used here include aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as diethyl ether, tetrahydrofuran, dioxane, monoglyme, diglyme and the like; halogenated hydrocarbons such as dichloromethane, dichloroethane, chloroform, carbon tetrachloride and the like; fatty acid such as acetic acid and the like; esters such as ethyl acetate, methyl acetate and the like; ketones such as acetone, methyl ethyl ketone and the like; acetonitrile, pyridine, DMF, DMSO, hexamethylphosphoric acid triamide and a mixed solvent thereof and the like.

[0085] Examples of the acid include mineral acid such as hydrobromic acid, hydrochloric acid, conc. sulfuric acid and the like, fatty acid such as formic acid, acetic acid and the like, organic acid such as p-toluenesulfonic acid and the like, Lewis acid such as aluminum chloride, zinc chloride, iron chloride, tin chloride, boron trifluoride, boron tribromide and the like, iodide such as sodium iodide, potassium iodide and the like, a mixture of the above-mentioned Lewis acid and iodide and the like.

[0086] Such acid is preferably used in an amount of generally 0.1- to 15-fold molar amount, preferably 0.5- to 10-fold molar amount, relative to compound (I). When the reaction is performed without solvent, an acid is generally used in an excess amount.

[0087] This reaction is performed generally at 0 - 150°C, preferably about 0 - 100°C, and generally completes in about 0.5 - 75 hr.

[0088] The starting compound used for each of the above-mentioned reaction schemes may be a preferable salt, and the object compound obtained in each reaction may form a preferable salt. The preferable salt thereof may be similar to the preferable salts of compound (I) shown below.

[0089] The preferable salt of compound (I) is a pharmaceutically acceptable salt and, for example, metal salts such as alkali metal salt (e.g., sodium salt, potassium salt etc.), alkaline earth metal salt (e.g., calcium salt, magnesium salt etc.) and the like; salts with inorganic bases such as ammonium salt, alkali metal carbonate (e.g., lithium carbonate, potassium carbonate, sodium carbonate, cesium carbonate etc.), alkali metal hydrogen carbonate (e.g., lithium hydrogen carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate etc.), alkali metal hydroxide (e.g., lithium hydroxide, sodium hydroxide, potassium hydroxide, cesium hydroxide etc.) and the like; salts with organic bases such as tri(lower)alkylamine (e.g., trimethylamine, triethylamine, N-ethyldiisopropylamine etc.), pyridine, quinoline, piperidine, imidazole, picoline, dimethylaminopyridine, dimethylaniline, N-(lower)alkyl-morpholine (e.g., N-methylmorpholine etc.), 1,5-diazabicyclo[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO) and the like; salts with inorganic acids such as hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, phosphate and the like; salts with organic acids such as formate, acetate, propionate, oxalate, malonate, succinate, fumarate, maleate, lactate, malate, citrate, tartrate, carbonate, picrate, methanesulfonate, ethanesulfonate, p-toluenesulfonate, glutamate, pamoate and the like; and the like can be mentioned.

[0090] In the following, compound (I) and a salt thereof are sometimes to be generically referred to as the compound of the present invention.

[0091] In addition, a compound wherein a solvate (e.g., hydrate, ethanolate etc.) is added to a starting material or object compound shown in each reaction scheme is also encompassed in each formula. As a preferable solvate, hydrate can be mentioned.

[0092] Each object compound obtained in each of the above-mentioned reaction schemes can be isolated and purified from the reaction mixture by for example, cooling the reaction mixture, applying an isolation operation of filtration, concentration, extraction and the like to separate a crude reaction product, and applying a general purification operation such as column chromatography, recrystallization and the like.

[0093] Compound (I) naturally encompasses isomers such as a geometric isomer, a stereoisomer, an optical isomer and the like.

[0094] Compound (I) usable in the present invention is also encompasses same compounds labeled with the isotope, wherein one or plural atoms is(are) replaced by one or plural atoms having a particular atomic mass or mass number. Examples of the isotope that can be incorporated into compound (I) include hydrogen, carbon, nitrogen, oxygen, sulfur, fluorine and chlorine isotopes such as ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{18}F, ^{36}Cl and the like. Compound (I) labeled with particular isotope, which contains the above-mentioned isotope and/or other isotope of other atom, for example, compound (I) incorporating a radioactive isotope such as ^{3}H, ^{14}C and the like, is useful for drug tissue distribution assay and/or substrate tissue distribution assay. Tritiated (i.e., ^{3}H) or carbon-14 (i.e., ^{14}C) isotope are particularly preferred because of easiness of preparation and detectability. Furthermore, substitution with a heavier isotope such as deuterium (i.e., ^{2}H) and the like is expected to provide improved metabolic stability and particular therapeutic advantage attributable to increased in vivo half-time or decreased amount of necessary administration. An isotope-labeled compound of compound (I) can be generally prepared according to the method disclosed in WO2006/112464, by substituting a non-isotope-labeled reagent with an easily available isotope-labeled reagent.

[0095] Compound (I) may be a pharmaceutically acceptable cocrystal or a cocrystal salt. Here, the cocrystal or cocrystal salt means a crystalline substance, which is constituted from two or more kinds of specific solids each having different physical properties (e.g., structure, melting point, heat of fusion and the like) at room temperature. The cocrystal and cocrystal salt can be produced by applying a cocrystallization method known per se.

[0096] Compound (I) and a salt thereof are used in the form of a general pharmaceutical preparation. Such preparation is prepared using a diluent or excipient generally used such as filler, extender, binder, humidifying agent, disintegrant, surface activating agent, lubricant and the like. The pharmaceutical preparation can have various forms depending on the treatment object, and representative examples include tablet, pill, powder, liquid, suspension, emulsion, granule, capsule, suppository, injection (liquid, suspension etc.) and the like.

[0097] For formulation of a tablet, various ones conventionally known as a carrier in this field can be widely used. Examples thereof include excipients such as lactose, sucrose, sodium chloride, glucose, urea, starch, calcium carbonate, kaolin, crystalline cellulose, silicic acid and the like, binders such as water, ethanol, propanol, simple syrup, glucose solution, starch solution, gelatin solution, carboxymethylcellulose, shellac, methylcellulose, potassium phosphate, polyvinylpyrrolidone and the like, disintegrants such as dry starch, sodium alginate, agar powder, laminaran powder, sodium hydrogen carbonate, calcium carbonate, polyoxyethylene sorbitan fatty acid esters, sodium lauryl sulfate, stearic acid monoglyceride, starch, lactose and the like, disintegration inhibitors such as sucrose, stearin, cacao butter, hydrogenation oil and the like, absorption promoters such as quaternary ammonium base, sodium lauryl sulfate and the like, moisturizers such as glycerol, starch and the like, adsorbent such as starch, lactose, kaolin, bentonite, colloidal silicic acid and the like, lubricants such as purified talc, stearate, boric acid powder, polyethylene glycol and the like; and the like. Where necessary, the tablet can take the form of a tablet having a general coating, for example, sugar-coated tablet, gelatin-coated tablet, enteric tablet, film-coated tablet or double-compressed tablet, or multi-layer tablet.

[0098] For formulation of a pill, various ones conventionally known as a carrier in this field can be widely used. Examples thereof include excipients such as glucose, lactose, starch, cacao butter, hydrogenated vegetable oil, kaolin, talc and the like, binders such as gum arabic powder, tragacanth powder, gelatin, ethanol and the like, disintegrants such as laminaran, agar and the like; and the like.

[0099] For formulation of a suppository, various ones conventionally known as a carrier in this field can be widely used. Examples thereof include polyethylene glycol, cacao butter, higher alcohol, higher alcohol esters, gelatin, semi-synthetic glyceride and the like.

[0100] A capsule is prepared by a conventional method by generally mixing an active ingredient compound with various carriers mentioned above and filling the mixture in a hard gelatin capsule, a soft capsule and the like.

[0101] For formulation of an injection, a liquid, an emulsion and a suspension are preferably sterilized and isotonic with blood. For formulation into such form, various ones conventionally known as a diluent in this field can be widely used. Examples thereof include water, ethyl alcohol, macrogol, propylene glycol, ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, polyoxyethylene sorbitan fatty acid esters and the like.

[0102] In this case, sodium chloride, glucose or glycerol in an amount sufficient for the preparation of an isotonic solution may be contained in a pharmaceutical preparation, or general solubilizing agent, buffering agent, soothing agent and the like may be further added. Where necessary, colorant, preservative, fragrant material, flavor, sweetening agent

and the like and other pharmaceutical products may be further contained in the pharmaceutical preparation.

[0103] The amount of compound (I) or a salt thereof to be contained in the pharmaceutical preparation of the present invention is not particularly limited and is appropriately selected from a wide range. It is generally about 1 - 70 wt%, preferably about 1 - 30 wt%, of the preparation composition.

[0104] The administration method of the pharmaceutical preparation of the present invention is not particularly limited, and a method suitable for various dosage forms, age, sex and other conditions of patients, level of disease and the like is employed for administration. For example, tablet, pill, liquid, suspension, emulsion, granule and capsule are orally administered. An injection is intravenously administered singly or as a mixture with a general fluid replacement such as glucose, amino acid and the like. Where necessary, it is administered singly by intramuscular, intradermal, subcutaneous or intraperitoneal administration. A suppository is intrarectally administered.

[0105] While the dose of the pharmaceutical preparation of the present invention is appropriately selected according to use, age, sex and other conditions of patients, level of disease and the like, the amount of the active ingredient compound is generally about 0.1 - 10 mg per day and per 1 kg body weight. The active ingredient compound in the range of about 1 - 200 mg is desirably contained in a unit administration form of preparation.

Effect of the Invention

[0106] The compound of the present invention has a D_2 receptor partial agonist effect, a 5-HT_{2A} receptor antagonist effect and a serotonin uptake inhibitory effect (or serotonin reuptake inhibitory effect).

[0107] The D_2 receptor partial agonist effect suppresses dopaminergic (DA) neurotransmission when it is enhanced, and accelerates the DAergic neurotransmission when it is lowered and thus has a function to stabilize the DA neurotransmission to a normal state (dopamine system stabilizer). According to this function, excellent clinically improving effect on the abnormal DA neurotransmission (enhancement and lowering), for example, improving effect on positive and negative symptoms, improving effect on cognitive impairment, improving effect on depressive symptom etc. are developed without causing side effects (see Michio Toru: Clinical Psychiatry, vol. 46, pages 855 - 864 (2004), Tetsuro Kikuchi and Tsuyoshi Hirose: Brain Science, vol. 25, pages 579 - 583 (2004), and Harrison, T. S. and Perry, C. M.: Drugs 64: 1715-1736, 2004).

[0108] 5-HT_{2A} receptor antagonist effect reduces extrapyramidal side effects, develops superior clinical effects, and is effective, for example, for improvement of negative symptoms, improvement of cognitive impairment, improvement of depressive symptom, improvement of insomnia and the like (see Jun Ishigooka and Ken Inada: Japanese Journal of Clinical Psychopharmacology, vol. 4, pages 1653 - 1664 (2001), Mitsukuni Murasaki: Japanese Journal of Clinical Psychopharmacology, vol. 1, pages 5 - 22 (1998), Pullar, I.A. et al.: Eur. J. Pharmacol., 407: 39-46, 2000, and Meltzer, H. Y. et al.: Prog. Neuro-psychopharmacol. Biol. Psychiatry 27: 1159-1172, 2003).

[0109] Serotonin uptake inhibitory effect (or serotonin reuptake inhibitory effect) is effective, for example, for improvement of depressive symptom (see Mitsukuni Murasaki: Japanese Journal of Clinical Psychopharmacology, vol. 1, pages 5 - 22 (1998)).

[0110] The compound of the present invention is excellent in all of these three effects, or remarkably excellent in one or two of these effects.

[0111] In addition, some of the compounds of the present invention have α_1 receptor antagonist effect in addition to the above-mentioned effects. The α_1 receptor antagonist effect is effective for improving positive symptoms of schizophrenia (see Svensson, T. H.: Prog. Neuro-psychopharmacol. Biol. Psychiatry 27: 1145-1158, 2003).

[0112] Therefore, the compound of the present invention has a wide treatment spectrum for and excellent clinical effect on schizophrenia and other central nervous system diseases.

[0113] Accordingly, the compound, the medicament, and pharmaceutical composition of the present invention are extremely effective for the improvement of various central nervous system disorders including schizophrenia, treatment-resistant, refractory or chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder (e.g., bipolar disorder type I and bipolar disorder type II), mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder (e.g., panic attack, panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, generalized anxiety disorder, acute stress disorder, etc.), somatoform disorder (e.g., hysteria, somatization disorder, conversion disorder, pain disorder, hypochondriasis, etc.), factitious disorder, dissociative disorder, sexual disorder (e.g., sexual dysfunction, sexual desire disorder, sexual arousal disorder, erectile dysfunction, etc.), eating disorder (e.g., anorexia nervosa, bulimia nervosa, etc.), sleep disorder, adjustment disorder, substance-related disorder (e.g., alcohol abuse, alcohol intoxication and drug addiction, stimulant intoxication, narcotism, etc.), anhedonia (e.g., anhedonia, anhedonia, iatrogenic anhedonia, anhedonia of a psychic or mental cause, anhedonia associated with depression, anhedonia associated with schizophrenia, etc.), delirium, cognitive impairment, cognitive impairment associated with Alzheimer's disease, Parkinson's disease, and other neurodegenerative diseases, cognitive impairment caused by Alzheimer's disease, Parkinson's disease and associated neurodegenerative diseases, cognitive impairment in schiz-

ophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autistic disorder (autism), Tourette's disorder, tic disorder, attention deficit hyperactivity disorder, conduct disorder, Down's syndrome and the like.

[0114] Moreover, the compound of the present invention scarcely shows side effects and is superior in the tolerability and safety.

[0115] Furthermore, the compound of the present invention is markedly superior in the solubility in oil such as sesame oil and benzyl benzoate, and can be applied to an oil injection. An oil preparation of the compound of the present invention shows superior blood concentration sustainability. Since the compound of the present invention changes, in blood, to a compound (compound (1)) disclosed in patent document 1, the compound of the present invention is also superior in the long-term maintenance of the blood concentration of compound (1) having desired efficacy.

[0116] In addition, the compound of the present invention is easily crystallized, superior in the operability, and also superior in the chemical stability.

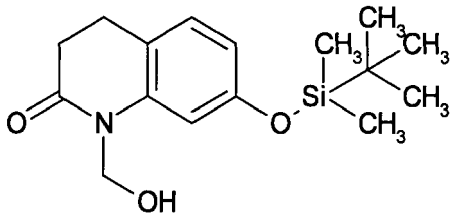
[0117] In addition, the compound (I) of the present invention can exert effects such as decreasing the amount of administration, improving side effects, enhancing therapeutic efficacy or the like which could not attained by conventional treatment by administering with at least one clinically used drug(s) selected from the group consisting of (1) mood stabilizers, (2) serotonin reuptake inhibitors, (3) norepinephrine reuptake inhibitors, (4) serotonin and norepinephrine reuptake inhibitors and (5) antidepressants.

[0118] The present invention is explained in more detail in the following by referring to Reference Example, Example and Experimental Example, which are not to be construed as limitative.

Reference Example 1

Synthesis of 7-(tert-butyldimethylsilanyloxy)-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one

[0119]

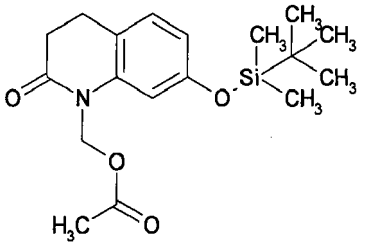


[0120] 7-(tert-Butyl-dimethylsilanyloxy)-3,4-dihydro-1H-quinolin-2-one (830 mg) was suspended in DMF (13 ml), formaldehyde (4.3 ml) and triethylamine (0.083 ml) were added, and the mixture was stirred at 80°C overnight. After cooling to room temperature, water was added, and the mixture was extracted with ethyl acetate, dried over sodium sulfate, and purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=2:1) to give the title compound (36 mg) as white crystals.

Reference Example 2

Synthesis of acetic acid 7-(tert-butyldimethylsilanyloxy)-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0121]



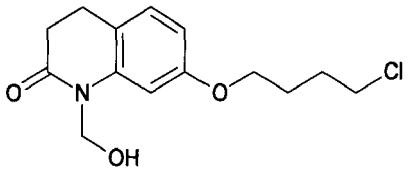
[0122] To a solution of 7-(tert-butyldimethylsilanyloxy)-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (37 mg) obtained in Reference Example 1 in dichloromethane were added pyridine (0.049 ml) and acetyl chloride (0.022 ml) and the mixture was stirred at room temperature overnight, and concentrated under reduced pressure. The residue was

purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=2:1) to give the title compound (26 mg) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 0.20 (s, 6H), 0.99 (s, 9H), 2.10 (s, 3H), 2.65-2.72 (m, 2H), 2.83-2.89 (m, 2H), 5.89 (brs, 2H), 6.51-6.56 (m, 2H), 6.99-7.04 (m, 1H)

Reference Example 3

Synthesis of 7-(4-chlorobutoxy)-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one

[0123]

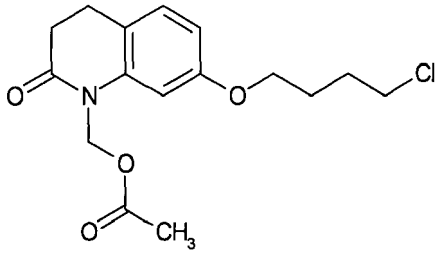


[0124] The compound was synthesized in the same manner as in Reference Example 1.

Reference Example 4

Synthesis of acetic acid 7-(4-chlorobutoxy)-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0125]

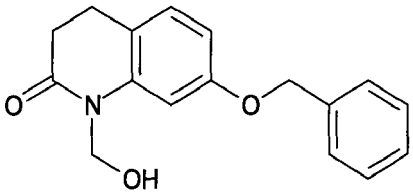


[0126] The compound was synthesized in the same manner as in Reference Example 2.
^{1}H-NMR ($CDCl_3$) δ: 1.90-2.03 (m, 4H), 2.12 (s, 3H), 2.64-2.72 (m, 2H), 2.84-2.90(m, 2H), 3.63 (t, J = 6.2 Hz, 2H), 3.99 (t, J = 5.7 Hz, 2H), 5.91 (brs, 2H), 6.58 (dd, J = 2.3, 8.2 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 7.08 (d, J = 8.2 Hz, 1H)

Reference Example 5

Synthesis of 7-benzyloxy-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one

[0127]

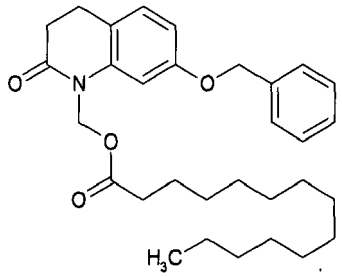


[0128] The compound was synthesized in the same manner as in Reference Example 1.

Reference Example 6

Synthesis of tetradecanoic acid 7-benzyloxy-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0129]

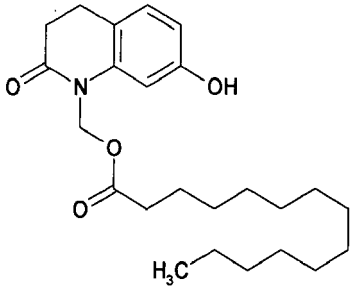


[0130] The compound was synthesized in the same manner as in Reference Example 2.

Reference Example 7

Synthesis of tetradecanoic acid 7-hydroxy-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0131]

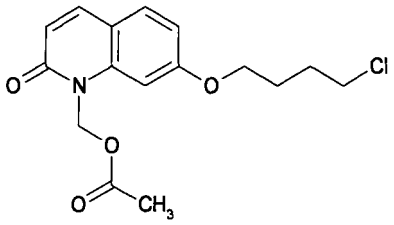


[0132] To a solution of tetradecanoic acid 7-benzyloxy-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester (528 mg) obtained in Reference Example 6 in ethanol (10 ml) was added 10% palladium carbon (53 mg), and the mixture was substituted with hydrogen and stirred at room temperature for 2.5 hr. The catalyst was filtered off, and the residue was concentrated under reduced pressure and purified by moderate-pressure silica gel column chromatography (ethyl acetate). After concentration under reduced pressure, the residue was recrystallized from hexane-ethyl acetate to give the title compound (209 mg) as a white powder.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.8 Hz, 3H), 1.20-1.35 (m, 20H), 1.58-1.68 (m, 2H), 2.35 (t, J = 7.6 Hz, 2H), 2.65-2.71 (m, 2H), 2.82-2.88 (m, 2H), 5.05 (brs, 1H), 5.90 (brs, 2H), 6.53 (dd, J = 2.4, 8.1 Hz, 1H), 6.56 (d, J = 2.4 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H)

Reference Example 8

Synthesis of acetic acid 7-(4-chlorobutoxy)-2-oxo-2H-quinolin-1-ylmethyl ester

[0133]

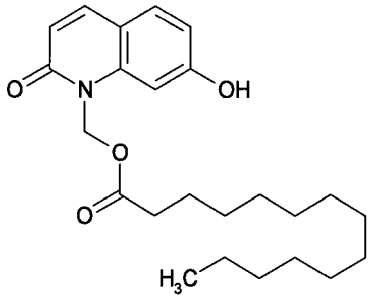


[0134] Acetic acid 7-(4-chlorobutoxy)-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester (339 mg) obtained in Reference Example 4 was dissolved in tetrahydrofuran (10 ml), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (709 mg) was added, and the mixture was stirred at room temperature for 2 days. To the reaction mixture was added aqueous sodium hydrogen carbonate solution and the mixture was stirred, filtered, and the filtrate was extracted with methylene chloride, dried over sodium sulfate, and concentrated under reduced pressure, and the residue was purified by moderate-pressure silica gel column chromatography (ethyl acetate) and concentrated under reduced pressure to give the title compound (299 mg) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.94-2.04 (m, 4H), 2.13 (s, 3H), 3.60-3.68 (m, 2H), 4.05-4.12 (m, 2H), 6.32 (brs, 2H), 6.53 (d, J = 9.5 Hz, 1H), 6.83 (dd, J = 2.2, 8.6 Hz, 1H), 6.89 (d, J = 2.2 Hz, 1H), 7.46 (d, J = 8.6 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Reference Example 9

Synthesis of tetradecanoic acid 7-hydroxy-2-oxo-2H-quinolin-1-ylmethyl ester

[0135]

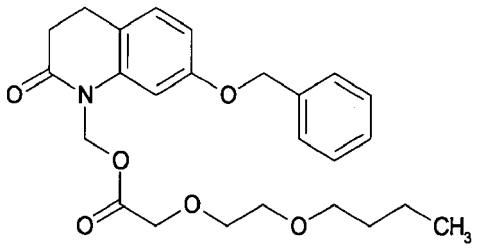


[0136] The compound was synthesized in the same manner as in Reference Example 8.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.8 Hz, 3H), 1.17-1.32 (m, 20H), 1.55-1.70 (m, 2H), 2.35 (t, J = 7.6 Hz, 2H), 6.31 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.55-6.68 (m, 1H), 6.78-6.82 (m, 1H), 6.84-6.87 (m, 1H), 7.43 (d, J = 8.5Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Reference Example 10

Synthesis of (2-butoxy ethoxy)-acetic acid 7-benzyloxy-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0137]



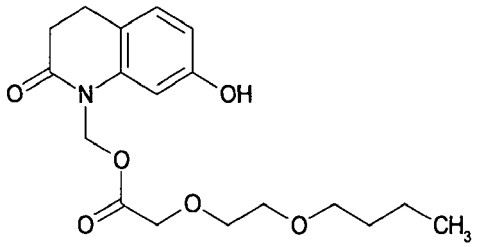
[0138] To a solution (20 ml) of 7-benzyloxy-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (760 mg) obtained in Reference Example 5, (2-butoxy ethoxy)acetic acid (473 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

(771 mg) in methylene chloride was added 4-dimethylaminopyridine (65.5 mg), and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. This was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1), and concentrated under reduced pressure to give the title compound (765 mg) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J = 7.4 Hz, 3H), 1.29-1.40 (m, 2H), 1.50-1.59 (m, 2H), 2.64-2.71 (m, 2H), 2.82-2.90 (m, 2H), 3.44 (t, J = 6.7 Hz, 2H), 3.57-3.63 (m, 2H), 3.70-3.75 (m, 2H), 4.18 (s, 2H), 5.06 (s, 2H), 5.95 (brs, 2H), 6.64-6.70 (m, 2H), 7.07 (d, J = 8.0 Hz, 1H), 7.30-7.45 (m, 5H)

Reference Example 11

Synthesis of (2-butoxy ethoxy)-acetic acid 7-hydroxy-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0139]

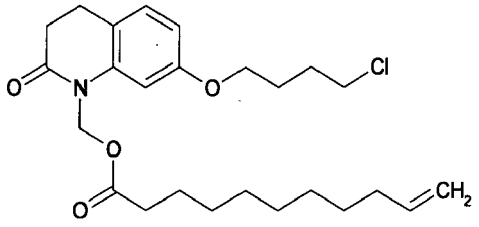


[0140] The compound was synthesized in the same manner as in Reference Example 7.
^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J = 7.4 Hz, 3H), 1.29-1.40 (m, 2H), 1.52-1.61 (m, 2H), 2.64-2.72 (m, 2H), 2.81-2.88 (m, 2H), 3.49 (t, J = 6.8 Hz, 2H), 3.62-3.67 (m, 2H), 3.71-3.76 (m, 2H), 4.19 (s, 2H), 5.98 (brs, 2H), 6.42-6.53 (m, 1H), 6.57 (dd, J = 2.3, 8.1 Hz, 1H), 6.65 (d, J = 2.3 Hz, 1H), 7.02 (d, J = 8.1 Hz, 1H)

Reference Example 12

Synthesis of undec-10-enoic acid 7-(4-chlorobutoxy)-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0141]

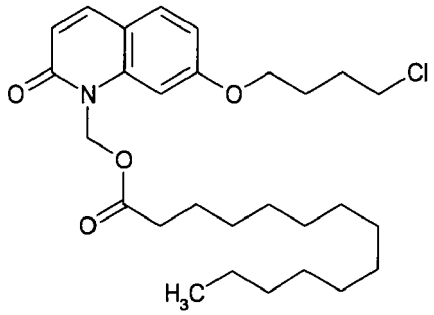


[0142] The compound was synthesized in the same manner as in Reference Example 10.
^{1}H-NMR ($CDCl_3$) δ: 1.23-1.40 (m, 10H), 1.57-1.68 (m, 2H), 1.90-2.07 (m, 6H), 2.35 (t, J = 7.5 Hz, 2H), 2.65-2.71 (m, 2H), 2.83-2.89 (m, 2H), 3.62 (t, J = 6.2 Hz, 2H), 3.98 (t, J = 6.8 Hz, 2H), 4.90-4.95 (m, 1H), 4.95-5.02 (m, 1H), 5.74-5.86 (m, 1H), 5.91 (brs, 2H), 6.58 (dd, J = 2.3, 8.1 Hz, 1H), 6.61 (d, J = 2.3 Hz, 1H), 7.07 (d, J = 8.1 Hz, 1H)

Reference Example 13

Synthesis of tetradecanoic acid 7-(4-chlorobutoxy)-2-oxo-2H-quinolin-1-ylmethyl ester

[0143]

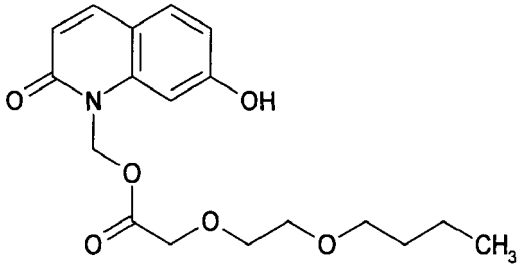


[0144] To a solution (5 ml) of tetradecanoic acid 7-hydroxy-2-oxo-2H-quinolin-1-ylmethyl ester (208 mg) obtained in Reference Example 9 in dimethylformamide were added 1-bromo-4-chlorobutane (0.358 ml) and potassium carbonate (107 mg) and the mixture was stirred at room temperature for 2 days. To the reaction mixture was added aqueous ammonium chloride solution, and the mixture was extracted with ethyl acetate. This was dried over sodium sulfate, and concentrated to give a crude product. The crude product was purified by silica gel column chromatography (hexane:ethyl acetate=1:0 to 2:1) to give the title compound (216 mg) as a white powder.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.9 Hz, 3H), 1.18-1.33 (m, 20H), 1.56-1.67 (m, 2H), 1.94-2.04 (m, 4H), 2.36 (t, J = 8.5 Hz, 2H), 3.61-3.66 (m, 2H), 4.04-4.10 (m, 2H), 6.33 (brs, 2H), 6.53 (d, J = 9.4 Hz, 1H), 6.82 (dd, J = 2.2, 8.6Hz, 1H), 6.88 (d, J = 2.2 Hz, 1H), 7.45 (d, J = 8.6 Hz, 1H), 7.63 (d, J = 9.4 Hz, 1H)

Reference Example 14

Synthesis of (2-butoxy-ethoxy)-acetic acid 7-hydroxy-2-oxo-2H-quinolin-1-ylmethyl ester

[0145]

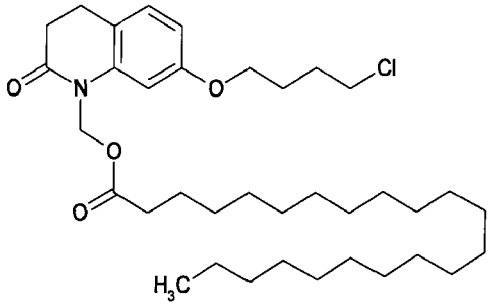


[0146] The compound was synthesized in the same manner as in Reference Example 8.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 7.3 Hz, 3H), 1.22-1.38 (m, 2H), 1.48-1.59 (m, 2H), 3.40-3.50 (m, 2H), 3.58-3.64 (m, 2H), 3.67-3.73 (m, 2H), 4.18 (s, 2H), 6.39 (brs, 2H), 6.50 (d, J = 9.4 Hz, 1H), 6.81-6.87 (m, 1H), 6.90-6.94 (m, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.64 (d, J = 9.5 Hz, 1H)

Reference Example 15

Synthesis of docosanoic acid 7-(4-chlorobutoxy)-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0147]

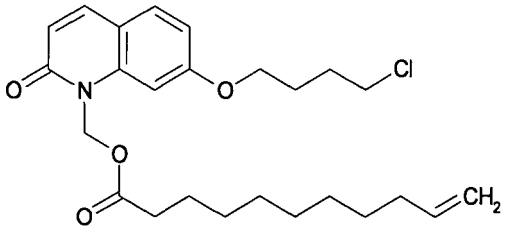


[0148] The compound was synthesized in the same manner as in Reference Example 12.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.8 Hz, 3H), 1.19-1.35 (m, 36H), 1.58-1.68 (m, 2H), 1.89-2.03 (m, 4H), 2.35 (t, J = 7.6 Hz, 2H), 2.64-2.72 (m, 2H), 2.82-2.90 (m, 2H), 3.62 (t, J = 6.2 Hz, 2H), 3.98 (t, J = 5.6 Hz, 2H), 5.91 (brs, 2H), 6.58 (dd, J = 2.3, 8.2 Hz, 1H), 6.60 (d, J = 2.3 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H)

Reference Example 16

Synthesis of undec-10-enoic acid 7-(4-chlorobutoxy)-2-oxo-2H-quinolin-1-ylmethyl ester

[0149]

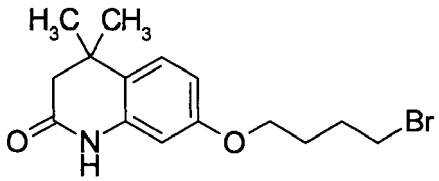


[0150] The compound was synthesized in the same manner as in Reference Example 8.
^{1}H-NMR ($CDCl_3$) δ: 1.20-1.39 (m, 10H), 1.57-1.67 (m, 2H), 1.95-2.05 (m, 6H), 2.36 (t, J = 7.5 Hz, 2H), 3.61-3.66 (m, 2H), 4.04-4.10 (m, 2H), 4.90-4.95 (m, 1H), 4.95-5.01 (m, 1H), 5.74-5.85 (m, 1H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.83 (dd, J = 2.2, 8.6 Hz, 1H), 6.88 (d, J = 2.2 Hz, 1H), 7.45 (d, J = 8.6 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Reference Example 17

Synthesis of 7-(4-bromobutoxy)-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one

[0151]

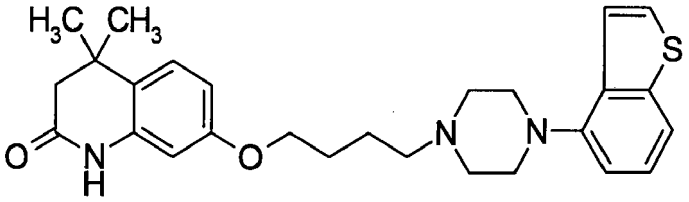


[0152] To a solution (20 ml) of 7-hydroxy-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (0.4 g) in DMF were added 1,4-dibromobutane (0.75 ml) and potassium carbonate (0.35 g) and the mixture was stirred at 60°C for 6 hr. After cooling to room temperature, water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (dichloromethane:methanol=100:1→50:1) to give the title compound (0.6 g) as a colorless solid.
^{1}H-NMR ($CDCl_3$) δ: 1.30 (6H, s), 1.88-1.98 (2H, m), 2.02-2.10 (2H, m), 2.47 (2H, s), 3.48 (2H, t, J=6.6Hz), 3.97 (2H, t, J=6.0Hz), 6.32 (1H, d, J=2.5Hz), 6.57 (1H, dd, J=8.5, 2.5Hz), 7.18 (1H, d, J=8.5Hz), 8.11 (1H, brs)

Reference Example 18

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one

[0153]

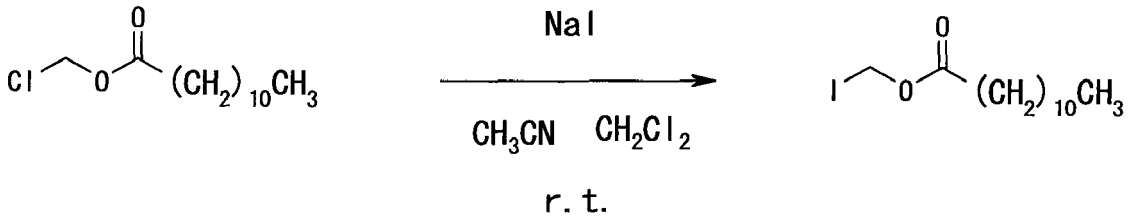


[0154] To a solution (20 ml) of 7-(4-bromobutoxy)-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (0.6 g) obtained in Reference Example 17 in DMF were added 1-benzo[b]thiophen-4-ylpiperazine hydrochloride (0.52 g) and potassium carbonate (0.64 g) and the mixture was stirred at 60°C for 6 hr. After cooling to room temperature, water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (dichloromethane:methanol=100:1→50:1) and crystallized from ethanol to give the title compound (0.33 g) as a white powder. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (6H, s), 1.68-1.78 (2H, m), 1.80-1.90 (2H, m), 2.46 (2H, s), 2.52 (2H, t, J=7.4Hz), 2.72 (4H, m), 3.19 (4H, m), 3.98 (2H, t, J=6.2Hz), 6.30 (1H, d, J=2.5Hz), 6.59 (1H, dd, J=8.5, 2.5Hz), 6.90 (1H, d, J=7.2Hz), 7.18 (1H, d, J=8.5Hz), 7.27 (1H, t, J=7.8Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.1Hz), 7.69 (1H, brs)

Reference Example 19

Synthesis of iodomethyldodecanoate

[0155]

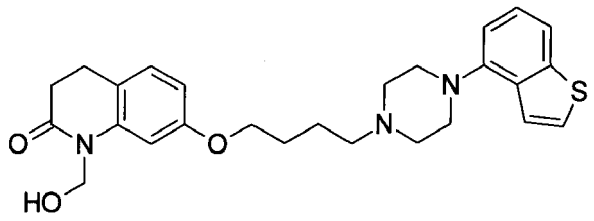


[0156] To a solution of chloromethyl dodecanoate[61413-67-0] (800 mg) in dichloromethane (10 ml) and acetonitrile (10 ml) was added sodium iodide (1.45 g), and the mixture was stirred at room temperature for 3 days. The solvent was evaporated under reduced pressure, water was added, and the mixture was extracted with dichloromethane, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to give iodomethyldbdecanoate (1.05 g).
oil: brown
^{1}H-NMR ($CDCl_3$) δ ppm : 0.88 (3H, t, J=7.0 Hz), 1.20-1.40 (16H, m), 1.50-1.70 (2H, m), 2.30-2.40 (2H, m), 5.91 (2H, s)

Example 1

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one

[0157]

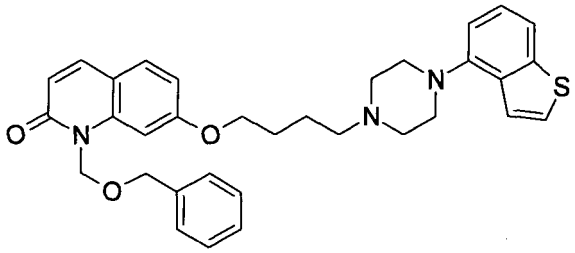


[0158] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (1 g) synthesized in the same manner as in WO2006/112464 (Example 11) in DMF (10 ml) were added 37% aqueous formalin solution (3.7 ml) and triethylamine (0.05 ml), and the mixture was heated at 80°C for 20 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane:methanol=30:1) to give a mixture (1 g, 3:2) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one and 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.80 (2H, m), 1.80-1.90 (2H, m), 2.48-2.55 (2H, m), 2.58-2.66 (2H, m), 2.66-2.78 (4H, m), 2.78-2.85 (1.2H, m), 2.86-2.92 (0.8H, m), 3.14-3.25 (4H, m), 3.94-4.40 (2H, m), 5.36 (1.2H, s), 6.31(0.4H, d, J=2.3Hz), 6.53 (0.4H, dd, J=2.4, 8.3Hz), 6.58 (0.6H, dd, J=2.4, 8.2Hz), 6.86 (0.6H, d, J=2.4Hz), 6.89 (1H, d, J=7.2Hz), 7.20-7.80 (1H, m), 7.27 (1H, t, J=8.4Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0Hz), 7.74-7.80 (0.4H, br)

Example 2

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-benzyloxymethyl-1H-quinolin-2-one

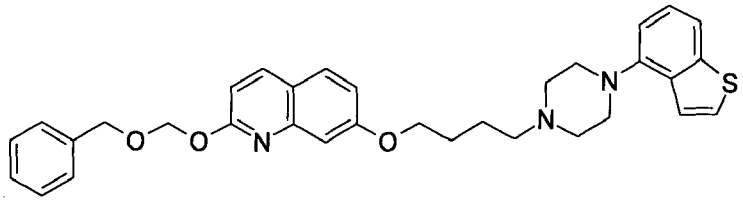
[0159]



Example 3

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-benzyloxymethoxy-quinoline

[0160]



[0161] 7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one (1.0 g, 2.31 mmol) synthesized in the same manner as in WO2006/112464 (Example 1) was suspended in tetrahydrofuran (THF) (20 ml) and, under a nitrogen atmosphere, sodium hydride (55% oil) (0.15 g, 3.44 mmol) was added and the mixture was stirred with heating under reflux for 30 min. The mixture was ice-cooled, benzylchloromethylether (0.48 ml, 3.46 mmol) was added, and the mixture was stirred at room temperature for 3 hr. To the reaction mixture was added ice water to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=100:0 to 0:100). The first fraction was concentrated under reduced pressure to give 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-benzyloxymethoxy-quinoline (0.15 g) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.83 (2H, m), 1.88-1.97 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.79 (4H, m), 3.15-3.25 (4H, m), 4.14 (2H, t, J=6.5Hz), 4.83 (2H, s), 5.78 (2H, s), 6.80 (1H, d, J=8.5Hz), 6.89 (1H, dd, J=0.5Hz, J=7.5Hz), 7.04 (1H, dd, J=2.5Hz, J=9.0Hz), 7.21 (1H, d, J=2.5Hz), 7.24-7.43 (8H, m), 7.54 (1H, d, J=8.0Hz), 7.60 (1H, d, J=8.0Hz), 7.94 (1H, d, J=8.5Hz)

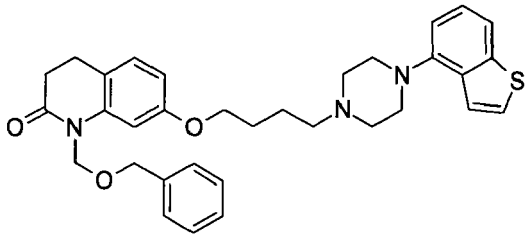
[0162] The second fraction was concentrated to dryness under reduced pressure to give 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-benzyloxymethyl-1H-quinolin-2-one (0.86 g) as a white amorphous solid.
^{1}H-NMR ($CDCl_3$) δ: 1.71-1.81 (2H, m), 1.85-1.94 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.78 (4H, m), 3.13-3.25 (4H, m),

4.09 (2H, t, J=6.0Hz), 4.67 (2H, s), 5.84 (2H, s), 6.50 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.5Hz, J=8.5Hz), 6.89 (1H, dd, J=0.5Hz, J=7.5Hz), 7.10 (1H, d, J=2.0Hz), 7.22-7.46 (9H, m), 7.55 (1H, d, J=8.0Hz), 7.60 (1H, d, J=9.5Hz)

Example 4

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-benzyloxymethyl-3,4-dihydro-1H-quinolin-2-one

[0163]

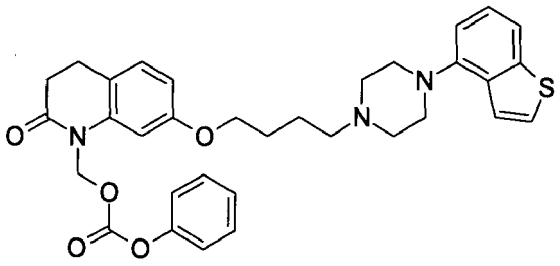


[0164] 7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (1.0 g, 2.30 mmol) synthesized in the same manner as in WO2006/112464 (Example 11) was suspended in tetrahydrofuran (THF) (20 ml) and, under a nitrogen atmosphere, sodium hydride (55% oil) (0.15 g, 3.44 mmol) was added, and the mixture was stirred with heating under reflux for 30 min. The mixture was ice-cooled, benzylchloromethylether (0.48 ml, 3.46 mmol) was added, and the mixture was stirred at room temperature for 3 hr. To the reaction mixture was added ice water to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=100:0 to 0:100) and concentrated under reduced pressure to give the title compound (yield 0.95 g, 74%) as a pale-yellow oil.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.90 (4H, m), 2.51 (2H, t, J=7.5Hz), 2.59-2.76 (6H, m), 2.78-2.85 (2H, m), 3.13-3.24 (4H, m), 3.98 (2H, t, J=6.0Hz), 4.66 (2H, s), 5.44 (2H, s), 6.08 (1H, dd, J=2.5Hz, J=8.0Hz), 6.89 (1H, dd, J=0.5Hz, J=7.5Hz), 7.00 (1H, d, J=2.5Hz), 7.03 (1H, d, J=8.0Hz), 7.23-7.43 (8H, m), 7.55 (1H, d, J=8.0Hz)

Example 5

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester

[0165]



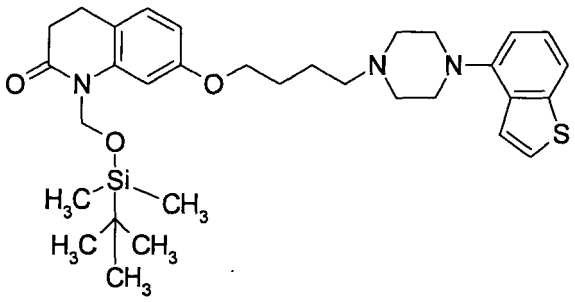
[0166] 7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (1.0 g, 2.30 mmol) synthesized in the same manner as in WO2006/112464 (Example 11) was suspended in tetrahydrofuran (THF) (20 ml) and, under a nitrogen atmosphere, sodium hydride (55% oil) (0.11 g, 2.52 mmol) was added, and the mixture was stirred with heating under reflux for 30 min. The mixture was cooled to -70°C, chloromethylphenylcarbonate (0.64 g, 3.43 mmol) was added, and the mixture was stirred at -70°C for 3 hr. Water was added to the reaction mixture to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=100:0 to 0:100) and concentrated under reduced pressure to give the title compound (yield 0.95 g, 74%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.91 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.85-2.92 (2H, m), 3.14-3.24 (4H, m),

4.01 (2H, t, J=6.5Hz), 6.06 (2H, s), 6.62 (1H, dd, J=2.5Hz, J=8.5Hz), 6.75 (1H, d, J=2.5Hz), 6.86-6.91 (1H, m), 7.09 (1H, d, J=8.5Hz), 7.19-7.29 (5H, m), 7.34-7.44 (3H, m), 7.55 (1H, d, J=8.0Hz)

Example 6

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-(tert-butyldimethylsilanyloxymethyl)-3,4-dihydro-1H-quinolin-2-one

[0167]

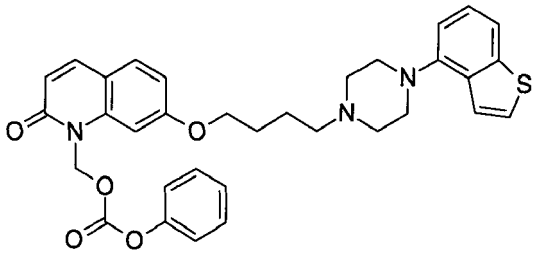


[0168] To a solution (15 ml) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (1.5 g) synthesized in the same manner as in WO2006/112464 (Example 11) in dimethylformamide (DMF) were added 37% aqueous formalin solution (5.5 ml) and a catalytic amount of triethylamine (0.08 ml) and the mixture was stirred at 80°C for 20 hr. After cooling to room temperature, and water was added to the reaction mixture. The obtained insoluble material was collected by filtration, dried, and dissolved in dichloromethane (15 ml). Imidazole (0.313 g) and tert-butylchlorodimethylsilane (0.519 g) were added, and the mixture was stirred at room temperature for 1.5 hr. Methanol was added, and the mixture was concentrated. This was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 2:1) to give the title compound (yield 550 mg, 41.3%) as a colorless amorphous solid.
^{1}H-NMR ($CDCl_3$) δ: 0.14 (6H, s), 0.90 (9H, s), 1.70-1.80 (2H, m), 1.80-1.92 (2H, m), 2.42 (2H, t, J=7.5Hz), 2.58-2.64 (2H, m), 2.68-2.76 (4H, m), 2.78-2.84 (2H, m), 3.14-3.24 (4H, m), 4.00 (2H, t, J=6.3Hz), 5.45 (2H, s), 6.58 (1H, dd, J=8.2Hz, 2.5Hz), 6.76 (1H, dd, J=7.6Hz, 0.6Hz), 7.00-7.04 (2H, m), 7.27 (1H, t, J=7.8Hz), 7.36-7.42 (2H, m), 7.54 (1H, d, J=8.1Hz)

Example 7

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester

[0169]

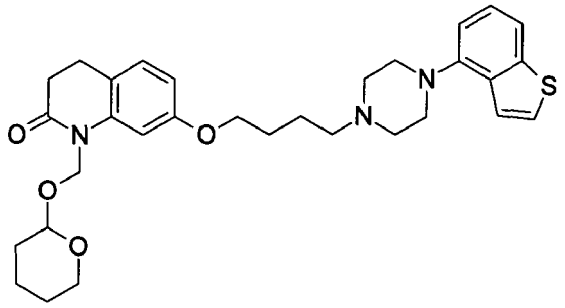


[0170] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.71-1.80 (2H, m), 1.85-1.95 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.65-2.76 (4H, m), 3.14-3.23 (4H, m), 4.08-4.14 (2H, m), 6.46 (2H, brs), 6.53 (1H, d, J=9.5Hz), 6.84-6.91 (2H, m), 6.97 (1H, d, J=2.0Hz), 7.18-7.30 (4H, m), 7.35-7.43 (4H, m), 7.47 (1H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.64 (1H, d, J=9.5Hz)

Example 8

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-(tetrahydropyran-2-yloxymethyl)-3,4-dihydro-1H-quinolin-2-one

[0171]

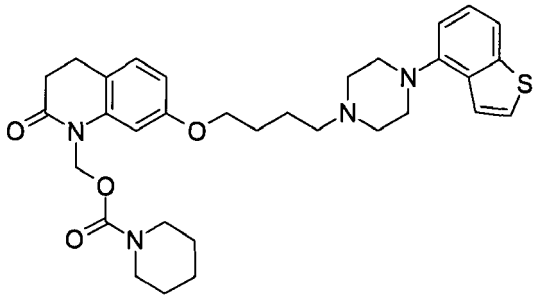


[0172] A solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (0.26 g), which is a mixture with 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one, was suspended in dichloromethane (10 ml), 3,4-dihydro-2H-pyran (0.08 ml) was added, p-toluenesulfonic acid hydrate (0.11 g) was added with stirring under ice-cooling, and the mixture was stirred at room temperature overnight. With stirring under ice-cooling, aqueous sodium hydrogen carbonate solution was added to the reaction mixture, and the mixture was extracted with dichloromethane, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane:methanol=60:1) to give 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-(tetrahydro-2H-pyran-2-yloxy)methyl-3,4-dihydro-1H-quinolin-2-one (180 mg).
^{1}H-NMR ($CDCl_3$) δ:1.50-1.80 (10H, m), 2.40-2.90 (6H, m), 2.72 (4H, brs), 3.20 (4H, brs), 3.40-4.00 (2H, m), 4.01 (2H, t, J=6.2Hz), 4.90-5.30 (3H, m), 6.58 (1H, dd, J=8.2Hz, 2.4Hz), 6.90 (1H, d, J=7.6Hz), 6.95 (1H, d, J=2.4Hz), 7.04 (1H, d, J=8.2Hz), 7.27 (1H, t, J=7.9Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.1Hz)

Example 9

Synthesis of piperidine-1-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0173]



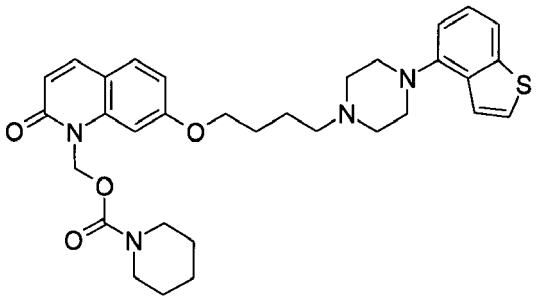
[0174] To a solution (3 ml) of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester (0.29 g) synthesized in the same manner as in Example 5 in THF were added piperidine (0.5 ml) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.05 ml), and the mixture was stirred at room temperature for 16 hr. Water was added and the reaction mixture was extracted with ethyl acetate, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure basic silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:1) to remove phenol, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1) to give the title compound (yield 0.21 g, 74%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.40-1.62 (6H, m), 1.69-1.90 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.62-2.79 (6H, m), 2.81-2.90 (2H, m),

3.13-3.26 (4H, m), 3.31-3.51 (4H, m), 3.99 (2H, t, J=6.0Hz), 5.93 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.0Hz), 6.78 (1H, d, J=2.5Hz), 6.86-6.92 (1H, m), 7.05 (1H, d, J=8.5Hz), 7.23-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, dd, J=0.5Hz, 5.5Hz), 7.54 (1H, d, J=8.0Hz)

Example 10

Synthesis of piperidine-1-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0175]

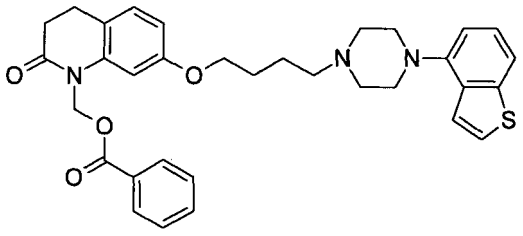


[0176] To a solution (5 ml) of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester (0.44 g) synthesized in the same manner as in Example 7 in THF was added piperidine (0.76 ml), and the mixture was stirred at room temperature for 3.5 days. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure basic silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:1) to give the title compound (0.44 g, yield quantitative) as a colorless amorphous solid.
^{1}H-NMR ($CDCl_3$) δ: 1.38-1.61 (6H, m), 1.72-1.82 (2H, m), 1.85-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.80 (4H, m), 3.14-3.25 (4H, m), 3.29-3.52 (4H, m), 4.10 (2H, t, J=6.0Hz), 6.36 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, 8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.12 (1H, t, J=2.0Hz), 7.23-7.31 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 11

Synthesis of benzoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0177]



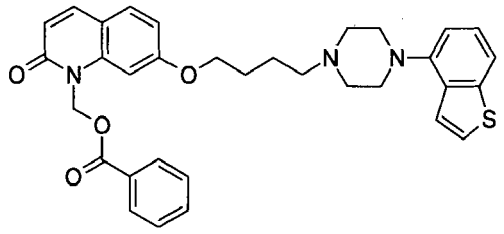
[0178] Sodium hydride (55% oil) (0.15 g, 2.52 mmol) was suspended in tetrahydrofuran (THF) (20 ml) and, under a nitrogen atmosphere, 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (1.0 g, 2.30 mmol) synthesized in the same manner as in WO2006/112464 (Example 11) was added, and the mixture was stirred with heating under reflux for 25 min. The mixture was cooled to 0°C, chloromethyl benzoate (0.627 g, 3.67 mmol) was added, and the mixture was stirred at room temperature for 2.5 hr. Under ice-cooling, aqueous ammonium chloride was added to the reaction mixture to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 2:3) and concentrated under reduced pressure to give the title compound (yield 1.132 g, 86.55%) as a colorless amorphous solid.

^{1}H-NMR ($CDCl_3$) δ: 1.64-1.75 (m, 2H), 1.77-1.86 (m, 2H), 2.44-2.51 (m, 2H), 2.61-2.77 (m, 6H), 2.87-2.93 (m, 2H), 3.11-3.22 (m, 4H), 3.97 (t, J = 6.3 Hz, 2H), 6.17 (brs, 2H), 6.61 (dd, J = 2.4, 8.3 Hz, 1H), 6.74 (d, J = 2.4 Hz, 1H), 6.84-6.91 (m, 1H), 7.09 (d, J = 8.3 Hz, 1H), 7.27 (dd, = 7.7, 7.7 Hz, 1H), 7.37-7.46 (m, 4H), 7.51-7.58 (m, 2H), 8.00-8.07 (m, 2H)

Example 12

Synthesis of benzoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0179]

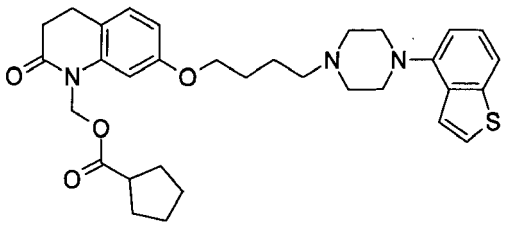


[0180] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.67-1.78 (m, 2H), 1.81-1.91 (m, 2H), 2.45-2.53 (m, 2H), 2.63-2.75 (m, 4H), 3.11-3.22 (m, 4H), 4.07 (t, J = 6.3 Hz, 2H), 6.56 (d, J = 9.5Hz, 1H), 6.59 (brs, 2H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.86-6.90 (m, 1H), 6.98 (d, J = 2.2 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.44 (m, 4H), 7.46 (d, J = 8.6 Hz, 1H), 7.51-7.59 (m, 2H), 7.65 (d, J = 9.5Hz, 1H), 8.02-8.07 (m, 2H)

Example 13

Synthesis of cyclopentanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0181]

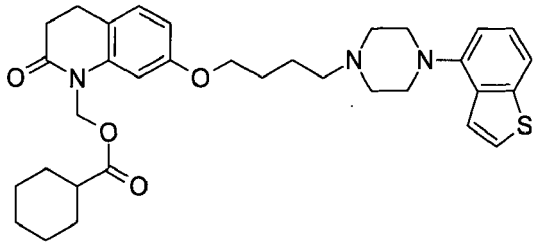


[0182] To a solution (20 ml) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (962 mg, 2.066 mmol) synthesized in the same manner as in Example 1, cyclopentanecarboxylic acid (0.448 ml, 4.13 mmol), 2-chloro-1,3-dimethylimidazolium chloride (768 mg, 4.55 mmol) in methylene chloride was added triethylamine (1.267 ml, 9.09 mmol), and the mixture was stirred at room temperature for 1 hr. 2-Chloro-1,3-dimethyl-imidazolium chloride (768 mg, 4.55 mmol) was added, and the mixture was heated under reflux for 1 hr. After cooling to room temperature, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. This was purified by moderate-pressure basic silica gel column (hexane:ethyl acetate=1:3) and concentrated under reduced pressure to give the title compound (yield 261 mg, 22.49%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.50-1.63 (m, 2H), 1.63-1.79 (m, 4H), 1.79-1.95 (m, 6H), 2.52 (t, J = 7.4 Hz, 2H), 2.64-2.83 (m, 7H), 2.83-2.89 (m, 2H), 3.13-3.25 (m, 4H), 3.98 (d, J = 6.2 Hz, 2H), 5.91 (brs, 2H), 6.57-6.61 (m, 2H), 6.89 (d, J = 7.6 Hz, 1H), 7.04-7.09 (m, 1H), 7.27 (dd, J = 7.8, 7.8Hz, 1H), 7.36-7.43 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H)

Example 14

Synthesis of cyclohexanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0183]

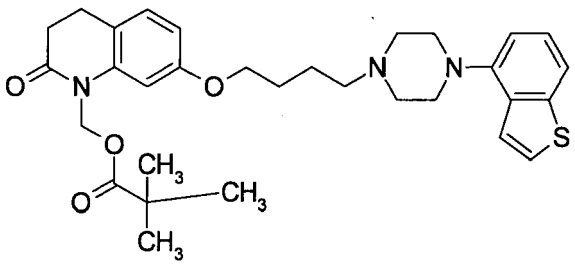


[0184] To a solution (15 ml) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (550 mg) synthesized in the same manner as in Example 1 in dichloromethane was added pyridine (0.287 ml), cyclohexanecarbonyl chloride (0.158 ml) with stirring under ice-cooling and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:3), and concentrated under reduced pressure. The residue was purified by basic silica gel column chromatography, and concentrated to dryness under reduced pressure to give the title compound (yield 172 mg, 25.3%) as a colorless amorphous solid.
^{1}H-NMR ($CDCl_3$) δ:1.15-1.32 (m, 3H), 1.40-1.53 (m, 2H), 1.57-1.65 (m, 1H), 1.68-1.79 (m, 4H), 1.81-1.96 (m, 4H), 2.36 (tt, J = 3.6, 11.2 Hz, 1H), 2.52 (t, J = 7.5 Hz, 2H), 2.65-2.76 (m, 6H), 2.83-2.90 (m, 2H), 3.15-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.91 (brs, 2H), 6.56-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.05-7.09 (m, 1H), 7.27 (dd, J = 7.7, 7.7 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 15

Synthesis of 2,2-dimethylpropionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0185]

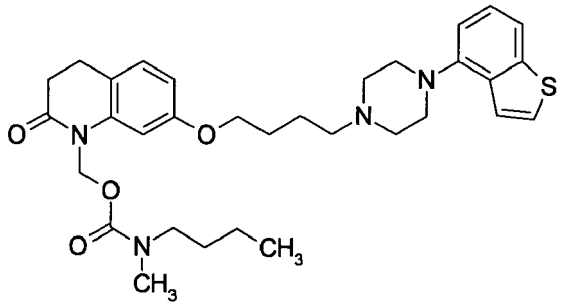


[0186] In the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.22 (s, 9H), 1.68-1.90 (m, 4H), 2.48-2.55 (m, 2H), 2.65-2.76 (m, 6H), 2.82-2.89 (m, 2H), 3.13-3.24 (m, 4H), 3.97 (t, J = 6.2 Hz, 2H), 5.90 (s, 2H), 6.57-6.62 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1Hz, 1H), 7.27 (dd, J = 7.7. 7.7 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.1 Hz, 1H)

Example 16

Synthesis of N-butyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0187]



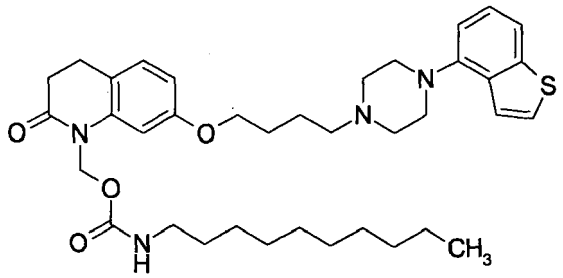
[0188] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: {0.82 (t, J=7.0Hz), 0.94 (t, J=7.0Hz) total 3H (1 : 1)}, 1.14-1.58 (4H, m), 1.64-1.91 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.63-2.78 (6H, m), 2.81-2.96 (5H, m), 3.13-3.33 (6H, m), 3.99 (2H, t, J=6.0Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.0Hz, 8.0Hz), 6.77 (1H, d, J=6.0Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.0Hz), 7.27 (1H, dd, J=8.0Hz, 8.0Hz), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=7.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 17

Synthesis of N-decylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0189]



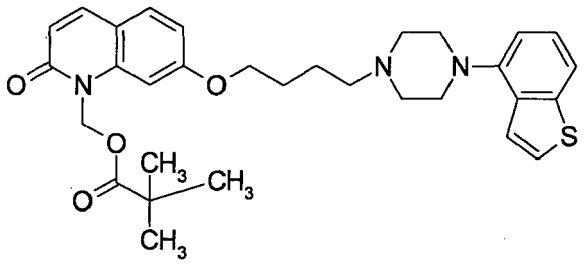
[0190] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0Hz), 1.16-1.34 (14H, m), 1.42-1.53 (2H, m), 1.69-1.89 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.62-2.77 (6H, m), 2.80-2.88 (2H, m), 3.12-3.25 (6H, m), 4.00 (2H, t, J=6.0Hz), 4.85 (1H, t, J=5.5Hz), 5.91 (2H, s), 6.59 (1H, dd, J=2.0Hz, 8.0Hz), 6.79 (1H, d, J=2.0Hz), 6.86-6.91 (1H, m), 7.05 (1H, d, J=8.0Hz), 7.27 (1H, dd, J=8.0Hz, 8.0Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.0Hz)

Example 18

Synthesis of 2,2-dimethylpropionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0191]

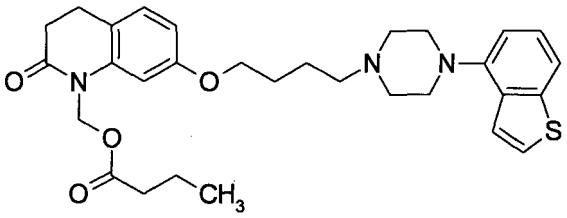


[0192] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.20 (s, 9H), 1.71-1.81 (m, 2H), 1.85-1.95 (m, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.67-2.78 (m, 4H), 3.15-3.24 (m, 4H), 4.06 (t, J = 6.2 Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.80 (d, J = 2.2 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.88-6.91 (m, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 19

Synthesis of butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0193]

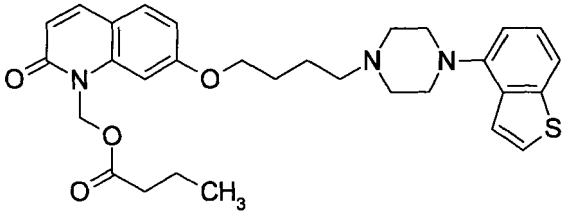


[0194] In the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.96 (t, J = 7.4 Hz, 3H), 1.63-1.79 (m, 4H), 1.80-1.90 (m, 2H), 2.35 (t, J = 7.4Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.64-2.77 (m, 6H), 2.82-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.99 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8Hz, 1H), 7.37-7.44 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 20

Synthesis of butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0195]

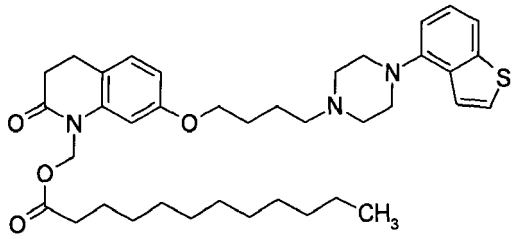


[0196] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.94 (t, J = 7.4 Hz, 3H), 1.62-1.72 (m, 2H), 1.72-1.82 (m, 2H), 1.86-1.96 (m, 2H), 2.35 (t, J =7.4 Hz, 2H), 2.54 (t, J = 7.4Hz, 2H), 2.65-2.78 (m, 4H), 3.13-3.25 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 21

Synthesis of dodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0197]

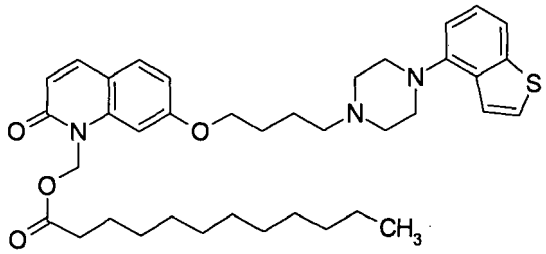


[0198] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.8 Hz), 1.20-1.36 (16H, m), 1.58-1.69 (2H, m), 1.69-1.80 (2H, m), 1.80-1.90 (2H, m), 2.36 (2H, t, J=7.6 Hz), 2.52 (2H, t, J=7.4 Hz), 2.64-2.76 (6H, m), 2.82-2.90 (2H, m), 3.14-3.26 (4H, br), 3.98 (2H, t, J=6.2 Hz), 5.92 (2H, brs), 6.56-6.64 (2H, m), 6.89 (1H, d, J=7.6 Hz), 7.07 (1H, d, J=8.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.40 (2H, dd, J=5.6, 12.6 Hz), 7.55 (1H, d, J=8.0 Hz)

Example 22

Synthesis of dodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0199]

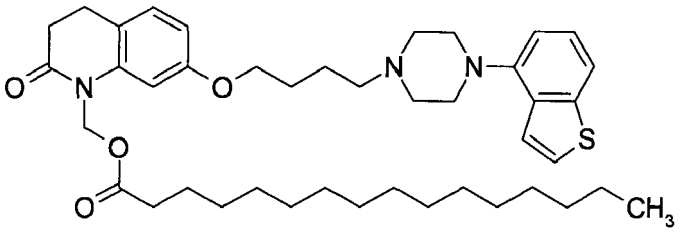


[0200] To a solution (5 ml) of dodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester (150 mg) synthesized in the same manner as in Example 21 in THF was added trifluoroacetic acid (TFA) (0.11 ml), then to a solution (3 ml) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.27 g) in THF was added, and the mixture was stirred at room temperature for 3 days. To the reaction mixture were added water and sodium carbonate, and the mixture was extracted with dichloromethane, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (ethyl acetate) to give the title compound (yield 50 mg, 33.4%) as a brown oil.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.9 Hz), 1.20-1.34 (16H, m), 1.55-1.68 (2H, m), 1.72-1.82 (2H, m), 1.85-1.94 (2H, m), 2.36 (2H, t, J=7.5 Hz), 2.50-2.60 (2H, m), 2.73 (4H, m), 3.20 (4H, m), 4.08 (2H, t, J=5.3 Hz), 6.34 (2H,brs), 6.52 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.5 Hz), 6.86-6.92 (2H, m), 7.24-7.30 (1H, m), 7.40 (2H, dd, J=5.6, 10.9 Hz), 7.45 (1H, d, J=8.6 Hz), 7.55 (1H, d, J=8.0 Hz), 7.62 (1H, d, J=9.5Hz)

Example 23

Synthesis of hexadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0201]

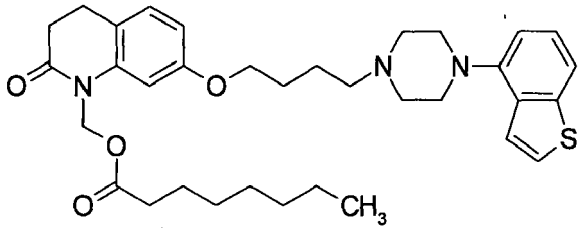


[0202] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.8, 3H), 1.18-1.34 (m, 26H), 1.57-1.80 (m, 4H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 2.63-2.77 (m, 6H), 2.83-2.89 (m, 2H), 3.15-3.25 (m, 2H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.59 (dd, J = 2.3, 8.1 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 24

Synthesis of octanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0203]

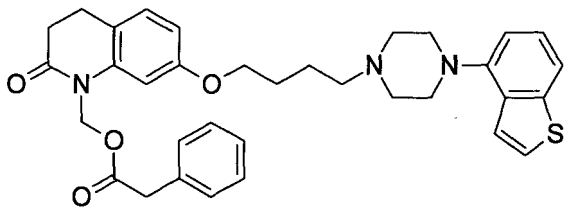


[0204] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.86 (t, J = 6.9Hz, 3H), 1.19-1.35 (m, 8H), 1.59-1.68 (m, 2H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 2.65-2.78 (m, 6H), 2.83-2.89 (m, 2H), 3.14-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J = 2.2, 8.1 Hz, 1H), 6.62 (d, J = 2.2, 1H), 6.88-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.1 Hz, 1H)

Example 25

Synthesis of phenylacetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0205]

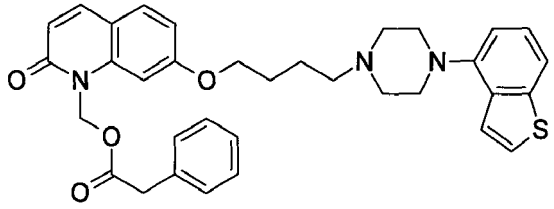


[0206] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.62-1.86 (m, 4H), 2.52 (t, J = 7.4 Hz, 2H), 2.65-2.77 (m, 6H), 2.82-2.88 (m, 2H), 3.14-3.25 (m, 4H), 3.68 (s, 2H), 3.85 (t, J = 6.2 Hz, 2H), 5.94 (brs, 2H), 6.51 (d, J = 2.3 Hz, 1H), 6.58 (dd, J = 2.3, 8.2 Hz, 1H), 6.88-6.92 (m, 1H), 7.06 (d, J = 8.2 Hz, 1H), 7.23-7.34 (m, 6H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.1 Hz, 1H)

Example 26

Synthesis of phenylacetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0207]

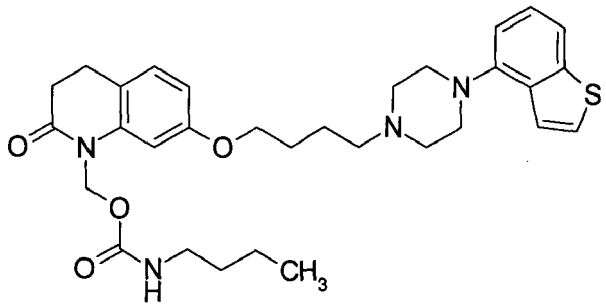


[0208] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) 5: 1.65-1.88 (m, 4H), 2.52 (t, J = 7.4 Hz, 2H), 2.64-2.78 (m, 4H), 3.14-3.25 (m, 4H), 3.67 (s, 2H), 3.87 (t, J = 6.2 Hz, 2H), 6.35 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.72 (d, J = 2.1 Hz, 1H), 6.82 (dd, J = 2.1, 8.6 Hz, 1H), 6.84-6.92 (m, 1H), 7.22-7.31 (m, 6H), 7.37-7.46 (m, 3H), 7.55 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 27

Synthesis of N-butylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0209]

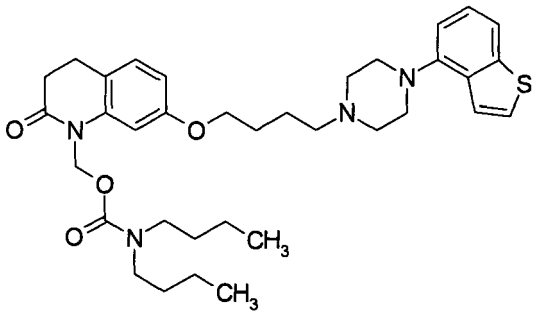


[0210] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, t, J=7.5Hz), 1.24-1.40 (2H, m), 1.43-1.53 (2H, m), 1.69-1.80 (2H, m), 1.81-1.91 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.82-2.89 (2H, m), 3.13-3.27 (6H, m), 4.00 (2H, t, J=6.0Hz), 4.74-4.82 (1H, m), 5.92 (2H, s), 6.59 (1H, dd, J=2.0Hz, 8.0Hz), 6.79 (1H, d, J=6.0Hz), 6.89 (1H, d, J=7.5Hz), 7.05 (1H, d, J=8.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 28

Synthesis of N,N-dibutylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0211]



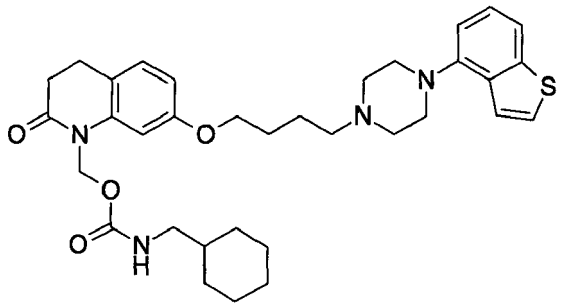
[0212] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.80 (3H, t, J=7.0Hz), 0.93 (3H, t, J=7.0Hz), 1.13-1.58 (8H, m), 1.68-1.90 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.62-2.78 (6H, m), 2.80-2.89 (2H, m), 3.09-3.30 (8H, m), 3.98 (2H, t, J=6.0Hz), 5.93 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.76 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 29

Synthesis of N-cyclohexylmethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0213]



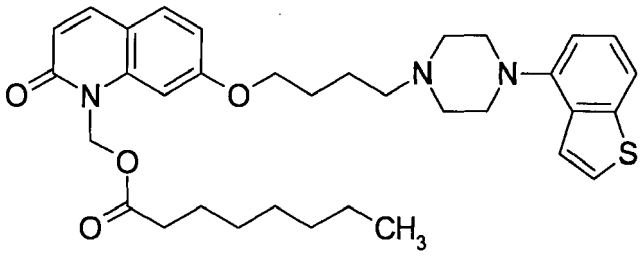
[0214] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.81-0.98 (2H, m), 1.07-1.30 (3H, m), 1.36-1.50 (1H, m), 1.59-1.80 (7H, m), 1.81-1.91 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.63-2.78 (6H, m), 2.81-2.89 (2H, m), 3.05 (2H, J=6.5Hz), 3.14-3.24 (4H, m), 4.00 (2H, t, J=6.0Hz), 4.84 (1H, t, J=5.5Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.80 (1H, d, J=2.0Hz), 6.87-6.92 (1H, m), 7.05 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.37-7.44 (2H, m), 7.55 (1H, d, J=8.0Hz)

Example 30

Synthesis of octanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0215]

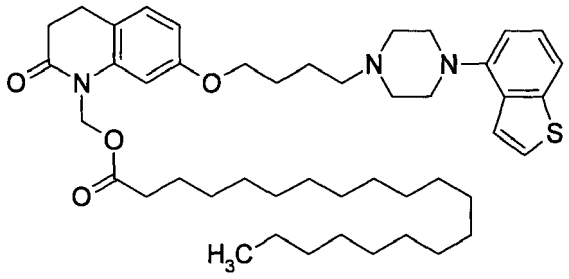


[0216] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.85 (t, J = 6.9 Hz, 3H), 1.16-1.33 (m, 8H), 1.57-1.68 (m, 2H), 1.74-1.96 (m, 4H), 2.36 (t, J = 7.5 Hz, 2H), 2.52-2.63 (m, 2H), 2.69-2.85 (m, 4H), 3.15-3.29 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.1, 8.6 Hz, 1H), 6.86-6.92 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.42 (m, 2H), 7.45 (d, J = 8.6Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 31

Synthesis of icosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0217]

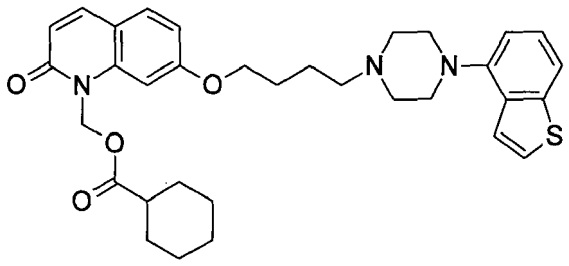


[0218] To a solution (6 ml) of arachidic acid (1048 mg, 3.35 mmol) in 1,2-dichloroethane was added thionyl chloride (1.217 ml, 16.77 mmol), and the mixture was heated under reflux, and concentrated under reduced pressure to give acid chloride. To a solution (15 ml) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (781 mg, 1.677 mmol) synthesized in the same manner as in Example 1 in dichloromethane were added pyridine (1.357 ml, 16.77 mmol) and the above-mentioned acid chloride, and the mixture was stirred at room temperature for 3 hr. The organic layer was dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:1), and concentrated under reduced pressure. The residue was purified by basic silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:1), and concentrated to dryness under reduced pressure to give the title compound (yield 856 mg, 67%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.8 Hz, 3H), 1.19-1.35 (m, 32H), 1.57-1.68 (m, 2H), 1.69-1.79 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.6 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.89 (m, 2H), 3.14-3.25 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J = 2.3, 8.1 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.1 Hz, 1H)

Example 32

Synthesis of cyclohexanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0219]

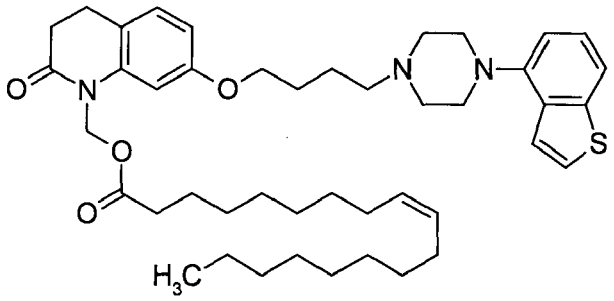


[0220] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.14-1.31 (m, 3H), 1.39-1.52 (m, 2H), 1.54-1.65 (m, 1H), 1.67-1.82 (m, 4H), 1.84-1.95 (m, 4H), 2.31-2.41 (m, 1H), 2.54 (t, J = 7.6 Hz, 2H), 2.65-2.79 (m, 4H), 3.13-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.86 (m, 2H), 6.89 (d, J = 7.6 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.47 (m, 3H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 33

Synthesis of (Z)-octadec-9-enoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0221]

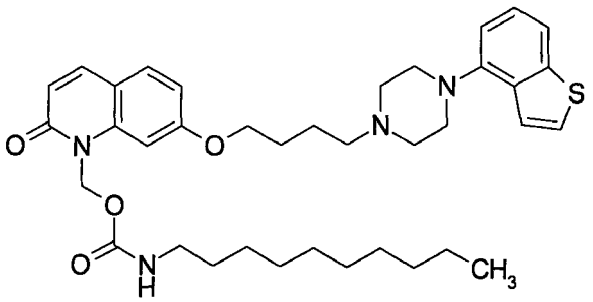


[0222] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.87 (t, J = 6.8 Hz, 3H), 1.20-1.36 (m, 20H), 1.58-1.68 (m, 2H), 1.69-1.79 (m, 2H), 1.80-1.90 (m, 2H), 1.93-2.07 (m, 4H), 2.36 (t, J = 7.5 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.79 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.99 (t, J = 6.3 Hz, 2H), 5.28-5.40 (m, 2H), 5.92 (brs, 2H), 6.60 (dd, J = 2.3. 8.1 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 34

Synthesis of N-decylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0223]

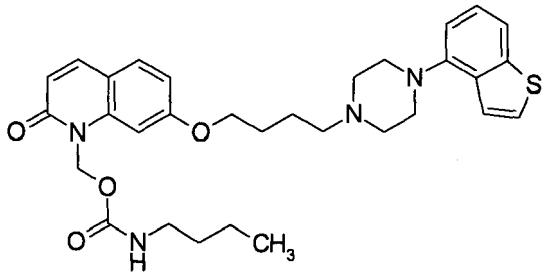


[0224] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0Hz), 1.16-1.35 (12H, m), 1.42-1.53 (4H, m), 1.72-1.83 (2H, m), 1.86-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.67-2.80 (4H, m), 3.13-3.28 (6H, m), 4.11 (2H, t, J=6.0Hz), 4.87 (1H, t, J=5.5Hz), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.92 (1H, m), 7.16 (1H, d, J=1.5Hz), 7.24-7.30 (1H, m), 7.36-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 35

Synthesis of N-butylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0225]

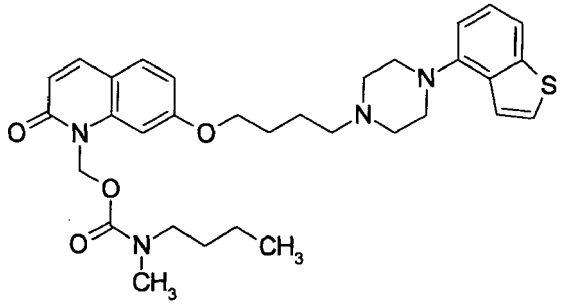


[0226] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.91 (3H, t, J=7.5Hz), 1.28-1.39 (2H, m), 1.43-1.53 (2H, m), 1.73-1.82 (2H, m), 1.87-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.67-2.78 (4H, m), 3.15-3.24 (6H, m), 4.11 (2H, t, J=6.0Hz), 4.88 (1H, t, J=5.5Hz), 6.32 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.15 (1H, d, J=1.5Hz), 7.24-7.30 (1H, m), 7.37-7.45 (3H, m), 7.55 (1H, d; J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 36

Synthesis of N-butyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0227]



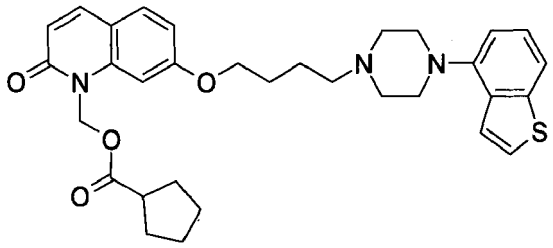
[0228] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: {0.87 (t, J=7.5Hz), 0.94 (t, J=7.5Hz) total 3H (1 : 1)}, 1.08-1.19 (1H, m), 1.26-1.43 (2H, m), 1.47-1.57 (1H, m), 1.72-1.83 (2H, m), 1.85-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.79 (4H, m), {2.82 (s), 2.92 (s) total 3H (1 : 1)}, 3.12-3.25 (5H, m), 3.30 (1H, t, J=7.5Hz), 4.10 (2H, t, J=6.0Hz), 6.35 (2H, s), 6.52 (1H, dd, J=1.5Hz, J=9.5Hz), 6.83 (1H, dd, J=1.5Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.10 (1H, d, J=16.5Hz), 7.25-7.30 (1H, m), 7.37-7.45 (3H, m), 7.55

(1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 37

Synthesis of cyclopentanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0229]



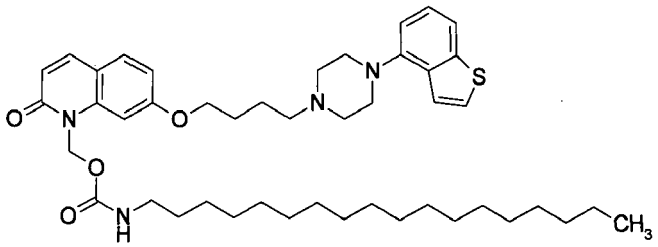
[0230] To a solution (10 ml) of cyclopentanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester (252 mg) synthesized in the same manner as in Example 13 in THF was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (509 mg), and the mixture was stirred at room temperature stirred for 2 days. To the reaction mixture were added water and sodium carbonate, and the mixture was extracted with dichloromethane, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1) and further by NH silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1) to give the title compound (yield 38 mg, 15%) as a colorless amorphous solid.

^{1}H-NMR ($CDCl_3$) δ:1.50-1.62 (m, 2H), 1.62-1.95 (m, 10H), 2.54 (t, J = 7.5Hz, 2H), 2.67-2.83 (m, 5H), 3.14-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.86 (m, 2H), 6.89 (d, J = 7.4 Hz, 1H), 7.27 (t, J = 7.9, 7.9 Hz, 1H), 7.37-7.47 (m, 3H), 7.55 (d, J = 7.9 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 38

Synthesis of N-octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0231]



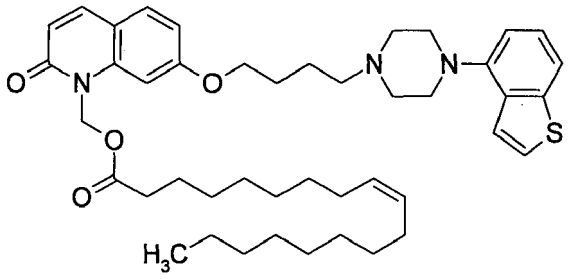
[0232] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0Hz), 1.13-1.34 (30H, m), 1.43-1.53 (2H, m), 1.73-1.83 (2H, m), 1.85-1.965 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.79 (4H, m), 3.13-3.25 (6H, m), 4.12 (2H, t, J=6.0Hz), 4.85 (1H, t, J=5.5Hz), 6.33 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.16 (1H, d, J=1.5Hz), 7.24-7.30 (1H, m), 7.36-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 39

Synthesis of (Z)-octadec-9-enoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0233]

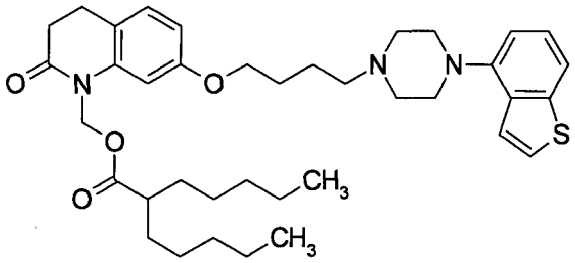


[0234] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6.8 Hz, 3H), 1.18-1.35 (m, 20H), 1.57-1.68 (m, 2H), 1.72-1.82 (m, 2H), 1.86-2.04 (m, 6H), 2.36 (t, J = 7.4 Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.67-2.79 (m, 4H), 3.14-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 5.26-5.39 (m, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (t, J = 7.9 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 40

Synthesis of 2-pentylheptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0235]

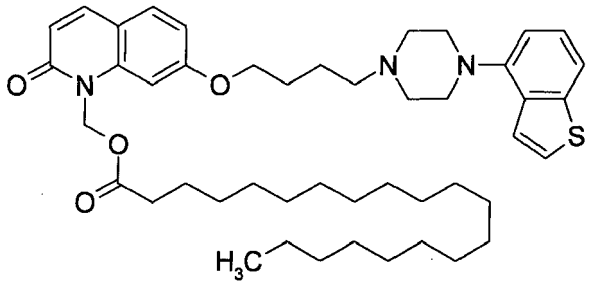


[0236] In the same manner as in Example 31, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.85 (t, 6H), 1.17-1.31 (m, 12H), 1.37-1.49 (m, 2H), 1.55-1.78 (m, 4H), 1.79-1.89 (m, 2H), 2.32-2.41 (m, 1H), 2.52 (t, J = 7.4 Hz, 2H), 2.64-2.77 (m, 6H), 2.82-2.89 (m, 2H), 3.13-3.24 (m, 4H), 3.97 (t, J = 6.2 Hz, 2H), 5.94 (brs, 2H), 6.59 (dd, J = 2.3, 8.2 Hz, 1H), 6.63 (d, J = 2.3 Hz, 1H), 6.87-6.92 (m, 1H), 7.06 (d, J = 8.2Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H),

Example 41

Synthesis of icosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0237]

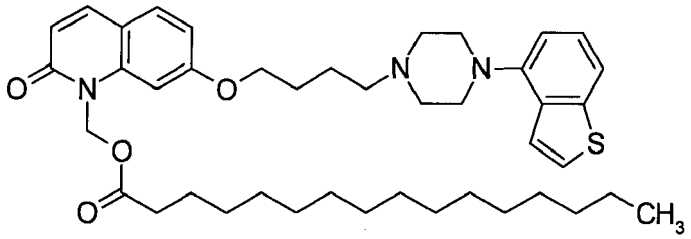


[0238] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.88 (t, J = 6.8 Hz, 3H), 1.18-1.33 (m, 32H), 1.58-1.67 (m, 2H), 1.72-1.82 (m, 2H), 1.86-1.96 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.67-2.77 (m, 4H), 3.14-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.1, 8.6 Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.36-7.43 (m, 2H), 7.44 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 42

Synthesis of hexadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0239]

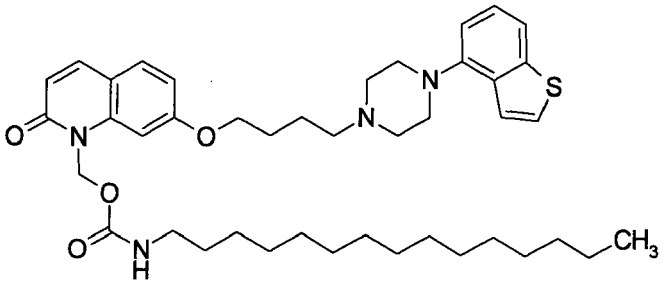


[0240] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6.8 Hz, 3H), 1.18-1.32 (m, 24H), 1.58-1.67 (m, 2H), 1.72-1.95 (m, 4H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.78 (m, 4H), 3.14-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.36-7.43 (m, 2H), 7.44 (d, J = 9.5 Hz, 1H), 7.55 (d, J = 8.6 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 43

Synthesis of N-pentadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0241]



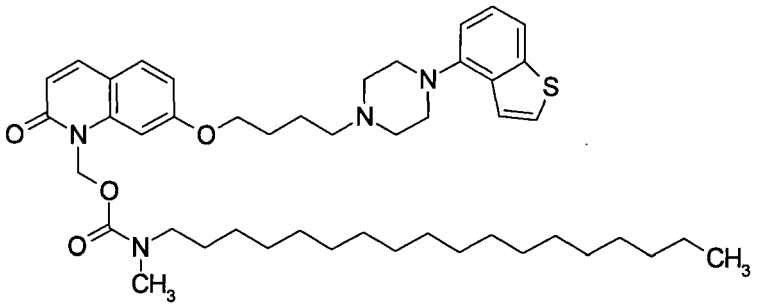
[0242] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title

compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0Hz), 1.16-1.33 (24H, m), 1.42-1.53 (2H, m), 1.72-1.83 (2H, m), 1.86-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.67-2.78 (4H, m), 3.14-3.24 (6H, m), 4.11 (2H, t, J=6.0Hz), 4.86 (1H, t, J=5.5Hz), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J= 8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.39 (1H, d, J=1.5Hz), 7.24-7.29 (1H, m), 7.37-7.44 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 44

Synthesis of N-methyl-N-octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0243]

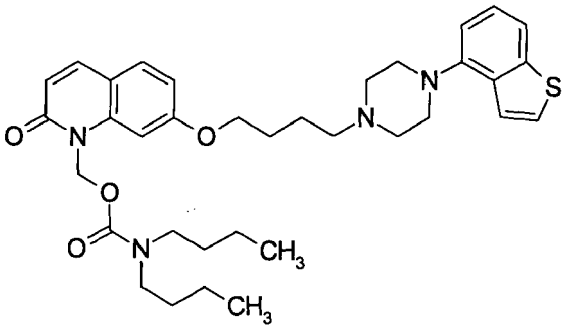


[0244] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0Hz), 1.01-1.32 (30H, m), 1.33-1.43 (1H, m), 1.47-1.58 (1H, m), 1.72-1.83 (2H, m), 1.85-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.78 (4H, m), {2.82 (s), 2.93 (s) total 3H (1 : 1)}, 3.12-3.24 (5H, m), 3.25-3.32 (1H, m), 4.09 (2H, t, J=5.5Hz), 6.36 (2H, s), 6.52 (1H, dd, J=2.0Hz, J=9.5Hz), 6.83 (1H, d, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.10 (1H, d, J=17.5Hz), 7.24-7.30 (1H, m), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.66 (1H, dd, J=4.0Hz, J=9.5Hz)

Example 45

Synthesis of N,N-dibutylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0245]



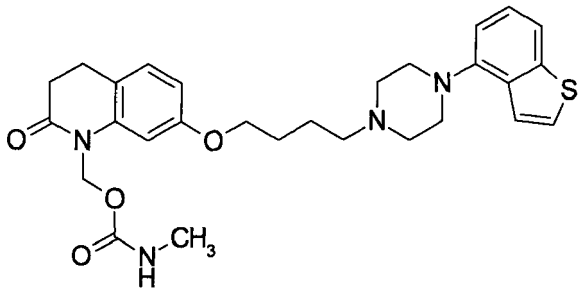
[0246] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.72 (3H, t, J=7.5Hz), 0.93 (3H, t, J=7.5Hz), 1.06-1.19 (2H, m), 1.24-1.42 (4H, m), 1.48-1.59 (2H, m), 1.72-1.83 (2H, m), 1.85-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.83 (4H, m), 3.12 (2H, t, J=7.5Hz), 3.15-3.23 (4H, m), 3.26 (2H, J=7.5Hz), 4.09 (2H, t, J=6.0Hz), 6.36 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz),

6.90 (1H, d, J=7.5Hz), 7.07 (1H, d, J=2.0Hz), 7.25-7.31 (1H, m), 7.37-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 46

Synthesis of N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0247]

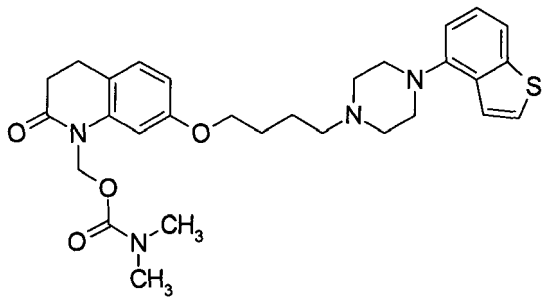


[0248] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.70-1.80 (2H, m), 1.81-1.91 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.63-2.77 (6H, m), 2.79-2.89 (5H, m), 3.14-3.24 (4H, m), 4.00 (2H, t, J=6.0Hz), 4.75 (1H, d, J=4.0Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.78 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 47

Synthesis of N,N-dimethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0249]

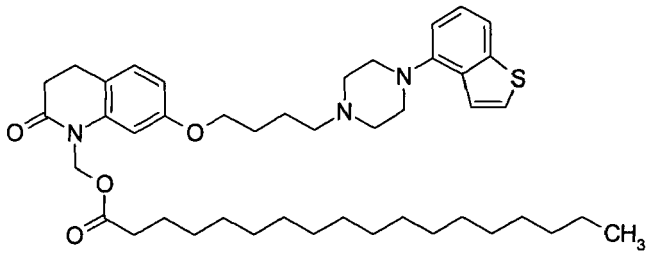


[0250] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.79 (2H, m), 1.81-1.90 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.83-2.91 (2H, m), 2.88 (3H, s), 2.95 (3H, s), 3.14-3.24 (4H, m), 4.00 (2H, t, J=6.5Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.78 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.42 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 48

Synthesis of octadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-yl-methyl ester

[0251]

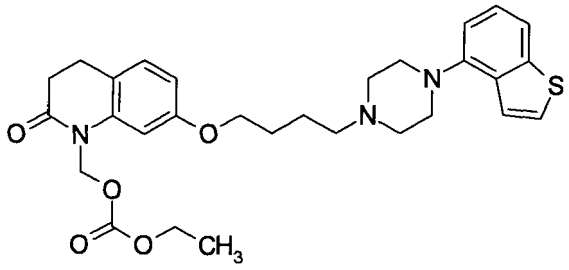


[0252] To a solution (20 ml) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-3,4-dihydro-1H-quinolin-2-one (640 mg, 2.066 mmol) synthesized in the same manner as in Example 1, stearic acid (587 mg, 2.062 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (395 mg, 2.062 mmol) in methylene chloride was added 4-dimethylaminopyridine (33.6 mg, 0.275 mmol), and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate. This was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1) and further by basic silica gel column chromatography (hexane:ethyl acetate=1:0 to 0:1) and concentrated under reduced pressure to give the title compound (yield 649 mg, 64.5%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ:0.88 (t, J = 6.9 Hz, 3H), 1.18-1.35 (m, 28H), 1.59-1.68 (m, 2H), 1.69-1.79 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.65-2.76 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J = 2.2, 8.1 Hz, 1H), 6.62 (d, J = 2.2 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 49

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester ethyl ester

[0253]

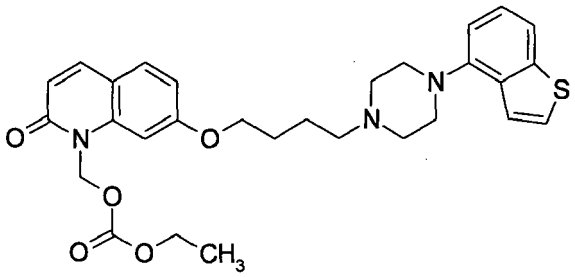


[0254] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, t, J=7.2 Hz), 1.70-1.80 (2H, m), 1.80-1.90 (2H, m), 2.52 (2H, t, J=7.4 Hz), 2.65-2.73 (2H, m), 2.72 (4H, m), 2.86 (2H, t, J=7.2 Hz), 3.14-3.24 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.25 (2H, q, J=7.2 Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.3, 8.3 Hz), 6.69 (1H, d, J=2.3 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.37-7.43 (2H, m), 7.55 (1H, d, J=8.1 Hz)

Example 50

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester ethyl ester

[0255]

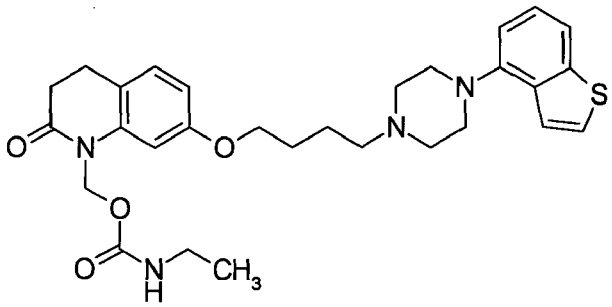


[0256] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) 5: 1.31 (3H, t, J=7.1 Hz), 1.72-1.84 (2H, m), 1.84-1.96 (2H, m), 2.56 (2H, t, J=7.4 Hz), 2.70-2.80 (4H, m), 3.16-3.26 (4H, m), 4.10 (2H, t, J=6.2 Hz), 4.26 (2H, q, J=7.1 Hz), 6.35 (2H,brs), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.88-6.95 (2H, m), 7.27 (1H, t, J=7.8 Hz), 7.37-7.41 (2H, m), 7.44 (1H, d, J=8.6 Hz), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 51

Synthesis of N-ethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0257]

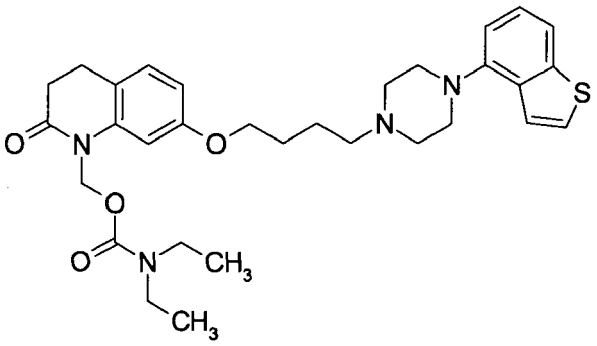


[0258] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.14 (3H, t, J=7.0Hz), 1.69-1.80 (2H, m), 1.81-1.90 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.61-2.79 (6H, m), 2.81-2.90 (2H, m), 3.09-3.31 (6H, m), 4.00 (2H, t, J=6.0Hz), 4.73-4.84 (1H, m), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.79 (1H, d, J=2.0Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.37-7.44 (2H, m), 7.55 (1H, d, J=8.0Hz)

Example 52

Synthesis of N,N-diethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0259]

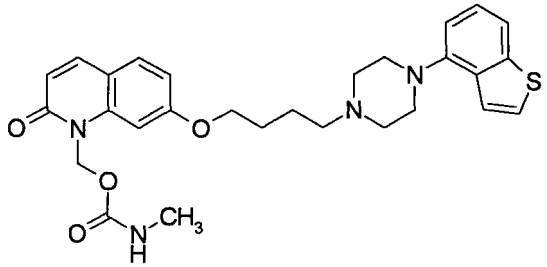


[0260] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.00-1.19 (6H, m), 1.66-1.79 (2H, m), 1.80-1.91 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.63-2.78 (6H, m), 2.82-2.90 (2H, m), 3.14-3.38 (8H, m), 3.99 (2H, t, J=6.0Hz), 5.93 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.77 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 53

Synthesis of N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0261]

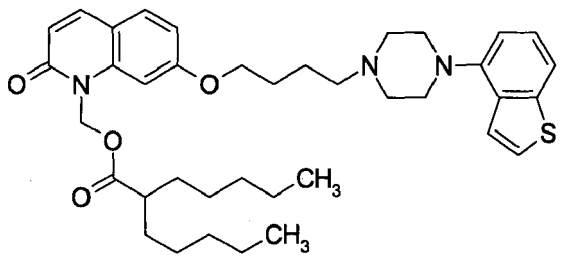


[0262] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.84 (2H, m), 1.85-1.96 (2H, m), 2.55 (2H, t, J=7.5Hz), 2.66-2.78 (4H, m), {2.82 (s), 2.84 (s) total 3H (1: 1)}, 3.13-3.26 (4H, m), 4.12 (2H, t, J=6.0Hz), 4.76-4.86 (1H, m), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.15 (1H, d, J=2.0Hz), 7.24-7.31 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 54

Synthesis of 2-pentylheptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0263]

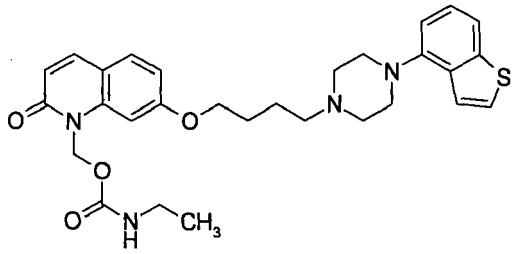


[0264] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.80 (t, J = 6.5 Hz, 6H), 1.13-1.24 (m, 12H), 1.37-1.48 (m, 2H), 1.54-1.66 (m, 2H), 1.71-1.81 (m, 2H), 1.85-1.95 (m, 2H), 2.33-2.43 (m, 1H), 2.54 (t, J = 7.4 Hz, 2H), 2.64-2.79 (m, 4H), 3.13-3.26 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.36 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.83 (dd, J = 2.1, 8.6 Hz, 1H), 6.87-6.93 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.44 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J=9.5Hz, 1H)

Example 55

Synthesis of N-ethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0265]

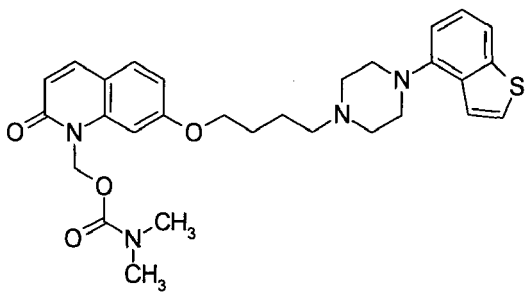


[0266] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.14 (3H, t, J=7.0Hz), 1.72-1.82 (2H, m), 1.85-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.78 (4H, m), 3.13-3.30 (6H, m), 4.12 (2H, t, J=6.0Hz), 4.80-4.89 (1H, m), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.92 (1H, m), 7.13-7.17 (1H, m), 7.24-7.30 (1H, m), 7.37-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 56

Synthesis of N,N-dimethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0267]

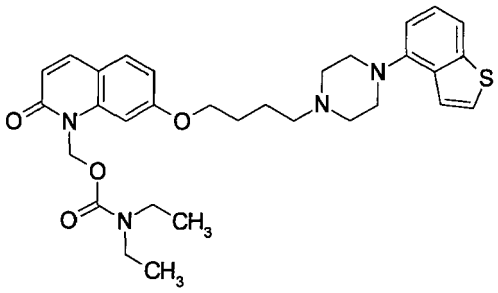


[0268] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.82 (2H, m), 1.86-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.67-2.78 (4H, m), 2.86 (3H, s), 2.96 (3H, s), 3.15-3.24 (4H, m), 4.10 (2H, t, J=6.0Hz), 6.35 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.12 (1H, d, J=2.0Hz), 7.24-7.31 (1H, m), 7.37-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 57

Synthesis of N,N-diethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0269]

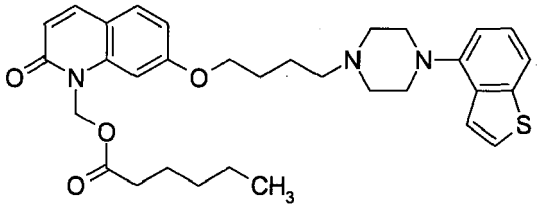


[0270] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.01 (3H, t, J=7.0Hz), 1.15 (3H, t, J=7.0Hz), 1.72-1.82 (2H, m), 1.84-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.64-2.808 (4H, m), 3.11-3.26 (6H, m), 3.34 (2H, q, J=7.0Hz), 4.09 (2H, t, J=6.0Hz), 6.36 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.92 (1H, m), 7.09 (1H, d, J=2.0Hz), 7.24-7.31 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 58

Synthesis of hexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0271]

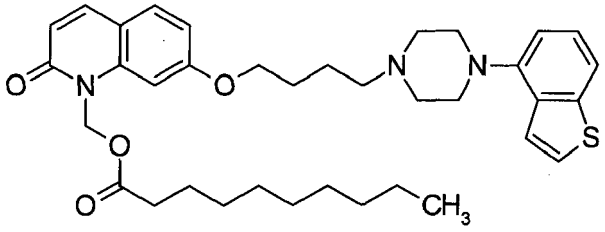


[0272] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.85 (t, J = 6.8 Hz, 3H), 1.25-1.33 (m, 4H), 1.58-1.69 (m, 2H), 1.70-1.85 (m, 2H), 1.85-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.4 Hz, 2H), 2.67-2.78 (m, 4H), 3.15-3.25 (m, 4H), 4.08 (t, J=6.2Hz, 2H), 6.34 (brs, 2H), 6.52 (d,J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.84-6.92 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 59

Synthesis of decanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0273]

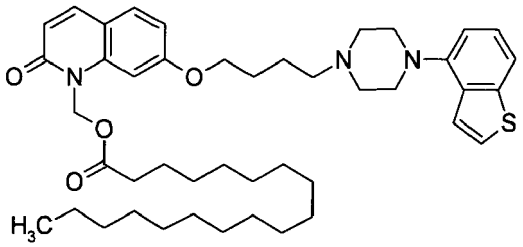


[0274] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1) and in the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.86 (t, J = 6.8Hz, 3H), 1.17-1.32 (m, 12H), 1.57-1.68 (m, 2H), 1.72-1.82 (m, 2H), 1.85-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.65-2.78 (m, 4H), 3.13-3.25 (m, 4H), 4.08 (t, J=6.2Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (d, J = 2.2, 8.6 Hz, 1H), 6.86-6.92 (m, 2H), 7.27 (dd, J =7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5Hz, 1H)

Example 60

Synthesis of octadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0275]

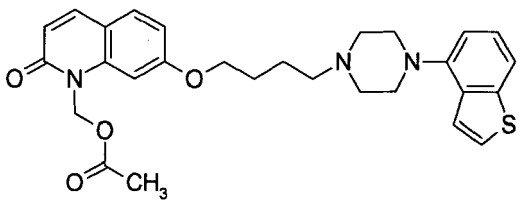


[0276] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ:0.88 (t, J = 6.8 Hz, 3H), 1.18-1.33 (m, 28H), 1.58-1.67 (m, 2H), 1.72-1.82 (m, 2H), 1.85-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.79 (m, 4H), 3.14-3.25 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J=9.5Hz, 1H), 6.84 (dd, J=2.2, 8.6 Hz, 1H), 6.87-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 61

Synthesis of acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0277]



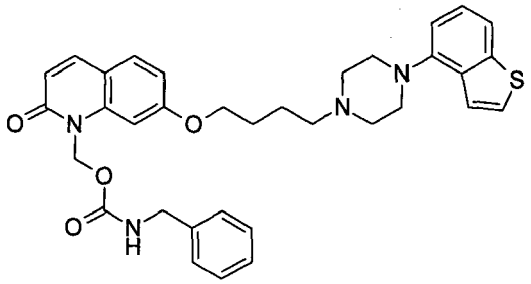
[0278] Acetic acid 7-(4-chlorobutoxy)-2-oxo-2H-quinolin-1-ylmethyl ester (299 mg), 1-benzo[b]thiophen-4-ylpiperazine

hydrochloride (235 mg), potassium carbonate (319 mg) and sodium iodide (152 mg) were suspended in DMF (5 ml), and this was stirred at 70°C for 3 hr and further at 80°C for 4 hr. After cooling to room temperature, to the reaction mixture was added aqueous ammonium chloride solution, and the mixture was extracted with ethyl acetate, dried over sodium sulfate, and concentrated under reduced pressure. The residue was purified by moderate-pressure silica gel column chromatography (hexane:ethyl acetate=1:0 to 1:9) and further by basic silica gel column chromatography, and concentrated under reduced pressure to give the title compound (132 mg) as a colorless amorphous solid.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.83 (m, 2H), 1.84-1.95 (m, 2H), 2.13 (s, 3H), 2.54 (t, J = 7.4 Hz, 2H), 2.68 -2.77 (m, 4H), 3.15-3.24 (m, 4H), 4.09 (t, J=6.3Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.85 (dd, J = 2.2, 8.6 Hz, 1H), 6.87-6.92 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 62

Synthesis of N-benzylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0279]

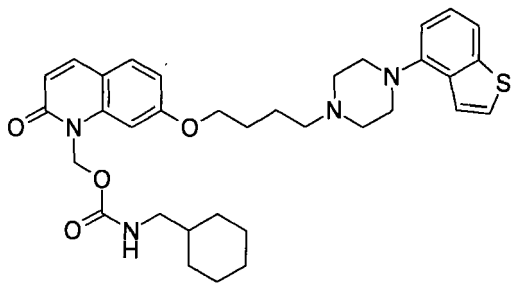


[0280] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.80 (2H, m), 1.82-1.92 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.77 (4H, m), 3.11-3.24 (4H, m), 4.07 (2H, t, J=6.0Hz), 4.41 (2H, t, J=6.0Hz), 5.26 (1H, t, J=6.0Hz), 6.37 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.88 (1H, d, J=7.0Hz), 7.15 (1H, d, J=1.5Hz), 7.23-7.34 (6H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.43 (1H, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 63

Synthesis of N-cyclohexylmethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0281]



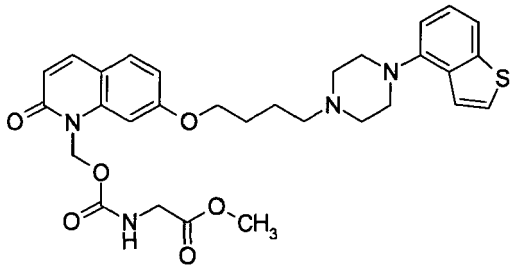
[0282] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.83-0.97 (2H, m), 1.02-1.28 (3H, m), 1.36-1.50 (1H, m), 1.54-1.84 (7H, m), 1.86-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.81 (4H, m), 3.05 (2H, t, J=6.5Hz), 3.13-3.27 (4H, m), 4.11 (2H, t, J=6.0Hz), 4.90 (1H, t, J=6.0Hz), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.16 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.37-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 64

Synthesis of {7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethoxycarbonylamino}acetic acid methyl ester

[0283]

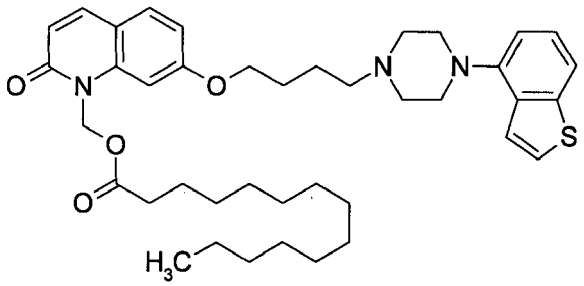


[0284] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.84 (2H, m), 1.86-1.94 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.81 (4H, m), 3.12-3.27 (4H, m), 3.74 (3H, s), 4.00 (2H, d, J=5.5Hz), 4.11 (2H, t, J=6.0Hz), 5.34-5.44 (1H, m), 6.36 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.92 (1H, m), 7.09 (1H, d, J=2.0Hz), 7.25-7.30 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 65

Synthesis of tetradecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0285]

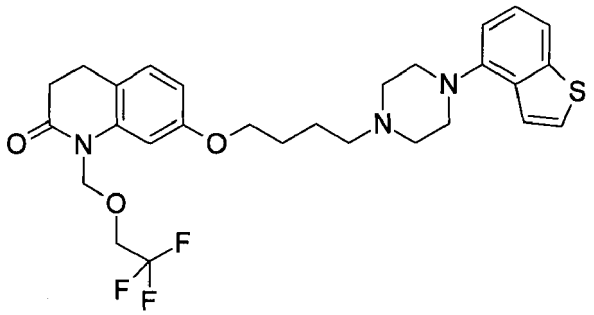


[0286] In the same manner as in Example 61, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6. 8Hz, 3H), 1.18-1.33 (m, 20H), 1.58-1.68 (m, 2H), 1.72-1.82 (m, 2H), 1.84-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.79 (m, 4H), 3.13-3.25 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.87-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J=8.6Hz, 1H), 7.55 (d, J=8.1Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 66

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-(2,2,2-trifluoroethoxymethyl)-3,4-dihydro-1H-quinolin-2-one

[0287]

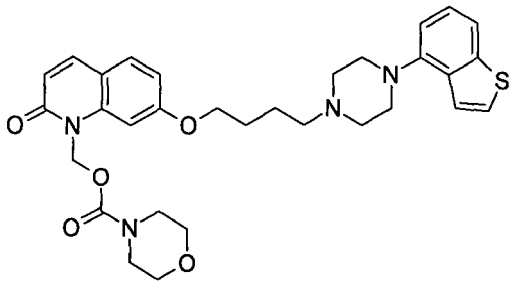


[0288] 2,2,2-Trifluoroethanol (0.10 ml) was dissolved in anhydrous THF (3 ml) under a nitrogen atmosphere and sodium hydride (about 55% oil) (60 mg) was added under ice-cooling. The reaction mixture was stirred at room temperature for 30 min under a nitrogen atmosphere. The obtained solution was ice-cooled again and, under a nitrogen atmosphere, a solution (3 ml) of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester (0.25 g) obtained in Example 5 in anhydrous THF was added using a cannula. The reaction mixture was stirred at room temperature for 18 hr under a nitrogen atmosphere. To the reaction mixture was added ice water to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated by filtration. The obtained residue was purified by silica gel column chromatography (ethyl acetate) to give the title compound (90 mg) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.93 (4H, m), 2.47-2.56 (2H, m), 2.64-2.76 (6H, m), 2.80-2.87 (2H, m), 3.13-3.25 (4H, m), 3.93-4.14 (4H, m), 5.42 (2H, s), 6.61 (1H, dd, J=2.5Hz, J=8.5Hz), 6.86-6.91 (2H, m), 7.05 (1H, d, J=8.5Hz), 7.24-7.28 (1H, m), 7.37 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.54 (1H, d, J=8.0Hz)

Example 67

Synthesis of morpholine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0289]

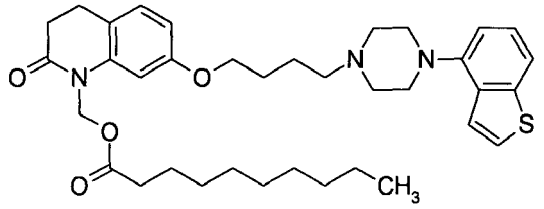


[0290] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.82 (2H, m), 1.87-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.80 (4H, m), 3.16-3.34 (4H, m), 3.37-3.73 (8H, m), 4.10 (2H, d, J=6.0Hz), 6.37 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.09 (1H, d, J=2.5Hz), 7.24-7.30 (1H, m), 7.37-7.43 (2H, m), 7.45 (1H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.63 (1H, d, J=9.5Hz)

Example 68

Synthesis of decanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0291]

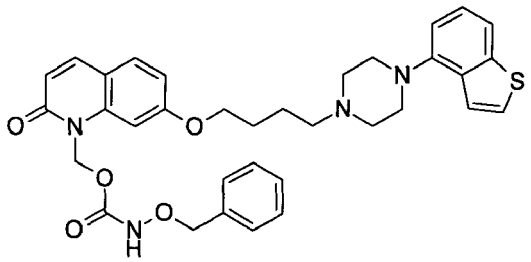


[0292] In the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6. 8Hz, 3H), 1.20-1.34 (m, 12H), 1.58-1.68 (m, 2H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.6 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.89 (m, 2H), 3.13-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J=2.2, 8.1 Hz, 1H), 6.62(d, J = 2.2 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 69

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl benzyloxycarbamate

[0293]

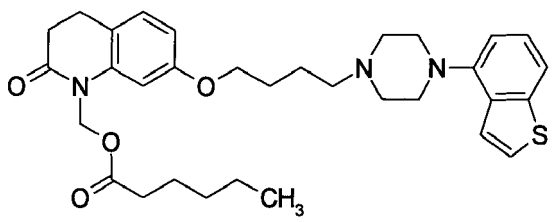


[0294] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.67-1.79 (2H, m), 1.81-1.92 (2H, m), 2.49 (2H, t, J=7.5Hz), 2.60-2.74 (4H, m), 3.07-3.21 (4H, m), 4.05 (2H, d, J=6.0Hz), 4.85 (2H, s), 6.37 (2H, s), 6.46 (1H, d, J=9.5Hz), 6.80-6.88 (2H, m), 7.03 (1H, d, J=2.0Hz), 7.23-7.45 (9H, m), 7.54 (1H, d, J=8.0Hz), 7.58 (1H, d, J=9.5Hz), 8.11 (1H, s)

Example 70

Synthesis of hexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-l-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0295]

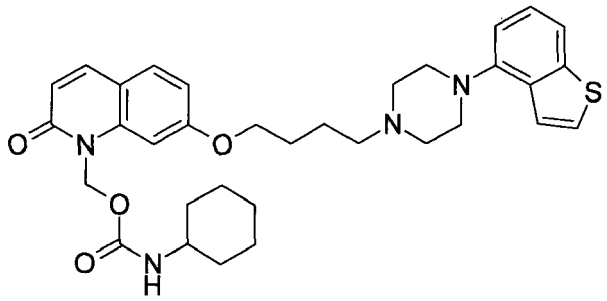


[0296] In the same manner as in Example 11, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0. 88 (t, J=6.9Hz, 3H), 1.26-1.34 (m, 4H), 1.59-1.69 (m, 2H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.53 (t, J = 7.4 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.89 (m, 2H), 3.14-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J = 2.2, 8.1 Hz, 1H), 6.62 (d, J = 2.2 Hz, 1H), 6.88-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 71

Synthesis of N-cyclohexylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0297]

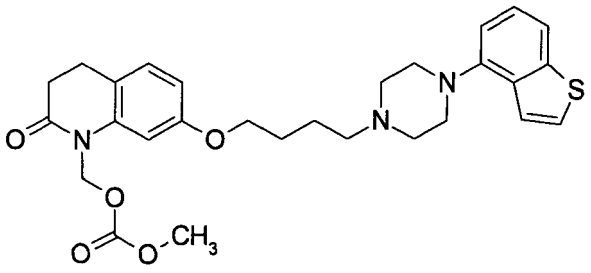


[0298] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.02-1.22 (3H, m), 1.24-1.41 (2H, m), 1.52-1.97 (9H, m), 2.54 (2H, t, J=7.5Hz), 2.64-2.82 (4H, m), 3.11-3.28 (4H, m), 3.45-3.59 (1H, m), 4.11 (2H, t, J=6.0Hz), 4.83 (1H, d, J=8.0Hz), 6.31 (2H, s), 6.50 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.14 (1H, brs), 7.24-7.30 (1H, m), 7.36-7.45 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.60 (1H, d, J=9.5Hz)

Example 72

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester methyl ester

[0299]

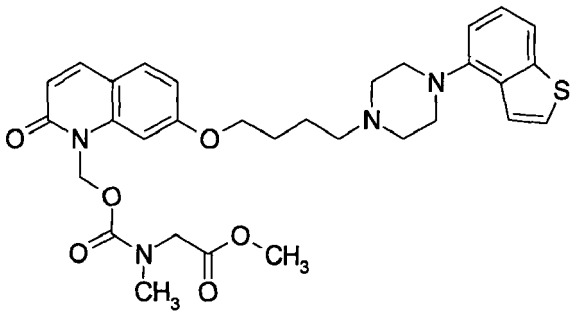


[0300] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.80 (2H, m), 1.80-1.90 (2H, m), 2.52 (2H, t, J=7.4 Hz), 2.64-2.78 (6H, m), 2.86 (2H, t, J=7.0 Hz), 3.14-3.24 (4H, br), 3.83 (3H, s), 4.00 (2H, t, J=6.2 Hz), 5.95 (2H, brs), 6.59 (1H, dd, J=2.4, 8.2 Hz), 6.69 (1H, d, J=2.2 Hz), 6.90 (1H, d, J=7.4 Hz), 7.06 (1H, d, J=8.2 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0 Hz)

Example 73

Synthesis of ({7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethoxycarbonyl}methylamino)acetic acid methyl ester

[0301]

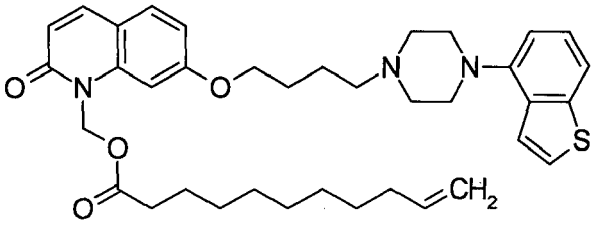


[0302] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.83 (2H, m), 1.85-1.97 (2H, m), 2.50-2.60 (2H, m), 2.66-2.81 (4H, m), {2.92 (s), 3.02(s) total 3H (1:1)}, 3.14-3.27 (4H, m), {3.53 (s), 3.74 (s) total 3H (1:1)}, 3.91 (1H, s), 4.06 (1H, s), 4.07-4.17 (2H, m), 6.33 (1H, s), 6.38 (1H, s), {6.50 (d, J=9.5Hz), 6.52 (d, J=9.5Hz total 1H (1:1)}, 6.80-6.86 (1H, m), {6.88 (brs), 6.90 (brs) total 1H (1:1)}, {6.98 (d, J=2.0Hz), 7.06 (d, J=2.0Hz) total 1H (1:1)}, 7.24-7.30 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), {7.61 (d, J=9.5Hz), 7.63 (d, J=9.0Hz) total 1H (1:1)}

Example 74

Synthesis of undec-10-enoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0303]

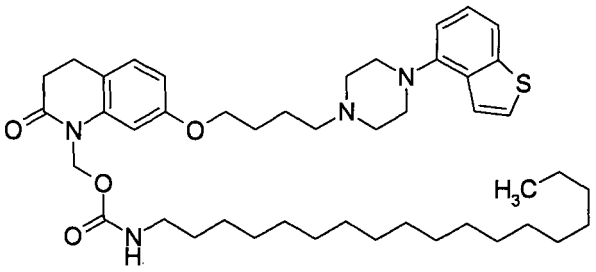


[0304] In the same manner as in Example 61, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.19-1.38 (m, 10H), 1.58-1.67 (m, 2H), 1.72-1.82 (m, 2H), 1.86-1.95 (m, 2H), 1.97-2.06 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.79 (m, 4H), 3.15-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 4.88-4.94 (m, 1H), 4.94-5.02 (m, 1H), 5.73-5.85 (m, 1H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.87-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 75

Synthesis of N-octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0305]

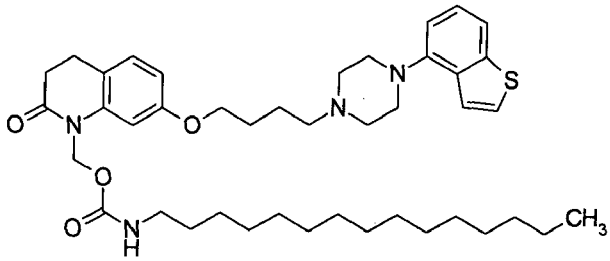


[0306] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0. 88 (3H, t, J=7.0Hz), 1.16-1.35 (30H, m), 1.42-1.54 (2H, m), 1.70-1.80 (2H, m), 1.81-1.90 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.62-2.78 (6H, m), 2.81-2.90 (2H, m), 3.12-3.27 (6H, m), 4.00 (2H, t, J=6.0Hz), 4.79 (1H, t, J=5.5Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.0Hz), 6.80 (1H, d, J=2.0Hz), 6.89 (1H, d, J=7.5Hz), 7.05 (1H, d, J=8.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 76

Synthesis of N-pentadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0307]

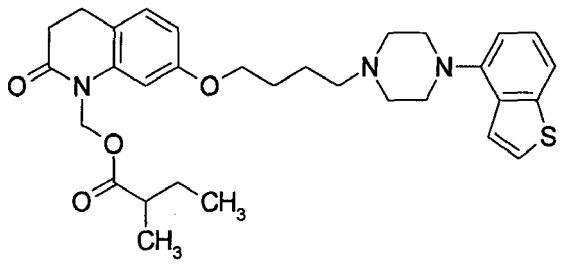


[0308] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7.0Hz), 1.16-1.35 (24H, m), 1.43-1.53 (2H, m), 1.69-1.80 (2H, m), 1.81-1.90 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.63-2.77 (6H, m), 2.81-2.90 (2H, m), 3.14-3.25 (6H, m), 4.00 (2H, t, J=6.0Hz), 4.80 (1H, t, J=5.5Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.0Hz), 6.80 (1H, d, J=2.0Hz), 6.89 (1H, d, J=7.5Hz), 7.05 (1H, d, J=8.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, dd, J=0.5Hz, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 77

Synthesis of 2-methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0309]



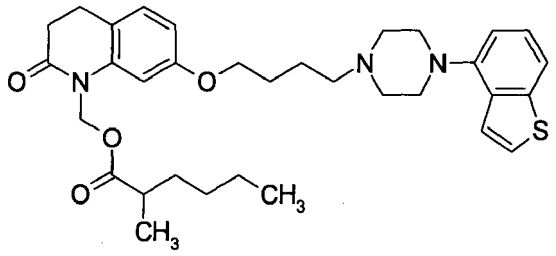
[0310] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.91 (t, J = 7.4 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H), 1.42-1.55 (m, 1H), 1.64-1.92 (m, 5H), 2.43 (m, 1H),

2.52 (t, J = 7.5 Hz, 2H), 2.64-2.79 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.63 (m, 2H), 6.90 (d, J = 7.4 Hz, 1H), 7.07 (d, J = 8.3 Hz, 1H), 7.27 (dd, J = 7.8 Hz, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 78

Synthesis of 2-methylhexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0311]

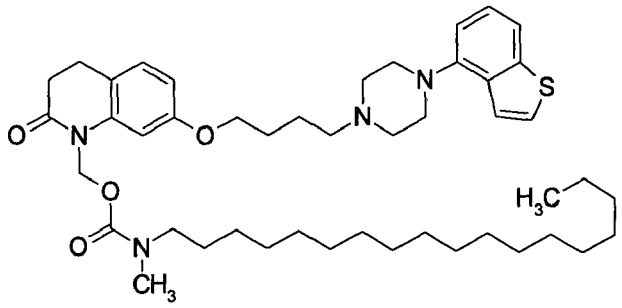


[0312] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.86 (t, J = 6.9 Hz, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.23-1.32 (m, 4H), 1.36-1.48 (m, 1H), 1.58-1.79 (m, 3H), 1.79-1.89 (m, 2H), 2.43-2.56 (m, 3H), 2.64-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.62 (m, 2H), 6.90 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H)

Example 79

Synthesis of N-methyl-N-octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0313]

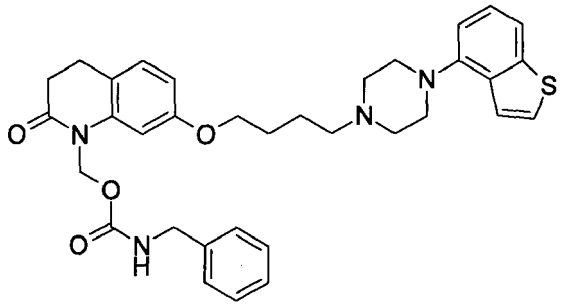


[0314] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0. 88 (3H, t, J=7.0Hz), 1.10-1.34 (30H, m), 1.38-1.57 (2H, m), 1.68-1.90 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.63-2.79 (6H, m), 2.81-2.95 (5H, m), 3.13-3.31 (6H, m), 3.99 (2H, t, J=5.5Hz), 5.93 (2H, s), 6.59 (1H, d, J=8.0Hz), 6.77 (1H, d, J=8.0Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.0Hz), 7.24-7.31 (1H, m), 7.36-7.43 (2H, m), 7.55 (1H, d, J=8.0Hz)

Example 80

Synthesis of N-benzylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0315]

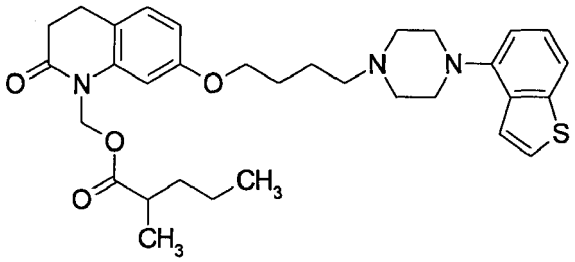


[0316] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.89 (4H, m), 2.51 (2H, t, J=7.5Hz), 2.63-2.77 (6H, m), 2.86 (2H, t, J=7.5Hz), 3.13-3.25 (4H, m), 3.98 (2H, t, J=6.0Hz), 4.40 (2H, t, J=6.0Hz), 5.10-5.18 (1H, m), 5.97 (2H, s), 6.59 (1H, dd, J=2.5Hz, J=8.5Hz), 6.80 (1H, d, J=2.0Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.23-7.35 (6H, m), 7.37-7.43 (2H, m), 7.55 (1H, d, J=8.0Hz)

Example 81

Synthesis of 2-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0317]

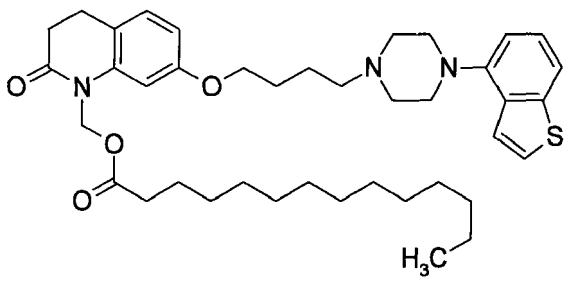


[0318] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0. 88 (t, J = 7.2 Hz, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.28-1.46 (m, 3H), 1.61-1.68 (m, 1H), 1.68-1.79 (m, 2H), 1.79-1.90 (m, 2H), 2.45-2.56 (m, 3H), 2.64-2.78 (m, 6H), 2.82-2.90 (m, 2H), 3.12-3.25 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.56-6.62 (m, 2H), 6.90 (d, J = 7.6 Hz, 1H), 7.04-7.10 (m, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.38 (d, J - 5.5 Hz, 1H), 7.41 (d, J = 5.5 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H)

Example 82

Synthesis of tetradecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0319]

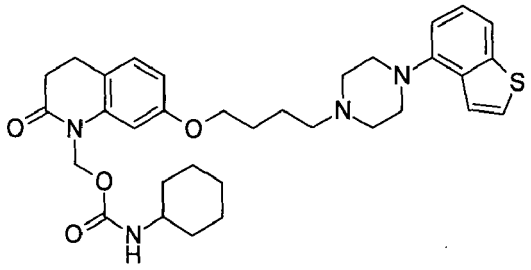


[0320] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6. 8 Hz, 3H), 1.20-1.33 (m, 20H), 1.57-1.68 (m, 2H), 1.69-1.79 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.6 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.65-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.60 (dd, J=2.2, 8.1 Hz, 1H), 6.62 (d, J = 2.2 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.24-7.30 (m, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H)

Example 83

Synthesis of N-cyclohexylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0321]

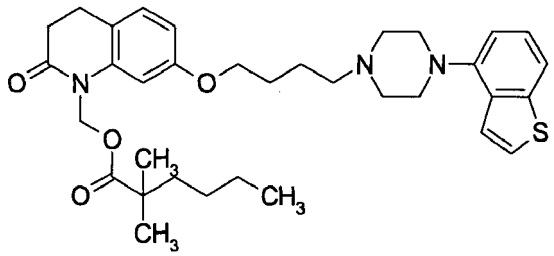


[0322] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.05-1.21 (4H, m), 1.25-1.43 (2H, m), 1.63-1.93 (8H, m), 2.52 (2H, t, J=7.5Hz), 2.63-2.78 (6H, m), 2.81-2.90 (2H, m), 3.14-3.26 (4H, m), 3.46-3.58 (1H, m), 4.00 (2H, t, J=6.0Hz), 4.71 (1H, d, J=8.0Hz), 5.91 (2H, s), 6.59 (1H, dd, J=2.0Hz, J=8.0Hz), 6.79 (1H, d, J=2.0Hz), 6.90 (1H, dd, J=0.5Hz, J=7.5Hz), 7.05 (1H, d, J=8.0Hz), 7.24-7.31 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, dd, J=0.5Hz, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 84

Synthesis of 2,2-dimethylhexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0323]

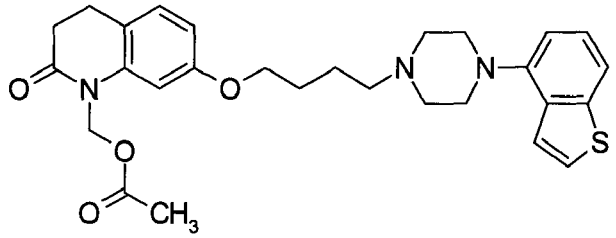


[0324] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.84 (t, J = 6.9 Hz, 3H), 1.14-1.29 (m, 4H), 1.17 (s, 6H), 1.47-1.54 (m, 2H), 1.68-1.78 (m, 2H), 1.79-1.89 (m, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.65-2.76 (m, 6H), 2.83-2.89 (m, 2H), 3.15-3.23 (m, 4H), 3.97 (d, J = 6.3 Hz, 2H), 5.91 (brs, 2H), 6.57-6.62 (m, 2H), 6.88-6.92 (m, 1H), 7.07 (d, J = 8.2 Hz, 1H), 7.27 (dd, J = 7.8 Hz, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 85

Synthesis of acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0325]

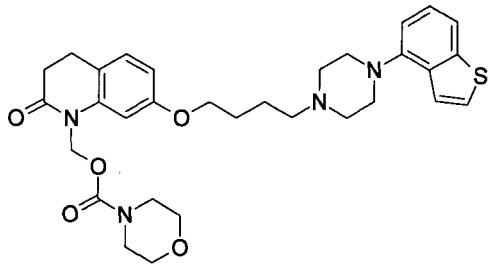


[0326] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.64-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.12 (s, 3H), 2.53 (t, J = 7.3 Hz, 2H), 2.65-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.13-3.24 (m, 4H), 3.99 (t, J = 6.2 Hz, 2H), 5.91 (brs, 2H), 6.60 (dd, J=2.3, 8.2 Hz, 1H), 6.63 (d, J=2.3Hz, 1H), 6.90 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H), 7.24-7.30 (m, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H)

Example 86

Synthesis of morpholine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0327]

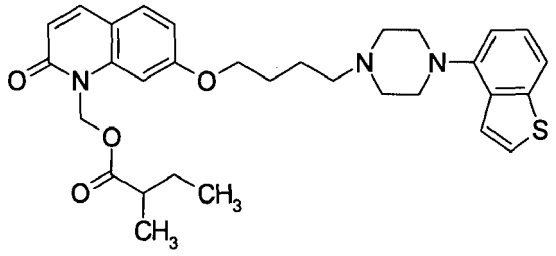


[0328] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.79 (2H, m), 1.81-1.90 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.64-2.78 (6H, m), 2.83-2.90 (2H, m), 3.13-3.25 (4H, m), 3.38-3.55 (4H, m), 3.56-3.74 (4H, m), 4.00 (2H, t, J=6.5Hz), 5.94 (2H, s), 6.60 (1H, dd, J=2.5Hz, J=8.5Hz), 6.74 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.07 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.39 (1H, d, J=5.5Hz), 7.41 (1H, dd, J=0.5Hz, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 87

Synthesis of 2-methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0329]



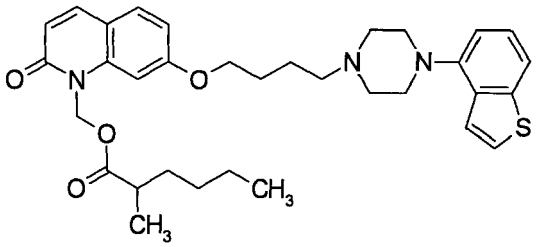
[0330] In the same manner as in Example 22, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.89 (t, J = 7.5 Hz, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.42-1.54 (m, 1H), 1.60-1.81 (m, 3H), 1.85-1.95 (m, 2H), 2.44 (dt, J = 7.0, 7.0 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 2.64-2.79 (m, 4H), 3.15-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.87 (m, 2H), 6.87-6.92 (m, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 88

Synthesis of 2-methylhexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0331]

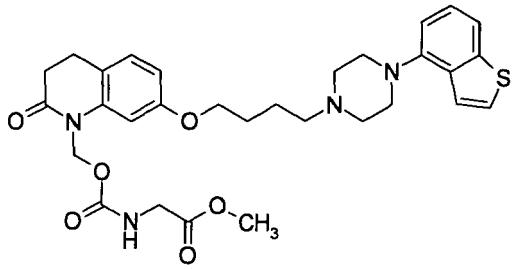


[0332] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.81 (t, J = 7.0 Hz, 3H), 1.15 (d, J = 7.0 Hz, 3H), 1.18-1.29 (m, 4H), 1.35-1.47 (m, 1H), 1.59-1.81 (m, 3H), 1.85-1.94 (m, 2H), 2.44-2.58 (m, 3H), 2.65-2.80 (m, 4H), 3.13-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.87 (m, 2H), 6.87-6.92 (m, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 89

Synthesis of {7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethoxycarbonylamino}acetic acid methyl ester

[0333]

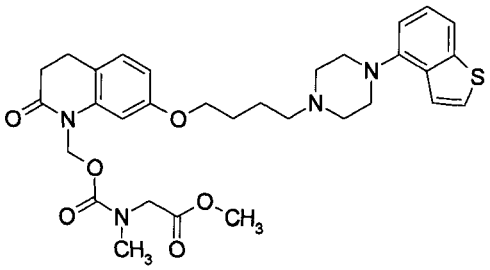


[0334] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.70-1.79 (2H, m), 1.81-1.90 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.82-2.89 (2H, m), 3.14-3.24 (4H, m), 3.75 (3H, s), 3.97-4.05 (4H, m), 4.34 (1H, t, J=5.0Hz), 5.95 (2H, s), 6.60 (1H, dd, J=2.0Hz, J=8.5Hz), 6.77 (1H, d, J=2.0Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.31 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 90

Synthesis of ({7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethoxycarbonyl}methylamino)acetic acid methyl ester

[0335]

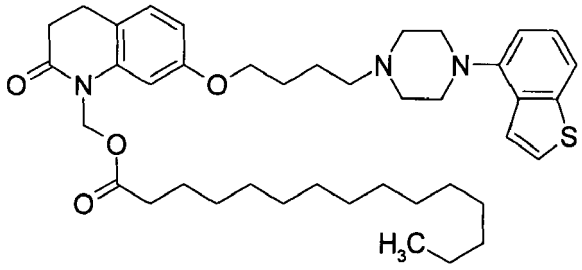


[0336] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.70-1.79 (2H, m), 1.81-1.91 (2H, m), 2.49-2.57 (2H, m), 2.63-2.78 (6H, m), 2.81-2.90 (2H, m), {3.64 (s), 3.75 (s) tota13H (1:1)}, 3.14-3.25 (4H, m), {3.64 (s), 3.75 (s) total 3H (1:1)}, 3.93 (s, 1H), 3.97-4.04 (2H, m), 4.06 (1H, s), 5.91 (1H, s), 5.96 (1H, s), 6.56-6.63 (1H, m), {6.68 (d, J=2.0Hz), 6.77 (d, J=2.0Hz) total 1H (1:1)}, 6.90 (1H, d, J=7.5Hz), 7.06 (1H, dd, J=8.0Hz, J=8.0Hz), 7.24-7.31 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 91

Synthesis of pentadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0337]

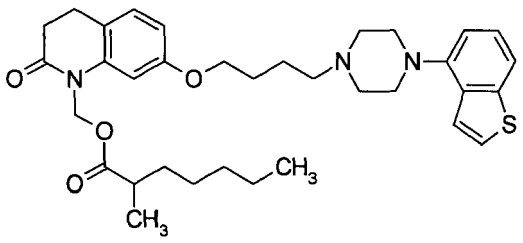


[0338] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6.8 Hz, 3H), 1.17-1.35 (m, 22H), 1.55-1.68 (m, 2H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.36 (t, J = 7.6 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.76 (m, 6H), 2.83-2.89 (m, 2H), 3.13-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.59 (dd, J = 2.3, 8.2 Hz, 1H), 6.62 (d, J = 2.3 Hz, 1H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.2 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 92

Synthesis of 2-methylheptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0339]



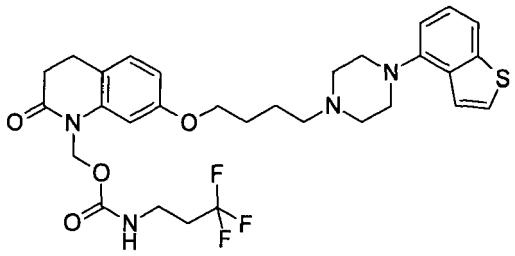
[0340] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.85 (t, J = 6. 8Hz, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.19-1.34 (m, 6H), 1.34-1.47 (m, 1H), 1.60-1.79

(m, 3H), 1.79-1.90 (m, 2H), 2.42-2.56 (m, 3H), 2.64-2.78 (m, 6H), 2.82-2.90 (m, 2H), 3.12-3.26 (m, 4H), 3.97 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.62 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 93

Synthesis of N-(3,3,3-trifluoropropyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0341]

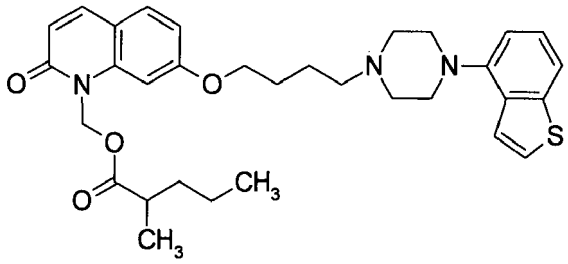


[0342] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.79 (2H, m), 1.80-1.90 (2H, m), 2.29-2.43 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.61-2.77 (6H, m), 2.79-2.89 (2H, m), 3.13-3.26 (4H, m), 3.46 (2H, dt, J=6.5Hz, J=6.5Hz), 3.99 (2H, t, J=6.0Hz), 5.20 (1H, t, J=6.0Hz), 5.92 (2H, s), 6.59 (1H, dd, J=2.0Hz, J=8.5Hz), 6.74 (1H, d, J=2.0Hz), 6.89 (1H, d, J=7.5Hz), 7.05 (1H, d, J=8.5Hz), 7.23-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.54 (1H, d, J=8.0Hz)

Example 94

Synthesis of 2-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0343]

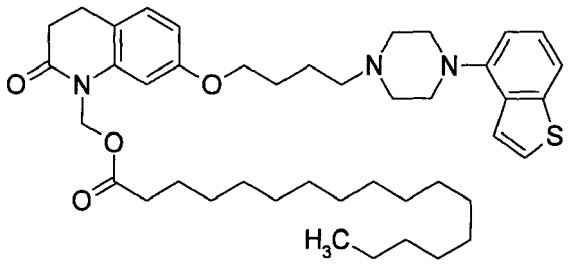


[0344] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.86 (t, J = 7.2 Hz, 3H), 1.15 (d, J = 7.0 Hz, 3H), 1.23-1.45 (m, 3H), 1.59-1.82 (m, 3H), 1.85-1.95 (m, 2H), 2.46-2.58 (m, 3H), 2.65-2.79 (m, 4H), 3.14-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.4 Hz, 1H), 6.82-6.87 (m, 2H), 6.90 (d, J = 7.6 Hz, 1H), 7.25-7.30 (m, 1H), 7.39 (d, J = 5.5 Hz, 1H), 7.42 (d, J = 5.5 Hz, 1H), 7.43-7.47 (m, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 95

Synthesis of heptadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0345]

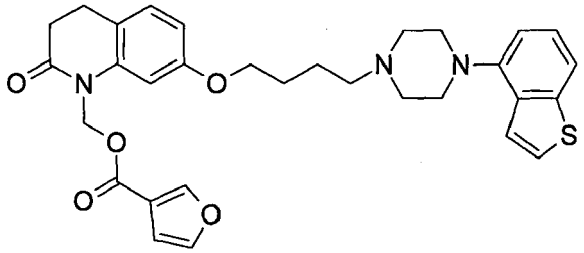


[0346] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, J = 6.9 Hz, 3H), 1.16-1.35 (m, 26H), 1.57-1.68 (m, 2H), 1.68-1.79 (m, 2H), 1.79-1.90 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.52 (d, J = 7.4 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.24 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 96

Synthesis of furan-3-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0347]

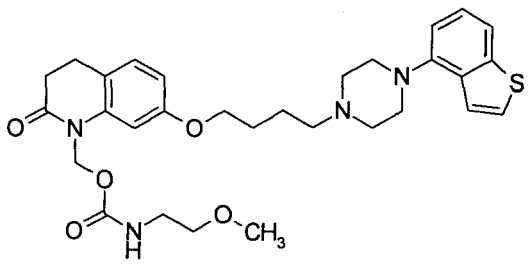


[0348] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.64-1.77 (m, 2H), 1.78-1.88 (m, 2H), 2.50 (t, J = 7.5 Hz, 2H), 2.63-2.75 (m, 6H), 2.85-2.92 (m, 2H), 3.12-3.23 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 6.09 (brs, 2H), 6.60 (dd, J=2.3, 8.3 Hz, 1H), 6.71 (d, J=2.3Hz, 1H), 6.74-6.77 (m, 1H), 6.87-6.91 (m, 1H), 7.09 (d, J = 8.3 Hz, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.37-7.43 (m, 3H), 7.55 (d, J = 7.9 Hz, 1H), 8.01-8.05 (m, 1H)

Example 97

Synthesis of N-(2-methoxyethyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0349]



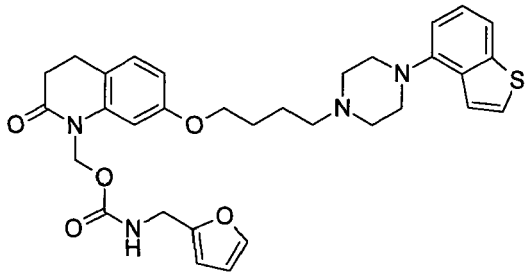
[0350] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10,

the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.91 (4H, m), 2.53 (2H, t, J=7.5Hz), 2.62-2.78 (6H, m), 2.81-2.91 (2H, m), 3.13-3.26 (4H, m), 3.33 (3H, s), 3.35-3.48 (4H, m), 4.00 (2H, t, J=6.0Hz), 5.12-5.21 (1H, m), 5.92 (2H, s), 6.59 (1H, dd, J=2.0Hz, J=8.0Hz), 6.78 (1H, d, J=2.0Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.42 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 98

Synthesis of N-furan-2-yl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0351]

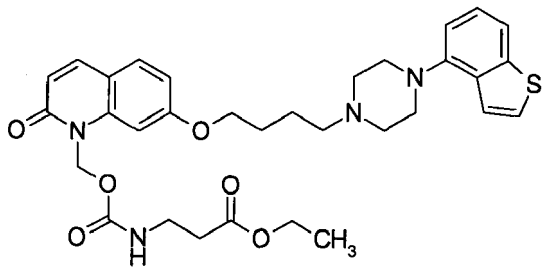


[0352] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 5 and in the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.90 (4H, m), 2.52 (2H, t, J=7.5Hz), 2.62-2.77 (6H, m), 2.81-2.90 (2H, m), 3.12-3.27 (4H, m), 3.99 (2H, t, J=6.0Hz), 4.39 (2H, d, J=6.0Hz), 5.11-5.19 (1H, m), 5.95 (2H, s), 6.23 (1H, brs), 6.30 (1H, brs), 6.59 (1H, dd, J=2.5Hz, J=8.0Hz), 6.77 (1H, d, J=2.5Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.0Hz), 7.24-7.30 (1H, m), 7.34 (1H, brs), 7.38 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.55 (1H, d, J=8.0Hz)

Example 99

Synthesis of 3-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethoxycarbonylamino}-propionic acid ethyl ester

[0353]

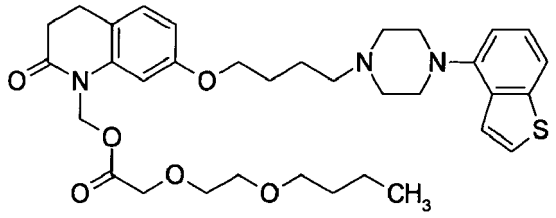


[0354] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, t, J=7.0Hz), 1.73-1.83 (2H, m), 1.86-1.96 (2H, m), 2.49-2.59 (4H, m), 2.66-2.80 (4H, m), 3.15-3.27 (4H, m), 3.45-3.53 (2H, m), 4.07-4.15 (4H, m), 5.36-5.43 (1H, m), 6.32 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.11 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 100

Synthesis of (2-butoxyethoxy)acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0355]

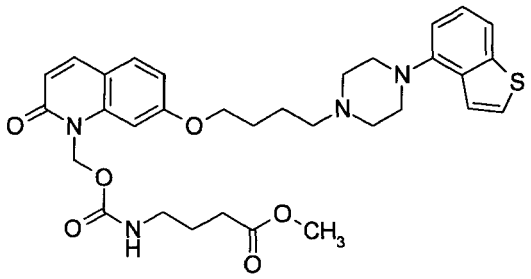


[0356] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J = 7.4 Hz, 3H), 1.29-1.40 (m, 2H), 1.50-1.59 (m, 2H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.53 (t, J = 7.4 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.13-3.24 (m, 4H), 3.45 (t, J =7.7 Hz, 2H), 3.58-3.63 (m, 2H), 3.71-3.76 (m, 2H), 3.98 (t, J = 6.2 Hz, 2H), 4.22 (s, 2H), 5.99 (brs, 2H), 6.57-6.62 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 7.8 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.36-7.44 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 101

Synthesis of 4-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethoxycarbonylamino}butyric acid methyl ester

[0357]

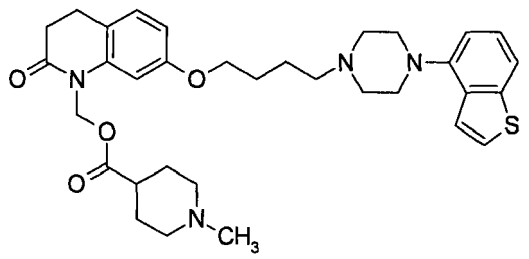


[0358] Using carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester synthesized in the same manner as in Example 7 and in the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.95 (6H, m), 2.36 (2H, t, J=7.0Hz), 2.54 (2H, t, J=7.5Hz), 2.66-2.80 (4H, m), 3.116-3.31 (6H, m), 3.64 (3H, s), 4.11 (2H, t, J=6.0Hz) 5.06 (1H, t, J=6.0Hz), 6.32 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.12 (1H, d, J=1.5Hz), 7.24-7.30 (1H, m), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 102

Synthesis of 1-methylpiperidine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0359]

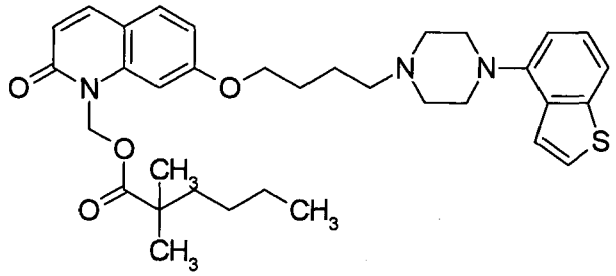


[0360] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.58-2.06 (m, 10H), 2.04 (s, 3H), 2.28-2.40 (m, 1H), 2.52 (t, J = 7.4 Hz, 2H), 2.63-2.82 (m, 8H), 2.82-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.97 (t, J = 6.3 Hz, 2H), 5.93 (brs, 2H), 6.56-6.62 (m, 2H), 6.88-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 103

Synthesis of 2,2-dimethylhexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0361]

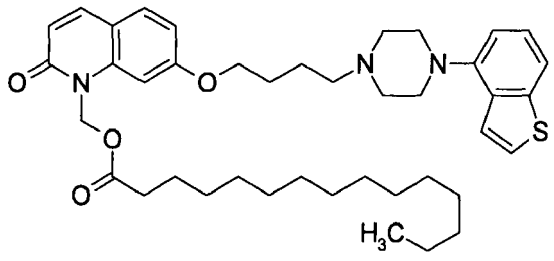


[0362] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.77 (t, J = 6.8 Hz, 3H), 1.09-1.20 (m, 10H), 1.42-1.52 (m, 2H), 1.68-1.95 (m, 4H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.78 (m, 4H), 3.14-3.25 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.86 (m, 2H), 6.87-6.92 (m, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.36-7.37 (m, 3H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 104

Synthesis of pentadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0363]

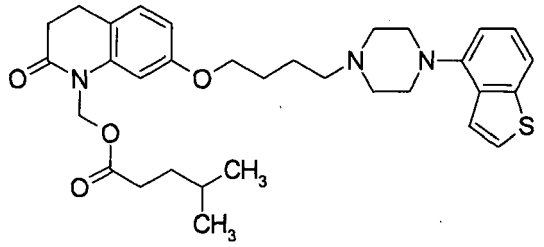


[0364] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6. 8 Hz, 3H), 1.16-1.34 (m, 22H), 1.57-1.67 (m, 2H), 1.67-1.82 (m, 2H), 1.85-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.65-2.79 (m, 4H), 3.13-3.25 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J=9.5Hz, 1H), 6.84 (dd, J=2.2, 8.6 Hz, 1H), 6.86-6.92 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 105

Synthesis of 4-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0365]

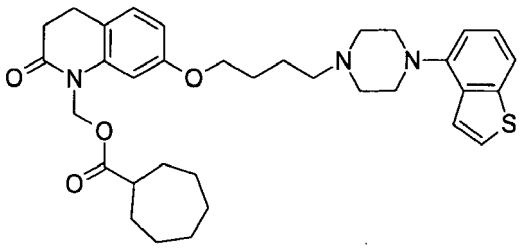


[0366] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, J = 6.3 Hz, 6H), 1.51-1.63 (m, 3H), 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.33-2.40 (m, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.65-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.24 (m, 4H), 3.99 (t, J = 6.2 Hz, 2H), 5.91 (brs, 2H), 6.57-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.0 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.1 Hz, 1H)

Example 106

Synthesis of cycloheptanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0367]

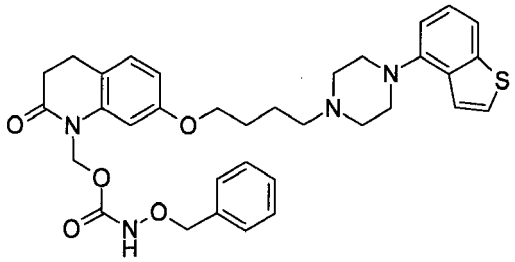


[0368] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.40-1.59 (m, 6H), 1.64-1.79 (m, 6H), 1.80-1.90 (m, 2H), 1.90-1.99 (m, 2H), 2.48-2.59 (m,3H), 2.64-2.78 (m, 6H), 2.82-2.90 (m, 2H), 3.14-3.23 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 5.91 (brs, 2H), 6.57-6.63 (m, 2H), 6.90 (d, J = 7.3 Hz, 1H), 7.05-7.09 (m, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H)

Example 107

Synthesis of benzyloxycarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0369]

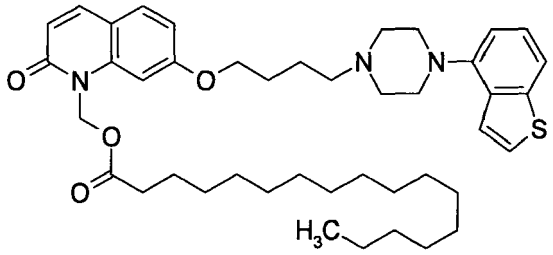


[0370] In the same manner as in Example 9, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.67-1.89 (4H, m), 2.51 (2H, t, J=7.5Hz), 2.61-2.76 (6H, m), 2.81-2.90 (2H, m), 3.10-3.23 (4H, m), 4.00 (2H, t, J=6.0Hz), 4.87 (2H, s), 6.00 (2H, s), 6.60 (1H, dd, J=2.5Hz, J=8.5Hz), 6.73 (1H, d, J=2.5Hz), 6.86-6.91 (1H, m), 7.07 (1H, d, J=8.5Hz), 7.24-7.42 (8H, m), 7.55 (1H, d, J=8.0Hz), 7.59 (1H, brs)

Example 108

Synthesis of heptadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0371]

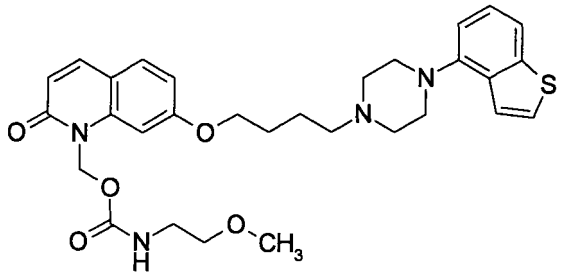


[0372] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (t, J = 6.9 Hz, 3H), 1.17-1.33 (m, 26H), 1.57-1.67 (m, 2H), 1.69-1.82 (m, 2H), 1.85-1.95 (m, 2H), 2.36 (t, J = 7.5 Hz, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.67-2.77 (m, 4H), 3.14-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J=9.5Hz, 1H), 6.84 (dd, J=2.2, 8.6 Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.36-7.43 (m, 2H), 7.44 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 109

Synthesis of N-(2-methoxyethyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0373]



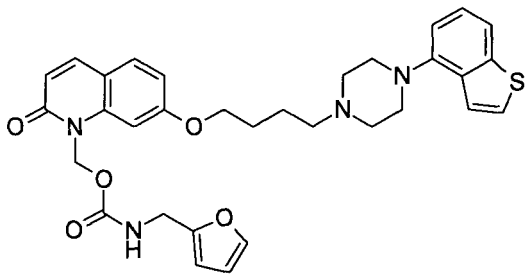
[0374] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.83 (2H, m), 1.86-1.96 (2H, m), 2.55 (2H, t, J=7.5Hz), 2.67-2.80 (4H, m), 3.16-3.25 (4H, m), 3.32 (3H, s), 3.36-3.47 (4H, m), 4.11 (2H, d, J=6.0Hz), 5.17-5.24 (1H, m), 6.33 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.13 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.37-7.47 (3H, m), 7.55 (1H,

d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 110

Synthesis of N-furan-2-yl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0375]

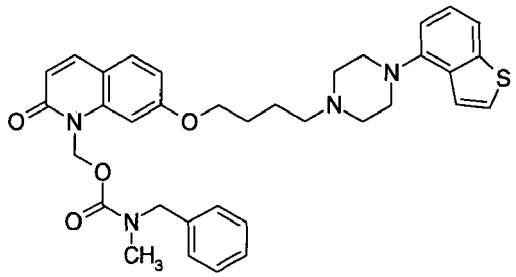


[0376] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.71-1.82 (2H, m), 1.83-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.80 (4H, m), 3.13-3.28 (4H, m), 4.10 (2H, t, J=6.0Hz), 4.39 (2H, d, J=6.0Hz), 5.19-5.29 (1H, m), 6.21 (1H, d, J=3.0Hz), 6.30 (1H, d, J=3.0Hz), 6.36 (2H, s), 6.50 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.91 (1H, m), 7.12 (1H, d, J=1.5Hz), 7.24-7.30 (1H, m), 7.33 (1H, brs), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 111

Synthesis of N-benzyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0377]

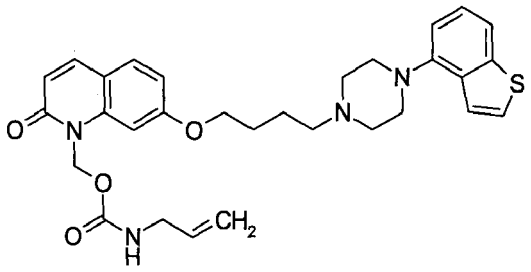


[0378] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.79 (2H, m), 1.82-1.92 (2H, m), 2.53 (2H, t, J=7.0Hz), 2.64-2.76 (4H, m), {2.80 (s), 2.93 (s) total 3H (1:1)}, 3.13-3.25 (4H, m), 4.02 (1H, t, J=6.0Hz), 4.08 (1H, t, J=6.0Hz), 4.37 (1H, s), 4.52 (1H, s), 6.41 (1H, s), 6.43 (1H, s), 6.52 (1H, dd, J=8.5Hz, J=8.5Hz), 6.80-6.91 (2H, m), {6.99-7.09 (m), 7.14-7.19 (m) total 3H (1:1)}, 7.21-7.35 (4H, m), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, dd, J=9.0Hz, J=9.0Hz)

Example 112

Synthesis of N-allylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0379]

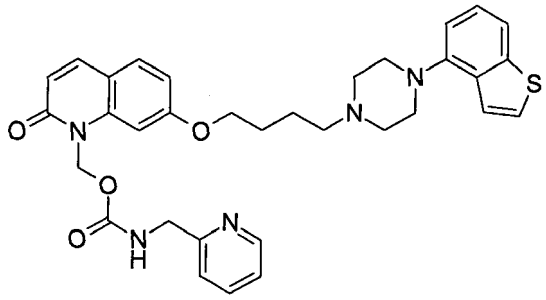


[0380] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.73-1.83 (2H, m), 1.85-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.64-2.80 (4H, m), 3.13-3.26 (4H, m), 3.84 (2H, t, J=5.5Hz), 4.11 (2H, t, J=6.0Hz), 4.91-5.01 (1H, m), 5.08-5.24 (2H, m), 5.77-5.90 (1H, m), 6.35 (2H, s), 6.51 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.14 (1H, brs), 7.24-7.30 (1H, m), 7.37-7.47 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 113

Synthesis of N-pyridin-2-yl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0381]

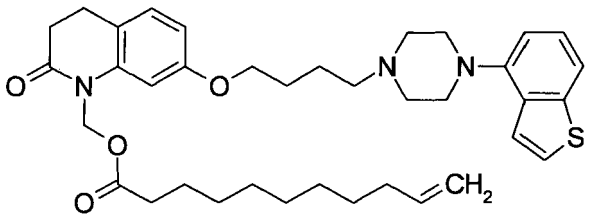


[0382] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.64-1.81 (2H, m), 1.83-1.93 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.66-2.80 (4H, m), 3.12-3.25 (4H, m), 4.08 (2H, t, J=6.0Hz), 4.53 (2H, d, J=5.0Hz), 6.01 (1H, t, J=5.0Hz), 6.38 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.88 (1H, d, J=7.5Hz), 7.03-7.19 (2H, m), 7.21-7.30 (2H, m), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.59-7.67 (2H, m), 8.40-8.57 (1H, m)

Example 114

Synthesis of undec-10-enoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0383]



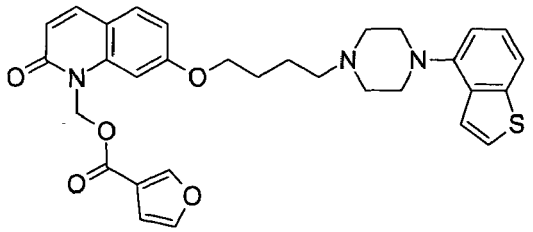
[0384] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.21-1.40 (m, 10H), 1.54-1.68 (m, 2H), 1.68-1.79 (m, 2H), 1.79-1.90 (m, 2H), 1.97-2.06 (m, 2H), 2.36 (t, J = 9.5 Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 2.64-2.76 (m, 6H), 2.83-2.96 (m, 2H), 3.14-3.23 (m, 4H), 3.99 (t, J =

6.3 Hz, 2H), 4.89-4.94 (m, 1H), 4.94-5.02 (m, 1H), 5.73-5.86 (m, 1H), 5.92 (brs, 2H), 6.57-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.07 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.36-7.43 (m, 2H), 7.55 (d, J = 7.9 Hz, 1H)

Example 115

Synthesis of furan-3-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0385]

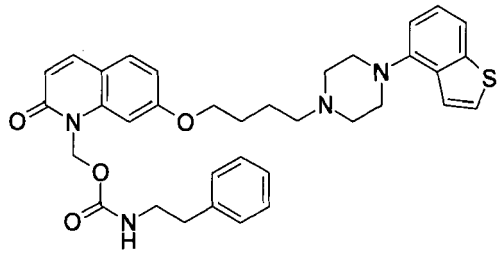


[0386] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.67-1.81 (m, 2H), 1.81-1.97 (m, 2H), 2.52 (dd, J = 7.5 Hz, 2H), 2.62-2.78 (m, 4H), 3.11-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.51 (brs, 2H), 6.54 (d, J = 9.5 Hz, 1H), 6.74-6.77 (m, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.96 (d, J = 2.2 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 3H), 7.46 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 9.5 Hz, 1H), 8.01-8.04 (m, 1H)

Example 116

Synthesis of N-phenethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0387]

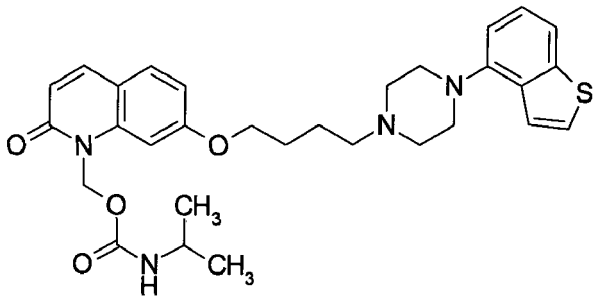


[0388] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.71-1.82 (2H, m), 1.85-1.96 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.63-2.77 (4H, m), 2.81 (2H, t, J=7.0Hz), 3.13-3.26 (4H, m), 3.44-3.52 (2H, m), 4.11 (2H, t, J=6.0Hz), 4.90 (1H, t, J=5.5Hz), 6.32 (2H, s), 6.50 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.88 (1H, d, J=7.5Hz), 7.12-7.34 (7H, m), 7.37-7.47 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 117

Synthesis of N-isopropyl-carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0389]

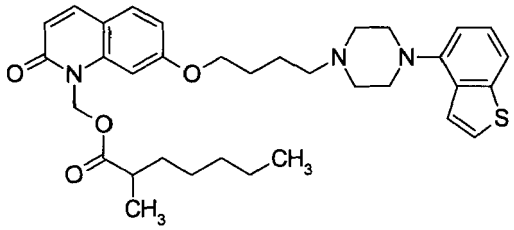


[0390] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.15 (6H, d, J=6.5Hz), 1.72-1.82 (2H, m), 1.85-1.94 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.66-2.78 (4H, m), 3.12-3.26 (4H, m), 3.78-3.90 (1H, m), 4.10 (2H, d, J=6.0Hz), 4.93 (1H, d, J=7.5Hz), 6.29 (2H, s), 6.48 (1H, d, J=9.5Hz), 6.82 (1H, dd, J=2.0Hz, J=8.5Hz), 6.88 (1H, d, J=7.5Hz), 7.13 (1H, brs), 7.26 (1H, dd, J=8.0Hz, J=8.0Hz), 7.35-7.44 (3H, m), 7.54 (1H, d, J=8.0Hz), 7.57 (1H, d, J=9.5Hz)

Example 118

Synthesis of 2-methylheptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0391]

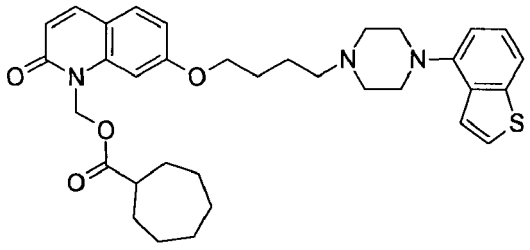


[0392] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.81 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 7.0 Hz, 3H), 1.17-1.30 (m, 6H), 1.35-1.46 (m, 1H), 1.58-1.71 (m, 1H), 1.71-1.82 (m, 2H), 1.82-1.98 (m, 2H), 2.43-2.58 (m, 3H), 2.66-2.79 (m, 4H), 3.14-3.25 (m, 4H), 4.07 (d, J = 6.2 Hz, 2H), 6.35 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.5 Hz, 1H), 6.85-6.92 (m, 2H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.37-7.43 (m, 2H), 7.44 (d, J = 8.5 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 119

Synthesis of cycloheptanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0393]



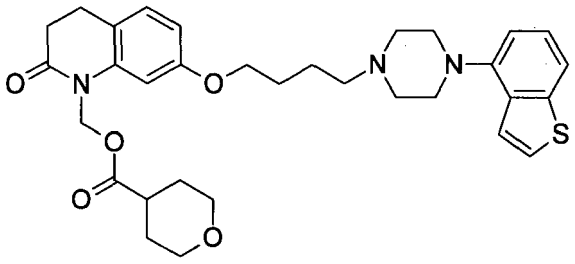
[0394] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.37-1.58 (m, 6H), 1.62-1.81 (m, 6H), 1.84-1.97 (m, 4H), 2.50-2.58 (m, 3H), 2.67-2.79 (m, 4H), 3.15-3.25 (m, 4H), 4.07 (t, J = 6.2Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.82-6.86 (m, 2H), 6.87-6.92 (m, 1H),

7.27 (dd, J = 8.0, 8.0 Hz, 1H), 7.37-7.43 (m, 2H), 7.43-7.47 (m, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 120

Synthesis of tetrahydropyran-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0395]

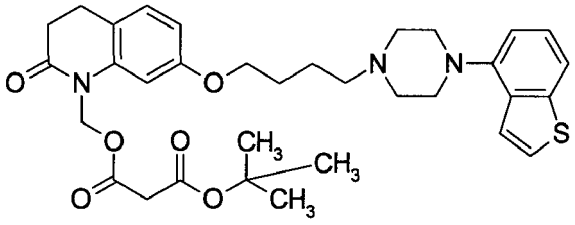


[0396] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.90 (m, 8H), 2.52 (t, J = 7.4 Hz, 2H), 2.56-2.65 (m, 1H), 2.65-2.77 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.37-3.45 (m, 2H), 3.90-4.01 (m,4H), 5.94 (brs, 2H), 6.57 (d, J = 2.2 Hz, 1H), 6.60 (d,J = 2.2, 8.2 Hz, 1H), 6.90 (d, J = 7.6 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H), 7.24-7.30 (m, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.42 d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H)

Example 121

Synthesis of malonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester tert-butyl ester

[0397]

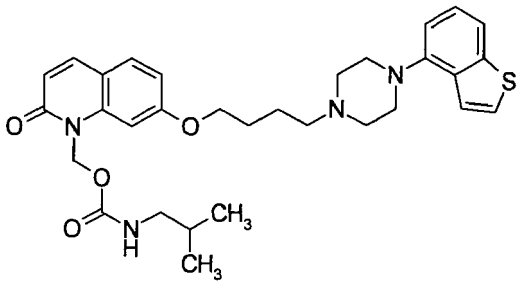


[0398] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.44 (s, 9H), 1.69-1.80 (m, 2H), 1.80-1.89 (m, 2H), 2.52 (d, J = 7.4 Hz, 2H), 2.64-2.79 (m, 6H), 2.83-2.90 (m, 2H), 3.14-3.25 (m, 4H), 3.35 (s, 2H), 4.01 (t, J = 6.2 Hz, 2H), 5.96 (brs, 2H), 6.00 (dd, J = 2.3, 8.2 Hz, 1H), 6.67 (d, J = 2.3 Hz, 1H), 6.90 (d, J = 7.4Hz, 1H), 7.07 (d, J = 8.2Hz, 1H), 7.25-7.30 (m, 1H), 7.37-7.43 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H).

Example 122

Synthesis of N-isobutylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0399]

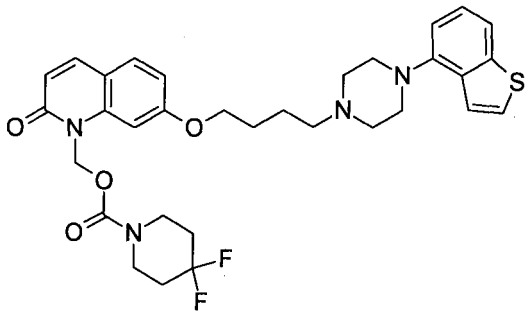


[0400] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.86-0.93 (6H, m), 1.69-1.82 (3H, m), 1.84-1.94 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.78 (4H, m), 3.03 (2H, t, J=6.5Hz), 3.13-3.25 (4H, m), 4.10 (2H, d, J=6.0Hz), 5.09 (1H, t, J=6.0Hz), 6.32 (2H, s), 6.49 (1H, d, J=9.5Hz), 6.82 (1H, dd, J=2.0Hz, J=8.5Hz), 6.86-6.91 (1H, m), 7.13 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.36-7.44 (3H, m), 7.54 (1H, d, J=8.0Hz), 7.58 (1H, d, J=9.5Hz)

Example 123

Synthesis of 4,4-difluoropiperidine-1-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0401]

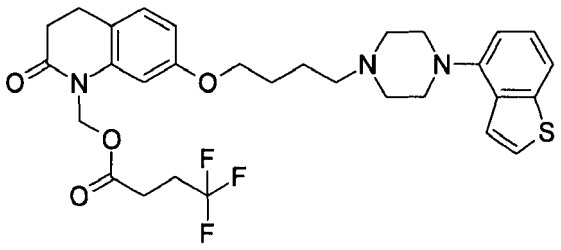


[0402] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-2.07 (8H, m), 2.54 (2H, t, J=7.5Hz), 2.64-2.78 (4H, m), 3.13-3.25 (4H, m), 3.48-3.71 (4H, m), 4.10 (2H, d, J=6.0Hz), 6.36 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.85 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 7.06 (1H, d, J=2.0Hz), 7.27 (1H, dd, J=8.0Hz, J=8.0Hz), 7.39 (1H, d, J=5.5Hz), 7.41 (1H, d, J=5.5Hz), 7.45 (1H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.63 (1H, d, J=9.5Hz)

Example 124

Synthesis of 4,4,4-trifluorobutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0403]

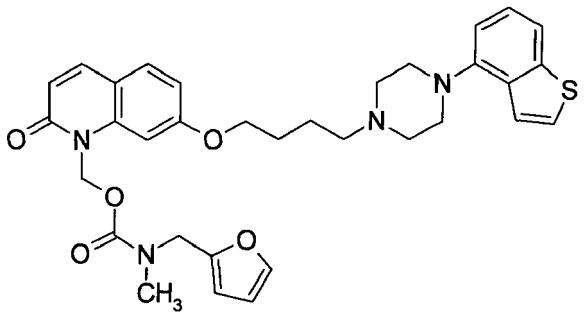


[0404] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.80 (m, 2H), 1.80-1.90 (m, 2H), 2.43-2.57 (m, 4H), 2.62-2.77 (m, 8H), 2.83-2.90 (m, 2H), 3.13-3.24 (m, 4H), 3.99 (t, J = 6.2Hz, 2H), 5.95 (brs, 2H), 6.57-6.63 (m, 2H), 6.87-6.92 (m, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.42 (m, 2H), 7.55 (d, J= 8.1 Hz, 1H)

Example 125

Synthesis of N-furan-2-ylmethyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0405]

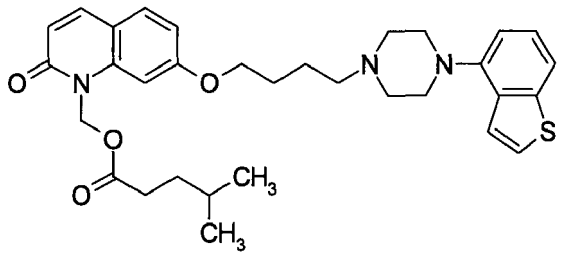


[0406] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.82 (2H, m), 1.84-1.94 (2H, m), 2.53 (2H, t, J=7.5Hz), 2.65-2.78 (4H, m), {2.84 (s), 2.97 (s) total 3H (1:1)}, 3.13-3.26 (4H, m), 4.05 (1H, d, J=6.0Hz), 4.10 (1H, t, J=6.0Hz), 4.31 (1H, s), 4.49 (1H, s), {6.02 (d, J=2.5Hz), 6.24 (d, J=2.5Hz) total 1H (1:1)}, {6.17 (brs), 6.32 (brs) total 1H (1:1)}, 6.39 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), {7.02 (brs), 7.12 (brs) total 1H (1:1)}, {7.19 (brs), 7.36 (brs) total 1H (1:1)}, 7.24-7.31 (1H, m), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.62 (1H, d, J=9.5Hz)

Example 126

Synthesis of 4-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0407]

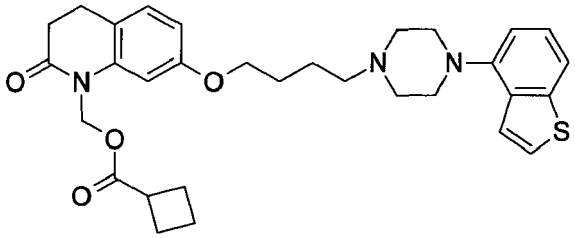


[0408] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (d, J = 6.3 Hz, 6H), 1.50-1.62 (m, 3H), 1.70-1.82 (m, 2H), 1.86-1.95 (m, 2H), 2.33-2.40 (m, 2H), 2.54 (t, J = 7.5 Hz, 2H), 2.66-2.79 (m, 4H), 3.14-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.33 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.86-6.91 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.45 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 127

Synthesis of cyclobutanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0409]

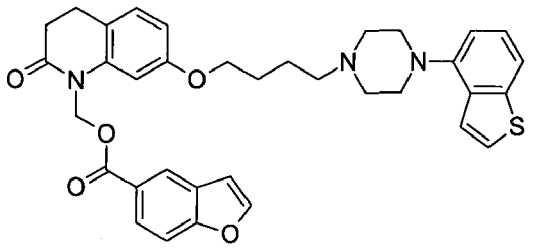


[0410] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.79 (m, 2H), 1.80-2.03 (m, 4H), 2.15-2.25 (m, 2H), 2.25-2.37 (m, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.77 (m, 6H), 2.83-2.89 (m, 2H), 3.13-3.24 (m, 5H), 3.98 (t, J = 6.2 Hz, 2H), 5.92 (brs, 2H), 6.57-6.62 (m, 2H), 6.90 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 7.24-7.30 (m, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H)

Example 128

Synthesis of benzofuran-5-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0411]

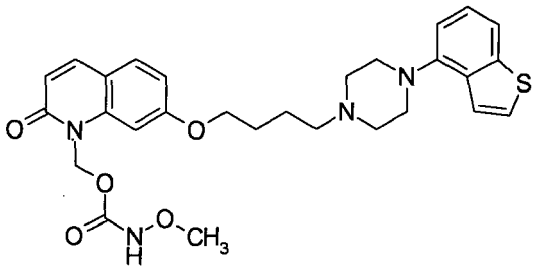


[0412] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.62-1.74 (m, 2H), 1.75-1.86 (m, 2H), 2.46 (t, J = 7.5 Hz, 2H), 2.58-2.71 (m, 4H), 2.71-2.79 (m, 2H), 2.82-2.93 (m, 2H), 3.07-3.20 (m, 4H), 3.96 (t, J = 6.3 Hz, 2H), 6.19 (brs, 2H), 6.61 (dd, J = 2.3, 8.3 Hz, 1H), 6.77 (d, J = 2.3 Hz, 1H), 6.79-6.83 (m, 1H), 6.85-6.90 (m, 1H), 7.10 (d, J = 8.3 Hz, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.36-7.41 (m, 2H), 7.52 (d, J = 8.7 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 2.2 Hz, 1H), 8.03 (dd, J = 1.7, 8.7 Hz, 1H). 8.36 (d, J = 1.7 Hz, 1H)

Example 129

Synthesis of N-methoxycarbamic acid (7-{4-[4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}-2-oxo-2H-quinolin-1-yl)methyl

[0413]

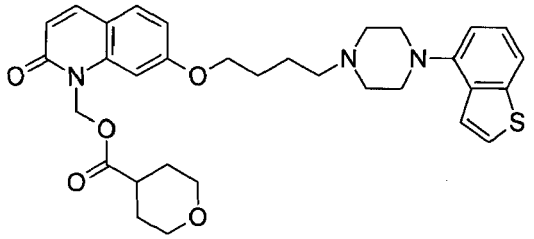


[0414] In the same manner as in Example 10, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.82 (2H, m), 1.84-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.79 (4H, m), 3.13-3.26 (4H, m), {3.51(s), 3.73 (s) total 3H (1:3)}, 4.07-4.17 (2H, m), {6.33 (s), 6.39 (s) total 2H (1:3)}, 6.48-6.53 (1H, m), 6.80-6.88 (2H, m), {7.05 (d, J=2.0Hz), 7.13 (d, J=2.0Hz) total 1H (3:1)}, 7.24-7.30 (1H, m), 7.37-7.47 (3H, m), 7.55 (1H, d, J=8.0Hz), {7.58 (brs), 7.83 (brs) total 1H (1:3)}, 7.62 (1H, d, J=9.5Hz)

Example 130

Synthesis of tetrahydropyran-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0415]

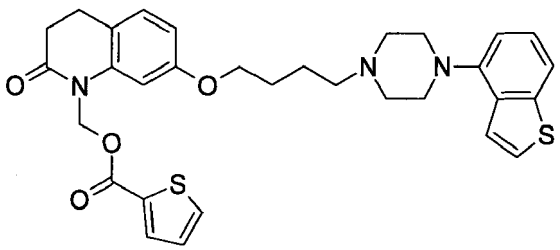


[0416] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.71-1.95 (m, 8H), 2.54 (t, J = 7.5 Hz, 2H), 2.57-2.66 (m, 1H), 2.67-2.79 (m, 4H), 3.14-3.25 (m, 4H), 3.34-3.43 (m, 2H), 3.93 (dt, J = 3.6, 7.6 Hz, 2H), 4.08 (t, J = 6.3 Hz, 2H), 6.35 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.81-6.87 (m, 2H), 6.87-6.92 (m, 1H), 7.27 (dd, J =7.9, 7.9 Hz, 1H), 7.39 (d, J = 5.5 Hz, 1H), 7.42 (d, J = 5.5 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 131

Synthesis of thiophene-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0417]

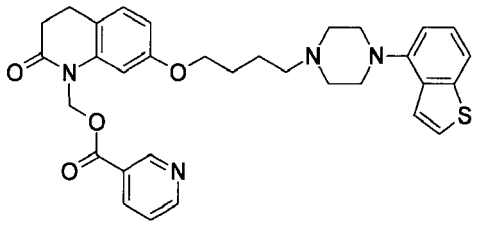


[0418] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.66-1.76 (m, 2H), 1.77-1.89 (m, 2H), 2.50 (t, J = 7.5 Hz, 2H), 2.62-2.76 (m, 6H), 2.85-2.92 (m, 2H), 3.10-3.23 (m, 4H), 3.98 (t, J = 6.2 Hz, 2H), 6.14 (brs, 2H), 6.61 (dd, J = 2.3, 8.2 Hz, 1H), 6.75 (d, J = 2.3 Hz, 1H), 6.86-6.91 (m, 1H), 7.05-7.11 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.53-7.58 (m, 2H), 7.82 (dd, J = 1.2, 3.8 Hz, 1H)

Example 132

Synthesis of nicotinic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0419]

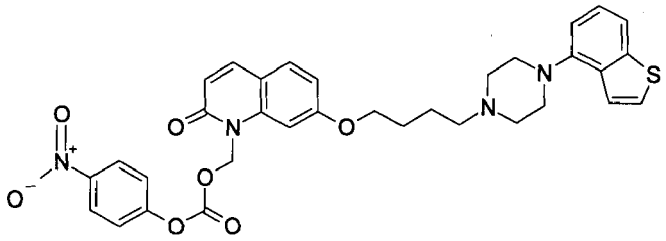


[0420] In the same manner as in Example 48, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.64-1.76 (m, 2H), 1.77-1.88 (m, 2H), 2.49 (t, J = 7.5 Hz, 2H), 2.61-2.78 (m, 6H), 2.87-2.94 (m, 2H), 3.10-3.24 (m, 4H), 3.98 (t, J = 6.3 Hz, 2H), 6.19 (brs, 2H), 6.62 (dd, J = 2.3, 8.3 Hz, 1H), 6.72 (d, J = 2.3 Hz, 1H), 6.88 (d, J = 7.5 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.35-7.42 (m, 3H), 7.55 (d, J = 8.0 Hz, 1H), 8.30 (ddd, J = 2.0, 2.0, 8.0 Hz, 1H), 8.77 (dd, J = 1.7 Hz, 4.9 Hz, 1H), 9.21-9.25 (m, 1H)

Example 133

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester 4-nitrophenyl ester

[0421]

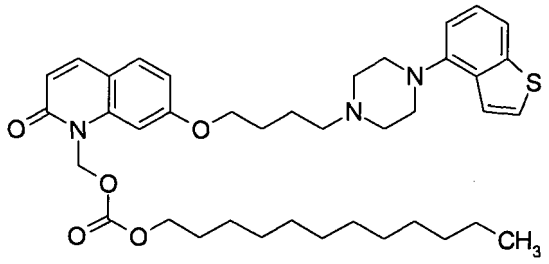


[0422] 7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one (2.0 g) was suspended in anhydrous THF (40 ml) under a nitrogen atmosphere, and sodium hydride (about 55% oil) (0.22 g) was added. The mixture was refluxed for 30 min under a nitrogen atmosphere. The obtained solution was cooled to was cooled to -70°C, and a solution (20 ml) of chloromethyl-4-nitrophenyl carbonate (1.50 g) in anhydrous THF with cannula. The reaction mixture was stirred at room temperature for 3 hr. Water was added to the reaction mixture to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated by filtration. The obtained residue was purified by silica gel column chromatography (ethyl acetate) to give the component (Rf value: 0.62, ethyl acetate, 0.67 g) as a pale-yellow amorphous compound. The obtained compound was used for the next reaction step without further purification.

Example 134

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester dodecyl ester

[0423]



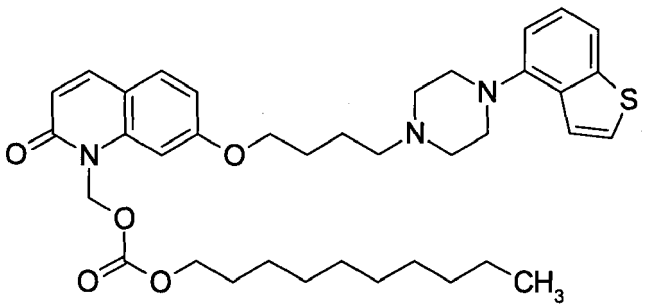
[0424] 1-Dodecanol (0.10 g) was dissolved in anhydrous THF (5 ml) under a nitrogen atmosphere and sodium hydride (about 55% oil) (25 mg) was added under ice-cooling with stirring. The reaction mixture was stirred at room temperature for 30 min under a nitrogen atmosphere, and then the mixture was ice-cooled. To the mixture was added a solution (5ml) of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester 4-nitrophenyl ester obtained in Example 133 (0.33 g) in anhydrous THF using a cannula. Under a nitrogen atmosphere, the reaction mixture was stirred with ice-cooling for 2 hr, and at room temperature for 1 hr. Water was added to the reaction mixture to discontinue the reaction, and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and concentrated by filtration. The obtained residue was purified by silica gel column chromatography (ethyl acetate:hexane =1:1) to give the title compound (0.14 g) as a colorless oil.

^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0Hz), 1.17-1.38 (18H, m), 1.59-1.70 (2H, m), 1.73-1.82 (2H, m), 1.86-1.95 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.69-2.78 (4H, m), 3.16-3.24 (4H, m), 4.10 (2H, t, J=6.0Hz), 4.18 (2H, t, J=6.5Hz), 6.35 (2H, brs), 6.50 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 6.93 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.42 (1H, d, J=5.5Hz), 7.44 (1H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 135

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester decyl ester

[0425]

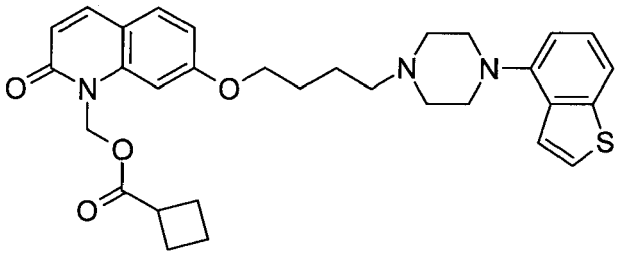


[0426] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1), and in the same manner as in Example 5, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0Hz), 1.17-1.38 (14H, m), 1.62-1.70 (2H, m), 1.72-1.83 (2H, m), 1.86-1.96 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.64-2.81 (4H, m), 3.12-3.26 (4H, m), 4.07-4.13 (2H, m), 4.18 (2H, t, J=6.5Hz), 6.35 (2H, brs), 6.50(1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.89 (1H, d, J=7.5Hz), 6.93 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.42 (1H, d, J=5.5Hz), 7.44 (1H, d, J=8.5Hz), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=9.5Hz)

Example 136

[0427] Synthesis of cyclobutanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

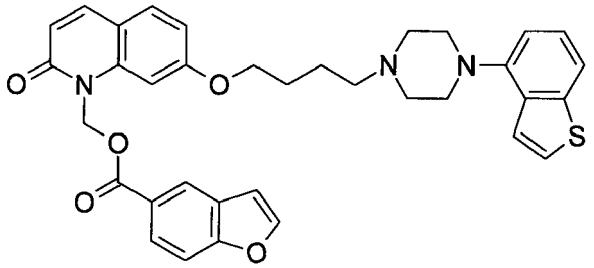


[0428] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.66-1.84 (m, 2H), 1.84-2.05 (m, 4H), 2.14-2.24 (m, 2H), 2.24-2.36 (m, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.65-2.80 (m, 4H), 3.12-3.26 (m, 5H), 4.08 (t, J = 6.2 Hz, 2H), 6.34 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.5 Hz, 1H), 6.87 (d, J = 2.2 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 7.24-7.30 (m, 1H), 7.39 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.44 (d, J = 8.5 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 9.5 Hz, 1H)

Example 137

Synthesis of benzofuran-5-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-yl-methyl ester

[0429]

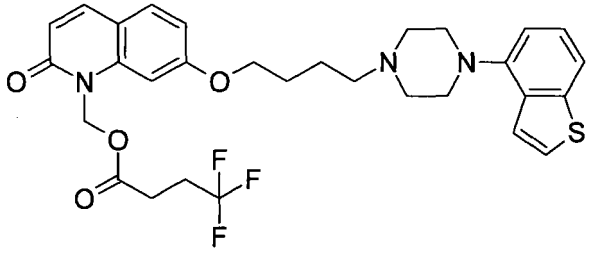


[0430] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.66-1.78 (m, 2H),1.78-1.92 (m, 2H), 2.48 (t, J = 7.4 Hz, 2H), 2.59-2.74 (m, 4H), 3.10-3.20 (m, 4H), 4.07 (t, J = 6.2 Hz, 2H), 6.57 (d, J = 9.5 Hz, 1H), 6.61 (brs, 2H), 6.76-6.81 (m, 1H), 6.84 (dd, J = 2.1, 8.6 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 7.00-7.04 (m, 1H), 7.27 (dd, J =7.9, 7.9 Hz, 1H), 7.37-7.42 (m, 2H), 7.47 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 8.7 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.62-7.69 (m, 2H), 8.03 (dd, J = 1.7, 8.7 Hz, 1H), 8.35 (d, J = 1.7 Hz, 1H)

Example 138

Synthesis of 4,4,4-trifluorobutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0431]



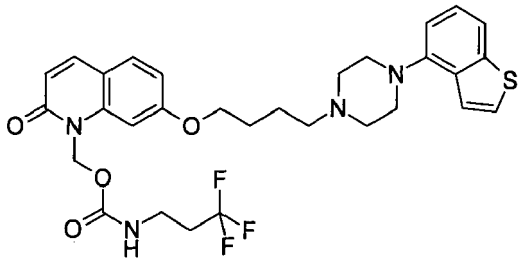
[0432] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.82 (m, 2H), 1.86-1.96 (m, 2H), 2.43-2.58 (m, 4H), 2.62-2.69 (m, 2H), 2.69-2.79 (m,4H),

3.14-3.26 (m, 4H), 4.08 (t, J = 6.2Hz, 2H), 6.36 (brs, 2H), 6.52 (d, J = 9.5 Hz, 1H), 6.83-6.88 (m, 2H), 6.88-6.92 (m, 1H), 7.27 (dd, J = 7.9, 7.9 Hz, 1H), 7.37-7.43 (m, 2H), 7.46 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 9.5 Hz, 1H)

Example 139

Synthesis of N-(3,3,3-trifluoropropyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0433]

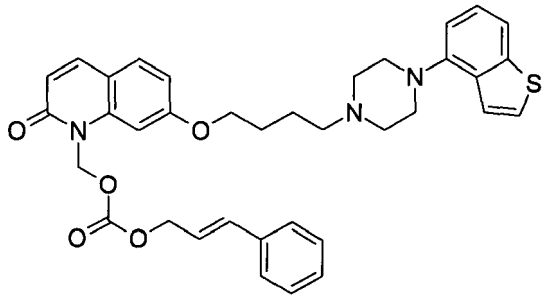


[0434] In the same manner as in Example 134, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.95 (4H, m), 2.30-2.44 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.65-2.82 (4H, m), 3.13-3.26 (4H, m), 3.48 (2H, dt, J=6.5Hz, J=6.5Hz), 4.04-4.14 (2H, m), 5.32-5.39 (1H, m), 6.31 (2H, s), 6.48 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, J=8.5Hz), 6.86-6.91 (1H, m), 7.07 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.37-7.44 (3H, m), 7.54 (1H, d, J=8.0Hz), 7.58 (1H, d, J=9.5Hz)

Example 140

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester (E)-3-phenyl-allyl ester

[0435]

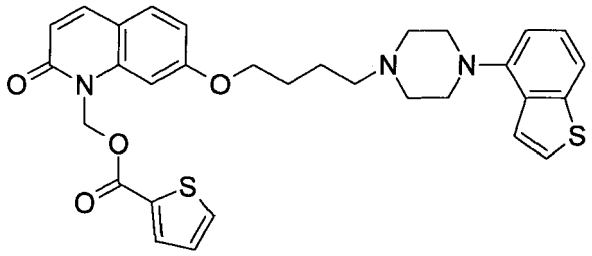


[0436] In the same manner as in Example 134, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.80 (2H, m), 1.82-1.94 (2H, m), 2.51 (2H, t, J=7.5Hz), 2.63-2.77 (4H, m), 3.12-3.24 (4H, m), 4.05-4.11 (2H, m), 4.34 (1H, dd, J=1.0Hz, J=6.5Hz), 4.83 (1H, dd, J=1.0Hz, J=6.5Hz), 6.16-6.30 (1H, m), 6.38 (2H, brs), 6.50 (1H, dd, J=2.0Hz, J=9.5Hz), 6.57-6.70 (1H, m), 6.80-6.85 (1H, m), 6.87(1H, brd, J=7.5Hz), 6.93 (1H, brs), 7.20-7.46 (9H, m), 7.54 (1H, d, J=8.0Hz), 7.59 (1H, dd, J=3.5Hz, J=9.5Hz)

Example 141

Synthesis of thiophene-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0437]

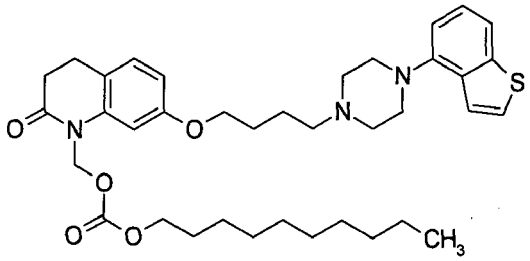


[0438] In the same manner as in Example 22, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.66-1.82 (m, 2H), 1.84-1.93 (m, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.64-2.77 (m, 4H), 3.12-3.24 (m, 4H), 4.08 (t, J = 6.2 Hz, 2H), 6.52-6.60 (m, 3H), 6.84 (dd, J = 2.1, 8.6 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 7.00 (d, J = 2.1 Hz, 1H), 7.07 (dd, J = 3.8, 4.9 Hz, 1H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.38 (d, J = 5.6 Hz, 1H), 7.41 (d, J = 5.6 Hz, 1H), 7.45 (d, J = 8.6 Hz, 1H), 7.53-7.59 (m, 2H), 7.64 (d, J = 9.5 Hz, 1H), 7.82 (dd, J = 1.2, 3.8 Hz, 1H)

Example 142

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester decyl ester

[0439]

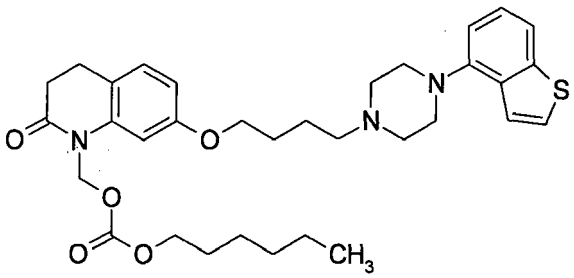


[0440] In the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0Hz), 1.19-1.41 (14H, m), 1.62-1.80 (4H, m), 1.82-1.91 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.82-2.90 (2H, m), 3.14-3.24 (4H, m), 4.00 (2H, t, J=6.0Hz), 4.17 (2H, t, J=6.5Hz), 5.94 (2H, s), 6.59 (1H, dd, J=2.5Hz, J=8.5Hz), 6.69 (1H, dd, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.25-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.40-7.43 (1H, m), 7.55 (1H, d, J=8.0Hz)

Example 143

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester hexyl ester

[0441]



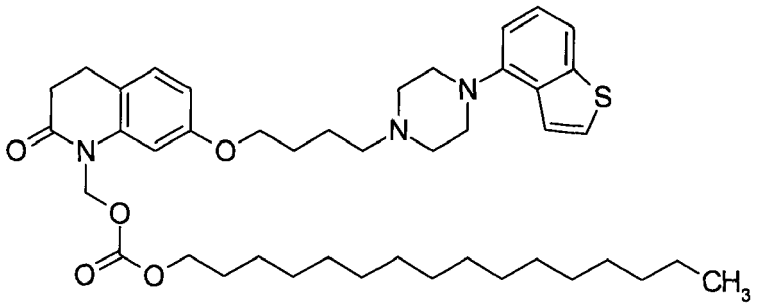
[0442] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.9 Hz), 1.20-1.90 (12H, m), 2.52 (2H, t, J=7.4 Hz), 2.60-2.80 (6H, m), 2.83-2.88 (2H,

m), 3.20 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.18 (2H, t, J=6. Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.4, 8.2 Hz), 6.69 (1H, d, J=2.3 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.3 Hz), 7.20-7.30 (1H, m), 7.35-7.45 (2H, m), 7.55 (1H, d, J=8.0 Hz)

Example 144

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester hexadecyl ester

[0443]

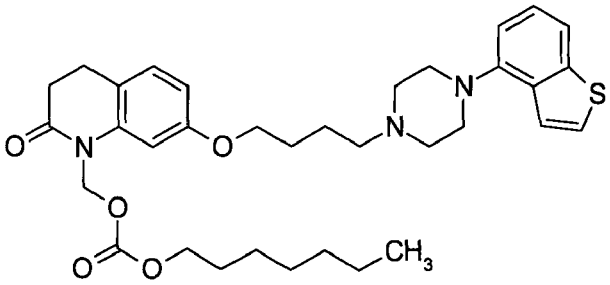


[0444] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.8 Hz), 1.20-1.90 (32H, m), 2.53 (2H, t, J=7.4 Hz), 2.64-2.78 (6H, m), 2.80-2.90 (2H, m), 3.20 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.17 (2H, t, J=6.8 Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.3, 8.3 Hz), 6.69 (1H, d, J=2.3 Hz), 6.89 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.3 Hz), 7.27 (1H, t, J=7.8 Hz), 7.35-7.45 (2H, m), 7.54 (1H, d, J=8.0 Hz)

Example 145

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester heptyl ester

[0445]

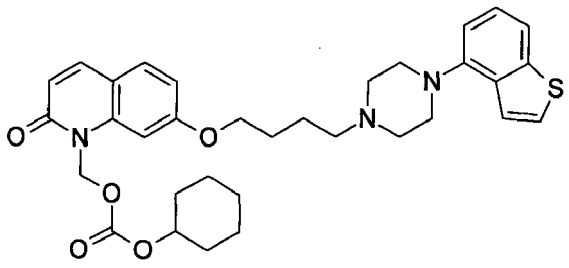


[0446] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=7.0 Hz), 1.22-1.40 (6H, m), 1.52-1.90 (8H, m), 2.53 (2H, t, J=7.4 Hz), 2.64-2.78 (6H, m), 2.86 (2H, t, J=7.2 Hz), 3.20 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.17 (2H, t, J=6.8 Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.4, 8.3 Hz), 6.69 (1H, d, J=2.3 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.2 Hz), 7.27 (1H, t, J=7.8 Hz), 7.35-7.45 (2H, m), 7.55 (1H, d, J=8.1 Hz)

Example 146

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester cyclohexyl ester

[0447]

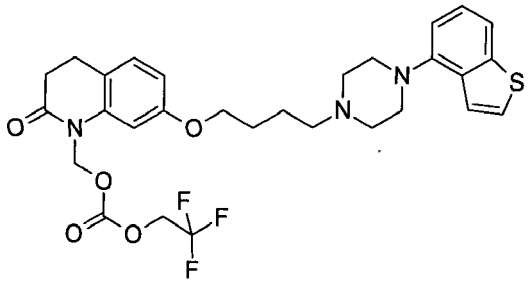


[0448] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one synthesized in the same manner as in WO2006/112464 (Example 1), and in the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.17-1.28 (1H, m), 1.29-1.41 (2H, m), 1.42-1.57 (3H, m), 1.68-1.82 (4H, m), 1.84-1.98 (4H, m), 2.53 (2H, t, J=7.5Hz), 2.64-2.80 (4H, m), 3.12-3.26 (4H, m), 4.09 (2H, t, J=6.0Hz), 4.64-4.72 (1H, m), 6.34 (2H, s), 6.49 (1H, d, J=9.5Hz), 6.83 (1H, dd, J=2.0Hz, 8.5Hz), 6.89 (1H, d, J=7.5Hz), 6.92 (1H, d, J=2.0Hz), 7.23-7.30 (1H, m), 7.36-7.44 (3H, m), 7.54 (1H, d, J=8.0Hz), 7.59 (1H, d, J=9.5Hz)

Example 147

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester 2,2,2-trifluoro-ethyl ester

[0449]

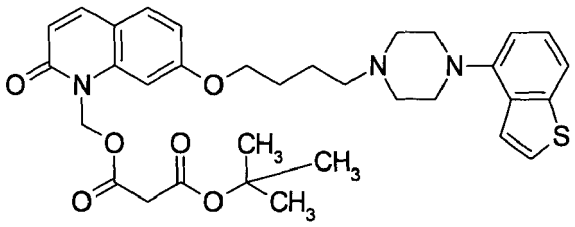


[0450] In the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.69-1.79 (2H, m), 1.81-1.90 (2H, m), 2.51 (2H, t, J=7.5Hz), 2.63-2.76 (6H, m), 2.81-2.90 (2H, m), 3.13-3.26 (4H, m), 3.99 (2H, t, J=6.0Hz), 4.55 (2H, q, J=8.0Hz), 6.00 (2H, s), 6.61 (1H, dd, J=2.5Hz, 8.0Hz), 6.65 (1H, d, J=2.5Hz), 6.86-6.91 (1H, m), 7.07 (1H, d, J=8.5Hz), 7.23-7.29 (1H, m), 7.37 (1H, d, J=5.5Hz), 7.39-7.43 (1H, m), 7.54 (1H, d, J=8.0Hz)

Example 148

Synthesis of malonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester tert-butyl ester

[0451]



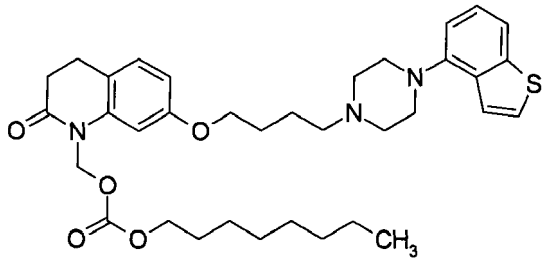
[0452] In the same manner as in Example 22, the title compound was obtained.

^{1}H-NMR ($CDCl_3$) δ: 1.38 (s, 9H), 1.69-1.83 (m, 2H), 1.85-1.95 (m, 2H), 2.55 (t, J = 7.4 Hz, 2H), 2.67-2.79 (m, 4H), 3.14-3.25 (m, 4H), 3.35 (s, 2H), 4.13 (t, J = 6.1 Hz, 2H), 6.37 (brs, 2H), 6.51 (d, J = 9.5 Hz, 1H), 6.84 (dd, J = 2.2, 8.6 Hz, 1H), 6.87-6.92 (m, 2H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 7.37-7.43 (m, 2H), 7.44 (d, J = 8.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 9.5 Hz, 1H)

Example 149

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester octyl ester

[0453]

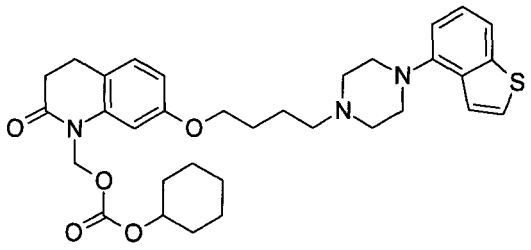


[0454] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.8 Hz), 1.20-1.40 (8H, m), 1.60-1.90 (8H, m), 2.53 (2H, t, J=7.4 Hz), 2.64-2.78 (6H, m), 2.86 (2H, t, J=6.8 Hz), 3.20 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.17 (2H, t, J=6.8 Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.3, 8.2 Hz), 6.69 (1H, d, J=2.3 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.0 Hz)

Example 150

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-l-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester cyclohexyl ester

[0455]

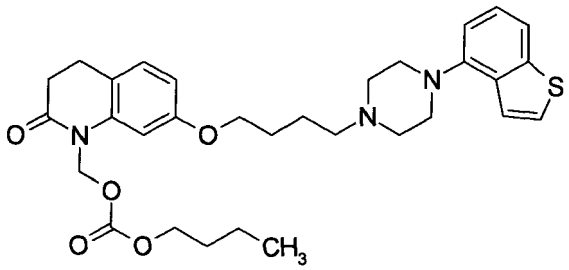


[0456] In the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.17-1.28 (1H, m), 1.29-1.41 (2H, m), 1.43-1.58 (3H, m), 1.68-1.79 (4H, m), 1.80-1.89 (2H, m), 1.90-1.99 (2H, m), 2.52 (2H, t, J=7.5Hz), 2.64-2.77 (6H, m), 2.82-2.89 (2H, m), 3.14-3.25 (4H, m), 4.00 (2H, t, J=6.0Hz), 4.62-4.71 (1H, m), 5.94 (2H, s), 6.59 (1H, dd, J=2.5Hz, 8.5Hz), 6.69 (1H, d, J=2.5Hz), 6.90 (1H, d, J=7.5Hz), 7.06 (1H, d, J=8.5Hz), 7.24-7.30 (1H, m), 7.38 (1H, d, J=5.5Hz), 7.40-7.44 (1H, m), 7.55 (1H, d, J=8.0Hz)

Example 151

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester butyl ester

[0457]

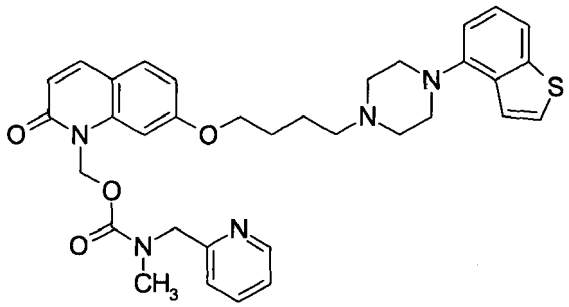


[0458] In the same manner as in Example 5, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, t, J=7.4 Hz), 1.34-1.46 (2H, m), 1.60-1.90 (6H, m), 2.52 (2H, t, J=7.4 Hz), 2.64-2.76 (6H, m), 2.82-2.88 (2H, m), 3.16-3.26 (4H, br), 4.00 (2H, t, J=6.2 Hz), 4.19 (2H, t, J=6.7Hz), 5.94 (2H,brs), 6.59 (1H, dd, J=2.3, 8.2 Hz), 6.69 (1H, d, J=2.3 Hz), 6.89 (1H, d, J=7.6 Hz), 7.06 (1H, d, J=8.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.1 Hz)

Example 152

Synthesis of N-methyl-N-pyridin-2-ylmethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0459]

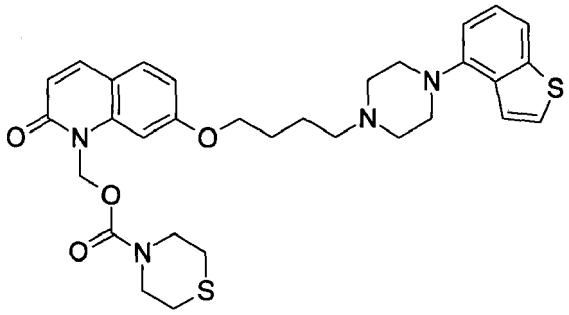


[0460] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.68-1.81 (2H, m), 1.82-1.94 (2H, m), 2.47-2.58 (2H, m), 2.64-2.78 (4H, m), {2.91 (s), 3.06 (s) total 3H (1:1)}, 3.13-3.25 (4H, m), 4.00-4.10 (2H, m), 4.47 (1H, s), 4.65 (1H, s), 6.37 (1H, brs), 6.43 (1H, brs), {6.48 (d, J=9.5Hz), 6.53 (d, J=9.5Hz) total 1H (1:1)}, 6.78-6.97 (2H, m), 6.99-7.05 (1H, m), 7.13-7.21 (1H, m), 7.23-7.31 (2H, m), 7.36-7.47 (3H, m), 7.52-7.68 (3H, m), {8.38 (d, J=4.5Hz), 8.54 (d, J=4.5Hz) total 1H (1:1)}

Example 153

Synthesis of thiomorpholine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

[0461]

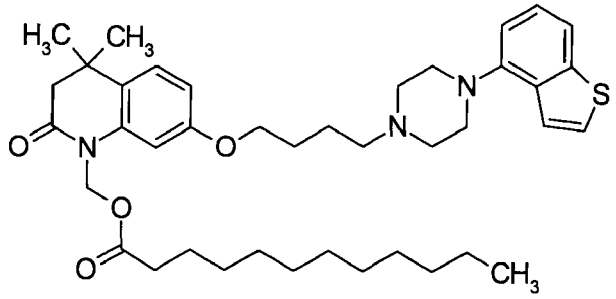


[0462] In the same manner as in Example 14, the title compound was obtained.
^{1}H-NMR ($CDCl_3$) δ: 1.72-1.82 (2H, m), 1.86-1.95 (2H, m), 2.45-2.52 (2H, m), 2.54 (2H, t, J=7.5Hz), 2.58-2.64 (2H, m), 2.68-2.79 (4H, m), 3.15-3.26 (4H, m), 3.63-3.72 (2H, m), 3.73-3.83 (2H, m), 4.10 (2H, d, J=6.5Hz), 6.36 (2H, s), 6.52 (1H, d, J=9.5Hz), 6.84 (1H, dd, J=2.0Hz, J=8.5Hz), 6.87-6.92 (1H, m), 7.06 (1H, d, J=2.0Hz), 7.24-7.30 (1H, m), 7.37-7.47 (3H, m), 7.55 (1H, d, J=8.0Hz), 7.63 (1H, d, J=9.5Hz)

Example 154

Synthesis of dodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-l-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0463]

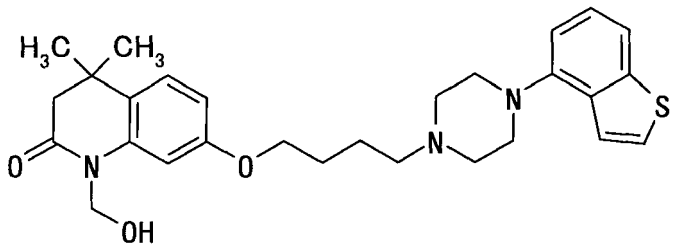


[0464] Using 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one obtained in Reference Example 18, the title compound was synthesized in the same manner as in Example 5.
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.9 Hz), 1.20-1.32 (22H, m), 1.56-1.68 (2H, m), 1.68-1.80 (2H, m), 1.80-1.90 (2H, m), 2.35 (2H, t, J=7.5 Hz), 2.50-2.56 (4H, m), 2.68-2.76 (4H, m), 3.14-3.24 (4H, m), 3.99 (2H, t, J=6.2 Hz), 5.97 (2H,brs), 6.62-6.68 (2H, m), 6.89 (1H, d, J=7.6 Hz), 7.20 (1H, d, J=8.3 Hz), 7.27 (1H, t, J=7.8 Hz), 7.40 (2H, dd, J=5.6, 12.5 Hz), 7.54 (1H, d, J=8.0 Hz)

Example 155

Synthesis of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one

[0465]



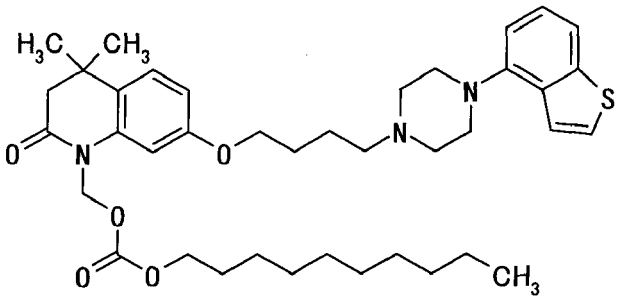
[0466] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (0.4 g) obtained in Reference Example 18 in DMF (10 ml) were added 37% aqueous formalin solution (1.5 ml) and triethylamine (0.02 ml), and the mixture was heated at 80°C for 10 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure to give a mixture (0.46 g, 1:3) of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one and 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one.
amorphous: colorless
^{1}H-NMR ($CDCl_3$) δ: 1.26 (3H, t, J=7.2Hz), 1.27 (1.5H, s), 1.29 (4.5H, s), 1.68-1.78 (2H, m), 1.78-1.90 (2H, m), 2.46 (1.5H, s), 2.48 (0.5H, s), 2.52 (2H, t, J=7.4Hz), 2.72 (4H, m), 3.19 (4H, m), 3.95-4.05 (2H, m), 5.41 (0.5H, s), 6.36(0.75H, d, J=2.5Hz), 6.58 (0.75H, dd, J=2.5, 8.5Hz), 6.64 (0.25H, dd, J=2.4, 8.5Hz), 6.87-6.92 (1.25H, m), 7.17 (0.75H, d,

J=8.5Hz), 7.18 (0.25H, d, J=8.5Hz), 7.27 (1H, t, J=7.8Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.0Hz), 8.32 (0.75H, brs)

Example 156

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester decyl ester

[0467]

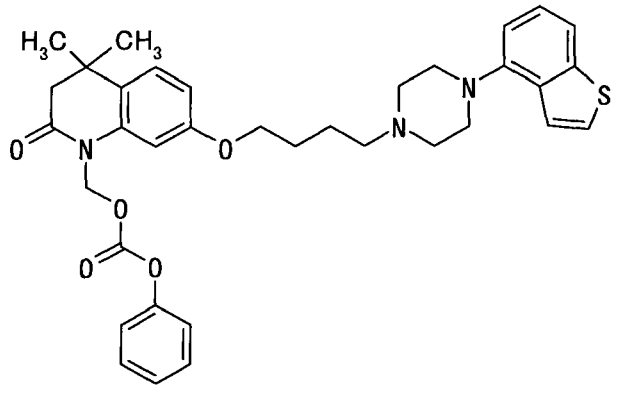


[0468] 7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-hydroxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (460 mg), which is a mixture with 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one obtained in Example 155, was suspended in methylene chloride (10 ml), pyridine (0.06 ml) and decyl chloroformate (103 mg) were added, and the mixture was stirred under ice-cooling for 4 hr. Water was added to the reaction mixture, and the mixture was extracted with methylene chloride, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester decyl ester (108 mg).
colorless oil
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.8 Hz), 1.20-1.40 (20H, m), 1.62-1.70 (2H, m), 1.70-1.80 (2H, m), 1.80-1.90 (2H, m), 2.50-2.56 (4H, m), 2.73 (4H, m), 3.20 (4H, m), 4.00 (2H, t, J=6.2 Hz), 4.17 (2H, t, J=6.8 Hz), 5.99 (2H, s), 6.65 (1H, dd, J=2.4, 8.5 Hz), 6.71 (1H, d, J=2.3 Hz), 6.89 (1H, d, J=7.6 Hz), 7.20 (1H, d, J=8.4 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.1 Hz)

Example 157

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester

[0469]



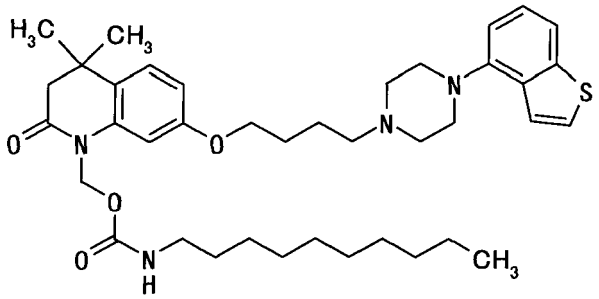
[0470] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (0.38 g) obtained in Reference Example 18 in THF (10 ml) was added 60% sodium hydride (40 mg) with stirring under ice-cooling, and the mixture was heated under reflux for 0.5 hr. Thereafter, with stirring under ice-cooling, a solution

of chloromethyl phenylcarbonate (0.23 g) in THF (1 ml) was added dropwise, and the mixture was stirred at room temperature overnight. With stirring under ice-cooling, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=1:1) to give carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester phenyl ester (130 mg).
colorless oil
^{1}H-NMR ($CDCl_3$) δ: 1.30 (6H, s), 1.68-1.90 (4H, m), 2.46-2.56 (2H, m), 2.57 (2H, s), 2.68-2.78 (4H, br), 3.14-3.24 (4H, br), 4.02 (2H, t, J=6.2 Hz), 6.11 (2H, s), 6.68 (1H, dd, J=2.4, 8.5 Hz), 6.75 (1H, d, J=2.4 Hz), 6.89 (1H, d, J=7.6 Hz), 7.16-7.46 (9H, m), 7.55 (1H, d, J=8.0 Hz).

Example 158

Synthesis of N-decylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

[0471]

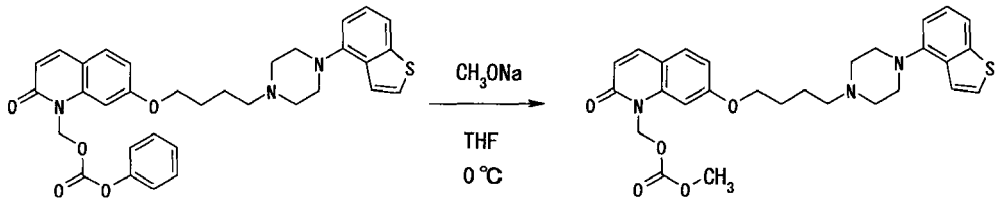


[0472] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one (0.21 g) obtained in Reference Example 18 in THF (10 ml) was added with stirring under ice-cooling 60% sodium hydride (27 mg), and the mixture was heated under reflux for 0.5 hr. Thereafter, with stirring under ice-cooling, a solution of chloromethyl phenylcarbonate (0.17 g) in THF (1 ml) was added dropwise, and the mixture was stirred at room temperature overnight. With stirring under ice-cooling, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure. To a solution of the obtained residue in THF (10 ml) was added decylamine (0.5 ml), and the mixture was stirred at room temperature overnight. With stirring under ice-cooling, water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give N-decylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)-butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester (126 mg).
yellow oil
^{1}H-NMR ($CDCl_3$) δ: 0.87 (3H, t, J=6.8 Hz), 1.18-1.34 (20H, m), 1.42-1.52 (2H, m), 1.70-1.80 (2H, m), 1.80-1.90 (2H, m), 2.48-2.56 (4H, m), 2.66-2.78 (4H, br), 3.12-3.24 (6H, m), 4.01 (2H, t, J=6.1 Hz), 4.76-4.84 (1H, m), 5.96 (2H, s), 6.64 (1H, dd, J=2.3, 8.5 Hz), 6.81 (1H, d, J=2.0 Hz), 6.89 (1H, d, J=7.6 Hz), 7.19 (1H, d, J=8.5 Hz), 7.24-7.30 (1H, m), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0 Hz)

Example 163

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester methyl ester

[0473]

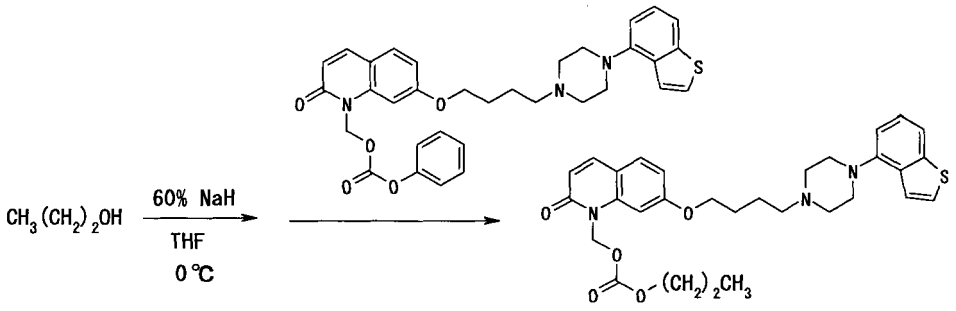


[0474] To a solution of n-hexylalcohol (50.5 mg) in tetrahydrofuran (5 ml) was added with stirring under ice-cooling 60% sodium hydride (18 mg) by small portions, and the mixture was stirred at the same temperature for 0.5 hr, to a solution of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester (240 mg) in tetrahydrofuran (1 ml) was added with stirring under ice-cooling sodium methoxide (30 mg), and the mixture was stirred for 3 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate) to give carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester methyl ester (42 mg).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 1.72-1.84 (2H, m), 1.85-1.96 (2H, m), 2.55 (2H, t, J=7.4 Hz), 2.68-2.80 (4H, br), 3.14-3.26 (4H, br), 3.83 (3H, s), 4.10 (2H, t, J=6.2 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.92 (1H, d, J=2.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.50 (1H, d, J=8.0 Hz), 7.60 (1H, d, J=9.5 Hz)

Example 165

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester propyl ester

[0475]

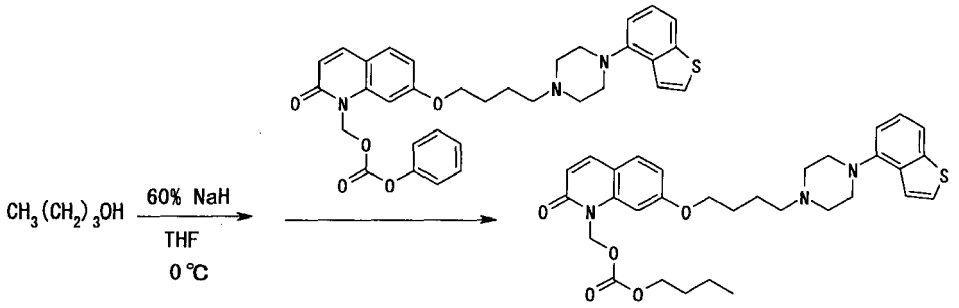


[0476] In the same manner as in Example 175, the compound was obtained (yield 78 mg, 27.5%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ ppm : 0.94 (3H, t, J=7.4 Hz), 1.58-1.84 (4H, m), 1.84-1.96 (2H, m), 2.54 (2H, t, J=7.5 Hz), 2.66-2.80 (4H, br), 3.14-3.28 (4H, br), 4.09 (2H, t, J=6.0 Hz), 4.15 (2H, t, J=6.7 Hz), 6.34 (2H, s), 6.49 (1H, d, J=9.5 Hz), 6.83 (1H, dd, J=2.1, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.0 Hz), 7.26 (1H, t, J=7.8 Hz), 7.36-7.44 (3H, m), 7.54 (1H, d, J=8.0 Hz), 7.62 (1H, d, J=9.5 Hz)

Example 168

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester butyl ester

[0477]

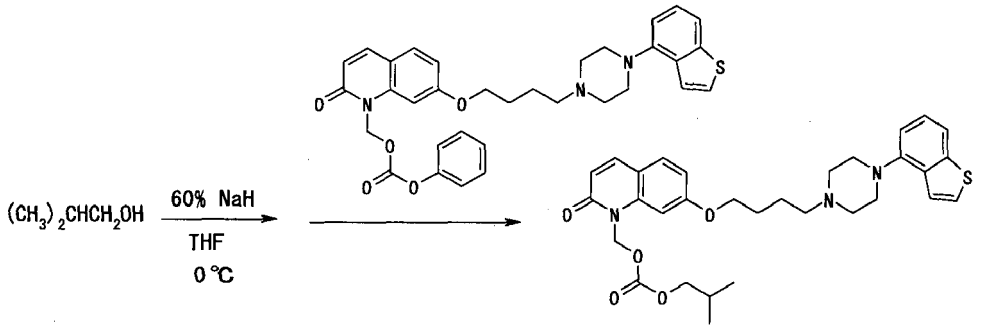


[0478] In the same manner as in Example 175, the compound was obtained (yield 47 mg, 14.3%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ ppm : 0.92 (3H, t, J=7.4 Hz), 1.32-1.44 (2H, m), 1.60-1.70 (2H, m), 1.72-1.84 (2H, m), 1.86-1.96 (2H, m), 2.55 (2H, t, J=7.5 Hz), 2.68-2.80 (4H, br), 3.16-3.26 (4H, br), 4.06-4.15 (2H, m), 4.20 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.7 Hz), 6.93 (1H, d, J=2.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 170

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester isobutyl ester

[0479]

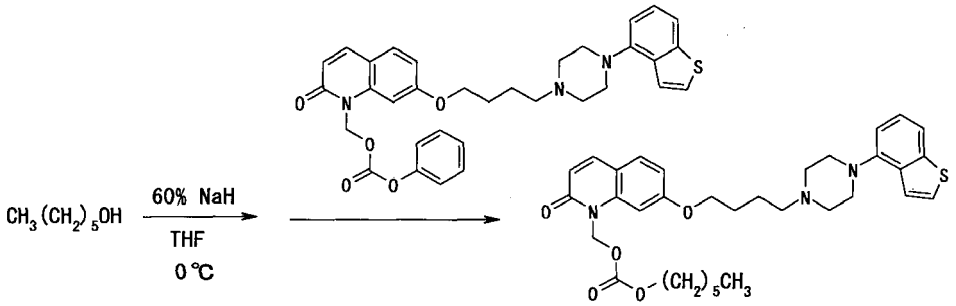


[0480] In the same manner as in Example 175, the compound was obtained (yield 48 mg, 14.6%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ ppm : 0.94 (6H, d, J=6.7 Hz), 1.70-2.04 (5H, m), 2.55 (2H, t, J=7.4 Hz), 2.66-2.80 (4H, br), 3.14-3.24 (4H, br), 3.98 (2H, d, J=6.6 Hz), 4.10 (2H, t, J=6.2 Hz), 6.35 (2H, s), 6.51 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.37-7.46 (3H, m), 7.55 (1H, d, J=8.1 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 175

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester hexyl ester

[0481]

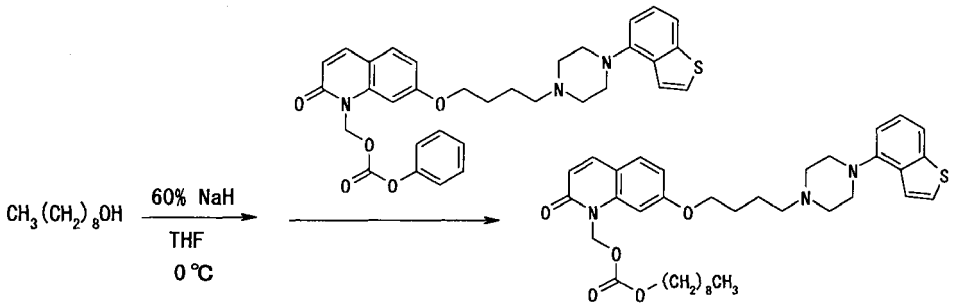


[0482] To a solution of n-hexylalcohol (50.5 mg) in tetrahydrofuran (5 ml) was added with stirring under ice-cooling 60% sodium hydride (18 mg) by small portions, and the mixture was stirred at the same temperature for 0.5 hr, a solution of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester phenyl ester (240 mg) in tetrahydrofuran (1 ml) was added dropwise, and the mixture was stirred under ice-cooling for 3 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate) to give carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester hexyl ester (30 mg).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=6.9 Hz), 1.20-1.40 (6H, m), 1.60-1.72 (2H, m), 1.72-1.84 (2H, m), 1.84-2.00 (2H, m), 2.55 (2H, t, J=7.4 Hz), 2.65-2.82 (4H, br), 3.10-3.28 (4H, br), 4.10 (2H, t, J=6.2 Hz), 4.19 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.6 Hz)

Example 177

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester nonyl ester

[0483]

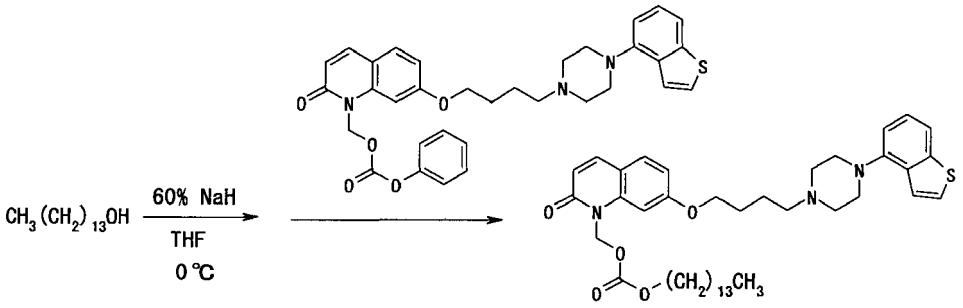


[0484] In the same manner as in Example 175, the compound was obtained (yield 40 mg, 10.8%) as a colorless oil.
^{1}H-NMR ($CDCl_3$) δ ppm : 0.86 (3H, t, J=6.9 Hz), 1.20-1.40 (12H, m), 1.60-1.70 (2H, m), 1.72-1.82 (2H, m), 1.85-1.95 (2H, m), 2.55 (2H, t, J=7.4 Hz), 2.68-2.78 (4H, br), 3.14-3.28 (4H, br), 4.06-4.14 (2H, m), 4.18 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.1, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 179

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester tetradecyl ester

[0485]

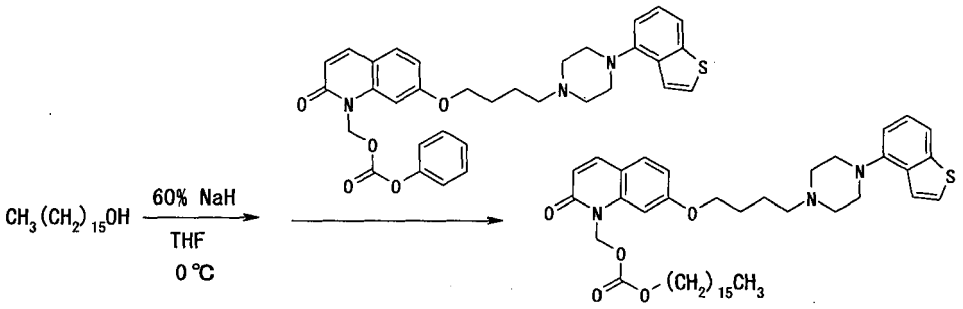


[0486] In the same manner as in Example 175, the colorless amorphous compound was obtained (yield 33 mg, 9.3%). ^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=6.9 Hz), 1.20-1.40 (22H, m), 1.55-1.95 (6H, m), 2.56 (2H, t, J=7.4 Hz), 2.68-2.80 (4H, br), 3.15-3.25 (4H, br), 4.10 (2H, t, J=6.2 Hz), 4.18 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 180

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester hexadecyl ester

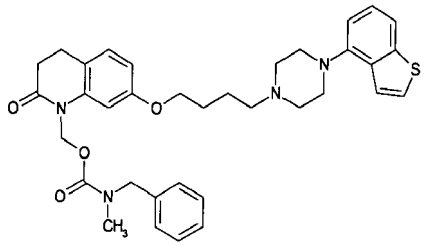
[0487]



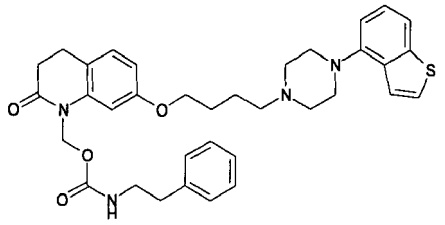
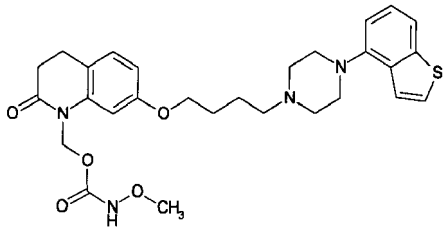
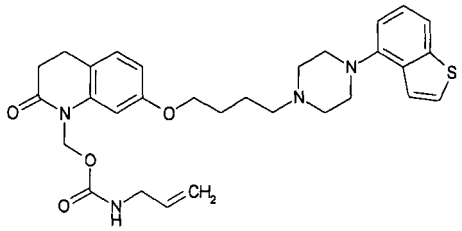
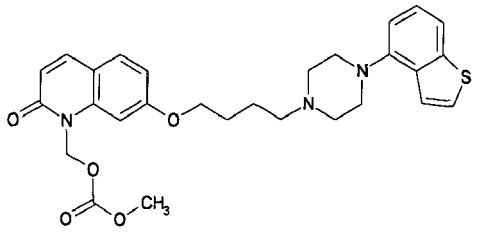
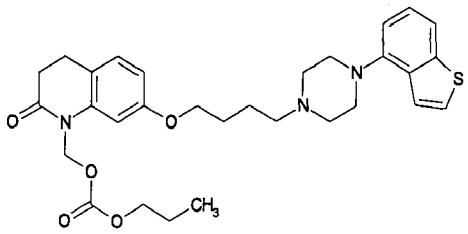
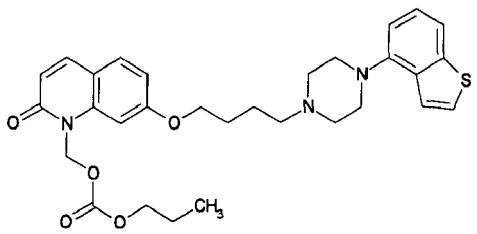
[0488] In the same manner as in Example 175, the colorless amorphous compound was obtained (yield 48 mg, 15%). ^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=6. Hz), 1.20-1.38 (26H, m), 1.60-1.96 (6H, m), 2.55 (2H, t, J=7.4 Hz), 2.70-2.80 (4H, br), 3.16-3.24 (4H, br), 4.10 (2H, t, J=6.2 Hz), 4.18 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.0 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.1 Hz), 7.61 (1H, d, J=9.5 Hz)

[0489] In the same manner as in the above-mentioned Examples, the compounds described in the following Table 1 can be synthesized.

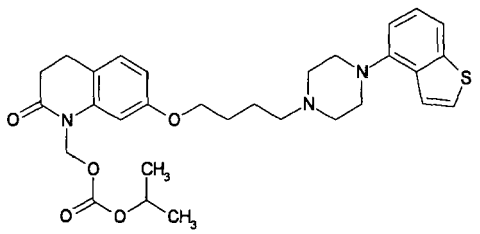
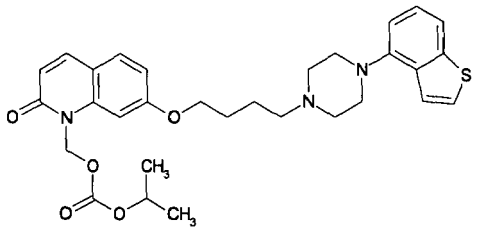
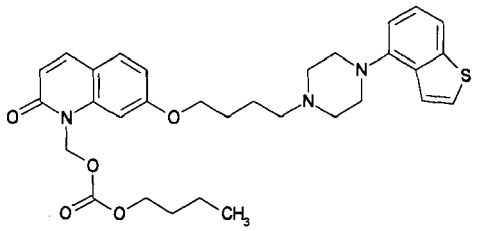
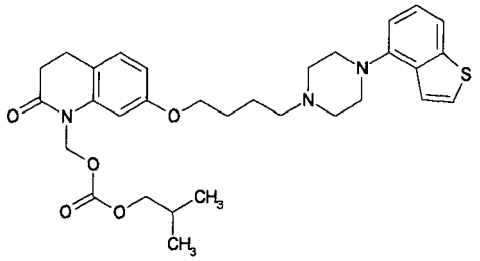
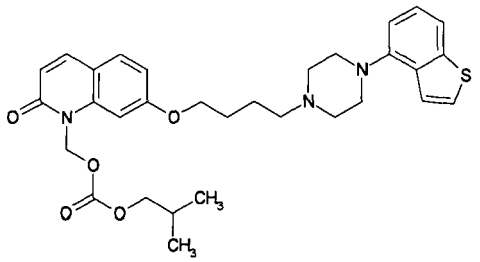
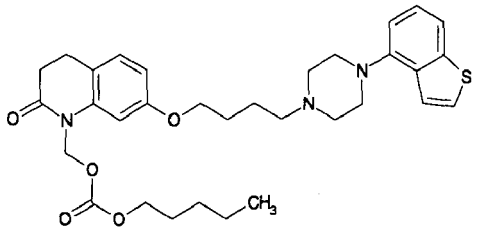
Table 1

Example	Structure Formula	
159		N-Benzyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

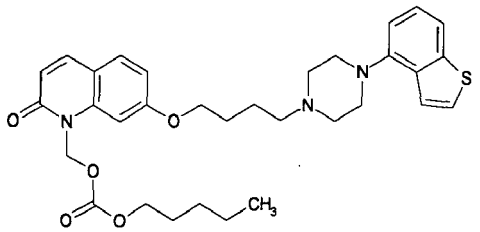
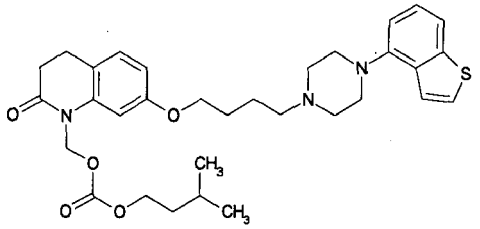
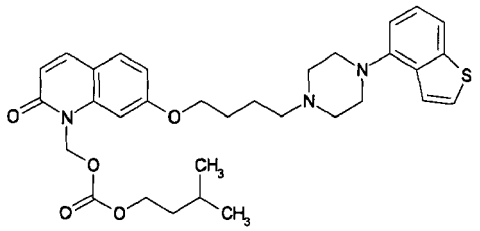
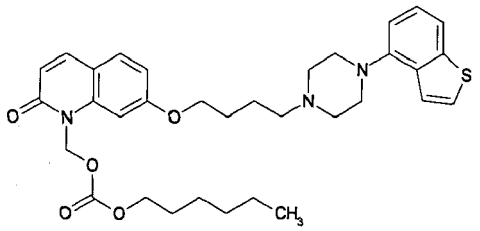
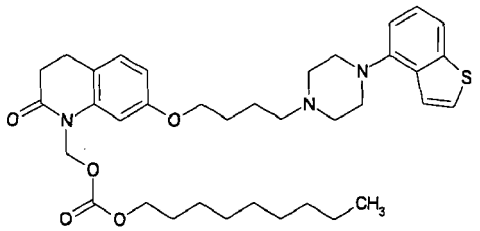
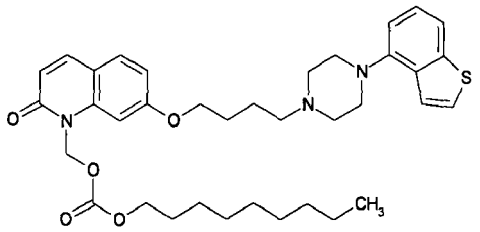
(continued)

Example	Structure Formula	
160		N-Phenethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
161		(7-{4-[4-(Benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}-2-oxo-3,4-dihydro-2H-quinolin-1-yl)methyl N-methoxycarbamate
162		N-Allylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
163		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester methyl ester
164		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester propyl ester
165		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester propyl ester

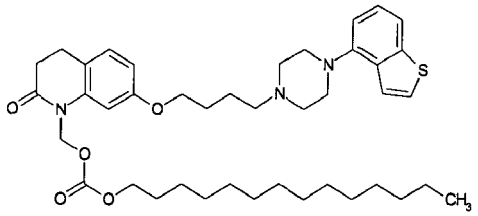
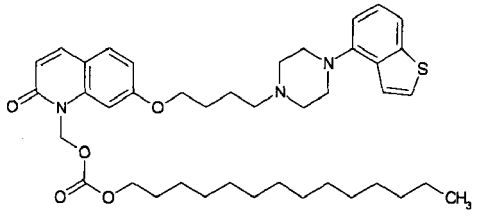
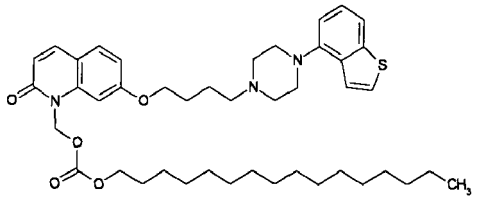
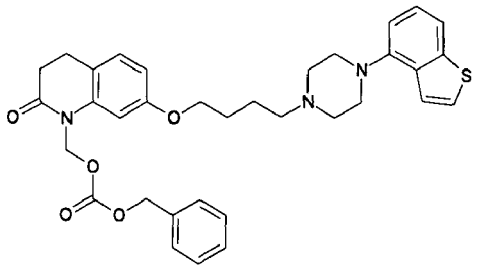
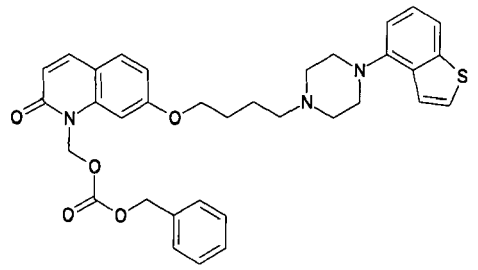
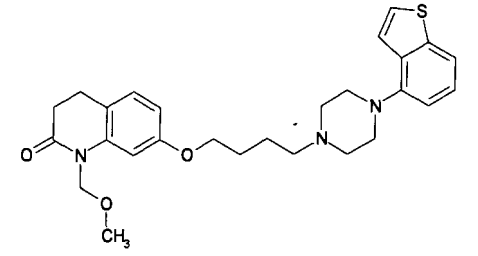
(continued)

Example	Structure Formula	
166		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester isopropyl ester
167		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester isopropyl ester
168		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester butyl ester
169		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester isobutyl ester
170		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester isobutyl ester
171		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester pentyl ester

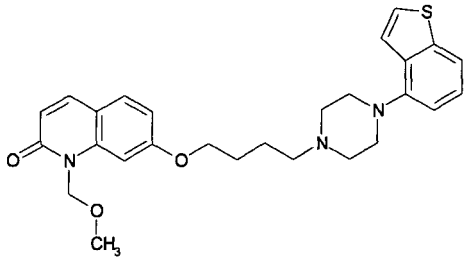
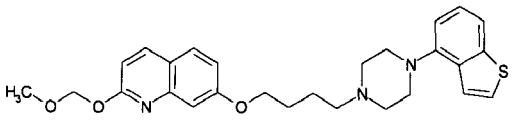
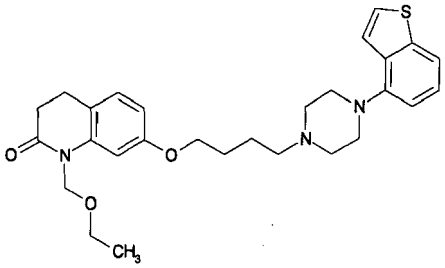
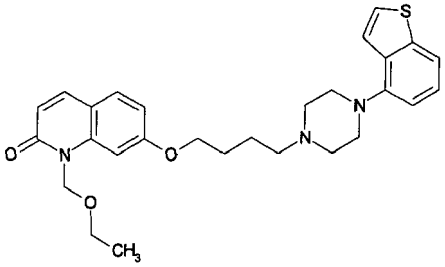
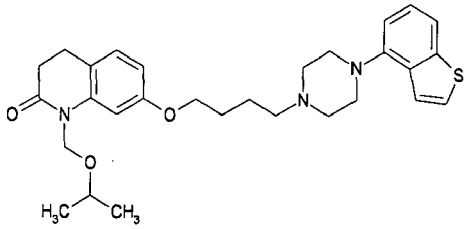
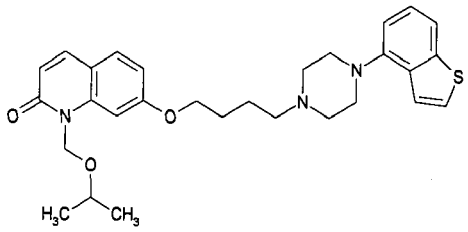
(continued)

Example	Structure Formula	
172		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester pentyl ester
173		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester 3-methylbutyl ester
174		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester 3-methylbutyl ester
175		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester hexyl ester
176		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester nonyl ester
177		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester nonyl ester

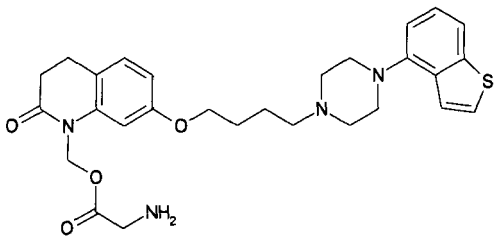
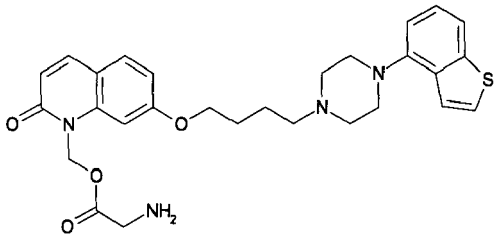
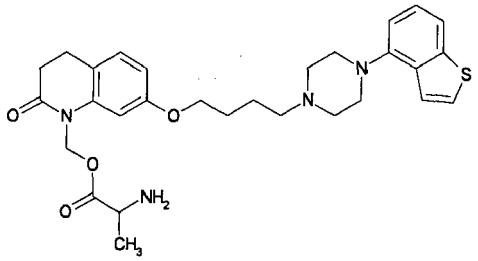
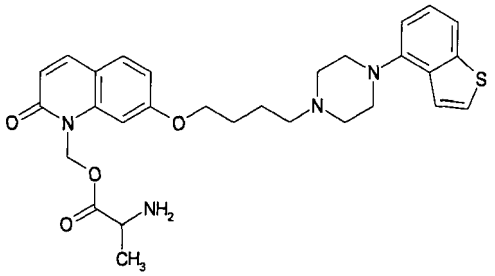
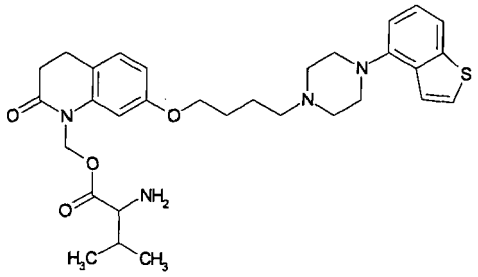
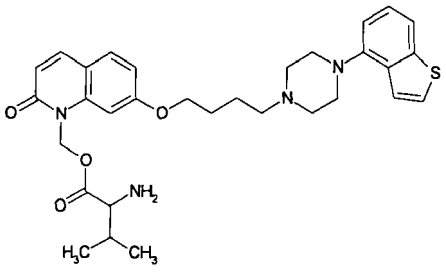
(continued)

Example	Structure Formula	
178		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester tetradecyl ester
179		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester tetradecyl ester
180		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester hexadecyl ester
181		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester benzyl ester
182		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester benzyl ester
183		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-methoxymethyl-3,4-dihydro-1H-quinolin-2-one

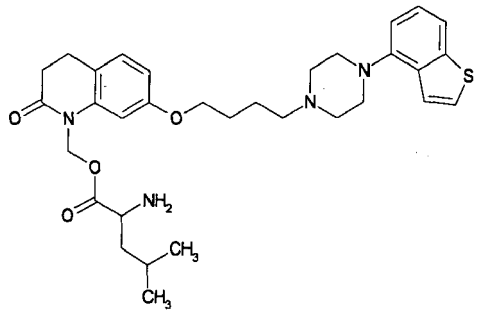
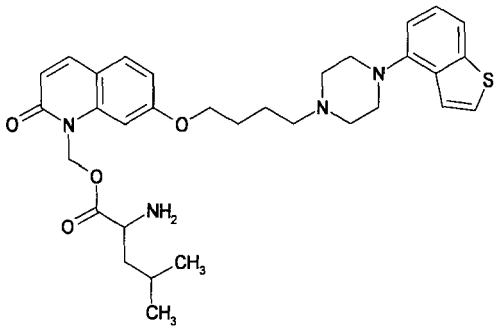
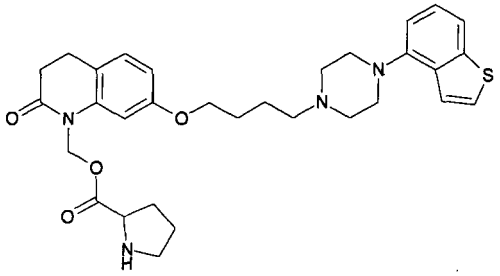
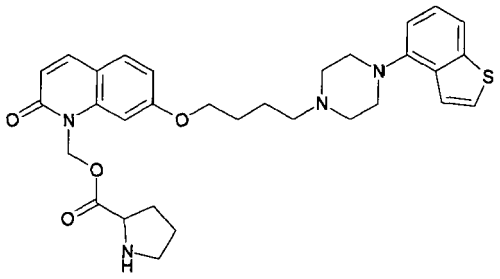
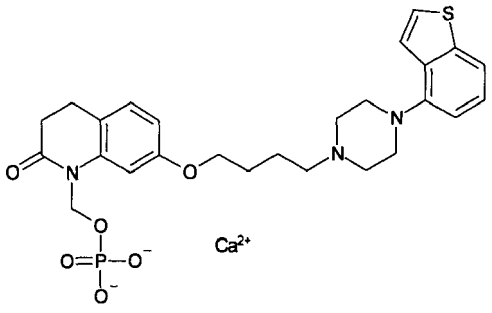
(continued)

Example	Structure Formula	
184		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-methoxymethyl-1H-quinolin-2-one
185		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-methoxymethoxyquinoline
186		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-ethoxymethyl-3,4-dihydro-1H-quinolin-2-one
187		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-ethoxymethyl-1H-quinolin-2-one
188		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-isopropoxymethyl-3,4-dihydro-1 H-quinolin-2-one
189		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-isopropoxymethyl-1H-quinolin-2-one

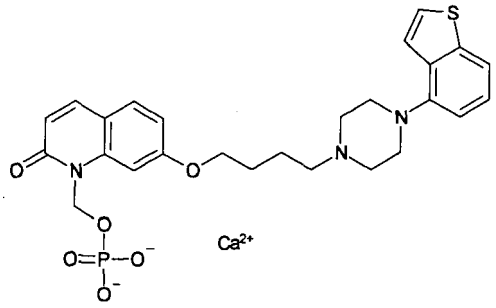
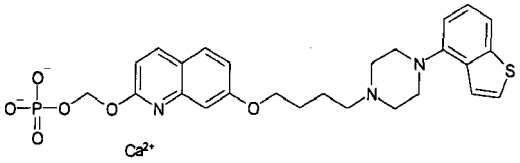
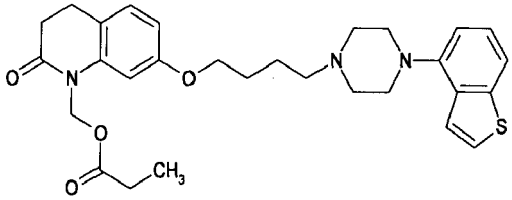
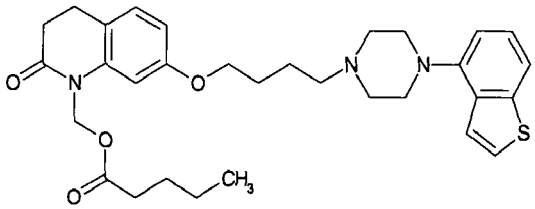
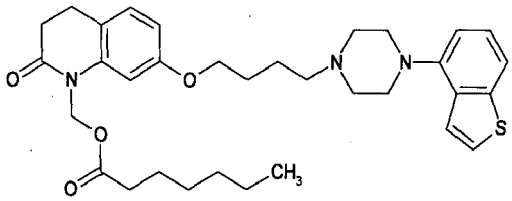
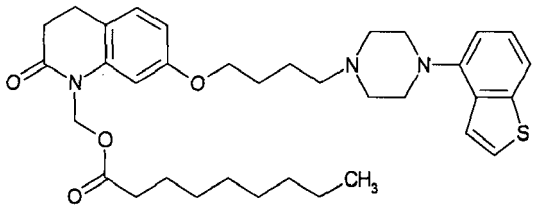
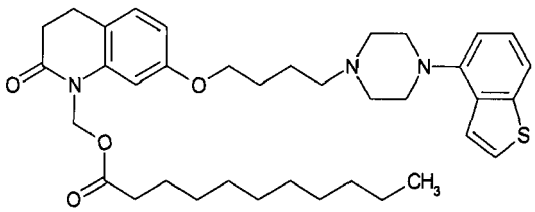
(continued)

Example	Structure Formula	
190		Aminoacetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
191		Aminoacetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
192		2-Aminopropionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
193		2-Aminopropionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
194		2-Amino-3-methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
195		2-Amino-3-methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

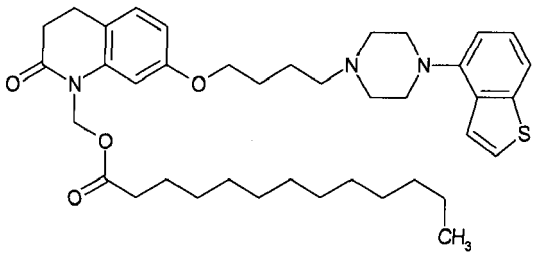
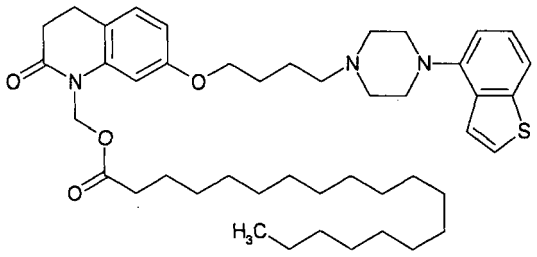
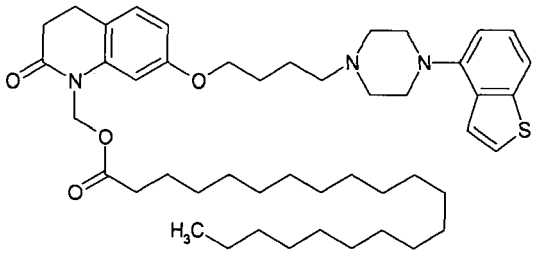
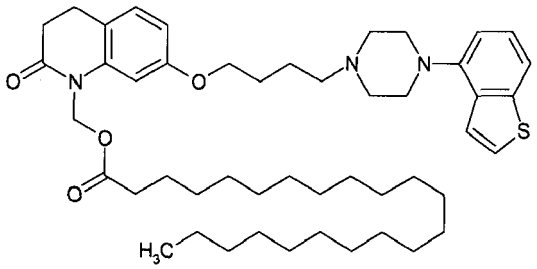
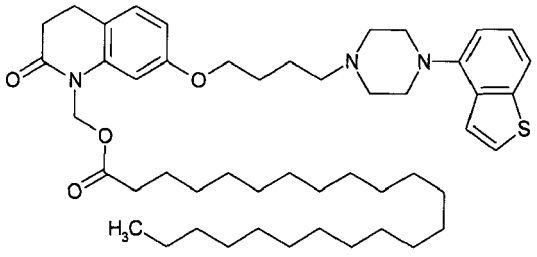
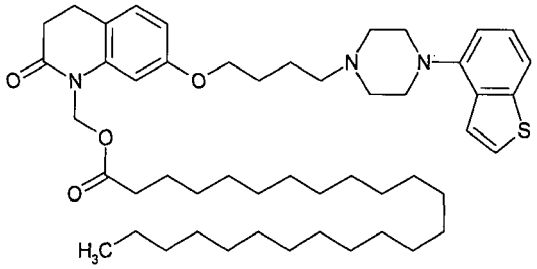
(continued)

Example	Structure Formula	
196		2-Amino-4-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
197		2-Amino-4-methylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
198		Pyrrolidine-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
199		Pyrrolidine-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
200		Calcium {7-[4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}-2-oxo-3,4-dihydro-2H-quinolin-1-yl)methyl phosphate

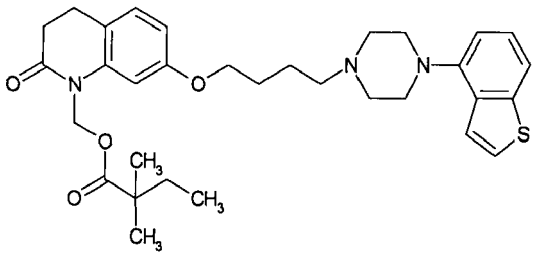
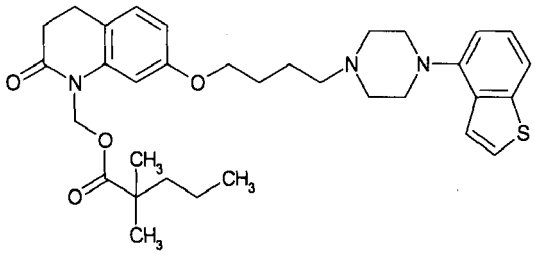
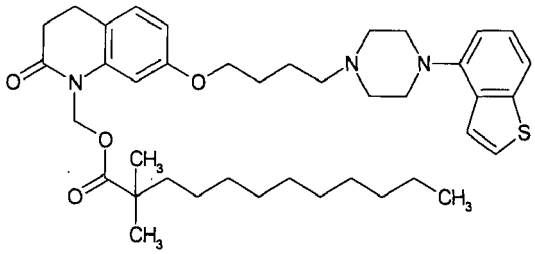
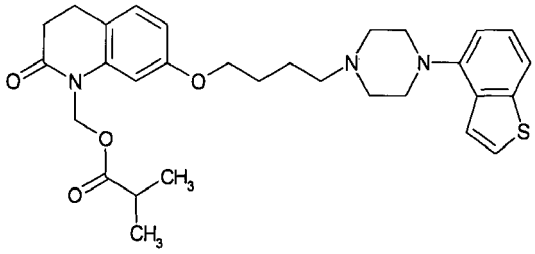
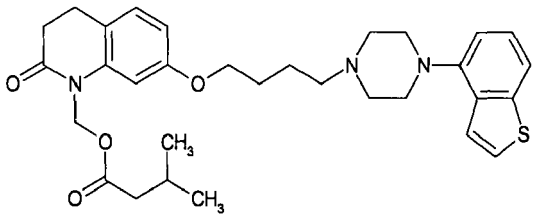
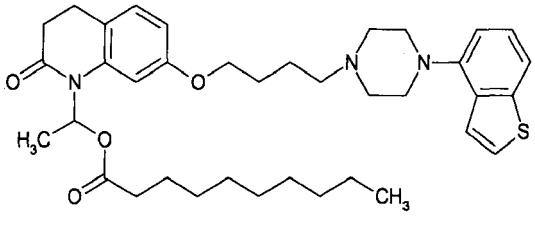
(continued)

Example	Structure Formula	
201		Calcium {7-[4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}-2-oxo-2H-quinolin-1-yl)methyl phosphate
202		Calcium (7-{4-[4-(benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}quinolin-2-yloxy)methyl phosphate
203		Propionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
204		Pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
205		Heptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
206		Nonanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
207		Undecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

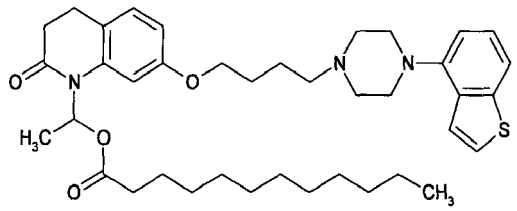
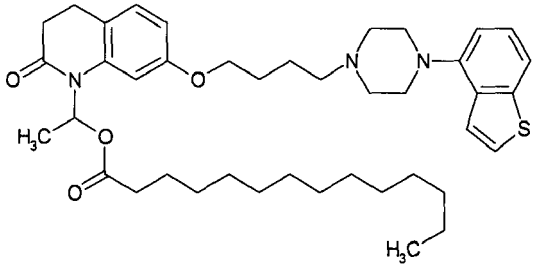
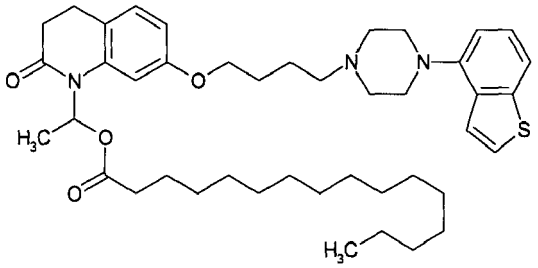
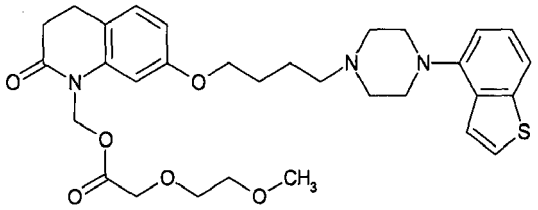
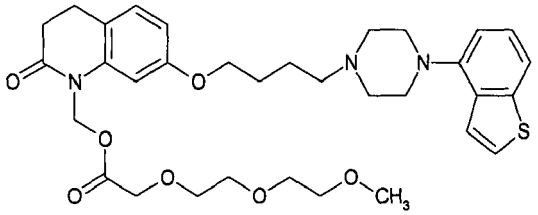
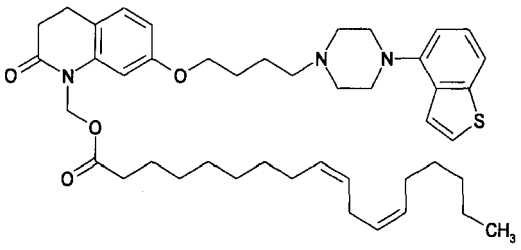
(continued)

Example	Structure Formula	
208		Tridecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
209		Nonadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
210		Henicosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
211		Docosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
212		Tricosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
213		Tetracosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

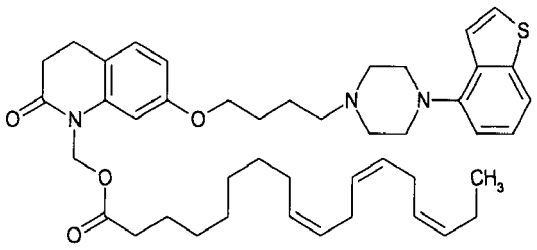
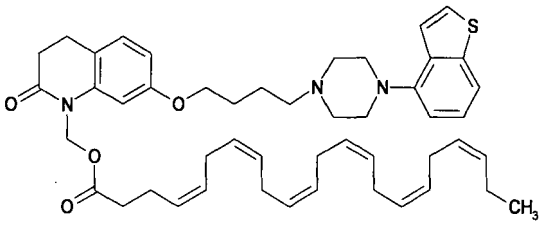
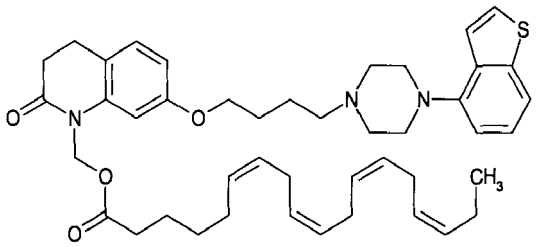
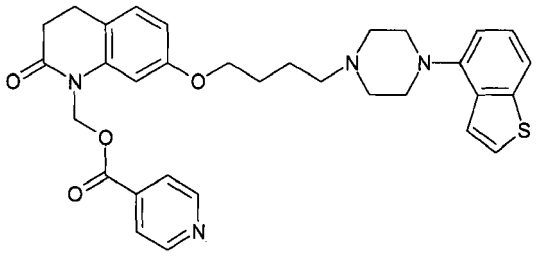
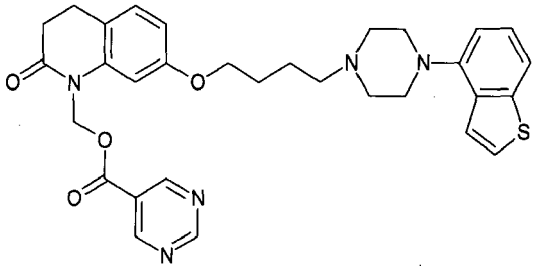
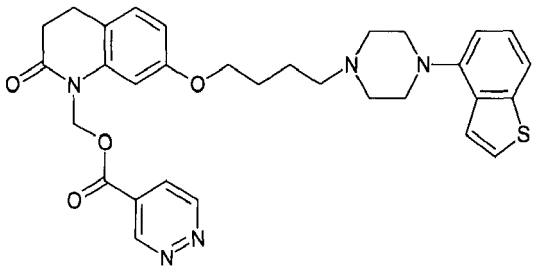
(continued)

Example	Structure Formula	
214		2,2-Dimethylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
215		2,2-Dimethylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
216		2,2-Dimethyldodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
217		Isobutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
218		3-Methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
219		Decanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-yl}ethyl ester

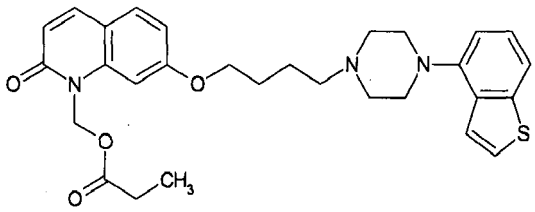
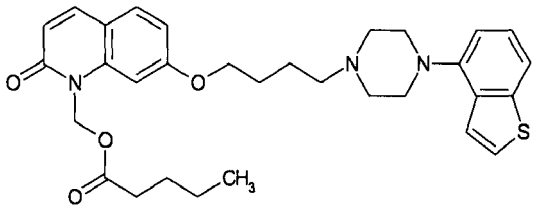
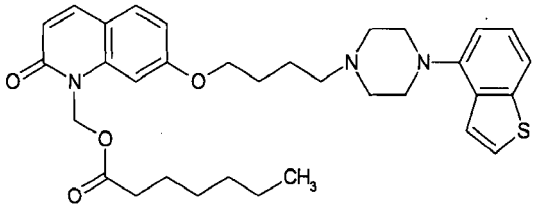
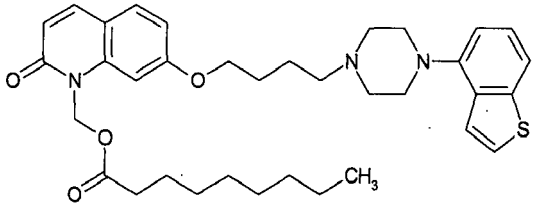
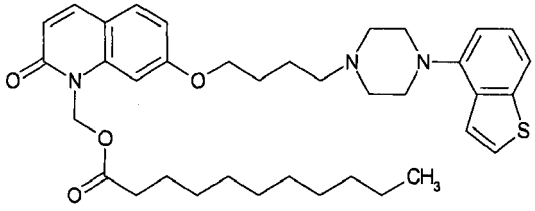
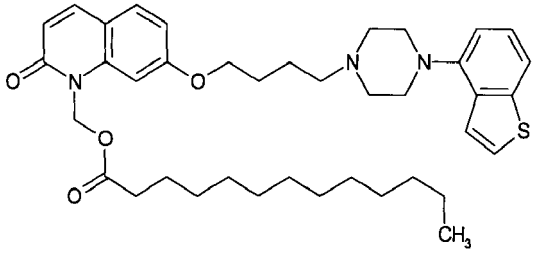
(continued)

Example	Structure Formula	
220		Dodecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-yl}ethyl ester
221		Tetradecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-yl}ethyl ester
222		Hexadecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-yl}ethyl ester
223		(2-Methoxyethoxy)acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
224		[2-(2-Methoxyethoxy)ethoxy]acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
225		(9Z,12Z)-Octadeca-9,12-dienoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

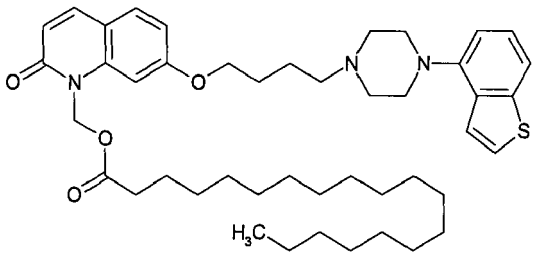
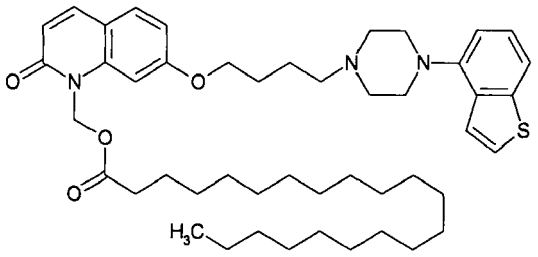
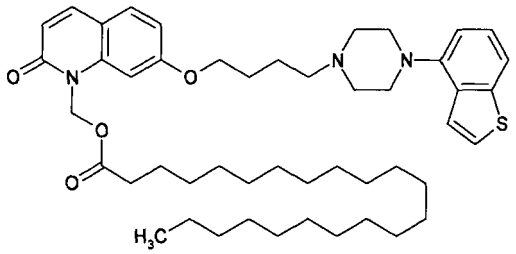
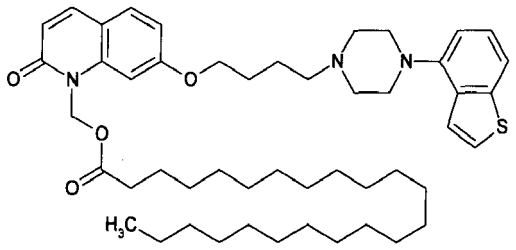
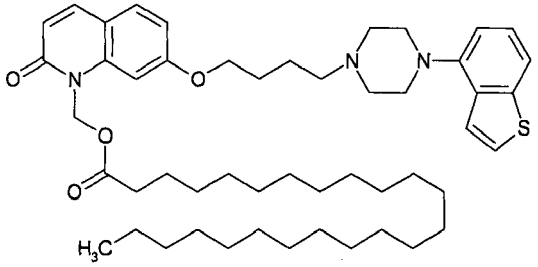
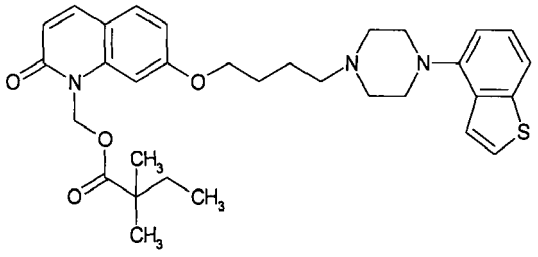
(continued)

Example	Structure Formula	
226		(9Z,12Z,15Z)-Octadeca-9,12,15-trienoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
227		(4Z, 7Z, 10Z, 13Z, 16Z, 19Z)-Docosa-4,7,10,13,16,19-hexaenoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
228		(6Z,9Z,12Z,15Z)-Octadeca-6,9,12,15-tetraenoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
229		Isonicotinic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
230		Pyrimidine-5-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
231		Pyridazine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

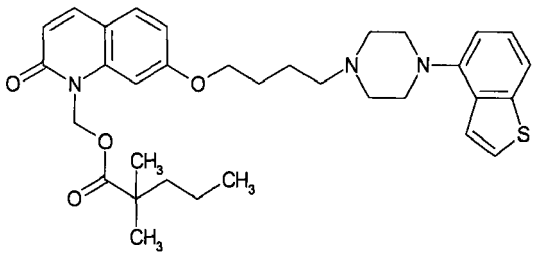
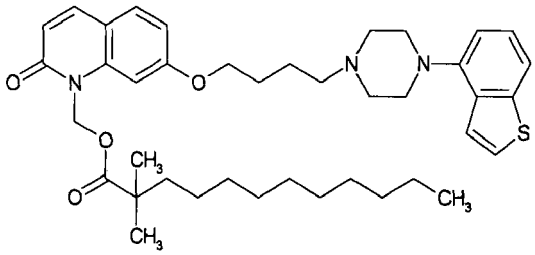
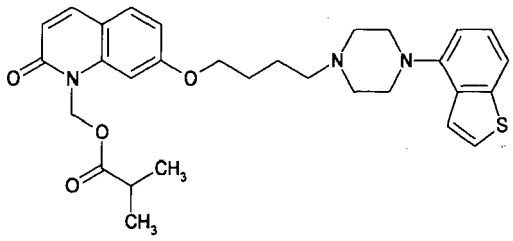
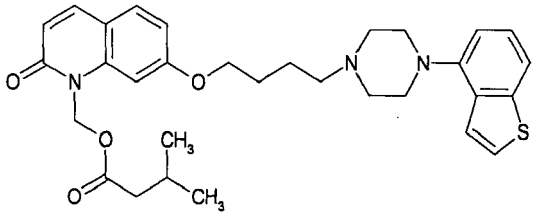
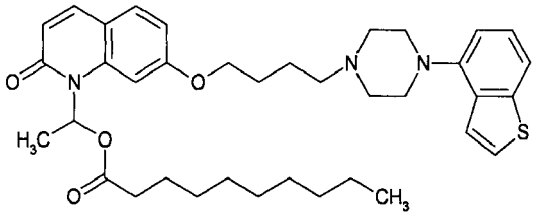
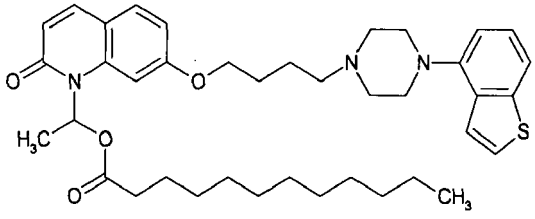
(continued)

Example	Structure Formula	
232		Propionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
233		Pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
234		Heptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
235		Nonanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
236		Undecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
237		Tridecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

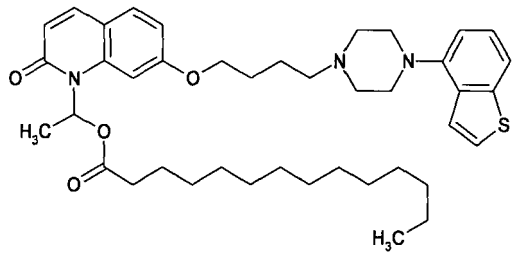
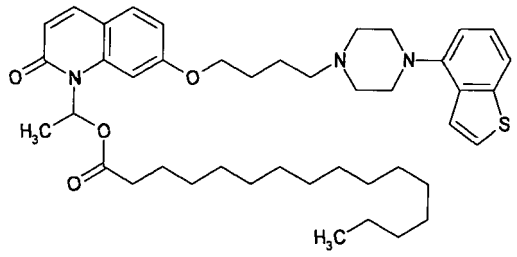
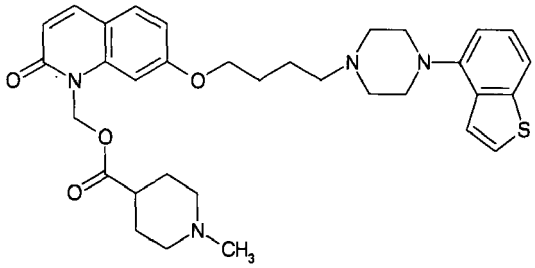
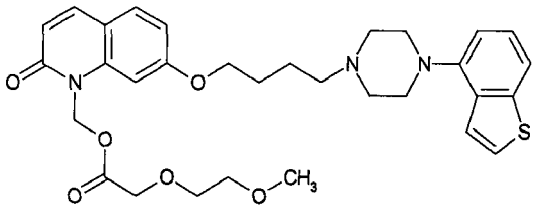
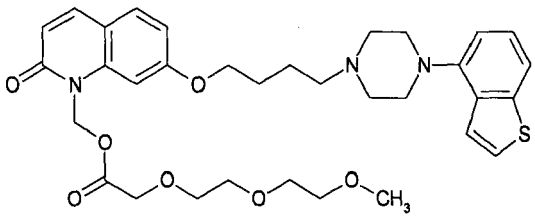
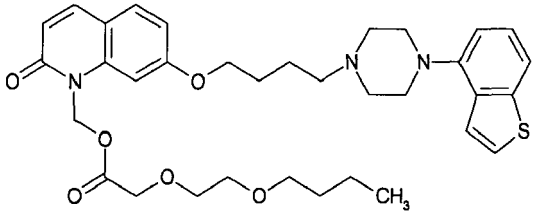
(continued)

Example	Structure Formula	
238		Nonadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
239		Henicosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
240		Docosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
241		Tricosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
242		Tetracosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
243		2,2-Dimethylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

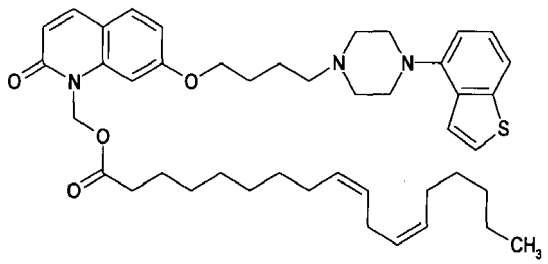
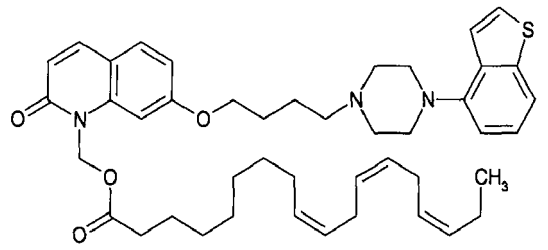
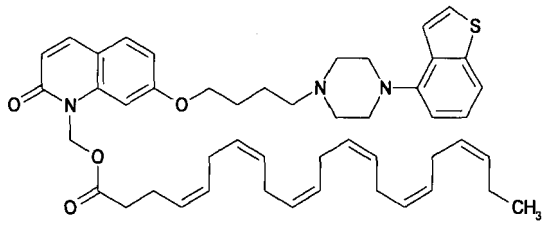
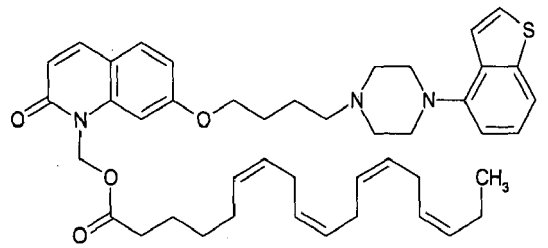
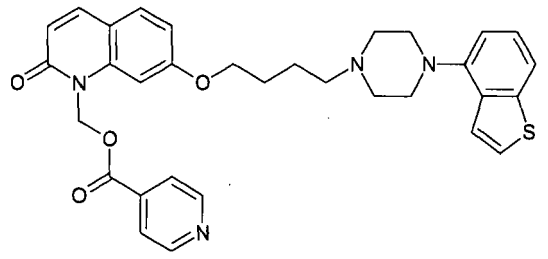
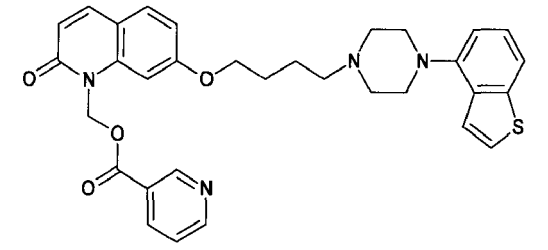
(continued)

Example	Structure Formula	
244		2,2-Dimethylpentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
245		2,2-Dimethyldodecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
246		Isobutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
247		3-Methylbutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
248		Decanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-yl}ethyl ester
249		Dodecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-yl}ethyl ester

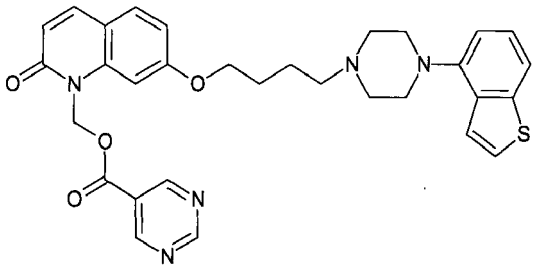
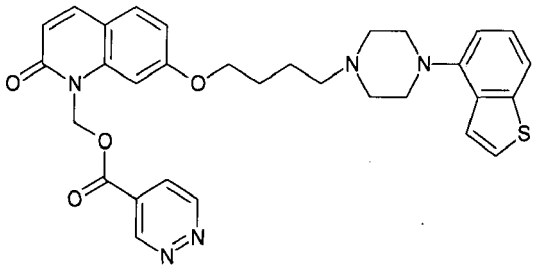
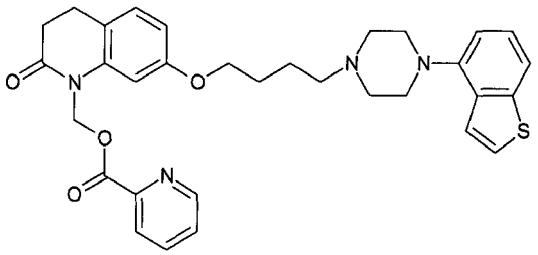
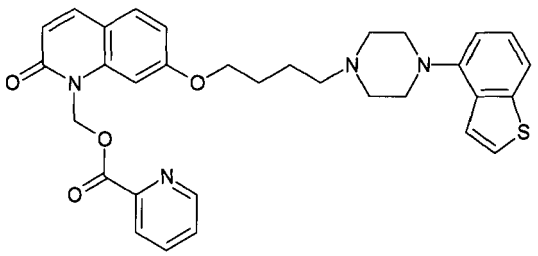
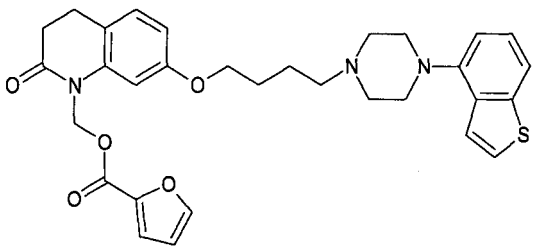
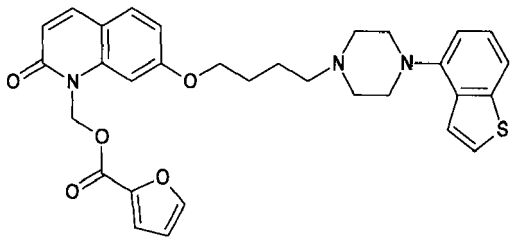
(continued)

Example	Structure Formula	
250		Tetradecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-yl}ethyl ester
251		Hexadecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-yl}ethyl ester
252		1-Methylpiperidine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
253		(2-Methoxyethoxy)acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
254		[2-(2-Methoxyethoxy)ethoxy]acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
255		(2-Butoxyethoxy)acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

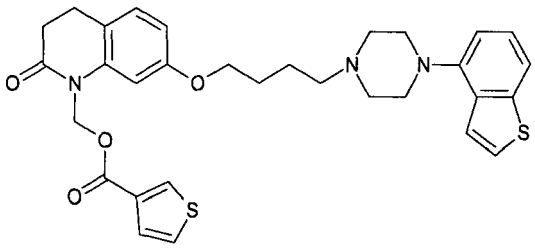
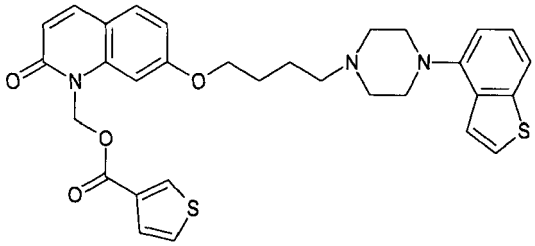
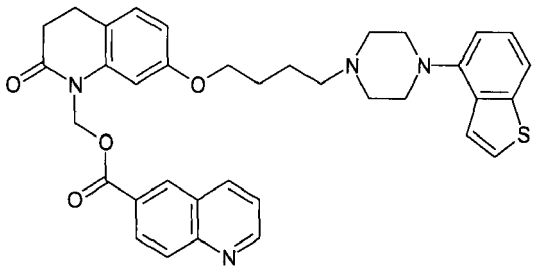
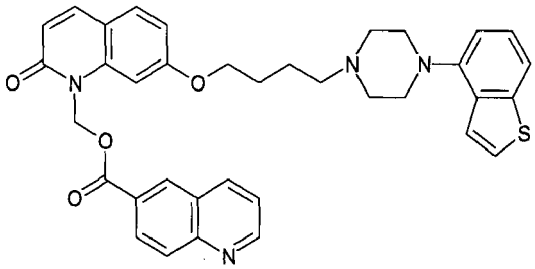
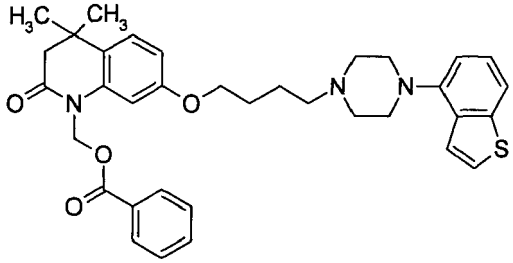
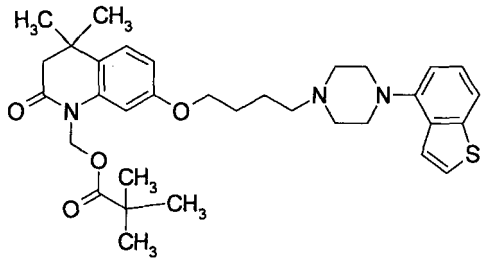
(continued)

Example	Structure Formula	
256		(9Z,12Z)-Octadeca-9,12-dienoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
257		(9Z,12Z,15Z)-Octadeca-9,12,15-trienoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
258		(4Z,7Z,10Z,13Z,16Z,19Z)-Docosa-4,7,10,13,16,19-hexaenoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
259		(6Z,9Z,12Z,15Z)-Octadeca-6,9,12,15-tetraenoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
260		Isonicotinic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
261		Nicotinic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

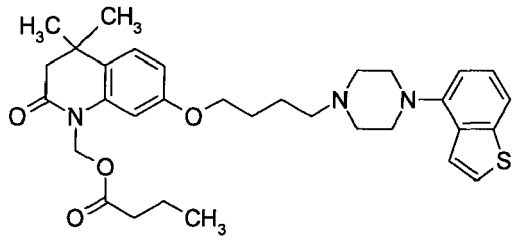
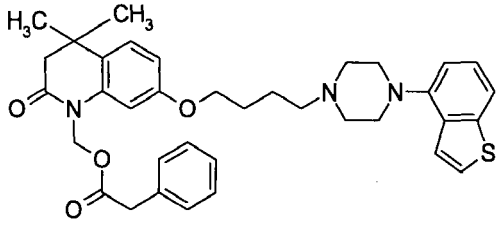
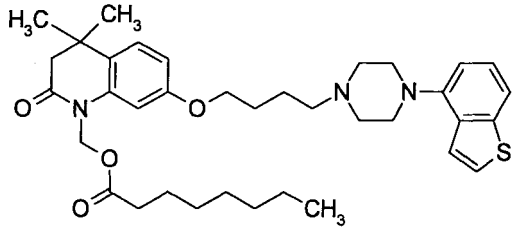
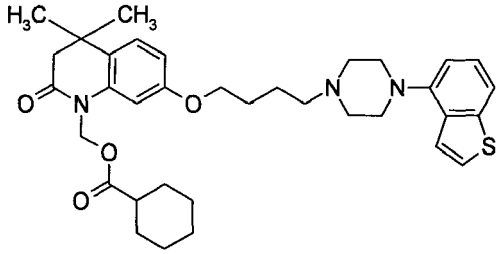
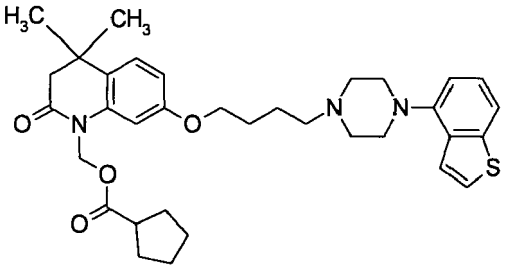
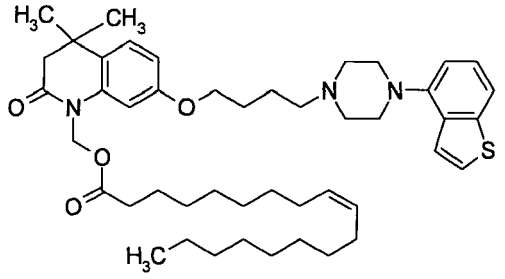
(continued)

Example	Structure Formula	
262		Pyrimidine-5-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
263		Pyridazine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
264		Pyridine-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
265		Pyridine-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
266		Furan-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
267		Furan-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester

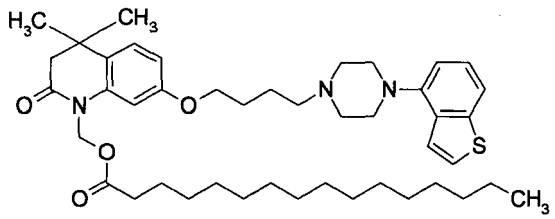
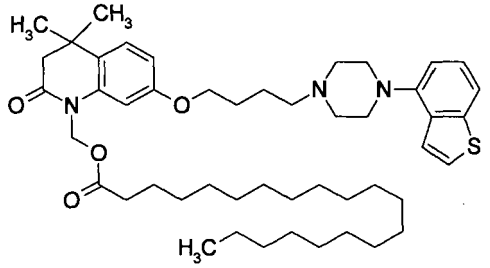
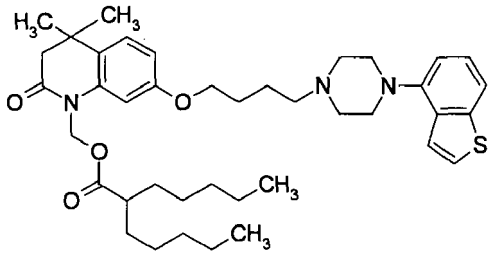
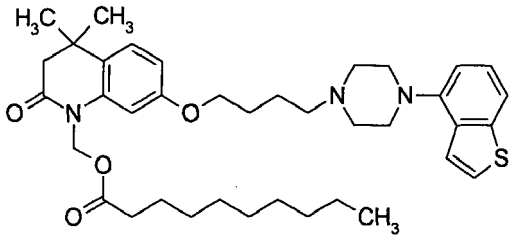
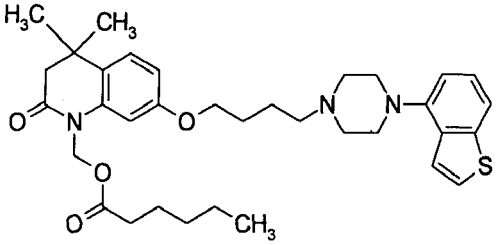
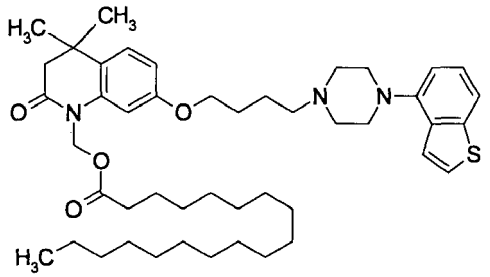
(continued)

Example	Structure Formula	
268		Thiophene-3-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
269		Thiophene-3-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
270		Quinoline-6-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
271		Quinoline-6-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester
272		Benzoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
273		2,2-Dimethylpropionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

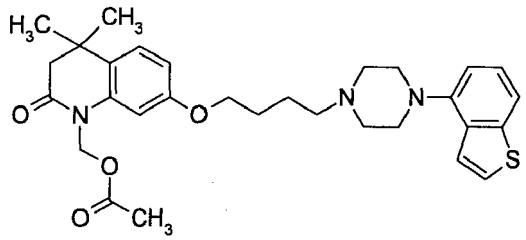
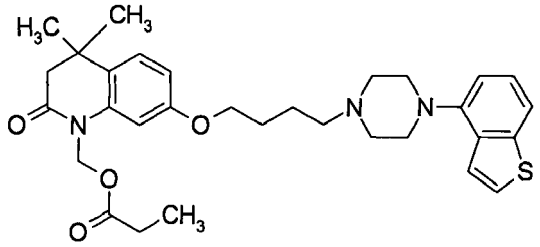
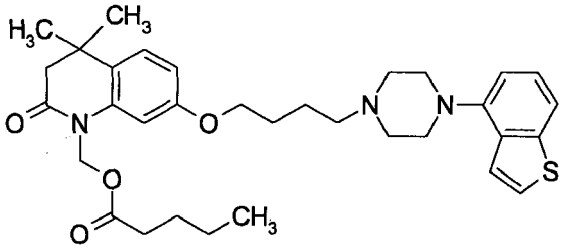
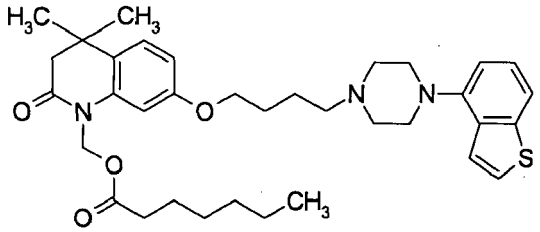
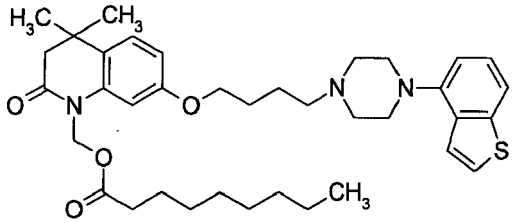
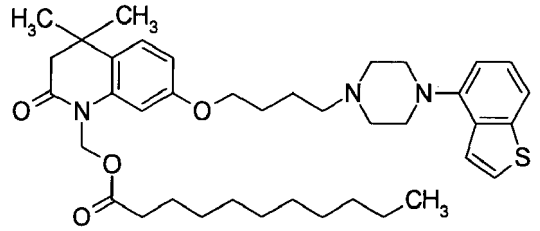
(continued)

Example	Structure Formula	
274		Butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
275		Phenylacetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
276		Octanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
277		Cyclohexanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
278		Cyclopentanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
279		(Z)-Octadec-9-enoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

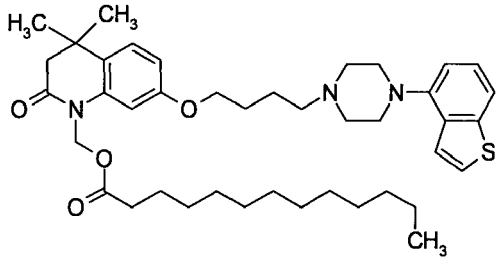
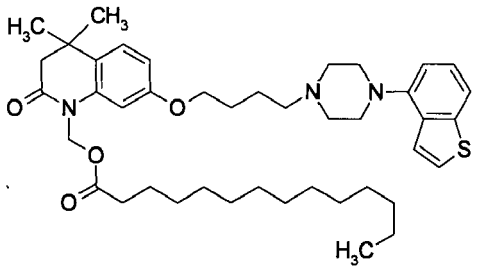
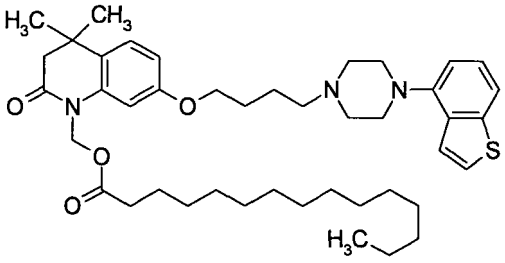
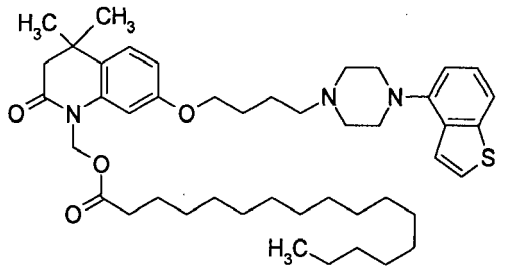
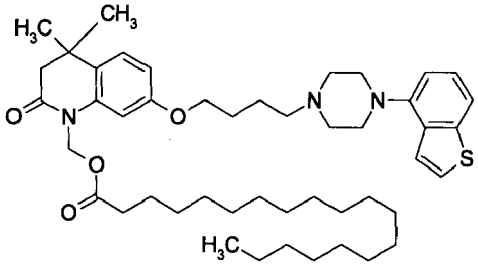
(continued)

Example	Structure Formula	
280		Hexadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
281		Icosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
282		2-Pentyl-heptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
283		Decanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
284		Hexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
285		Octadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

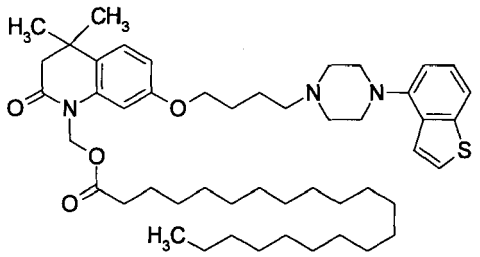
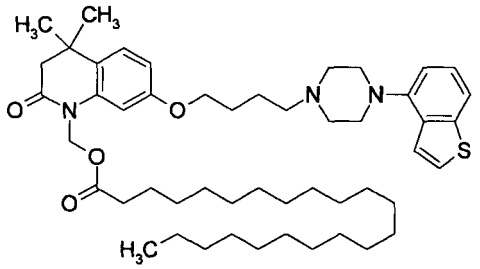
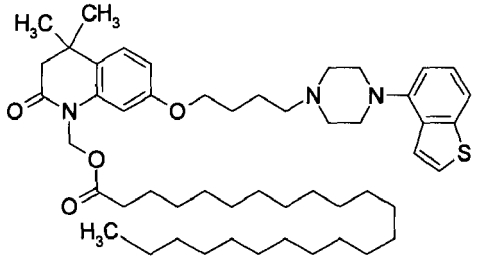
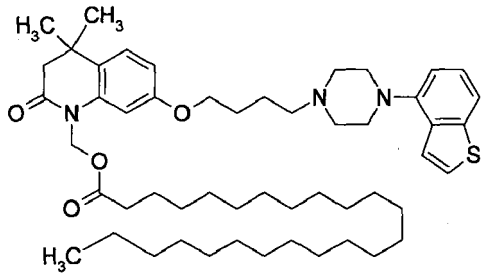
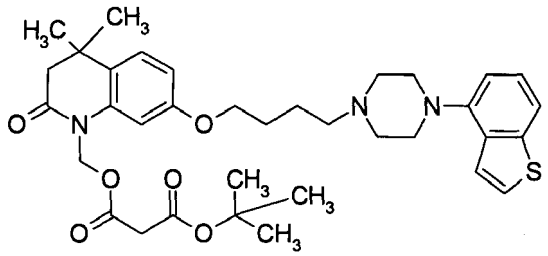
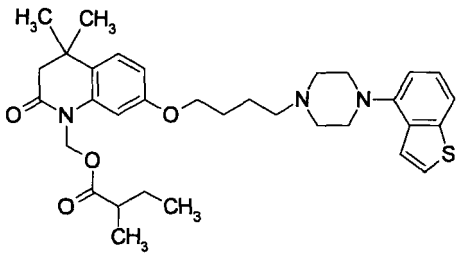
(continued)

Example	Structure Formula	
286		Acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
287		Propionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
288		Pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
289		Heptanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
290		Nonanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
291		Undecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

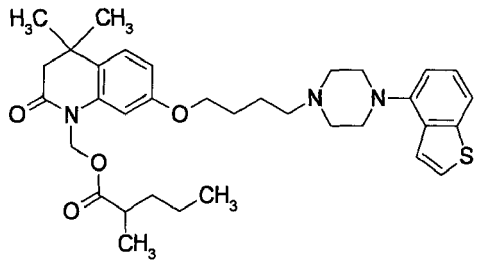
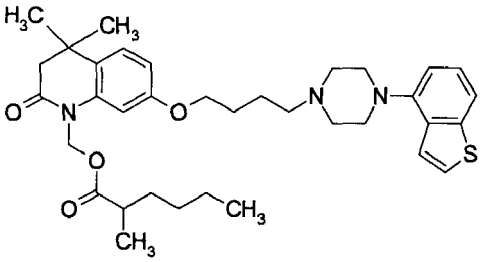
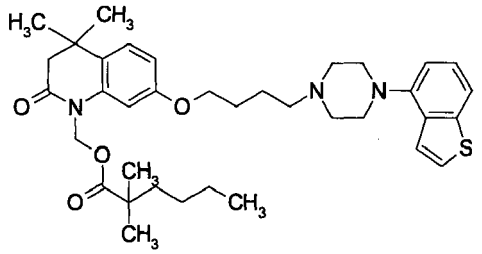
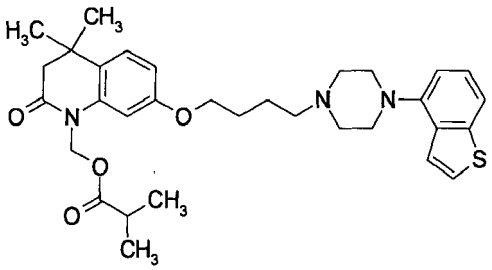
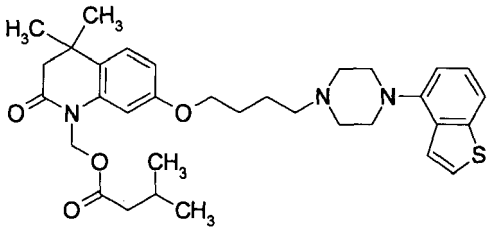
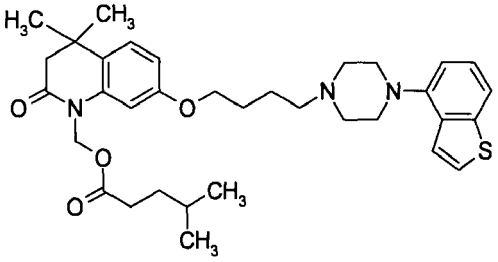
(continued)

Example	Structure Formula	
292		Tridecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
293		Tetradecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
294		Pentadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
295		Heptadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
296		Nonadecanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

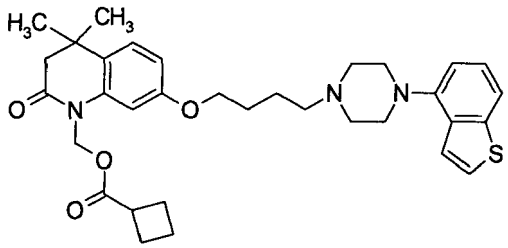
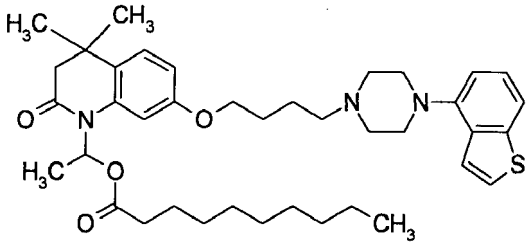
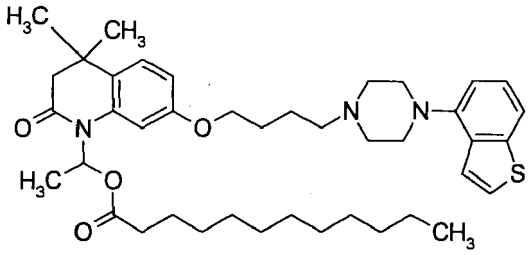
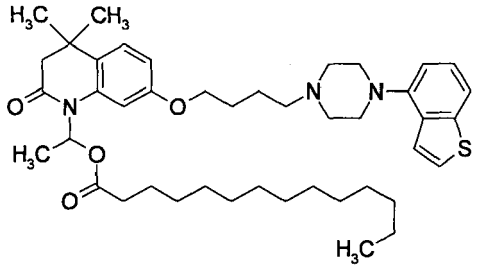
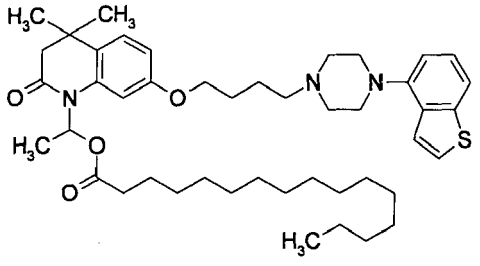
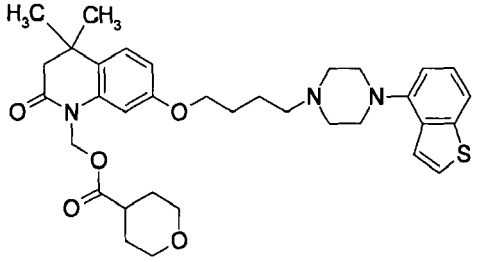
(continued)

Example	Structure Formula	
297		Henicosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
298		Docosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
299		Tricosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
300		Tetracosanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
301		Malonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester tert-butyl ester
302		2-Methyl-butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

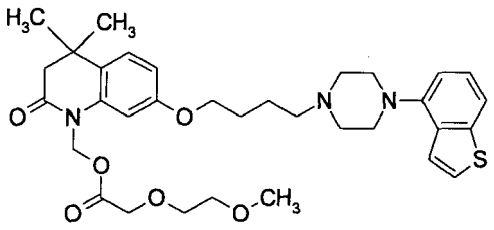
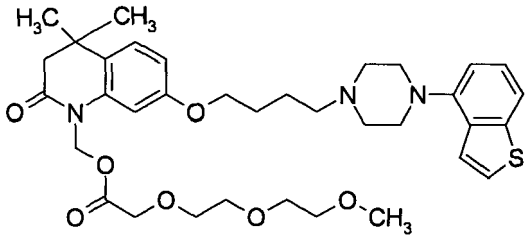
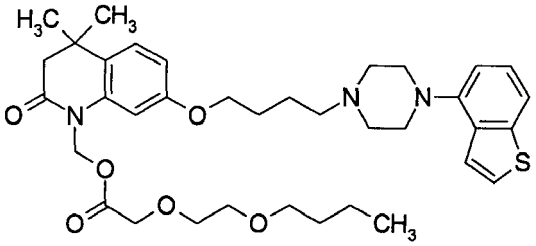
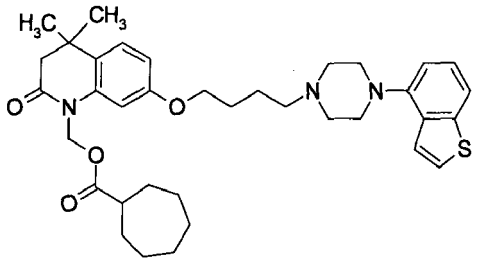
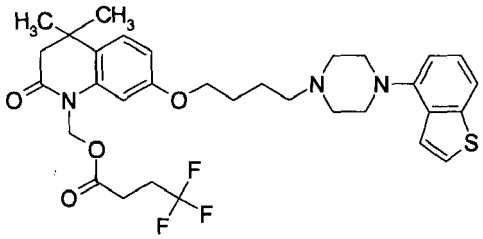
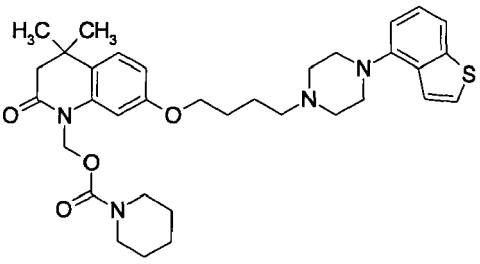
(continued)

Example	Structure Formula	
303		2-Methyl-pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
304		2-Methyl-hexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
305		2,2-Dimethyl-hexanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
306		Isobutyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
307		3-Methyl-butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
308		4-Methyl-pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

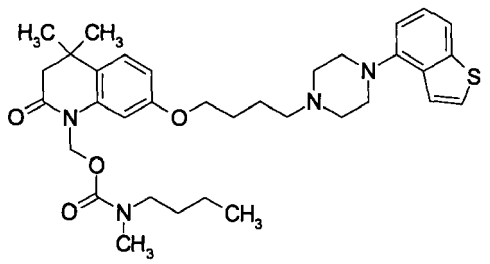
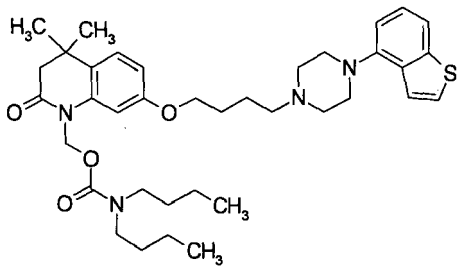
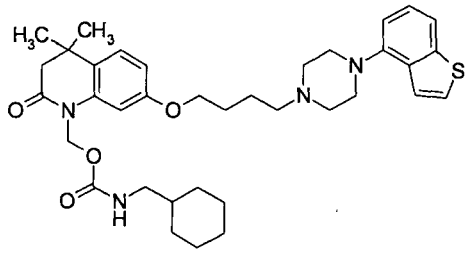
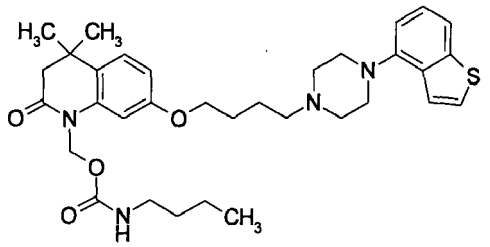
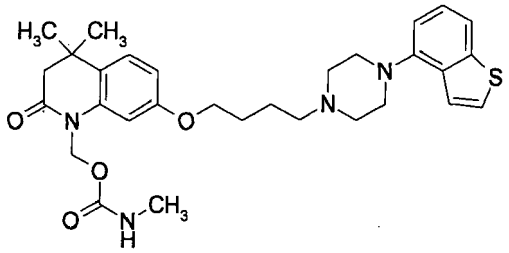
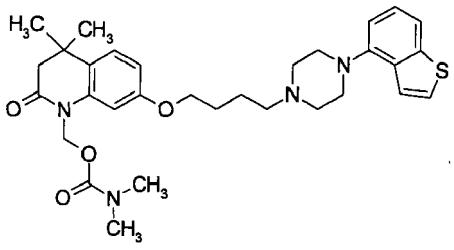
(continued)

Example	Structure Formula	
309		Cyclobutanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
310		Decanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl}-ethyl ester
311		Dodecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl}-ethyl ester
312		Tetradecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl}-ethyl ester
313		Hexadecanoic acid 1-{7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl}-ethyl ester
314		Tetrahydro-pyran-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

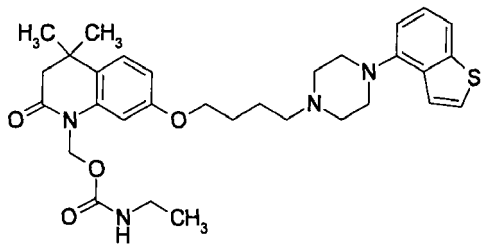
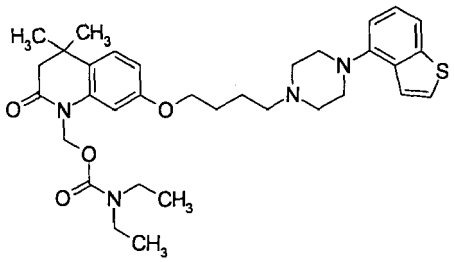
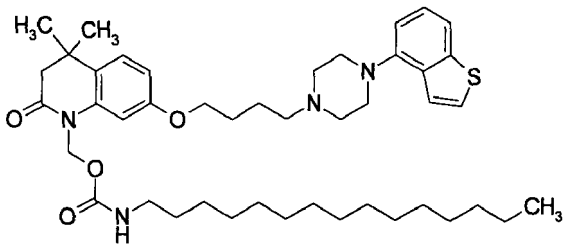
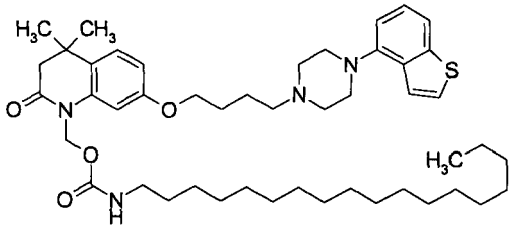
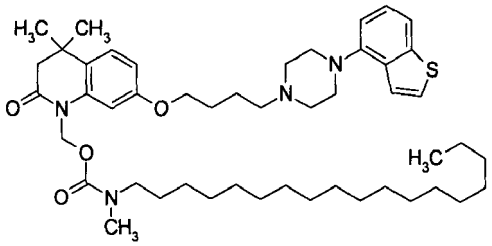
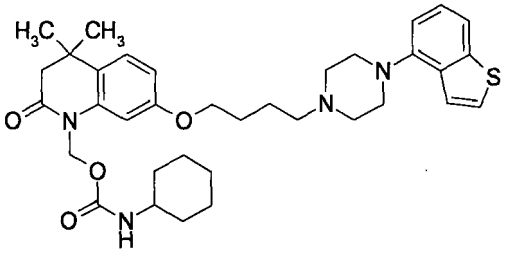
(continued)

Example	Structure Formula	
315		(2-Methoxy-ethoxy)-acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
316		[2-(2-Methoxy-ethoxy)-ethoxy]-acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
317		(2-Butoxy-ethoxy)-acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
318		Cycloheptanecarboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
319		4,4,4-Trifluoro-butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
320		Piperidine-1-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

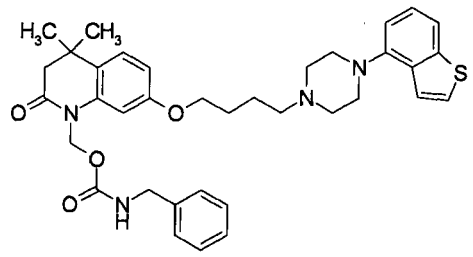
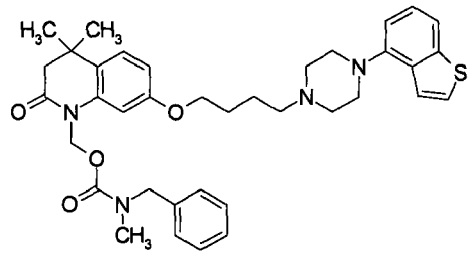
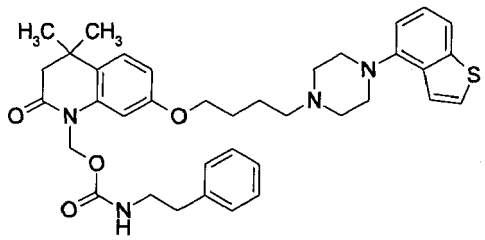
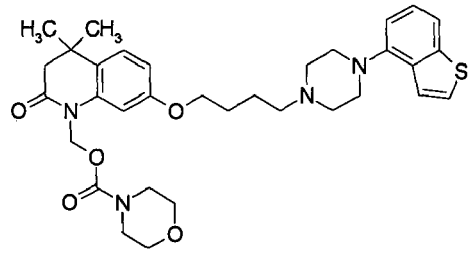
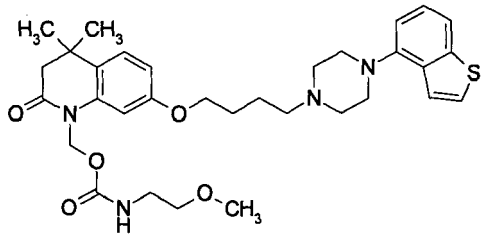
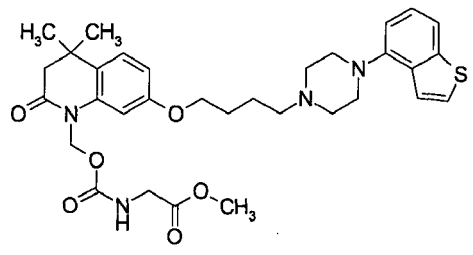
(continued)

Example	Structure Formula	
321		N-Butyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
322		N,N-Dibutylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
323		N-Cyclohexylmethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
324		N-Butylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
325		N-Methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
326		N,N-Dimethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

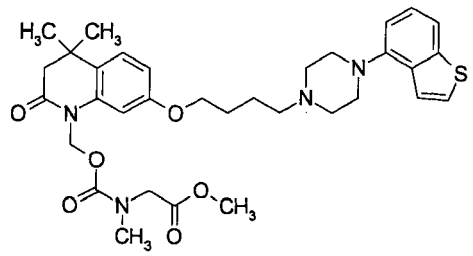
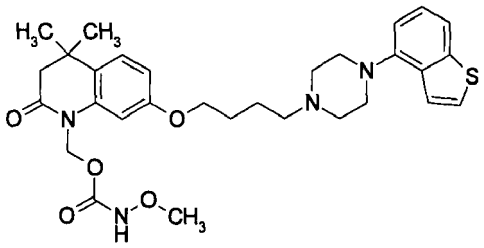
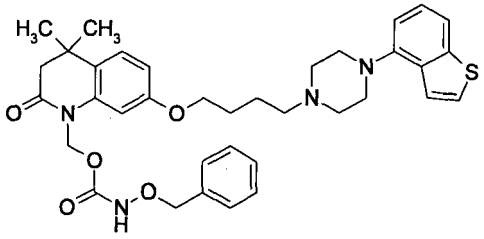
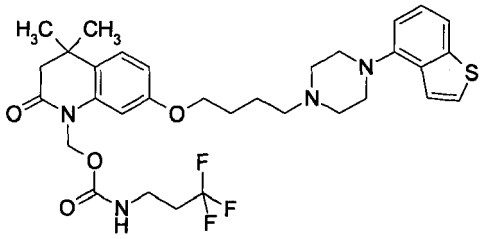
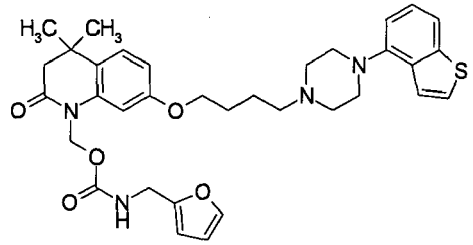
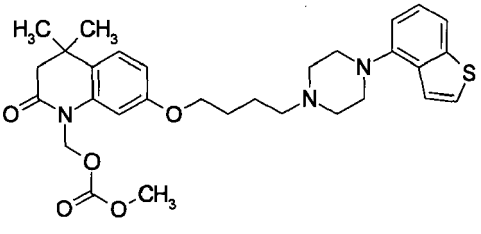
(continued)

Example	Structure Formula	
327		N-Ethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
328		N,N-Diethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
329		N-Pentadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
330		N-Octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
331		N-Methyl-N-octadecylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
332		N-Cyclohexylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

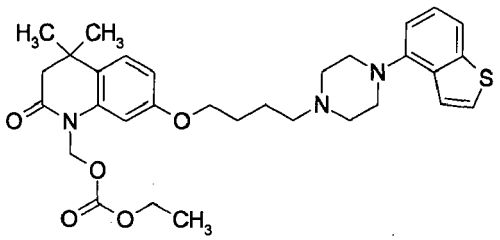
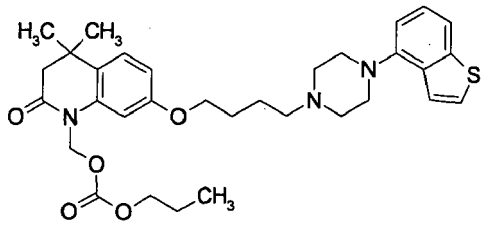
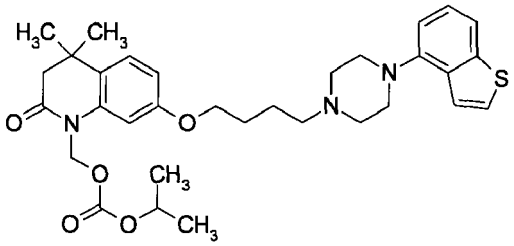
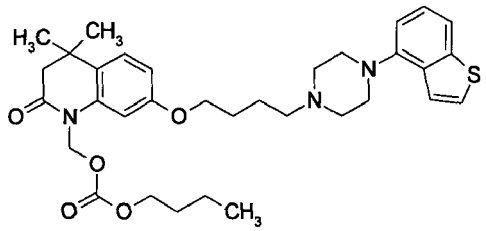
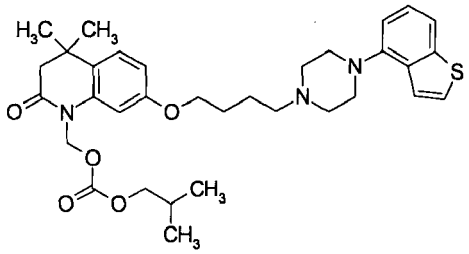
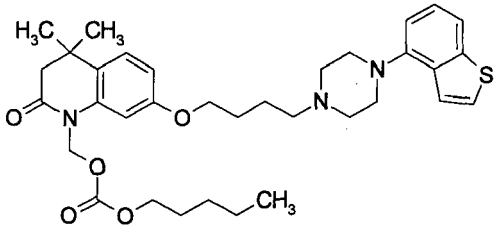
(continued)

Example	Structure Formula	
333		N-Benzylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
334		N-Benzyl-N-methylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
335		N-Phenethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
336		Morpholine-4-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
337		N-(2-Methoxyethyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
338		{7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethoxycarbonylamino}acetic acid methyl ester

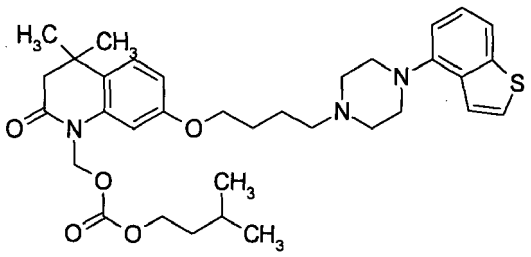
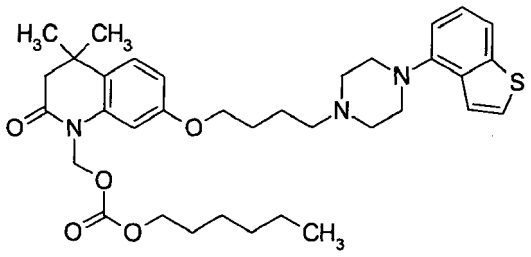
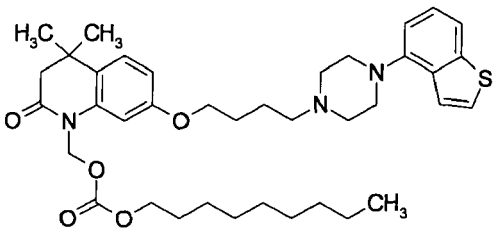
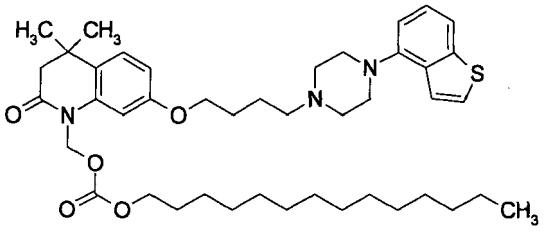
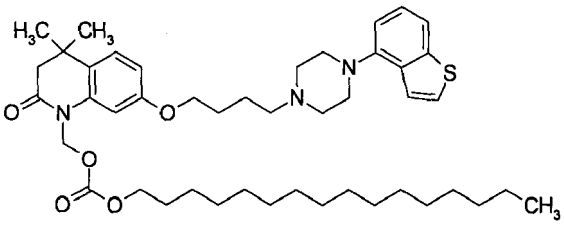
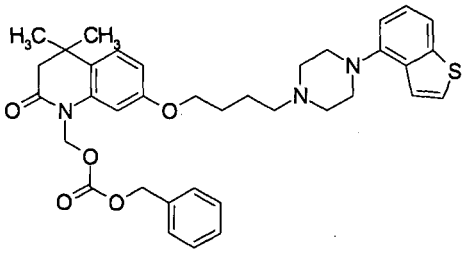
(continued)

Example	Structure Formula	
339		({7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethoxycarbonyl}-methyl-amino)acetic acid methyl ester
340		(7-{4-[4-(Benzo[b]thiophen-4-yl)piperazin-1-yl]butoxy}-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl)methyl N-methoxycarbamate
341		7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl N-benzyloxycarbamate
342		N-(3,3,3-Trifluoro-propyl)carbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
343		N-Furan-2-ylmethylcarbamic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
344		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester methyl ester

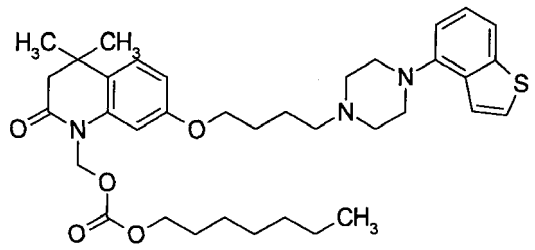
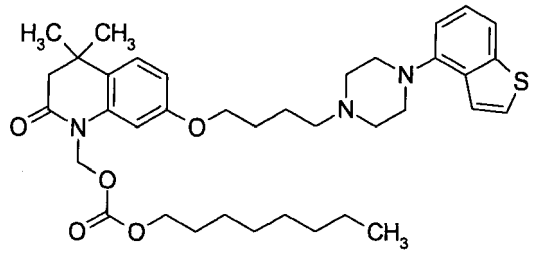
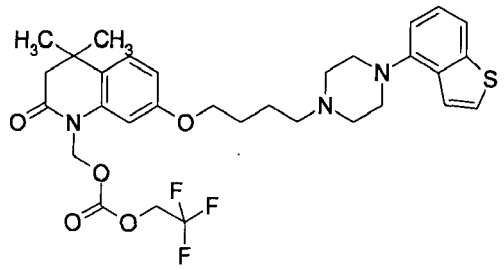
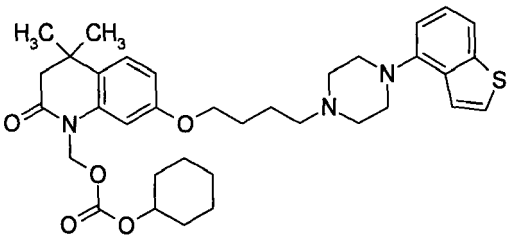
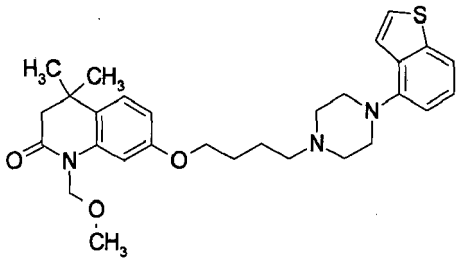
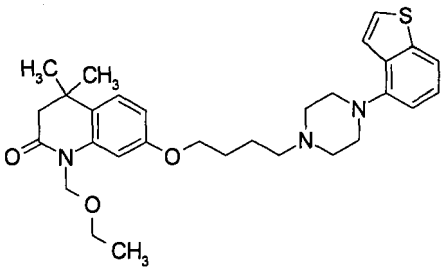
(continued)

Example	Structure Formula	
345		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester ethyl ester
346		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester propyl ester
347		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester isopropyl ester
348		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester butyl ester
349		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihyd ro-2H-quinolin-1-ylmethyl ester isobutyl ester
350		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester pentyl ester

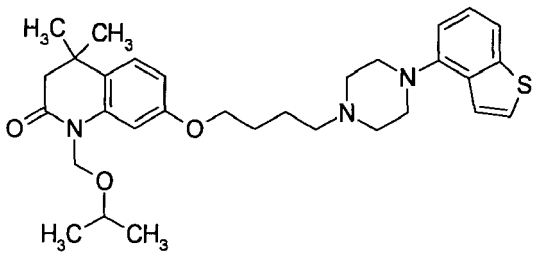
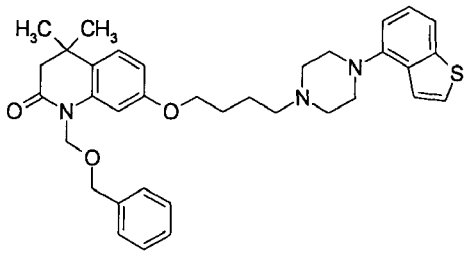
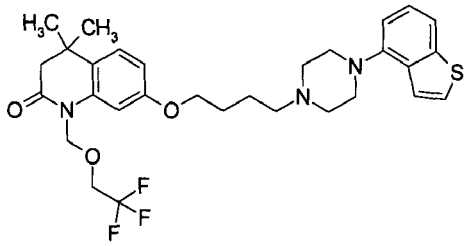
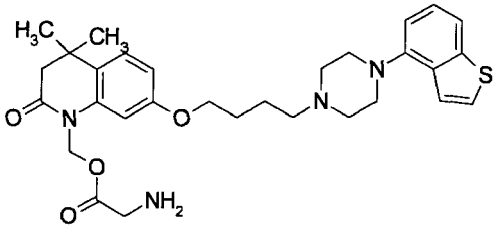
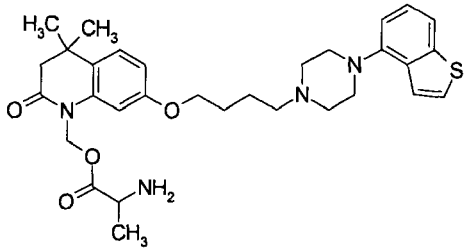
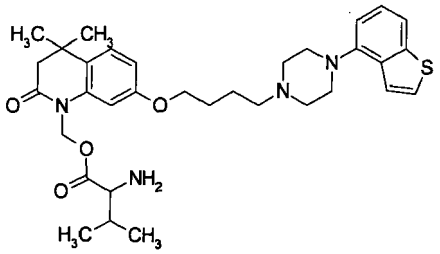
(continued)

Example	Structure Formula	
351		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester 3-methyl-butyl ester
352		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester hexyl ester
353		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester nonyl ester
354		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester tetradecyl ester
355		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester hexadecyl ester
356		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester benzyl ester

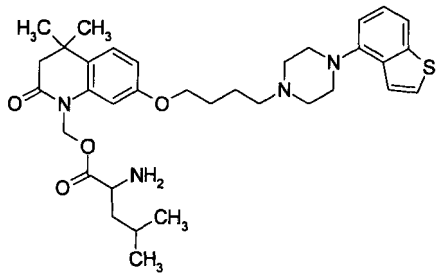
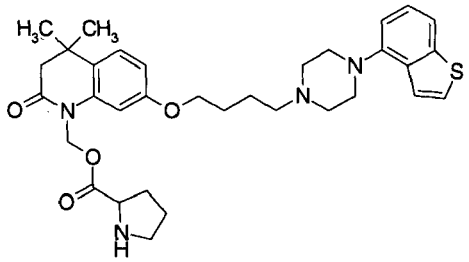
(continued)

Example	Structure Formula	
357		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester heptyl ester
358		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester octyl ester
359		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester 2,2,2-trifluoro-ethyl ester
360		Carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester cyclohexyl ester
361		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-methoxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one
362		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-ethoxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one

(continued)

Example	Structure Formula	
363		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-isopropoxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one
364		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-benzyloxymethyl-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one
365		7-[4-(4-Benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-1-(2,2,2-trifluoro-ethoxymethyl)-3,4-dihydro-1H-quinolin-2-one
366		Amino-acetic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
367		2-Amino-propionic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
368		2-Amino-3-methyl-butyric acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

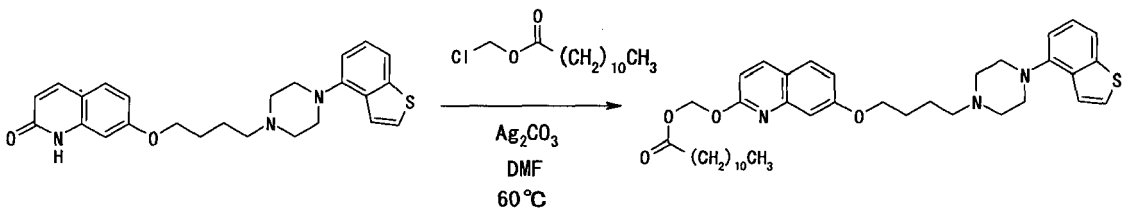
(continued)

Example	Structure Formula	
369		2-Amino-4-methyl-pentanoic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester
370		Pyrrolidine-2-carboxylic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-ylmethyl ester

Example 371

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl dodecanoate

[0490]



[0491] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (800 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dimethylformamide (30 ml) was added silver carbonate (I) (0.76 g), chloromethyldodecanoate[61413-67-0] (1.15 g) was added, and the mixture was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl dodecanoate (22 mg).

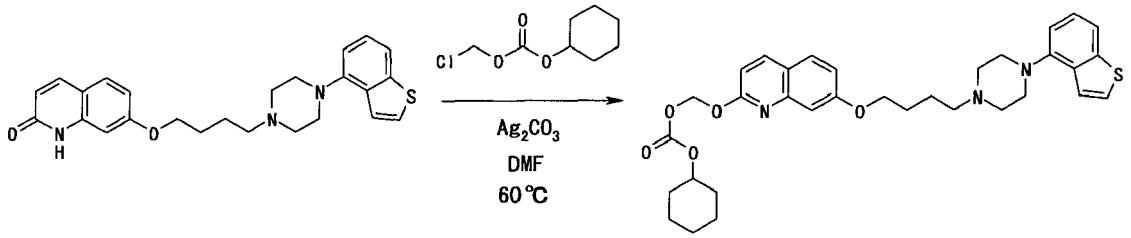
oil: colorless

^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=7.1 Hz), 1.16-2.10 (18H, m), 2.36 (2H, t, J=7.5 Hz), 2.58 (2H, t, J=7.5 Hz), 2.76 (4H, br), 3.21 (4H, br), 4.15 (2H, t, J=6.3 Hz), 6.25 (2H, s), 6.80 (1H, d, J=8.7 Hz), 6.90 (1H, d, J=7.4 Hz), 7.06 (1H, dd, J=2.5, 8.8 Hz), 7.22 (1H, d, J=2.3 Hz), Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=8.8 Hz), 7.96 (1H, d, J=8.7 Hz)

Example 372

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl cyclohexyl carbonate

[0492]

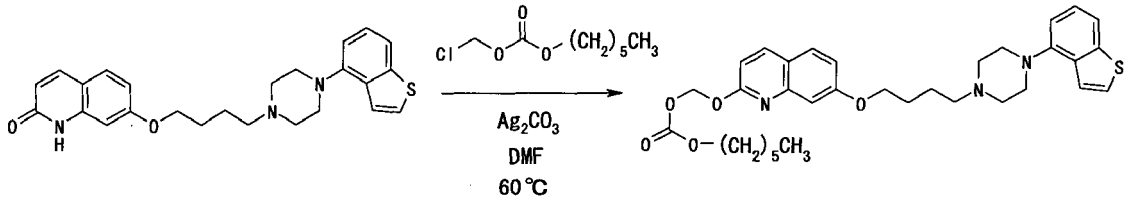


[0493] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one(700 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dimethylformamide (20 ml) was added silver carbonate (I) (0.53 g), chloromethyl cyclohexyl carbonate[40510-86-9] (0.68 g) was added, and the mixture was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl cyclohexyl carbonate (60 mg).
amorphous: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 1.10-2.00 (14H, m), 2.56 (2H, t, J=7.5 Hz), 2.75 (4H, br), 3.21 (4H, br), 4.14 (2H, t, J=6.3 Hz), 4.64-4.74 (1H, m), 6.27 (2H, s), 6.82 (1H, d, J=8.7 Hz), 6.90 (1H, d, J=7.2 Hz), 7.06 (1H, dd, J=2.5, 8.8 Hz), 7.20-7.30 (2H, m), 7.35-7.45 (2H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=8.9 Hz), 7.96 (1H, d, J=8.7 Hz)

Example 373

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethylhexyl carbonate

[0494]

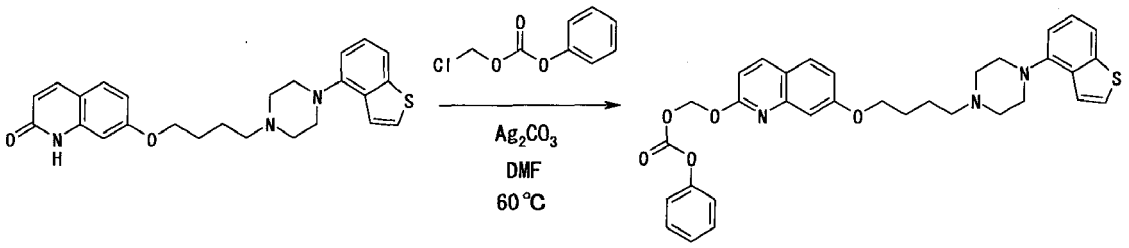


[0495] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (730 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dimethylformamide (20 ml) was added silver carbonate (I) (0.56 g), chloromethyl hexyl carbonate[663597-51-1] (0.72 g) was added, and the mixture was stirred at 60°C for 10 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl hexyl carbonate (95 mg).
oil: yellow
^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=6.9 Hz), 1.20-1.40 (6H, m), 1.60-1.70 (2H, m), 1.74-1.84 (2H, m), 1.88-1.98 (2H, m), 2.57 (2H, t, J=7.6 Hz), 2.76 (4H, br), 3.21 (4H, br), 4.14 (2H, t, J=6.3 Hz), 4.19 (2H, t, J=6.7 Hz), 6.27 (2H, s), 6.82 (1H, d, J=8.7 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, dd, J=2.5, 8.8 Hz), 7.23 (1H, d, J=2.4 Hz), Hz), 7.27 (1H, t, J=7.9 Hz), 7.35-7.45 (2H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=8.8 Hz), 7.96 (1H, d, J=8.7 Hz)

Example 374

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethylphenyl carbonate

[0496]

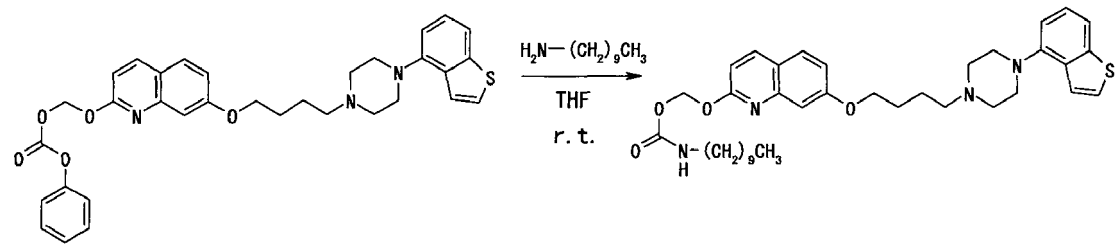


[0497] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (1.5 g) synthesized in the same manner as in WO2006/112464 (Example 1) in dimethylformamide (50 ml) was added silver carbonate (I) (1.14 g), chloromethyl phenyl carbonate[35180-03-1] (1.42 g) was added, and the mixture was stirred at 60°C for 4 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl phenyl carbonate (20 mg).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 1.70-2.10 (4H, m), 2.59 (2H, t, J=7.4 Hz), 2.78 (4H, br), 3.22 (4H, br), 4.10-4.18 (2H, m), 6.38 (2H, s), 6.80-6.95 (4H, m), 7.08 (1H, dd, J=2.4, 8.8 Hz), 7.18-7.45 (7H, m), 7.55 (1H, d, J=8.0Hz), 7.63 (1H, d, J=8.9 Hz), 8.00 (1H, d, J=8.7 Hz)

Example 375

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyldecyl carbamate

[0498]

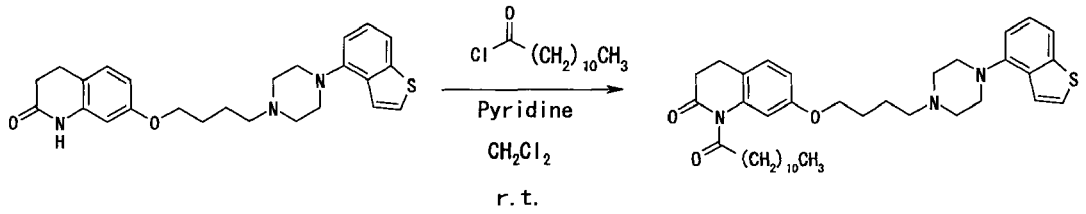


[0499] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl phenyl carbonate (20 mg) synthesized in the same manner as in Example 374 in THF (10 ml) was added decylamine[2016-57-1] (0.1 ml), and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, and dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=2:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yloxymethyl decyl carbamate (18 mg).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 0.87 (3H, t, J=6.9 Hz), 1.10-2.40 (20H, m), 2.58 (2H, t, J=7.4 Hz), 2.76 (4H, br), 3.16-3.26 (6H, m), 4.15 (2H, t, J=6.3 Hz), 4.83 (1H, t, J=5.4 Hz), 6.23 (2H, s), 6.82 (1H, d, J=8.7 Hz), 6.90 (1H, d, J=7.6 Hz), 7.06 (1H, dd, J=2.5, 8.8 Hz), 7.23 (1H, d, J=2.4 Hz), Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0Hz), 7.61 (1H, d, J=8.8 Hz), 7.95 (1H, d, J=8.7 Hz)

Example 376

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1-dodecanoyl-3,4-dihydroquinolin-2(1H)-one

[0500]

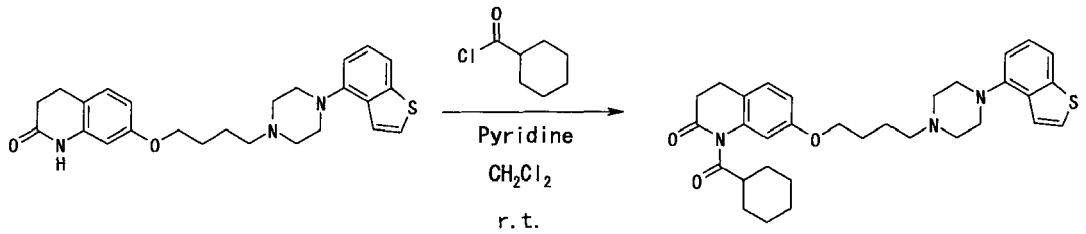


[0501] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-3,4-dihydro-1H-quinolin-2-one (0.3 g) synthesized in the same manner as in WO2006/112464 (Example 11) in methylene chloride (10 ml) was added pyridine (0.11 ml), with stirring under ice-cooling, dodecanoylchloride (0.24 ml) was added, and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with methylene chloride, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate) to give 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1-dodecanoyl-3,4-dihydro-1H-quinolin-2-one (0.4 g).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 0.88 (3H, t, J=6.8 Hz), 1.20-1.40 (16H, m), 1.68-1.90 (6H, m), 2.54 (2H, t, J=7.4 Hz), 2.65-2.80 (6H, m), 2.80-2.88 (2H, m), 2.97 (2H, t, J=7.6 Hz), 3.16-3.26 (4H, m), 3.97 (2H, t, J=6.2 Hz), 6.67 (1H, dd, J=2.4, 8.3 Hz), 6.83 (1H, dd, J=0.6, 7.7 Hz), 7.08 (1H, d, J=8.3 Hz), 7.27 (1H, t, J=7.8 Hz), 7.37-7.43 (2H, m), 7.55 (1H, d, J=8.0 Hz)

Example 377

Synthesis of 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cyclohexanecarbonyl)-3,4-dihydroquinolin-2(1H)-one

[0502]

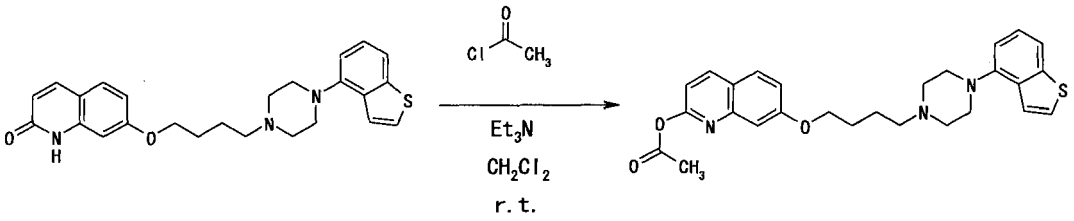


[0503] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-3,4-dihydro-1H-quinolin-2-one (1 g) synthesized in the same manner as in WO2006/112464 (Example 11) in dichloromethane (30 ml) was added pyridine (0.37 ml), with stirring under ice-cooling, cyclohexanecarbonyl chloride (0.46 ml) was added and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=9:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1-(cyclohexanecarbonyl)-3,4-dihydroquinolin-2(1H)-one (1.2 g). oil: yellow
^{1}H-NMR ($CDCl_3$) δ ppm : 1.20-2.25 (14H, m), 2.53 (2H, t, J=7.5 Hz), 2.64-2.78 (6H, m), 2.84-2.90 (2H, m), 3.12-3.24 (5H, m), 3.97 (2H, t, J=6.2 Hz), 6.59 (1H, d, J=2.3Hz), 6.63 (1H, dd, J=2.4, 8.3 Hz), 6.90 (1H, d, J=7.4 Hz), 7.08 (1H, d, J=8.3 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.0 Hz)

Example 378

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]quinolin-2-yl acetate

[0504]

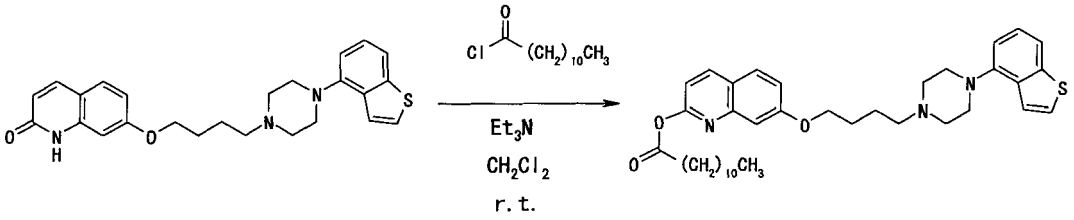


[0505] To a solution of 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-1H-quinolin-2-one (3.14 g) synthesized in the same manner as in WO2006/112464 (Example 1) in methylene chloride (32 mL) were added with stirring under ice-cooling triethylamine (4.0 mL) and acetyl chloride (1.5 mL), and the mixture was stirred at room temperature for 39 hr. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (methylene chloride :ethyl acetate=7:3→1:9) to give 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]quinolin-2-yl acetate (1.24 g).
oil: yellow
^{1}H-NMR ($CDCl_3$) δ ppm : 1.62-1.81 (2H, m), 1.81-2.00 (2H, m), 2.39 (3H, s), 2.54 (2H, t, J=7.5 Hz), 2.67-2.86 (4H, m), 3.10-3.29 (4H, m), 4.15 (2H, t, J=6.3 Hz), 6.90 (1H, d, J=7.5 Hz), 7.05 (1H, d, J=8.5 Hz), 7.10-7.29 (3H, m), 7.29-7.48 (2H, m), 7.55 (1H, d, J=7.8Hz), 7.72 (1H, d, J=9.0Hz), 8.15 (1H, d, J=8.5 Hz)

Example 379

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl dodecanoate

[0506]

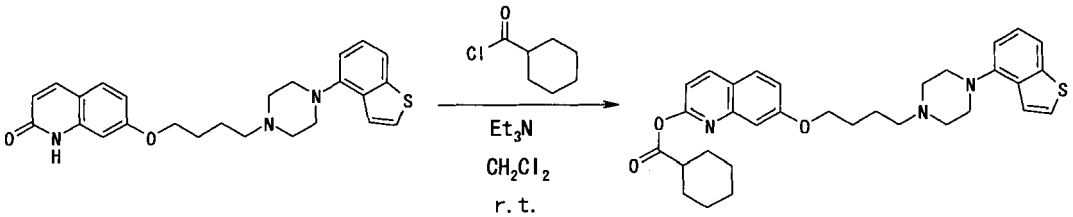


[0507] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (800 mg) in dichloromethane (20 ml) synthesized in the same manner as in WO2006/112464 (Example 1) was added triethylamine (0.77 ml), with stirring under ice-cooling, dodecanoylchloride (1.1 ml) was added and the mixture was stirred at room temperature for 4 hr. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl dodecanoate (1.34 g).
oil: yellow
^{1}H-NMR ($CDCl_3$) δ ppm : 0.88 (3H, t, J=6.8 Hz), 1.20-1.50 (16H, m), 1.72-1.86 (4H, m), 1.86-1.98 (2H, m), 2.55 (2H, t, J=7.6 Hz), 2.66 (2H, t, J=7.6 Hz), 2.75 (4H, br), 3.20 (4H, br), 4. 14 (2H, t, J=6.3 Hz), 6.90 (1H, d, J=7.5 Hz), 7.04 (1H, d, J=8.6 Hz), 7.19 (1H, dd, J=2.4, 8.9 Hz), 7.27 (1H, t, J=7.8 Hz), 7.33 (1H, d, J=2.4 Hz), 7.36-7.44 (2H, m), 7.55 (1H, d, J=8.1 Hz), 7.71 (1H, d, J=9.0 Hz), 8.14 (1H, d, J=8.6 Hz)

Example 380

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl cyclohexanecarboxylate

[0508]

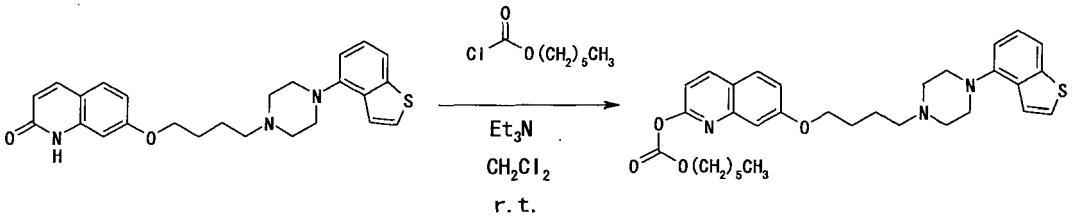


[0509] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (800 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dichloromethane (20 ml) was added triethylamine (0.64 ml), with stirring under ice-cooling, cyclohexanecarbonyl chloride (0.49 ml) was added and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=4:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl cyclohexanecarboxylate (1.08 g).
oil: yellow
^{1}H-NMR ($CDCl_3$) δ ppm : 1.20-2.20 (14H, m), 2.54 (2H, t, J=7.5 Hz), 2.60-2.80 (5H, m), 3.20 (4H, br), 4.08-4.18 (2H, m), 6.89 (1H, d, J=7.6 Hz), 7.01 (1H, d, J=8.6 Hz), 7.18 (1H, dd, J=2.5, 8.9 Hz), 7.27 (1H, t, J=7.8 Hz), 7.34 (1H, d, J=2.4 Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.0 Hz), 7.70 (1H, d, J=8.9 Hz), 8.12 (1H, d, J=8.6 Hz)

Example 381

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl hexyl carbonate

[0510]

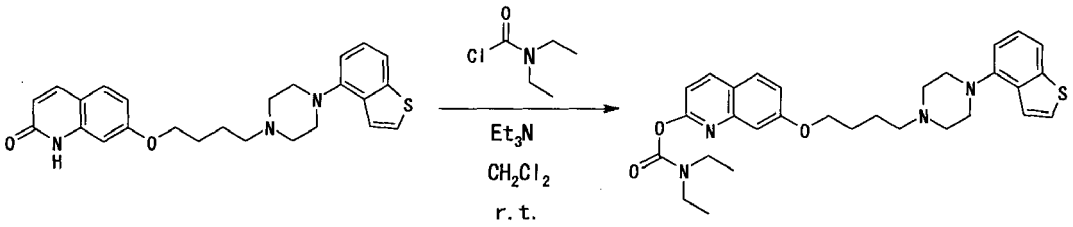


[0511] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (800 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dichloromethane (20 ml) was added triethylamine(0.65 ml), with stirring under ice-cooling, hexylchloroformate (0.6 g) was added at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=1:2) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl hexyl carbonate (1.09 g).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 0.91 (3H, t, J=7.0 Hz), 1.30-1.50 (6H, m), 1.70-1.84 (4H, m), 1.88-1.98 (2H, m), 2.54 (2H, t, J=7.5 Hz), 2.72 (4H, br), 3.20 (4H, br), 4.15 (2H, t, J=6.4 Hz), 4.30 (2H, t, J=6.7 Hz), 6.90 (1H, dd, J=0.4, 7.6 Hz), 7.08 (1H, d, J=8.6 Hz), 7.20 (1H, dd, J=2.4, 8.9 Hz), 7.27 (1H, t, J=7.8 Hz), 7.33 (1H, d, J=2.4 Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=8.0 Hz), 7.72 (1H, d, J=9.0 Hz), 8.15 (1H, d, J=8.6 Hz)

Example 382

Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl diethylcarbamate

[0512]

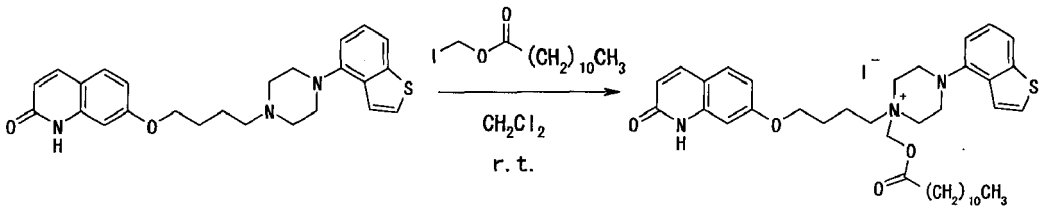


[0513] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (800 mg) synthesized in the same manner as in WO2006/112464 (Example 1) in dichloromethane (20 ml) was added triethylamine (0.65 ml), with stirring under ice-cooling, diethylcarbamoylchloride (0.5 g) was added and the mixture was stirred at room temperature overnight. Water was added to the reaction mixture and the mixture was extracted with ethyl acetate. The organic layer was dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate:n-hexane=20:1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-quinolin-2-yl diethylcarbamate (120 mg).
oil: colorless
^{1}H-NMR ($CDCl_3$) δ ppm : 1.23 (3H, t, J=7.1 Hz), 1.30 (3H, t, J=7. Hz), 1.72-1.84 (2H, m), 1.86-1.98 (2H, m), 2.54 (2H, t, J=7.5 Hz), 2.73 (4H, br), 3.20 (4H, br), 3.43 (2H, q, J=7.0 Hz), 3.52 (2H, q, J=7.1 Hz), 4.13 (2H, t, J=6.3 Hz), 6.89 (1H, d, J=7.2 Hz), 7.08 (1H, d, J=8.6 Hz), 7.16 (1H, dd, J=2.5, 8.9 Hz), 7.26 (1H, t, J=7.8 Hz), 7.34 (1H, d, J=2.4 Hz), 7.36-7.44 (2H, m), 7.54 (1H, d, J=7.9 Hz), 7.68 (1H, d, J=8.9 Hz), 8.09 (1H, d, J=8.6 Hz)

Example 383

Synthesis of 4-(benzo[b]thiophen-4-yl)-1-(dodecanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide

[0514]

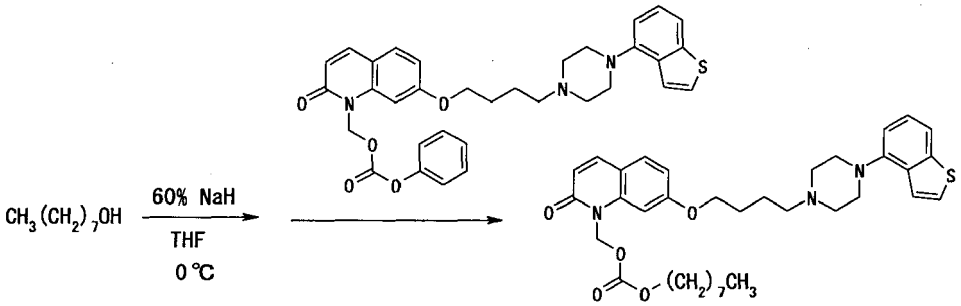


[0515] To a solution of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (0.85 g) synthesized in the same manner as in WO2006/112464 (Example 1) in dichloromethane (20 ml) was added iodomethyldodecanoate (1 g) synthesized in the same manner as in Reference Example 19, and the mixture was stirred at room temperature overnight. The solvent was evaporated under reduced pressure, ether was added and the mixture was left standing. The obtained crystals were collected by filtration to give 4-(benzo[b]thiophen-4-yl)-1-(dodecanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide (1.07 g).
powder :yellow
^{1}H-NMR (DMSO-d_6) δ ppm : 0.84 (3H, t, J=6.8 Hz) , 1.10-2.56 (24H, m), 3.44-3.56 (4H, m), 3.60-3.90 (6H, m), 4.09 (2H, t, J=5.5 Hz), 5.57 (2H, s), 6.31 (1H, d, J=9.4 Hz), 6.80-6.86 (2H, m), 7.05 (1H, d, J=7.6 Hz), 7.35 (1H, t, J=7.9 Hz), 7.54 (1H, d, J=5.5 Hz), 7.56-7.62 (1H, m), 7.68-7.86 (3H, m), 11.63 (1H, s)

Example 384

Synthesis of (7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl octyl carbonate

[0516]

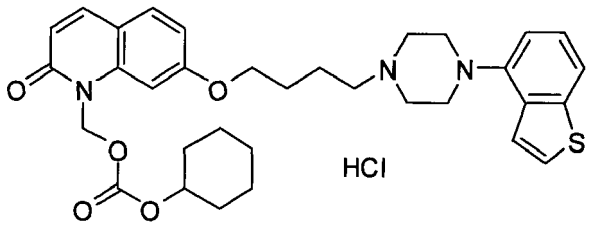


[0517] In the same manner as in Example 175, the compound was obtained (yield 25 mg, 8.7%) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ ppm : 0.86 (3H, t, J=6.9 Hz), 1.16-1.40 (10H, m), 1.58-1.72 (2H, m), 1.72-1.84 (2H, m), 1.85-1.95 (2H, m), 2.55 (2H, t, J=7.5 Hz), 2.68-2.80 (4H, br), 3.14-3.26 (4H, br), 4.10 (2H, t, J=6.2 Hz), 4.18 (2H, t, J=6.7 Hz), 6.35 (2H, s), 6.50 (1H, d, J=9.5 Hz), 6.84 (1H, dd, J=2.2, 8.6 Hz), 6.89 (1H, d, J=7.6 Hz), 6.93 (1H, d, J=2.1 Hz), 7.27 (1H, t, J=7.8 Hz), 7.36-7.46 (3H, m), 7.55 (1H, d, J=8.0 Hz), 7.61 (1H, d, J=9.5 Hz)

Example 385

Synthesis of carbonic acid 7-[4-(4-benzo[b]thiophen-4-ylpiperazin-1-yl)butoxy]-2-oxo-2H-quinolin-1-ylmethyl ester cyclohexyl ester hydrochloride

[0518]



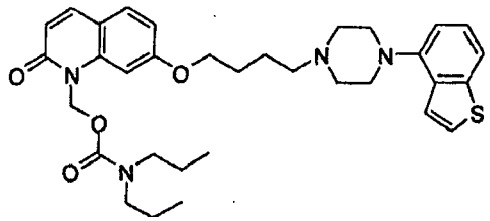
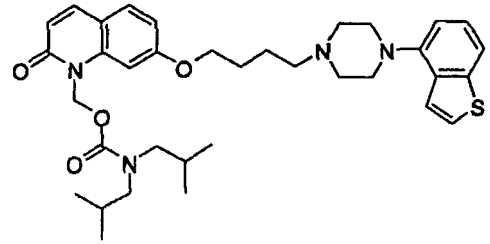
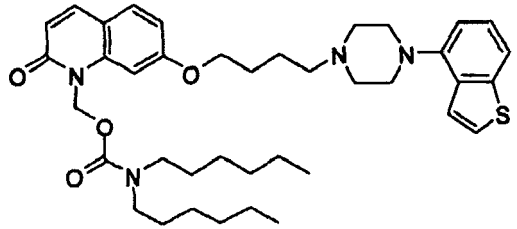
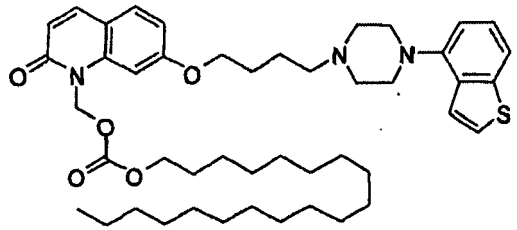
[0519] Sodium hydride (55% oil) (0.962 g, 22.04 mmol) was suspended in tetrahydrofuran (THF) (200 ml), 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (8.31 g, 19.17 mmol) was added and the mixture was stirred at 50°C for 1 hr. The mixture was cooled to 0°C, chloromethyl cyclohexyl carbonate (4.80 g, 24.92 mmol) was added dropwise and the mixture was stirred at room temperature overnight. After cooling to 0°C, excess 2N hydrochloric acid was added to quench the reaction. The precipitated solid was collected by filtration and dried. In addition, the filtrate was extracted with ethyl acetate. The organic layer was concentrated and purified by moderate-pressure silica gel column chromatography (methylene chloride: methanol =100:0 to 20:1). Likewise, the solid was purified by moderate-pressure silica gel column chromatography. Concentration under reduced pressure gave the title compound (yield, 5.04 g, 42%) as a white solid.

^{1}H-NMR (DMSO-d_6) δ ppm : 1.16 (m, 6H), 1.59-1.69 (m, 2H), 1.80 (m, 6H), 3.00-3.60 (m, 10H), 4.19 (t, J = 5.9 Hz, 2H), 4.57-4.65 (m, 1H), 6.29 (s, 2H), 6.42 (d, J = 9.5 Hz, 1H), 6.97 (dd, J = 2.3, 8.5 Hz, 1H), 6.98 (dd, J = 1.8, 7.7 Hz, 1H), 7.04 (d, J = 2.3 Hz, 1H), 7.31 (dd, J = 7.7, 7.7 Hz, 1H), 7.43 (dd, J = 1.8, 5.5 Hz, 1H), 7.63-7.71 (m, 3H), 7.86 (d, J = 9.5 Hz, 1H).

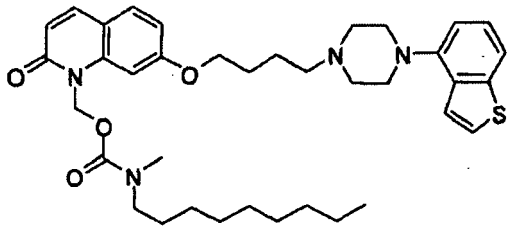
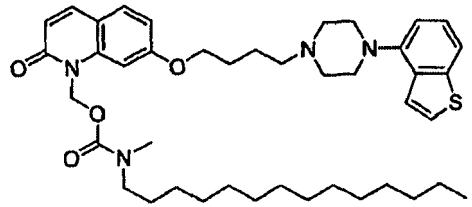
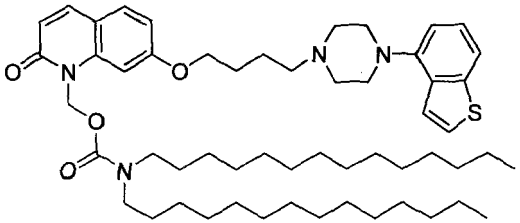
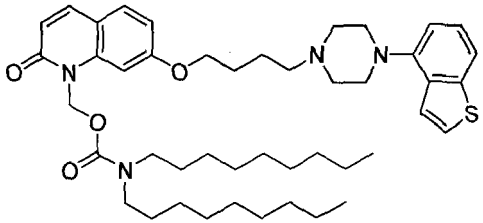
[0520] In the same manner as in the above-mentioned Examples, the compounds described in the following Table 2 can be synthesized.

[0521] (Examples not falling within the scope of the invention as claimed are marked with an asterisk (*))

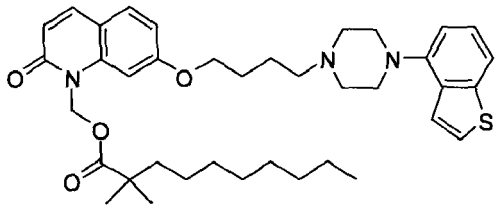
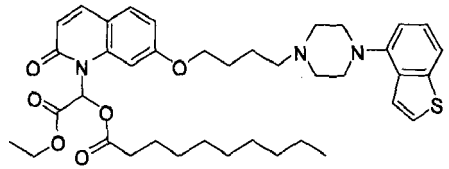
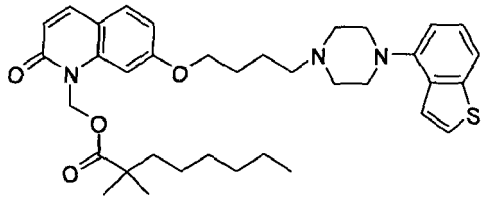
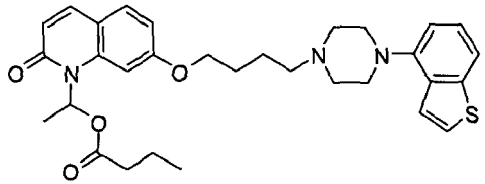
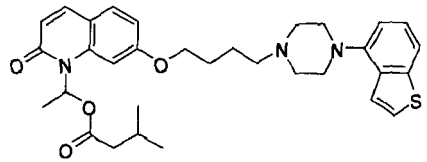
Table 2

Example	Structure Formula	
386		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl dipropylcarbamate
387		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl diisobutylcarbamate
388		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl dihexylcarbamate
389		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl nonadecylcarbonate

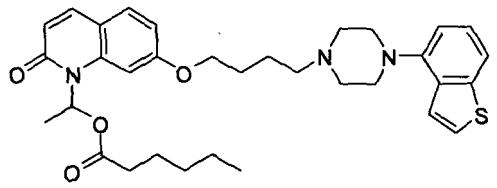
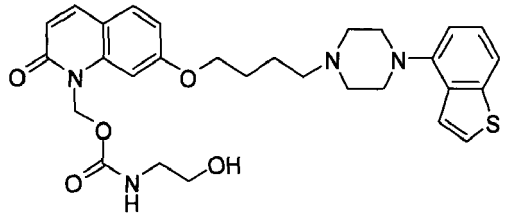
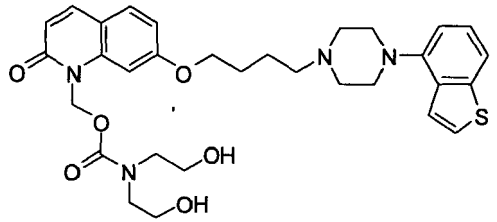
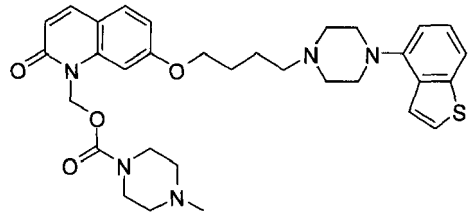
(continued)

Example	Structure Formula	
390		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl methyl(nonyl)carbamate
391		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl methyl(tetradecyl)carbamate
392		(7-(4-(4-(benzo[b]hiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl ditetradecylcarbamate
393		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl dinonylcarbamate

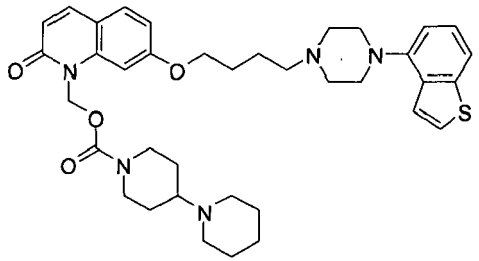
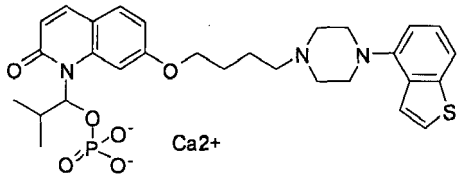
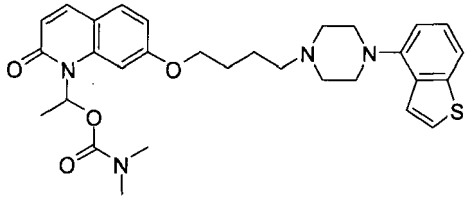
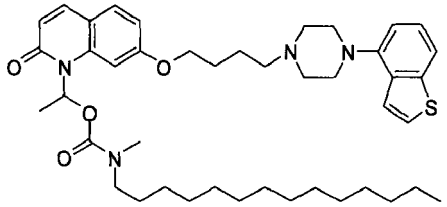
(continued)

Example	Structure Formula	
394		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 2,2-dimethyldecanoate
395		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-ethoxy-2-oxoethyl decanoate
396		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 2,2-dimethyloctanoate
397		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl butyrate
398		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl 3-methylbutanoate

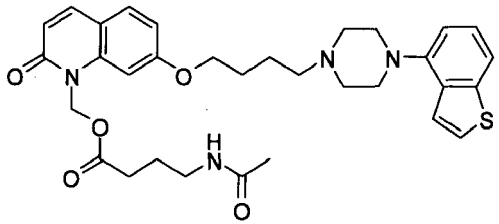
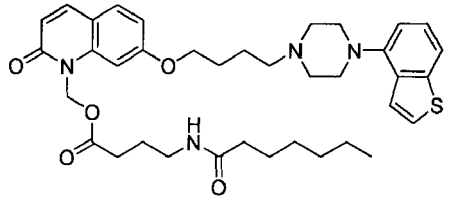
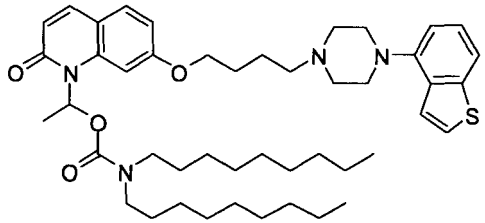
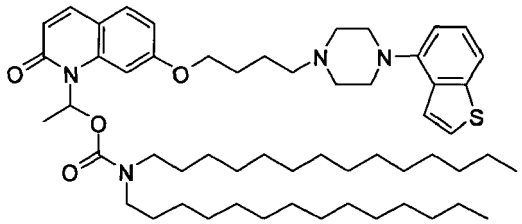
(continued)

Example	Structure Formula	
399		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl hexanoate
400		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 2-hydroxyethylcarbamate
401		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl bis(2-hydroxyethyl)carbamate
402		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 4-methylpiperazine-1-carboxylate

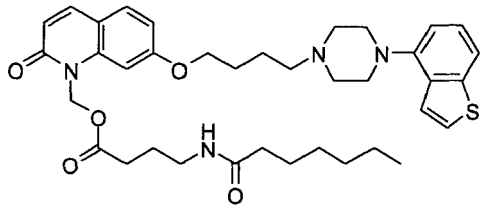
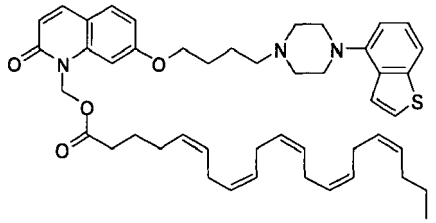
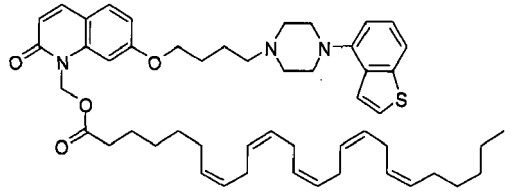
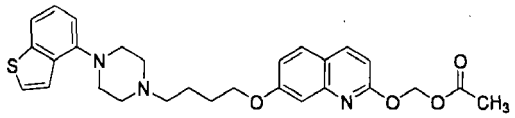
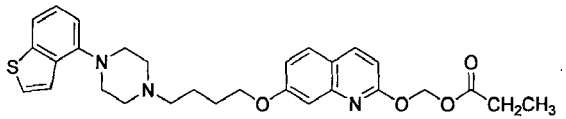
(continued)

Example	Structure Formula	
403		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 1,4'-bipiperidine-1'-carboxylate
404		calcium 1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-methylpropyl phosphate
405		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl dimethylcarbamate
406		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl methyl(tetradecyl)carbamate

(continued)

Example	Structure Formula	
407		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 4-acetamidobutanoate
408		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 4-heptanamidobutanoate
409		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl dinonylcarbamate
410		1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)ethyl ditetradecylcarbamate

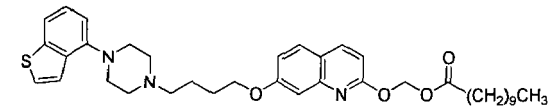
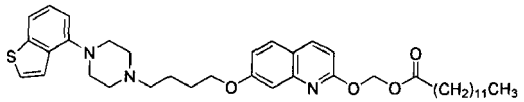
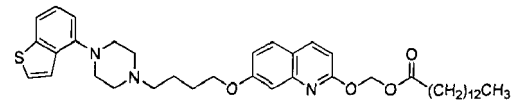
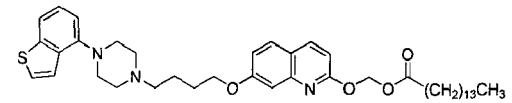
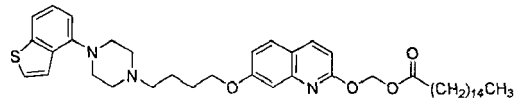
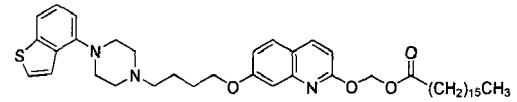
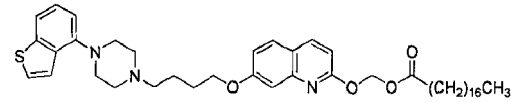
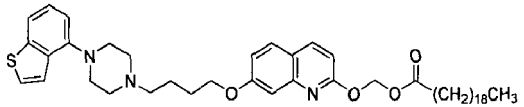
(continued)

Example	Structure Formula	
411		(7-(4-(4-(benzo[b]thiophen-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl 4-heptanamidobutanoate
412		(5Z,8Z,11Z,14Z,17Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl henicosa-5,8,11,14,17-pentaenoate
413		(7Z, 10Z, 13Z, 16Z, 19Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)methyl pentacosa-7,10,13,16,19-pentaenoate
414		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl acetate
415		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl propionate

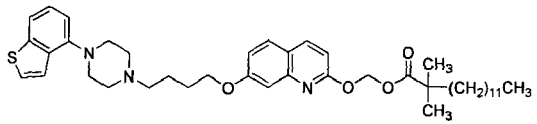
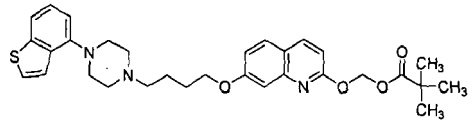
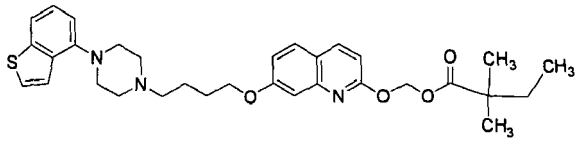
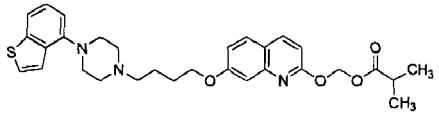
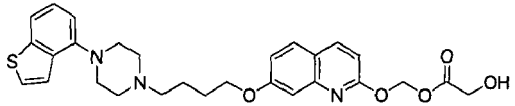
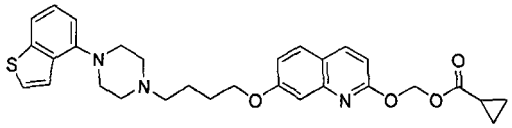
(continued)

Example	Structure Formula	
416		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl butyrate
417		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl pentanoate
418		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl hexanoate
419		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl heptanoate
420		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl octanoate
421		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl nonanoate
422		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl decanoate

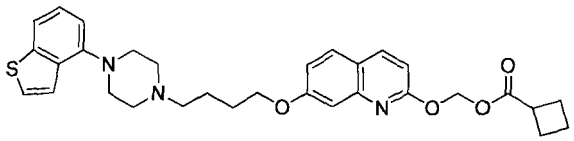
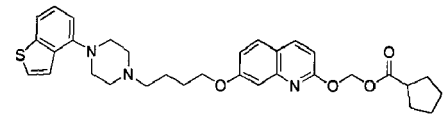
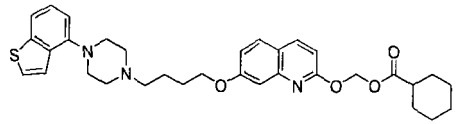
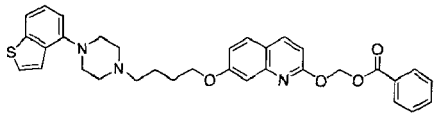
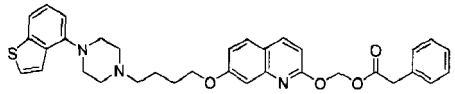
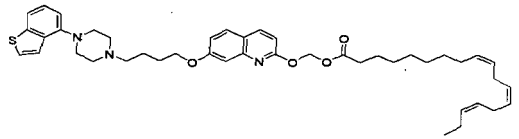
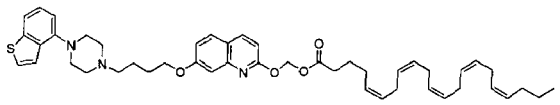
(continued)

Example	Structure Formula	
423		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl undecanoate
424		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl tridecanoate
425		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl tetradecanoate
426		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl pentadecanoate
427		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl palmitate
428		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl heptadecanoate
429		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl stearate
430		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl icosanoate

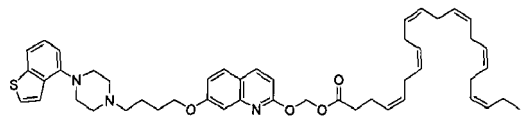
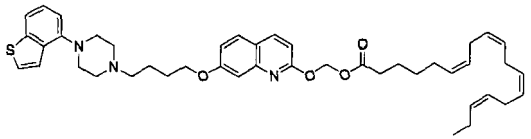
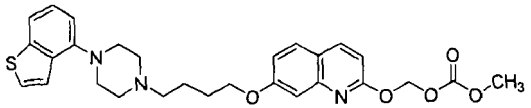
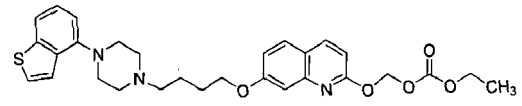
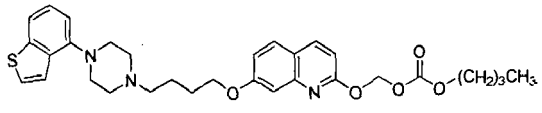
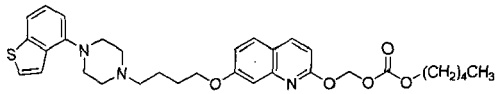
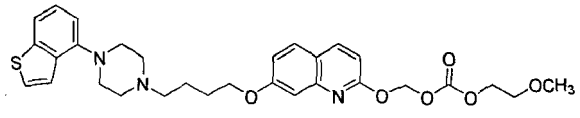
(continued)

Example	Structure Formula	
431		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 2,2-dimethyltetradecanoate
432		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl pivalate
433		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 2,2-dimethylbutanoate
434		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl isobutyrate
435		(7-(4-(4-(benzo[b]thiophen-4.-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 2-hydroxyacetate
436		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl cyclopropanecarboxylate

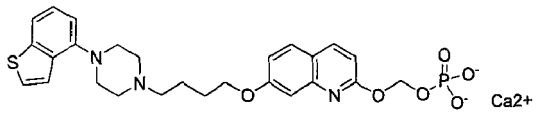
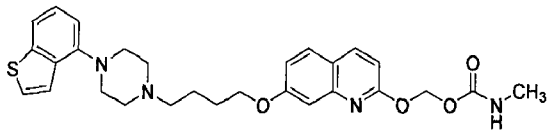
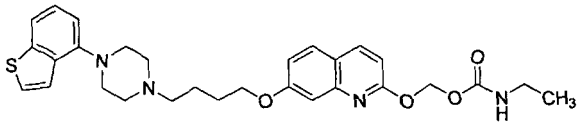
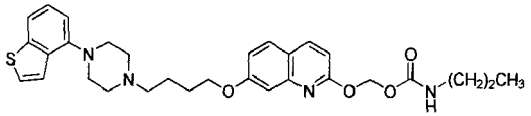
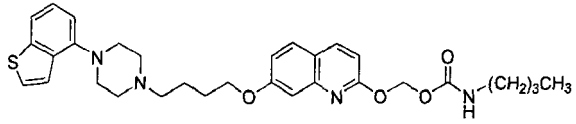
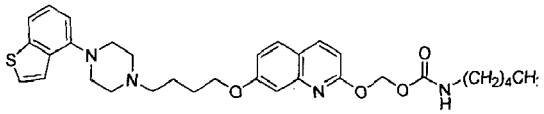
(continued)

Example	Structure Formula	
437		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl cyclobutanecarboxylate
438		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl cyclopentanecarboxylate
439		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl cyclohexanecarboxylate
440		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl benzoate
441		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 2-phenylacetate
442		(9Z,12Z,15Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl octadeca-9,12,15-trienoate
443		(5Z,8Z,11Z,14Z,17Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl henicosa-5,8,11,14,17-pentaenoate

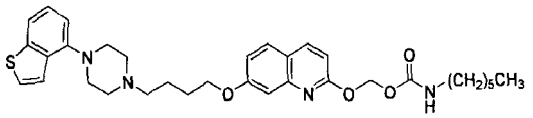
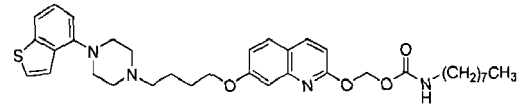
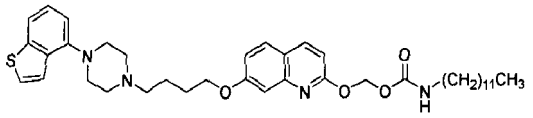
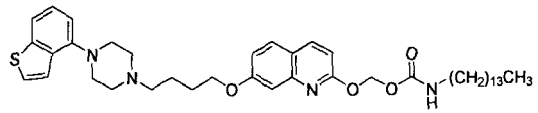
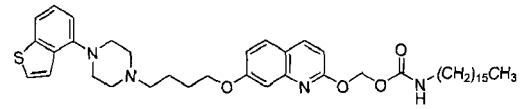
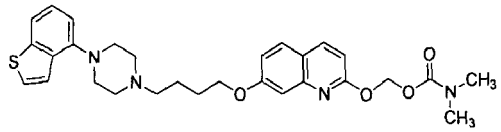
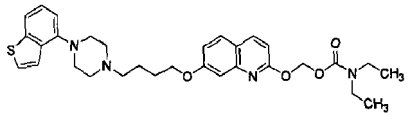
(continued)

Example	Structure Formula	
444		(4Z,7Z,10Z, 13Z, 16Z, 19Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl docosa-4,7,10,13,16,19-hexaenoate
445		(6Z,9Z,12Z,15Z)-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl octadeca-6,9,12,15-tetraenoate
446		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl methyl carbonate
447		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl ethyl carbonate
448		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl butyl carbonate
449		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl pentyl carbonate
450		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 2-methoxyethyl carbonate

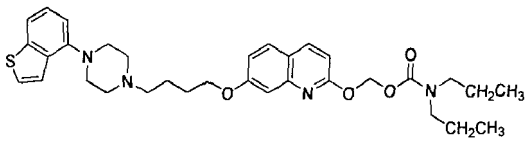
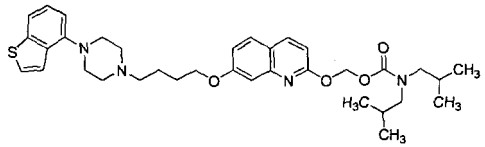
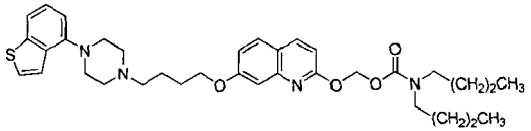
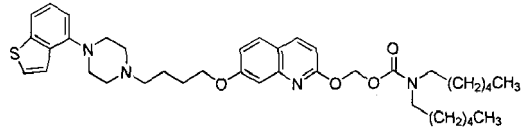
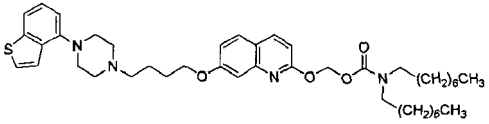
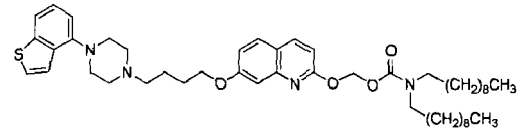
(continued)

Example	Structure Formula	
451		calcium (7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl phosphate
452		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl methylcarbamate
453		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl ethylcarbamate
454		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl propylcarbamate
455		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl butylcarbamate
456		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl pentylcarbamate

(continued)

Example	Structure Formula	
457		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl hexylcarbamate
458		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl octylcarbamate
459		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dodecylcarbamate
460		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl tetradecylcarbamate
461		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl hexadecylcarbamate
462		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dimethylcarbamate
463		(7-(4-(4-(benzo[b]thiophen-4.-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl diethylcarbamate

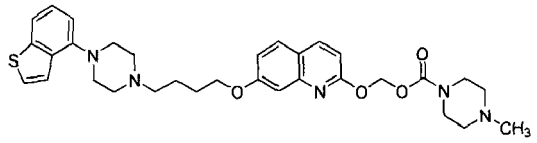
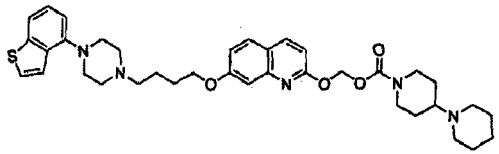
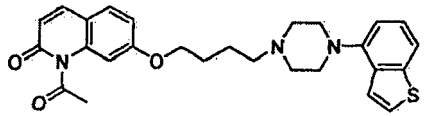
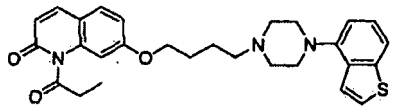
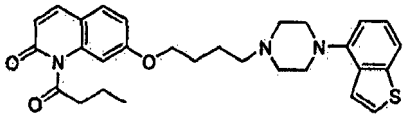
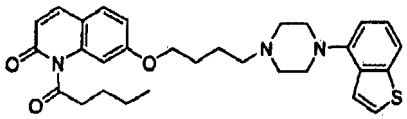
(continued)

Example	Structure Formula	
464		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dipropylcarbamate
465		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl diisobutylcarbamate
466		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dibutylcarbamate
467		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dihexylcarbamate
468		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dioctylcarbamate
469		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl didecylcarbamate

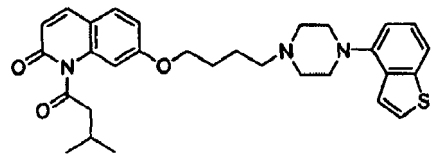
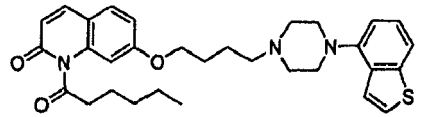
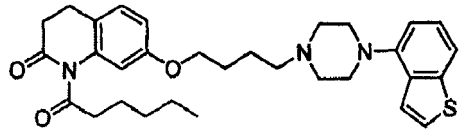
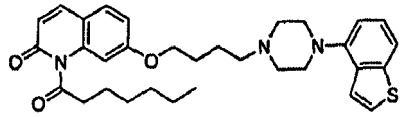
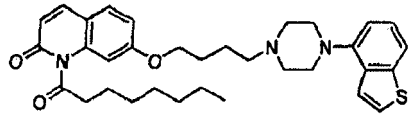
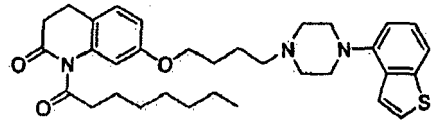
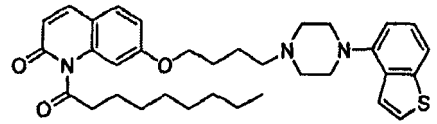
(continued)

Example	Structure Formula	
470		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl didodecylcarbamate
471		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl ditetradecylcarbamate
472		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl dihexadecylcarbamate
473		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl bis(2-hydroxyethyl)carbamate
474		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl piperidine-1-carboxylate

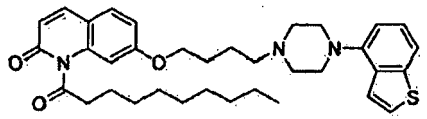
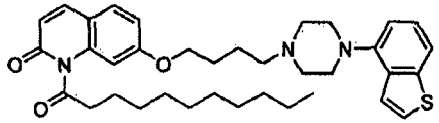
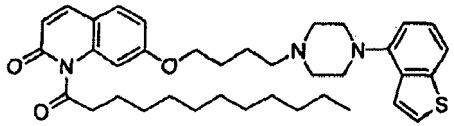
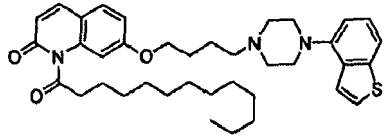
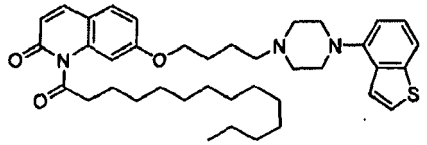
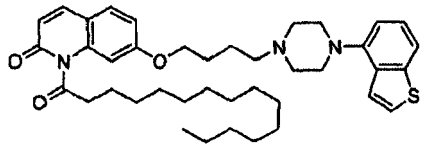
(continued)

Example	Structure Formula	
475		(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl 4-methylpiperazine-1-carboxylate
476		(7-(4-(4-(benzo[b]thiophen-4-yl)pipecazin-1-yl)butoxy)quinolin-2-yloxy)methyl 1,4'-bipiperidine-1'-carboxylate
477 *		1-acetyl-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one
478 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-propionylquinolin-2(1H)-one
479 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-butyrylquinolin-2(1H)-one
480 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-pentanoylquinolin-2(1H)-one

(continued)

Example	Structure Formula	
481 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(3-methylbutanoyl)quinolin-2(1 H)-one
482 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-hexanoylquinolin-2(1H)-one
483 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-hexanoyl-3,4-dihydroquinolin-2(1 H)-one
484 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-heptanoylquinolin-2(1H)-one
485 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-octanoylquinolin-2(1 H)-one
486 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-octanoyl-3,4-dihydroquinolin-2(1H)-one
487 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-nonanoylquinolin-2(1H)-one

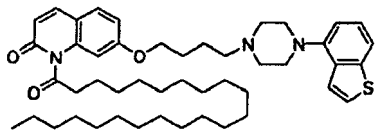
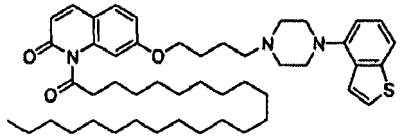
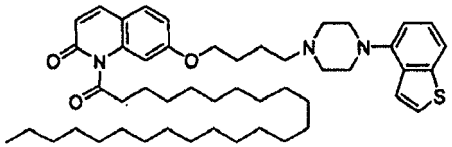
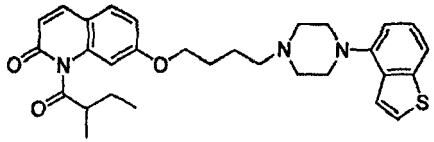
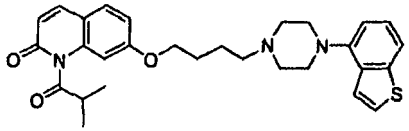
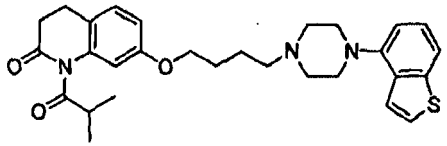
(continued)

Example	Structure Formula	
488 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-decanoylquinolin-2(1H)-one
489 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-undecanoylquinolin-2(1H)-one
490 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-dodecanoylquinolin-2(1H)-one
491 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-tridecanoylquinolin-2(1H)-one
492 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-tetradecanoylquinolin-2(1H)-one
493 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-pentadecanoylquinolin-2(1H)-one

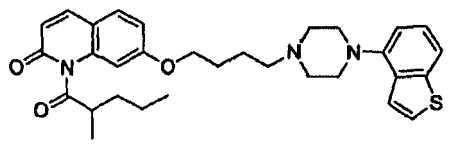
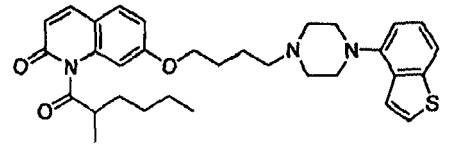
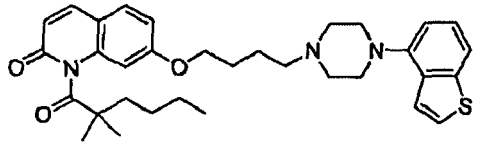
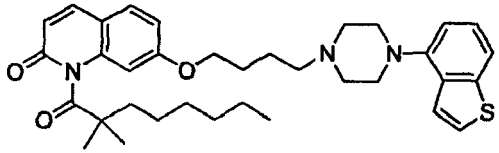
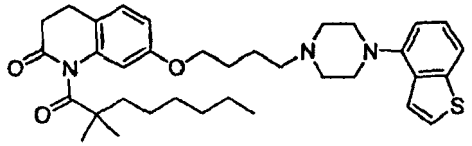
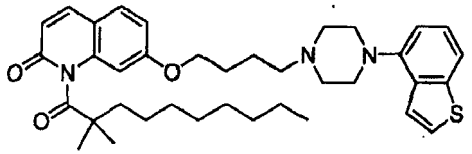
(continued)

Example	Structure Formula	
494 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-palmitoylquinolin-2(1H)-one
495 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-heptadecanoylquinolin-2(1H)-one
496 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-stearoylquinolin-2(1H)-one
497 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-nonadecanoylquinolin-2(1H)-one
498 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-icosanoylquinolin-2(1H)-one
499 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-henicosanoylquinolin-2(1H)-one

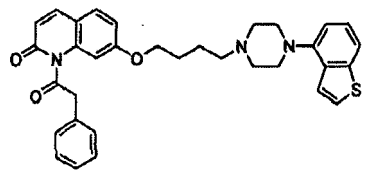
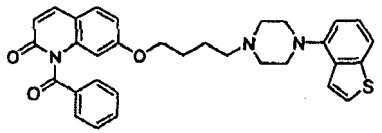
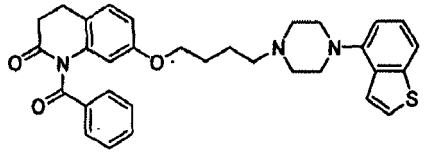
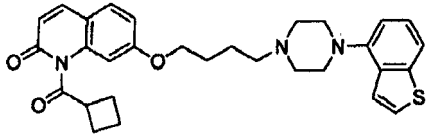
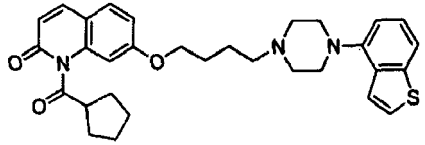
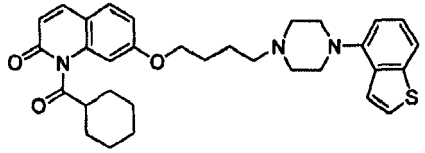
(continued)

Example	Structure Formula	
500 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-docosanoylquinolin-2(1H)-one
501 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-tricosanoylquinolin-2(1H)-one
502 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-tetracosanoylquinolin-2(1H)-one
503 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-methylbutanoyl)quinolin-2(1 H)-one
504 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-isobutyrylquinolin-2(1H)-one
505 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-isobutyryl-3,4-dihydroquinolin-2(1H)-one

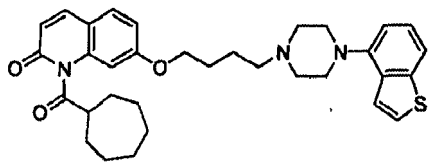
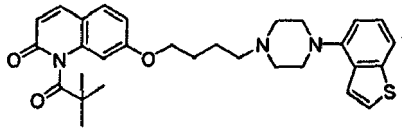
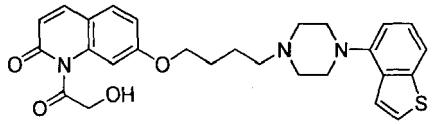
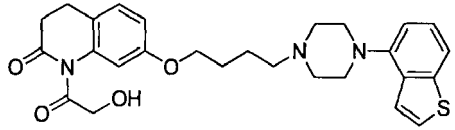
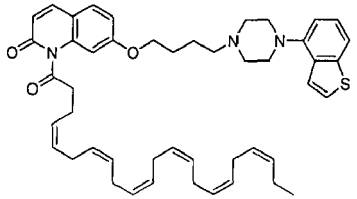
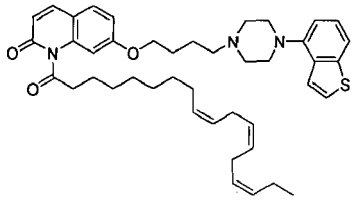
(continued)

Example	Structure Formula	
506 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-methylpentanoyl)quinolin-2(1H)-one
507 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-methylhexanoyl)quinolin-2(1H)-one
508 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2,2-dimethylhexanoyl)quinolin-2(1H)-one
509 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2,2-dimethyloctanoyl)quinolin-2(1H)-one
510 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2,2-dimethyloctanoyl)-3,4-dihydroquinolin-2(1H)-one
511 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2,2-dimethyldecanoyl)quinolin-2(1H)-one

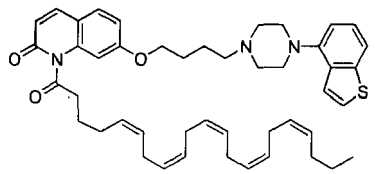
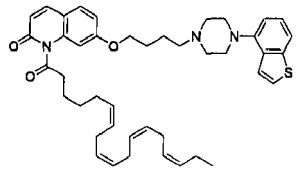
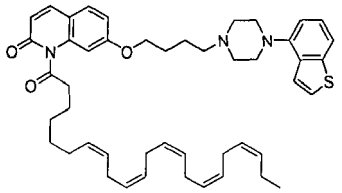
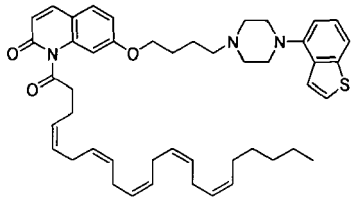
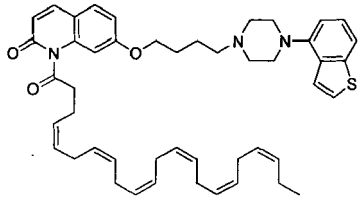
(continued)

Example	Structure Formula	
512		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-phenylacetyl)quinolin-2(1H)-one
513 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-benzoylquinolin-2(1H)-one
514 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-benzoyl-3,4-dihydroquinolin-2(1H)-one
515		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cyclobutanecarbonyl)quinoli n-2(1H)-one
516		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cyclopentanecarbonyl)quinol in-2(1H)-one
517		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cyclohexanecarbonyl)quinoli n-2(1H)-one

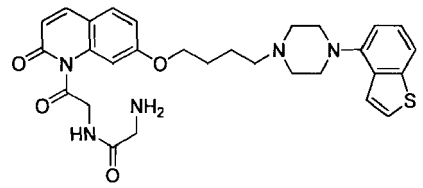
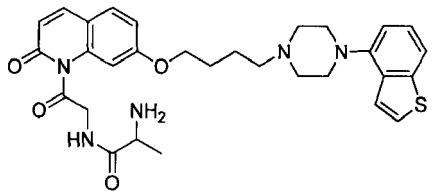
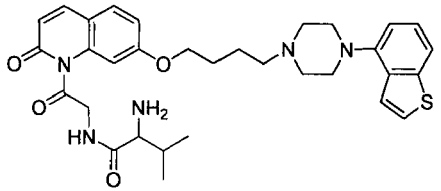
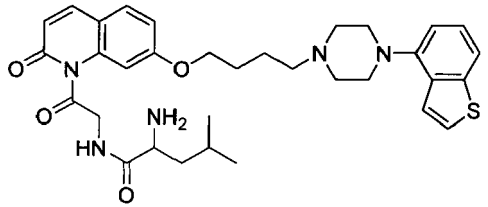
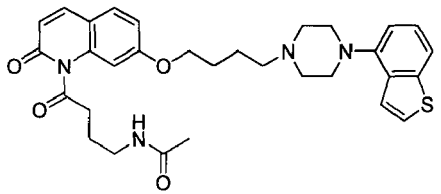
(continued)

Example	Structure Formula	
518		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cycloheptanecarbonyl)quinol in-2(1H)-one
519 *		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-pivaloylquinolin-2(1H)-one
520		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-hydroxyacetyl)quinolin-2(1H)-one
521		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-hydroxyacetyl)-3,4-dihydroquinolin-2(1H)-one
522		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(4Z,7Z,10Z,13Z,16Z,19Z)-docosa-4,7,10,13,16,19-hexaenoylquinolin-2(1H)-one
523		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(9Z,12Z,15Z)-octadeca-9,12,15-trienoylquinolin-2(1H)-one

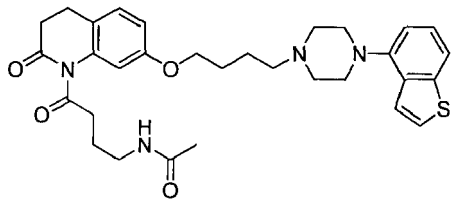
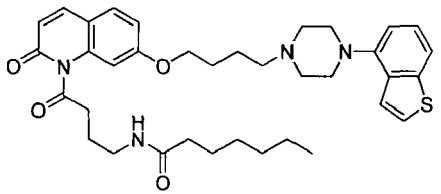
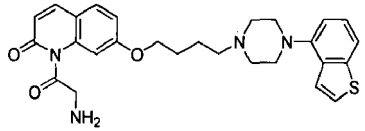
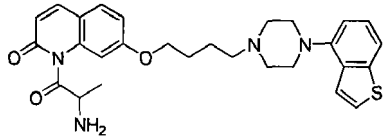
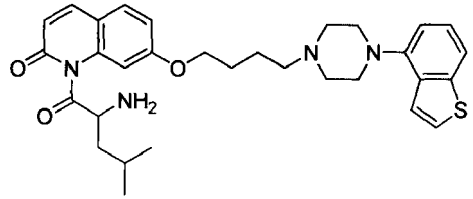
(continued)

Example	Structure Formula	
524		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(5Z,8Z,11Z,14Z,17Z)-henicosa-5,8,11,14,17-pentaenoylquinolin-2(1H)-one
525		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(6Z,9Z,12Z,15Z)-octadeca-6,9,12,15-tetraenoylquinolin-2(1H)-one
526		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(7Z,10Z,13Z,16Z,19Z)-docosa-7,10,13,16,19-pentaenoylquinolin-2(1H)-one
527		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(4Z,7Z,10Z,13Z,16Z)-docosa-4,7,10,13,16-pentaenoylquinolin-2(1H)-one
528		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(4Z,7Z,10Z,13Z,16Z,19Z)-docosa-4,7,10,13,16,19-hexaenoylquinolin-2(1H)-one

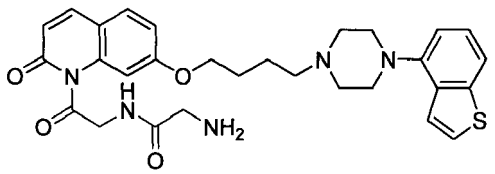
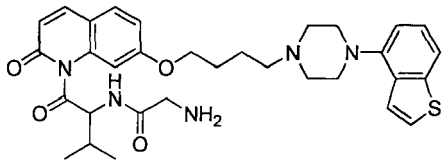
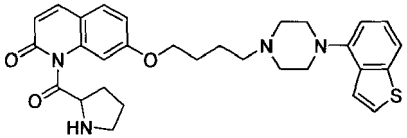
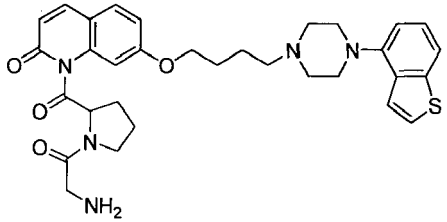
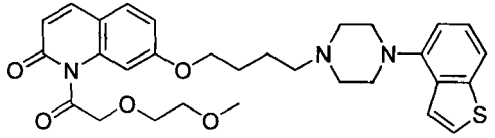
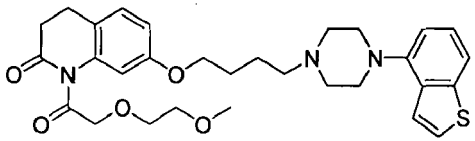
(continued)

Example	Structure Formula	
529		2-amino-N-(2-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-oxoethyl)acetamide
530		2-amino-N-(2-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-oxoethyl)propanamide
531		2-amino-N-(2-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-oxoethyl)-3-methylbutanamide
532		2-amino-N-(2-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-2-oxoethyl)-4-methylpentanamide
533		N-(4-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-4-oxobutyl)acetamide

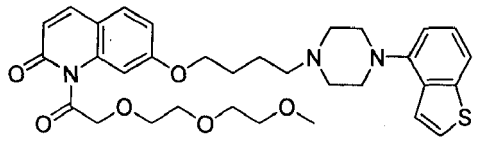
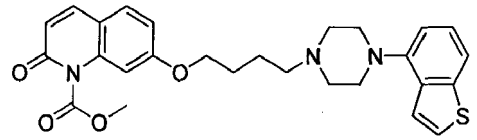
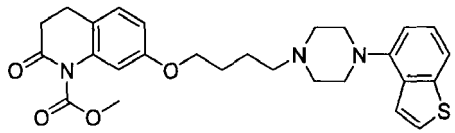
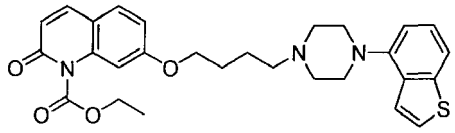
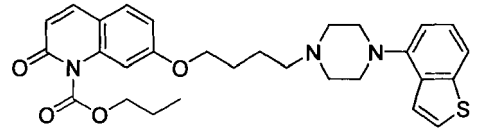
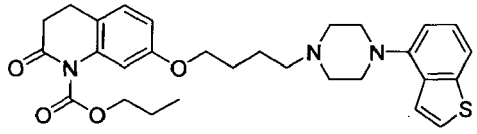
(continued)

Example	Structure Formula	
534		N-(4-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)-4-oxobutyl)acetamide
535		N-(4-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-4-oxobutyl)heptanamide
536		1-(2-aminoacetyl)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one
537		1-(2-aminopropanoyl)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one
538		1-(2-amino-4-methylpentanoyl)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one

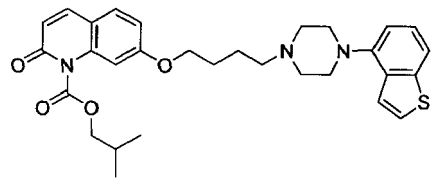
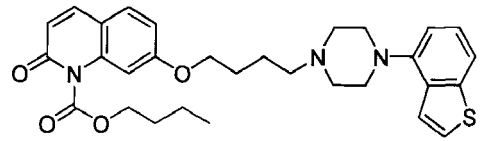
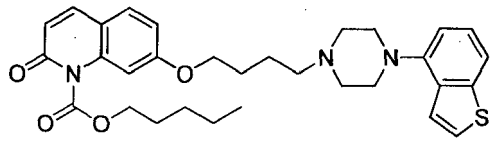
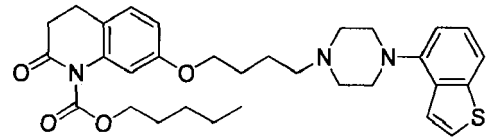
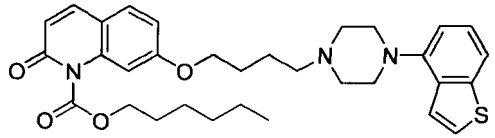
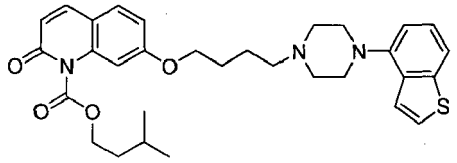
(continued)

Example	Structure Formula	
539		2-amino-N-(2-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)-2-oxoethyl)acetamide
540		2-amino-N-(1-(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl)-3-methyl-1-oxobutan-2-yl)acetamide
541		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(pyrrolidine-2-carbonyl)quinolin-2(1H)-one
542		1-(1-(2-aminoacetyl)pyrrolidine-2-carbonyl)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one
543		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-(2-methoxyethoxy)acetyl)quinoli n-2(1H)-one
544		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-(2-methoxyethoxy)acetyl)-3,4-dihydroquinolin-2(1H)-one

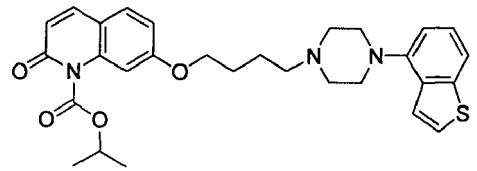
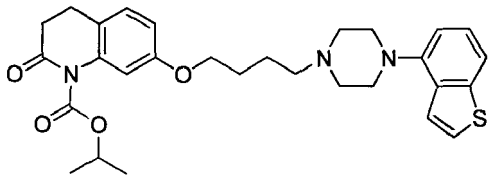
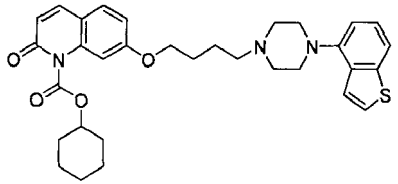
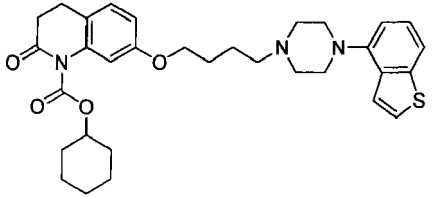
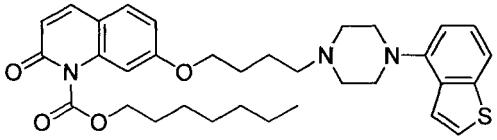
(continued)

Example	Structure Formula	
545		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(2-(2-(2-methoxyethoxy)ethoxy)acetyl)quinolin-2(1H)-one
546		methyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
547		methyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate
548		ethyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
549		propyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
550		propyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate

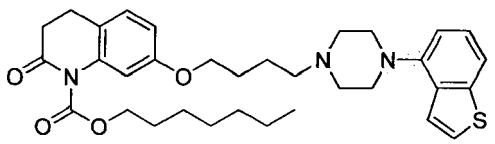
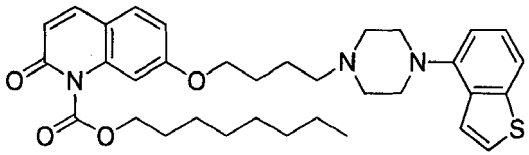
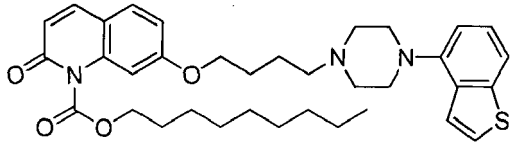
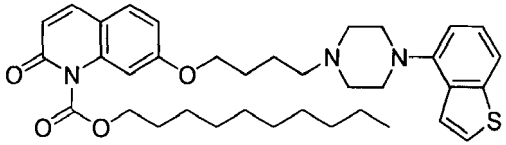
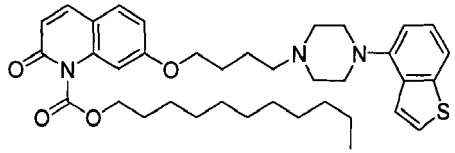
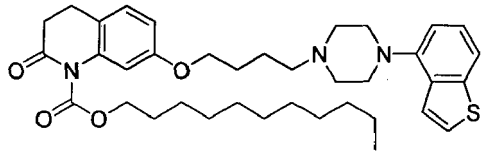
(continued)

Example	Structure Formula	
551		isobutyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
552		butyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
553		pentyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
554		pentyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate
555		hexyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
556		isopentyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate

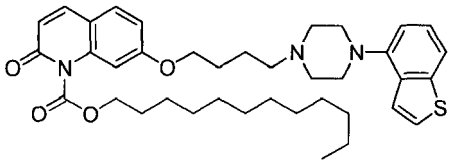
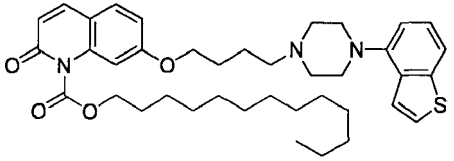
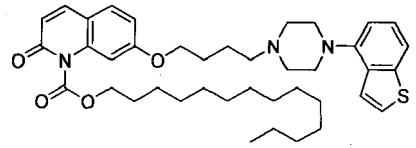
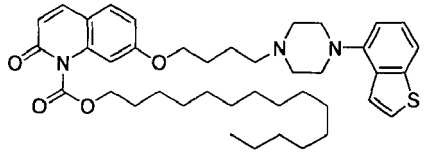
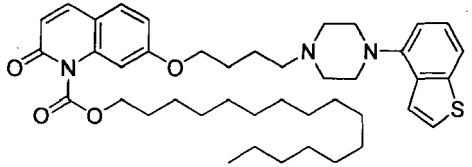
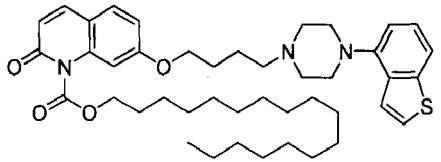
(continued)

Example	Structure Formula	
557		isopropyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
558		isopropyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate
559		cyclohexyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
560		cyclohexyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate
561		heptyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate

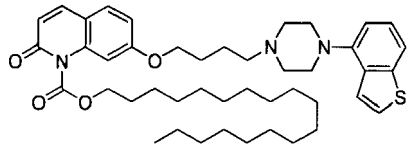
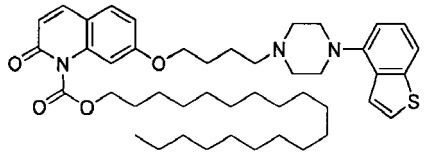
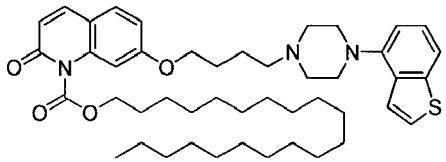
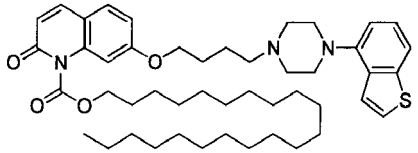
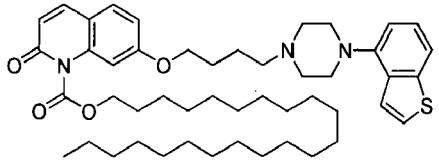
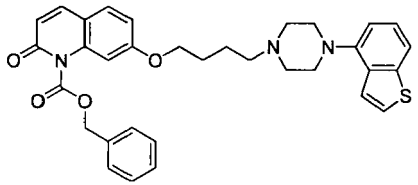
(continued)

Example	Structure Formula	
562		heptyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate
563		octyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
564		nonyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
565		decyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1 (2H)-carboxylate
566		undecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
567		undecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate

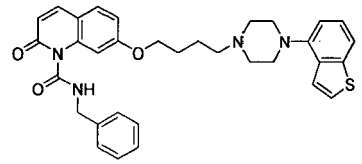
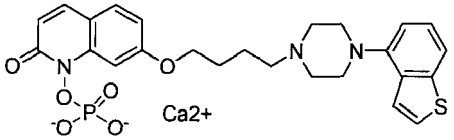
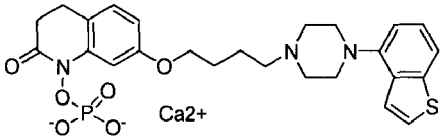
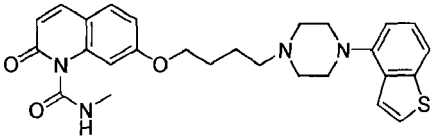
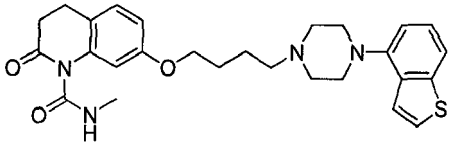
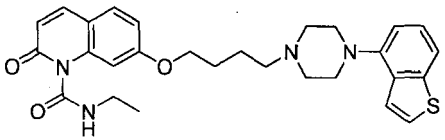
(continued)

Example	Structure Formula	
568		dodecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
569		tridecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
570		tetradecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
571		pentadecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
572		hexadecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
573		heptadecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate

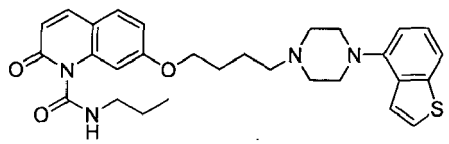
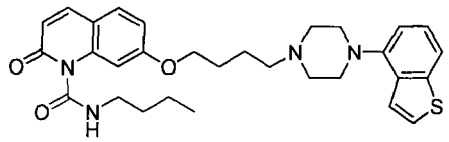
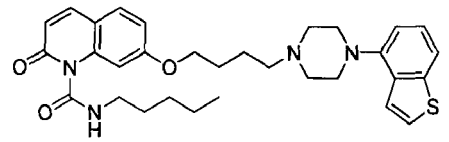
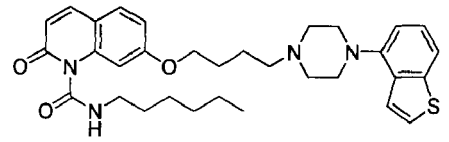
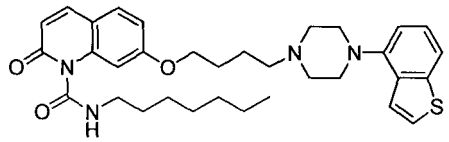
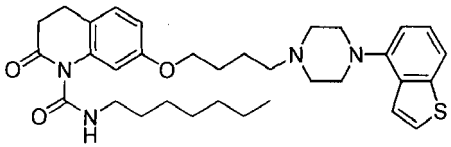
(continued)

Example	Structure Formula	
574		octadecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
575		nonadecyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
576		icosyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
577		henicosyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
578		docosyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate
579		benzyl 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinoline-1(2H)-carboxylate

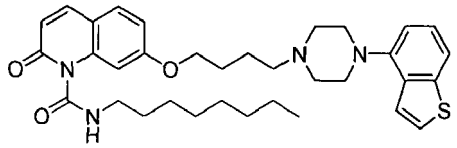
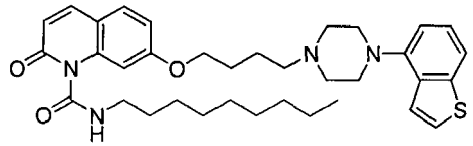
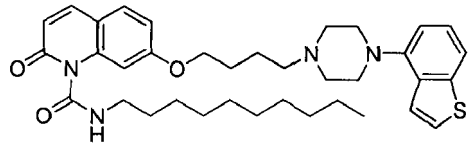
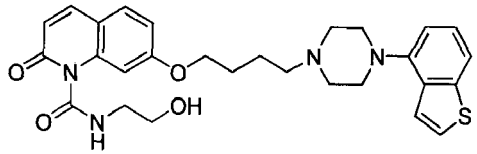
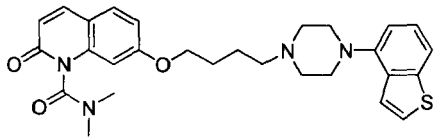
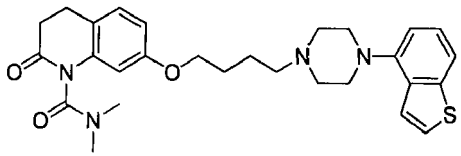
(continued)

Example	Structure Formula	
580		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-benzyl-2-oxoquinoline-1 (2H)-carboxamide
581		calcium 7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1(2H)-yl phosphate
582		calcium7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl phosphate
583		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-methyl-2-oxoquinoline-1 (2H)-carboxamide
584		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-methyl-2-oxo-3,4-dihydroquinoline-1 (2H)-carboxamide
585		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-ethyl-2-oxoquinoline-1 (2H)-carboxamide

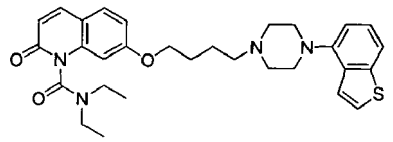
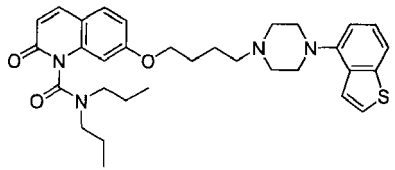
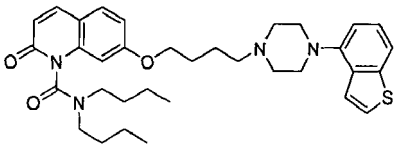
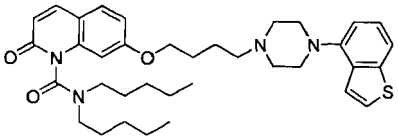
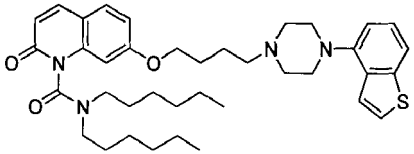
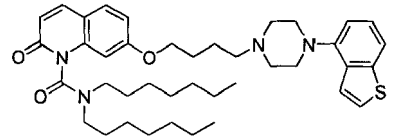
(continued)

Example	Structure Formula	
586		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-N-propylquinoline-1 (2H)-carboxamide
587		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-butyl-2-oxoquinoline-1 (2H)-carboxamide
588		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-N-pentylquinoline-1(2H)-carboxamide
589		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-hexyl-2-oxoquinoline-1(2H)-carboxamide
590		7-(4-(4-(benzo[b]hiophen-4-yl)piperazin-1-yl)butoxy)-N-heptyl-2-oxoquinoline-1 (2H)-carboxamide
591		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-heptyl-2-oxo-3,4-dihydroquinoline-1 (2H)-carboxamide

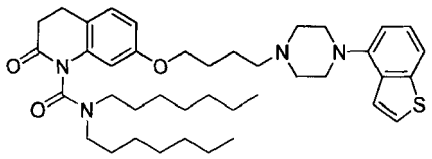
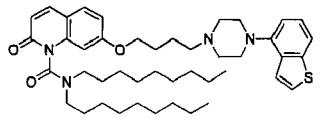
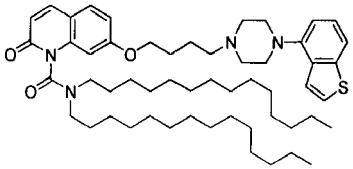
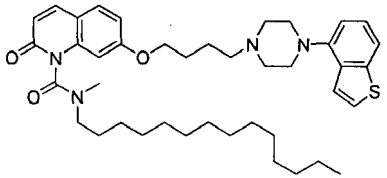
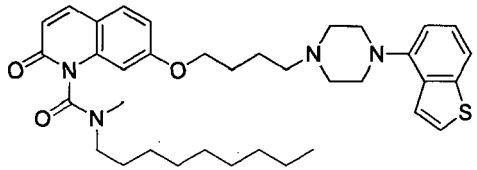
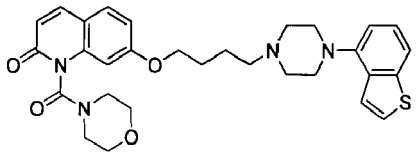
(continued)

Example	Structure Formula	
592		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-octyl-2-oxoquinoline-1 (2H)-carboxamide
593		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-nonyl-2-oxoquinoline-1 (2H)-carboxamide
594		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-decyl-2-oxoquinoline-1 (2H)-carboxamide
595		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-(2-hydroxyethyl)-2-oxoquinoline-1 (2H)-carboxamide
596		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dimethyl-2-oxoquinoline-1(2H)-carboxamide
597		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dimethyl-2-oxo-3,4-dihydroquinoline-1(2H)-carboxamide

(continued)

Example	Structure Formula	
598		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-diethyl-2-oxoquinoline-1 (2H)-carboxamide
599		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-N,N-dipropylquinoline-1 (2H)-carboxamide
600		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dibutyl-2-oxoquinoline-1 (2H)-carboxamide
601		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-N,N-dipentylquinoline-1(2H)-carboxamide
602		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dihexyl-2-oxoquinoline-1(2H)-carboxamide
603		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-diheptyl-2-oxoquinoline-1(2H)-carboxamide

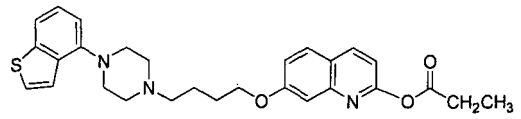
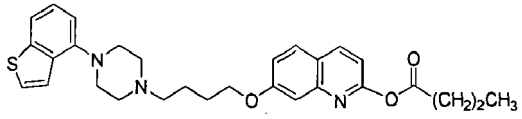
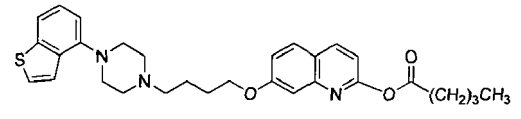
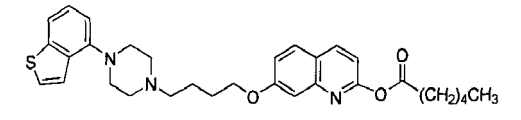
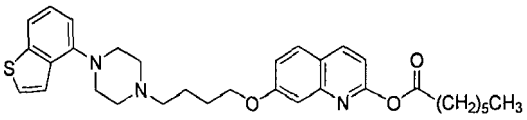
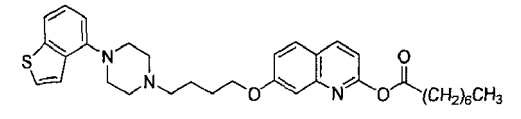
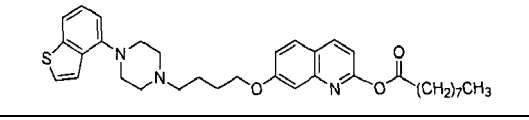
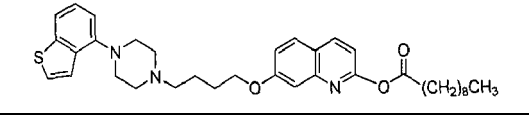
(continued)

Example	Structure Formula	
604		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-diheptyl-2-oxo-3,4-dihydroquinoline-1(2H)-carboxamide
605		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dinonyl-2-oxoquinoline-1(2H)-carboxamide
606		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-N,N-ditetradecylquinoline-1(2H)-carboxamide
607		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-methyl-2-oxo-N-tetradecylquinoline-1(2H)-carboxamide
608		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N-methyl-N-nonyl-2-oxoquinoline-1(2H)-carboxamide
609		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(morpholino-4-carbonyl)quinolin-2(1H)-one

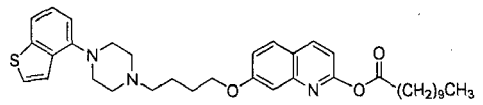
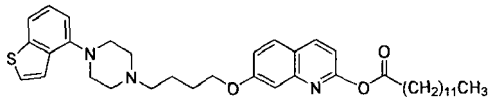
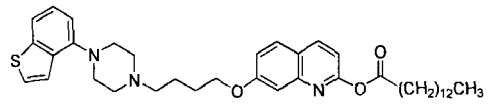
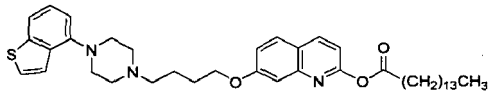
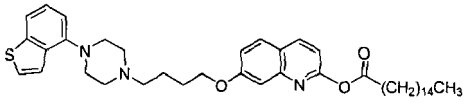
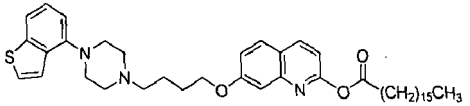
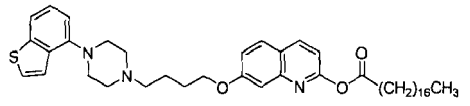
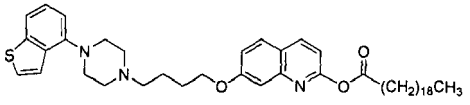
(continued)

Example	Structure Formula	
610		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(morpholine-4-carbonyl)-3,4-dihydroquinolin-2(1H)-one
611		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-bis(2-hydroxyethyl)-2-oxoquinoline-1(2H)-carboxamide
612		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-N,N-dibenzyl-2-oxoquinoline-1(2H)-carboxamide
613		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(4-methylpiperazine-1-carbonyl)quinolin-2(1H)-one
614		1-(1,4'-bipiperidine-1'-carbonyl)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2(1H)-one
615		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-1-(cyclopropanecarbonyl)quinol in-2(1H)-one

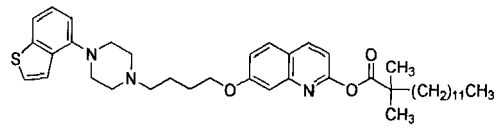
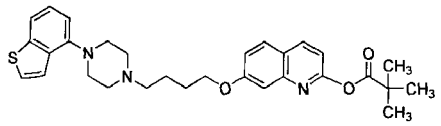
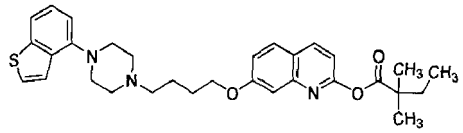
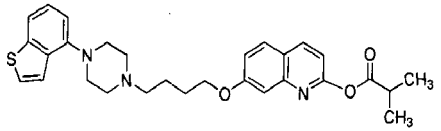
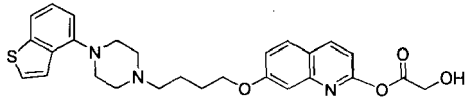
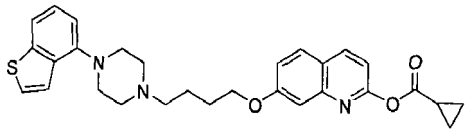
(continued)

Example	Structure Formula	
616		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl propionate
617		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl butyrate
618		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl pentanoate
619		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl hexanoate
620		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl heptanoate
621		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl octanoate
622		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl nonanoate
623		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl decanoate

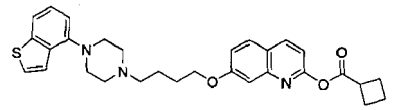
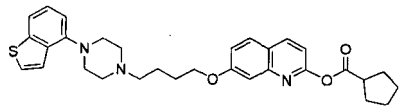
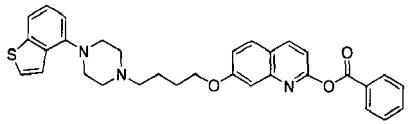
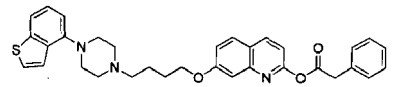
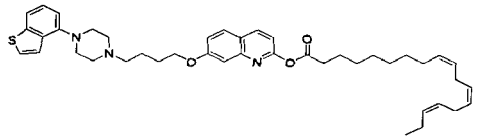
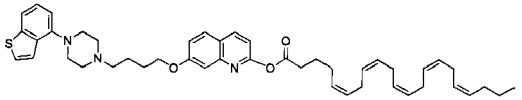
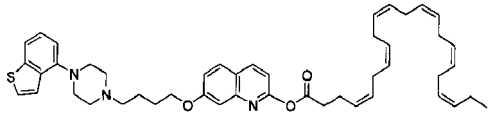
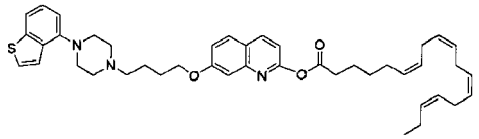
(continued)

Example	Structure Formula	
624		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl undecanoate
625		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl tridecanoate
626		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl tetradecanoate
627		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl pentadecanoate
628		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl palmitate
629		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl heptadecanoate
630		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl stearate
631		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl icosanoate

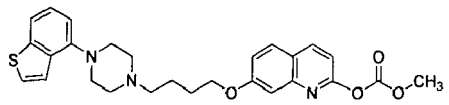
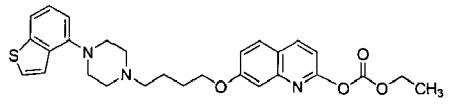
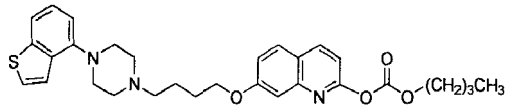
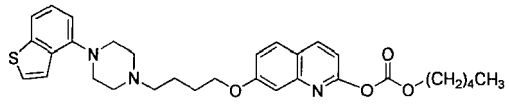
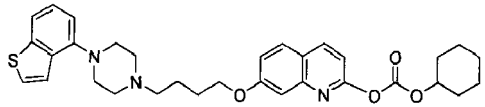
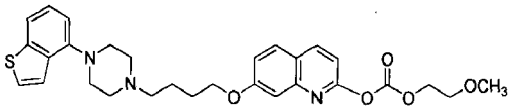
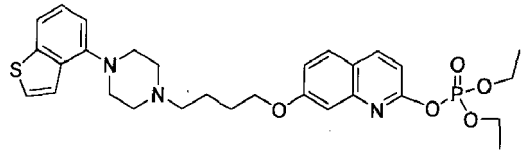
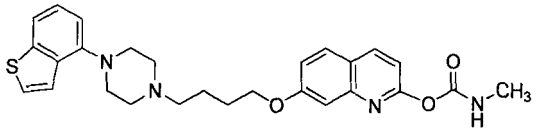
(continued)

Example	Structure Formula	
632		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 2,2-dimethyltetradecanoate
633		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl pivalate
634		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 2,2-dimethylbutanoate
635		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl isobutyrate
636		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 2-hydroxyacetate
637		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl cyclopropanecarboxylate

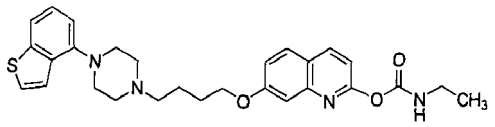
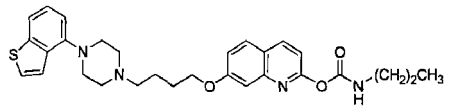
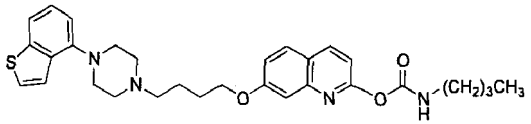
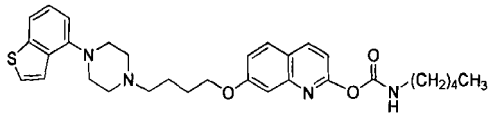
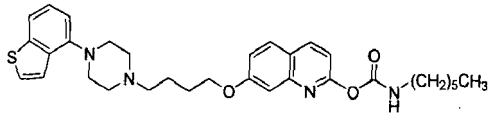
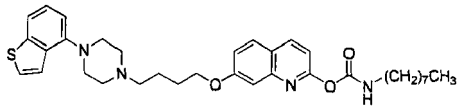
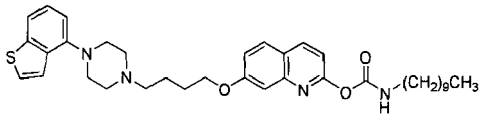
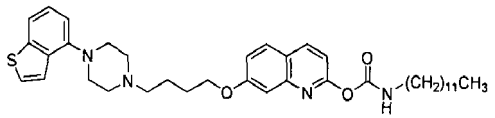
(continued)

Example	Structure Formula	
638		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl cyclobutanecarboxylate
639		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl cyclopentanecarboxylate
640		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl benzoate
641		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 2-phenylacetate
642		(9Z,12Z,15Z)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl octadeca-9,12,15-trienoate
643		(5Z,8Z,11Z,14Z,17Z)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl henicosa-5,8,11,14,17-pentaenoate
644		(4Z,7Z,10Z,13Z,16Z,19Z)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl docosa-4,7,10,13,16,19-hexaenoate
645		(6Z,9Z,12Z,15Z)-7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl octadeca-6,9,12,15-tetraenoate

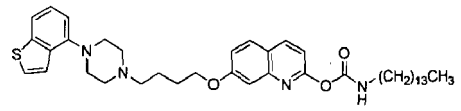
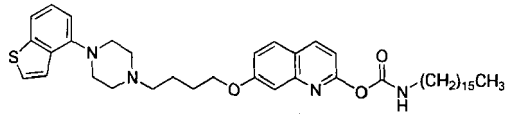
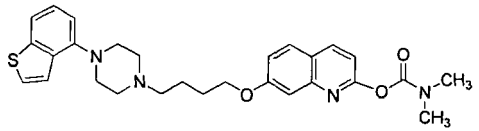
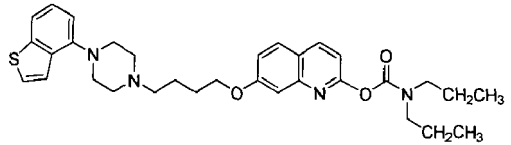
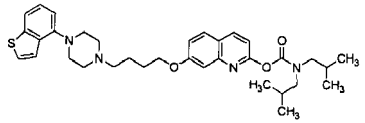
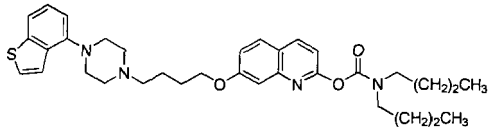
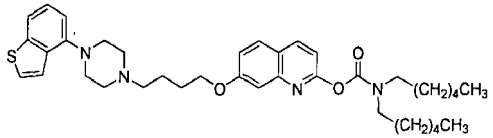
(continued)

Example	Structure Formula	
646		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl methyl carbonate
647		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl ethyl carbonate
648		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl butyl carbonate
649		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl pentyl carbonate
650		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl cyclohexyl carbonate
651		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 2-methoxyethyl carbonate
652		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl diethyl phosphate
653		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl methylcarbamate

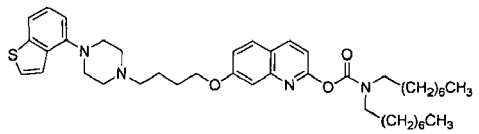
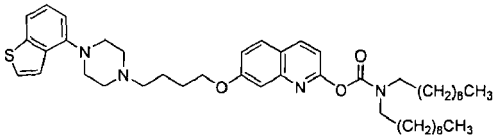
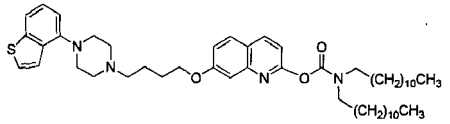
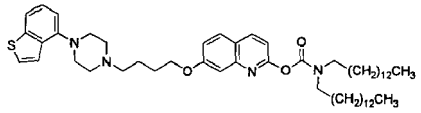
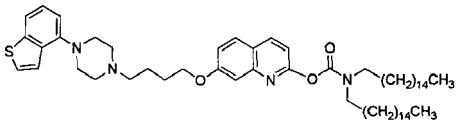
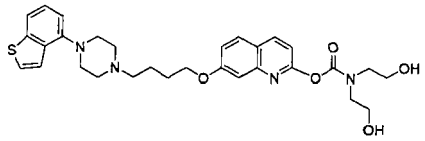
(continued)

Example	Structure Formula	
654		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl ethylcarbamate
655		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl propylcarbamate
656		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl butylcarbamate
657		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl pentylcarbamate
658		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl hexylcarbamate
659		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl octylcarbamate
660		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl decylcarbamate
661		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dodecylcarbamate

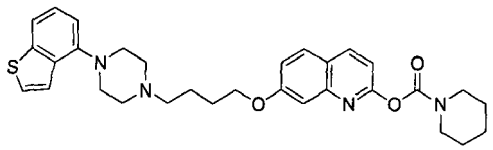
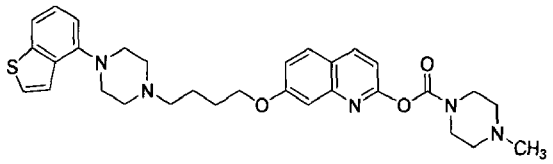
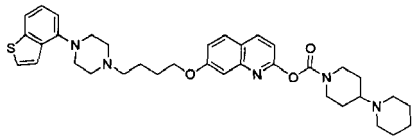
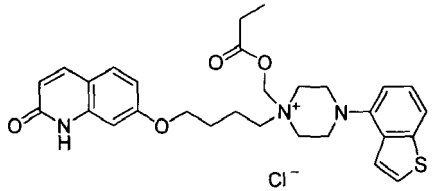
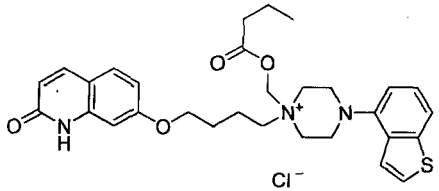
(continued)

Example	Structure Formula	
662		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl tetradecylcarbamate
663		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl hexadecylcarbamate
664		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dimethylcarbamate
665		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dipropylcarbamate
666		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl diisobutylcarbamate
667		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dibutylcarbamate
668		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dihexylcarbamate

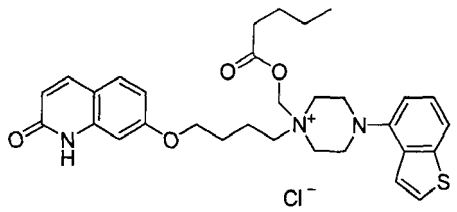
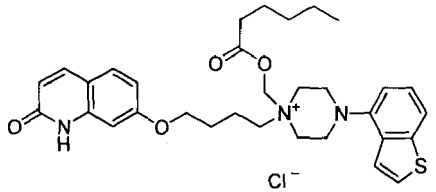
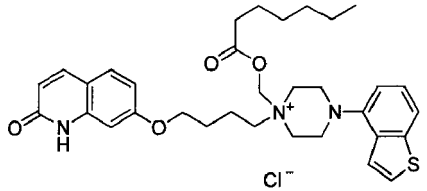
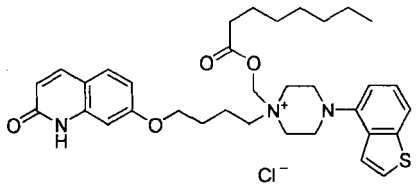
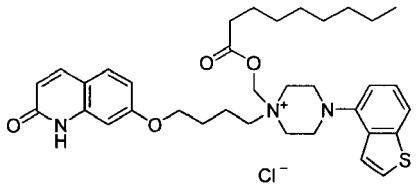
(continued)

Example	Structure Formula	
669		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dioctylcarbamate
670		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl didecylcarbamate
671		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)q uinolin-2-yl didodecylcarbamate
672		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl ditetradecylcarbamate
673		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl dihexadecylcarbamate
674		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl bis(2-hydroxyethyl)carbamate

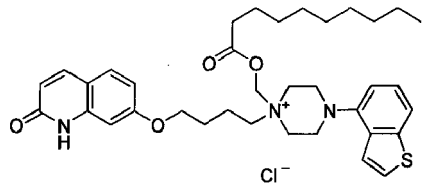
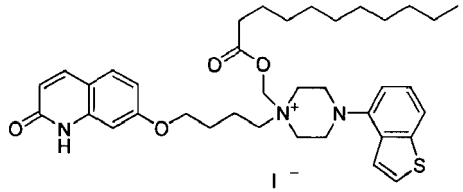
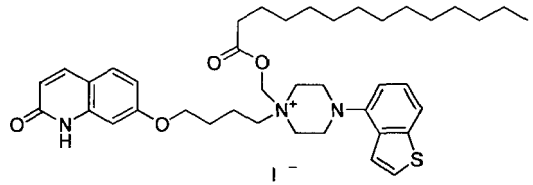
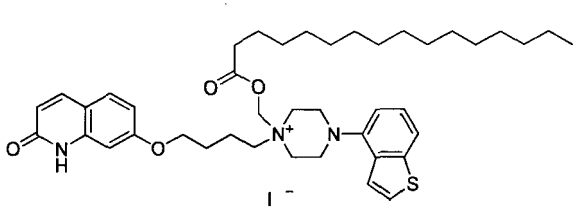
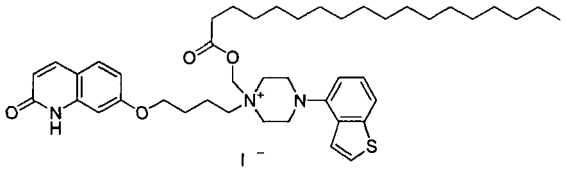
(continued)

Example	Structure Formula	
675		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl piperidine-1-carboxylate
676		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 4-methylpiperazine-1-carboxylate
677		7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl 1,4'-bipiperidine-1'-carboxylate
678		4-(benzo[b]thiophen4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(propionyloxymethyl)piperazi n-1-ium chloride
679		4-(benzo[b]thiophen-4-yl)-1-(butyryfoxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride

(continued)

Example	Structure Formula	
680		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(pentanoyloxymethyl)piperazi n-1-ium chloride
681		4-(benzo[b]thiophen-4-yl)-1-(hexanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
682		4-(benzo[b]thiophen-4-yl)-1-(heptanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
683		4-(benzo[b]thiophen-4-yl)-1-(octanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
684		4-(benzo[b]thiophen-4-yl)-1-(nonanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride

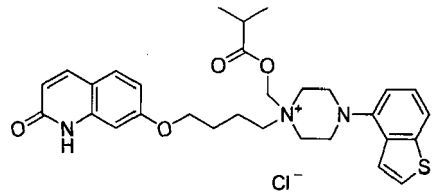
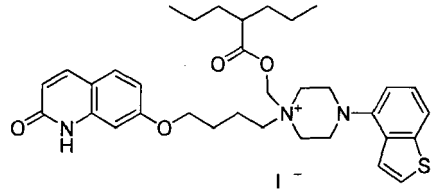
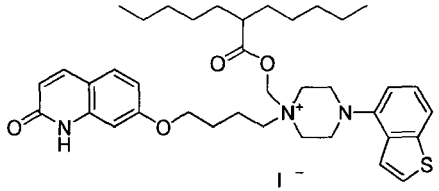
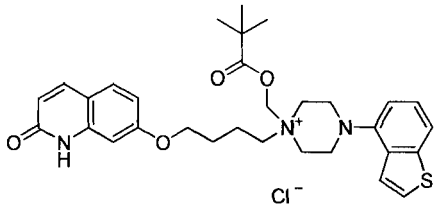
(continued)

Example	Structure Formula	
685		4-(benzo[b]thiophen-4-yl)-1-(decanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
686		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(undecanoyloxymethyl)pipera zin-1-ium iodide
687		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(tetradecanoyloxymethyl)pipe razin-1-ium iodide
688		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(palmitoyloxymethyl)piperazin -1-ium iodide
689		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(stearoyloxymethyl)piperazin-1-ium iodide

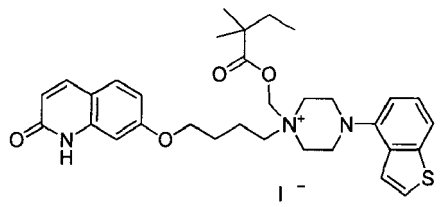
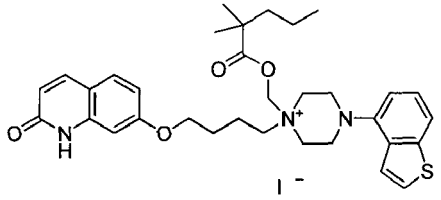
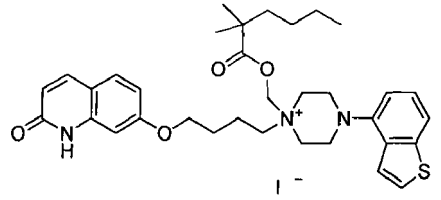
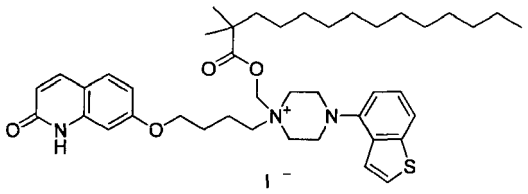
(continued)

Example	Structure Formula	
690		4-(benzo[b]thiophen-4-yl)-1-(icosanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
691		4-(benzo[b]thiophen-4-yl)-1-(docosanoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
692		4-(benzo[b]thiophen-4-yl)-1-(cyclopentanecarbonyloxyme thyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
693		4-(benzo[b]thiophen-4-yl)-1-(cyclohexanecarbonyloxymet hyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide

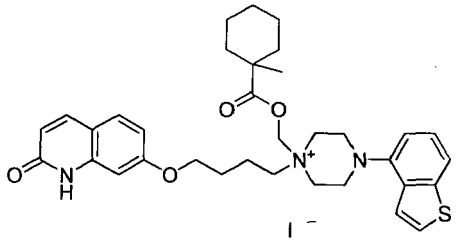
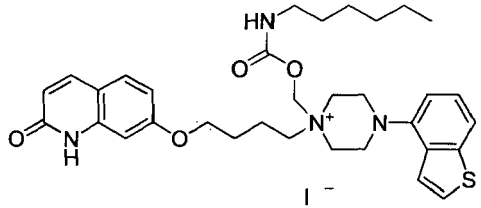
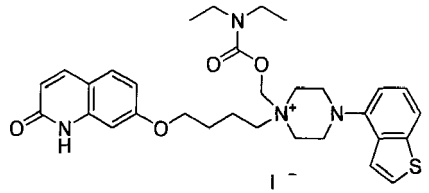
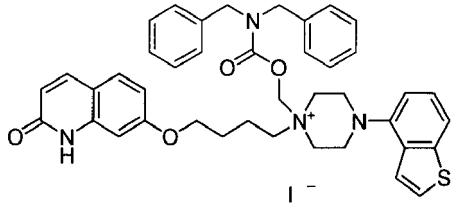
(continued)

Example	Structure Formula	
694		4-(benzo[b]thiophen-4-yl)-1-(isobutyryloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
695		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-((2-propylpentanoyloxy)methyl)pi perazin-1-ium iodide
696		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-((2-pentylheptanoyloxy)methyl)pi perazin-1-ium iodide
697		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(pivaloyloxymethyl)piperazin-1-ium chloride

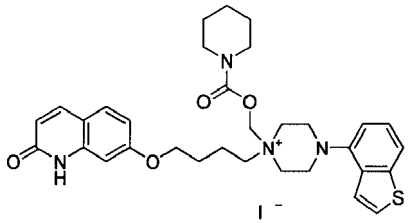
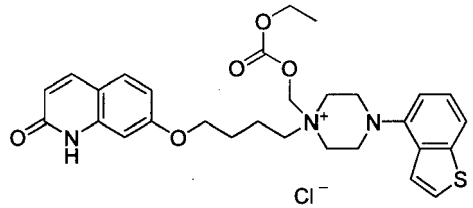
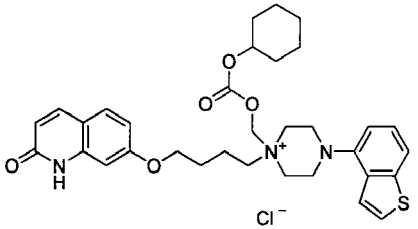
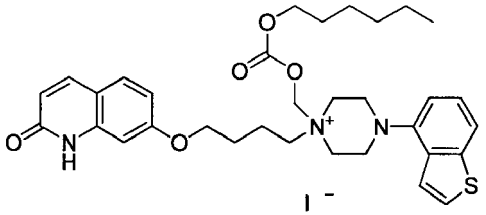
(continued)

Example	Structure Formula	
698		4-(benzo[b]thiophen-4-yl)-1-((2,2-dimethylbutanoyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
699		4-(benzo[b]thiophen-4-yl)-1-((2,2-dimethylpentanoyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
700		4-(benzo(b]thiophen-4-yl)-1-((2,2-dimethylhexanoyloxy)methyl) -1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
701		4-(benzo[b]thiophen-4-yl)-1-((2,2-dimethyltetradecanoyloxy)me thyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide

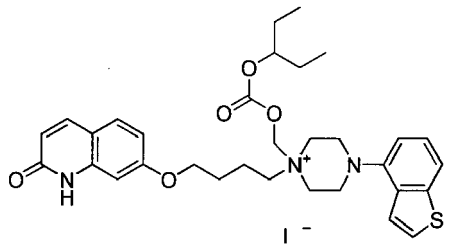
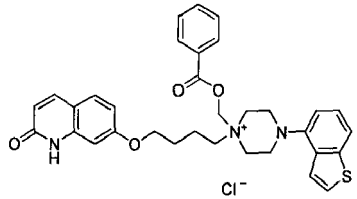
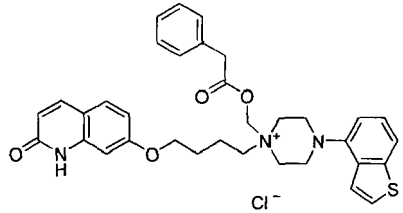
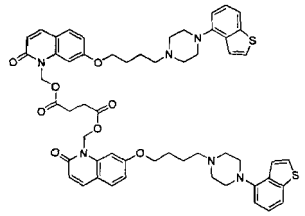
(continued)

Example	Structure Formula	
702		4-(benzo[b]thiophen-4-yl)-1-((1-methylcyclohexanecarbonylo xy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
703		4-(benzo[b]thiophen-4-yl)-1-((hexylcarbamoyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
704		4-(benzo[b]thiophen-4-yl)-1-((diethylcarbamoyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide
705		4-(benzo[b]thiophen-4-yl)-1-((dibenzylcarbamoyloxy)meth yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide

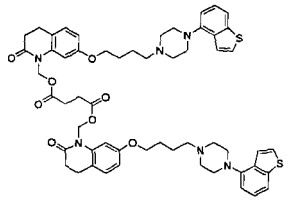
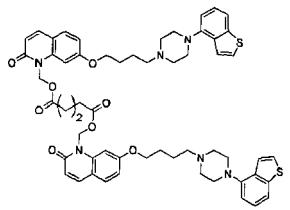
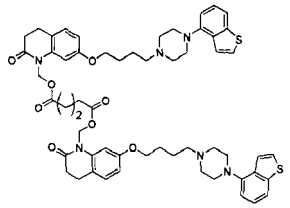
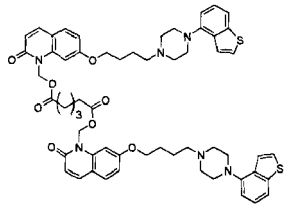
(continued)

Example	Structure Formula	
706		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-((piperidine-1-carbonyloxy)methyl)piperazin -1-ium iodide
707		4-(benzo[b]thiophen-4-yl)-1-((ethoxycarbonyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
708		4-(benzo[b]thiophen-4-yl)-1-((cyclohexyloxycarbonyloxy) methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
709		4-(benzo[b]thiophen-4-yl)-1-((hexyloxycarbonyloxy)methyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium iodide

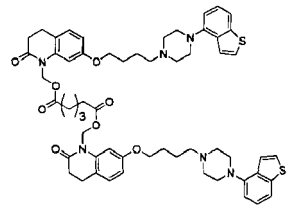
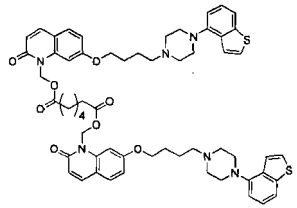
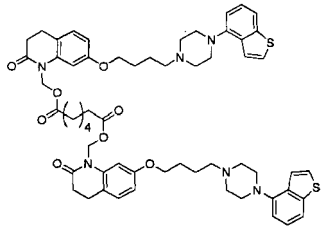
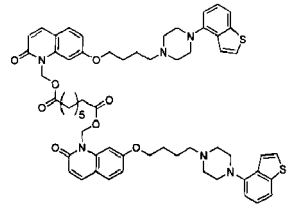
(continued)

Example	Structure Formula	
710		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-(((pentan-3-yloxy)carbonyloxy)methyl)pip erazin-1-ium iodide
711		4-(benzo[b]thiophen-4-yl)-1-(benzoyloxymethyl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)piperazin-1-ium chloride
712		4-(benzo[b]thiophen-4-yl)-1-(4-(2-oxo-1,2-dihydroquinolin-7-yloxy)butyl)-1-((2-phenylacetoxy)methyl)pipera zin-1-ium chloride
713		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) succinate

(continued)

Example	Structure Formula	
714		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) succinate
715		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) glutarate
716		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) glutarate
717		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) adipate

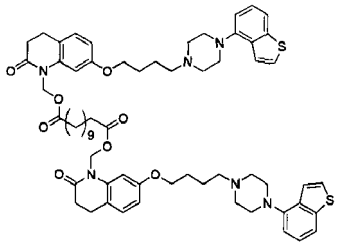
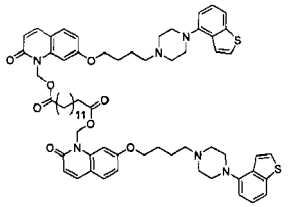
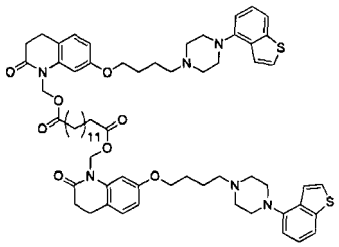
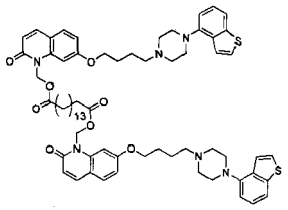
(continued)

Example	Structure Formula	
718		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) adipate
719		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) heptanedioate
720		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) heptanedioate
721		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) octanedioate

(continued)

Example	Structure Formula	
722		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) octanedioate
723		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) decanedioate
724		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) decanedioate
725		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) dodecanedioate

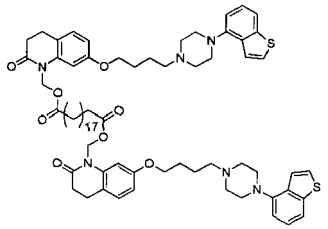
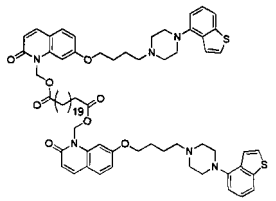
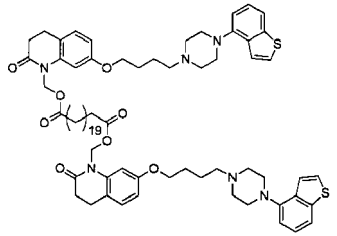
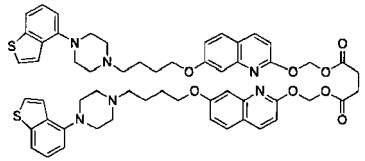
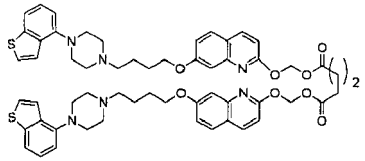
(continued)

Example	Structure Formula	
726		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) dodecanedioate
727		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) tetradecanedioate
728		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) tetradecanedioate
729		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) hexadecanedioate

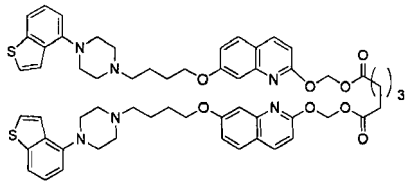
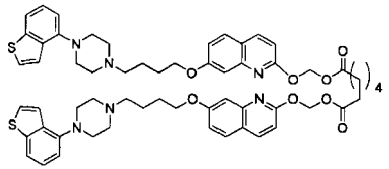
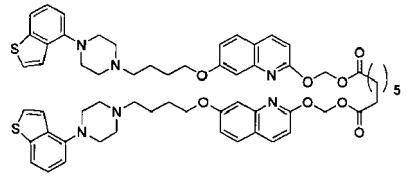
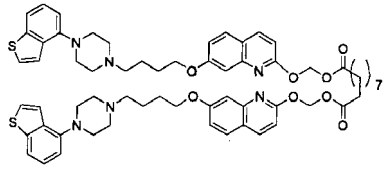
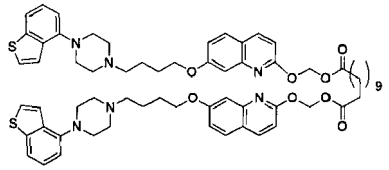
(continued)

Example	Structure Formula	
730		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) hexadecanedioate
731		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) octadecanedioate
732		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) octadecanedioate
733		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) icosanedioate

(continued)

Example	Structure Formula	
734		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) icosanedioate
735		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxoquinolin-1 (2H)-yl)methyl) docosanedioate
736		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)-2-oxo-3,4-dihydroquinolin-1(2H)-yl)methyl) docosanedioate
737		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) succinate
738		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) glutarate

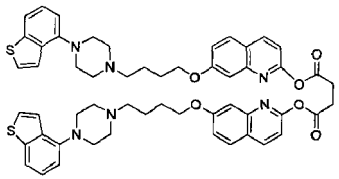
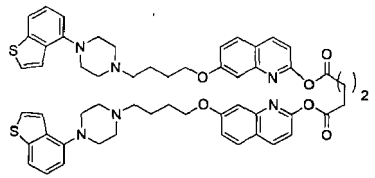
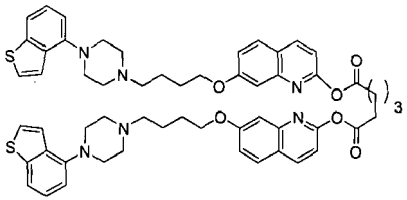
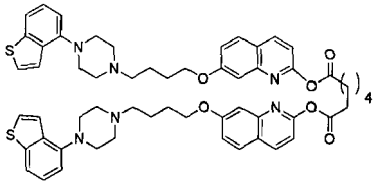
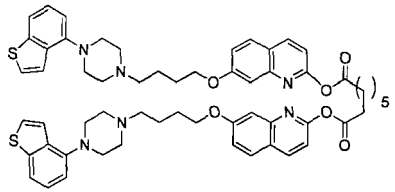
(continued)

Example	Structure Formula	
739		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) adipate
740		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) heptanedioate
741		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) octanedioate
742		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) decanedioate
743		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) dodecanedioate

(continued)

Example	Structure Formula	
744		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) tetradecanedioate
745		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) hexadecanedioate
746		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) octadecanedioate
747		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) icosanedioate
748		bis((7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yloxy)methyl) docosanedioate

(continued)

Example	Structure Formula	
749		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) succinate
750		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) glutarate
751		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) adipate
752		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) heptanedioate
753		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) octanedioate

(continued)

Example	Structure Formula	
754		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) decanedioate
755		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) dodecanedioate
756		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) tetradecanedioate
757		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) hexadecanedioate
758		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) octadecanedioate

(continued)

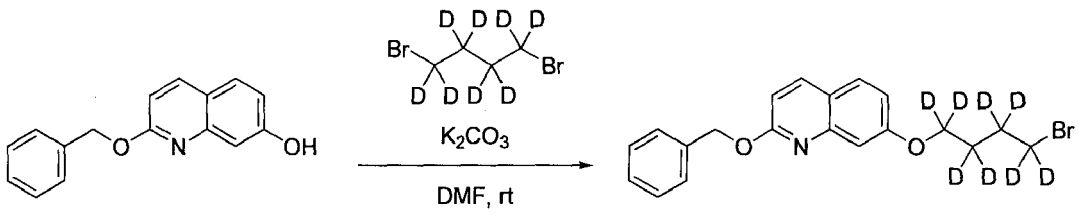
Example	Structure Formula	
759		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) icosanedioate
760		bis(7-(4-(4-(benzo[b]thiophen-4-yl)piperazin-1-yl)butoxy)quinolin-2-yl) docosanedioate
*example not falling within the scope of the invention as claimed		

[0522] Example A: Synthesis of deuteride of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one
A-1: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

(synthesis method 1)

step 1: Synthesis of 2-benzyloxy-7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)quinoline

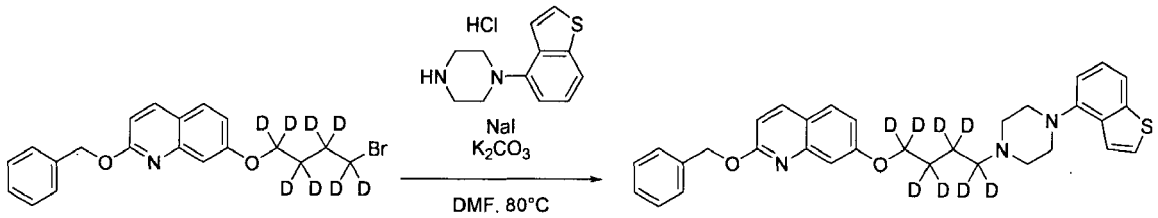
[0523]



[0524] To a mixture of 2-benzyloxy-7-hydroxy quinoline (2.52 g) and potassium carbonate (1.67 g) in dimethylformamide (25 ml) was added 1,4-dibromobutane-d_8 (99.6 atom % D: 2.4 ml), and the mixture was stirred at room temperature overnight. To the reaction mixture was added water, ethyl acetate, the insoluble material was filtered off, and the filtrate was partitioned, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate=10:0→9:1) to give 2-benzyloxy-7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)quinoline (3.14 g).
2-benzyloxy-7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)quinoline : white powder, ^{1}H-NMR ($CDCl_3$) δ: 5.52 (2H, s), 6.81 (1H, d, J=8.7Hz), 7.02 (1H, dd, J=8.8, 2.5Hz), 7.21 (1H, d, J=2.5Hz), 7.29-7.47 (3H, m), 7.49-7.56 (2H, m), 7.60 (1H, d, J=8.8Hz), 7.91 (1H, d, J=8.7Hz)

step 2: Synthesis of 2-benzyloxy-7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]quinoline

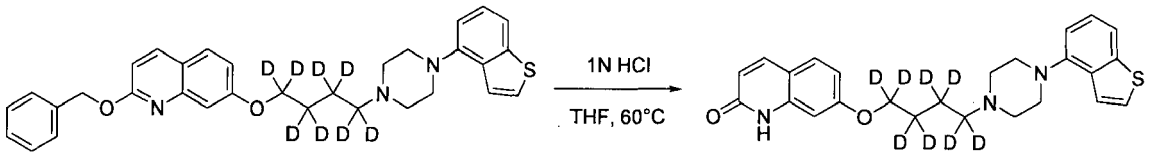
[0525]



[0526] A mixture of 2-benzyloxy-7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)quinoline (3.14 g), 1-benzothiophene-4-piperazine hydrochloride (2.43 g), sodium iodide (1.31 g) and potassium carbonate (2.64 g) in dimethylformamide (60 ml) was stirred at 80°C for 5 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane:ethyl acetate=7:3→5:5) to give 2-benzyloxy-7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]quinoline (3.73 g).
2-benzyloxy-7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]quinoline: pale-yellow amorphous solid, ^{1}H-NMR ($CDCl_3$) δ: 2.64-2.83 (4H, m), 3.14-3.25 (4H, m), 5.53 (2H, s), 6.81 (1H, d, J=8.8Hz), 6.89 (1H, d, J=7.6Hz), 7.03-7.08 (1H, m), 7.25-7.49 (7H, m), 7.50-7.63 (4H, m), 7.91 (1H, d, J=8.8Hz)

step 3: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

[0527]

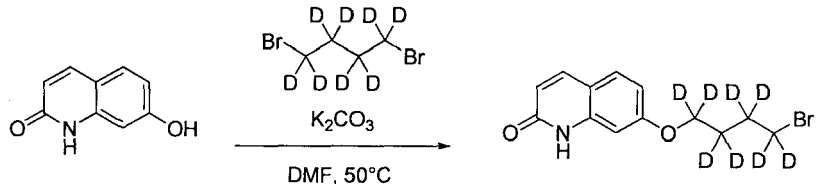


[0528] A mixture of 2-benzyloxy-7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]quinoline (3.73 g) and 1N hydrochloric acid (35.1 ml) in tetrahydrofuran (60 ml) was stirred at 60°C for 4 hr, and ice-cooled. Ice water was added, and the mixture was stirred. The precipitated solid was collected by filtration, washed with water and dried under reduced pressure. To a mixture of the obtained powder in ethanol (70 ml) was added under ice-cooling 1N sodium hydroxide to basify the mixture. The solvent was evaporated under reduced pressure and the residue was washed with water, and recrystallized from a mixture of ethanol and water to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one (2.29 g). 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one : white powder, ^{1}H-NMR (DMSO-d_6) δ: 2.54-2.67 (4H, m), 2.91-3.15 (4H, m), 6.29 (1H, d, J=9.5Hz), 6.75-6.83 (2H, m), 6.88 (1H, d, J=7.6Hz), 7.21-7.30 (1H, m), 7.39 (1H, d, J=5.5Hz), 7.50-7.66 (2H, m), 7.69 (1H, d, J=5.5Hz), 7.80 (1H, d, J=9.5Hz), 11.58 (1H, s)

(synthesis method 2)

step 1: Synthesis of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one

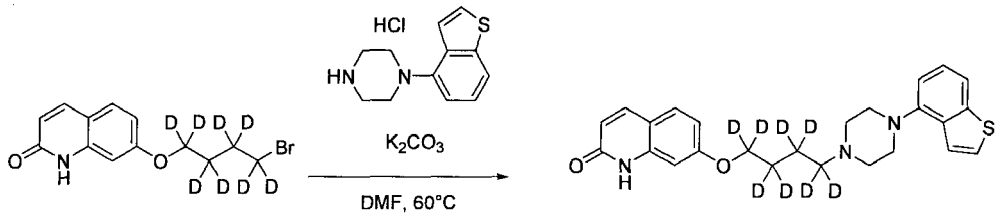
[0529]



[0530] To a mixture of 7-hydroxy-1H-quinolin-2-one [70500-72-0] (0.72 g) and potassium carbonate (0.68 g) in dimethylformamide (20 ml) was added 1,4-dibromobutane-d_8 (99.6 atom % D: 3 g), and the mixture was stirred at 50°C for 5 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 100 : 1) to give 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one (1.1 g). 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one : white powder like, ^{1}H-NMR ($CDCl_3$) δ: 6.56 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 7.45 (1H, d, J=8.6Hz), 7.74 (1H, d, J=9.4Hz), 12.33 (1H, brs).

step 2: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

[0531]



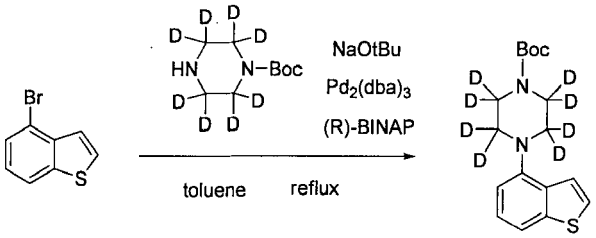
[0532] A mixture of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one (0.4 g), 1-benzothiophene-4-piperazine hydrochloride (0.37 g), potassium carbonate (0.45 g) and dimethylformamide (20 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one (0.3 g).
7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one same as that synthesized in synthesis method 1 was obtained.

white powder m.p. 177 - 179°C (recrystallized from EtOH)

A-2: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

step 1: Synthesis of tert-butyl 4-(benzo[b]thiophen-4-yl)piperazine-2,2,3,3,5,5,6,6-de-1-carboxylate

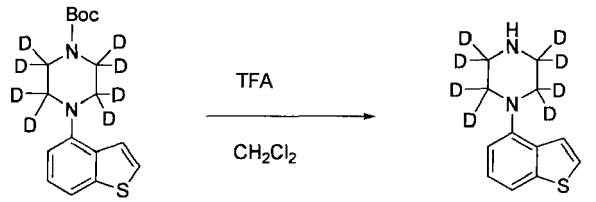
[0533]



[0534] A mixture of 4-bromo-benzo[b]thiophene [5118-13-8] (0.55 g), tert-butyl 1-piperazine-2,2,3,3,5,5,6,6-d_8-carboxylate (98.3 atom % D :0.5 g), sodium t-butoxide (0.25 g), (R)-(+)-BINAP (30 mg), tris(dibenzylideneacetone)dipalladium(0) (30 mg) and toluene (20 ml) was heated under reflux under an argon atmosphere for 3 hr. Water was poured into the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (ethyl acetate : n-hexane = 1 : 100) to give tert-butyl 4-(benzo[b]thiophen-4-yl)piperazine-2,2,3,3,5,5,6,6-d_8-1-carboxylate (0.41 g).
tert-butyl 4-(benzo[b]thiophen-4-yl)piperazine-2,2,3,3,5,5,6,6-d_8-1-carboxylate:
yellow powder
^{1}H-NMR ($CDCl_3$) δ: 1.50 (9H, s), 3.03-3.09 (0.06H, br), 3.59-3.65 (0.06H, br), 6.87 (1H, dd, J=0.8, 7.7Hz), 7.28 (1H, t, J=7.8Hz), 7.41 (2H, s), 7.57 (1H, d, J=8.0Hz).
Confirmed by ^{1}H-NMR ($CDCl_3$): at least 98 atom % D.

step 2: Synthesis of 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8

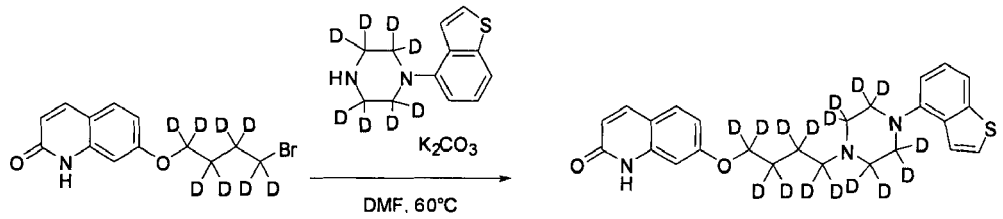
[0535]



[0536] To a solution of tert-butyl 4-(benzo[b]thiophen-4-yl)piperazine-2,2,3,3,5,5,6,6-d_8-1-carboxylate (0.57 g) in dichloromethane (5 ml) was added trifluoroacetic acid (1 ml) and the mixture was stirred at room temperature for 3 hr. Water was poured into the reaction mixture, alkalified with aqueous sodium hydroxide solution, and the mixture was extracted with dichloromethane, washed with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (basic silica gel, ethyl acetate : methanol= 20 : 1) to give 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8 (0.31 g).
1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8: oil brown
^{1}H-NMR ($CDCl_3$) δ: 3.06-3.10 (0.13H, br), 6.88 (1H, dd, J=0.8, 7.6Hz), 7.27 (1H, t, J=7.8Hz), 7.38 (1H, d, J=5.4Hz), 7.42 (1H, dd, J=0.7, 5.5Hz), 7.54 (1H, d, J=8.1Hz).
Confirmed by ^{1}H-NMR ($CDCl_3$): at least 98 atom % D.

step 3: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

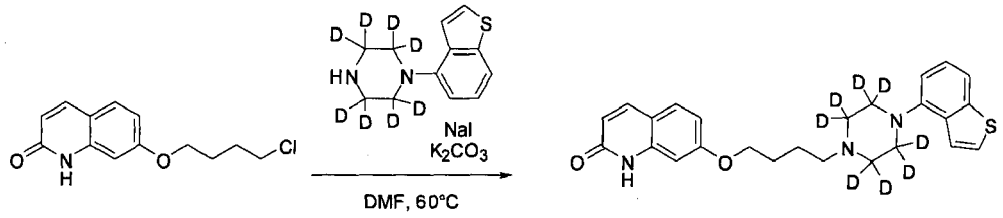
[0537]



[0538] A mixture of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one (633 mg) obtained in Example A-1, synthesis method 2, step 1, 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8 (471 mg) obtained in this Example, step 2, potassium carbonate (374 mg) and dimethylformamide (20 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one (0.45 g). 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one: yellow powder m.p. 176 - 178°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ: 2.64-2.72 (0.06H, m), 3.02-3.20 (0.06H, m), 6.55 (1H, d, J = 9.4Hz), 6.79-6.86 (2H, m), 6.89 (1H, dd, J = 0.7, 7.6Hz), 7.26 (1H, t, J = 7.8Hz), 7.36-7.46 (3H, m), 7.54 (1H, d, J = 8.0Hz), 7.72 (1H, d, J = 9.4Hz), 12.34 (1H, brs).

A-3: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_e)-butoxy]-1H-quinolin-2-one

[0539]

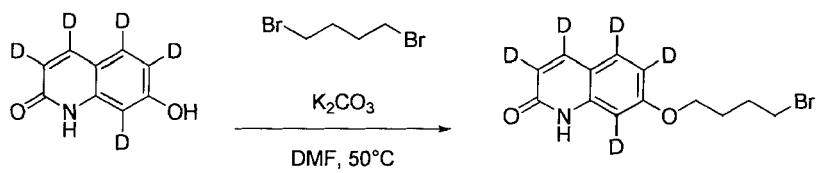


[0540] A mixture of 7-(4-chlorobutoxy)-1H-quinolin-2-one (340 mg), 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8 (310 mg) obtained in Example A-2, step 2, sodium iodide (220 mg), potassium carbonate (240 mg) and dimethylformamide (10 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy]-1H-quinolin-2-one (0.31 g). 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy]-1H-quinolin-2-one: yellow powder m.p. 175.5 - 177°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) 5: 1.70-1.84 (2H, m), 1.84-1.96 (2H, m), 2.54 (2H, t, J = 7.5Hz), 2.66-2.72 (0.06H, m), 3.14-3.18 (0.06H, m), 4.12 (2H, t, J = 6.2Hz), 6.54 (1H, d, J = 9.4Hz), 6.79-6.86 (2H, m), 6.89 (1H, dd, J = 0.6, 7.6Hz), 7.26 (1H, t, J = 7.9Hz), 7.36-7.48 (3H, m), 7.54 (1H, d, J = 8.0Hz), 7.72 (1H, d, J = 9.4Hz), 12.27 (1H, brs).

A-4: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8) -butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5

step 1: Synthesis of 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5

[0541]

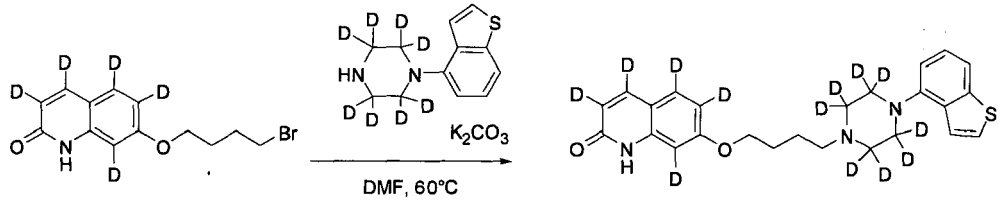


[0542] To a mixture of 7-hydroxy-1H-quinolin-2-one-3,4,5,6,8-d_5 (99 atom % D: 3 g) obtained by a deuteration reaction

(Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 7-hydroxy-1H-quinolin-2-one [70500-72-0] and potassium carbonate (3 g) in dimethylformamide (120 ml) was added 1,4-dibromobutane (6.5 ml), and the mixture was stirred at 50°C for 4 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 100 : 1) to give 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5 (3.45 g). 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5 . white powder like
^{1}H-NMR ($CDCl_3$) δ ppm: 1.94-2.05 (2H, m), 2.05-2.15 (2H, m), 3.51(2H, t, J=6.5Hz), 4.10(2H, t, J=6.0Hz), 6.55 (0.01H, s), 6.79-6.81 (2H, m), 7.52 (0.008H, s), 7.73 (0.008H, s), 11.89 (1H, brs).

step 2: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8) butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5

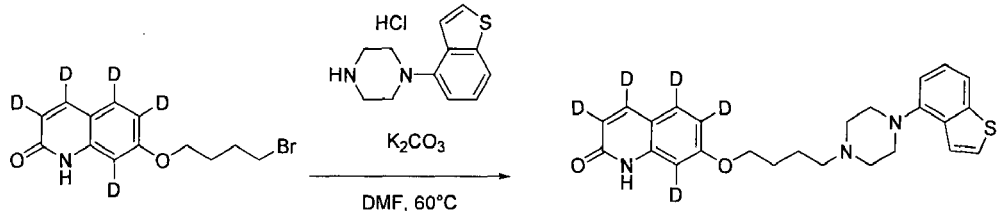
[0543]



[0544] A mixture of 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.6 g), 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8 (0.5 g), potassium carbonate (360 mg) and dimethylformamide (20 ml) was stirred at 60°C for 5 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d8))-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.45 g).
7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 175.5 - 177.5°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 1.70-1.84 (2H, m), 1.80-1.96 (2H, m), 2.54 (2H, t, J = 7.4Hz), 2.66-2.72 (<0.07H, br), 3.14-3.20 (<0.06H, br), 4.12 (2H, t, J = 6.2Hz), 6.54 (<0.008H, s), 6.82 (<0.025H, d, J = 5.7Hz), 6.89 (1H, dd, J = 0.6, 7.7Hz), 7.26 (1H, t, J = 7.9Hz), 7.38 (1H, d, J = 5.5Hz), 7.42 (1H, d, J = 5.9Hz), 7.54 (1H, d, J = 8.0Hz), 7.72 (<0.01H, s), 12.10 (1H, brs).

A-5: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5

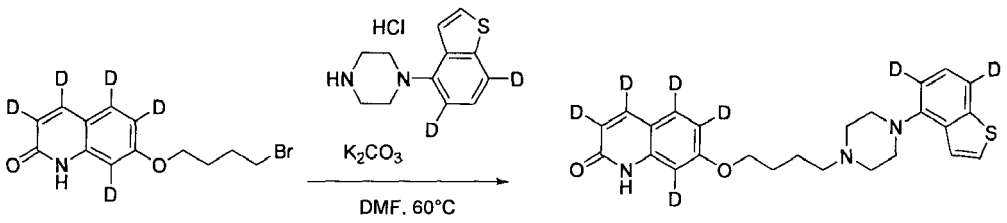
[0545]



[0546] A mixture of 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.6 g) obtained in Example A-4, step 1, 1-benzothiophene-4-piperazine hydrochloride (0.56 g), potassium carbonate (690 mg) and dimethylformamide (20 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.5 g). 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 177 - 179°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 1.70-1.85 (2H, m), 1.85-1.95 (2H, m), 2.54 (2H, t, J = 7.4Hz), 2.66-2.82 (4H, br), 3.14-3.28 (4H, br), 4.08-4.12 (2H, m), 6.54 (<0.01H, s), 6.83 (<0.02H, d, J = 10.3Hz), 6.89 (1H, d, J = 7.7Hz), 7.26 (1H, t, J = 7.8Hz), 7.36 (1H, d, J = 5.5Hz), 7.42 (1H, dd, J =0.6, 5.5Hz), 7.54 (1H, d, J=8.0Hz), 7.72 (<0.01H, s), 12.24 (1H, brs).

A-6: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5

[0547]

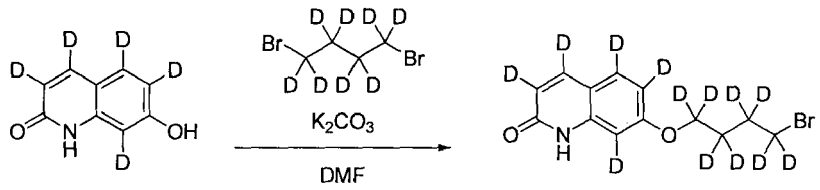


[0548] A mixture of 7-(4-bromobutoxy)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.6 g) obtained in Example A-4, step 1, 1-benzo[b]thiophen-4-yl-5,7-d_2-piperazine hydrochloride (0.56 g) obtained by a deuteration reaction (Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 1-benzothiophene-4-piperazine hydrochloride, potassium carbonate (690 mg) and dimethylformamide (20 ml) was stirred at 60°C for 5 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.42 g).
7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 176.5 - 178.5°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 1.70-1.98 (4H, m), 2.54 (2H, t, J = 7.4Hz), 2.66-2.80 (4H, br), 3.14-3.26 (4H, br), 4.12 (2H, t, J = 6.1Hz), 6.54 (<0.01H, s), 6.83 (<0.02H, d, J = 10.0Hz), 6.89 (<0.01H, d, J = 7.7Hz), 7.08(<0.02H, m), 7.25-7.28 (1H, m), 7.38 (0.89H, d, J = 5.5Hz), 7.42 (1H, d, J =5.5Hz), 7.54 (0.06H, d, J = 8.1Hz), 7.72 (<0.01H, s), 12.23 (1H, brs).

A-7: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d5

step 1: Synthesis of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one-3,4,5,6,8-d_5

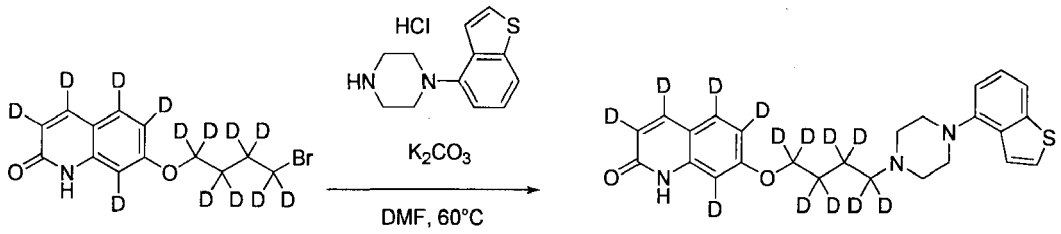
[0549]



[0550] To a mixture of 7-hydroxy-1H-quinolin-2-one-3,4,5,6,8-d_5 (99 atom % D: 1.65 g) obtained by a deuteration reaction (Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 7-hydroxy-1H-quinolin-2-one [70500-72-0] and potassium carbonate (1.51 g) in dimethylformamide (40 ml) was added 1,4-dibromobutane-d_8 (99.6 atom % D: 5.55 g), and the mixture was stirred at 50°C for 4 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 100 : 1) to give 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one-3,4,5,6,8-d_5 (1.1 g).
7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one-3,4,5,6,8-d_5 : white powder like, ^{1}H-NMR ($CDCl_3$) δ ppm: 6.55 (0.008H, s), 6.81 (0.021H, d, J=9.6Hz), 7.45 (0.008H, s), 7.74 (0.008H, s), 12.28(1H, brs).

step 2: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5

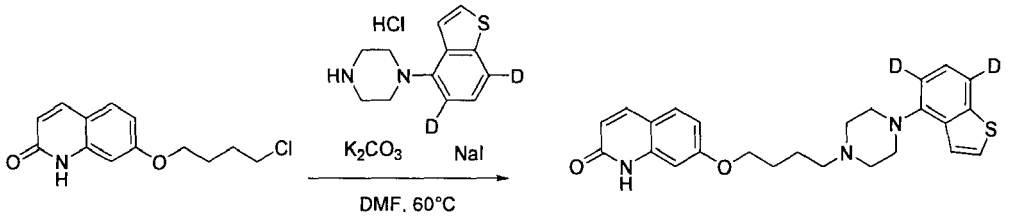
[0551]



[0552] A mixture of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.5 g) obtained in this Example, step 1, 1-benzothiophene-4-piperazine hydrochloride (0.45 g), potassium carbonate (0.56 g) and dimethylformamide (20 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.24 g).
7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 176 - 177.5°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 2.60-2.84 (4H, br), 3.10-3.28 (4H, br), 6.54 (<0.007H, s), 6.82 (<0.02H, d, J = 6.0Hz), 6.89 (1H, dd, J = 0.5,7.6Hz), 7.27 (1H, t, J = 7.8Hz), 7.38 (1H, d, J = 5.6Hz), 7.42 (1H, dd, J =0.5, 5.6Hz), 7.54 (1H, d, J = 8.0Hz), 7.72 (<0.009H, s), 12.13 (1H, brs).

A-8: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one

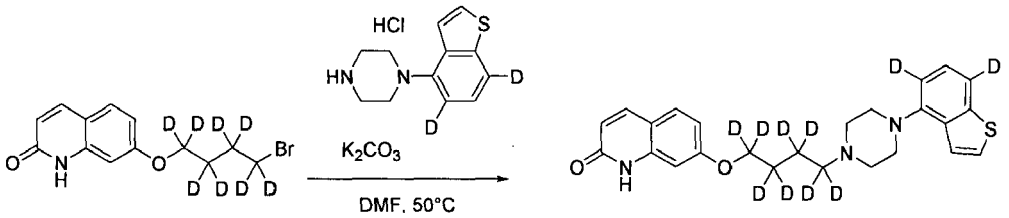
[0553]



[0554] A mixture of 7-(4-chlorobutoxy)-1H-quinolin-2-one (0.5 g), 1-benzo[b]thiophen-4-yl-5,7-d_2-piperazine hydrochloride (0.56 g) obtained by a deuteration reaction (Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 1-benzothiophene-4-piperazine hydrochloride, sodium iodide (0.33 g), potassium carbonate (690 mg) and dimethylformamide (20 ml) was stirred at 60°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (0.31 g).
7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy]-1H-quinolin-2-one: white powder m.p. 179.5 - 181.5°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 1.68-1.84 (2H, m), 1.84-1.96 (2H, m), 2.54 (2H, t, J = 7.4Hz), 2.66-2.80 (4H, br), 3.16-3.26 (4H, br), 4.12 (2H, t, J = 6.2Hz), 6.54 (1H, d, J =9.4Hz), 6.78-6.86 (2H, m), 6.90 (<0.02H, d, J = 7.7Hz), 7.25-7.28 (1H, m), 7.38 (0.82H, d, J = 5.6Hz), 7.40-7.48 (2H, m), 7.54 (0.05H, d, J=8.6Hz), 7.72 (1H, d, J=9.4Hz), 12.09 (1H, brs).

A-9: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one

[0555]



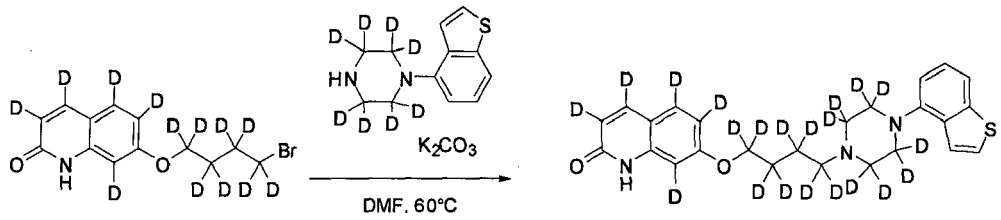
[0556] A mixture of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one (0.5 g) obtained in Example A-1, synthesis method 2, step 1, 1-benzo[b]thiophen-4-yl-5,7-d_2-piperazine hydrochloride (0.46 g) obtained by a deuteration reaction (Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 1-benzothiophene-4-piperazine hydrochloride, potassium carbonate (0.57 g) and dimethylformamide (20 ml) was stirred at 50°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one (0.35 g).

7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one: white powder m.p. 176.5 - 178.5°C (recrystallized from EtOH)

^{1}H-NMR ($CDCl_3$) δ ppm : 2.66-2.80 (4H, br), 3.10-3.28 (4H, br), 6.55 (1H, d, J =9.4Hz), 6.81 (1H, dd, J = 2.4, 8.6Hz), 6.85 (1H, d, J = 2.3Hz), 6.89 (<0.04H, d, J =7.7Hz), 7.24-7.28 (1H, m), 7.38 (0.85H, d, J=5.6Hz), 7.40-7.46(2H, m), 7.54 (0.06H, dd, J = 0.5, 8.0Hz), 7.72 (1H, d, J = 9.4Hz), 12.47 (1H, brs).

A-10: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5

[0557]

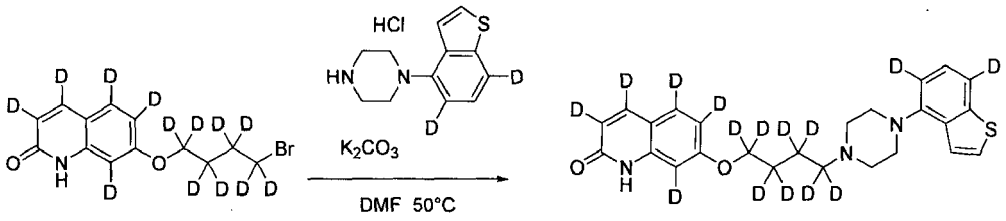


[0558] A mixture of 7-(4-bromobutoxy-l,1,2,2,3,3,4,4-dg)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.6 g) obtained in Example A-7, step 1, 1-benzo[b]thiophen-4-yl-piperazine-2,2,3,3,5,5,6,6-d_8 (0.57 g) obtained in Example A-2, step 2, potassium carbonate (380 mg) and dimethylformamide (20 ml) was stirred at 60°C for 5 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane : methanol= 30 : 1) to give 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.45 g).

7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl-2,2,3,3,5,5,6,6-d_8)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 175.5 - 177.5°C (recrystallized from EtOH) ^{1}H-NMR ($CDCl_3$) δ ppm : 2.64-2.72 (<0.06H, br), 3.14-3.20 (<0.06H, br), 6.54 (<0.01H, s), 6.80-6.86 (<0.04H, m), 6.89 (1H, dd, J = 0.8, 7.6Hz), 7.26 (1H, t, J = 7.9Hz), 7.38 (1H, d, J = 5.5Hz), 7.41 (1H, dd, J = 0.7, 5.6Hz), 7.54 (1H, d, J = 8.0Hz), 7.72 (<0.01H, s), 12.35 (1H, brs).

A-11: Synthesis of 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5

[0559]

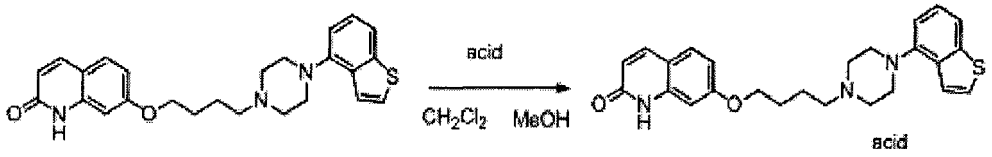


[0560] A mixture of 7-(4-bromobutoxy-1,1,2,2,3,3,4,4-d_8)-1H-quinolin-2-one-3,4,5,6,8-d_5 (0.5 g) obtained in Example A-7, step 1, 1-benzo[b]thiophen-4-yl-5,7-d_2-piperazine hydrochloride (0.46 g) obtained by a deuteration reaction (Org. Lett. 2004, 6, 1485.; Bull. Chem. Soc. Jpn. 2008, 81, 278.) of 1-benzothiophene-4-piperazine hydrochloride, potassium carbonate (0.56 g) and dimethylformamide (20 ml) was stirred at 50°C for 6 hr. Water was added to the reaction mixture, and the mixture was extracted with ethyl acetate, washed with water, and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (dichloromethane :

methanol= 30 : 1) to give 7-[4-(4-benzo [b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinoline-2-one-3,4,5,6,8-d_5 (0.34 g). 7-[4-(4-benzo[b]thiophen-4-yl-5,7-d_2-piperazin-1-yl)-butoxy-1,1,2,2,3,3,4,4-d_8]-1H-quinolin-2-one-3,4,5,6,8-d_5: white powder m.p. 175.5 - 177.5°C (recrystallized from EtOH)
^{1}H-NMR ($CDCl_3$) δ ppm : 2.66-2.80 (4H, br), 3.14-3.26 (4H, br), 6.54 (<0.01H, s), 6.83 (<0.02H, d, J = 11.2Hz), 6.89 (<0.01H, d, J = 7.6Hz), 7.06-7.10 (<0.02H, m), 7.25-7.28 (1H, m), 7.38 (0.86H, d, J = 5.6Hz), 7.42 (1H, d, J =5.6Hz), 7.54 (<0.05H, dd, J = 0.6, 8.0Hz), 7.72 (<0.01H, s), 12.28 (1H, brs).

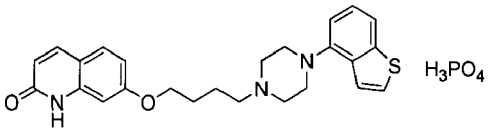
Example B: Synthesis of salt of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one

[0561]



phosphate:

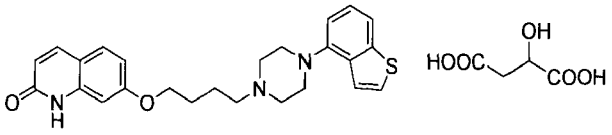
[0562] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (15 g) in dichloromethane (100 ml) and methanol (100 ml) was warmed to 60°C, dissolved, and phosphoric acid (4.39 g) was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one phosphate (17.9 g).
[0563] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one phosphate (17.5 g) was recrystallized from ethanol (550 ml) and water (550 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one phosphate (14.4 g).



[0564] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one phosphate : colorless crystals : m.p. 226 - 228°C (recrystallized from EtOH - H_2O)
^{1}H-NMR (DMSO-d_6) δ ppm : 1.66-1.76 (2H, m), 1.76-1.86 (2H, m), 2.63 (2H, t, J=7.0Hz), 2.76-2.86 (4H, br), 3.08-3.18 (4H, br), 4.07 (2H, t, J=6.2Hz), 6.30 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.90 (1H, d, J=7.4Hz), 7.28 (1H, t, J=7.8Hz), 7.42 (1H, d, J=5.5Hz), 7.56 (1H, d, J=9.4Hz), 7.63 (1H, d, J=8.0Hz), 7.71 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.2-12.2 (1H, br).

DL-malate:

[0565] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (15 g) in dichloromethane (100 ml) and methanol (100 ml) was warmed to 60°C, dissolved, and DL-malic acid (5.11 g) dissolved in water (10 ml) was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one DL-malate (20 g).
[0566] 7-[4-(4-Benzo[blthiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one DL-malate (20 g) was recrystallized from ethanol (350 ml) and water (50 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one DL-malate (14.5 g).



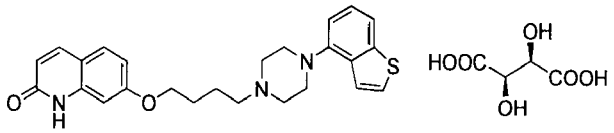
[0567] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one DL-malate: colorless crystal: m.p. 136 - 139°C (recrystallized from EtOH - H_2O)

^{1}H-NMR (DMSO-d_6) δ ppm : 1.64-1.76 (2H, m), 1.76-1.86 (2H, m), 2.62 (2H, t, J=7.1Hz), 2.74-2.86 (4H, br), 3.06-3.18 (4H, br), 4.06 (2H, t, J=6.0Hz), 4.21 (2H, s), 6.30 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.90 (1H, d, J=7.4Hz), 7.28 (1H, t, J=7.8Hz), 7.42 (1H, d, J=5.5Hz), 7.56 (1H, d, J=9.3Hz), 7.63 (1H, d, J=8.0Hz), 7.71 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.59 (1H, brs).

L (+)-tartrate :

[0568] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (15 g) in dichloromethane (100 ml) and methanol (100 ml) was heated to 60°C, dissolved, and L(+)-tartaric acid (5.72 g) dissolved in water (10 ml) was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one L(+)-tartrate (19.3 g).

[0569] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one L(+)-tartrate (19.3 g) was recrystallized from ethanol (700 ml) and water (250 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one L(+)-tartrate (16.5 g).



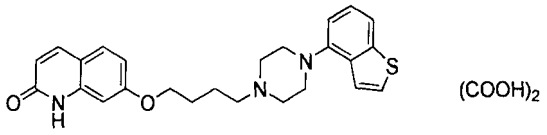
[0570] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one L(+)-tartrate: colorless crystal: m.p. 198 - 203°C (recrystallized from EtOH - H_2O)

^{1}H-NMR (DMSO-d_6) δ ppm : 1.64-1.76 (2H, m), 1.76-1.86 (2H, m), 2.41 (1H, dd, J=6.7, 15.6Hz), 2.59 (1H, dd, J=6.4, 15.6Hz), 2.66 (2H, t, J=7.2Hz), 2.78-2.88 (4H, br), 3.06-3.18 (4H, br), 4.07 (2H, t, J=6.2Hz), 4.16 (1H, t, J=6.5Hz), 6.30 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.90 (1H, d, J=7.2Hz), 7.29 (1H, t, J=7.8Hz), 7.43 (1H, dd, J=0.6, 5.5Hz), 7.56 (1H, d, J=9.3Hz), 7.63 (1H, d, J=8.0Hz), 7.71 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.59 (1H, brs).

oxalate:

[0571] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (3 g) in dichloromethane (20 ml) and methanol (20 ml) was warmed to 60°C, dissolved, and oxalic acid (0.69 g) dissolved in methanol (5 ml) was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one oxalate (3.3 g).

[0572] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one oxalate (1 g) was recrystallized from ethanol (20 ml) and water (20 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one oxalate (0.8 g).



[0573] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one oxalate : colorless crystal: m.p. 126.5 - 128°C (recrystallized from EtOH - H_2O)

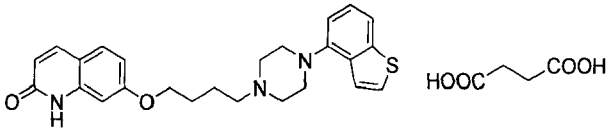
^{1}H-NMR (DMSO-d_6) δ ppm : 1.78-1.90 (4H, br) , 3.06-3.14 (2H, br) , 3.24-3.36 (4H, br), 3.62-4.24 (6H, br), 6.31 (1H, d, J=9.4Hz), 6.78-6.86 (2H, m), 6.95 (1H, d, J=7.4Hz), 7.31 (1H, t, J=7.9Hz), 7.48 (1H, dd, J=0.4, 5.6Hz), 7.57 (1H, d, J=9.4Hz), 7.69 (1H, d, J=8.1Hz), 7.75 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.62 (1H, brs).

succinate:

[0574] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (2 g) in dichloromethane (20 ml) and methanol (20 ml) was warmed to 60°C, dissolved, and succinic acid (0.6 g) dissolved in methanol-water was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one succinate (2.4 g).

[0575] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one succinate (1 g) was recrystallized from ethanol (20 ml) and water (8 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one succi-

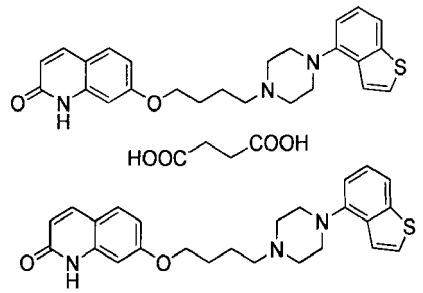
nate (0.74 g).



[0576] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one succinate: colorless crystal: m.p. 158.5 - 160°C (recrystallized from EtOH - H_2O)
^{1}H-NMR (DMSO-d_6) δ ppm : 1.60-1.70 (2H, m), 1.76-1.86 (2H, m), 2.41 (4H, s), 2.44-2.50 (2H, m), 2.60-2.70 (4H, br), 3.04-3.10 (4H, br), 4.06 (2H, t, J=6.4Hz), 6.29 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.89 (1H, d, J=7.3Hz), 7.27 (1H, t, J=7.8Hz), 7.40 (1H, dd, J=0.4, 5.6Hz), 7.56 (1H, d, J=9.3Hz), 7.61 (1H, d, J=8.0Hz), 7.69 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.58 (1H, brs).

1/2 succinate:

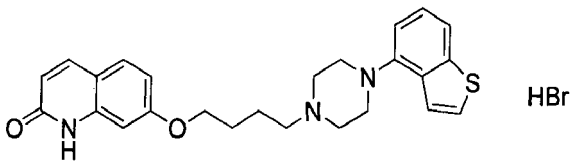
[0577] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (2 g) in dichloromethane (20 ml) and methanol (20 ml) was warmed to 60°C, dissolved, and succinic acid (0.3 g) dissolved in methanol-water was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 succinate (1.84 g).
[0578] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 succinate (1 g) was recrystallized from ethanol (20 ml) and water (5 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 succinate (0.69 g).



[0579] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 succinate: colorless crystal: m.p. 158 - 160°C (recrystallized from EtOH - H_2O)
^{1}H-NMR (DMSO-d_6) δ ppm : 1.60-1.70 (2H, m), 1.76-1.86 (2H, m), 2.41 (2H, s), 2.47 (2H, t, J=7.2Hz), 2.60-2.70 (4H, br), 3.02-3.10 (4H, br), 4.06 (2H, t, J=6.4Hz), 6.30 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.88 (1H, d, J=7.3Hz), 7.28 (1H, t, J=7.8Hz), 7.40 (1H, dd, J=0.4, 5.5Hz), 7.56 (1H, d, J=9.4Hz), 7.61 (1H, d, J=7.6Hz), 7.69 (1H, d, J=5.5Hz), 7.80 (1H, d, J=9.5Hz), 11.59 (1H, brs).

hydrobromide:

[0580] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (2 g) in dichloromethane (20 ml) and methanol (20 ml) was warmed to 60°C, dissolved, and a solution of 47% hydrobromic acid (0.86 g) in methanol was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one hydrobromide (2.2 g).
[0581] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one hydrobromide (1 g) was recrystallized from ethanol (20 ml) and water (5 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one hydrobromide (0.81 g).

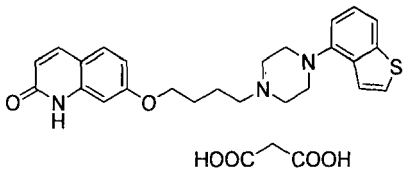


[0582] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one hydrobromide: colorless crystal: m.p. 223 - 228°C (recrystallized from EtOH - H_2O)
^{1}H-NMR (DMSO-d_6) δ ppm : 1.80-2.00 (4H, br), 3.06-3.20 (2H, m), 3.26-3.40 (4H, br), 3.50-3.74 (4H, m), 4.09 (2H, t, J=5.4Hz), 6.31 (1H, d, J=9.4Hz), 6.80-6.86 (2H, m), 6.99 (1H, d, J=7.6Hz), 7.33 (1H, t, J=7.9Hz), 7.51 (1H, d, J=5.5Hz), 7.59 (1H, d, J=9.2Hz), 7.72 (1H, d, J=8.0Hz), 7.78 (1H, d, J=5.5Hz), 7.82 (1H, d, J=9.5Hz), 9.65 (1H, brs), 11.62 (1H, s).

malonate:

[0583] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (2 g) in dichloromethane (20 ml) and methanol (20 ml) was warmed to 60°C, dissolved, and malonic acid(0.53 g) dissolved in methanol was added at room temperature. The precipitated crystals were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one malonate (2.4 g).

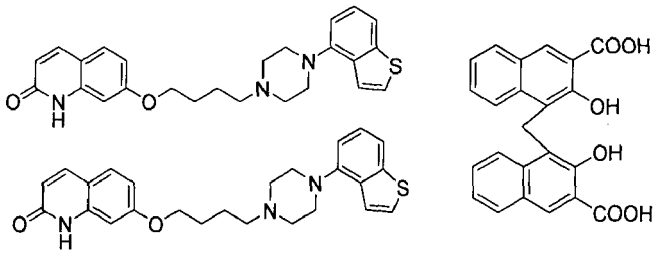
[0584] 7-[4-(4-Benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one malonate (1 g) was recrystallized from ethanol (4 ml) and water (10 ml) to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one malonate (0.72 g).



[0585] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one malonate: colorless crystal: m.p. 134 - 136°C (recrystallized from EtOH - H_2O)
^{1}H-NMR (DMSO-d_6) δ ppm : 1.68-1.88 (4H, m), 2.82 (2H, brs), 2.92-3.08 (6H, m), 3.12-3.22 (4H, br), 4.07 (2H, t, J=5.8Hz), 6.30 (1H, d, J=9.4Hz), 6.78-6.84 (2H, m), 6.93 (1H, d, J=7.6Hz), 7.30 (1H, t, J=7.8Hz), 7.45 (1H, d, J=5.5Hz), 7.57 (1H, d, J=9.4Hz), 7.66 (1H, d, J=8.1Hz), 7.73 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 11.60 (1H, brs).

1/2 pamoate:

[0586] A suspension of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one (1 g) in dimethylformamide (10 ml) and acetonitrile (10 ml) was warmed to give a solution, and pamoic acid (0.49 g) was added. The mixture was warmed to 60°C, dissolved, and the mixture was stood at room temperature. Water was added, the suspended substances were collected by filtration, and dried to give 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 pamoate (1.5 g).



[0587] 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)-butoxy]-1H-quinolin-2-one 1/2 pamoate: yellow amorphous
^{1}H-NMR (DMSO-d_6) δ ppm : 1.78-1.92 (4H, m), 3.4-3.8 (10H, br), 4.05-4.12 (2H, m), 4.71 (1H, s), 6.31 (1H, d, J=9.5Hz), 6.78-6.84 (2H, m), 6.96 (1H, d, J=7.6Hz), 7.04 (1H, t, J=7.4Hz), 7.13-7.19 (1H, m), 7.31 (1H, t, J=7.8Hz), 7.49 (1H, d, J=5.5Hz), 7.56 (1H, d, J=8.7Hz), 7.69 (2H, d, J=8.0Hz), 7.76 (1H, d, J=5.5Hz), 7.81 (1H, d, J=9.5Hz), 8.18 (1H, d,

J=8.6Hz), 8.25 (1H, s), 11.63 (1H, brs).

Experimental Example 1

[0588] Each of the Example compounds was examined for the solubility in oil (sesame oil, benzyl benzoate).

[0589] For the specific gravity of an oil, the following values were applied.
sesame oil (specific gravity: 0.914 - 0.921)
benzyl benzoate (specific gravity: 1.123) (method)

[0590] Example compound is measured in a microtube and an oil (sesame oil, or, benzyl benzoate) in an amount to make the concentration 10 mg/0.1 ml is added. After stirring, the solubility is evaluated by visual observation. When the compound is not dissolved, the mixture is heated, and the solubility is evaluated after cooling.

[0591] The results are shown in Table 3 and Table 4. In the Tables, ○ means soluble.

Table 3

Example No.	Sesame oil
Example 17	○
Example 21	○
Example 28	○
Example 44	○
Example 45	○
Example 52	○
Example 57	○
Example 60	○
Example 75	○
Example 76	○
Example 79	○
Example 134	○
Example 135	○
Example 142	○
Example 144	○
Example 149	○
Example 150	○
Example 154	○
Example 156	○
Example 158	○
Example 177	○
Example 179	○
Example 180	○
Example 373	○
Example 379	○
Example 380	○
Example 381	○
Example 384	○

Table 4

Example No.	benzyl benzoate
Example 9	○
Example 10	○
Example 11	○
Example 12	○
Example 13	○
Example 14	○
Example 15	○
Example 16	○
Example 17	○
Example 18	○
Example 19	○
Example 20	○
Example 21	○
Example 22	○
Example 23	○
Example 24	○
Example 25	○
Example 26	○
Example 27	○
Example 28	○
Example 29	○
Example 30	○
Example 31	○
Example 32	○
Example 33	○
Example 34	○
Example 35	○
Example 36	○
Example 37	○
Example 38	○
Example 39	○
Example 40	○
Example 41	○
Example 42	○
Example 43	○
Example 44	○
Example 45	○

(continued)

Example No.	benzyl benzoate
Example 46	○
Example 47	○
Example 48	○
Example 49	○
Example 50	○
Example 51	○
Example 52	○
Example 53	○
Example 54	○
Example 55	○
Example 56	○
Example 57	○
Example 58	○
Example 59	○
Example 60	○
Example 61	○
Example 62	○
Example 63	○
Example 64	○
Example 65	○
Example 67	○
Example 68	○
Example 69	○
Example 70	○
Example 71	○
Example 72	○
Example 73	○
Example 74	○
Example 75	○
Example 76	○
Example 77	○
Example 78	○
Example 79	○
Example 80	○
Example 81	○
Example 82	○
Example 83	○
Example 84	○

(continued)

Example No.	benzyl benzoate
Example 85	○
Example 86	○
Example 87	○
Example 88	○
Example 89	○
Example 90	○
Example 91	○
Example 92	○
Example 93	○
Example 94	○
Example 95	○
Example 96	○
Example 97	○
Example 98	○
Example 99	○
Example 100	○
Example 101	○
Example 102	○
Example 103	○
Example 104	○
Example 105	○
Example 106	○
Example 107	○
Example 108	○
Example 109	○
Example 110	○
Example 111	○
Example 112	○
Example 113	○
Example 114	○
Example 115	○
Example 116	○
Example 117	○
Example 118	○
Example 119	○
Example 120	○
Example 121	○
Example 122	○

(continued)

Example No.	benzyl benzoate
Example 123	○
Example 124	○
Example 125	○
Example 126	○
Example 127	○
Example 128	○
Example 129	○
Example 130	○
Example 131	○
Example 132	○
Example 134	○
Example 135	○
Example 136	○
Example 137	○
Example 139	○
Example 140	○
Example 141	○
Example 142	○
Example 143	○
Example 144	○
Example 145	○
Example 146	○
Example 147	○
Example 148	○
Example 149	○
Example 150	○
Example 151	○
Example 152	○
Example 153	○
Example 154	○
Example 156	○
Example 158	○
Example 163	○
Example 165	○
Example 168	○
Example 170	○
Example 175	○
Example 177	○

(continued)

Example No.	benzyl benzoate
Example 179	○
Example 180	○
Example 371	○
Example 372	○
Example 373	○
Example 379	○
Example 380	○
Example 381	○
Example 382	○
Example 384	○

Experimental Example 2; pharmacokinetics of intramuscular preparations

[0592] A suspended fine particle preparation used as a sustainable injection requires re-suspending before administration, and the particle surface area markedly affects the drug release profile. Thus, the particle size after re-suspending needs to be strictly controlled, so that coagulation and the like will not occur.

[0593] On the other hand, since an oil-soluble preparation contains a drug completely dissolved therein, re-suspending before administration is not necessary and, since the drug is released depending on the oil-water distribution coefficient, control of the particle size is not necessary. Furthermore, since sterilization by filtration, which has been unattainable for suspended fine particle preparations, has become possible, a preparation can be prepared more conveniently.

[0594] Since the compound disclosed in patent document 1 shows low solubility in an oil base material such as benzyl benzoate and the like, an oil-soluble preparation cannot be produced. When a soluble preparation is produced, an aqueous base material using a solubilizing agent such as Captisol (Sulfobutylether-β-cyclodextrin) and the like needs to be used. In contrast, since the compound of the present invention shows high solubility in an oil base material, an oil-soluble preparation can be produced.

[0595] Thus, an oil-soluble preparation of the compound of the present invention and an water soluble preparation of the compound disclosed in patent document 1 were prepared, intramuscularly administered to rats and pharmacokinetics of these preparations were evaluated.

Animal

[0596] 7-week-old male rats were purchased from CHARLES RIVER LABORATORIES JAPAN, INC, preliminarily bred and rats weighing 265.2 g - 288.6 g were used for the experiment. The experiment was performed under the conditions of no fasting, free access to water and feed, and the following breeding environment. Rats per cage: 4, temperature: 23±2°C, humidity: 60±10%, light-on time: 7:00 - 19:00

Production method of preparation

[0597] As the compound disclosed in patent document 1, used was 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one (control compound) disclosed in Example 1 that expresses desired efficacy. A water-soluble preparation was obtained by dissolving the control compound in aqueous 15% Captisol and 0.78% tartaric acid solution to a concentration of 0.5%, and the pH was adjusted to 4.3 with 5N aqueous sodium hydroxide solution.

[0598] An oil-soluble preparation was obtained by dissolving the compound of the present invention disclosed in Example 146 in benzyl benzoate to a concentration of 15%, and adjusted.

Methods of administration and blood sampling

[0599] Under isoflurane anesthesia, non-fasting male rats were intramuscularly administered at left leg region (about 4 mm depth) using a syringe with 24G needle. The dose is as described below.

Test preparation 1: low dose of oil-soluble preparation of the compound of the present invention: 25 mg/kg (based on control compound)
Test preparation 2: high dose of oil-soluble preparation of the compound of the present invention: 50 mg/kg (based on control compound)
Test preparation 3: water-soluble preparation of control compound: 0.1 mg/kg

[0600] The test preparation was administered to the rats. For test preparation 3, about 0.3 mL each of blood samples were collected from the jugular vein 5 min, 15 min, 30 min, 1 hr, 2 hr, 4 hr and 20 hr later. For test preparations 1 and 2, about 0.3 mL each of blood samples were collected from the jugular vein 6 hr, 1 day, 3 days, 7 days, 14 days, 21 days and 28 days later. For collection of blood samples, a 1 mL syringe treated with EDTA-lithium fluoride-heparin was used. The collected blood was preserved under ice-cooling, the plasma was rapidly separated by centrifugation, and the concentration of the control compound was quantified by LCMS. The pharmacokinetics parameters such as Cmax, Tmax, AUClast, AUCinf, t1/2 and the like were determined by WinNonlin Professional Version 6.1 (model-independent method, Pharsight corporation).

Results

[0601] The results are shown in Fig. 1 (blood concentration profile of control compound after administration of test preparations 1, 2 and 3) and Table 5 (pharmacokinetics parameters of test preparations 1, 2 and 3).

[Table 5]

	Cmax (μg/mL)	Tmax (day)	AUClast (μg·day/mL)	AUCinf (μg·day/mL)	t1/2 (day)
Test preparation 1	0.0258	5.00	0.270	0.473	27.99
Test preparation 2	0.0423	5.31	0.480	0.621	16.99
Test preparation 3	0.0629	0.01	0.003	0.003	0.05
Each parameter shows mean value (n=4)					

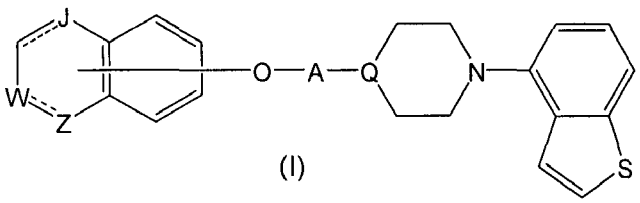
Discussion

[0602] In test preparation 3, the control compound disappeared immediately after intramuscular administration. On the other hand, in test preparations 1 and 2, the control compound showed a sustained blood concentration profile. Therefrom it was shown that the improved solubility of the compound of the present invention in an oily substrate has enabled the production of a dissolution preparation that shows blood concentration sustainability of the compound of patent document 1.

[0603] This application is based on application No. 61/532,393 filed in United States of America (filing date; September 8, 2011).

Claims

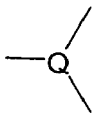
1. A heterocyclic compound represented by the formula (I)



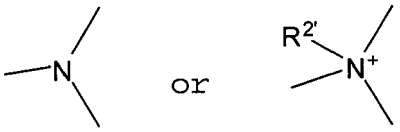
(I)

wherein

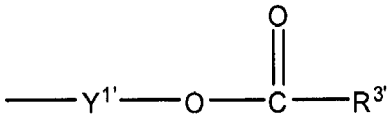
A is a C1-6 alkylene group;



in the monocyclic heterocycle containing Q is



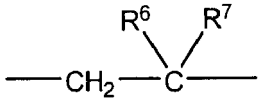
wherein
$R^{2'}$ is the following group



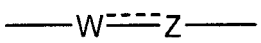
wherein
$Y^{1'}$ is a C1-6 alkylene group,
$R^{3'}$ is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group optionally substituted by a C1-6 alkyl group,
(3) a phenyl group,
(4) a phenyl C1-6 alkyl group
(5) a C1-6 alkoxy group,
(6) a C3-20 cycloalkyloxy group,
(7) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a phenyl C1-6 alkyl group, or
(8) a piperidyl group optionally having a piperidyl group;

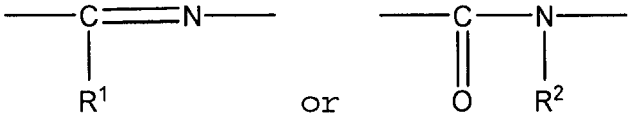
at the 3-position and the 4-position of the bicyclic heterocycle skeleton containing Z and W is -CH=CH- or



wherein R^6 and R^7 are the same or different and each is a hydrogen or a C1-6 alkyl group;



is

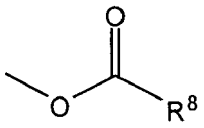


wherein

R^1 is

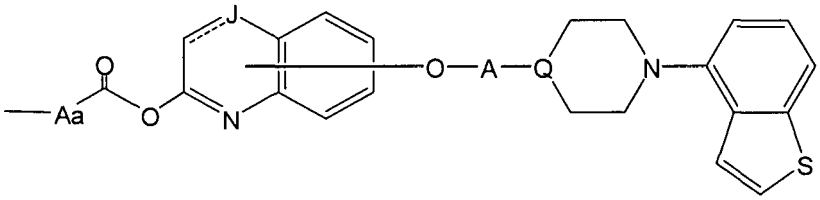
a C1-6 alkoxy C1-6 alkoxy group,
a phosphonooxy C1-6 alkoxy group,
a phenyl C1-6 alkoxy C1-6 alkoxy group,
a phosphonooxy group optionally having 1 or 2 C1-6 alkyl groups,

the following group

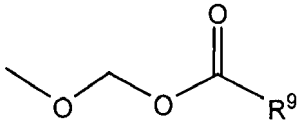


wherein
R^8 is

(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a phenyl group,
(5) a phenyl C1-6 alkyl group,
(6) a C2-30 alkenyl group,
(7) a C1-6 alkoxy group,
(8) a C3-20 cycloalkyloxy group,
(9) a C1-6 alkoxy C1-6 alkoxy group,
(10) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group,
(11) a piperidyl group optionally having a piperidyl group,
(12) a piperazinyl group optionally having a C1-6 alkyl group, or
(13) the following group



wherein Aa is a C1-30 alkylene group, and other symbols are as defined above, or
the following group

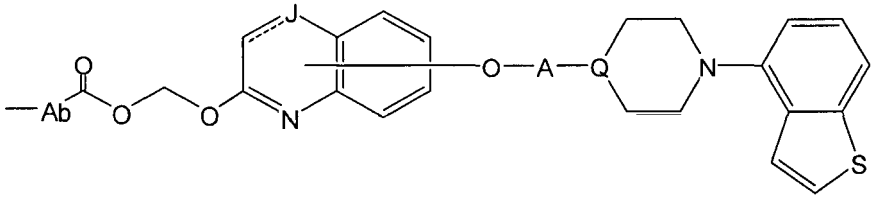


wherein

R^9 is

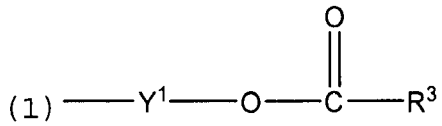
(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,

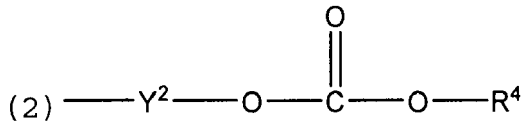
(3) a C3-20 cycloalkyl group,
(4) a phenyl group,
(5) a phenyl C1-6 alkyl group,
(6) a C2-30 alkenyl group,
(7) a C1-6 alkoxy group,
(8) a C3-20 cycloalkyloxy group,
(9) a C1-6 alkoxy C1-6 alkoxy group,
(10) a phenyloxy group,
(11) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group,
(12) a piperidyl group optionally having a piperidyl group,
(13) a piperazinyl group optionally having a C1-6 alkyl group, or
(14) the following group

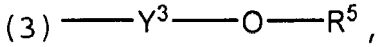


wherein Ab is a C1-30 alkylene group, and other symbols are as defined above;

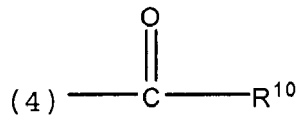
R^2 is a hydrogen or
the following group







or



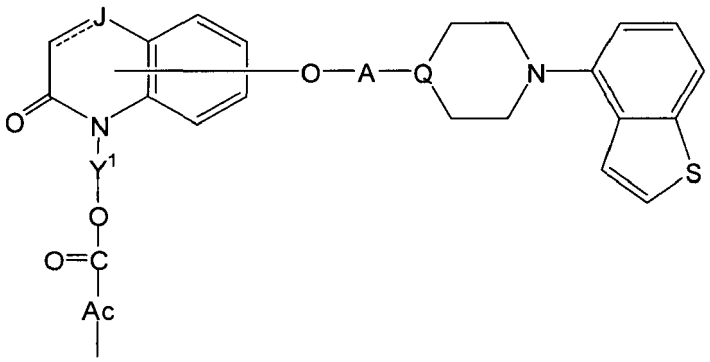
wherein
Y^1 is a C1-6 alkylene group optionally substituted by

(1) a C1-6 alkoxycarbonyl group or
(2) a C1-6 alkyl group,

Y^2 is a C1-6 alkylene group,
Y^3 is a single bond or a C1-6 alkylene group optionally substituted by a C1-6 alkyl group,

R^3 is

(1) a C1-30 alkyl group,
(2) a halogen-substituted C1-6 alkyl group,
(3) a C2-30 alkenyl group,
(4) an amino C1-6 alkyl group,
(5) a C3-20 cycloalkyl group,
(6) a phenyl group,
(7) a phenyl C1-6 alkyl group,
(8) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group and a piperidyl group,
(9) a halogen-substituted piperidyl group,
(10) a morpholinyl group,
(11) a pyrrolidinyl group,
(12) a tetrahydropyranyl group,
(13) a furyl group,
(14) a thienyl group,
(15) a pyridyl group,
(16) a pyrimidinyl group,
(17) a pyridazinyl group,
(18) a benzofuryl group,
(19) a quinolyl group,
(20) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(21) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(22) a C1-6 alkoxy C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(23) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group, a C3-20 cycloalkyl group, a C3-20 cycloalkyl C1-6 alkyl group, a C2-6 alkenyl group, a halogen-substituted C1-6 alkyl group, a C1-6 alkoxy group, a C1-6 alkoxy C1-6 alkyl group, a C1-6 alkoxycarbonyl C1-6 alkyl group, a phenyl C1-6 alkyl group, a phenyl C1-6 alkoxy group, a furyl C1-6 alkyl group, a pyridyl C1-6 alkyl group, a hydroxy-substituted C1-6 alkyl group,
(24) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group,
(25) a piperazinyl group optionally having a C1-6 alkyl group, or
(26) the following group



wherein Ac is a C1-30 alkylene group, and other symbols are as defined above,

R^4 is

(1) a C1-30 alkyl group,
(2) a phenyl group,
(3) a phenyl C1-6 alkyl group,
(4) a halogen-substituted C1-6 alkyl group, or
(5) a C3-20 cycloalkyl group,

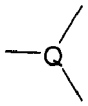
R^5 is

(1) a hydrogen,
(2) a C1-6 alkyl group,
(3) a halogen-substituted C1-6 alkyl group,
(4) a phenyl C1-6 alkyl group,
(5) a phenyl C1-6 alkoxy C1-6 alkyl group,
(6) a tri-C1-6 alkylsilyl group,
(7) a tetrahydropyranyl group, or
(8) a phosphono group,

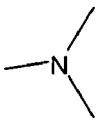
R^{10} is

(2) a C2-30 alkenyl group,
(4) a phenyl C1-6 alkyl group,
(5) a hydroxy-substituted C1-6 alkyl group,
(6) a C3-20 cycloalkyl group,
(7) an amino C1-6 alkyl group optionally having 1 or 2 substituents selected from the group consisting of an amino C1-6 alkylcarbonyl group and a C1-6 alkylcarbonyl group,
(8) a pyrrolidinyl group optionally having an amino C1-6 alkylcarbonyl group,
(9) an alkoxy group,
(10) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(11) a C1-6 alkoxy C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group,
(12) a phenyl C1-6 alkoxy group,
(13) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group, a hydroxy-substituted C1-6 alkyl group and a phenyl C1-6 alkyl group,
(14) a morpholino group,
(15) a piperazinyl group optionally having a C1-6 alkyl group,
(16) a piperidyl group optionally having a piperidyl group, or
(17) a C3-20 cycloalkyloxy group;

provided when



is

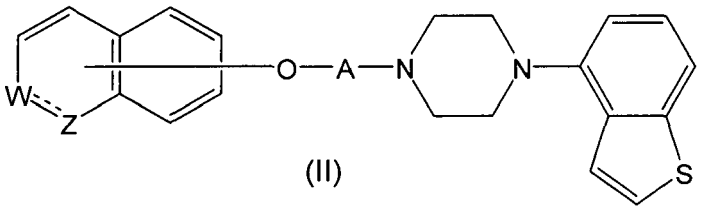


,

then
R^2 is not a hydrogen,

or a salt thereof.

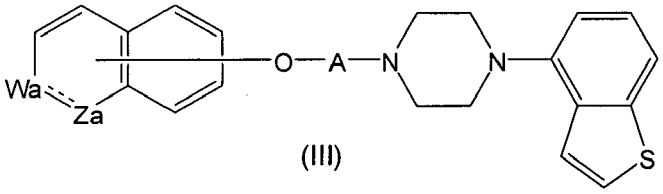
2. The heterocyclic compound according to claim 1, which is represented by the formula (II)



(II)

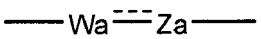
wherein each symbol is as defined in claim 1, or a salt thereof.

3. The heterocyclic compound according to claim 1, which is represented by the formula (III)

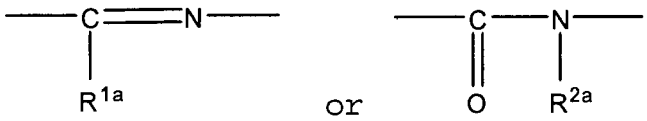


(III)

wherein

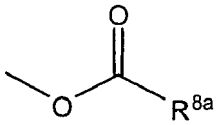


is



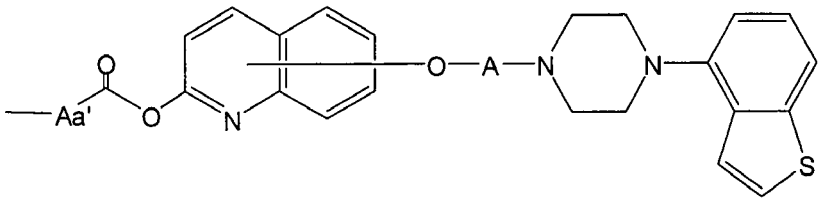
wherein

R^{1a} is the following group



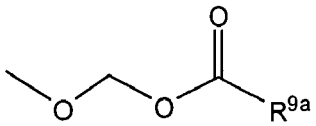
wherein
R^{8a} is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a C1-6 alkoxy group,
(4) a C3-20 cycloalkyloxy group,
(5) a C1-6 alkoxy C1-6 alkoxy group,
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group, or
(7) the following group



wherein Aa' is a C1-30 alkylene group, and other symbol is as defined in claim 1, or

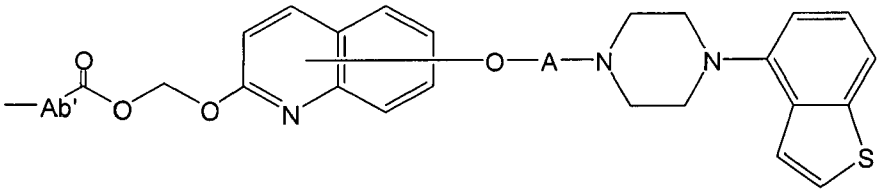
the following group



wherein

R^{9a} is

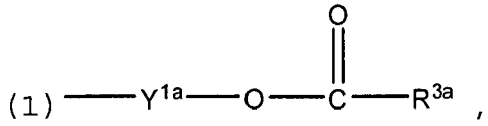
(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a C1-6 alkoxy group,
(5) a C3-20 cycloalkyloxy group,
(6) a C1-6 alkoxy C1-6 alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group,
(9) a piperidyl group optionally having a piperidyl group,
(10) a piperazinyl group optionally having a C1-6 alkyl group, or
(11) the following group



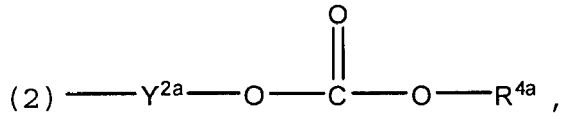
wherein Ab' is a C1-30 alkylene group, and other symbol is as defined in claim 1;

R^{2a} is

the following group

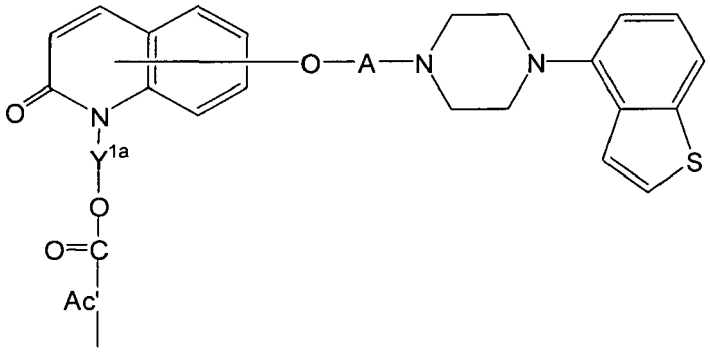


or



wherein
Y^{1a} is a C1-6 alkylene group,
Y^{2a} is a C1-6 alkylene group,
R^{3a} is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group,
(4) a tetrahydropyranyl group,
(5) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(6) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group
(7) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group, or
(8) the following group



wherein Ac' is a C1-30 alkylene group, Y^{1a} is a C1-6 alkylene group and other symbols are as defined in claim 1,

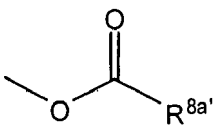
R^{4a} is

(1) a C1-30 alkyl group, or
(2) a C3-20 cycloalkyl group; and

A is a C1-6 alkylene group,

or a salt thereof.

4. The heterocyclic compound according to claim 2, wherein R^1 is the following group

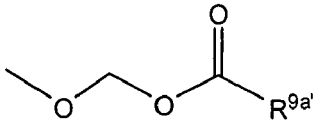


wherein

$R^{8a'}$ is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group,
(3) a C1-6 alkoxy group,
(4) a C3-20 cycloalkyloxy group,
(5) a C1-6 alkoxy C1-6 alkoxy group, or
(6) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group and a hydroxy-substituted C1-6 alkyl group, or

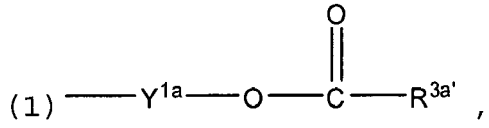
the following group



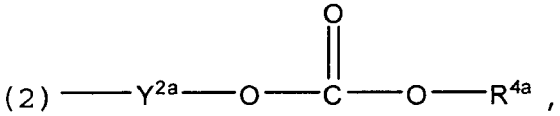
wherein
$R^{9a'}$ is

(1) a C1-30 alkyl group,
(2) a hydroxy-substituted C1-6 alkyl group,
(3) a C3-20 cycloalkyl group,
(4) a C1-6 alkoxy group,
(5) a C3-20 cycloalkyloxy group,
(6) a C1-6 alkoxy C1-6 alkoxy group,
(7) a phenyloxy group,
(8) an amino group optionally having 1 or 2 substituents selected from the group consisting of a C1-30 alkyl group,
(9) a piperidyl group optionally having a piperidyl group, or
(10) a piperazinyl group optionally having a C1-6 alkyl group; R^2 is

the following group



or



wherein
Y^{1a} is a C1-6 alkylene group,
Y^{2a} is a C1-6 alkylene group,
$R^{3a'}$ is

(1) a C1-30 alkyl group,
(2) a C3-20 cycloalkyl group
(3) a piperidyl group optionally having 1 or 2 substituents selected from the group consisting of a C1-6 alkyl group,
(4) a tetrahydropyranyl group,
(5) a C1-6 alkoxycarbonyl C1-6 alkyl group,
(6) a C1-6 alkoxy C1-6 alkoxy C1-6 alkyl group

(7) an amino C1-6 alkyl group optionally having a C1-6 alkylcarbonyl group,

R^{4a} is

(1) a C1-30 alkyl group, or
(2) a C3-20 cycloalkyl group;

or a salt thereof.

5. A pharmaceutical composition comprising the heterocyclic compound according to claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent and/or a carrier.

6. A prophylactic and/or therapeutic agent for a central neurological disease, comprising the heterocyclic compound according to claim 1 or a pharmaceutically acceptable salt thereof as an active ingredient.

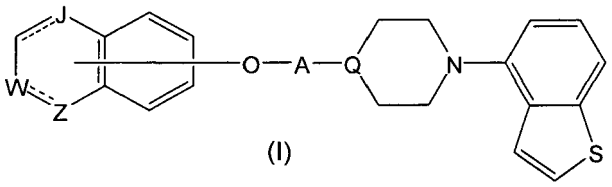
7. The agent according to claim 6, wherein the central neurological disease is selected from the group consisting of schizophrenia, treatment-resistant, refractory or chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, adjustment disorder, substance-related disorder, anhedonia, delirium, Alzheimer's disease, Parkinson disease, cognitive impairment, cognitive impairment associated with neurodegenerative diseases, cognitive impairment caused by neurodegenerative diseases, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autistic disorder, Tourette's disorder, tic disorder, attention deficit hyperactivity disorder, conduct disorder and Down's syndrome.

8. The heterocyclic compound according to claim 1 or a pharmaceutically acceptable salt thereof for use as a medicament.

9. The heterocyclic compound according to claim 1 or a pharmaceutically acceptable salt thereof for use in preventing and/or treating a central neurological disease.

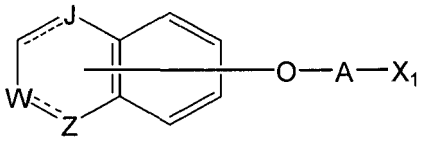
10. The heterocyclic compound or pharmaceutically acceptable salt thereof for use according to claim 9, wherein the central neurological disease is selected from the group consisting of schizophrenia, treatment-resistant, refractory or chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, adjustment disorder, substance-related disorder, anhedonia, delirium, Alzheimer's disease, Parkinson disease, cognitive impairment, cognitive impairment associated with neurodegenerative diseases, cognitive impairment caused by neurodegenerative diseases, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autistic disorder, Tourette's disorder, tic disorder, attention deficit hyperactivity disorder, conduct disorder and Down's syndrome.

11. A method of producing a heterocyclic compound represented by the formula (I)

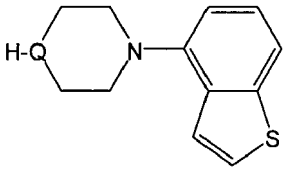


(I)

wherein each symbol is as defined in claim 1,
or a salt thereof, comprising reacting a compound represented by
the formula



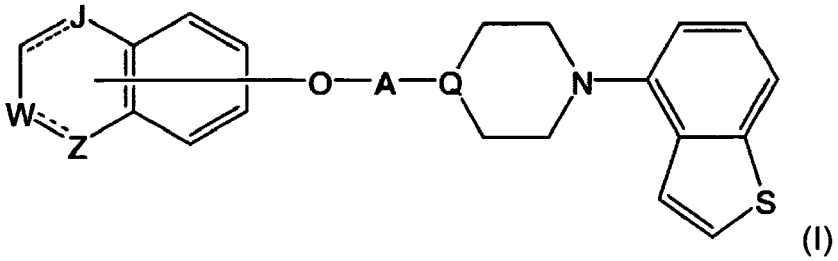
wherein X_1 is a halogen atom or a group that causes a substitution reaction similar to that by a halogen atom, and other symbols are as defined in claim 1, or a salt thereof, with a compound represented by



wherein Q is as defined in claim 1, or a salt thereof.

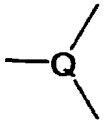
Patentansprüche

1. Heterocyclische Verbindung der Formel (I):



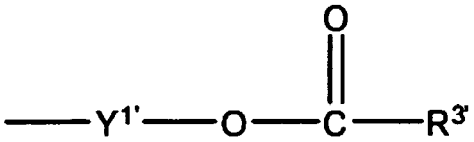
worin:

A eine C_{1-6}-Alkylengruppe ist;



in dem monocyclischen Heterocyclus, enthaltend Q,

ist, worin:
$R^{2'}$ die nachstehende Gruppe ist:



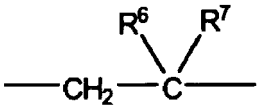
worin:

y1' eine C_{1-6}-Alkylengruppe ist,
$R^{3'}$ ist:

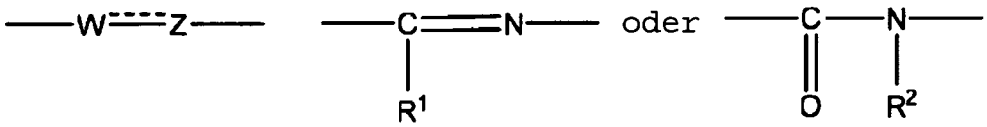
(1) eine C_{1-30}-Alkylgruppe,
(2) eine C_{3-20}-Cycloalkylgruppe, die gegebenenfalls mit einer C_{1-6}-Alkylgruppe substituiert ist,
(3) eine Phenylgruppe,
(4) eine Phenyl-C_{1-6}-alkyl-Gruppe
(5) eine C_{1-6}-Alkoxygruppe,
(6) eine C_{3-20}-Cycloalkyloxygruppe,
(7) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe und einer Phenyl-C_{1-6}-alkyl-Gruppe, aufweist oder
(8) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist;

an der 3-Position und der 4-Position des bicyclischen Heterocyclus-Skeletts, enthaltend Z und W,

- CH=CH- oder



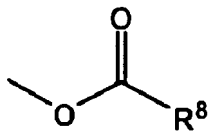
ist, worin R^6 und R^7 gleich oder verschieden sind und jeweils Wasserstoff oder eine C_{1-6}-Alkylgruppe sind;



ist,

worin:
R^1 ist:

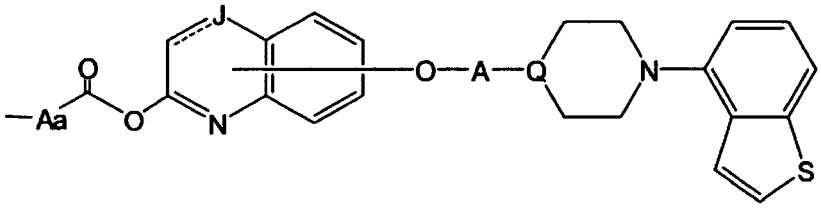
eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-Gruppe,
eine Phosphonooxy-C_{1-6}-alkoxy-Gruppe,
eine Phenyl-C_{1-6}-alkoxy-C_{1-}alkoxy-Gruppe,
eine Phosphonooxygruppe, die gegebenenfalls 1 oder 2 C_{1-6}-Alkylgruppen aufweist,
die nachstehende Gruppe



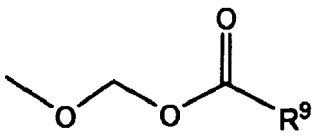
worin:

R^8 ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine Hydroxy-substituierte C_{1-6}-Alkylgruppe,
(3) eine C_{3-20}-Cycloalkylgruppe,
(4) eine Phenylgruppe,
(5) eine Phenyl-C_{1-6}-alkyl-Gruppe,
(6) eine C_{2-30}-Alkenylgruppe,
(7) eine C_{1-6}-Alkoxygruppe,
(8) eine C_{3-20}-Cycloalkyloxygruppe,
(9) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-Gruppe,
(10) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe und einer Hydroxy-substituierten C_{1-6}-Alkylgruppe, aufweist,
(11) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist,
(12) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist, oder
(13) die nachstehende Gruppe



worin Aa eine C_{1-30}-Alkylengruppe ist und die anderen Symbole wie vorstehend definiert sind, oder die nachstehende Gruppe:

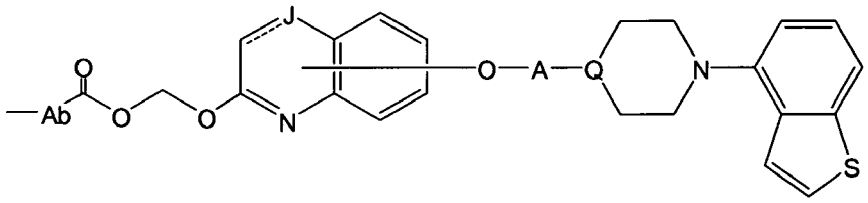


worin:

R^9 ist:

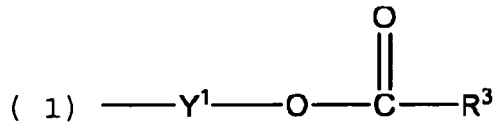
(1) eine C_{1-30}-Alkylgruppe,
(2) eine Hydroxy-substituierte C_{1-6}-Alkylgruppe,
(3) eine C_{3-20}-Cycloalkylgruppe,
(4) eine Phenylgruppe,
(5) eine Phenyl-C_{1-6}-alkyl-Gruppe,
(6) eine C_{2-30}-Alkenylgruppe,
(7) eine C_{1-6}-Alkoxygruppe,
(8) eine C_{3-20}-Cycloalkyloxygruppe,
(9) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-Gruppe,
(10) eine Phenyloxygruppe,
(11) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe und einer Hydroxy-substituierten C_{1-6}-Alkylgruppe, aufweist,

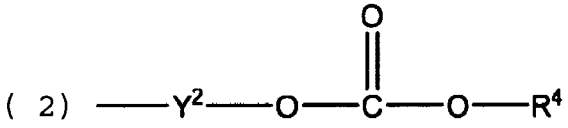
(12) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist,
(13) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist, oder
(14) die nachstehende Gruppe:



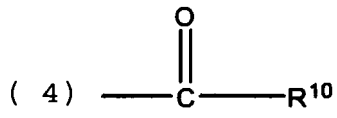
worin Ab eine C_{1-30}-Alkylengruppe ist und die anderen Symbole wie vorstehend definiert sind;

R^2 Wasserstoff oder die nachstehende Gruppe ist:





(3) Y^3 O R^5 oder



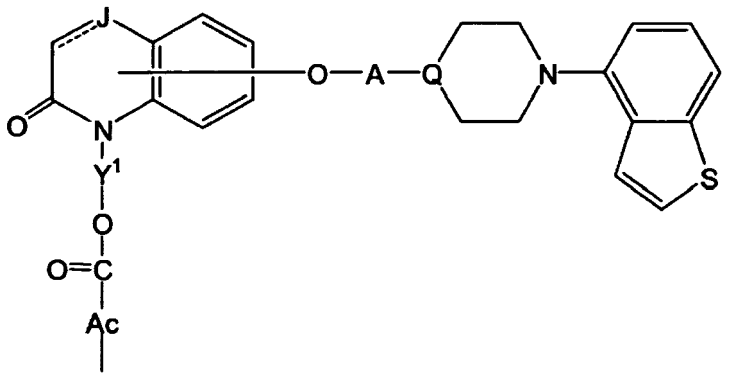
worin:
Y^1 eine C_{1-6}-Alkylengruppe ist, gegebenenfalls substituiert durch

(1) eine C_{1-6}-Alkoxycarbonylgruppe oder
(2) eine C_{1-6}-Alkylgruppe,

Y^2 eine C_{1-6}-Alkylengruppe ist,
Y^3 eine Einfachbindung oder eine C_{1-6}-Alkylengruppe ist, die gegebenenfalls durch eine C_{1-6}-Alkylgruppe substituiert ist,
R^3 ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine Halogen-substituierte C_{1-6}-Alkylgruppe,
(3) eine C_{2-30}-Alkenylgruppe,
(4) eine Amino-C_{1-6}-alkyl-Gruppe,
(5) eine C_{3-20}-Cycloalkylgruppe,
(6) eine Phenylgruppe,
(7) eine Phenyl-C_{1-6}-alkyl-Gruppe,
(8) eine Piperidylgruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-6}-Alkylgruppe und einer Piperidylgruppe, aufweist,
(9) eine Halogen-substituierte Piperidylgruppe,
(10) eine Morpholinylgruppe,
(11) eine Pyrrolidinylgruppe,

(12) eine Tetrahydropyranylgruppe,
(13) eine Furylgruppe,
(14) eine Thienylgruppe,
(15) eine Pyridylgruppe,
(16) eine Pyrimidinylgruppe,
(17) eine Pyridazinylgruppe,
(18) eine Benzofurylgruppe,
(19) eine Chinolylgruppe,
(20) eine C_{1-6}-Alkoxycarbonyl-C_{1-6}-alkyl-Gruppe,
(21) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(22) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(23) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe, einer C_{3-20}-Cycloalkylgruppe, einer C_{3-20}-Cycloalkyl-C_{1-6}-alkyl-Gruppe, einer C_{2-6}-Alkenylgruppe, einer Halogen-substituierten C_{1-6}-Alkylgruppe, einer C_{1-6}-Alkoxygruppe, einer C_{1-6}-Alkoxy-C_{1-6}-alkyl-Gruppe, einer C_{1-6}-Alkoxycarbonyl-C_{1-6}-alkyl-Gruppe, einer Phenyl-C_{1-6}-alkyl-Gruppe, einer Phenyl-C_{1-6}-alkoxy-Gruppe, einer Furyl-C_{1-6}-alkyl-Gruppe, einer Pyridyl-C_{1-6}-alkyl-Gruppe und einer Hydroxy-substituierten C_{1-6}-Alkylgruppe, aufweist,
(24) eine Amino-C_{1-6}-alkyl-Gruppe, die gegebenenfalls eine C_{1-6}-Alkylcarbonylgruppe aufweist,
(25) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist, oder
(26) die nachstehende Gruppe



worin Ac eine C_{1-30}-Alkylengruppe ist und die anderen Symbole wie vorstehend definiert sind,
R^4 ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine Phenylgruppe,
(3) eine Phenyl-C_{1-6}-alkyl-Gruppe,
(4) eine Halogen-substituierte C_{1-6}-Alkylgruppe oder
(5) eine C_{3-20}-Cycloalkylgruppe,

R^5 ist:

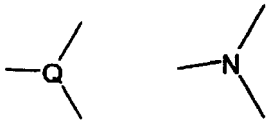
(1) Wasserstoff,
(2) eine C_{1-6}-Alkylgruppe,
(3) eine Halogen-substituierte C_{1-6}-Alkylgruppe,
(4) eine Phenyl-C_{1-6}-alkyl-Gruppe,
(5) eine Phenyl-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(6) eine Tri-C_{1-6}-alkylsilyl-Gruppe,
(7) eine Tetrahydropyranylgruppe oder
(8) eine Phosphonogruppe,

R^{10} ist

(2) eine C_{2-30}-Alkenylgruppe,
(4) eine Phenyl-C_{1-6}-alkyl-Gruppe,

(5) eine Hydroxy-substituierte C_{1-6}-Alkylgruppe,
(6) eine C_{3-20}-Cycloalkylgruppe,
(7) eine Amino-C_{1-6}-alkyl-Gruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer Amino-C_{1-6}-alkylcarbonyl-Gruppe und einer C_{1-6}-Alkylcarbonylgruppe, aufweist,
(8) eine Pyrrolidinylgruppe, die gegebenenfalls eine Amino-C_{1-6}-alkylcarbonyl-Gruppe aufweist,
(9) eine Alkoxygruppe,
(10) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(11) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(12) eine Phenyl-C_{1-6}-alkoxy-Gruppe,
(13) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe, einer Hydroxy-substituierten C_{1-6}-Alkylgruppe und einer Phenyl-C_{1-6}-alkyl-Gruppe, aufweist,
(14) eine Morpholinogruppe,
(15) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist,
(16) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist, oder
(17) eine C_{3-20}-Cycloalkyloxygruppe;

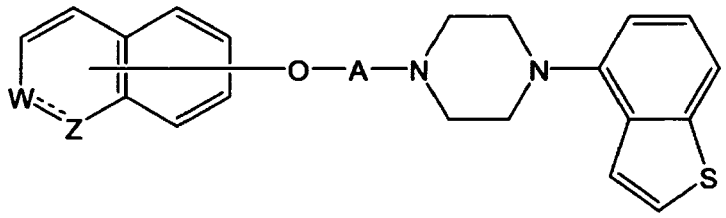
vorausgesetzt, dass, wenn



ist, dann R^2 kein Wasserstoff ist,

oder ein Salz davon.

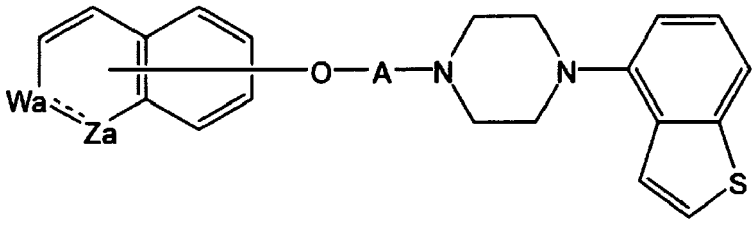
2. Heterocyclische Verbindung gemäss Anspruch 1, die durch die Formel (II) dargestellt ist:



(II)

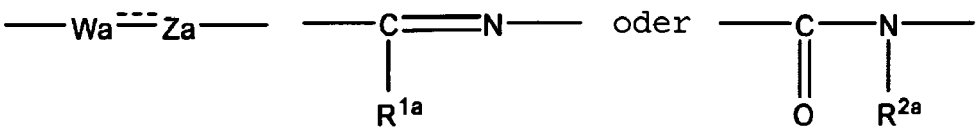
worin jedes Symbol wie in Anspruch 1 definiert ist, oder ein Salz davon.

3. Heterocyclische Verbindung gemäss Anspruch 1, die durch die Formel (III) dargestellt ist:



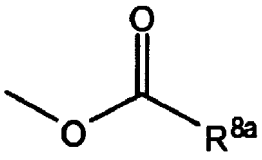
(III)

worin



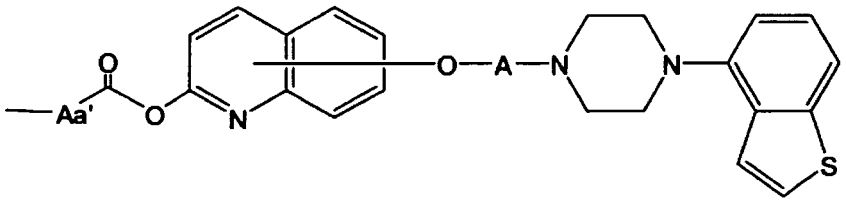
ist,
worin:

R^{1a} die nachstehende Gruppe ist:

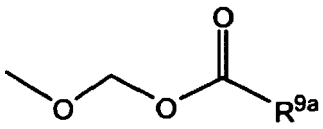


worin
R^{8a} ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine C_{3-20}-Cycloalkylgruppe,
(3) eine C_{1-6}-Alkoxygruppe,
(4) eine C_{3-20}-Cycloalkyloxygruppe,
(5) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-Gruppe,
(6) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe und einer Hydroxy-substituierten C_{1-6}-Alkylgruppe, aufweist, oder
(7) die nachstehende Gruppe



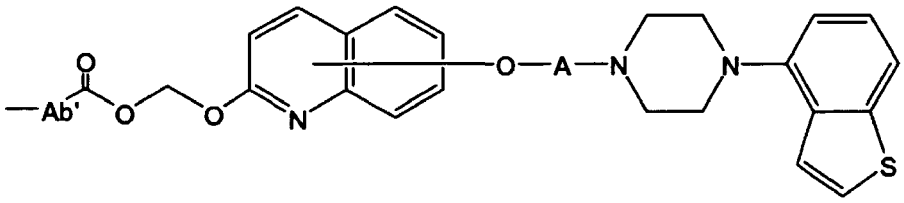
worin Aa' eine C_{1-30}-Alkylengruppe ist und die anderen Symbole wie in Anspruch 1 definiert sind,
oder
die nachstehende Gruppe



worin
R^{9a} ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine Hydroxy-substituierte C_{1-6}-Alkylgruppe,
(3) eine C_{3-20}-Cycloalkylgruppe,
(4) eine C_{1-6}-Alkoxygruppe,
(5) eine C_{3-20}-Cycloalkyloxygruppe,
(6) eine C_{1-6}-Alkoxy-C_{1-}-alkoxy-Gruppe,
(7) eine Phenyloxygruppe,
(8) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend

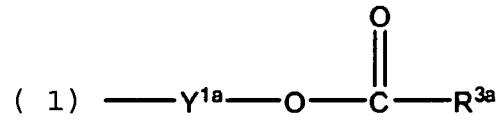
aus einer C_{1-30}-Alkylgruppe, aufweist,
(9) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist,
(10) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist, oder
(11) die nachstehende Gruppe



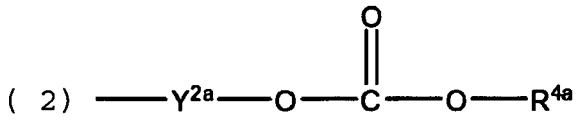
worin Ab' eine C_{1-30}-Alkylengruppe ist und die anderen Symbole wie in Anspruch 1 definiert sind;

R^{2a} ist:

die nachstehende Gruppe



oder

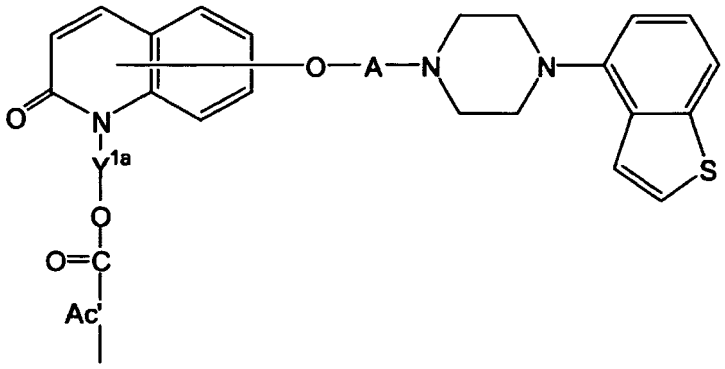


worin

Y^{1a} eine C_{1-6}-Alkylengruppe ist,
Y^{2a} eine C_{1-6}-Alkylengruppe ist,

R^{3a} ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine C_{3-20}-Cycloalkylgruppe,
(3) eine Piperidylgruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-6}-Alkylgruppe, aufweist,
(4) eine Tetrahydropyranylgruppe,
(5) eine C_{1-6}-Alkoxycarbonyl-C_{1-6}-alkyl-Gruppe,
(6) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(7) eine Amino-C_{1-6}-alkyl-Gruppe, die gegebenenfalls eine C_{1-6}-Alkylcarbonylgruppe aufweist, oder
(8) die nachstehende Gruppe



worin Ac' eine C_{1-30}-Alkylengruppe ist, Y^{1a} eine C_{1-6}-Alkylengruppe ist und die anderen Symbole wie in Anspruch 1 definiert sind,

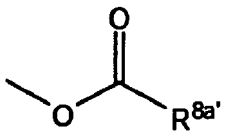
R^{4a} ist:

(1) eine C_{1-30}-Alkylgruppe oder
(2) eine C_{3-20}-Cycloalkylgruppe; und

A eine C_{1-6}-Alkylengruppe,
oder ein Salz davon.

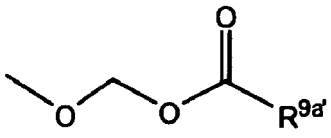
4. Heterocyclische Verbindung gemäss Anspruch 2, worin R^1 ist:

die nachstehende Gruppe



worin
$R^{8a'}$ ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine C_{3-20}-Cycloalkylgruppe,
(3) eine C_{1-6}-Alkoxygruppe,
(4) eine C_{3-20}-Ccloalkyloxygruppe,
(5) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-Gruppe oder
(6) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe und einer Hydroxy-substituierten C_{1-6}-Alkylgruppe, aufweist, oder die nachstehende Gruppe



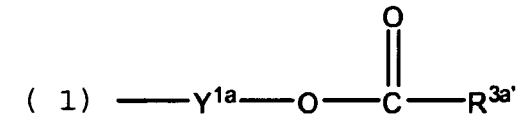
worin
$R^{9a'}$ ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine Hydroxy-substituierte C_{1-6}-Alkylgruppe,
(3) eine C_{3-20}-Cycloalkylgruppe,

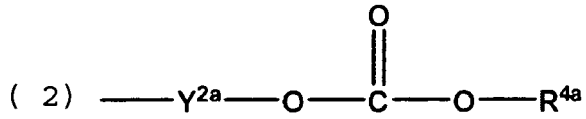
(4) eine C_{1-6}-Alkoxygruppe,
(5) eine C_{3-20}-Cycloalkyloxygruppe,
(6) eine C_{1-6}-Alkoxy-C_{1-}-alkoxy-Gruppe,
(7) eine Phenyloxygruppe,
(8) eine Aminogruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-30}-Alkylgruppe, aufweist,
(9) eine Piperidylgruppe, die gegebenenfalls eine Piperidylgruppe aufweist, oder
(10) eine Piperazinylgruppe, die gegebenenfalls eine C_{1-6}-Alkylgruppe aufweist;

R^2 ist:

die nachstehende Gruppe



oder



worin

Y^{1a} eine C_{1-6}-Alkylengruppe ist,
Y^{2a} eine C_{1-6}-Alkylengruppe ist,

$R^{3a'}$ ist:

(1) eine C_{1-30}-Alkylgruppe,
(2) eine C_{3-20}-Cycloalkylgruppe
(3) eine Piperidylgruppe, die gegebenenfalls 1 oder 2 Substituenten, ausgewählt aus der Gruppe bestehend aus einer C_{1-6}-Alkylgruppe, aufweist,
(4) eine Tetrahydropyranylgruppe,
(5) eine C_{1-6}-Alkoxycarbonyl-C_{1-6}-alkyl-Gruppe,
(6) eine C_{1-6}-Alkoxy-C_{1-6}-alkoxy-C_{1-6}-alkyl-Gruppe,
(7) eine Amino-C_{1-6}-alkyl-Gruppe, die gegebenenfalls eine C_{1-6}-Alkylcarbonylgruppe aufweist,

R^{4a} ist:

(1) eine C_{1-30}-Alkylgruppe oder
(2) eine C_{3-20}-Cycloalkylgruppe;

oder ein Salz davon.

5. Pharmazeutische Zusammensetzung, umfassend die heterocyclische Verbindung gemäss Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon und ein(en) pharmazeutisch annehmbare(s/n) Verdünnungsmittel und/oder Träger.

6. Prophylaktisches und/oder therapeutisches Mittel für eine zentral-neurologische Erkrankung, umfassend die heterocyclische Verbindung gemäss Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon als Wirkstoff.

7. Mittel gemäss Anspruch 6, wobei die zentral-neurologische Erkrankung aus der Gruppe bestehend aus Schizophrenie, behandlungsresistenter, refraktärer oder chronischer Schizophrenie, emotionaler Störung, psychotischer Störung, Stimmungsstörung, bipolarer Störung, Manie, Depression, endogener Depression, schwerer Depression,

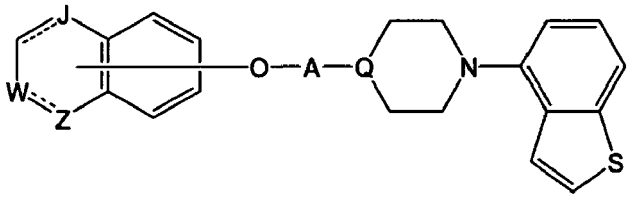
melancholischer und behandlungsresistenter Depression, Dysthymie, cyclothymer Störung, Angststörung, somatoformer Störung, artifizieller Störung, dissoziativer Störung, sexueller Störung, Essstörung, Schlafstörung, Anpassungsstörung, substanzbezogener Störung, Anhedonie, Delirium, Alzheimer-Krankheit, Parkinson-Krankheit, kognitiver Beeinträchtigung, kognitiver Beeinträchtigung in Verbindung mit neurodegenerativen Erkrankungen, durch neurodegenerative Krankheiten verursachter kognitiver Beeinträchtigung, kognitiver Beeinträchtigung bei Schizophrenie, durch behandlungsresistente, refraktäre oder chronische Schizophrenie verursachter kognitiver Beeinträchtigung, Erbrechen, Reisekrankheit, Übergewicht, Migräne, Schmerzen, geistiger Behinderung, Autismus, Tourette-Syndrom, Tic-Störung, Aufmerksamkeits-Defizit-Hyperaktivitäts-Störung, Verhaltensstörung und Down-Syndrom ausgewählt ist.

8. Heterocyclische Verbindung gemäss Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon zur Verwendung als Arzneimittel.

9. Heterocyclische Verbindung gemäss Anspruch 1 oder ein pharmazeutisch annehmbares Salz davon zur Verwendung bei der Prävention und/oder Behandlung einer zentralen neurologischen Erkrankung.

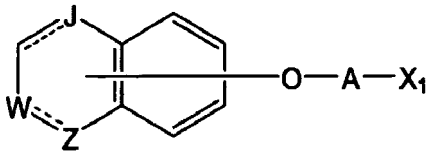
10. Heterocyclische Verbindung oder ein pharmazeutisch annehmbares Salz davon gemäss Anspruch 9, wobei die zentrale neurologische Erkrankung aus der Gruppe bestehend aus Schizophrenie, behandlungsresistenter, refraktärer oder chronischer Schizophrenie, emotionaler Störung, psychotischer Störung, Stimmungsstörung, bipolarer Störung, Manie, Depression, endogener Depression, schwerer Depression, melancholischer und behandlungsresistenter Depression, Dysthymie, cyclothymer Störung, Angststörung, somatoformer Störung, artifizieller Störung, dissoziativer Störung, sexueller Störung, Essstörung, Schlafstörung, Anpassungsstörung, substanzbezogener Störung, Anhedonie, Delirium, Alzheimer-Krankheit, Parkinson-Krankheit, kognitiver Beeinträchtigung, kognitiver Beeinträchtigung in Verbindung mit neurodegenerativen Erkrankungen, durch neurodegenerative Krankheiten verursachter kognitiver Beeinträchtigung, kognitiver Beeinträchtigung bei Schizophrenie, durch behandlungsresistente, refraktäre oder chronische Schizophrenie verursachter kognitiver Beeinträchtigung, Erbrechen, Reisekrankheit, Übergewicht, Migräne, Schmerzen, geistiger Behinderung, Autismus, Tourette-Syndrom, Tic-Störung, Aufmerksamkeits-Defizit-Hyperaktivitäts-Störung, Verhaltensstörung und Down-Syndrom ausgewählt ist.

11. Verfahren zur Herstellung einer heterocyclischen Verbindung der Formel (I):

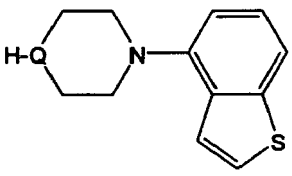


(I)

worin jedes Symbol wie in Anspruch 1 definiert ist, oder eines Salzes davon, umfassend die Umsetzung einer Verbindung der Formel:



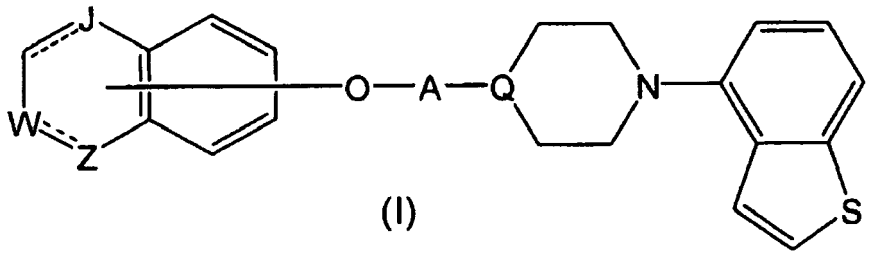
worin X_1 ein Halogenatom oder eine Gruppe ist, die eine Substitutionsreaktion ähnlich der durch ein Halogenatom bewirkt, und die anderen Symbole wie in Anspruch 1 definiert sind, oder eines Salzes davon mit einer Verbindung, dargestellt durch:



worin Q wie in Anspruch 1 definiert ist, oder einem Salz davon.

Revendications

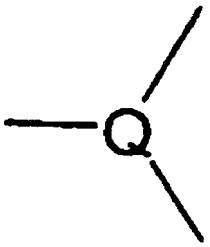
1. Composé hétérocyclique représenté par la formule (I)



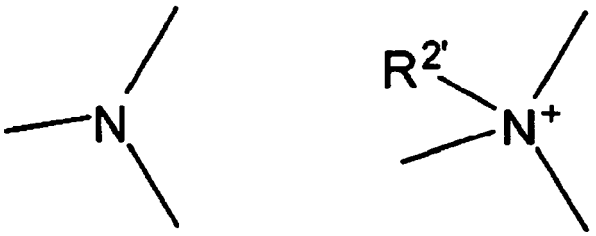
(I)

dans laquelle

A est un groupe C1-6 alcylène ;

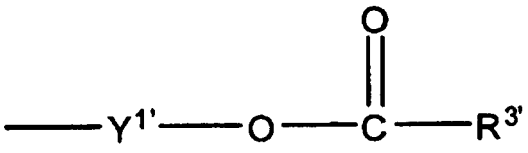


dans l'hétérocycle monocyclique contenant Q est



ou

dans lequel
$R^{2'}$ est le groupe suivant



dans lequel

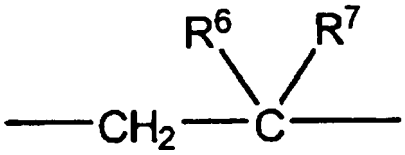
$Y^{1'}$ est un groupe C1-6 alcylène,

$R^{3'}$ est

(1) un groupe C1-30 alkyle,

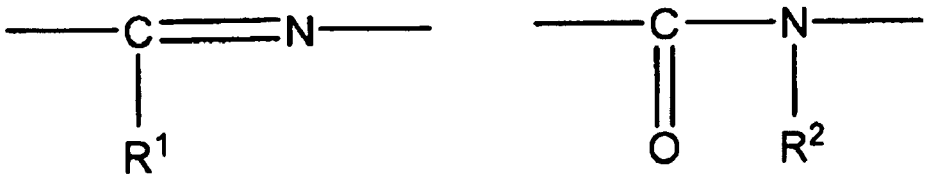
(2) un groupe C3-20 cycloalkyle éventuellement substitué par un groupe C1-6 alkyle,
(3) un groupe phényle,
(4) un groupe phényle C1-6 alkyle,
(5) un groupe C1-6 alcoxy,
(6) un groupe C3-20 cycloalcoxy,
(7) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle et un groupe phényle C1-6 alkyle, ou
(8) un groupe pipéridyle ayant éventuellement un groupe pipéridyle ;

en position 3 et en position 4 du squelette de l'hétérocycle bicyclique contenant Z et W est un-CH=CH- ou



dans lequel R^6 et R^7 sont identiques ou différents et chacun est un hydrogène ou un groupe C1-6 alkyle ;

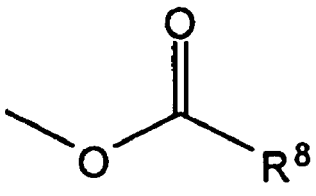
est



ou

dans lequel

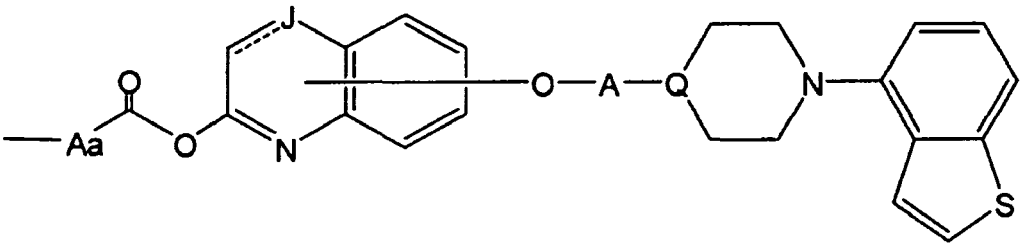
R^1 est
un groupe C1-6 alcoxy C1-6 alcoxy,
un groupe phosphonooxy C1-6 alcoxy,
un groupe phényle C1-6 alcoxy C1-6 alcoxy,
un groupe phosphonooxy ayant éventuellement ayant 1 ou 2 groupes C1-6 alkyle,
le groupe suivant



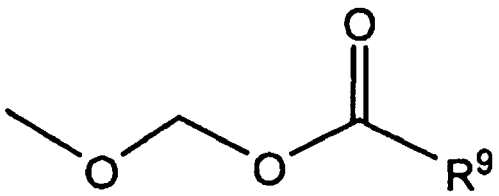
dans lequel
R^8 est

(1) un groupe C1-30 alkyle
(2) un groupe hydroxy-substitué C1-6 alkyle,
(3) un groupe C3-20 cycloalkyle,

(4) un groupe phényle
(5) un groupe phényle C1-6 alkyle,
(6) un groupe C2-30 alcényle,
(7) un groupe C1-6 alcoxy,
(8) un groupe C3-20 cycloalcoxy,
(9) un groupe C1-6 alcoxy C1-6 alcoxy,
(10) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle, et d'un groupe C1-6 alkyle hydroxy-substitué,
(11) un groupe pipéridyle ayant éventuellement un groupe pipéridyle,
(12) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,
ou
(13) le groupe suivant



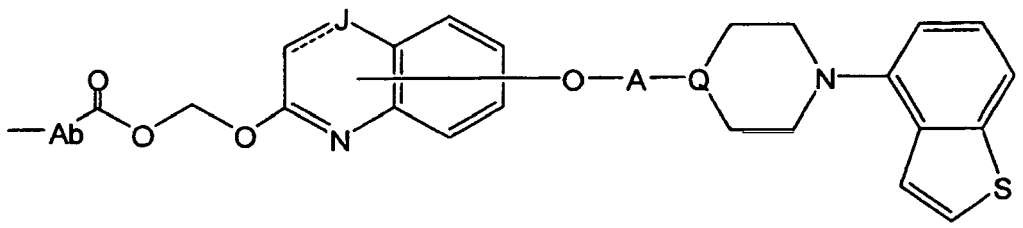
dans lequel Aa est un groupe C1-30 alcylène, et les autres symboles sont comme définis ci-dessus, ou le groupe suivant



dans lequel

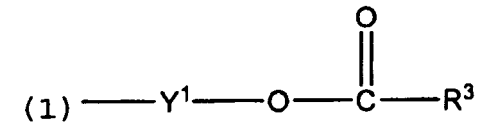
R^9 est

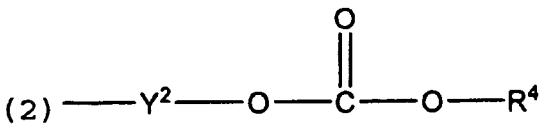
(1) un groupe C1-30 alkyle,
(2) un groupe C1-6 alkyle hydroxy-substitué,
(3) un groupe C3-20 cycloalkyle,
(4) un groupe phényle,
(5) un groupe phényle C1-6 alkyle,
(6) un groupe C2-30 alcényle,
(7) un groupe C1-6 alcoxy,
(8) un groupe C3-20 cycloalkyloxy,
(9) un groupe C1-6 alcoxy C1-6 alcoxy,
(10) un groupe phényloxy,
(11) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle et d'un groupe C1-6 alkyle hydroxy-substitué,
(12) un groupe pipéridyle ayant éventuellement un groupe pipéridyle,
(13) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,
ou
(14) le groupe suivant



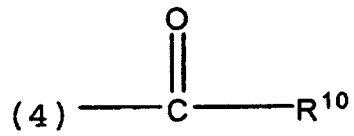
Dans lequel Ab est un groupe C1-30 alcylène, et les autres symboles sont comme définis ci-dessus ;

R^2 est un hydrogène ou
le groupe suivant





(3)-Y^3-O-R^5,
ou



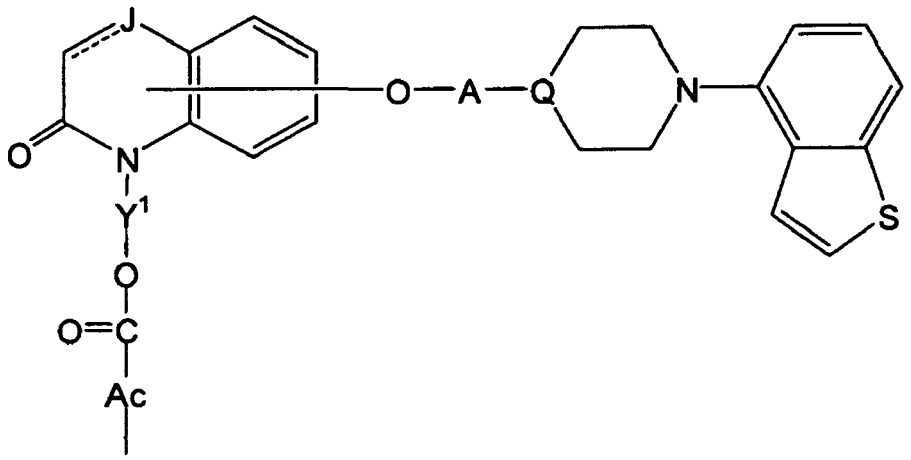
dans lequel
Y^1 est un groupe C1-6 alcylène, éventuellement substitué par

(1) un groupe C1-6 alcoxycarbonyle, ou
(2) un groupe C1-6 alkyle,

Y^2 est un groupe C1-6 alcylène,
Y^3 est une liaison simple ou un groupe C1-6 alcylène éventuellement substitué par un groupe C1-6 alkyle,
R^3 est

(1) un groupe C1-30 alkyle,
(2) un groupe C1-6 alkyle halogéno-substitué,
(3) un groupe C2-30 alcényle
(4) un groupe amino C1-6 alkyle,
(5) un groupe C3-20 cycloalkyle,
(6) un groupe phényle,
(7) un groupe phényle C1-6 alkyle,
(8) un groupe pipéridyle ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-6 alkyle et d'un groupe pipéridyle,
(9) un groupe pipéridyle halogéno-substitué,
(10) un groupe morpholinyle,
(11) un groupe pyrrolidinyle,
(12) un groupe tétrahydropyranyle,

(13) un groupe furyle,
(14) un groupe thiényle,
(15) un groupe pyridyle,
(16) un groupe pyrimidinyle,
(17) un groupe pyridazinyle,
(18) un groupe benzofuryle,
(19) un groupe quinolyle,
(20) un groupe C1-6 alcoxycarbonyle C1-6 alkyle,
(21) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(22) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(23) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle, un groupe C3-20 cycloalkyle, un groupe C3-20 cycloalkyle C1-6 alkyle, un groupe C2-6 alcényle, un groupe C1-6 alkyle halogéno-substitué, un groupe C1-6 alcoxy, un groupe C1-6 alcoxy C1-6 alkyle, un groupe C1-6 alcoxycarbonyle C1-6 alkyle, un groupe phényle C1-6 alkyle, un groupe phényle C1-6 alcoxy, un groupe furyle C1-6 alkyle, un groupe pyridyle C1-6 alkyle, un groupe C1-6 alkyle hydroxy-substitué,
(24) un groupe amino C1-6 alkyle ayant éventuellement un groupe C1-6 alkylcarbonyle,
(25) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,
ou
(26) le groupe suivant



dans lequel Ac est un groupe C1-30 alcylène, et les autres symboles sont comme définis ci-dessus,

R^4 est

(1) un groupe C1-30 alkyle,
(2) un groupe phényle,
(3) un groupe phényle C1-6 alkyle
(4) un groupe C1-6 alkyle halogéno-substitué, ou
(5) un groupe C3-20 cycloalkyle,

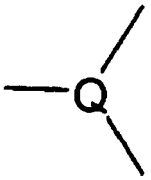
R^5 est

(1) un hydrogène
(2) un groupe C1-6 alkyle,
(3) un groupe C1-6 alkyle halogéno-substitué,
(4) un groupe phényle C1-6 alkyle,
(5) un groupe phényle C1-6 alcoxy C1-6 alkyle,
(6) un groupe tri-C1-6 alkylsilyle,
(7) un groupe tétrahydropyranyle ou
(8) un groupe phosphono,

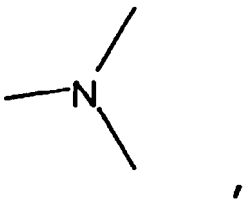
R^{10} est

(2) un groupe C2-30 alcényle,
(4) un groupe phényle C1-6 alkyle,
(5) un groupe C1-6 alkyle hydroxy-substitué,
(6) un groupe C3-20 cycloalkyle,
(7) un groupe amino C1-6 alkyle ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe amino C1-6 alkylcarbonyle et d'un groupe C1-6 alkylcarbonyle,
(8) un groupe pyrrolidinyle ayant éventuellement un groupe amino C1-6 alkylcarbonyle,
(9) un groupe alcoxy,
(10) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(11) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(12) un groupe phényle C1-6 alcoxy,
(13) un groupe amino ayant éventuellement 1 ou 2 substituants, choisis dans le groupe constitué d'un groupe C1-30 alkyle, un groupe C1-6 alkyle hydroxy-substitué, et un groupe phényle C1-6 alkyle,
(14) un groupe morpholino,
(15) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,
(16) un groupe pipéridyle ayant éventuellement un groupe pipéridyle, ou
(17) un groupe C3-20 cycloalkyloxy ;

à condition que, lorsque



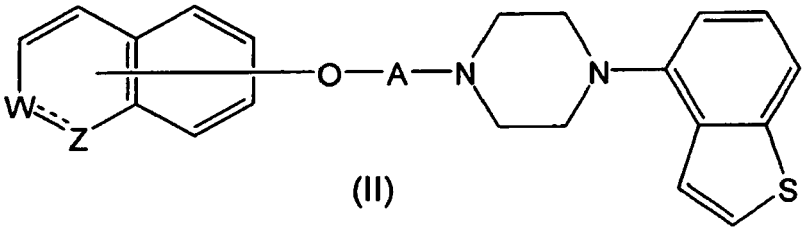
est



alors
R^2 ne soit pas un hydrogène,

ou son sel.

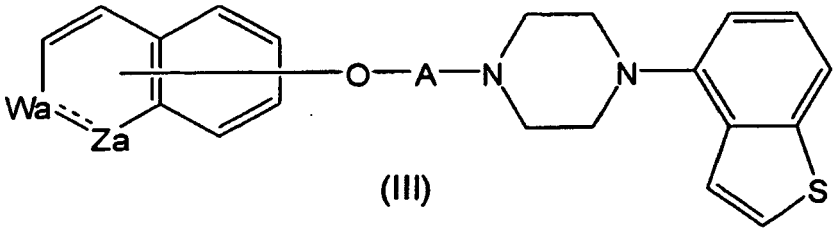
2. Composé hétérocyclique selon la revendication 1, qui est représenté par la formule (II)



(II)

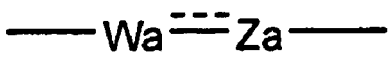
dans laquelle chaque symbole est comme défini dans la revendication 1, ou son sel.

3. Composé hétérocyclique selon la revendication 1, qui est représenté par la formule (III)

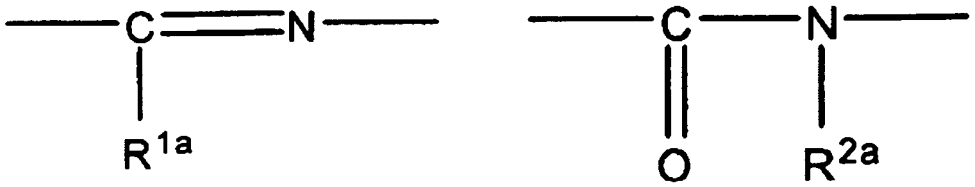


(III)

dans laquelle



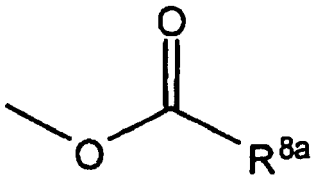
est



ou

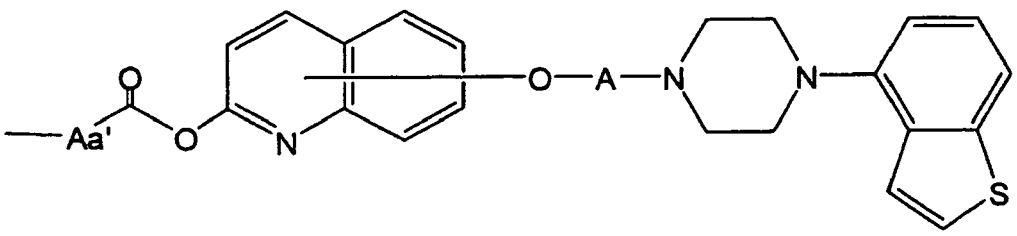
dans laquelle

R^{1a} est le groupe suivant

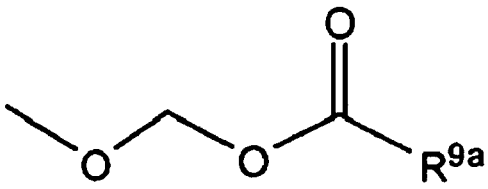


dans lequel
R^{8a} est

(1) un groupe C1-30 alkyle,
(2) un groupe C3-20 cycloalkyle,
(3) un groupe C1-6 alcoxy,
(4) un groupe C3-20 cycloalkyloxy,
(5) un groupe C1-6 alcoxy C1-6 alcoxy,
(6) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle et d'un groupe C1-6 alkyle hydroxy-substitué ou
(7) le groupe suivant



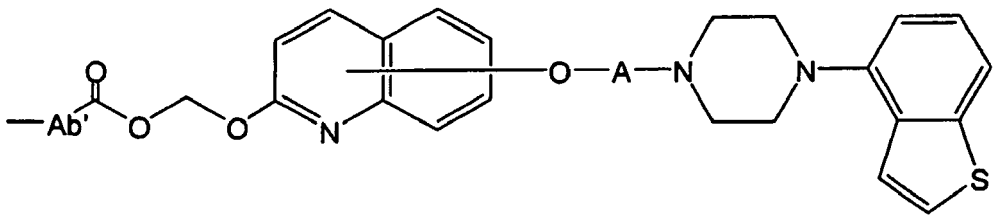
dans lequel Aa' est un groupe C1-30 alcylène, et les autres symboles sont comme définis à la revendication 1 ou
le groupe suivant



dans lequel

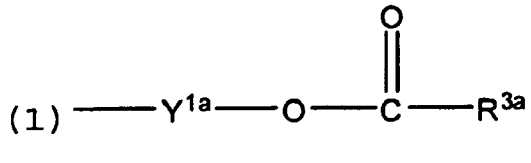
R^{9a} est

(1) un groupe C1-30 alkyle,
(2) un groupe C1-6 alkyle hydroxy-substitué
(3) un groupe C3-20 cycloalkyle,
(4) un groupe C1-6 alcoxy,
(5) un groupe C3-20 cycloalkyloxy,
(6) un groupe C1-6 alcoxy C1-6 alcoxy,
(7) un groupe phényloxy,
(8) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle,
(9) un groupe pipéridyle ayant éventuellement un groupe pipéridyle,
(10) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,
ou
(11) le groupe suivant



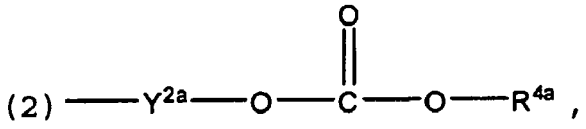
dans lequel Ab' est un groupe C1-30 alcylène, et les autres symboles sont comme définis dans la revendication 1 ;

R^{2a} est
le groupe suivant



,

ou



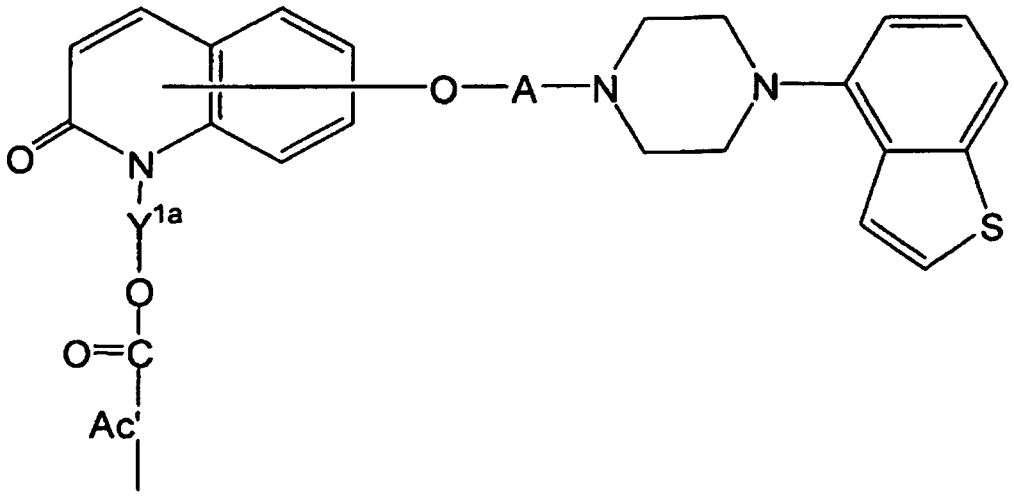
,

dans lequel

Y^{1a} est un groupe C1-6 alcylène,
Y^{2a} est un groupe C1-6 alcylène,

R^{3a} est

(1) un groupe C1-30 alkyle,
(2) un groupe C3-20 cycloalkyle,
(3) un groupe pipéridyle ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-6 alkyle,
(4) un groupe tétrahydropyranyle,
(5) un groupe C1-6 alcoxycarbonyle C1-6 alkyle,
(6) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(7) un groupe amino C1-6 alkyle ayant éventuellement un groupe C1-6 alkylcarbonyle, ou
(8) le groupe suivant



dans lequel Ac' est un groupe C1-30 alcylène, Y^{1a} est un groupe C1-6 alcylène ou les autres symboles sont comme définis dans la revendication 1,

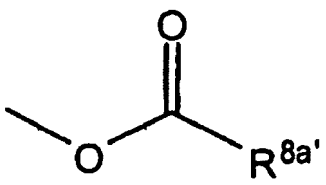
R^{4a} est

(1) un groupe C1-30 alkyle, ou
(2) un groupe C3-20 cycloalkyle, et

A est un groupe C1-6 alcylène,

ou son sel.

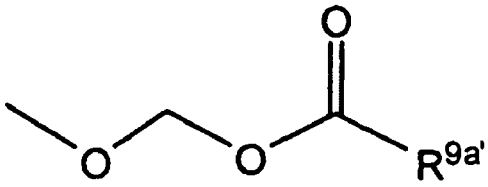
4. Composé hétérocyclique selon la revendication 2, dans lequel R^1 est le groupe suivant



dans lequel

$R^{8a'}$ est

(1) un groupe C1-30 alkyle,
(2) un groupe C3-20 cycloalkyle,
(3) un groupe C1-6 alcoxy,
(4) un groupe C3-20 cycloalkyloxy,
(5) un groupe C1-6 alcoxy C1-6 alcoxy, ou
(6) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 et d'un groupe C1-6 alkyle hydroxy-substitué, ou
le groupe suivant

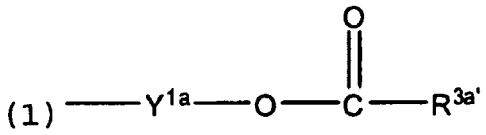


dans lequel

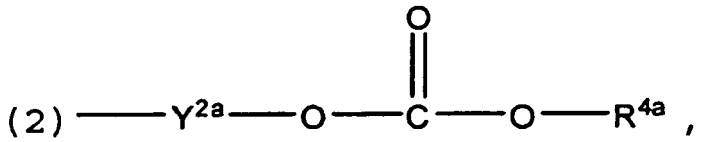
$R^{9a'}$ est

(1) un groupe C1-30 alkyle,
(2) un groupe C1-6 alkyle hydroxy-substitué,
(3) un groupe C3-20 cycloalkyle,
(4) un groupe C1-6 alcoxy,
(5) un groupe C3-20 cycloalkyloxy,
(6) un groupe C1-6 alcoxy C1-6 alcoxy,
(7) un groupe phényloxy,
(8) un groupe amino ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-30 alkyle,
(9) un groupe pipéridyle ayant éventuellement un groupe pipéridyle, ou
(10) un groupe pipérazinyle ayant éventuellement un groupe C1-6 alkyle,

R^2 est
le groupe suivant



ou



dans lequel

Y^{1a} est un groupe C1-6 alcylène,
Y^{2a} est un groupe C1-6 alcylène

$R^{3a'}$ est

(1) un groupe C1-30 alkyle,
(2) un groupe C3-20 cycloalkyle,
(3) un groupe pipéridyle ayant éventuellement 1 ou 2 substituants choisis dans le groupe constitué d'un groupe C1-6 alkyle,
(4) un groupe tétrahydropyranyle,
(5) un groupe C1-6 alcoxycarbonyle C1-6 alkyle,
(6) un groupe C1-6 alcoxy C1-6 alcoxy C1-6 alkyle,
(7) un groupe amino C1-6 alkyle ayant éventuellement un groupe C1-6 alkylcarbonyle,

R^{4a} est

(1) un groupe C1-30 alkyle ou
(2) un groupe C3-20 cycloalkyle,

ou son sel.

5. Composition pharmaceutique comprenant le composé hétérocyclique selon la revendication 1 ou son sel pharmaceutiquement acceptable, et un diluant et/ou un excipient pharmaceutiquement acceptable.

6. Agent prophylactique et/ou thérapeutique pour une maladie neurologique centrale, comprenant le composé hétérocyclique selon la revendication 1 ou son sel pharmaceutiquement acceptable comme ingrédient actif.

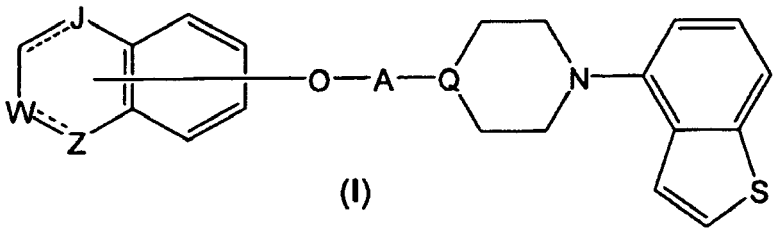
7. Agent selon la revendication 6, dans lequel la maladie neurologique centrale est choisie dans le groupe constitué de la schizophrénie, la schizophrénie résistante au traitement, réfractaire ou chronique, la perturbation émotionnelle, le trouble psychotique, les troubles de l'humeur, les troubles bipolaires, les manies, la dépression, la dépression endogène, la dépression majeure, la dépression mélancolique et résistante au traitement, le trouble dysthymique, le trouble cyclothymique, le trouble de l'anxiété, le trouble somatoforme, le trouble factice, le trouble dissociatif, le trouble sexuel, le trouble de l'appétit, le trouble du sommeil, le trouble de l'adaptation, le trouble lié à une substance, l'anhédonie, le délire, la maladie d'Alzheimer, la maladie de Parkinson, l'altération cognitive, l'altération cognitive associée à des maladies neurodégénératives, l'altération cognitive provoquée par des maladies neurodégénératives, l'altération cognitive dans la schizophrénie, l'altération cognitive provoquée par une schizophrénie résistante au traitement, réfractaire ou chronique, les vomissements, le mal des transports, l'obésité, la migraine, la douleur, le retard mental, les troubles de l'autisme, le syndrome de Tourette, les tics, les troubles de l'hyperactivité avec déficit de l'attention, les troubles du comportement et le syndrome de Down.

8. Composé hétérocyclique selon la revendication 1 ou son sel pharmaceutiquement acceptable pour utilisation en tant que médicament.

9. Composé hétérocyclique selon la revendication 1 ou son sel pharmaceutiquement acceptable pour utilisation dans la prévention et/ou le traitement d'une maladie neurologique centrale.

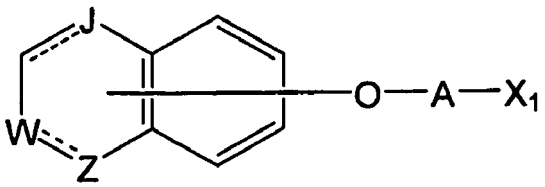
10. Composé hétérocyclique ou son sel pharmaceutiquement acceptable pour utilisation selon la revendication 9, dans lequel la maladie neurologique centrale est choisie dans le groupe constitué de la schizophrénie, la schizophrénie résistante au traitement, réfractaire ou chronique, la perturbation émotionnelle, le trouble psychotique, les troubles de l'humeur, les troubles bipolaires, les manies, la dépression, la dépression endogène, la dépression majeure, la dépression mélancolique et résistante au traitement, le trouble dysthymique, le trouble cyclothymique, le trouble de l'anxiété, le trouble somatoforme, le trouble factice, le trouble dissociatif, le trouble sexuel, le trouble de l'appétit, le trouble du sommeil, le trouble de l'adaptation, le trouble lié à une substance, l'anhédonie, le délire, la maladie d'Alzheimer, la maladie de Parkinson, l'altération cognitive, l'altération cognitive associée à des maladies neurodégénératives, l'altération cognitive provoquée par des maladies neurodégénératives, l'altération cognitive dans la schizophrénie, l'altération cognitive provoquée par une schizophrénie résistante au traitement, réfractaire ou chronique, les vomissements, le mal des transports, l'obésité, la migraine, la douleur, le retard mental, les troubles de l'autisme, le syndrome de Tourette, les tics, les troubles de l'hyperactivité avec déficit de l'attention, les troubles du comportement et le syndrome de Down.

11. Procédé de production d'un composé hétérocyclique représenté par la formule (I)

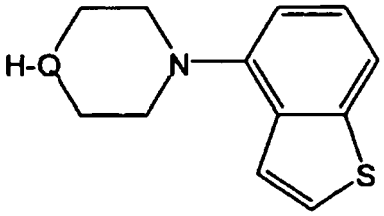


(I)

dans laquelle chaque symbole est comme défini à la revendication 1,
ou son sel, comprenant la mise en réaction d'un composé représenté par la formule

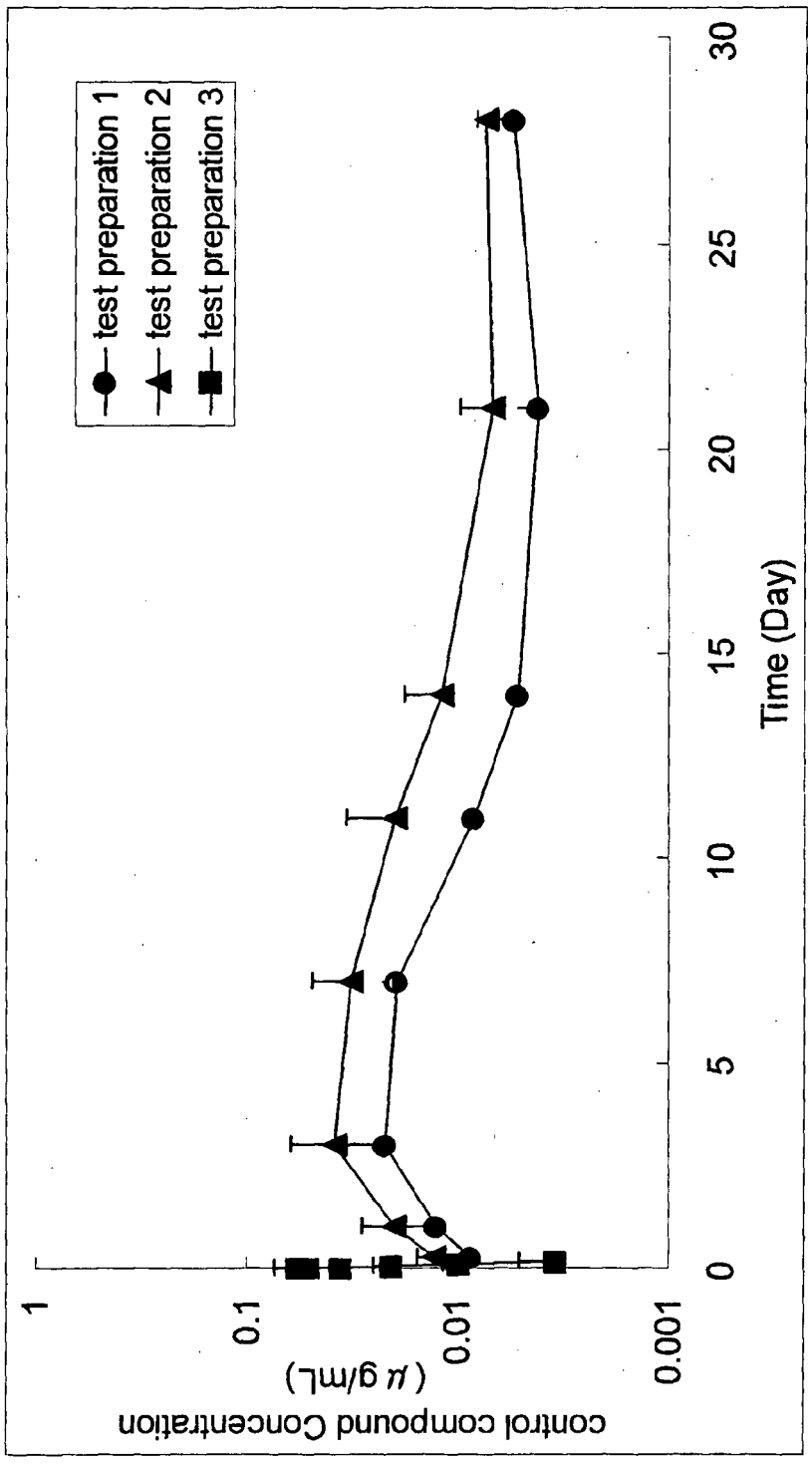


dans laquelle X_1 est un atome d'halogène ou un groupe qui provoque une réaction de substitution similaire à celle obtenue par un atome d'halogène, et les autres symboles sont comme définis dans la revendication 1, ou son sel, avec un composé représenté par



dans laquelle Q est comme défini dans la revendication 1 ou son sel.

FIG. 1


test preparation 1
test preparation 2
test preparation 3
control compound Concentration
(μ g/mL)
1
0.1
0.01
0.001
0
5
10
15
20
25
30
Time (Day)

REFERENCES CITED IN THE DESCRIPTION

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