DESCRIPTION

Title of the Invention: 1,3,4,8-TETRAHYDRO-2H-PYRIDO[1,2-A]PYRAZINE DERIVATIVE AND USE OF SAME AS HIV INTEGRASE INHIBITOR

TECHNICAL FIELD

[0001]

The present invention relates to a novel 1,3,4,8-tetrahydro-2H-pyrido[1,2-a]pyrazine derivative useful as an anti-HIV agent, a pharmaceutically acceptable salt thereof, and a solvate thereof. In addition, the present invention relates to a pharmaceutical composition comprising the derivative or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier; an anti-HIV agent, an HIV integrase inhibitor and the like, comprising the derivative or a pharmaceutically acceptable salt thereof, or a solvate thereof as an active ingredient; an anti-HIV agent comprising a combination of the derivative or a pharmaceutically acceptable salt thereof, or a solvate thereof, and one or more kinds of other anti-HIV active substances; and the like.

Background Art

[0002]

HIV (Human Immunodeficiency Virus (type 1)) belonging to retrovirus is a causative virus of AIDS (Acquired Immunodeficiency Syndrome).

HIV targets CD4 positive cell groups such as helper T cell, macrophage and dendritic cell and destroys these immunocompetent cells to cause immunodeficiency.

Accordingly, a medicament that eradicates HIV in a living organism or suppresses its growth is effective for the prophylaxis or treatment of AIDS.

[0003]

HIV possesses a bimolecular RNA gene in a shell, which is covered with an envelope protein. The RNA codes for several enzymes (protease, reverse transcriptase, integrase)

characteristic of the virus and the like. Translated reverse transcriptase and integrase are present in the shell, and protease is present inside and outside the shell.

HIV contacts and invades a host cell, causes uncoating, and releases a complex of RNA and integrase and the like into the cytoplasm. From the RNA, DNA is transcribed by reverse transcriptase, and a full length double stranded DNA is produced. The DNA moves into the nucleus of the host cell and is incorporated by integrase into the DNA of the host cell. The incorporated DNA is converted to an mRNA by polymerase of the host cell, from which mRNA various proteins necessary for forming a virus are synthesized by HIV protease and the like, and a virus particle is finally formed, which then undergoes budding and its release.

[0004]

These virus specific enzymes are considered to be essential for the growth of HIV. These enzymes are drawing attention as the target of the development of antiviral agents, and several anti-HIV agents have been already developed.

For example, zidovudine, didanosine, lamivudine and the like have been already on the market as reverse transcriptase inhibitors, and indinavir, nelfinavir and the like as protease inhibitors.

In addition, a multiple drug combination therapy using these medicaments in combination (to be also referred to as HAART (highly active antiretroviral therapy)) is also used. For example, 3 agent combination therapy using two agents from reverse transcriptase inhibitors (zidovudine and lamivudine, or tenofovir and emtricitabine), and a non-nucleic acid reverse transcriptase inhibitor (efavirenz), or a protease inhibitor (lopinavir, fosamprenavir or atazanavir) in combination with ritonavir, and the like is used in clinical practice, and such multiple drug combination therapy is becoming the mainstream of the AIDS treatment.

However, some of these medicaments are known to cause side effects such as liver function failure, central nervous disorders (e.g., vertigo), and the like. In addition, acquisition of resistance to a medicament causes a problem. Even worse, emergence of an HIV that shows multiple drug resistance in a multiple drug combination therapy has been known.

[0005]

Under the circumstances, a further development of a novel medicament, particularly a development of an anti-HIV agent based on a new mechanism, has been desired, wherein a development of an anti-HIV agent having an integrase inhibitory activity is expected, because an integrase characteristic of retrovirus is an essential enzyme for the growth of HIV.

SUMMARY OF THE INVENTION

Problems to be Solved by the Invention

[0006]

From the findings obtained from pharmacological studies and clinical results heretofore, an anti-HIV agent is effective for the prophylaxis or treatment of AIDS, and particularly a compound having an integrase inhibitory activity can be an effective anti-HIV agent.

Therefore, the present invention aims at provision of a compound having an anti-HIV activity, particularly a compound having an integrase inhibitory activity.

Means of Solving the Problems

[0007]

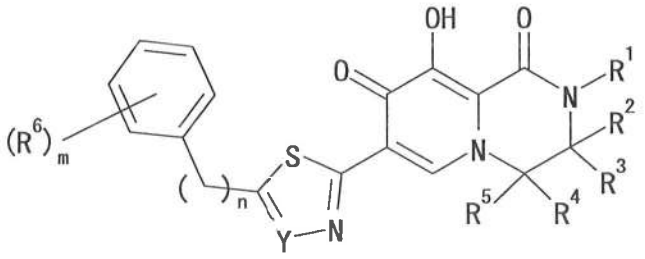
The present inventors have conducted intensive studies in an attempt to find a compound having an anti-HIV action, particularly a compound having an integrase inhibitory action, and completed the present invention.

More specifically, the present invention provides the following.

[1] A compound represented by the following formula [I] or a

pharmaceutically acceptable salt thereof, or a solvate thereof (sometimes to be abbreviated as "the compound of the present invention" in the present specification):

[0008]



[I]

[0009]

wherein

R^1 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

(2) a C_{3-8} cycloalkyl group, or

(3) a saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom,

R^2, R^3, R^4 and R^5 are the same or different and each is

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$ wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by

the same or different 1 to 5 substituents selected from the following group B,

(4) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group A, or

(5) a cyano group,

or

R^2 and R^3, or R^4 and R^5 optionally form, together with the carbon atom bonded thereto,

i) C_{3-8} cycloalkane, or

ii) a saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom,

wherein R^2, R^3, R^4 and R^5 are not hydrogen atoms at the same time,

R^6 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 halogen atoms,

(2) a C_{1-6} alkoxy group,

(3) a halogen atom, or

(4) a C_{3-8} cycloalkyl group,

Y is

(1) CH, or

(2) a nitrogen atom,

m is an integer of 1 to 5, and when m is an integer of 2 to 5, then each R^6 may be the same or different, and

n is an integer of 1 to 3,

group A:

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^{A1} and R^{A2} optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the following group B,

(b) a hydroxyl group,

(c) a C_{1-6} alkoxy group,

(d) a C_{1-6} alkoxy-C_{1-6} alkoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group,

(iii) a C_{1-6} alkyl-carbonyl group, or

(iv) a C_{1-6} alkyl-sulfonyl group, or

R^{A3} and R^{A4} optionally form, together with the nitrogen atom bonded thereto, a hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by 1 or 2 oxo groups,

(g) a carboxyl group,

(h) a C_{1-6} alkyl-sulfonyl group, and

(i) a C_{1-6} alkyl-carbonyl group;

group B:

(a) a hydroxyl group,

(b) a C_{1-6} alkoxy group,

(c) a C_{1-6} alkoxy-C_{1-6} alkyl group

(d) a C_{3-8} cycloalkyl group, and

(e) an oxo group.

[2] The compound of the above-mentioned [1], wherein R^1 is a C_{1-6} alkyl group optionally substituted by the same or different 1

to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[3] The compound of the above-mentioned [2], wherein R^1 is a C_{1-6} alkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[4] The compound of the above-mentioned [2], wherein R^1 is a C_{1-6} alkyl group substituted by a C_{3-8} cycloalkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[5] The compound of the above-mentioned [1], wherein R^1 is a C_{3-8} cycloalkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[6] The compound of the above-mentioned [1], wherein one of R^2, R^3, R^4 and R^5 is $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[7] The compound of the above-mentioned [1], wherein one of R^2, R^3, R^4 and R^5 is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A, or a pharmaceutically acceptable salt thereof, or a solvate

thereof.

[8] The compound of the above-mentioned [1], wherein R^6 is a halogen atom, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[9] The compound of the above-mentioned [1], wherein Y is CH, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

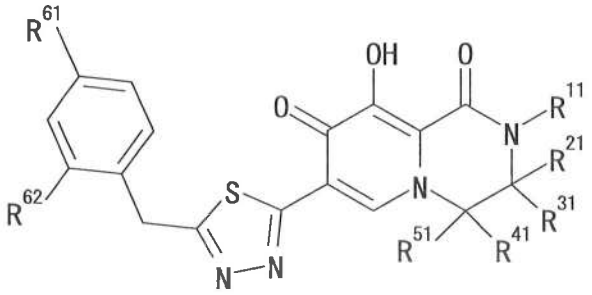
[10] The compound of the above-mentioned [1], wherein Y is a nitrogen atom, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[11] The compound of the above-mentioned [1], wherein m is 1 or 2, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[12] The compound of the above-mentioned [1], wherein n is 1, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[13] The compound of the above-mentioned [1], which is represented by the following formula [I-1], or a pharmaceutically acceptable salt thereof, or a solvate thereof:

[0010]



[I-1]

[0011]

wherein

R^{11} is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group, or

(2) a C_{3-8} cycloalkyl group,

R^{21}, R^{31}, R^{41} and R^{51} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

wherein R^{21}, R^{31}, R^{41} and R^{51} are not hydrogen atoms at the same time,

R^{61} is a halogen atom, and

R^{62} is a hydrogen atom or a halogen atom.

[14] The compound of the above-mentioned [13], wherein R^{21} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A, and

R^{31}, R^{41} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[15] The compound of the above-mentioned [13], wherein R^{21} is a C_{1-6} alkyl group, and

R^{31}, R^{41} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[16] The compound of the above-mentioned [13], wherein R^{41} is a C_{1-6} alkyl group optionally substituted by the same or different

1 to 5 substituents selected from group A, and

R^{21}, R^{31} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[17] The compound of the above-mentioned [13], wherein R^{21} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

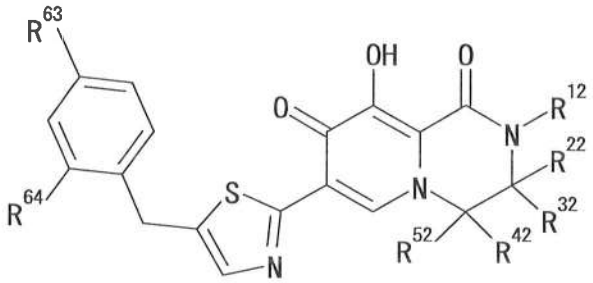
R^{41} is a C_{1-6} alkyl group, and

R^{31} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[18] The compound of the above-mentioned [1], which is represented by the following formula [I-2], or a pharmaceutically acceptable salt thereof, or a solvate thereof:

[0012]



[I-2]

[0013]

wherein

R^{12} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

R^{22}, R^{32}, R^{42} and R^{52} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B,

or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

wherein R^{22}, R^{32}, R^{42} and R^{52} are not hydrogen atoms at the same time,

R^{63} is a halogen atom, and

R^{64} is a hydrogen atom or a halogen atom.

[19] The compound of the above-mentioned [18], wherein R^{42} is -$CO-NR^aR^b$

wherein R^a and R^b form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B,

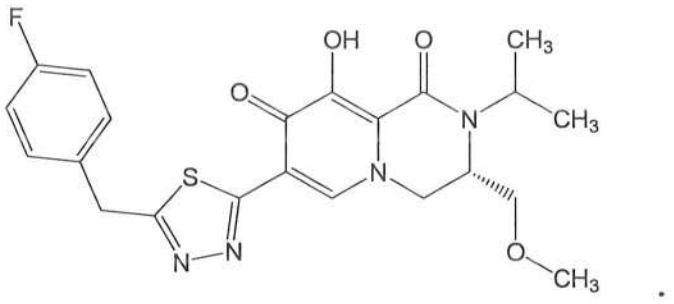
R^{52} is a C_{1-6} alkyl group, and

R^{22} and R^{32} is a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[20] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

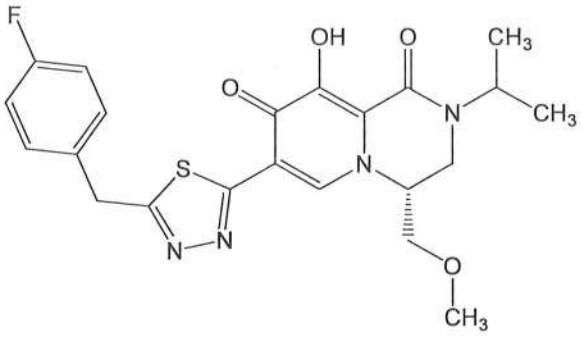
[0014]



[0015]

[21] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

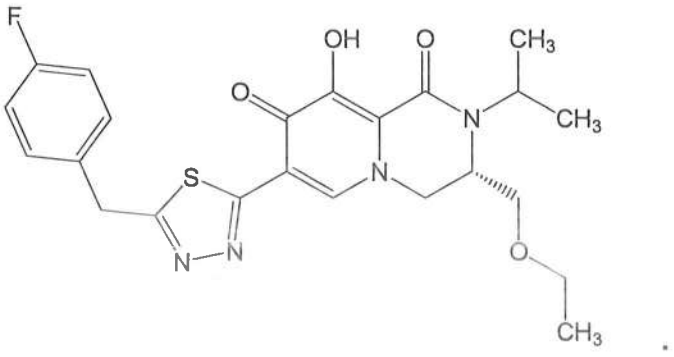
[0016]



[0017]

[22] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

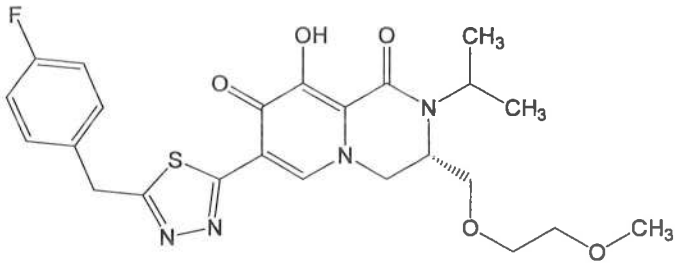
[0018]



[0019]

[23] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

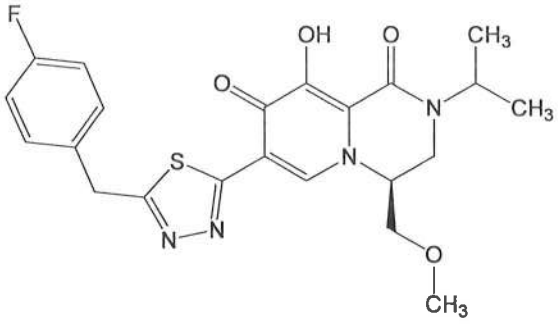
[0020]



[0021]

[24] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

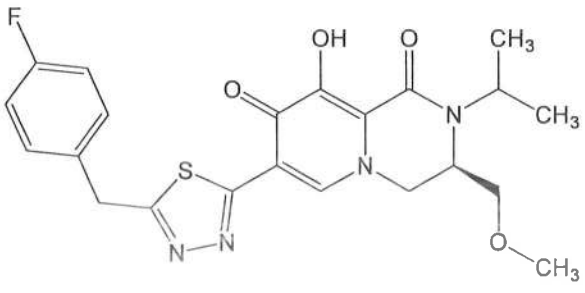
[0022]



[0023]

[25] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

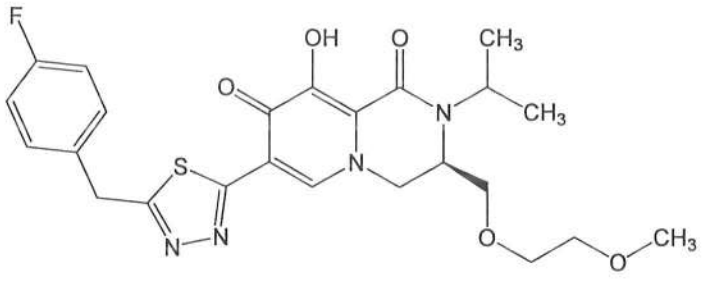
[0024]



[0025]

[26] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

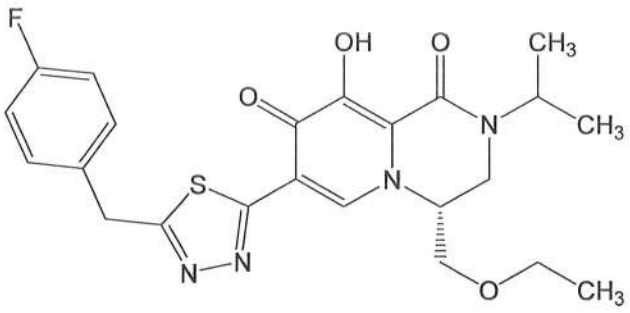
[0026]



[0027]

[27] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

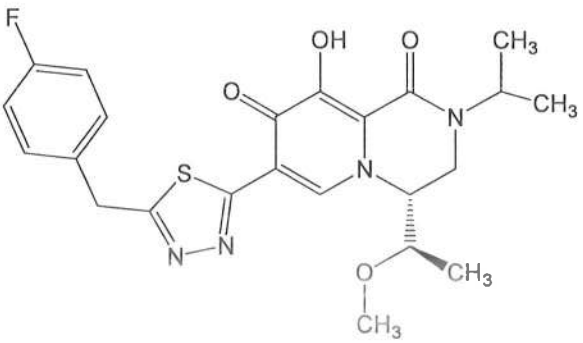
[0028]



[0029]

[28] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

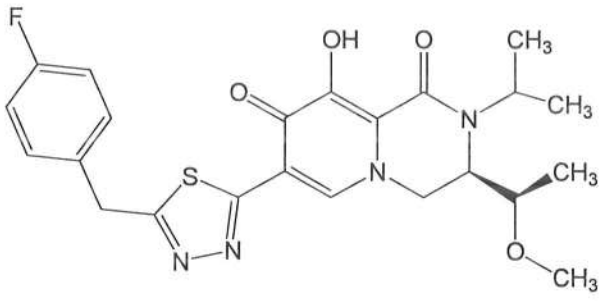
[0030]



[0031]

[29] The compound of the above-mentioned [1], which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:

[0032]



[0033]

[30] A pharmaceutical composition comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[31] An anti-HIV agent comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

[32] An HIV integrase inhibitor comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

[33] An anti-HIV agent comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, in combination with one or more other kinds of anti-HIV active substances.

[34] Use of the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, for the production of an anti-HIV agent.

[35] Use of the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, for the production of an HIV integrase inhibitor.

[36] A method for the prophylaxis or treatment of an HIV infectious disease in a mammal, which comprises administering an effective amount of the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, to said mammal.

[37] The method of the above-mentioned [36], which further comprises administering an effective amount of one or more other kinds of anti-HIV active substances to the mammal.

[38] A method for inhibiting HIV integrase in a mammal, which comprises administering an effective amount of the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, to said mammal.

[39] An anti-HIV composition comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[40] A pharmaceutical composition for inhibiting HIV integrase, comprising the compound of any one of the above-mentioned [1] to [29] or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[41] A commercial package comprising the pharmaceutical composition of the above-mentioned [30] and a written matter associated therewith, which states that the pharmaceutical composition can or should be used for treating HIV.

[42] A kit comprising the pharmaceutical composition of the above-mentioned [30] and a written matter associated therewith, which states that the pharmaceutical composition can or should be used for treating HIV.

Effect of the Invention

[0034]

The compound of the present invention can be medicaments effective for the prophylaxis or treatment of HIV infections or AIDS, as anti-HIV agents, having an HIV integrase inhibitory activity. In addition, by a combined use with other anti-HIV agent(s) such as protease inhibitor, reverse transcriptase inhibitor and the like, they can be more effective anti-HIV agents. Furthermore, having high inhibitory activity specific for integrase, they can be medicaments safe for human body with a fewer side effects.

Description of Embodiments

[0035]

The definitions of respective substituents and respective moieties used in the present specification are as follows.

[0036]

The "halogen atom" is a fluorine atom, a chlorine atom, a bromine atom or an iodine atom.

[0037]

The "C_{1-6} alkyl group" is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, preferably a straight chain or branched chain alkyl group having 1 to 4 carbon atoms. Specific examples include a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isopentyl group, a 1,1-dimethylpropyl group, a 1,2-dimethylpropyl group, a 2,2-dimethylpropyl group, a 1-ethylpropyl group, a hexyl group and the like.

[0038]

The "C_{1-6} alkoxy group" is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, preferably a straight chain or branched chain alkoxy group having 1 to 4 carbon atoms. Specific examples include a methoxy group, an ethoxy group, a propoxy group, an isopropyloxy group, a butoxy group, an isobutyloxy group, a tert-butyloxy group, a pentyloxy group, a hexyloxy group and the like.

[0039]

The "C_{1-6} alkoxy-C_{1-6} alkyl group" is that wherein the alkoxy moiety is the "C_{1-6} alkoxy group" defined above, and the alkyl moiety is the "C_{1-6} alkyl group" defined above. Preferred is a C_{1-6} alkoxy-C_{1-6} alkyl group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 4 carbon atoms, and the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 4 carbon atoms. Examples of the C_{1-6} alkoxy-C_{1-6} alkyl group include a methoxymethyl group, a methoxyethyl group, a methoxypropyl

group, a methoxybutyl group, a methoxypentyl group, a methoxyhexyl group, an ethoxymethyl group, an ethoxyethyl group, an ethoxypropyl group, an ethoxybutyl group, an ethoxypentyl group, an ethoxyhexyl group, a propoxymethyl group, a propoxyethyl group, a propoxypropyl group, a propoxybutyl group, a propoxypentyl group, a propoxyhexyl group, a butoxymethyl group, a butoxyethyl group, a butoxypropyl group, a butoxybutyl group, a butoxypentyl group, a butoxyhexyl group, a pentyloxymethyl group, a pentyloxyethyl group, a pentyloxypropyl group, a pentyloxybutyl group, a pentyloxypentyl group, a pentyloxyhexyl group, a hexyloxymethyl group, a hexyloxyethyl group, a hexyloxypropyl group, a hexyloxybutyl group, a hexyloxypentyl group, a hexyloxyhexyl group and the like.

[0040]

The "C_{1-6} alkoxy-C_{1-6} alkoxy group" is that wherein the C_{1-6} alkoxy moiety is the "C_{1-6} alkoxy group" defined above, preferably a straight chain or branched chain alkoxy group having 1 to 4 carbon atoms. Examples thereof include a methoxymethoxy group, a methoxyethoxy group, a methoxypropoxy group, a methoxybutoxy group, a methoxypentyloxy group, a methoxyhexyloxy group, an ethoxymethoxy group, an ethoxyethoxy group, an ethoxypropoxy group, an ethoxybutoxy group, an ethoxypentyloxy group, an ethoxyhexyloxy group, a propoxymethoxy group, a propoxyethoxy group, a propoxypropoxy group, a propoxybutoxy group, a propoxypentyloxy group, a propoxyhexyloxy group, a butoxymethoxy group, a butoxyethoxy group, a butoxypropoxy group, a butoxybutoxy group, a butoxypentyloxy group, a butoxyhexyloxy group, a pentyloxymethoxy group, a pentyloxyethoxy group, a pentyloxypropoxy group, a pentyloxybutoxy group, a pentyloxypentyloxy group, a pentyloxyhexyloxy group, a hexyloxymethoxy group, a hexyloxyethoxy group, a hexyloxypropoxy group, a hexyloxybutoxy group, a hexyloxypentyloxy group, a hexyloxyhexyloxy group and the like.

[0041]

The "C_{1-6} alkyl-carbonyl group" is an alkyl-carbonyl group wherein the C_{1-6} alkyl moiety is the "C_{1-6} alkyl group" defined above, preferably a straight chain or branched chain alkyl group having 1 to 4 carbon atoms. Examples thereof include a methylcarbonyl group, an ethylcarbonyl group, a propylcarbonyl group, an isopropylcarbonyl group, a butylcarbonyl group, an isobutylcarbonyl group, a sec-butylcarbonyl group, a tert-butylcarbonyl group, a pentylcarbonyl group, an isopentylcarbonyl group, a 1,1-dimethylpropylcarbonyl group, a hexylcarbonyl group and the like.

[0042]

The "C_{1-6} alkyl-sulfonyl group" is an alkyl-sulfonyl group wherein the C_{1-6} alkyl moiety is the "C_{1-6} alkyl group" defined above, preferably a straight chain or branched chain alkyl group having 1 to 4 carbon atoms. Examples thereof include a methylsulfonyl group, an ethylsulfonyl group, a propylsulfonyl group, an isopropylsulfonyl group, a butylsulfonyl group, an isobutylsulfonyl group, a sec-butylsulfonyl group, a tert-butylsulfonyl group, a pentylsulfonyl group, an isopentylsulfonyl group, a 1,1-dimethylpropylsulfonyl group, a hexylsulfonyl group and the like.

[0043]

The "C_{3-8} cycloalkyl group" is a saturated cycloalkyl group having 3 to 8 carbon atoms, preferably 3 to 5 carbon atoms, and examples thereof include a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group and the like.

[0044]

The "C_{3-8} cycloalkane" is saturated cycloalkane having 3 to 8 carbon atoms, preferably 3 to 5 carbon atoms, and examples thereof include cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane and the like.

[0045]

The "hetero ring" means a saturated or unsaturated (including partially unsaturated and completely unsaturated) monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, or a fused ring of the hetero rings, or a fused ring of a carbon ring selected from benzene, cyclopentane and cyclohexane, and the hetero ring.

[0046]

Examples of the above-mentioned "saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom" include a 4- to 7-membered saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and the like. Specific examples thereof include azetidine, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, imidazolidine, pyrazolidine, 1,3-dioxolane, 1,3-oxathioran, oxazolidine, thiazolidine, piperidine, piperazine, tetrahydropyran, tetrahydrothiopyran, dioxane, morpholine, thiomorpholine and the like.

[0047]

Examples of the above-mentioned "unsaturated (including partially unsaturated and completely unsaturated) monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom" include a 4- to 7-membered unsaturated (including partially unsaturated and completely unsaturated) monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and the like. Specific examples thereof include pyrroline, furan, thiophene, imidazole, imidazoline, pyrazole, oxazole, isoxazole, thiazole, isothiazole, 1,2,4-triazole, 1,2,3-triazole, tetrazole, 1,3,4-oxadiazole, 1,2,4-oxadiazole, 1,3,4-thiadiazole, 1,2,4-thiadiazole, furazan, pyridine, pyrimidine, 3,4-dihydropyrimidine, pyridazine, pyrazine,

1,3,5-triazine, pyrazoline, oxazoline, isooxazoline, thiazoline, isothiazoline, pyran and the like.

[0048]

Examples of the above-mentioned "fused ring of the hetero rings, or fused ring of a carbon ring selected from benzene, cyclopentane and cyclohexane, and the hetero ring" include indole, isoindole, benzimidazole, indazole, benzothiazole, benzofuran, isobenzofuran, indolizine, quinoline, isoquinoline, 1,2-dihydroquinoline, quinazoline, quinoxaline, cinnoline, phthalazine, quinolizidine, purine, pteridine, indoline, isoindoline, 5,6,7,8-tetrahydroquinoline, 1,2,3,4-tetrahydroquinoline, 1,3-benzodioxolane, 3,4-methylenedioxypyridine, 4,5-ethylenedioxypyrimidine, chromene, chromane, isochromane, 1,2,4-benzotriazine and the like.

[0049]

The "saturated monocyclic hetero ring" formed by R^a and R^b together with the nitrogen atom bonded thereto means a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and examples thereof include a 4- to 7-membered (e.g., 4- to 6-membered) saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 (e.g., 1 to 3, preferably 1) hetero atoms selected from nitrogen atom, oxygen atom and sulfur atom, and the like. Specific examples of the saturated monocyclic hetero ring include those exemplified as the above-mentioned "saturated monocyclic hetero ring containing, beside carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom", which contain, beside carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

The saturated monocyclic hetero ring is optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from the following group B.

[0050]

The "saturated monocyclic hetero ring" formed by R^2 and R^3, or R^4 and R^5, together with the carbon atom bonded thereto means a saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and examples thereof include a 5- to 7-membered (e.g., 6-membered) saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 (e.g., 1 to 3, preferably 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and the like. Specific examples of the saturated monocyclic hetero ring include those similar to the saturated monocyclic hetero rings exemplified as the above-mentioned "saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom".

[0051]

The "saturated monocyclic hetero ring" formed by R^{A1} and R^{A2} together with the nitrogen atom bonded thereto means a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and examples thereof include a 4- to 6-membered saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 (e.g., 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom and the like. Specific examples of the saturated monocyclic hetero ring include those exemplified as the above-mentioned "saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom", which optionally contain, besides carbon atom and one nitrogen atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

The saturated monocyclic hetero ring is optionally substituted by the same or different 1 to 5 substituents

selected from the following group B.

[0052]

The "hetero ring" formed by R^{A3} and R^{A4} together with the nitrogen atom bonded thereto means a hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and examples thereof include a 4- to 6-membered (e.g., 5-membered) monocyclic hetero ring, a 8- to 10-membered (e.g., 9-membered) fused cyclic hetero ring and the like, optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom. Specific examples of the hetero ring include those exemplified as the above-mentioned "hetero ring", which optionally contain, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

The hetero ring is optionally substituted by 1 or 2 oxo groups.

[0053]

The "saturated monocyclic heterocyclic group" for R^1 means a saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and examples thereof include a 5- or 6-membered saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 (e.g., 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and the like. Specific examples of the saturated monocyclic heterocyclic group include groups derived from those exemplified as the above-mentioned "saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom", which optionally contain, besides carbon atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom and the like. Examples thereof include a pyrrolidinyl group, a

tetrahydrofuryl (e.g., 3-tetrahydrofuryl) group, a tetrahydrothienyl group, an imidazolidinyl group, a pyrazolidinyl group, a 1,3-dioxolanyl group, a 1,3-oxathioranyl group, an oxazolidinyl group, a thiazolidinyl group, a piperidinyl group, a piperazinyl group, a tetrahydropyranyl group, a tetrahydrothiopyranyl group, a dioxanyl group, a morpholinyl group, a thiomorpholinyl group and the like.

[0054]

The "group A" includes the following substituents (a) to (i).

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^{A1} and R^{A2} optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the following group B,

(b) a hydroxyl group,

(c) a C_{1-6} alkoxy group,

(d) a C_{1-6} alkoxy-C_{1-6} alkoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group,

(iii) a C_{1-6} alkyl-carbonyl group, or

(iv) a C_{1-6} alkyl-sulfonyl group, or

R^{A3} and R^{A4} optionally form, together with the nitrogen atom bonded thereto, a hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by 1 or 2 oxo groups,

(g) a carboxyl group,

(h) a C_{1-6} alkyl-sulfonyl group, and

(i) a C_{1-6} alkyl-carbonyl group.

[0055]

The "C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A" is that wherein the "C_{1-6} alkyl group" defined above is optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from "group A" defined above, and includes an unsubstituted C_{1-6} alkyl group.

[0056]

The "group B" includes the following substituents (a) to (e).

(a) a hydroxyl group,

(b) a C_{1-6} alkoxy group,

(c) a C_{1-6} alkoxy-C_{1-6} alkyl group,

(d) a C_{3-8} cycloalkyl group, and

(e) an oxo group.

[0057]

The "C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B" is that wherein the "C_{1-6} alkyl group" defined above is optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from the "group B" defined above, and includes an unsubstituted C_{1-6} alkyl group.

[0058]

The "saturated monocyclic hetero ring is optionally substituted by the same or different 1 to 5 substituents

selected from group B" for R^a and R^b, or R^{A1} and R^{A2} means that the "saturated monocyclic hetero ring" defined above which is formed by R^a and R^b, or R^{A1} and R^{A2} together with the nitrogen atom bonded thereto is optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from the "group B" defined above, and includes an unsubstituted saturated monocyclic hetero ring.

[0059]

In the above-mentioned formula [I], preferable groups are as described below.

[0060]

R^1 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

(2) a C_{3-8} cycloalkyl group, or

(3) a saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

[0061]

Preferable embodiment of R^1 is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group.

More preferable embodiment of R^1 is a C_{1-6} alkyl group.

A different, more preferable embodiment of R^1 is a C_{1-6} alkyl group substituted by a C_{3-8} cycloalkyl group.

[0062]

A different, preferable embodiment of R^1 is a C_{3-8} cycloalkyl group.

[0063]

Further different preferable embodiments of R^1 are

(1) a C_{1-6} alkyl group optionally substituted by the same or

different 1 to 3 C_{3-8} cycloalkyl groups,

(2) a C_{3-8} cycloalkyl group,

(3) a 5- or 6-membered saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 (e.g., 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and the like.

Of these, preferred are a methyl group, a cyclopropylmethyl group, an ethyl group, a 1-cyclopropylethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a 1,2-dimethylpropyl group, a 2,2-dimethylpropyl group, a 1-ethylpropyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a tetrahydrofuryl (e.g., 3-tetrahydrofuryl) group and the like.

[0064]

R^2, R^3, R^4 and R^5 are the same or different and each is

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B,

(4) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A, or

(5) a cyano group.

[0065]

In a preferable embodiment of R^2, R^3, R^4 and R^5, one of R^2, R^3, R^4 and R^5 is $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B.

[0066]

In another preferable embodiment of R^2, R^3, R^4 and R^5, one of R^2, R^3, R^4 and R^5 is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A.

[0067]

Further preferable embodiments of R^2, R^3, R^4 and R^5 are respectively shown below.

[0068]

As R^2, preferred are

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom, and

(ii) a C_{1-6} alkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a 4- to 7-membered (e.g., 4- to 6-

membered) saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 (e.g., 1 to 3, preferably 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom,

(4) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 3 (e.g., 1) substituents selected from

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom, or

(ii) a C_{1-6} alkyl group,

(b) a hydroxyl group,

(c) a C_{1-6} alkoxy group,

(d) a C_{1-6} alkoxy-C_{1-6} alkoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group,

(iii) a C_{1-6} alkyl-carbonyl group, or

(iv) a C_{1-6} alkyl-sulfonyl group, and

(g) a carboxyl group, and

(5) a cyano group.

As R^2, more preferred are

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a methyl group,

(ii') an ethyl group,

(ii") an isopropyl group, or

(ii"') a tert-butyl group, or

R^a and R^b optionally form, together with the nitrogen

atom bonded thereto, a saturated monocyclic hetero ring selected from azetidine, pyrrolidine and morpholine,

(4) a methyl group, an ethyl group, a propyl goroup, or an isopropyl group, which is optionally substituted by the same or different 1 to 3 (e.g., 1) substituents selected from

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom, or

(ii) a methyl group,

(b) a hydroxyl group,

(c) a methoxy group,

(c') an ethoxy group,

(c'') an isopropoxy group,

(d) a methoxyethoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is a hydrogen atom, a methyl group, a methylcarbonyl group, an isopropylcarbonyl group, a tert-butylcarbonyl group, a 1,1-dimethylpropylcarbonyl group or a methylsulfonyl group, and

(g) a carboxyl group, and

(5) a cyano group.

[0069]

As R^3, preferred are

(1) a hydrogen atom, and

(2) a C_{1-6} alkyl group optionally substituted by a C_{1-6} alkoxy group.

As R^3, more preferred are a hydrogen atom, a methyl group and a methoxymethyl group.

[0070]

As R^4, preferred are

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from a C_{1-6} alkoxy group and a C_{3-8} cycloalkyl group, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring which is a 4- to 7-membered (e.g., 4- to 6-membered) saturated monocyclic hetero ring which is optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 (e.g., 1 to 3, preferably 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents selected from (a) a hydroxyl group, (b) a C_{1-6} alkoxy group, (c) a C_{1-6} alkoxy-C_{1-6} alkyl group and (d) an oxo group,

(4) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) substituents

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is selected from

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 (e.g., 1 to 3, preferably 1) C_{1-6} alkoxy groups, or

(iii) a C_{3-8} cycloalkyl group, or

R^{A1} and R^{A2} optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring which is a 4- to 6-membered saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 (e.g., 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by a C_{1-6} alkoxy group,

(b) a hydroxyl group,

(c) a C_{1-6} alkoxy group,

(d) a C_{1-6} alkoxy-C_{1-6} alkoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group,

(iii) a C_{1-6} alkyl-carbonyl group, or

(iv) a C_{1-6} alkyl-sulfonyl group, or

R^{A3} and R^{A4} optionally form, together with the nitrogen atom bonded thereto, a hetero ring which is a 4- to 7-membered (e.g., 6-membered) monocyclic hetero ring, or a 8- to 10-membered (e.g., 9-membered) fused cyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by 1 or 2 oxo groups,

(g) a carboxyl group,

(h) a C_{1-6} alkyl-sulfonyl group, and

(i) a C_{1-6} alkyl-carbonyl group, and

(5) a cyano group.

As R^4, more preferred are

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a methyl group, an ethyl group, an isopropyl group or an isobutyl group, which is optionally substituted by the same or different one substituent selected from a methoxy group and a cyclopropyl group, or

(iii) a cyclopropyl group, or

R^a and R^b optionally form, together with the nitrogen

atom bonded thereto, a saturated monocyclic hetero ring selected from azetidine, pyrrolidine, piperidine and morpholine, which is optionally substituted by one substituent selected from a hydroxyl group, a methoxy group, a methoxymethyl group and an oxo group,

(4) a methyl group, an ethyl group, a propyl group, an isopropyl group or a tert-butyl group, which is optionally substituted by one or two substituents selected from

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom,

(ii) a methyl group, an ethyl group, an isopropyl group or an isobutyl group, which is optionally substituted by a methoxy group, or

(iii) a cyclopropyl group, or

R^{A1} and R^{A2} optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring selected from azetidine, piperidine and morpholine, and optionally substituted by a methoxy group,

(b) a hydroxyl group,

(c) a methoxy group,

(c') an ethoxy group,

(c") a propoxy group,

(c"') an isopropoxy group,

(c"") a butoxy group,

(d) a methoxyethoxy group,

(d') an ethoxyethoxy group,

(d") a methoxypropoxy group,

(d"') a methoxyisopropoxy group,

(d"") an isopropoxyethoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is a hydrogen atom, a methyl group, an ethyl group, an

isopropyl group, a methylcarbonyl group, an ethylcarbonyl group, an isopropylcarbonyl group, a methylsulfonyl group or a tert-butylsulfonyl group, or

R^{A3} and R^{A4} optionally form, together with the nitrogen atom bonded thereto, pyrazole, triazole (e.g., 1,2,4-triazole), tetrazole, oxazolidine or isoindoline, which is optionally substituted by 1 or 2 oxo groups,

(g) a carboxyl group,

(h) a methylsulfonyl group, and

(i) a methylcarbonyl group, and

(5) a cyano group.

[0071]

As R^5, preferred are a hydrogen atom and a C_{1-6} alkyl group optionally substituted by one substituent selected from a C_{1-6} alkoxy group and a C_{1-6} alkoxy-C_{1-6} alkoxy group.

As R^5, more preferred are a hydrogen atom and a methyl group or an ethyl group, which is optionally substituted by one substituent selected from a methoxy group and a methoxyethoxy group.

[0072]

R^2 and R^3, or R^4 and R^5 optionally form, together with the carbon atom bonded thereto, i) C_{3-8} cycloalkane or ii) a saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

As the ring formed by R^2 and R^3, or R^4 and R^5 together with the carbon atom bonded thereto, preferred are

i) C_{3-8} cycloalkane, and

ii) a 5- to 7-membered (e.g., 6-membered) saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 (e.g., 1 to 3, preferably 1) hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom.

As the ring formed by R^2 and R^3, or R^4 and R^5 together with the carbon atom bonded thereto, more preferred are cyclopropane and tetrahydropyran.

[0073]

Here, R^2, R^3, R^4 and R^5 are not hydrogen atoms at the same time.

[0074]

R^6 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 (e.g., 1 to 3) halogen atoms,

(2) a C_{1-6} alkoxy group,

(3) a halogen atom, or

(4) a C_{3-8} cycloalkyl group.

As R^6, preferred is a halogen atom.

Other preferable embodiments of R^6 are a methyl group, a trifluoromethyl group, a methoxy group, an ethoxy group, a fluorine atom, a chlorine atom, a bromine atom and a cyclopropyl group.

[0075]

Y is

(1) CH, or

(2) a nitrogen atom.

As Y, preferred is CH.

Other preferable embodiment of Y is a nitrogen atom.

[0076]

m is an integer of 1 to 5, and when m is an integer of 2 to 5, the above-mentioned R^6 may be the same or different.

As m, preferred is 1 to 3.

As m, more preferred is 1 or 2.

[0077]

n is an integer of 1 to 3.

As n, preferred is 1.

[0078]

In the above-mentioned formula [I-1], preferable groups are as described below.

[0079]

R^{11} is

(1) a C_{1-6} alkyl group optionally substituted by the same or

different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group, or

(2) a C_{3-8} cycloalkyl group.

As R^{11}, those exemplified as the preferable embodiments of R^1 in the above-mentioned formula (I), which are within the scope of R^{11}, are preferable.

[0080]

R^{21}, R^{31}, R^{41} and R^{51} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, and

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A.

[0081]

As R^{21}, preferred is a hydrogen atom.

Other preferable embodiment of R^{21} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A. More preferred is a C_{1-6} alkyl group.

Examples of yet other preferable embodiment of R^{21} include those exemplified as the preferable embodiments of R^2

in the above-mentioned formula (I), which are within the scope of R^{21}.

[0082]

As R^{31}, preferred is a hydrogen atom.

Examples of other preferable embodiment of R^{31} include those exemplified as the preferable embodiments of R^3 in the above-mentioned formula (I), which are within the scope of R^{31}.

[0083]

As R^{41}, preferred is a hydrogen atom.

Other preferable embodiment of R^{41} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A. More preferred is a C_{1-6} alkyl group.

Examples of yet other preferable embodiment of R^{41} include those exemplified as the preferable embodiments of R^4 in the above-mentioned formula (I), those contained within the scope of R^{41}.

[0084]

As R^{51}, preferred is a hydrogen atom.

Other preferable embodiments of R^{51} are those exemplified as the preferable embodiments of R^5 in the above-mentioned formula (I), which are within the scope of R^{51}.

[0085]

Here, R^{21}, R^{31}, R^{41} and R^{51} are not hydrogen atoms at the same time.

[0086]

R^{61} is a halogen atom.

As R^{61}, preferred are a fluorine atom and a chlorine atom.

[0087]

R^{62} is a hydrogen atom or a halogen atom.

As R^{62}, preferred are a hydrogen atom, a fluorine atom and a bromine atom.

[0088]

In the above-mentioned formula [I-2], preferable groups are as described below.

[0089]

R^{12} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group.

As R^{12}, those exemplified as the preferable embodiments of R^1 in the above-mentioned formula (I), which are within the scope of R^{12}, are preferable.

[0090]

R^{22}, R^{32}, R^{42} and R^{52} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group A.

[0091]

As R^{22}, preferred is a hydrogen atom.

Other preferable embodiments of R^{22} are those exemplified as the preferable embodiments of R^2 in the above-mentioned formula (I), which are within the scope of R^{22}.

[0092]

As R^{32}, preferred is a hydrogen atom.

Other preferable embodiments of R^{32} are those exemplified as the preferable embodiments of R^3 in the above-mentioned formula (I), which are within the scope of R^{32}.

[0093]

As R^{42}, preferred is $-CO-NR^aR^b$

wherein R^a and R^b form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the above-mentioned group B.

Other preferable embodiments of R^{42} are those exemplified as the preferable embodiments of R^4 in the above-mentioned formula (I), which are within the scope of R^{42}.

[0094]

As R^{52}, preferred is a C_{1-6} alkyl group.

Other preferable embodiments of R^{52} are those exemplified as the preferable embodiments of R^5 in the above-mentioned formula (I), which are within the scope of R^{52}.

[0095]

Here, R^{22}, R^{32}, R^{42} and R^{52} are not hydrogen atoms at the same time.

[0096]

R^{63} is a halogen atom.

As R^{63}, preferred is a fluorine atom.

[0097]

R^{64} is a hydrogen atom or a halogen atom.

As R^{64}, preferred are a hydrogen atom and a fluorine atom.

[0098]

As the compound of the present invention, compounds represented by the above-mentioned formula [I], the formula [I-1] and the formula [I-2], and compounds described in the following Examples are preferable.

[0099]

A pharmaceutically acceptable salt of the "compounds represented by the above-mentioned formula [I], the formula [I-1] and the formula [I-2]" (hereinafter to be also referred to as the compound of the present invention) may be any salt as long as it forms an atoxic salt with the compound of the present invention. Examples thereof include a salt with an inorganic acid, a salt with an organic acid, a salt with an inorganic base, a salt with an organic base, a salt with an amino acid and the like.

Examples of the salt with an inorganic acid include salts with hydrochloric acid, nitric acid, sulfuric acid, phosphoric acid, hydrobromic acid and the like.

Examples of the salt with an organic acid include salts with oxalic acid, malonic acid, maleic acid, citric acid, fumaric acid, lactic acid, malic acid, succinic acid, tartaric acid, acetic acid, trifluoroacetic acid, gluconic acid, ascorbic acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid and the like.

Examples of the salt with an inorganic base include sodium salt, potassium salt, calcium salt, magnesium salt, ammonium salt and the like.

Examples of the salt with an organic base include salts with methylamine, diethylamine, trimethylamine, triethylamine, ethanolamine, diethanolamine, triethanolamine, ethylenediamine, tris(hydroxymethyl)methylamine, dicyclohexylamine, N,N'-dibenzylethylenediamine, guanidine, pyridine, picoline, choline, cinchonine, meglumine and the like.

Examples of the salt with an amino acid include salts with lysine, arginine, aspartic acid, glutamic acid and the like.

[0100]

Each salt can be obtained by reacting a compound represented by the formula [I], the formula [I-1] and the formula [I-2] with an inorganic base, an organic base, an

inorganic acid, an organic acid or an amino acid according to a method known per se.

[0101]

In the present invention, as the pharmaceutically acceptable salt of the compounds represented by the formula [I], the formula [I-1] and the formula [I-2], preferred are salts with hydrochloric acid (e.g., 1 hydrochloride, 2 hydrochloride), salts with hydrobromic acid (e.g., 1 hydrobromide, 2 hydrobromide), and sodium salt.

[0102]

The "solvate" is a compound represented by the formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof, with which a molecule of a solvent is coordinated, and also encompasses hydrates (also referred to as water-containing compound). The solvate is preferably a pharmaceutically acceptable solvate, such as a 1 hydrate, a 1/2 hydrate, a 2 hydrate, a 1 hydrate of sodium salt, a 1 methanolate, a 1 ethanolate, a 1 acetonitrilate, a 2/3 ethanolate of 2 hydrochloride of the compound represented by the formula [I], the formula [I-1] and the formula [I-2] and the like.

[0103]

A solvate of a compound represented by the formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof can be obtained according to a method known per se.

[0104]

In addition, there can be various isomers of compounds represented by the above-mentioned formulas [I], [I-1] and [I-2]. For example, when E form and Z form are present as geometric isomers, and when an asymmetric carbon atom is present, enantiomers and diastereomers are present as stereo isomers based on them. In addition, when axial chirality is present, stereo isomers based thereon are present. Where necessary, tautomers can be present. Accordingly, all of such

isomers and mixtures thereof are encompassed in the scope of the present invention. As the compound of the present invention, one isolated and purified from various isomers, by-products, metabolites or prodrugs is preferable, and one having a purity of not less than 90% is preferable and one having a purity of not less than 95% is more preferable.

[0105]

In addition, the compounds represented by the formula [I], the formula [I-1] and the formula [I-2] may be crystal or amorphous.

[0106]

In addition, a compound represented by the formula [I], the formula [I-1] and the formula [I-2] may be labeled with an isotope (e.g., ^{3}H, ^{14}C, ^{35}S etc.).

[0107]

As the compounds represented by the formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof, or a solvate thereof, compounds represented by the formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof, or a solvate thereof, which is substantially purified, is preferable. More preferred is compounds represented by the formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof, or a solvate thereof, which has been purified to a purity of not less than 80%.

[0108]

In the present invention, a prodrug of a compound represented by the formula [I], the formula [I-1] and the formula [I-2] can also be a useful medicament.

[0109]

A "prodrug" is a derivative of the compound of the present invention, which has a chemically or metabolically decomposable group and which restores to the original compound to show its inherent efficacy after administration to the body by, for example, hydrolysis, solvolysis or decomposition under

physiological conditions. It includes a complex and a salt, not involving a covalent bond.

[0110]

The prodrug is utilized, for example, for improving absorption by oral administration or targeting of a target site.

[0111]

Examples of the site to be modified include highly reactive functional groups in the compound of the present invention, such as hydroxyl group, carboxyl group, amino group and the like.

[0112]

Examples of the hydroxyl-modifying group include acetyl group, propionyl group, isobutyryl group, pivaloyl group, palmitoyl group, benzoyl group, 4-methylbenzoyl group, dimethylcarbamoyl group, dimethylaminomethylcarbonyl group, sulfo group, alanyl group, fumaryl group and the like. In addition, a sodium salt of 3-carboxybenzoyl group, 2-carboxyethylcarbonyl group and the like can also be used.

Examples of the carboxyl-modifying group include methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, tert-butyl group, pivaloyloxymethyl group, carboxymethyl group, dimethylaminomethyl group, 1-(acetyloxy)ethyl group, 1-(ethoxycarbonyloxy)ethyl group, 1-(isopropyloxycarbonyloxy)ethyl group, 1-(cyclohexyloxycarbonyloxy)ethyl group, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl group, benzyl group, phenyl group, o-tolyl group, morpholinoethyl group, N,N-diethylcarbamoylmethyl group, phthalidyl group and the like.

Examples of the amino-modifying group include hexylcarbamoyl group, 3-methylthio-1-(acetylamino)propylcarbonyl group, 1-sulfo-1-(3-ethoxy-4-hydroxyphenyl)methyl group, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl group and the like.

[0113]

Examples of the "pharmaceutical composition" include oral preparations such as tablet, capsule, granule, powder, troche, syrup, emulsion, suspension and the like, and parenteral agents such as external preparation, suppository, injection, eye drop, transnasal agent, pulmonary preparation and the like.

[0114]

The pharmaceutical composition of the present invention (e.g., an anti-HIV composition, a pharmaceutical composition for HIV integrase inhibitory etc.) is produced by appropriately admixing a suitable amount of a compound represented by the formula [I], the formula [I-1] or the formula [I-2] of the present invention or a salt thereof, or a solvate thereof with at least one kind of a pharmaceutically acceptable carrier according to a method known per se in the technical field of pharmaceutical preparations. The content of the compound represented by the formula [I], the formula [I-1] or the formula [I-2] of the present invention or a salt thereof, or a solvate thereof in the pharmaceutical composition varies depending on the dosage form, the dose and the like, and the like. It is, for example, 0.1 to 100 wt% of the whole composition.

Examples of the "pharmaceutically acceptable carrier" include various organic or inorganic carrier substances conventionally used as preparation materials such as excipient, disintegrant, binder, fluidizer, lubricant and the like for solid dosage forms, and solvent, solubilizing agent, suspending agent, isotonicity agent, buffering agent, soothing agent and the like for liquid preparations. Where necessary, additives such as preservative, antioxidant, colorant, sweetening agent and the like are used.

Examples of the "excipient" include lactose, sucrose, D-mannitol, D-solbitol, cornstarch, dextrin, microcrystalline cellulose, crystalline cellulose, carmellose, carmellose calcium, sodium carboxymethyl starch, low-substituted hydroxypropylcellulose, gum arabic and the like.

Examples of the "disintegrant" include carmellose, carmellose calcium, carmellose sodium, sodium carboxymethyl starch, croscarmellose sodium, crospovidone, low-substituted hydroxypropylcellulose, hydroxypropylmethylcellulose, crystalline cellulose and the like.

Examples of the "binder" include hydroxypropylcellulose, hydroxypropylmethylcellulose, povidone, crystalline cellulose, sucrose, dextrin, starch, gelatin, carmellose sodium, gum arabic and the like.

Examples of the "fluidizer" include light anhydrous silicic acid, magnesium stearate and the like.

Examples of the "lubricant" include magnesium stearate, calcium stearate, talc and the like.

Examples of the "solvent" include purified water, ethanol, propylene glycol, macrogol, sesame oil, corn oil, olive oil and the like.

Examples of the "solubilizing agent" include propylene glycol, D-mannitol, benzyl benzoate, ethanol, triethanolamine, sodium carbonate, sodium citrate and the like.

Examples of the "suspending agent" include benzalkonium chloride, carmellose, hydroxypropylcellulose, propylene glycol, povidone, methylcellulose, glycerol monostearate and the like.

Examples of the "isotonicity agent" include glucose, D-sorbitol, sodium chloride, D-mannitol and the like.

Examples of the "buffering agent" include sodium hydrogen phosphate, sodium acetate, sodium carbonate, sodium citrate and the like.

Examples of the "soothing agent" include benzyl alcohol and the like.

Examples of the "preservative" include ethyl parahydroxybenzoate, chlorobutanol, benzyl alcohol, sodium dehydroacetate, sorbic acid and the like.

Examples of the "antioxidant" include sodium sulfite, ascorbic acid and the like.

Examples of the "colorant" include food colors (e.g.,

Food Color Red No. 2 or 3, Food Color yellow 4 or 5 etc.), β-carotene and the like.

Examples of the "sweetening agent" include saccharin sodium, dipotassium glycyrrhizinate, aspartame and the like.

[0115]

The pharmaceutical composition of the present invention can be administered not only to human but also to mammals other than human (e.g., mouse, rat, hamster, guinea pig, rabbit, cat, dog, swine, bovine, horse, sheep, monkey etc.) orally or parenterally (e.g., topical, rectal, intravenous administration etc.). While the dose varies depending on the subject of administration, disease, symptom, dosage form, administration route and the like, for example, the dose for oral administration to an adult patient (body weight: about 60 kg) is generally within the scope of about 1 mg to 1 g per day, based on the compound of the present invention as an active ingredient. The amount can be administered in one to several portions.

[0116]

The compounds represented by the above-mentioned formula [I], the formula [I-1] and the formula [I-2] or a pharmaceutically acceptable salt thereof, or a solvate thereof inhibits HIV integrase, and can be used as an active ingredient of a therapeutic agent or prophylactic agent for HIV infection.

To "inhibit HIV integrase" means to specifically inhibit the function as HIV integrase to eliminate or attenuate the activity thereof. For example, it means to specifically inhibit the function of HIV integrase under the conditions of the below-mentioned Experimental Example 1. As the "inhibition of HIV integrase", preferred is "inhibition of human HIV integrase". As the "HIV integrase inhibitor", preferred is a "human HIV integrase inhibitor".

The compounds represented by the above-mentioned formula [I], the formula [I-1] and the formula [I-2] or a

pharmaceutically acceptable salt thereof, or a solvate thereof can be used in combination (hereinafter to be referred to as combination use) with other single or plural medicaments (hereinafter to be also referred to as a concomitant drug) by a conventional method generally employed in the medicament field.

The administration frequency of the compounds represented by the above-mentioned formula [I], the formula [I-1] and the formula [I-2], or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a concomitant drug is not limited, and they may be administered as a combined agent to the subject of administration, or the two may be administered simultaneously or at certain time intervals. In addition, they may be used as a medicament in the form of a kit containing the pharmaceutical composition of the present invention and a concomitant drug. The dose of the concomitant drug may be determined according to the dosage used clinically, and can be appropriately determined depending on the subject of administration, disease, symptom, dosage form, administration route, administration time, combination and the like. The administration form of the concomitant drug is not particularly limited, and the compound of the present invention or a salt thereof, or a solvate thereof and the concomitant drug need only be combined.

[0117]

An anti-HIV agent is generally required to sustain its effect for a long time, so that can be effective not only for temporal suppression of viral growth but also prohibition of viral re-growth. This means that a prolonged administration is necessary and that a high single dose may be frequently inevitable to sustain effect for a longer period through the night. Such prolonged and high dose administration increases the risk of causing side effects.

[0118]

In view of this, one of the preferable embodiments of the

compound of the present invention is such compound permitting high absorption by oral administration, and such compound capable of maintaining blood concentration of the administered compound for an extended period of time.

[0119]

In addition to the above-mentioned, preferable embodiments of the compound of the present invention are a compound having fine pharmacological activity (e.g., a compound having strong HIV integrase inhibitory activity, a compound having high anti-HIV activity), a compound having fine bioavailability (e.g., a compound having high cellular membrane permeability, a compound stable to metabolic enzyme, a compound with low binding ability to protein and the like), a compound having an anti-HIV activity against HIV having G140S/Q148H mutation, and the like.

[0120]

Of the compounds of the present invention, a compound having high pharmacological activity (concretely, IC_{50} of HIV integrase inhibitory activity is less than 0.1 μM, preferably less than 0.01 μM) and high oral absorption, whose blood concentration is maintained for a long time after administration, is more preferable.

[0121]

Using the above-mentioned compound, dose and/or frequency of administration of the compound of the present invention to human are/is expected to be decreased. Preferable administration frequency is not more than twice a day, more preferably, not more than once a day (e.g., once a day, once in two days, etc.).

[0122]

The compound of the present invention can be used for the improvement of viremia due to HIV and/or maintenance of improved condition thereof, prophylaxis and treatment of virus infections, particularly, an HIV infection and/or maintenance of improved condition thereof.

[0123]

As an index of the "treatment", "improvement" or "effect", a decrease in the virus level or HIV RNA level in the body, particularly in blood, can be used.

[0124]

The "prophylaxis of HIV infection" includes administration of a medicament to a person with suspected or possible HIV infection (infection due to transfusion, infection from mother to child), and the like.

[0125]

By the "prophylaxis of AIDS" is meant, for example, administration of a medicament to an individual who tested HIV positive but has not yet developed the disease state of AIDS; administration of a medicament to an individual who shows an improved disease state of AIDS after treatment but who carries HIV still to be eradicated and whose relapse of AIDS is worried; administration of a medicament before infection with HIV out of a fear of possible infection; and the like.

[0126]

Examples of the "other anti-HIV agents" and "other anti-HIV active substances" to be used for a multiple drug combination therapy include an anti-HIV antibody or other antibody, an HIV vaccine or other vaccine, immunostimulants such as interferon, interferon agonist and the like, a ribozyme against HIV, an HIV antisense drug, an HIV reverse transcriptase inhibitor, an HIV protease inhibitor, an HIV integrase inhibitor, an inhibitor of attachment between a receptor (CD4, CXCR4, CCR5 and the like) of a host cell recognized by virus and the virus (CCR5 antagonist and the like), a DNA polymerase inhibitor or DNA synthesis inhibitor, a medicament acting on HIVp24, an HIV fusion inhibitor, an IL-2 agonist or antagonist, a TNF-α antagonist, an α-glucosidase inhibitor, a purine nucleoside phosphorylase inhibitor, an apoptosis agonist or inhibitor, a cholinesterase inhibitor, an immunomodulator and the like.

[0127]

Specific examples of the HIV reverse transcriptase inhibitor include Retrovir(R) (zidovudine), Epivir(R) (lamivudine), Zerit(R) (sanilvudine), Videx(R) (didanosine), Hivid(R) (zalcitabine), Ziagen(R) (abacavir sulfate), Viramune(R) (nevirapine), Stocrin(R) (efavirenz), Rescriptor(R) (delavirdine mesylate), Combivir(R) (zidovudine+lamivudine), Trizivir(R) (abacavir sulfate+lamivudine+zidovudine), Coactinon(R) (emivirine), Phosphonovir(R), Coviracil(R), alovudine (3'-fluoro-3'-deoxythymidine), Thiovir (thiophosphonoformic acid), Capravirin (5-[(3,5-dichlorophenyl)thio]-4-isopropyl-1-(4-pyridylmethyl)imidazole-2-methanol carbamic acid), Tenofovir disoproxil fumarate ((R)-[[2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl]phosphonic acid bis(isopropoxycarbonyloxymethyl)ester fumarate), DPC-083 ((4S)-6-chloro-4-[(1E)-cyclopropylethenyl]-3,4-dihydro-4-trifluoromethyl-2(1H)-quinazolinone), DPC-961 ((4S)-6-chloro-4-(cyclopropylethynyl)-3,4-dihydro-4-(trifluoromethyl)-2(1H)-quinazolinone), DAPD ((-)-β-D-2,6-diaminopurine dioxolane), Immunocal, MSK-055, MSA-254, MSH-143, NV-01, TMC-120, DPC-817, GS-7340, TMC-125, SPD-754, D-A4FC, capravirine, UC-781, emtricitabine, alovudine, Phosphazid, BCH-10618, DPC-083, Etravirine, BCH-13520, MIV-210, Abacavir sulfate/lamivudine, GS-7340, GW-5634, GW-695634, TMC-278 and the like, wherein (R) means a registered trademark (hereinafter the same) and the names of other medicaments are general names.

[0128]

Specific examples of the HIV protease inhibitor include Crixivan(R) (indinavir sulfate ethanolate), saquinavir, Invirase(R) (saquinavir mesylate), Norvir(R) (ritonavir), Viracept(R) (nelfinavir mesylate), lopinavir, Prozei(R) (amprenavir), Kaletra(R) (ritonavir+lopinavir), mozenavir dimesylate ([4R-(4α,5α,6β)]-1,3-bis[(3-aminophenyl)methyl]-hexahydro-5,6-dihydroxy-4,7-bis(phenylmethyl)-2H-1,3-diazepin-

2-one dimethanesulfonate), tipranavir (3'-[(1R)-1-[(6R)-5,6-dihydro-4-hydroxy-2-oxo-6-phenylethyl-6-propyl-2H-pyran-3-yl]propyl]-5-(trifluoromethyl)-2-pyridinesulfonamide), lasinavir (N-[5(S)-(tert-butoxycarbonylamino)-4(S)-hydroxy-6-phenyl-2(R)-(2,3,4-trimethoxybenzyl)hexanoyl]-L-valine 2-methoxyethylenamide), KNI-272 ((R)-N-tert-butyl-3-[(2S,3S)-2-hydroxy-3-N-[(R)-2-N-(isoquinolin-5-yloxyacetyl)amino-3-methylthiopropanoyl]amino-4-phenylbutanoyl]-5,5-dimethyl-1,3-thiazolidine-4-carboxamide), GW-433908, TMC-126, DPC-681, buckminsterfullerene, MK-944A (MK944 (N-(2(R)-hydroxy-1(S)-indanyl)-2(R)-phenylmethyl-4(S)-hydroxy-5-[4-(2-benzo[b]furanylmethyl)-2(S)-(tert-butylcarbamoyl)piperazin-1-yl]pentanamide)+indinavir sulfate), JE-2147 ([2(S)-oxo-4-phenylmethyl-3(S)-[(2-methyl-3-oxy)phenylcarbonylamino]-1-oxabutyl]-4-[(2-methylphenyl)methylamino]carbonyl-4(R)-5,5-dimethyl-1,3-thiazole), BMS-232632 (dimethyl (3S,8S,9S,12S)-3,12-bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6-[[4-(2-pyridinyl)phenyl]methyl]-2,5,6,10,13-pentaazatetradecanedicarboxylate), DMP-850 ((4R,5S,6S,7R)-1-(3-amino-1H-indazol-5-ylmethyl)-4,7-dibenzyl-3-butyl-5,6-dihydroxyperhydro-1,3-diazepin-2-one), DMP-851, RO-0334649, Nar-DG-35, R-944, VX-385, TMC-114, Tipranavir, Fosamprenavir sodium, Fosamprenavir calcium, Darunavir, GW-0385, R-944, RO-033-4649, AG-1859 and the like.

[0129]

The HIV integrase inhibitor is exemplified by S-1360, L-870810 and the like, the DNA polymerase inhibitor or DNA synthesis inhibitor is exemplified by Foscavir(R), ACH-126443 (L-2',3'-didehydro-dideoxy-5-fluorocytidine), entecavir ((1S,3S,4S)-9-[4-hydroxy-3-(hydroxymethyl)-2-methylenecyclopentyl]guanine), calanolide A ([10R-(10α,11β,12α)]-11,12-dihydro-12-hydroxy-6,6,10,11-tetramethyl-4-propyl-2H,6H,10H-benzo[1,2-b:3,4-b':5,6-b"]tripyran-2-one), calanolide B, NSC-674447 (1,1'-azobisformamide), Iscador (viscum alubm extract), Rubitecan and the like, the HIV

antisense drug is exemplified by HGTV-43, GEM-92 and the like, the anti-HIV antibody or other antibody is exemplified by NM-01, PRO-367, KD-247, Cytolin(R), TNX-355 (CD4 antibody), AGT-1, PRO-140 (CCR5 antibody), Anti-CTLA-4MAb and the like, the HIV vaccine or other vaccine is exemplified by ALVAC(R), AIDSVAX(R), Remune(R), HIV gp41 vaccine, HIV gp120 vaccine, HIV gp140 vaccine, HIV gp160 vaccine, HIV p17 vaccine, HIV p24 vaccine, HIV p55 vaccine, AlphaVax Vector System, canarypox gp160 vaccine, AntiTat, MVA-F6 Nef vaccine, HIV rev vaccine, C4-V3 peptide, p2249f, VIR-201, HGP-30W, TBC-3B, PARTICLE-3B, Antiferon (interferon-α vaccine) and the like, the interferon or interferon agonist is exemplified by Sumiferon(R), MultiFeron(R), interferon-τ, Reticulose, human leukocyte interferon α and the like, the CCR5 antagonist is exemplified by SCH-351125 and the like, the medicament acting on HIV p24 is exemplified by GPG-NH2 (glycyl-prolyl-glycinamide) and the like, the HIV fusion inhibitor is exemplified by FP-21399 (1,4-bis[3-[(2,4-dichlorophenyl)carbonylamino]-2-oxo-5,8-disodium sulfonyl]naphthyl-2,5-dimethoxyphenyl-1,4-dihydrazone), T-1249, Synthetic Polymeric Construction No3, pentafuside, FP-21399, PRO-542, Enfuvirtide and the like, the IL-2 agonist or antagonist is exemplified by interleukin-2, Imunace(R), Proleukin(R), Multikine(R), Ontak(R) and the like, the TNF-α antagonist is exemplified by Thalomid(R) (thalidomide), Remicade(R) (infliximab), curdlan sulfate and the like, the α-glucosidase inhibitor is exemplified by Bucast(R) and the like, the purine nucleoside phosphorylase inhibitor is exemplified by peldesine (2-amino-4-oxo-3H,5H-7-[(3-pyridyl)methyl]pyrrolo[3,2-d]pyrimidine) and the like, the apoptosis agonist or inhibitor is exemplified by Arkin Z(R), Panavir(R), Coenzyme Q10 (2-deca(3-methyl-2-butenylene)-5,6-dimethoxy-3-methyl-p-benzoquinone) and the like, the cholinesterase inhibitor is exemplified by Cognex(R) and the like, and the immunomodulator is exemplified by Imunox(R), Prokine(R), Met-enkephalin (6-de-L-arginine-7-de-L-arginine-8-

de-L-valinamide-adrenorphin), WF-10 (10-fold dilute tetrachlorodecaoxide solution), Perthon, PRO-542, SCH-D, UK-427857, AMD-070, AK-602, TK-303 (Elvitegravir) and the like.

[0130]

In addition, Neurotropin(R), Lidakol(R), Ancer 20(R), Ampligen(R), Anticort(R), Inactivin(R), PRO-2000, Rev M10 gene, HIV specific cytotoxic T cell (CTL immunotherapy, ACTG protocol 080 therapy, CD4-ζ gene therapy), SCA binding protein, RBC-CD4 complex, Motexafin gadolinium, GEM-92, CNI-1493, (±)-FTC, Ushercell, D2S, BufferGel(R), VivaGel(R), Glyminox vaginal gel, sodium lauryl sulfate, 2F5, 2F5/2G12, VRX-496, Ad5gag2, BG-777, IGIV-C, BILR-255 and the like are exemplified.

[0131]

The compound of the present invention can be combined with one or more (e.g., 1 or 2) kinds of other anti-HIV active substances (to be also referred to as other anti-HIV agents), and used as an anti-HIV agent and the like for the prophylaxis or treatment of HIV infection. As the "other anti-HIV agents" and "other anti-HIV active substances" to be used for a multiple drug combination therapy with the compound of the present invention, preferred are an HIV reverse transcriptase inhibitor and an HIV protease inhibitor. Two or three, or even a greater number of medicaments can be used in combination, wherein a combination of medicaments having different action mechanisms is one of the preferable embodiments. In addition, selection of medicaments free of side effect duplication is preferable.

[0132]

Specific examples of the combination of medicaments include a combination of a group consisting of efavirenz, tenofovir, emtricitabine, indinavir, nelfinavir, atazanavir, ritonavir + indinavir, ritonavir + lopinavir, ritonavir + saquinavir, didanosine + lamivudine, zidovudine + didanosine, stavudine + didanosine, zidovudine + lamivudine, stavudine + lamivudine and tenofovir + emtricitabine, and the compound of

the present invention (Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents. August 13, 2001). Particularly preferred is a combined use of two agents with efavirenz, indinavir, nelfinavir, tenofovir, emtricitabine, zidovudine or lamivudine, and a combined use of three agents with zidovudine + lamivudine, tenofovir + lamivudine, tenofovir + zidovudine, tenofovir + efavirenz, tenofovir + nelfinavir, tenofovir + indinavir, tenofovir + emtricitabine, emtricitabine + lamivudine, emtricitabine + zidovudine, emtricitabine + efavirenz, emtricitabine + nelfinavir, emtricitabine + indinavir, nelfinavir + lamivudine, nelfinavir + zidovudine, nelfinavir + efavirenz, nelfinavir + indinavir, efavirenz + lamivudine, efavirenz + zidovudine or efavirenz + indinavir.

[0133]

In the case of combined administration, the compound of the present invention can be administered simultaneously with a medicament to be used in combination (hereinafter concomitant drug) or administered at certain time intervals. In the case of combined administration, a pharmaceutical composition comprising the compound of the present invention and a concomitant drug can be administered. Alternatively, a pharmaceutical composition comprising the compound of the present invention and a pharmaceutical composition comprising a concomitant drug may be administered separately. The administration route of the compound of the present invention and that of the concomitant drug may be the same or different.

[0134]

In the case of a combined administration, the compound of the present invention can be administered once a day or several times a day in a single dose of 0.01 mg to 1 g, or may be administered at a smaller dose. The concomitant drug can be administered at a dose generally used for the prevention or treatment of an HIV infection, for example, at a single dose of 0.01 mg to 0.3 g. Alternatively, it may be administered in

a smaller dose.

[0135]

Now, production methods of the compound of the present invention are specifically explained. However, the present invention is not limited to these production methods. For production of the compound of the present invention, the order of reactions can be appropriately changed. The reactions may be performed from a reasonable step or a reasonable substitution moiety. In addition, an appropriate substituent conversion (conversion or further modification of substituent) step may be inserted between respective steps. When a reactive functional group is present, protection and deprotection may be appropriately performed. Furthermore, to promote the progress of reactions, reagents other than those exemplified below may be used as appropriate. The starting compounds whose production methods are not described are commercially available or can be easily prepared by a combination of known synthesis reactions. The compound obtained in each step can be purified by conventional methods such as distillation, recrystallization, column chromatography and the like. In some cases, the next step may be performed without isolation and purification.

In the following production methods, the "room temperature" means 1 to 40°C.

[0136]

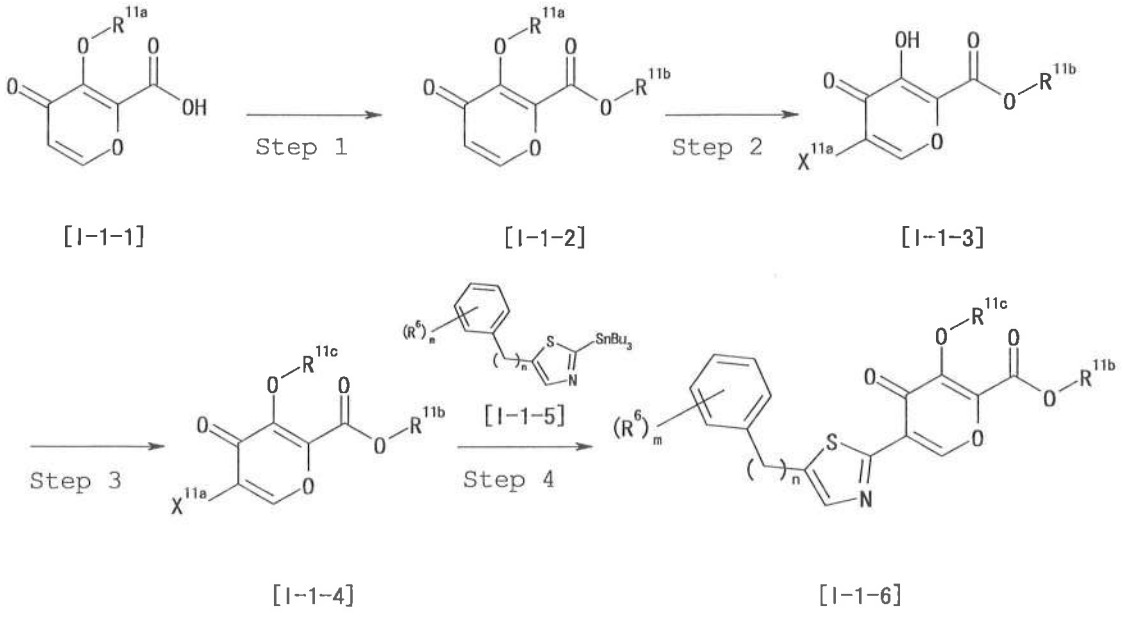
Production method I

[0137]

Production method I-1

Of compounds [I-3-1] in the below-mentioned production method I-3, compound [I-1-6] which is compound [I-3-1] wherein Y is CH can be synthesized by the following method.

[0138]



[I-1-1] [I-1-2] [I-1-3]

[I-1-4] [I-1-6]

[0139]

wherein R^{11a} and R^{11c} are the same or different and each is a hydroxyl-protecting group such as an acetyl group, a benzyl group, a methyl group, an ethyl group, an isopropyl group, a trimethylsilyl group, a triethylsilyl group, a tert-butyldimethylsilyl group, a triisopropylsilyl group, a tert-butyldiphenylsilyl group and the like, R^{11b} is a carboxyl-protecting group such as a methyl group, an ethyl group, a benzyl group, a tert-butyl group and the like, X^{11a} is a halogen atom such as a chlorine atom, a bromine atom and the like, and other symbols are each as described above.

[0140]

Step 1

Compound [I-1-2] can be obtained by introducing a protecting group into the carboxyl group of compound [I-1-1] according to a known method.

For example, when R^{11b} is a methyl group, compound [I-1-2] can be obtained by reacting compound [I-1-1] with trimethylsilyldiazomethane at a low temperature to room temperature in a single or mixed solvent such as tetrahydrofuran (THF), toluene, methanol, ethanol and the like.

[0141]

Step 2

Compound [I-1-3] can be obtained by introducing a halogen atom X^{11a} into compound [I-1-2] according to a known method.

For example, when X^{11a} is a bromine atom, compound [I-1-3] can be obtained by reacting compound [I-1-2] with a bromination reagent (e.g., bromine, trimethylphenylammonium tribromide etc.) at room temperature to under heating in a solvent such as chloroform, methylene chloride, acetic acid and the like.

[0142]

Step 3

Compound [I-1-4] can be obtained by introducing a protecting group into a hydroxyl group of compound [I-1-3] according to a known method.

For example, when R^{11c} is a benzyl group, compound [I-1-4] can be obtained by reacting compound [I-1-3] with benzyl halide (e.g., benzyl chloride, benzyl bromide etc.) at room temperature to under heating in the presence of a base such as potassium acetate, potassium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, potassium phosphate, triethylamine, sodium hydrogen phosphate, cesium carbonate, sodium hydride, potassium t-butoxide, lithiumdiisopropylamide (LDA) and the like in a solvent such as N,N-dimethylformamide (DMF), dimethylacetamide (DMA), acetonitrile, 1,2-dimethoxyethane, THF, toluene and the like.

[0143]

Step 4

Compound [I-1-6] can be obtained by subjecting compound [I-1-4] to a coupling reaction with compound [I-1-5] in the presence of a palladium catalyst (e.g., tris(dibenzylideneacetone)dipalladium(0), tetrakis(triphenylphosphine)palladium(0) and bis(triphenylphosphine)palladium(II) dichloride etc.) at room temperature to under heating in a solvent such as DMF, DMA, acetonitrile, toluene, 1,4-dioxane and the like. For preferable progress of the reaction, a ligand (e.g., tri(2-

furyl)phosphine, tributylphosphine etc.) may be further added.

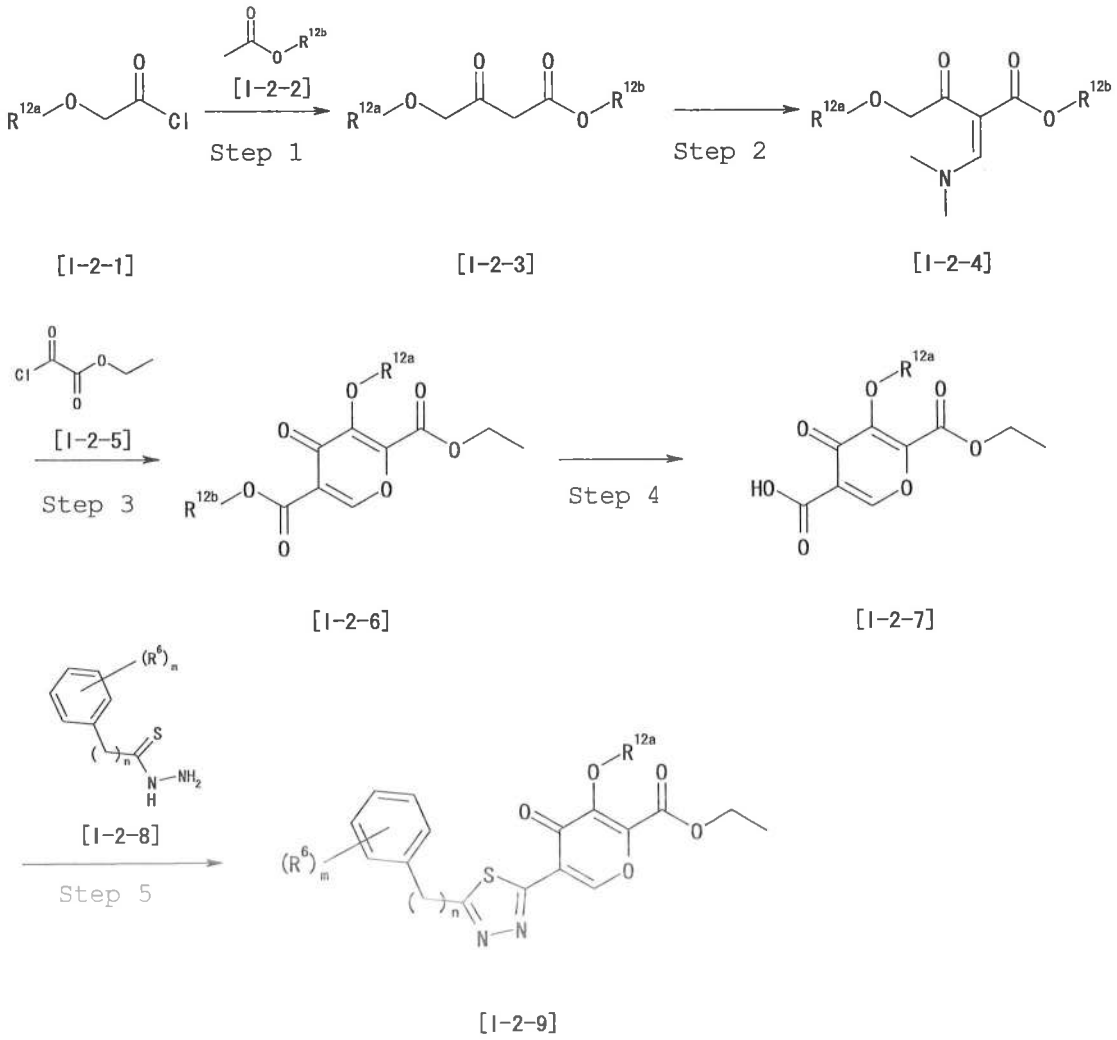
For example, compound [I-1-5] wherein n is 1 can be obtained in the same manner as in step 1R-2 and step 1R-3 of the below-mentioned Reference Example 1.

[0144]

Production method I-2

Of compounds [I-3-1] in the below-mentioned production method I-3, compound [I-2-9] which is compound [I-3-1] wherein Y is a nitrogen atom and R^{13b} is an ethyl group can be synthesized by the following method.

[0145]



[0146]

wherein R^{12a} is a hydroxyl-protecting group such as acetyl group, benzyl group, methyl group, ethyl group, isopropyl group, trimethylsilyl group, triethylsilyl group, tert-

butyldimethylsilyl group, triisopropylsilyl group, tert-butyldiphenylsilyl group and the like, R^{12b} is a carboxyl-protecting group such as methyl group, ethyl group, benzyl group, tert-butyl group and the like, and other symbols are each as described above.

[0147]

Step 1

Compound [I-2-3] can be obtained by reacting compound [I-2-1] with compound [I-2-2] at -78°C to room temperature conditions in a solvent such as DMF, DMA, dimethyl sulfoxide (DMSO), THF, toluene and the like, in the presence of a base such as sodium hydride, lithiumdiisopropylamide (LDA), lithium hexamethyldisilazide (LHMDS) and the like.

[0148]

Step 2

Compound [I-2-4] can be obtained by reacting Compound [I-2-3] with N,N-dimethylformamidedimethylacetal at room temperature to under heating in a solvent such as DMF, acetonitrile, THF, chloroform, ethyl acetate, methylene chloride, toluene and the like.

[0149]

Step 3

Compound [I-2-6] can be obtained by adding a base such as sodium hydride, LDA, LHMDS and the like to a solution of Compound [I-2-4] dissolved in a solvent such as DMF, DMA, DMSO, THF, toluene and the like at -78°C to room temperature, reacting the compound with compound [I-2-5] and treating same with triethylamine, diisopropylethylamine or the like.

[0150]

Step 4

Compound [I-2-7] can be obtained by removing the carboxyl-protecting group R^{12b} of compound [I-2-6] by a known method. For example, when the protecting group is a tert-butyl group, compound [I-2-7] can be obtained by stirring compound [I-2-6] at a low temperature to under heating in a single or

mixed solvent of hexane, chloroform, methylene chloride, ethyl acetate, toluene, 1,2-dimethoxyethane, 1,4-dioxane, THF, methanol, ethanol, 2-propanol, DMSO, DMF, DMA, acetonitrile, water and the like in the presence of acid such as p-toluenesulfonic acid, methanesulfonic acid, boron trifluoride, boron trichloride, boron tribromide, aluminum trichloride, hydrochloric acid, hydrogen bromide, phosphoric acid, sulfuric acid, acetic acid, trifluoroacetic acid and the like.

[0151]

Step 5

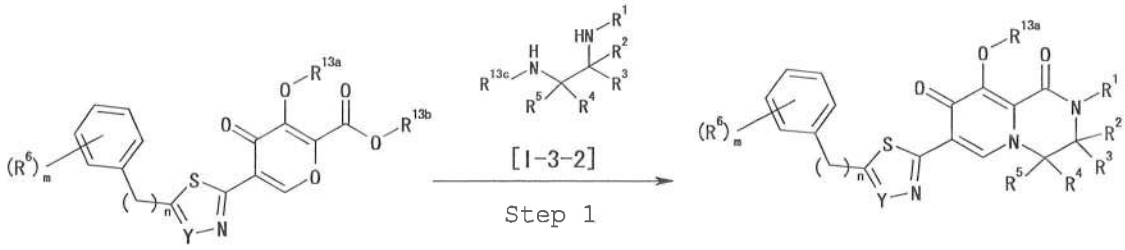
Compound [I-2-9] can be obtained by converting compound [I-2-7] to acid chloride by a known method, and further reacting the compound with compound [I-2-8]. Specifically, compound [I-2-9] can be obtained by converting compound [I-2-7] to acid chloride with a chlorinating agent such as oxalyl chloride, thionyl chloride, phosphorus trichloride and the like at a low temperature to room temperature in a single or mixed solvent of hexane, chloroform, methylene chloride, ethyl acetate, toluene, 1,2-dimethoxyethane, 1,4-dioxane, THF and the like in the presence of a catalytic amount of DMF where necessary, and reacting the compound with compound [I-2-8].

[0152]

production method I-3

A compound represented by the above-mentioned formula [I] can be synthesized by the following method.

[0153]

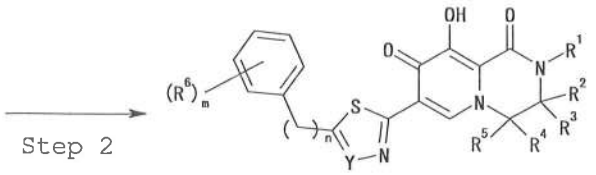


[I-3-1]

[I-3-2]

Step 1

[I-3-3]



Step 2

[I]

[0154]

wherein R^{13a} is a hydroxyl-protecting group such as acetyl group, benzyl group, methyl group, ethyl group, isopropyl group, trimethylsilyl group, triethylsilyl group, tert-butyldimethylsilyl group, triisopropylsilyl group, tert-butyldiphenylsilyl group and the like, R^{13b} is a carboxyl-protecting group such as methyl group, ethyl group, benzyl group, tert-butyl group and the like, R^{13c} is an amino-protecting group such as benzyloxycarbonyl group, tert-butoxycarbonyl group, benzyl group and the like, and other symbols are each as described above.

[0155]

Step 1

Compound [I-3-3] can be obtained by reacting compound [I-3-1] with compound [I-3-2], wherein amino-protecting group R^{13c} is removed in advance according to a known method at room temperature to under heating in a single or mixed solvent of chloroform, dichloromethane, DMF, DMA, DMSO, acetonitrile, 1,2-dimethoxyethane, THF, toluene, water and the like, and cyclizing the compound in the presence of a base such as triethylamine, diisopropylamine, diisopropylethylamine, diazabicycloundecene, sodium carbonate, potassium carbonate,

sodium hydrogen carbonate and the like. The cyclization reaction can also be performed in the presence of acid such as acetic acid, p-toluenesulfonic acid, methanesulfonic acid, boron trifluoride, boron trichloride, boron tribromide, hydrochloric acid, hydrogen bromide, phosphoric acid, sulfuric acid and the like.

[0156]

Step 2

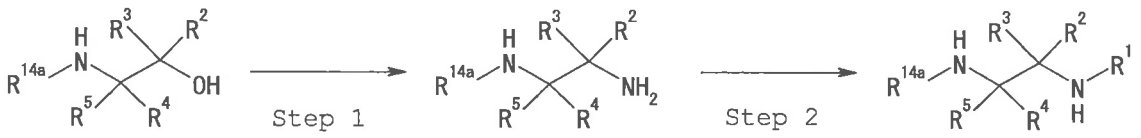
Compound [I] can be obtained by removing the hydroxyl-protecting group R^{13a} of compound [I-3-3] by a known method. For example, when the protecting group is a benzyl group, compound [I] can be obtained by stirring compound [I-3-3] at a low temperature to room temperature in a single or mixed solvent of hexane, chloroform, methylene chloride, ethyl acetate, toluene, methanol, ethanol, 2-propanol, THF, 1,4-dioxane, acetonitrile, water and the like, in the presence of acid such as hydrochloric acid, sulfuric acid, hydrogen bromide, phosphoric acid, acetic acid, trifluoroacetic acid and the like. The acid may be used as a solvent.

[0157]

Production method I-4

Compound [I-3-2] in the above-mentioned production method I-3 (corresponding to the following compound [I-4-3]) can be synthesized by the following method.

[0158]



[I-4-1] [I-4-2] [I-4-3]

[0159]

wherein R^{14a} is an amino-protecting group such as benzyloxycarbonyl group, tert-butoxycarbonyl group, benzyl group and the like, and other symbols are each as described above.

[0160]

Step 1

Compound [I-4-1] obtainable from a commercially available compound by a known method is reacted with phthalimide at a low temperature to under heating in a single or mixed solvent of THF, methylene chloride, chloroform, DMF, ethyl acetate, toluene and the like in the presence of a phosphorus reagent such as triphenylphosphine, diphenyl(2-pyridyl)phosphine, tributylphosphine, tri-tert-butylphosphine and the like and an azo compound such as diisopropylazodicarboxylate, diethylazodicarboxylate, N,N,N',N'-tetramethylazodicarboxamide, 1,1'-(azodicarbonyl)dipiperidine and the like, and the obtained compound is further treated with hydrazine to remove a phthaloyl group to give amine compound [I-4-2].

[0161]

Step 2

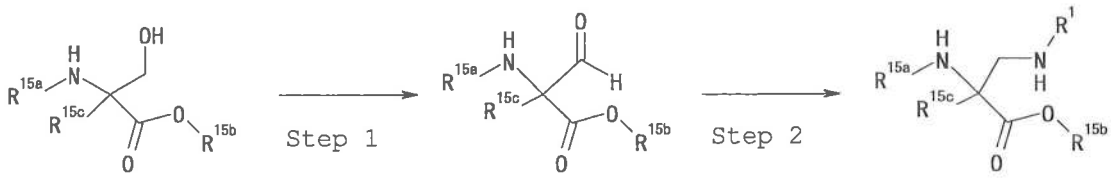
Compound [I-4-2] is reacted with a ketone compound or aldehyde compound at a low temperature to room temperature in a solvent such as DMF, acetonitrile, THF, chloroform, ethyl acetate, methylene chloride, toluene and the like, and the mixture is stirred in the presence of a reducing agent such as sodium borohydride, sodium triacetoxyborohydride and the like to introduce substituent R^1 into the amino group of compound [I-4-2], whereby compound [I-4-3] can be obtained.

[0162]

Production method I-5

Of compounds [I-3-2] in the above production method I-3, a compound, which is compound [I-3-2] wherein particularly R^2 and R^3 are each a hydrogen atom, one of R^4 and R^5 is a carboxyl group or $-CO-NR^aR^b$ wherein R^a and R^b are as described above, and the other is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the aforementioned group A, can be synthesized by the following method.

[0163]



[I-5-1] [I-5-2] [I-5-3]

[0164]

wherein R^{15a} is an amino-protecting group such as benzyloxycarbonyl group, tert-butoxycarbonyl group, benzyl group and the like, R^{15b} is a carboxyl-protecting group such as methyl group, ethyl group, benzyl group, tert-butyl group and the like, R^{15c} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the aforementioned group A, and other symbols are each as described above.

[0165]

Step 1

Compound [I-5-2] can be obtained by oxidizing the hydroxyl group of compound [I-5-1] obtainable from a commercially available compound by a known method, to a aldehyde group by a chromium oxide-pyridine complex (e.g., pyridinium chlorochromate, pyridinium dichromate and the like), a metal oxidant (e.g., chromium oxide, silver carbonate, manganese dioxide and the like), by DMSO oxidization using various DMSO activators such as oxalyl chloride, trifluoroacetic anhydride, acetic anhydride, dicyclohexylcarbodiimide (DCC), sulfur trioxide-pyridine complex and the like, Dess-Martin oxidization and the like according to a known method.

[0166]

Step 2

Compound [I-5-3] can be obtained by subjecting the aldehyde group of compound [I-5-2] to a reductive amination under similar conditions as in production method I-4, step 2. The obtained compound [I-5-3] is cyclized by the above-mentioned method, and the carboxyl-protecting group R^{15b} is

removed by a known method and, where necessary, the resulting compound is reacted with an amine compound by a known method to give the object compound.

[0167]

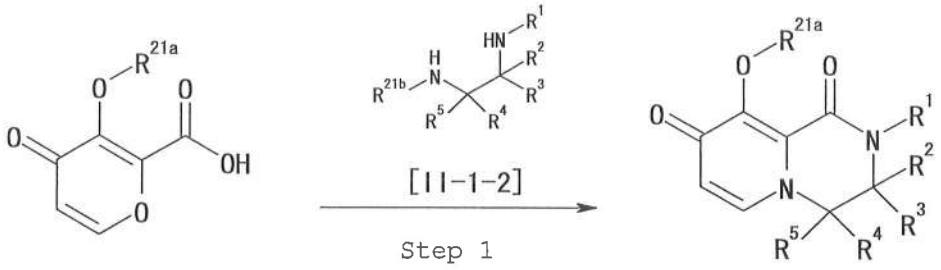
Production method II

[0168]

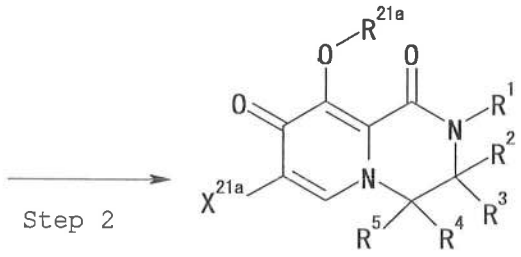
Production method II-1

Of the compounds represented by the above-mentioned formula [I], compound [II-1-6], which is compound [I] wherein Y is CH can be synthesized by the following method.

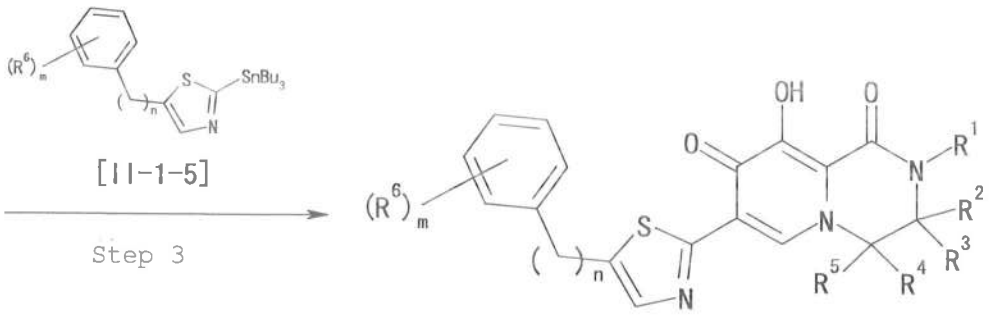
[0169]



[II-1-1] [II-1-3]



[II-1-4]



[II-1-6]

[0170]

wherein R^{21a} is a hydroxyl-protecting group such as acetyl group, benzyl group, methyl group, ethyl group, isopropyl group, trimethylsilyl group, triethylsilyl group, tert-butyldimethylsilyl group, triisopropylsilyl group, tert-butyldiphenylsilyl group and the like, R^{21b} is an amino-protecting group such as benzyloxycarbonyl group, tert-butoxycarbonyl group, benzyl group and the like, X^{21a} is a leaving group such as a halogen atom (e.g., fluorine atom, chlorine atom, bromine atom, iodine atom and the like), p-toluenesulfonyloxy group (OTs), methanesulfonyloxy group (OMs), trifluoromethanesulfonyloxy group (OTf) and the like, and other symbols are each as described above.

[0171]

Step 1

Compound [II-1-3] can be obtained by converting compound [II-1-1] to acid chloride by a known method at a low temperature to under heating, reacting the acid chloride with compound [II-1-2], removing the amino-protecting group R^{21b}, and stirring the mixture in the presence of a base such as potassium acetate, potassium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, potassium phosphate, triethylamine, diisopropylethylamine, sodium hydrogen phosphate, cesium carbonate and the like.

Compound [II-1-2] can be obtained by a method similar to that of Production method I-4.

[0172]

Step 2

Compound [II-1-4] can be obtained by introducing leaving group X^{21a} into compound [II-1-3] by a known method.

For example, when the leaving group X^{21a} is a bromine atom, the bromine atom is introduced into compound [II-1-3] by a method similar to that in production method I-1, step 2 to give compound [II-1-4].

[0173]

Step 3

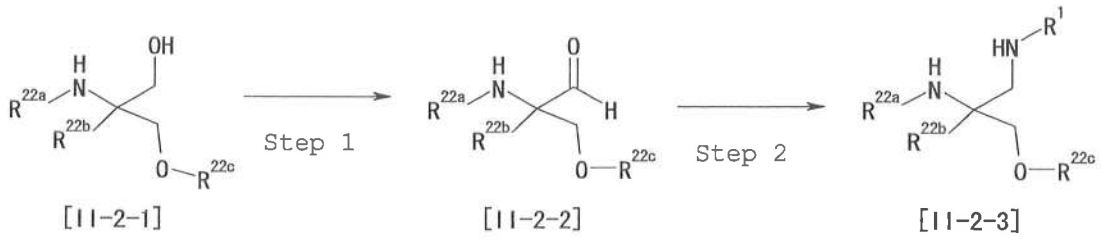
Compound [II-1-4] is reacted with compound [II-1-5] by a method similar to that of production method I-1, step 4, and the hydroxyl-protecting group R^{21a} is removed by a method similar to that of production method I-3, step 2, whereby compound [II-1-6] can be obtained.

[0174]

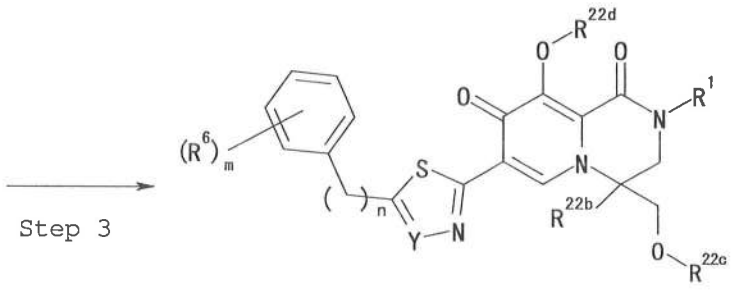
Production method II-2

Of the compounds represented by the above-mentioned formula [I], a compound, which is compound [I] wherein particularly R^2 and R^3 are each a hydrogen atom, and one of R^4 and R^5 is a methyl group substituted by $-NR^{A3}R^{A4}$ wherein R^{A3} and ^{A4} are as described above, and the other is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the aforementioned group A, can be synthesized by the following method.

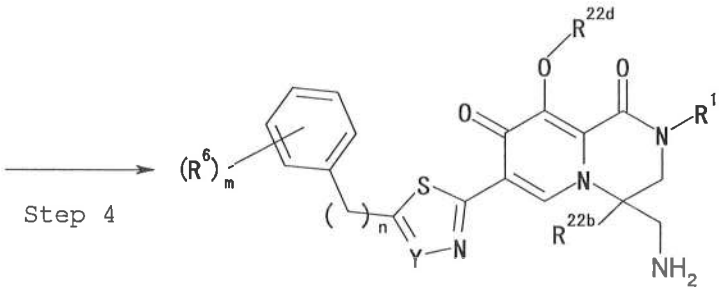
[0175]



[II-2-1] [II-2-2] [II-2-3]



[II-2-4]



[II-2-5]

[0176]

wherein R^{22a} is an amino-protecting group such as benzyloxycarbonyl group, tert-butoxycarbonyl group, benzyl group and the like, R^{22b} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the aforementioned group A, R^{22c} and R^{22d} are the same or different, and each is a hydroxyl-protecting group such as acetyl group, benzyl group, methyl group, ethyl group, isopropyl group, trimethylsilyl group, triethylsilyl group, tert-butyldimethylsilyl group, triisopropylsilyl group, tert-butyldiphenylsilyl group and the like, and other symbols are each as described above.

[0177]

Step 1

The hydroxyl group of compound [II-2-1] is oxidized, by a

known method to give aldehyde group, whereby compound [II-2-2] can be obtained. The known method is the same as the one indicated for, for example, the production method I-5, step 1.

[0178]

Step 2

Compound [II-2-3] can be obtained by subjecting compound [II-2-2] to reductive amination by the same method as in the production method I-5, step 2.

[0179]

Step 3

Compound [II-2-4] can be obtained from compound [II-2-3] by the same method as in production method II-1, step 1 to step 3.

[0180]

Step 4

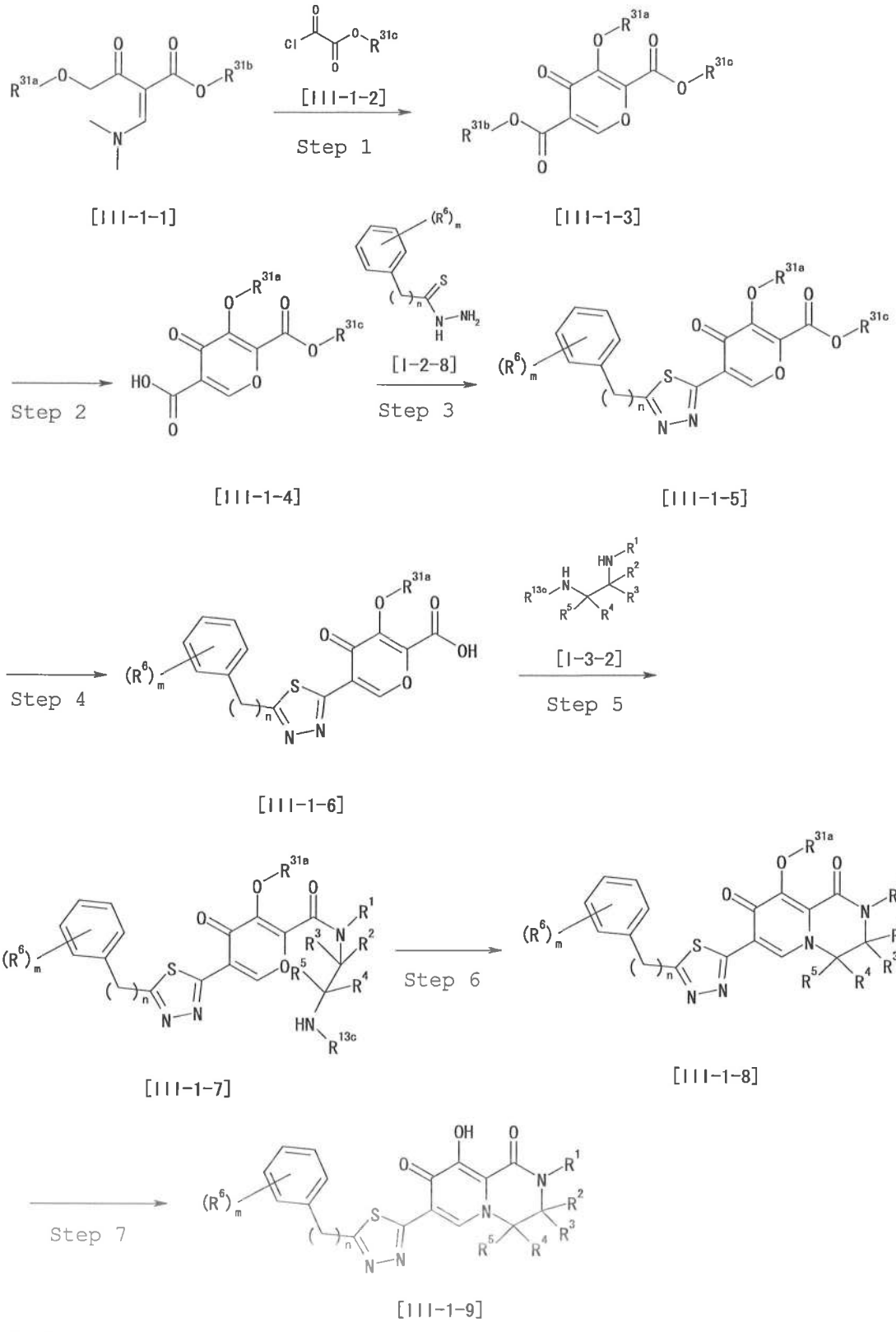
The hydroxyl-protecting group R^{22c} of compound [II-2-4] is removed by a known method, and the hydroxyl group is appropriately subjected to substituent conversion to a leaving group (OTs, OMs, OTf etc.). After reaction with potassium phthalimide, and the phthaloyl group is removed by a method similar to production method I-4, step 1 to give compound [II-2-5]. The obtained compound [II-2-5] is subjected to an appropriately combination of removal of hydroxyl-protecting group R^{22d} by a method similar to production method I-3, step 2, and modification of amino group of compound [II-2-5] by a known method to give the object compound.

[0181]

Production method III

Of compounds represented by the above-mentioned formula [I], compound [III-1-9], which is compound [I] wherein Y is a nitrogen atom can be synthesized by the following method.

[0182]



[0183]

wherein R^{31a} is a hydroxyl-protecting group such as acetyl group, benzyl group, methyl group, ethyl group, isopropyl group, trimethylsilyl group, triethylsilyl group, tert-butyldimethylsilyl group, triisopropylsilyl group, tert-

butyldiphenylsilyl group and the like, R^{31b} and R^{31c} are the same or different and each is a carboxyl-protecting group such as methyl group, ethyl group, benzyl group, tert-butyl group and the like, and other symbols are each as described above.

[0184]

Step 1

Compound [III-1-3] can be obtained by reacting compound [III-1-1] with compound [III-1-2] by a method similar to production method I-2, step 3.

[0185]

Step 2

Compound [III-1-4] can be obtained by removing the carboxyl-protecting group R^{31b} of compound [III-1-3] by a method similar to production method I-2, step 4.

[0186]

Step 3

Compound [III-1-5] can be obtained by reacting compound [III-1-4] with compound [I-2-8] by a method similar to production method I-2, step 5.

[0187]

Step 4

Compound [III-1-6] can be obtained by removing the carboxyl-protecting group R^{31c} of compound [III-1-5] by a known method.

[0188]

Step 5

Compound [III-1-7] can be obtained by converting compound [III-1-6] to acid chloride by a method similar to production method I-2, step 5, and reacting the acid chloride with compound [I-3-2] in a solvent such as hexane, chloroform, methylene chloride, ethyl acetate, toluene, 1,2-dimethoxyethane, 1,4-dioxane, THF and the like in the presence of a base such as potassium acetate, potassium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, potassium phosphate, triethylamine, diisopropylethylamine,

sodium hydrogen phosphate, cesium carbonate and the like.

[0189]

Step 6

Compound [III-1-8] can be obtained by removing the amino-protecting group R^{13c} of compound [III-1-7] by a known method, and performing cyclization by a method similar to a cyclization reaction of production method II-1, step 1 in the presence of a base.

[0190]

Step 7

Compound [III-1-9] can be obtained by removing the hydroxyl-protecting group R^{31a} of compound [III-1-8] by a known method. For example, when the protecting group is a benzyl group, a method similar to production method I-3, step 2 can be used.

Examples

[0191]

Now, the production methods of the compound of the present invention are specifically explained by referring to Examples, which are not to be construed as limitative.

The abbreviations used in the Examples mean the following.

Bn: benzyl group

Boc: tert-butoxycarbonyl group

Et: ethyl group

Me: methyl group

Ms: methanesulfonyl group

TBS: tert-butyldimethylsilyl group

TFA: trifluoroacetic acid

THP: tetrahydropyranyl group

Z: benzyloxycarbonyl group

In addition, the following ^{1}H-NMR values were measured by resolution 400 MHz.

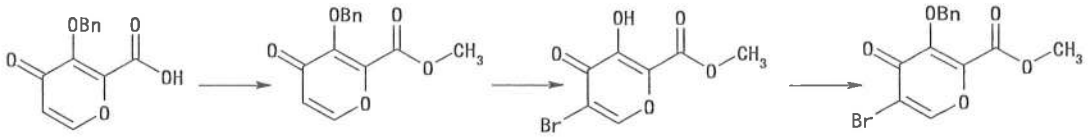
[0192]

Reference Example 1

[0193]

step 1R-1

[0194]



[0195]

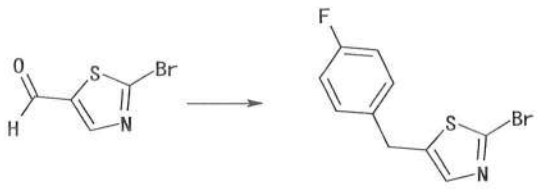
3-benzyloxy-4-oxo-4H-pyran-2-carboxylic acid (11.43 g) was suspended in methanol (20 mL)-tetrahydrofuran (80 mL), 2M (trimethylsilyl)diazomethane/hexane solution (46.4 mL) was added dropwise under ice-cooling, and the mixture was stirred at room temperature for 1.5 hr. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in chloroform (80 mL). Thereto was added bromine (23 mL) and the mixture was stirred for 2 days at 75°C. The mixture was allowed to cool to room temperature, hexane was added and the precipitated solid was collected by filtration. The obtained solid was dissolved in dimethylformamide (54 mL), potassium carbonate (7.1 g) and benzyl bromide (5.6 mL) were added, and the mixture was stirred at 80°C for 40 min. The mixture was allowed to cool to room temperature and filtered. The filtrate was concentrated and 1N aqueous hydrochloric acid solution was added to the obtained residue. The mixture was extracted twice with ethyl acetate. The combined ethyl acetate layer was washed with saturated brine, dried, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:20 - 1:4), the eluate was concentrated, and the precipitated crystals were collected by filtration to give the object compound (7.65 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.11 (s, 1H), 7.49-7.44 (m, 2H), 7.40-7.32 (m, 3H), 5.32 (s, 2H), 3.89 (s, 3H).

[0196]

step 1R-2

[0197]



[0198]

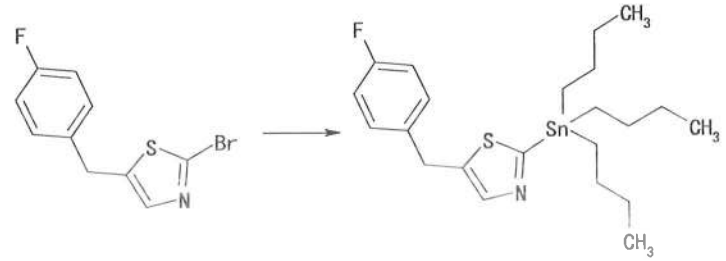
To a solution of 2-bromothiazole-5-carbaldehyde (14 g) in THF (300 mL) was added dropwise 1M (4-fluorophenyl)magnesium bromide/THF solution (80 mL) at -78°C, and the mixture was stirred for 1 hr. Saturated aqueous ammonium chloride solution was added, and the mixture was allowed to cool to room temperature, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried, and concentrated. Trifluoroacetic acid (100 mL) and triethylsilane (58 mL) were added to the obtained residue, and the mixture was stirred for 100 min at 75°C. The mixture was allowed to cool to room temperature and concentrated, and the residue was purified by silica gel column chromatography (ethyl acetate:hexane=1:50 - 1:9) to give the object compound (16.8 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.31-7.29 (m, 1H), 7.21-7.14 (m, 2H), 7.05-6.98 (m, 2H), 4.07 (s, 2H).

[0199]

step 1R-3

[0200]



[0201]

To a solution of the compound (3.2 g) obtained in step 1R-2 in THF (50 mL) was added dropwise 1.6M n-butyllithium/hexane solution (8.1 mL) at -78°C and the mixture was stirred for 10 min. Tributyltin chloride (3.5 mL) was added, and the mixture was stirred at -78°C for 30 min and at

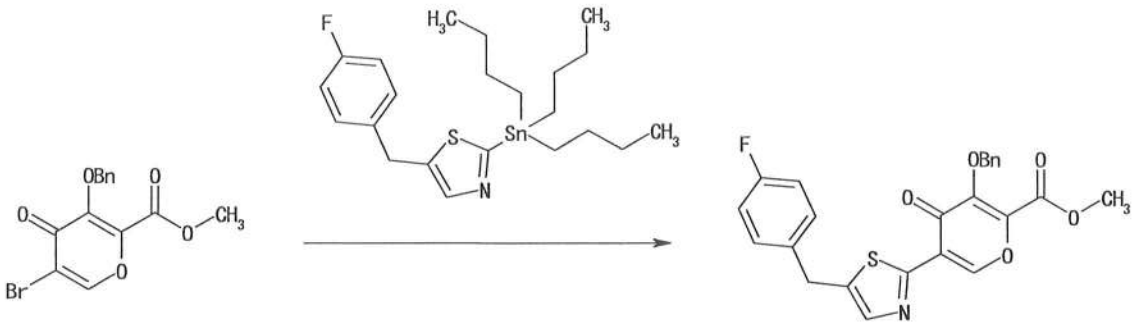
room temperature for 30 min. Ice-cold water was added and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried, and concentrated to give the object compound (6.2 g) described in the above-mentioned scheme as a crude product.

^{1}H-NMR (THF) δ: 7.76-7.74 (m, 1H), 7.25-7.21 (m, 2H), 7.03-6.97 (m, 2H), 4.19 (s, 2H), 1.65-1.56 (m, 6H), 1.40-1.28 (m, 6H), 1.20-1.13 (m, 6H), 0.91-0.85 (m, 9H).

[0202]

step 1R-4

[0203]



[0204]

Under an argon stream, tris(dibenzylideneacetone)dipalladium(0) (84 mg) and tri(2-furyl)phosphine (85 mg) were suspended in toluene (1.5 mL), and the suspension was stirred at room temperature for 15 min. The compound (890 mg) obtained in step 1R-3 and the compound (310 mg) obtained in step 1R-1 were added, and the mixture was stirred at 80°C for 1 hr. The obtained reaction mixture was filtered through celite, and concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:20 - 1:4) to give the object compound (190 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.91 (s, 1H), 7.62-7.61 (m, 1H), 7.51-7.45 (m, 2H), 7.40-7.32 (m, 3H), 7.25-7.19 (m, 2H), 7.04-6.97 (m, 2H), 5.37 (s, 2H), 4.19 (s, 2H), 3.91 (s, 3H).

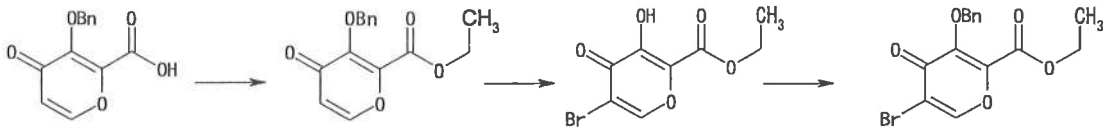
[0205]

Reference Example 2

[0206]

step 2R-1

[0207]



[0208]

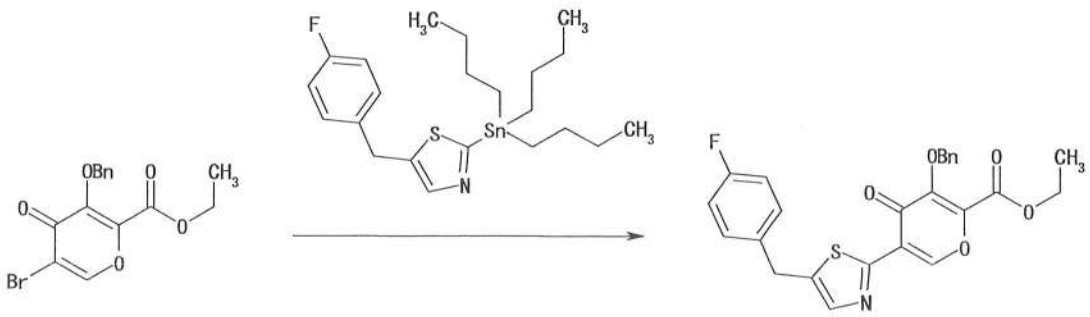
In the same manner as in step 1R-1 except that 3-benzyloxy-4-oxo-4H-pyran-2-carboxylic acid (15.0 g) was ethylated with iodoethane, the object compound (10.97 g) described in the above-mentioned scheme was obtained.

^{1}H-NMR ($CDCl_3$) δ: 8.11 (s, 1H), 7.50-7.46 (m, 2H), 7.40-7.32 (m, 3H), 5.31 (s, 2H), 4.36 (q, 2H, J = 7.2 Hz), 1.33 (t, 3H, J = 7.2 Hz).

[0209]

step 2R-2

[0210]



[0211]

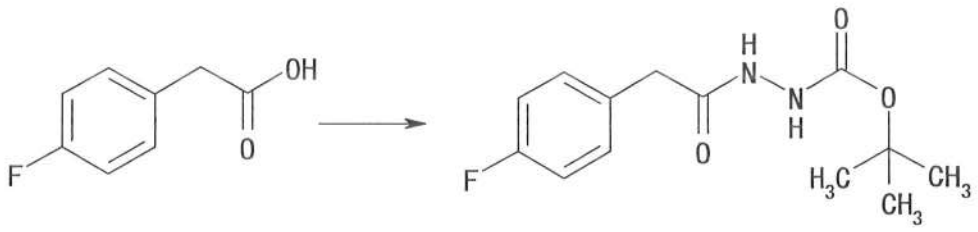
In the same manner as in step 1R-4, the object compound (1.0 g) described in the above-mentioned scheme was obtained from the compound (1.2 g) obtained in step 2R-1.

^{1}H-NMR ($CDCl_3$) δ: 8.91 (s, 1H), 7.62-7.61 (m, 1H), 7.51-7.47 (m, 2H), 7.39-7.31 (m, 3H), 7.25-7.20 (m, 2H), 7.04-6.97 (m, 2H), 5.37 (s, 2H), 4.38 (q, 2H, J = 7.2 Hz), 4.19 (s, 2H), 1.34 (t, 3H, J = 7.2 Hz).

[0212]

Reference Example 3

[0213]



[0214]

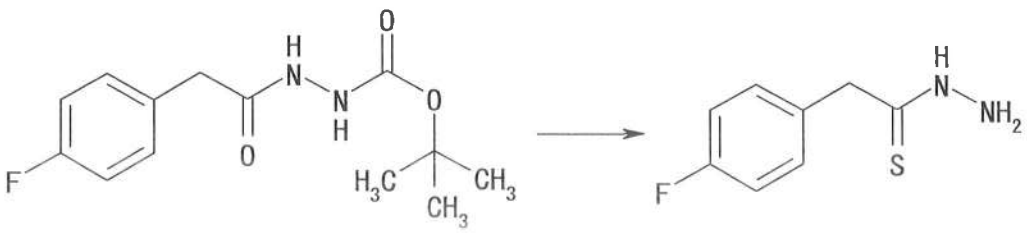
step 3R-1

To a solution of 4-fluorophenylacetic acid (25 g) and tert-butyl carbazate (22.5 g) in DMF (200 mL) were added 1-hydroxybenzotriazole hydrate (HOBT·H_2O (27.3 g)) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC·HCl (34.1 g)), and the mixture was stirred at room temperature overnight. Saturated aqueous sodium hydrogen carbonate solution was added, and the mixture was stirred for a while and extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution and saturated brine, dried over magnesium sulfate, and concentrated to give the object compound (32.3 g) described in the above-mentioned scheme as a crude product.

[0215]

step 3R-2

[0216]



[0217]

To a solution of the compound (32.3 g) obtained in step 3R-1 in THF (300 mL) was added a Lawesson reagent (48.7 g), and the mixture was stirred at 50°C overnight and allowed to cool. The reaction mixture was poured into a stirred saturated aqueous sodium hydrogen carbonate solution by small portions, and the mixture was stirred at room temperature for 30 min.

The mixture was extracted twice with ethyl acetate, and the organic layer was washed with saturated aqueous sodium hydrogen carbonate solution and saturated brine, dried over magnesium sulfate, and concentrated. To the residue was added 4N hydrochloric acid/dioxane solution (300 mL), and the mixture was stirred at room temperature for 1 hr. The precipitated salt was collected by filtration, and dissolved in water (200 mL), and the solution was neutralized with sodium hydrogen carbonate and extracted twice with ethyl acetate. The organic layer was washed with saturated brine, dried over sodium sulfate, and concentrated. To the residue was added ethyl acetate/hexane (1:4) solution and the mixture was slurry washed. The residue was collected by filtration, and dried to give the object compound (15.78 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.27-8.03 (br m, 1H), 7.26-7.20 (m, 2H), 7.10-7.03 (m, 2H), 4.88-4.75 (br m, 2H), 4.08 (s, 2H).

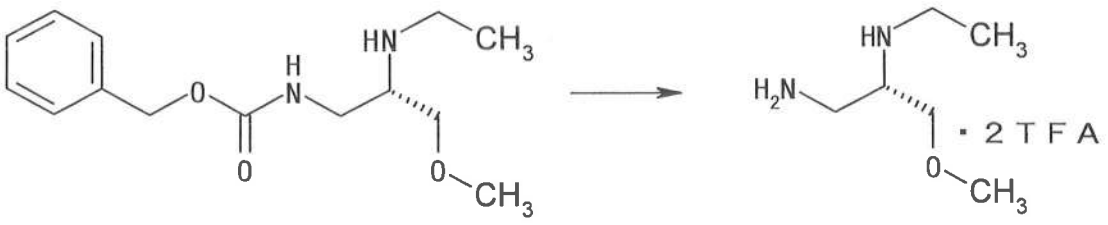
[0218]

Example 1

[0219]

step 1-1

[0220]



[0221]

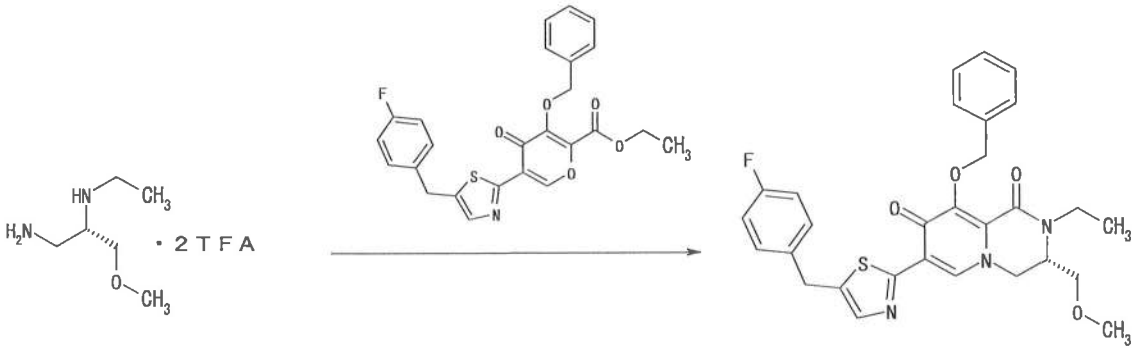
To a solution of (S)-2-ethylamino-3-methoxypropylcarbamic acid benzyl ester (76 mg) in methanol (10 mL) was added a 7.5% palladium-carbon catalyst (100 mg), and the reaction mixture was stirred under a moderate-pressure (0.4 MPa) in a hydrogen atmosphere at room temperature for 3 hr. The reaction mixture was filtered through celite, trifluoroacetic acid (1 mL) was added and the mixture was concentrated to give the object

compound (133 mg) described in the above-mentioned scheme as a crude product.

[0222]

step 1-2

[0223]



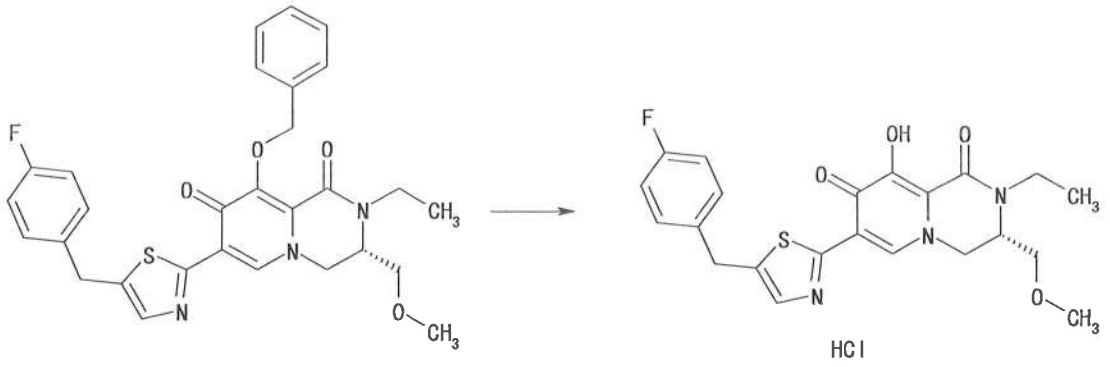
[0224]

To a solution of the compound (55 mg) obtained in step 1-1 in tetrahydrofuran (1.5 mL) was added diisopropylethylamine (160 μL), and the mixture was stirred for 10 min. A solution of the compound (46 mg) obtained in Reference Example 2 in tetrahydrofuran (1 mL) was added, and the mixture was stirred at room temperature for 30 min. The reaction mixture was concentrated, toluene (4 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (200 μL) were added, and the mixture was stirred at 110°C for 15 min. Acetic acid (500 μL) was added, and the mixture was stirred at 110°C for 1 hr. The reaction mixture was allowed to cool to room temperature, and diluted with ethyl acetate. The mixture was washed with 5% aqueous potassium hydrogen sulfate solution, dried and concentrated, and the concentrate was purified by silica gel thin layer chromatography (ethyl acetate:methanol=20:1) to give the object compound (56 mg) described in the above-mentioned scheme.

[0225]

step 1-3

[0226]



[0227]

Compound (56 mg) obtained in step 1-2 was dissolved in trifluoroacetic acid (1.0 mL), and the mixture was stood at room temperature for 1 hr. The reaction solution was concentrated, ethyl acetate was added and the mixture was concentrated. Ethyl acetate, 4N hydrochloric acid/ethyl acetate solution, and hexane were added to allow crystallization to give the object compound (28 mg) described in the above-mentioned scheme.

^{1}H-NMR (DMSO-d_6) δ: 12.30 (br s, 1H), 8.64 (s, 1H), 7.66 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.57 (d, 1H, J=13.5 Hz), 4.39 (dd, 1H, J=13.5, 3.9 Hz), 4.19 (s, 2H), 4.12-4.10 (m 1H), 3.87-3.80 (m, 1H), 3.53-3.44 (m, 2H), 3.27-3.22 (m, 1H), 3.20 (s, 3H), 1.18 (t, 3H, J=7.1 Hz).

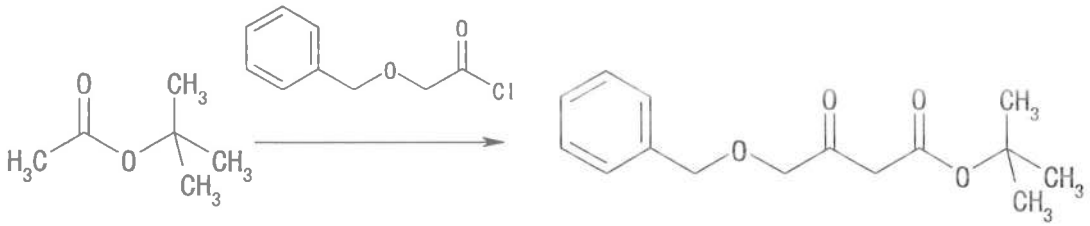
[0228]

Example 2

[0229]

step 2-1

[0230]



[0231]

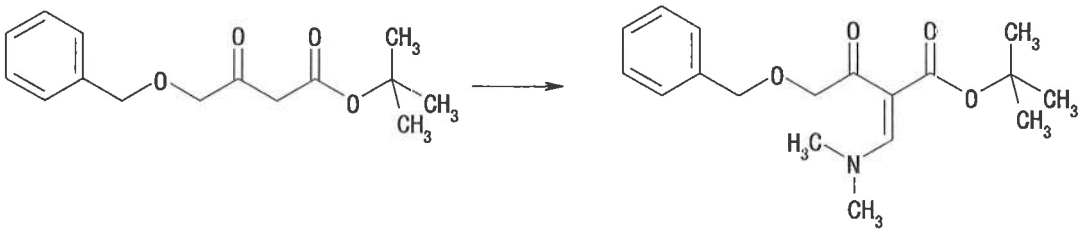
Under nitrogen, a solution of 1M lithium bis(trimethylsilyl)amide-THF/ethylbenzene (100 mL) in THF (100 mL) was cooled to -70°C, and tert-butyl acetate (13.5 mL) was

added dropwise under stirring. After stirring for 15 min, benzyloxyacetyl chloride (7.52 mL) was added dropwise. After stirring for 1 hr, 2N aqueous hydrochloric acid solution was added to the reaction mixture until its pH reached 3 and the mixture was allowed to warm to room temperature. The mixture was extracted with ethyl acetate, and the organic layer was washed with 2N aqueous hydrochloric acid solution and saturated brine, dried over sodium sulfate and concentrated. The above operation was repeated, and the both were combined to give the object compound (40.3 g) described in the above-mentioned scheme as a crude product.

[0232]

step 2-2

[0233]



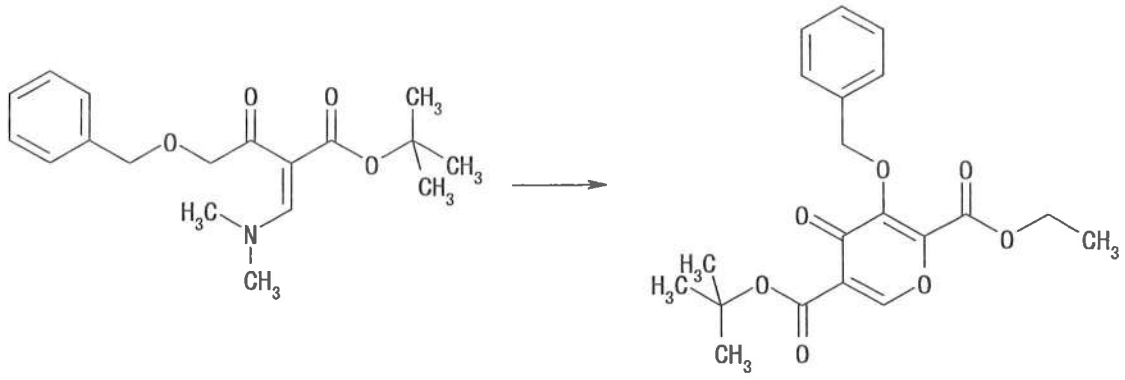
[0234]

To a solution of the compound (38 g) obtained in step 2-1 in toluene (80 mL) was added dimethylformamidedimethylacetal (38 mL), and the mixture was stirred at 100°C for 1 hr. The mixture was allowed to cool, and concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:2 - ethyl acetate) to give the object compound (11.3 g) described in the above-mentioned scheme. ^{1}H-NMR ($CDCl_3$) δ: 7.66 (s, 1H), 7.40-7.13 (m, 5H), 4.60 (s, 2H), 4.42 (s, 2H), 3.40-2.65 (m, 6H), 1.45 (s, 9H).

[0235]

step 2-3

[0236]



[0237]

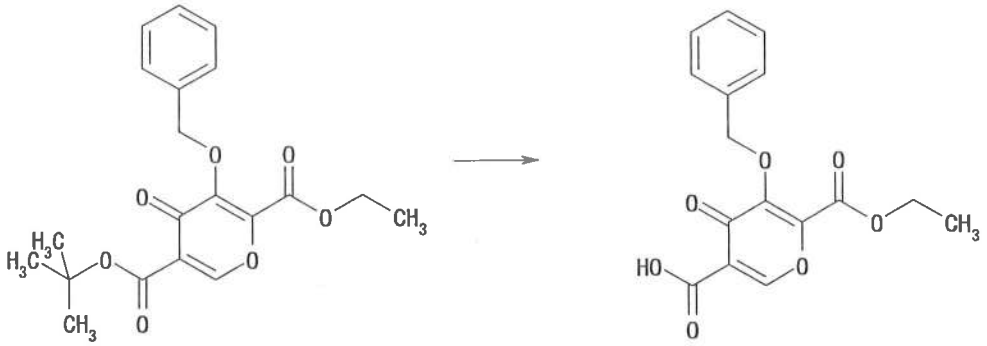
Under nitrogen, a solution of 1M lithium bis(trimethylsilyl)amide-THF/ethylbenzene (42.5 mL) in THF (150 mL) was cooled to -70°C, and a solution of the compound (11.3 g) obtained in step 2-2 in THF (50 mL) was added dropwise over 3 min under stirring. After stirring for 20 min, ethyl chloroglyoxylate (4.75 mL) was added at once. After stirring for 25 min, saturated aqueous potassium hydrogen sulfate solution and ethyl acetate were added and the mixture was allowed to warm to room temperature. The organic layer was separated, washed with saturated brine, dried over sodium sulfate, and concentrated. Toluene was added to the residue, and the mixture was concentrated once. Toluene (100 mL) and triethylamine (10 mL) were added and the mixture was stirred at room temperature. One hour later, the mixture was concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:6 - 1:3) to give the object compound (6.03 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.39 (s, 1H), 7.51-7.47 (m, 2H), 7.39-7.30 (m, 3H), 5.32 (s, 2H), 4.34 (q, 2H, J = 7.2 Hz), 1.57 (s, 9H), 1.31 (t, 3H, J = 7.2 Hz).

[0238]

step 2-4

[0239]



[0240]

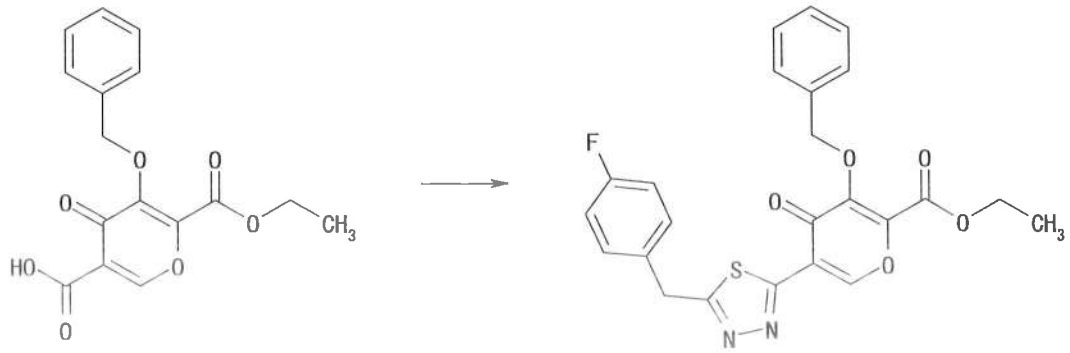
To a solution of the compound (18.7 g) obtained in step 2-3 in ethyl acetate (20 mL) was added 4N hydrochloric acid/ethyl acetate (200 mL) under stirring, and the mixture was stirred at room temperature for 1 hr. To the reaction mixture was added hexane (1 L), the mixture was stirred for a while, and the crystals were collected by filtration, and dried to give the object compound (11.1 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 13.03 (s, 1H), 8.80 (s, 1H), 7.47-7.43 (m, 2H), 7.41-7.35 (m, 3H), 5.38 (s, 2H), 4.40 (q, 2H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz).

[0241]

step 2-5

[0242]



[0243]

To a solution of the compound (6 g) obtained in step 2-4 in toluene (80 mL) were added oxalyl chloride (3.27 mL) and dimethylformamide (0.04 mL) under stirring, and the mixture was stirred at room temperature for 2 hr. The reaction mixture was concentrated, chloroform (100 ml) and the compound (5.22

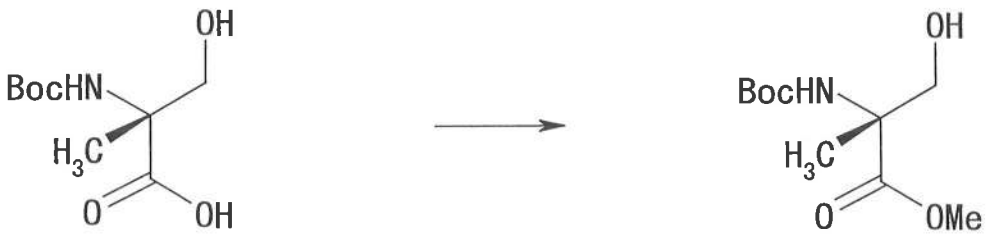
g) obtained in Reference Example 3 were added, and the mixture was stirred at room temperature overnight. 5% Aqueous potassium hydrogen sulfate solution was added, and the mixture was extracted twice with chloroform. The organic layer was washed with 5% aqueous potassium hydrogen sulfate solution and saturated brine, dried over magnesium sulfate, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:4 - 1:3), ethyl acetate/hexane (1:3) solution was added, and the mixture was slurry washed. The residue was collected by filtration, and dried to give the object compound (6.348 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.07 (s, 1H), 7.49-7.44 (m, 2H), 7.39-7.28 (m, 5H), 7.07-7.00 (m, 2H), 5.35 (s, 2H), 4.46 (s, 2H), 4.39 (q, 2H, J = 7.1 Hz), 1.34 (t, 3H, J = 7.1 Hz).

[0244]

step 2-6

[0245]



[0246]

To a solution of (R)-2-tert-butoxycarbonylamino-3-hydroxy-2-methylpropionic acid (5.00 g) in dimethylformamide (50 mL) were added potassium carbonate (6.31 g) and iodomethane (2.84 mL), and the mixture was stirred at room temperature for 3 hr. Water (100 mL) was added, and the mixture was extracted with ethyl acetate (150 mL). The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution (100 mL), dried and concentrated to give the object compound (5.06 g) described in the above-mentioned scheme.

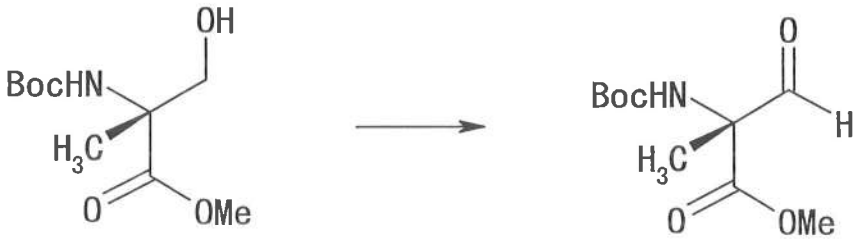
^{1}H-NMR ($CDCl_3$) δ: 5.29 (br s, 1H), 3.99 (dd, 1H, J = 11.6, 6.0

Hz), 3.83-3.73 (m, 1H), 3.78 (s, 3H), 3.23 (br s, 1H), 1.48 (s, 3H), 1.45 (s, 9H).

[0247]

step 2-7

[0248]



[0249]

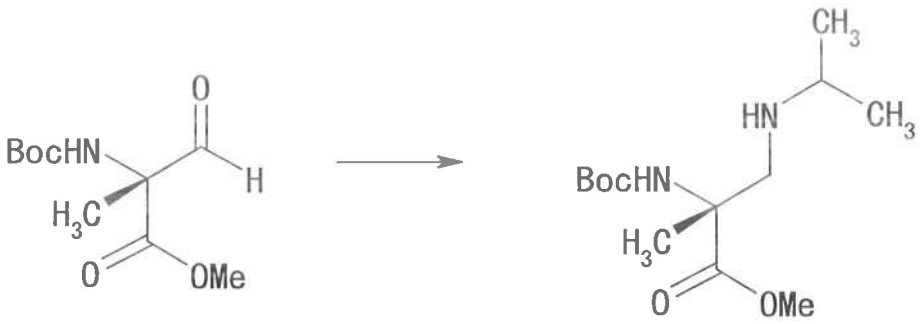
To a solution of the compound (2.50 g) obtained in step 2-6 in dimethyl sulfoxide (25 mL) were added triethylamine (2.25 mL) and a pyridine-sulfur trioxide complex (2.62 g), and the mixture was stirred at room temperature for 1 hr. 1N Aqueous hydrochloric acid solution (100 mL) was added, and the mixture was extracted with ethyl acetate (200 mL). The organic layer was washed successively with 1N aqueous hydrochloric acid solution (100 mL) and saturated aqueous sodium hydrogen carbonate solution (100 mL), dried and concentrated to give the object compound (1.22 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.57 (s, 1H), 5.63 (br s, 1H), 3.81 (s, 3H), 1.57 (s, 3H), 1.45 (s, 9H).

[0250]

step 2-8

[0251]



[0252]

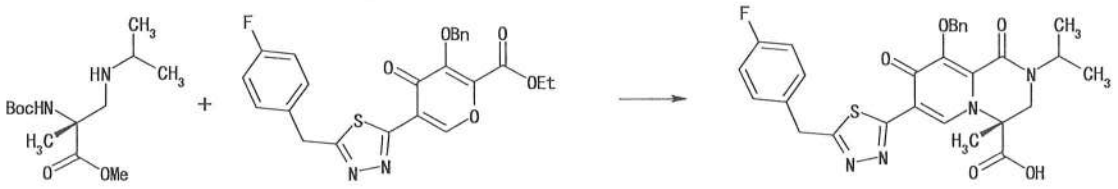
To a solution of the compound (660 mg) obtained in step 2-7 in chloroform (7.0 mL) were added isopropylamine (368 μL), acetic acid (245 μL) and sodium triacetoxyborohydride (955 mg), and the mixture was stirred at room temperature for 18 hr. Saturated aqueous sodium hydrogen carbonate solution (30 mL) and chloroform (50 mL) were added and the mixture was partitioned. The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution (30 mL), dried and concentrated. The concentrate was purified by silica gel column chromatography (chloroform:methanol=10:1) to give the object compound (764 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 5.74 (br s, 1H), 3.74 (s, 3H), 2.89 (br s, 2H), 2.73 (sep, 1H, J = 6.2 Hz), 1.52 (s, 3H), 1.44 (s, 9H), 1.02 (d, 3H, J = 6.2 Hz), 1.02 (d, 3H, J = 6.2 Hz).

[0253]

step 2-9

[0254]



[0255]

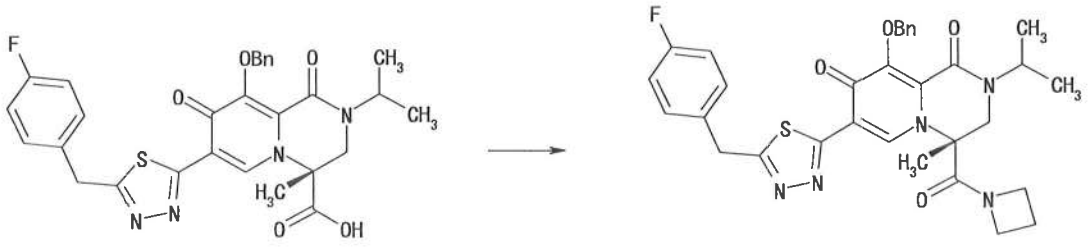
The compound (155 mg) obtained in step 2-8 was dissolved in trifluoroacetic acid solution (1.0 mL), and the mixture was stirred at room temperature for 30 min. The mixture was concentrated, chloroform was added, and the mixture was concentrated. This operation was performed twice. Toluene (5 mL), diisopropylethylamine (395 μL) and the compound (200 mg) obtained in step 2-5 were added, and the mixture was stirred at room temperature for 30 min. Toluene (5 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (100 μL) were added, and the mixture was stirred at 120°C for 1 hr. The reaction mixture was allowed to cool to room temperature, acetic acid (1.0 mL) was added, and the mixture was further stirred at 110°C for 1

hr. 2N Aqueous hydrochloric acid solution (30 mL) was added, and the mixture was extracted with ethyl acetate (60 mL). The organic layer was dried and concentrated, toluene was added, and this operation was repeated twice to give the object compound (263 mg) described in the above-mentioned scheme.
^{1}H-NMR ($CDCl_3$) δ: 8.87 (s, 1H), 7.59 (d, 2H, J = 7.0 Hz), 7.41-7.13 (m, 4H), 7.08-6.98 (m, 3H), 5.46 (d, 1H, J = 10.0 Hz), 5.23 (d, 1H, J = 10.0 Hz), 4.86 (sep, 1H, J = 6.3 Hz), 4.44 (s, 2H), 3.85 (d, 1H, J = 13.5 Hz), 3.44 (d, 1H, J = 13.5 Hz), 1.96 (s, 3H), 1.14 (d, 3H, J = 6.3 Hz), 1.12 (d, 3H, J = 6.3 Hz).

[0256]

step 2-10

[0257]



[0258]

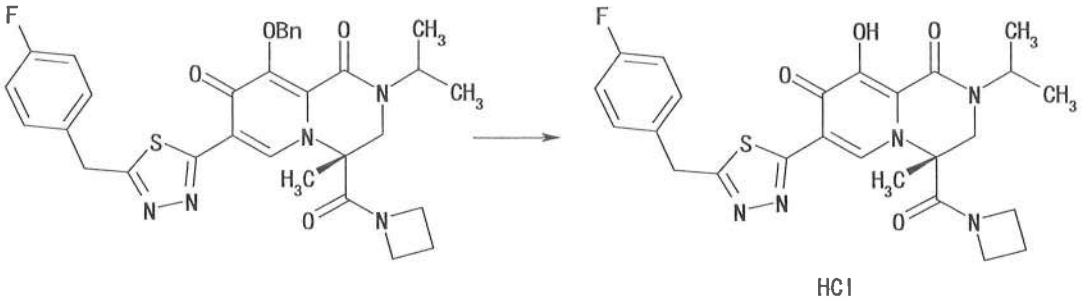
To a solution of the compound (40.0 mg) obtained in step 2-9, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (28.0 mg) and 1-hydroxybenzotriazole hydrate (22.0 mg) in dimethylformamide (400 μL) was added azetidine (20 μL), and the mixture was stirred at room temperature for 18 hr. Saturated aqueous sodium hydrogen carbonate solution (10 mL) was added, and the mixture was extracted with ethyl acetate (25 mL). The organic layer was washed successively with 1N aqueous hydrochloric acid solution (10 mL) and saturated aqueous sodium hydrogen carbonate solution (10 mL), dried and concentrated. The concentrate was purified by silica gel thin layer chromatography (chloroform:methanol=15:1) to give the object compound (26.7 mg) described in the above-mentioned scheme.
^{1}H-NMR ($CDCl_3$) δ: 8.99 (s, 1H), 7.64-7.58 (m, 2H), 7.36-7.27 (m,

5H), 7.07-6.99 (m, 2H), 5.53 (d, 1H, J = 10.0 Hz), 5.39 (d, 1H, J = 10.0 Hz), 4.82 (sep, 1H, J = 6.7 Hz), 4.46 (s, 2H), 4.10-3.92 (m, 2H), 3.97 (d, 1H, J = 13.4 Hz), 3.75-3.66 (m, 1H), 3.61-3.51 (m, 1H), 3.27 (d, 1H, J = 13.4 Hz), 2.19-2.05 (m, 2H), 1.97 (s, 3H), 1.15 (d, 6H, J = 6.7 Hz).

[0259]

step 2-11

[0260]



[0261]

The compound (25.0 mg) obtained in step 2-10 was dissolved in trifluoroacetic acid (1.0 mL), and the mixture was stirred at room temperature for 30 min. The reaction solution was concentrated, chloroform was added, and the mixture was concentrated. 4N Hydrochloric acid/ethyl acetate solution was added, and the mixture was concentrated. Crystallization from ethyl acetate-hexane gave the object compound (17.2 mg) described in the above-mentioned scheme. ^{1}H-NMR (DMSO-d_6) δ: 12.91 (br s, 1H), 8.71 (s, 1H), 7.46-7.38 (m, 2H), 7.23-7.15 (m, 2H), 4.70 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.29-4.18 (br m, 1H), 4.02 (d, 1H, J = 13.9 Hz), 3.90-3.81 (br m, 2H), 3.80-3.72 (br m, 1H), 3.71 (d, 1H, J = 13.9 Hz), 2.16-2.04 (br m, 2H), 1.99 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).

[0262]

Example 3

[0263]

step 3-1

[0264]



[0265]

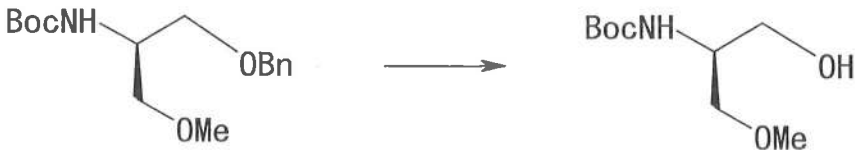
To a solution of (R)-1-benzyloxymethyl-2-hydroxyethylcarbamic acid tert-butyl ester (5.0 g) and 2,6-di-tert-butylpyridine (8.0 mL) in chloroform (50 mL) were added iodomethane (1.33 mL) and silver(I) trifluoromethanesulfonate (6.85 g) under ice-cooling, and the mixture was stirred for 30 min, and further stirred at room temperature for 1 hr. The reaction suspension was filtered through celite, and concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:20 - 1:4) to give the object compound (2.8 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.38-7.27 (m, 5H), 4.97-4.85 (m, 1H), 4.53 (s, 2H), 4.00-3.81 (m, 1H), 3.59 (dd, 1H, J = 9.4, 4.2 Hz), 3.51 (dd, 1H, J = 9.4, 5.8 Hz), 3.51 (dd, 1H, J = 9.4, 4.4 Hz), 3.44 (dd, 1H, J = 9.4, 6.0 Hz), 3.34 (s, 3H), 1.44 (s, 9H).

[0266]

step 3-2

[0267]



[0268]

To a solution of the compound (2.8 g) obtained in step 3-1 in methanol (100 mL) was added a 7.5% palladium-carbon catalyst (1.4 g), and the mixture was stirred at room temperature for 17 hr under a hydrogen atmosphere and moderate pressure (0.4 MPa). The reaction mixture was filtered through celite and concentrated to give the object compound (2.05 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 5.22-5.10 (m, 1H), 3.84-3.64 (m, 3H), 3.60-

3.49 (m, 2H), 3.37 (s, 3H), 2.73-2.55 (m, 1H), 1.45 (s, 9H).

[0269]

step 3-3

[0270]



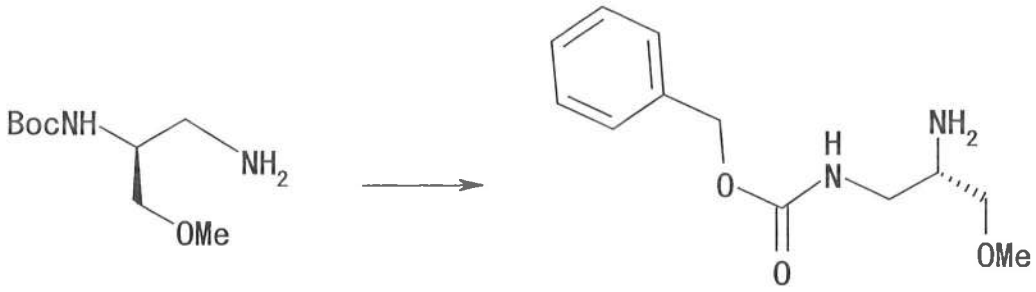
[0271]

To a solution of the compound (1.6 g) obtained in step 3-2, phthalimide (1.38 g) and triphenylphosphine (2.47 g) in tetrahydrofuran (20 mL) was added dropwise 2.2M diethyl azodicarboxylate/toluene solution (4.3 mL) under ice-cooling, and the mixture was stirred at room temperature for 20 min. The reaction mixture was concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:10 - 1:2). The obtained solid was dissolved in ethanol (30 mL)-toluene (30 mL), hydrazine monohydrate (1.6 mL) was added, and the mixture was stirred at 80°C for 40 min. The mixture was allowed to cool to room temperature, the solid was filtered off, and the filtrate was concentrated. Toluene was added to the residue, and the precipitated solid was filtered off. The filtrate was concentrated to give the object compound (1.3 g) described in the above-mentioned scheme. ^{1}H-NMR ($CDCl_3$) δ: 5.08-4.89 (m, 1H), 3.71-3.63 (m, 1H), 3.50 (dd, 1H, J = 9.5, 3.7 Hz), 3.40 (dd, 1H, J = 9.5, 5.1 Hz), 3.35 (s, 3H), 2.84 (dd, 1H, J = 13.0, 6.0 Hz), 2.80 (dd, 1H, J= 13.0, 6.0 Hz), 1.45 (s, 9H).

[0272]

step 3-4

[0273]



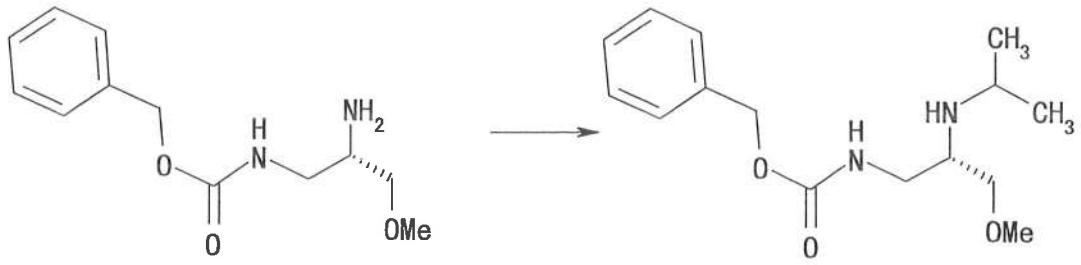
[0274]

To a solution of the compound (0.8 g) obtained in step 3-3 in dioxane (8 mL) was added saturated aqueous sodium hydrogen carbonate solution (2 mL), benzyl chloroformate (0.84 mL) was added dropwise under ice-cooling, and the mixture was stirred for 40 min, and at room temperature for 10 min. Water (15 mL) was added, and the mixture was extracted with ethyl acetate. The extract was dried, and concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:10 - 1:2). To the obtained solid was added 4N hydrochloric acid/dioxane solution (5 mL), and the mixture was stirred at room temperature for 30 min. The reaction mixture was concentrated, and the residue was dissolved in chloroform. Saturated aqueous sodium hydrogen carbonate solution (2 mL) was added, and the mixture was stirred. The mixture was extracted with chloroform, and the organic layer was dried and concentrated to give the object compound (639 mg) described in the above-mentioned scheme.
^{1}H-NMR ($CDCl_3$) δ: 7.39-7.28 (m, 5H), 5.27-5.20 (m, 1H), 5.10 (s, 2H), 3.41-3.24 (m, 3H), 3.35 (s, 3H), 3.18-3.01 (m, 2H), 1.39 (br s, 2H).

[0275]

step 3-5

[0276]



[0277]

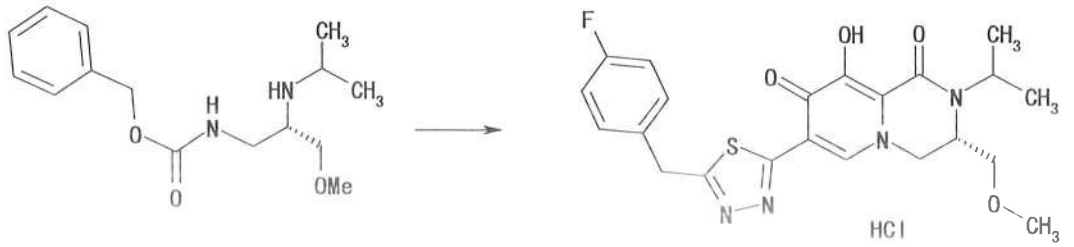
To a solution of the compound (150 mg) obtained in step 3-4 in chloroform (4 mL) were added acetone (70 μL), acetic acid (54 μL) and sodium triacetoxyborohydride (200 mg) under ice-cooling, and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with chloroform, saturated aqueous sodium hydrogen carbonate solution was added, and the mixture was stirred. The chloroform layer was washed with saturated brine, dried, and concentrated to give the object compound (156 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.39-7.28 (m, 5H), 5.39-5.29 (m, 1H), 5.10 (s, 2H), 3.42-3.28 (m, 3H), 3.33 (s, 3H), 3.22-3.14 (m, 1H), 2.96-2.82 (m, 2H), 1.04 (d, 3H, J = 6.8 Hz), 1.02 (d, 3H, J = 6.8 Hz).

[0278]

step 3-6

[0279]



[0280]

In the same manner as in step 2-9 and step 2-11, the object compound (17.0 mg) described in the above-mentioned scheme was obtained from the compound (156 mg) obtained in step 3-5. For removal of the amino-protecting group (benzyloxycarbonyl group) of the compound obtained in step 3-5,

a known method was used according to the protecting group. ^{1}H-NMR (DMSO-d_6) δ: 8.84 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.14 (m, 2H), 4.66 (d, 1H, J = 13.2 Hz), 4.47 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 4.34 (dd, 1H, J = 13.5, 3.7 Hz), 4.22-4.17 (m, 1H), 3.49 (dd, 1H, J = 10.6, 4.3 Hz), 3.39 (dd, 1H, J = 10.6, 7.5 Hz), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).

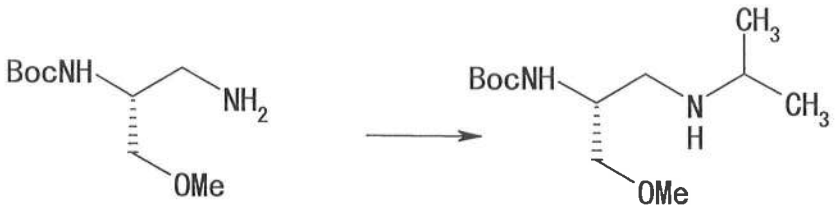
[0281]

Example 4

[0282]

step 4-1

[0283]



[0284]

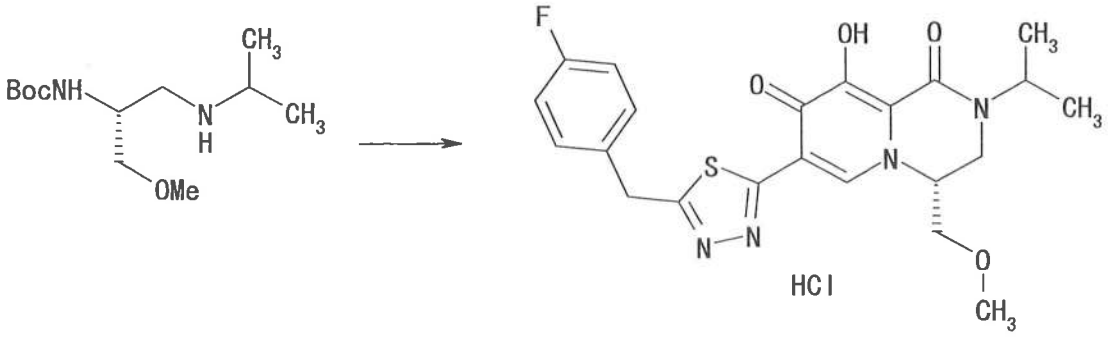
To a solution of (R)-1-aminomethyl-2-methoxyethylcarbamic acid tert-butyl ester (1.0 g) produced from (S)-1-benzyloxymethyl-2-hydroxyethylcarbamic acid tert-butyl ester in the same manner as in Example 3, step 3-1 to step 3-3 in chloroform (15 mL) were added acetone (432 μL) and acetic acid (337 μL) under ice-cooling, sodium triacetoxyborohydride (1.25 g) was added at room temperature, and the mixture was stirred at room temperature for 14 hr. To the reaction mixture was added saturated aqueous sodium hydrogen carbonate solution, and the mixture was extracted 3 times with chloroform. The combined chloroform layer was dried, and concentrated, and the concentrate was purified by silica gel column chromatography (chloroform:methanol=50:1 - 7:1) to give the object compound (1.12 g) described in the above-mentioned scheme. ^{1}H-NMR ($CDCl_3$) δ: 5.09-4.90 (m, 1H), 3.81-3.69 (m, 1H), 3.49 (dd, 1H, J = 9.5, 4.0 Hz), 3.43-3.37 (m, 1H), 3.34 (s, 3H), 2.82-2.68 (m, 3H), 1.45 (s, 9H), 1.04 (d, 3H, J = 6.4 Hz),

1.03 (d, 3H, J = 6.4 Hz).

[0285]

step 4-2

[0286]



[0287]

In the same manner as in step 2-9 and step 2-11 (known deprotection and condensation reactions may be omitted as necessary), the object compound (10.8 mg) described in the above-mentioned scheme was obtained from the compound (19.0 mg) obtained in step 4-1.

^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.80 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.15 (m, 2H), 5.01-4.93 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.8, 4.1 Hz), 3.75 (dd, 1H, J = 13.8, 1.3 Hz), 3.65-3.54 (m, 2H), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).

[0288]

Example 5

[0289]

step 5-1

[0290]



[0291]

In the same manner as in step 3-3, the object compound (1.0 g) described in the above-mentioned scheme was obtained from (S)-2-hydroxy-1-methylethylcarbamic acid tert-butyl ester

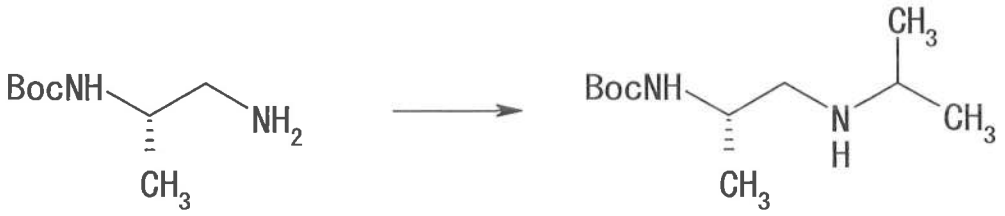
(1.4 g).

^{1}H-NMR ($CDCl_3$) δ: 4.68-4.49 (m, 1H), 3.71-3.58 (m, 1H), 2.74 (dd, 1H, J = 13.0, 4.9 Hz), 2.62 (dd, 1H, J = 13.0, 6.5 Hz), 1.45 (s, 9H), 1.12 (d, 3H, J= 6.7 Hz).

[0292]

step 5-2

[0293]



[0294]

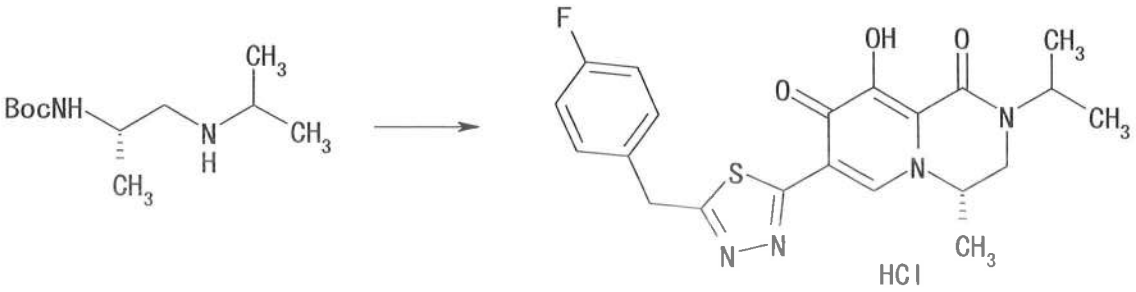
In the same manner as in step 4-1, the object compound (180 mg) described in the above-mentioned scheme was obtained from the compound (190 mg) obtained in step 5-1.

^{1}H-NMR ($CDCl_3$) δ: 4.91-4.66 (m, 1H), 3.81-3.66 (m, 1H), 2.81 (sep, 1H, J = 6.4 Hz), 2.66 (dd, 1H, J = 12.0, 4.9 Hz), 2.60 (dd, 1H, J = 12.0, 6.7 Hz), 1.45 (s, 9H), 1.14 (d, 3H, J = 6.6 Hz), 1.06 (d, 6H, J = 6.4 Hz).

[0295]

step 5-3

[0296]



[0297]

In the same manner as in step 2-9 and step 2-11, the object compound (27.5 mg) described in the above-mentioned scheme was obtained from the compound (30.0 mg) obtained in step 5-2.

^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.91 (s, 1H), 7.45-7.38

(m, 2H), 7.22-7.15 (m, 2H), 4.92 (ddd, 1H, J = 6.8, 3.5, 2.2 Hz), 4.80 (t, 1H, J = 6.8 Hz), 4.47 (s, 2H), 3.81 (dd, 1H, J = 13.5, 3.5 Hz), 3.63 (dd, 1H, J = 13.5, 2.2 Hz), 1.39 (d, 3H, J = 6.8 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz).

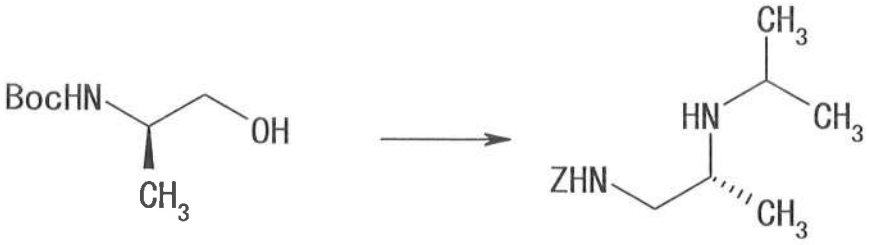
[0298]

Example 6

[0299]

step 6-1

[0300]



[0301]

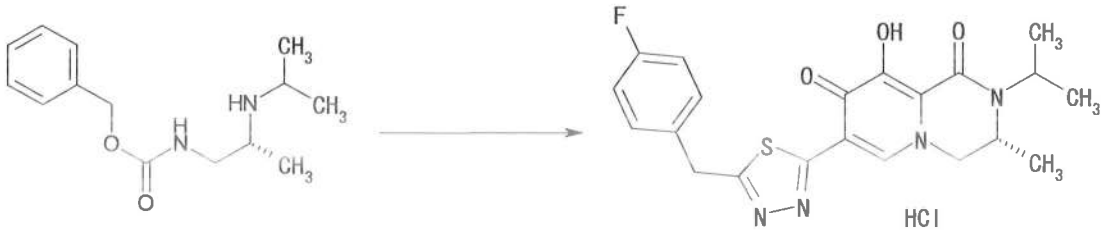
In the same manner as in step 3-3 to step 3-5, the object compound (105 mg) described in the above-mentioned scheme was obtained from (R)-2-hydroxy-1-methylethylcarbamic acid tert-butyl ester (2.0 g).

^{1}H-NMR ($CDCl_3$) δ: 7.40-7.28 (m, 5H), 5.28 (br s, 1H), 5.10 (s, 2H), 3.29-3.17 (m, 1H), 3.02-2.92 (m, 1H), 2.92-2.80 (m, 2H), 1.04 (d, 6H, J = 6.3 Hz), 0.99 (d, 3H, J = 6.0 Hz).

[0302]

step 6-2

[0303]



[0304]

In the same manner as in step 2-9 and step 2-11 (known deprotection and condensation reactions may be omitted as necessary), the object compound (16.6 mg) described in the above-mentioned scheme was obtained from the compound (105 mg)

obtained in step 6-1. For removal of the amino-protecting group (benzyloxycarbonyl group) of the compound obtained in step 6-1, a known method was used according to the protecting group.

^{1}H-NMR (DMSO-d_6) δ: 12.54 (br s, 1H), 8.85 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.62-4.53 (m, 1H), 4.51-4.44 (m, 3H), 4.32 (dd, 1H, J = 13.1, 3.4 Hz), 4.26-4.18 (m, 1H), 1.27 (d, 3H, J = 6.7 Hz), 1.26 (d, 3H, J = 6.7 Hz), 1.21 (d, 3H, J = 6.5 Hz).

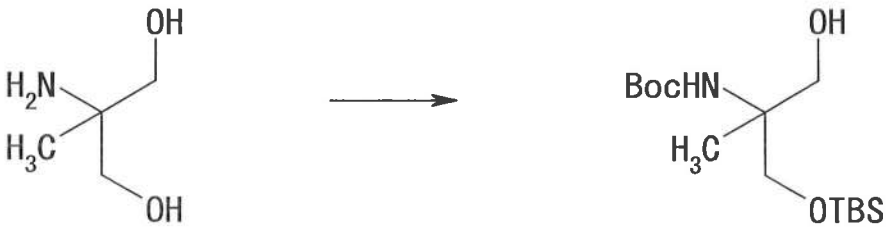
[0305]

Example 7

[0306]

step 7-1

[0307]



[0308]

2-Amino-2-methyl-1,3-propanediol (20.0 g) was suspended in tetrahydrofuran (400 mL), and di-tert-butyl dicarbonate (41.6 g) was added. The mixture was stirred at room temperature for 3 hr and concentrated. Dimethylformamide (200 mL) was added to dissolve the concentrate again, imidazole (13.0 g) and tert-butylchlorodimethylsilane (29.3 g) were added, and the mixture was stirred at room temperature for 15 hr. Water (500 mL) was added, and the mixture was extracted with ethyl acetate (800 mL). The organic layer was washed with water (400 mL), dried, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:10) to give the object compound (35.9 g) described in the above-mentioned scheme.

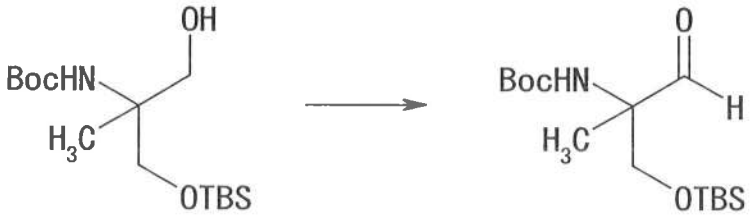
^{1}H-NMR ($CDCl_3$) δ: 5.13 (br s, 1H), 4.00 (br s, 1H), 3.77 (d, 1H, J = 9.7 Hz), 3.70 (dd, 1H, J = 11.4, 4.2 Hz), 3.61 (d, 1H, J =

9.7 Hz), 3.55 (dd, 1H, J = 11.4, 8.4 Hz), 1.44 (s, 9H), 1.19 (s, 3H), 0.90 (s, 9H), 0.07 (s, 6H).

[0309]

step 7-2

[0310]



[0311]

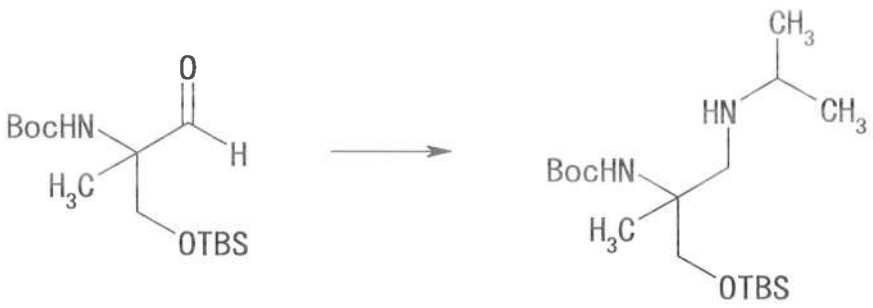
To a solution of the compound (15.5 g) obtained in step 7-1 in dimethyl sulfoxide (120 mL) were added triethylamine (8.12 mL) and a sulfur trioxide-pyridine complex (11.9 g), and the mixture was stirred at room temperature for 3 hr. 1N Aqueous hydrochloric acid solution (300 mL) was added, and the mixture was extracted with ethyl acetate (700 mL). The organic layer was washed successively with 1N aqueous hydrochloric acid solution (150 mL) and saturated aqueous sodium hydrogen carbonate solution (200 mL), dried, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:20) to give the object compound (11.0 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.49 (s, 1H), 5.29 (br s, 1H), 3.86-3.71 (br m, 2H), 1.45 (s, 9H), 1.34 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H).

[0312]

step 7-3

[0313]



[0314]

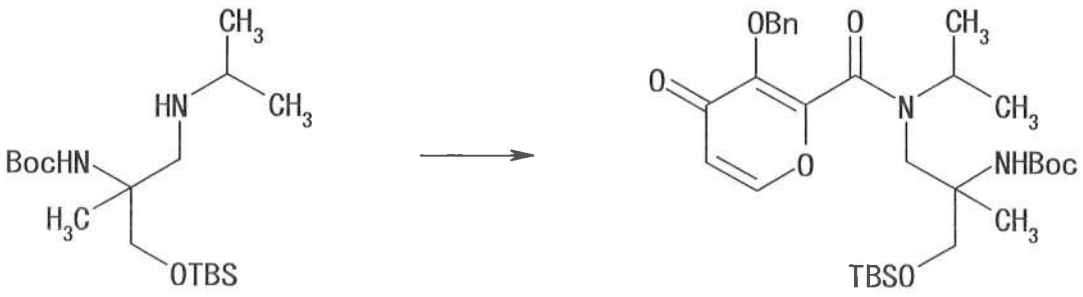
To a solution of the compound (11.0 g) obtained in step 7-2 in chloroform (110 mL) were added isopropylamine (4.46 mL), acetic acid (2.97 mL) and sodium triacetoxyborohydride (11.6 g), and the mixture was stirred at room temperature for 15 hr. The mixture was partitioned between saturated aqueous sodium hydrogen carbonate solution (150 mL) and chloroform (200 mL). The organic layer was washed twice with saturated aqueous sodium hydrogen carbonate solution (100 mL), dried, and concentrated. The concentrate was purified by silica gel column chromatography (chloroform:methanol=10:1) to give the object compound (14.1 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 5.43 (br s, 1H), 3.73 (d, 1H, J = 9.6 Hz), 3.58 (d, 1H, J = 9.6 Hz), 2.80-2.66 (m, 2H), 2.55 (d, 1H, J = 11.6 Hz), 1.43 (s, 9H), 1.24 (s, 3H), 1.05 (br s, 6H), 0.89 (s, 9H), 0.05 (s, 6H).

[0315]

step 7-4

[0316]



[0317]

To a solution of 3-benzyloxy-4-oxo-4H-pyran-2-carboxylic acid (5.00 g) in toluene (100 mL) were added triethylamine (3.40 mL) and thionyl chloride (1.78 mL) at 0°C, and the mixture was stirred at 0°C for 30 min. The precipitated salt was filtered off, the filtrate was concentrated, and the concentrate was dissolved in tetrahydrofuran (40 mL). This tetrahydrofuran solution was added dropwise to a solution of the compound (10.3 g) obtained in step 7-3 and pyridine (30 mL) in tetrahydrofuran (60 mL) at 0°C, and the mixture was

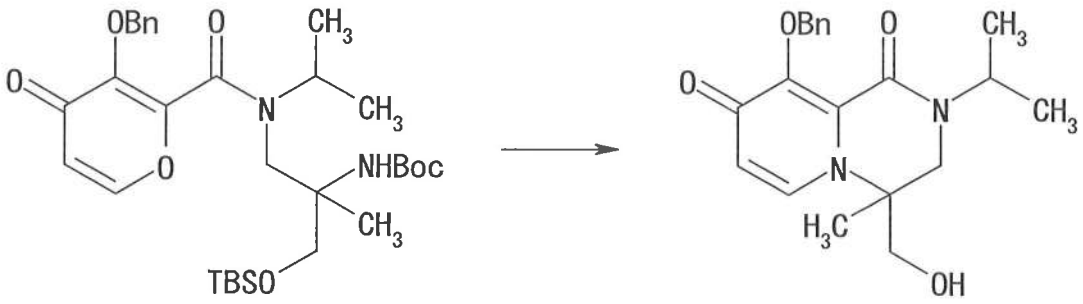
stirred at room temperature for 30 min. The reaction mixture was concentrated, toluene was added and the mixture was concentrated. This operation was performed twice. 1N Aqueous hydrochloric acid solution (150 mL) was added, and the mixture was extracted with ethyl acetate (250 mL). The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution (100 mL), dried, and concentrated. The concentrate was purified by silica gel column chromatography (chloroform:methanol=50:1) to give the object compound (9.65 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.74-7.66 (m, 1H), 7.46-7.28 (m, 5H), 6.50-6.42 (m, 1H), 5.96 (br s, 1H), 5.28-5.14 (m, 2H), 4.02-3.33 (m, 5H), 1.47-1.37 (m, 9H), 1.29-1.00 (m, 9H), 0.95-0.83 (m, 9H), 0.13-0.03 (m, 6H).

[0318]

step 7-5

[0319]



[0320]

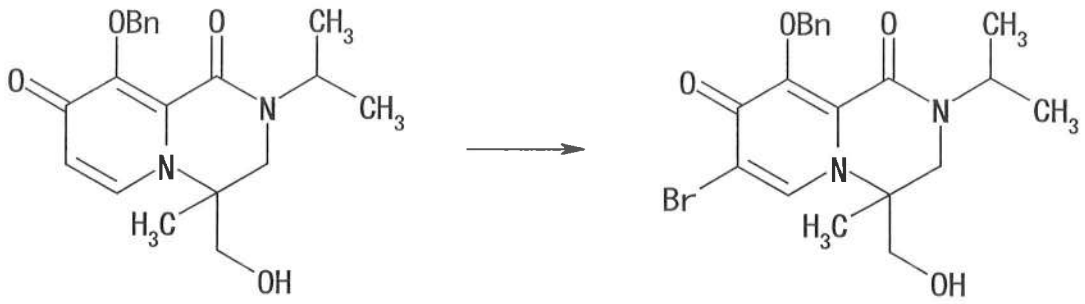
To the compound (9.65 g) obtained in step 7-4 was added 4N hydrochloric acid/ethyl acetate solution (100 mL), and the mixture was stirred at room temperature for 30 min. This was concentrated, ethanol (400 mL) and saturated aqueous sodium hydrogen carbonate solution (100 mL) were added, and the mixture was stirred at room temperature for 18 hr. The insoluble material was filtered off, and the filtrate was concentrated. Water (100 mL) was added, and the mixture was extracted twice with chloroform (200 mL, 100 mL). The organic layer was dried, and concentrated, and the concentrate was purified by silica gel column chromatography

(chloroform:methanol=30:1 - 20:1 - 10:1) to give the object compound (2.20 g) described in the above-mentioned scheme. ^{1}H-NMR ($CDCl_3$) δ: 7.52 (d, 2H, J = 7.9 Hz), 7.48 (d, 1H, J = 7.9 Hz), 7.37-7.22 (m, 3H), 6.25 (d, 1H, J = 7.9 Hz), 5.79 (br s, 1H), 5.20 (d, 1H, J = 10.0 Hz), 5.17 (d, 1H, J = 10.0 Hz), 4.85 (sep, 1H, J = 6.5 Hz), 3.80 (d, 1H, J = 12.1 Hz), 3.61 (d, 1H, J = 12.1 Hz), 3.35 (d, 1H, J = 14.2 Hz), 3.14 (d, 1H, J = 14.2 Hz), 1.47 (s, 3H), 1.12 (d, 3H, J = 6.5 Hz), 1.11 (d, 3H, J = 6.5 Hz).

[0321]

step 7-6

[0322]



[0323]

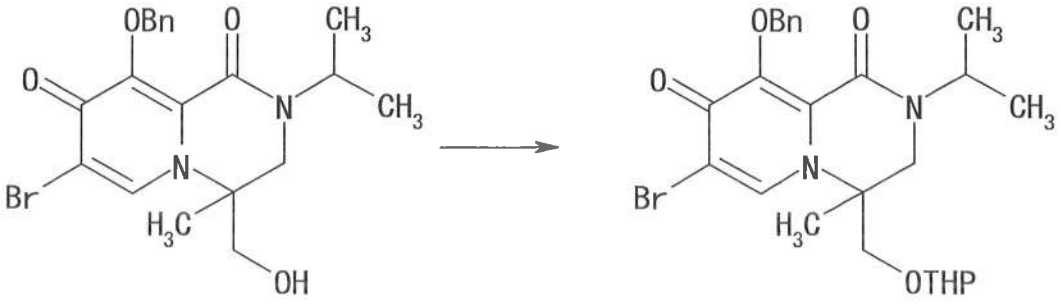
The compound (2.20 g) obtained in step 7-5, trimethylphenylammonium tribromide (3.48 g) and sodium hydrogen carbonate (1.04 g) were dissolved in 2:1 chloroform-methanol (60 mL), and the mixture was stirred at room temperature for 30 min. Saturated aqueous sodium hydrogen carbonate solution (100 mL) was added, and the mixture was extracted with chloroform (200 mL). The organic layer was washed successively with 1N aqueous hydrochloric acid solution (100 mL) and saturated aqueous sodium hydrogen carbonate solution (100 mL), dried, and concentrated to give the object compound (2.23 g) described in the above-mentioned scheme. ^{1}H-NMR (DMSO-d_6) δ: 8.22 (s, 1H), 7.53 (d, 2H, J = 7.0 Hz), 7.41-7.27 (m, 3H), 5.48 (br s, 1H), 5.10 (d, 1H, J = 10.2 Hz), 5.03 (d, 1H, J = 10.2 Hz), 4.67 (sep, 1H, J = 6.7 Hz), 3.66 (d, 1H, J = 11.6 Hz), 3.59 (d, 1H, J = 11.6 Hz), 3.56 (d, 1H, J = 14.2 Hz), 3.45 (d, 1H, J = 14.2 Hz), 1.48 (s, 3H), 1.11 (d, 6H,

J = 6.7 Hz).

[0324]

step 7-7

[0325]



[0326]

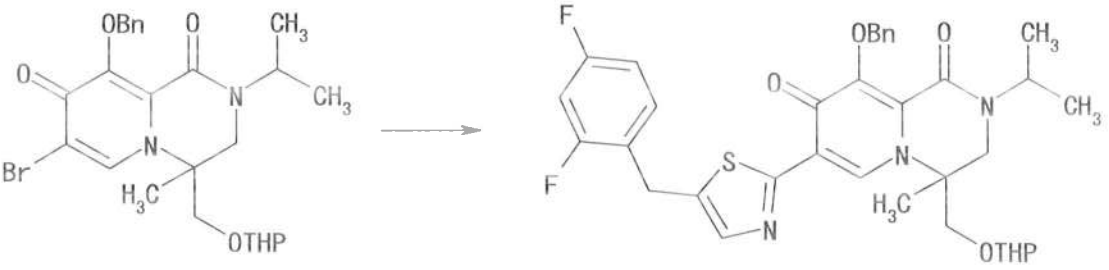
To a solution of the compound (2.12 g) obtained in step 7-6 in chloroform (45 mL) were added 3,4-dihydro-2H-pyran (882 μL) and camphorsulfonic acid (56 mg), and the mixture was stirred at room temperature for 2 hr. The reaction mixture was concentrated, and the concentrate was purified by silica gel column chromatography (chloroform:methanol=30:1) to give the object compound (2.23 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.91-7.89 (m, 1H), 7.72-7.66 (m, 2H), 7.37-7.27 (m, 3H), 5.41-5.36 (m, 1H), 5.27-5.17 (m, 1H), 5.02-4.92 (m, 1H), 4.61-4.48 (m, 1H), 3.92-3.81 (m, 1H), 3.79-3.27 (m, 5H), 1.78-1.48 (m, 9H), 1.20-1.14 (m, 6H).

[0327]

step 7-8

[0328]



[0329]

The compound (250 mg) obtained in step 7-7, tris(dibenzylideneacetone)dipalladium (44 mg), tri(2-

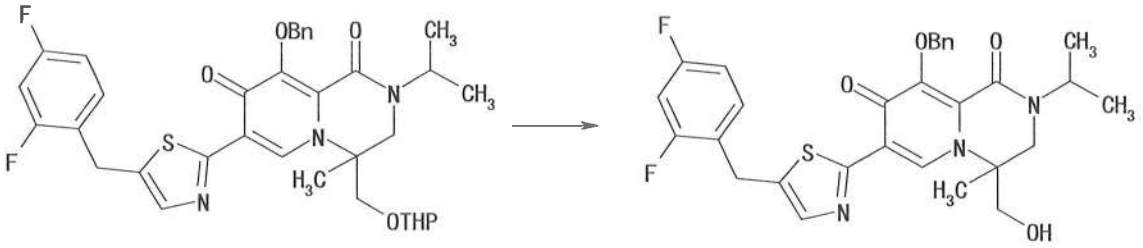
furyl)phosphine (45 mg) and 5-(2,4-difluorobenzyl)-2-tributylstanylthiazole (835 mg) were dissolved in dioxane (5.0 mL), and the mixture was heated in a microwave apparatus at 110°C for 40 min. This operation was performed twice using the same amounts, and the reaction mixtures were combined and concentrated. The concentrate was purified by silica gel column chromatography (chloroform:methanol=30:1) to give the object compound (682 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.78-8.74 (m, 1H), 7.72-7.67 (m, 2H), 7.60-7.56 (m, 1H), 7.37-7.17 (m, 4H), 6.86-6.71 (m, 2H), 5.52-5.46 (m, 1H), 5.34-5.25 (m, 1H), 5.03-4.93 (m, 1H), 4.62-4.53 (m, 1H), 4.20-4.14 (m, 2H), 4.02-3.87 (m, 1H), 3.77-3.43 (m, 5H), 3.36-3.26 (m, 1H), 1.78-1.42 (m, 8H), 1.21-1.13 (m, 6H).

[0330]

step 7-9

[0331]



[0332]

The compound (682 mg) obtained in step 7-8 was dissolved in tetrahydrofuran-methanol-water (4:1:1, 6.0 mL). Acetic acid (2.0 mL) was added, and the mixture was stirred at 80°C for 30 hr. The reaction mixture was concentrated, toluene was added, and the mixture was concentrated. This operation was performed twice, and the concentrate was purified by silica gel column chromatography (chloroform:methanol=40:1) to give the object compound (390 mg) described in the above-mentioned scheme.

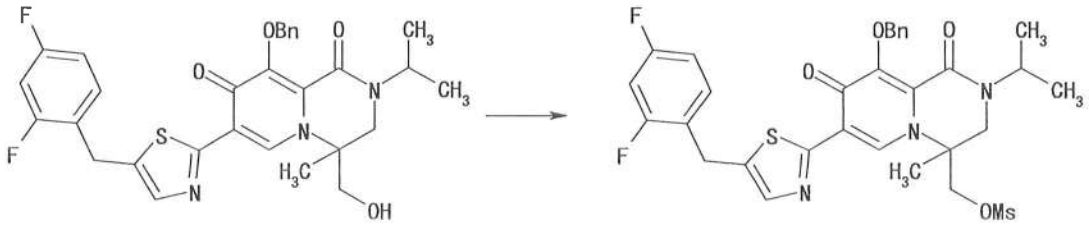
^{1}H-NMR ($CDCl_3$) δ: 8.66 (s, 1H), 7.67-7.62 (m, 2H), 7.51 (s, 1H), 7.36-7.25 (m, 3H), 7.24-7.15 (m, 1H), 6.84-6.75 (m, 2H), 5.40 (d, 1H, J = 9.7 Hz), 5.29 (d, 1H, J = 9.7 Hz), 4.93 (sep, 1H, J = 6.7 Hz), 4.14 (s, 2H), 3.86 (s, 2H), 3.51 (d, 1H, J = 13.9

Hz), 3.25 (d, 1H, J = 13.9 Hz), 1.65 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.15 (d, 3H, J = 6.7 Hz).

[0333]

step 7-10

[0334]



[0335]

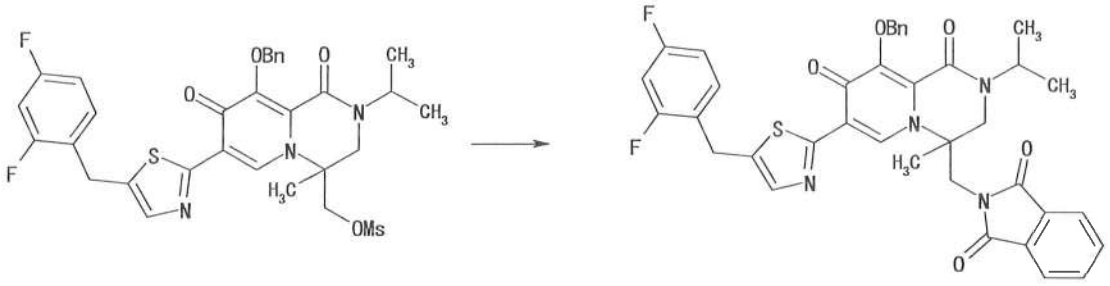
To a solution of the compound (250 mg) obtained in step 7-9 in chloroform (5.0 mL) were added triethylamine (93 μL) and methanesulfonyl chloride (41 μL) at 0°C, and the mixture was stirred at 0°C for 1 hr. Triethylamine (93 μL) and methanesulfonyl chloride (41 μL) were added, and the mixture was further stirred at 0°C for 1 hr. Saturated aqueous sodium hydrogen carbonate solution (20 mL) was added, and the mixture was extracted with chloroform (40 mL). The organic layer was washed with 1N aqueous hydrochloric acid solution (20 mL), dried, and concentrated to give the object compound (295 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 7.68-7.61 (m, 4H), 7.40-7.20 (m, 4H), 6.92-6.82 (m, 2H), 5.45 (d, 1H, J = 9.8 Hz), 5.32 (d, 1H, J = 9.8 Hz), 4.98 (sep, 1H, J = 6.8 Hz), 4.80 (br s, 1H), 4.50 (d, 1H, J = 10.1 Hz), 4.19 (s, 2H), 3.58 (d, 1H, J = 14.1 Hz), 3.37 (d, 1H, J = 14.1 Hz), 3.20 (br s, 3H), 1.85 (s, 3H), 1.22 (d, 3H, J = 6.8 Hz), 1.19 (d, 3H, J = 6.8 Hz).

[0336]

step 7-11

[0337]



[0338]

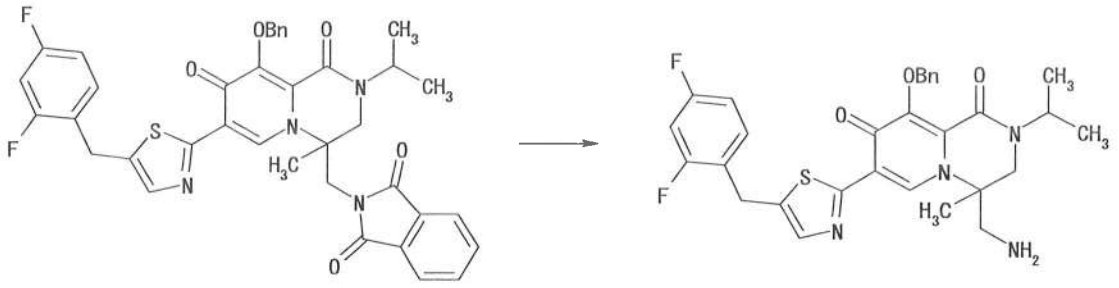
The compound (30 mg) obtained in step 7-10 and potassium phthalimide (26 mg) were dissolved in dimethylformamide (1.0 mL), and the mixture was heated in a microwave apparatus at 150°C for 2 hr. This operation was performed two more times using the compound (115 mg) obtained in step 7-10, potassium phthalimide (100 mg) and dimethylformamide (4.0 mL), and all the reaction mixtures were combined. Water (30 mL) was added, and the mixture was extracted with ethyl acetate (60 mL). The organic layer was washed successively with 1N aqueous hydrochloric acid solution (30 mL) and saturated aqueous sodium hydrogen carbonate solution (30 mL), dried and concentrated. The concentrate was purified by silica gel column chromatography (chloroform:methanol=30:1) to give the object compound (277 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.45 (s, 1H), 7.91-7.58 (m, 7H), 7.40-7.14 (m, 4H), 6.85-6.76 (m, 2H), 5.60 (d, 1H, J = 9.7 Hz), 5.31 (d, 1H, J = 9.7 Hz), 5.07 (sep, 1H, J = 6.7 Hz), 4.21 (d, 1H, J = 14.4 Hz), 4.12 (s, 2H), 3.88 (d, 1H, J = 14.4 Hz), 3.58 (d, 1H, J = 13.9 Hz), 3.47 (d, 1H, J = 13.9 Hz), 1.78 (s, 3H), 1.29 (d, 3H, J = 6.7 Hz), 1.21 (d, 3H, J = 6.7 Hz).

[0339]

step 7-12

[0340]



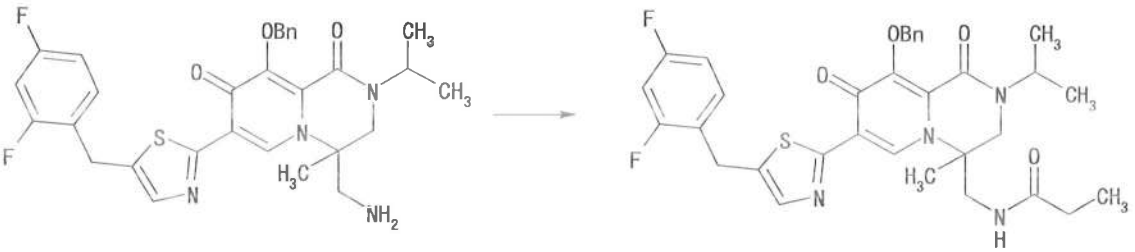
[0341]

To a solution of the compound (277 mg) obtained in step 7-11 in 1:1 ethanol-toluene (6.0 mL) was added hydrazine monohydrate (60 μL), and the mixture was stirred at 80°C for 3 hr. Furthermore, hydrazine monohydrate (60 μL) was added, and the mixture was stirred at 80°C for 2 hr. The precipitate was filtered off, and the filtrate was concentrated, and the concentrate was purified by silica gel column chromatography (chloroform:methanol=30:1 - 20:1) to give the object compound (104 mg) described in the above-mentioned scheme.
^{1}H-NMR ($CDCl_3$) δ: 8.71 (s, 1H), 7.71-7.63 (m, 2H), 7.59 (s, 1H), 7.38-7.27 (m, 3H), 7.25-7.16 (m, 1H), 6.85-6.76 (m, 2H), 5.53 (d, 1H, J = 9.7 Hz), 5.26 (d, 1H, J = 9.7 Hz), 4.97 (sep, 1H, J = 6.7 Hz), 4.18 (s, 2H), 3.51 (d, 1H, J = 13.9 Hz), 3.32 (d, 1H, J = 13.9 Hz), 3.05 (d, 1H, J = 13.7 Hz), 2.98 (d, 1H, J = 13.7 Hz), 1.67 (s, 3H), 1.20 (d, 3H, J = 6.7 Hz), 1.18 (d, 3H, J = 6.7 Hz).

[0342]

step 7-13

[0343]



[0344]

To a solution of the compound (20.0 mg) obtained in step 7-12 in chloroform (400 μL) were added triethylamine (9.9 μL) and propionyl chloride (4.8 μL), and the mixture was stirred at

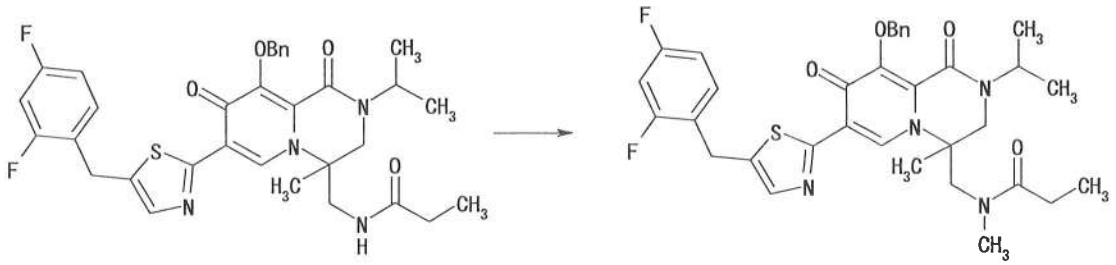
room temperature for 1 hr. The obtained reaction mixture was directly purified by silica gel thin layer chromatography (chloroform:methanol=10:1) to give the object compound (14.2 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.58 (s, 1H), 7.64-7.59 (m, 2H), 7.52 (s, 1H), 7.36-7.27 (m, 3H), 7.25-7.17 (m, 1H), 6.86-6.78 (m, 2H), 6.21 (br s, 1H), 5.40 (d, 1H, J = 9.7 Hz), 5.28 (d, 1H, J = 9.7 Hz), 4.96 (sep, 1H, J = 6.7 Hz), 4.15 (s, 2H), 3.76 (dd, 1H, J = 14.7, 7.1 Hz), 3.55 (dd, 1H, J = 14.7, 6.4 Hz), 3.39 (d, 1H, J = 13.7 Hz), 3.35 (d, 1H, J = 13.7 Hz), 2.28 (dt, 2H, J = 14.5, 6.6 Hz), 1.61 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz), 1.14 (t, 3H, J = 7.7 Hz).

[0345]

step 7-14

[0346]



[0347]

To a solution of the compound (14.0 mg) obtained in step 7-13 in tetrahydrofuran (1.0 mL) were added excess amounts of iodomethane and potassium tert-butoxide at 0°C (until disappearance of starting materials). The obtained reaction mixture was directly purified by silica gel thin layer chromatography (chloroform:methanol=15:1) to give the object compound (5.6 mg) described in the above-mentioned scheme.

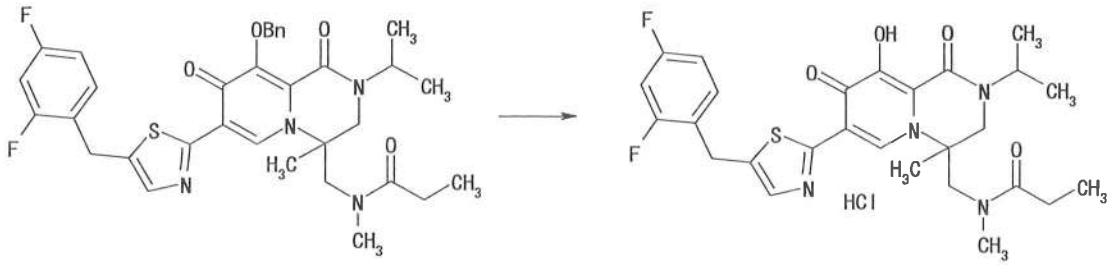
^{1}H-NMR ($CDCl_3$) δ: 8.60 (s, 1H), 7.68-7.63 (m, 2H), 7.58 (s, 1H), 7.36-7.27 (m, 3H), 7.25-7.19 (m, 1H), 6.86-6.77 (m, 2H), 5.58 (d, 1H, J = 10.0 Hz), 5.32 (d, 1H, J = 10.0 Hz), 4.98 (sep, 1H, J = 6.7 Hz), 4.28 (d, 1H, J = 14.4 Hz), 4.19 (s, 2H), 3.47 (d, 1H, J = 14.2 Hz), 3.32 (d, 1H, J = 14.2 Hz), 3.12 (d, 1H, J = 14.4 Hz), 2.54 (s, 3H), 2.37 (dq, 1H, J = 15.5, 7.0 Hz), 2.30

(dq, 1H, J = 15.5, 7.0 Hz), 1.69 (s, 3H), 1.21 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz), 1.15 (t, 3H, J = 7.0 Hz).

[0348]

step 7-15

[0349]



[0350]

The compound (5.6 mg) obtained in step 7-14 was dissolved in trifluoroacetic acid (1.0 mL), and the mixture was stirred at room temperature for 1 hr. The reaction solution was concentrated, chloroform was added, and the mixture was concentrated. 4N Hydrochloric acid/ethyl acetate solution was added, and the mixture was concentrated. Crystallization from ethyl acetate-hexane gave the object compound (3.2 mg) described in the above-mentioned scheme.

^{1}H-NMR (DMSO-d_6) δ: 13.18 (br s, 1H), 8.41 (s, 1H), 7.65 (s, 1H), 7.44 (td, 1H, J = 8.8, 6.7 Hz), 7.25 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.07 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.80 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.83 (d, 1H, J = 14.1 Hz), 3.78 (d, 1H, J = 13.7 Hz), 3.68 (d, 1H, J = 13.7 Hz), 3.51 (d, 1H, J = 14.1 Hz), 2.77 (s, 3H), 2.16-2.03 (m, 2H), 1.67 (s, 3H), 1.22 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz), 0.69 (t, 3H, J = 7.3 Hz).

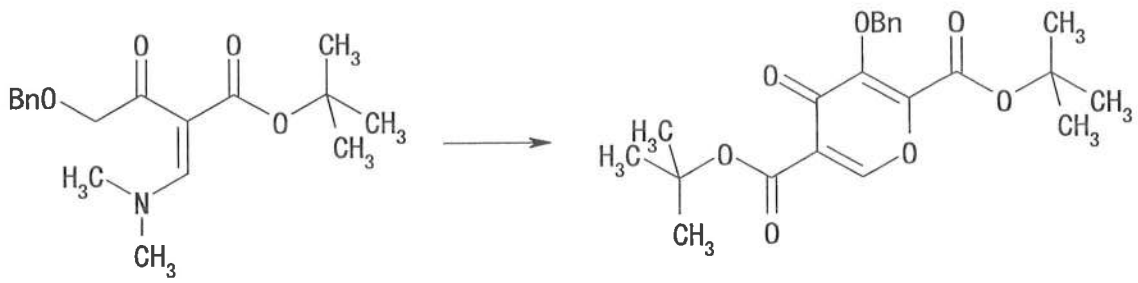
[0351]

Example 8

[0352]

step 8-1

[0353]



[0354]

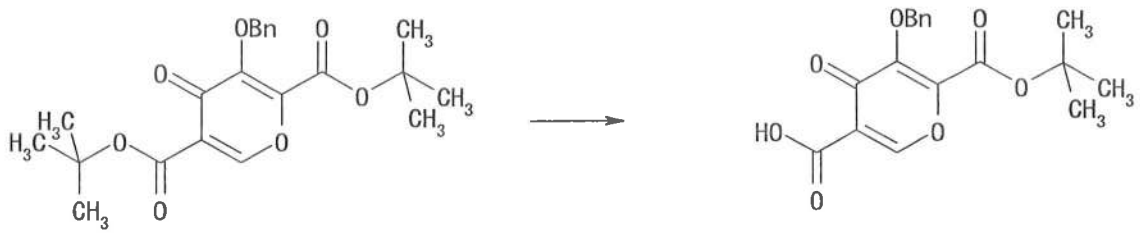
Under nitrogen, a solution of 1.6M lithium hexamethyldisilazide-THF (11.73 mL) in THF (100 mL) was cooled to -78°C, and a solution of the compound (5 g) obtained in step 2-2 in THF (15 mL) was added dropwise over 2 min under stirring. After stirring for 13 min, tert-butyl chloroglyoxylate (3.58 mL) was added at once. After stirring for 25 min, saturated aqueous potassium hydrogen sulfate solution and ethyl acetate were added, and the mixture was allowed to warm to room temperature. The organic layer was separated, washed with saturated aqueous potassium hydrogen sulfate solution and saturated brine, dried over sodium sulfate, and concentrated. Toluene was added to the residue, and the mixture was concentrated once. Toluene (100 mL) and triethylamine (10 mL) were added and the mixture was stirred at room temperature, and concentrated 30 min later. The above-mentioned operation was repeated once more, and the both were combined and purified by silica gel column chromatography (ethyl acetate:hexane=1:9 - 1:6) to give the object compound (4.496 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.37 (s, 1H), 7.52-7.49 (m, 2H), 7.39-7.29 (m, 3H), 5.27 (s, 2H), 1.57 (s, 9H), 1.51 (s, 9H).

[0355]

step 8-2

[0356]



[0357]

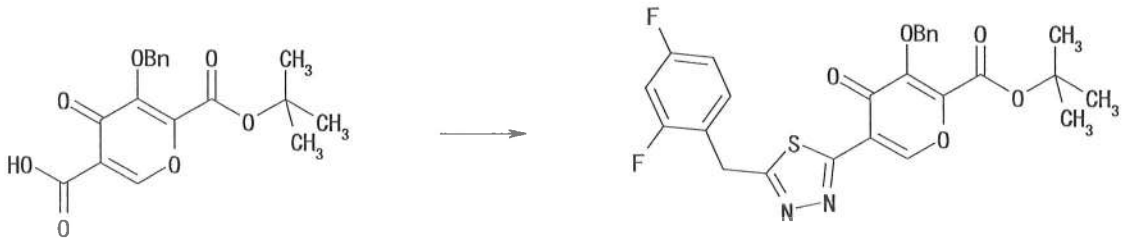
To a solution of the compound (4.49 g) obtained in step 8-1 in dioxane (5 mL) was added 4N hydrochloric acid/dioxane solution (20 mL) with stirring, and the mixture was stirred at room temperature for 20 min. The reaction mixture was concentrated, ethyl acetate/hexane (1:4) solution was added and the mixture was slurry washed. The residue was collected by filtration, and dried to give the object compound (3.30 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.78 (s, 1H), 7.48-7.44 (m, 2H), 7.41-7.34 (m, 3H), 5.34 (s, 2H), 1.54 (s, 9H).

[0358]

step 8-3

[0359]



[0360]

To a solution of the compound (1 g) obtained in step 8-2 in toluene (20 mL)/chloroform (5 mL) were added oxalyl chloride (0.326 mL) and dimethylformamide (0.01 mL) under stirring, and the mixture was stirred at room temperature for 30 min. The reaction mixture was concentrated, THF (20 mL) was added, and the mixture was cooled to -78°C under nitrogen. Triethylamine (1.21 mL) and (2,4-difluorophenyl)thioacetic acid hydrazide (555 mg) were added, and the temperature of the mixture was raised slowly. After 25 min, ethyl acetate and water were added, and the mixture was warmed to room

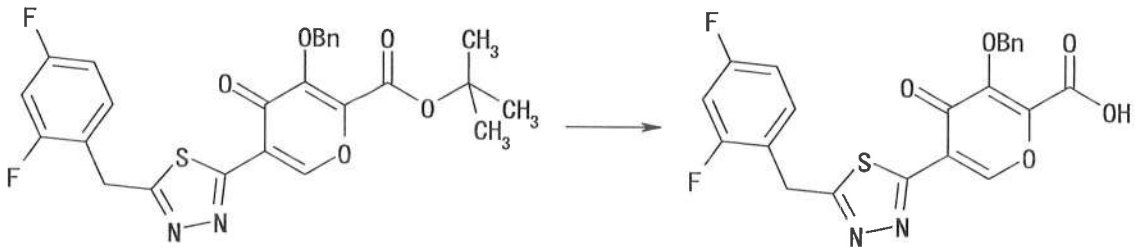
temperature. The mixture was extracted twice with ethyl acetate, and the organic layer was washed with saturated brine, dried over sodium sulfate, and concentrated. To the residue was added acetic acid (20 mL), and the mixture was stirred at 100°C for 2 hr. The mixture was allowed to cool to room temperature, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:9 - 1:4) to give the object compound (112 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.05 (s, 1H), 7.50-7.46 (m, 1H), 7.39-7.18 (m, 5H), 6.91-6.80 (m, 2H), 5.32 (s, 2H), 4.49 (s, 2H), 1.53 (s, 9H).

[0361]

step 8-4

[0362]



[0363]

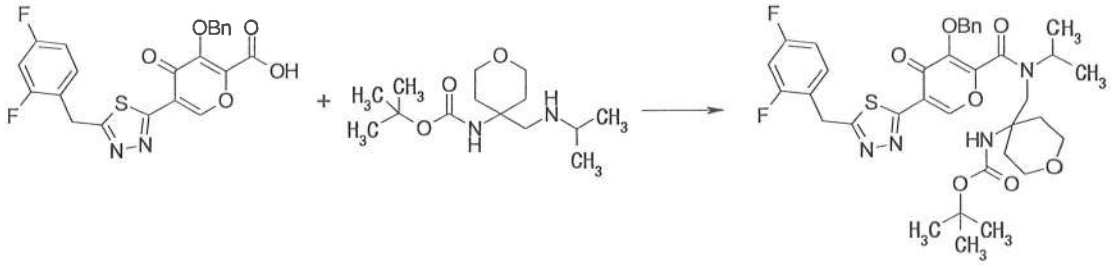
A solution of the compound (1.01 g) obtained in step 8-3 in formic acid (20 mL) was stirred at room temperature for 2 hr. The reaction mixture was concentrated, ethyl acetate/hexane (1:4) solution was added and the mixture was slurry washed. The crystals were collected by filtration. The mother liquor was concentrated, formic acid (20 mL) was added, and the mixture was stirred at room temperature for 3 hr. The reaction mixture was concentrated, ethyl acetate/hexane (1:4) solution was added and the mixture was slurry washed. The crystals were collected by filtration. The both crystals were combined and dried to give the object compound (238 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.13 (s, 1H), 7.43-7.18 (m, 6H), 6.93-6.79 (m, 2H), 5.67 (s, 2H), 4.51 (s, 2H).

[0364]

step 8-5

[0365]



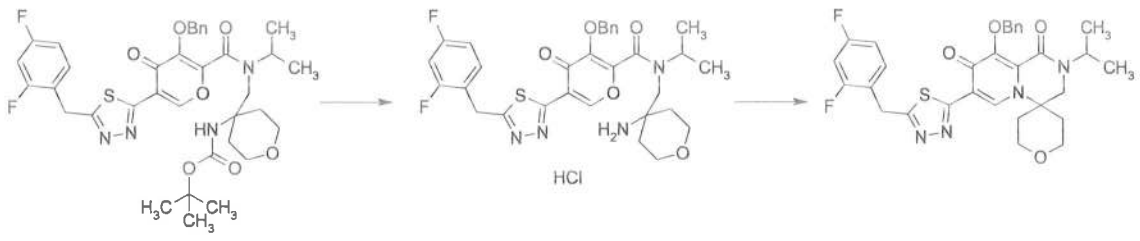
[0366]

To a solution of the compound (69 mg) obtained in step 8-4 in N,N-dimethylformamide (1.5 mL) were added O-(7-azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) (86 mg), 1-hydroxy-7-azabenzotriazole (HOAt) (31 mg), triethylamine (1.1 mL) and [4-(isopropylaminomethyl)tetrahydropyran-4-yl]carbamic acid tert-butyl ester (49 mg) under ice-cooling, and the mixture was stirred at room temperature overnight. To the reaction mixture was added 5% aqueous potassium hydrogen sulfate solution, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution, dried, and concentrated. The concentrate was purified by silica gel thin layer chromatography (chloroform:methanol=10:1) to give the object compound (18 mg) described in the above-mentioned scheme.

[0367]

step 8-6

[0368]



[0369]

To the compound (18 mg) obtained in step 8-5 was added 4N

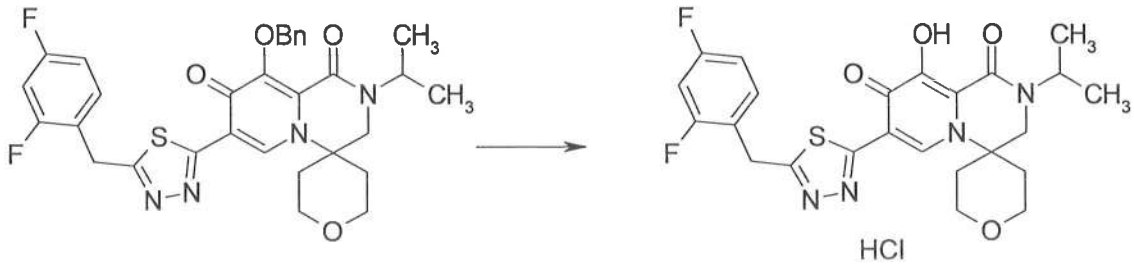
hydrochloric acid/dioxane solution (1 mL), and the mixture was left standing at room temperature for 1.5 hr. The reaction mixture was concentrated, 2-propanol (6 mL), water (0.6 mL) and saturated aqueous sodium hydrogen carbonate solution (0.6 mL) were added, and the mixture was stirred with heating at 100°C for 4 hr. The mixture was allowed to cool to room temperature once, left standing overnight, and stirred again with heating at 100°C for 8 hr. To the reaction mixture was added saturated brine, and the mixture was extracted with ethyl acetate, dried and concentrated. The concentrate was purified by silica gel thin layer chromatography (chloroform:methanol=10:1) to give the object compound (10 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 9.05 (s, 1H), 7.66-7.62 (m, 2H), 7.38-7.28 (m, 4H), 6.88-6.81 (m, 2H), 5.38 (s, 2H), 4.97 (sep, 1H, J = 7.0 Hz), 4.47 (s, 2H), 4.11-4.04 (m, 2H), 3.74-3.65 (m, 2H), 3.55 (s, 2H), 2.45-2.36 (m, 2H), 2.01-1.94 (m, 2H), 1.22 (d, 6H, J = 7.0 Hz).

[0370]

step 8-7

[0371]



[0372]

The compound (10 mg) obtained in step 8-6 was dissolved in trifluoroacetic acid (1.0 mL), and the mixture was stood at room temperature for 50 min. Trifluoroacetic acid solution was concentrated, 4N hydrochloric acid/dioxane solution was added and the mixture was concentrated. Toluene was added and the mixture was concentrated. The obtained residue was crystallized from ethyl acetate (0.5 mL)-hexane (2 mL) to give

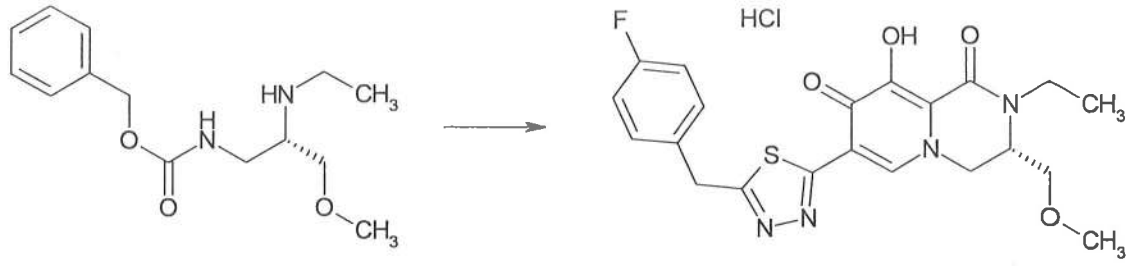
the object compound (4.7 mg) described in the above-mentioned scheme.

^{1}H-NMR (DMSO-d_6) δ: 13.25 (br s, 1H), 8.88 (s, 1H), 7.58-7.50 (m, 1H), 7.32-7.25 (m, 1H), 7.15-7.09 (m, 1H), 4.83 (sep, 1H, J = 6.9 Hz), 4.50 (s, 2H), 3.89-3.82 (m, 2H), 3.88 (br s, 2H), 3.80-3.73 (m, 2H), 2.31-2.22 (m, 2H), 2.01-1.94 (m, 2H), 1.23 (d, 6H, J = 6.9 Hz).

[0373]

Example 9

[0374]



[0375]

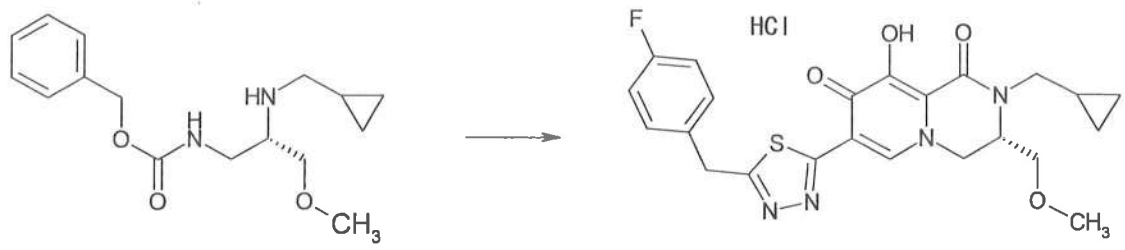
In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (18.0 mg) described in the above-mentioned scheme was obtained from ((S)-2-ethylamino-3-methoxypropyl)carbamic acid benzyl ester (80 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.64-12.34 (m, 1H), 8.83 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.64 (dd, 1H, J = 13.4, 1.5 Hz), 4.47 (s, 2H), 4.42 (dd, 1H, J = 13.4, 4.4 Hz), 4.17-4.11 (m, 1H), 3.86 (dq, 1H, J = 14.0, 7.0 Hz), 3.54 (dd, 1H, J = 10.4, 4.9 Hz), 3.50 (dd, 1H, J = 10.4, 6.3 Hz), 3.27 (dq, 1H, J = 14.0, 7.0 Hz), 3.22 (s, 3H), 1.20 (t, 3H, J = 7.0 Hz).

[0376]

Example 10

[0377]



[0378]

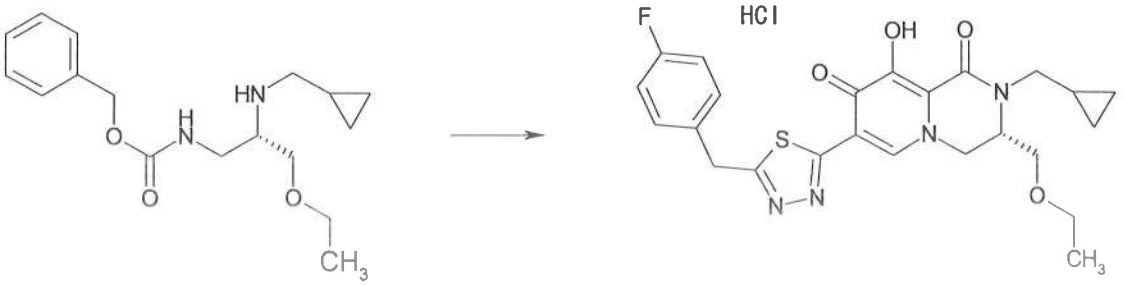
In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (10.7 mg) described in the above-mentioned scheme was obtained from ((S)-2-cyclopropylmethylamino-3-methoxypropyl)carbamic acid benzyl ester (36 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.46 (br s, 1H), 8.85 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.67 (dd, 1H, J = 13.7, 1.6 Hz), 4.47 (s, 2H), 4.45 (dd, 1H, J = 13.7, 3.9 Hz), 4.27-4.20 (m, 1H), 3.69 (dd, 1H, J = 14.0, 7.0 Hz), 3.58 (dd, 1H, J = 10.3, 4.8 Hz), 3.51 (dd, 1H, J = 10.3, 6.5 Hz), 3.21 (dd, 1H, J = 14.0, 7.0 Hz), 3.21 (s, 3H), 1.21-1.10 (m, 1H), 0.59-0.47 (m, 2H), 0.44-0.36 (m, 1H), 0.36-0.27 (m, 1H).

[0379]

Example 11

[0380]



[0381]

In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (32.0 mg) described in the above-mentioned scheme was obtained from ((S)-2-cyclopropylmethylamino-3-ethoxypropyl)carbamic acid benzyl

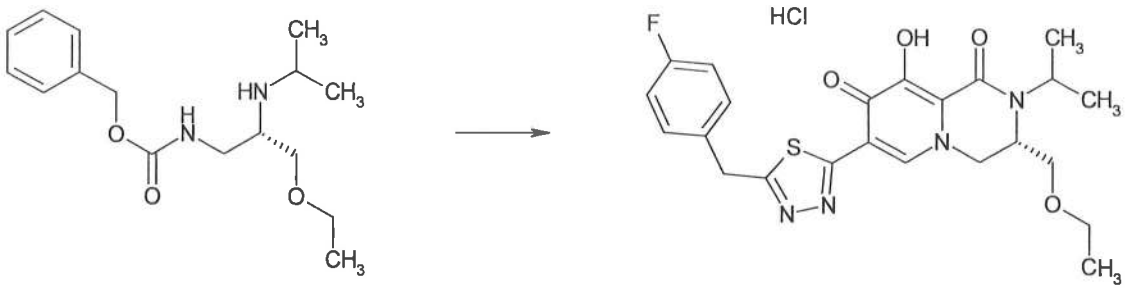
ester (295 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.84 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.15 (m, 2H), 4.67 (d, 1H, J=12.3 Hz), 4.46 (s, 2H), 4.46-4.42 (m, 1H), 4.22-4.19 (m, 2H), 3.67 (dd, 1H, J=14.2, 7.2 Hz), 3.61 (dd, 1H, J=10.4, 4.4 Hz), 3.55 (dd, 1H, J=10.4, 6.2 Hz), 3.40-3.32 (m, 2H), 3.21 (dd, 1H, J=14.2, 7.0 Hz), 0.94 (t, 3H, J=7.0 Hz), 0.54-0.46 (m, 2H), 0.41-0.37 (m, 1H), 0.33-0.27 (m, 1H).

[0382]

Example 12

[0383]



[0384]

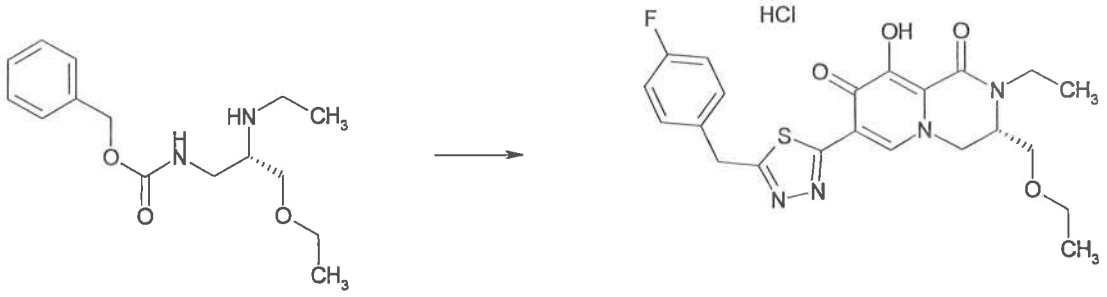
In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (35.0 mg) described in the above-mentioned scheme was obtained from ((S)-3-ethoxy-2-isopropylaminopropyl)carbamic acid benzyl ester (230 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.40 (br s, 1H), 8.85 (s, 1H), 7.43-7.40 (m, 2H), 7.22-7.16 (m, 2H), 4.67, (d, 1H, J=11.9 Hz), 4.51-4.47 (m, 1H), 4.47 (s, 2H), 4.35 (dd, 1H, J=13.3, 3.9 Hz), 4.20-4.16 (m, 1H), 3.54 (dd, 1H, J=10.5, 4.1 Hz), 3.45-3.32 (m, 3H), 1.30 (d, 3H, J=4.6 Hz), 1.28 (d, 3H, J=4.6 Hz), 0.96 (t, 3H, J=7.0 Hz).

[0385]

Example 13

[0386]



[0387]

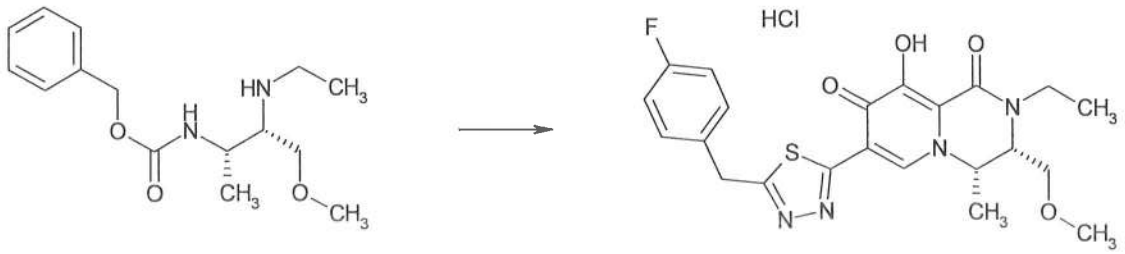
In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (37.0 mg) described in the above-mentioned scheme was obtained from ((S)-3-ethoxy-2-ethylaminopropyl)carbamic acid benzyl ester (250 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.84 (s, 1H), 7.43-7.40 (m, 2H), 7.22-7.16 (m, 2H), 4.67, (dd, 1H, J=13.5, 1.5 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J=13.5, 4.2 Hz), 4.14-4.11 (m, 1H), 3.91-3.82 (m, 1H), 3.60-3.53 (m, 2H), 3.41-3.34 (m, 2H), 3.31-3.23 (m, 1H), 1.20 (t, 3H, J=7.2 Hz), 0.96 (t, 3H, J=7.0Hz).

[0388]

Example 14

[0389]



[0390]

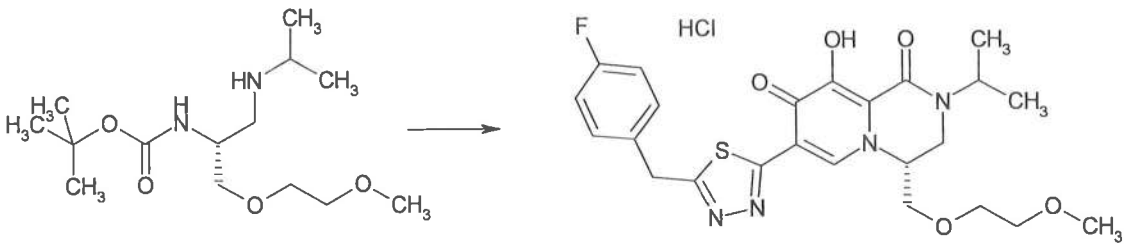
In the same manner as in step 2-9 (amino-protecting group was removed by a known method according to the protecting group) and step 2-11, the object compound (32.9 mg) described in the above-mentioned scheme was obtained from ((1S,2S)-2-ethylamino-3-methoxy-1-methylpropyl)carbamic acid benzyl ester (51 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.62 (s, 1H), 7.42-7.38 (m, 2H), 7.20-7.16 (m, 2H), 4.77-4.71 (m, 1H), 4.47 (s, 2H), 4.14 (q, 1H, J=4.0 Hz), 3.92-3.84 (m, 1H), 3.59 (d, 2H, J=4.4 Hz), 3.33-3.26 (m, 1H), 3.18 (s, 3H), 1.64 (d, 3H, J=6.5 Hz), 1.21 (t, 3H, J=7.1 Hz).

[0391]

Example 15

[0392]



[0393]

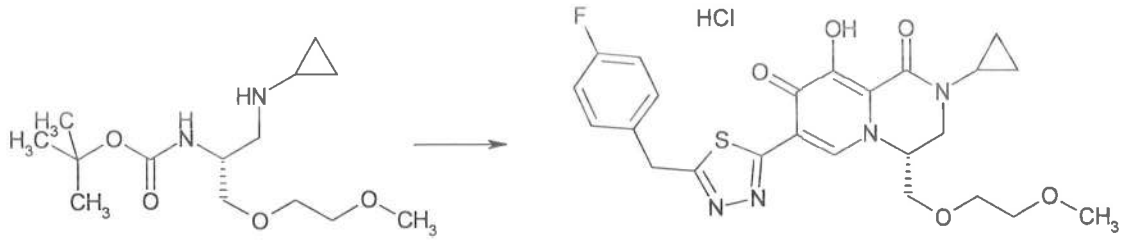
In the same manner as in step 2-9 and step 2-11, the object compound (6.2 mg) described in the above-mentioned scheme was obtained from [(R)-2-isopropylamino-1-((2-methoxyethoxy)methyl)ethyl]carbamic acid tert-butyl ester (19.3 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.82 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.15 (m, 2H), 4.99-4.91 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.8, 4.1 Hz), 3.78-3.68 (m, 2H), 3.64 (dd, 1H, J = 10.4, 7.7 Hz), 3.58-3.45 (m, 2H), 3.34 (t, 2H, J = 4.5 Hz), 3.11 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).

[0394]

Example 16

[0395]



[0396]

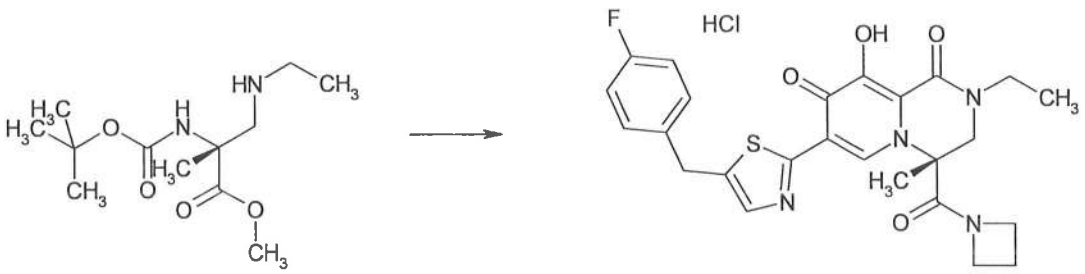
In the same manner as in step 2-9 and step 2-11, the object compound (10.7 mg) described in the above-mentioned scheme was obtained from [(R)-2-cyclopropylamino-1-((2-methoxyethoxy)methyl)ethyl]carbamic acid tert-butyl ester (16 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 8.81 (s, 1H), 7.45-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.92-4.84 (br m, 1H), 4.47 (s, 2H), 4.09-3.99 (m, 1H), 3.74-3.57 (m, 3H), 3.56-3.44 (m, 2H), 3.34 (t, 2H, J = 4.6 Hz), 3.13 (s, 3H), 2.94-2.84 (m, 1H), 0.97-0.67 (m, 4H).

[0397]

Example 17

[0398]



[0399]

In the same manner as in step 2-9 to step 2-11, the object compound (39 mg) described in the above-mentioned scheme was obtained from (R)-2-tert-butoxycarbonylamino-3-ethylamino-2-methylpropionic acid methyl ester (60 mg) obtainable from a commercially available compound by a known method.

^{1}H-NMR (DMSO-d_6) δ: 12.69 (m, 1H), 8.60 (s, 1H), 7.69 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.12 (m, 2H), 4.20 (s, 2H), 4.18-4.13 (m, 1H), 4.01 (d, 1H, J=13.5 Hz), 3.89 (d, 1H, J=13.5 Hz), 3.87-3.80 (m, 2H), 3.67-3.61 (m, 1H), 3.54-3.44 (m, 2H), 2.12-2.04 (m, 2H), 1.91 (s, 3H), 1.10 (t, 3H, J=7.2 Hz).

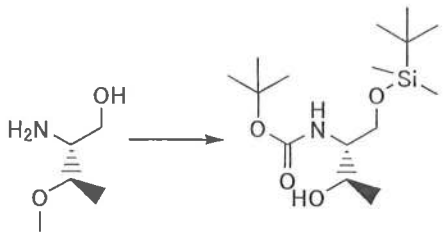
[0400]

Example 340

[0401]

step 340-1

[0402]



[0403]

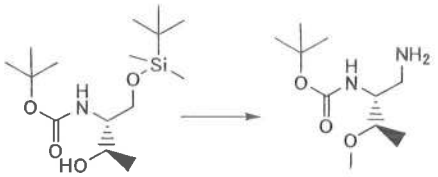
To a solution of L-threoninol (2.05 g) in chloroform (14 mL) were added di-tert-butyl dicarbonate (4.26 g) and saturated aqueous sodium hydrogen carbonate solution (10 mL) and the mixture was stirred at room temperature for 3 hr and left standing for 3 days. To the reaction mixture was added saturated brine, and the mixture was extracted with chloroform. The organic layer was dried, and concentrated. The obtained residue was dissolved in dimethylformamide (40 mL) and, under ice-cooling, imidazole (2.97 g) and tert-butylchlorodimethylsilane (1.49 g) were added, and the mixture was stirred at room temperature for 45 min. Water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried, and concentrated. The concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:10 - 1:3) to give the object compound (2.39 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 5.18 (d, 1H, J = 8.2 Hz), 4.18-4.14 (m, 1H), 3.89 (dd, 1H, J = 10.4, 3.3 Hz), 3.82 (dd, 1H, J = 10.4, 2.6 Hz), 3.48-3.45 (m, 1H), 3.29 (s, 1H), 1.46 (s, 9H), 1.18 (d, 3H, J = 6.2 Hz), 0.90 (s, 9H), 0.08 (s, 6H).

[0404]

step 340-2

[0405]



[0406]

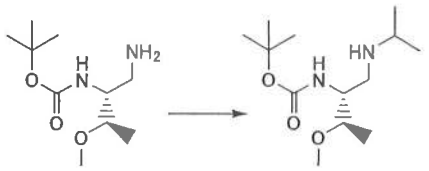
To a solution of the compound (2.39 g) obtained in step 340-1 in toluene (12 mL) were added tetrabutylammonium hydrogen sulfate (76 mg), 50% aqueous sodium hydroxide solution (8 mL) and methyl sulfate (922 μL) under ice-cooling, and the mixture was stirred at room temperature for 90 min. Ice water was added, and the mixture was extracted with toluene. The organic layer was washed with saturated brine, dried, and concentrated. The obtained residue was dissolved in tetrahydrofuran (20 mL), 1.0M tetrabutylammonium fluoride/tetrahydrofuran solution (8.16 mL) was added and the mixture was stirred at room temperature for 100 min. Water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried and concentrated. Toluene was added and the mixture was concentrated again. To a solution of the obtained residue in tetrahydrofuran (40 mL) were added phthalimide (1.85 g) and triphenylphosphine (3.30 g), 2.2M diethyl azodicarboxylate/toluene solution (5.05 mL) was added dropwise under ice-cooling, and the mixture was stirred at room temperature for 90 min. The reaction mixture was concentrated, and the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=1:10 - 1:2). The obtained solid was dissolved in ethanol (60 mL)-toluene (60 mL), hydrazine monohydrate (2.05 mL) was added, and the mixture was stirred at 80°C for 4 hr. The mixture was allowed to cool to room temperature, the solid was filtered off, and the filtrate was concentrated. Toluene was added to the residue, and the precipitated solid was filtered off. The filtrate was concentrated to give the object compound (1.54 g) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 4.82 (br s, 1H), 3.52-3.45 (m, 2H), 3.31 (s, 3H), 2.81 (dd, 2H, J = 13.0, 6.0 Hz), 2.76 (dd, 2H, J = 13.0, 7.1 Hz), 1.51 (br s, 2H), 1.15 (d, 3H, J = 6.2 Hz).

[0407]

step 340-3

[0408]



[0409]

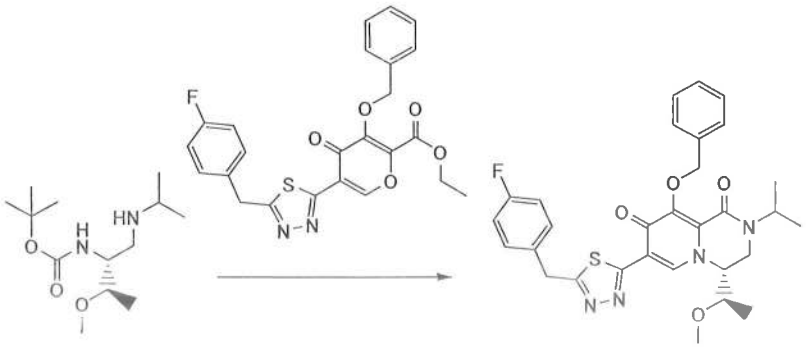
To a solution of the compound (187 mg) obtained in step 340-2 in chloroform (3 mL) were added acetone (76 μL), acetic acid (59 μL) and sodium triacetoxyborohydride (218 mg) under ice-cooling, and the mixture was stirred at room temperature for 5 hr. The reaction mixture was diluted with chloroform, saturated aqueous sodium hydrogen carbonate solution was added and the mixture was stirred. The chloroform layer was dried and concentrated to give the object compound (190 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 4.84 (br s, 1H), 3.59-3.50 (m, 2H), 3.32 (s, 3H), 2.83-2.66 (m, 3H), 1.51 (br s, 1H), 1.14 (d, 3H, J = 6.4 Hz), 1.04 (d, 3H, J = 6.4 Hz), 1.04 (d, 3H, J = 6.4 Hz).

[0410]

step 340-4

[0411]



[0412]

The compound (190 mg) obtained in step 340-3 was dissolved in trifluoroacetic acid (2.0 mL), and the mixture was stood at room temperature for 20 min. Trifluoroacetic acid solution was concentrated, tetrahydrofuran (1.58 mL) and diisopropylethylamine (636 μL) were added to give a solution.

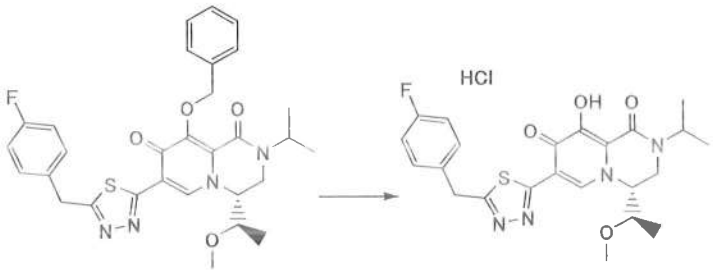
To a solution of the compound (75 mg) obtained in step 2-5 in tetrahydrofuran (500 μL) was added the above-mentioned solution (634 μL), and the mixture was stirred at room temperature for 15 min. Toluene (6 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (250 μL) were added and the mixture was stirred at 100°C for 20 min. Acetic acid (750 μL) was added and the mixture was stirred at 100°C for 1 hr. The reaction mixture was allowed to cool to room temperature, 5% aqueous potassium hydrogen sulfate solution was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogen carbonate solution and saturated brine, dried, and concentrated. The concentrate was purified by silica gel thin layer chromatography (ethyl acetate:methanol=15:1) to give the object compound (73 mg) described in the above-mentioned scheme.

^{1}H-NMR ($CDCl_3$) δ: 8.65 (s, 1H), 7.65-7.62 (m, 2H), 7.35-7.25 (m, 5H), 7.04-6.98 (m, 2H), 5.51 (d, 1H, J = 9.9 Hz), 5.24 (d, 1H, J = 9.9 Hz), 4.94 (sep, 1H, J = 6.8 Hz), 4.43 (s, 2H), 3.93-3.89 (m, 1H), 3.67 (dd, 1H, J = 14.2, 3.9 Hz), 3.47 (dq, 1H, J = 8.8, 6.0 Hz), 3.42 (dd, 1H, J = 14.2, 1.5 Hz), 3.15 (s, 3H), 1.29 (d, 3H, J = 6.0 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.14 (d, 3H, J = 6.8 Hz).

[0413]

step 340-5

[0414]



[0415]

The compound (72 mg) obtained in step 340-4 was dissolved in trifluoroacetic acid (1.0 mL), and the mixture was stood at room temperature for 4 hr. Trifluoroacetic acid solution was

concentrated, toluene was added and the mixture was concentrated. Ethyl acetate, 4N hydrochloric acid/ethyl acetate solution, and hexane were added to allow crystallization to give the object compound (65 mg) described in the above-mentioned scheme.

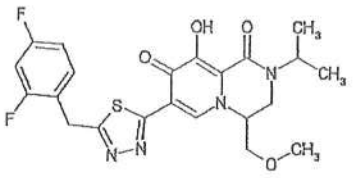
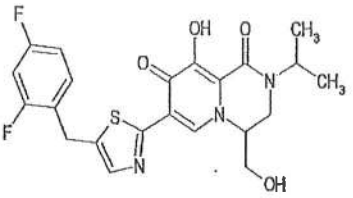
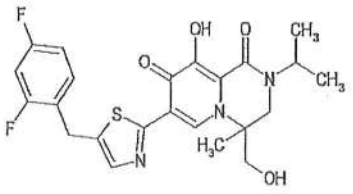
^{1}H-NMR (DMSO-D_6) δ: 12.82 (br s, 1H), 8.72 (s, 1H), 7.44-7.41 (m, 2H), 7.21-7.17 (m, 2H), 4.77 (sep, 1H, J = 6.6 Hz), 4.65 (ddd, 1H, J = 8.2, 4.1, 0.9 Hz), 4.47 (s, 2H), 3.88 (dd, 1H, J = 14.0, 4.1 Hz), 3.76 (dd, 1H, J = 14.0, 0.9 Hz), 3.52 (dq, 1H, J = 8.2, 6.2 Hz), 3.03 (s, 3H), 1.21 (d, 3H, J = 6.2 Hz), 1.20 (d, 3H, J = 6.6 Hz), 1.17 (d, 3H, J = 6.6 Hz).

[0416]

The compounds of Examples 18 to 465 shown in the following Tables were produced in the same manner as in the above-mentioned Examples 1 to 17 and 340, or by using other conventional methods where necessary. The structural formulas and property data of the compounds of Examples 18 to 465 are shown in the following Tables.

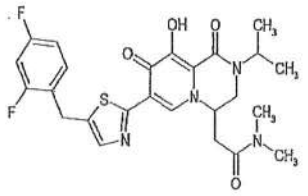
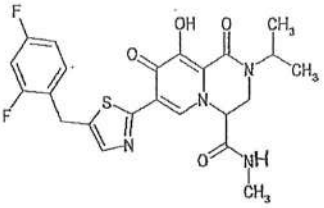
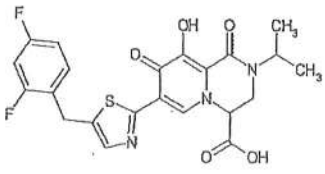
[0417]

[Table 1-1]

No.	structural formula	salt	^{1}H-NMR
18		—	^{1}H-NMR (DMSO-d_6) δ : 12.82 (s, 1H), 8.80 (s, 1H), 7.54 (td, 1H, J = 8.8, 6.7 Hz), 7.29 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.12 (tdd, 1H, J = 8.8, 2.6 0.9 Hz), 5.01-4.93 (br m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.9, 3.9 Hz), 3.75 (dd, 1H, J = 13.9, 1.4 Hz), 3.62 (dd, 1H, J = 10.2, 5.8 Hz), 3.57 (dd, 1H, J = 10.2, 7.7 Hz), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
19		—	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.58 (s, 1H), 7.64 (s, 1H), 7.45 (td, 1H, J = 8.8, 6.8 Hz), 7.24 (ddd, 1H, J = 10.6, 9.7, 2.9 Hz), 7.07 (tdd, 1H, J = 8.8, 2.9, 1.0 Hz), 4.75 (sep, 1H, J = 6.6 Hz), 4.69-4.59 (br m, 1H), 4.21 (s, 2H), 3.81 (dd, 1H, J = 13.5, 3.7 Hz), 3.72 (dd, 1H, J = 13.5, 1.5 Hz), 3.67 (dd, 1H, J = 11.7, 5.3 Hz), 3.53 (dd, 1H, J = 11.7, 8.6 Hz), 1.16 (d, 3H, J = 6.6 Hz), 1.15 (d, 3H, J = 6.6 Hz).
20		—	^{1}H-NMR (DMSO-d_6) δ : 13.11 (br s, 1H), 8.60 (s, 1H), 7.66 (s, 1H), 7.44 (td, 1H, J = 8.7, 6.7 Hz), 7.24 (ddd, 1H, J = 10.4, 9.3, 2.8 Hz), 7.07 (tdd, 1H, J = 8.7, 2.8, 0.9 Hz), 4.79 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.89 (d, 1H, J = 14.1 Hz), 3.79 (d, 1H, J = 14.1 Hz), 3.72 (d, 1H, J = 13.7 Hz), 3.63 (d, 1H, J = 13.7 Hz), 1.58 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).

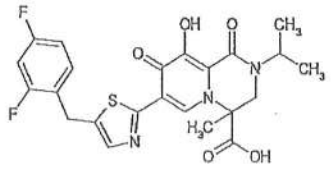
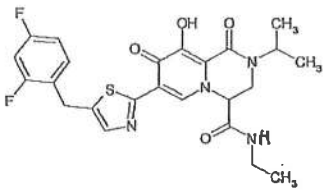
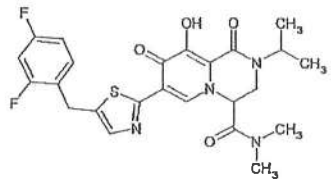
[0418]

[Table 1-2]

No.	structural formula	salt	^{1}H-NMR
21		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.67 (s, 1H), 8.71 (s, 1H), 7.65 (s, 1H), 7.49–7.41 (m, 1H), 7.33–7.20 (m, 1H), 7.11–7.02 (m, 1H), 5.11–5.02 (m, 1H), 4.84–4.73 (m, 1H), 4.21 (s, 2H), 3.87–3.73 (m, 2H), 2.89–2.82 (m, 2H), 2.86 (s, 3H), 2.79 (s, 3H), 1.13 (d, 3H, J = 7.0 Hz), 1.13 (d, 3H, J = 6.7 Hz).
22		—	^{1}H-NMR (DMSO-d_6) δ : 12.37 (s, 1H), 8.66 (s, 1H), 8.25 (q, 1H, J = 4.4 Hz), 7.64 (s, 1H), 7.45 (td, 1H, J = 8.6, 6.5 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.8 Hz), 7.07 (tdd, 1H, J = 8.6, 2.8, 0.9 Hz), 5.52–5.46 (br m, 1H), 4.69 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.02 (dd, 1H, J = 13.9, 2.1 Hz), 3.94 (dd, 1H, J = 13.9, 3.5 Hz), 2.61 (d, 3H, J = 4.4 Hz), 1.12 (d, 3H, J = 6.7 Hz), 1.03 (d, 3H, J = 6.7 Hz).
23		—	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.75 (s, 1H), 7.65 (s, 1H), 7.46 (td, 1H, J = 8.8, 7.1 Hz), 7.24 (ddd, 1H, J = 10.6, 9.7, 2.4 Hz), 7.07 (tdd, 1H, J = 8.8, 2.4, 0.9 Hz), 5.71–5.66 (br m, 1H), 4.73 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.03 (dd, 1H, J = 13.5, 2.6 Hz), 3.95 (dd, 1H, J = 13.5, 4.0 Hz), 1.16 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).

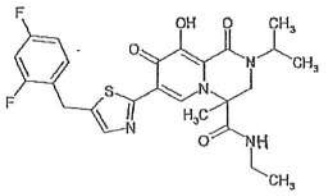
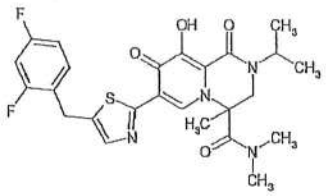
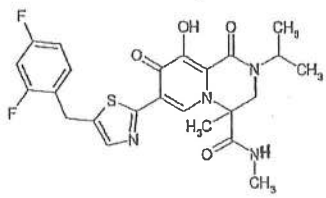
[0419]

[Table 1-3]

No.	structural formula	salt	^{1}H-NMR
24		—	^{1}H-NMR (DMSO-d_6) δ: 12.90 (br s, 1H), 8.59 (s, 1H), 7.66 (s, 1H), 7.44 (td, 1H, J = 9.0, 7.3 Hz), 7.24 (ddd, 1H, J = 10.8, 9.3, 2.4 Hz), 7.07 (tdd, 1H, J = 9.0, 2.4, 1.0 Hz), 4.72 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.05 (d, 2H, J = 13.2 Hz), 3.74 (d, 1H, J = 13.2 Hz), 1.92 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).
25		—	^{1}H-NMR (DMSO-d_6) δ: 12.39 (s, 1H), 8.66 (s, 1H), 8.36 (t, 1H, J = 5.4 Hz), 7.64 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.6 Hz), 7.25 (ddd, 1H, J = 10.4, 9.3, 2.6 Hz), 7.07 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 5.50–5.43 (br m, 1H), 4.70 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.03 (dd, 1H, J = 13.9, 1.6 Hz), 3.95 (dd, 1H, J = 13.9, 3.7 Hz), 3.09 (qd, 2H, J = 7.4, 5.4 Hz), 1.13 (d, 3H, J = 6.7 Hz), 1.05 (d, 3H, J = 6.7 Hz), 1.02 (t, 3H, J = 7.4 Hz).
26		—	^{1}H-NMR (DMSO-d_6) δ: 12.32 (br s, 1H), 8.71 (s, 1H), 7.63 (s, 1H), 7.46 (td, 1H, J = 8.7, 6.6 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.7, 2.6, 1.2 Hz), 6.05–6.00 (br m, 1H), 4.71 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.98 (dd, 1H, J = 14.4, 3.9 Hz), 3.80 (dd, 1H, J = 14.4, 1.4 Hz), 3.17 (s, 3H), 2.82 (s, 3H), 1.14 (d, 3H, J = 6.7 Hz), 0.98 (d, 3H, J = 6.7 Hz).

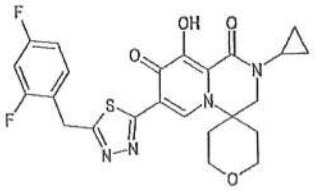
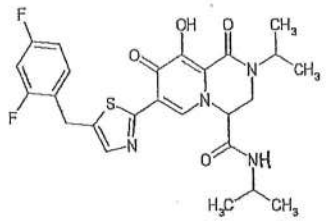
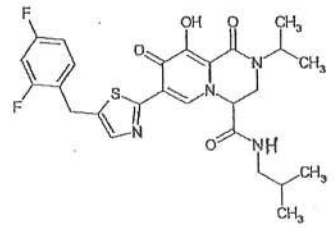
[0420]

[Table 1-4]

No.	structural formula	salt	^{1}H-NMR
27		—	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.50 (s, 1H), 8.13 (t, 1H, J = 5.4 Hz), 7.66 (s, 1H), 7.44 (td, 1H, J = 8.7, 6.7 Hz), 7.24 (ddd, 1H, J = 10.4, 9.3, 2.7 Hz), 7.07 (tdd, 1H, J = 8.7, 2.7, 0.9 Hz), 4.71 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.08 (d, 1H, J = 13.8 Hz), 3.78 (d, 1H, J = 13.8 Hz), 3.17-2.98 (m, 2H), 1.92 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz), 1.00 (t, 3H, J = 7.2 Hz).
28		—	^{1}H-NMR (DMSO-d_6) δ: 12.85 (s, 1H), 8.42 (s, 1H), 7.66 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.7 Hz), 7.24 (ddd, 1H, J = 10.4, 9.7, 2.8 Hz), 7.07 (tdd, 1H, J = 8.7, 2.8, 0.9 Hz), 4.73 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.12 (d, 1H, J = 14.1 Hz), 3.79 (d, 1H, J = 14.1 Hz), 2.93 (br s, 6H), 1.97 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).
29		—	^{1}H-NMR (DMSO-d_6) δ: 12.78 (s, 1H), 8.51 (s, 1H), 8.05 (q, 1H, J = 4.2 Hz), 7.66 (s, 1H), 7.44 (td, 1H, J = 8.7, 6.6 Hz), 7.24 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.05 (d, 1H, J = 13.7 Hz), 3.78 (d, 1H, J = 13.7 Hz), 2.59 (d, 3H, J = 4.2 Hz), 1.92 (s, 3H), 1.14 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).

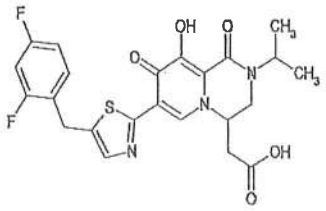
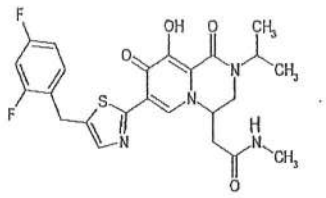
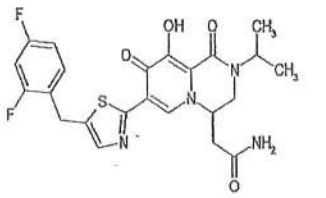
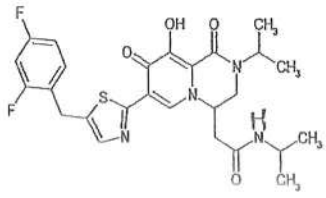
[0421]

[Table 1-5]

No.	structural formula	salt	^{1}H-NMR
30		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.17 (br s, 1H), 8.87 (s, 1H), 7.54 (td, 1H, J = 8.5, 6.9 Hz), 7.29 (ddd, 1H, J = 10.5, 9.3, 2.4 Hz), 7.11 (tdd, 1H, J = 8.5, 2.4, 1.2 Hz), 4.49 (s, 2H), 3.90 (s, 2H), 3.88–3.81 (m, 2H), 3.74–3.66 (m, 2H), 2.98 (ddt, 1H, J = 7.3, 6.9, 4.0 Hz), 2.28–2.19 (m, 2H), 1.98–1.91 (m, 2H), 0.93–0.80 (m, 4H).
31		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.65 (s, 1H), 8.30 (d, 1H, J = 7.4 Hz), 7.64 (s, 1H), 7.45 (td, 1H, J = 8.6, 6.5 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.6, 2.6, 0.9 Hz), 5.46–5.41 (br m, 1H), 4.71 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.03 (dd, 1H, J = 14.0, 1.9 Hz), 3.95 (dd, 1H, J = 14.0, 3.6 Hz), 3.85–3.74 (m, 1H), 1.13 (d, 3H, J = 6.7 Hz), 1.09 (d, 3H, J = 6.7 Hz), 1.07 (d, 3H, J = 7.0 Hz), 1.05 (d, 3H, J = 7.0 Hz).
32		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.40 (br s, 1H), 8.68 (s, 1H), 8.31 (dd, 1H, J = 6.2, 5.7 Hz), 7.64 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.6 Hz), 7.24 (ddd, 1H, J = 10.4, 9.3, 2.8 Hz), 7.07 (tdd, 1H, J = 8.7, 2.8, 1.2 Hz), 5.51–5.46 (br m, 1H), 4.68 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.04 (dd, 1H, J = 14.1, 2.1 Hz), 3.94 (dd, 1H, J = 14.1, 3.6 Hz), 2.97 (ddd, 1H, J = 12.8, 6.6, 6.2 Hz), 2.78 (ddd, 1H, J = 12.8, 6.6, 5.7 Hz), 1.67 (sep, 1H, J = 6.5 Hz), 1.12 (d, 3H, J = 6.7 Hz), 1.04 (d, 3H, J = 6.7 Hz), 0.83 (d, 3H, J = 6.5 Hz), 0.82 (d, 3H, J = 6.5 Hz).

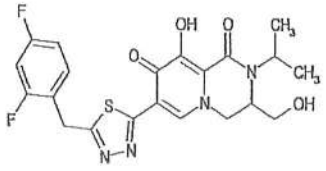
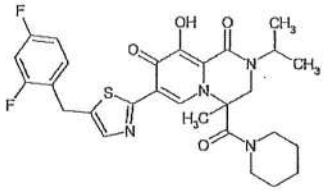
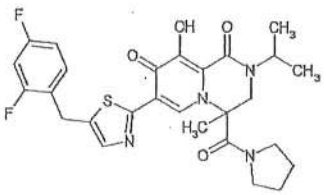
[0422]

[Table 1-6]

No.	structural formula	salt	^{1}H-NMR
33		—	^{1}H-NMR (DMSO-d_6) δ: 8.69 (s, 1H), 7.65 (s, 1H), 7.50-7.40 (m, 1H), 7.33-7.20 (m, 1H), 7.11-7.03 (m, 1H), 5.16-5.04 (m, 1H), 4.84-4.71 (m, 1H), 4.21 (s, 2H), 3.89-3.68 (m, 2H), 2.92-2.64 (m, 2H), 1.15 (t, 6H, J = 6.3 Hz).
34		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.64 (br s, 1H), 8.54 (s, 1H), 7.95-7.87 (m, 1H), 7.64 (s, 1H), 7.50-7.41 (m, 1H), 7.33-7.20 (m, 1H), 7.12-7.03 (m, 1H), 5.08-4.99 (m, 1H), 4.84-4.74 (m, 1H), 4.21 (s, 2H), 3.88-3.65 (m, 2H), 2.70-2.54 (m, 2H), 2.45 (d, 3H, J = 4.4 Hz), 1.17 (d, 3H, J = 6.5 Hz), 1.14 (d, 3H, J = 7.2 Hz).
35		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.58 (s, 1H), 7.65 (s, 1H), 7.49-7.38 (m, 2H), 7.28-7.19 (m, 1H), 7.11-7.03 (m, 1H), 7.00 (br s, 1H), 5.07-4.97 (m, 1H), 4.85-4.73 (m, 1H), 4.21 (s, 2H), 3.91-3.65 (m, 2H), 2.71-2.51 (m, 2H), 1.18 (d, 3H, J = 7.0 Hz), 1.15 (d, 3H, J = 7.2 Hz).
36		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.46 (s, 1H), 7.85 (d, 1H, J = 7.7 Hz), 7.63 (s, 1H), 7.48-7.39 (m, 1H), 7.29-7.19 (m, 1H), 7.12-7.03 (m, 1H), 5.05-4.94 (m, 1H), 4.86-4.74 (m, 1H), 4.20 (s, 2H), 3.88-3.60 (m, 3H), 2.70-2.46 (m, 2H), 1.18 (d, 3H, J = 7.0 Hz), 1.15 (d, 3H, J = 7.2 Hz), 0.92 (d, 3H, J = 6.7 Hz), 0.69 (d, 3H, J = 6.7 Hz).

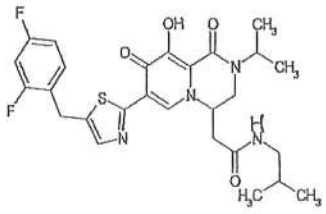
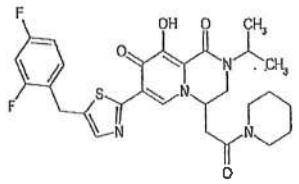
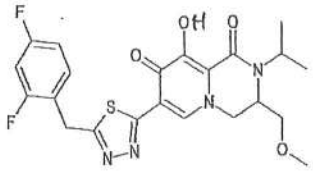
[0423]

[Table 1-7]

No.	structural formula	salt	^{1}H-NMR
37		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.80 (s, 1H), 7.57–7.49 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.67 (dd, 1H, J = 13.2, 1.4 Hz), 4.51 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.34 (dd, 1H, J = 13.2, 3.5 Hz), 4.00–3.93 (m, 1H), 3.57 (dd, 1H, J = 11.5, 3.5 Hz), 3.36 (dd, 1H, J = 11.5, 8.1 Hz), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).
38		—	^{1}H-NMR (DMSO-d_6) δ: 12.97 (br s, 1H), 8.38 (s, 1H), 7.67 (s, 1H), 7.45 (td, 1H, J = 8.8, 6.6 Hz), 7.25 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.07 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.75 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.03 (d, 1H, J = 13.9 Hz), 3.80 (d, 1H, J = 13.9 Hz), 3.56–3.35 (br m, 4H), 1.90 (s, 3H), 1.59–1.50 (br m, 2H), 1.49–1.40 (br m, 4H), 1.18 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).
39		—	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.52 (s, 1H), 7.66 (s, 1H), 7.45 (td, 1H, J = 8.8, 6.6 Hz), 7.24 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.11 (d, 1H, J = 13.9 Hz), 3.74 (d, 1H, J = 13.9 Hz), 3.64–3.54 (br m, 1H), 3.42–3.32 (br m, 1H), 3.32–3.22 (br m, 1H), 3.15–3.05 (br m, 1H), 2.00 (s, 3H), 1.94–1.82 (br m, 1H), 1.79–1.57 (br m, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.07 (d, 3H, J = 6.7 Hz).

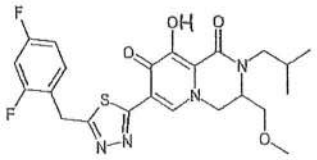
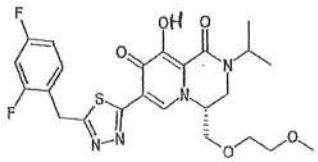
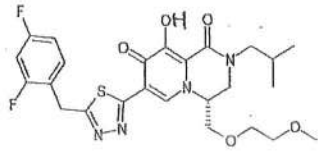
[0424]

[Table 1-8]

No.	structural formula	salt	^{1}H-NMR
40		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.92–12.53 (m, 1H), 8.44 (s, 1H), 7.97 (t, 1H, J = 6.3 Hz), 7.64 (s, 1H), 7.49–7.40 (m, 1H), 7.29–7.19 (m, 1H), 7.12–7.02 (m, 1H), 5.10–4.98 (m, 1H), 4.86–4.75 (m, 1H), 4.21 (s, 2H), 3.90–3.81 (m, 1H), 3.75–3.67 (m, 1H), 2.92–2.82 (m, 1H), 2.77–2.66 (m, 1H), 2.61–2.48 (m, 2H), 1.44–1.30 (m, 1H), 1.18 (d, 3H, J = 7.2 Hz), 1.15 (d, 3H, J = 7.2 Hz), 0.54 (d, 3H, J = 6.7 Hz), 0.50 (d, 3H, J = 7.2 Hz).
41		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.88–12.50 (m, 1H), 8.68 (s, 1H), 7.65 (s, 1H), 7.49–7.40 (m, 1H), 7.28–7.20 (m, 1H), 7.11–7.03 (m, 1H), 5.11–5.03 (m, 1H), 4.84–4.73 (m, 1H), 4.21 (s, 2H), 3.88–3.73 (m, 2H), 3.54–3.19 (m, 4H), 2.87 (d, 2H, J = 7.0 Hz), 1.59–1.43 (m, 2H), 1.42–1.29 (m, 4H), 1.13 (d, 3H, J = 6.7 Hz), 1.13 (d, 3H, J = 6.5 Hz).
42		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.45 (br s, 1H), 8.84 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.07 (m, 1H), 4.66 (dd, 1H, J = 13.4, 1.6 Hz), 4.49 (s, 2H), 4.47 (sep, 1H, J = 6.8 Hz), 4.35 (dd, 1H, J = 13.4, 3.7 Hz), 4.23–4.17 (m, 1H), 3.49 (dd, 1H, J = 10.2, 4.2 Hz), 3.39 (dd, 1H, J = 10.2, 7.4 Hz), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz).

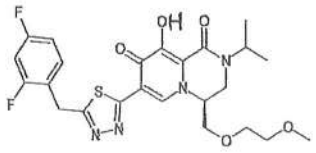
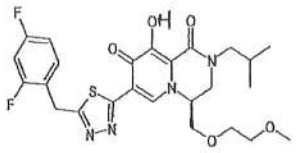
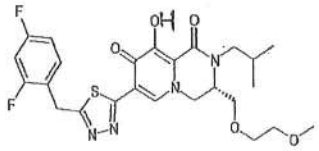
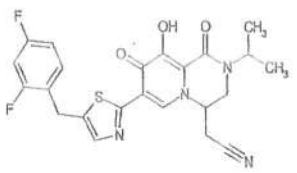
[0425]

[Table 1-9]

No.	structural formula	salt	^{1}H-NMR
43		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.54 (br s, 1H), 8.83 (s, 1H), 7.57–7.49 (m, 1H), 7.32–7.25 (m, 1H), 7.14–7.07 (m, 1H), 4.65 (dd, 1H, J = 13.4, 1.4 Hz), 4.48 (s, 2H), 4.47 (dd, 1H, J = 13.4, 4.3 Hz), 4.10–4.04 (m, 1H), 3.80 (dd, 1H, J = 13.3, 8.0 Hz), 3.53 (dd, 1H, J = 10.4, 5.1 Hz), 3.49 (dd, 1H, J = 10.4, 6.3 Hz), 3.20 (s, 3H), 2.94 (dd, 1H, J = 13.3, 7.1 Hz), 2.08 (ddsep, 1H, J = 8.0, 7.1, 6.7 Hz), 0.95 (d, 3H, J = 6.7 Hz), 0.89 (d, 3H, J = 6.7 Hz).
44		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.81 (s, 1H), 7.59–7.49 (m, 1H), 7.33–7.23 (m, 1H), 7.16–7.07 (m, 1H), 4.99–4.90 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 3.93–3.60 (m, 4H), 3.58–3.44 (m, 2H), 3.33 (t, 2H, J = 4.6 Hz), 3.11 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
45		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.80 (s, 1H), 7.59–7.50 (m, 1H), 7.35–7.24 (m, 1H), 7.16–7.07 (m, 1H), 4.97–4.86 (m, 1H), 4.49 (s, 2H), 4.06 (dd, 1H, J = 13.7, 4.2 Hz), 3.80–3.66 (m, 3H), 3.59–3.46 (m, 3H), 3.36–3.31 (m, 2H), 3.22 (dd, 1H, J = 7.1, 12.6 Hz), 3.11 (s, 3H), 2.00 (sept, 1H, J = 6.6 Hz), 0.91 (d, 6H, J = 6.6 Hz).

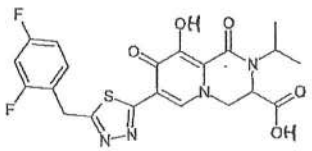
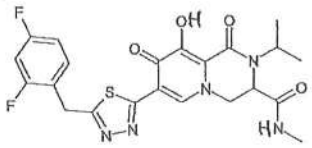
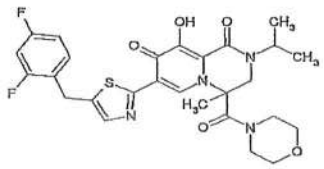
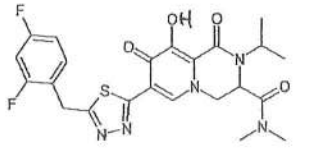
[0426]

[Table 1-10]

No.	structural formula	salt	^{1}H-NMR
46		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.84 (br s, 1H), 8.81 (s, 1H), 7.59–7.49 (m, 1H), 7.33–7.23 (m, 1H), 7.16–7.07 (m, 1H), 4.99–4.90 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 3.93–3.60 (m, 4H), 3.58–3.44 (m, 2H), 3.33 (t, 2H, J = 4.6 Hz), 3.11 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
47		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.80 (br s, 1H), 8.80 (s, 1H), 7.59–7.50 (m, 1H), 7.35–7.24 (m, 1H), 7.16–7.07 (m, 1H), 4.97–4.86 (m, 1H), 4.49 (s, 2H), 4.06 (dd, 1H, J = 13.7, 4.2 Hz), 3.80–3.66 (m, 3H), 3.59–3.46 (m, 3H), 3.36–3.31 (m, 2H), 3.22 (dd, 1H, J = 7.1, 12.6 Hz), 3.11 (s, 3H), 2.00 (sept, 1H, J = 6.6 Hz), 0.91 (d, 6H, J = 6.6 Hz).
48		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.55 (br s, 1H), 8.81 (s, 1H), 7.59–7.49 (m, 1H), 7.35–7.24 (m, 1H), 7.16–7.07 (m, 1H), 4.65 (d, 1H, J = 13.2 Hz), 4.53–4.45 (m, 1H), 4.48 (s, 2H), 4.09–4.01 (m, 1H), 3.80 (dd, 1H, J = 13.4, 7.9 Hz), 3.67–3.57 (m, 2H), 3.50–3.39 (m, 2H), 3.30–3.24 (m, 2H), 3.08 (s, 3H), 2.95 (dd, 1H, J = 13.4, 7.0 Hz), 2.14–2.01 (m, 1H), 0.95 (d, 3H, J = 6.5 Hz), 0.90 (d, 3H, J = 6.7 Hz).
49		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.73 (br s, 1H), 8.80 (s, 1H), 7.67 (s, 1H), 7.51–7.42 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.03 (m, 1H), 5.27–5.17 (m, 1H), 4.85–4.72 (m, 1H), 4.22 (s, 2H), 3.96–3.65 (m, 2H), 3.34–3.20 (m, 2H), 1.20 (d, 3H, J = 7.2 Hz), 1.14 (d, 3H, J = 7.0 Hz).

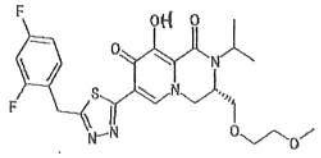
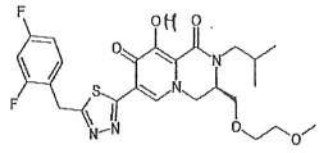
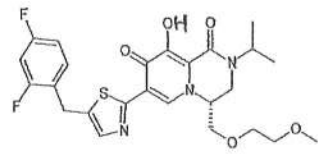
[0427]

[Table 1-11]

No.	structural formula	salt	^{1}H-NMR
50		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.38 (s, 1H), 8.95 (s, 1H), 7.57–7.50 (m, 1H), 7.32–7.25 (m, 1H), 7.14–7.08 (m, 1H), 5.00–4.91 (m, 2H), 4.73 (sep, 1H, J = 6.6 Hz), 4.52 (dd, 1H, J = 13.6, 3.9 Hz), 4.48 (s, 2H), 1.24 (d, 3H, J = 6.6 Hz), 1.13 (d, 3H, J = 6.6 Hz).
51		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (s, 1H), 8.80 (s, 1H), 8.31 (q, 1H, J = 4.6 Hz), 7.57–7.49 (m, 1H), 7.33–7.24 (m, 1H), 7.14–7.07 (m, 1H), 4.76 (d, 1H, J = 14.2 Hz), 4.73 (sep, 1H, J = 6.8 Hz), 4.60 (d, 1H, J = 4.0 Hz), 4.54 (dd, 1H, J = 14.2, 4.0 Hz), 4.48 (s, 2H), 2.60 (d, 3H, J = 4.6 Hz), 1.21 (d, 3H, J = 6.8 Hz), 1.04 (d, 3H, J = 6.8 Hz).
52		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.95 (br s, 1H), 8.39 (s, 1H), 7.68 (s, 1H), 7.45 (td, 1H, J = 8.6, 6.7 Hz), 7.25 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.07 (tdd, 1H, J = 8.6, 2.6, 0.9 Hz), 4.75 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.02 (d, 1H, J = 14.4 Hz), 3.81 (d, 1H, J = 14.4 Hz), 3.60–3.41 (br m, 8H), 1.91 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
53		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.57 (s, 1H), 8.81 (s, 1H), 7.57–7.49 (m, 1H), 7.32–7.25 (m, 1H), 7.14–7.07 (m, 1H), 5.17 (d, 1H, J = 3.0 Hz), 4.80 (d, 1H, J = 13.7 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.52–4.46 (m, 1H), 4.48 (s, 2H), 3.20 (s, 3H), 2.81 (s, 3H), 1.24 (d, 3H, J = 6.7 Hz), 1.00 (d, 3H, J = 6.7 Hz).

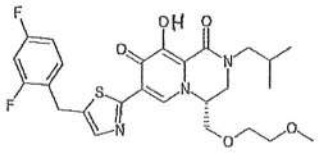
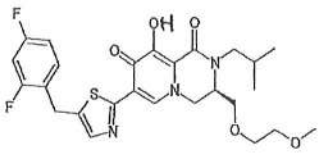
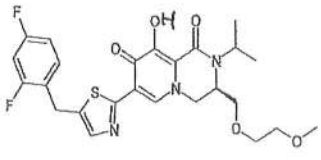
[0428]

[Table 1-12]

No.	structural formula	salt	^{1}H-NMR
54		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.44 (br s, 1H), 8.81 (s, 1H), 7.59–7.48 (m, 1H), 7.34–7.23 (m, 1H), 7.16–7.06 (m, 1H), 4.69–4.61 (m, 1H), 4.53–4.43 (m, 1H), 4.48 (s, 2H), 4.36 (dd, 1H, J = 7.2, 13.4 Hz), 4.23–4.14 (m, 1H), 3.51–3.40 (m, 4H), 3.33–3.25 (m, 2H), 3.08 (s, 3H), 1.28 (d, 3H, J = 6.7 Hz), 1.29 (d, 3H, J = 6.5 Hz).
55		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.55 (br s, 1H), 8.81 (s, 1H), 7.59–7.49 (m, 1H), 7.35–7.24 (m, 1H), 7.16–7.07 (m, 1H), 4.65 (d, 1H, J = 13.2 Hz), 4.53–4.45 (m, 1H), 4.48 (s, 2H), 4.09–4.01 (m, 1H), 3.80 (dd, 1H, J = 13.4, 7.9 Hz), 3.67–3.57 (m, 2H), 3.50–3.39 (m, 2H), 3.30–3.24 (m, 2H), 3.08 (s, 3H), 2.95 (dd, 1H, J = 13.4, 7.0 Hz), 2.14–2.01 (m, 1H), 0.95 (d, 3H, J = 6.5 Hz), 0.90 (d, 3H, J = 6.7 Hz).
56		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.70 (br s, 1H), 8.65 (s, 1H), 7.65 (s, 1H), 7.49–7.42 (m, 1H), 7.28–7.21 (m, 1H), 7.10–7.04 (m, 1H), 4.93–4.87 (m, 1H), 4.77 (sep, 1H, J = 6.9 Hz), 4.21 (s, 2H), 3.82 (dd, 1H, J = 13.7, 4.0 Hz), 3.76–3.67 (m, 2H), 3.62 (dd, 1H, J = 10.5, 7.7 Hz), 3.56–3.45 (m, 2H), 3.35–3.32 (m, 2H), 3.12 (s, 3H), 1.16 (d, 3H, J = 6.9 Hz), 1.15 (d, 3H, J = 6.9 Hz).

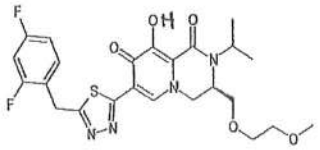
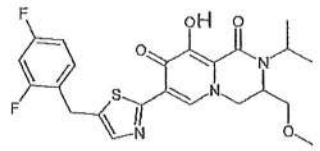
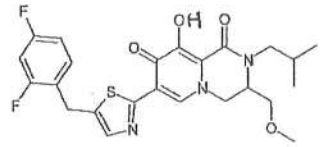
[0429]

[Table 1-13]

No.	structural formula	salt	^{1}H-NMR
57		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.66 (br s, 1H), 8.64 (s, 1H), 7.65 (s, 1H), 7.49–7.42 (m, 1H), 7.28–7.21 (m, 1H), 7.10–7.04 (m, 1H), 4.90–4.82 (m, 1H), 4.21 (s, 2H), 4.04 (dd, 1H, J = 13.7, 4.4 Hz), 3.78–3.64 (m, 3H), 3.56–3.45 (m, 2H), 3.45–3.28 (m, 3H), 3.21 (dd, 1H, J = 13.3, 6.9 Hz), 3.11 (s, 3H), 2.05–1.94 (m, 1H), 0.91 (d, 6H, J = 6.4 Hz).
58		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.40 (br s, 1H), 8.63 (s, 1H), 7.64 (s, 1H), 7.49–7.41 (m, 1H), 7.28–7.20 (m, 1H), 7.11–7.04 (m, 1H), 4.62–4.55 (m, 1H), 4.46 (dd, 1H, J = 13.8, 4.4 Hz), 4.21 (s, 2H), 4.06–4.00 (m, 1H), 3.80 (dd, 1H, J = 13.4, 7.7 Hz), 3.64–3.54 (m, 2H), 3.50–3.40 (m, 2H), 3.33–3.24 (m, 2H), 3.10 (s, 3H), 2.94 (dd, 1H, J = 13.4, 7.1 Hz), 2.12–2.03 (m, 1H), 0.95 (d, 3H, J = 6.7 Hz), 0.89 (d, 3H, J = 6.7 Hz).
59		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.30 (br s, 1H), 8.62 (s, 1H), 7.64 (s, 1H), 7.50–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.03 (m, 1H), 4.62–4.55 (m, 1H), 4.48 (sep, 1H, J = 6.7 Hz), 4.36–4.31 (m, 1H), 4.21 (s, 2H), 4.19–4.14 (m, 1H), 3.58 (dd, 1H, J = 10.3, 4.1 Hz), 3.52–3.39 (m, 3H), 3.33–3.27 (m, 2H), 3.10 (s, 3H), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).

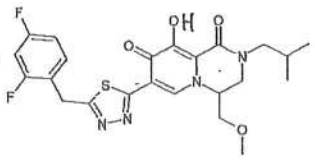
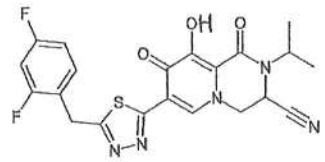
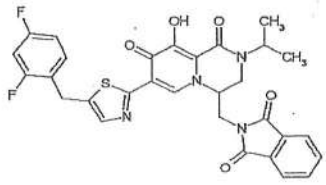
[0430]

[Table 1-14]

No.	structural formula	salt	^{1}H-NMR
60		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.44 (br s, 1H), 8.81 (s, 1H), 7.59–7.48 (m, 1H), 7.34–7.23 (m, 1H), 7.16–7.06 (m, 1H), 4.69–4.61 (m, 1H), 4.53–4.43 (m, 1H), 4.48 (s, 2H), 4.36 (dd, 1H, J = 7.2, 13.4 Hz), 4.23–4.14 (m, 1H), 3.51–3.40 (m, 4H), 3.33–3.25 (m, 2H), 3.08 (s, 3H), 1.28 (d, 3H, J = 6.7 Hz), 1.29 (d, 3H, J = 6.5 Hz).
61		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.66 (s, 1H), 7.49–7.41 (m, 1H), 7.29–7.21 (m, 1H), 7.11–7.03 (m, 1H), 4.60 (dd, 1H, J = 13.4, 1.4 Hz), 4.47 (sep, 1H, J = 6.8Hz), 4.33 (dd, 1H, J = 13.4, 3.7 Hz), 4.22 (s, 2H), 4.14–4.10 (m, 1H), 3.48 (dd, 1H, J = 10.3, 4.3 Hz), 3.36 (dd, 1H, J = 10.3, 7.7 Hz), 3.21 (s, 3H), 1.29 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz).
62		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 8.65 (s, 1H), 7.65 (s, 1H), 7.50–7.41 (m, 1H), 7.30–7.21 (m, 1H), 7.11–7.03 (m, 1H), 4.59 (dd, 1H, J = 13.7, 1.2 Hz), 4.46 (dd, 1H, J = 13.7, 4.2 Hz), 4.21 (s, 2H), 4.08–4.01 (m, 1H), 3.80 (dd, 1H, J = 13.2, 7.9 Hz), 3.52 (dd, 1H, J = 10.4, 5.4 Hz), 3.48 (dd, 1H, J = 10.4, 6.4 Hz), 3.20 (s, 3H), 2.93 (dd, 1H, J = 13.2, 7.2 Hz), 2.08 (tt, 1H, J = 6.7, 6.7 Hz), 0.95 (d, 3H, J = 6.7 Hz), 0.89 (d, 3H, J = 6.7 Hz).

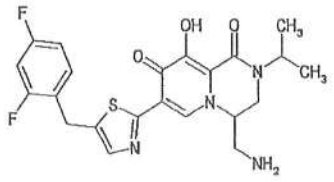
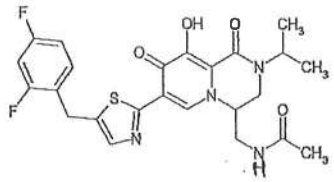
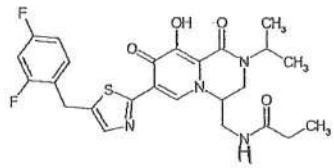
[0431]

[Table 1-15]

No.	structural formula	salt	^{1}H-NMR
63		HCl	^{1}H-NMR ($CDCl_3$) δ : 12.78 (br s, 1H), 9.36 (s, 1H), 7.38–7.30 (m, 1H), 6.92–6.84 (m, 2H), 4.58–4.51 (m, 1H), 4.48 (s, 2H), 4.05–3.98 (m, 1H), 3.76–3.63 (m, 3H), 3.51 (dd, 1H, J = 13.4, 7.9 Hz), 3.39 (s, 3H), 3.29 (dd, 1H, J = 13.4, 7.0 Hz), 2.09–1.99 (m, 1H), 1.00 (d, 3H, J = 6.7 Hz), 0.99 (d, 3H, J = 6.7 Hz).
64		HCl	^{1}H-NMR (DMSO-d_6) δ : 9.03 (s, 1H), 7.59–7.51 (m, 1H), 7.33–7.25 (m, 1H), 7.16–7.08 (m, 1H), 5.66 (dd, 1H, J = 3.0, 1.9 Hz), 5.07 (dd, 1H, J = 13.8, 1.9 Hz), 4.78 (sep, 1H, J = 6.8 Hz), 4.61 (dd, 1H, J = 13.8, 3.0 Hz), 4.51 (s, 2H), 1.31 (d, 3H, J = 6.8 Hz), 1.24 (d, 3H, J = 6.8 Hz).
65		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.31 (s, 1H), 7.78–7.73 (m, 2H), 7.72–7.67 (m, 2H), 7.38 (td, 1H, J = 8.8, 6.8 Hz), 7.36 (s, 1H), 7.25 (ddd, 1H, J = 10.4, 9.0, 2.6 Hz), 7.08 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.99–4.91 (br m, 1H), 4.80 (sep, 1H, J = 6.7 Hz), 4.13 (s, 2H), 4.04 (dd, 1H, J = 14.3, 4.6 Hz), 3.96 (dd, 1H, J = 13.9, 2.0 Hz), 3.89 (dd, 1H, J = 13.9, 4.0 Hz), 3.82 (dd, 1H, J = 14.3, 9.3 Hz), 1.27 (d, 3H, J = 6.7 Hz), 1.19 (d, 3H, J = 6.7 Hz).

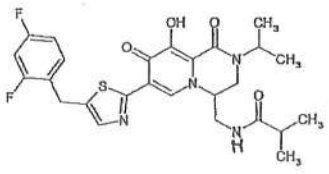
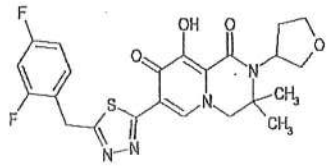
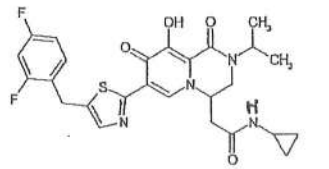
[0432]

[Table 1-16]

No.	structural formula	salt	^{1}H-NMR
66		2HCl	^{1}H-NMR (DMSO-d_6) δ: 12.56 (br s, 1H), 8.70 (s, 1H), 8.25–8.13 (br m, 2H), 7.66 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.7 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.08 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.95–4.86 (br m, 1H), 4.76 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 3.90 (dd, 1H, J = 13.8, 3.6 Hz), 3.84 (dd, 1H, J = 13.8, 1.9 Hz), 3.35–3.24 (br m, 1H), 3.22–3.09 (br m, 1H), 1.19 (d, 3H, J = 6.7 Hz), 1.15 (d, 3H, J = 6.7 Hz).
67		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.39 (s, 1H), 8.05 (t, 1H, J = 6.0 Hz), 7.64 (s, 1H), 7.46 (td, 1H, J = 8.8, 7.0 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.08 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.77 (sep, 1H, J = 6.7 Hz), 4.67–4.59 (br m, 1H), 4.21 (s, 2H), 3.84 (dd, 1H, J = 13.8, 3.8 Hz), 3.74 (dd, 1H, J = 13.8, 0.9 Hz), 3.41–3.27 (m, 2H), 1.66 (s, 3H), 1.19 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
68		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.36 (s, 1H), 7.97 (t, 1H, J = 6.0 Hz), 7.62 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.7 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.08 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.77 (sep, 1H, J = 6.7 Hz), 4.68–4.60 (br m, 1H), 4.21 (s, 2H), 3.84 (dd, 1H, J = 13.7, 3.9 Hz), 3.75 (dd, 1H, J = 13.7, 1.4 Hz), 3.40–3.29 (m, 2H), 1.96–1.86 (m, 2H), 1.19 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz), 0.78 (t, 3H, J = 7.5 Hz).

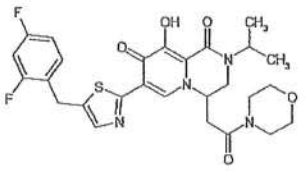
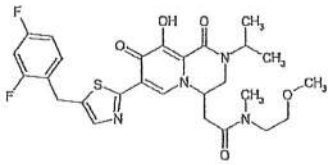
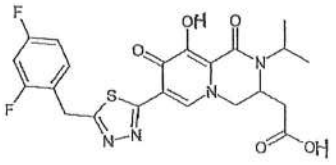
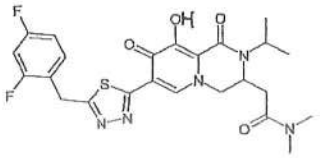
[0433]

[Table 1-17]

No.	structural formula	salt	^{1}H-NMR
69		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.66 (s, 1H), 8.33 (s, 1H), 7.93 (t, 1H, J = 6.0 Hz), 7.61 (s, 1H), 7.43 (td, 1H, J = 8.7, 6.6 Hz), 7.25 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.78 (sep, 1H, J = 6.7 Hz), 4.69–4.61 (br m, 1H), 4.20 (s, 2H), 3.84 (dd, 1H, J = 13.7, 3.9 Hz), 3.74 (dd, 1H, J = 13.7, 1.4 Hz), 3.38–3.32 (m, 2H), 2.15 (sep, 1H, J = 6.7 Hz), 1.19 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz), 0.85 (d, 3H, J = 6.7 Hz), 0.73 (d, 3H, J = 6.7 Hz).
70		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.55 (br s, 1H), 8.75 (s, 1H), 7.58–7.50 (m, 1H), 7.34–7.24 (m, 1H), 7.16–7.07 (m, 1H), 4.49 (s, 2H), 4.43–4.30 (m, 3H), 4.03 (q, 1H, J = 7.8 Hz), 3.92–3.48 (m, 3H), 2.36–2.26 (m, 1H), 2.12–2.00 (m, 1H), 1.39 (s, 3H), 1.36 (s, 3H).
71		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.64 (br s, 1H), 8.49 (s, 1H), 8.04 (d, 1H, J = 3.9 Hz), 7.65 (s, 1H), 7.50–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.11–7.03 (m, 1H), 5.07–4.96 (m, 1H), 4.84–4.72 (m, 1H), 4.21 (s, 2H), 3.87–3.59 (m, 2H), 2.71–2.30 (m, 3H), 1.15 (t, 6H, J = 7.4 Hz), 0.55–0.35 (m, 2H), 0.24–0.06 (m, 2H).

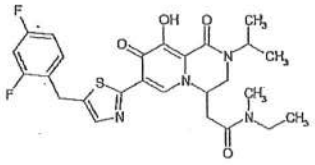
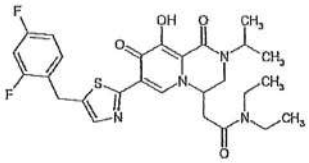
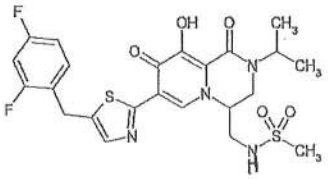
[0434]

[Table 1-18]

No.	structural formula	salt	^{1}H-NMR
72		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.69 (br s, 1H), 8.70 (s, 1H), 7.65 (s, 1H), 7.49–7.39 (m, 1H), 7.29–7.19 (m, 1H), 7.11–7.00 (m, 1H), 5.14–5.01 (m, 1H), 4.86–4.71 (m, 1H), 4.21 (s, 2H), 3.91–3.67 (m, 2H), 3.51–3.22 (m, 8H), 2.91 (d, 2H, J = 6.5 Hz), 1.14 (d, 3H, J = 6.7 Hz), 1.13 (d, 3H, J = 6.7 Hz).
73		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.69 (s, 1.0H), 7.65 (s, 1.0H), 7.49–7.40 (m, 1.0H), 7.29–7.19 (m, 1.0H), 7.11–7.02 (m, 1.0H), 5.13–5.03 (m, 1.0H), 4.84–4.72 (m, 1.0H), 4.21 (s, 2.0H), 3.88–3.55 (m, 2.0H), 3.55–3.25 (m, 4.0H), 3.15 (s, 1.5H), 3.12 (s, 1.5H), 3.02–2.82 (m, 2.0H), 2.88 (s, 1.5H), 2.79 (s, 1.5H), 1.13 (d, 6.0H, J = 6.5 Hz).
74		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.85 (s, 1H), 7.57–7.50 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.62–4.56 (m, 1H), 4.53–4.30 (m, 3H), 4.49 (s, 2H), 2.69–2.45 (m, 2H), 1.30 (d, 3H, J = 7.2 Hz), 1.28 (d, 3H, J = 7.2 Hz).
75		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (s, 1H), 8.80 (s, 1H), 7.57–7.49 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.57–4.46 (m, 2H), 4.48 (s, 2H), 4.45–4.34 (m, 2H), 2.84 (s, 3H), 2.83 (s, 3H), 2.81–2.54 (m, 2H), 1.28 (d, 3H, J = 6.8 Hz), 1.25 (d, 3H, J = 6.8 Hz).

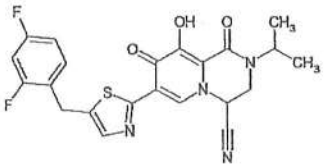
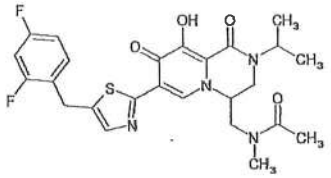
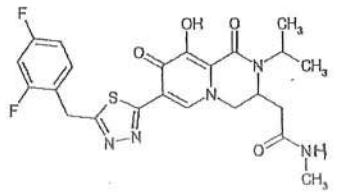
[0435]

[Table 1-19]

No.	structural formula	salt	^{1}H-NMR
76		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.81–12.55 (m, 1H), 8.70 (d, 1H, J = 3.7 Hz), 7.65 (s, 1H), 7.50–7.40 (m, 1H), 7.29–7.19 (m, 1H), 7.11–7.03 (m, 1H), 5.13–5.02 (m, 1H), 4.86–4.72 (m, 1H), 4.21 (s, 2H), 3.88–3.73 (m, 2H), 3.42–3.10 (m, 3H), 2.90–2.80 (m, 1H), 2.83 (s, 1.8H), 2.76 (s, 1.2H), 1.13 (d, 3H, J = 7.0 Hz), 1.12 (d, 3H, J = 6.7 Hz), 0.99 (t, 1.2H, J = 7.2 Hz), 0.93 (t, 1.8H, J = 7.4 Hz).
77		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.67 (br s, 1H), 8.68 (s, 1H), 7.65 (s, 1H), 7.50–7.40 (m, 1H), 7.29–7.19 (m, 1H), 7.12–7.03 (m, 1H), 5.14–5.04 (m, 1H), 4.85–4.73 (m, 1H), 4.21 (s, 2H), 3.90–3.76 (m, 2H), 3.35–3.10 (m, 4H), 2.84 (d, 2H, J = 6.7 Hz), 1.13 (t, 6H, J = 6.7 Hz), 0.98 (t, 3H, J = 7.4 Hz), 0.94 (t, 3H, J = 7.4 Hz).
78		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.66 (br s, 1H), 8.57 (s, 1H), 7.65 (s, 1H), 7.45 (td, 1H, J = 8.7, 6.6 Hz), 7.36 (dd, 1H, J = 6.7, 6.1 Hz), 7.24 (ddd, 1H, J = 10.4, 9.5, 2.8 Hz), 7.07 (tdd, 1H, J = 8.7, 2.8, 0.9 Hz), 4.75 (sep, 1H, J = 6.7 Hz), 4.71–4.63 (br m, 1H), 4.21 (s, 2H), 3.85 (dd, 1H, J = 13.8, 4.1 Hz), 3.75 (dd, 1H, J = 13.8, 1.2 Hz), 3.38 (ddd, 1H, J = 14.1, 6.1, 5.6 Hz), 3.16 (ddd, 1H, J = 14.1, 9.0, 6.7 Hz), 2.89 (s, 3H), 1.21 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).

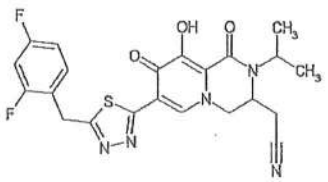
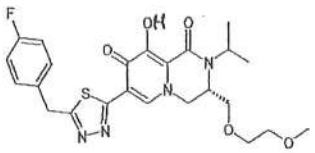
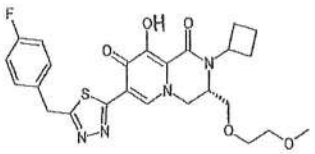
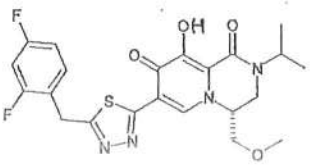
[0436]

[Table 1-20]

No.	structural formula	salt	^{1}H-NMR
79		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.94 (s, 1H), 7.70 (s, 1H), 7.47 (td, 1H, J = 8.6, 6.8 Hz), 7.25 (ddd, 1H, J = 10.1, 9.5, 2.6 Hz), 7.08 (tdd, 1H, J = 8.6, 2.6, 1.1 Hz), 6.30-6.25 (br m, 1H), 4.80 (sep, 1H, J = 6.8 Hz), 4.24 (dd, 1H, J = 14.1, 2.0 Hz), 4.23 (s, 2H), 4.02 (dd, 1H, J = 14.1, 3.5 Hz), 1.23 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz).
80		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.35 (s, 1H), 7.64 (s, 1H), 7.46 (td, 1H, J = 8.8, 7.1 Hz), 7.25 (ddd, 1H, J = 10.6, 9.5, 2.6 Hz), 7.08 (tdd, 1H, J = 8.8, 2.6, 1.3 Hz), 4.92-4.84 (br m, 1H), 4.78 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.87 (dd, 1H, J = 14.1, 4.4 Hz), 3.83 (dd, 1H, J = 14.1, 10.8 Hz), 3.71 (dd, 1H, J = 13.9, 1.1 Hz), 3.39 (dd, 1H, J = 13.9, 4.0 Hz), 2.90 (s, 3H), 1.77 (s, 3H), 1.19 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
81		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (s, 1H), 8.80 (s, 1H), 7.92 (q, 1H, J = 4.4 Hz), 7.57-7.50 (m, 1H), 7.33-7.26 (m, 1H), 7.15-7.08 (m, 1H), 4.53-4.30 (m, 4H), 4.49 (s, 2H), 2.56 (d, 3H, J = 4.4 Hz), 2.44-2.37 (m, 2H), 1.29 (d, 3H, J = 6.8 Hz), 1.27 (d, 3H, J = 6.8 Hz).

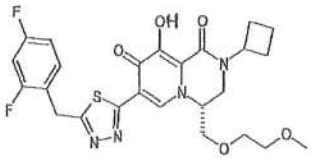
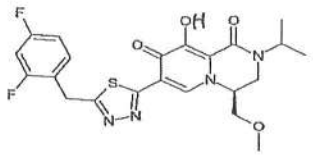
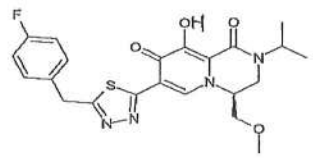
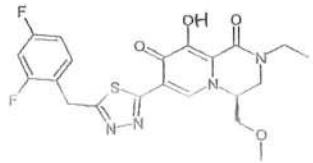
[0437]

[Table 1-21]

No.	structural formula	salt	^{1}H-NMR
82		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.88 (s, 1H), 7.58-7.50 (m, 1H), 7.32-7.25 (m, 1H), 7.15-7.08 (m, 1H), 4.64 (d, 1H, J = 13.2 Hz), 4.54-4.41 (m, 3H), 4.49 (s, 2H), 3.12 (dd, 1H, J = 17.5, 7.0 Hz), 3.01 (dd, 1H, J = 17.5, 4.2 Hz), 1.31 (d, 3H, J = 6.8 Hz), 1.31 (d, 3H, J = 6.8 Hz).
83		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.82 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.68-4.62 (m, 1H), 4.55-4.42 (m, 1H), 4.47 (s, 2H), 4.36 (dd, 1H, J = 13.1, 3.6 Hz), 4.23-4.13 (m, 1H), 3.52-3.39 (m, 4H), 3.32-3.25 (m, 2H), 3.09 (s, 3H), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).
84		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.48 (br s, 1H), 8.82 (s, 1H), 7.44-7.36 (m, 2H), 7.22-7.15 (m, 2H), 4.70-4.64 (m, 1H), 4.61-4.50 (m, 1H), 4.47 (s, 2H), 4.45-4.37 (m, 1H), 4.31-4.23 (m, 1H), 3.58-3.39 (m, 4H), 3.31-3.25 (m, 2H), 3.09 (s, 3H), 2.37-2.12 (m, 4H), 1.75-1.62 (m, 2H).
85		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.82 (s, 1H), 8.80 (s, 1H), 7.54 (td, 1H, J = 8.8, 6.7 Hz), 7.29 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.12 (tdd, 1H, J = 8.8, 2.6 0.9 Hz), 5.01-4.93 (br m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.9, 3.9 Hz), 3.75 (dd, 1H, J = 13.9, 1.4 Hz), 3.62 (dd, 1H, J = 10.2, 5.8 Hz), 3.57 (dd, 1H, J = 10.2, 7.7 Hz), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).

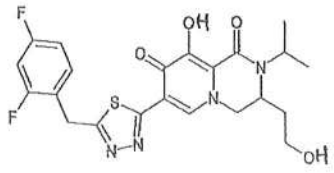
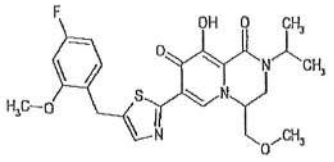
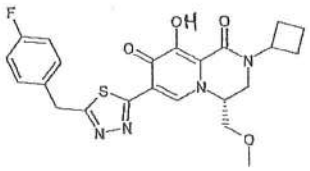
[0438]

[Table 1-22]

No.	structural formula	salt	^{1}H-NMR
86		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.73 (br s, 1H), 8.82 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 5.00–4.84 (m, 2H), 4.49 (s, 2H), 3.98–3.87 (m, 2H), 3.74 (dd, 1H, J = 10.4, 6.0 Hz), 3.64 (dd, 1H, J = 10.4, 7.4 Hz), 3.58–3.46 (m, 2H), 3.34 (t, 2H, J = 4.6 Hz), 3.12 (s, 3H), 2.34–2.03 (m, 4H), 1.76–1.65 (m, 2H).
87		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.80 (s, 1H), 7.59–7.49 (m, 1H), 7.35–7.24 (m, 1H), 7.16–7.07 (m, 1H), 5.01–4.93 (m, 1H), 4.77 (t, 1H, J = 6.7 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.7, 3.9 Hz), 3.75 (dd, 1H, J = 13.7, 2.5 Hz), 3.62 (dd, 1H, J = 10.2, 5.8 Hz), 3.57 (dd, 1H, J = 10.2, 7.7 Hz), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
88		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.80 (s, 1H), 7.45–7.39 (m, 2H), 7.22–7.15 (m, 2H), 5.01–4.94 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.7, 3.9 Hz), 3.75 (dd, 1H, J = 13.7, 1.6 Hz), 3.62 (dd, 1H, J = 10.4, 5.8 Hz), 3.57 (dd, 1H, J = 10.4, 7.7 Hz), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
89		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (br s, 1H), 8.78 (s, 1H), 7.58–7.50 (m, 1H), 7.32–7.26 (m, 1H), 7.14–7.08 (m, 1H), 4.99–4.89 (m, 1H), 4.49 (s, 2H), 4.07 (dd, 1H, J = 13.7, 4.4 Hz), 3.74–3.56 (m, 4H), 3.44–3.33 (m, 1H), 3.25 (s, 3H), 1.14 (t, 3H, J = 7.2 Hz).

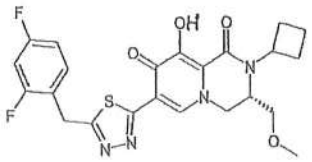
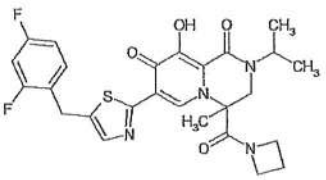
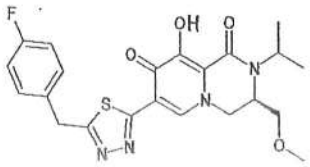
[0439]

[Table 1-23]

No.	structural formula	salt	^{1}H-NMR
90		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.47 (s, 1H), 8.87 (s, 1H), 7.57–7.49 (m, 1H), 7.32–7.24 (m, 1H), 7.15–7.07 (m, 1H), 4.66 (dd, 1H, J = 13.5, 1.7 Hz), 4.53 (sep, 1H, J = 6.8 Hz), 4.49 (s, 2H), 4.35–4.28 (m, 1H), 4.14–4.07 (m, 1H), 3.62–3.47 (m, 2H), 1.81–1.51 (m, 2H), 1.29 (d, 6H, J = 6.8 Hz).
91		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76–12.55 (br m, 1H), 8.61 (s, 1H), 7.61 (s, 1H), 7.25 (dd, 1H, J = 8.5, 6.9 Hz), 6.92 (dd, 1H, J = 11.3, 2.4 Hz), 6.73 (td, 1H, J = 8.5, 2.4 Hz), 4.94–4.86 (br m, 1H), 4.77 (sep, 1H, J = 6.9 Hz), 4.09 (s, 2H), 3.84–3.79 (m, 1H), 3.83 (s, 3H), 3.76–3.69 (m, 1H), 3.60 (dd, 1H, J = 10.5, 5.6 Hz), 3.54 (dd, 1H, J = 10.5, 7.7 Hz), 3.23 (s, 3H), 1.16 (d, 3H, J = 6.9 Hz), 1.15 (d, 3H, J = 6.9 Hz).
92		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.70 (br s, 1H), 8.81 (s, 1H), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 5.02–4.85 (m, 2H), 4.47 (s, 2H), 3.98–3.87 (m, 2H), 3.65 (dd, 1H, J = 10.3, 5.8 Hz), 3.57 (dd, 1H, J = 10.3, 7.5 Hz), 3.25 (s, 3H), 2.31–2.04 (m, 4H), 1.77–1.65 (m, 2H).

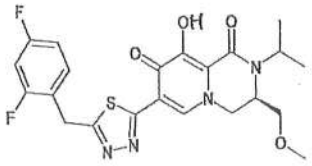
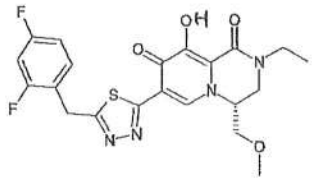
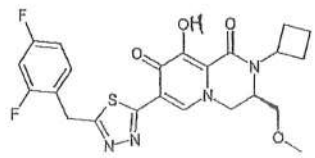
[0440]

[Table 1-24]

No.	structural formula	salt	^{1}H-NMR
93		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.84 (s, 1H), 7.57–7.49 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.07 (m, 1H), 4.68 (d, 1H, J = 13.2 Hz), 4.60–4.49 (m, 1H), 4.48 (s, 2H), 4.41 (dd, 1H, J = 13.2, 3.7 Hz), 4.32–4.25 (m, 1H), 3.43 (dd, 1H, J = 10.4, 4.6 Hz), 3.39 (dd, 1H, J = 10.4, 6.8 Hz), 3.21 (s, 3H), 2.39–2.11 (m, 4H), 1.77–1.63 (m, 2H).
94		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.79 (br s, 1H), 8.60 (s, 1H), 7.67 (s, 1H), 7.45 (td, 1H, J = 8.2, 6.0 Hz), 7.24 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.07 (tdd, 1H, J = 8.2, 2.6, 0.9 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.22 (s, 2H), 4.19–4.14 (br m, 1H), 4.09 (d, 1H, J = 14.1 Hz), 4.00 (d, 1H, J = 14.1 Hz), 3.88–3.81 (br m, 2H), 3.74–3.69 (br m, 1H), 2.14–2.04 (br m, 2H), 1.94 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.13 (d, 3H, J = 6.7 Hz).
95		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.84 (s, 1H), 7.43–7.38 (m, 2H), 7.21–7.14 (m, 2H), 4.66 (d, 1H, J = 13.2 Hz), 4.47 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 4.34 (dd, 1H, J = 13.5, 3.7 Hz), 4.22–4.17 (m, 1H), 3.49 (dd, 1H, J = 10.6, 4.3 Hz), 3.39 (dd, 1H, J = 10.6, 7.5 Hz), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).

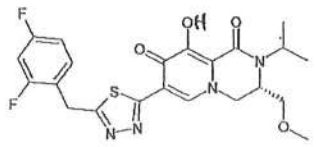
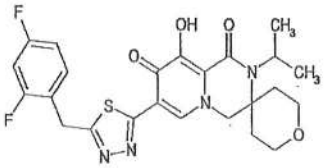
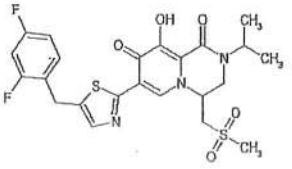
[0441]

[Table 1-25]

No.	structural formula	salt	^{1}H-NMR
96		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.45 (br s, 1H), 8.84 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.07 (m, 1H), 4.66 (dd, 1H, J = 13.4, 1.6 Hz), 4.49 (s, 2H), 4.47 (sep, 1H, J = 6.8 Hz), 4.35 (dd, 1H, J = 13.4, 3.7 Hz), 4.23–4.17 (m, 1H), 3.49 (dd, 1H, J = 10.2, 4.2 Hz), 3.39 (dd, 1H, J = 10.2, 7.4 Hz), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz).
97		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (br s, 1H), 8.78 (s, 1H), 7.58–7.50 (m, 1H), 7.32–7.26 (m, 1H), 7.14–7.08 (m, 1H), 4.99–4.89 (m, 1H), 4.49 (s, 2H), 4.07 (dd, 1H, J = 13.7, 4.4 Hz), 3.74–3.56 (m, 4H), 3.44–3.33 (m, 1H), 3.25 (s, 3H), 1.14 (t, 3H, J = 7.2 Hz).
98		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.51 (br s, 1H), 8.84 (s, 1H), 7.58–7.49 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.71–4.64 (m, 1H), 4.60–4.46 (m, 3H), 4.41 (dd, 1H, J = 13.7, 3.9 Hz), 4.31–4.25 (m, 1H), 3.46–3.36 (m, 2H), 3.21 (s, 3H), 2.37–2.12 (m, 4H), 1.77–1.64 (m, 2H).

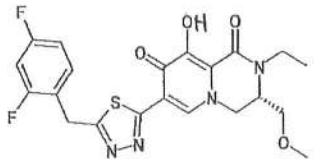
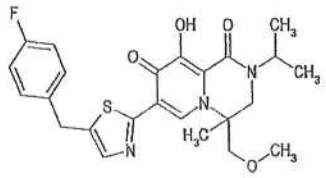
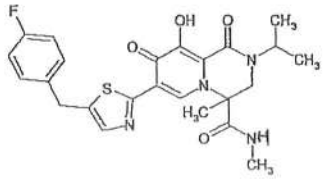
[0442]

[Table 1-26]

No.	structural formula	salt	^{1}H-NMR
99		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.46 (br s, 1H), 8.84 (s, 1H), 7.57-7.50 (m, 1H), 7.32-7.25 (m, 1H), 7.15-7.08 (m, 1H), 4.66 (dd, 1H, J = 13.2, 1.6 Hz), 4.52-4.42 (m, 1H), 4.49 (s, 2H), 4.35 (dd, 1H, J = 13.2, 4.0 Hz), 4.23-4.17 (m, 1H), 3.49 (dd, 1H, J = 10.4, 4.3 Hz), 3.39 (dd, 1H, J = 10.4, 7.5 Hz), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz).
100		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.56 (br s, 1H), 9.02 (s, 1H), 7.53 (td, 1H, J = 8.5, 6.4 Hz), 7.29 (ddd, 1H, J = 10.5, 9.7, 2.4 Hz), 7.12 (tdd, 1H, J = 8.5, 2.4, 1.2 Hz), 4.72 (s, 2H), 4.49 (s, 2H), 4.16-4.02 (br m, 1H), 3.82-3.78 (m, 2H), 3.74-3.66 (m, 2H), 2.21-2.13 (m, 2H), 1.64-1.58 (m, 2H), 1.43 (d, 6H, J = 6.4 Hz).
101		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.66 (br s, 1H), 8.66 (s, 1H), 7.66 (s, 1H), 7.51-7.40 (m, 1H), 7.29-7.20 (m, 1H), 7.11-7.03 (m, 1H), 5.45-5.34 (m, 1H), 4.83-4.70 (m, 1H), 4.21 (s, 2H), 3.95-3.85 (m, 2H), 3.81-3.59 (m, 2H), 3.05 (s, 3H), 1.20 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).

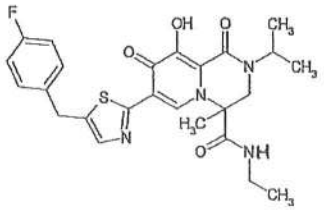
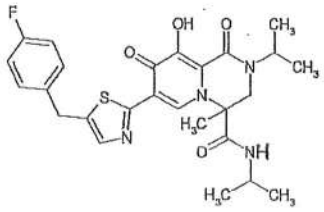
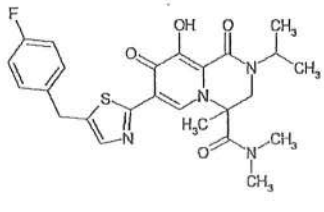
[0443]

[Table 1-27]

No.	structural formula	salt	^{1}H-NMR
102		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.83 (s, 1H), 7.57-7.50 (m, 1H), 7.33-7.25 (m, 1H), 7.15-7.08 (m, 1H), 4.64 (dd, 1H, J = 13.7, 1.6 Hz), 4.49 (s, 2H), 4.43 (dd, 1H, J = 13.7, 4.1 Hz), 4.17-4.12 (m, 1H), 3.86 (dq, 1H, J = 13.4, 7.0 Hz), 3.54 (dd, 1H, J = 10.2, 5.1 Hz), 3.50 (dd, 1H, J = 10.2, 6.3 Hz), 3.27 (dq, 1H, J = 13.4, 7.0 Hz), 3.21 (s, 3H), 1.18 (t, 3H, J = 7.0 Hz).
103		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.61 (s, 1H), 7.70 (s, 1H), 7.36-7.29 (m, 2H), 7.18-7.11 (m, 2H), 4.80 (sep, 1H, J = 6.7 Hz), 4.20 (s, 2H), 3.74 (d, 1H, J = 13.7 Hz), 3.64 (d, 1H, J = 10.4 Hz), 3.64 (d, 1H, J = 13.7 Hz), 3.58 (d, 1H, J = 10.4 Hz), 3.24 (s, 3H), 1.63 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).
104		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.53 (s, 1H), 8.14 (q, 1H, J = 4.4 Hz), 7.69 (s, 1H), 7.36-7.30 (m, 2H), 7.18-7.11 (m, 2H), 4.70 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.09 (d, 1H, J = 13.9 Hz), 3.77 (d, 1H, J = 13.9 Hz), 2.60 (d, 3H, J = 4.4 Hz), 1.93 (s, 3H), 1.14 (d, 3H, J = 6.7 Hz), 1.09 (d, 3H, J = 6.7 Hz).

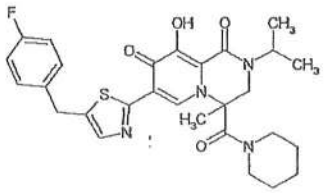
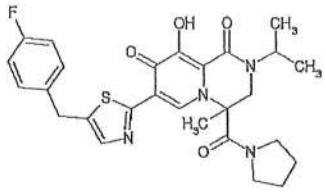
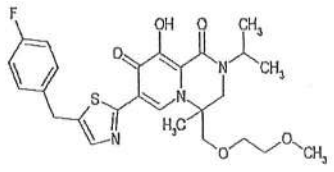
[0444]

[Table 1-28]

No.	structural formula	salt	^{1}H-NMR
105		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.52 (s, 1H), 8.18 (t, 1H, J = 5.2 Hz), 7.68 (s, 1H), 7.36-7.30 (m, 2H), 7.18-7.11 (m, 2H), 4.71 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.11 (d, 1H, J = 13.9 Hz), 3.78 (d, 1H, J = 13.9 Hz), 3.18-2.98 (m, 2H), 1.92 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz), 1.00 (t, 3H, J = 7.2 Hz).
106		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.50 (s, 1H), 8.07 (d, 1H, J = 7.4 Hz), 7.68 (s, 1H), 7.36-7.30 (m, 2H), 7.18-7.11 (m, 2H), 4.72 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.16 (d, 1H, J = 14.1 Hz), 3.81 (sep, 1H, J = 6.7 Hz), 3.79 (d, 1H, J = 14.1 Hz), 1.93 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.15 (d, 3H, J = 6.7 Hz), 1.07 (d, 3H, J = 6.7 Hz), 1.06 (d, 3H, J = 6.7 Hz).
107		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (s, 1H), 8.43 (s, 1H), 7.69 (s, 1H), 7.37-7.29 (m, 2H), 7.19-7.11 (m, 2H), 4.73 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.12 (d, 1H, J = 14.1 Hz), 3.79 (d, 1H, J = 14.1 Hz), 2.93 (s, 6H), 1.98 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).

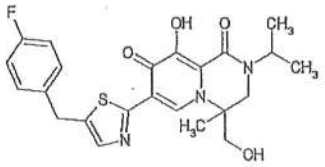
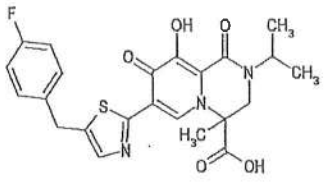
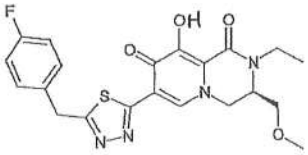
[0445]

[Table 1-29]

No.	structural formula	salt	^{1}H-NMR
108		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.96 (br s, 1H), 8.39 (s, 1H), 7.69 (s, 1H), 7.37–7.30 (m, 2H), 7.19–7.11 (m, 2H), 4.75 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.03 (d, 1H, J = 14.4 Hz), 3.80 (d, 1H, J = 14.4 Hz), 3.56–3.37 (br m, 4H), 1.90 (s, 3H), 1.59–1.50 (br m, 2H), 1.50–1.41 (br m, 4H), 1.18 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).
109		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.79 (br s, 1H), 8.54 (s, 1H), 7.69 (s, 1H), 7.37–7.30 (m, 2H), 7.19–7.11 (m, 2H), 4.70 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.12 (d, 1H, J = 14.1 Hz), 3.75 (d, 1H, J = 14.1 Hz), 3.65–3.53 (br m, 1H), 3.43–3.33 (br m, 1H), 3.33–3.23 (br m, 1H), 3.16–3.05 (br m, 1H), 2.01 (s, 3H), 1.94–1.84 (br m, 1H), 1.81–1.56 (br m, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).
110		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.12 (s, 1H), 8.63 (s, 1H), 7.69 (s, 1H), 7.36–7.30 (m, 2H), 7.18–7.11 (m, 2H), 4.79 (sep, 1H, J = 6.7 Hz), 4.20 (s, 2H), 3.74 (d, 1H, J = 10.2 Hz), 3.73 (d, 1H, J = 13.9 Hz), 3.66 (d, 1H, J = 10.2 Hz), 3.65 (d, 1H, J = 13.9 Hz), 3.54–3.42 (m, 2H), 3.38–3.30 (m, 2H), 3.11 (s, 3H), 1.63 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).

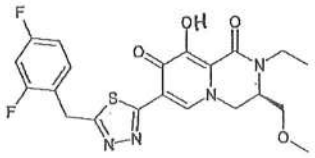
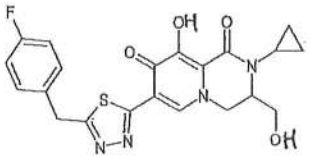
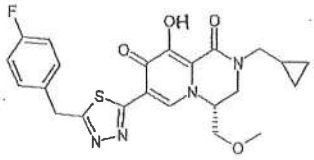
[0446]

[Table 1-30]

No.	structural formula	salt	^{1}H-NMR
111		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.14 (s, 1H), 8.63 (s, 1H), 7.69 (s, 1H), 7.36–7.30 (m, 2H), 7.18–7.11 (m, 2H), 4.79 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.72 (d, 1H, J = 13.7 Hz), 3.64 (d, 1H, J = 13.7 Hz), 3.61 (s, 2H), 1.59 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).
112		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.87 (br s, 1H), 8.61 (s, 1H), 7.70 (s, 1H), 7.37–7.30 (m, 2H), 7.18–7.11 (m, 2H), 4.73 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.06 (d, 1H, J = 13.7 Hz), 3.80 (d, 1H, J = 13.7 Hz), 1.98 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.14 (d, 3H, J = 6.7 Hz).
113		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.64–12.34 (m, 1H), 8.83 (s, 1H), 7.44–7.37 (m, 2H), 7.22–7.14 (m, 2H), 4.64 (dd, 1H, J = 13.4, 1.5 Hz), 4.47 (s, 2H), 4.42 (dd, 1H, J = 13.4, 4.4 Hz), 4.17–4.11 (m, 1H), 3.86 (dq, 1H, J = 14.0, 7.0 Hz), 3.54 (dd, 1H, J = 10.4, 4.9 Hz), 3.50 (dd, 1H, J = 10.4, 6.3 Hz), 3.27 (dq, 1H, J = 14.0, 7.0 Hz), 3.22 (s, 3H), 1.20 (t, 3H, J = 7.0 Hz).

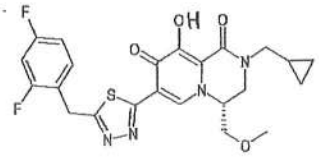
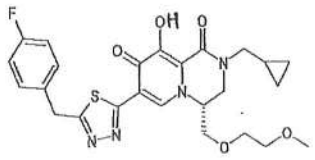
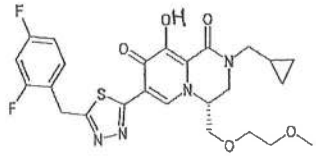
[0447]

[Table 1-31]

No.	structural formula	salt	^{1}H-NMR
114		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.83 (s, 1H), 7.57–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.64 (dd, 1H, J = 13.7, 1.6 Hz), 4.49 (s, 2H), 4.43 (dd, 1H, J = 13.7, 4.1 Hz), 4.17–4.12 (m, 1H), 3.86 (dq, 1H, J = 13.4, 7.0 Hz), 3.54 (dd, 1H, J = 10.2, 5.1 Hz), 3.50 (dd, 1H, J = 10.2, 6.3 Hz), 3.27 (dq, 1H, J = 13.4, 7.0 Hz), 3.21 (s, 3H), 1.18 (t, 3H, J = 7.0 Hz).
115		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (br s, 1H), 8.79 (s, 1H), 7.44–7.37 (m, 2H), 7.22–7.15 (m, 2H), 4.61 (dd, 1H, J = 13.6, 1.6 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J = 13.6, 4.2 Hz), 3.86–3.80 (m, 1H), 3.62 (dd, 1H, J = 11.5, 3.8 Hz), 3.52 (dd, 1H, J = 11.5, 7.1 Hz), 2.95–2.88 (m, 1H), 1.03–0.94 (m, 1H), 0.90–0.83 (m, 1H), 0.83–0.72 (m, 2H).
116		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (s, 1H), 8.79 (s, 1H), 7.46–7.38 (m, 2H), 7.24–7.15 (m, 2H), 5.02–4.90 (m, 1H), 4.47 (s, 2H), 4.12 (dd, 1H, J = 13.7, 3.9 Hz), 3.87–3.79 (m, 1H), 3.73–3.58 (m, 2H), 3.45 (dd, 1H, J = 14.0, 7.3 Hz), 3.31 (dd, 1H, J = 14.0, 6.8 Hz), 3.26 (s, 3H), 1.15–1.03 (m, 1H), 0.58–0.46 (m, 2H), 0.39–0.26 (m, 2H).

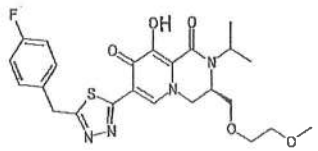
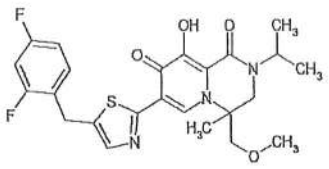
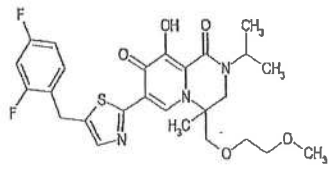
[0448]

[Table 1-32]

No.	structural formula	salt	^{1}H-NMR
117		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (br s, 1H), 8.79 (s, 1H), 7.59–7.50 (m, 1H), 7.33–7.26 (m, 1H), 7.15–7.08 (m, 1H), 4.99–4.92 (m, 1H), 4.49 (s, 2H), 4.12 (dd, 1H, J = 13.8, 4.3 Hz), 3.87–3.80 (m, 1H), 3.69 (dd, 1H, J = 10.4, 5.6 Hz), 3.62 (dd, 1H, J = 10.4, 7.9 Hz), 3.45 (dd, 1H, J = 13.8, 7.3 Hz), 3.31 (dd, 1H, J = 13.9, 7.0 Hz), 3.26 (s, 3H), 1.14–1.03 (m, 1H), 0.57–0.46 (m, 2H), 0.39–0.27 (m, 2H).
118		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.76 (s, 1H), 8.80 (s, 1H), 7.45–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.96–4.89 (m, 1H), 4.47 (s, 2H), 4.11 (dd, 1H, J = 13.7, 4.2 Hz), 3.84 (dd, 1H, J = 13.7, 1.2 Hz), 3.78 (dd, 1H, J = 10.5, 5.6 Hz), 3.70 (dd, 1H, J = 10.5, 7.7 Hz), 3.59–3.39 (m, 3H), 3.37–3.29 (m, 3H), 3.10 (s, 3H), 1.13–1.04 (m, 1H), 0.58–0.46 (m, 2H), 0.38–0.27 (m, 2H).
119		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (br s, 1H), 8.80 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.16–7.08 (m, 1H), 4.97–4.89 (m, 1H), 4.49 (s, 2H), 4.12 (dd, 1H, J = 13.7, 4.4 Hz), 3.84 (dd, 1H, J = 13.7, 1.2 Hz), 3.78 (dd, 1H, J = 10.5, 5.6 Hz), 3.70 (dd, 1H, J = 10.5, 7.7 Hz), 3.59–3.40 (m, 3H), 3.37–3.29 (m, 3H), 3.10 (s, 3H), 1.14–1.04 (m, 1H), 0.58–0.47 (m, 2H), 0.38–0.27 (m, 2H).

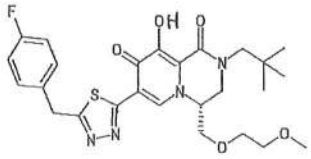
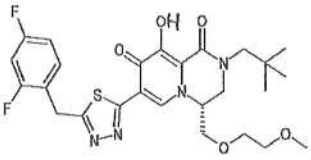
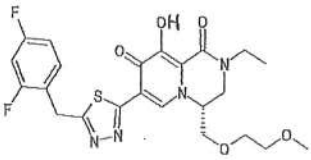
[0449]

[Table 1-33]

No.	structural formula	salt	^{1}H-NMR
120		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 8.82 (s, 1H), 7.44–7.37 (m, 2H), 7.22–7.14 (m, 2H), 4.65 (d, 1H, J = 12.5 Hz), 4.55–4.42 (m, 1H), 4.47 (s, 2H), 4.36 (dd, 1H, J = 13.1, 3.6 Hz), 4.23–4.13 (m, 1H), 3.52–3.39 (m, 4H), 3.32–3.25 (m, 2H), 3.09 (s, 3H), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).
121		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.10 (br s, 1H), 8.58 (s, 1H), 7.66 (s, 1H), 7.44 (td, 1H, J = 8.7, 6.7 Hz), 7.23 (ddd, 1H, J = 10.4, 9.5, 2.6 Hz), 7.06 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.78 (sep, 1H, J = 6.7 Hz), 4.20 (s, 2H), 3.73 (d, 1H, J = 13.9 Hz), 3.63 (d, 1H, J = 13.9 Hz), 3.63 (d, 1H, J = 10.2 Hz), 3.56 (d, 1H, J = 10.2 Hz), 3.22 (s, 3H), 1.61 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
122		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.12 (br s, 1H), 8.62 (s, 1H), 7.67 (s, 1H), 7.45 (td, 1H, J = 8.8, 7.0 Hz), 7.25 (ddd, 1H, J = 10.4, 9.3, 2.6 Hz), 7.07 (tdd, 1H, J = 8.8, 2.6, 1.0 Hz), 4.79 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.78–3.70 (m, 2H), 3.66 (d, 1H, J = 10.2 Hz), 3.65 (d, 1H, J = 13.9 Hz), 3.54–3.42 (m, 2H), 3.37–3.29 (m, 2H), 3.11 (s, 3H), 1.63 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).

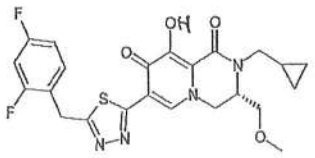
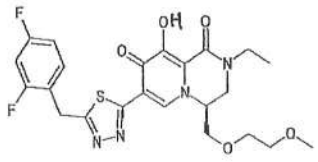
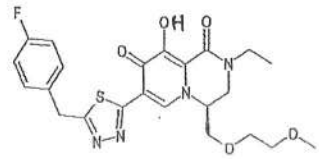
[0450]

[Table 1-34]

No.	structural formula	salt	^{1}H-NMR
123		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (s, 1H), 8.82 (s, 1H), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.93–4.86 (m, 1H), 4.47 (s, 2H), 4.19 (dd, 1H, J = 13.7, 4.2 Hz), 3.82 (dd, 1H, J = 10.4, 5.6 Hz), 3.78–3.70 (m, 2H), 3.58–3.47 (m, 2H), 3.42 (d, 1H, J = 13.4 Hz), 3.35–3.31 (m, 2H), 3.23 (d, 1H, J = 13.4 Hz), 3.11 (s, 3H), 0.98 (s, 9H).
124		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.80 (s, 1H), 7.57–7.50 (m, 1H), 7.32–7.24 (m, 1H), 7.14–7.07 (m, 1H), 4.92–4.85 (m, 1H), 4.48 (s, 2H), 4.18 (dd, 1H, J = 13.7, 4.2 Hz), 3.81 (dd, 1H, J = 10.6, 5.7 Hz), 3.76–3.69 (m, 2H), 3.56–3.46 (m, 2H), 3.41 (d, 1H, J = 13.4 Hz), 3.34–3.30 (m, 2H), 3.22 (d, 1H, J = 13.4 Hz), 3.09 (s, 3H), 0.97 (s, 9H).
125		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.79 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.96–4.88 (m, 1H), 4.49 (s, 2H), 4.07 (dd, 1H, J = 13.6, 4.3 Hz), 3.79–3.59 (m, 4H), 3.57–3.45 (m, 2H), 3.45–3.36 (m, 1H), 3.33 (t, 2H, J = 4.6 Hz), 3.10 (s, 3H), 1.15 (t, 3H, J = 7.2 Hz).

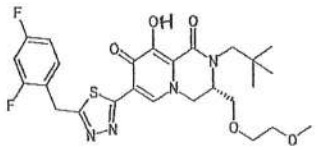
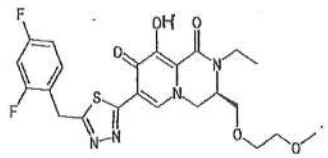
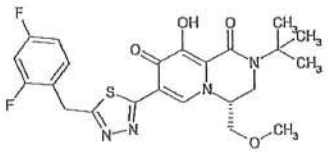
[0451]

[Table 1-35]

No.	structural formula	salt	^{1}H-NMR
126		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.47 (br s, 1H), 8.83 (s, 1H), 7.56–7.49 (m, 1H), 7.32–7.24 (m, 1H), 7.14–7.07 (m, 1H), 4.66 (dd, 1H, J = 13.4, 1.6 Hz), 4.48 (s, 2H), 4.44 (dd, 1H, J = 13.4, 4.2 Hz), 4.25–4.20 (m, 1H), 3.68 (dd, 1H, J = 14.0, 7.0 Hz), 3.57 (dd, 1H, J = 10.2, 4.6 Hz), 3.50 (dd, 1H, J = 10.2, 6.5 Hz), 3.20 (dd, 1H, J = 14.0, 7.0 Hz), 3.20 (s, 3H), 1.20–1.09 (m, 1H), 0.58–0.46 (m, 2H), 0.43–0.35 (m, 1H), 0.35–0.27 (m, 1H).
127		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.78 (br s, 1H), 8.79 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.96–4.88 (m, 1H), 4.49 (s, 2H), 4.07 (dd, 1H, J = 13.6, 4.3 Hz), 3.79–3.59 (m, 4H), 3.57–3.45 (m, 2H), 3.45–3.36 (m, 1H), 3.33 (t, 2H, J = 4.6 Hz), 3.10 (s, 3H), 1.15 (t, 3H, J = 7.2 Hz).
128		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.80 (s, 1H), 7.44–7.39 (m, 2H), 7.22–7.15 (m, 2H), 4.95–4.88 (m, 1H), 4.47 (s, 2H), 4.07 (dd, 1H, J = 13.6, 4.3 Hz), 3.78–3.60 (m, 4H), 3.57–3.46 (m, 2H), 3.43–3.37 (m, 1H), 3.33 (t, 2H, J = 4.6 Hz), 3.10 (s, 3H), 1.15 (t, 3H, J = 7.2 Hz).

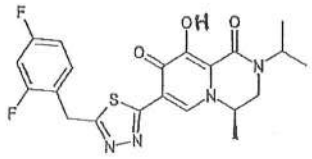
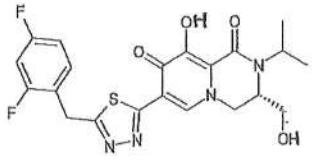
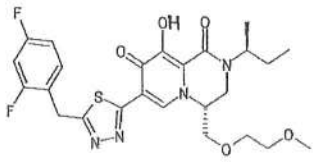
[0452]

[Table 1-36]

No.	structural formula	salt	^{1}H-NMR
129		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.67 (s, 1H), 8.83 (s, 1H), 7.59–7.49 (m, 1H), 7.34–7.25 (m, 1H), 7.16–7.07 (m, 1H), 4.70–4.55 (m, 2H), 4.49 (s, 2H), 4.03–3.97 (br m, 1H), 3.95 (d, 1H, J = 13.4 Hz), 3.66–3.59 (m, 2H), 3.47–3.41 (m, 2H), 3.27–3.22 (m, 2H), 3.07 (s, 3H), 2.85 (d, 1H, J = 13.4 Hz), 0.98 (s, 9H).
130		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.50 (s, 1H), 8.80 (s, 1H), 7.59–7.49 (m, 1H), 7.34–7.25 (m, 1H), 7.15–7.07 (m, 1H), 4.68–4.59 (m, 1H), 4.48 (s, 2H), 4.43 (dd, 1H, J = 13.4, 4.2 Hz), 4.17–4.09 (m, 1H), 3.86 (td, 1H, J = 13.9, 7.0 Hz), 3.67–3.56 (m, 2H), 3.52–3.41 (m, 2H), 3.34–3.22 (m, 3H), 3.09 (s, 3H), 1.20 (t, 3H, J = 7.0 Hz).
131		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.97–12.84 (br m, 1H), 8.76 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.92–4.85 (br m, 1H), 4.48 (s, 2H), 3.98–3.84 (m, 2H), 3.67 (dd, 1H, J = 10.1, 5.6 Hz), 3.59 (dd, 1H, J = 10.1, 7.7 Hz), 3.28 (s, 3H), 1.48 (s, 9H).

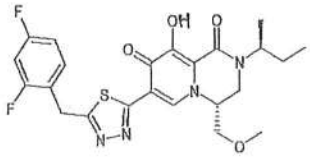
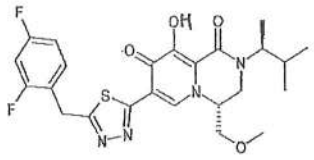
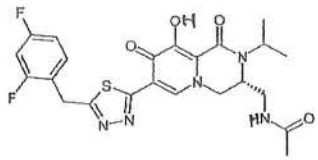
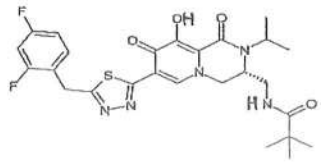
[0453]

[Table 1-37]

No.	structural formula	salt	^{1}H-NMR
132		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.79 (br s, 1H), 8.90 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.97–4.88 (m, 1H), 4.84–4.74 (m, 1H), 4.49 (s, 2H), 3.81 (dd, 1H, J = 13.5, 3.7 Hz), 3.63 (dd, 1H, J = 13.5, 2.2 Hz), 1.39 (d, 3H, J = 6.6 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz).
133		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.48 (s, 1H), 8.80 (s, 1H), 7.57–7.50 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.67 (d, 1H, J = 13.1 Hz), 4.51 (sep, 1H, J = 6.8 Hz), 4.49 (s, 2H), 4.34 (dd, 1H, J = 13.1, 3.7 Hz), 4.00–3.93 (m, 1H), 3.57 (dd, 1H, J = 11.4, 3.7 Hz), 3.37 (dd, 1H, J = 11.4, 8.3 Hz), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).
134		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.88 (br s, 1H), 8.83–8.80 (m, 1H), 7.59–7.50 (m, 1H), 7.33–7.24 (m, 1H), 7.16–7.08 (m, 1H), 5.01–4.90 (br m, 1H), 4.60–4.50 (m, 1H), 4.49 (s, 2H), 3.87–3.63 (m, 4H), 3.57–3.46 (m, 2H), 3.35–3.30 (m, 2H), 3.12–3.10 (m, 3H), 1.59–1.48 (m, 2H), 1.15 (d, 3H, J = 6.7 Hz), 0.91–0.78 (m, 3H).

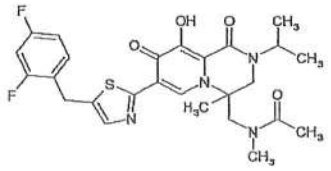
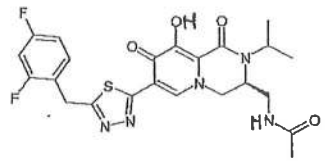
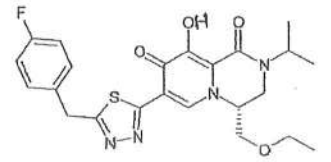
[0454]

[Table 1-38]

No.	structural formula	salt	^{1}H-NMR
135		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.89 (br s, 1H), 8.81 (s, 1H), 7.59–7.50 (m, 1H), 7.34–7.25 (m, 1H), 7.16–7.06 (m, 1H), 5.03–4.92 (br m, 1H), 4.59–4.50 (m, 1H), 4.49 (s, 2H), 3.73–3.54 (m, 4H), 3.26–3.23 (m, 3H), 1.61–1.45 (m, 2H), 1.15 (d, 3H, J = 6.7 Hz), 0.91–0.80 (m, 3H),
136		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.96 (br s, 1H), 8.82 (s, 1H), 7.59–7.49 (m, 1H), 7.35–7.24 (m, 1H), 7.17–7.06 (m, 1H), 5.04–4.91 (m, 1H), 4.49 (s, 2H), 4.30–3.57 (m, 5H), 3.27–3.22 (m, 3H), 1.87–1.69 (m, 1H), 1.17 (d, 3H, J = 6.8 Hz), 0.97–0.79 (m, 6H).
137		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.71 (s, 1H), 8.23–8.17 (m, 1H), 7.58–7.50 (m, 1H), 7.33–7.26 (m, 1H), 7.15–7.08 (m, 1H), 4.58 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.43 (dd, 1H, J = 13.0, 1.3 Hz), 4.31 (dd, 1H, J = 13.0, 3.0 Hz), 3.97–3.91 (m, 1H), 3.45–3.36 (m, 1H), 2.97–2.86 (m, 1H), 1.80 (s, 3H), 1.34 (d, 3H, J = 6.7 Hz), 1.27 (d, 3H, J = 6.7 Hz).
138		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.49 (br s, 1H), 8.72 (s, 1H), 7.88–7.83 (m, 1H), 7.57–7.50 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.57 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.38–4.28 (m, 2H), 3.99–3.92 (m, 1H), 3.38–3.29 (m, 1H), 3.04–2.95 (m, 1H), 1.38 (d, 3H, J = 6.7 Hz), 1.29 (d, 3H, J = 6.7 Hz), 1.08 (s, 9H).

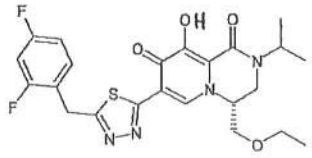
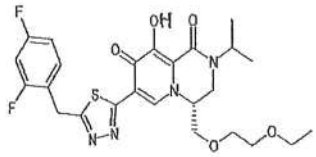
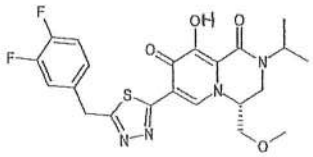
[0455]

[Table 1-39]

No.	structural formula	salt	^{1}H-NMR
139		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.18 (br s, 1H), 8.47 (s, 1H), 7.67 (s, 1H), 7.46 (td, 1H, J = 8.8, 6.6 Hz), 7.25 (ddd, 1H, J = 10.4, 9.3, 2.6 Hz), 7.08 (tdd, 1H, J = 8.8, 2.6, 0.9 Hz), 4.79 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 3.79 (d, 1H, J = 13.9 Hz), 3.74 (d, 1H, J = 14.6 Hz), 3.68 (d, 1H, J = 13.9 Hz), 3.57 (d, 1H, J = 14.6 Hz), 2.75 (s, 3H), 1.81 (s, 3H), 1.67 (s, 3H), 1.22 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).
140		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 8.71 (s, 1H), 8.22–8.17 (m, 1H), 7.57–7.50 (m, 1H), 7.33–7.26 (m, 1H), 7.15–7.08 (m, 1H), 4.58 (sep, 1H, J = 6.8 Hz), 4.49 (s, 2H), 4.43 (d, 1H, J = 13.0 Hz), 4.30 (dd, 1H, J = 13.0, 3.0 Hz), 3.98–3.91 (m, 1H), 2.96–2.86 (m, 1H), 2.56–2.50 (m, 1H), 1.80 (s, 3H), 1.34 (d, 3H, J = 6.8 Hz), 1.27 (d, 3H, J = 6.8 Hz).
141		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (s, 1H), 8.82 (s, 1H), 7.45–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.99–4.91 (m, 1H), 4.77 (sep, 1H, J = 6.8 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.8, 4.1 Hz), 3.75 (dd, 1H, J = 13.8, 1.7 Hz), 3.66 (dd, 1H, J = 10.4, 6.0 Hz), 3.59 (dd, 1H, J = 10.4, 7.5 Hz), 3.50–3.34 (m, 2H), 1.17 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz), 1.02 (t, 3H, J = 7.1 Hz).

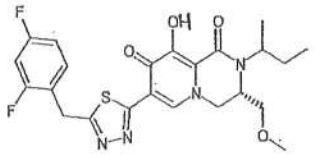
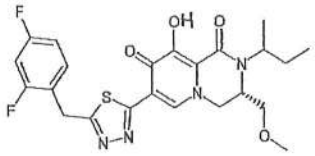
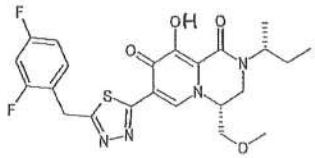
[0456]

[Table 1-40]

No.	structural formula	salt	^{1}H-NMR
142		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.81 (s, 1H), 7.58–7.51 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.07 (m, 1H), 4.98–4.91 (m, 1H), 4.77 (sep, 1H, J = 6.8 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.7, 4.0 Hz), 3.78–3.73 (m, 1H), 3.69–3.56 (m, 2H), 3.50–3.34 (m, 2H), 1.17 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz), 1.02 (t, 3H, J = 7.1 Hz).
143		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.80 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.99–4.92 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 3.84 (dd, 1H, J = 13.8, 4.1 Hz), 3.79–3.68 (m, 2H), 3.65 (dd, 1H, J = 10.4, 7.9 Hz), 3.56–3.44 (m, 2H), 3.38–3.34 (m, 2H), 3.30–3.22 (m, 2H), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz), 0.91 (t, 3H, J = 7.0 Hz).
144		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.81 (s, 1H), 7.52–7.38 (m, 2H), 7.26–7.21 (m, 1H), 5.00–4.94 (m, 1H), 4.77 (sep, 1H, J = 6.9 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.7, 4.0 Hz), 3.75 (dd, 1H, J = 13.7, 1.2 Hz), 3.66–3.54 (m, 2H), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.9 Hz), 1.16 (d, 3H, J = 6.9 Hz).

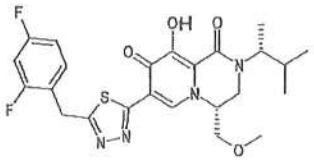
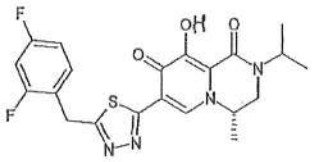
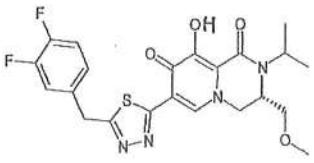
[0457]

[Table 1-41]

No.	structural formula	salt	^{1}H-NMR
145		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.45 (br s, 1H), 8.85 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.71–4.65 (m, 1H), 4.49 (s, 2H), 4.38–4.27 (m, 2H), 4.17–4.11 (m, 1H), 3.50 (dd, 1H, J = 10.5, 4.1 Hz), 3.39 (dd, 1H, J = 10.5, 7.7 Hz), 3.20 (s, 3H), 1.78–1.59 (m, 2H), 1.25 (d, 3H, J = 6.8 Hz), 0.86 (t, 3H, J = 7.4 Hz).
146		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.83 (s, 1H), 7.57–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.65 (dd, 1H, J = 13.5, 1.1 Hz), 4.49 (s, 2H), 4.38 (dd, 1H, J = 13.5, 4.1 Hz), 4.15–4.03 (m, 2H), 3.50 (dd, 1H, J = 10.1, 4.2 Hz), 3.42 (dd, 1H, J = 10.1, 7.1 Hz), 3.20 (s, 3H), 1.83–1.73 (m, 1H), 1.63–1.53 (m, 1H), 1.33 (d, 3H, J = 6.8 Hz), 0.91 (t, 3H, J = 7.4 Hz).
147		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.81 (s, 1H), 7.59–7.49 (m, 1H), 7.33–7.25 (m, 1H), 7.16–7.08 (m, 1H), 5.05–4.86 (br m, 1H), 4.60–4.50 (m, 1H), 4.49 (s, 2H), 3.87–3.56 (m, 4H), 3.25–3.25 (m, 3H), 1.54–1.50 (m, 2H), 1.15 (d, 3H, J = 6.5 Hz), 0.91–0.80 (m, 3H).

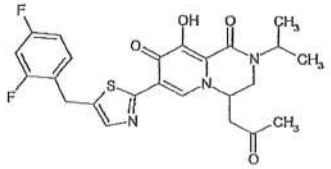
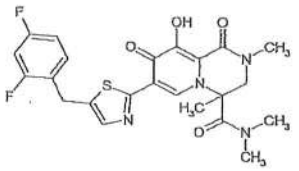
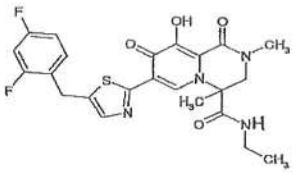
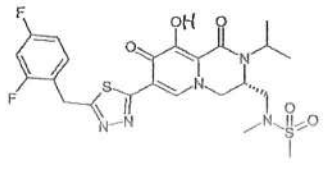
[0458]

[Table 1-42]

No.	structural formula	salt	^{1}H-NMR
148		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.87 (br s, 1H), 8.81 (s, 1H), 7.58–7.52 (m, 1H), 7.32–7.27 (m, 1H), 7.16–7.07 (m, 1H), 5.05–4.90 (m, 1H), 4.49 (s, 2H), 4.32–4.20 (m, 1H), 3.90–3.57 (m, 4H), 3.26–3.24 (m, 3H), 1.87–1.69 (m, 1H), 1.19–1.10 (m, 3H), 0.97–0.79 (m, 6H).
149		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.90 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.97–4.88 (m, 1H), 4.84–4.74 (m, 1H), 4.49 (s, 2H), 3.81 (dd, 1H, J = 13.5, 3.7 Hz), 3.63 (dd, 1H, J = 13.5, 2.2 Hz), 1.39 (d, 3H, J = 6.6 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.16 (d, 3H, J = 6.8 Hz).
150		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.44 (br s, 1H), 8.85 (s, 1H), 7.53–7.37 (m, 2H), 7.26–7.19 (m, 1H), 4.66 (dd, 1H, J = 13.5, 1.5 Hz), 4.51–4.43 (m, 1H), 4.49 (s, 2H), 4.38–4.32 (m, 1H), 4.23–4.17 (m, 1H), 3.49 (dd, 1H, J = 10.4, 4.4 Hz), 3.39 (dd, 1H, J = 10.4, 7.5 Hz), 3.22 (s, 3H), 1.30 (d, 3H, J = 6.6 Hz), 1.29 (d, 3H, J = 6.8 Hz).

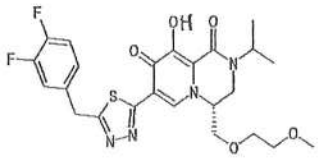
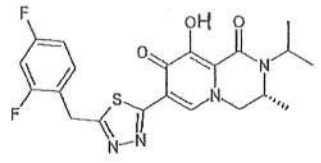
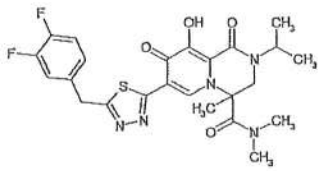
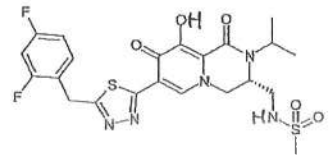
[0459]

[Table 1-43]

No.	structural formula	salt	^{1}H-NMR
151		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.86-12.34 (m, 1H), 8.68 (s, 1H), 7.66 (s, 1H), 7.49-7.39 (m, 1H), 7.29-7.20 (m, 1H), 7.11-7.02 (m, 1H), 5.12-5.03 (m, 1H), 4.84-4.70 (m, 1H), 4.21 (s, 2H), 3.82-3.55 (m, 2H), 3.15-2.96 (m, 2H), 2.08 (s, 3H), 1.17-1.09 (m, 6H).
152		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.43 (s, 1H), 7.68 (s, 1H), 7.50-7.41 (m, 1H), 7.29-7.20 (m, 1H), 7.11-7.03 (m, 1H), 4.24-4.16 (m, 1H), 4.22 (s, 2H), 3.91 (d, 1H, J = 13.9 Hz), 3.07 (s, 3H), 2.89 (s, 6H), 1.92 (s, 3H).
153		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.64 (br s, 1H), 8.53 (s, 1H), 8.34-8.23 (m, 1H), 7.68 (s, 1H), 7.50-7.40 (m, 1H), 7.30-7.20 (m, 1H), 7.13-7.02 (m, 1H), 4.23 (s, 2H), 4.12 (d, 1H, J = 14.1 Hz), 4.01 (d, 1H, J = 14.1 Hz), 3.17-2.97 (m, 2H), 3.03 (s, 3H), 1.87 (s, 3H), 0.99 (t, 3H, J = 7.4 Hz).
154		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.32 (s, 1H), 8.79 (s, 1H), 7.58-7.50 (m, 1H), 7.32-7.25 (m, 1H), 7.15-7.08 (m, 1H), 4.60 (d, 1H, J = 13.0 Hz), 4.55 (sep, 1H, J = 6.8 Hz), 4.48 (s, 2H), 4.35 (dd, 1H, J = 13.0, 3.0 Hz), 4.27-4.20 (m, 1H), 3.26 (dd, 1H, J = 13.7, 10.5 Hz), 2.99 (dd, 1H, J = 13.7, 3.0 Hz), 2.87 (s, 3H), 2.84 (s, 3H), 1.30 (d, 6H, J = 6.8 Hz).

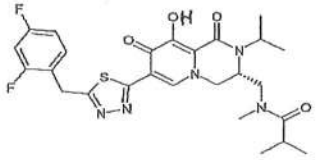
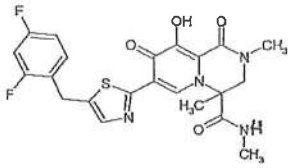
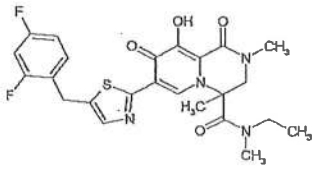
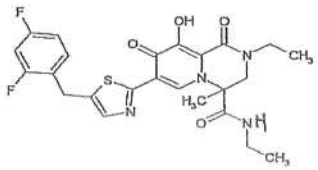
[0460]

[Table 1-44]

No.	structural formula	salt	^{1}H-NMR
155		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.83 (br s, 1H), 8.82 (s, 1H), 7.52–7.37 (m, 2H), 7.27–7.20 (m, 1H), 4.99–4.91 (m, 1H), 4.77 (sep, 1H, J = 6.9 Hz), 4.49 (s, 2H), 3.84 (dd, 1H, J = 13.7, 4.0 Hz), 3.79–3.69 (m, 2H), 3.64 (dd, 1H, J = 10.5, 7.7 Hz), 3.58–3.45 (m, 2H), 3.34 (t, 2H, J = 4.6 Hz), 3.11 (s, 3H), 1.17 (d, 3H, J = 6.9 Hz), 1.16 (d, 3H, J = 6.9 Hz).
156		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.84 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.62–4.53 (m, 1H), 4.51–4.45 (m, 3H), 4.32 (dd, 1H, J = 13.1, 3.4 Hz), 4.26–4.18 (m, 1H), 1.27 (d, 3H, J = 6.9 Hz), 1.26 (d, 3H, J = 6.9 Hz), 1.21 (d, 3H, J = 6.4 Hz).
157		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.96 (s, 1H), 8.56 (s, 1H), 7.53–7.19 (m, 3H), 4.80–4.66 (m, 1H), 4.50 (s, 2H), 4.15 (d, 1H, J = 14.3 Hz), 3.82 (d, 1H, J = 14.3 Hz), 3.09–2.83 (m, 6H), 2.04 (s, 3H), 1.18 (d, 3H, J = 7.1 Hz), 1.11 (d, 3H, J = 7.1 Hz).
158		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.35 (s, 1H), 8.75 (s, 1H), 7.57–7.49 (m, 2H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.61–4.53 (m, 2H), 4.49 (s, 2H), 4.40–4.33 (m, 1H), 4.00–3.93 (m, 1H), 3.21–3.12 (m, 1H), 3.02–2.92 (m, 1H), 2.90 (s, 3H), 1.30 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).

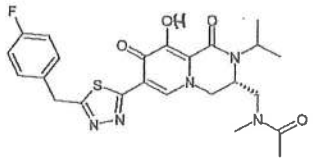
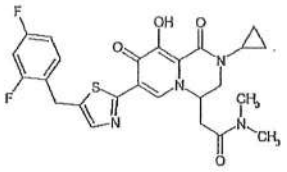
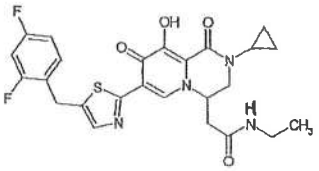
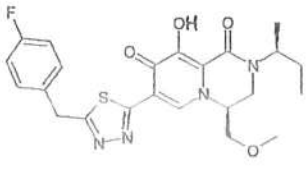
[0461]

[Table 1-45]

No.	structural formula	salt	^{1}H-NMR
159		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.39 (br s, 1H), 8.83 (s, 1H), 7.58–7.49 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.56 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.42–4.28 (m, 2H), 4.26–4.18 (m, 1H), 3.41–3.36 (m, 2H), 3.04 (s, 3H), 2.83 (t, 1H, J = 6.7 Hz), 1.34 (d, 3H, J = 6.7 Hz), 1.29 (d, 3H, J = 6.7 Hz), 1.00 (d, 3H, J = 6.7 Hz), 0.99 (d, 3H, J = 6.7 Hz).
160		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.67 (br s, 1H), 8.53 (s, 1H), 8.12–8.02 (m, 1H), 7.67 (s, 1H), 7.49–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.02 (m, 1H), 4.22 (s, 2H), 4.07 (d, 1H, J = 14.1 Hz), 3.99 (d, 1H, J = 14.1 Hz), 3.03 (s, 3H), 2.60 (d, 3H, J = 4.6 Hz), 1.86 (s, 3H).
161		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (br s, 1H), 8.41 (s, 1H), 7.66 (s, 1H), 7.50–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.03 (m, 1H), 4.22 (s, 2H), 4.17 (d, 1H, J = 13.9 Hz), 3.91 (d, 1H, J = 13.9 Hz), 3.46–3.17 (m, 2H), 3.06 (s, 3H), 2.84 (s, 3H), 1.90 (s, 3H), 0.99 (t, 3H, J = 7.4 Hz).
162		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.52 (s, 1H), 8.31–8.22 (m, 1H), 7.67 (s, 1H), 7.50–7.39 (m, 1H), 7.31–7.19 (m, 1H), 7.13–7.03 (m, 1H), 4.22 (s, 2H), 4.14 (d, 1H, J = 13.7 Hz), 3.99 (d, 1H, J = 13.7 Hz), 3.66–3.28 (m, 2H), 3.15–3.00 (m, 2H), 1.89 (s, 3H), 1.11 (t, 3H, J = 7.4 Hz), 0.99 (t, 3H, J = 7.4 Hz).

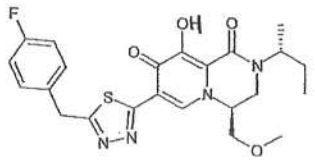
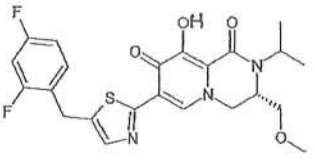
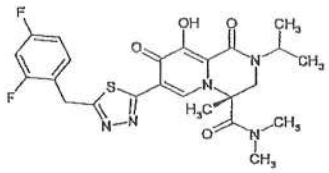
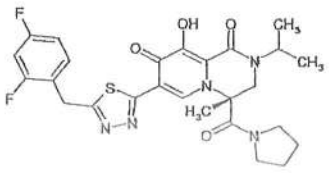
[0462]

[Table 1-46]

No.	structural formula	salt	^{1}H-NMR
163		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.34 (br s, 1H), 8.78 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.55 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 4.43 (d, 1H, J = 12.4 Hz), 4.38–4.27 (m, 1H), 4.25–4.17 (m, 1H), 3.44 (dd, 1H, J = 13.3, 10.0 Hz), 3.34–3.28 (m, 1H), 3.00 (s, 3H), 1.99 (s, 3H), 1.33 (d, 3H, J = 6.7 Hz), 1.29 (d, 3H, J = 6.7 Hz).
164		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.71 (s, 1H), 7.66 (s, 1H), 7.49–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.03 (m, 1H), 5.06–4.95 (m, 1H), 4.21 (s, 2H), 4.04 (dd, 1H, J = 13.4, 3.5 Hz), 3.68–3.60 (m, 1H), 2.97–2.88 (m, 1H), 2.88–2.82 (m, 2H), 2.87 (s, 3H), 2.79 (s, 3H), 0.96–0.83 (m, 2H), 0.83–0.72 (m, 1H), 0.67–0.55 (m, 1H).
165		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.52 (s, 1H), 7.99 (t, 1H, J = 4.9 Hz), 7.65 (s, 1H), 7.49–7.40 (m, 1H), 7.29–7.20 (m, 1H), 7.12–7.03 (m, 1H), 5.00–4.89 (m, 1H), 4.21 (s, 2H), 4.03 (dd, 1H, J = 13.9, 3.9 Hz), 3.58–3.50 (m, 1H), 3.03–2.83 (m, 3H), 2.56 (d, 2H, J = 7.4 Hz), 1.01–0.71 (m, 4H), 0.80 (t, 3H, J = 7.2 Hz).
166		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.81 (s, 1H), 7.47–7.36 (m, 2H), 7.23–7.12 (m, 2H), 5.04–4.91 (m, 1H), 4.60–4.49 (m, 1H), 4.47 (s, 2H), 3.88–3.54 (m, 4H), 3.27–3.23 (m, 3H), 1.61–1.46 (m, 2H), 1.15 (d, 3H, J = 6.4 Hz), 0.91–0.80 (m, 3H).

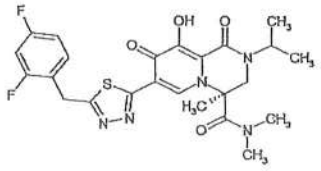
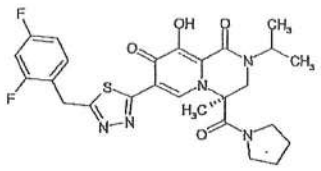
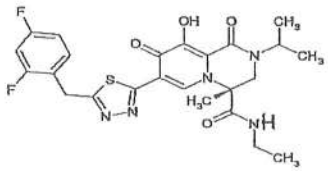
[0463]

[Table 1-47]

No.	structural formula	salt	^{1}H-NMR
167		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.81 (s, 1H), 7.46–7.38 (m, 2H), 7.23–7.14 (m, 2H), 5.02–4.92 (m, 1H), 4.60–4.49 (m, 1H), 4.47 (s, 2H), 3.89–3.54 (m, 4H), 3.27–3.23 (m, 3H), 1.59–1.47 (m, 2H), 1.15 (d, 3H, J = 6.4 Hz), 0.91–0.80 (m, 3H).
168		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.66 (s, 1H), 7.65 (s, 1H), 7.49–7.40 (m, 1H), 7.30–7.20 (m, 1H), 7.12–7.02 (m, 1H), 4.64–4.56 (m, 1H), 4.47 (sep, 1H, J = 6.7 Hz), 4.33 (dd, 1H, J = 13.3, 3.6 Hz), 4.24–4.14 (m, 3H), 3.48 (dd, 1H, J = 10.2, 4.2 Hz), 3.36 (dd, 1H, J = 10.2, 7.7 Hz), 3.21 (s, 3H), 1.29 (d, 3H, J = 6.7 Hz), 1.28 (d, 3H, J = 6.7 Hz).
169		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.96 (br s, 1H), 8.55 (s, 1H), 7.54 (td, 1H, J = 8.6, 6.6 Hz), 7.29 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.11 (tdd, 1H, J = 8.6, 2.6, 0.9 Hz), 4.73 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.15 (d, 1H, J = 14.4 Hz), 3.82 (d, 1H, J = 14.4 Hz), 2.95 (br s, 6H), 2.03 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).
170		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.91 (br s, 1H), 8.64 (s, 1H), 7.54 (td, 1H, J = 8.8, 6.6 Hz), 7.29 (ddd, 1H, J = 10.4, 9.5, 2.8 Hz), 7.12 (tdd, 1H, J = 8.8, 2.8, 1.2 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.14 (d, 1H, J = 14.1 Hz), 3.77 (d, 1H, J = 14.1 Hz), 3.71–3.50 (br m, 2H), 3.36–3.24 (br m, 1H), 3.21–3.08 (br m, 1H), 2.06 (s, 3H), 1.97–1.86 (br m, 1H), 1.83–1.59 (br m, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).

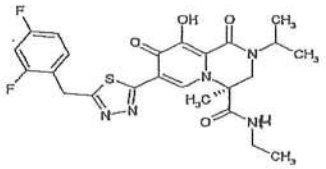
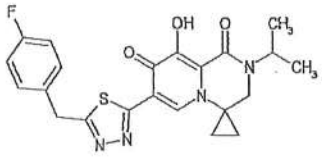
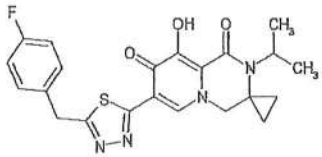
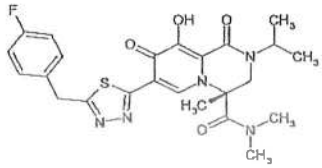
[0464]

[Table 1-48]

No.	structural formula	salt	^{1}H-NMR
171		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.96 (br s, 1H), 8.55 (s, 1H), 7.54 (td, 1H, J = 8.6, 6.6 Hz), 7.29 (ddd, 1H, J = 10.2, 9.3, 2.6 Hz), 7.11 (tdd, 1H, J = 8.6, 2.6, 0.9 Hz), 4.73 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.15 (d, 1H, J = 14.4 Hz), 3.82 (d, 1H, J = 14.4 Hz), 2.95 (br s, 6H), 2.03 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).
172		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.91 (br s, 1H), 8.64 (s, 1H), 7.54 (td, 1H, J = 8.8, 6.6 Hz), 7.29 (ddd, 1H, J = 10.4, 9.5, 2.8 Hz), 7.12 (tdd, 1H, J = 8.8, 2.8, 1.2 Hz), 4.70 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.14 (d, 1H, J = 14.1 Hz), 3.77 (d, 1H, J = 14.1 Hz), 3.71–3.50 (br m, 2H), 3.36–3.24 (br m, 1H), 3.21–3.08 (br m, 1H), 2.06 (s, 3H), 1.97–1.86 (br m, 1H), 1.83–1.59 (br m, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).
173		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.93 (br s, 1H), 8.62 (s, 1H), 8.19 (t, 1H, J = 5.2 Hz), 7.54 (td, 1H, J = 8.7, 6.6 Hz), 7.29 (ddd, 1H, J = 10.4, 9.3, 2.6 Hz), 7.12 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.71 (sep, 1H, J = 6.7 Hz), 4.50 (s, 2H), 4.11 (d, 1H, J = 13.9 Hz), 3.80 (d, 1H, J = 13.9 Hz), 3.18–2.98 (m, 2H), 1.96 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.12 (d, 3H, J = 6.7 Hz), 1.00 (t, 3H, J = 7.2 Hz).

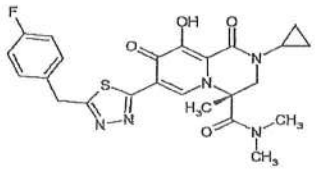
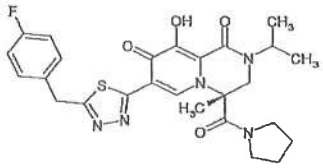
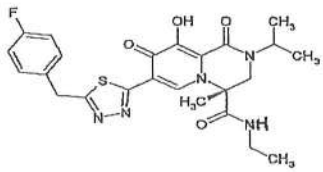
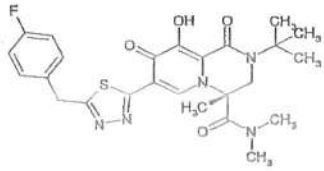
[0465]

[Table 1-49]

No.	structural formula	salt	^{1}H-NMR
174		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.93 (br s, 1H), 8.62 (s, 1H), 8.19 (t, 1H, J = 5.2 Hz), 7.54 (td, 1H, J = 8.7, 6.6 Hz), 7.29 (ddd, 1H, J = 10.4, 9.3, 2.6 Hz), 7.12 (tdd, 1H, J = 8.7, 2.6, 0.9 Hz), 4.71 (sep, 1H, J = 6.7 Hz), 4.50 (s, 2H), 4.11 (d, 1H, J = 13.9 Hz), 3.80 (d, 1H, J = 13.9 Hz), 3.18-2.98 (m, 2H), 1.96 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.12 (d, 3H, J = 6.7 Hz), 1.00 (t, 3H, J = 7.2 Hz).
175		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.43 (s, 1H), 7.42-7.37 (m, 2H), 7.21-7.15 (m, 2H), 4.76 (sep, 1H, J = 6.9 Hz), 4.46 (s, 2H), 3.66 (s, 2H), 1.66-1.61 (m, 2H), 1.13-1.18 (m, 2H), 1.16 (d, 6H, J = 6.9 Hz).
176		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.67 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.47 (s, 2H), 4.31 (s, 2H), 4.15 (sep, 1H, J = 6.9 Hz), 1.35-1.29 (m, 2H), 1.32 (d, 6H, J = 6.9 Hz), 1.07-1.02 (m, 2H).
177		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.95 (s, 1H), 8.55 (s, 1H), 7.44-7.36 (m, 2H), 7.21-7.15 (m, 2H), 4.73 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.15 (d, 1H, J = 14.1 Hz), 3.82 (d, 1H, J = 14.1 Hz), 3.07-2.81 (br m, 6H), 2.04 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).

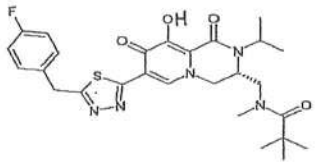
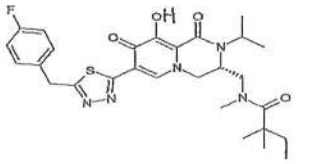
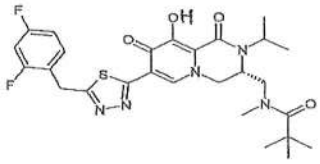
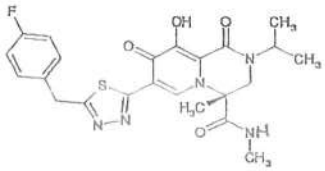
[0466]

[Table 1-50]

No.	structural formula	salt	^{1}H-NMR
178		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.87 (s, 1H), 8.55 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.48 (s, 2H), 4.15 (d, 1H, J = 13.9 Hz), 3.85 (d, 1H, J = 13.9 Hz), 2.95-2.83 (m, 1H), 2.89 (s, 6H), 1.97 (s, 3H), 0.95-0.80 (m, 2H), 0.76-0.62 (m, 2H).
179		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.90 (s, 1H), 8.65 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.15 (m, 2H), 4.70 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.14 (d, 1H, J = 13.9 Hz), 3.77 (d, 1H, J = 13.9 Hz), 3.72-3.62 (br m, 1H), 3.36-3.23 (br m, 2H), 3.20-3.09 (br m, 1H), 2.06 (s, 3H), 1.98-1.84 (br m, 1H), 1.83-1.59 (br m, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).
180		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.92 (s, 1H), 8.62 (s, 1H), 8.17 (t, 1H, J = 5.2 Hz), 7.44-7.37 (m, 2H), 7.23-7.15 (m, 2H), 4.71 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.10 (d, 1H, J = 13.9 Hz), 3.80 (d, 1H, J = 13.9 Hz), 3.18-2.99 (m, 2H), 1.96 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.12 (d, 3H, J = 6.7 Hz), 1.01 (t, 3H, J = 7.2 Hz).
181		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.98 (br s, 1H), 8.59 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.15 (m, 2H), 4.47 (s, 2H), 4.32 (d, 1H, J = 14.4 Hz), 3.82 (d, 1H, J = 14.4 Hz), 2.90 (s, 6H), 2.03 (s, 3H), 1.45 (s, 9H).

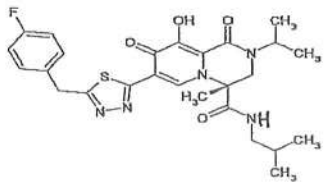
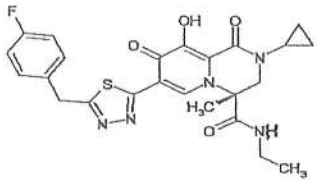
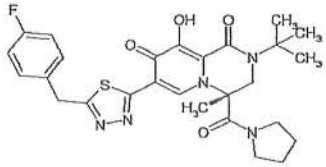
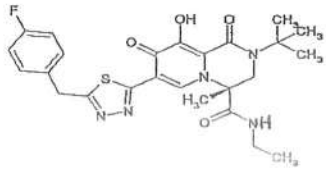
[0467]

[Table 1-51]

No.	structural formula	salt	^{1}H-NMR
182		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.91 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.55 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 4.43–4.29 (m, 2H), 4.26–4.19 (m, 1H), 3.47 (dd, 1H, J = 13.3, 4.0 Hz), 3.28 (dd, 1H, J = 13.3, 10.0 Hz), 3.12 (s, 3H), 1.35 (d, 3H, J = 6.7 Hz), 1.30 (d, 3H, J = 6.7 Hz), 1.20 (s, 9H).
183		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.92 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.55 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 4.38–4.33 (m, 2H), 4.22–4.16 (m, 1H), 3.47 (dd, 1H, J = 13.5, 3.5 Hz), 3.28 (dd, 1H, J = 13.5, 10.0 Hz), 3.12 (s, 3H), 1.65–1.57 (m, 2H), 1.35 (d, 3H, J = 6.7 Hz), 1.30 (d, 3H, J = 6.7 Hz), 1.17 (s, 3H), 1.16 (s, 3H), 0.79 (t, 3H, J = 7.5 Hz).
184		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.41 (br s, 1H), 8.90 (s, 1H), 7.58–7.50 (m, 1H), 7.32–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.56 (sep, 1H, J = 6.6 Hz), 4.49 (s, 2H), 4.41–4.29 (m, 2H), 4.27–4.18 (m, 1H), 3.48–3.44 (m, 1H), 3.29 (dd, 1H, J = 13.5, 10.0 Hz), 3.12 (s, 3H), 1.35 (d, 3H, J = 6.7 Hz), 1.30 (d, 3H, J = 6.7 Hz), 1.20 (s, 9H).
185		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.90 (br s, 1H), 8.63 (s, 1H), 8.12 (q, 1H, J = 4.4 Hz), 7.45–7.37 (m, 2H), 7.23–7.15 (m, 2H), 4.70 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.08 (d, 1H, J = 13.9 Hz), 3.80 (d, 1H, J = 13.9 Hz), 2.59 (d, 3H, J = 4.4 Hz), 1.97 (s, 3H), 1.15 (d, 3H, J = 6.7 Hz), 1.09 (d, 3H, J = 6.7 Hz).

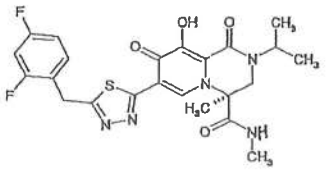
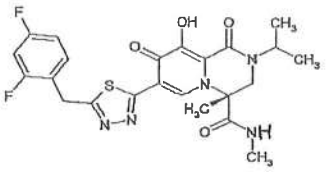
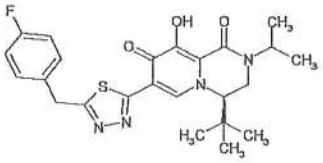
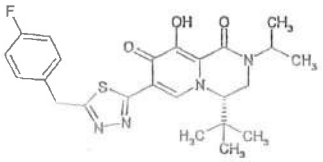
[0468]

[Table 1-52]

No.	structural formula	salt	^{1}H-NMR
186		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.93 (br s, 1H), 8.64 (s, 1H), 8.09 (t, 1H, J = 6.0 Hz), 7.43–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.69 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.14 (d, 1H, J = 13.9 Hz), 3.79 (d, 1H, J = 13.9 Hz), 3.10–3.01 (m, 1H), 2.71–2.62 (m, 1H), 1.97 (s, 3H), 1.75–1.61 (m, 1H), 1.15 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz), 0.79 (d, 6H, J = 6.7 Hz).
187		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.62 (s, 1H), 8.19 (t, 1H, J = 5.2 Hz), 7.45–7.36 (m, 2H), 7.22–7.15 (m, 2H), 4.48 (s, 2H), 4.00 (d, 1H, J = 13.7 Hz), 3.96 (d, 1H, J = 13.7 Hz), 3.11–3.02 (m, 2H), 2.88 (sep, 1H, J = 3.9 Hz), 1.92 (s, 3H), 0.98 (t, 3H, J = 7.0 Hz), 0.96–0.89 (m, 1H), 0.85–0.69 (m, 2H), 0.65–0.56 (m, 1H).
188		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.93 (br s, 1H), 8.69 (s, 1H), 7.45–7.39 (m, 2H), 7.22–7.15 (m, 2H), 4.48 (s, 2H), 4.32 (d, 1H, J = 13.9 Hz), 3.77 (d, 1H, J = 13.9 Hz), 3.44–3.23 (br m, 4H), 2.01 (s, 3H), 1.92–1.54 (br m, 4H), 1.44 (s, 9H).
189		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.98 (br s, 1H), 8.59 (s, 1H), 8.19 (t, 1H, J = 7.0 Hz), 7.44–7.37 (m, 2H), 7.23–7.15 (m, 2H), 4.48 (s, 2H), 4.23 (d, 1H, J = 13.7 Hz), 3.83 (d, 1H, J = 13.7 Hz), 3.10 (dq, 2H, J = 7.0, 7.0 Hz), 1.94 (s, 3H), 1.45 (s, 9H), 1.02 (t, 3H, J = 7.0 Hz).

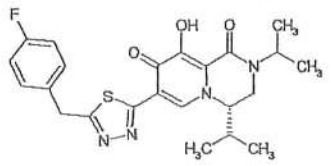
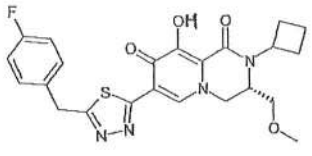
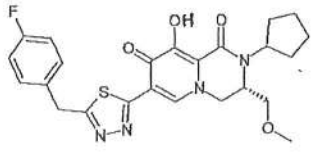
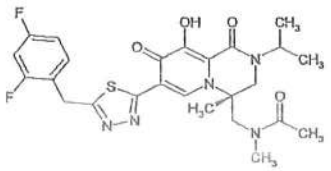
[0469]

[Table 1-53]

No.	structural formula	salt	^{1}H-NMR
190		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.90 (br s, 1H), 8.62 (s, 1H), 8.10 (q, 1H, J = 4.4 Hz), 7.53 (td, 1H, J = 8.6, 6.5 Hz), 7.28 (ddd, 1H, J = 10.2, 9.5, 2.6 Hz), 7.11 (tdd, 1H, J = 8.6, 2.6, 1.1 Hz), 4.69 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.06 (d, 1H, J = 13.9 Hz), 3.78 (d, 1H, J = 13.9 Hz), 2.58 (d, 3H, J = 4.4 Hz), 1.95 (s, 3H), 1.13 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).
191		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.90 (br s, 1H), 8.62 (s, 1H), 8.10 (q, 1H, J = 4.4 Hz), 7.53 (td, 1H, J = 8.6, 6.5 Hz), 7.28 (ddd, 1H, J = 10.2, 9.5, 2.6 Hz), 7.11 (tdd, 1H, J = 8.6, 2.6, 1.1 Hz), 4.69 (sep, 1H, J = 6.7 Hz), 4.49 (s, 2H), 4.06 (d, 1H, J = 13.9 Hz), 3.78 (d, 1H, J = 13.9 Hz), 2.58 (d, 3H, J = 4.4 Hz), 1.95 (s, 3H), 1.13 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J = 6.7 Hz).
192		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.88 (br s, 1H), 8.82 (s, 1H), 7.45–7.39 (m, 2H), 7.22–7.16 (m, 2H), 4.77 (sep, 1H, J = 6.9 Hz), 4.63–4.59 (m, 1H), 4.47 (s, 2H), 3.89–3.82 (m, 2H), 1.27 (d, 3H, J = 6.9 Hz), 1.19 (d, 3H, J = 6.9 Hz), 0.96 (s, 9H).
193		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.88 (br s, 1H), 8.82 (s, 1H), 7.45–7.39 (m, 2H), 7.22–7.16 (m, 2H), 4.77 (sep, 1H, J = 6.9 Hz), 4.63–4.59 (m, 1H), 4.47 (s, 2H), 3.89–3.83 (m, 2H), 1.28 (d, 3H, J = 6.9 Hz), 1.19 (d, 3H, J = 6.9 Hz), 0.96 (s, 9H).

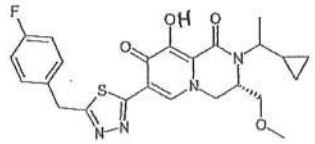
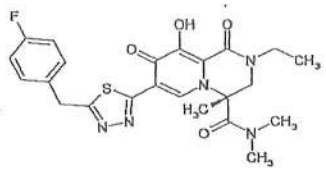
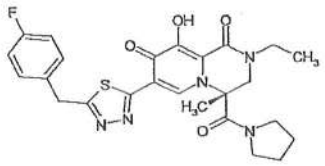
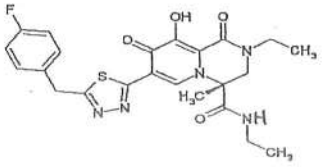
[0470]

[Table 1-54]

No.	structural formula	salt	^{1}H-NMR
194		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (br s, 1H), 8.90 (s, 1H), 7.45-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.79-4.79 (sep, 1H, J = 6.7 Hz), 4.50-4.43 (m, 1H), 4.47 (s, 2H), 3.86-3.78 (m, 2H), 2.03-1.92 (m, 1H), 1.20 (d, 3H, J = 6.7 Hz), 1.18 (d, 3H, J = 6.7 Hz), 1.04 (d, 3H, J = 6.7 Hz), 0.69 (d, 3H, J = 6.7 Hz).
195		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.49 (br s, 1H), 8.85 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.68 (dd, 1H, J = 13.5, 1.3 Hz), 4.61-4.49 (m, 1H), 4.47 (s, 2H), 4.41 (dd, 1H, J = 13.5, 4.0 Hz), 4.31-4.25 (m, 1H), 3.43 (dd, 1H, J = 10.6, 5.0 Hz), 3.39 (dd, 1H, J = 10.6, 6.8 Hz), 3.21 (s, 3H), 2.38-2.11 (m, 4H), 1.77-1.64 (m, 2H).
196		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.49 (br s, 1H), 8.85 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.15 (m, 2H), 4.65 (dd, 1H, J = 13.7, 1.5 Hz), 4.47 (s, 2H), 4.44-4.34 (m, 2H), 4.20-4.13 (m, 1H), 3.47 (dd, 1H, J = 10.4, 4.6 Hz), 3.41 (dd, 1H, J = 10.4, 7.3 Hz), 3.21 (s, 3H), 1.95-1.72 (m, 6H), 1.63-1.49 (m, 2H).
197		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.29 (br s, 1H), 8.52 (s, 1H), 7.60-7.50 (m, 1H), 7.36-7.25 (m, 1H), 7.17-7.08 (m, 1H), 4.86-4.73 (m, 1H), 4.49 (s, 2H), 3.91-3.64 (m, 4H), 2.82 (s, 3H), 1.81 (s, 3H), 1.71 (s, 3H), 1.23 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 7.0 Hz).

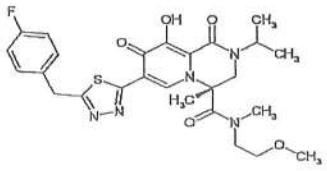
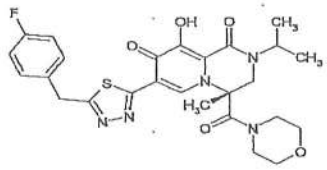
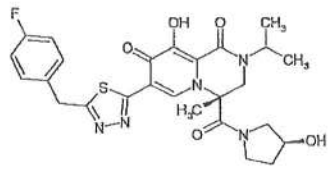
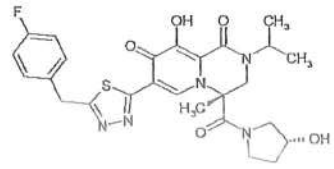
[0471]

[Table 1-55]

No.	structural formula	salt	^{1}H-NMR
198		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.88 (s, 1H), 7.45–7.37 (m, 2H), 7.23–7.15 (m, 2H), 4.70 (d, 1H, J = 13.0 Hz), 4.47 (s, 2H), 4.39–4.27 (m, 2H), 3.73–3.61 (m, 2H), 3.49–3.41 (m, 1H), 3.22 (s, 3H), 1.34 (d, 3H, J = 6.7 Hz), 1.26–1.13 (m, 1H), 0.69–0.60 (m, 1H), 0.54–0.45 (m, 1H), 0.42–0.27 (m, 2H).
199		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.87 (s, 1H), 8.56 (s, 1H), 7.45–7.37 (m, 2H), 7.23–7.15 (m, 2H), 4.48 (s, 2H), 4.21 (d, 1H, J = 13.9 Hz), 3.98 (d, 1H, J = 13.9 Hz), 3.53 (q, 2H, J = 7.0 Hz), 2.50 (s, 6H), 2.01 (s, 3H), 1.11 (t, 3H, J = 7.0 Hz).
200		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.67 (s, 1H), 7.45–7.39 (m, 2H), 7.22–7.15 (m, 2H), 4.48 (s, 2H), 4.19 (d, 1H, J = 13.9 Hz), 3.96 (d, 1H, J = 13.9 Hz), 3.59–3.25 (br m, 3H), 3.53 (dq, 1H, J = 14.0, 7.0 Hz), 3.49 (dq, 1H, J = 14.0, 7.0 Hz), 3.12–2.96 (br m, 1H), 2.01 (s, 3H), 1.96–1.48 (m, 4H), 1.09 (t, 3H, J = 7.0 Hz).
201		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.62 (s, 1H), 8.26 (t, 1H, J = 5.6 Hz), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.48 (s, 2H), 4.13 (d, 1H, J = 13.9 Hz), 4.01 (d, 1H, J = 13.9 Hz), 3.62 (dq, 1H, J = 14.2, 7.1 Hz), 3.36 (dq, 1H, J = 14.2, 7.1 Hz), 3.14–3.04 (m, 2H), 1.93 (s, 3H), 1.11 (t, 3H, J = 7.1 Hz), 1.00 (t, 3H, J = 7.1 Hz).

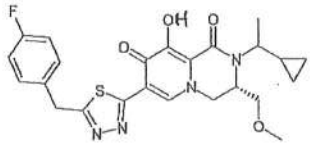
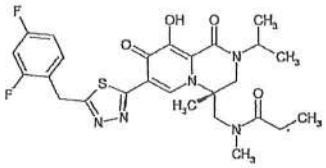
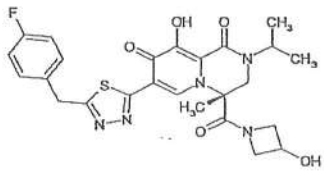
[0472]

[Table 1-56]

No.	structural formula	salt	^{1}H-NMR
202		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.00 (br s, 1H), 8.57 (s, 1H), 7.45–7.37 (m, 2H), 7.22–7.15 (m, 2H), 4.72 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.18 (d, 1H, J = 14.4 Hz), 3.81 (d, 1H, J = 14.4 Hz), 3.64 (br s, 3H), 3.42 (t, 2H, J = 5.3 Hz), 3.20 (s, 3H), 3.05–2.92 (br m, 2H), 2.02 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.13 (d, 3H, J = 6.7 Hz).
203		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.06 (br s, 1H), 8.52 (s, 1H), 7.46–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.75 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.05 (d, 1H, J = 14.4 Hz), 3.84 (d, 1H, J = 14.4 Hz), 3.62–3.48 (br m, 8H), 1.98 (s, 3H), 1.18 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
204		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.95 (br s, 1H), 8.68–8.61 (m, 1H), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.69 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.23–4.15 (br m, 1H), 4.11 (d, 1H, J = 13.9 Hz), 3.76 (d, 1H, J = 13.9 Hz), 3.69–3.59 (br m, 1H), 3.46–3.36 (br m, 2H), 3.30–2.88 (br m, 1H), 2.09–2.00 (m, 3H), 2.02–1.55 (br m, 2H), 1.21–1.06 (m, 6H).
205		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.91 (br s, 1H), 8.71–8.61 (m, 1H), 7.46–7.37 (m, 2H), 7.24–7.14 (m, 2H), 4.69 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.33–4.13 (br m, 2H), 4.08 (d, 1H, J = 13.9 Hz), 3.77 (d, 1H, J = 13.9 Hz), 3.51–3.15 (br m, 3H), 2.14–2.01 (m, 3H), 1.89–1.61 (br m, 2H), 1.21–1.02 (m, 6H).

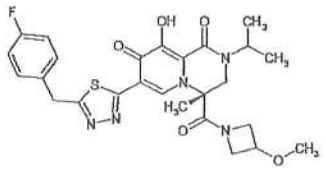
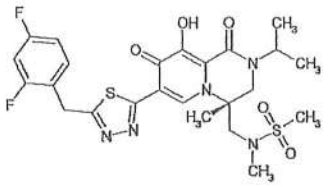
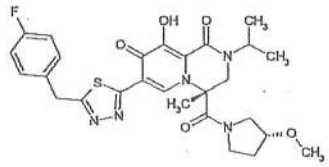
[0473]

[Table 1-57]

No.	structural formula	salt	^{1}H-NMR
206		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.87 (s, 1H), 7.44–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.72 (d, 1H, J = 12.3 Hz), 4.47 (s, 2H), 4.43–4.33 (m, 2H), 3.67–3.58 (m, 1H), 3.57–3.51 (m, 1H), 3.47–3.40 (m, 1H), 3.22 (s, 3H), 1.34 (d, 3H, J = 6.7 Hz), 1.31–1.21 (m, 1H), 0.68–0.59 (m, 1H), 0.54–0.46 (m, 1H), 0.44–0.36 (m, 1H), 0.32–0.24 (m, 1H).
207		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.31 (br s, 1H), 8.48 (s, 1H), 7.59–7.49 (m, 1H), 7.38–7.22 (m, 1H), 7.20–7.05 (m, 1H), 4.87–4.73 (m, 1H), 4.48 (s, 2H), 4.02–3.86 (m, 1H), 3.80 (d, 1H, J = 13.7 Hz), 3.71 (d, 1H, J = 13.7 Hz), 3.47–3.32 (m, 1H), 2.85 (s, 3H), 2.17–2.04 (m, 2H), 1.71 (s, 3H), 1.23 (d, 3H, J = 7.0 Hz), 1.17 (d, 3H, J = 7.0 Hz), 0.65 (t, 3H, J = 7.4 Hz).
208		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.93 (br s, 1H), 8.72 (s, 1H), 7.45–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.69 (sep, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.44–4.27 (br m, 2H), 4.11–3.82 (br m, 2H), 4.02 (d, 1H, J = 13.9 Hz), 3.72 (d, 1H, J = 13.9 Hz), 3.64–3.40 (br m, 1H), 1.99 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.12 (d, 3H, J = 6.7 Hz).

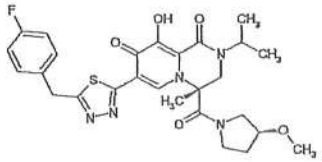
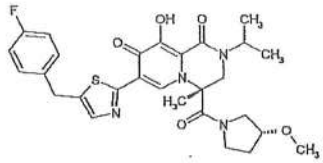
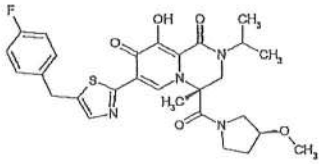
[0474]

[Table 1-58]

No.	structural formula	salt	^{1}H-NMR
209		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.89 (br s, 1H), 8.71 (s, 1H), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.70 (sep, 1H, J = 6.8 Hz), 4.48 (s, 2H), 4.22–3.90 (br m, 4H), 4.00 (d, 1H, J = 13.9 Hz), 3.74–3.57 (br m, 1H), 3.74 (d, 1H, J = 13.9 Hz), 3.14 (s, 3H), 2.00 (s, 3H), 1.19–1.09 (m, 6H).
210		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.30 (s, 1H), 8.60 (s, 1H), 7.56–7.50 (m, 1H), 7.35–7.25 (m, 1H), 7.13–7.08 (m, 1H), 4.80–4.74 (m, 1H), 4.47 (s, 2H), 3.75 (s, 2H), 3.48–3.30 (m, 2H), 2.84 (s, 3H), 2.57 (s, 3H), 1.74 (s, 3H), 1.24 (d, 3H, J=6.7 Hz), 1.15 (d, 3H, J=6.7 Hz).
211		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.91 (s, 0.5H), 12.86 (s, 0.5H), 8.68 (s, 0.5H), 8.60 (s, 0.5H), 7.42–7.38 (m, 2H), 7.20–7.15 (m, 2H), 4.72–4.65 (m, 1H), 4.47 (s, 2H), 4.16 (d, 0.5H, J = 13.7Hz), 4.08 (d, 0.5H, J = 13.7 Hz), 4.00–3.98 (m, 0.5H), 3.86–3.84 (m, 0.5H) 3.81–3.74 (m, 2H), 3.51–3.33 (m, 3H), 3.17 (s, 3H), 2.54–2.49 (m, 2H), 2.07 (s, 3H), 1.15 (d, 3H, J=6.7 Hz), 1.05 (d, 3H, J=6.7 Hz).

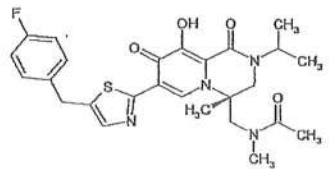
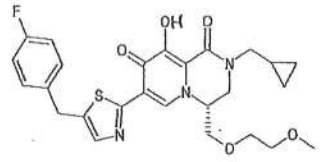
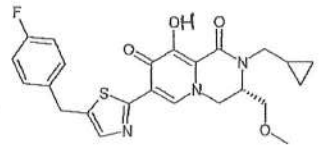
[0475]

[Table 1-59]

No.	structural formula	salt	^{1}H-NMR
212		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.94 (s, 1H), 8.66 (s, 0.5H), 8.62 (s, 0.5H), 7.42–7.38 (m, 2H), 7.20–7.15 (m, 2H), 4.70–4.65 (m, 1H), 4.47 (s, 2H), 4.11–4.06 (m, 1H), 3.93–3.90 (m, 1H), 3.87–3.84 (m, 1H), 3.81–3.75 (m, 1H) 3.69–3.65 (m, 1H), 3.62–3.45 (m, 1H), 3.17 (s, 1.5H), 3.15 (s, 1.5H), 3.10–3.06 (m, 1H), 2.07 (s, 1.5H), 2.05 (s, 1.5H), 1.99–1.96 (m, 1H), 1.79–1.76 (m, 1H), 1.16 (d, 3H, J=6.7 Hz), 1.06 (d, 3H, J=6.7 Hz).
213		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.55 (s, 0.5H), 8.48 (s, 0.5H), 7.67 (s, 1H), 7.34–7.29 (m, 2H), 7.17–7.11 (m, 2H), 4.71–4.65 (m, 1H), 4.25–4.04 (m, 1H), 4.20 (s, 2H), 3.98–3.86 (m, 0.5H), 3.85–3.84 (m, 0.5H), 3.78–3.68 (m, 2H), 3.50–3.25 (m, 2H), 3.17 (s, 1.5H), 3.15 (s, 1.5H), 2.54–2.49 (m, 1H), 2.02 (s, 3H), 1.91–1.85 (m, 1H), 1.78–1.71 (m, 1H), 1.15 (d, 3H, J = 6.7 Hz), 1.05 (d, 3H, J=6.7 Hz).
214		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.54 (s, 0.5H), 8.50 (s, 0.5H), 7.68 (s, 1H), 7.34–7.31 (m, 2H), 7.17–7.11 (m, 2H), 4.71–4.65 (m, 1H), 4.20 (s, 2H), 4.07 (dd, 1H, J=13.9, 5.3 Hz), 3.90–3.85 (m, 1H), 3.75 (dd, 1H, J=13.9, 7.4 Hz), 3.59–3.36 (m, 3H), 3.15 (s, 3H), 2.54–2.49 (m, 1H), 2.02 (s, 1.5H), 1.99 (s, 1.5H), 1.99–1.97 (m, 1H), 1.78–1.71 (m, 1H), 1.16 (d, 3H, J = 6.7 Hz), 1.08 (d, 3H, J=6.7 Hz).

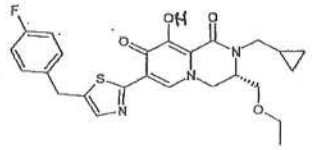
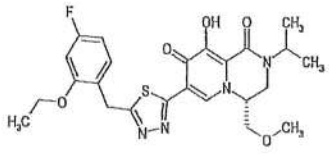
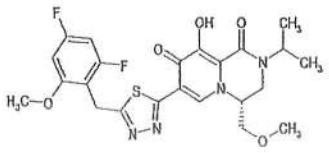
[0476]

[Table 1-60]

No.	structural formula	salt	^{1}H-NMR
215		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.20 (br s, 1H), 8.44 (s, 1H), 7.67 (s, 1H), 7.35–7.31 (m, 2H), 7.16–7.11 (m, 2H), 4.81–4.74 (m, 1H), 4.19 (s, 2H), 3.79–3.65 (m, 3H), 3.57 (d, 1H, J=14.4 Hz), 2.74 (s, 3H), 1.81 (s, 3H), 1.66 (s, 3H), 1.21 (d, 3H, J=6.7 Hz), 1.15 (d, 3H, J=6.7 Hz).
216		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.60 (br s, 1H), 8.63 (s, 1H), 7.66 (s, 1H), 7.35–7.30 (m, 2H), 7.17–7.11 (m, 2H), 4.89–4.85 (m, 1H), 4.19 (s, 2H), 4.08 (dd, 1H, J=13.7, 4.2 Hz), 3.81 (d, 1H, J=13.7 Hz), 3.57 (dd, 1H, J=10.5, 5.7 Hz), 3.66 (dd, 1H, J=10.5, 7.9 Hz), 3.56–3.39 (m, 3H), 3.33–3.27 (m, 3H), 3.10 (s, 3H), 1.10–1.04 (m, 1H), 0.55–0.46 (m, 2H), 0.36–0.26 (m, 2H).
217		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.30 (br s, 1H), 8.65 (s, 1H), 7.66 (s, 1H), 7.34–7.30 (m, 2H), 7.16–7.11 (m, 2H), 4.60 (d, 1H, J=13.2 Hz), 4.42 (dd, 1H, J=13.2, 3.9 Hz), 4.24–4.19 (m, 1H), 4.19 (s, 2H), 3.67 (dd, 1H, J=14.2, 7.0 Hz), 3.55 (dd, 1H, J=10.3, 4.8 Hz), 3.47 (dd, 1H, J=10.3, 7.0 Hz), 3.20 (s, 3H), 3.19 (dd, 1H, J=14.2, 7.4 Hz), 1.18–1.12 (m, 1H), 0.55–0.46 (m, 2H), 0.41–0.37 (m, 1H), 0.31–0.28 (m, 1H).

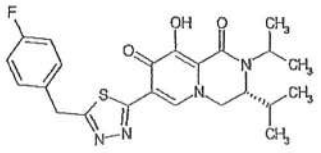
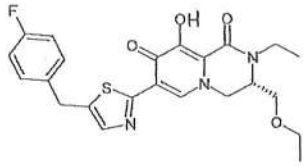
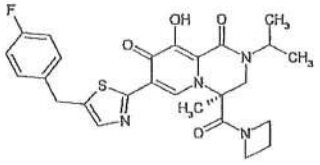
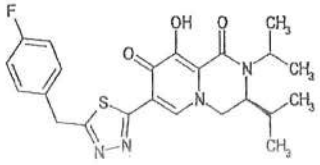
[0477]

[Table 1-61]

No.	structural formula	salt	^{1}H-NMR
218		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.30 (br s, 1H), 8.65 (s, 1H), 7.66 (s, 1H), 7.34-7.31 (m, 2H), 7.16-7.11 (m, 2H), 4.61 (d, 1H, J=13.5 Hz), 4.42 (dd, 1H, J=13.5, 4.2 Hz), 4.24-4.19 (m, 1H), 4.19 (s, 2H), 3.67 (dd, 1H, J=14.0, 7.1 Hz), 3.60 (dd, 1H, J=10.3, 4.2 Hz), 3.52 (dd, 1H, J=10.3, 6.4 Hz), 3.42-3.30 (m, 2H), 3.20 (dd, 1H, J=14.0, 7.0 Hz), 1.16-1.11 (m, 1H), 0.95 (t, 3H, J=7.0 Hz), 0.56-0.46 (m, 2H), 0.41-0.37 (m, 1H), 0.31-0.27 (m, 1H).
219		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.78 (s, 1H), 7.35 (dd, 1H, J = 8.4, 7.0 Hz), 6.93 (dd, 1H, J = 11.4, 2.6 Hz), 6.74 (td, 1H, J = 8.4, 2.6 Hz), 4.97-4.93 (m, 1H), 4.79-4.72, (m, 1H), 4.33 (s, 2H), 4.06 (q, 2H, J=7.0 Hz), 3.79-3.65 (m, 2H), 3.61 (dd, 1H, J=10.3, 5.7 Hz), 3.55 (dd, 1H, J=10.3, 7.7 Hz), 3.23 (s, 3H), 1.31 (t, 3H, J=7.0 Hz), 1.15 (d, 3H, J=2.3 Hz), 1.14 (d, 3H, J=2.3 Hz).
220		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.76 (s, 1H), 6.93-6.87 (m, 2H), 4.97-4.93 (m, 1H), 4.79-4.72 (m, 1H), 4.33 (s, 2H), 3.85 (s, 3H), 3.84-3.72 (m, 2H), 3.61 (dd, 1H, J=10.3, 5.7 Hz), 3.55 (dd, 1H, J=10.3, 7.8 Hz), 3.23 (s, 3H), 1.15 (d, 3H, J=2.3 Hz), 1.14 (d, 3H, J=2.3 Hz).

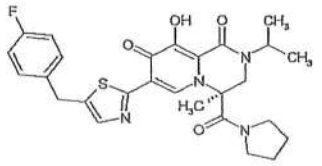
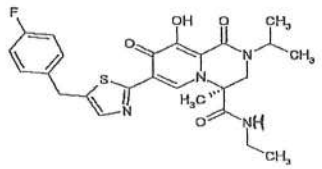
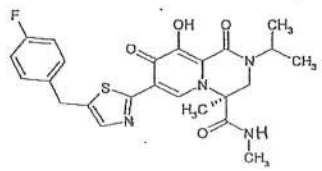
[0478]

[Table 1-62]

No.	structural formula	salt	^{1}H-NMR
221		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 9.02 (s, 1H), 7.43–7.39 (m, 2H), 7.21–7.16 (m, 2H), 4.76 (d, 1H, J=13.3 Hz), 4.47 (s, 2H), 4.30 (dd, 1H, J=13.3, 4.6 Hz), 4.21–4.14 (m, 1H), 3.83 (br t, 1H, J=4.6 Hz), 2.04–1.99 (m, 1H), 1.39 (d, 3H, J=6.9 Hz), 1.35 (d, 3H, J=6.9 Hz), 1.05 (d, 3H, J=6.9Hz), 0.64 (d, 3H, J=6.9 Hz).
222		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.30 (br s, 1H), 8.65 (s, 1H), 7.67 (s, 1H), 7.35–7.31 (m, 2H), 7.18–7.13 (m, 2H), 4.59, (br d, 1H, J=13.3 Hz), 4.41 (dd, 1H, J=13.3, 4.1 Hz), 4.20 (s, 2H), 4.12–4.09 (m, 1H), 3.89–3.84 (m, 1H), 3.58–3.50 (m, 2H), 3.41–3.34 (m, 2H), 3.29–3.24 (m, 1H), 1.20 (t, 3H, J=7.2 Hz), 0.97 (t, 3H, J=7.0Hz).
223		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (m, 1H), 8.59 (s, 1H), 7.69 (s, 1H), 7.34–7.30 (m, 2H), 7.17–7.11 (m, 2H), 4.72–4.65 (m, 1H), 4.20 (s, 2H), 4.20–4.13 (m, 1H), 4.00 (d, 1H, J=13.5 Hz), 3.86–3.80 (m, 2H), 3.75–3.66 (m, 2H), 2.12–2.03 (m, 2H), 1.93 (s, 3H), 1.14 (d, 3H, J=6.7 Hz), 1.12 (d, 3H, J=6.7 Hz).
224		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.55 (br s, 1H), 9.02 (s, 1H), 7.43–7.39 (m, 2H), 7.21–7.16 (m, 2H), 4.76 (d, 1H, J=13.3 Hz), 4.47 (s, 2H), 4.30 (dd, 1H, J=13.3, 4.6 Hz), 4.21–4.14 (m, 1H), 3.83 (br t, 1H, J=4.6 Hz), 2.04–1.99 (m, 1H), 1.39 (d, 3H, J = 6.9 Hz), 1.35 (d, 3H, J=6.9 Hz), 1.05 (d, 3H, J=6.9 Hz), 0.64 (d, 3H, J=6.9 Hz).

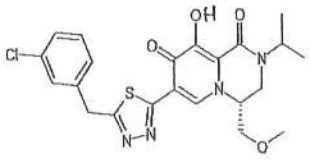
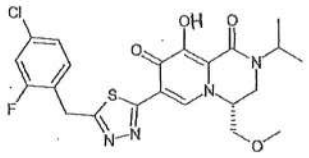
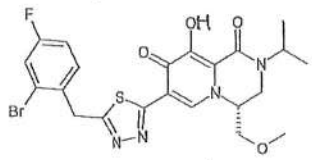
[0479]

[Table 1-63]

No.	structural formula	salt	^{1}H-NMR
225		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.78 (s, 1H), 8.52 (s, 1H), 7.67 (s, 1H), 7.34–7.30 (m, 2H), 7.16–7.12 (m, 2H), 4.72–4.66 (m, 1H), 4.19 (s, 2H), 4.11 (d, 1H, J=13.9 Hz), 3.74 (d, 1H, J=13.9 Hz), 3.41–3.25 (m, 1H), 3.13–3.06 (m, 1H), 3.81–3.74 (m, 2H), 2.00 (s, 3H), 1.92–1.84 (m, 1H), 1.75–1.61 (m, 3H), 1.15 (d, 3H, J=6.7 Hz), 1.07 (d, 3H, J=6.7 Hz).
226		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.81 (br s, 1H), 8.51 (s, 1H), 8.20 (br t, 1H, J=5.5 Hz), 7.67 (s, 1H), 7.34–7.30 (m, 2H), 7.16–7.11 (m, 2H), 4.73–4.66 (m, 1H), 4.20 (s, 2H), 4.11 (d, 1H, J=13.7 Hz), 3.77 (d, 1H, J=13.7 Hz), 3.13–2.99 (m, 2H), 1.92 (s, 3H), 1.14 (d, 3H, J=6.7 Hz), 1.10 (d, 3H, J=6.7 Hz), 0.99 (t, 3H, J=7.2 Hz).
227		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.80 (br s, 1H), 8.54 (s, 1H), 8.22 (d, 1H, J=4.4 Hz), 7.69 (s, 1H), 7.34–7.30 (m, 2H), 7.16–7.12 (m, 2H), 4.73–4.66 (m, 1H), 4.20 (s, 2H), 4.13 (d, 1H, J=13.7 Hz), 3.78 (d, 1H, J=13.7 Hz), 2.57 (d, 3H, J=4.4 Hz), 1.93 (s, 3H), 1.13 (d, 3H, J=7.0 Hz), 1.08 (d, 3H, J=7.0 Hz).

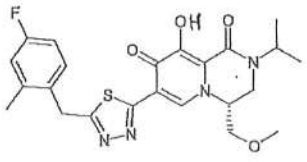
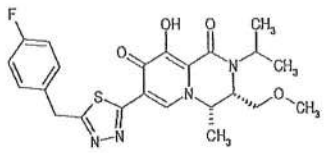
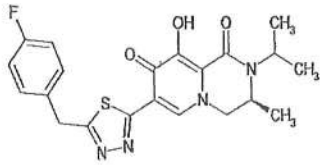
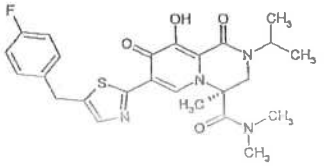
[0480]

[Table 1-64]

No.	structural formula	salt	^{1}H-NMR
228		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.85 (br s, 1H), 8.81 (s, 1H), 7.48-7.46 (m, 1H), 7.42-7.33 (m, 3H), 4.98-4.96 (m, 1H), 4.80-4.73 (m, 1H), 4.50 (s, 2H), 3.84 (dd, 1H, J=13.8, 4.1 Hz), 3.75 (br d, 1H, J=13.8 Hz), 3.63 (dd, 1H, J=10.4, 5.7 Hz), 3.57 (dd, 1H, J=10.4, 7.5 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).
229		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.83 (br s, 1H), 8.80 (s, 1H), 7.51 (t, 1H, J=8.3 Hz), 7.48 (dd, 1H, J=8.3, 2.0 Hz), 7.32 (dd, 1H, J=8.3, 2.0 Hz), 5.00-4.95 (m, 1H), 4.80-4.74 (m, 1H), 4.50 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.0 Hz), 3.75 (dd, 1H, J=13.7, 1.6 Hz), 3.62 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).
230		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.83 (br s, 1H), 8.79 (s, 1H), 7.66 (dd, 1H, J=8.7, 2.6 Hz), 7.61 (dd, 1H, J=8.7, 6.0 Hz), 7.32 (td, 1H, J=8.7, 2.6 Hz), 4.99-4.95 (m, 1H), 4.80-4.74 (m, 1H), 4.57 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.0 Hz), 3.75 (dd, 1H, J=13.7, 1.6 Hz), 3.62 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).

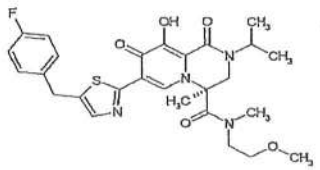
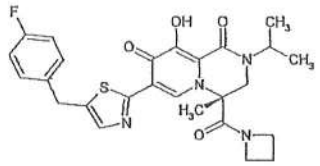
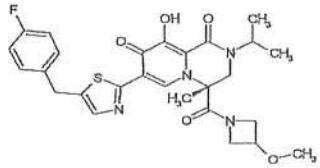
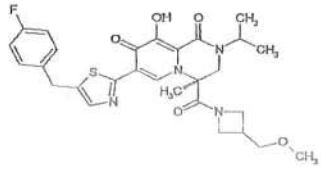
[0481]

[Table 1-65]

No.	structural formula	salt	^{1}H-NMR
231		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.80 (br s, 1H), 8.79 (s, 1H), 7.37 (dd, 1H, J=8.5, 6.1 Hz), 7.10-7.01 (m, 2H), 4.99-4.95 (m, 1H), 4.80-4.74 (m, 1H), 4.45 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.1 Hz), 3.75 (br d, 1H, J=13.7 Hz), 3.62 (dd, 1H, J=10.4, 5.7 Hz), 3.57 (dd, 1H, J=10.4, 7.6 Hz), 3.25 (s, 3H), 2.29 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).
232		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (br s, 1H), 8.56 (s, 1H), 7.42-7.38 (m, 2H), 7.20-7.16 (m, 2H), 4.66-4.64 (m, 1H), 4.47 (s, 2H), 4.45-4.40 (m, 1H), 4.08-4.05 (m, 1H), 3.56 (dd, 1H, J=11.3, 3.2 Hz), 3.50 (dd, 1H, J=11.3, 4.2 Hz), 3.11 (s, 3H), 1.75 (d, 3H, J=6.5 Hz), 1.33 (d, 3H, J=6.0 Hz), 1.32 (d, 3H, J=6.0 Hz).
233		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.54 (br s, 1H), 8.85 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.62-4.53 (m, 1H), 4.51-4.44 (m, 3H), 4.32 (dd, 1H, J = 13.1, 3.4 Hz), 4.26-4.18 (m, 1H), 1.27 (d, 3H, J = 6.7 Hz), 1.26 (d, 3H, J = 6.7 Hz), 1.21 (d, 3H, J = 6.5 Hz).
234		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.85 (s, 1H), 8.43 (s, 1H), 7.69 (s, 1H), 7.37-7.29 (m, 2H), 7.19-7.11 (m, 2H), 4.73 (sep, 1H, J = 6.7 Hz), 4.21 (s, 2H), 4.12 (d, 1H, J = 14.1 Hz), 3.79 (d, 1H, J = 14.1 Hz), 2.93 (s, 6H), 1.98 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.11 (d, 3H, J = 6.7 Hz).

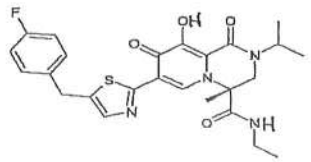
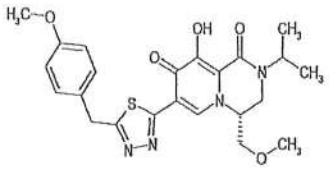
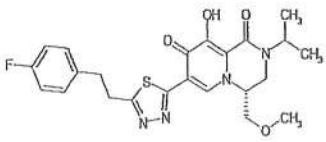
[0482]

[Table 1-66]

No.	structural formula	salt	^{1}H-NMR
235		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.89 (br s, 1H), 8.46 (s, 1H), 7.69 (s, 1H), 7.34-7.31 (m, 2H), 7.16-7.12 (m, 2H), 4.74-4.68 (m, 1H), 4.20 (s, 2H), 4.15 (d, 1H, J = 14.2 Hz), 3.78 (d, 1H, J = 14.2 Hz), 3.60-3.53 (m, 1H), 3.40 (br t, 2H, J = 5.2 Hz), 3.36-3.28 (m, 1H), 3.18 (s, 3H), 2.95 (br s, 3H), 1.97 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.12 (d, 3H, J = 6.7 Hz).
236		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.80 (m, 1H), 8.59 (s, 1H), 7.69 (s, 1H), 7.34-7.30 (m, 2H), 7.17-7.11 (m, 2H), 4.72-4.65 (m, 1H), 4.20 (s, 2H), 4.20-4.13 (m, 1H), 4.00 (d, 1H, J=13.5 Hz), 3.86-3.80 (m, 2H), 3.75-3.66 (m, 2H), 2.12-2.03 (m, 2H), 1.93 (s, 3H), 1.14 (d, 3H, J=6.7 Hz), 1.12 (d, 3H, J=6.7 Hz).
237		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.55 (s, 1H), 7.69 (s, 1H), 7.34-7.30 (m, 2H), 7.17-7.11 (m, 2H), 4.72-4.66 (m, 1H), 4.20 (s, 2H), 4.17-3.96 (m, 4H), 3.73-3.53 (m, 3H), 3.12 (s, 3H), 2.95 (s, 3H), 1.18-1.07 (m, 6H).
238		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.80 (br s, 1H), 8.58-8.53 (m, 1H), 7.69-7.68 (m, 1H), 7.34-7.30 (m, 2H), 7.16-7.12 (m, 2H), 4.72-4.66 (m, 2H), 4.20 (s, 2H), 3.99-3.84 (m, 2H), 3.78-3.67 (m, 1H), 3.60-3.47 (m, 2H), 3.36-3.33 (m, 2H), 3.27-3.25 (m, 1H), 3.28-3.16 (m, 3H), 1.93 (s, 3H), 1.15-1.10 (m, 6H).

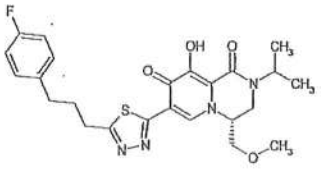
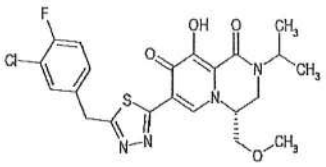
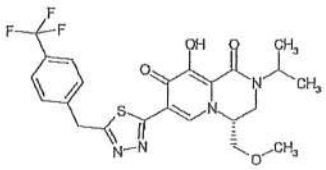
[0483]

[Table 1-67]

No.	structural formula	salt	^{1}H-NMR
239		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.51 (s, 1H), 8.20 (br t, 1H, J=5.5 Hz), 7.67 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.73-4.66 (m, 1H), 4.20 (s, 2H), 4.11 (d, 1H, J=13.7 Hz), 3.77 (d, 1H, J=13.7 Hz), 3.13-2.99 (m, 2H), 1.92 (s, 3H), 1.14 (d, 3H, J=6.7 Hz), 1.10 (d, 3H, J=6.7 Hz), 0.99 (t, 3H, J=7.2 Hz).
240		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.80 (s, 1H), 7.29 (d, 2H, J=8.9 Hz), 6.92 (d, 2H, J=8.9 Hz), 4.99-4.94 (m, 1H), 4.80-4.73 (m, 1H), 4.39 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.0 Hz), 3.75 (d, 1H, J=13.7 Hz), 3.74 (s, 3H), 3.62 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.4 Hz), 1.15 (d, 3H, J=2.4 Hz).
241		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.80 (s, 1H), 7.32 (dd, 2H, J=8.5, 5.6 Hz), 7.11 (t, 2H, J=8.5 Hz), 4.98-4.94 (m, 1H), 4.81-4.74 (m, 1H), 3.84 (dd, 1H, J=13.9, 3.8 Hz), 3.76 (d, 1H, J=13.9 Hz), 3.63 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.5 Hz), 3.41 (t, 2H, J=7.7 Hz), 3.26 (s, 3H), 3.09 (t, 2H, J=7.7 Hz), 1.17 (d, 3H, J=1.6 Hz), 1.15 (d, 3H, J=1.6 Hz).

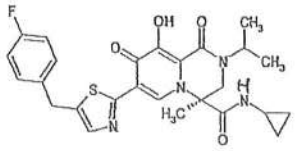
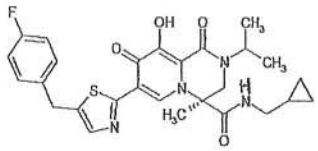
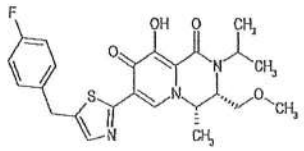
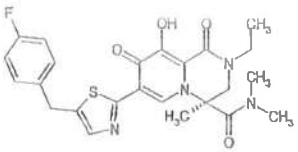
[0484]

[Table 1-68]

No.	structural formula	salt	^{1}H-NMR
242		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.81 (s, 1H), 7.28 (dd, 2H, J=8.5, 5.6 Hz), 7.11 (t, 2H, J=8.5 Hz), 4.98-4.94 (m, 1H), 4.81-4.74 (m, 1H), 3.85 (dd, 1H, J=13.9, 4.0 Hz), 3.76 (dd, 1H, J=13.9, 1.4 Hz), 3.63 (dd, 1H, J=10.3, 5.8 Hz), 3.58 (dd, 1H, J=10.3, 7.7 Hz), 3.26 (s, 3H), 3.10 (t, 2H, J=7.7 Hz), 2.68 (t, 2H, J=7.7 Hz), 2.09-2.01 (m, 2H), 1.18 (d, 3H, J=2.0 Hz), 1.16 (d, 3H, J=2.0 Hz).
243		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.81 (s, 1H), 7.65-7.63 (m, 1H), 7.41-7.39 (m, 2H), 5.00-4.95 (m, 1H), 4.80-4.74 (m, 1H), 4.50 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.0 Hz), 3.76 (dd, 1H, J=13.7, 1.6 Hz), 3.63 (dd, 1H, J=10.1, 5.6 Hz), 3.57 (dd, 1H, J=10.1, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).
244		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.81 (s, 1H), 7.73 (d, 2H, J=8.1 Hz), 7.60 (d, 2H, J=8.1 Hz), 4.99-4.94 (m, 1H), 4.80-4.73 (m, 1H), 4.61 (s, 2H), 3.84 (dd, 1H, J=13.7, 4.0 Hz), 3.76 (dd, 1H, J=13.7, 1.6 Hz), 3.63 (dd, 1H, J=10.1, 5.6 Hz), 3.57 (dd, 1H, J=10.1, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).

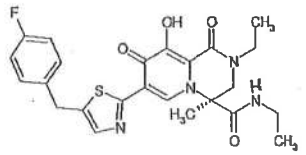
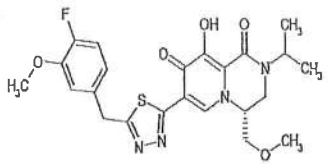
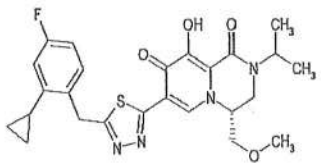
[0485]

[Table 1-69]

No.	structural formula	salt	^{1}H-NMR
245		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.79 (br s, 1H), 8.48 (s, 1H), 8.34-8.33 (m, 1H), 7.67 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.12 (m, 2H), 4.73-4.67 (m, 1H), 4.20 (s, 2H), 4.06 (d, 1H, J=13.7 Hz), 3.78 (d, 1H, J=13.7 Hz), 3.61-3.44 (m, 1H), 1.90 (s, 3H), 1.13 (d, 3H, J=6.7 Hz), 1.09 (d, 3H, J=6.7 Hz), 0.62 (d, 2H, J=7.4 Hz), 0.46-0.41 (m, 2H).
246		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.82 (br s, 1H), 8.51 (s, 1H), 8.28 (t, 1H, J=5.5 Hz), 7.67 (s, 1H), 7.33-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.73-4.66 (m, 1H), 4.20 (s, 2H), 4.15 (d, 1H, J=13.9 Hz), 3.78 (d, 1H, J=13.9 Hz), 2.98-2.84 (m, 2H), 1.93 (s, 3H), 1.14 (d, 3H, J=7.2 Hz), 1.12 (d, 3H, J=7.2 Hz), 0.89-0.85 (m, 1H), 0.40-0.37 (m, 2H), 0.14-0.10 (m, 2H).
247		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.70 (br s, 1H), 8.51 (s, 1H), 7.71 (s, 1H), 7.34-7.30 (m, 2H), 7.18-7.12 (m, 2H), 4.64-4.62 (m, 1H), 4.45-4.49 (m, 1H), 4.21 (s, 2H), 4.06-4.02 (m, 1H), 3.53 (dd, 1H, J=11.1, 3.4 Hz), 3.48 (dd, 1H, J=11.1, 4.2 Hz), 3.11 (s, 3H), 1.72 (d, 3H, J=6.5 Hz), 1.33 (d, 3H, J=5.6 Hz), 1.31 (d, 3H, J=5.6 Hz).
248		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.44 (s, 1H), 7.68 (s, 1H), 7.37-7.29 (m, 2H), 7.16-7.11 (m, 2H), 4.20 (s, 2H), 4.19 (d, 1H, J = 14.1 Hz), 3.93 (d, 1H, J = 14.1 Hz), 3.56-3.44 (m, 2H), 2.90 (s, 6H), 1.94 (s, 3H), 1.10 (s, 3H, J=7.2 Hz).

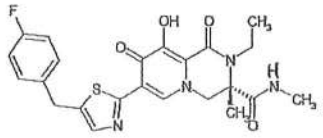
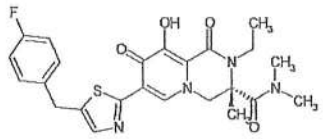
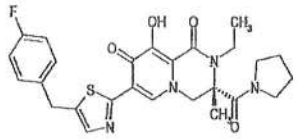
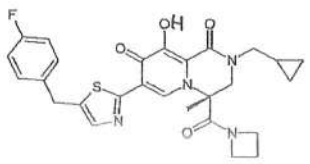
[0486]

[Table 1-70]

No.	structural formula	salt	^{1}H-NMR
249		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.50 (s, 1H), 8.20 (br t, 1H, J=5.1 Hz), 7.67 (s, 1H), 7.33–7.30 (m, 2H), 7.16–7.11 (m, 2H), 4.20 (s, 2H), 4.09 (d, 1H, J = 13.7 Hz), 3.97 (d, 1H, J = 13.7 Hz), 3.64–3.55 (m, 1H), 3.38–3.32 (m, 1H), 3.11–3.04 (m, 2H), 1.88 (s, 3H), 1.10 (s, 3H, J=7.2 Hz), 0.98 (s, 3H, J=7.2 Hz).
250		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.81 (s, 1H), 7.23–7.16 (m, 2H), 6.94–6.90 (m, 1H), 4.99–4.95 (m, 1H), 4.80–4.74 (m, 1H), 4.45 (s, 2H), 3.86–3.83 (m, 1H), 3.83 (s, 3H), 3.76 (dd, 1H, J=13.9, 1.4 Hz), 3.63 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).
251		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.79 (s, 1H), 7.38 (dd, 1H, J=8.5, 6.5 Hz), 7.02 (td, 1H, 8.5, 2.8 Hz), 6.81 (dd, 1H, J=8.5, 2.8 Hz), 4.98–4.94 (m, 1H), 4.78–4.64 (m, 1H), 4.60 (s, 2H), 3.83 (dd, 1H, J=13.7, 4.0 Hz), 3.75 (dd, 1H, J=13.7, 1.4 Hz), 3.62 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 2.06–1.99 (m, 1H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz), 0.90–0.84 (m, 2H), 0.66–0.63 (m, 2H).

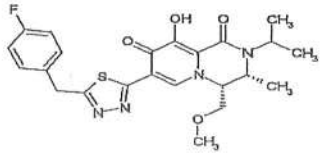
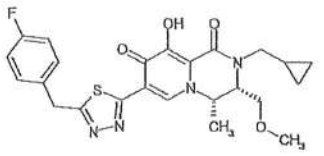
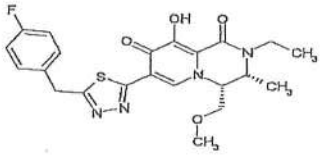
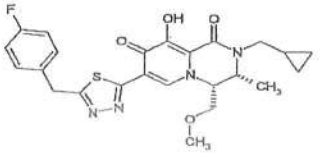
[0487]

[Table 1-71]

No.	structural formula	salt	^{1}H-NMR
252		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.40 (br s, 1H), 8.52 (s, 1H), 8.09-8.05 (m, 1H), 7.65 (s, 1H), 7.34-7.29 (m, 2H), 7.16-7.10 (m, 2H), 4.67 (d, 1H, J=13.5 Hz), 4.37 (d, 1H, J=13.5 Hz), 4.19 (s, 2H), 3.76-3.68 (m, 1H), 3.38-3.29 (m, 1H), 2.54 (d, 3H, J=4.4 Hz), 1.65 (s, 3H), 1.51 (t, 3H, J=7.1 Hz).
253		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.40 (br s, 1H), 8.68 (s, 1H), 7.66 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.86 (d, 1H, J=14.1 Hz), 4.46 (d, 1H, J=14.1 Hz), 4.19 (s, 2H), 3.78-3.69 (m, 1H), 3.18-3.09 (m, 1H), 2.99 (br s, 6H), 1.71 (s, 3H), 1.19 (t, 3H, J=7.1 Hz).
254		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 8.69 (s, 1H), 7.65 (s, 1H), 7.34-7.29 (m, 2H), 7.16-7.11 (m, 2H), 4.86 (d, 1H, J=13.9 Hz), 4.46 (d, 1H, J=13.9 Hz), 4.30-4.03 (m, 1H), 4.19 (s, 2H), 3.78-3.68 (m, 2H), 3.46-3.17 (m, 3H), 1.98-1.78 (m, 4H), 1.73 (s, 3H), 1.17 (t, 3H, J=7.1 Hz).
255		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.70 (br s, 1H), 8.61 (s, 1H), 7.70 (s, 1H), 7.35-7.32 (m, 2H), 7.17-7.13 (m, 2H), 4.21 (s, 2H), 4.21-4.17 (m, 1H), 4.11 (d, 1H, J=13.7 Hz), 3.96 (d, 1H, J=13.7 Hz), 3.89-3.82 (m, 2H), 3.78-3.73 (m, 1H), 3.46 (dd, 1H, J=13.9, 6.9 Hz), 3.25 (dd, 1H, J=13.9, 7.5 Hz), 2.14-2.06 (m, 2H), 1.94 (s, 3H), 1.09-1.03 (m, 1H), 0.52-0.49 (m, 2H), 0.34-0.31 (m, 2H).

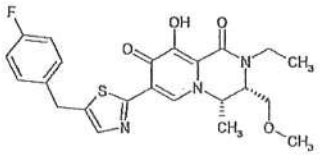
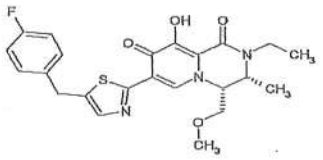
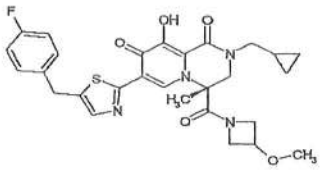
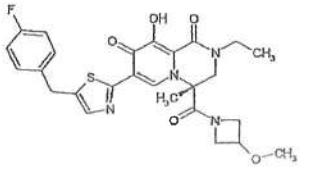
[0488]

[Table 1-72]

No.	structural formula	salt	^{1}H-NMR
256		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.78 (s, 1H), 7.42-7.39 (m, 2H), 7.20-7.16 (m, 2H), 4.72-4.70 (m, 1H), 4.60-4.53 (m, 1H), 4.47 (s, 2H), 4.18-4.10 (m, 2H), 3.94 (dd, 1H, J=11.9, 2.2 Hz), 3.46 (s, 3H), 1.29 (d, 3H, J=6.9 Hz), 1.27 (d, 3H, J=6.9 Hz), 1.05 (d, 3H, J=6.5 Hz).
257		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.76 (br s, 1H), 8.62 (s, 1H), 7.42-7.38 (m, 2H), 7.20-7.16 (m, 2H), 4.77-4.74 (m, 1H), 4.47 (s, 2H), 4.19 (q, 1H, J=4.0 Hz), 3.71 (dd, 1H, J=14.1, 7.3 Hz), 3.62 (d, 2H, J=4.4 Hz), 3.23 (dd, 1H, J=14.1, 6.9 Hz), 3.16 (s, 3H), 1.69 (d, 3H, J=6.9 Hz), 1.22-1.16 (m, 1H), 0.58-0.48 (m, 2H), 0.44-0.39 (m, 1H), 0.34-0.29 (m, 1H).
258		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.82 (br s, 1H), 8.72 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.84-4.79 (m, 1H), 4.47 (s, 2H), 4.26-4.21 (m, 1H), 3.89-3.76 (m, 3H), 3.33 (s, 3H), 3.33-3.26 (m, 1H), 1.24 (d, 3H, J=6.9 Hz), 1.17 (t, 3H, J=7.3 Hz).
259		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.78 (br s, 1H), 8.74 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.85-4.81 (m, 1H), 4.47 (s, 2H), 4.30-4.24 (m, 1H), 3.93 (dd, 1H, J=11.5, 8.5 Hz), 3.85 (dd, 1H, J=11.5, 3.0 Hz), 3.56 (dd, 1H, J=14.1, 7.5 Hz), 3.37 (s, 3H), 3.30 (dd, 1H, J=14.1, 6.9 Hz), 1.24 (d, 3H, J=6.9 Hz), 1.15-1.09 (m, 1H), 0.58-0.48 (m, 2H), 0.41-0.30 (m, 2H).

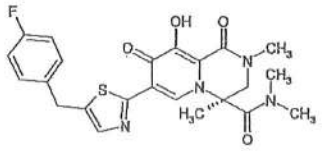
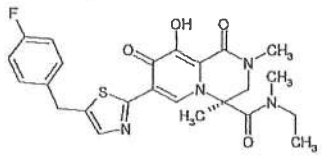
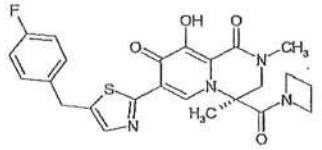
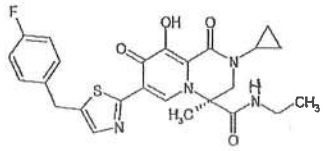
[0489]

[Table 1-73]

No.	structural formula	salt	^{1}H-NMR
260		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.67 (br s, 1H), 8.53 (s, 1H), 7.69 (s, 1H), 7.33-7.29 (m, 2H), 7.17-7.11 (m, 2H), 4.73-4.67 (m, 1H), 4.19 (s, 2H), 4.10 (q, 1H, J=4.1 Hz), 3.90-3.83 (m, 1H), 3.56 (d, 2H, J=4.6 Hz), 3.33-3.32 (m, 1H), 3.16 (s, 3H), 1.61 (d, 3H, J=6.5 Hz), 1.20 (t, 3H, J=7.1 Hz).
261		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.59 (s, 1H), 7.67 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.79-4.75 (m, 1H), 4.22-4.19 (m, 1H), 4.19 (s, 2H), 3.85-3.73 (m, 3H), 3.31 (s, 3H), 3.31-3.24 (m, 1H), 1.22 (d, 3H, J=6.7 Hz), 1.15 (t, 3H, J=7.1 Hz).
262		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.71 (br s, 1H), 8.60 (s, 1H), 7.70 (s, 1H), 7.35-7.31 (m, 2H), 7.16-7.12 (m, 2H), 4.41-4.38 (m, 1H), 4.20 (s, 2H), 4.10-4.02 (m, 4H), 3.98 (d, 1H, J=13.7 Hz), 3.68-3.59 (m, 1H), 3.43-3.35 (m, 1H), 3.32-3.26 (m, 1H), 3.13 (s, 3H), 1.94 (s, 3H), 1.07-1.00 (m, 1H), 0.53-0.45 (m, 2H), 0.34-0.28 (m, 2H).
263		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.60 (s, 1H), 7.69 (s, 1H), 7.34-7.31 (m, 2H), 7.14 (br t, 2H, J=8.8 Hz), 4.39-4.36 (m, 1H), 4.20 (s, 2H), 4.11-3.90 (m, 5H), 3.69-3.65 (m, 1H), 3.57-3.40 (m, 2H), 3.12 (s, 3H), 1.92 (s, 3H), 1.09 (t, 3H, J=6.6 Hz).

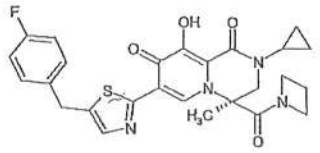
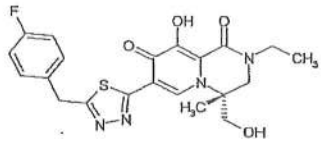
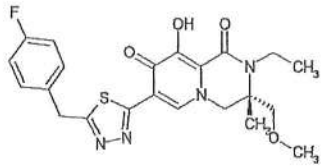
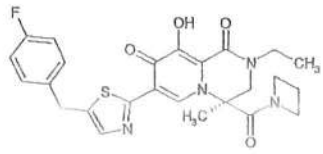
[0490]

[Table 1-74]

No.	structural formula	salt	^{1}H-NMR
264		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (s, 1H), 8.41 (s, 1H), 7.68 (s, 1H), 7.32 (dd, 2H, J=8.2, 5.9 Hz), 7.16-7.13 (m, 2H), 4.19 (s, 2H), 4.18 (d, 1H, J = 13.9 Hz), 3.90 (d, 1H, J = 13.9 Hz), 3.05 (s, 3H), 2.88 (s, 6H), 1.91 (s, 3H).
265		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (s, 1H), 8.40 (s, 1H), 7.67 (s, 1H), 7.35-7.29 (m, 2H), 7.16-7.11 (m, 2H), 4.19 (s, 2H), 4.17 (d, 1H, J = 13.9 Hz), 3.89 (d, 1H, J = 13.9 Hz), 3.43-3.35 (m, 1H), 3.28-3.19 (m, 1H), 3.05 (s, 3H), 2.83 (s, 3H), 1.89 (s, 3H), 0.98 (t, 3H, J=7.1 Hz).
266		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.66 (br s, 1H), 8.62 (s, 1H), 7.70 (s, 1H), 7.34-7.31 (m, 2H), 7.16-7.12 (m, 2H), 4.20 (s, 2H), 4.18-4.11 (m, 1H), 4.04-3.97 (m, 1H), 3.91-3.82 (m, 2H), 3.28-3.19 (m, 1H), 3.64-3.57 (m, 1H), 3.03 (s, 3H), 2.09-2.03 (m, 2H), 1.90 (s, 3H).
267		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.73 (br s, 1H), 8.50 (s, 1H), 8.18 (br t, 1H, J=5.6 Hz), 7.67 (s, 1H), 7.34-7.29 (m, 2H), 7.17-7.11 (m, 2H), 4.20 (s, 2H), 3.99 (d, 1H, J=13.7 Hz), 3.93 (d, 1H, J=13.7 Hz), 3.08-3.01 (m, 2H), 2.87-2.84 (m, 1H), 1.87 (s, 3H), 0.96 (t, 3H, J=7.2 Hz), 0.94-0.89 (m, 1H), 0.81-0.69 (m, 2H), 0.62-0.56 (m, 1H).

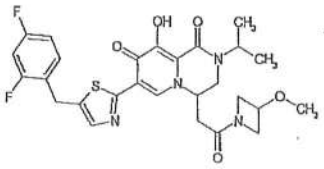
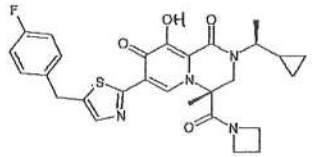
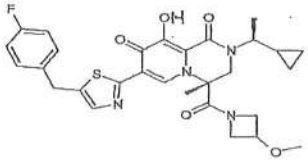
[0491]

[Table 1-75]

No.	structural formula	salt	^{1}H-NMR
268		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.70 (br s, 1H), 8.61 (s, 1H), 7.69 (s, 1H), 7.34-7.30 (m, 2H), 7.16-7.11 (m, 2H), 4.20 (s, 2H), 4.07-4.01 (m, 1H), 3.92 (d, 1H, J=13.2 Hz), 3.87-3.82 (m, 2H), 3.80 (d, 1H, J=13.2 Hz), 3.50-3.42 (m, 1H), 2.89-2.84 (m, 1H), 2.08-2.00 (m, 2H), 1.89 (s, 3H), 0.91-0.85 (m, 1H), 0.82-0.73 (m, 2H), 0.67-0.61 (m, 1H).
269		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.18 (br s, 1H), 8.67 (s, 1H), 7.42-7.38 (m, 2H), 7.20-7.14 (m, 2H), 4.46 (s, 2H), 3.83 (d, 1H, J=13.7 Hz), 3.74 (d, 1H, J=13.7 Hz), 3.64 (d, 1H, J=11.8 Hz), 3.62 (d, 1H, J=11.8 Hz), 3.60-3.44 (m, 3H), 1.59 (s, 3H), 1.15 (t, 3H, J=7.2 Hz).
270		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.75 (s, 1H), 7.41-7.38 (m, 2H), 7.20-7.15 (m, 2H), 4.53 (d, 1H, J=13.7 Hz), 4.46 (s, 2H), 4.30 (d, 1H, J=13.7 Hz), 3.68-3.59 (m, 1H), 3.51 (d, 1H, J=10.4 Hz), 3.48-3.43 (m, 2H), 3.20 (s, 3H), 1.35 (s, 3H), 1.19 (t, 3H, J=7.1 Hz).
271		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.61 (s, 1H), 7.69 (s, 1H), 7.34-7.31 (m, 2H), 7.16-7.12 (m, 2H), 4.20 (s, 2H), 4.17-4.15 (m, 1H), 4.02 (d, 1H, J=13.5 Hz), 4.00-3.87 (m, 2H), 3.89 (d, 1H, J=13.5 Hz), 3.65-3.63 (m, 1H), 3.54-3.44 (m, 2H), 2.10-2.06 (m, 2H), 1.91 (s, 3H), 1.10 (t, 3H, J=7.1 Hz).

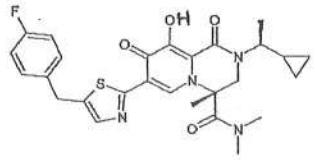
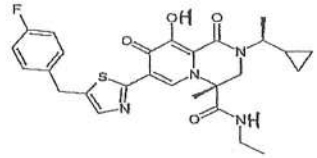
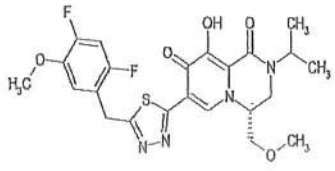
[0492]

[Table 1-76]

No.	structural formula	salt	^{1}H-NMR
272		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.65 (br s, 1H), 8.66 (s, 1H), 7.64 (s, 1H), 7.47–7.41 (m, 1H), 7.24 (dt, 1H, J=14.0, 5.0 Hz), 7.06 (td, 1H, J=8.5, 2.3 Hz), 5.10–5.03 (m, 1H), 4.80–4.73 (m, 1H), 4.20 (s, 2H), 4.18–4.04 (m, 2H), 3.98–3.85 (m, 1H), 3.87–3.71 (m, 3H), 3.61–3.53 (m, 1H), 3.15 (s, 1.5H), 3.08 (s, 1.5H), 2.66–2.58 (m, 2H), 1.15–1.11 (m, 6H).
273		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.83 (br s, 1H), 8.59 (s, 1H), 7.70 (s, 1H), 7.35–7.32 (m, 2H), 7.17–7.13 (m, 2H), 4.21 (s, 2H), 4.21–4.17 (m, 1H), 4.14 (d, 1H, J=13.7 Hz), 3.93–3.76 (m, 5H), 2.16–2.08 (m, 2H), 1.97 (s, 3H), 1.24 (d, 3H, J=6.8 Hz), 1.13–1.10 (m, 1H), 0.64–0.58 (m, 1H), 0.43–0.38 (m, 2H), 0.20–0.15 (m, 1H).
274		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.81 (br s, 1H), 8.58 (s, 1H), 7.70 (s, 1H), 7.35–7.32 (m, 2H), 7.17–7.13 (m, 2H), 4.21 (s, 2H), 4.21–4.14 (m, 3H), 4.06–4.00 (m, 1H), 3.87–3.64 (m, 4H), 3.15 (s, 3H), 1.98 (s, 3H), 1.24 (d, 3H, J=6.6 Hz), 1.13–1.09 (m, 1H), 0.61–0.57 (m, 1H), 0.49–0.36 (m, 2H), 0.15–0.07 (m, 1H).

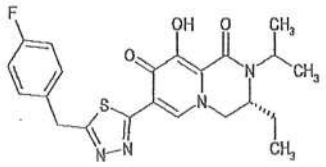
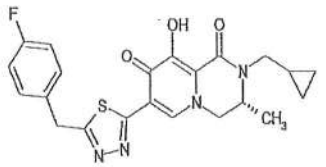
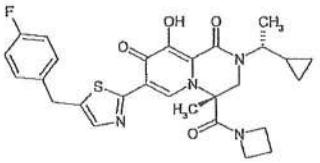
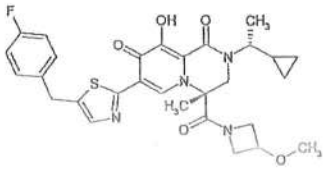
[0493]

[Table 1-77]

No.	structural formula	salt	^{1}H-NMR
275		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.48 (s, 1H), 7.69 (s, 1H), 7.35–7.32 (m, 2H), 7.17–7.13 (m, 2H), 4.31 (d, 1H, J=14.3 Hz), 4.21 (s, 2H), 3.93 (d, 1H, J=14.3 Hz), 3.83–3.75 (m, 1H), 2.98 (br s, 6H), 2.05 (s, 3H), 1.25 (d, 3H, J=6.8 Hz), 1.10–1.03 (m, 1H), 0.64–0.58 (m, 1H), 0.42–0.33 (m, 2H), 0.12–0.08 (m, 1H).
276		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.86 (br s, 1H), 8.52 (s, 1H), 8.21 (t, 1H, J=5.4 Hz), 7.69 (s, 1H), 7.36–7.31 (m, 2H), 7.18–7.13 (m, 2H), 4.29 (d, 1H, J=13.7 Hz), 4.21 (s, 2H), 3.87 (d, 1H, J=13.7 Hz), 3.81–3.73 (m, 1H), 3.20–3.14 (m, 1H), 3.02–2.96 (m, 1H), 1.94 (s, 3H), 1.24 (d, 3H, J=6.8 Hz), 1.13–1.07 (m, 1H), 1.01 (t, 3H, J=7.2 Hz), 0.62–0.57 (m, 1H), 0.37–0.31 (m, 2H), 0.18–0.12 (m, 1H).
277		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.80 (s, 1H), 7.38–7.32 (m, 2H), 4.99–4.97 (m, 1H), 4.80–4.74 (m, 1H), 4.46 (s, 2H), 3.84 (dd, 1H, J=13.5, 4.2 Hz), 3.83 (s, 3H), 3.75 (dd, 1H, J=13.5, 1.2 Hz), 3.63 (dd, 1H, J=10.3, 5.8 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.25 (s, 3H), 1.17 (d, 3H, J=2.0 Hz), 1.15 (d, 3H, J=2.0 Hz).

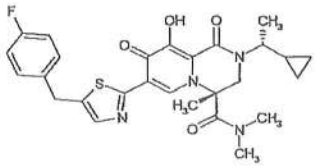
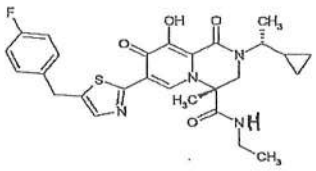
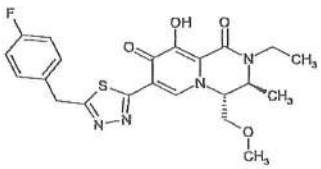
[0494]

[Table 1-78]

No.	structural formula	salt	^{1}H-NMR
278		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.45 (br s, 1H), 8.98 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.71-4.67 (m, 1H), 4.56-4.49 (m, 1H), 4.47 (s, 2H), 4.30-4.25 (m, 1H), 3.93-3.90 (m, 1H), 1.65-1.61 (m, 1H), 1.46-1.38 (m, 1H), 1.29 (d, 3H, J=2.4 Hz), 1.27 (d, 3H, J=2.0 Hz), 0.92 (t, 3H, J=7.5 Hz).
279		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.60 (br s, 1H), 8.84 (s, 1H), 7.43-7.38 (m, 2H), 7.20-7.15 (m, 2H), 4.50-4.46 (m, 1H), 4.46 (s, 2H), 4.41 (dd, 1H, J=13.1, 3.6 Hz), 4.20-4.17 (m, 1H), 3.57 (dd, 1H, J=14.0, 7.1 Hz), 3.22 (dd, 1H, J=14.0, 7.0 Hz), 1.24 (d, 3H, J=6.5 Hz), 1.14-1.10 (m, 1H), 0.56-0.47 (m, 2H), 0.39-0.36 (m, 1H), 0.33-0.29 (m, 1H).
280		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (br s, 1H), 8.61 (s, 1H), 7.70 (s, 1H), 7.35-7.32 (m, 2H), 7.18-7.13 (m, 2H), 4.21 (s, 2H), 4.21-4.13 (m, 2H), 3.86-3.73 (m, 5H), 2.14-2.06 (m, 2H), 1.96 (s, 3H), 1.20 (d, 3H, J=6.6 Hz), 1.15-1.07 (m, 1H), 0.64-0.58 (m, 1H), 0.45-0.38 (m, 2H), 0.23-0.20 (m, 1H).
281		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.74 (br s, 1H), 8.60 (s, 1H), 7.70 (s, 1H), 7.36-7.32 (m, 2H), 7.17-7.13 (m, 2H), 4.21 (s, 2H), 4.15-4.04 (m, 4H), 3.89-3.78 (m, 2H), 3.68-3.58 (m, 2H), 3.15 (s, 1.5H), 3.14 (s, 1.5H), 1.98 (s, 3H), 1.19-1.11 (m, 4H), 0.61-0.57 (m, 1H), 0.49-0.38 (m, 2H), 0.22-0.19 (m, 1H).

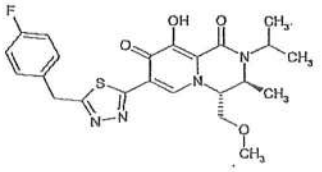
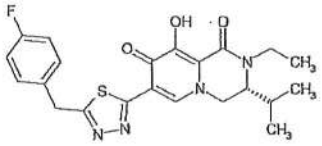
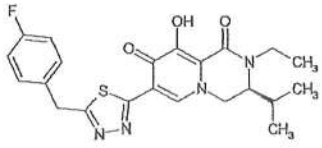
[0495]

[Table 1-79]

No.	structural formula	salt	^{1}H-NMR
282		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.84 (br s, 1H), 8.42 (s, 1H), 7.69 (s, 1H), 7.35–7.32 (m, 2H), 7.18–7.12 (m, 2H), 4.24 (d, 1H, J=14.3 Hz), 4.21 (s, 2H), 3.93 (d, 1H, J=14.3 Hz), 3.89–3.81 (m, 1H), 2.94 (br s, 6H), 1.99 (s, 3H), 1.19 (d, 3H, J=6.6 Hz), 1.15–1.09 (m, 1H), 0.63–0.58 (m, 1H), 0.48–0.39 (m, 2H), 0.26–0.22 (m, 1H).
283		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.77 (br s, 1H), 8.53 (s, 1H), 8.25 (t, 1H, J=5.4 Hz), 7.69 (s, 1H), 7.35–7.32 (m, 2H), 7.17–7.13 (m, 2H), 4.29 (d, 1H, J=13.9 Hz), 4.21 (s, 2H), 3.92 (d, 1H, J=13.9 Hz), 3.89–3.83 (m, 1H), 3.16–3.02 (m, 2H), 1.95 (s, 3H), 1.18 (d, 3H, J=6.8 Hz), 1.03–1.01 (m, 1H), 1.01 (t, 3H, J=7.2 Hz), 0.62–0.58 (m, 1H), 0.47–0.39 (m, 2H), 0.24–0.19 (m, 1H).
284		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.66 (br s, 1H), 8.82 (s, 1H), 7.43–7.39 (m, 2H), 7.21–7.16 (m, 2H), 4.83 (br t, 1H, J=6.6 Hz), 4.48 (s, 2H), 4.04 (q, 1H, J=6.2 Hz), 3.95–3.86 (m, 1H), 3.64 (dd, 1H, J=10.4, 5.3 Hz), 3.53 (dd, 1H, J=10.4, 7.9 Hz), 3.24 (s, 3H), 3.16–3.07 (m, 1H), 1.26 (d, 3H, J=6.6 Hz), 1.16 (t, 3H, J=7.1 Hz).

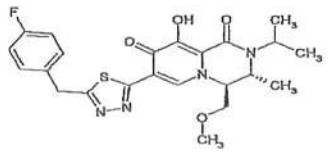
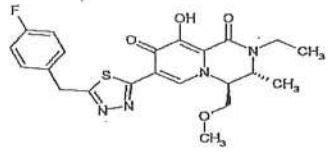
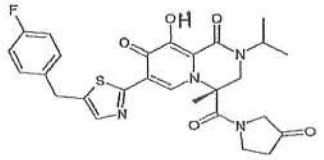
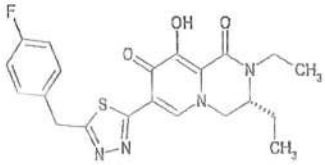
[0496]

[Table 1-80]

No.	structural formula	salt	^{1}H-NMR
285		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.67 (br s, 1H), 8.82 (s, 1H), 7.43-7.39 (m, 2H), 7.22-7.15 (m, 2H), 4.82 (br t, 1H, J=6.0 Hz), 4.65-4.58 (m, 1H), 4.48 (s, 2H), 4.16 (q, 1H, J=6.5 Hz), 3.60 (dd, 1H, J=10.3, 5.4 Hz), 3.49 (dd, 1H, J=10.3, 7.9 Hz), 3.24 (s, 3H), 1.27 (d, 3H, J=2.0 Hz), 1.26 (d, 3H, J=2.0 Hz), 1.21 (t, 3H, J=6.8 Hz).
286		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.53 (br s, 1H), 9.01 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.15 (m, 2H), 4.75 (d, 1H, J=13.8 Hz), 4.47 (s, 2H), 4.34 (dd, 1H, J=13.8, 4.3 Hz), 4.01 (td, 1H, J=13.8, 6.9 Hz), 3.74 (br t, 1H, J=5.0 Hz), 3.74 (td, 1H, J=13.8, 6.9 Hz), 1.92 (td, 1H, J=13.8, 6.9 Hz), 1.20 (t, 3H, J = 6.9 Hz), 0.99 (d, 3H, J=6.9 Hz), 0.79 (d, 3H, J=6.9 Hz).
287		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.53 (br s, 1H), 9.01 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.15 (m, 2H), 4.75 (d, 1H, J=13.8 Hz), 4.47 (s, 2H), 4.34 (dd, 1H, J=13.8, 4.3 Hz), 4.01 (td, 1H, J=13.8, 6.9 Hz), 3.74 (br t, 1H, J=5.0 Hz), 3.74 (td, 1H, J=13.8, 6.9 Hz), 1.92 (td, 1H, J=13.8, 6.9 Hz), 1.20 (t, 3H, J = 6.9 Hz), 0.99 (d, 3H, J=6.9 Hz), 0.79 (d, 3H, J=6.9 Hz).

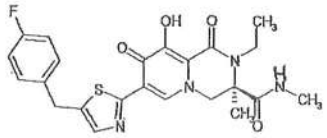
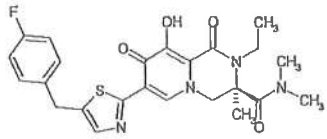
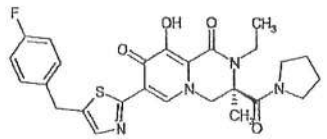
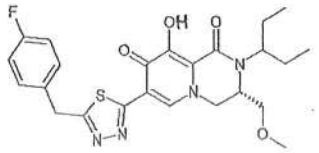
[0497]

[Table 1-81]

No.	structural formula	salt	^{1}H-NMR
288		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.67 (br s, 1H), 8.82 (s, 1H), 7.43-7.39 (m, 2H), 7.22-7.15 (m, 2H), 4.82 (br t, 1H, J=6.0 Hz), 4.65-4.58 (m, 1H), 4.48 (s, 2H), 4.16 (q, 1H, J=6.5 Hz), 3.60 (dd, 1H, J=10.3, 5.4 Hz), 3.49 (dd, 1H, J=10.3, 7.9 Hz), 3.24 (s, 3H), 1.27 (d, 3H, J=2.0 Hz), 1.26 (d, 3H, J=2.0 Hz), 1.21 (t, 3H, J=6.8 Hz).
289		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.66 (br s, 1H), 8.82 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.83 (br t, 1H, J=6.6 Hz), 4.48 (s, 2H), 4.04 (q, 1H, J=6.2 Hz), 3.95-3.86 (m, 1H), 3.64 (dd, 1H, J=10.4, 5.3 Hz), 3.53 (dd, 1H, J=10.4, 7.9 Hz), 3.24 (s, 3H), 3.16-3.07 (m, 1H), 1.26 (d, 3H, J=6.6 Hz), 1.16 (t, 3H, J=7.1 Hz).
290		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.86 (br s, 1H), 8.56 (s, 1H), 7.70 (s, 1H), 7.37-7.31 (m, 2H), 7.19-7.12 (m, 2H), 4.73-4.66 (m, 1H), 4.21 (s, 2H), 4.19-4.07 (m, 2H), 3.86-3.70 (m, 6H), 2.03 (s, 3H), 1.17 (d, 3H, J = 6.5 Hz), 1.10 (d, 3H, J=6.5 Hz).
291		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.53 (br s, 1H), 8.96 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.65 (d, 1H, J=13.5 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J=13.5, 3.8 Hz), 3.92-3.84 (m, 2H), 3.24-3.16 (m, 1H), 1.72-1.66 (m, 1H), 1.51-1.41 (m, 1H), 1.20 (t, 3H, J=7.3 Hz), 0.92 (t, 3H, J=7.5 Hz).

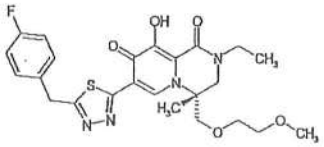
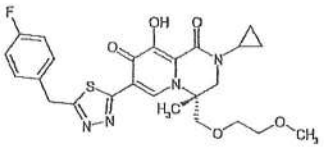
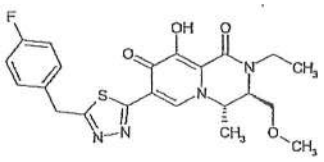
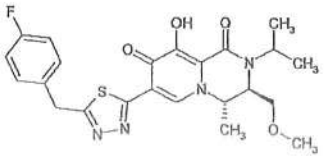
[0498]

[Table 1-82]

No.	structural formula	salt	^{1}H-NMR
292		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.40 (br s, 1H), 8.52 (s, 1H), 8.09–8.05 (m, 1H), 7.65 (s, 1H), 7.34–7.29 (m, 2H), 7.16–7.10 (m, 2H), 4.67 (d, 1H, J=13.5 Hz), 4.37 (d, 1H, J=13.5 Hz), 4.19 (s, 2H), 3.76–3.68 (m, 1H), 3.38–3.29 (m, 1H), 2.54 (d, 3H, J=4.4 Hz), 1.65 (s, 3H), 1.51 (t, 3H, J=7.1 Hz).
293		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.40 (br s, 1H), 8.68 (s, 1H), 7.66 (s, 1H), 7.34–7.30 (m, 2H), 7.16–7.11 (m, 2H), 4.86 (d, 1H, J=14.1 Hz), 4.46 (d, 1H, J=14.1 Hz), 4.19 (s, 2H), 3.78–3.69 (m, 1H), 3.18–3.09 (m, 1H), 2.99 (br s, 6H), 1.71 (s, 3H), 1.19 (t, 3H, J=7.1 Hz).
294		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.69 (s, 1H), 7.65 (s, 1H), 7.34–7.29 (m, 2H), 7.16–7.11 (m, 2H), 4.86 (d, 1H, J=13.9 Hz), 4.46 (d, 1H, J=13.9 Hz), 4.30–4.03 (m, 1H), 4.19 (s, 2H), 3.78–3.68 (m, 2H), 3.46–3.17 (m, 3H), 1.98–1.78 (m, 4H), 1.73 (s, 3H), 1.17 (t, 3H, J=7.1 Hz).
295		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.46 (br s, 1H), 8.84 (s, 1H), 7.43–7.39 (m, 2H), 7.20–7.15 (m, 2H), 4.68 (d, 1H, J=13.5 Hz), 4.46 (s, 2H), 4.36 (dd, 1H, J=13.5, 3.7 Hz), 4.08–4.00 (m, 2H), 3.49 (dd, 1H, J=10.2, 3.9 Hz), 3.41 (dd, 1H, J=10.2, 7.0 Hz), 3.17 (s, 3H), 1.77–1.59 (m, 4H), 0.90 (t, 3H, J=7.3 Hz), 0.85 (t, 3H, J=7.3 Hz).

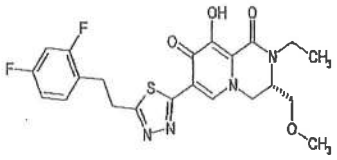
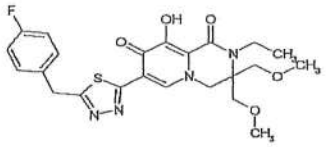
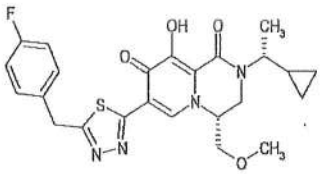
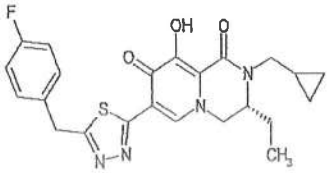
[0499]

[Table 1-83]

No.	structural formula	salt	^{1}H-NMR
296		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.19 (br s, 1H), 8.71 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.47 (s, 2H), 3.86-3.76 (m, 3H), 3.70 (d, 1H, J=10.4 Hz), 3.63-3.45 (m, 4H), 3.35-3.33 (m, 2H), 3.11 (s, 3H), 1.64 (s, 3H), 1.17 (t, 3H, J=7.2 Hz).
297		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.21 (br s, 1H), 8.71 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.47 (s, 2H), 3.80-3.63 (m, 4H), 3.51-3.44 (m, 2H), 3.35-3.33 (m, 2H), 3.12 (s, 3H), 2.95-2.90 (m, 1H), 1.62 (s, 3H), 0.93-0.76 (m, 4H).
298		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.51 (br s, 1H), 8.93 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.91 (q, 1H, J=6.8 Hz), 4.48 (s, 2H), 4.04-3.95 (m, 2H), 3.52 (dd, 1H, J=10.3, 5.2 Hz), 3.46 (dd, 1H, J=10.3, 6.5 Hz), 3.22 (s, 3H), 3.20-3.13 (m, 1H), 1.42 (d, 3H, J=6.6 Hz), 1.19 (t, 3H, J=7.1 Hz).
299		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.95 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.95 (q, 1H, J=6.5 Hz), 4.58-4.51 (m, 1H), 4.48 (s, 2H), 4.07-4.04 (m, 1H), 3.50 (dd, 1H, J=10.5, 4.1 Hz), 3.36 (dd, 1H, J=10.5, 7.9 Hz), 3.22 (s, 3H), 1.39 (d, 3H, J=6.8 Hz), 1.29 (d, 3H, J=5.0 Hz), 1.27 (d, 3H, J=5.0 Hz).

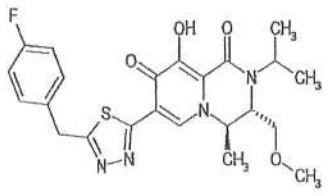
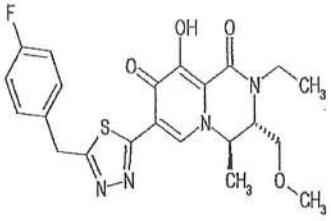
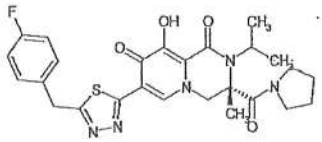
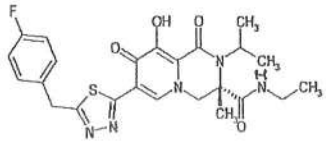
[0500]

[Table 1-84]

No.	structural formula	salt	^{1}H-NMR
300		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.82 (s, 1H), 7.39 (dd, 1H, J=15.3, 8.7 Hz), 7.22-7.16 (m, 1H), 7.02 (td, 1H, J=8.7, 2.4 Hz), 4.63 (d, 1H, J=13.3 Hz), 4.42 (dd, 1H, J=13.3, 4.3 Hz), 4.17-4.13 (m, 1H), 3.87 (td, 1H, J=14.0, 7.1 Hz), 3.56-3.49 (m, 2H), 3.40 (t, 2H, J=7.5 Hz), 3.32-3.25 (m, 1H), 3.22 (s, 3H), 3.09 (t, 2H, J=7.5 Hz), 1.21 (t, 3H, J=7.1 Hz).
301		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.61 (br s, 1H), 8.78 (s, 1H), 7.42-7.39 (m, 2H), 7.20-7.16 (m, 2H), 4.51 (s, 2H), 4.47 (s, 2H), 3.65-3.53 (m, 6H), 3.26 (s, 6H), 1.19 (t, 3H, J=7.1 Hz).
302		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (br s, 1H), 8.80 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.15 (m, 2H), 4.99-4.95 (m, 1H), 4.46 (s, 2H), 3.99-3.84 (m, 3H), 3.63 (dd, 1H, J=10.3, 5.7 Hz), 3.57 (dd, 1H, J=10.3, 7.7 Hz), 3.24 (s, 3H), 1.22 (d, 3H, J=7.0 Hz), 1.08-1.00 (m, 1H), 0.61-0.55 (m, 1H), 0.47-0.36 (m, 2H), 0.23-0.18 (m, 1H).
303		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.97 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.69 (d, 1H, J=13.3 Hz), 4.48 (s, 2H), 4.38 (dd, 1H, J=13.3, 3.4 Hz), 3.95-3.93 (m, 1H), 3.69 (dd, 1H, J=13.9, 7.1 Hz), 3.16 (dd, 1H, J=13.9 7.2 Hz), 1.79-1.72 (m, 1H), 1.48-1.40 (m, 1H), 1.19-1.12 (m, 1H), 0.93 (t, 3H, J=7.4 Hz), 0.55-0.48 (m, 2H), 0.42-0.37 (m, 1H), 0.34-0.30 (m, 1H).

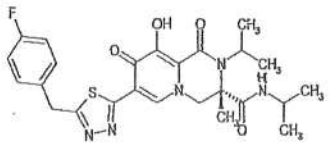
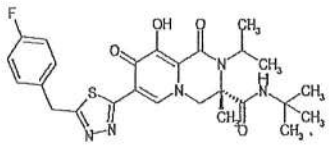
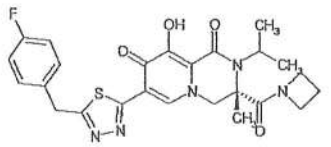
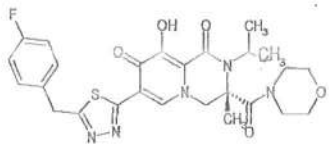
[0501]

[Table 1-85]

No.	structural formula	salt	^{1}H-NMR
304		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.95 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.95 (q, 1H, J=6.5 Hz), 4.58-4.51 (m, 1H), 4.48 (s, 2H), 4.07-4.04 (m, 1H), 3.50 (dd, 1H, J=10.5, 4.1 Hz), 3.36 (dd, 1H, J=10.5, 7.9 Hz), 3.22 (s, 3H), 1.39 (d, 3H, J=6.8 Hz), 1.29 (d, 3H, J=5.0 Hz), 1.27 (d, 3H, J=5.0 Hz).
305		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.51 (br s, 1H), 8.93 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.91 (q, 1H, J=6.8 Hz), 4.48 (s, 2H), 4.04-3.95 (m, 2H), 3.52 (dd, 1H, J=10.3, 5.2 Hz), 3.46 (dd, 1H, J=10.3, 6.5 Hz), 3.22 (s, 3H), 3.20-3.13 (m, 1H), 1.42 (d, 3H, J=6.6 Hz), 1.19 (t, 3H, J=7.1 Hz).
306		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.70 (br s, 1H), 8.86 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.80 (d, 1H, J = 14.0 Hz), 4.49 (d, 1H, J = 14.0 Hz), 4.47 (s, 2H), 4.11-3.06 (m, 4H), 3.60 (sep, 1H, J = 6.6 Hz), 2.06-1.63 (m, 4H), 1.73 (s, 3H), 1.46 (d, 3H, J = 6.6 Hz), 1.43 (d, 3H, J = 6.6 Hz).
307		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.65 (br s, 1H), 8.74 (s, 1H), 8.31 (t, 1H, J = 5.5 Hz), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.58 (d, 1H, J = 13.5 Hz), 4.48 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 3.53 (sep, 1H, J = 6.6 Hz), 3.20-3.09 (m, 2H), 1.58 (s, 3H), 1.48 (d, 3H, J = 6.6 Hz), 1.41 (d, 3H, J = 6.6 Hz), 1.01 (t, 3H, J = 7.2 Hz).

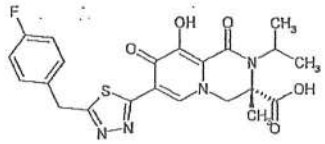
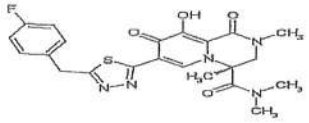
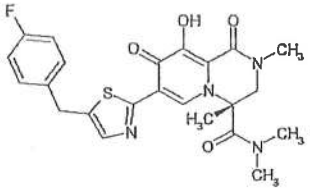
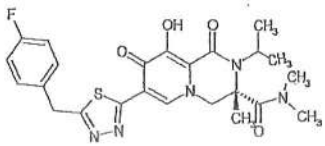
[0502]

[Table 1-86]

No.	structural formula	salt	^{1}H-NMR
308		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.74 (s, 1H), 8.11 (d, 1H, J = 7.7 Hz), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.61 (d, 1H, J = 14.0 Hz), 4.49 (d, 1H, J = 14.0 Hz), 4.47 (s, 2H), 3.91 (sep, 1H, J = 6.6 Hz), 3.48 (sep, 1H, J = 6.6 Hz), 1.55 (s, 3H), 1.51 (d, 3H, J = 6.6 Hz), 1.41 (d, 3H, J = 6.6 Hz), 1.09 (d, 3H, J = 6.6 Hz), 1.06 (d, 3H, J = 6.6 Hz).
309		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (br s, 1H), 8.75 (s, 1H), 7.77 (s, 1H), 7.44–7.37 (m, 2H), 7.22–7.15 (m, 2H), 4.67 (d, 1H, J = 13.5 Hz), 4.49 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 3.40 (sep, 1H, J = 6.7 Hz), 1.54 (d, 3H, J = 6.7 Hz), 1.50 (s, 3H), 1.41 (d, 3H, J = 6.7 Hz), 1.29 (s, 9H).
310		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.66 (br s, 1H), 8.85 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.68–3.76 (m, 4H), 4.64 (d, 1H, J = 13.9 Hz), 4.47 (s, 2H), 4.46 (d, 1H, J = 13.9 Hz), 3.69 (sep, 1H, J = 6.7 Hz), 2.28–2.15 (m, 2H), 1.66 (s, 3H), 1.44 (d, 3H, J = 6.7 Hz), 1.43 (d, 3H, J = 6.7 Hz).
311		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.67 (br s, 1H), 8.81 (s, 1H), 7.45–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.71 (d, 1H, J = 14.0 Hz), 4.58 (d, 1H, J = 14.0 Hz), 4.47 (s, 2H), 3.75–3.40 (m, 9H), 1.66 (s, 3H), 1.53 (d, 3H, J = 6.6 Hz), 1.42 (d, 3H, J = 6.6 Hz).

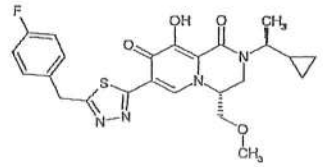
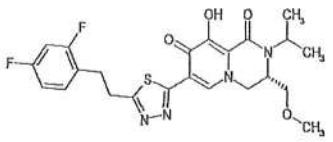
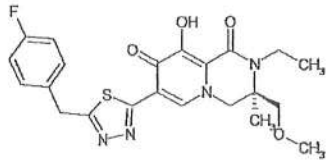
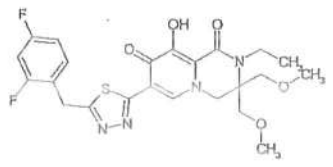
[0503]

[Table 1-87]

No.	structural formula	salt	^{1}H-NMR
312		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.99 (br s, 1H), 12.50 (br s, 1H), 8.83 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.13 (m, 2H), 4.78 (d, 1H, J = 14.0 Hz), 4.49 (d, 1H, J = 14.0 Hz), 4.47 (s, 2H), 3.85 (sep, 1H, J = 6.8 Hz), 1.66 (s, 3H), 1.49 (d, 3H, J = 6.8 Hz), 1.45 (d, 3H, J = 6.8 Hz).
313		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.88 (br s, 1H), 8.55 (s, 1H), 7.45-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.48 (s, 2H), 4.21 (d, 1H, J = 14.0 Hz), 3.96 (d, 1H, J = 14.0 Hz), 3.07 (s, 3H), 2.91 (s, 6H), 1.98 (s, 3H).
314		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (br s, 1H), 8.42 (s, 1H), 7.69 (s, 1H), 7.36-7.30 (m, 2H), 7.18-7.11 (m, 2H), 4.21 (s, 2H), 4.20 (d, 1H, J = 13.9 Hz), 3.91 (d, 1H, J = 13.9 Hz), 3.07 (s, 3H), 2.89 (s, 6H), 1.92 (s, 3H).
315		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.70 (br s, 1H), 8.84 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.16 (m, 2H), 4.80 (d, 1H, J = 13.9 Hz), 4.53 (d, 1H, J = 13.9 Hz), 4.47 (s, 2H), 3.45 (sep, 1H, J = 6.6 Hz), 3.08 (s, 6H), 1.65 (s, 3H), 1.49 (d, 3H, J = 6.6 Hz), 1.42 (d, 3H, J = 6.6 Hz).

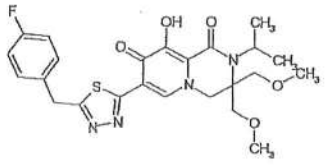
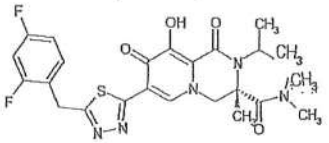
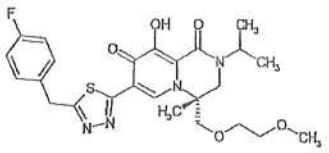
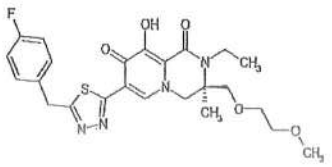
[0504]

[Table 1-88]

No.	structural formula	salt	^{1}H-NMR
316		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.80 (s, 1H), 7.45-7.39 (m, 2H), 7.23-7.15 (m, 2H), 5.06-4.97 (m, 1H), 4.48 (s, 2H), 3.94-3.91 (m, 2H), 3.90-3.80 (m, 1H), 3.72-3.58 (m, 2H), 3.26 (s, 3H), 1.23 (d, 3H, J = 6.8 Hz), 1.18-1.07 (m, 1H), 0.66-0.57 (m, 1H), 0.50-0.37 (m, 2H), 0.31-0.20 (m, 1H).
317		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.84 (s, 1H), 7.44-7.36 (m, 1H), 7.23-7.15 (m, 1H), 7.06-6.98 (m, 1H), 4.66 (dd, 1H, J = 13.6, 1.4 Hz), 4.48 (sep, 1H, J = 6.8 Hz), 4.35 (dd, 1H, J = 13.6, 3.6 Hz), 4.24-4.17 (m, 1H), 3.50 (dd, 1H, J = 10.4, 4.2 Hz), 3.44-3.37 (m, 3H), 3.22 (s, 3H), 3.09 (t, 2H, J = 7.5 Hz), 1.30 (d, 3H, J = 6.8 Hz), 1.29 (d, 3H, J = 6.8 Hz).
318		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.76 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.15 (m, 2H), 4.55 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 4.31 (d, 1H, J = 13.5 Hz), 3.71-3.59 (m, 1H), 3.56-3.42 (m, 3H), 3.21 (s, 3H), 1.37 (s, 3H), 1.20 (t, 3H, J = 7.1 Hz).
319		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.63 (br s, 1H), 8.77 (s, 1H), 7.58-7.48 (m, 1H), 7.33-7.25 (m, 1H), 7.16-7.08 (m, 1H), 4.52 (s, 2H), 4.49 (s, 2H), 3.63 (d, 2H, J = 10.6 Hz), 3.58 (q, 2H, J = 7.1 Hz), 3.54 (d, 2H, J = 10.6 Hz), 3.26 (s, 6H), 1.19 (t, 3H, J = 7.1 Hz).

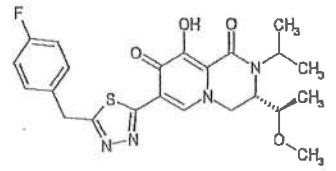
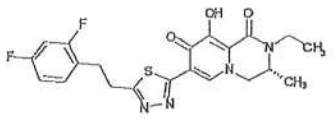
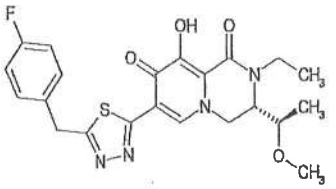
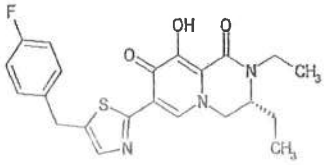
[0505]

[Table 1-89]

No.	structural formula	salt	^{1}H-NMR
320		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.74 (br s, 1H), 8.74 (s, 1H), 7.44–7.37 (m, 2H), 7.22–7.14 (m, 2H), 4.50 (s, 2H), 4.47 (s, 2H), 3.94 (sep, 1H, J = 6.6 Hz), 3.66 (d, 2H, J = 10.6 Hz), 3.51 (d, 2H, J = 10.6 Hz), 3.27 (s, 6H), 1.45 (d, 6H, J = 6.6 Hz).
321		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.71 (br s, 1H), 8.83 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.26 (m, 1H), 7.15–7.08 (m, 1H), 4.80 (d, 1H, J = 14.0 Hz), 4.54 (d, 1H, J = 14.0 Hz), 4.49 (s, 2H), 3.45 (sep, 1H, J = 6.7 Hz), 3.07 (s, 6H), 1.65 (s, 3H), 1.49 (d, 3H, J = 6.7 Hz), 1.42 (d, 3H, J = 6.7 Hz).
322		HCl	^{1}H-NMR (DMSO-d_6) δ : 13.25 (br s, 1H), 8.71 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.79 (sep, 1H, J = 6.8 Hz), 4.47 (s, 2H), 3.80–3.73 (m, 2H), 3.71–3.64 (m, 2H), 3.55–3.43 (m, 2H), 3.37–3.31 (m, 2H), 3.11 (s, 3H), 1.65 (s, 3H), 1.18 (d, 3H, J = 6.8 Hz), 1.18 (d, 3H, J = 6.8 Hz).
323		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.69 (br s, 1H), 8.73 (s, 1H), 7.44–7.38 (m, 2H), 7.23–7.15 (m, 2H), 4.55 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 4.31 (d, 1H, J = 13.5 Hz), 3.71–3.46 (m, 4H), 3.46–3.42 (m, 2H), 3.29–3.24 (m, 2H), 3.07 (s, 3H), 1.37 (s, 3H), 1.20 (t, 3H, J = 7.1 Hz).

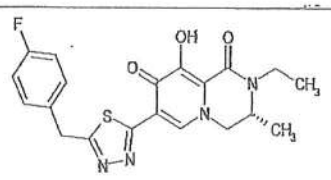
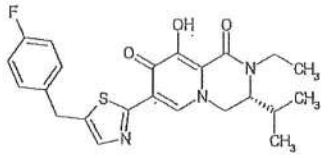
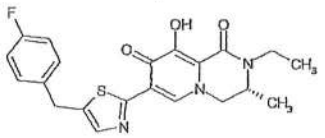
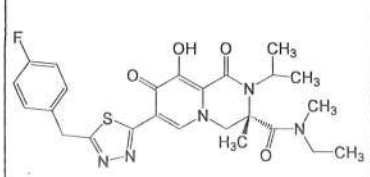
[0506]

[Table 1-90]

No.	structural formula	salt	^{1}H-NMR
324		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.52 (br s, 1H), 8.91 (s, 1H), 7.44-7.36 (m, 2H), 7.22-7.14 (m, 2H), 4.82 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 4.35 (sep, 1H, J = 6.8 Hz), 4.30 (dd, 1H, J = 13.5, 4.5 Hz), 4.01-3.96 (m, 1H), 3.64-3.55 (m, 1H), 3.05 (s, 3H), 1.35 (d, 3H, J = 6.8 Hz), 1.33 (d, 3H, J = 6.8 Hz), 1.19 (d, 3H, J = 6.2 Hz).
325		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.64 (br s, 1H), 8.83 (s, 1H), 7.44-7.35 (m, 1H), 7.23-7.15 (m, 1H), 7.05-6.98 (m, 1H), 4.50-4.37 (m, 2H), 4.16-4.07 (m, 1H), 3.88-3.76 (m, 1H), 3.40 (t, 2H, J = 7.5 Hz), 3.30-3.19 (m, 1H), 3.10 (t, 2H, J = 7.5 Hz), 1.24 (d, 3H, J = 6.6 Hz), 1.20 (t, 3H, J = 7.2 Hz).
326		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.50 (br s, 1H), 8.91 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.15 (m, 2H), 4.80 (d, 1H, J = 13.5 Hz), 4.47 (s, 2H), 4.36 (dd, 1H, J = 13.5, 4.6 Hz), 4.00-3.87 (m, 2H), 3.66-3.58 (m, 1H), 3.31-3.18 (m, 1H), 3.08 (s, 3H), 1.21 (t, 3H, J = 7.1 Hz), 1.16 (d, 3H, J = 6.4 Hz).
327		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.42 (br s, 1H), 8.76 (s, 1H), 7.67 (s, 1H), 7.36-7.30 (m, 2H), 7.19-7.11 (m, 2H), 4.61 (d, 1H, J = 13.2 Hz), 4.33 (dd, 1H, J = 13.2, 3.7 Hz), 4.20 (s, 2H), 3.95-3.83 (m, 1H), 3.88-3.80 (m, 1H), 3.22-3.11 (m, 1H), 1.74-1.62 (m, 1H), 1.50-1.36 (m, 1H), 1.20 (t, 3H, J = 7.2 Hz), 0.91 (t, 3H, J = 7.4 Hz).

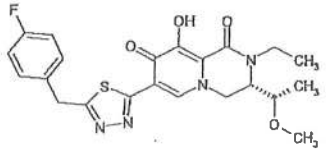
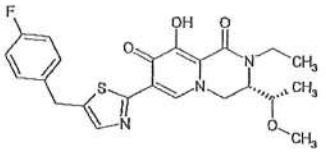
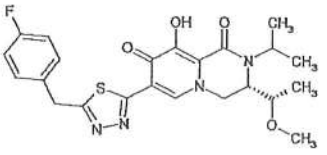
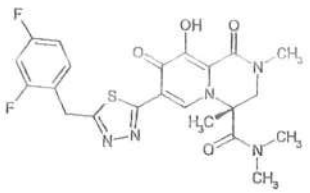
[0507]

[Table 1-91]

No.	structural formula	salt	^{1}H-NMR
328		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.62 (br s, 1H), 8.84 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.49-4.35 (m, 2H), 4.47 (s, 2H), 4.15-4.07 (m, 1H), 3.87-3.75 (m, 1H), 3.31-3.18 (m, 1H), 1.26-1.14 (m, 6H).
329		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.33 (br s, 1H), 8.82 (s, 1H), 7.67 (s, 1H), 7.37-7.30 (m, 2H), 7.18-7.11 (m, 2H), 4.71 (d, 1H, J = 13.9 Hz), 4.32 (dd, 1H, J = 13.9, 4.4 Hz), 4.20 (s, 2H), 4.07-3.94 (m, 1H), 3.75-3.69 (m, 1H), 3.16-3.04 (m, 1H), 1.97-1.85 (m, 1H), 1.20 (t, 3H, J = 7.1 Hz), 0.98 (d, 3H, J = 6.8 Hz), 0.78 (d, 3H, J = 6.8 Hz).
330		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.52 (br s, 1H), 8.66 (s, 1H), 7.67 (s, 1H), 7.37-7.30 (m, 2H), 7.19-7.11 (m, 2H), 4.46-4.33 (m, 2H), 4.20 (s, 2H), 4.14-4.04 (m, 1H), 3.86-3.75 (m, 1H), 3.29-3.18 (m, 1H), 1.22 (d, 3H, J = 6.6 Hz), 1.19 (t, 3H, J = 7.2 Hz).
331		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.68 (br s, 1H), 8.83 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.77 (d, 1H, J = 13.7 Hz), 4.55 (d, 1H, J = 13.7 Hz), 4.47 (s, 2H), 4.16-3.03 (m, 5H), 3.44 (sep, 1H, J = 6.6 Hz), 1.63 (s, 3H), 1.49 (d, 3H, J = 6.6 Hz), 1.42 (d, 3H, J = 6.6 Hz), 1.09-1.00 (m, 3H).

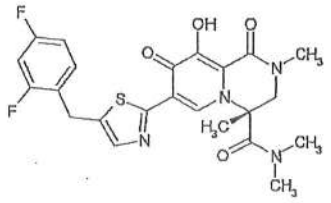
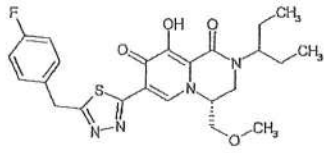
[0508]

[Table 1-92]

No.	structural formula	salt	^{1}H-NMR
332		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.50 (br s, 1H), 8.95 (s, 1H), 7.44–7.36 (m, 2H), 7.22–7.15 (m, 2H), 4.69 (dd, 1H, J = 14.0, 1.5 Hz), 4.47 (s, 2H), 4.39 (dd, 1H, J = 14.0, 4.2 Hz), 4.04–3.98 (m, 1H), 3.97–3.92 (m, 1H), 3.51–3.43 (m, 1H), 3.26–3.18 (m, 1H), 3.18 (s, 3H), 1.19 (t, 3H, J = 7.2 Hz), 1.10 (d, 3H, J = 6.2 Hz).
333		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.76 (s, 1H), 7.67 (s, 1H), 7.36–7.30 (m, 2H), 7.18–7.11 (m, 2H), 4.64 (dd, 1H, J = 13.6, 1.5 Hz), 4.37 (dd, 1H, J = 13.6, 4.0 Hz), 4.20 (s, 2H), 4.06–3.97 (m, 1H), 3.95–3.90 (m, 1H), 3.51–3.40 (m, 1H), 3.27–3.19 (m, 1H), 3.19 (s, 3H), 1.19 (t, 3H, J = 6.8 Hz), 1.08 (d, 3H, J = 6.4 Hz).
334		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.47 (br s, 1H), 8.96 (s, 1H), 7.44–7.38 (m, 2H), 7.22–7.15 (m, 2H), 4.68 (dd, 1H, J = 13.9, 1.3 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J = 13.9, 3.5 Hz), 4.14–4.06 (m, 1H), 3.98–3.93 (m, 1H), 3.41 (sep, 1H, J = 6.7 Hz), 3.24 (s, 3H), 1.39 (d, 3H, J = 6.7 Hz), 1.34 (d, 3H, J = 6.7 Hz), 1.02 (d, 3H, J = 6.3 Hz).
335		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.85 (br s, 1H), 8.54 (s, 1H), 7.58–7.50 (m, 1H), 7.33–7.25 (m, 1H), 7.15–7.08 (m, 1H), 4.49 (s, 2H), 4.21 (d, 1H, J = 13.9 Hz), 3.97 (d, 1H, J = 13.9 Hz), 3.07 (s, 3H), 2.91 (s, 6H), 1.97 (s, 3H).

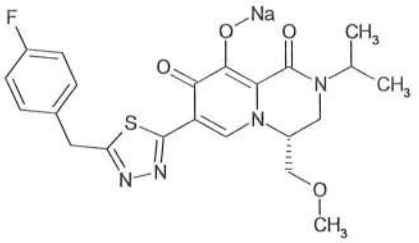
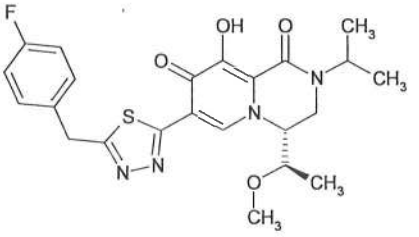
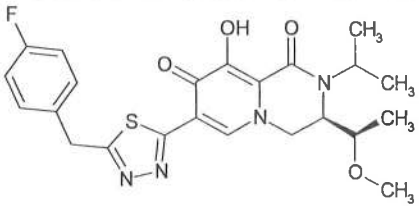
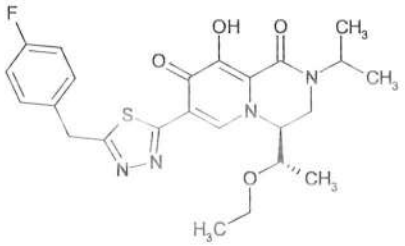
[0509]

[Table 1-93]

No.	structural formula	salt	^{1}H-NMR
336		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.75 (br s, 1H), 8.46 (s, 1H), 7.69 (s, 1H), 7.50–7.42 (m, 1H), 7.29–7.21 (m, 1H), 7.11–7.05 (m, 1H), 4.22 (s, 2H), 4.21 (d, 1H, J = 14.0 Hz), 3.93 (d, 1H, J = 14.0 Hz), 3.07 (s, 3H), 2.89 (s, 6H), 1.93 (s, 3H).
337		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.86 (br s, 1H), 8.83 (s, 1H), 7.45–7.39 (m, 2H), 7.23–7.16 (m, 2H), 5.02–4.94 (m, 1H), 4.47 (s, 2H), 4.40–4.29 (m, 1H), 3.83–3.56 (m, 4H), 3.26 (s, 3H), 1.64–1.43 (m, 4H), 0.92–0.78 (m, 6H).

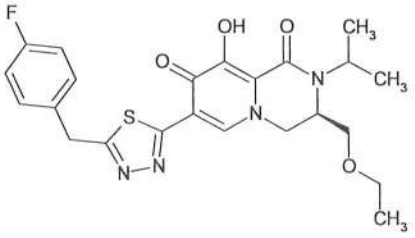
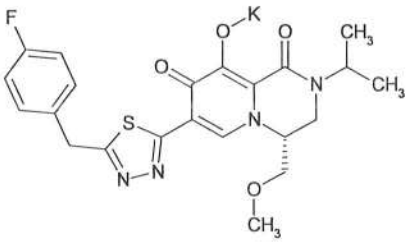
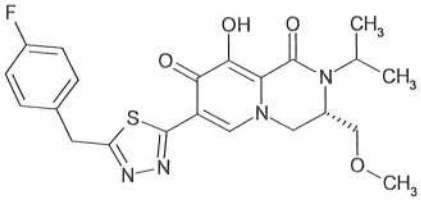
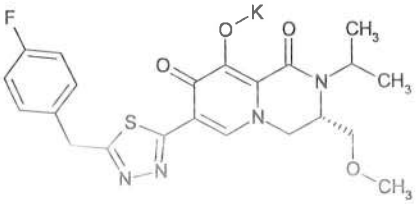
[0510]

[Table 1-94]

No.	structural formula	salt	^{1}H-NMR
338		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.92 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.78 (quint, 1H, J = 6.9 Hz), 4.71 (ddd, 1H, J = 6.4, 4.0, 1.6 Hz), 4.47 (s, 2H), 3.87 (dd, 1H, J = 13.7, 1.6 Hz), 3.78 (dd, 1H, J = 13.7, 4.0 Hz), 3.58 (dq, 1H, J = 6.4, 6.0 Hz), 3.22 (s, 3H), 1.19 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.9 Hz), 1.03 (d, 3H, J = 6.0 Hz).
339			^{1}H-NMR (DMSO-d_6) δ: 8.21 (s, 1H), 7.42-7.39 (m, 2H), 7.20-7.16 (m, 2H), 4.85 (quint, 1H, J = 6.6 Hz), 4.71-4.65 (m, 1H), 4.41 (s, 2H), 3.58-3.53 (m, 3H), 3.48-3.44 (m, 1H), 3.24 (s, 3H), 1.09 (d, 6H, J = 6.6 Hz).
340		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.72 (s, 1H), 7.44-7.41 (m, 2H), 7.21-7.17 (m, 2H), 4.77 (sep, 1H, J = 6.6 Hz), 4.65 (ddd, 1H, J = 8.2, 4.1, 0.9 Hz), 4.47 (s, 2H), 3.88 (dd, 1H, J = 14.0, 4.1 Hz), 3.76 (dd, 1H, J = 14.0, 0.9 Hz), 3.52 (dq, 1H, J = 8.2, 6.2 Hz), 3.03 (s, 3H), 1.21 (d, 3H, J = 6.2 Hz), 1.20 (d, 3H, J = 6.6 Hz), 1.17 (d, 3H, J = 6.6 Hz).
341		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.95 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.68 (dd, 1H, J = 13.8, 1.5 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J = 13.8, 3.9 Hz), 4.10 (quint, 1H, J = 6.6 Hz), 3.96 (ddd, 1H, J = 6.6, 3.9, 1.5 Hz), 3.41 (dq, 1H, J = 6.6, 6.4 Hz), 3.24 (s, 3H), 1.39 (d, 3H, J = 6.6 Hz), 1.34 (d, 3H, J = 6.6 Hz), 1.02 (d, 3H, J = 6.4 Hz).
342		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.72 (s, 1H), 7.45-7.41 (m, 3H), 7.22-7.17 (m, 2H), 4.77 (quint, 1H, J = 6.8 Hz), 4.60 (ddd, 1H, J = 8.4, 4.2, 0.9 Hz), 4.47 (s, 2H), 3.88 (dd, 1H, J = 14.3, 4.2 Hz), 3.74 (dd, 1H, J = 14.3, 0.9 Hz), 3.56 (dq, 1H, J = 8.4, 6.2 Hz), 3.41 (dq, 1H, J = 9.5, 7.1 Hz), 2.91 (dq, 1H, J = 9.5, 7.1 Hz), 1.22 (d, 3H, J = 6.2 Hz), 1.20 (d, 3H, J = 6.8 Hz), 1.17 (d, 3H, J = 6.8 Hz), 0.75 (t, 3H, J = 7.1 Hz).

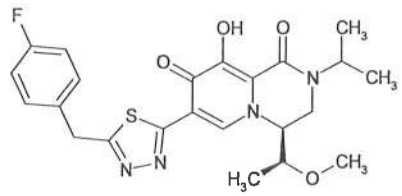
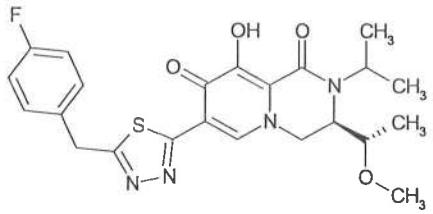
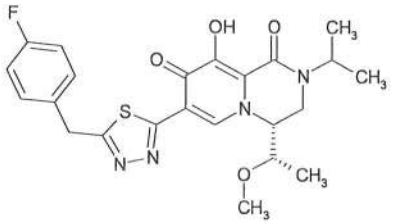
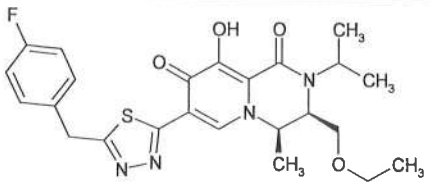
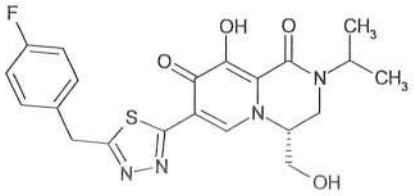
[0511]

[Table 1-95]

No.	structural formula	salt	^{1}H-NMR
343		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.85 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.15 (m, 2H), 4.66 (dd, 1H, J = 12.4, 1.5 Hz), 4.48 (sep, 1H, J = 6.6 Hz), 4.47 (s, 2H), 4.35 (dd, 1H, J = 13.2, 3.7 Hz), 4.20-4.16 (m, 1H), 3.54 (dd, 1H, J = 10.5, 4.1 Hz), 3.45-3.30 (m, 3H), 1.30 (d, 3H, J = 6.6 Hz), 1.28 (d, 3H, J = 6.6 Hz), 0.96 (t, 3H, J = 6.9 Hz).
344			^{1}H-NMR (DMSO-d_6) δ: 12.81 (s, 1H), 8.80 (s, 1H), 7.44-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.99-4.95 (m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.7, 3.9 Hz), 3.75 (dd, 1H, J = 13.9, 1.6 Hz), 3.63 (dd, 1H, J = 10.2, 6.0 Hz), 3.57 (dd, 1H, J = 10.2, 7.7 Hz), 3.25 (s, 3H), 1.16 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
345			^{1}H-NMR (DMSO-d_6) δ: 8.10 (s, 1H), 7.41-7.36 (m, 2H), 7.20-7.14 (m, 2H), 4.83 (quint, 1H, J = 6.7 Hz), 4.62-4.57 (m, 1H), 4.38 (s, 2H), 3.57-3.44 (m, 4H), 3.25 (s, 3H), 1.05 (d, 6H, J = 6.7 Hz).
346			^{1}H-NMR (DMSO-d_6) δ: 12.44 (br s, 1H), 8.85 (s, 1H), 7.44-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.70-4.61 (m, 1H), 4.54-4.41 (m, 1H), 4.47 (s, 2H), 4.39-4.30 (m, 1H), 4.25-4.14 (m, 1H), 3.53-3.34 (m, 2H), 3.21 (s, 3H), 1.30 (d, 3H, J = 6.3 Hz), 1.28 (d, 3H, J = 6.3 Hz).
347			^{1}H-NMR (DMSO-d_6) δ: 8.02 (br s, 1H), 7.42-7.33 (m, 2H), 7.21-7.13 (m, 2H), 4.73-4.59 (m, 1H), 4.38 (s, 2H), 4.34-4.22 (m, 1H), 4.07-3.96 (m, 1H), 3.89-3.78 (m, 1H), 3.30-3.05 (m, 2H), 3.24 (s, 3H), 1.13 (d, 3H, J = 7.0 Hz), 1.06 (d, 3H, J = 7.0 Hz).

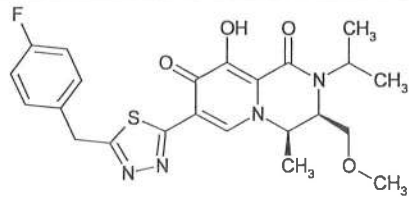
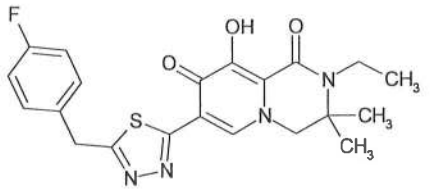
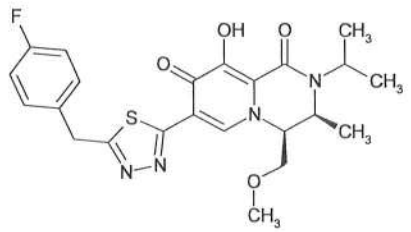
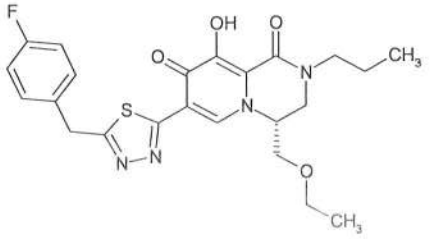
[0512]

[Table 1-96]

No.	structural formula	salt	^{1}H-NMR
348		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.72 (s, 1H), 7.47-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.83-4.71 (m, 1H), 4.69-4.60 (m, 1H), 4.47 (s, 2H), 3.88 (dd, 1H, J = 14.1, 3.7 Hz), 3.81-3.71 (m, 1H), 3.56-3.47 (m, 1H), 3.03 (s, 3H), 1.24-1.13 (m, 9H).
349		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.52 (s, 1H), 8.90 (s, 1H), 7.40 (dd, 2H, J = 8.3, 5.6 Hz), 7.17 (dd, 2H, J = 8.3, 8.4 Hz), 4.81 (d, 1H, J = 14.1 Hz), 4.46 (s, 2H), 4.38-4.27 (m, 2H), 3.98 (s, 1H), 3.62-3.56 (m, 1H), 3.04 (s, 3H), 1.33 (t, 6H, J = 6.0 Hz), 1.18 (d, 3H, J = 7.0 Hz).
350		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.91 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.15 (m, 2H), 4.78 (quint, 1H, J = 6.9 Hz), 4.70 (dd, 1H, J = 6.4, 4.2 Hz), 4.47 (s, 2H), 3.86 (d, 1H, J = 13.7 Hz), 3.77 (dd, 1H, J = 13.7, 4.2 Hz), 3.58 (dq, 1H, J = 6.4, 6.0 Hz), 3.21 (s, 3H), 1.19 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.9 Hz), 1.02 (d, 3H, J = 6.0 Hz).
351		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.56 (s, 1H), 7.44-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.70-4.60 (m, 1H), 4.50-4.38 (m, 1H), 4.47 (s, 2H), 4.08-4.02 (m, 1H), 3.61 (dd, 1H, J = 11.1, 3.7 Hz), 3.53 (dd, 1H, J = 11.1, 3.9 Hz), 3.27 (q, 2H, J = 7.4 Hz), 1.75 (d, 3H, J = 6.5 Hz), 1.32 (t, 6H, J = 7.0 Hz), 0.82 (t, 3H, J = 7.0 Hz).
352			^{1}H-NMR (DMSO-d_6) δ: 12.79 (br s, 1H), 8.74 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.15 (m, 2H), 5.32-5.23 (m, 1H), 4.81-4.65 (m, 2H), 4.47 (s, 2H), 3.86-3.64 (m, 3H), 3.60-3.51 (m, 1H), 1.16 (d, 3H, J = 6.7 Hz), 1.15 (d, 3H, J = 6.7 Hz).

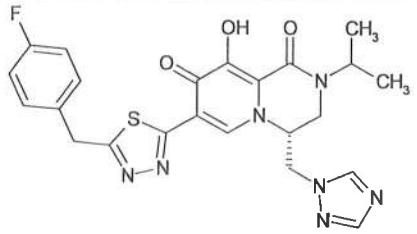
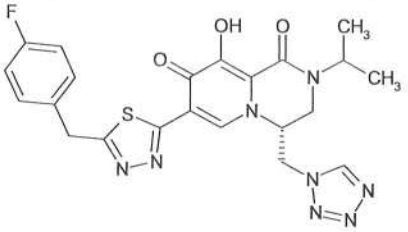
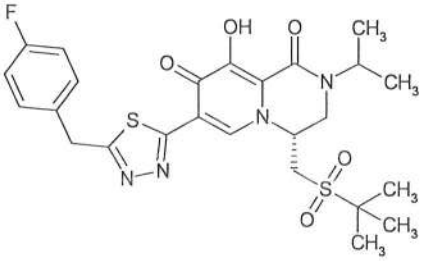
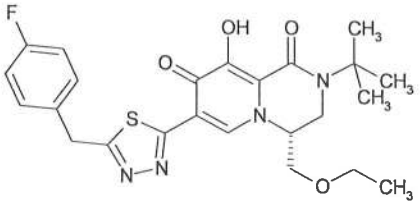
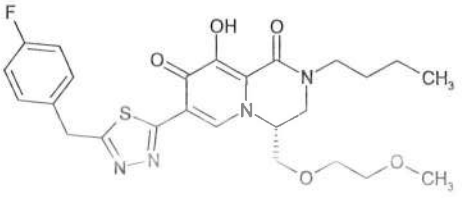
[0513]

[Table 1-97]

No.	structural formula	salt	^{1}H-NMR
353		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.56 (s, 1H), 7.44-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.70-4.59 (m, 1H), 4.49-4.37 (m, 1H), 4.47 (s, 2H), 4.11-4.03 (m, 1H), 3.59-3.46 (m, 2H), 3.11 (s, 3H), 1.75 (d, 3H, J = 6.5 Hz), 1.32 (t, 6H, J = 6.5 Hz).
354		HBr	^{1}H-NMR (DMSO-D_6) δ: 8.80 (s, 1H), 7.43-7.37 (m, 2H), 7.21-7.14 (m, 2H), 4.70-4.64 (m, 1H), 4.55-4.44 (m, 3H), 4.33 (dd, 1H, J = 13.3, 3.6 Hz), 3.99-3.93 (m, 1H), 3.56 (dd, 1H, J = 11.4, 3.7 Hz), 3.35 (dd, 1H, J = 11.4, 8.1 Hz), 1.28 (d, 3H, J = 6.7 Hz), 1.27 (d, 3H, J = 6.7 Hz).
355		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.76 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.47 (s, 2H), 4.34 (s, 2H), 3.55 (q, 2H, J = 7.1 Hz), 1.36 (s, 6H), 1.19 (t, 3H, J = 7.1 Hz).
356		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (s, 1H), 8.77 (s, 1H), 7.42-7.36 (m, 2H), 7.21-7.14 (m, 2H), 4.71 (ddd, 1H, J = 8.0, 2.2, 2.0 Hz), 4.56 (quint, 1H, J = 6.9 Hz), 4.46 (s, 2H), 4.19-4.09 (m, 2H), 3.93 (dd, 1H, J = 11.7, 2.2 Hz), 3.45 (s, 3H), 1.29 (d, 3H, J=6.9 Hz), 1.27 (d, 3H, J=6.9 Hz), 1.04 (d, 3H, J = 6.5 Hz).
357		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (s, 1H), 8.80 (s, 1H), 7.41 (tt, 2H, J = 8.7, 3.1 Hz), 7.18 (tt, 2H, J = 8.9, 2.5 Hz), 4.94-4.88 (m, 1H), 4.46 (s, 2H), 4.06 (dd, 1H, J = 13.8, 4.3 Hz), 3.73-3.67 (m, 2H), 3.64-3.52 (m, 2H), 3.49-3.27 (m, 3H), 1.63-1.53 (m, 2H), 1.01 (t, 3H, J = 7.0 Hz), 0.89 (t, 3H, J = 8.2 Hz).

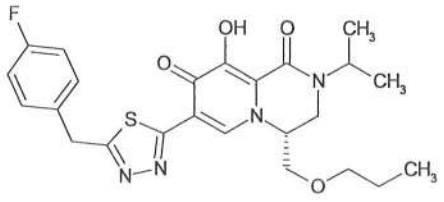
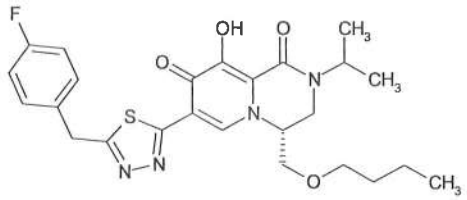
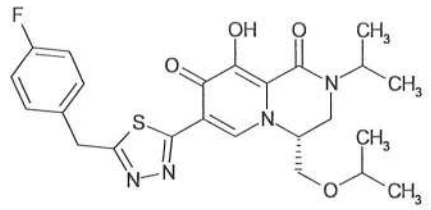
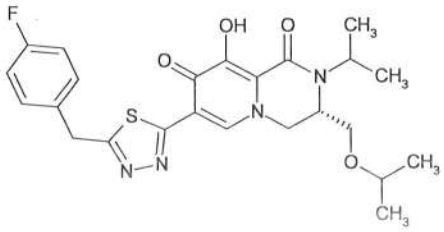
[0514]

[Table 1-98]

No.	structural formula	salt	^{1}H-NMR
358		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.90 (br s, 1H), 8.37 (s, 1H), 8.07 (s, 1H), 8.00 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.13 (m, 2H), 5.28-5.18 (m, 1H), 4.89-4.60 (m, 3H), 4.44 (s, 2H), 3.98-3.83 (m, 2H), 1.25 (d, 3H, J = 6.7 Hz), 1.18 (d, 3H, J = 6.7 Hz).
359		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.88 (br s, 1H), 8.99 (s, 1H), 8.20 (s, 1H), 7.46-7.37 (m, 2H), 7.24-7.14 (m, 2H), 5.48-5.38 (m, 1H), 5.37-5.19 (m, 2H), 4.84-4.72 (m, 1H), 4.45 (s, 2H), 3.96 (d, 2H, J = 3.0 Hz), 1.25 (d, 3H, J = 6.7 Hz), 1.17 (d, 3H, J = 6.7 Hz).
360		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.75 (s, 1H), 7.45-7.37 (m, 2H), 7.22-7.14 (m, 2H), 5.52-5.41 (m, 1H), 4.81-4.71 (m, 1H), 4.47 (s, 2H), 3.98-3.81 (m, 2H), 3.66 (d, 2H, J = 7.0 Hz), 1.29 (s, 9H), 1.21 (d, 3H, J = 6.5 Hz), 1.15 (d, 3H, J = 6.5 Hz).
361		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.94 (s, 1H), 8.80 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.15 (m, 2H), 4.89-4.85 (m, 1H), 4.47 (s, 2H), 3.96 (dd, 1H, J = 14.0, 1.5 Hz), 3.87 (dd, 1H, J = 14.0, 3.0 Hz), 3.70 (dd, 1H, J = 10.2, 6.7 Hz), 3.62 (dd, 1H, J = 10.2, 7.5 Hz), 3.50-3.41 (m, 2H), 1.49 (s, 9H), 1.05 (t, 3H, J = 6.9 Hz).
362		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.80 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.94-4.89 (m, 1H), 4.47 (s, 2H), 4.06 (dd, 1H, J = 13.6, 4.3 Hz), 3.77-3.72 (m, 2H), 3.70-3.46 (m, 5H), 3.38-3.31 (m, 3H), 3.11 (s, 3H), 1.60-1.52 (m, 2H), 1.37-1.27 (m, 2H), 0.92 (t, 3H, J = 7.4 Hz).

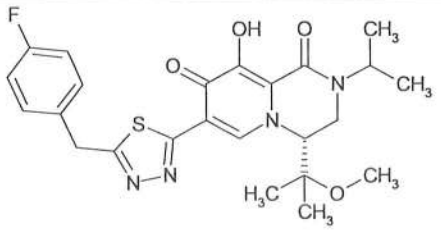
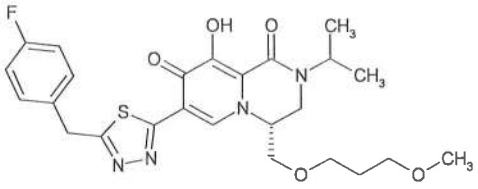
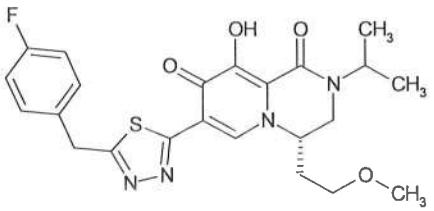
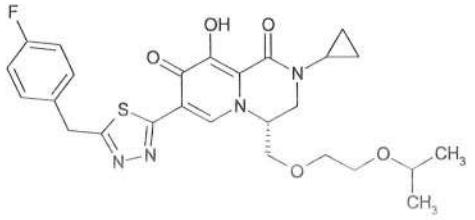
[0515]

[Table 1-99]

No.	structural formula	salt	^{1}H-NMR
363		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.82 (s, 1H), 7.46-7.38 (m, 2H), 7.24-7.14 (m, 2H), 5.01-4.91 (br m, 1H), 4.77 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.88-3.54 (m, 4H), 3.41-3.24 (m, 2H), 1.41 (td, 2H, J = 13.9, 7.2 Hz), 1.17 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz), 0.74 (t, 3H, J = 7.2 Hz).
364		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.80 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.13 (m, 2H), 4.99-4.89 (m, 1H), 4.76 (sep, 1H, J = 7.0), 4.46 (s, 2H), 3.88-3.52 (m, 4H), 3.43-3.24 (m, 2H), 1.40-1.29 (m, 2H), 1.22-1.09 (m, 8H), 0.69 (t, 3H, J = 7.3 Hz).
365		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.83 (s, 1H), 7.46-7.38 (m, 2H), 7.23-7.15 (m, 2H), 4.94-4.71 (m, 2H), 4.47 (s, 2H), 3.85-3.45 (m, 5H), 1.21-1.12 (m, 6H), 1.02 (d, 3H, J = 6.0 Hz), 0.96 (d, 3H, J = 6.3 Hz).
366			^{1}H-NMR (DMSO-d_6) δ: 12.77 (s, 1H), 8.80 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.14 (m, 2H), 4.91-4.83 (m, 1H), 4.83-4.73 (m, 2H), 4.47 (s, 2H), 3.86 (dd, 1H, J = 14.1, 3.5 Hz), 3.76-3.67 (m, 1H), 3.54-3.43 (m, 1H), 1.96-1.71 (m, 2H), 1.19 (d, 3H, J = 7.0 Hz), 1.16 (d, 3H, J = 6.7 Hz).
367		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 8.84 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.69-4.63 (m, 1H), 4.53-4.44 (m, 3H), 4.35 (dd, 1H, J = 13.3, 4.0 Hz), 4.18-4.11 (m, 1H), 3.55 (dd, 1H, J = 10.5, 3.6 Hz), 3.48-3.39 (m, 2H), 1.30 (d, 3H, J = 6.9 Hz), 1.28 (d, 3H, J = 6.9 Hz), 0.95-0.90 (m, 6H).

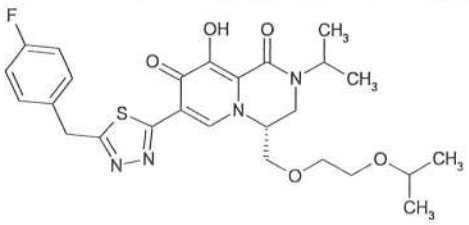
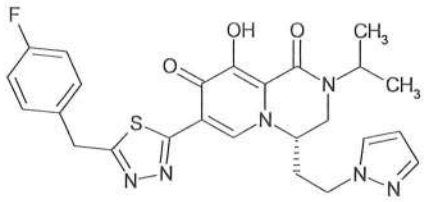
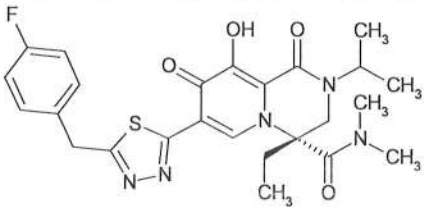
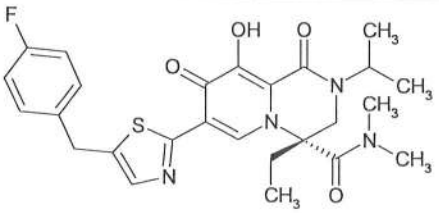
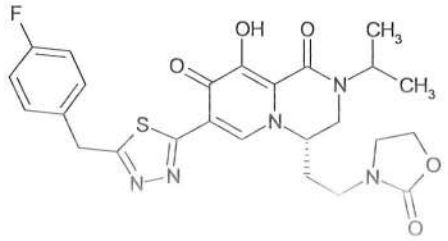
[0516]

[Table 1-100]

No.	structural formula	salt	^{1}H-NMR
368		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.78 (s, 1H), 7.44-7.40 (m, 2H), 7.22-7.16 (m, 2H), 4.74-4.70 (m, 1H), 4.74 (quint, 1H, J = 7.1 Hz), 4.47 (s, 2H), 3.91-3.82 (m, 2H), 3.05 (s, 3H), 1.20 (d, 3H, J = 7.1 Hz), 1.19 (s, 3H), 1.18 (d, 3H, J = 7.1 Hz), 1.10 (s, 3H).
369		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.81 (s, 1H), 7.44-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.95 (s, 1H), 4.80-4.73 (m, 1H), 4.47 (s, 2H), 3.85 (dd, 1H, J = 13.7, 4.0 Hz), 3.75 (d, 1H, J = 13.7 Hz), 3.67 (dd, 1H, J = 10.3, 5.4 Hz), 3.58 (dd, 1H, J = 10.3, 7.7 Hz), 3.45 (dt, 1H, J = 11.4, 4.6 Hz), 3.34 (dt, 1H, J = 11.4, 4.8 Hz), 3.20-3.13 (m, 2H), 3.00 (s, 3H), 1.64-1.58 (m, 2H), 1.16 (dd, 6H, J = 6.9, 2.4 Hz).
370		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.72 (s, 1H), 7.46-7.38 (m, 2H), 7.24-7.15 (m, 2H), 4.91-4.81 (m, 1H), 4.84-4.72 (m, 1H), 4.47 (s, 2H), 3.89-3.65 (m, 2H), 3.45-3.35 (m, 1H), 3.20-3.07 (m, 1H), 3.18 (s, 3H), 2.07-1.93 (m, 1H), 1.93-1.80 (m, 1H), 1.18 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
371		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.75 (s, 1H), 7.47-7.37 (m, 2H), 7.24-7.15 (m, 2H), 4.91-4.73 (m, 2H), 4.47 (s, 2H), 3.90-3.63 (m, 2H), 3.58-3.01 (m, 4H), 2.11-1.79 (m, 2H), 1.19 (d, 3H, J = 7.2 Hz), 1.16 (d, 3H, J = 7.2 Hz), 1.03 (t, 3H, J = 7.2 Hz).
372		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (br s, 1H), 8.80 (s, 1H), 7.44-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.93-4.84 (m, 1H), 4.47 (s, 2H), 4.04 (dd, 1H, J = 13.7, 4.0 Hz), 3.69 (dd, 1H, J = 10.5, 5.6 Hz), 3.66-3.59 (m, 2H), 3.53-3.32 (m, 5H), 2.93-2.85 (m, 1H), 0.96-0.69 (m, 4H), 0.93 (d, 3H, J = 6.0 Hz), 0.90 (d, 3H, J = 6.0 Hz).

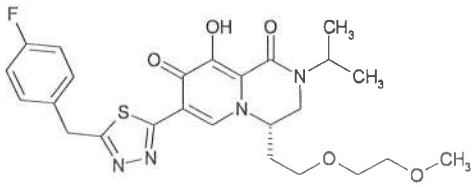
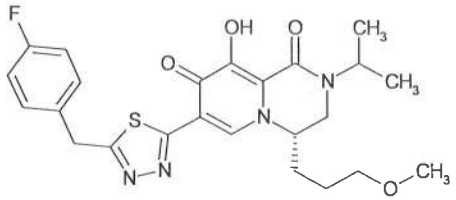
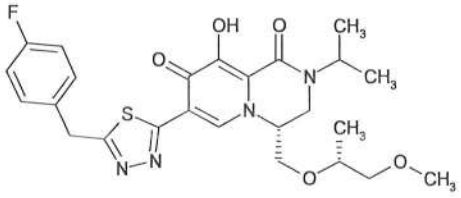
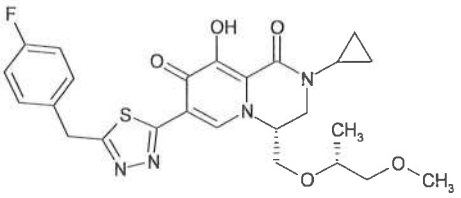
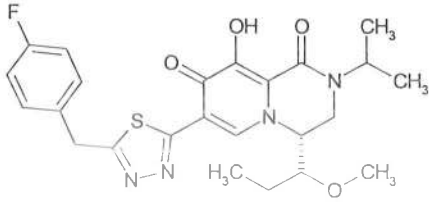
[0517]

[Table 1-101]

No.	structural formula	salt	^{1}H-NMR
373		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.80 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 5.00-4.91 (m, 1H), 4.77 (sep, 1H, J = 6.9 Hz), 4.47 (s, 2H), 3.84 (dd, 1H, J = 13.7, 4.0 Hz), 3.80-3.74 (m, 1H), 3.71 (dd, 1H, J = 10.3, 5.8 Hz), 3.65 (dd, 1H, J = 10.3, 7.9 Hz), 3.54-3.32 (m, 5H), 1.17 (d, 3H, J = 6.9 Hz), 1.16 (d, 3H, J = 6.9 Hz), 0.92 (d, 3H, J = 6.0 Hz), 0.89 (d, 3H, J = 6.0 Hz).
374		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.89 (s, 1H), 7.70 (d, 1H, J = 2.2 Hz), 7.45 (d, 1H, J = 1.8 Hz), 7.44-7.39 (m, 2H), 7.22-7.16 (m, 2H), 6.20 (dd, 1H, J = 2.2, 1.8 Hz), 4.86-4.82 (m, 1H), 4.78 (quint, 1H, J = 7.1 Hz), 4.47 (s, 2H), 4.26-4.14 (m, 2H), 3.84 (dd, 1H, J = 13.6, 3.6 Hz), 3.68 (dd, 1H, J = 13.6, 0.9 Hz), 2.27-2.20 (m, 2H), 1.18 (d, 3H, J = 7.1 Hz), 1.14 (d, 3H, J = 7.1 Hz).
375		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.19 (br s, 1H), 8.41 (s, 1H), 7.46-7.38 (m, 2H), 7.23-7.14 (m, 2H), 4.80-4.68 (m, 1H), 4.47 (s, 2H), 4.08 (d, 1H, J = 14.1 Hz), 3.81 (d, 1H, J = 14.1 Hz), 2.93 (s, 6H), 2.61-2.11 (m, 2H), 1.19 (d, 3H, J = 7.0 Hz), 1.16 (d, 3H, J = 7.0 Hz), 0.91 (t, 3H, J = 7.2 Hz).
376		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.09 (br s, 1H), 8.30 (s, 1H), 7.70 (s, 1H), 7.38-7.28 (m, 2H), 7.19-7.10 (m, 2H), 4.80-4.69 (m, 1H), 4.20 (s, 2H), 4.06 (d, 1H, J = 14.1 Hz), 3.78 (d, 1H, J = 14.1 Hz), 2.91 (s, 6H), 2.47-2.07 (m, 2H), 1.22-1.12 (m, 6H), 0.87 (t, 3H, J = 7.2 Hz).
377		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.96 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.87-4.80 (m, 1H), 4.80 (quint, 1H, J = 6.6 Hz), 4.47 (s, 2H), 4.23 (t, 2H, J = 7.9 Hz), 3.87-3.82 (m, 1H), 3.76-3.73 (m, 1H), 3.57-3.46 (m, 2H), 3.33-3.25 (m, 1H), 3.19-3.11 (m, 1H), 1.95 (dt, 2H, J = 7.1, 7.9 Hz), 1.22 (d, 3H, J = 6.6 Hz), 1.16 (d, 3H, J = 6.6 Hz).

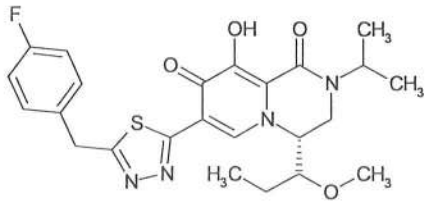
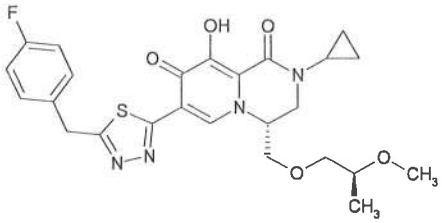
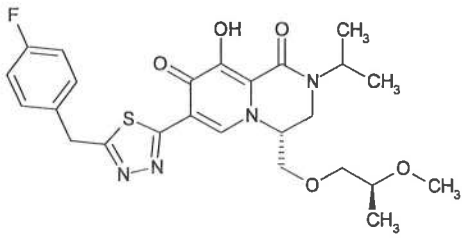
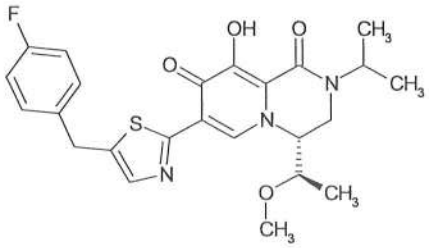
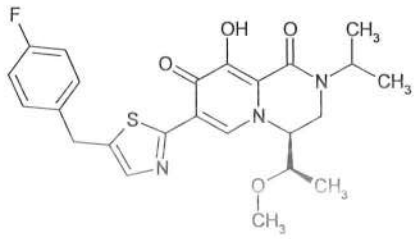
[0518]

[Table 1-102]

No.	structural formula	salt	^{1}H-NMR
378		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (br s, 1H), 8.75 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.88-4.83 (m, 1H), 4.78 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.85 (dd, 1H, J = 13.6, 3.6 Hz), 3.73 (dd, 1H, J = 13.6, 0.9 Hz), 3.53-3.48 (m, 1H), 3.45-3.31 (m, 4H), 3.29-3.18 (m, 1H), 3.15 (s, 3H), 2.04-1.96 (m, 1H), 1.91-1.83 (m, 1H), 1.19 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
379		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.78 (br s, 1H), 8.91 (s, 1H), 7.44-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.83-4.81 (m, 1H), 4.79 (sep, 1H, J = 6.7 Hz), 4.47 (s, 2H), 3.83 (dd, 1H, J = 13.8, 3.6 Hz), 3.72 (dd, 1H, J = 13.8, 1.5 Hz), 3.35-3.22 (m, 2H), 3.18 (s, 3H), 1.81-1.71 (m, 1H), 1.70-1.58 (m, 2H), 1.37-1.33 (m, 1H), 1.18 (d, 3H, J = 6.7 Hz), 1.16 (d, 3H, J = 6.7 Hz).
380		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.83 (s, 1H), 7.46-7.39 (m, 2H), 7.23-7.15 (m, 2H), 4.92-4.83 (br m, 1H), 4.81-4.70 (m, 1H), 4.47 (s, 2H), 3.85-3.62 (m, 4H), 3.59-3.48 (m, 1H), 3.26-3.18 (m, 2H), 3.17 (s, 3H), 1.21-1.12 (m, 6H), 0.91 (d, 3H, J = 6.5 Hz).
381		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.85 (br s, 1H), 8.83 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.15 (m, 2H), 4.86-4.76 (br m, 1H), 4.47 (s, 2H), 4.02 (dd, 1H, J = 13.4, 4.2 Hz), 3.77-3.58 (m, 3H), 3.57-3.48 (m, 1H), 3.26-3.19 (m, 2H), 3.18 (s, 3H), 2.93-2.84 (m, 1H), 0.92 (d, 3H, J = 6.3 Hz), 0.91-0.70 (m, 4H).
382		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.71 (s, 1H), 7.44-7.42 (m, 2H), 7.21-7.17 (m, 2H), 4.78 (quint, 1H, J = 6.9 Hz), 4.70 (dd, 1H, J = 9.0, 3.7 Hz), 4.47 (s, 2H), 3.87 (dd, 1H, J = 14.5, 3.7 Hz), 3.74 (d, 1H, J = 14.5 Hz), 3.32 (ddd, 1H, J = 9.0, 3.6, 6.0 Hz), 2.96 (s, 3H), 1.79-1.70 (m, 1H), 1.54-1.43 (m, 1H), 1.19 (dd, 6H, J = 10.9, 6.9 Hz), 0.94 (t, 3H, J = 7.5 Hz).

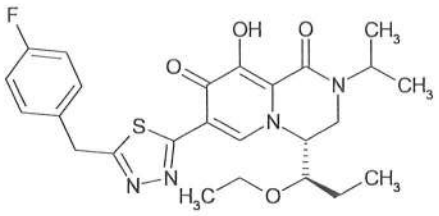
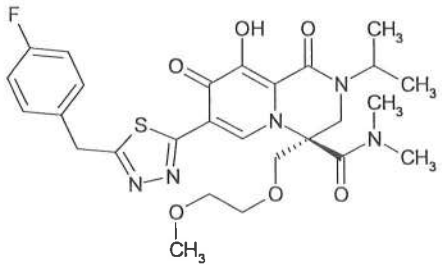
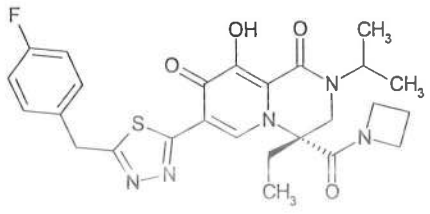
[0519]

[Table 1-103]

No.	structural formula	salt	^{1}H-NMR
383		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.88 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.86-4.82 (m, 1H), 4.77 (quint, 1H, J = 6.9 Hz), 4.47 (s, 2H), 3.83-3.78 (m, 2H), 3.47-3.42 (m, 1H), 3.18 (s, 3H), 1.53-1.47 (m, 1H), 1.33-1.25 (m, 1H), 1.19 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.9 Hz), 0.87 (t, 3H, J = 7.5 Hz).
384		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.82 (br s, 1H), 8.81 (s, 1H), 7.46-7.36 (m, 2H), 7.23-7.15 (m, 2H), 4.93-4.86 (m, 1H), 4.47 (s, 2H), 4.04 (dd, 1H, J = 13.2, 4.2 Hz), 3.75-3.57 (m, 3H), 3.39-3.25 (m, 3H), 3.10 (s, 3H), 2.92-2.87 (m, 1H), 0.93 (d, 3H, J = 5.8 Hz), 0.91-0.67 (m, 4H).
385		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.84 (br s, 1H), 8.82 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.15 (m, 2H), 5.00-4.92 (br m, 1H), 4.83-4.72 (m, 1H), 4.47 (s, 2H), 3.89-3.59 (m, 4H), 3.41-3.24 (m, 3H), 3.09 (s, 3H), 1.17 (d, 3H, J = 6.7 Hz), 1.15 (d, 3H, J = 6.7 Hz), 0.93 (d, 3H, J = 6.3 Hz).
386		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.69 (br s, 1H), 8.56 (s, 1H), 7.66 (s, 1H), 7.39-7.30 (m, 2H), 7.19-7.11 (m, 2H), 4.83-4.71 (m, 1H), 4.63-4.54 (m, 1H), 4.20 (s, 2H), 3.86 (dd, 1H, J = 14.1, 4.2 Hz), 3.78-3.70 (m, 1H), 3.55-3.45 (m, 1H), 3.02 (s, 3H), 1.23-1.14 (m, 9H).
387		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.74 (s, 1H), 7.68 (s, 1H), 7.37-7.30 (m, 2H), 7.19-7.11 (m, 2H), 4.84-4.73 (m, 1H), 4.69-4.63 (m, 1H), 4.20 (s, 2H), 3.89-3.81 (m, 1H), 3.76 (dd, 1H, J = 13.7, 4.0 Hz), 3.60-3.52 (m, 1H), 3.22 (s, 3H), 1.21-1.15 (m, 6H), 1.00 (d, 3H, J = 6.0 Hz).

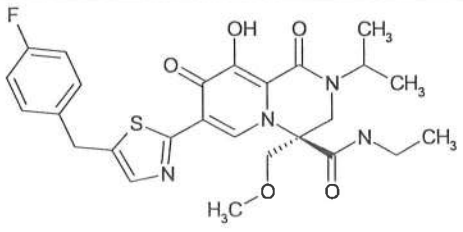
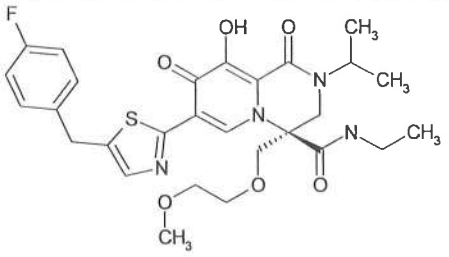
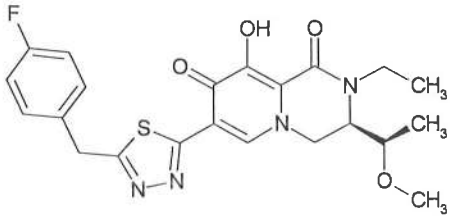
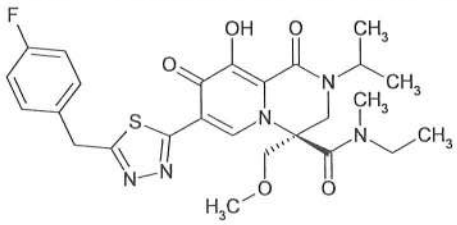
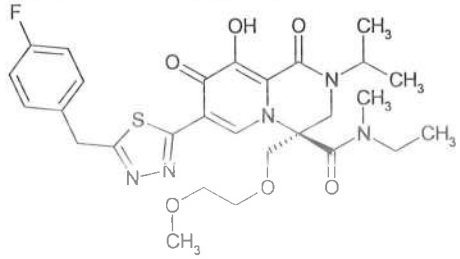
[0520]

[Table 1-104]

No.	structural formula	salt	^{1}H-NMR
388		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.74 (s, 1H), 7.68 (s, 1H), 7.37-7.31 (m, 2H), 7.18-7.11 (m, 2H), 4.84-4.73 (m, 1H), 4.69-4.63 (m, 1H), 4.20 (s, 2H), 3.89-3.81 (m, 1H), 3.76 (dd, 1H, J = 13.7, 4.0 Hz), 3.60-3.51 (m, 1H), 3.22 (s, 3H), 1.21-1.14 (m, 6H), 1.00 (d, 3H, J = 6.0 Hz).
389		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.81 (s, 1H), 8.73 (s, 1H), 7.45-7.42 (m, 2H), 7.21-7.18 (m, 2H), 4.82-4.75 (m, 1H), 4.65 (dd, 1H, J = 9.1, 2.6 Hz), 4.47 (s, 3H), 3.87 (dd, 1H, J = 13.3, 3.8 Hz), 3.74 (d, 1H, J = 13.3 Hz), 3.39-3.27 (m, 2H), 2.77-2.73 (m, 1H), 1.79-1.70 (m, 1H), 1.51-1.43 (m, 1H), 1.20 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.9 Hz), 0.96 (t, 3H, J = 7.5 Hz), 0.74 (t, 3H, J = 6.9 Hz).
390		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (s, 1H), 7.44-7.42 (m, 2H), 7.21-7.17 (m, 2H), 4.62 (d, 1H, J = 5.6 Hz), 4.47 (s, 2H), 4.05 (dd, 1H, J = 13.9, 3.8 Hz), 3.57 (d, 1H, J = 13.3 Hz), 3.47-3.45 (m, 1H), 3.34 (dd, 1H, J = 9.3, 6.9 Hz), 2.94 (dd, 1H, J = 7.7, 3.6 Hz), 2.86 (dd, 1H, J = 9.3, 7.3 Hz), 1.55-1.38 (m, 2H), 0.94 (t, 3H, J = 7.0 Hz), 0.78 (t, 3H, J = 6.5 Hz), 0.42-0.36 (m, 1H), 0.34-0.27 (m, 2H), 0.24-0.20 (m, 1H).
391		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.90 (s, 1H), 8.86 (s, 1H), 7.47-7.37 (m, 2H), 7.23-7.15 (m, 2H), 4.81-4.65 (m, 1H), 4.47 (s, 2H), 4.41 (d, 1H, J = 12.1 Hz), 4.25 (d, 1H, J = 12.1 Hz), 4.06 (d, 1H, J = 14.1 Hz), 3.81 (d, 1H, J = 14.1 Hz), 3.75-3.63 (m, 2H), 3.62-3.36 (m, 2H), 3.21 (s, 3H), 3.11-2.73 (m, 6H), 1.16 (d, 3H, J = 6.8 Hz), 1.10 (d, 3H, J = 6.8 Hz).
392		HCl	^{1}H-NMR (DMSO-d_6) δ: 13.04 (s, 1H), 8.69 (s, 1H), 7.46-7.38 (m, 2H), 7.23-7.14 (m, 2H), 4.76-4.62 (m, 1H), 4.48 (s, 2H), 4.18-4.04 (m, 1H), 3.98 (d, 1H, J = 13.5 Hz), 3.94-3.82 (m, 2H), 3.78 (d, 1H, J = 13.5 Hz), 3.70-3.57 (m, 1H), 2.50-2.22 (m, 2H), 2.15-2.00 (m, 2H), 1.16 (t, 6H, J = 6.8 Hz), 1.03 (t, 3H, J = 7.5 Hz).

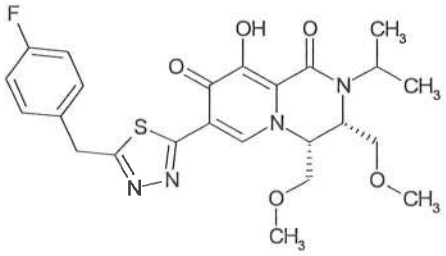
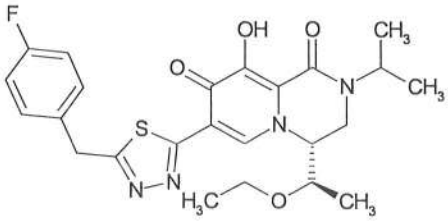
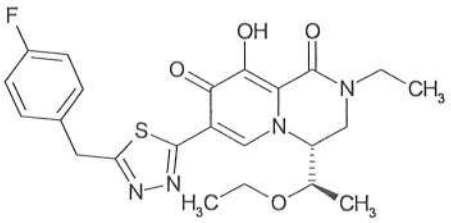
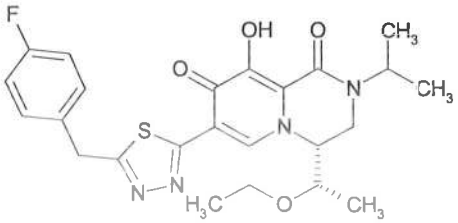
[0521]

[Table 1-105]

No.	structural formula	salt	^{1}H-NMR
393		HCl	^{1}H-NMR (DMSO-d_6) δ : 8.80 (s, 1H), 8.16 (t, 1H, J = 5.5 Hz), 7.67 (s, 1H), 7.38-7.28 (m, 2H), 7.19-7.10 (m, 2H), 4.76-4.63 (m, 1H), 4.20 (s, 2H), 4.17 (d, 1H, J = 11.9 Hz), 4.12 (d, 1H, J = 11.9 Hz), 4.03 (d, 1H, J = 13.9 Hz), 3.76 (d, 1H, J = 13.9 Hz), 3.40 (s, 3H), 3.21-2.92 (m, 2H), 1.13 (d, 3H, J = 6.8 Hz), 1.10 (d, 3H, J = 6.8 Hz), 0.99 (t, 3H, J = 7.5 Hz).
394		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.88 (s, 1H), 8.17 (t, 1H, J = 5.1 Hz), 7.66 (s, 1H), 7.37-7.29 (m, 2H), 7.19-7.10 (m, 2H), 4.76-4.64 (m, 1H), 4.33-4.16 (m, 2H), 4.20 (s, 2H), 4.04 (d, 1H, J = 13.9 Hz), 3.78 (d, 1H, J = 13.9 Hz), 3.72-3.66 (m, 2H), 3.57-3.50 (m, 2H), 3.25 (s, 3H), 3.20-2.96 (m, 2H), 1.14 (d, 3H, J = 6.8 Hz), 1.10 (d, 3H, J = 6.8 Hz), 1.04 (t, 3H, J = 7.3 Hz).
395		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.95 (s, 1H), 7.44-7.36 (m, 2H), 7.22-7.15 (m, 2H), 4.69 (dd, 1H, J = 14.0, 1.5 Hz), 4.47 (s, 2H), 4.39 (dd, 1H, J = 14.0, 4.2 Hz), 4.04-3.98 (m, 1H), 3.97-3.92 (m, 1H), 3.51-3.43 (m, 1H), 3.26-3.18 (m, 1H), 3.18 (s, 3H), 1.19 (t, 3H, J = 7.2 Hz), 1.10 (d, 3H, J = 6.2 Hz).
396		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.92 (s, 1H), 8.77 (s, 1H), 7.47-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.79-4.66 (m, 1H), 4.47 (s, 2H), 4.28 (d, 1H, J = 11.9 Hz), 4.12 (d, 1H, J = 11.9 Hz), 4.06 (d, 1H, J = 14.3 Hz), 3.82 (d, 1H, J = 14.3 Hz), 3.47-3.29 (m, 5H), 3.05-2.78 (m, 3H), 1.16 (d, 3H, J = 7.1 Hz), 1.12 (d, 3H, J = 7.1 Hz), 1.08-0.97 (m, 3H).
397		HCl	^{1}H-NMR (DMSO-d_6) δ : 12.93 (s, 1H), 8.85 (s, 1H), 7.48-7.34 (m, 2H), 7.24-7.13 (m, 2H), 4.77-4.65 (m, 1H), 4.47 (s, 2H), 4.38 (d, 1H, J = 11.9 Hz), 4.23 (d, 1H, J = 11.9 Hz), 4.06 (d, 1H, J = 14.3 Hz), 3.82 (d, 1H, J = 14.3 Hz), 3.73-3.24 (m, 6H), 3.19 (s, 3H), 3.06-2.84 (m, 3H), 1.16 (d, 3H, J = 6.6 Hz), 1.12 (d, 3H, J = 6.6 Hz), 1.07-0.94 (m, 3H).

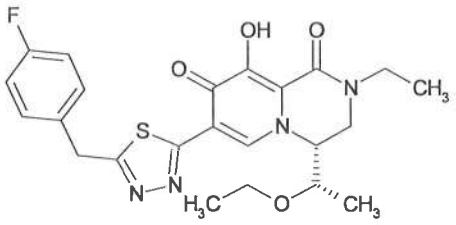
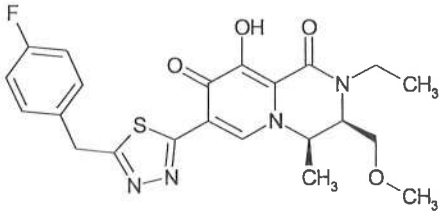
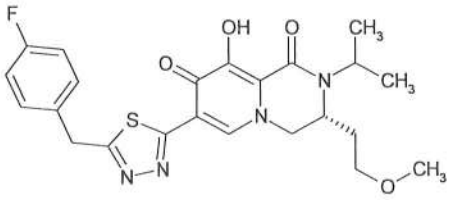
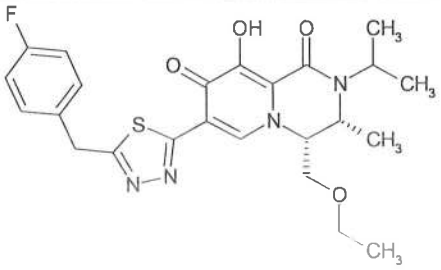
[0522]

[Table 1-106]

No.	structural formula	salt	^{1}H-NMR
398		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.69 (br s, 1H), 8.78 (s, 1H), 7.44-7.36 (m, 2H), 7.22-7.14 (m, 2H), 4.84-4.79 (m, 1H), 4.47 (s, 2H), 4.46-4.37 (m, 1H), 4.22-4.13 (m, 2H), 4.01 (dd, 1H, J = 11.9, 2.2 Hz), 3.49-3.39 (m, 2H), 3.46 (s, 3H), 3.14 (s, 3H), 1.33 (d, 3H, J = 6.9 Hz), 1.30 (d, 3H, J = 6.9 Hz).
399		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (s, 1H), 8.73 (s, 1H), 7.47-7.39 (m, 2H), 7.23-7.15 (m, 2H), 4.60-4.52 (m, 1H), 4.47 (s, 2H), 4.06 (dd, 1H, J = 14.1, 4.0 Hz), 3.65-3.55 (m, 2H), 3.47-3.36 (m, 1H), 3.02-2.88 (m, 2H), 1.16 (d, 3H, J = 6.2 Hz), 0.94-0.82 (m, 3H), 0.79 (t, 3H, J = 7.3 Hz), 0.75-0.64 (m, 1H).
400		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (s, 1H), 8.72 (s, 1H), 7.47-7.39 (m, 2H), 7.24-7.15 (m, 2H), 4.84-4.71 (m, 1H), 4.60 (dd, 1H, J = 8.6, 2.6 Hz), 4.47 (s, 2H), 3.88 (dd, 1H, J = 14.3, 4.0 Hz), 3.75 (d, 1H, J = 13.9 Hz), 3.58-3.53 (m, 1H), 3.46-3.34 (m, 1H), 2.97-2.85 (m, 1H), 1.26-1.14 (m, 9H), 0.75 (t, 3H, J = 6.9 Hz).
401		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.72 (s, 1H), 7.47-7.39 (m, 2H), 7.24-7.15 (m, 2H), 4.60-4.53 (m, 1H), 4.47 (s, 2H), 4.11 (dd, 1H, J = 14.1, 4.2 Hz), 3.75 (d, 1H, J = 13.5 Hz), 3.65-3.37 (m, 4H), 3.00-2.90 (m, 1H), 1.22 (d, 3H, J = 6.2 Hz), 1.16 (t, 3H, J = 7.1 Hz), 0.77 (t, 3H, J = 6.9 Hz).
402		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.90 (s, 1H), 8.32 (s, 1H), 7.44-7.40 (m, 2H), 7.22-7.17 (m, 2H), 4.81-4.74 (m, 1H), 4.71 (t, 1H, J = 4.8 Hz), 4.47 (s, 2H), 3.87 (d, 1H, J = 12.5 Hz), 3.78 (dd, 1H, J = 13.9, 4.2 Hz), 3.71-3.65 (m, 1H), 3.57-3.50 (m, 1H), 3.17-3.10 (m, 1H), 1.19 (t, 6H, J = 7.0 Hz), 1.06 (d, 3H, J = 6.0 Hz), 1.02 (t, 3H, J = 6.9 Hz).

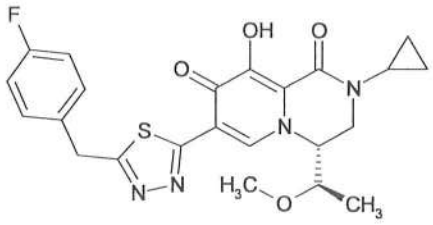
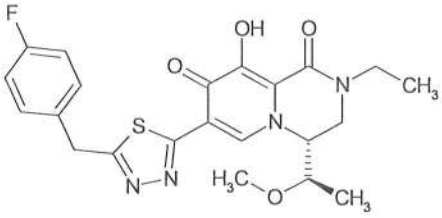
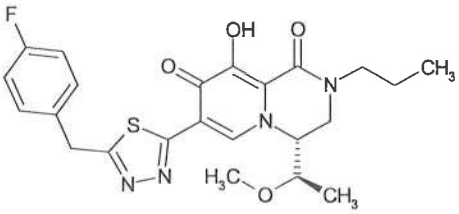
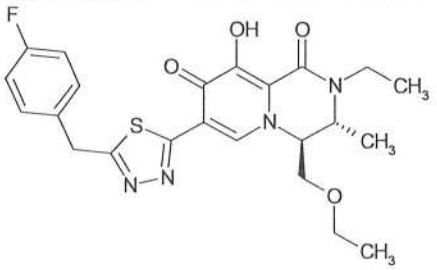
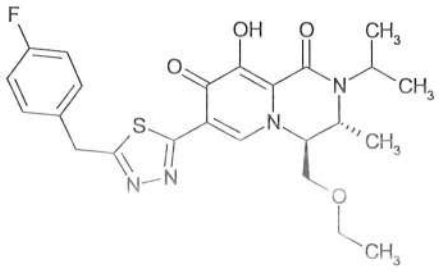
[0523]

[Table 1-107]

No.	structural formula	salt	^{1}H-NMR
403		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.91 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.69 (t, 1H, J = 4.6 Hz), 4.47 (s, 2H), 4.02 (dd, 1H, J = 14.1, 4.4 Hz), 3.84 (d, 1H, J = 13.7 Hz), 3.73-3.67 (m, 1H), 3.65-3.58 (m, 1H), 3.56-3.39 (m, 2H), 3.21-3.15 (m, 1H), 1.16 (t, 3H, J = 7.1 Hz), 1.07 (d, 3H, J = 6.0 Hz), 1.01 (t, 3H, J = 6.9 Hz).
404		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.90 (s, 1H), 7.43-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.66 (t, 1H, J = 4.4 Hz), 4.47 (s, 2H), 3.98 (dd, 1H, J = 13.9, 4.2 Hz), 3.74-3.65 (m, 2H), 3.56-3.48 (m, 1H), 3.20-3.14 (m, 1H), 2.92-2.87 (m, 1H), 1.04 (d, 3H, J = 7.0 Hz), 1.02 (t, 3H, J = 7.2 Hz), 0.94-0.89 (m, 1H), 0.87-0.80 (m, 2H), 0.75-0.70 (m, 1H).
405		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.62 (s, 1H), 7.42-7.38 (m, 2H), 7.20-7.16 (m, 2H), 4.77-4.71 (m, 1H), 4.47 (s, 2H), 4.14 (q, 1H, J=4.0 Hz), 3.92-3.84 (m, 1H), 3.59 (d, 2H, J=4.4 Hz), 3.33-3.26 (m, 1H), 3.18 (s, 3H), 1.64 (d, 3H, J=6.5 Hz), 1.21 (t, 3H, J=7.1 Hz).
406		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.44 (br s, 1H), 8.89 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.66-4.60 (m, 1H), 4.56-4.45 (m, 3H), 4.34-4.27 (m, 1H), 4.10-4.04 (m, 1H), 3.50-3.36 (m, 2H), 3.24 (s, 3H), 1.89-1.79 (m, 1H), 1.73-1.62 (m, 1H), 1.28 (d, 6H, J = 6.9 Hz).
407		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.88 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.15 (m, 2H), 4.71-4.66 (m, 1H), 4.62-4.52 (m, 1H), 4.47 (s, 2H), 4.21-4.07 (m, 2H), 3.99 (dd, 1H, J = 11.7, 2.0 Hz), 3.71-3.62 (m, 2H), 1.32-1.22 (m, 9H), 1.05 (d, 3H, J = 6.4 Hz).

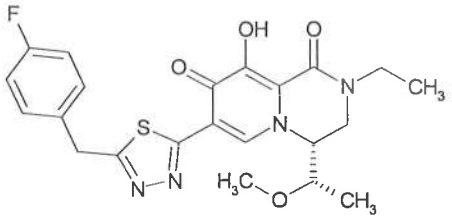
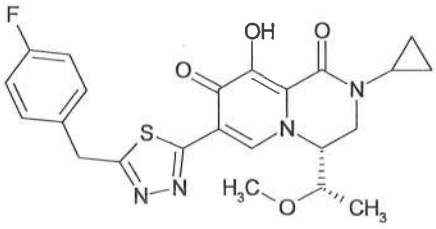
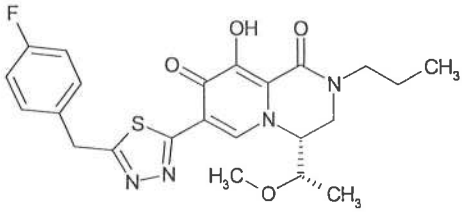
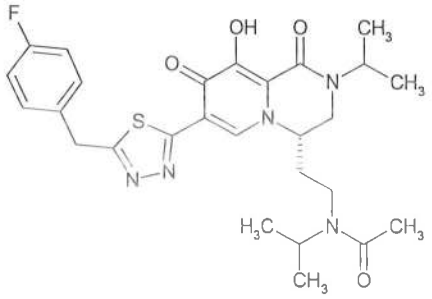
[0524]

[Table 1-108]

No.	structural formula	salt	^{1}H-NMR
408		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.73 (s, 1H), 8.72 (s, 1H), 7.44-7.40 (m, 2H), 7.22-7.16 (m, 2H), 4.64-4.55 (m, 1H), 4.47 (s, 2H), 4.06 (dd, 1H, J = 14.1, 4.2 Hz), 3.66-3.49 (m, 2H), 3.06 (s, 3H), 2.96-2.86 (m, 1H), 1.15 (d, 3H, J = 6.0 Hz), 0.96-0.78 (m, 3H), 0.75-0.63 (m, 1H).
409		HCl	^{1}H-NMR (DMSO-D_6) δ: 12.73 (br s, 1H), 8.71 (s, 1H), 7.47-7.39 (m, 2H), 7.24-7.15 (m, 2H), 4.66-4.56 (m, 1H), 4.47 (s, 2H), 4.11 (dd, 1H, J = 14.1, 4.2 Hz), 3.76 (d, 1H, J = 13.7 Hz), 3.66-3.42 (m, 3H), 3.06 (s, 3H), 1.21 (d, 3H, J = 5.7 Hz), 1.16 (t, 3H, J = 7.3 Hz).
410		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.71 (s, 1H), 7.47-7.39 (m, 2H), 7.24-7.15 (m, 2H), 4.65-4.57 (m, 1H), 4.47 (s, 2H), 4.10 (dd, 1H, J = 14.1, 4.0 Hz), 3.77 (d, 1H, J = 14.8 Hz), 3.59-3.38 (m, 3H), 3.05 (s, 3H), 1.60 (dt, 2H, J = 7.4, 7.4 Hz), 1.21 (d, 3H, J = 6.2 Hz), 0.90 (t, 3H, J = 7.4 Hz).
411		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.67 (s, 1H), 8.83 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.14 (m, 2H), 4.81 (t, 1H, J = 6.3 Hz), 4.48 (s, 2H), 4.09-3.99 (m, 1H), 3.97-3.85 (m, 1H), 3.68 (dd, 1H, J = 10.6, 5.7 Hz), 3.55 (dd, 1H, J = 10.6, 7.6 Hz), 3.51-3.30 (m, 2H), 3.19-3.06 (m, 1H), 1.27 (d, 3H, J = 6.6 Hz), 1.17 (t, 3H, J = 6.8 Hz), 1.01 (t, 3H, J = 7.3 Hz).
412		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.68 (br s, 1H), 8.83 (s, 1H), 7.46-7.37 (m, 2H), 7.23-7.15 (m, 2H), 4.85-4.76 (m, 1H), 4.67-4.57 (m, 1H), 4.48 (s, 2H), 4.20-4.10 (m, 1H), 3.64 (dd, 1H, J = 10.5, 5.8 Hz), 3.56-3.32 (m, 3H), 1.31-1.18 (m, 9H), 1.02 (t, 3H, J = 7.1 Hz).

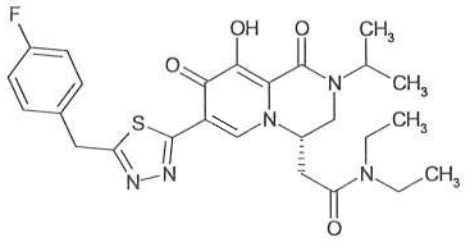
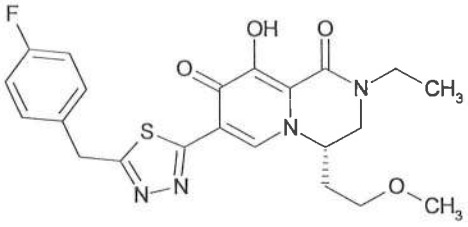
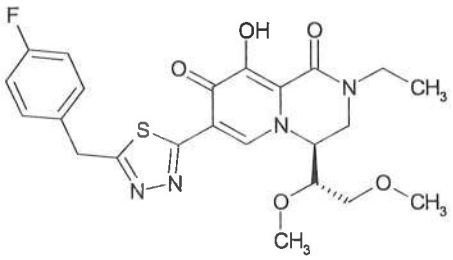
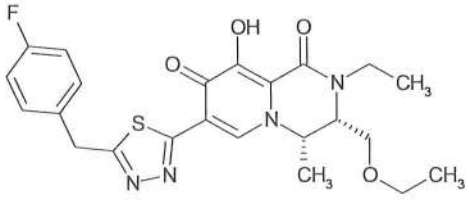
[0525]

[Table 1-109]

No.	structural formula	salt	^{1}H-NMR
413		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.70 (s, 1H), 8.87 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.69 (t, 1H, J = 4.4 Hz), 4.47 (s, 2H), 4.09-4.04 (m, 1H), 3.76 (d, 1H, J = 12.9 Hz), 3.66-3.60 (m, 1H), 3.23 (s, 3H), 3.07 (s, 3H), 1.04 (d, 3H, J = 6.4 Hz).
414		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (s, 1H), 8.90 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.17 (m, 2H), 4.69 (t, 1H, J = 4.4 Hz), 4.47 (s, 2H), 4.05-4.00 (m, 1H), 3.83 (d, 1H, J = 13.3 Hz), 3.67-3.59 (m, 2H), 3.45-3.39 (m, 1H), 3.23 (s, 3H), 1.16 (t, 3H, J = 7.1 Hz), 1.04 (d, 3H, J = 6.0 Hz).
415		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (s, 1H), 8.89 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.66 (t, 1H, J = 4.6 Hz), 4.47 (s, 2H), 3.98 (dd, 1H, J = 13.7, 4.0 Hz), 3.71 (d, 1H, J = 12.5 Hz), 3.59-3.53 (m, 1H), 3.22 (s, 3H), 2.94-2.88 (m, 1H), 1.02 (d, 3H, J = 6.0 Hz), 0.95-0.89 (m, 1H), 0.85-0.80 (m, 2H), 0.75-0.69 (m, 1H).
416		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (s, 1H), 8.90 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.69 (t, 1H, J = 4.8 Hz), 4.47 (s, 2H), 4.01 (dd, 1H, J = 13.9, 4.2 Hz), 3.83 (d, 1H, J = 12.9 Hz), 3.64-3.58 (m, 1H), 3.55-3.48 (m, 1H), 3.41-3.34 (m, 1H), 3.21 (s, 3H), 1.63-1.58 (m, 2H), 1.05 (d, 3H, J = 6.0 Hz), 0.91 (t, 3H, J = 7.3 Hz).
417		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.86 (s, 1H), 7.44-7.35 (m, 2H), 7.19-7.09 (m, 2H), 4.86-4.68 (m, 2H), 4.45 (s, 2H), 3.90-3.80 (m, 1H), 3.76-3.67 (m, 1H), 3.46-2.59 (m, 3H), 2.14-1.65 (m, 5H), 1.24 (d, 3H, J = 7.1 Hz), 1.19 (d, 3H, J = 7.1 Hz), 1.14-0.98 (m, 6H).

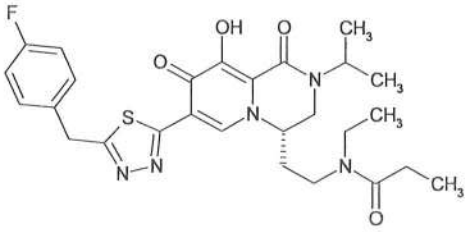
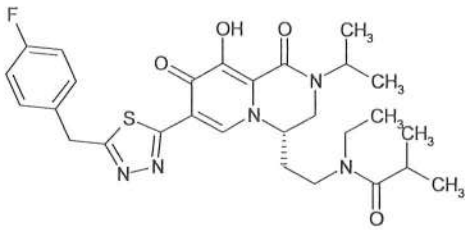
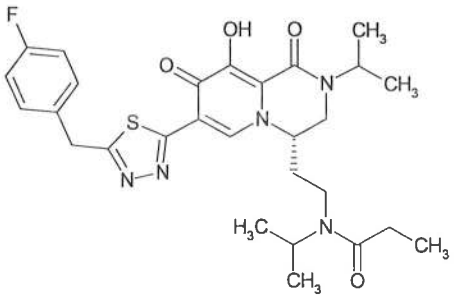
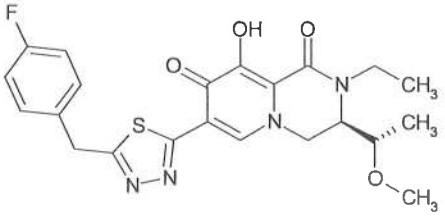
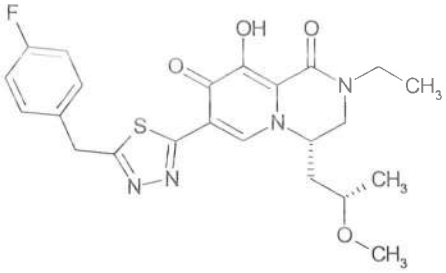
[0526]

[Table 1-110]

No.	structural formula	salt	^{1}H-NMR
418		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.84 (s, 1H), 7.46-7.36 (m, 2H), 7.23-7.14 (m, 2H), 5.21-5.10 (m, 1H), 4.86-4.73 (m, 1H), 4.47 (s, 2H), 3.84 (d, 2H, J = 2.2 Hz), 3.37-3.11 (m, 4H), 2.87 (d, 2H, J = 7.1 Hz), 1.13 (t, 6H, J = 7.3 Hz), 0.99 (t, 3H, J = 7.1 Hz), 0.95 (t, 3H, J = 7.1 Hz).
419		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.73 (s, 1H), 7.47-7.38 (m, 2H), 7.23-7.15 (m, 2H), 4.89-4.76 (m, 1H), 4.47 (s, 2H), 4.20-3.99 (m, 2H), 3.72-3.57 (m, 2H), 3.51-3.32 (m, 2H), 3.18 (s, 3H), 2.15-1.83 (m, 2H), 1.16 (t, 3H, J = 7.3 Hz).
420		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.75 (br s, 1H), 8.64 (s, 1H), 7.46-7.39 (m, 2H), 7.22-7.15 (m, 2H), 4.77-4.71 (m, 1H), 4.47 (s, 2H), 4.11 (dd, 1H, J = 13.7, 4.0 Hz), 3.77-3.71 (m, 1H), 3.64-3.44 (m, 5H), 3.33 (s, 3H), 3.10 (s, 3H), 1.20-1.13 (m, 3H).
421		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.61 (s, 1H), 7.46-7.34 (m, 2H), 7.24-7.14 (m, 2H), 4.81-4.69 (m, 1H), 4.47 (s, 2H), 4.15-4.08 (m, 1H), 3.90 (td, 1H, J = 13.9, 7.0 Hz), 3.64 (d, 2H, J = 4.2 Hz), 3.38-3.21 (m, 3H), 1.65 (d, 3H, J = 7.0 Hz), 1.22 (t, 3H, J = 7.3 Hz), 0.89 (t, 3H, J = 6.8 Hz).
422		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (br s, 1H), 8.55 (s, 1H), 7.45-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.72-4.61 (m, 1H), 4.49-4.38 (m, 1H), 4.47 (s, 2H), 4.09-4.02 (m, 1H), 3.61 (dd, 1H, J = 11.1, 3.0 Hz), 3.54 (dd, 1H, J = 11.1, 3.9 Hz), 3.27 (q, 2H, J = 7.0 Hz), 1.75 (d, 3H, J = 6.6 Hz), 1.32 (t, 6H, J = 6.8 Hz), 0.82 (t, 3H, J = 7.0 Hz).

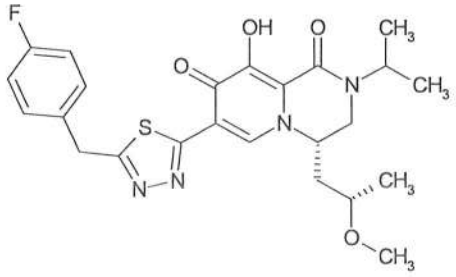
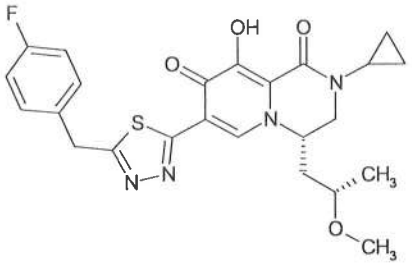
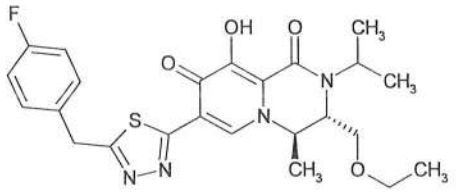
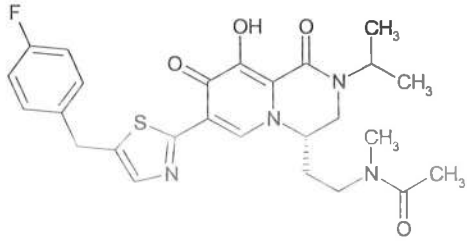
[0527]

[Table 1-111]

No.	structural formula	salt	^{1}H-NMR
423		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.83 (s, 1H), 7.44-7.35 (m, 2H), 7.18-7.09 (m, 2H), 4.84-4.66 (m, 2H), 4.45 (s, 2H), 3.90-3.79 (m, 1H), 3.77-3.64 (m, 1H), 3.48-2.60 (m, 4H), 2.33-2.17 (m, 2H), 2.08-1.77 (m, 2H), 1.24 (d, 3H, J = 6.4 Hz), 1.19 (d, 3H, J = 6.6 Hz), 1.12-1.00 (m, 3H), 0.97 (t, 3H, J = 7.7 Hz).
424		HCl	^{1}H-NMR (DMSO-d_6) δ: 9.02 (s, 0.25H), 8.94 (s, 0.75H), 7.46-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.95-4.66 (br m, 2H), 4.47 (s, 2H), 3.92-3.67 (m, 2H), 3.53-2.98 (br m, 4H), 2.87-2.53 (br m, 1H), 2.14-1.63 (br m, 2H), 1.29-0.86 (br m, 15H).
425		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.86 (s, 1H), 7.44-7.35 (m, 2H), 7.19-7.08 (m, 2H), 4.85-4.69 (m, 2H), 4.45 (s, 2H), 4.22-3.98 (m, 2H), 3.90-3.80 (m, 1H), 3.78-3.68 (m, 1H), 3.13-3.00 (m, 1H), 2.35-2.15 (m, 2H), 2.09-1.93 (m, 1H), 1.87-1.71 (m, 1H), 1.24 (d, 3H, J = 6.6 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.07 (t, 6H, J = 6.4 Hz), 0.96 (t, 3H, J = 7.3 Hz).
426		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.49 (s, 1H), 8.91 (s, 1H), 7.42-7.39 (m, 2H), 7.20-7.16 (m, 2H), 4.80 (d, 1H, J = 13.3 Hz), 4.47 (s, 2H), 4.36 (dd, 1H, J = 13.7, 4.8 Hz), 3.96-3.89 (m, 2H), 3.65-3.60 (m, 1H), 3.28-3.20 (m, 1H), 3.08 (s, 3H), 1.21 (t, 3H, J = 7.1 Hz), 1.16 (d, 3H, J = 6.4 Hz).
427		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.65 (s, 1H), 7.44-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.88-4.84 (m, 1H), 4.46 (s, 2H), 4.08 (dd, 1H, J = 13.5, 3.8 Hz), 3.65-3.62 (m, 1H), 3.62 (dq, 1H, J = 13.7, 7.3 Hz), 3.45 (dq, 1H, J = 13.7, 7.3 Hz), 3.21 (s, 3H), 3.02-2.97 (m, 1H), 1.93-1.78 (m, 2H), 1.16 (t, 3H, J = 7.3 Hz), 1.04 (d, 3H, J = 6.0 Hz).

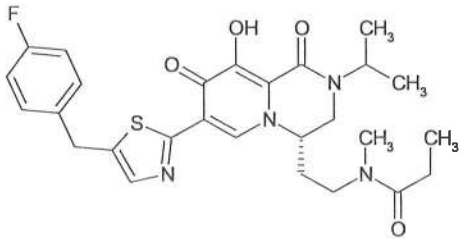
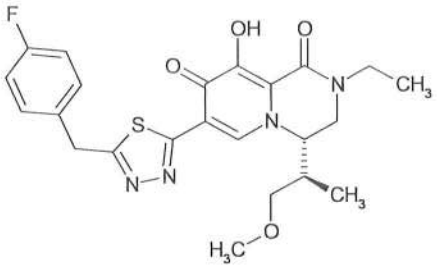
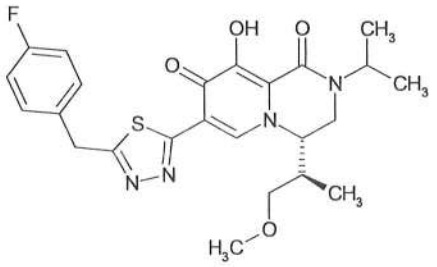
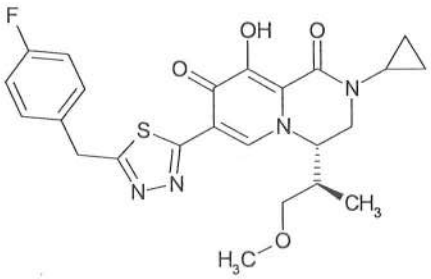
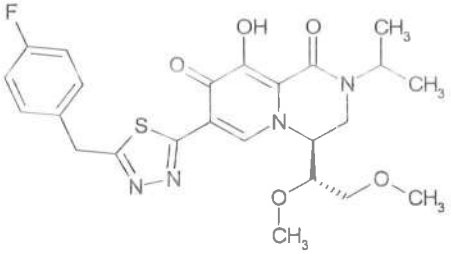
[0528]

[Table 1-112]

No.	structural formula	salt	^{1}H-NMR
428		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (s, 1H), 8.64 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.17 (m, 2H), 4.91-4.87 (m, 1H), 4.78 (sep, 1H, J = 6.8 Hz), 4.46 (s, 2H), 3.84 (dd, 1H, J = 13.5, 3.6 Hz), 3.68 (dd, 1H, J = 13.5, 1.3 Hz), 3.22 (s, 3H), 2.99-2.95 (m, 1H), 1.86 (ddd, 1H, J = 14.6, 9.9, 3.1 Hz), 1.77 (ddd, 1H, J = 14.6, 10.4, 4.9 Hz), 1.18 (d, 3H, J = 6.8 Hz), 1.15 (d, 3H, J = 6.8 Hz), 1.04 (d, 3H, J = 6.0 Hz).
429		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (br s, 1H), 8.65 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.85-4.80 (m, 1H), 4.46 (s, 2H), 4.02 (dd, 1H, J = 13.2, 3.7 Hz), 3.54 (dd, 1H, J = 13.2, 0.9 Hz), 3.21 (s, 3H), 3.03-2.96 (m, 1H), 2.97-2.91 (m, 1H), 1.85-1.75 (m, 2H), 1.03 (d, 3H, J = 6.0 Hz), 0.95-0.72 (m, 4H).
430		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.95 (s, 1H), 7.45-7.37 (m, 2H), 7.23-7.14 (m, 2H), 5.01-4.90 (m, 1H), 4.56 (sep, 1H, J = 6.8 Hz), 4.48 (s, 2H), 4.08-4.01 (m, 1H), 3.55 (dd, 1H, J = 10.5, 3.9 Hz), 3.45-3.31 (m, 3H), 1.40 (d, 3H, J = 6.6 Hz), 1.29 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz), 0.98 (t, 3H, J = 6.9 Hz).
431		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (br s, 1H), 8.93 (s, 1H), 7.45-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.92 (q, 1H, J = 6.7 Hz), 4.48 (s, 2H), 4.04-3.96 (m, 2H), 3.59-3.47 (m, 2H), 3.44-3.31 (m, 2H), 3.22-3.09 (m, 1H), 1.42 (d, 3H, J = 6.7 Hz), 1.20 (t, 3H, J = 7.1 Hz), 0.97 (t, 3H, J = 6.9 Hz).
432		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.80-8.74 (m, 1H), 7.68 (s, 1H), 7.38-7.29 (m, 2H), 7.20-7.10 (m, 2H), 4.97-4.55 (m, 2H), 4.20 (s, 2H), 3.92-3.60 (m, 2H), 3.60-3.02 (m, 2H), 2.93 (s, 2H), 2.72 (s, 1H), 2.08-1.59 (m, 5H), 1.22 (d, 3H, J = 7.1 Hz), 1.16 (d, 3H, J = 6.4 Hz).

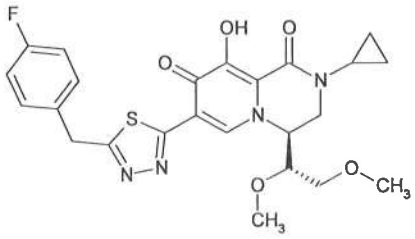
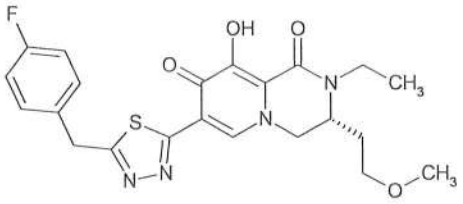
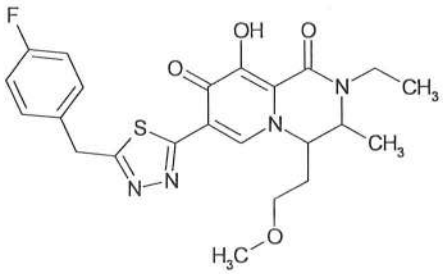
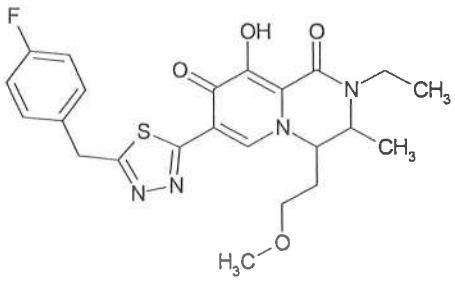
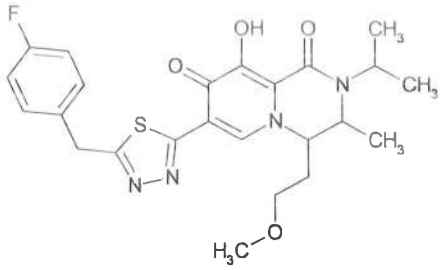
[0529]

[Table 1-113]

No.	structural formula	salt	^{1}H-NMR
433		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.66 (s, 1H), 7.61 (s, 1H), 7.36-7.27 (m, 2H), 7.16-7.04 (m, 2H), 4.84-4.56 (m, 2H), 4.19 (s, 2H), 3.88-3.76 (m, 1H), 3.75-3.63 (m, 1H), 3.52-3.14 (m, 2H), 3.03-2.70 (m, 3H), 2.33-2.17 (m, 2H), 2.06-1.76 (m, 2H), 1.24 (d, 3H, J = 6.6 Hz), 1.19 (d, 3H, J = 6.6 Hz), 0.96 (t, 3H, J = 7.5 Hz).
434		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.63 (br s, 1H), 8.73 (s, 1H), 7.44-7.41 (m, 2H), 7.21-7.17 (m, 2H), 4.60-4.55 (m, 1H), 4.47 (s, 2H), 4.05 (dd, 1H, J = 13.9, 3.4 Hz), 3.78 (dd, 1H, J = 13.9, 1.1 Hz), 3.63 (dq, 1H, J = 13.5, 7.1 Hz), 3.48 (dq, 1H, J = 13.5, 7.1 Hz), 3.18 (dd, 1H, J = 9.9, 4.2 Hz), 3.02 (s, 3H), 2.88 (dd, 1H, J = 9.9, 3.4 Hz), 2.11-2.04 (m, 1H), 1.16 (t, 3H, J = 7.1 Hz), 1.07 (d, 3H, J = 6.8 Hz).
435		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.75 (s, 1H), 7.44-7.41 (m, 2H), 7.22-7.17 (m, 2H), 4.79 (sep, 1H, J = 6.8 Hz), 4.60-4.57 (m, 1H), 4.46 (s, 2H), 3.82 (dd, 1H, J = 14.3, 3.5 Hz), 3.77 (dd, 1H, J = 14.3, 1.3 Hz), 3.16 (dd, 1H, J = 9.9, 4.1 Hz), 2.99 (s, 3H), 2.83 (dd, 1H, J = 9.9, 3.3 Hz), 2.06-2.02 (m, 1H), 1.20 (d, 3H, J = 6.8 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.08 (d, 3H, J = 6.8 Hz).
436		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.64 (br s, 1H), 8.73 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.17 (m, 2H), 4.57-4.54 (m, 1H), 4.46 (s, 2H), 4.01 (dd, 1H, J = 13.7, 3.6 Hz), 3.61 (dd, 1H, J = 13.7, 1.2 Hz), 3.17 (dd, 1H, J = 9.9, 4.4 Hz), 3.02 (s, 3H), 2.98-2.92 (m, 1H), 2.88 (dd, 1H, J = 9.9, 3.4 Hz), 2.07-1.99 (m, 1H), 1.03 (d, 3H, J = 6.9 Hz), 0.93-0.81 (m, 3H), 0.72-0.65 (m, 1H).
437		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.83 (br s, 1H), 8.65 (s, 1H), 7.46-7.40 (m, 2H), 7.22-7.16 (m, 2H), 4.83-4.71 (m, 2H), 4.47 (s, 2H), 3.93-3.86 (m, 1H), 3.79-3.73 (m, 1H), 3.60-3.47 (m, 3H), 3.33 (s, 3H), 3.08 (s, 3H), 1.22 (d, 3H, J = 6.9 Hz), 1.18 (d, 3H, J = 6.9 Hz).

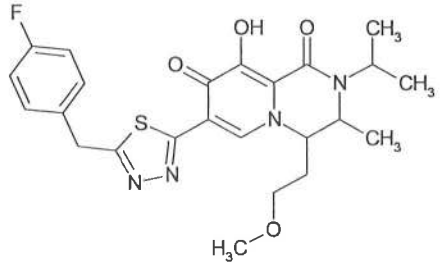
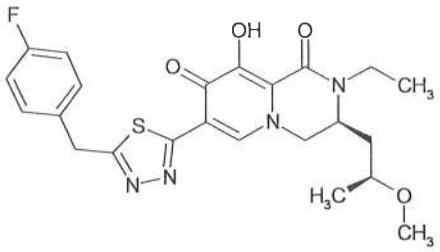
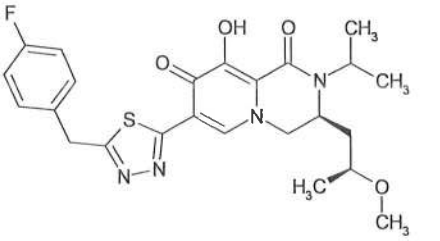
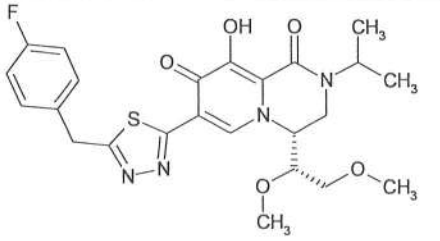
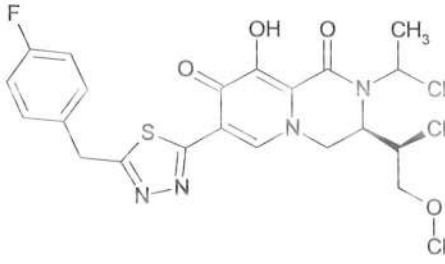
[0530]

[Table 1-114]

No.	structural formula	salt	^{1}H-NMR
438		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.74 (br s, 1H), 8.64 (s, 1H), 7.46-7.39 (m, 2H), 7.22-7.15 (m, 2H), 4.76-4.70 (m, 1H), 4.47 (s, 2H), 4.10-4.02 (m, 1H), 3.67-3.60 (m, 1H), 3.60-3.53 (m, 1H), 3.48 (dd, 1H, J = 10.9, 4.0 Hz), 3.43 (dd, 1H, J = 10.9, 5.2 Hz), 3.32 (s, 3H), 3.10 (s, 3H), 2.96-2.88 (m, 1H), 0.95-0.73 (m, 4H).
439		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.46 (br s, 1H), 8.87 (s, 1H), 7.45-7.36 (m, 2H), 7.23-7.14 (m, 2H), 4.65-4.56 (m, 1H), 4.47 (s, 2H), 4.38 (dd, 1H, J = 13.7, 3.6 Hz), 4.07-3.98 (m, 1H), 3.91 (td, 1H, J = 13.9, 7.1 Hz), 3.48-3.33 (m, 2H), 3.23 (s, 3H), 3.11 (td, 1H, J = 13.9, 7.1 Hz), 1.91-1.79 (m, 1H), 1.79-1.67 (m, 1H), 1.20 (t, 3H, J = 7.1 Hz).
440	 racemate, containing two kinds of diatereomers of Example No. 441	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.63 (s, 1H), 8.76 (s, 1H), 7.44-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.66 (dd, 1H, J = 9.7, 4.4 Hz), 4.47 (s, 2H), 3.97 (dd, 1H, J = 13.9, 6.2 Hz), 3.92-3.86 (m, 1H), 3.41-3.36 (m, 1H), 3.17-3.10 (m, 5H), 2.08-2.01 (m, 1H), 1.87-1.80 (m, 1H), 1.24 (d, 3H, J = 6.4 Hz), 1.19 (t, 3H, J = 7.1 Hz).
441	 racemate, containing two kinds of diatereomers of Example No. 440	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.77 (s, 1H), 8.64 (s, 1H), 7.44-7.40 (m, 2H), 7.22-7.17 (m, 2H), 4.71-4.67 (m, 1H), 4.47 (s, 2H), 4.33-4.27 (m, 1H), 3.76 (td, 1H, J = 14.1, 7.1 Hz), 3.43-3.36 (m, 2H), 3.15 (s, 3H), 3.12-3.05 (m, 1H), 2.09-2.02 (m, 1H), 1.94-1.84 (m, 1H), 1.33 (d, 3H, J = 5.2 Hz), 1.14 (t, 3H, J = 7.1 Hz).
442	 racemate, containing two kinds of diatereomers of Example No. 443	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.65 (s, 1H), 8.75 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.17 (m, 2H), 4.67-4.58 (m, 2H), 4.47 (s, 2H), 4.10-4.04 (m, 1H), 3.42-3.37 (m, 1H), 3.17 (s, 3H), 3.15-3.09 (m, 1H), 2.05-1.97 (m, 1H), 1.82-1.75 (m, 1H), 1.28-1.23 (m, 9H).

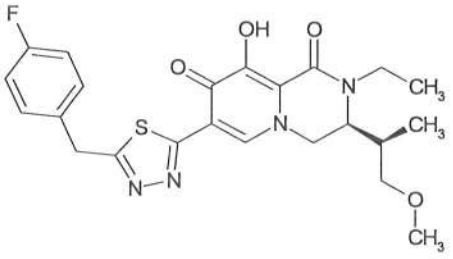
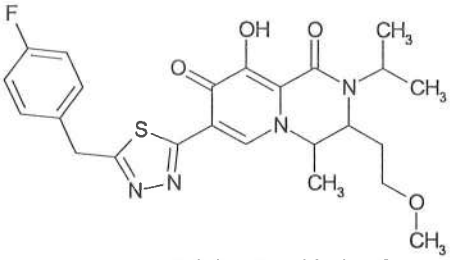
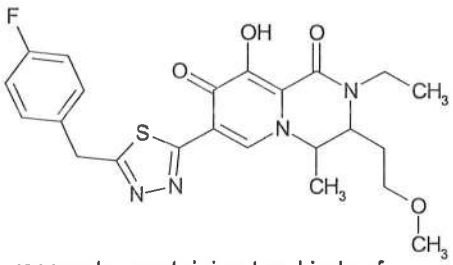
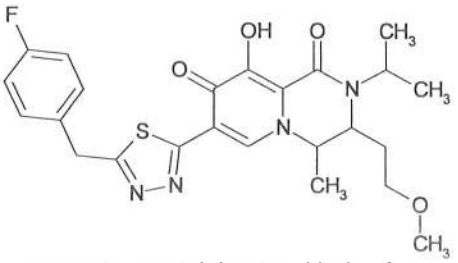
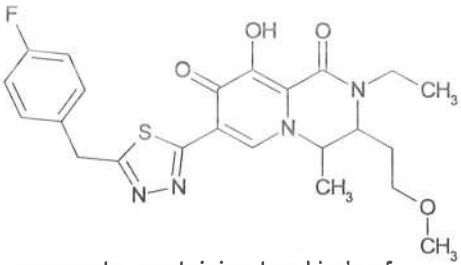
[0531]

[Table 1-115]

No.	structural formula	salt	^{1}H-NMR
443	 racemate, containing two kinds of diatereomers of Example No. 442	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.76 (s, 1H), 8.65 (s, 1H), 7.42-7.39 (m, 2H), 7.20-7.16 (m, 2H), 4.56-4.51 (m, 2H), 4.47 (s, 2H), 4.09-4.03 (m, 1H), 3.63-3.54 (m, 2H), 3.31 (s, 3H), 2.50-2.48 (m, 1H), 2.12-2.06 (m, 1H), 1.30 (d, 3H, J = 7.0 Hz), 1.28 (d, 3H, J = 7.0 Hz), 1.09 (d, 3H, J = 6.0 Hz).
444		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.48 (br s, 1H), 8.80 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.55 (dd, 1H, J = 13.2, 1.5 Hz), 4.47 (s, 2H), 4.38 (dd, 1H, J = 13.2, 3.5 Hz), 4.08-4.04 (m, 1H), 3.98 (dq, 1H, J = 13.5, 7.1 Hz), 3.42-3.37 (m, 1H), 3.20 (s, 3H), 3.06 (dq, 1H, J = 13.5, 7.1 Hz), 1.71-1.59 (m, 2H), 1.20 (t, 3H, J = 7.1 Hz), 1.06 (d, 3H, J = 6.2 Hz).
445		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.81 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.57 (dd, 1H, J = 13.2, 1.3 Hz), 4.47 (s, 2H), 4.45 (sep, 1H, J = 6.8 Hz), 4.31 (dd, 1H, J = 13.2, 3.3 Hz), 4.11-4.06 (m, 1H), 3.50-3.45 (m, 1H), 3.19 (s, 3H), 1.68-1.57 (m, 2H), 1.31 (d, 3H, J = 6.8 Hz), 1.28 (d, 3H, J = 6.8 Hz), 1.08 (d, 3H, J = 6.2 Hz).
446		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.75 (s, 1H), 7.45-7.39 (m, 2H), 7.22-7.16 (m, 2H), 4.86-4.75 (m, 2H), 4.47 (s, 2H), 3.86-3.80 (m, 1H), 3.76 (dd, 1H, J = 13.3, 3.6 Hz), 3.61 (dd, 1H, J = 11.7, 2.8 Hz), 3.58-3.51 (m, 1H), 3.30 (s, 3H), 3.18 (s, 3H), 2.97 (dd, 1H, J = 11.7, 2.8 Hz), 1.20 (d, 3H, J = 6.9 Hz), 1.17 (d, 3H, J = 6.9 Hz).
447		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.47 (br s, 1H), 8.99 (s, 1H), 7.44-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.73 (d, 1H, J = 13.7 Hz), 4.47 (s, 2H), 4.34 (dd, 1H, J = 13.7, 4.4 Hz), 4.23-4.14 (m, 1H), 4.05-4.00 (m, 1H), 3.46 (dd, 1H, J = 9.7, 8.1 Hz), 3.37 (dd, 1H, J = 9.7, 5.2 Hz), 3.30 (s, 3H), 2.22-2.11 (m, 1H), 1.38 (d, 3H, J = 6.9 Hz), 1.34 (d, 3H, J = 6.9 Hz), 0.60 (d, 3H, J = 7.3 Hz).

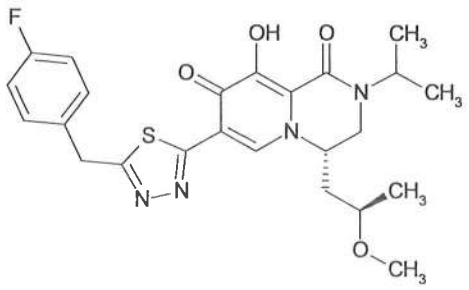
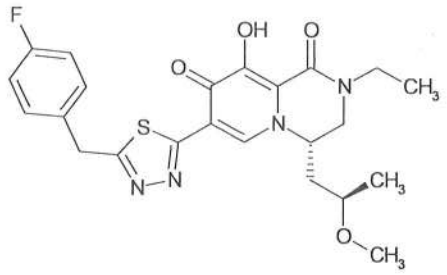
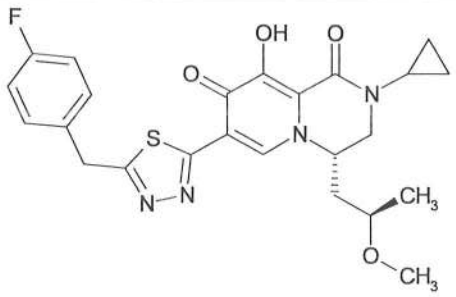
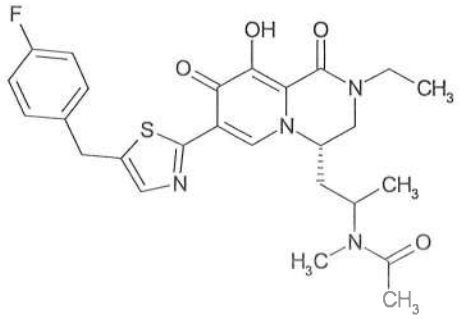
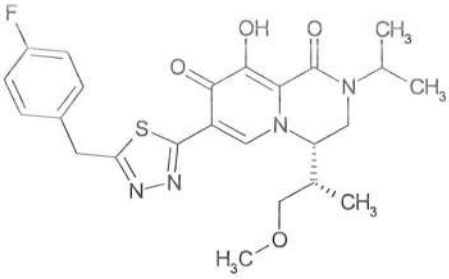
[0532]

[Table 1-116]

No.	structural formula	salt	^{1}H-NMR
448		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.42 (br s, 1H), 9.00 (s, 1H), 7.44-7.37 (m, 2H), 7.22-7.14 (m, 2H), 4.76-4.68 (m, 1H), 4.47 (s, 2H), 4.37 (dd, 1H, J = 14.1, 4.0 Hz), 4.07-3.96 (m, 1H), 3.93-3.86 (m, 1H), 3.38-3.28 (m, 2H), 3.26 (s, 3H), 3.11-2.99 (m, 1H), 2.05-1.95 (m, 1H), 1.19 (t, 3H, J = 7.1 Hz), 0.81 (d, 3H, J = 6.9 Hz).
449	 racemate, containing two kinds of diatereomers of Example No. 451	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (s, 1H), 8.57 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.65-4.59 (m, 1H), 4.47 (s, 2H), 4.30-4.24 (m, 1H), 4.01-3.96 (m, 1H), 3.33-3.24 (m, 2H), 3.11 (s, 3H), 1.92-1.86 (m, 1H), 1.70 (d, 3H, J = 6.4 Hz), 1.66-1.59 (m, 1H), 1.38 (d, 3H, J = 6.9 Hz), 1.33 (d, 3H, J = 6.9 Hz).
450	 racemate, containing two kinds of diatereomers of Example No. 452	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.52 (s, 1H), 8.93 (s, 1H), 7.43-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.88-4.84 (m, 1H), 4.48 (s, 2H), 4.08-4.02 (m, 1H), 3.83 (t, 1H, J = 7.1 Hz), 3.44-3.37 (m, 2H), 3.23 (s, 3H), 3.04-2.96 (m, 1H), 1.84-1.73 (m, 2H), 1.41 (d, 3H, J = 6.9 Hz), 1.19 (t, 3H, J = 7.0 Hz).
451	 racemate, containing two kinds of diatereomers of Example No. 449	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.50 (s, 1H), 8.95 (s, 1H), 7.42-7.38 (m, 2H), 7.21-7.16 (m, 2H), 4.91 (dd, 1H, J = 12.7, 5.8 Hz), 4.61-4.54 (m, 1H), 4.48 (s, 2H), 3.88 (d, 1H, J = 8.9 Hz), 3.50-3.39 (m, 2H), 3.24 (s, 3H), 1.91-1.85 (m, 1H), 1.69-1.61 (m, 1H), 1.39 (d, 3H, J = 6.9 Hz), 1.28 (d, 3H, J = 6.4 Hz), 1.26 (d, 3H, J = 6.4 Hz).
452	 racemate, containing two kinds of diatereomers of Example No. 450	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.70 (s, 1H), 8.65 (s, 1H), 7.42-7.38 (m, 2H), 7.22-7.15 (m, 2H), 4.75-4.70 (m, 1H), 4.47 (s, 2H), 4.08-3.96 (m, 2H), 3.37-3.31 (m, 2H), 3.20 (s, 3H), 3.15-3.07 (m, 1H), 1.94-1.87 (m, 1H), 1.68-1.58 (m, 4H), 1.20 (t, 3H, J = 7.1 Hz).

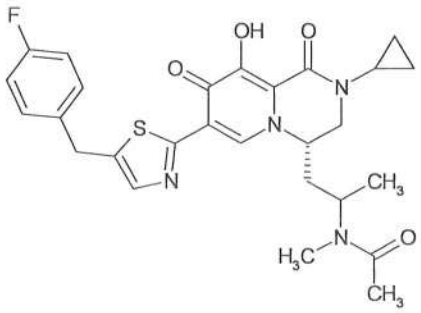
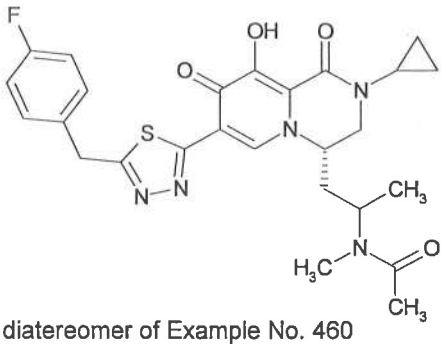
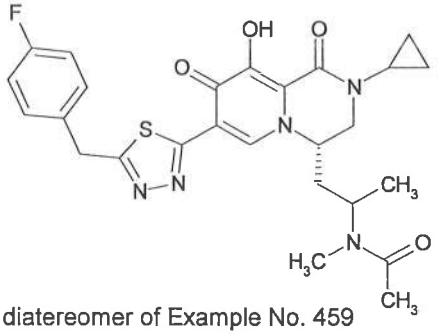
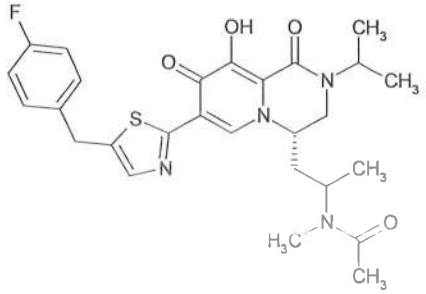
[0533]

[Table 1-117]

No.	structural formula	salt	^{1}H-NMR
453		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (br s, 1H), 8.81 (s, 1H), 7.45-7.39 (m, 2H), 7.23-7.15 (m, 2H), 4.95-4.88 (m, 1H), 4.78 (sep, 1H, J = 6.9 Hz), 4.47 (s, 2H), 3.81 (dd, 1H, J = 13.5, 3.4 Hz), 3.74-3.65 (m, 1H), 3.58-3.48 (m, 1H), 3.03 (s, 3H), 1.88-1.80 (m, 1H), 1.78-1.68 (m, 1H), 1.19 (d, 3H, J = 6.9 Hz), 1.16 (d, 3H, J = 6.9 Hz), 1.07 (d, 3H, J = 6.0 Hz).
454		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.67 (br s, 1H), 8.82 (s, 1H), 7.45-7.38 (m, 2H), 7.23-7.14 (m, 2H), 4.93-4.83 (m, 1H), 4.47 (s, 2H), 4.05 (dd, 1H, J = 13.5, 3.8 Hz), 3.71-3.42 (m, 4H), 3.05 (s, 3H), 1.95-1.86 (m, 1H), 1.82-1.71 (m, 1H), 1.16 (t, 3H, J = 7.1 Hz), 1.09 (d, 3H, J = 6.0 Hz).
455		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.82 (s, 1H), 7.43-7.40 (m, 2H), 7.21-7.16 (m, 2H), 4.88-4.83 (m, 1H), 4.46 (s, 2H), 3.98 (dd, 1H, J = 13.3, 3.6 Hz), 3.53 (dd, 1H, J = 13.3, 1.8 Hz), 3.52-3.46 (m, 1H), 3.02 (s, 3H), 2.98-2.93 (m, 1H), 1.86 (ddd, 1H, J = 14.3, 6.2, 2.6 Hz), 1.71 (ddd, 1H, J = 14.3, 8.8, 7.9 Hz), 1.08 (d, 3H, J = 6.0 Hz), 0.94-0.79 (m, 3H), 0.75-0.70 (m, 1H).
456	 diatereomer of Example No. 463	HCl	^{1}H-NMR (DMSO-d_6) δ: 8.66 (s, 0.7H), 8.50 (s, 0.3H), 7.70-7.64 (m, 1.0H), 7.37-7.30 (m, 2.0H), 7.19-7.11 (m, 2.0H), 4.70-4.62 (m, 0.3H), 4.59-4.51 (m, 0.7H), 4.44-4.34 (m, 0.7H), 4.20 (s, 2.0H), 4.08-3.99 (m, 1.0H), 3.80-3.70 (m, 0.3H), 3.69-3.47 (m, 3.0H), 2.80 (s, 2.1H), 2.69 (s, 0.9H), 2.12-1.86 (m, 4.3H), 1.83-1.73 (m, 0.7H), 1.22-1.12 (m, 3.0H), 1.05 (d, 0.9H, J = 6.4 Hz), 1.00 (d, 2.1H, J = 6.4 Hz).
457		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.80 (br s, 1H), 8.82 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.77 (sep, 1H, J = 6.9 Hz), 4.69-4.65 (m, 1H), 4.47 (s, 2H), 3.86 (d, 2H, J = 2.8 Hz), 3.37 (d, 2H, J = 5.2 Hz), 3.28 (s, 3H), 2.22-2.15 (m, 1H), 1.21 (d, 3H, J = 6.9 Hz), 1.18 (d, 3H, J = 6.9 Hz), 0.66 (d, 3H, J = 6.9 Hz).

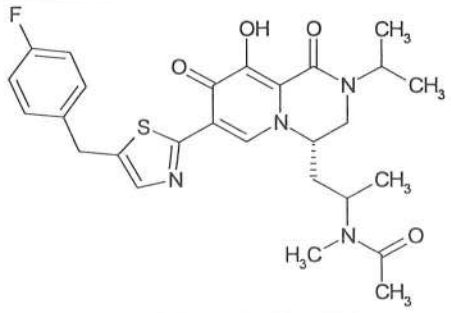
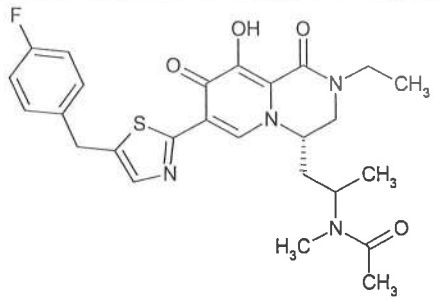
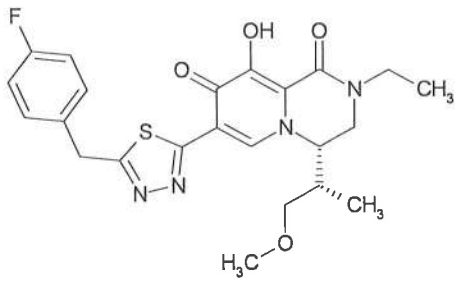
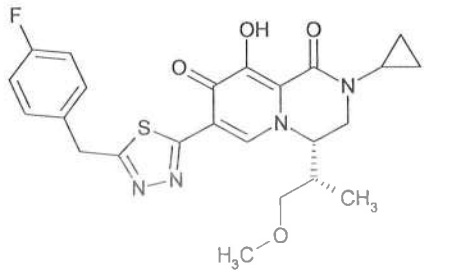
[0534]

[Table 1-118]

No.	structural formula	salt	^{1}H-NMR
458		HCl	^{1}H-NMR (DMSO-d_6) δ: 8.63 (s, 0.67H), 8.46 (s, 0.33H), 7.71-7.61 (m, 1H), 7.39-7.28 (m, 2H), 7.21-7.10 (m, 2H), 4.67-4.31 (m, 2H), 4.26-4.16 (m, 2H), 4.07-3.42 (br m, 2H), 3.03-2.56 (br m, 4H), 2.14-1.59 (m, 5H), 1.28-0.60 (m, 7H).
459	 diatereomer of Example No. 460	HCl	^{1}H-NMR (DMSO-d_6) δ: 9.18-8.08 (m, 1H), 7.49-7.10 (m, 4H), 5.28-3.81 (m, 6H), 3.07-2.45 (m, 4H), 2.36-1.64 (m, 5H), 1.38-0.32 (m, 7H).
460	 diatereomer of Example No. 459	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (br s, 1H), 8.92-8.63 (m, 1H), 7.47-7.37 (m, 2H), 7.24-7.13 (m, 2H), 4.80-4.19 (m, 4H), 4.10-3.39 (m, 2H), 3.04-2.48 (m, 4H), 2.15-1.61 (m, 5H), 1.18-0.59 (m, 7H).
461	 diatereomer of Example No. 462	HCl	^{1}H-NMR (DMSO-d_6) δ: 8.63 (s, 1H), 7.68 (s, 1H), 7.37-7.29 (m, 2H), 7.19-7.10 (m, 2H), 4.90-4.65 (m, 2H), 4.61-4.45 (m, 1H), 4.20 (s, 2H), 3.89-3.55 (m, 2H), 2.81 (s, 3H), 2.00 (s, 3H), 1.95-1.76 (m, 2H), 1.29-1.11 (br m, 6H), 1.02 (d, 3H, J = 7.1 Hz).

[0535]

[Table 1-119]

No.	structural formula	salt	^{1}H-NMR
462	 diatereomer of Example No. 461	HCl	^{1}H-NMR (DMSO-d_6) δ: 8.63 (s, 0.75H), 8.44 (s, 0.25H), 7.69-7.63 (m, 1H), 7.39-7.29 (m, 2H), 7.19-7.10 (m, 2H), 4.85-3.97 (m, 3H), 4.20 (s, 2H), 3.85-3.54 (m, 2H), 2.81 (s, 2.25H), 2.72 (s, 0.75H), 2.06-1.61 (m, 5H), 1.33-1.08 (m, 6H), 1.08-0.93 (m, 3H).
463	 diatereomer of Example No. 456	HCl	^{1}H-NMR (DMSO-d_6) δ: 12.58 (br s, 1.0H), 8.62 (s, 0.9H), 8.58 (s, 0.1H), 7.68 (s, 0.9H), 7.67 (s, 0.1H), 7.36-7.30 (m, 2.0H), 7.18-7.11 (m, 2.0H), 4.76-4.65 (m, 1.0H), 4.57-4.49 (m, 1.0H), 4.20 (s, 2.0H), 3.99-3.93 (m, 1.0H), 3.75-3.59 (m, 1.9H), 3.59-3.38 (m, 1.1H), 2.80 (s, 2.7H), 2.58 (s, 0.3H), 1.98 (s, 2.7H), 1.92-1.83 (m, 2.3H), 1.22-1.13 (m, 3.3H), 1.03 (d, 2.7H, J = 6.9 Hz).
464		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.72 (br s, 1H), 8.81 (s, 1H), 7.44-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.65-4.62 (m, 1H), 4.47 (s, 2H), 4.09 (dd, 1H, J = 13.7, 4.0 Hz), 3.82 (dd, 1H, J = 13.7, 0.8 Hz), 3.58 (dq, 1H, J = 13.3, 7.3 Hz), 3.53 (dq, 1H, J = 13.3, 7.3 Hz), 3.37 (dd, 1H, J = 9.7, 4.8 Hz), 3.32 (dd, 1H, J = 9.7, 6.4 Hz), 3.26 (s, 3H), 2.24-2.17 (m, 1H), 1.17 (t, 3H, J = 7.3 Hz), 0.72 (d, 3H, J = 6.9 Hz).
465		HCl	^{1}H-NMR (DMSO-d_6) δ: 12.71 (br s, 1H), 8.81 (s, 1H), 7.43-7.39 (m, 2H), 7.21-7.16 (m, 2H), 4.64-4.61 (m, 1H), 4.47 (s, 2H), 4.01 (dd, 1H, J = 13.7, 4.0 Hz), 3.72 (dd, 1H, J = 13.7, 1.2 Hz), 3.34-3.29 (m, 2H), 3.27 (s, 3H), 2.98-2.92 (m, 1H), 2.20-2.14 (m, 1H), 0.90-0.79 (m, 4H), 0.67 (d, 3H, J = 6.9 Hz).

[0536]

Experimental Example 1

The following explains evaluation methods of the HIV integrase inhibitory activity of the compound of the present invention.

[0537]

(i) Construction of recombinant integrase gene expression system

A full-length gene sequence (Accession No.: M19921) of HIV-1 pNL4-3 integrase was inserted into restriction enzyme *Nde* I and *Xho* I sites of plasmid pET21a(+) (manufactured by Novagen) to construct an integrase expression vector pET21a-IN-Wild type.

[0538]

(ii) Production and purification of integrase protein

Escherichia coli recombinant BL21(DE3) transformed with plasmid pET21a-IN-Wild type obtained in (i) was shake cultured at 30°C in a liquid medium containing ampicillin. When the culture reached the logarithmic growth phase, isopropyl-β-D-thiogalactopyranoside was added to promote expression of integrase gene. The culture was continued for 5 hr to promote accumulation of the integrase protein. The recombinant *E. coli* was collected in pellets by centrifugal separation and preserved at -80°C.

This *Escherichia coli* was suspended in Lysis buffer (50 mM Tris-HCl (pH 7.6), 10 mM $MgCl_2$, 5 mM DTT), and disrupted by repeating treatments of pressurization and depressurization, and insoluble fraction was collected by centrifugation at 4°C, 18,000 rpm for 60 min. This was suspended in Lysis buffer containing a protease inhibitor, 1.25 mM sodium chloride and 10 mM CHAPS were added, and the mixture was stirred at 4°C for 30 min. Water-soluble fraction was collected by centrifugation at 4°C, 9,000 rpm for 30 min. The obtained fraction was diluted with a column buffer (50 mM Tris-HCl (pH 7.6), 1 mM DTT, 10% Glycerol, 10 mM CHAPS) to 5-fold, and the mixture was applied to heparin column (HiPrep 16/10 Heparin FF column: manufactured by GE Healthcare Bio-Sciences). Using a column buffer containing 1M NaCl, a protein was eluted with 0-1M NaCl concentration gradient, and an eluted fraction containing an integrase protein was collected. The obtained fraction was

diluted 5-fold with a column buffer (50 mM Tris-HCl (pH 7.6), 1 mM DTT, 10% Glycerol, 10 mM CHAPS), and the mixture was applied to cation exchange column (Mono-S column: manufactured by GE Healthcare Bio-Sciences). Using a column buffer containing 1M NaCl, a protein was eluted with 0-1M NaCl concentration gradient, and an eluted fraction containing an integrase protein was collected. The obtained fractions of the integrase protein were collected, and preserved at -80°C.

[0539]

(iii) Preparation of DNA solution

The following DNA synthesized by FASMAC was dissolved in TE buffer (10 mM Tris-hydrochloric acid (pH 8.0), 1 mM EDTA) and mixed with donor DNA, target DNA, and each complementary strand (+ and - strands) to 1 μM. The mixture was heated at 95°C for 5 min, 80°C for 10 min, 70°C for 10 min, 60°C for 10 min, 50°C for 10 min and 40°C for 10 min and kept at 25°C to give a double stranded DNA, which was used for the test.

Donor DNA (+ strand having biotin attached to the 5′ terminal)

Donor + strand: 5′-Biotin-ACC CTT TTA GTC AGT GTG GAA AAT CTC TAG CA-3′ (SEQ ID NO:1)

Donor - strand: 5′-ACT GCT AGA GAT TTT CCA CAC TGA CTA AAA G-3′ (SEQ ID NO:2)

Target DNA (+, - strands both having digoxigenin attached to the 3′ terminal)

Target + strand: 5′-TGA CCA AGG GCT AAT TCA CT-Dig-3′ (SEQ ID NO:3)

Target - strand: 5′-AGT GAA TTA GCC CTT GGT CA-Dig-3′ (SEQ ID NO:4)

[0540]

(iv) Determination of enzyme (HIV integrase) inhibitory activity

The donor DNA was diluted with TE buffer to 20 nM, of which 50 μL was added to each well of streptavidin-coated black plate (manufactured by PIAS Corporation) and allowed to adsorb

at 37°C for 20 min. The plate was washed with phosphate buffer (Dulbecco's PBS, Sanko Junyaku Co., Ltd.) containing 0.1% Tween 20 and phosphate buffer. Then, an enzyme reaction mixture (70 μL), a test substance (10 μL) diluted with the enzyme reaction mixture and 0.75 μM integrase protein (10 μL) were added to each well and the mixture was reacted at 37°C for 60 min.

composition of enzyme reaction mixture: 30 mM MOPS (3-morpholinopropanesulfonic acid), 5 mM magnesium chloride, 3 mM DTT (dithiothreitol), 0.1 mg/mL BSA (bovine serum albumin), 5% glycerol, 10% DMSO (dimethyl sulfoxide), 0.01% Tween 20.

Then, 25 nM target DNA (10 μL) was added, and the mixture was reacted at 37°C for 20 min and washed with phosphate buffer containing 0.1% Tween 20 to stop the reaction.

Then, 100 mU/mL peroxidase labeled anti-digoxigenin antibody solution (Roche, 100 μL) was added, and the mixture was reacted at 37°C for 60 min, followed by washing with phosphate buffer containing 0.1% Tween 20.

Then, peroxidase fluorescence substrate solution (manufactured by PIAS Corporation, 100 μL) was added, and the mixture was reacted at room temperature for 20 min to 30 min. A reaction quenching liquid (manufactured by PIAS Corporation, 100 μL) was added to discontinue the reaction, and fluorescence intensity at excitation wavelength 325 nm/fluorescence wavelength 420 nm was measured.

[0541]

The HIV integrase inhibitory activity (IC_{50}) of the compound of the present invention was calculated from the inhibition rate according to the following formula:

inhibition rate (%)=[1-(Object-Blank)/(Control-Blank)]×100

Object: fluorescence intensity of well in the presence of test compound

Control: fluorescence intensity of well in the absence of test compound

Blank: fluorescence intensity of well in the absence of test compound and integrase protein

The results are shown in the following Tables.

[0542]

[Table 2-1]

Example No.	inhibitory activity IC_{50} (μM)
2	0.013
3	0.0085
4	0.01
5	0.0074
6	0.0056
7	0.013
8	0.0089
9	0.0091
10	0.0088
11	0.0064
12	0.0073
13	0.0064
14	0.01
15	0.013
16	0.02
17	0.0079
18	0.0082
19	0.0081
20	0.017

[0543]

[Table 2-2]

Example No.	inhibitory activity IC_{50} (μM)
21	0.0094
22	0.007
23	0.012
24	0.023
25	0.011
26	0.0076
27	0.01
28	0.015
29	0.01
30	0.009
31	0.0083
32	0.0077
33	0.0062
34	0.0082
35	0.0067
36	0.013
37	0.0063
38	0.012
39	0.01
40	0.013

[0544]

[Table 2-3]

Example No.	inhibitory activity IC_{50} (μM)
41	0.0072
42	0.0034
43	0.0046
44	0.0081
45	0.011
46	0.011
47	0.012
48	0.0069
49	0.0051
50	0.0064
51	0.0057
52	0.013
53	0.01
54	0.0075
55	0.021
56	0.01
57	0.011
58	0.017
59	0.012
60	0.017

[0545]

[Table 2-4]

Example No.	inhibitory activity IC_{50} (μM)
61	0.0066
62	0.0092
63	0.0083
64	0.0061
65	0.013
66	0.0064
67	0.0076
68	0.0098
69	0.013
70	0.0089
71	0.011
72	0.011
73	0.0077
74	0.0057
75	0.0091
76	0.0083
77	0.011
78	0.0089
79	0.0064
80	0.0098

[0546]

[Table 2-5]

Example No.	inhibitory activity IC_{50} (μM)
81	0.0075
82	0.0049
83	0.0071
84	0.011
85	0.0075
86	0.0095
87	0.0077
88	0.0087
89	0.008
90	0.0067
92	0.0087
93	0.0078
94	0.0088
95	0.0095
96	0.0067
97	0.0066
98	0.0075
99	0.0061
100	0.0081
101	0.0064

[0547]

[Table 2-6]

Example No.	inhibitory activity IC_{50} (μM)
102	0.0071
103	0.018
104	0.015
105	0.017
106	0.02
107	0.019
108	0.018
109	0.021
110	0.023
111	0.02
112	0.019
113	0.013
114	0.0081
115	0.012
116	0.0096
117	0.0094
118	0.013
119	0.011
120	0.015
121	0.016

[0548]

[Table 2-7]

Example No.	inhibitory activity $IC_{50}(\mu M)$
122	0.019
123	0.027
124	0.015
125	0.011
126	0.0073
127	0.014
128	0.019
129	0.012
130	0.013
131	0.013
132	0.0091
133	0.0074
134	0.016
135	0.012
136	0.011
137	0.0086
138	0.011
139	0.012
140	0.0058
141	0.008

[0549]

[Table 2-8]

Example No.	inhibitory activity IC_{50} (μM)
142	0.0064
143	0.0069
144	0.0077
145	0.0056
146	0.0059
147	0.0083
148	0.0098
149	0.0059
150	0.0061
151	0.0054
152	0.0059
153	0.0058
154	0.0073
155	0.01
156	0.0046
157	0.029
158	0.0054
159	0.0066
160	0.0061
161	0.0078

[0550]

[Table 2-9]

Example No.	inhibitory activity $IC_{50}(\mu M)$
162	0.0071
163	0.0077
164	0.0065
165	0.0074
166	0.012
167	0.01
168	0.0058
169	0.012
170	0.012
171	0.016
172	0.014
173	0.016
174	0.014
175	0.0095
176	0.0085
177	0.017
178	0.02
179	0.019
180	0.01
181	0.014

[0551]

[Table 2-10]

Example No.	inhibitory activity IC_{50} (μM)
182	0.0097
183	0.01
184	0.006
185	0.015
186	0.018
187	0.019
188	0.018
189	0.02
190	0.011
191	0.012
192	0.015
193	0.011
194	0.0082
195	0.0059
196	0.0067
197	0.014
198	0.0057
199	0.0084
200	0.0096
201	0.0095

[0552]

[Table 2-11]

Example No.	inhibitory activity $IC_{50}(\mu M)$
202	0.013
203	0.013
204	0.013
205	0.013
206	0.0059
207	0.024
208	0.012
209	0.012
210	0.023
211	0.016
212	0.014
213	0.015
214	0.016
217	0.0053
218	0.0065
219	0.015
220	0.0068
221	0.0084
222	0.0065
223	0.012

[0553]

[Table 2-12]

Example No.	inhibitory activity IC_{50} (μM)
224	0.0073
225	0.018
226	0.013
227	0.013
228	0.011
229	0.012
230	0.069
231	0.011
232	0.015
233	0.0064
234	0.018
235	0.016
236	0.013
237	0.013
238	0.018
239	0.016
240	0.052
241	0.014
242	0.013
243	0.0076

[0554]

[Table 2-13]

Example No.	inhibitory activity IC_{50} (μM)
244	0.074
245	0.0081
246	0.0084
247	0.01
248	0.014
249	0.012
250	0.017
251	0.011
252	0.0092
253	0.0077
254	0.0076
255	0.009
256	0.0082
257	0.0091
258	0.0093
259	0.009
260	0.012
261	0.011
262	0.01
263	0.009

[0555]

[Table 2-14]

Example No.	inhibitory activity IC_{50} (μM)
264	0.0085
265	0.0093
266	0.011
267	0.011
268	0.015
269	0.0094
270	0.0095
271	0.011
272	0.0089
273	0.014
274	0.012
275	0.014
276	0.016
277	0.012
278	0.0099
279	0.0063
280	0.016
281	0.016
282	0.015
283	0.018

[0556]

[Table 2-15]

Example No.	inhibitory activity IC_{50} (μM)
284	0.011
285	0.011
286	0.0078
287	0.008
288	0.0088
289	0.01
290	0.014
291	0.0087
292	0.0073
293	0.0096
294	0.011
295	0.012
296	0.019

[0557]

[Table 2-16]

Example No.	inhibitory activity IC_{50} (μM)
297	0.02
298	0.009
299	0.0098
300	0.009
301	0.008
302	0.0099
303	0.0058
304	0.0091
305	0.0095
306	0.01
307	0.011
308	0.013
309	0.0088
310	0.0099
311	0.0097
312	0.012
313	0.0097
314	0.0079
315	0.0088

[0558]

[Table 2-17]

Example No.	inhibitory activity IC_{50} (μM)
316	0.012
317	0.0098
318	0.0065
319	0.0058
320	0.0094
321	0.007
323	0.014

[0559]

[Table 2-18]

Example No.	inhibitory activity IC_{50} (μM)
327	0.0059
328	0.0071
329	0.0061
330	0.0064
331	0.0093
332	0.012
333	0.0075
334	0.0091
335	0.0098
336	0.0072
337	0.017
338	0.0071
353	0.013
354	0.0080
355	0.0066
356	0.0089
357	0.0073
358	0.012
359	0.0048
360	0.011

[0560]

[Table 2-19]

Example No.	inhibitory activity IC_{50} (μM)
361	0.015
362	0.010
363	0.0087
364	0.010
365	0.012
382	0.0087
383	0.0079
384	0.012
385	0.0082
386	0.015
387	0.011
388	0.0086
389	0.014
391	0.024
392	0.011
393	0.015
394	0.014
395	0.010
396	0.015
397	0.019

[0561]

Experimental Example 2 Evaluation of antiviral activity

The effect of combined use of the compound of the present invention and existent anti-HIV agents can be determined in the following manner.

For example, the effect of combined use of two agents from existent nucleoside reverse transcriptase inhibitors (zidovudine, lamivudine, tenofovir), non-nucleoside reverse transcriptase inhibitors (efavirenz) or protease inhibitors (indinavir, nelfinavir) and test substance A and the like are evaluated using CEM-SS cells infected with HIV-1 IIIB by XTT method.

In addition, the effect of combined use of three agents of test substance A, zidovudine and lamivudine, or test substance A, tenofovir and lamivudine, and the like is evaluated.

[0562]

Prior to the combined use test, IC_{50} and CC_{50} of each medicament alone are measured. 5 concentrates of medicament A and 9 concentrates of medicament B, determined based on these results, are combined to evaluate the effect of combined use of two agents. For combined use of three agents, a high concentrated medicament B and a medicament C are mixed and medicament A and concentration thereof are combined for evaluation.

The test results of the test substance and concomitant drug alone or in combination thereof are analyzed based on the programs of Prichard and Shipman MacSynergy II version 2.01 and Deltagraph version 1.5d. A three-dimensional plot is drawn from % inhibition at the concentrations of each combined medicament, the obtained from 3 times of tests, with 95% (or 68%, 99%) confidence limits, and the effect of the combined use is evaluated based on the numerical values of $\mu M^2\%$ calculated therefrom. The criteria of evaluation are shown in the following.

Definition of interaction $\mu M^2\%$

Strong synergistic action	>100
Slight synergistic action	+51 - +100
Additive action	+50 - -50
Slight antagonistic action	-51 - -100
Strong antagonistic action	<-100

[0563]

Experimental Example 3 Metabolism stability test

Metabolism stability test in liver microsome

Liver microsome of human or animal species (rat or monkey) (manufactured by Xenotech LLC (Lenexa, KS, USA), 20 mg protein/mL) (2.5 μL) and NADPH-generating system coenzyme solution (β-nicotinamide adenine dinucleotide phosphate: 5.2 mM, D-glucose-6-phosphate: 13.2 mM, magnesium chloride: 13.2 mM, glucose-6-phosphate dehydrogenase: 1.8 U/mL) (50 μL) are suspended in 100 mM potassium phosphate buffer (pH 7.4, 147.5 μL), and mixed with a test substance (2 μL) dissolved in acetonitrile containing 0.5% DMSO. After incubation at 37°C for 0, 10 and 60 min, acetonitrile containing formic acid (final concentrated 0.1%) is added and the mixture is centrifuged. The test substance (unchanged form) in the supernatant is measured by high performance liquid chromatography/Mass Spectrometry (LC/MS). The residual ratio (%) is calculated from the obtained measurement values according to the following formula.

residual ratio (%) = amount of test substance after incubation (0, 10 or 60 min)/amount of test substance at incubation 0 min x 100

Preferred as the compound of the present invention is a compound with a residual ratio at 60 min later of not less than 40%, more preferably not less than 60%, further preferably not less than 80%.

[0564]

Formulation Example is given below. This example is merely for the exemplification purpose and does not limit the invention.

Formulation Example

(a)	compound of Example 1	10	g
(b)	lactose	50	g
(c)	corn starch	15	g
(d)	sodium carboxymethylcellulose	44	g
(e)	magnesium stearate	1	g

The entire amounts of (a), (b) and (c) and 30 g of (d) are kneaded with water, dried in vacuo and granulated. The obtained granules are mixed with 14 g of (d) and 1 g of (e) and processed into tablets with a tableting machine to give 1000 tablets each containing 10 mg of (a).

Industrial Applicability

[0565]

The compounds of the present invention show a high inhibitory activity against HIV integrase.

Therefore, these compounds can be medicaments effective for, for example, the prophylaxis or treatment of AIDS, as integrase inhibitors, antiviral agents, anti-HIV agents and the like, having an HIV integrase inhibitory activity. In addition, by a combined use with other anti-HIV agent(s) such as protease inhibitor, reverse transcriptase inhibitor and the like, they can be more effective anti-HIV agents. Furthermore, having high inhibitory activity specific for integrase, they can be medicaments safe for human body with a fewer side effects.

Sequence Listing Free Text

[0566]

SEQ ID NO: 1: Donor+ chain for HIV integrase activity measurement

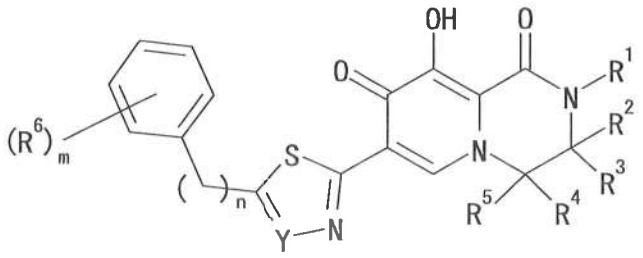
SEQ ID NO: 2: Donor- chain for HIV integrase activity measurement

SEQ ID NO: 3: Target+ chain for HIV integrase activity measurement

SEQ ID NO: 4: Target- chain for HIV integrase activity measurement

Claims

[Claim 1] A compound represented by the following formula [I] or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[I]

wherein

R^1 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

(2) a C_{3-8} cycloalkyl group, or

(3) a saturated monocyclic heterocyclic group containing, besides carbon atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom,

R^2, R^3, R^4 and R^5 are the same or different and each is

(1) a hydrogen atom,

(2) a carboxyl group,

(3) $-CO-NR^aR^b$ wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by

the same or different 1 to 5 substituents selected from the following group B,

(4) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group A, or

(5) a cyano group,

or

R^2 and R^3, or R^4 and R^5 optionally form, together with the carbon atom bonded thereto,

i) C_{3-8} cycloalkane, or

ii) a saturated monocyclic hetero ring containing, besides carbon atom, 1 to 6 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom,

wherein R^2, R^3, R^4 and R^5 are not hydrogen atoms at the same time,

R^6 is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 halogen atoms,

(2) a C_{1-6} alkoxy group,

(3) a halogen atom, or

(4) a C_{3-8} cycloalkyl group,

Y is

(1) CH, or

(2) a nitrogen atom,

m is an integer of 1 to 5, and when m is an integer of 2 to 5, then each R^6 may be the same or different, and

n is an integer of 1 to 3,

group A:

(a) $-CO-NR^{A1}R^{A2}$

wherein R^{A1} and R^{A2} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from the following group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^{A1} and R^{A2} optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 3 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from the following group B,

(b) a hydroxyl group,

(c) a C_{1-6} alkoxy group,

(d) a C_{1-6} alkoxy-C_{1-6} alkoxy group,

(e) a cyano group,

(f) $-NR^{A3}R^{A4}$

wherein R^{A3} and R^{A4} are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group,

(iii) a C_{1-6} alkyl-carbonyl group, or

(iv) a C_{1-6} alkyl-sulfonyl group, or

R^{A3} and R^{A4} optionally form, together with the nitrogen atom bonded thereto, a hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by 1 or 2 oxo groups,

(g) a carboxyl group,

(h) a C_{1-6} alkyl-sulfonyl group, and

(i) a C_{1-6} alkyl-carbonyl group;

group B:

(a) a hydroxyl group,

(b) a C_{1-6} alkoxy group,

(c) a C_{1-6} alkoxy-C_{1-6} alkyl group

(d) a C_{3-8} cycloalkyl group, and

(e) an oxo group.

[Claim 2] The compound according to claim 1, wherein R^1 is a C_{1-6} alkyl group optionally substituted by the same or different 1

to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 3] The compound according to claim 2, wherein R^1 is a C_{1-6} alkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 4] The compound according to claim 2, wherein R^1 is a C_{1-6} alkyl group substituted by a C_{3-8} cycloalkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 5] The compound according to claim 1, wherein R^1 is a C_{3-8} cycloalkyl group, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 6] The compound according to claim 1, wherein one of R^2, R^3, R^4 and R^5 is $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 7] The compound according to claim 1, wherein one of R^2, R^3, R^4 and R^5 is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A, or a pharmaceutically acceptable salt thereof, or a solvate

thereof.

[Claim 8] The compound according to claim 1, wherein R^6 is a halogen atom, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

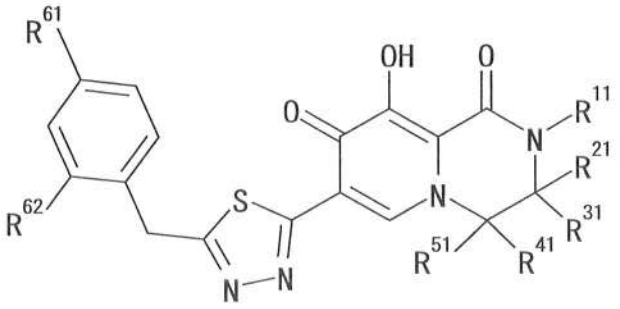
[Claim 9] The compound according to claim 1, wherein Y is CH, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 10] The compound according to claim 1, wherein Y is a nitrogen atom, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 11] The compound according to claim 1, wherein m is 1 or 2, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 12] The compound according to claim 1, wherein n is 1, or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 13] The compound according to claim 1, which is represented by the following formula [I-1], or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[I-1]

wherein

R^{11} is

(1) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group, or

(2) a C_{3-8} cycloalkyl group,

R^{21}, R^{31}, R^{41} and R^{51} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

wherein R^{21}, R^{31}, R^{41} and R^{51} are not hydrogen atoms at the same time,

R^{61} is a halogen atom, and

R^{62} is a hydrogen atom or a halogen atom.

[Claim 14] The compound according to claim 13, wherein R^{21} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A, and

R^{31}, R^{41} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 15] The compound according to claim 13, wherein R^{21} is a C_{1-6} alkyl group, and

R^{31}, R^{41} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 16] The compound according to claim 13, wherein R^{41} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A, and

R^{21}, R^{31} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

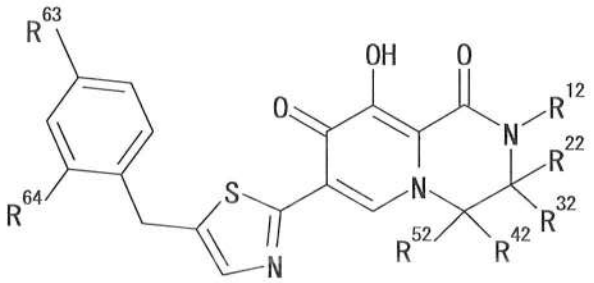
[Claim 17] The compound according to claim 13, wherein R^{21} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

R^{41} is a C_{1-6} alkyl group, and

R^{31} and R^{51} are each a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

[Claim 18] The compound according to claim 1, which is represented by the following formula [I-2], or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[I-2]

wherein

R^{12} is a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from

(i) a C_{3-8} cycloalkyl group, and

(ii) a C_{1-6} alkoxy group,

R^{22}, R^{32}, R^{42} and R^{52} are the same or different and each is

(1) a hydrogen atom,

(2) $-CO-NR^aR^b$

wherein R^a and R^b are the same or different and each is

(i) a hydrogen atom,

(ii) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(iii) a C_{3-8} cycloalkyl group, or

R^a and R^b optionally form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring

optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B, or

(3) a C_{1-6} alkyl group optionally substituted by the same or different 1 to 5 substituents selected from group A,

wherein R^{22}, R^{32}, R^{42} and R^{52} are not hydrogen atoms at the same time,

R^{63} is a halogen atom, and

R^{64} is a hydrogen atom or a halogen atom.

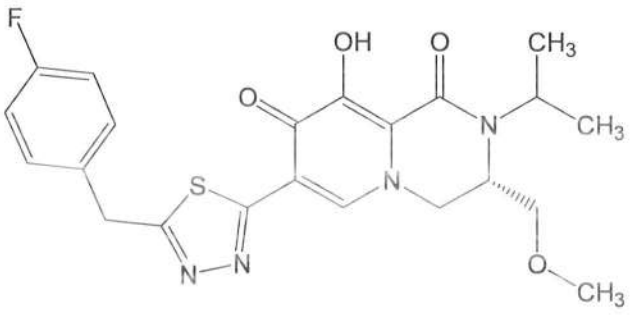
[Claim 19] The compound according to claim 18, wherein R^{42} is -CO-NR^aR^b wherein R^a and R^b form, together with the nitrogen atom bonded thereto, a saturated monocyclic hetero ring optionally containing, besides carbon atom and one nitrogen atom, 1 to 5 hetero atoms selected from a nitrogen atom, an oxygen atom and a sulfur atom, and optionally substituted by the same or different 1 to 5 substituents selected from group B,

R^{52} is a C_{1-6} alkyl group, and

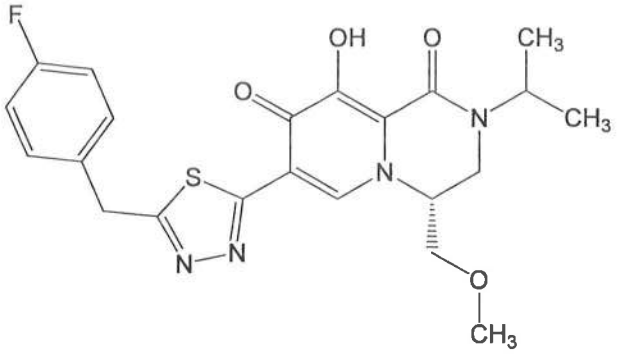
R^{22} and R^{32} is a hydrogen atom,

or a pharmaceutically acceptable salt thereof, or a solvate thereof.

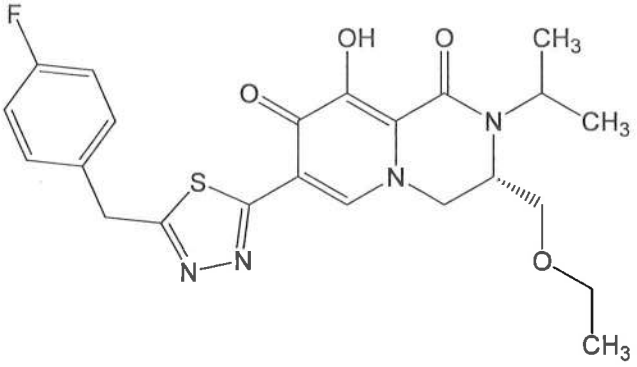
[Claim 20] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



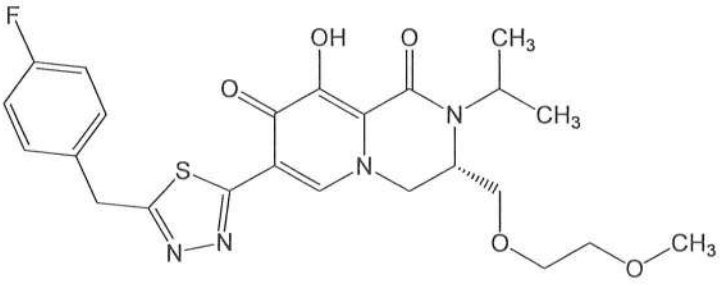
[Claim 21] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



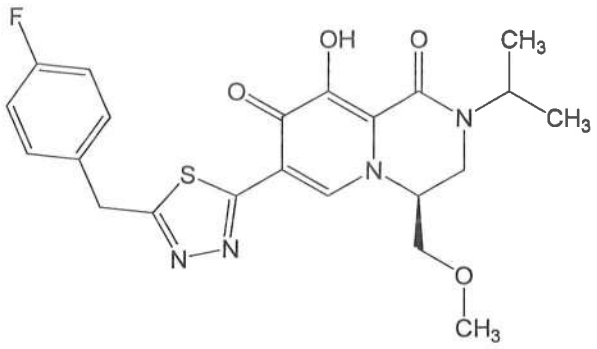
[Claim 22] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



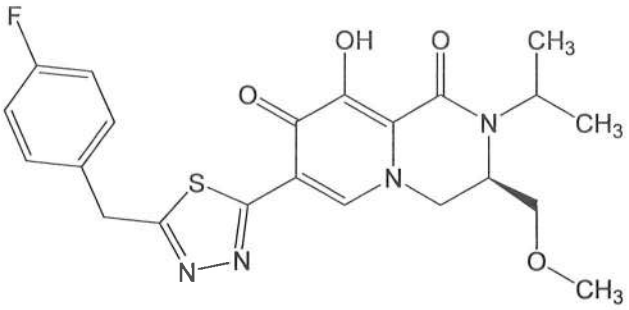
[Claim 23] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



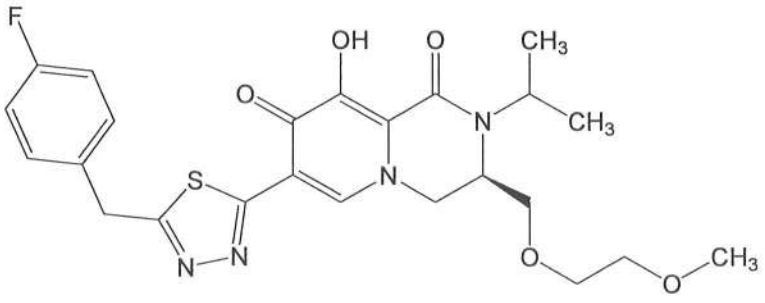
[Claim 24] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



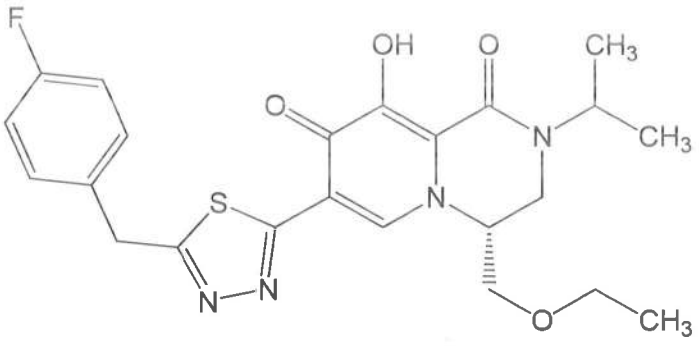
[Claim 25] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



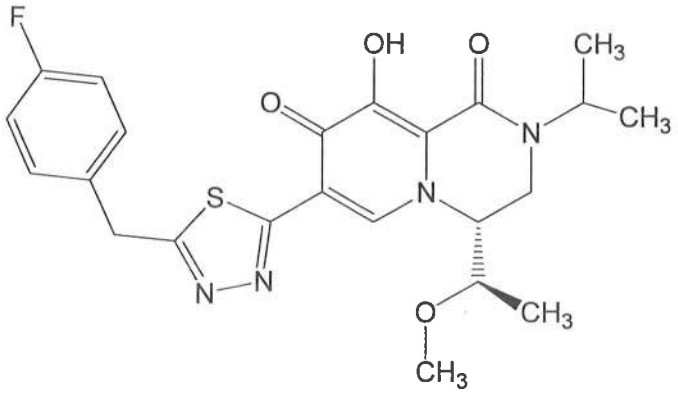
[Claim 26] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



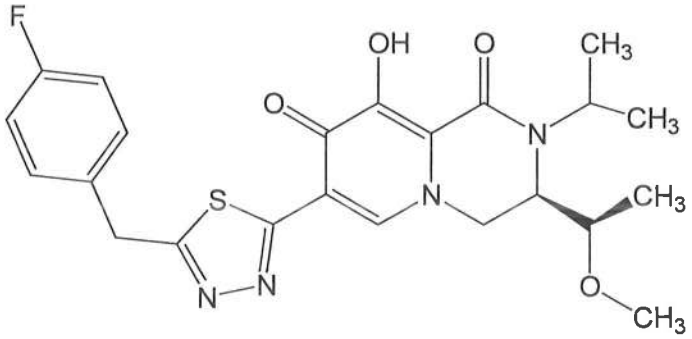
[Claim 27] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[Claim 28] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[Claim 29] The compound according to claim 1, which is represented by the formula, or a pharmaceutically acceptable salt thereof, or a solvate thereof:



[Claim 30] A pharmaceutical composition comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[Claim 31] An anti-HIV agent comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

[Claim 32] An HIV integrase inhibitor comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, as an active ingredient.

[Claim 33] An anti-HIV agent comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, in combination with one or

more other kinds of anti-HIV active substances.

[Claim 34] Use of the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, for the production of an anti-HIV agent.

[Claim 35] Use of the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, for the production of an HIV integrase inhibitor.

[Claim 36] A method for the prophylaxis or treatment of an HIV infectious disease in a mammal, which comprises administering an effective amount of the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, to said mammal.

[Claim 37] The method according to claim 36, which further comprises administering an effective amount of one or more other kinds of anti-HIV active substances to the mammal.

[Claim 38] A method for inhibiting HIV integrase in a mammal, which comprises administering an effective amount of the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, to said mammal.

[Claim 39] An anti-HIV composition comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[Claim 40] A pharmaceutical composition for inhibiting HIV integrase, comprising the compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof, or a solvate thereof, and a pharmaceutically acceptable carrier.

[Claim 41] A commercial package comprising the pharmaceutical composition according to claim 30 and a written matter associated therewith, which states that the pharmaceutical composition can or should be used for treating HIV.

[Claim 42] A kit comprising the pharmaceutical composition

according to claim 30 and a written matter associated therewith, which states that the pharmaceutical composition can or should be used for treating HIV.

SEQUENCE LISTING

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