

DESCRIPTION

HETEROCYCLIC JANUS KINASE 3 INHIBITORS

5 The present invention relates to a novel condensed heterocyclic compound and to a medicament containing the compound as an active ingredient, and more particularly, to an immune disease treating agent.

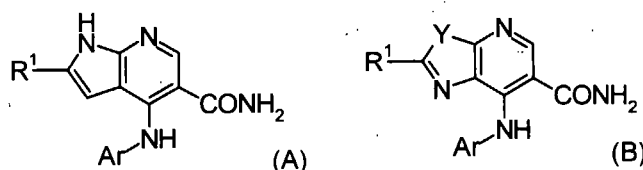
10 BACKGROUND ART

 Janus kinase 3 (hereafter referred to as JAK3) is a family of protein kinases. Although kinases in this family, other than JAK3, are expressed in a wide range of tissues, JAK3 is expressed locally in hematopoietic cells. This does not
15 contradict the fact that JAK3 plays an important role in signal transmission via various receptors, such as interleukin (hereafter referred to as IL) -2, IL-4, IL-7, IL-9, IL-15, and IL-21 by noncovalent association with the common γ chain (refer to nonpatent literature 1 and nonpatent literature 2).

20 In XSCID (X-linked severe combined immunodeficiency) patient populations, JAK3 protein level lowers or a genetic defect is found in the common γ chain. It is indicated that this problem occurs because immunosuppression blocks JAK3-dependent signaling pathways (refer to nonpatent
25 literature 3 and nonpatent literature 4). Animal experiments

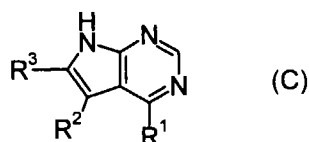
have shown that JAK3 not only plays an important role in maturation of B-lymphocytes and T-lymphocytes but also in maintaining the function of T-cells. Hence, it is expected that diseases involving proliferative abnormality of T-cells, such as rejection during organ/tissue transplantation and autoimmune diseases, can be treated by controlling immune response through this mechanism.

On the other hand, a pyrrolopyridine derivative (patent literature 1) represented by formula (A) or (B) or an imidazopyridine derivative (refer to patent literature 2) is known as a compound having JAK3 inhibition activity.



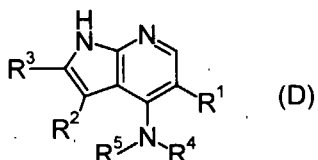
(For the symbols in the formulas, refer to the corresponding patent publications.)

Furthermore, a pyrrolopyrimidine derivative (refer to patent literature 3, patent literature 4, patent literature 5, and patent literature 6) represented by formula (C) is also known as a compound having JAK3 inhibition activity.



(For the symbols in the formula, refer to the corresponding patent publications.)

Still further, a pyrrolopyridine derivative (refer to patent literature 7) represented by formula (D) is also known as a compound having JAK3 inhibition activity.



5 (For the symbols in the formula, refer to the corresponding patent publication:)

However, in any literature, the compound according to the present invention is not disclosed specifically.

[Nonpatent literature 1] J. J. O'shea et al, Cell, Vol. 109
10 (suppl.), S121, 2002

[Nonpatent literature 2] K. Ozaki et al, Science, Vol. 298,
p. 1630, 2002

[Nonpatent literature 3] P. Macchi et al, Nature, Vol. 377,
p. 65, 1995

15 [Nonpatent literature 4] S. M. Russell et al, Science, Vol.
270, p. 797, 1995

[Patent literature 1] WO 2004/099205

[Patent literature 2] WO 2004/099204

[Patent literature 3] WO 99/065908

20 [Patent literature 4] WO 99/065909

[Patent literature 5] WO 01/042246

[Patent literature 6] WO 02/000661

[Patent literature 7] WO 2006/069080

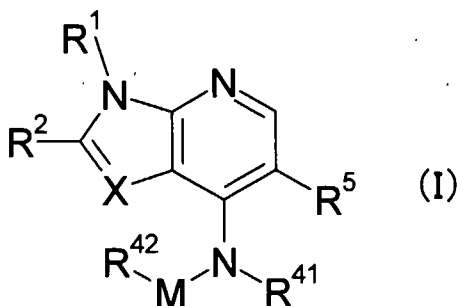
DISCLOSURE OF THE INVENTION

PROBLEM TO BE SOLVED BY THE INVENTION

As a result of intensive studies with an object of providing a useful pharmaceutical composition having JAK3 inhibition activity, the inventors have found that a novel condensed heterocyclic compound has an excellent JAK3 inhibition activity, and have completed the present invention.

More specifically, the present invention provides a novel condensed heterocyclic compound represented by the following formula (I) or pharmaceutically acceptable salts thereof, and a pharmaceutical composition containing the compound, more particularly, a pharmaceutical composition serving as an agent for treating and/or preventing autoimmune diseases, inflammatory diseases, and allergic diseases.

The condensed heterocyclic compound is a condensed pyridine compound represented by the following formula (I):



wherein

X is N or CR³,

M is (CH₂)_m; m is 0 or 1,

R¹ is -H or lower alkyl which may be substituted,

R^2 is -H or lower alkyl which may be substituted,

R^3 is -H, halogen, or lower alkyl which may be substituted,

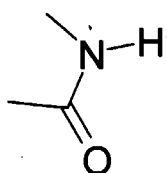
R^{41} is -H or heteroaryl which may be substituted,

5 R^{42} is a bridged ring group which may be substituted,

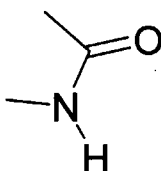
R^5 is a group selected from the group consisting of halogen, cyano, acyl, acylamino, lower alkyl, lower alkenyl, -O-lower alkyl, 5- or 6-membered heterocycloalkyl, 5- or 6-membered heterocycloalkenyl, and 5-membered heteroaryl,
10 each of which may be substituted,

provided that when R^5 is 5-membered heteroaryl, X is $-CR^3$,

or R^{41} and R^5 may be linked via a specific functional group to form bivalent groups shown below:

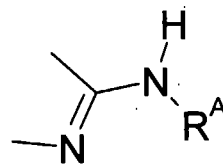


(I-A)



(I-B)

or



(I-C)

15 wherein R^A is -H or acyl which may be substituted, or pharmaceutically acceptable salts thereof.

EFFECT OF THE INVENTION

The compound according to the present invention has JAK3
20 inhibition activity and is thus useful as an active ingredient of an agent for treating and/or preventing diseases caused by

undesirable cytokine signal transmission (e.g., rejection during organ/tissue transplantation, autoimmune diseases, asthma, atopic dermatitis, Alzheimer's disease, and atherosclerotic disease), or diseases caused by abnormal
5 cytokine signal transmission (e.g., cancer and leukemia).

BEST MODES FOR CARRYING OUT THE INVENTION

The compound according to the present invention represented by the formula (I) is characterized in its chemical
10 structure that the compound has a cross-linked amine and also has a skeleton in which 5- and 6-membered heterocycles are condensed, just as in 1H-pyrrolo[2,3-b]pyridine, 1H-imidazo[4,5-b]pyridine, or pyrazolo[1,5-a]pyrimidine, and is further characterized in pharmacology that the compound has
15 a JAK3 inhibition activity.

The present invention is described below in detail.

The term "alkyl" in this specification is a straight or branched monovalent group.

The term "lower alkyl" in the specification is a C₁-C₆
20 straight or branched alkyl and may include, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, n-pentyl, neopentyl, and n-hexyl, preferably methyl, ethyl, n-propyl, isopropyl, and isobutyl, and particularly preferably methyl and ethyl.

25 The term "lower alkenyl" in the specification is C₂-C₆

straight or branched alkenyl having a double bond at each possible site, and may include, such as ethenyl (vinyl), 1-propenyl, 2-propenyl (allyl), 1-methylethen-1-yl, 1-buten-1-yl, 2-buten-1-yl, 3-buten-1-yl, 1-methyl-1-propen-1-yl, 2-methyl-1-propen-1-yl, 1-methyl-2-propen-1-yl, and 2-methyl-2-propen-1-yl, preferably 1-methyl-2-propen-1-yl.

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

10 The term "cycloalkyl" is a C₃-C₈ monovalent nonaromatic carbocyclic group, and may partially have unsaturated bonds or may be condensed with a benzene ring. However, bridged cycloc hydrocarbons are excluded. Cycloalkyl may include, such as cyclopropyl, cyclobutyl, cyclohexyl, cycloheptyl, 15 cyclooctyl, cyclobutenyl, cyclohexenyl, cyclooctadienyl, indanyl, and tetrahydronaphthyl, preferably cyclohexyl.

The term "heterocycloalkyl" is a 5- to 6-membered nonaromatic saturated heterocycle which may have one or more identical or different hetero atoms selected from the group consisting of nitrogen atoms, oxygen atoms, and sulfur atoms 20 which may be oxidized. Heterocycloalkyl may be partially unsaturated or may be condensed with a benzene ring. However, aza-bridged cyclic hydrocarbons are excluded. Heterocycloalkyl may include, such as aziridinyl, azetidiny, 25 pyrrolizinyl, piperidinyl, homopiperidinyl, morpholinyl,

thiomorpholinyl, piperazinyl, tetrahydrofuranyl,
tetrahydrothiophenyl, dihydrooxazolyl, tetrahydropyranyl,
tetrahydrothiopyranyl, indolynyl, tetrahydroquinolyl,
tetrahydroisoquinolyl, and benzoxazinyl, preferably
5 dihydrooxazolyl, oxadiazolyl, oxadiazolanyl, and furanyl.

The term "heterocycloalkenyl" is partially substituted
"heterocycloalkyl".

The term "cyclic amino" is, among groups defined in
"heterocycloalkyl" a monovalent 3- to 8-membered nonaromatic
10 cyclic amine which has at least one nitrogen atom, and may have
one or more identical or different hetero atoms selected from
the group consisting of nitrogen atoms, oxygen atoms, and
sulfur atoms which may be oxidized, wherein at least one
nitrogen atom has a bond. However, aza-bridged cyclic
15 hydrocarbons are excluded. The "Cyclic amino" may include,
such as aziridino, azetidino, pyrrolidino, piperidino,
homopiperidino, morpholino, thiomorpholino, and piperazino.

The term "aryl" is an aromatic hydrocarbon group and may
include, phenyl, naphthyl, and indenyl, preferably C₆-C₁₀ aryl,
20 and more preferably phenyl.

The term "heteroaryl" is a monovalent 5- or 6-membered
aromatic heterocyclic group having one or more identical or
different hetero atoms selected from the group consisting of
nitrogen, oxygen and sulfur atoms, and may be condensed with
25 a benzene ring. "Heteroaryl" may include, such as pyridyl,

pyrazinyl, pyrimidinyl, pyridazinyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, thienyl, furyl, oxadiazolyl, thiadiazolyl, quinolyl, isoquinolyl, benzothiazolyl, benzoxazolyl, indolyl, indazolyl, quinoxalyl, and quinazolyl, preferably pyridazinyl, pyridyl, pyrazinyl, thiazolyl, pyrazolyl, and thioxazolyl.

The term "bridged ring group" means "bridged cyclic hydrocarbon" and "aza-bridged cyclic hydrocarbon".

The term "bridged cyclic hydrocarbon" is a saturated or unsaturated, bicyclic or polycyclic bridged hydrocarbon group having two or three C₃-C₁₀ cycloalkyl rings. Non bridged cycloalkyls are excluded. Bicyclic or polycyclic C₄-C₁₆ bridged hydrocarbon groups are particularly preferable. Bridged cyclic hydrocarbon may include, such as bicyclo[2.1.1]hexyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl, bicyclo[4.3.1]decyl, bicyclo[3.3.1]nonyl, bornyl, bornenyl, norbornyl, norbornenyl, 6,6-dimethylbicyclo[3.1.1]heptyl, tricyclobutyl, and adamantyl, preferably adamantyl or bicyclo[2.2.1]heptyl.

The term "aza-bridged cyclic hydrocarbon" is a saturated or unsaturated, bicyclic or polycyclic bridged hydrocarbon group in which at least one of atoms constituting a ring is a nitrogen atom. Non bridged heterocycloalkyls are excluded. Bicyclic or polycyclic C₄-C₁₆ aza-bridged hydrocarbon groups

are particularly preferable. The term "aza-bridged cyclic hydrocarbon" may include, such as azanorbornyl, quinuclidinyl, isoquinuclidinyl, tropanyl, azabicyclo[3.2.1]octanyl, azabicyclo[2.2.1]heptanyl, 2-azabicyclo[3.2.1]octanyl, azabicyclo[3.2.1]octanyl, azabicyclo[3.2.2]nonanyl, azabicyclo[3.3.0]nonanyl, and azabicyclo[3.3.1]nonanyl, preferably tropanyl, 2-oxa-5-azabicyclo[2.2.1]hept-5-yl.

The term "acyl" means -C (=O) -lower alkyl, -C (=O) -cycloalkyl, -C (=O) -heterocycloalkyl, -C (=O) -aryl, -C (=O) -heteroaryl, carbamoyl, lower alkylcarbamoyl, -C (=O) -C (=O)-NH-lower alkyl, cycloalkylcarbamoyl, heterocycloalkylcarbamoyl, arylcarbamoyl, and heteroarylcarbamoyl. The term "lower alkyl," "cycloalkyl," "heterocycloalkyl," "aryl" and "heteroaryl" have the above-mentioned meanings.

X in the formula (I) is preferably CH.

R¹ in the formula (I) is preferably -H. R² in the formula (I) is preferably -H or CH₃, and more preferably -H.

R⁴¹ in the formula (I) is preferably -H.

Furthermore, R⁴² in the formula (I) is preferably adamantyl or tropanyl, each of which may be substituted with OH.

Still further, R⁵ in the formula (I) is preferably carbamoyl which may be substituted or -C(=O)-lower alkyl which may have OH more preferably -CONH₂ or hydroxyacetyl. As

another embodiment, R^{41} and R^5 are bonded via a specific functional group to form a cyclic structure described above, preferably formula (I-C).

As substituents which are allowed to be used for "which may be substituted" of R^1 , R^2 , R^3 , R^{41} , R^{42} and/or R^5 , the following groups described in items (a) to (g) are included:

- (a) Halogen
- (b) $-OH$, $-O-R^Z$, $-O$ -phenyl, $-OCO-R^Z$, $-OCONH-R^Z$, oxo ($=O$);
- (c) $-SH$, $-S-R^Z$, $-S$ -phenyl, $-S$ -heteroaryl, $-SO-R^Z$, $-SO$ -phenyl,
10 $-SO$ -heteroaryl, $-SO_3H$, $-SO_2-R^Z$, $-SO_2$ -phenyl,
 $-SO_2$ -heteroaryl, sulfamoyl which may be substituted with
one or two R^Z groups.
- (d) Amino which may be substituted with one or two R^Z groups,
 $-NHCO-R^Z$, $-NHCO$ -phenyl, $-NHCO_2-R^Z$, $-NHCONH_2$, $-NHCONH-R^Z$,
15 $-NHSO_2-R^0$, $-NHSO_2$ -phenyl, $-NHSO_2NH_2$, $-NO_2$, $=N-O-R^Z$;
- (e) $-CHO$, $-CO-R^Z$, $-CO_2H$, $-CO_2-R^Z$, carbamoyl which may be
substituted with one or two R^Z groups, $-CO$ -cyclic amino,
 $-COCO-R^Z$, cyano;
- (f) R^Z
- 20 (g) Phenyl which may be substituted with one or more groups
selected from the substituents described in the above items
(a) to (f), 5- or 6-membered heterocycloalkyl, 5- or 6-membered
heteroaryl, 5- or 6-membered heterocycloaryl.

R^Z in the above items (a) to (g) may include "cyano; $-OH$;
25 and lower alkyl which may be substituted with one to three

groups selected from the group consisting of -O-lower alkyl, -NH-lower alkyl, -CONH-lower alkyl, 5- or 6-membered heterocycloalkyl, and 5- or 6-membered heteroaryl."

The compound according to the present invention may include geometric isomers and tautomeric isomers depending on the type of constituent. In addition, the compound according to the present invention may have asymmetric carbon atoms. All of the isomers, including separated isomers and mixtures thereof, are included within the scope of the present invention. Furthermore, labeled compounds, that is, compounds obtained by substituting one or more atoms of the compound according to the present invention with radioactive or nonradioactive isotopes are also included in the scope of the present invention.

Furthermore, the pharmaceutically acceptable prodrug of the compound of the present invention is also included in the scope of the present invention. The pharmaceutically acceptable prodrug is a compound having a group that can be converted into amino group, hydroxyl group, carboxyl group, etc. through solvolysis or under physiological conditions. The groups described in Prog. Med., Vol. 5, p. 2157-2161, 1985 and "Iyakuhin No Kaihatsu (Development of Medicines)" (Hirokawa Pub. Co., 1990), Vol. 7, Molecular Design, p. 163-198 are taken as examples of groups forming such prodrugs.

The compound represented by the formula (I) may form acid

or base addition salts. These salts should only be pharmaceutically acceptable salts. More specifically, the salts may include an acid addition salt with an inorganic acid (e.g., hydrochloric acid, hydrobromic acid, hydriodic acid, sulfuric acid, nitric acid, and phosphoric acid), and an acid addition salt with an organic acid (e.g., formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, tartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid, aspartic acid, and glutamic acid); a salt with an inorganic base (e.g., sodium, potassium, magnesium, calcium, and aluminum), and a salt with an organic base (e.g., methylamine, ethylamine, ethanolamine, lysine, and ornithine); an ammonium salt; and the like.

Still further, various hydrates, solvates, and crystalline polymorphic forms of the compound represented by the formula (I) and salts thereof are also included in the scope of the present invention.

PROCESS

The compound according to the present invention can be produced using the characteristics based on the basic skeleton or the type of substituent thereof and by applying various known synthesis methods. During the production, protecting the relevant functional group with a suitable protective group or

replacing the relevant functional group with a group that can be easily converted into the functional group at the stage of a starting substance or an intermediate may occasionally be effective depending on the type of the functional group in production technology. This kind of functional group may include, for example, amino group, hydroxyl group, and carboxyl group. The protective group for such a functional group may include, for example, the protective groups described in "Protective Groups in Organic Synthesis (3rd. Ed, 1999)" written by T. W. Greene and P. G. Wuts, and one of these should only be selected and used as necessary depending on reaction conditions. In this kind of method, the desired component can be obtained by introducing the protective group, by carrying out reaction and by eliminating the protective group as necessary, or by converting the group into a desired group.

In addition, the prodrug of the compound according to the present invention can be produced by introducing a specific group or by carrying out reaction using the obtained compound represented by the formula (I) at the stage of a starting substance or an intermediate, just as in the case of the above-mentioned protective group. The reaction can be carried out using methods known to those skilled in the art, such as ordinary esterification, amidation, and dehydration.

The abbreviations used in the specification are as

follows:

Pr: Preparation number; Ex: Example number; Structure:

chemical structure; Rf-Syn: the number of an Example to which reference was made (the number indicates that the relevant

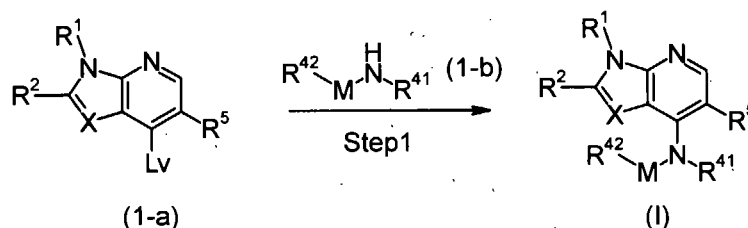
5 compound was produced according to a production method similar to that for producing the compound described in the Example designated by the number.); HPLC: high performance liquid

chromatography; TLC: thin layer chromatography; Rf: rate of flow value; Data: NMR data and/or MS data; $^1\text{H-NMR}$: ^1H -nuclear

10 magnetic resonance; MS: mass spectrometry; $(\text{M}+\text{H})^+$: $(\text{M}+\text{H})^+$;

$(\text{M}+\text{Na})^+$: $(\text{M}+\text{Na})^+$; $(\text{M}-\text{H})^-$: $(\text{M}-\text{H})^-$.

<First process>



[wherein R^1 , R^2 , R^{41} , R^{42} , R^5 , M and X are as defined above, and

15 Lv is a leaving group.]

In this process, the compound represented by the formula (I-a) and having a leaving group is reacted with the amine represented by the formula (I-b) to produce the compound according to the present invention represented by the formula

20 (I). The leaving group Lv may include halogen (e.g., chloro and bromo); sulfonyloxy (e.g., methanesulfonyloxy, ethanesulfonyloxy, benzenesulfonyloxy, p-toluenesulfonyloxy,

p-nitrobenzenesulfonyloxy, and trifluorometanesulfonyloxy);
etc.

In Step 1, the leaving group Lv of the compound
represented by the formula (I-a) is substituted with amine.

5 This reaction is carried out under atmospheric pressure or
under pressure in the absence of a solvent or in the presence
of a suitable solvent.

The solvent may include, for example, aromatic
hydrocarbons (e.g., toluene and xylene); ketones (e.g.,
10 acetone and methyl ethyl ketone); ethers (e.g., diethylether,
tetrahydrofuran (THF), dioxane, and diethoxyethane); alcohols
(e.g., methanol (MeOH), ethanol (EtOH), 2-propanol (i-PrOH),
and 1-butanol (n-BuOH)); halogenated hydrocarbons (e.g.,
dichloromethane, 1,2-dichloroethane, chloroform, and carbon
15 tetrachloride); acetonitrile; aprotic solvents (e.g.,
dimethylformamide (DMF), 1,3-dimethyl-2-imidazolidinone,
N-methylpyrrolidone (NMP), and dimethylsulfoxide (DMSO));
water; or a mixture of these. It is preferable that the
reaction is carried out in the presence of a base, and the base
20 may include, for example, alkaline carbonates (e.g., sodium
carbonate and potassium carbonate); alkaline
hydrogencarbonates (e.g., sodium hydrogencarbonate and
potassium hydrogencarbonate); alkoxides (e.g., sodium
methoxide, sodium ethoxide, and potassium t-butoxide);
25 tertiary amines (e.g., triethylamine, tributylamine, and

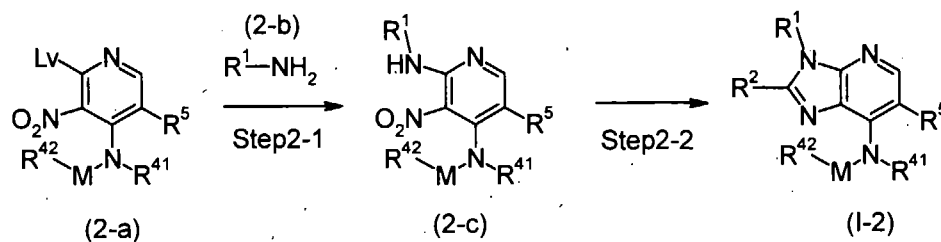
diisopropylethylamine); organic bases (e.g.,
1,8-diazabicyclo[5.4.0]undeca-7-ene, pyridine, and lutidine).
However, an excess amount of the compound (I-b) can also be
used. Although the reaction temperature differs depending on
5 the type of a starting compound and reaction conditions, the
reaction can usually be carried out at a temperature
approximately ranging from ambient temperature to the
refluxing temperature of a solvent. The reaction can also
usually be carried out in the presence of a base, such as sodium
10 hydroxide and sodium carbonate, in an organic solvent inert
to the reaction, such as N,N-dimethylformamide and
N,N-dimethylacetamide, under ambient temperature to heating.
In addition, the amine represented by the formula (I-b) can
also be used as a salt thereof for the reaction.

15 Furthermore, microwave irradiation can also be carried
out under heating. Still further, the reaction can also be
carried out by a coupling reaction using a phosphorus reagent,
such as 2-(di-t-butylphosphino)biphenyl, and a palladium
catalyst, such as palladium acetate, in the presence of a base,
20 such as cesium carbonate.

For the reaction, it is possible to use the methods
described in the Preparation(s) or the Example(s) of the
present specification or methods similar to those. The
compound represented by the formula (I-a) can thus be produced
25 using known methods, methods obvious to those skilled in the

art, or the methods described in the reference examples or the Examples of the present specification or methods similar to those.

<Second process>



[wherein R¹, R², R⁴¹, R⁴², R⁵, M and Lv are as defined forgoing.]

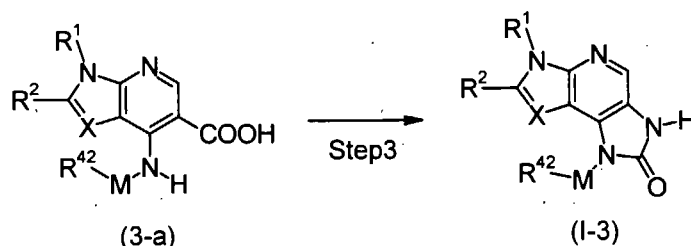
In this process, the nitropyridine compound represented by the formula (2-a) is reacted with the amine represented by the formula (2-b), and the leaving group at the second position is substituted with the amine to derive the aminonitropyridine compound represented by the formula (2-c). The derived compound is used to produce the compound according to the present invention represented by the formula (I-2).

The method used in Step 1 of the first process can be incorporated in Step 2-1. The amine represented by the formula (2-b) can also be used as a salt thereof for the reaction.

In Step 2-2 in the case that -R² is -H, an imidazole ring can be constructed by reacting an orthoformate, such as ethyl orthoformate, in the presence of an acid catalyst. It is desirable that the nitro group should be reduced before the orthoformate is used for the reaction. Furthermore, the method to be used in the case that the compound represented

by the formula (I-2) wherein $-R^2$ is not $-H$ is synthesized may include, for example, the method in which the amino group of the compound represented by the formula (2-c) is acylated in advance, the method in which tetraalkylorthocarbonate or
 5 alkylisothiocyanate is used instead of the orthoformate, and the method in which carboxylic acid or carboxylic anhydride is reacted with a strong acid, such as sulfonic acid. These actions can be carried out in a solvent inert to the reactions or in the absence of a solvent, under ambient temperature to
 10 heating or under heating and refluxing.

<Third process>



[wherein R^1 , R^2 , R^{42} , X , and M are as defined forgoing.]

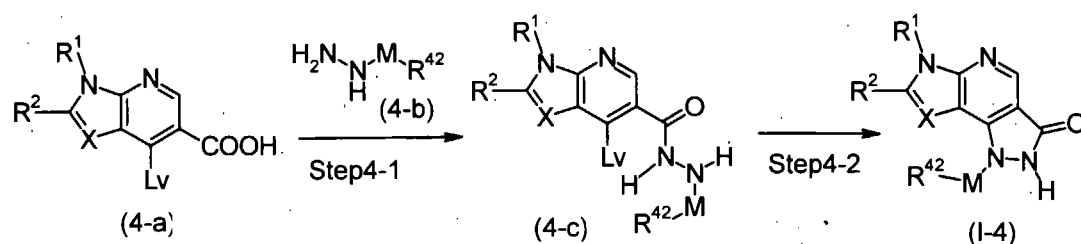
In this process, the compound according to the present
 15 invention represented by the formula (3-a) and having a carboxyl group is used as a starting compound to produce the compound according to the present invention represented by the formula (I-3).

In Step 3, the carboxyl group of the compound represented
 20 by the formula (3-a) is reacted with an azidation agent, such as diphenylphosphoryl azide (DPPA) and sodium azide, to construct an imidazolone ring according to the so-called

Curtius rearrangement reaction. It is advantageous that the reaction is carried out in the presence of a base.

Usually, triethylamine, pyridine, etc. can be used as a base, and the reaction can be carried out under ambient temperature to heating or under heating and refluxing.

<Fourth process>



[wherein R^1 , R^2 , R^{42} , M , X and Lv are as defined forgoing.]

In this process, the carboxylic compound represented by the formula (4-a) is reacted with the hydrazine derivative represented by the formula (4-b) to obtain the hydrazide represented by the formula (4-c). From the hydrazide, the compound according to the present invention represented by the formula (I-4) is produced.

Step 4-1 can be carried out similarly to the reaction in which the compound represented by the formula (4-a) and the compound represented by the formula (4-b) are condensed by amidation. The compound (4-a) can be used as a free acid for the reaction, and the reactive derivative thereof can also be used for the reaction. The reactive derivative of the compound (4-a) may include an acid halide (e.g., acid chloride and acid bromide); an ordinary ester (e.g., methyl ester, ethyl ester,

and benzyl ester); acid azide; an activated ester with
N-hydroxybenzotriazole (HOBt), p-nitrophenyl, or
N-hydroxysuccinimide); a symmetric acid anhydride; a mixed
acid anhydride with a halocarboxylic acid alkyl ester (e.g.,
5 alkyl halide carbonate), pivaloyl halide, p-toluenesulfonic
acid chloride, etc.; and a mixed acid anhydride, such as a
phosphoric acid-type mixed acid anhydride obtained by reaction
with diphenylphosphoryl chloride or N-methylmorpholine; etc.

When the compound (4-a) is reacted in the form of a free
10 acid or reacted without isolating the activated ester, it is
preferable to use a condensing agent, such as dicyclohexyl-
carbodiimide (DCC), 1,1'-carbonylbis-1H-imidazole (CDI),
diphenylphosphoryl azide (DPPA), diethylphosphoryl
cyanide (DEPC), and 1-ethyl-3-(3-dimethylaminopropyl)
15 carbodiimide hydrochloride (EDCI·HCl).

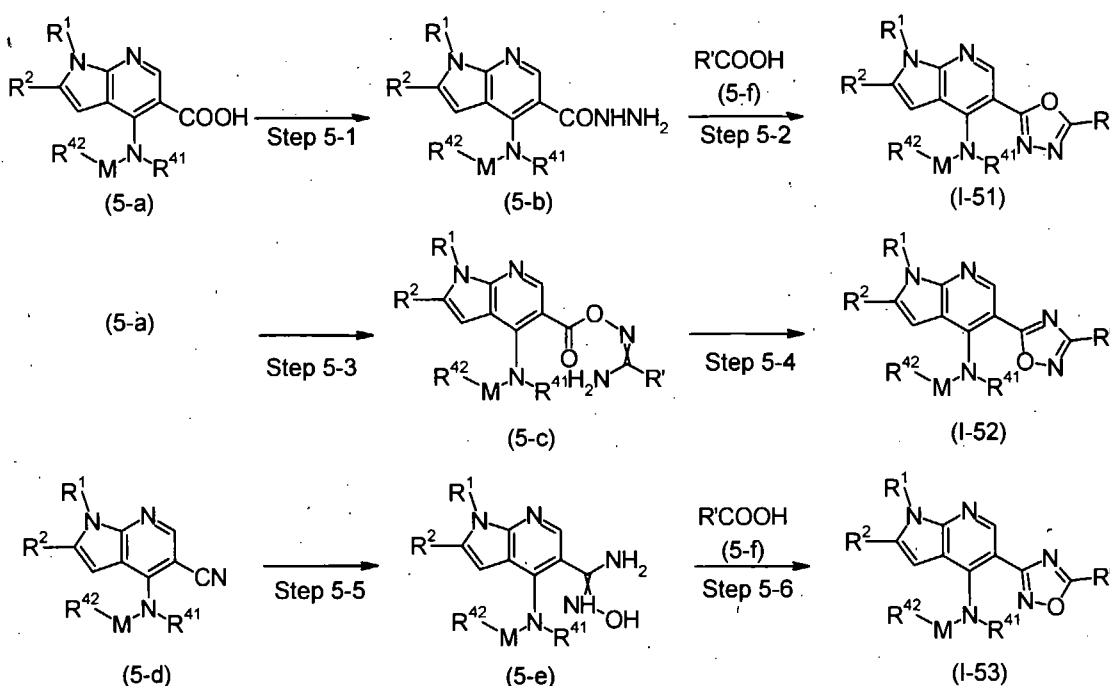
The reaction is carried out in an organic solvent inert
to the reaction, such as halogenated hydrocarbons, aromatic
hydrocarbons, ethers, esters (e.g., ethyl acetate),
acetonitrile, DMF, and DMSO, under cooling, under cooling to
20 ambient temperature, or under ambient temperature to heating,
although the conditions differ depending on the reactive
derivative or the condensing agent to be used.

In order to smoothly advance the reaction, it is
occasionally advantageous that an excess amount of the
25 compound (4-b) is used for the reaction or the reaction is
carried out in the presence of a base, such as

N-methylmorpholine, trimethylamine, triethylamine, diisopropylethylamine, N,N-dimethylaniline, pyridine, 4-(N,N-dimethylamino)pyridine, picoline, and lutidine. Pyridine can also be used as a solvent.

- 5 The method used in Step 1 of the first process can be incorporated in Step 4-2.

<Fifth process>



[wherein R^1 , R^2 , R^{41} , R^{42} and M are as defined above, R' is
 10 suitable substituent. The carboxylic acid represented by the formula (5-f) is a marketed product or can be prepared using a marketed product.]

In step 5-2, step 5-4 and step 5-6, a reaction for constructing an oxadiazole ring at R^5 is carried out.

- 15 In Step 5-1, a reaction for synthesizing an acid hydrazide from the carboxylic acid represented by the formula

(5-a) is carried out. Furthermore, the intermediate represented by the formula (5-c) can also be synthesized from the carboxylic acid represented by the formula (5-a). The reaction in Step 4-1 can be incorporated in each of these
5 reactions.

In Step 5-2, Step 5-4, and step 5-6, a reaction for constructing an oxadiazole ring is carried out under ambient temperature to heating. An organic base may be added to advance the reaction.

10 In Step 5-5, the aromatic nitrile compound represented by the formula (5-d) is reacted with hydroxylamine to obtain hydroxyamidine represented by the formula (5-e). The obtained hydroxyamidine is reacted with the carboxylic acid represented by the formula (5-f) to produce the compound according to the
15 present invention represented by the formula (I-53).

In Step 5-5, the reaction with free hydroxylamine or hydroxylamine hydrochloride is carried out in the presence of a base, whereby the hydroxyamidine represented by the formula (5-e) can be produced.

20 The reaction can be carried out in a solvent inert to the reaction. The solvent may include, for example, alcohols (e.g., methanol (MeOH), ethanol (EtOH), and 2-propanol (iPrOH)); aromatic hydrocarbons (e.g., toluene and xylene); ethers (e.g., diethylether, tetrahydrofuran (THF), dioxane,
25 and diethoxyethane); halogenated hydrocarbons (e.g.,

dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride); aprotic solvents (e.g., DMF, 1,3-dimethyl-2-imidazolidinone, and DMSO); water; or a mixture of these. Usually, alcohols are used for the reaction.

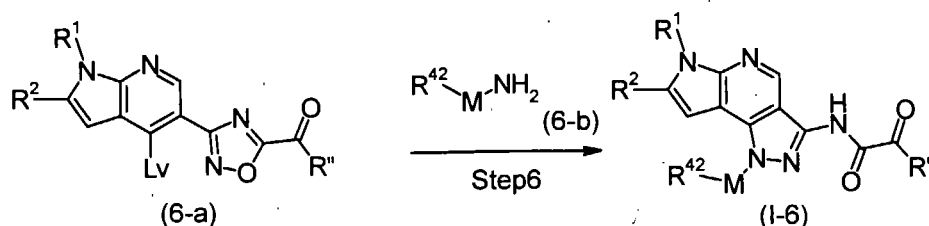
- 5 In the case that hydroxylamine hydrochloride is used for the reaction as described above, it is preferable that the reaction is carried out in the presence of a base, and the base may include, for example, alkaline carbonates (e.g., sodium carbonate and potassium carbonate); alkaline
- 10 hydrogencarbonates (e.g., sodium hydrogencarbonate and potassium hydrogencarbonate); alkoxides (e.g., sodium methoxide, sodium ethoxide, and potassium t-butoxide); tertiary amines (e.g., triethylamine and diisopropylethylamine); and organic bases (e.g.,
- 15 1,8-diazabicyclo[5.4.0]undeca-7-ene, pyridine, and lutidine). Although the reaction temperature differs depending on the type of a starting compound and reaction conditions, the reaction can usually be carried out at a temperature approximately ranging from ambient temperature to the
- 20 refluxing temperature of a solvent. The reaction can usually be carried out in the presence of a base, such as sodium carbonate, in an organic solvent inert to the reaction, such as methanol, under ambient temperature to heating.

- Step 5-6 consists of two stages: acylation of
- 25 hydroxyamidine and subsequent cyclization. The intermediate

producing method in Step 4-1 can be incorporated in the acylation in the first stage. However, the reaction is usually carried out under ambient temperature to heating, or under heating and refluxing. The cyclization in the second stage
5 can be carried out by isolating and purifying an acyl and by heating the acyl in an organic solvent inert to the reaction, such as ethanol and dioxane, in the presence or absence of a base. The base may include an inorganic base, such as sodium acetate, or an organic base, such as diisopropylethylamine.
10 The reaction consisting of the two stages can be carried out by one operation by performing ordinary acylation and then by directly heating the reaction mixture or by carrying out reaction under microwave irradiation.

The solvent may include, for example, aromatics (e.g.,
15 toluene, xylene, and pyridine); ethers (e.g., diethylether, tetrahydrofuran, dioxane, and diethoxyethane); halogenated hydrocarbons (e.g., dichloromethane, 1,2-dichloroethane, chloroform, and carbon tetrachloride); acetonitrile; aprotic solvents (e.g., DMF, N,N-dimethylacetamide (DMA),
20 1,3-dimethyl-2-imidazolidinone, N-methylpyrrolidone (NMP), and DMSO)); water; or a mixture of these. Although the reaction temperature differs depending on the type of a starting compound and reaction conditions, the reaction can be carried out under ambient temperature to heating.

<Sixth process>



[wherein R^1 , R^2 , R^{42} , M, and Lv are as defined above; R'' is suitable substituent.]

5 In Step 6, in the case that the compound represented by the formula (6-a) is reacted with the primary amine represented by the formula (6-b), after ipso substitution, the oxadiazole ring is opened to construct an aminopyrazolone ring. The reaction conditions described in Step 1 can be incorporated
10 herein as the reaction conditions. The reaction can be carrying out under ambient temperature to refluxing temperature.

In addition, some of the compounds represented by the formula (I) can also be produced from the compound according
15 to the present invention produced as described above by appropriately combining processes usually used by those skilled in the art, such as known alkylation, acylation, substitution, oxidation, reduction, hydrolysis, deprotection, halogenation, and Mannich reaction. For example, when the
20 compound according to the present invention wherein $-R^5$ is $-\text{CO}_2\text{H}$ is produced from the compound according to the present invention wherein R^5 is lower alkyloxycarbonyl, hydrolysis can

be used referring to the method described in "Jikken Kagaku Koza (Courses in Experimental Chemistry) (5th Ed., 2003)."

Moreover, when the compound according to the present invention wherein R⁵ is halogen is produced from the compound according

5 to the present invention wherein both R³ and R⁵ are -H,

halogenation can be used referring to the method described in

"Jikken Kagaku Koza (Courses in Experimental Chemistry) (5th Ed., 2003)."

Still further, when the compound according to the present invention wherein R³ is a lower alkyl substituted

10 with a group selected from the group consisting of mono(lower alkyl)amino, di(lower alkyl)amino, and cyclic amino is

produced from the compound according to the present invention

wherein R³ is -H, the Mannich reaction can be used referring

to the methods described in "Jikken Kagaku Koza (Courses in

15 Experimental Chemistry) (5th Ed., 2003)"; C. Mannich et al.,

Arch. Pharm., 1912, Vol. 250, p. 647; J. H. Brewster et al.,

Org. React., 1953, Vol. 7, p. 99; F. F. Blicke, Org. React.,

1942, Vol. 1, p. 303; K. W. Merz et al., Pharmazie, 1956, Vol.

11, p. 505; etc.

20 The processes capable of being usually used by those skilled in the art are not only used for the compound according to the present invention but can also be used for intermediates formed during production. The processes can also advance to subsequent processes.

25 The compound produced as described above is in a free

form or subjected to salt-forming processing using a conventional method and isolated and purified as a salt thereof. The isolation and purification are carried out by performing ordinary chemical operations, such as extraction, concentration, evaporation, crystallization, filtration, recrystallization, and various types of chromatography.

Various types of isomers can be isolated by utilizing the difference in physicochemical properties between the isomers using a conventional method. For example, a racemic mixture can be converted into an optically pure isomer using a general racemic resolution method, such as the method in which the racemic mixture is converted into a diastereomer salt with a general optically-active acid, such as tartaric acid, and subjected to optical resolution. Furthermore, the diastereomixture can be separated by fractional crystallization or various types of chromatography, for example. Still further, the optically-active compound can also be produced using a suitable optically-active material.

The pharmacological activity of the compound according to the present invention was verified by carrying out the following test.

Test example 1: JAK3 inhibition test

The JAK3 inhibition test was performed as described below according to the method of Okimoto et al.

(1) Preparation of human JAK3

Purified human JAK3 kinase domain was purchased from Carna Biosciences, Inc. (Kobe, Japan). This is obtained as described below. His-tag (41 kDa) was attached to the N-terminal of the 796-1124 (C-terminal) fragment of the human JAK3 protein (accession number #NM_000215), expressed using baculovirus expression system, and then purified using Ni-NTA affinity column chromatography.

(2) Measurement of JAK3 activity

As substrates, Biotin-Lyn-Substrate-2 (Biotin-XEQED EPEGF YFEWL EPE, X = ϵ -Acp (PEPTIDE INSTITUTE, INC., Osaka, Japan) and ATP were used. As an assay buffer, 15mM Tris-HCl pH 7.5 containing 0.01% Tween 20 and 2mM DTT was used. Normally, 20 μ L of a substrate solution (an assay buffer containing 627nM Biotin-Lyn-Substrate-2, 20 μ M ATP, and 25mM MgCl₂), an assay buffer containing 10 μ L of a substance to be tested, and 20 μ L of an enzyme solution were added to a microplate, and stirred sufficiently.

After incubation at ambient temperature for one hour, the plate was washed with a cleaning buffer (50mM Tris-HCl pH 7.5, 150mM NaCl, 0.02% Tween 20), and a blocking buffer (a cleaning buffer containing 0.1% bovine serum albumin) was added to the plate. After incubation at ambient temperature for 30 minutes, the blocking buffer was removed, and an HRP-PY-20 solution (obtained by diluting HRP-PY-20 solution with the blocking buffer 500 times) was added. After

incubation at ambient temperature for 30 minutes, the plate was washed four times, and a TMB substrate solution (Sigma) was added to the plate. After incubation at ambient temperature for four minutes, 1M sulfuric acid was added to stop the reaction. Enzyme activity was measured as absorbance at 450 nm. The efficacy of the test compound as a JAK3 inhibitor was expressed as an IC_{50} value.

The IC_{50} values described below are results obtained in the test.

The results of those tests are shown in the Table 1.
Table 1: JAK3 inhibitory activity of the compound of the present invention.

Table 1

Ex	IC_{50} (nM)	Ex	IC_{50} (nM)
29	2.3	379	1.2
32	1.9	384	0.28
33	2.1	405	0.65
34	0.17	426	2.3
121	1.1	434	0.86
122	0.43	484	0.31
133	4.4	498	1.3
143	0.69	543	0.33

It is verified that the compound according to the present invention has inhibition activity against JAK3 and is useful as an active ingredient of an agent for treating or preventing diseases caused by undesirable cytokine signal transmission (e.g., rejection during organ/tissue transplantation, autoimmune diseases, asthma, atopic dermatitis, Alzheimer's

disease, and atherosclerotic disease), or diseases caused by abnormal cytokine signal transmission (e.g., cancer and leukemia).

In addition, on the basis of the JAK3 inhibition activity, the compound according to the present invention is useful for treating and/or preventing the following diseases.

The pharmaceutical composition of the present invention comprising JAK3 inhibitor such as the compound (I) is useful as a therapeutic or prophylactic agent for diseases or conditions caused by undesirable cytokine signal transduction, such as rejection reaction in organ/tissue transplantation, autoimmune diseases, asthma, atopic dermatitis, Alzheimer's disease, atherosclerosis, tumors, myelomas, and leukemia as exemplified below:

rejection reactions by transplantation of organs or tissues such as the heart, kidney, liver, bone marrow, skin, cornea, lung, pancreas, islet, small intestine, limb, muscle, nerve, intervertebral disc, trachea, myoblast, cartilage, etc.; and graft-versus-host reactions following bone marrow transplantation; autoimmune diseases such as rheumatoid arthritis, systemic lupus, erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes and complications from diabetes, etc.

Furthermore, pharmaceutical preparations of the JAK3

inhibitor, such as the compound (I), are useful for the therapy or prophylaxis of the following diseases.

Inflammatory or hyperproliferative skin diseases or cutaneous manifestations of immunologically-mediated diseases (e.g., psoriasis, atopic dermatitis, contact dermatitis, eczematoid dermatitis, seborrheic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedema, vasculitides, erythema, dermal eosinophilia, lupus erythematosus, acne, alopecia areata, etc.);

autoimmune diseases of the eye (e.g., keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, herpetic keratitis, conical keratitis, corneal epithelial dystrophy, keratoleukoma, ocular premphigus, Mooren's ulcer, scleritis, Grave's ophthalmopathy, Vogt-Koyanagi-Harada syndrome, keratoconjunctivitis sicca (dry eye), phlyctenule, iridocyclitis, sarcoidosis, endocrine ophthalmopathy, etc.);

reversible obstructive airways diseases [asthma (e.g., bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, dust asthma, etc.), particularly chronic or inveterate asthma (e.g., late asthma, airway hyper-responsiveness, etc.), bronchitis, etc.]; mucosal or vascular inflammations (e.g., gastric ulcer, ischemic or thrombotic vascular injury, ischemic bowel diseases,

enteritis, necrotizing enterocolitis, intestinal damages associated with thermal burns, leukotriene B4-mediated diseases, etc.);

intestinal inflammations/allergies (e.g., coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease, ulcerative colitis, etc.);

food-related allergic diseases with symptomatic manifestation remote from the gastrointestinal tract (e.g., migraine, rhinitis, eczema, etc.);

autoimmune diseases and inflammatory conditions (e.g., primary mucosal edema, autoimmune atrophic gastritis, premature menopause, male sterility, juvenile diabetes mellitus, pemphigus vulgaris, pemphigoid, sympathetic ophthalmitis, lens-induced uveitis, idiopathic leukopenia, active chronic hepatitis, idiopathic cirrhosis, discoid lupus erythematosus, autoimmune orchitis, arthritis (e.g., arthritis deformans, etc.), polychondritis, etc.); allergic conjunctivitis.

Therefore, the pharmaceutical composition of the present invention is useful for the therapy and prophylaxis of liver diseases [e.g., immunogenic diseases (e.g., chronic autoimmune liver diseases such as autoimmune hepatic diseases, primary biliary cirrhosis, sclerosing cholangitis, etc.), partial liver resection, acute liver necrosis (e.g., necrosis caused by toxins, viral hepatitis, shock, anoxia, etc.),

hepatitis B, non-A/non-B hepatitis, hepatocirrhosis, hepatic failure (e.g., fulminant hepatitis, late-onset hepatitis, "acute-on-chronic" liver failure (acute liver failure on chronic liver diseases, etc.), etc.), etc.].

- 5 Pharmaceutical preparations of the JAK3 inhibitor, such as the compound (I), either from alone or in combination with one or more additional agents which may include but are not limited to cyclosporin A, tacrolimus, sirolimus, everolimus, micophenolate (e.g. Cellcept(R), Myfortic(R), etc.),
- 10 azathioprine, brequinar, leflunomide, sphingosine-1-phosphate receptor agonist (e.g. fingolimod, KRP-203, etc.), LEA-29Y, anti-IL-2 receptor antibody (e.g. daclizumab, etc.), anti-CD3 antibody (e.g. OKT3, etc.), Anti-T cell immunogloblin (e.g. AtGam, etc.) aspirin, CD28-B7 blocking
- 15 molecules (e.g. Belatacept, Abatacept, etc.), CD40-CD154 blocking molecules (e.g. Anti-CD40 antibody, etc.), protein kinase C inhibitor (e.g. AEB-071, etc.), acetaminophen, ibuprofen, naproxen, piroxicam, and anti inflammatory steroid (e.g. prednisolone or dexamethasone) may be administrated as
- 20 part of the same or separate dosage forms, via the same or different routes of administration, and on the same or different administration schedules according to standard pharmaceutical practice.

The pharmaceutical composition containing one or two or

25 more kinds of the compound represented by the formula (I) or

pharmaceutically acceptable salts thereof as an active ingredient can be prepared using carriers, excipients, and other additives usually used for pharmaceutical preparation.

Therapeutic administration can be accomplished either
5 by oral administration via tablets, pills, capsules, granules, powders, solutions, etc., or parenteral administration via intravenous or intramuscular injections, suppositories, transdermal agents, transnasal agents, inhalers, etc. The dose of the compound is determined appropriately in
10 consideration of the symptoms, age, sex, and the like of each patient to be treated. Usually, in the case of oral administration, a daily dose of approximately 0.001 to 100 mg/kg of the compound can be administered one or two to four times per day for an adult patient. When intravenous
15 administration is required depending on symptoms, a dose of 0.0001 to 10 mg/kg of the compound can usually be administered one to multiple times per day for an adult patient. In the case of inhalation, a dose of 0.0001 to 1 mg/kg of the compound can usually be administered one to multiple times per day for
20 an adult patient.

The solid composition for use in the oral administration according to the present invention is used in the form of tablets, powders, granules, etc. In such a solid composition, one or more active ingredients are mixed with at least one
25 inactive excipient, such as lactose, mannitol, glucose,

hydroxypropyl cellulose, microcrystalline cellulose, starch, polyvinyl pyrrolidone, and magnesium aluminometasilicate. According to a usual method, the composition may contain inactive additives, such as a lubricant (e.g., magnesium stearate), a disintegrating agent (e.g., carboxymethyl starch sodium), and a solubilization assisting agent. If necessary, tablets or pills may be coated with sugar or a film of a gastric or enteric coating substance.

The liquid composition for oral administration contains pharmaceutically acceptable emulsions, solutions, suspensions, syrups, or elixirs, and also contains a generally used inert diluent, such as purified water or ethanol. In addition to the inert diluent, the composition may also contain auxiliary agents, such as a solubilization assisting agent, a moistening agent, and a suspending agent, as well as sweeteners, flavors, aromatics, and antiseptics.

The injections for parenteral administration contain aseptic aqueous or non-aqueous solutions, suspensions, or emulsions. The diluent for use in the aqueous solutions may include, for example, distilled water for injection use and physiological saline. The diluent for use in the non-aqueous solutions may include, for example, propylene glycol, polyethylene glycol, plant oil (e.g., olive oil), alcohol (e.g., ethanol), and polysorbate 80 (official name). Such a composition may further contain additive agents, such as a

tonicity agent, an antiseptic, a moistening agent, an emulsifying agent, a dispersing agent, a stabilizing agent, and a solubilization assisting agent. These compositions are sterilized by filtration through a bacteria retaining filter, blending of a germicide, or irradiation. Furthermore, they may also be produced in the form of sterile solid compositions and dissolved or suspended in sterile water or a sterile solvent for injection use prior to their use.

The transmucosal agents, such as inhalers and transnasal agents, are used in the form of solid, liquid or semisolid and can be produced according to conventional known methods. For example, excipients (e.g., lactose and starch), pH adjusters, antiseptics, surface active agents, lubricants, stabilizers, thickeners, etc. may also be added as necessary. For administration, suitable devices for inhalation or insufflation can be used. For example, using known devices and sprayers, such as measuring inhalation devices, the compound can be administered independently or in the form of prescribed mixture powders. Furthermore, the compound combined with pharmaceutically acceptable carriers can also be administered in the form of solutions or suspensions. Dry powder inhalers and the like may be devices for single or multiple administrations, and dry powders or capsules containing powders can also be used. Still further, the devices may be in the form of a pressure aerosol spray or the

like that uses a suitable ejection agent, such as chlorofluoroalkane or hydrofluoroalkane, or a suitable gas, such as carbon dioxide.

The drug for external use may include ointments, plasters, 5 creams, jellies, patches, sprays, lotions, eye-drops, eye ointments, etc. The drug contains generally used ointment bases, lotion bases, aqueous or non-aqueous solutions, suspensions, emulsions, etc. The ointment bases or lotion bases may include, for example, polyethylene glycol, 10 carboxyvinal polymer, white vaseline, bleached bee wax, polyoxyethylene hydrogenated castor oil, glyceryl monostearate, stearyl alcohol, cetyl alcohol, lauromacrogol, and sorbitan sesquioleate.

15 EXAMPLES

Although the present invention is described below specifically by way of Examples, the present invention is not limited by these Examples at all. Starting compounds being used in Examples include novel substances, and the methods for 20 producing such starting compounds from known compounds are described by way of Preparations.

Preparation 1

The compounds in Preparations 1-1 to 1-25 shown in the 25 following table were produced by using the corresponding

starting compounds according to the method similar to that described in Example 1.

Table 2

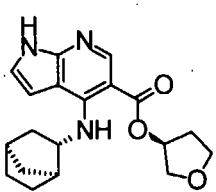
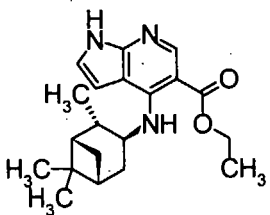
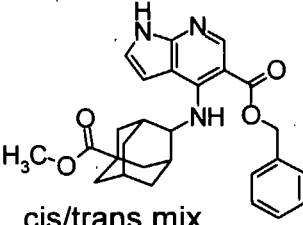
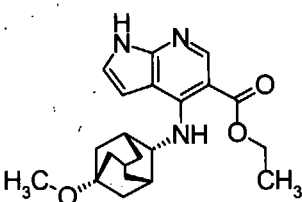
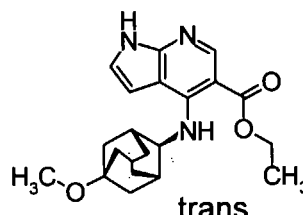
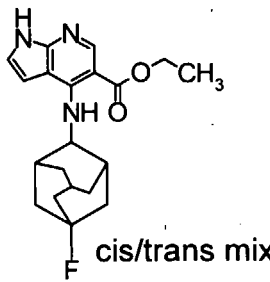
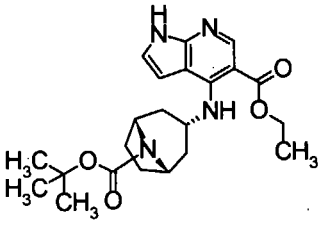
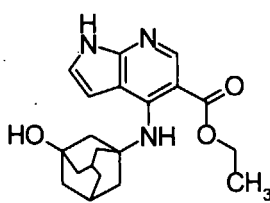
Pr	Structure	Pr	Structure
1-1		1-2	
1-3	 cis/trans mix	1-4	
1-5	 trans	1-6	 F cis/trans mix
1-7		1-8	

Table 2 (contd.)

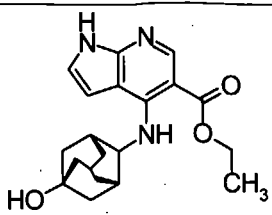
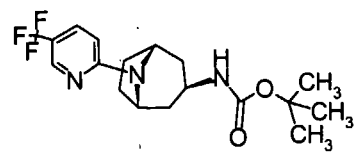
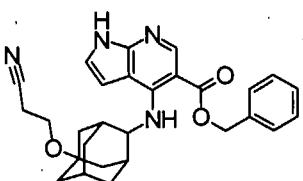
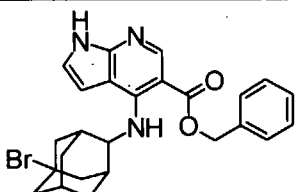
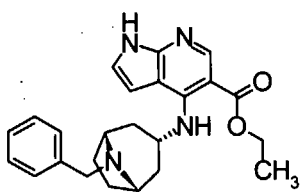
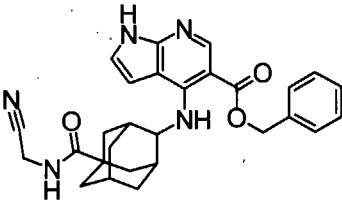
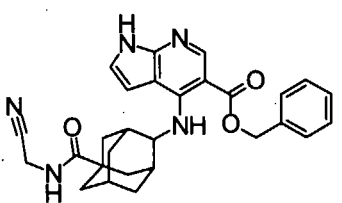
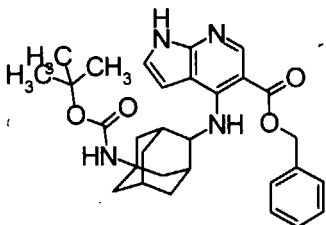
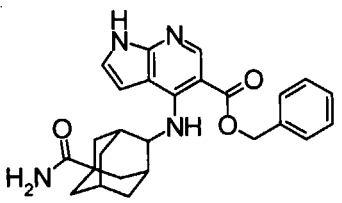
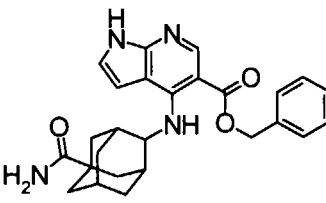
Pr	Structure	Pr	Structure
1-9	 cis/trans mix	1-10	
1-11	 cis or trans unknown	1-12	 cis or trans unknown
1-13		1-14	 diastereomer of 1-15 cis or trans unknown
1-15	 diastereomer of 1-14 cis or trans unknown	1-16	 cis/trans mix
1-17	 diastereomer of 1-18 cis or trans unknown	1-18	 diastereomer of 1-17 cis or trans unknown

Table 2 (contd.)

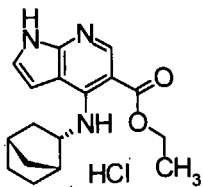
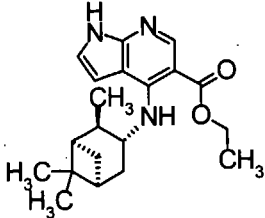
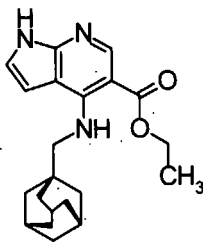
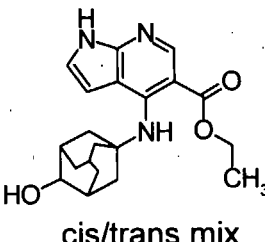
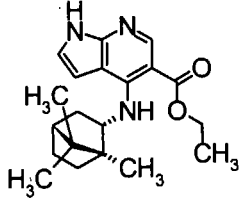
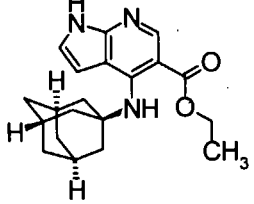
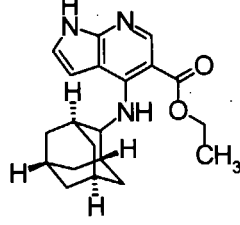
Pr	Structure	Pr	Structure
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1-21		1-22	
1-23		1-24	
1-25			

Table 3

Pr	Data
1-1	MS: 342 (M+H) +
1-2	MS: 342 (M+H) +
1-3	MS: 460 (M+H) +
1-4	MS: 370 (M+H) +
1-5	MS: 370 (M+H) +
1-6	MS: 358 (M+H) +
1-7	¹ H-NMR (400MHz, d6-DMSO) δ: 1.32 (3H, t, J=7.0Hz), 1.43 (9H, s), 1.73-1.87 (2H, m), 1.90-2.08 (4H, m), 2.18-2.33 (2H, m), 4.08-4.18 (2H, m), 4.28 (2H, q, J=7.0Hz), 4.37-4.47 (1H, m), 6.52-6.57 (1H, m), 7.13-7.18 (1H, m), 8.56 (1H, s), 9.39 (1H, d, J=7.6Hz), 11.67 (1H, s). MS: 415 (M+H) +

Table 3(contd.)

Pr	Data
1-8	¹ H-NMR (400MHz, d6-DMSO) δ : 0.32 (3H, t, J=7.1Hz), 0.48-3.13 (14H, m), 4.26 (2H, q, J=7.1Hz), 4.68 (1H, s), 6.71-6.72 (1H, m), 7.23-7.24 (1H, m), 8.60 (1H, s), 9.34 (1H, s), 11.69 (1H, s). MS: 356 (M+H) +
1-9	¹ H-NMR (400MHz, d6-DMSO) δ : 0.32 (3H, t, J=7.1Hz), 0.40-0.47 (2H, m), 1.95-2.17 (11H, m), 0.80-0.83 (1H, m), 4.26 (2H, q, J=7.1Hz), 4.73 (1H, d, J=2.9Hz), 6.76 (1H, dd, J=2.4Hz, 3.5Hz), 7.22 (1H, dd, J=2.6Hz, 3.3Hz), 8.60 (1H, s), 9.33 (1H, s), 11.68 (1H, s). MS: 356 (M+H) +
1-10	MS: 372 (M+H) +
1-11	MS: 471 (M+H) +
1-12	MS: 481 (M+H) +
1-13	MS: 405 (M+H) +
1-14	MS: 484 (M+H) +
1-15	MS: 484 (M+H) +
1-16	MS: 517 (M+H) +
1-17	MS: 445 (M+H) +
1-18	MS: 445 (M+H) +
1-19	MS: 300 (M+H) +
1-20	MS: 342 (M+H) +
1-21	MS: 354 (M+H) +
1-22	MS: 356 (M+H) +
1-23	MS: 342 (M+H) +
1-24	¹ H-NMR (400MHz, d6-DMSO) δ : 1.35 (3H, t, J=7.1Hz), 1.68-1.77 (6H, m), 2.10-2.18 (9H, m), 4.26 (2H, q, J=7.1Hz), 6.75 (1H, d, J=3.6Hz), 7.22 (1H, d, J=3.4Hz), 8.60 (1H, s), 9.34 (1H, s), 11.67 (1H, s). MS: 340 (M+H) +
1-25	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32 (3H, t, J=7.1Hz), 1.61-2.07 (16H, m), 4.29 (2H, q, J=7.1Hz), 4.48 (1H, d, J=3.5Hz), 7.18 (1H, d, J=3.2Hz), 9.36 (1H, d, J=8.0Hz), 11.67 (1H, s). MS: 340 (M+H) +

Preparation 2

To glycineamide hydrochloride (34 mg) were added a solution of ethyl 3-(4-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)-1,2,4-oxadiazole-5-carboxylate (60 mg) in 1-methyl-2-pyrrolidone (0.6 ml) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.092 ml), and the mixture was stirred at 70°C for 1 hour. After being left to cool, the reaction solution was directly purified by preparative HPLC (10mM NH₄HCO₃ + NH₃

(pH = 9.2):CH₃CN = 90:10 to 20:80). The active fraction was concentrated and dried to hardness to obtain 3-(4-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)-N-methyl-1,2,4-oxadiazole-5-carboxylate (23 mg) as a solid.

- 5 The compounds in Preparations 2-1 to 2-26 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 2.

Table 4

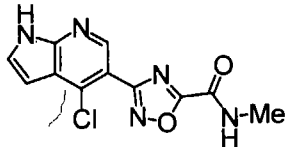
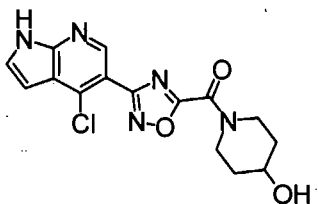
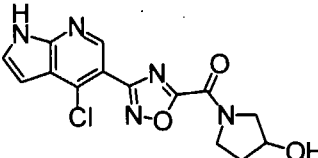
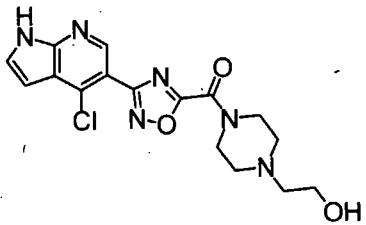
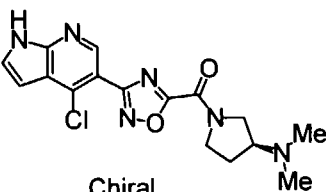
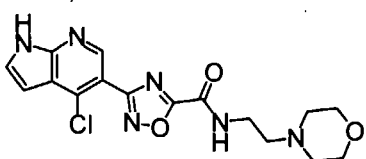
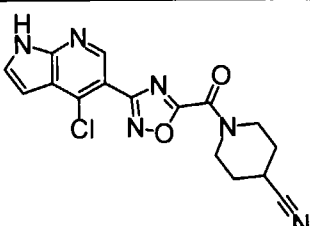
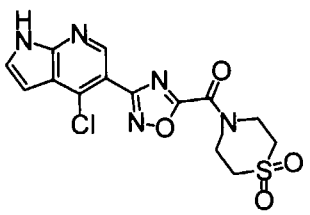
Pr	Structure	Pr	Structure
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2-2		2-3	
2-4	 Chiral	2-5	
2-6		2-7	

Table 4 (contd.)

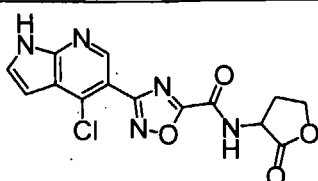
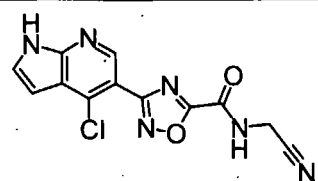
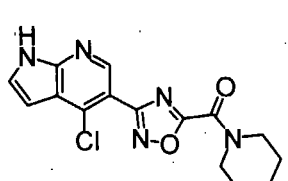
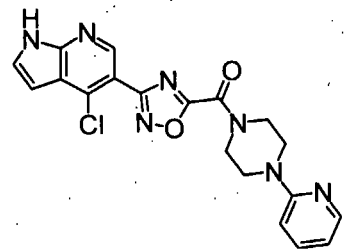
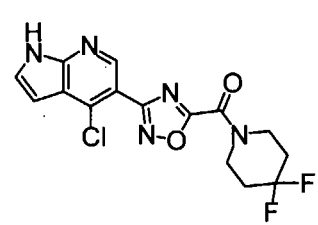
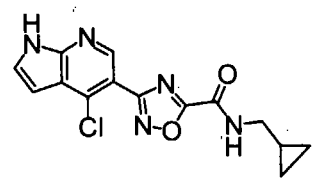
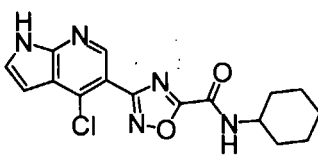
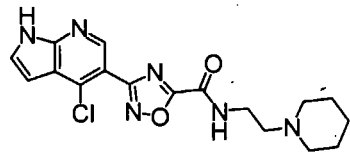
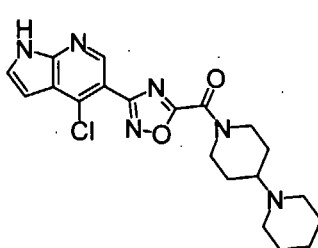
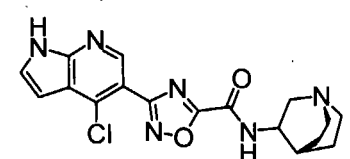
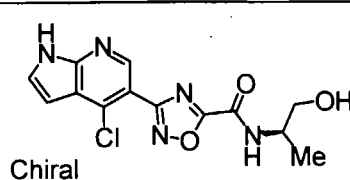
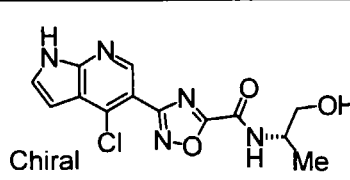
Pr	Structure	Pr	Structure
2-8		2-9	
2-10		2-11	
2-12		2-13	
2-14		2-15	
2-16		2-17	
2-18	 Chiral	2-19	 Chiral

Table 4 (contd.)

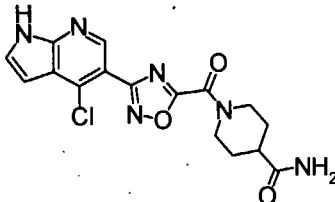
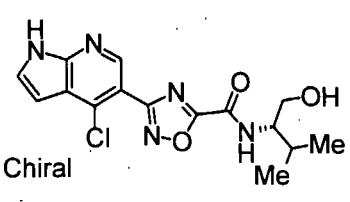
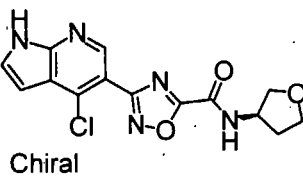
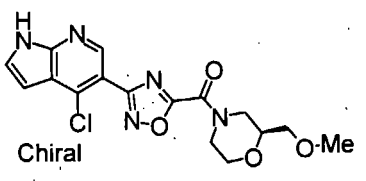
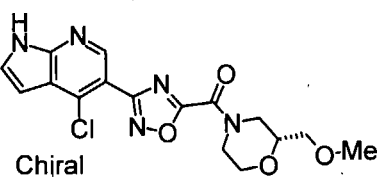
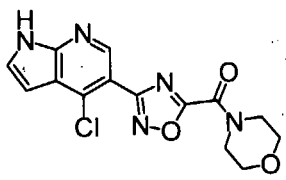
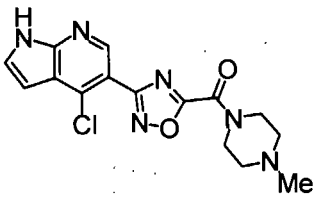
Pr	Structure	Pr	Structure
2-20		2-21	
2-22		2-23	
2-24		2-25	
2-26			

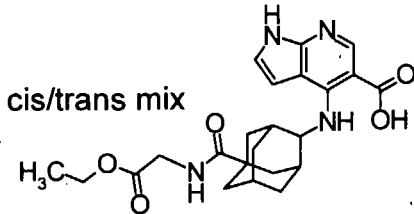
Table 5

Ex	MS data	Ex	MS data
2	MS: 278 (M+H) +	2-1	MS: 348 (M+H) +
2-2	MS: 334 (M+H) +	2-3	MS: 377 (M+H) +
2-4	MS: 361 (M+H) +	2-5	MS: 377 (M+H) +
2-6	MS: 357 (M+H) +	2-7	MS: 382 (M+H) +
2-8	MS: 348 (M+H) +	2-9	MS: 303 (M+H) +
2-10	MS: 332 (M+H) +	2-11	MS: 410 (M+H) +
2-12	MS: 368 (M+H) +	2-13	MS: 318 (M+H) +
2-14	MS: 346 (M+H) +	2-15	MS: 375 (M+H) +
2-16	MS: 415 (M+H) +	2-17	MS: 373 (M+H) +
2-18	MS: 322 (M+H) +	2-19	MS: 322 (M+H) +
2-20	MS: 375 (M+H) +	2-21	MS: 350 (M+H) +
2-22	MS: 334 (M+H) +	2-23	MS: 378 (M+H) +
2-24	MS: 378 (M+H) +	2-25	MS: 334 (M+H) +
2-26	MS: 347 (M+H) +		

Preparation 3

Benzyl 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (55 mg), ethyl {[(4-amino-1-adamantyl) carbonyl] amino}acetate (54 mg) and triethylamine (80 μ l) were dissolved in N-methyl-2-pyrrolidone (0.55 ml) and stirred at 180°C for 1 hour using a microwave reaction system. To the reaction solution were added ethyl acetate and water, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate), the obtained compound was dissolved in dioxane (1.1 ml) and methanol (1.1 ml), 10% palladium on carbon (50% wet) was added, and catalytic reduction was performed for 4 hours at ambient temperature at 1 atm. Methanol, dioxane, and 1M hydrochloric acid were added, and the precipitated solid was dissolved and filtered to remove the catalyst. The filtrate was concentrated under reduced pressure to obtain 4-({5-[(2-ethoxy-2-oxoethyl) carbamoyl]adamantan-2-yl}amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (18 mg).

Table 6

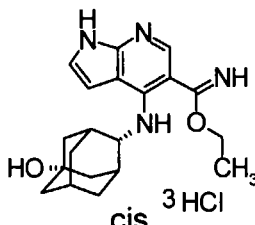
Pr	Structure	Data
3	cis/trans mix 	MS: 441 (M+H) +

Preparation 4

To a ethanol (3 ml) was added acetyl chloride carefully at 4°C. The reaction solution was stirred at 4°C for 30 minutes.

- 5 To the reaction solution were added a solution of 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (50 mg) in chloroform (0.5 ml) and 2M hydrochloric acid/ethanol solution (0.5 ml) dropwise. The reaction solution was stirred under ambient temperature for
- 10 18 hours. The reaction solution was concentrated under reduced pressure to obtain ethyl 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidate trihydrochloride (75 mg).

Table 7

Pr	Structure	Data
4		MS: 355 (M-3HCl+H) +

15 Preparation 5

The compounds in Preparations 5-1 to 5-32 shown in the

following table were produced using the corresponding starting compounds according to the method similar to that described in Example 3.

Table 8

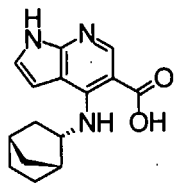
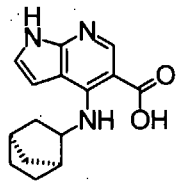
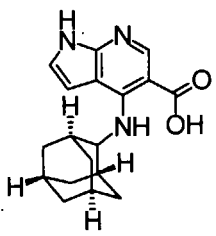
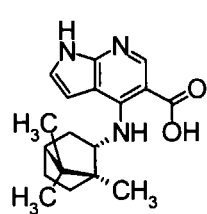
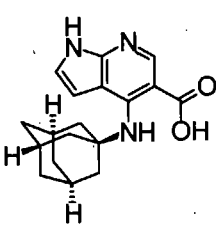
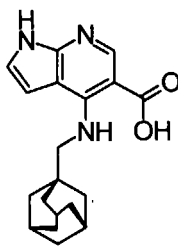
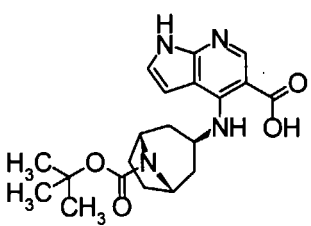
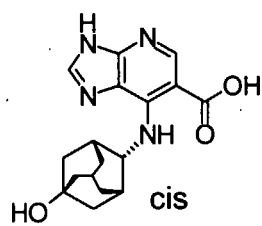
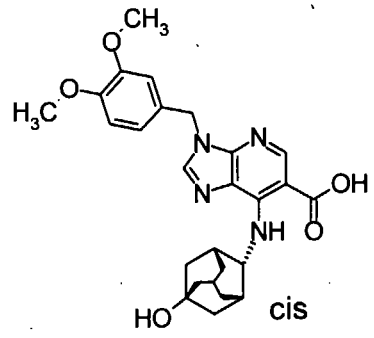
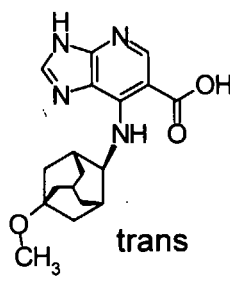
Pr	Structure	Pr	Structure
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5-3		5-4	
5-5		5-6	
5-7		5-8	
5-9		5-10	

Table 8 (contd.)

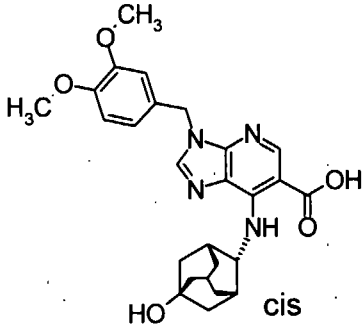
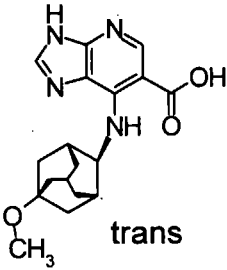
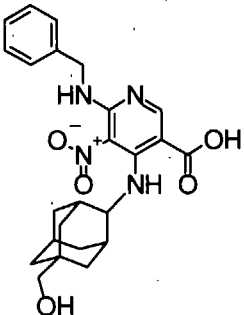
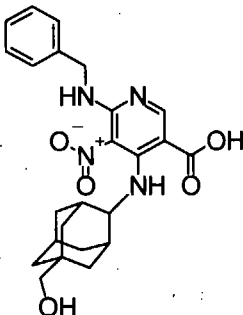
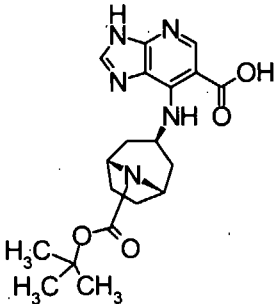
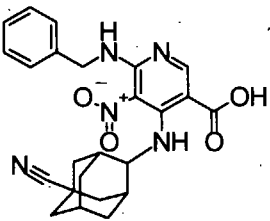
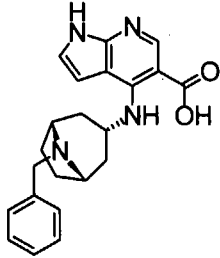
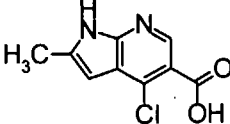
Pr	Structure	Pr	Structure
5-9		5-10	
5-11	 diastereomer of 5-12 cis or trans unknown	5-12	 diastereomer of 5-11 cis or trans unknown
5-13	 cis or trans unknown	5-14	 cis or trans unknown
5-15		5-16	

Table 8 (contd.)

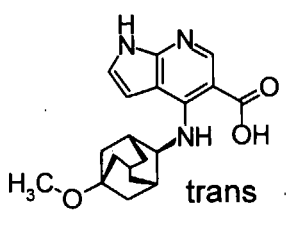
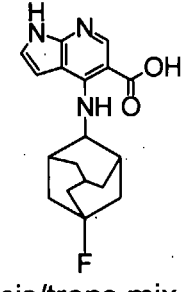
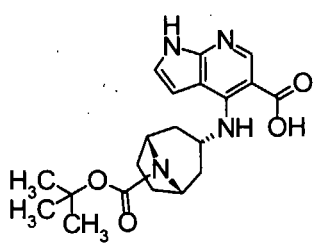
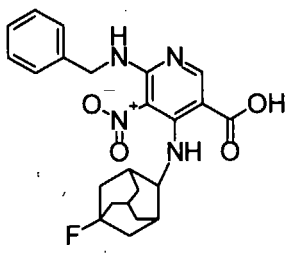
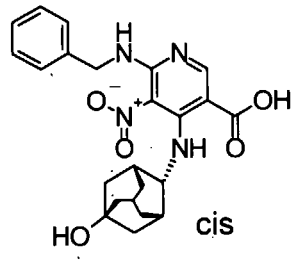
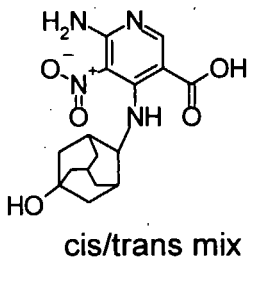
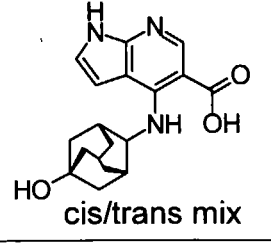
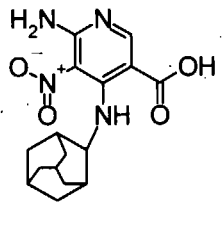
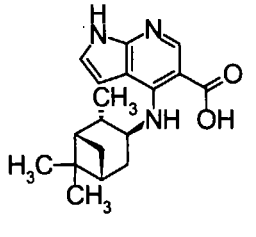
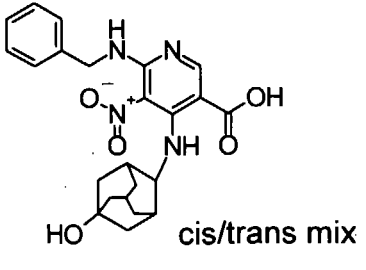
Pr	Structure	Pr	Structure
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5-19	 cis/trans mix	5-20	 cis/trans mix
5-21	 cis	5-22	 cis/trans mix
5-23	 cis/trans mix	5-24	 cis/trans mix
5-25	 cis/trans mix	5-26	 cis/trans mix

Table 8 (contd.)

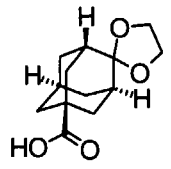
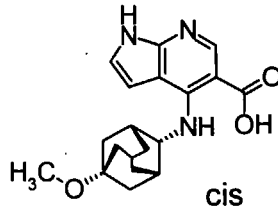
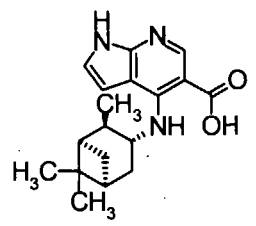
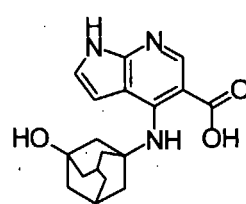
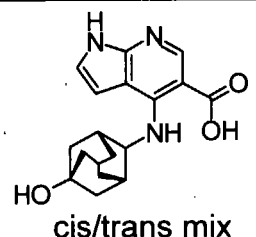
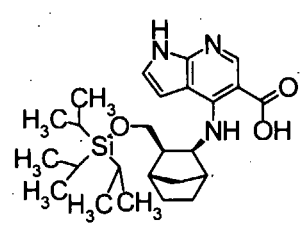
Pr	Structure	Pr	Structure
5-27		5-28	
5-29		5-30	
5-31		5-32	

Table 9

Pr	Data
5-1	MS: 272 (M+H) +
5-2	MS: 272 (M+H) +
5-3	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 1.60-2.06 (14H, m), 4.24 (1H, d, J=7.9Hz), 6.46 (1H, dd, J=1.3Hz, 3.3Hz), 7.16 (1H, dd, J=2.4 Hz, 3.2Hz), 8.52 (1H, s), 9.61 (1H, s), 11.59 (1H, s), 12.33 (1H, br) MS: 312 (M+H) +
5-4	MS: 314 (M+H) +
5-5	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 1.67-1.75 (6H, m), 2.09-2.16 (9H, m), 6.71 (1H, s), 7.16 (1H, s), 8.56 (1H, s), 9.76 (1H, br), 11.49 (1H, s) MS: 312 (M+H) +
5-6	MS: 326 (M+H) +
5-7	MS: 410 (M+Na) +
5-8	MS: 329 (M+H) +
5-9	MS: 479 (M+H) +
5-10	
5-11	MS: 475 (M+Na) +
5-12	
5-13	MS: 409 (M+Na) +
5-14	MS: 446 (M-H) -

Table 9 (contd.)

Pr	Data
5-15	MS: 377 (M+H) +
5-16	MS: 209 (M-H) -
5-17	MS: 342 (M+H) +
5-18	MS: 330 (M+H) +
5-19	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43 (9H, s), 1.70-1.88 (2H, m), 1.88-2.09 (4H, m), 2.14-2.33 (2H, m), 4.05-4.20 (2H, m), 4.34-4.46 (1H, m), 6.48-6.58 (1H, m), 7.09-7.17 (1H, m), 8.52 (1H, s), 9.67 (1H, d, J=6.2Hz), 11.62 (1H, s), 12.45 (1H, br). MS: 387 (M+H) +
5-20	MS: 463 (M+Na) +
5-21	MS: 437 (M-H) -
5-22	MS: 371 (M+Na) +
5-23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-1.46 (2H, m), 1.96-2.15 (1H, m), 2.44-2.55 (1H, m), 3.82 (1H, s), 4.71 (1H, s), 6.72-6.75 (1H, m), 7.19 (1H, t, J=2.9Hz), 8.56 (1H, s), 9.71 (1H, br), 11.57 (1H, s). MS: 328 (M+H) +
5-24	MS: 355 (M+Na) +
5-25	MS: 314 (M+H) +
5-26	MS: 437 (M-H) -
5-27	MS: 261 (M+H) +
5-28	MS: 342 (M+H) +
5-29	MS: 314 (M+H) +
5-30	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.68 (6H, m), 1.98 (6H, s), 2.26 (2H, s), 4.66 (1H, s), 6.68 (1H, dd, J=5.3Hz, 11.4Hz), 7.2 (1H, dd, J=2.5Hz, 3.0Hz), 8.57 (1H, s), 9.70 (1H, br), 11.58 (1H, s). MS: 328 (M+H) +
5-31	MS: 328 (M+H) +
5-32	MS: 458 (M+H) +

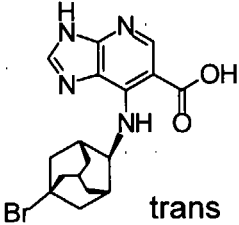
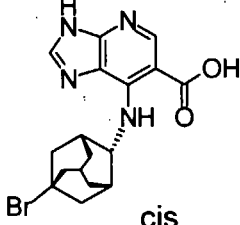
Preparation 6

To a ethyl 7-[(trans-5-hydroxyadamantan-2-yl) amino]-3H-imidazo[4,5-b]pyridine-6-carboxylate (50mg) was added 47% aqueous hydrobromic acid (0.75 ml), and the mixture was stirred at 120°C for 1 hour using a microwave reaction system. After the reaction solution was cooled, the pH was adjusted to 5 with aqueous potassium carbonate, and the obtained solid was collected by filtration and washed with

water to obtain 7-[(trans-5-bromoadamantan-2-yl)amino]-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (44 mg).

The compounds in Preparations 6-1 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 6.

Table 10

Pr	Structure	Data	Pr	Structure	Data
6	 trans	MS: 391, 393 (M+H)+	6-1	 cis	MS: 391, 393 (M+H)+

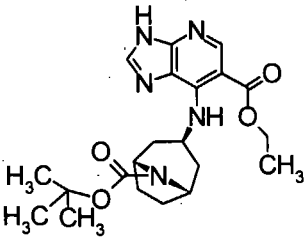
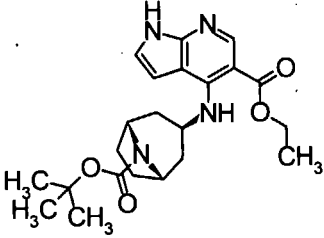
Preparation 7

A mixture of ethyl 7-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino]-3H-imidazo[4,5-b]pyridine-6-carboxylate (400 mg), di-t-butyl dicarbonate (203 mg), triethylamine (130 μ l), dioxane (4 ml) and water (4 ml) was stirred at ambient temperature for 1 hour. The mixture was diluted with ethyl acetate (5 ml) and water (20 ml). The resulting precipitate was collected by filtration (ethyl 7-[(3-exo)-8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]oct-3-ylamino]-3H-imidazo[4,5-b]pyridine-6-carboxylate, (200 mg)). The filtrate was diluted with ethyl acetate (50 ml) and extracted with ethyl acetate. The organic extracts were washed with brine, dried over sodium sulfate and concentrated. Recrystallization

from ethyl acetate/n-hexane gave ethyl 7-{[(3-exo)-8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-3H-imidazo[4,5-b]pyridine-6-carboxylate (100mg) as a white solid.

- 5 The compounds in Preparations 7-1 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 64.

Table 11

Pr	Structure	Data	Pr	Structure	Data
7		MS: 416 (M+H) +	7-1		MS: 415 (M+H) +

10 Preparation 8

The compounds in Preparations 8-1 to 8-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 44.

15 Table 12

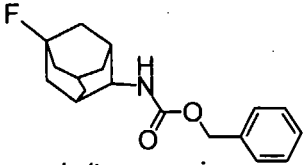
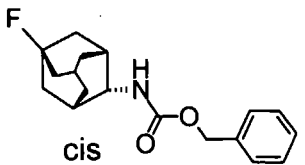
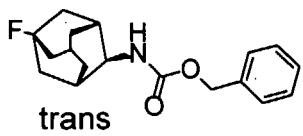
Pr	Structure	Data	Pr	Structure	Data
8-1	 cis/trans mix	MS: 326 (M+Na) +	8-2	 cis	MS: 326 (M+Na) +

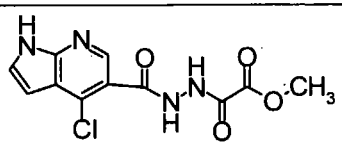
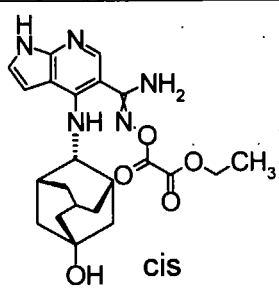
Table 12 (contd.)

Pr	Structure	Data
8-3	 trans	MS: 326 (M+Na) +

Preparation 9

The compounds in Preparations 9-1 to 9-2 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 10.

Table 13

Pr	Structure	Data
9-1		MS: 319 (M+Na) +
9-2	 cis	MS: 424 (M-H ₂ O+H) +

Preparation 10

The compounds in Preparations 10-1 to 10-18 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 4.

Table 14

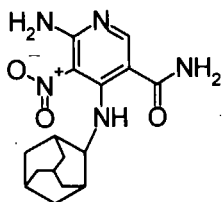
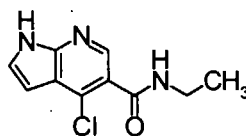
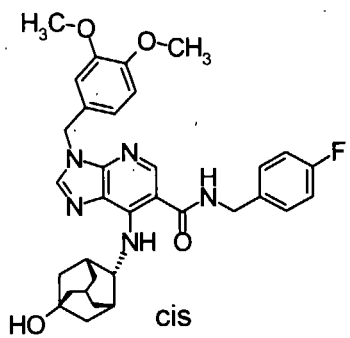
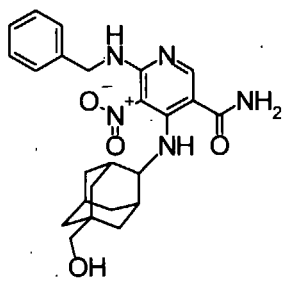
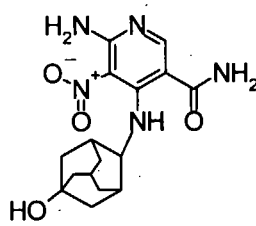
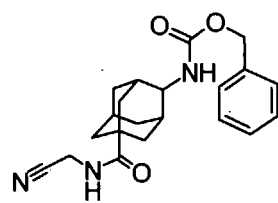
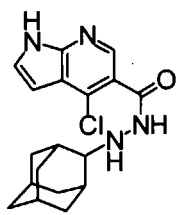
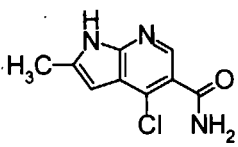
Pr	Structure	Pr	Structure
10-1		10-2	
10-3		10-4	 diastereomer of 10-18 cis or trans unknown
10-5	 cis/trans mix	10-6	 cis or trans unknown
10-7		10-8	

Table 14 (contd.)

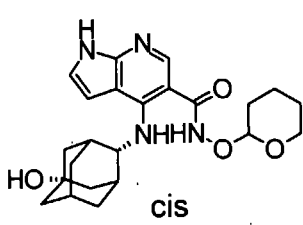
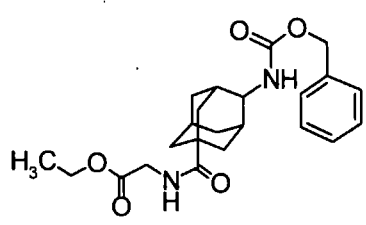
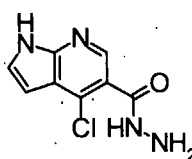
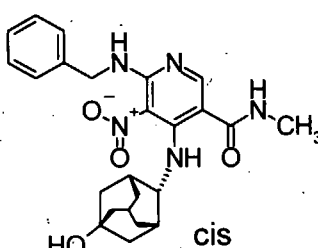
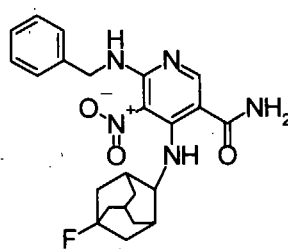
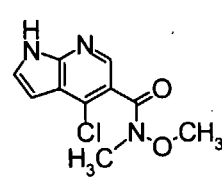
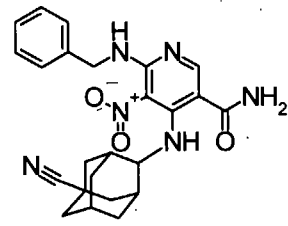
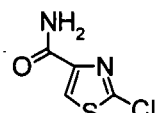
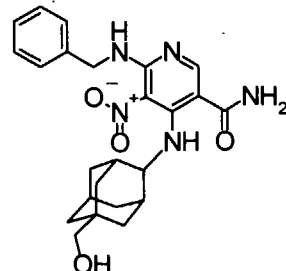
Pr	Structure	Pr	Structure
10-9	 cis	10-10	 cis or trans unknown
10-11		10-12	 cis
10-13	 cis/trans mix	10-14	
10-15	 cis or trans unknown	10-16	
10-17		10-18	 diastereomer of 10-4 cis or trans unknown

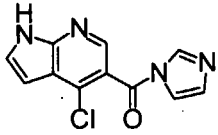
Table 15

Pr	Data
10-1	MS:332 (M+H) +
10-2	MS:246 (M+Na) +
10-3	MS:586 (M+H) +
10-4	MS:452 (M+H) +
10-5	MS:370 (M+Na) +
10-6	MS:368 (M+H) +
10-7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.45 (2H, m), 1.65-1.86 (8H, m), 1.94-1.97 (2H, m), 2.15-2.20 (2H, m), 3.08-3.11 (1H, m), 5.05-5.08 (1H, m), 6.55-6.57 (1H, m), 7.66-7.68 (1H, m), 8.19 (1H, s), 9.85 (1H, d, J=6.8Hz), 12.20 (1H, brs). MS:367 (M+Na) +
10-8	MS:232 (M+Na) +
10-9	MS:427 (M+H) +
10-10	MS:415 (M+H) +
10-11	MS:233 (M+Na) +
10-12	MS:474 (M+Na) +
10-13	MS:462 (M+Na) +
10-14	MS:262 (M+Na) +
10-15	MS:447 (M+H) +
10-16	
10-17	MS:232 (M+Na) +
10-18	MS:452 (M+H) +

Preparation 11

To a solution of 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (350 mg) in N,N-dimethylformamide (4 ml) were added N,N-carbonyl diimidazole (289 mg) and glycinemethylester hydrochloride (447 mg) successively under ambient temperature. The mixture was stirred at ambient temperature for 2 hours. To the reaction solution was added water. The precipitated solid was filtered, washed with water, and dried to obtain 4-chloro-5-(1H-imidazol-1-ylcarbonyl)-1H-pyrrolo[2,3-b]pyridine (325 mg) as a white solid.

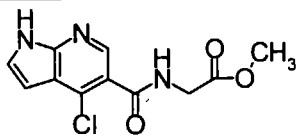
Table 16

Pr	Structure	Data
11		MS: 247 (M+H) ⁺ , 245 (M-H) ⁻

Preparation 12

To a solution of 4-chloro-5-(1H-imidazol-1-ylcarbonyl)-1H-pyrrolo[2,3-b]pyridine (300 mg) in N,N-dimethylformamide (3 ml) were added N-ethyl-N-isopropylpropane-2-amine (0.64 ml) and glycine methylester hydrochloride (305 mg) at ambient temperature. The mixture was warmed immediately to 60°C and stirred at 60°C for 2 hours. After to the reaction solution was added water, the mixture was stirred for 1 hour. The precipitated solid was filtered, washed with water, and dried to obtain methyl N-[(4-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)carbonyl]glycinate (267 mg) as a white solid.

Table 17

Pr	Structure	Data
12		MS: 290 (M+Na) ⁺

15 Preparation 13

To a solution of benzyl rel-[(1R,2S,3S,5s)-5-hydroxyadamantan-2-yl]carbamate (1.3 g) in dichloroethane (13 ml) were added trimethyloxonium tetrafluoroborate (1.28 g), 2,6-di-t-butyl-4-methylpyridine (2.21 g). The reaction

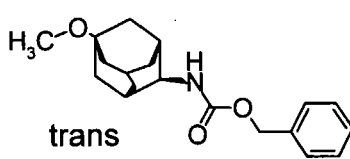
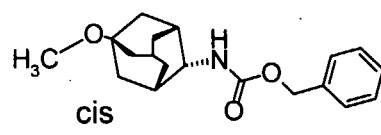
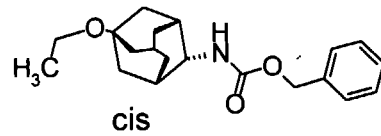
solution was refluxed for 3 hours. The reaction solution was concentrated under reduced pressure, ethyl acetate was added, and the insoluble matter was filtered. To the filtrate was added water, and the mixture was extracted with ethyl acetate.

- 5 The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane: ethyl acetate = 19:1 to 7:3) to obtain benzyl rel-[(1R,2S,3S,5s)-5-methoxyadamantan-2-yl]carbamate (540 mg) as a colorless oily matter.
- 10

The compounds in Preparations 13-1 to 13-2 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 13.

15

Table 18

Pr	Structure	Data
13	 trans	MS: 338 (M+Na) +
13-1	 cis	MS: 338 (M+Na) +
13-2	 cis	MS: 352 (M+Na) +

Preparation 14

The compounds in Preparations 14-1 to 14-6 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Examples 12 to Examples 14.

Table 19

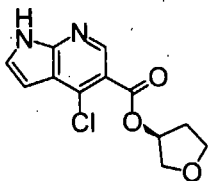
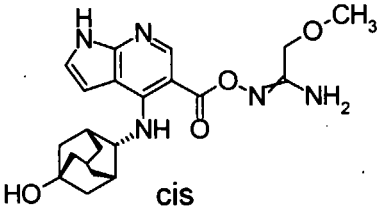
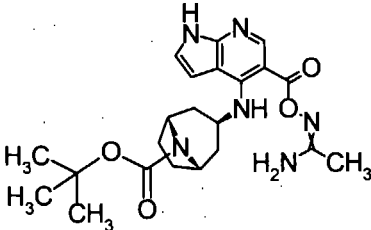
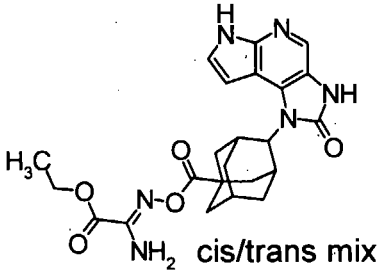
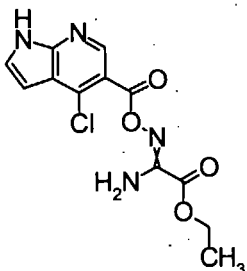
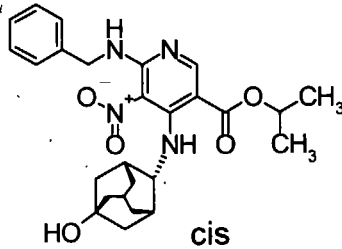
Pr	Structure	Pr	Structure
14-1		14-2	
14-3		14-4	
14-5		14-6	

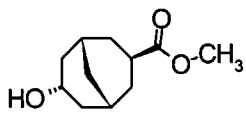
Table 20

Pr	Data
14-1	MS: 267 (M+H) +
14-2	MS: 414 (M+H) +
14-3	MS: 443 (M+H) +
14-4	MS: 467 (M+H) +
14-5	MS: 333 (M+Na) +
14-6	MS: 481 (M+H) +

Preparation 15

To a solution of (3-exo,7-endo)-7-hydroxybicyclo
[3.3.1]nonan-3-carboxylic acid (700 mg) in methanol (14 ml)
was added concentrated sulfuric acid (2 ml) dropwise, and the
5 reaction solution was refluxed for 1 hour. To the reaction
solution was added water, the mixture was extracted with ethyl
acetate. The organic layer was washed with water, saturated
aqueous sodium hydrogencarbonate, and brine, dried over
magnesium sulfate, and filtered. The filtrate was
10 concentrated under reduced pressure to obtain methyl-
(3-exo,7-endo)-7-hydroxybicyclo[3.3.1]nonan-3- carboxylate
(730 mg).

Table 21

Pr	Structure	Data
15		MS:221 (M+Na) +

Preparation 16

15 The compounds in Preparations 16-1 to 16-3 shown in the
following table were produced using the corresponding starting
compounds according to the method similar to that described
in Example 28.

Table 22

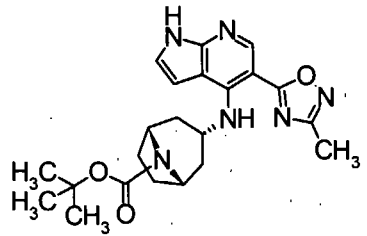
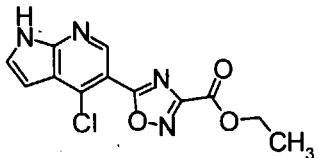
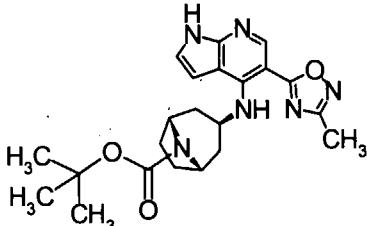
Pr	Structure	Pr	Structure
16-1		16-2	
16-3			

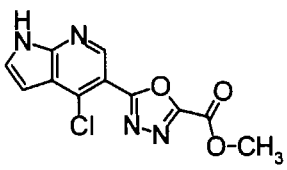
Table 23

Pr	Data
16-1	$^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$) δ : 1.44 (9H, s), 1.77-2.39 (8H, m), 2.42 (3H, s), 4.09-4.20 (2H, m), 4.48-4.57 (1H, m), 6.61-6.66 (1H, m), 7.21-7.26 (1H, m), 8.57 (1H, s), 9.16 (1H, d, $J=7.5\text{ Hz}$), 11.81 (1H, s). MS: 425 (M+H) +
16-2	MS: 315 (M+Na) +
16-3	MS: 425 (M+H) +

Preparation 17

- 5 The compound in Preparation 17 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Example 29.

Table 24

Pr	Structure	Data
17		MS: 301 (M+Na) +

Preparation 18

The compounds in Preparations 18-1 to 18-5 shown in the following table were produced using the corresponding starting compound according to the method similar to that described in

5 Example 30.

Table 25

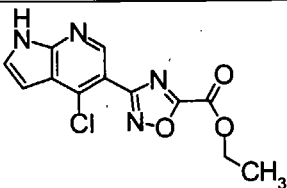
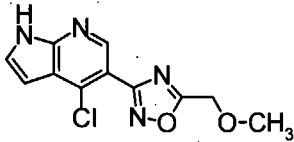
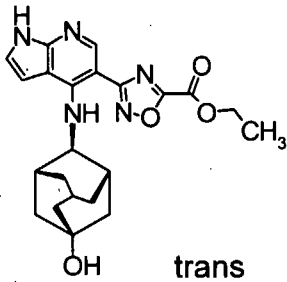
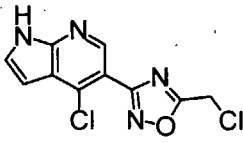
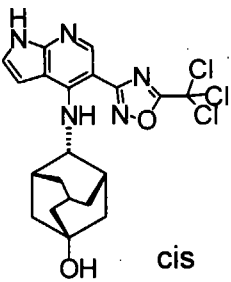
Pr	Structure	Pr	Structure
18-1		18-2	
18-3	 trans	18-4	
18-5	 cis		

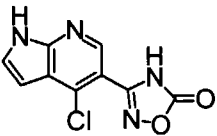
Table 26

Pr	Data
18-1	MS: 315 (M+Na) +
18-2	MS: 287 (M+Na) +
18-3	MS: 424 (M+H) +
18-4	MS: 291 (M+Na) +
18-5	MS: 468 (M+H) +

Preparation 19

To a solution of 4-chloro-N'-hydroxy-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidamide (100 mg) in N,N-dimethylformamide (1 ml) were added pyridine (58 μ l) and 2-ethylhexyl chlorocarbonate (92 μ l) at 4°C. The reaction solution was stirred at ambient temperature for 2 hours. To the reaction solution was added water. The precipitate was collected by filtration and dissolved in xylene (2 ml). The reaction solution was stirred at 160°C for 3 hours. To the reaction solution was added water, and the precipitate was collected by filtration to obtain 3-(4-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)-1,2,4-oxadiazol-5(4H)-one (63 mg) as a white solid.

Table 27

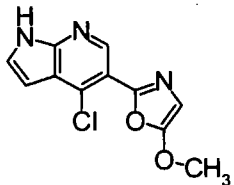
Pr	Structure	Data
19		MS: 235 (M-H) -

15 Preparation 20

To a solution of methyl N-[(4-chloro-1H-pyrrolo[2,3-b]pyridin-5-yl)carbonyl]glycinate (167 mg) in chloroform (5 ml) was added diphosphorus pentoxide (886 mg) under ambient temperature, and the mixture was refluxed for 18 hours. The reaction solution was cooled and added to saturated aqueous sodium hydrogencarbonate. The reaction solution was extracted with ethyl acetate. The organic layer was washed

with water. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by thin-layer silica gel column chromatography (chloroform:methanol = 15:1) to obtain
 5 4-chloro-5-(5-methoxy-1,3-oxazol-2-yl)-1H-pyrrolo[2,3-b]pyridine (45 mg) as a yellowish white solid.

Table 28

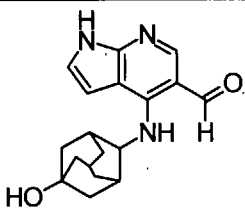
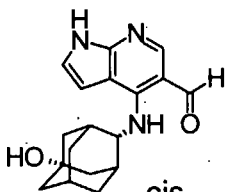
Pr	Structure	Data
20		MS: 250 (M+H) +

Preparation 21

To a solution of 4-[(5-hydroxyadamantan-2-yl)amino]-
 10 1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (150 mg) in tetrahydrofuran (3 ml) was added 1.01M diisobutylaluminum hydride/toluene solution (1.93 ml) at -78°C. The reaction solution was stirred for 18 hours under ambient temperature. To the reaction solution was added 1M hydrochloric acid under
 15 ice cooling, and the mixture was stirred for 30 minutes. The mixture was extracted with chloroform and washed with water. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to obtain
 20 4-[(5-hydroxyadamantan-2-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-carbaldehyde (100 mg) as a pale yellow amorphous substance.

The compound in Preparation 21-1 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Preparation 21.

5 Table 29

Pr	Structure	Data	Pr	Structure	Data
21	 cis/trans mix	MS: 312 (M+H) +	21-1	 cis	MS: 312 (M+H) +

Preparation 22

To a mixture of 6-(benzylamino)-1-(5-hydroxyadamantan-2-yl)-7-nitro-1,3-dihydro-2H-imidazo[4,5-c]pyridine-2-one (68mg) and methanol (1 ml) were added ammonium formate (197
10 mg) and 50% wet 10% palladium on carbon (33 mg) at ambient temperature. The mixture was refluxed for 5 hours. After the mixture was cooled, the catalyst was removed by filtration. The mother liquid was concentrated to obtain 6,7-diamino-1-(5-hydroxyadamantan-2-yl)-1,3-dihydro-2H-imidazo[4,5-
15 c]pyridine-2-one (54 mg).

The compounds in Preparations 22-1 to 22-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 22.

Table 30

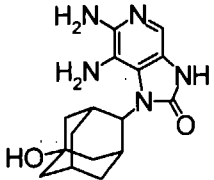
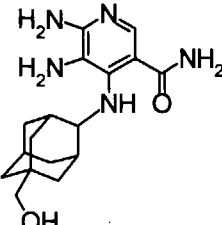
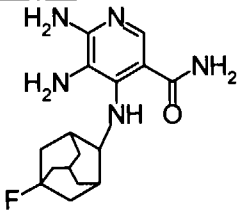
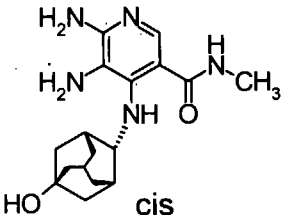
Pr	Structure	Pr	Structure
22	 cis or trans unknown	22-1	 cis or trans unknown
22-2	 cis/trans mix	22-3	 cis

Table 31

Pr	Data
22	MS: 316 (M+H) +
22-1	MS: 332 (M+H) +
22-2	MS: 320 (M+H) +
22-3	MS: 332 (M+H) +

Preparation 23

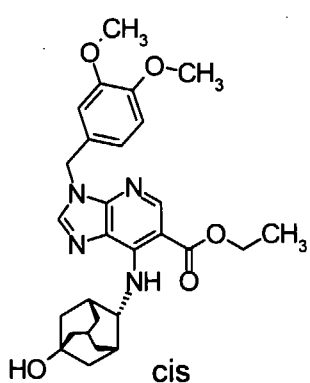
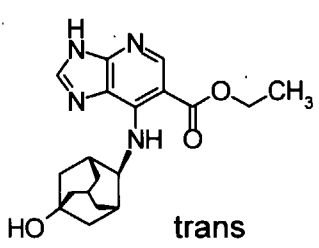
5 To a suspension of ethyl 6-[(3,4'-dimethoxybenzyl) amino]-4-[(cis-5-hydroxy adamantan-2-yl) amino]-5-nitronicotinate (2.73 g) in ethanol (40 ml) was added 10% palladium on carbon (50% wet) (550 mg). In hydrogen atmosphere, catalytic reduction was carried out at 80°C for 5 hours. After

10 the reaction solution was cooled to ambient temperature, the catalyst was filtered and washed with dioxane, and the solvent was evaporated under reduced pressure. To the residue were added ethyl orthoformate (17 ml) and concentrated hydrochloric acid (864 µl), and the mixture was stirred at ambient

temperature for overnight. The reaction solution was neutralized with saturated aqueous sodium hydrogencarbonate and extracted with ethyl acetate and tetrahydrofuran. The organic layer was washed with saturated brine, dried over magnesium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain ethyl 3-(3,4-dimethoxybenzyl)-7-[(cis-5-hydroxyadamantan-2-yl)amino]-3H-imidazo[4,5-b]pyridine-6-carboxylate (2.17 g).

The compound in Preparation 23-1 shown in the following table were produced using the corresponding starting compound according to the method similar to that described in Preparation 23.

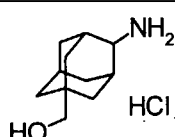
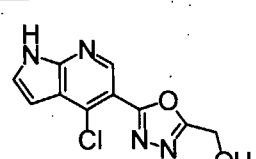
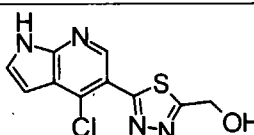
Table 32

Pr	Structure	Data	Pr	Structure	Data
23	 cis	MS: 507 (M+H) ⁺	23-1	 trans	MS: 357 (M+H) ⁺

Preparation 24

The compounds in Preparations 24-1 to 24-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 35.

Table 33

Pr	Structure	Data	Pr	Structure	Data
24-1	 cis/trans mix	MS: 182 (M+H) ⁺	24-2		MS: 299 (M+Na) ⁺
24-3		MS: 273 (M+Na) ⁺			

Preparation 25

To a reaction solution of N-Boc-nortropinone (1.38 g), benzylamine (0.803 ml) and acetic acid (0.35 ml) in dichloromethane (10 ml) and 1,2-dichloroethane (32 ml) was added sodium triacetoxyborohydride (1.95 g). And the mixture was stirred at ambient temperature for 2 hours. To the reaction mixture was added benzylamine (0.201 ml) and sodium triacetoxyborohydride (649 mg), and the mixture was stirred at 50°C for 3.5 hours. Furthermore, to the reaction mixture was added sodium triacetoxyborohydride (649 mg) and the mixture was stirred at 50°C for 3 hours. The reaction solvent was evaporated under reduced pressure. To the residue were added saturated aqueous sodium hydrogencarbonate and 1M

aqueous sodium hydroxide to alkalify the residue. The residue was extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium hydrogencarbonate, water, and saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain 3-(benzylamino)-8-azabicyclo[3.2.1]octane-8-carbamic acid t-butyl ester (1.78 g) as a white solid.

The compounds in Preparations 25-1 to 25-8 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 25.

Table 34

Pr	Structure	Pr	Structure
25		25-1	 diastereomer of 25-8 cis or trans unknown
25-2	 cis/trans mix	25-3	 cis/trans mix

Table 34 (contd.)

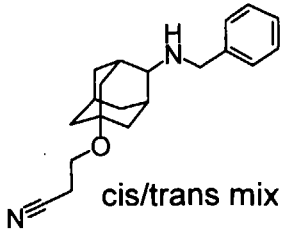
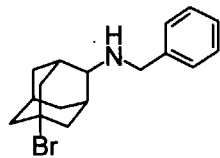
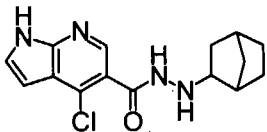
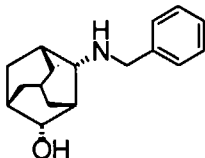
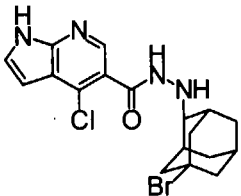
Pr	Structure	Pr	Structure
25-4	 cis/trans mix	25-5	 cis or trans unknown
25-6		25-7	
25-8	 diastereomer of 25-1 cis or trans unknown		

Table 35

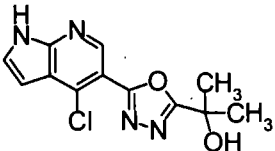
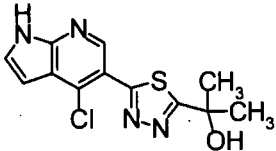
Pr	Data
25	¹ H-NMR (400MHz, CDCl ₃) δ: 1.35-1.66 (3H, m), 1.45 (9H, s), 1.86-2.22 (6H, m), 3.00 (1H, dd, J=6.0, 6.0Hz), 3.78 (2H, s), 4.04-4.28 (2H, m), 7.20-7.38 (5H, m)
25-1	MS: 423, 425 (M+H) +
25-2	MS: 383 (M+Na) +
25-3	MS: 357 (M+H) +
25-4	MS: 311 (M+H) +
25-5	MS: 320, 322 (M+H) +
25-6	MS: 327 (M+Na) +
25-7	MS: 258 (M+H) +
25-8	MS: 423, 425 (M+H) +

Preparation 26

- 5 The compounds in Preparations 26-1 to 26-2 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described

in Example 50.

Table 36

Pr.	Structure	Data	Pr.	Structure	Data
26-1		MS: 301 (M+Na) ⁺	26-2		MS: 317 (M+Na) ⁺

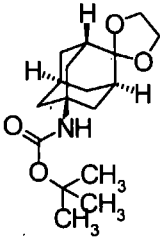
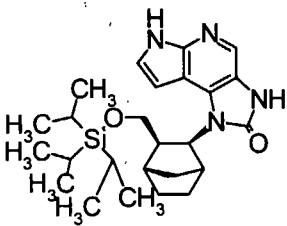
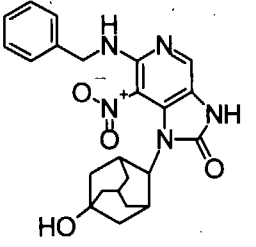
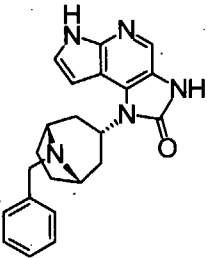
Preparation 27

To a solution of rel-(1'R,3'S,5'S,7's)-5'H-spiro[1,3-dioxolane-2,2'-tricyclo[3.3.1.1~3,7~]decane]-5'-carboxylic acid (100 mg) in toluene (1 ml) was added diphenylphosphate azide (99 μ l) and triethylamine (64 μ l). The mixture was stirred at 110°C for 2 hours. After the reaction solution was cooled to ambient temperature, water was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was dissolved in N,N-dimethylacetamide (1 ml), and potassium t-butoxide (49 mg) was added. The mixture was stirred at ambient temperature for overnight. To the reaction solution was added water, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over magnesium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate)

to obtain t-butyl rel-(1'R,3'S,5'S,7's)-5'H-spiro[1,3-dioxolane-2,2'-tricyclo[3.3.1.1~3,7~]decane]-5'-yl carbamate (40 mg).

The compounds in Preparations 27-1 to 27-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 27.

Table 37

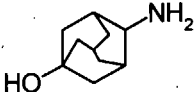
Pr	Structure	Data	Pr	Structure	Data
27		MS: 332 (M+Na) +	27-1		MS: 455 (M+H) +
27-2	 cis or trans unknown	MS: 436 (M+H) +	27-3		MS: 374 (M+H) +

Preparation 28

To a concentrated sulfuric acid (175 ml) was added 70% nitric acid (20 ml) dropwise under ice cooling, and 2-adamantamine hydrochloride (25 g) was added slowly at 10°C or less. The mixture was warmed to ambient temperature and stirred for 2 hours. The reaction solution was poured into

ice water, and the mixture was neutralized with 6M aqueous sodium hydroxide and extracted with dichloromethane four times. The organic layers were combined, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to
 5 obtain 4-aminoadamantan-1-ol (17.7 g).

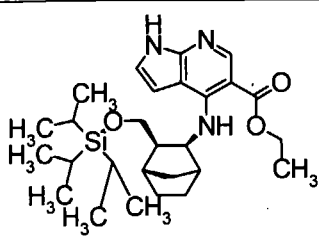
Table 38

Pr	Structure	Data
28	 cis/trans mix	MS:168 (M+H) +

Preparation 29

A mixture of ethyl 4-{{[3-exo(hydroxymethyl)bicyclo[2.2.1]heptyl-2-exo]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (54 mg), triisopropylsilyl chloride (52 μ l),
 10 imidazole (17 mg), and N,N-dimethylformamide (0.3 ml) was stirred at ambient temperature for 2 hours. The reaction solution was diluted with ethyl acetate (20 ml) and poured into saturated aqueous sodium hydrogencarbonate (15 ml). The
 15 mixture was extracted with ethyl acetate (15 ml) two times, and the extract was washed with brine (20 ml), dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate) to obtain ethyl
 20 4-{{[3-exo(triisopropylsilyl)oxy]methyl} bicyclo[2.2.1]heptyl-2-exo]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (76 mg) as a pale brown solid.

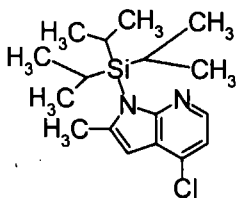
Table 39

Pr	Structure	Data
29		MS: 486 (M+H) +

Preparation 30

To a solution of 4-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine (0.85 g) in N,N-dimethylformamide (8.5 ml) was added 60% oil-suspended NaH (245 mg) under nitrogen atmosphere while being cooled in an ice water bath. The reaction solution was stirred at ambient temperature for 1 hour and cooled again in the ice water bath. To the reaction solution was added triisopropylsilyl chloride (1.3 ml) slowly dropwise for 10 or more minutes. The reaction solution was stirred for 3 hours at ambient temperature and diluted with ethyl acetate (30 ml). The solution was washed with saturated aqueous sodium hydrogencarbonate (30 ml) and brine (20 ml). The solution was dehydrated with anhydrous magnesium sulfate and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane) to obtain 4-chloro-2-methyl-1-(triisopropylsilyl)-pyrrolo[2,3-b]pyridine (1.45 g) as a colorless transparent liquid.

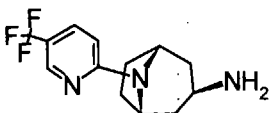
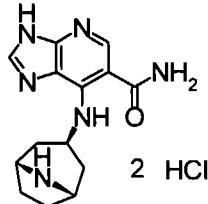
Table 40

Pr	Structure	Data
30		MS: 323 (M+H) +

Preparation 31

The compounds in Preparations 31-1 to 31-2 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 19.

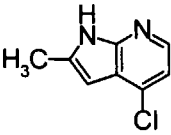
Table 41

Pr	Structure	Data	Pr	Structure	Data
31-1		MS: 272 (M+H) +	31-2		MS: 287 (M+H) +

Preparation 32

A mixture of 4-chloro-2-methyl-1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine (4.73 g), potassium carbonate (6.4 g), methanol (45 ml), and water (15 ml) was stirred at 90°C for 2 hours. After the mixture was cooled, the obtained needle crystals were filtered and washed with water to obtain 4-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine (1.85 g).

Table 42

Pr	Structure	Data
32		MS:167 (M+H) +

Preparation 33

To a solution of benzyl rel-[(1R,2S,3S,5s)-5-hydroxyadamantan-2-yl]carbamate (5.5 g) in methanol (55 ml) was added 10% palladium on carbon (50% wet) (1.1 g), and the mixture was stirred under hydrogen atmosphere at ambient temperature for 3 hours. After 10% palladium on carbon was removed with Celite, the filtrate was concentrated under reduced pressure to obtain rel-(1s,3R,4S,5S)-4-adamantamine-1-ol (3.8 g).

The compounds in Preparations 33-1 to 33-11 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 33.

Table 43

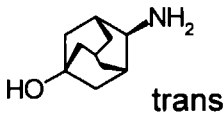
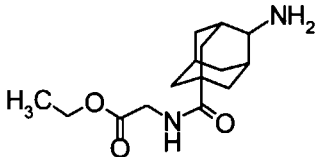
Pr	Structure	Pr	Structure
33	 trans	33-1	 diastereomer of 33-9 cis or trans unknown

Table 43 (contd.)

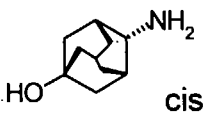
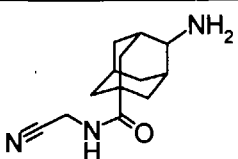
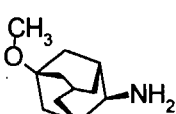
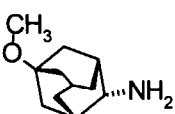
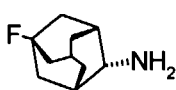
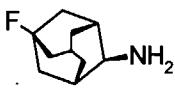
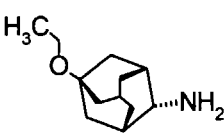
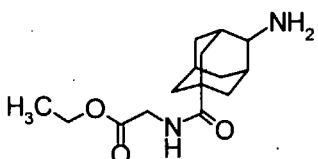
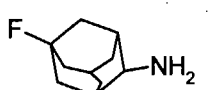
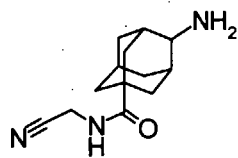
Pr	Structure	Pr	Structure
33-2	 cis	33-3	 diastereomer of 33-11 cis or trans unknown
33-4	 trans	33-5	 cis
33-6	 cis	33-7	 trans
33-8	 cis	33-9	 diastereomer of 33-1 cis or trans unknown
33-10	 cis/trans mix	33-11	 diastereomer of 33-3 cis or trans unknown

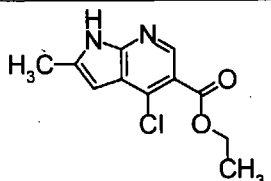
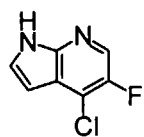
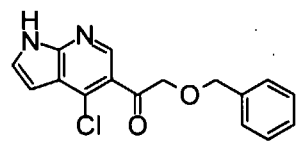
Table 44

Pr	Data	Pr	Data
33	MS:168 (M+H) +	33-1	MS:281 (M+H) +
33-2	MS:168 (M+H) +	33-3	MS:234 (M+H) +
33-4	MS:182 (M+H) +	33-5	MS:182 (M+H) +
33-6	MS:170 (M+H) +	33-7	MS:170 (M+H) +
33-8	MS:196 (M+H) +	33-9	MS:281 (M+H) +
33-10	MS:170 (M+H) +	33-11	MS:234 (M+H) +

Preparation 34

The compounds in Preparations 34-1 to 34-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 21.

Table 45

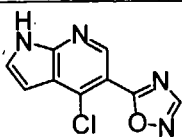
Pr	Structure	Data	Pr	Structure	Data
34-1		MS: 261 (M+Na) +	34-2		MS: 171 (M+H) +
34-3		MS: 323 (M+H) +			

Preparation 35

To a solution of ethyl 5-(4-chloro-1H-pyrrolo[2,3-b]pyridine-5-yl)-1,2,4-oxadiazole-3-carboxylate (350 mg) in ethanol (3.5 ml) was added 1M aqueous sodium hydroxide (1.79 ml), and the reaction solution was stirred at 50°C for 3 hours. The reaction solution was cooled to 4°C, and 1M hydrochloric acid was added to acidify the solution. The mixture was extracted with a mixture of chloroform and methanol (4:1) and

washed with water. The organic layer was dried over magnesium sulfate and then filtered. The filtrate was concentrated under reduced pressure to obtain 4-chloro-5-(1,2,4-oxadiazole-5-yl)-1H-pyrrolo[2,3-b]pyridine (215 mg) as a white solid.

Table 46

Pr	Structure	Data
35		MS:219 (M-H) +

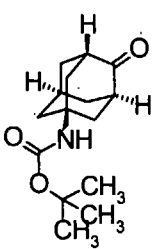
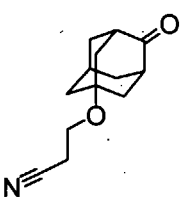
Preparation 36

t-Butyl rel-(1'R,3'S,5'S,7's)-5'H-spiro[1,3-dioxolane- 2,2'-tricyclo[3.3.1.1~3,7~]decane]-5'-yl carbamate (420 mg) was dissolved in tetrahydrofuran (4.2 ml) and water (4.2 ml), para-tosylic acid monohydrate (516 mg) was added, and the mixture was stirred at 60°C for 4 hours. The reaction solution was evaporated under reduced pressure, and saturated aqueous sodium hydrogencarbonate was added. The mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate) to obtain t-butyl (cis-4-oxadamantan-1-yl)carbamate (120 mg).

The compound in Preparation 36-1 shown in the following table was produced using the corresponding starting compound

according to the method similar to that described in Preparation 36.

Table 47

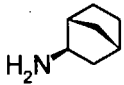
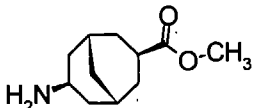
Pr	Structure	Data	Pr	Structure	Data
36		MS: 288 (M+H) +	36-1		MS: 220 (M+H) +

Preparation 37

5 To a reaction solution of 2-[(1R,2R,4S)-bicyclo
[2.2.1]hept-2-yl]-1H-isoindole-1,3(2H)-dione (1.4 g) in
tetrahydrofuran (28 ml) and ethanol (28 ml) was added 80%
aqueous hydrazine monohydrate (1.1 ml), and the mixture was
refluxed for 3 hours. After the reaction solution was cooled
10 to ambient temperature, insoluble matter was removed by
filtration. The filtrate was concentrated under reduced
pressure to reduce the amount of the solvent. To the residue
was added dichloromethane, and the mixture was washed with 1M
aqueous sodium hydroxide, dried over anhydrous magnesium
15 sulfate, and evaporated under reduced pressure. To the
residue was added methanol, the mixture was converted into
hydrochloride by adding 4M hydrochloric acid/dioxane solution,
concentrated under reduced pressure and dried to hardness to
obtain (1R,2R,4S)-bicyclo[2.2.1] heptane-2-amine
20 hydrochloride (0.6 g).

The compound in Preparation 37-1 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Preparation 37.

5 Table 48

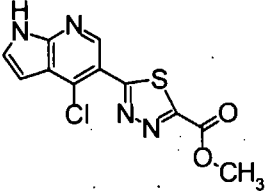
Pr	Structure	Data	Pr	Structure	Data
37	 HCl	MS: 112 (M+H) +	37-1		MS: 198 (M+H) +

Preparation 38

To a suspension of methyl (2-{{[4-chloro-6-(methylamino)-5-vinylpyridine-3-yl]carbonyl}hydrazino}(oxo)acetate (450 mg) in tetrahydrofuran (7 ml) and dioxane
 10 (7 ml) was added diphosphorus pentasulfide (383 mg) under cooling in an ice bath. After the mixture was stirred at ambient temperature for 5 hours. To the reaction mixture was added tetrahydrofuran (10 ml) and diphosphorus pentasulfide (190 mg). After the mixture was stirred at ambient temperature
 15 for 2 hours, water was added to the reaction solution, and the pH was adjusted to approximately 10 with aqueous sodium hydroxide, and the solution was extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The
 20 residue was purified by silica gel chromatography (chloroform:methanol) to obtain methyl-5-(4-chloro-1H-pyrrolo[2,3,b]pyridine-5-yl)-1,3,4-thiadiazole-2-

carboxylate (90 mg).

Table 49

Pr	Structure	Data
38		MS: 317 (M+H) +

Preparation 39

The compounds in Preparations 39-1 to 39-4 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Example 45.

Table 50

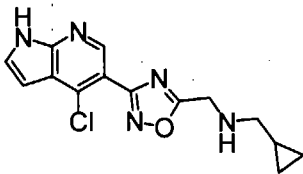
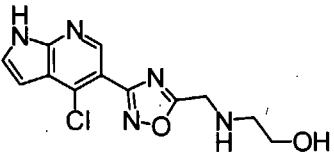
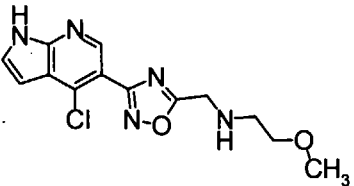
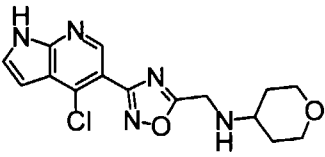
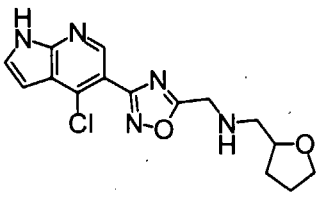
Pr	Structure	Data
39		MS: 304 (M+H) +, 326 (M+Na) +
39-1		MS: 316 (M+Na) +
39-2		MS: 330 (M+Na) +

Table 50 (contd.)

Pr	Structure	Data
39-3		MS: 356 (M+Na) +
39-4		MS: 356 (M+Na) +

Preparation 40

To a reaction solution of 4-Chloro-1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridine (2.26 g) in tetrahydrofuran (16 ml) was added sec-butyllithium (14.6 ml) dropwise in nitrogen atmosphere at -78°C. After the mixture was stirred at the same temperature for 30 minutes, a solution of benzyl chloroformate (2.1 ml) in tetrahydrofuran (16 ml) was added dropwise to the reaction mixture at -78°C.

Furthermore, the reaction solution was stirred at -78°C for 15 minutes, neutralized with saturated aqueous ammonium chloride (12 ml), and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was dissolved in tetrahydrofuran (17 ml), 1M tetrabutylammonium fluoride/tetrahydrofuran solution (16.9 ml) was added, and the mixture was stirred at ambient temperature for 3 hours. To the reaction solution were added

ethyl acetate and water, the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column

5 chromatography (n-hexane:ethyl acetate) to obtain benzyl 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (690 mg).

The compounds in Preparations 40-1 to 40-3 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described
10 in Preparation 40.

Table 51

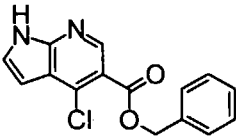
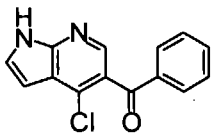
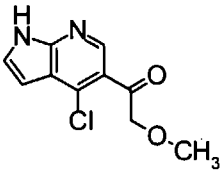
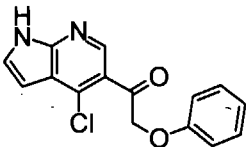
Pr	Structure	Pr	Structure
40		40-1	
40-2		40-3	

Table 52

Pr	Data
40	$^1\text{H-NMR}$ (d ₆ -DMSO) δ : 5.40 (2H, s), 6.6 (1H, d, J=1.8Hz), 7.35-7.39 (3H, m), 7.41-7.45 (2H, m), 7.71 (1H, d, J=3.5Hz), 8.75 (1H, s), 12.42 (1H, br). MS: (+): 297
40-1	MS: 279 (M+Na) +
40-2	MS: 247 (M+H) +
40-3	MS: 285 (M-H) -

Preparation 41

Into a 100 ml metal sealed tube were put a stirring rod,
ethyl 4-{[(3-exo)8-benzyl-8-azabicyclo[3.2.1]oct-3-yl]
amino}-6-chloro-5-nicotinic acid ester (1.5 g), 28% aqueous
5 ammonia (4.6 ml), and ethanol (7.5 ml). The tube was closed
and stirred at 90°C for 2 hours. After being cooled, the
reaction solution was diluted with methanol (20 ml) and
evaporated under reduced pressure. The residue was
recrystallized from ethyl acetate-methanol to obtain ethyl
10 6-amino-4-{[(3-exo)8-benzyl-8-azabicyclo[3.2.1]oct-3-yl]
amino}-5-nicotinic acid ester (1.3 g) as a yellow solid.

The compound in Preparation 41-1 shown in the following
table was produced using the corresponding starting compound
according to the method similar to that described in

15 Preparation 41.

Table 53

Pr	Structure	Data	Pr	Structure	Data
41		MS: 426 (M+H) ⁺	41-1		MS: 361 (M+H) ⁺
41-1		MS: 361 (M+H) ⁺			

Preparation 42

The compounds in Preparations 42-1 to 42-26 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described

5 in Example 7.

Table 5.4

Pr	Structure	Pr	Structure
42-1		42-2	
42-3		42-4	
42-5		42-6	
42-7		42-8	
42-9		42-10	

Table 54 (contd.)

Pr	Structure	Pr	Structure
42-11		42-12	
42-13		42-14	
42-15		42-16	
42-17		42-18	
42-19		42-20	
42-21		42-22	
42-23		42-24	

Table 54 (contd.)

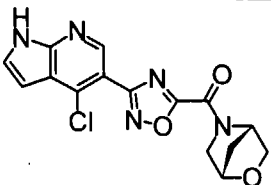
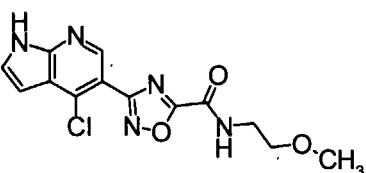
Pr	Structure	Pr	Structure
42-25		42-26	

Table 55

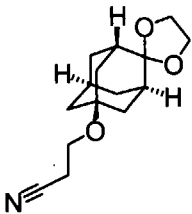
Pr	Data
42-1	MS: 348 (M+H) +
42-2	MS: 377 (M+H) +
42-3	MS: 316 (M+Na) +
42-4	MS: 370 (M+H) +
42-5	MS: 384 (M+Na) +
42-6	MS: 335 (M+H) +
42-7	MS: 375 (M+H) +
42-8	MS: 322 (M+H) +
42-9	MS: 308 (M+H) +
42-10	MS: 314 (M+Na) +
42-11	MS: 384 (M+Na) +
42-12	MS: 286 (M+Na) +
42-13	MS: 384 (M+Na) +
42-14	MS: 358 (M+Na) +
42-15	MS: 358 (M+Na) +
42-16	MS: 398 (M+Na) +
42-17	MS: 404 (M+Na) +
42-18	MS: 412 (M+Na) +
42-19	MS: 398 (M+Na) +
42-20	MS: 286 (M+Na) +
42-21	MS: 418 (M+Na) +, 394 (M-H) -
42-22	MS: 300 (M+Na) +
42-23	MS: 369 (M+Na) +
42-24	MS: 286 (M+Na) +
42-25	MS: 346 (M+H) +
42-26	MS: 322 (M+H) +, 344 (M+Na) +, 320 (M-H) -

Preparation 43

- 5 The compound in Preparation 43 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Example

41.

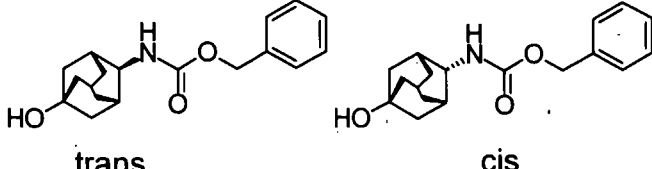
Table 56

Pr	Structure	Data
43		MS: 264 (M+H) +

Preparation 44

To a solution of 4-aminoadamantan-1-ol (8.9 g) in tetrahydrofuran (89 ml) were added benzyloxycarbonyl chloride (7.6 ml) and 1M aqueous sodium hydroxide (53.4 ml) dropwise successively under ice cooling, and the mixture was stirred for 3 hours under ice cooling. The reaction solution was poured into aqueous potassium hydrogensulfate, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate = 1:1 to 1:3) to obtain benzyl rel-[(1R,2S,3S,5s)-5-hydroxyadamantan-2-yl]carbamate (6.2 g) and benzyl rel-[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]carbamate (5.3 g).

Table 57

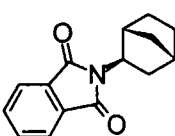
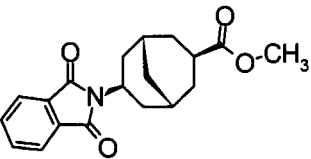
Pr	Structure	Data
44	 trans cis	MS: 324 (M+Na) + 324 (M+Na) +

Preparation 45

To a solution of (1R,2S,4S)-bicyclo[2.2.1]heptane-2-ol (1.0 g) in tetrahydrofuran (10 ml) were added phthalimide (1.4 g) and triphenylphosphine (2.6 g), and diethylazodicarboxylate (1.5 ml) dropwise under ice cooling. The mixture was warmed to ambient temperature and stirred for 24 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (n-hexane:ethyl acetate) = 100:0 to 95:5) to obtain 2-[(1R,2R,4S)-bicyclo[2.2.1]hept-2-yl]-1H-isoindole-1,3(2H)-dione (1.4 g) as a colorless solid.

The compound in Preparation 45-1 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Preparation 45.

Table 58

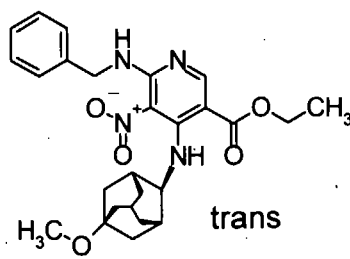
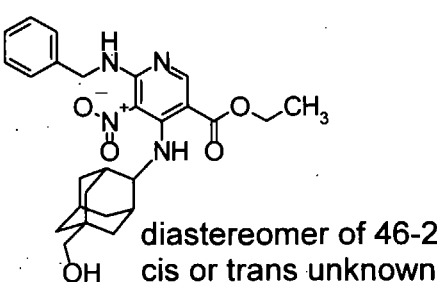
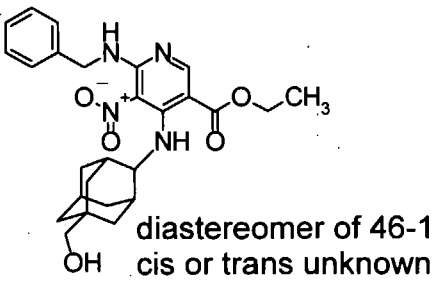
Pr	Structure	Data	Pr	Structure	Data
45		MS: 264 (M+Na) +	45-1		MS: 350 (M+Na) +

Preparation 46

A mixture of ethyl 6-chloro-4-([5-methoxyadamantan-2-yl]amino)-5-nicotinic acid ester (635 mg), benzylamine (253 μ l), diisopropylethylamine (270 μ l), and 2-propanol (3 ml) was subjected to microwave irradiation under nitrogen atmosphere and heated at 90°C for 30 minutes. After being cooled, the reaction solution was diluted with ethyl acetate (20 ml) and poured into 1/2 saturated aqueous ammonia chloride (20 ml). The mixture was extracted with ethyl acetate (20 ml) two times, washed with brine (30 ml), dehydrated with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane:ethyl acetate) to obtain ethyl 6-benzylamino-4-([5-methoxyadamantan-2-yl]amino)-5-nicotinic acid ester (550 mg) as an orange solid.

The compounds in Preparations 46-1 to 46-2 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 46.

Table 59

Pr	Structure	Data
46	 trans	MS: 481 (M+H) +
46-1	 diastereomer of 46-2 cis or trans unknown	MS: 481 (M+H) +
46-2	 diastereomer of 46-1 cis or trans unknown	MS: 481 (M+H) +

Preparation 47

A solution of 4-chloro-2-methyl-1-(triisopropylsilyl)-
 1H-pyrrolo[2,3-b]pyridine (525 mg) in tetrahydrofuran (10 ml)
 5 was cooled to -78°C under nitrogen atmosphere, and to the
 reaction mixture was added 0.99M sec-butyllithium/cyclohexane
 solution (4.1 ml) dropwise. After the mixture was stirred at
 -78°C, ethyl chlorocarbonate (389 µl) was added dropwise. The
 reaction solution was stirred at -78°C for 30 minutes,
 10 saturated aqueous ammonium chloride (20 ml) was added, and the
 temperature was returned to ambient temperature. The reaction

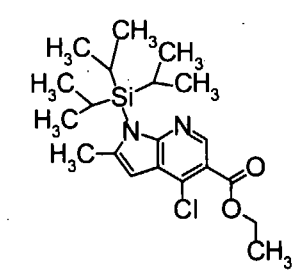
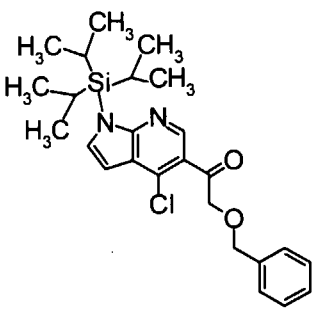
solution was transferred into a separating funnel and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was

5 purified by silica gel column chromatography (n-hexane) to obtain ethyl 4-chloro-2-methyl-1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (645 mg) as a colorless viscous liquid.

The compound in Preparation 47-1 shown in the following

10 table was produced using the corresponding starting compound according to the method similar to that described in Preparation 47.

Table 60

Pr	Structure	Data
47		MS: 417 (M+Na) +
47-1		

Preparation 48

A mixture of ethyl 4,6-dichloro-5-nitronicotinic acid ester (1 g), 2-adamantamine hydrochloride (708 mg), diisopropylethylamine (1.3 ml), and 2-propanol (4 ml) was subjected to microwave irradiation under nitrogen atmosphere, and heated at 90°C for 10 minutes. After being cooled, the reaction solution was diluted with ethyl acetate (20 ml), and poured into 1/2 saturated aqueous ammonium chloride (20 ml). The mixture was extracted with ethyl acetate (20 ml) two times, washed with brine (30 ml), dehydrated with anhydrous magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane: ethyl acetate) to obtain ethyl 4-(2-adamantylamino)-6-chloro-5-nicotinic acid ester (1.23 g) as an orange solid.

The compounds in Preparations 48-1 to 48-5 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 48.

Table 61

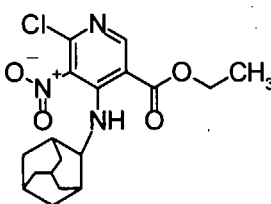
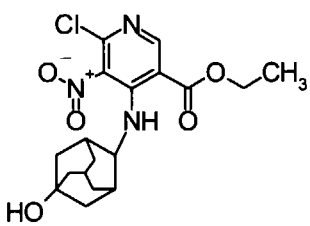
Pr	Structure	Pr	Structure
48		48-1	 cis/trans mix

Table 61 (contd.)

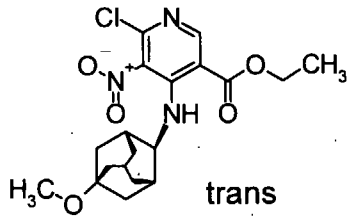
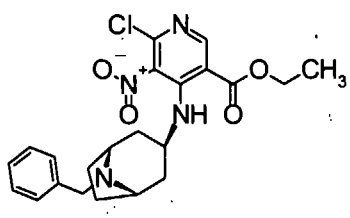
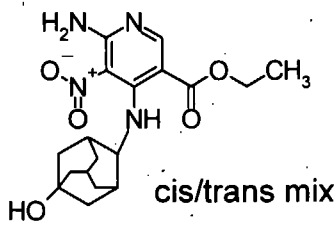
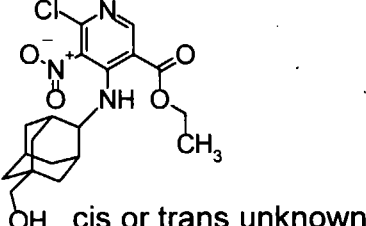
Pr	Structure	Pr	Structure
48-2	 trans	48-3	
48-4	 cis/trans mix	48-5	 cis or trans unknown

Table 62

Pr	Data
48	MS: 380 (M+H) +
48-1	MS: 396 (M+H) +
48-2	MS: 410 (M+H) +
48-3	MS: 445 (M+H) +
48-4	MS: 377 (M+H) +
48-5	MS: 410 (M+H) +

Preparation 49

A mixture of ethyl 4,6-dichloro-5-nitronicotinic acid
 5 ester (333 mg), 4-amino-1-adamantanol (200 mg),
 diisopropylethylamine (219 μ l), and isopropylalcohol (1 ml)
 was subjected to microwave irradiation under nitrogen
 atmosphere and heated at 90°C for 10 minutes. After the
 mixture was cooled, benzylamine (157 μ l) was added to the
 10 reaction solution, the mixture was subjected to microwave
 irradiation again and heated at 90°C for 10 minutes. After
 being cooled, the reaction solution was diluted with ethyl
 acetate (20 ml), poured into 1/2 saturated aqueous ammonium

chloride (20 ml), extracted with ethyl acetate (20 ml) two times, washed with brine (30 ml), dried over anhydrous magnesium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain ethyl 6-(benzylamino)-4-[(5-hydroxy-2-adamantyl)amino]-nicotinic acid ester (515 mg) as an orange solid.

The compounds in Preparations 49-1 to 49-5 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 49.

Table 63

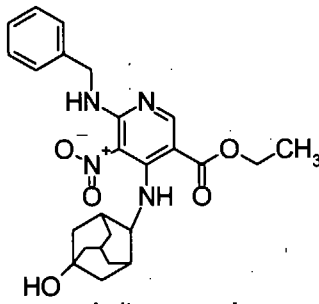
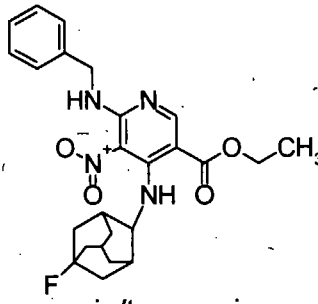
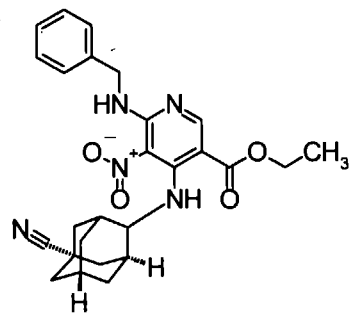
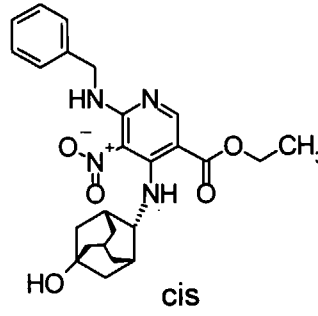
Pr	Structure	Pr	Structure
49	 cis/trans mix	49-1	 cis/trans mix
49-2	 cis or trans unknown	49-3	 cis

Table 63(contd.)

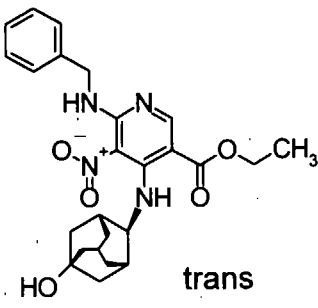
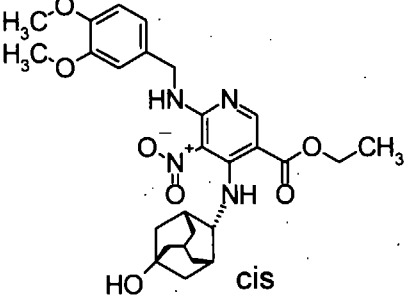
Pr	Structure	Pr	Structure
49-4	 trans	49-5	 cis

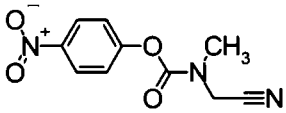
Table 64

Pr	Data
49	MS: 467 (M+H) +
49-1	MS: 469 (M+H) +
49-2	MS: 476 (M+H) +
49-3	MS: 467 (M+H) +
49-4	
49-5	MS: 527 (M+H) +

Preparation 50

The compound in Preparation 50 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Example 10.

Table 65

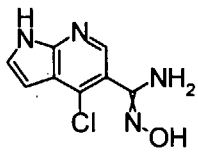
Pr	Structure
50	

Preparation 51

The compound in Preparation 51 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Example

28.

Table 66

Pr	Structure	Data
51		MS: 211 (M+H) +

Preparation 52

5 10% Palladium on carbon (50% wet) (40 mg) was added to a solution of benzyl 4-[(5-carbamoyladamantan-2-yl)amino]-1H-pyrrolo-[2,3-b]pyridine-5-carboxylate (183 mg) in methanol (5 ml) and 1,4-dioxane (5 ml), and hydrogenated under hydrogen atmosphere for 5 hours. Resulting precipitates were dissolved by tetrahydrofuran and filtered out the catalysts.

10 The filtrates were evaporated in vacuo to give 4-[(5-carbamoyladamantan-2-yl)amino]-1H-pyrrolo[2,3-b] pyridine-5-carboxylic acid (117 mg).

 The compounds in Preparations 52-1 to 52-17 shown in the following table were produced using the corresponding starting compounds according to the method similar to that described in Preparation 52.

15

Table 67

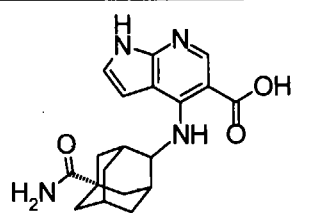
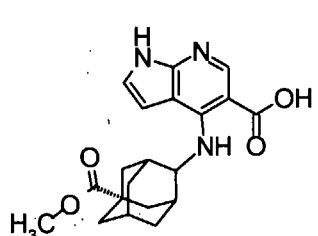
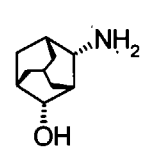
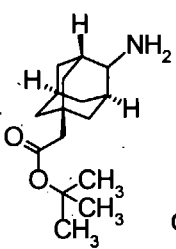
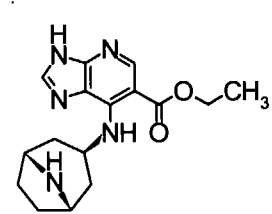
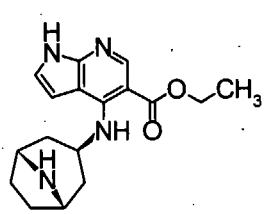
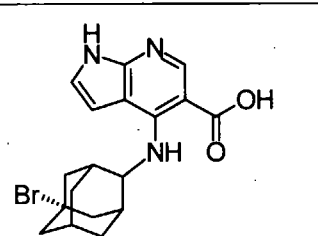
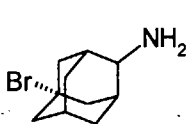
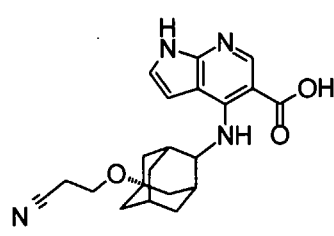
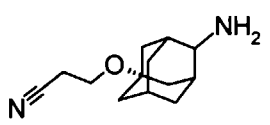
Pr	Structure	Pr	Structure
52-1	 diastereomer of 52-14 cis or trans unknown	52-2	 cis/trans mix
52-3		52-4	 cis/trans mix
52-5		52-6	
52-7	 cis or trans unknown	52-8	 cis or trans unknown
52-9	 cis or trans unknown	52-10	 cis/trans mix

Table 67 (contd.)

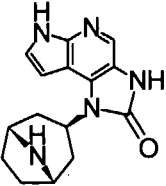
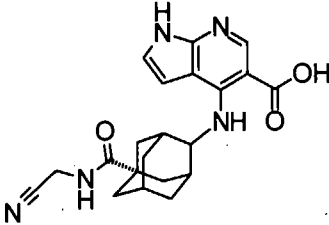
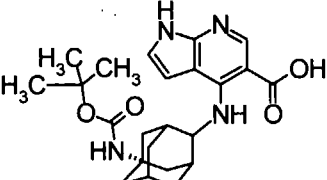
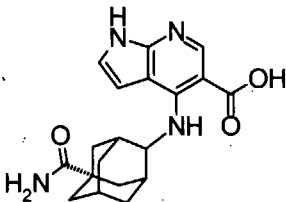
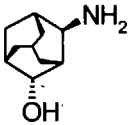
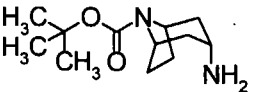
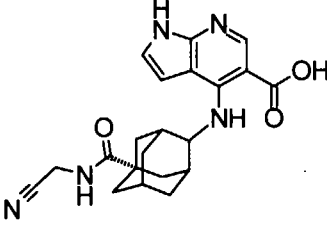
Pr	Structure	Pr	Structure
52-11		52-12	 diastereomer of 53-17 cis or trans unknown
52-13	 cis or trans unknown	52-14	 diastereomer of 53-1 cis or trans unknown
52-15		52-16	
52-17	 diastereomer of 53-12 cis or trans unknown		

Table 68

Pr	Data
52-1	MS: 355 (M+H) +
52-2	MS: 370 (M+H) +
52-3	MS: 168 (M+H) +.
52-4	MS: 267 (M+H) +
52-5	MS: 316 (M+H) +
52-6	MS: 313 (M-H) -

Table 68 (contd.)

Pr	Data
52-7	MS: 390, 392 (M+H) +
52-8	MS: 230, 232 (M+H) +
52-9	MS: 381 (M+H) +
52-10	MS: 221 (M+H) +
52-11	MS: 284 (M+H) +
52-12	MS: 394 (M+H) +
52-13	MS: 427 (M+H) +
52-14	MS: 355 (M+H) +
52-15	MS: 168 (M+H) +
52-16	¹ H-NMR (400MHz, CDCl ₃) δ : 1.46 (9H, s), 1.61-2.29 (10H, m), 3.33 (1H, dd, J=6.2, 6.2Hz), 4.06-4.29 (2H, m) MS: 227 (M+H) +
52-17	MS: 394 (M+H) +

Preparation 53

The compound in Preparation 53-1 to 53-4 shown in the following table was produced using the corresponding starting compound according to the method similar to that described in Example 16.

Table 69

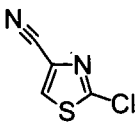
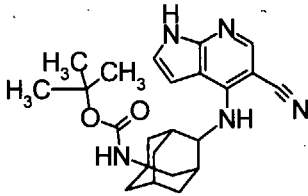
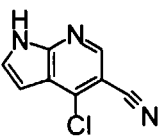
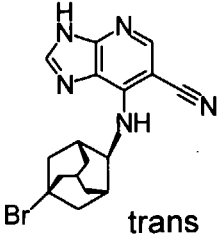
Pr	Structure	Pr	Structure
53-1		53-2	 cis/trans mix
53-3		53-4	 trans

Table 70

Pr	Structure
53-1	MS:143 (M-H) -
53-2	MS:430 (M+Na) +
53-3	MS:176 (M-H) -
53-4	MS:372, 374 (M+H) +

Example 1

5 To a solution of 5-(4-chloro-1H-pyrrolo[2,3-b]pyridine-5-yl)-N-methyl-1,3,4-oxadiazole-2-carboxamide (18 mg) in 1-methyl-2-pyrrolidone (0.18 ml) were added N,N-dibutyl-1-butaneamine (0.046 ml) and cis-(1S,3R,4R,5S)-4-aminoadamantan-1-ol (32.5 mg) under ambient temperature.

10 The mixture was heated immediately to 150°C and stirred for 2 hours. After the disappearance of the starting compound was ascertained, the residue was purified by silica gel column chromatography (chloroform:methanol = 97:3 to 85:15) to obtain

15 cis-5-(4-((1R,2R,3S,5s)-5-hydroxyadamantan-2-yl)amino)-1H-pyrrolo[2,3-b]pyridine-5-yl)-N-methyl-1,3,4-oxadiazole-2-carboxamide (19.8 mg) as a white solid.

Example 2

To 1-[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methaneamine (61 mg) were added a solution of 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (39 mg) in 1-methyl-2-pyrrolidone (0.6 ml), triethylamine (0.056 ml), and sodium iodide (3 mg), and the mixture was stirred at 130°C for 17 hours.

20 After the reaction mixture was left to cool, to the reaction

mixture were added N,N-dimethylformamide (0.3 ml) and water (0.1 ml), and the reaction mixture was dissolved. The reaction mixture was directly purified by preparative HPLC (10mM-NH₄HCO₃ + NH₃ (pH = 9.2):CH₃CN = 98:2 to 30:70). The active fraction

5 was concentrated and dried to hardness to obtain 4-
({[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl)methyl}a
mino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (33.5 mg) as a
solid.

Example 3

10 To a suspension methyl 4-(2-oxo-3,6-dihydropyrazolo
[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)adamantan-1-carboxy
late (40 mg) in methanol (0.4 ml) and dioxane (0.4 ml) was added
1M aqueous sodium hydroxide (0.22ml), and the suspension was
refluxed for 2 hours. The reaction solution was cooled to
15 ambient temperature, the pH was adjusted to 5 with 1M aqueous
hydrochloric acid and pH 4 buffer solution, and the reaction
solution was evaporated under reduced pressure. The obtained
solid was collected by filtration and washed with water to
obtain 4-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]
20 pyridine-1(2H)-yl)adamantan-1-carboxylic acid (32 mg).

Example 4

4-(2-Oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]
pyridine-1(2H)-yl)adamantan-1-carboxylic acid (50 mg) was
suspended in N,N-dimethyl formamide (1 ml). To the suspension
25 were added aminoacetonitrile hydrochloride (17 mg),

1-hydroxybenzotriazole (28 mg), diisopropylethylamine (62 μ l), and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (41 mg) successively, and the mixture was stirred overnight at ambient temperature. To the reaction solution were added ethyl acetate and water, and the organic layer was extracted. The organic layer was washed with saturated brine, dried over magnesium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain N-(cyanomethyl)-4-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)adamantan-1-carboxamide (23 mg).

Example 5

To a solution of 3-methylbenzoic acid (22.4 mg) in 1-methyl-2-pyrrolidone (0.6ml) were added 4-[(3-exo-8-azabicyclo[3.2.1]oct-3-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (42.8 mg) and 1-hydroxybenzotriazole (22.3 mg). Furthermore, 1M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide/1-methyl-2-pyrrolidone solution (0.225 ml) was added, and the mixture was stirred for 4 hours at 50°C. After being cooled, the reaction solution was directly purified by preparative HPLC system (10mM-NH₄HCO₃ + NH₃ (pH = 9.2):CH₃CN = 98:2 to 30:70). The active fraction was concentrated and dried to hardness to obtain 4-{[(3-exo)-8-(3-methylbenzoyl)-8-azabicyclo[3.2.1]oct-3-yl)amino]}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (34.8 mg) as a solid.

Example 6

To a solution of 2-aminoethanol (18.6 mg) in 1-methyl-2-pyrrolidone (0.6 ml) were added cis-4-
{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo
5 [2,3-b]pyridine-5-carboxylic acid (41 mg) and 1-
hydroxybenzotriazole (18.6 mg). Furthermore, 1-ethyl-3-
(3-dimethylaminopropyl)-carbodiimide/1-methyl-2-pyrrolidone
solution (0.188 ml) was added, and the mixture was stirred
for 6 hours at 60°C. After being cooled, the reaction solution
10 was directly purified by preparative HPLC (10mM-NH₄HCO₃ + NH₃
(pH = 9.2):CH₃CN = 98:2 to 30:70). The active fraction was
concentrated and dried to hardness to obtain 4-([(2r,5s)-
5-hydroxyadamantan-2-yl]amino)-N-(2-hydroxyethyl)-1H-pyrro
lo[2,3-b]pyridine-5-carboxamide (22.9 mg) as a solid.

15 Example 7

To a solution of ethyl 3-(4-([(2r,5s)-5-
hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-
yl)-1,2,4-oxadiazole-5-carboxylate (25 mg) in 1-methyl-2-
pyrrolidone (0.25 ml) was added 2-piperazin-1-ylethanol (8.5
20 mg) under ambient temperature. The mixture was immediately
warmed to 50°C and stirred for 0.5 hour. After the
disappearance of the starting compound was ascertained, the
residue was purified by silica gel column chromatography
(chloroform:methanol = 96:4 to 87:13) to obtain cis-
25 (1s,3R,4R,5S)-4-{[5-(5-{[4-(2-hydroxyethyl)piperazin-1-yl]

carbonyl}-1,2,4-oxadiazole-3-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (22.6 mg) as a yellowish white solid.

Example 8

5 To a solution of methylamine hydrochloride (4.7 mg) in 1-methyl-2-pyrrolidone (0.3 ml) were added ethyl cis-5-(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)-1,2,4-oxadiazole-5-carboxylate (14.8 mg) and diisopropylamine (0.0183 ml), and the mixture was
10 stirred for 6 hours at 90°C. After being cooled, the reaction solution was directly purified by preparative HPLC system (10 mM-NH₄HCO₃ + NH₃ (pH = 9.2):CH₃CN = 90:10 to 20:80). The active fraction was concentrated and dried to hardness to obtain
15 5-(4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)-N-methyl-1,2,4-oxadiazole-3-carboxamide (6.74 mg) as a solid.

Example 9

To a solution of cis-5-(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)-N-piperidine-4-yl-1,2,4-oxadiazole-3-carboxamide
20 dihydrochloride (20 mg) in 1-methyl-2-pyrrolidone (0.25 ml) were added N-ethyl-N-isopropylpropan-2-amine (0.025 ml) and acetic anhydride (0.043 ml) under ambient temperature, and the mixture was stirred for 1 hour. The residue was purified by
25 silica gel column chromatography (chloroform:methanol = 99:1

to 89:11) to obtain cis-N-(1-acetylpiperidine-4-yl)-5-(4-
{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo
[2,3-b]pyridine-5-yl)-1,2,4-oxadiazole-3- carboxamide (7.8
mg) as a yellowish white solid.

5 Example 10

To 1-(5-aminoadamantan-2-yl)-3,6-dihydroimidazo
[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one dihydrochloride (15
mg) were added dichloromethane-methanol and saturated aqueous
sodium hydrogencarbonate, and the organic layer was extracted.
10 The organic layer was dried over magnesium sulfate and filtered.
The filtrate was evaporated under reduced pressure. The
residue was suspended in dichloromethane (7.5 ml), and
triethylamine (13 µl) and propanoyl chloride (4 µl) were added.
The mixture was stirred overnight at ambient temperature. The
15 reaction solution was purified by NH silica gel column
chromatography (chloroform:methanol) to obtain N-[4-(2-oxo-
3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)
adamantan-1-yl]propanamide (2 mg).

Example 11

20 To a solution of cis-4-{[(1R,2R,3S,5s)-5-
hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-
carboxylic acid (30 mg) in N,N-dimethylformamide (0.21 ml)
were added N,N'-carbonyl diimidazole (22.3 mg) and 2M
dimethylamine/methanol solution (0.183 ml) successively under
25 ambient temperature. The mixture was stirred at ambient

temperature for 18 hours. Water was added to the reaction solution, and the reaction solution was filtered. The solid residue was washed with water and dried. The residue was purified by thin-layer silica gel column chromatography (chloroform: methanol = 10:1) to obtain methyl cis-4-
5 {[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo [2,3-b]pyridine-5-carboxylate (18 mg) as a yellowish white solid.

Example 12

10 To a suspension of rel-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (25 mg) in N,N-dimethylformamide (0.4 ml) were added potassium carbonate (15.8 mg) and 1-chloroacetone (0.0073 ml), and the mixture was stirred at ambient temperature
15 for 5 hours. The reaction solution was diluted with ethyl acetate, washed with water and saturated brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to
20 obtain rel-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid 2-oxopropyl ester (20.8 mg) as a white solid.

Example 13

To a suspension of rel-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-

25

carboxylic acid (45 mg), acetamide oxime (25.5 mg), and
1-hydroxybenzotriazole (27.9 mg) in N,N-dimethylformamide
(1.08 ml) were added triethylamine (0.077 ml) and N-[3-
(dimethylamino)propyl]-N'-ethylcarbodiimide hydrochloride
5 (39.5 mg). The mixture was stirred for 2 hours at 60°C. The
reaction solution was diluted with chloroform and ethanol,
washed with saturated brine, dried over anhydrous sodium
sulfate, and filtered. The filtrate was evaporated under
reduced pressure. The residue was purified by silica gel
10 column chromatography (chloroform:methanol) to obtain
rel-(1Z)-N'-{[(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]
amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)carbonyl]oxy}
ethanimidamide (38.9 mg) as white powder.

Example 14

15 To a solution of cis-4-{[(1R,2R,3S,5s)-5-
hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-
carboxylic acid (30 mg) in N,N-dimethylformamide (0.9 ml) were
added N,N'-carbonyldiimidazole (83 mg),
N-ethyl-N-isopropylpropane-2-amine (0.018 ml), and carbonic
20 acid-guanidine (1:2) (82.5 mg) successively under ambient
temperature. Furthermore, after 1-methyl-2-pyrrolidone (0.3
ml) was added, the mixture was immediately warmed to 60°C and
stirred for 5 hours. The mixture was evaporated under reduced
pressure and dried. The residue was purified by basic
25 thin-layer silica gel column chromatography (chloroform:

methanol = 6:1) to obtain cis-N-(diaminomethylene)-4-
{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-
1H-pyrrolo[2,3-b]pyridine-5-carboxamide (18.1 mg) as a
yellowish white solid.

5 Example 15

To a solution of cis-4-[(1R,2R,3S,5s)-5-
hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-
carboxylic acid (80 mg) in 1-methyl-2-pyrrolidone (0.8 ml) were
added (O-(7-azabenzotriazol-1-yl)-1,1,3,3-
10 tetramethyluronium hexafluorophosphate) (HATU) (139 mg),
N-ethyl-N-isopropylpropane-2-amine (0.17 ml), and hydrazine
carboxamide hydrochloride (32.7 mg) successively under ambient
temperature. The mixture was stirred for 3 hours at ambient
temperature. To the reaction solution were added ethyl acetate
15 and diisopropyl ether, and the mixture was filtered. The solid
residue was washed with ethyl acetate-diisopropyl ether and
dried to obtain cis-2-[(4-[(1R,2R,3S,5s)-5-
hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-yl
)carbonyl]hydrazinecarboxamide (90 mg) as a yellowish white
20 solid.

Example 16

4-(2-Oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]
pyridine-1(2H)-yl)adamantan-1-carboxamide (70 mg) was
suspended in N,N-dimethylformamide (1 ml), and
25 2,4,6-trichloro-1,3,5-triazine (37 mg) was added under ice.

cooling. The mixture was stirred at ambient temperature for 4 hours. To the reaction solution was added saturated aqueous sodium hydrogencarbonate, and the obtained solid was collected by filtration, washed with water and ethyl acetate to obtain
5 4-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)adamantan-1-carbonitrile (30 mg).

Example 17

To a solution of 5-(4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-yl)-1,2,4-oxadiazole
10 -3-carboxamide (30 mg) in tetrahydrofuran (1 ml) were added pyridine (37 μ l) and trifluoroacetic anhydride (64 μ l) under ice cooling, and the reaction solution was stirred under ambient temperature for 30 minutes. Water was added to the reaction solution, and the precipitate was collected by
15 filtration and dissolved in tetrahydrofuran (1 ml). To the reaction solution was added 1M aqueous sodium hydroxide (0.114 ml) under ice cooling, and the reaction solution was stirred for 1 hour under ambient temperature. The reaction solution was extracted with chloroform and washed with water. The
20 organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10) to obtain
5-(4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo
25 [2,3-b]pyridine-5-yl)-1,2,4-oxadiazole-3-carbonitrile (5

mg) as a white solid.

Example 18

t-Butyl [4-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo
[2,3-b]pyridine-1(2H)-yl)adamantan-1-yl]carbamate (118 mg)
5 was suspended in dioxane (1.2 ml). 4M hydrochloric
acid/dioxane (0.7 ml) was added, and the mixture was stirred
overnight at ambient temperature. To the reaction solution
was added ethyl acetate, and the obtained solid was collected
by filtration and washed with ethyl acetate to obtain
10 1-(5-adamantan-2-yl)-3,6-dihydroimidazo[4,5-d]pyrrolo
[2,3-b]pyridine-2(1H)-one dihydrochloride (108 mg).

Example 19

To 3-(3,4-dimethoxybenzyl)-N-(4-fluorobenzyl)-
7-((5-hydroxyadamantan-2-yl)amino)-3H-imidazo[4,5-b]
15 pyridine-6-carboxamide (170 mg) was added trifluoroacetic
acid (1.7 ml), and the mixture was stirred at ambient
temperature for overnight. The reaction solution was
neutralized with saturated aqueous sodium hydrogencarbonate
and extracted with ethyl acetate and tetrahydrofuran. The
20 organic layer was washed with saturated brine, dried over
magnesium sulfate, and filtered. The filtrate was evaporated
under reduced pressure. The residue was purified by silica
gel column chromatography (chloroform:methanol) to obtain
N-(4-fluorobenzyl)-7-((5-hydroxyadamantan-2-yl)amino)-
25 3H-imidazo[4,5-b]pyridine-6-carboxamide (31 mg).

Example 20

To a solution of 4-{[(2r,5s)-5-hydroxyadamantan-2-yl] amino}-N-(tetrahydro-2H-pyran-2-yloxy)-1H-pyrrolo[2,3-b] pyridine-5-carboxamide (35 mg) in ethanol (0.525 ml) was added
5 2M hydrochloric acid/ethanol solution (0.205 ml) under ambient temperature. The reaction solution was stirred under ambient temperature for 2 hours. To the reaction solution was added ethyl acetate, and the precipitate was collected by filtration to obtain N-hydroxy-4-{[(2r,5s)-5-hydroxyadamantan-2-yl] amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
10 hydrochloride (18 mg) as a white solid.

Example 21

To a solution of 3-{[(triisopropylsilyl)oxy]methyl} bicyclo[2.2.1]hept-2-yl]-3,6-dihydroimidazo[4,5-d]pyrrolo
15 [2,3-b]pyridine-2(1H)-one (45 mg) in tetrahydrofuran (0.15 ml) was added 1M tetrabutylammoniumfluoride/tetrahydrofuran solution (297 µl), and the mixture was stirred overnight at ambient temperature. The reaction solution was evaporated under reduced pressure. The residue was purified by silica
20 gel column chromatography (ethyl acetate:methanol) to obtain 1-[3-(hydroxymethyl)bicyclo[2.2.1]hept-2-yl]-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one (14.8 mg) as a white solid. To a solution of
rel-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl] amino}-1H-pyrrolo[2,3-b]pyridine-5-carbohydrazide in 1-methyl-2-
25

pyrrolidone (1 ml) were added triethyl orthoformate (340 μ l) and p-toluene sulfonic acid monohydrate (5.6 mg). After stirring at 120°C for 30 minutes, triethyl orthoformate (340 μ l) and p-toluene sulfonic acid monohydrate (5.6 mg) were added.

5 After the mixture was stirred at 120°C for 40 minutes, the reaction solution was extracted with 20% chloroform/methanol solution, and washed with saturated aqueous sodium bicarbonate. The organic layer was dried over magnesium sulfate and filtered. The filtrate was evaporated under reduced pressure. The

10 residue was purified by silica gel chromatography (chloroform:methanol) to obtain rel-(1s,3R,4R,5S)-4-
{[1-(diethoxymethyl)-5-(1,3,4-oxazole-2-yl)-1H-pyrrolo
[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (28 mg) and
rel-(1s,3R,4R,5S)-4-([5-(1,3,4-oxazole-2-yl)-1H-pyrrolo
15 [2,3-b]pyridine-4-yl]amino}adamantan-1-ol (70 mg).

Example 22

The cis-trans mixture of N-(cyanomethyl)-4-(2-oxo-3,6-dihydropyrazolo[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)adamantan-1-carboxylate was separated by HPLC (aqueous

20 (NH₄)HCO₃-aqueous ammonia (pH = 9.2):acetonitrile) to obtain a fraction (8 mg) having a peak with a short retention time and another fraction (15 mg) having a peak with a long retention time.

Example 23

4-(Adamantan-1-ylamino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (17 mg) and triethylamine (15 μ l) were dissolved in dioxane (0.5 ml). To the mixture was added diphenylphosphoryl azide (DPPA) (18 μ l) at 120°C under stirring. The mixture was stirred at the same temperature for 2 hours and cooled to ambient temperature. The obtained solid was collected by filtration and washed with acetonitrile to obtain (adamantan-1-yl)-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one (11 mg).

10 Example 24

To a mixture of 5,6-diamino-4-{cis-5-hydroxyl-2-adamantyl]amino}-N-methylnicotinamide (9 mg) and triethyl orthoformate (0.15 ml) was added concentrated hydrochloric acid (5 μ l), and the mixture was heated at 90°C for 3 hours. After being cooled, the reaction solution was diluted with ethyl acetate (10 ml), and saturated aqueous sodium hydrogencarbonate (10 ml) was added. The organic layer was extracted, dried over magnesium sulfate, and concentrated. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain 7-{[cis-5-hydroxyadamantan-2-yl]amino}-N-methyl-3H-imidazo[4,5-b]pyridine-6-carboxamide (0.5 mg) as a pale yellow solid.

Example 25

A mixture of acetic anhydride (897 μ l) and formic acid (342 μ l) was stirred at 60°C for 2 hours. After the mixture

was cooled, a solution of 4-(2-adamantylamino)-6-amino-5-nicotinamide (200 mg) in dichloromethane (1 ml) was added dropwise. The reaction mixture was stirred at ambient temperature for 1 hour and at 50°C for 2 hours. After being cooled, the reaction mixture was evaporated under reduced pressure. To the residue were added ethanol (2 ml), tetrahydrofuran (1 ml), and water (1 ml). Then, iron powder (169 mg) and ammonium chloride (16 mg) were added to the mixture. The mixture was stirred at 120°C for 6 hours. After being cooled, the mixture was evaporated under reduced pressure. To the residue was added saturated aqueous sodium hydroxide (10 ml), and the mixture was extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain 7-(2-adamantylamino)-3H-imidazo[4,5-b]pyridine-6-carboxamide (110 mg) as a white solid.

Example 26

To a mixture of isopropyl 6-(benzylamino)-4-{{cis-5-hydroxyadamantan-2-yl}amino}-5-nicotinate (90 mg), ammonium formate (236 mg), and methanol was added 10% palladium on carbon (50% wet) (40 mg), and the mixture was stirred for 5 hours under refluxing. After being cooled, the reaction mixture was filtered to remove catalyst. The filtrate was concentrated

under reduced pressure. To the residue were added triethyl orthoformate (0.6 ml) and concentrated hydrochloric acid (31 μ l), and the mixture was stirred at ambient temperature for 3 hours. After the reaction mixture was diluted with ethyl acetate (20 ml), saturated aqueous sodium hydrogencarbonate (20 ml) was added. The organic layer was extracted, dried over magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain isopropyl-rel-7-([(1R,2R,3S,5S)-5-hydroxyadamantan-2-yl]amino)-3H-imidazo[4,5-b]pyridine-6-carboxylate (45 mg) as a white solid.

Example 27

To a solution of 4-[(5-hydroxyadamantan-2-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (100 mg) in methanol (3 ml) were added hydroxylamine hydrochloride (34 mg) and sodium hydrogencarbonate (82 mg), and the reaction solution was stirred at 90°C for 18 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10) to obtain N'-hydroxy-4-([(2r,5s)-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidamide (32 mg) as a white solid and to obtain N'-hydroxy-4-([(2s,5r)-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidamide

(35 mg) as a white solid.

Example 28

A solution of rel-(1Z)-N'-{[(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridin-5-yl)carbonyl]oxy}ethanimidamide (16.2 mg) in N,N-dimethylformamide (0.4 mL) was stirred at 160 °C for 3 hours, then stirred at 165 °C for 1 hour. The reaction mixture was diluted with ethyl acetate, washed with 10% sodium chloride aqueous solution, water (three times), and brine, dried over magnesium sulfate, filtered and evaporated in vacuo. The residue was purified by silica gel column chromatography (chloroform:methanol, 15:1) to give rel-(1s,3R,4R,5S)-4-{[5-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino}adamantan-1-ol (6.0 mg) as a orange crystals.

Example 29

To a solution of rel-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carbohydrazide in 1-methyl-2-pyrrolidone (1 ml) were added triethyl orthoformate (340 µl) and p-toluene sulfonic acid monohydrate (5.6 mg). After the mixture was stirred at 120 °C for 30 minutes, triethyl orthoformate (340 µl) and p-toluene sulfonic acid monohydrate (5.6 mg) were added. After the mixture was stirred at 120 °C for 40 minutes, the reaction solution was extracted with 20% chloroform/ methanol solution and washed with saturated aqueous sodium bicarbonate. The

organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (chloroform:methanol) to obtain rel-(1s,3R,4R,5S)-4-{[1-(diethoxymethyl)-5-(1,3,4-oxazole-2-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (28mg) and to obtain rel-(1s,3R,4R,5S)-4-{[5-(1,3,4-oxazole-2-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (70 mg).

10 Example 30

To a solution of N'-hydroxy-4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboximidamide (45 mg) in dichloromethane (0.45 ml) were added pyridine (32 μ l) and acetic anhydride (19 μ l). The reaction solution was stirred under ambient temperature for 2 hours. To the reaction solution were further added pyridine (32 μ l) and acetic anhydride (19 μ l), and the reaction solution was stirred at 60°C for 2 hours. To the reaction solution was further added pyridine (0.5 ml), and the mixture was stirred at 90°C for 16 hours. The reaction solution was extracted with chloroform and washed with water. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10) to obtain (1s,4r)-4-{[5-(5-methyl-1,2,4-

oxadiazole-3-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}
adamantan-1-ol (10 mg) as a white solid.

Example 31

To a solution of N'-hydroxy-4-{[(2r,5s)-5-
5 hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-
carboxyimidamide (25 mg) in N,N-dimethylformamide (0.5 ml)
were added pyridine (9 μ l) and 2-ethylhexyl chlorocarbonate
(14 μ l) under ice cooling. The reaction solution was stirred
at ambient temperature for 2 hours. To the reaction solution
10 was added water. The mixture was extracted with chloroform
and washed with water. The organic layer was dried over
magnesium sulfate and filtered. The filtrate was concentrated
under reduced pressure. The residue was dissolved in
N,N-dimethylformamide (0.5 ml) and xylene (0.5 ml), and the
15 reaction solution was stirred at 150°C for 2 hours. After the
reaction solution was cooled to ambient temperature, the
precipitate was collected by filtration and washed with a small
amount of ethyl acetate to obtain (1s,4r)-4-(3-aminopyrazolo
[3,4-d]pyrrolo[2,3-b]pyridine-1(6H)-yl)adamantan-1-ol (8
20 mg) as a white solid.

Example 32

To a solution of 3-(4-chloro-1H-pyrrolo[2,3-b]
pyridine-5-yl)-N-(2-methoxyethyl)-1,2,4-oxadiazole-5-
carboxamide (35 mg) in 1-methyl-2-pyrrolidone (0.35 ml) were
25 added N,N-dibutyl-1-butanamine (0.078 ml) and cis-

(1S,3R,4R,5S)-4-aminoadamantan-1-ol (36 mg) under ambient temperature. The mixture was immediately heated to 190°C and stirred for 1 hour. After the disappearance of the starting compound was ascertained, water was added to the reaction solution, and the solution was filtered. The solid residue was washed with water and dried. The solid residue was purified by thin-layer silica gel column chromatography (chloroform:methanol = 12:1) to obtain cis-N-{1-[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]-1,6-dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridine-3-yl}-N'-(2-methoxyethyl)ethanediamide (18.1 mg) as a yellowish white solid.

Example 33

To a solution of 3-(4-chloro-1H-pyrrolo[2,3-b]pyridine-5-yl)-N-methyl-1,2,4-oxadiazole-5-carboxamide (14.2 mg) in 1-methyl-2-pyrrolidone (0.142 ml) were added N,N-dibutyl-1-butanamine (0.0487 ml) and cis-(1S,3R,4R,5S)-4-aminoadamantan-1-ol (25.7 mg). The mixture was stirred for 100 minutes using a microwave reaction system at 200°C. After being cooled, the reaction solution was directly purified by preparative HPLC system (10mM NH₄HCO₃ + NH₃ (pH = 9.2):CH₃CN = 95:5 to 20:80). The active fraction was concentrated to obtain cis-N-{1-[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]-1,6-dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridine-3-yl}-N'-methylethanediamide (11.1 mg) as a solid.

Example 34

To a suspension of 4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (60 mg) in toluene (0.6 ml) were added thiosemicarbazide (35.5 mg) and trifluoroacetic acid (0.15 ml), and the mixture was stirred at 70°C for 6 hours. To the mixture were further added thiosemicarbazide (35.5 mg) and trifluoroacetic acid (0.15 ml), and the mixture was stirred at 90°C for 51 hours. Furthermore, thiosemicarbazide (17.8 mg) was added, and the mixture was stirred at 90°C for 48 hours. The reaction solution was alkalified with saturated aqueous sodium hydrogencarbonate and extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain (1s,4r)-4-([5-(5-amino-1,3,4-thiadiazole-2-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino)adamantan-1-ol (8.3 mg) as a white solid.

Example 35

To a solution of ethyl 5-[4-(2-oxo-3,6-dihydroimidazo[2,3-b]pyridine-1(2H)-yl)adamantan-1-yl]-1,2,4-oxadiazole-3-carboxylate (30 mg) in tetrahydrofuran (1 ml) was added lithium aluminum hydride (10 mg) under ice cooling, and the mixture was stirred for 1 hour at ambient temperature. To the reaction solution was added 1M aqueous sodium hydroxide. The

mixture was stirred for 30 minutes at ambient temperature and extracted with chloroform. The organic layer was dried over magnesium sulfate and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain 1-{5-[3-(hydroxymethyl)-1,2,4-oxadiazole-5-yl]adamantan-2-yl}-3,6-dihydroimiazolo[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one (3 mg).

Example 36

To a solution of 4-{[(2r,5s)-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (27 mg) in ethanol (0.5 ml) were added 10% palladium on carbon (30 mg) and 2M hydrochloric acid/ethanol solution (0.5 ml). The reaction solution was stirred for 3 hours under hydrogen atmosphere at 60°C. The catalyst was filtered with Celite, and the filtrate was concentrated under reduced pressure to obtain (1s,4r)-4- {[5-(aminomethyl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol trihydrochloride (37 mg) as a white solid.

Example 37

To a solution of 1-(4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)ethanone (20 mg) in tetrahydrofuran (2.5 ml) was added lithium aluminum hydride (19.4 mg) under ambient temperature. Furthermore, the mixture was stirred at ambient temperature for 2 hours. After the

disappearance of the starting compound was ascertained, to the reaction solution were added water (19 μ l), 2M aqueous sodium hydroxide (19 μ l), and water (57 μ l) successively. The precipitated solid was removed by Celite filtration and washed with tetrahydrofuran. The filtrate was concentrated under reduced pressure and purified by thin-layer silica gel column chromatography (chloroform:methanol = 4:1) to obtain (1s,4r)-4-{[5-(1-hydroxyethyl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (9.1mg).

10 Example 38

To a solution of 4-{[(3-exo)-8-(5-nitropyridine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (25 mg) in methanol (0.5 ml) were added ammonium formate (38.6 mg) and palladium on carbon (50% wet) (1.3 mg), and the mixture was heated for 5 hours under refluxing. After the mixture was cooled to ambient temperature, the insoluble matter was removed by Celite filtration and washed with methanol. The filtrate was evaporated under reduced pressure and purified by thin-layer silica gel column chromatography (chloroform:methanol = 4:1) to obtain 4-{[(3-exo)-8-(5-aminopyridine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (12 mg).

Example 39

To a solution of N'-(5-bromoadamantan-2-yl)-4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carbohydrazide (200 mg) in 1-methyl-2-pyrrolidone (1.5 ml) was added triethylamine (0.2 ml), and the mixture was stirred at 200°C using a microwave reaction system for 2 hours. After the reaction solution was cooled, water was added to the reaction solution, and the mixture was extracted with chloroform. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol) to obtain 1-(5-bromoadamantan-2-yl)-1,6-dihydropyrazolo [3,4-d]pyrrolo[2,3-b]pyridine-3(2H)-one (91 mg).

Example 40

To a suspension of 4-([(2R,5S)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (50 mg) in a mixture of toluene (1.5 ml) and N,N'-dimethylformamide (1.5 ml) were added sodium azide (105 mg) and triethylamine hydrochloride (223 mg), and the mixture was stirred for at 100°C for 3 hours. To the reaction mixture was added sodium azide (210 mg) and triethylamine hydrochloride (446 mg), and the mixture was stirred at 100°C for 3.5 hours. The reaction solution was diluted with a mixture solvent of dichloromethane:methanol (= 10:1), and the organic layer was separated. Furthermore, the water layer was extracted with

a mixture solvent of dichloromethane: methanol (= 10:1) three times. The obtained organic layers were combined, dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (dichloromethane: methanol = 10:1) to obtain rel-(1s,3R,4R,5S)-4-{[5-(2H-tetrazole-5-yl)-1H-pyrrolo [2,3-b]pyridine-4-yl]amino}adamantan-1-ol (35 mg) as a solid.

Example 41

To 4-[(5-bromoadamantan-2-yl)amino]-1H-pyrrolo [2,3-b]pyridine-5-carboxamide (52 mg) were added ethylene cyanhydrin (250 µl) and triethylamine (56 µl), and the mixture was stirred for 20 minutes using a microwave reaction system at 150°C. The reaction solution was cooled and purified by silica gel column chromatography (chloroform:methanol). The obtained fraction was concentrated under reduced pressure, and water was added. The obtained solid was collected by filtration to obtain 4-{[5-(2-cyanoethoxy)adamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (16 mg).

Example 42

To a solution of 4-({5-[5-(trichloromethyl)-1,2,4-oxadiazole-3-yl]-1H-pyrrolo[2,3-b]pyridine-4-yl}amino)adamantan-1-ol (80 mg) in 1-methyl-2-pyrrolidinone (1.6 ml) was added ethylamine/methanol solution (2.0M) (1.7 ml) under ice cooling. The reaction solution was stirred for 5 hours

under ambient temperature. To the reaction solution were added ethyl acetate, tetrahydrofuran, and water. The mixture was extracted with a mixture solvent of tetrahydrofuran and ethyl acetate, and washed with saturated brine. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel (NH silica gel) column chromatography (chloroform:methanol = 100:0 to 91:9) to obtain 4-({5-[5-(ethylamino)-1,2,4-oxadiazole-3-yl]-1H-pyrrolo[2,3-b]pyridine-4-yl}amino)adamantan-1-ol (50 mg) as a yellow solid.

Example 43

4-[(5-Hydroxyadamantan-2-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (100 mg) was dissolved in 45% aqueous HBr (0.5 ml), and the mixture was refluxed for 1.5 hours. The reaction solution was cooled, and the obtained solid was collected by filtration and washed with water. The obtained solid was dissolved in dichloromethane and methanol, and purified by silica gel column chromatography (chloroform:methanol) to obtain 4-[5-bromoadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (85 mg).

Example 44

(5-Hydroxyadamantan-2-yl)-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one (92 mg) was suspended in dichloromethane, and diethyl aminosulfur trifluoride (DAST)

was added. The mixture was stirred at ambient temperature for 1 hour. The saturated aqueous sodium hydrogencarbonate and ethyl acetate were added. The obtained solid was collected by filtration and washed with diisopropyl ethylether to obtain
5 (5- fluoroadamantan-2-yl)-3,6-dihydroimidazo[4,5-d]pyrrolo [2,3-b]pyridine-2(1H)-one (34 mg).

Example 45

To a solution of cis-(1s,3R,4R,5S)-4-{[5-(2H-tetrazole-5-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino} adamantan-1-ol (55 mg) in 1-methyl-2-pyrrolidone (0.65 ml)
10 were added N-ethyl-N-isopropylpropane-2-amine (0.11 ml) and iodomethane (0.015 ml) under ambient temperature, and the mixture was stirred at ambient temperature for 4 hours. The residue was purified by silica gel column chromatography
15 (chloroform:methanol = 99:1 to 90:10) to obtain cis-(1s,3R,4R,5S)-4-{[5-(2-methyl-2H-tetrazol-5-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (19.5 mg) as a major product (having a larger R_f value obtained by TLC (chloroform-methanol = 10:1)) and to obtain cis-
20 (1s,3R,4R,5S)-4-{[5-(1-methyl-1H-tetrazole-5-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino}adamantan-1-ol (4.5 mg) as a minor product (having a smaller R_f value obtained by TLC (chloroform-methanol = 10:1)), the major and minor products each being obtained as a yellowish white solid.

25 Example 46

To a solution of 2-chloronicotinonitrile (56.7 mg) and 4-[(3-exo)-8-azabicyclo[3.2.1]oct-3-ylamino]-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (58.4 mg) in 1-methyl-2-pyrrolidone (0.6 ml) were added triethylamine (0.057 ml) and sodium iodide (3 mg), and the mixture was stirred for 10 hours at 130°C. After the reaction mixture was left to cool, 1-methyl-2-pyrrolidone (0.3 ml) was added to the reaction mixture, and the reaction mixture was dissolved. The mixture was directly purified by preparative HPLC system (10mM NH₄HCO₃ + NH₃ (pH = 9.2):CH₃CN = 98:2 to 60:40). The active fraction was concentrated and dried to hardness to obtain 4-[(3-exo)-8-(3-cyanopyridine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (10.1 mg) as a solid.

15 Example 47

To a solution of 4-[(3-exo)-8-(5-aminopyridine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (11 mg) in methanol/dichloromethane was added aqueous formalin (0.022 ml), and the mixture was stirred at ambient temperature for 0.5 hours. Sodium triacetoxyborohydride (30.9 mg) was further added, and the mixture was stirred for 16 hours at ambient temperature. To the reaction solution was added saturated aqueous sodium hydrogencarbonate, and the mixture was stirred for 30 minutes at ambient temperature and extracted with chloroform-methanol.

The extract was concentrated, and the obtained yellow oily matter was purified by thin-layer silica gel column chromatography (chloroform:methanol = 7:1) to obtain 4-([(3-exo)-8-(5-(dimethylamino)pyridine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (5.2mg) as a yellowish white solid.

Example 48

To a suspension of 4-[(3-endo)-8-azabicyclo[3.2.1]oct-3-ylamino]-1H-pyrrolo[2,3-b]pyridine-5-carboxamide dihydrochloride (25 mg) in 1,3-dimethyl-2-imidazolidinone (0.5 ml) was added triethylamine (0.029 ml). Furthermore, mesyl chloride (0.0059 ml) was added under ice cooling. After the mixture was stirred for 1 hour at ambient temperature, diluted aqueous sodium hydrogencarbonate was added, and the mixture was stirred. The precipitated white solid was collected by filtration, washed with water, and dried to obtain 4-([(3-endo)-8-(methylsulfonyl)-8-azabicyclo[3.2.1]oct-3-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (14.1 mg) as a white solid.

Example 49

To a solution of 1-[(3-exo)-8-azabicyclo[3.2.1]oct-3-yl]-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-2(1H)-one (12 mg) in N,N-dimethylacetamide (0.48 ml) and N,N-dimethylformamide (0.24 ml) were added N-ethyl-N-isopropylpropane-2-amine (0.015 ml) and 6-

chloronicotinonitrile (11.7 mg). The mixture was immediately heated to 90°C and stirred for 12 hours. After the disappearance of the starting compound was ascertained, the reaction solution was evaporated under reduced pressure and dried. The solid residue was purified by thin-layer silica gel column chromatography (chloroform:methanol = 8:1) to obtain 6-[(3-exo)-3-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridine-1(2H)-yl)-8-azabicyclo[3.2.1]oct-8-yl]nicotinonitrile (5.2 mg) as a yellowish white solid.

10 Example 50

To a solution of ethyl 3-(4-[(2r,5s)-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-yl)-1,2,4-oxadiazole-5-carboxylate (80 mg) in tetrahydrofuran (3.2 ml) was added 3M iodo(methyl)magnesium/diethyl ether solution (0.315 ml) under ice cooling, and the reaction solution was stirred for 16 hours under ambient temperature. To the reaction solution was further added 3M iodo(methyl)magnesium/diethyl ether solution (0.189 ml) under ice cooling. The reaction solution was stirred under ambient temperature for 16 hours. To the reaction solution was added water under ice cooling, and the mixture was stirred at the same temperature for 15 minutes. To the reaction solution were added chloroform and saturated aqueous ammonium chloride. The mixture was extracted with chloroform and washed with saturated brine. The organic layer was dried over magnesium sulfate and filtered.

The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10) to obtain rel-(1s,3R,4R,5S)-4-((5-[5-(1-hydroxy-1-methylethyl)-1,2,4-oxadiazole-3-yl]-1H-pyrrolo[2,3-b]pyridine-4-yl)amino)adamantan-1-ol (15 mg) as a white solid.

Example 51

To a solution of 4-{[(3-exo)-8-(5-bromopyrimidine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (22.2 mg) in N,N-dimethylformamide (0.67 ml) and 1,3-dimethyl-2-imidazolidinone (0.67 ml) were added tetrakis(triphenylphosphine)palladium (0) (5.8 mg) and dicyanozinc (17.7 mg). Reaction was carried out at 160°C using a microwave reaction system for 1 hour. To the reaction solution was added dichloromethane, and the mixture was filtered. The solid residue was washed with dichloromethane and dried. The solid residue was purified by thin-layer silica gel column chromatography (chloroform:methanol = 8:1) to obtain 4-{[(3-exo)-8-(5-cyanopyrimidine-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (15 mg) as a yellowish white solid.

Example 52

To a solution of 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (30 mg) in tetrahydrofuran (0.6 ml) was added diisobutylaluminum

hydride (0.99M toluene solution) (0.49 ml) at 5°C. The mixture was stirred for 2 hours at 5°C and further stirred for 3 hours at ambient temperature. To the reaction solution was added 6M aqueous hydrochloric acid (0.09 ml) at 5°C. The mixture was stirred for 0.5 hour at ambient temperature. Solid sodium hydroxide (23.3 mg) and magnesium sulfate were added, and the mixture was stirred for 0.5 hour at ambient temperature. The insoluble matter was removed by Celite filtration and washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and purified by thin-layer silica gel column chromatography (chloroform:methanol = 9:1) to obtain 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboaldehyde (18 mg) as a yellowish white solid.

15 Example 53

To a solution of 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboaldehyde (20 mg) in ethanol (0.6 ml) were added pyridine (0.052 ml) and O-methylhydroxyamine hydrochloride (32.1 mg), and the mixture was heated for 6 hours under refluxing. After being cooled to ambient temperature, the reaction solution was evaporated under reduced pressure, dried, and purified by thin-layer silica gel column chromatography (chloroform:methanol = 10:1) to obtain 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboaldehyde O-methyloxime (11

mg) as a yellowish white solid.

Example 54

To acetic acid (0.8 ml) were added pyrrolidine (0.013 ml) and para-formaldehyde (5.72 mg), and the mixture was stirred for 5 minutes at 60°C. To the reaction solution was added cis-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (40.0 mg) at 60°C, and the mixture was stirred at 60°C for 2 hours. The reaction solution was evaporated under reduced pressure, and toluene and N-ethyl-N-isopropylpropane-2-amine were added, and the mixture was subjected to azeotropy. The solid residue was purified by NH thin-layer silica gel column chromatography (chloroform:methanol = 10:1) to obtain cis-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-3-(pyrrolidine-1-ylmethyl)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (10.8 mg) as a yellowish white solid.

Example 55

To a solution of 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboaldehyde (40 mg) in tetrahydrofuran (1 ml) was added methyl (triphenylphosphoranylidene)acetate (56 mg), and the reaction solution was stirred at 80°C for 16 hours. To the reaction solution was further added methyl (triphenylphosphoranylidene)acetate (43 mg), and the reaction solution was stirred at 90°C for 3 hours. To the reaction

solution was further added methyl (triphenylphosphoranylidene)acetate (129 mg), and the reaction solution was stirred at 90°C for 16 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10) to obtain methyl (2E)-3-(4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-yl)acrylate (7 mg) as a yellow solid.

10 Example 56

To a solution of cis-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (50 mg) in N,N-dimethylformamide (0.6 ml) was added 1-chloro-2,5-pyrrolidinedione (18.4 mg) at ambient temperature. After the mixture was stirred at ambient temperature for 2 hours, water was added to the reaction solution, and the solution was filtered. The solid residue was washed with water and dried. The solid residue was purified by thin-layer silica gel column chromatography (chloroform: methanol = 4:1) to obtain cis-3-chloro-4-([(1R,2R,3S,5s)-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (5 mg) as a yellowish white solid.

Example 57

25 To a solution of N'-hydroxy-4-([(2r,5s)-5-

hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidamide (30 mg) in acetic acid (0.5 ml) was added acetic anhydride (11 µl), and the reaction solution was stirred for 30 minutes under ambient temperature. To the reaction solution was added 10% palladium on carbon (10 mg), and the mixture was stirred under hydrogen atmosphere at 50°C for 3 hours. After the reaction solution was cooled to ambient temperature, the catalyst was filtered off with Celite. The filtrate was concentrated under reduced pressure, and the residue was washed with acetonitrile under stirring. The precipitate was collected by filtration to obtain 4-{[(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimidamide acetate (20 mg) as a yellow solid.

15 Example 58

To a solution of cis-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (30 mg) in 1-methyl-2-pyrrolidone (0.18 ml) was added pyridine hydrochloride (10.6 mg) at ambient temperature. Reaction was carried out at 200°C for 1 hour using a microwave reaction system. To the reaction solution was added saturated aqueous sodium hydrogencarbonate, and the mixture was extracted with ethyl acetate and washed with water. The extract was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue

was purified by thin-layer silica gel column chromatography (chloroform:methanol = 10:1) to obtain cis-(1s,3R,4R,5S)-4-(1H-pyrrolo[2,3-b]pyridine-4-ylamino)adamantan-1-ol (14.1 mg) as a yellowish white solid.

5 Example 59

To a solution of cis-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxylic acid (30 mg) in N,N-dimethylformamide (0.1 ml) was added N,N'-carbonyldiimidazole (29.7 mg), and the mixture was
10 stirred for 0.5 hours at 60°C. To the reaction mixture was added methanesulfonamide (17.4 mg) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.027 ml). After being further stirred at 60°C for 3 hours, the reaction solution was concentrated under reduced pressure. The residue was purified by thin-layer
15 silica gel column chromatography (chloroform:methanol = 4:1) to obtain cis-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-N-(methylsulfonyl)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (7.8 mg) as a yellowish white solid.

Example 60

20 To a solution of cis-4-([(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (75 mg) in tetrahydrofuran (0.5 ml) and methanol (0.375 ml) was added 1,1-dimethoxy-N,N-dimethylmethaneamine (1.54 ml) at ambient temperature. After being stirred for 1
25 hour under heating and refluxing, the mixture was cooled to

ambient temperature and stirred for 1 hour. The precipitated solid was collected by filtration, washed and dried to obtain cis-N-[(dimethylamino)methylene]-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide (70 mg) as a white solid.

Example 61

A solution of cis-2-[(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)carbonyl]hydrazine carboxamide (30 mg) in a mixture of xylene (0.45 ml) and acetic acid (0.45 ml) was stirred at 120°C for 3 hours. Furthermore, 1-methyl-2-pyrrolidone (0.45 ml) was added, and the mixture was stirred at 150°C for 4 hours. The reaction solution was concentrated under reduced pressure and dried. The residue was purified by thin-layer silica gel column chromatography (chloroform:methanol = 10:1) to obtain cis-5-(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)-2,4-dihydro-3H-1,2,4-triazol-3-one (5.6 mg) as a product (having a higher R_f value obtained by TLC (chloroform-methanol = 10:1)) and to obtain cis-5-(4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-yl)-1,3,4-oxadiazole-2(3H)-one (8.9 mg) as another product (having a lower R_f value obtained by TLC (chloroform-methanol = 10:1)), these products each being obtained as a yellowish white solid.

Example 62

To a solution of ethyl 4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimide trihydrochloride (75 mg) in ethanol (1 ml) was added 1,2-ethanediamine (0.11 ml), the reaction solution was stirred at 120°C for 2 hours. The reaction solution was concentrated under reduced pressure, and the residue was purified by NH-silica gel column chromatography (chloroform:methanol = 100:0 to 95:5) to obtain (1s,4r)-4-([5-(4,5-dihydro-1H-imidazole-2-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino)adamantan-1-ol (17 mg) as a white solid.

Example 63

To a solution of ethyl 4-([(2r,5s)-5-hydroxyadamantan-2-yl]amino)-1H-pyrrolo[2,3-b]pyridine-5-carboxyimide trihydrochloride (150 mg) in ethanol (1.5 ml) were added 2-aminoethanol (78 µl) and triethylamine (0.225 ml), and the reaction solution was stirred at 110°C for 2 hours. The reaction solution was cooled to ambient temperature and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to 90:10). The obtained solid was washed with ethyl acetate under stirring and collected by filtration to obtain (1s,4r)-4-([5-(4,5-dihydro-1,3-oxazole-2-yl)-1H-pyrrolo[2,3-b]pyridine-4-yl]amino)adamantan-1-ol (5 mg) as a white solid.

Example 64

4-[(5-Hydroxyadamantan-2-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-carbonitrile (200 mg) and Raney nickel were added to ethanol (5 ml), and the reaction solution was stirred under hydrogen atmosphere at 60°C for 8 hours. The catalyst was
5 filtered off with Celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in dioxane (3 ml), and 1M aqueous sodium hydroxide (0.65 ml) was added. To the reaction solution was added di-t-butyl dicarbonate (0.22 ml) under ambient temperature, and the mixture was stirred for 16
10 hours. The reaction solution was extracted with chloroform and washed with water. The organic layer was dried over magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform:methanol = 100:0 to
15 90:10) to obtain t-butyl ({4-[(5-hydroxyadamantan-2-yl)amino]-1H-pyrrolo[2,3-b]pyridine-5-yl)methyl}carbamate (40 mg) as a pale yellow solid.

The compounds shown in the following Table 71 were produced according to the above-mentioned production methods,
20 the methods obvious to those skilled in the art, or modified methods of these. The tables 71 and 72 show the structures and physicochemical data of the compounds described in these Examples and also show the methods for producing the compounds.

Table 71

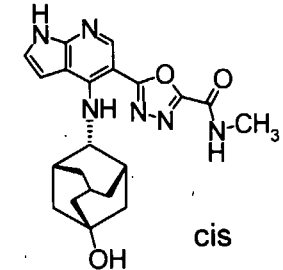
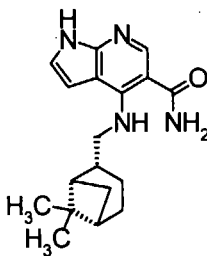
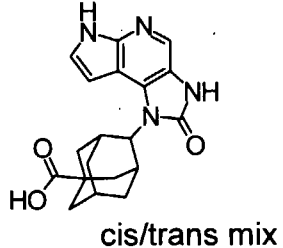
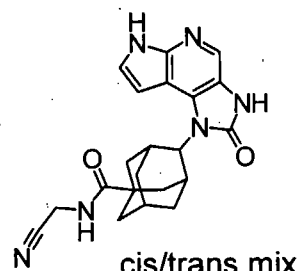
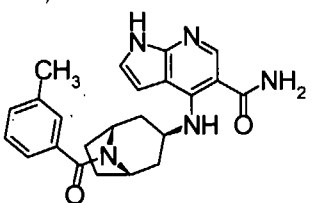
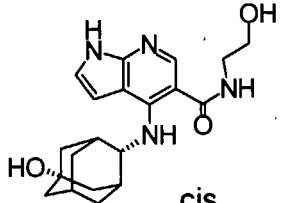
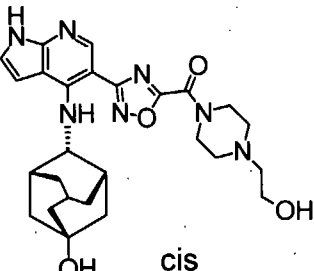
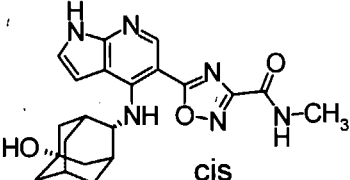
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5	 cis	6	 cis
7	 cis	8	 cis

Table 71 (contd.)

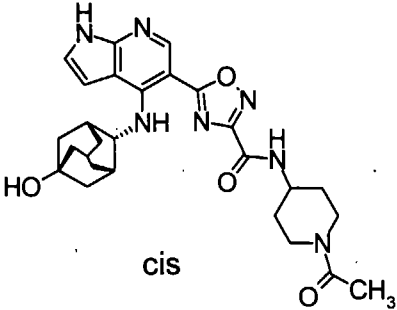
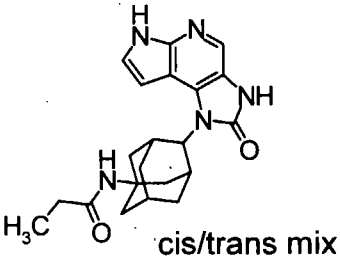
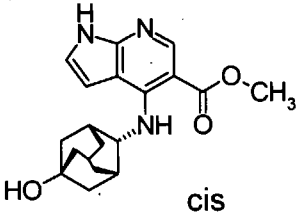
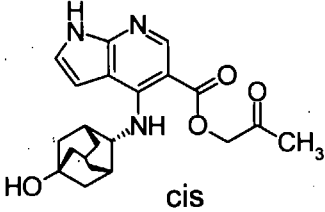
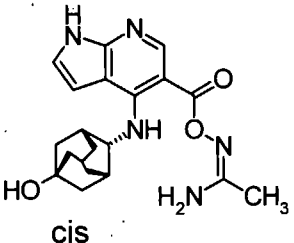
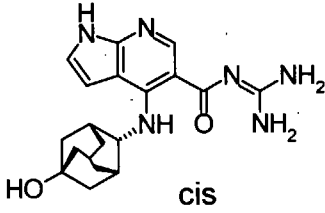
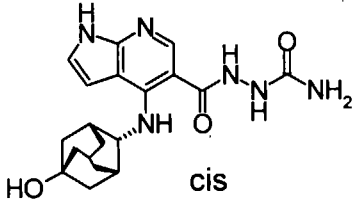
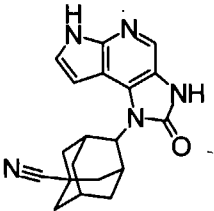
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11	 cis	12	 cis
13	 cis	14	 cis
15	 cis	16	 diastereomer of 365 cis or trans unknown

Table 71 (contd.)

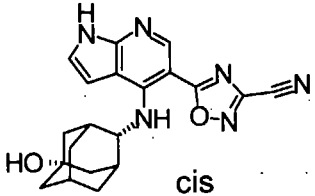
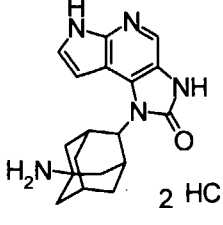
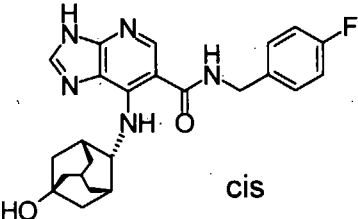
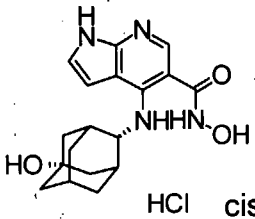
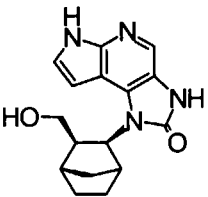
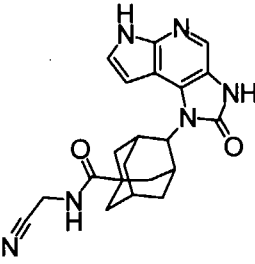
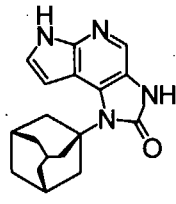
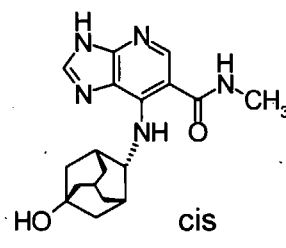
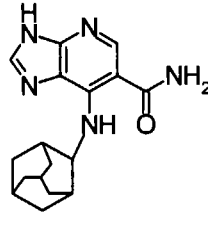
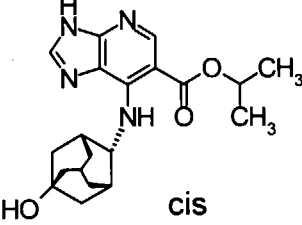
Ex	Structure	Ex	Structure
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19	 cis	20	 HCl cis
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25		26	 cis

Table 71 (contd.)

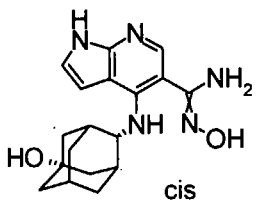
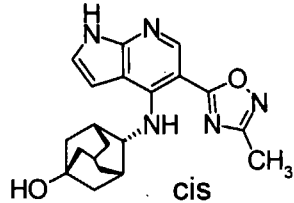
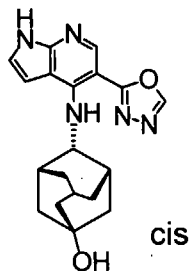
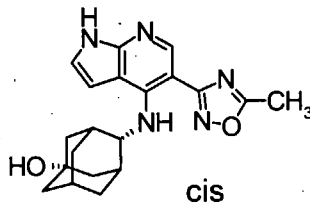
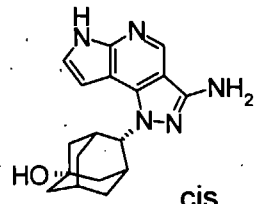
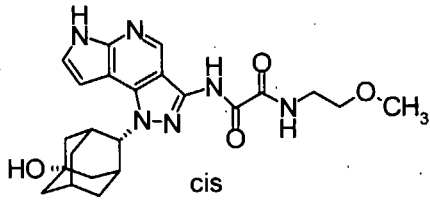
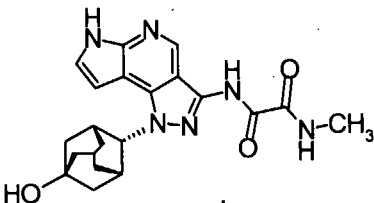
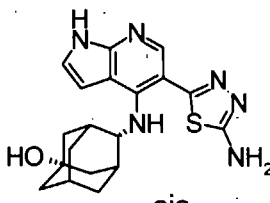
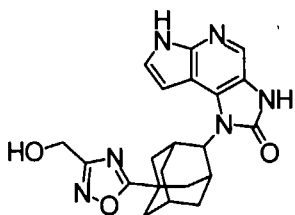
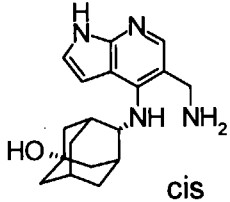
Ex	Structure	Ex	Structure
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29	 cis	30	 cis
31	 cis	32	 cis
33	 cis	34	 cis
35	 cis/trans mix	36	 cis

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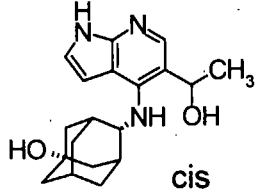
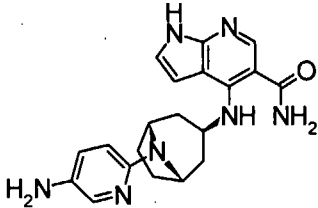
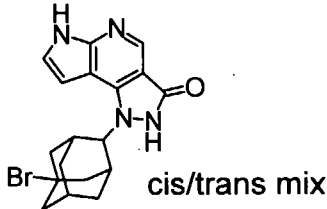
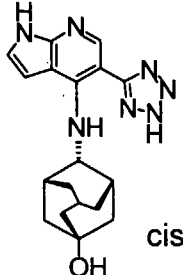
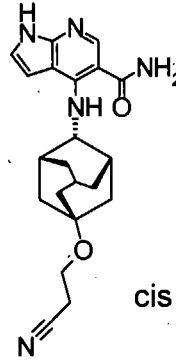
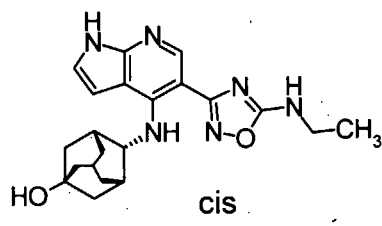
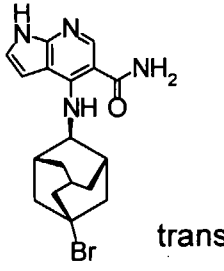
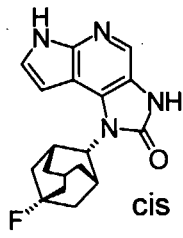
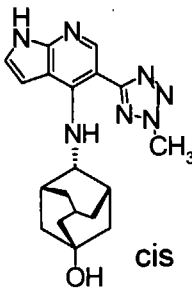
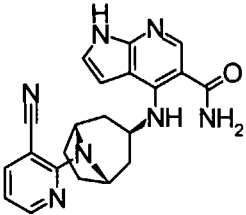
Ex	Structure	Ex	Structure
37	 cis	38	 cis
39	 cis/trans mix	40	 cis
41	 cis	42	 cis
43	 trans	44	 cis
45	 cis	46	 cis

Table 71(contd.)

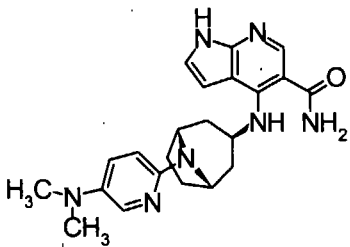
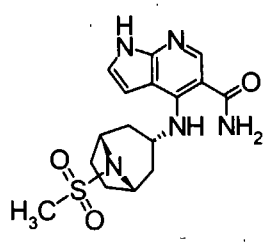
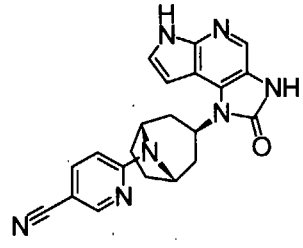
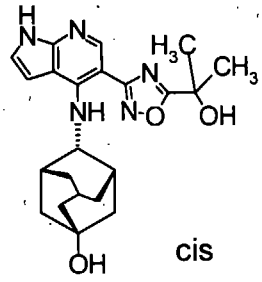
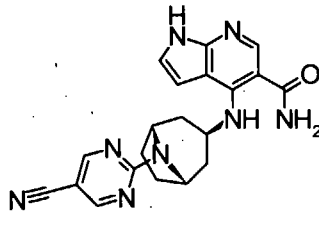
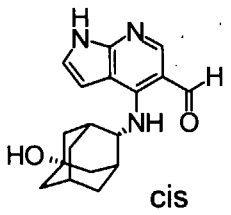
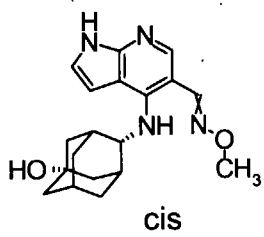
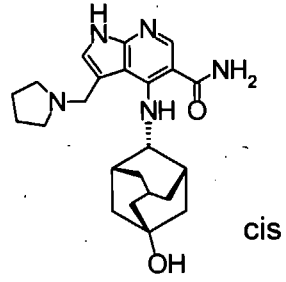
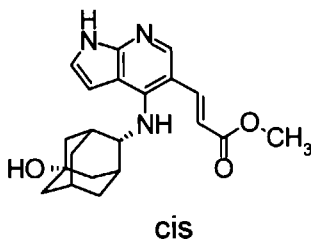
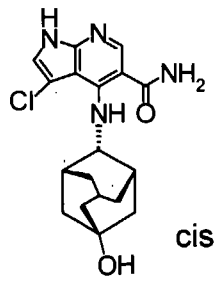
Ex	Structure	Ex	Structure
47		48	
49		50	
51		52	
53		54	
55		56	

Table 71 (contd.)

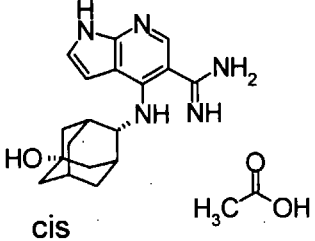
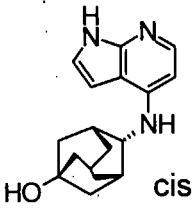
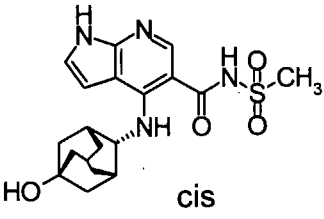
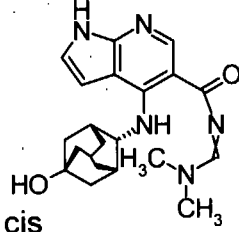
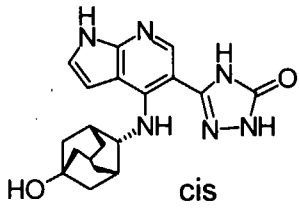
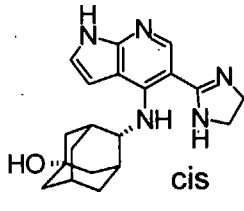
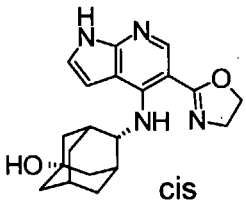
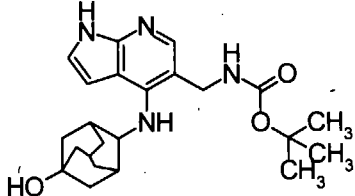
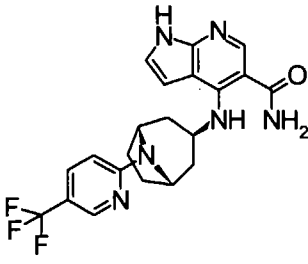
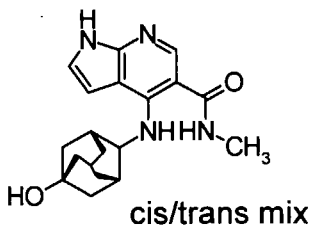
Ex	Structure	Ex	Structure
57	 cis	58	 cis
59	 cis	60	 cis
61	 cis	62	 cis
63	 cis	64	 cis/trans mix
65		66	 cis/trans mix

Table 71(contd.)

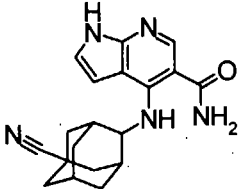
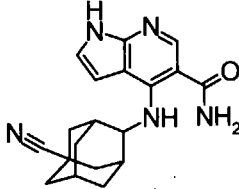
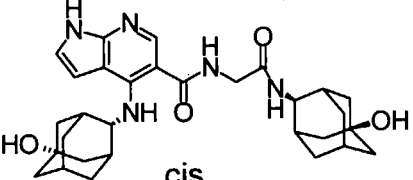
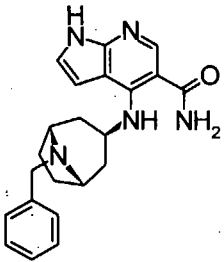
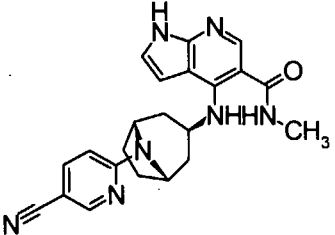
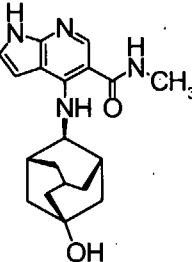
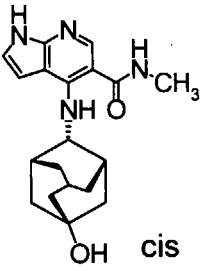
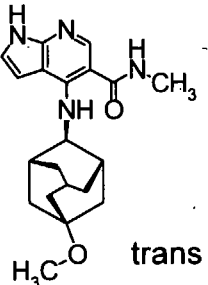
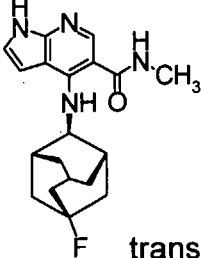
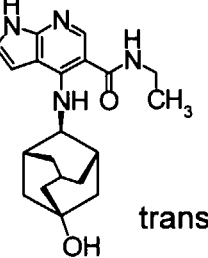
Ex	Structure	Ex	Structure
67	 diastereomer of 68 cis or trans unknown	68	 diastereomer of 67 cis or trans unknown
69	 cis	70	
71		72	 trans
73	 cis	74	 trans
75	 trans	76	 trans

Table 71 (contd.)

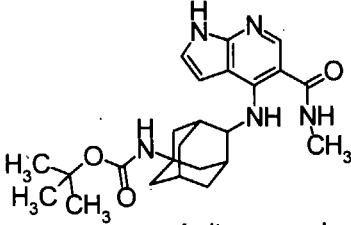
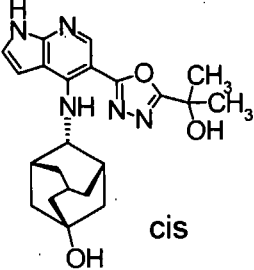
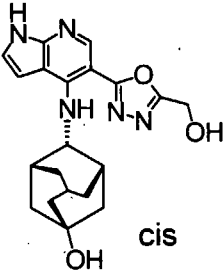
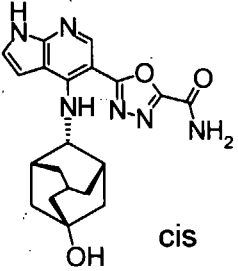
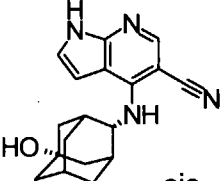
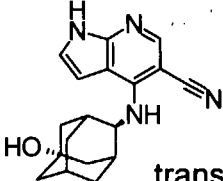
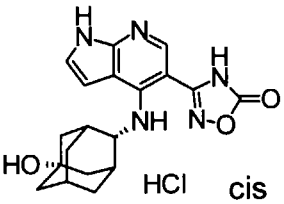
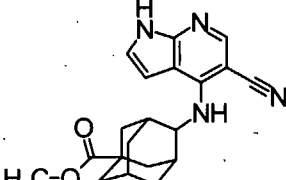
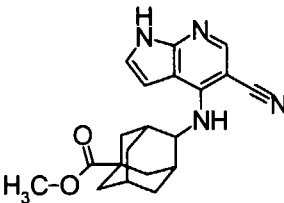
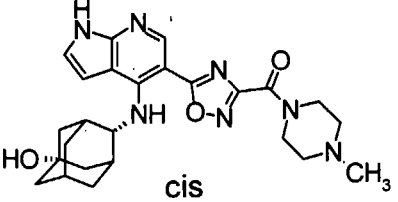
Ex	Structure	Ex	Structure
77	 cis/trans mix	78	 cis
79	 cis	80	 cis
81	 cis	82	 trans
83	 HCl cis	84	 diastereomer of 85 cis or trans unknown
85	 diastereomer of 84 cis or trans unknown	86	 cis

Table 71 (contd.)

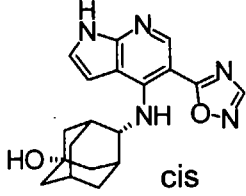
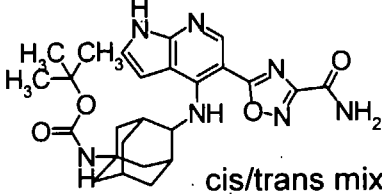
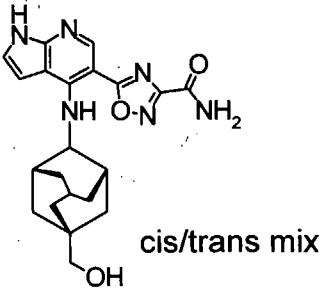
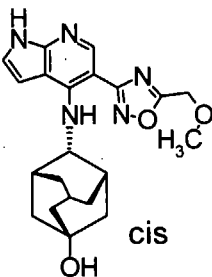
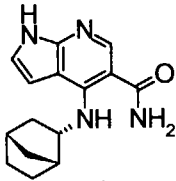
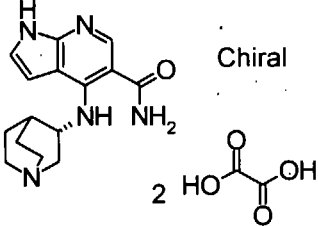
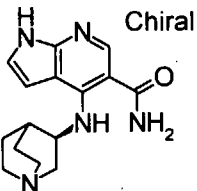
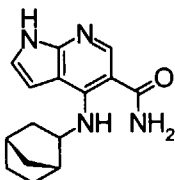
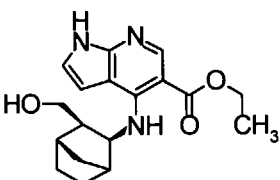
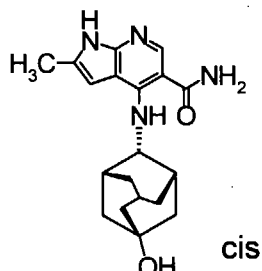
Ex	Structure	Ex	Structure
87	 cis	88	 cis/trans mix
89	 cis/trans mix	90	 cis
91		92	 Chiral
93	 Chiral	94	
95	 cis	96	 cis

Table 71 (contd.)

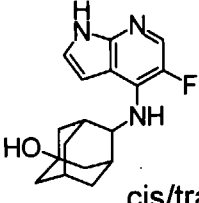
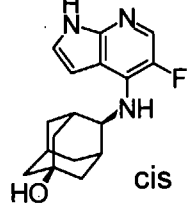
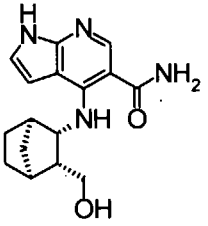
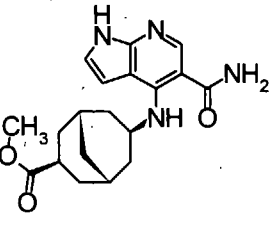
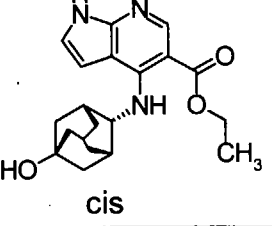
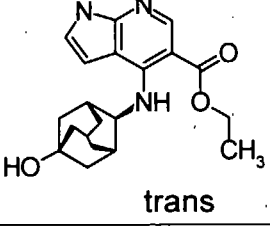
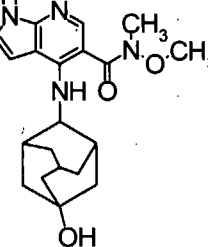
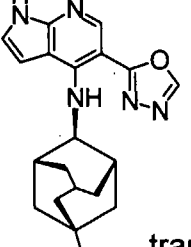
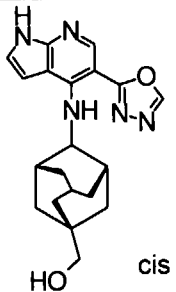
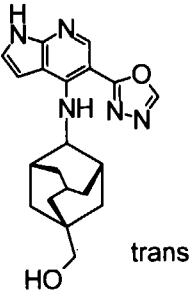
Ex	Structure	Ex	Structure
97	 cis/trans mix	98	 cis
99	 cis	100	 trans
101	 cis	102	 trans
103	 cis/trans mix	104	 trans
105	 cis	106	 trans

Table 71 (contd.)

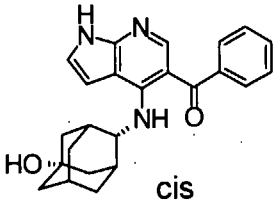
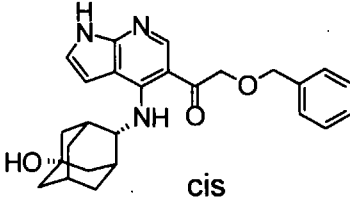
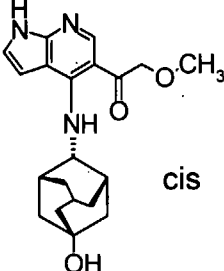
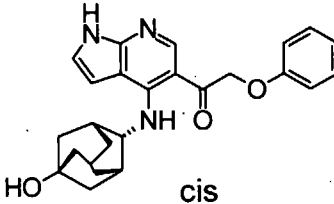
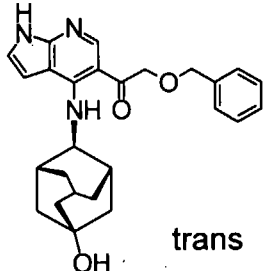
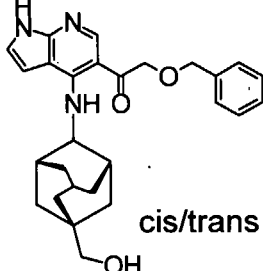
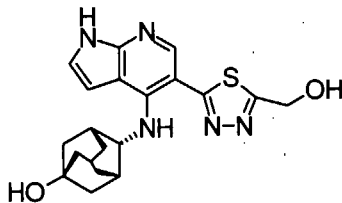
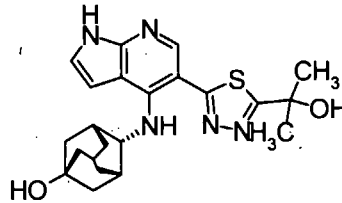
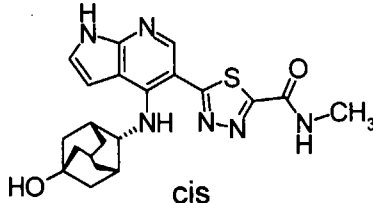
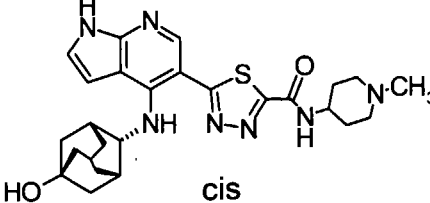
Ex	Structure	Ex	Structure
107	 cis	108	 cis
109	 cis	110	 cis
111	 trans	112	 cis/trans mix
113	 cis	114	 cis
115	 cis	116	 cis

Table 71 (contd.)

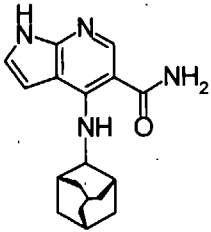
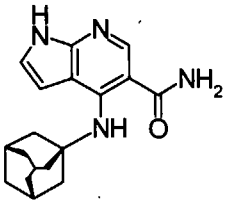
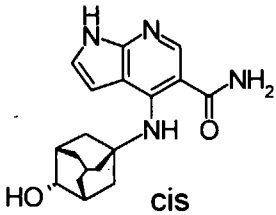
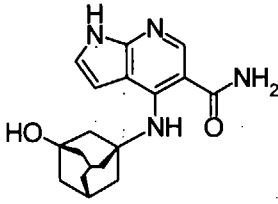
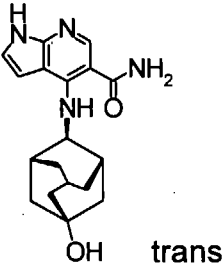
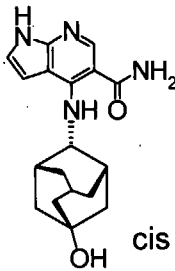
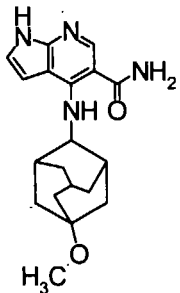
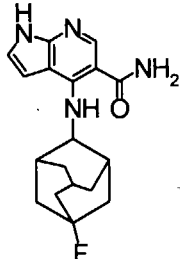
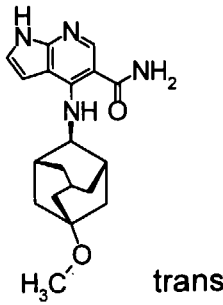
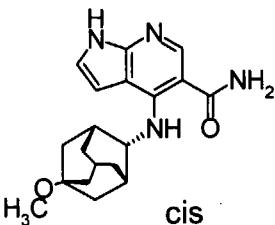
Ex	Structure	Ex	Structure
117		118	
119	 cis	120	
121	 trans	122	 cis
123	 H ₃ C cis/trans mix	124	 F cis/trans mix
125	 H ₃ C trans	126	 H ₃ C cis

Table 71 (contd.)

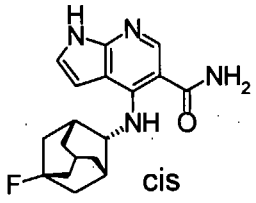
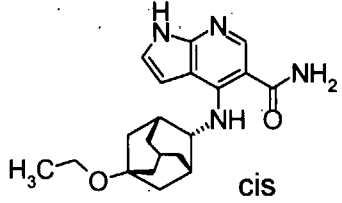
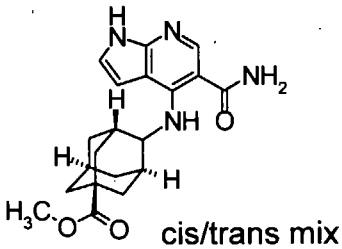
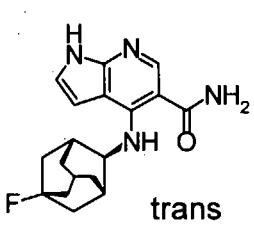
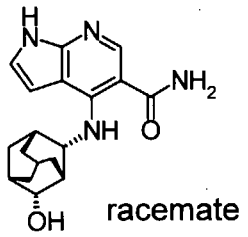
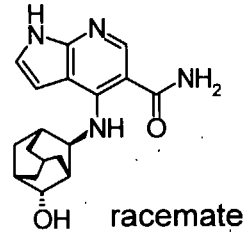
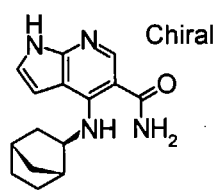
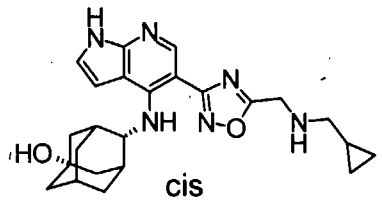
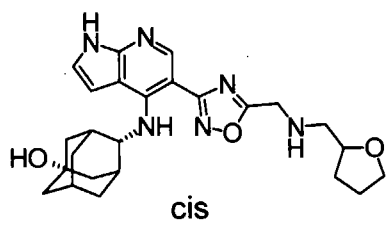
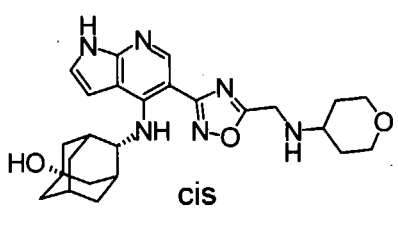
Ex	Structure	Ex	Structure
127	 cis	128	 cis
129	 cis/trans mix	130	 trans
131	 racemate	132	 racemate
133	 Chiral	134	 cis
135	 cis	136	 cis

Table 71 (contd.)

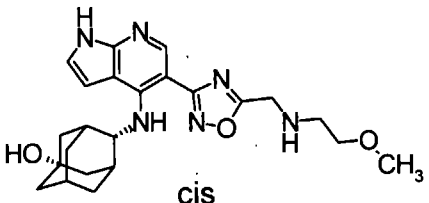
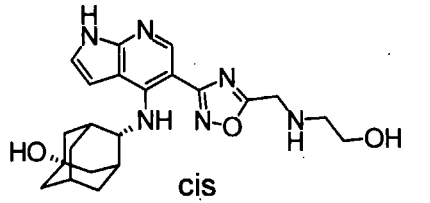
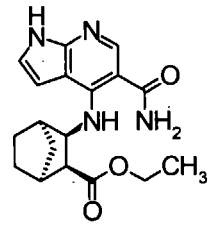
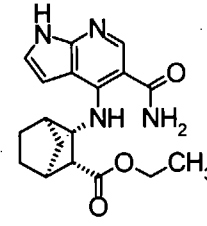
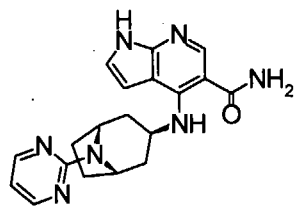
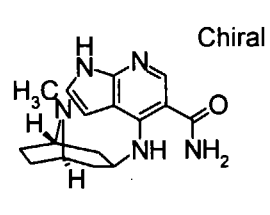
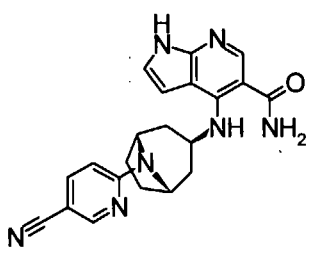
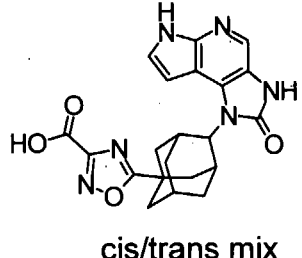
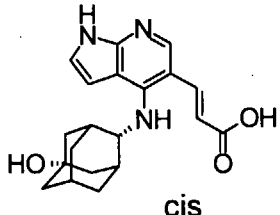
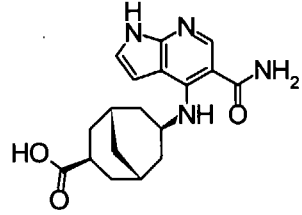
Ex	Structure	Ex	Structure
137	 cis	138	 cis
139	 cis	140	 cis
141	 cis	142	 Chiral
143	 cis	144	 cis/trans mix
145	 cis	146	 cis

Table 71(contd.)

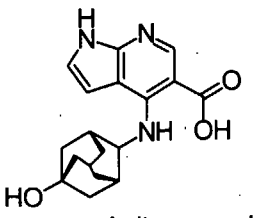
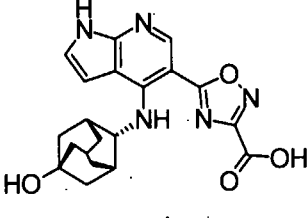
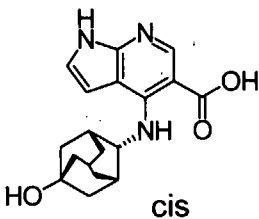
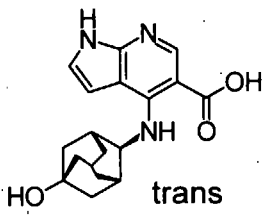
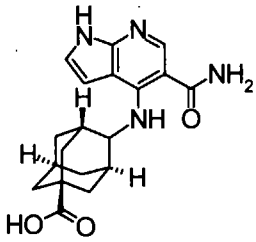
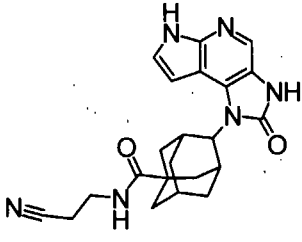
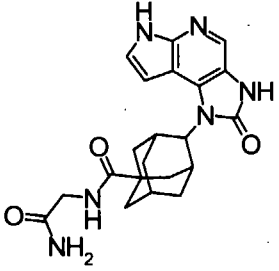
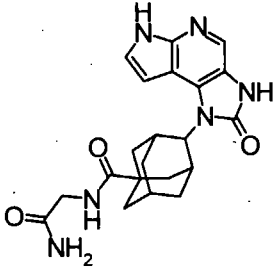
Ex.	Structure	Ex.	Structure
147	 cis/trans mix	148	 cis
149	 cis	150	 trans
151	 cis/trans mix	152	 cis/trans mix
153	 diastereomer of 154 cis or trans unknown	154	 diastereomer of 153 cis or trans unknown

Table 71 (contd.)

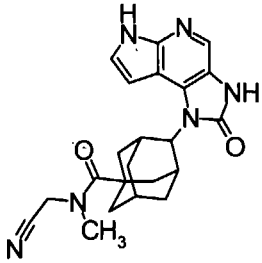
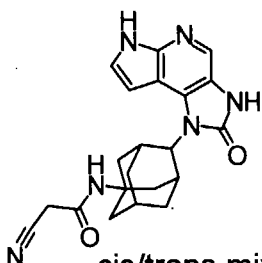
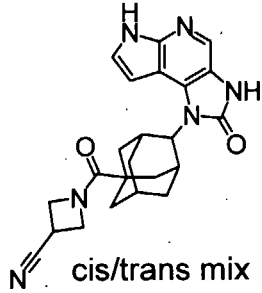
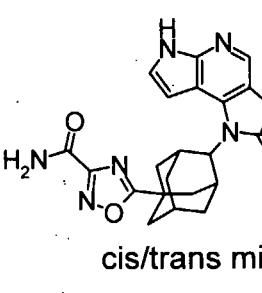
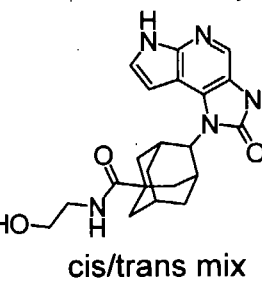
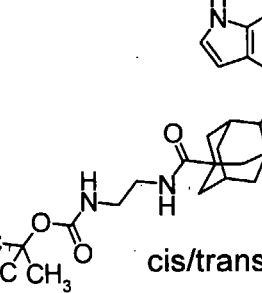
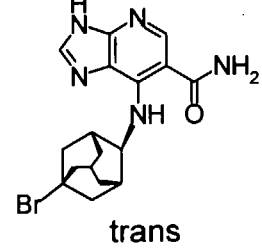
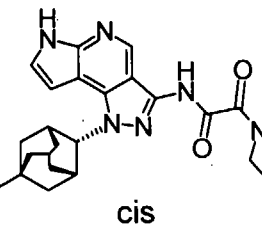
Ex	Structure	Ex	Structure
155	 cis/trans mix	156	 cis/trans mix
157	 cis/trans mix	158	 cis/trans mix
159	 cis/trans mix	160	 cis/trans mix
161	 trans	162	 cis

Table 71 (contd.)

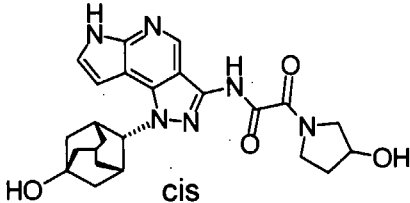
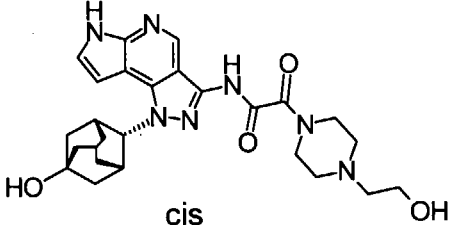
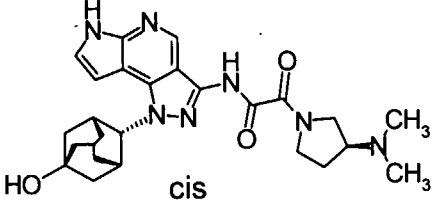
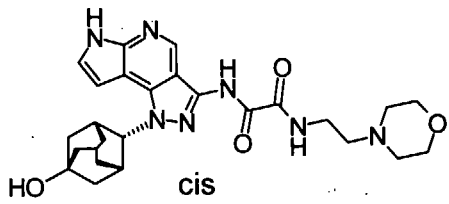
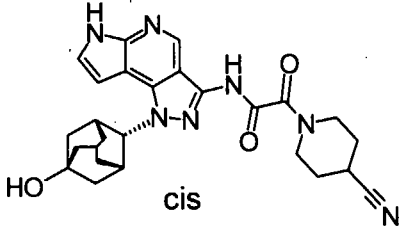
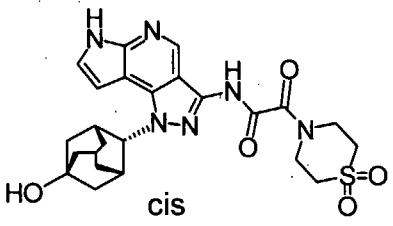
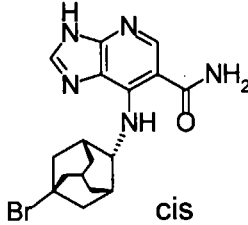
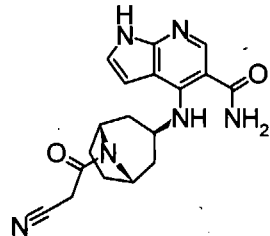
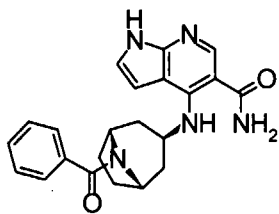
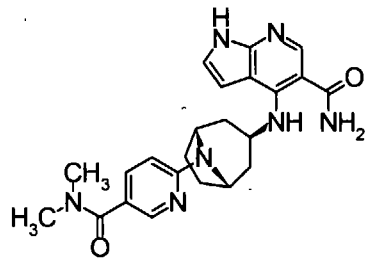
Ex	Structure	Ex	Structure
163	 cis	164	 cis
165	Chiral  cis	166	 cis
167	 cis	168	 cis
169	 cis	170	 cis
171	 cis	172	 cis

Table 71 (contd.)

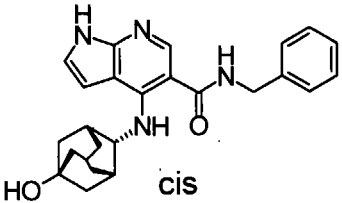
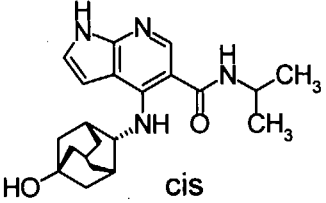
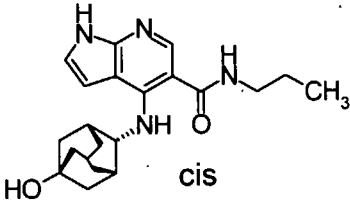
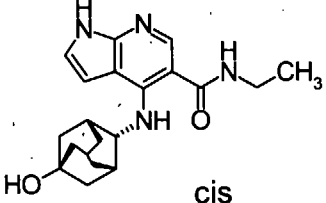
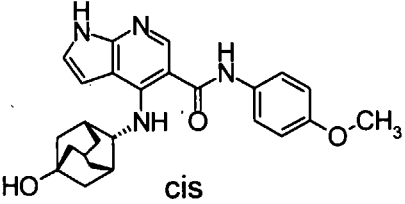
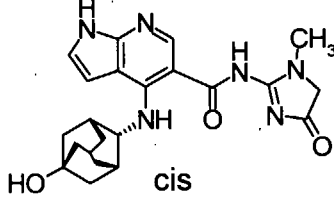
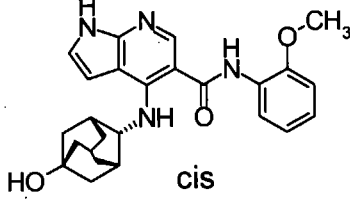
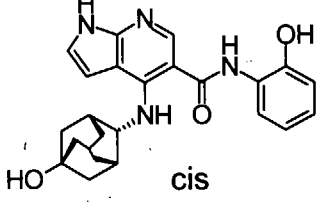
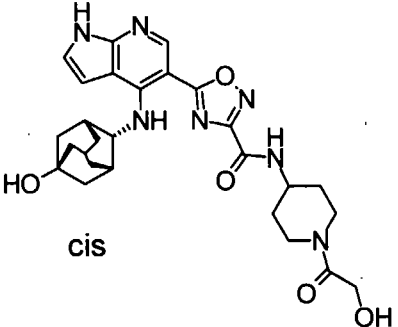
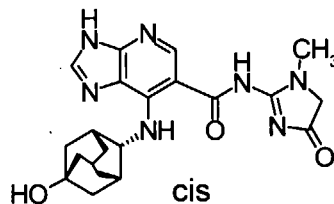
Ex	Structure	Ex	Structure
173	 cis	174	 cis
175	 cis	176	 cis
177	 cis	178	 cis
179	 cis	180	 cis
181	 cis	182	 cis

Table 71 (contd.)

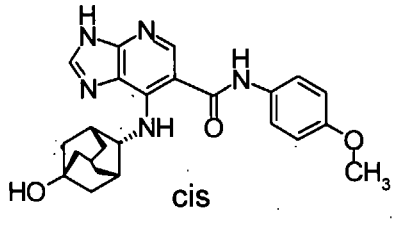
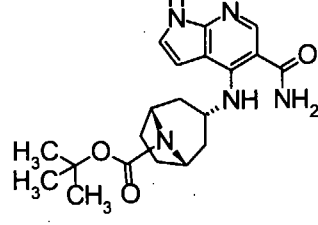
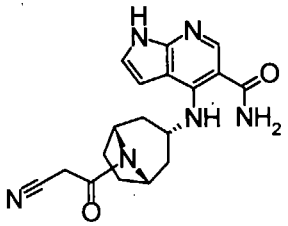
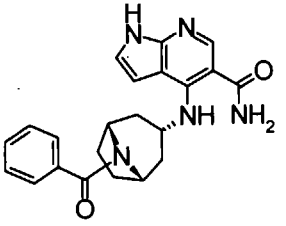
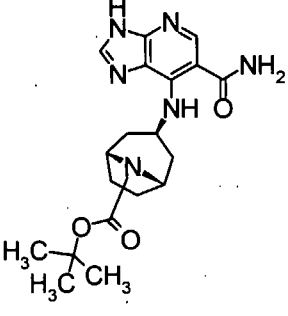
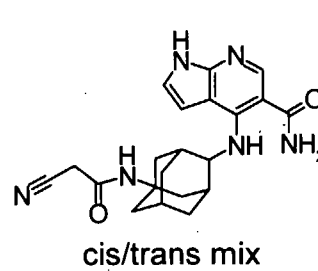
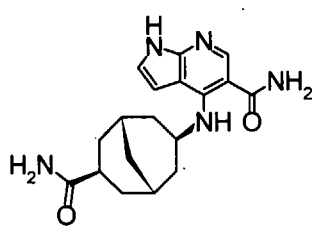
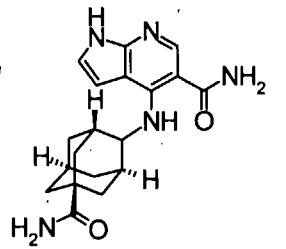
Ex	Structure	Ex	Structure
183	 cis	184	
185		186	
187		188	 cis/trans mix
189		190	 cis/trans mix

Table 71 (contd.)

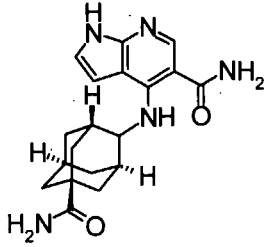
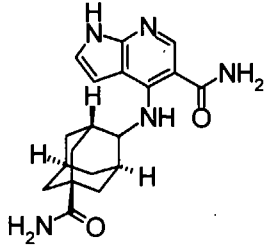
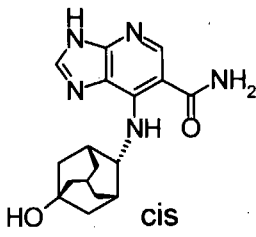
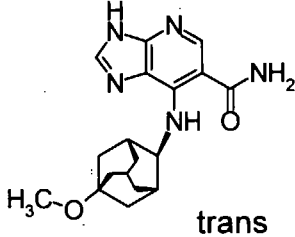
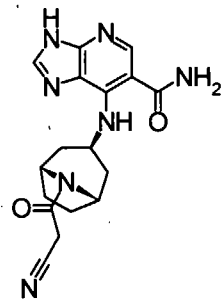
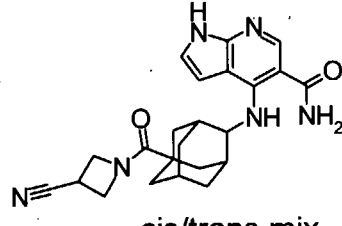
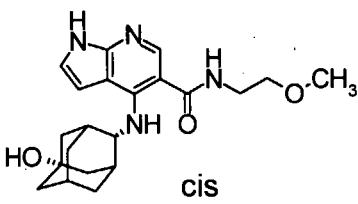
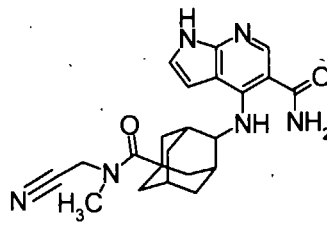
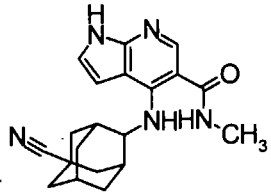
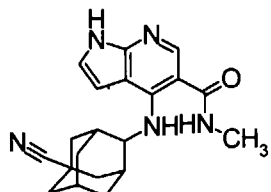
Ex	Structure	Ex	Structure
191	 diastereomer of 192 cis or trans unknown	192	 diastereomer of 191 cis or trans unknown
193	 cis	194	 trans
195		196	 cis/trans mix
197	 cis	198	 cis/trans mix
199	 diastereomer of 200 cis or trans unknown	200	 diastereomer of 199 cis or trans unknown

Table 71 (contd.)

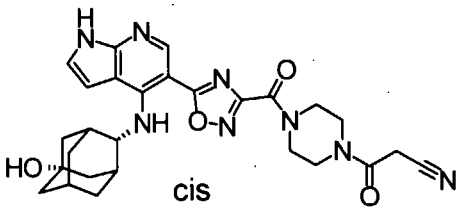
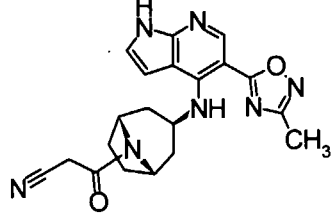
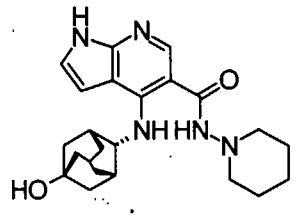
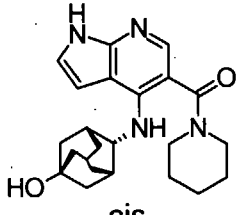
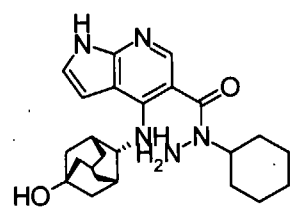
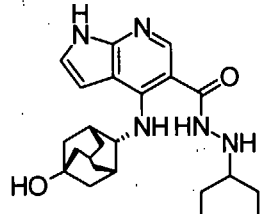
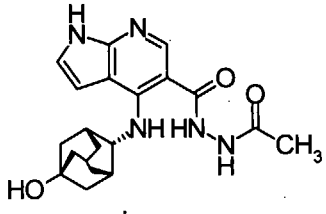
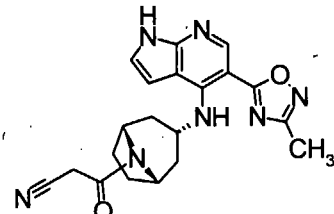
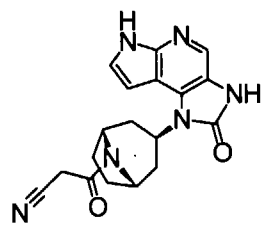
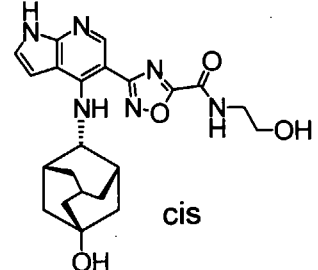
Ex	Structure	Ex	Structure
201	 cis	202	 cis
203	 cis	204	 cis
205	 cis	206	 cis
207	 cis	208	 cis
209	 cis	210	 cis

Table 71 (contd.)

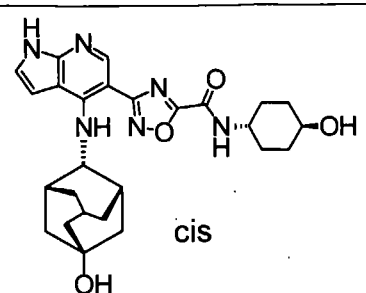
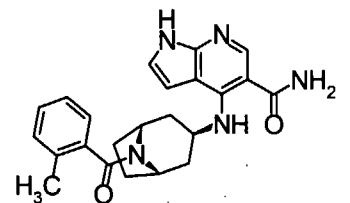
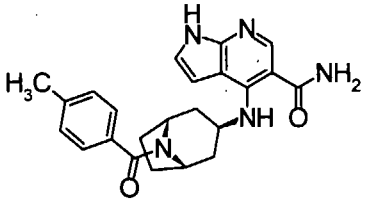
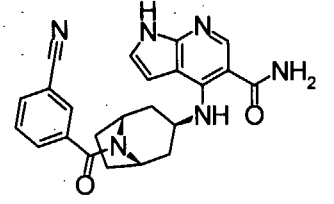
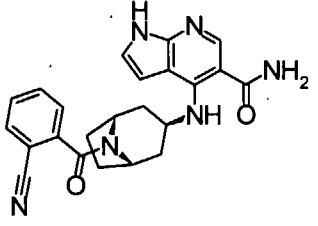
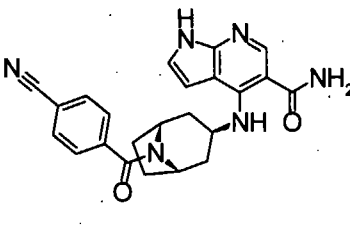
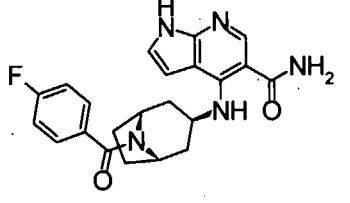
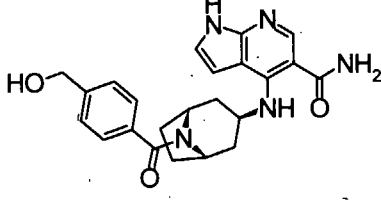
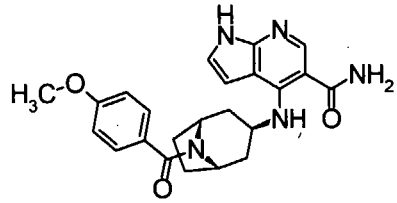
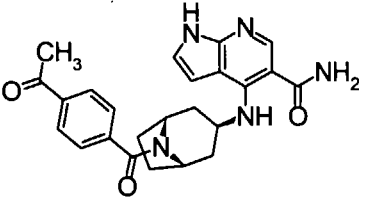
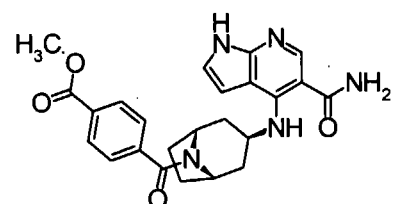
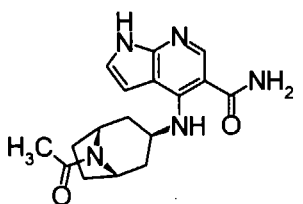
Ex	Structure	Ex	Structure
211	 cis	212	
213		214	
215		216	
217		218	
219		220	
221		222	

Table 71 (contd.)

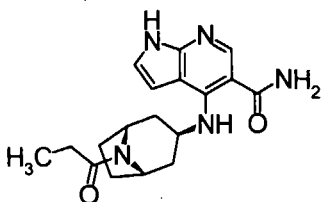
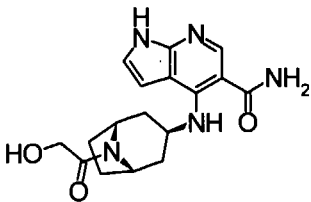
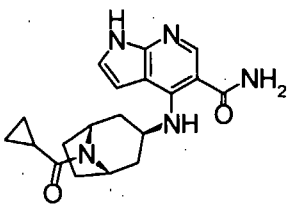
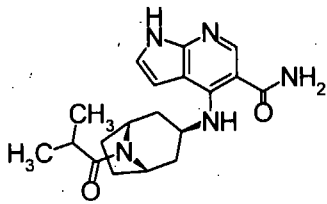
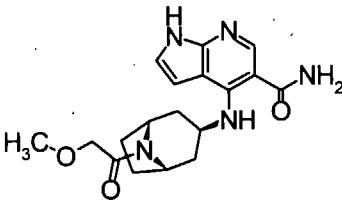
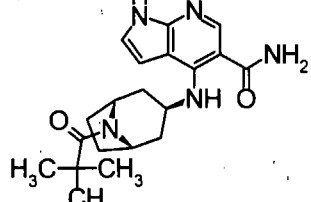
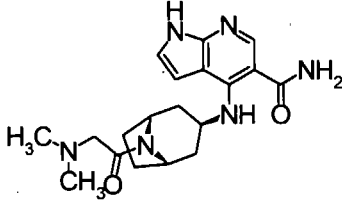
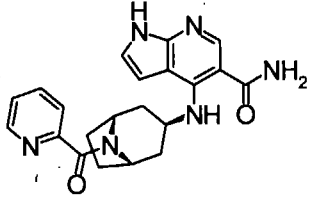
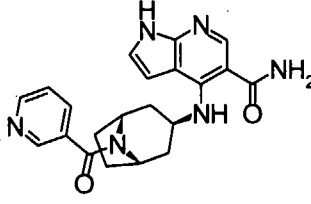
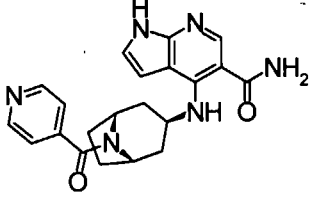
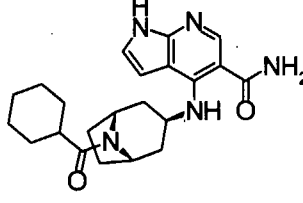
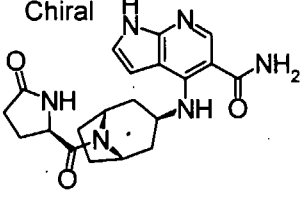
Ex	Structure	Ex	Structure
223		224	
225		226	
227		228	
229		230	
231		232	
233		234	

Table 71 (contd.)

Ex	Structure	Ex	Structure
235		236	
237		238	
239		240	
241		242	
243		244	
245		246	

Table 71 (contd.)

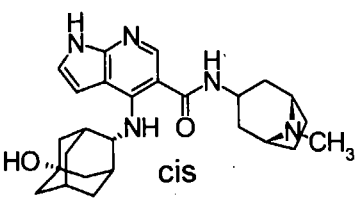
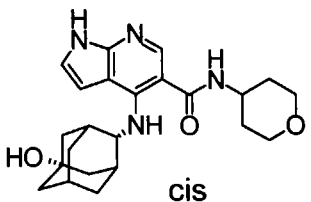
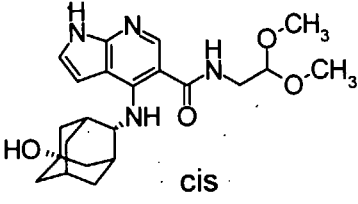
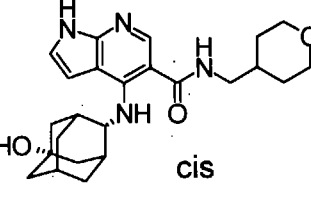
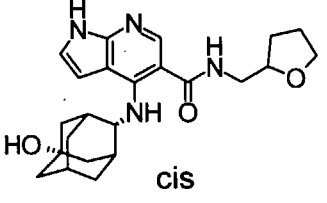
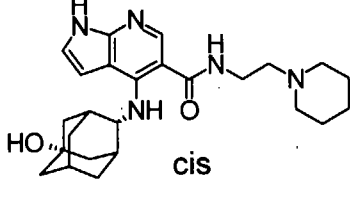
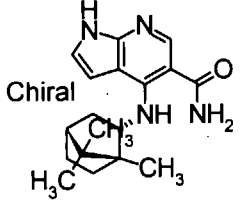
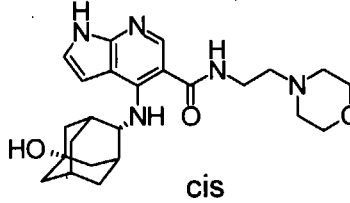
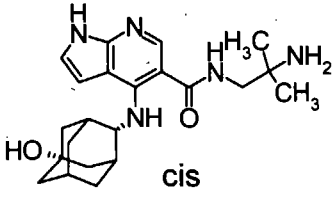
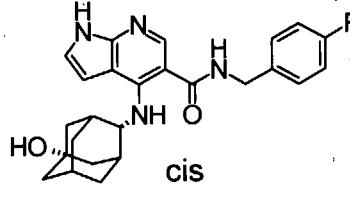
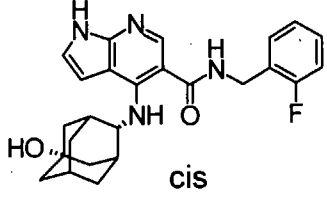
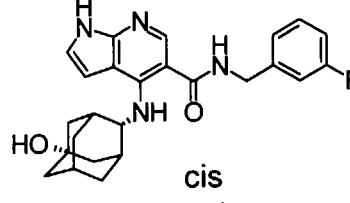
Ex	Structure	Ex	Structure
247	 cis	248	 cis
249	 cis	250	 cis
251	 cis	252	 cis
253	 Chiral	254	 cis
255	 cis	256	 cis
257	 cis	258	 cis

Table 71 (contd.)

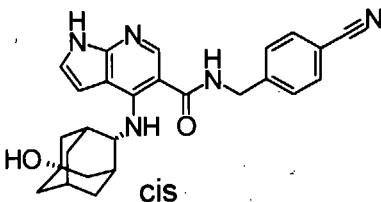
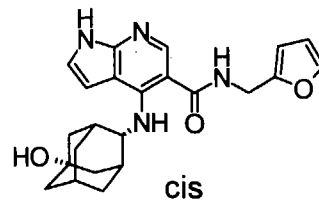
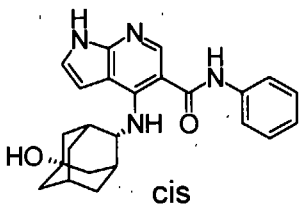
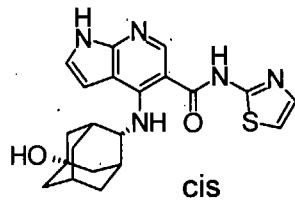
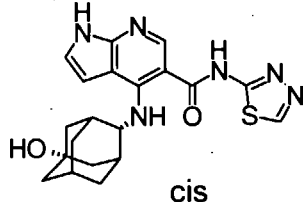
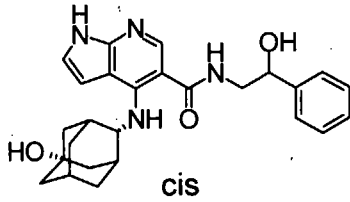
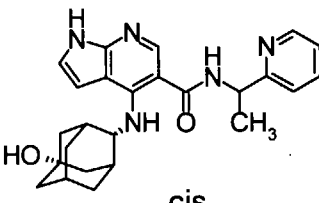
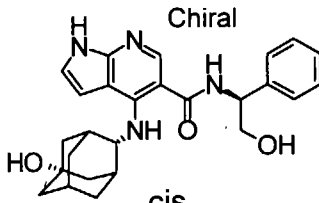
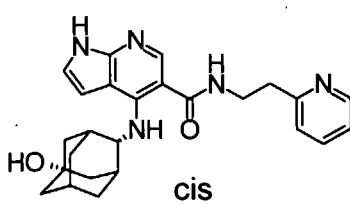
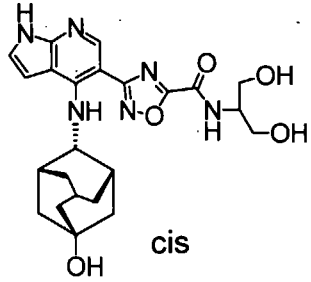
Ex	Structure	Ex	Structure
259	 cis	260	 cis
261	 cis	262	 cis
263	 cis	264	 cis
265	 cis	266	 cis
267	 cis	268	 cis

Table 71 (contd.)

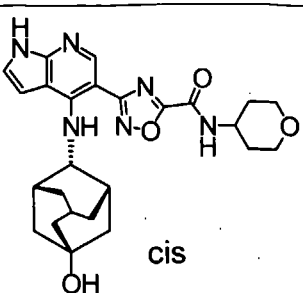
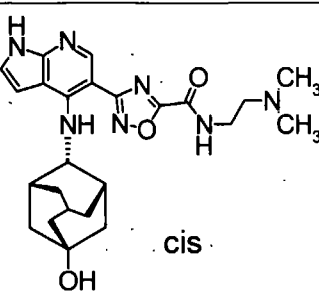
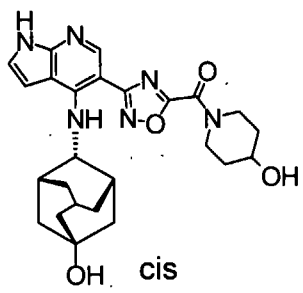
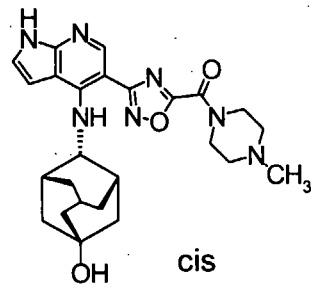
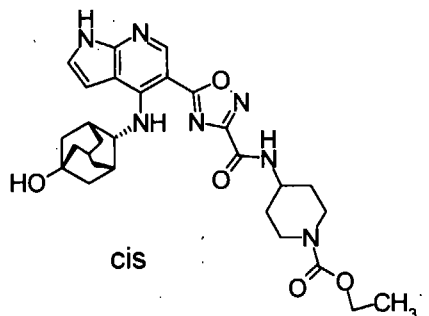
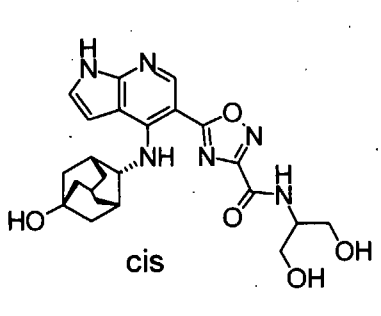
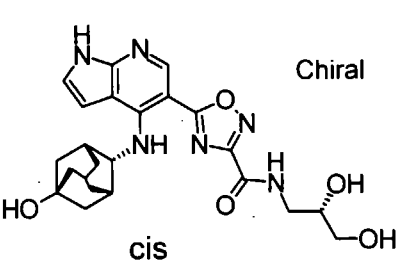
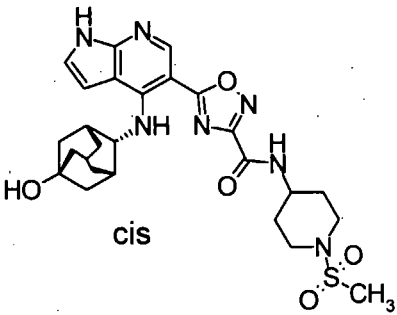
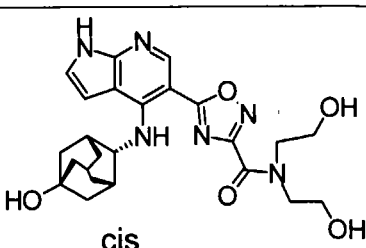
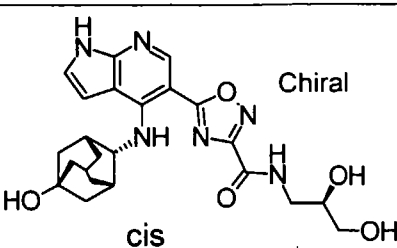
Ex	Structure	Ex	Structure
269	 cis	270	 cis
271	 cis	272	 cis
273	 cis	274	 cis
275	 cis Chiral	276	 cis
277	 cis	278	 cis Chiral

Table 71 (contd.)

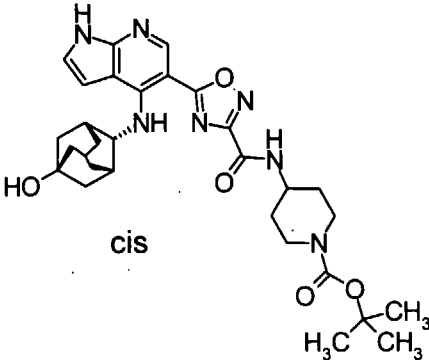
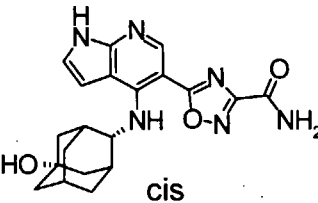
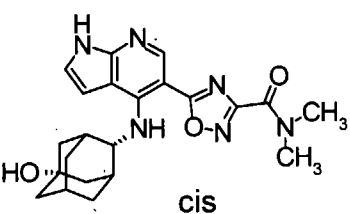
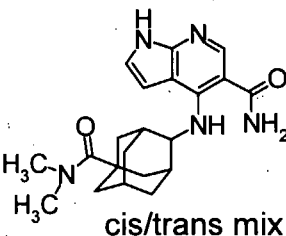
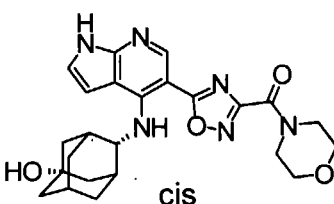
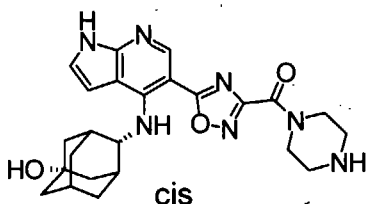
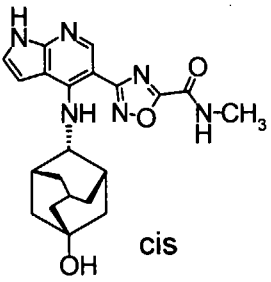
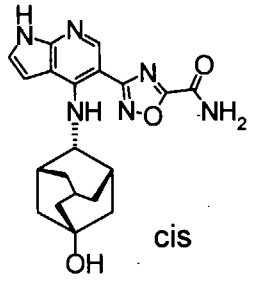
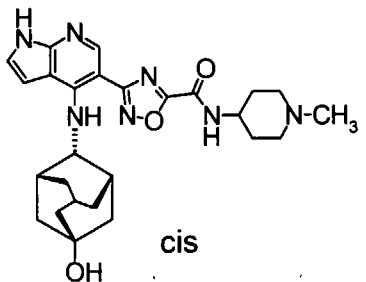
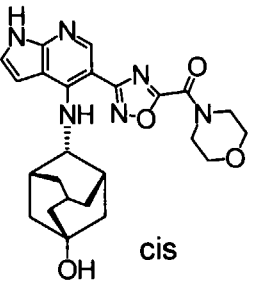
Ex	Structure	Ex	Structure
279	 cis	280	 cis
281	 cis	282	 cis/trans mix
283	 cis	284	 cis
285	 cis	286	 cis
287	 cis	288	 cis

Table 71 (contd.)

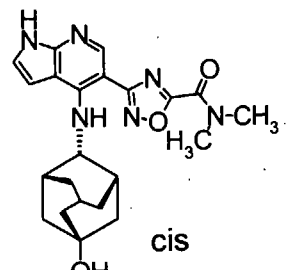
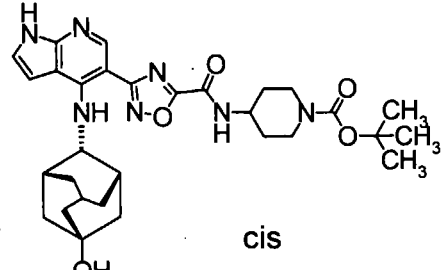
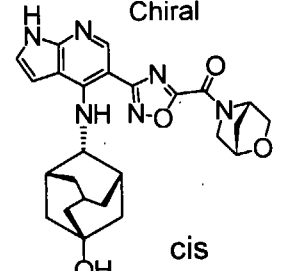
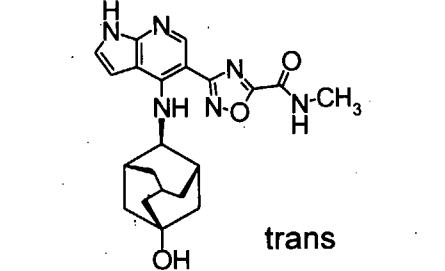
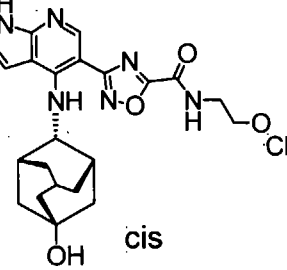
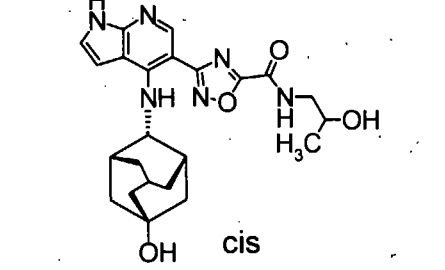
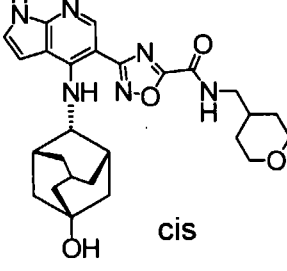
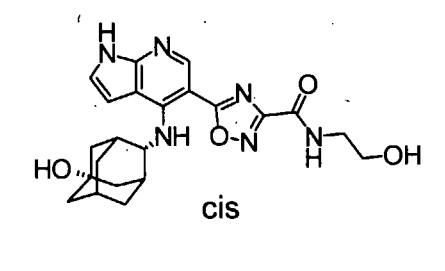
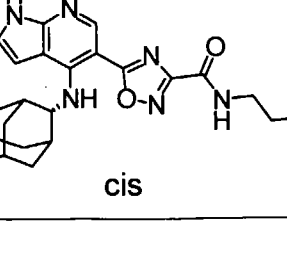
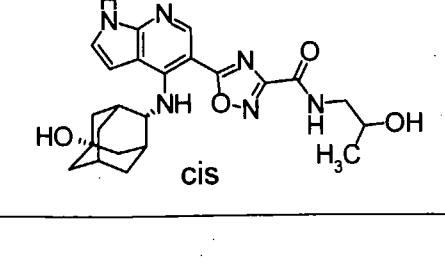
Ex	Structure	Ex	Structure
289	 cis	290	 cis
291	 Chiral cis	292	 trans
293	 cis	294	 cis
295	 cis	296	 cis
297	 cis	298	 cis

Table 71 (contd.)

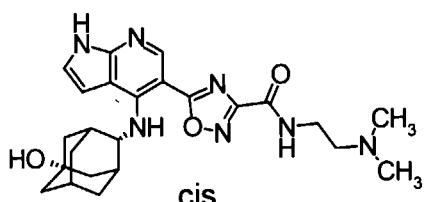
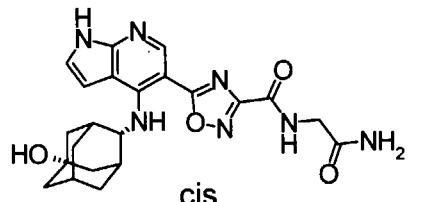
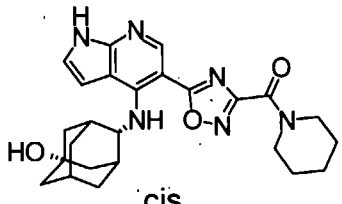
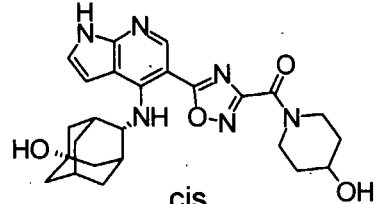
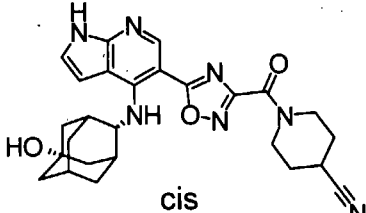
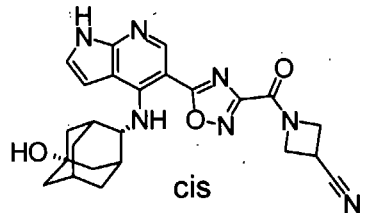
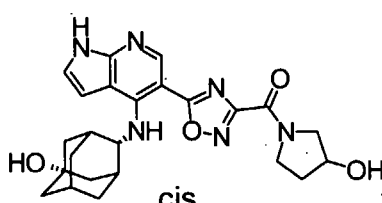
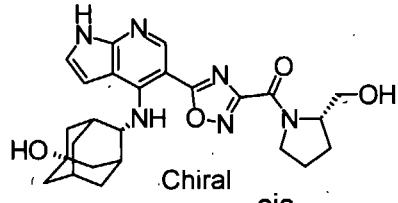
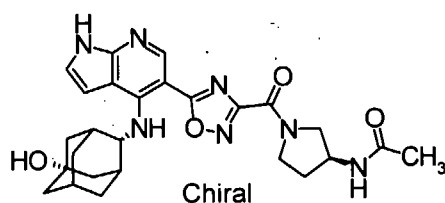
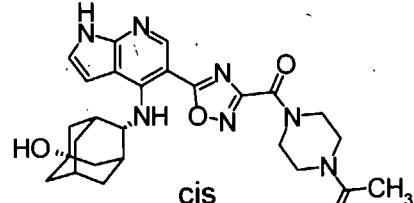
Ex	Structure	Ex	Structure
299	 cis	300	 cis
301	 cis	302	 cis
303	 cis	304	 cis
305	 cis	306	 Chiral cis
307	 Chiral cis	308	 cis

Table 71 (contd.)

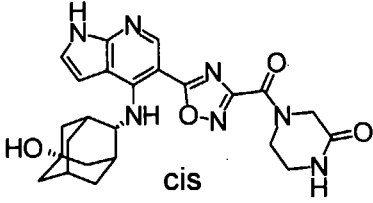
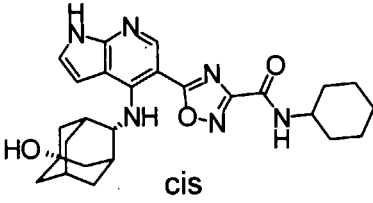
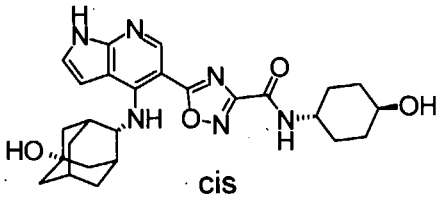
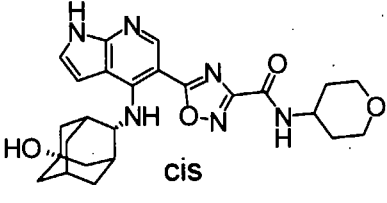
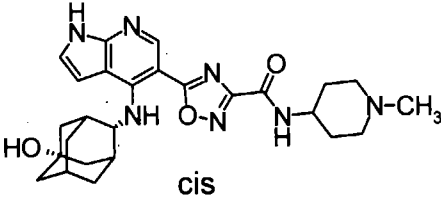
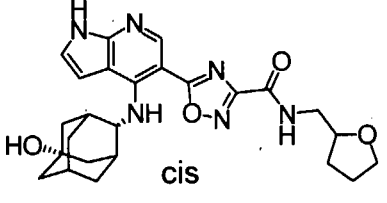
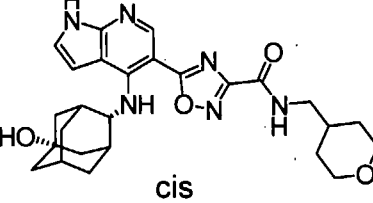
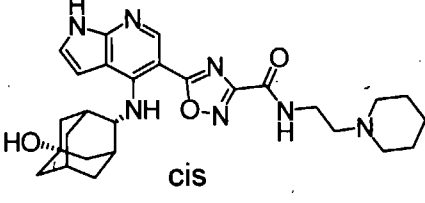
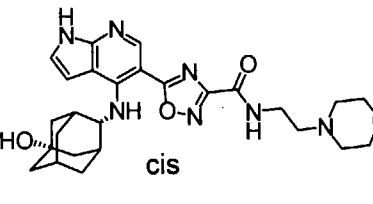
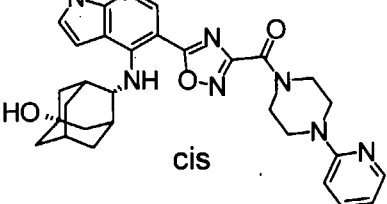
Ex	Structure	Ex	Structure
309	 cis	310	 cis
311	 cis	312	 cis
313	 cis	314	 cis
315	 cis	316	 cis
317	 cis	318	 cis

Table 71 (contd.)

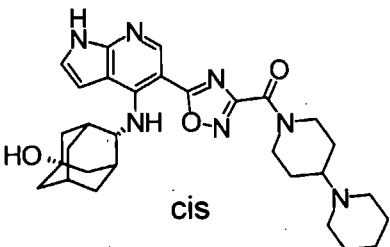
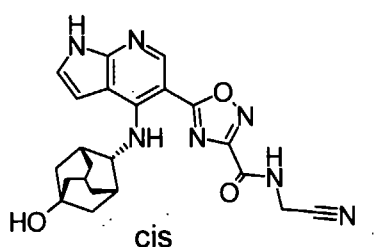
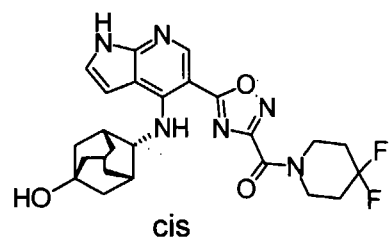
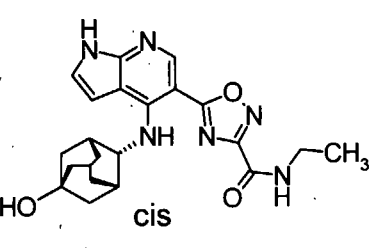
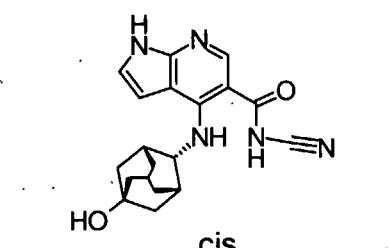
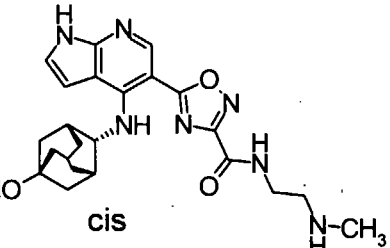
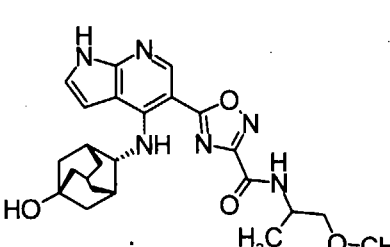
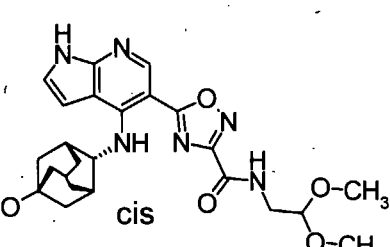
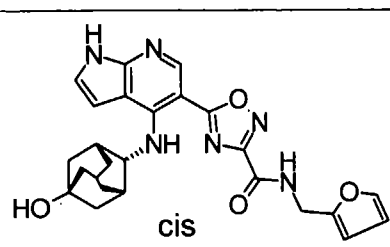
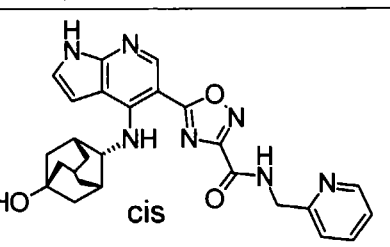
Ex	Structure	Ex	Structure
319	 cis	320	 cis
321	 cis	322	 cis
323	 cis	324	 cis
325	 cis	326	 cis
327	 cis	328	 cis

Table 71 (contd.)

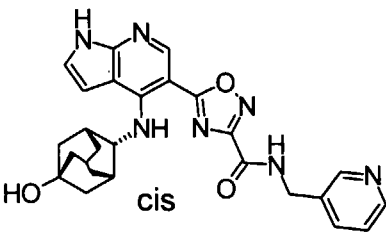
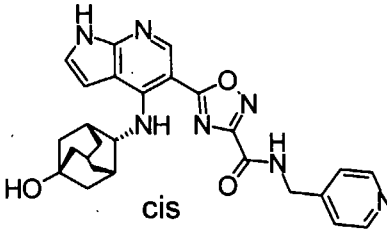
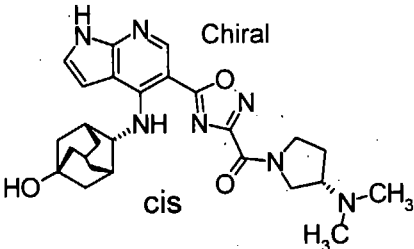
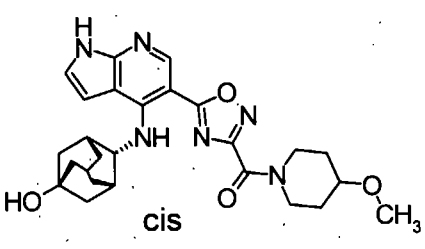
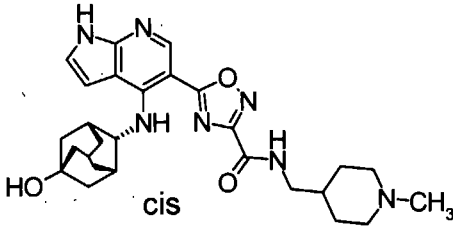
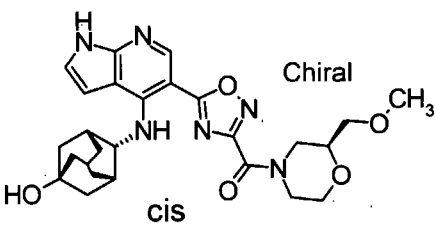
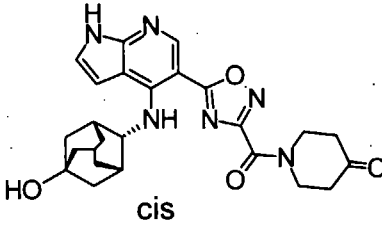
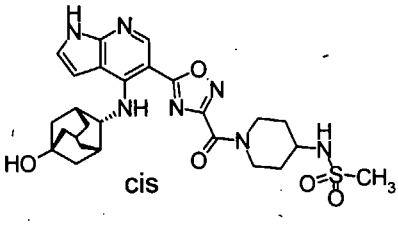
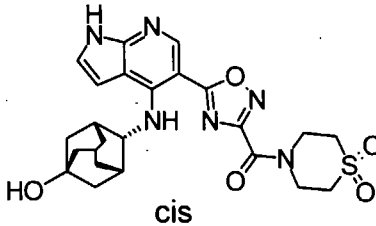
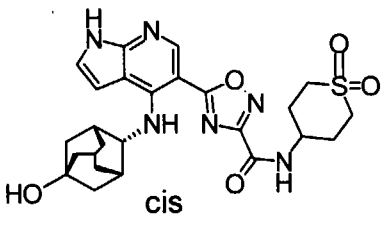
Ex	Structure	Ex	Structure
329		330	
331		332	
333		334	
335		336	
337		338	

Table 71 (contd.)

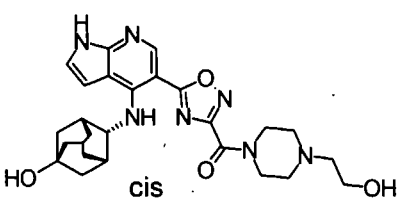
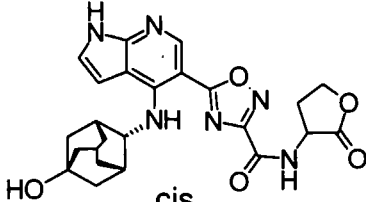
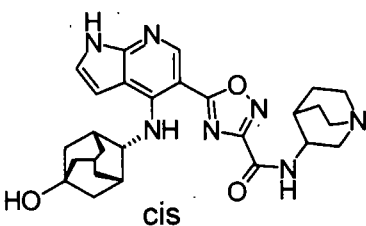
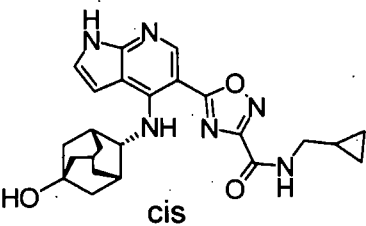
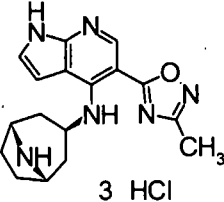
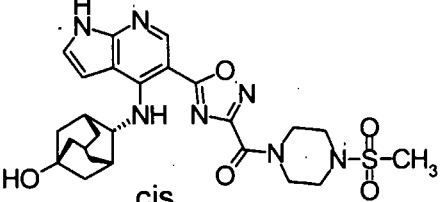
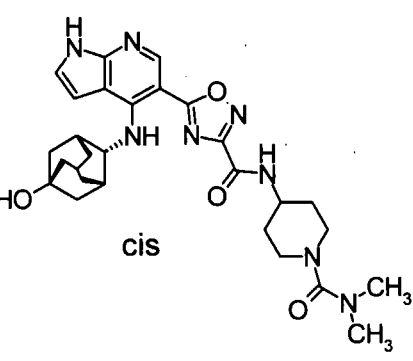
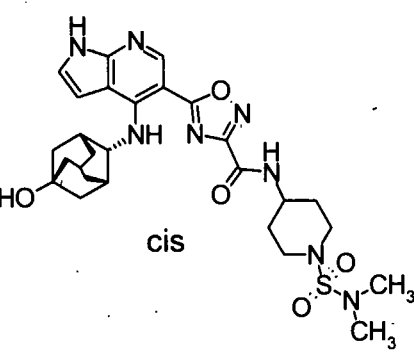
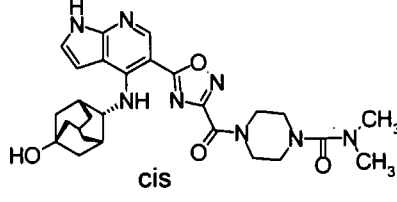
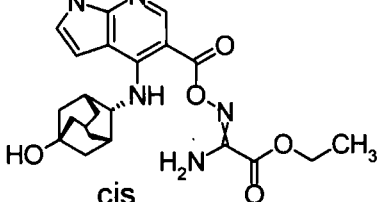
Ex	Structure	Ex	Structure
339	 cis	340	 cis
341	 cis	342	 cis
343	 3 HCl	344	 cis
345	 cis	346	 cis
347	 cis	348	 cis

Table 71 (contd.)

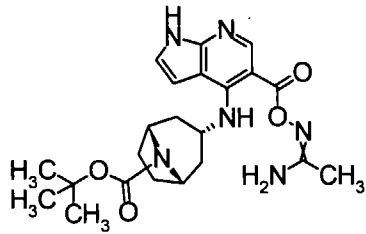
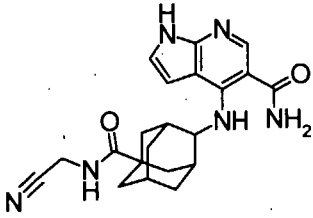
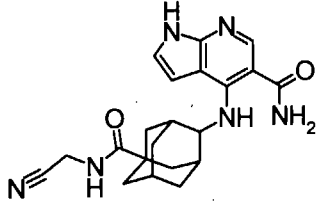
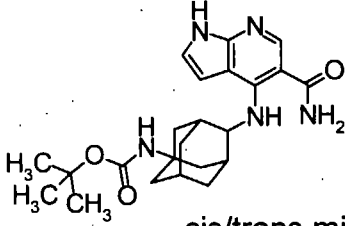
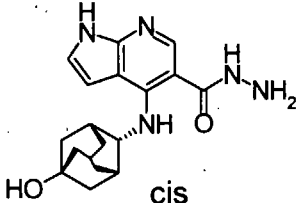
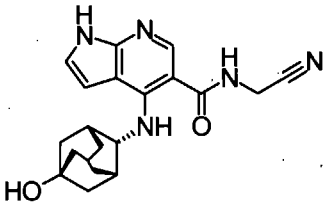
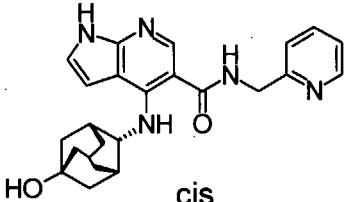
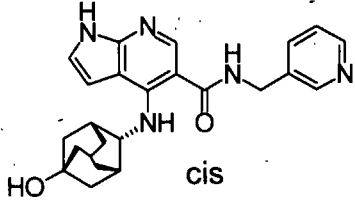
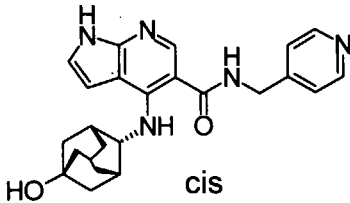
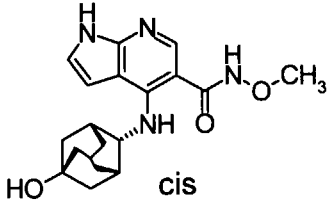
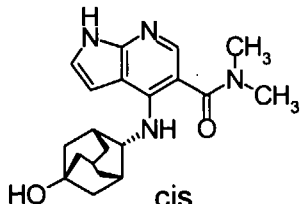
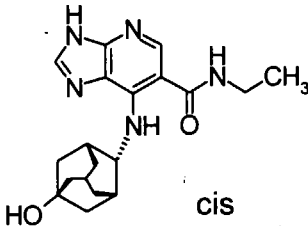
Ex	Structure	Ex	Structure
349		350	 diastereomer of 351 cis or trans unknown
351	 diastereomer of 350 cis or trans unknown	352	 cis/trans mix
353	 cis	354	 cis
355	 cis	356	 cis
357	 cis	358	 cis
359	 cis	360	 cis

Table 71 (contd.)

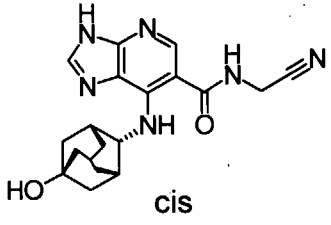
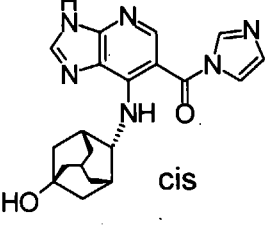
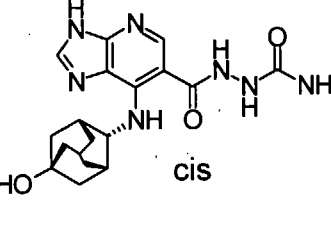
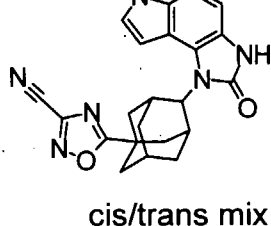
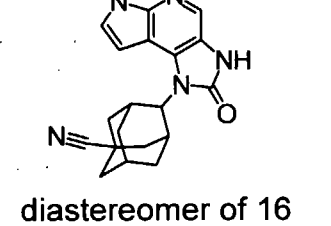
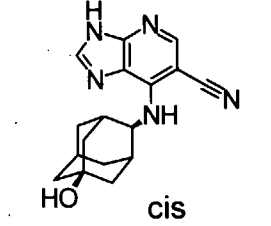
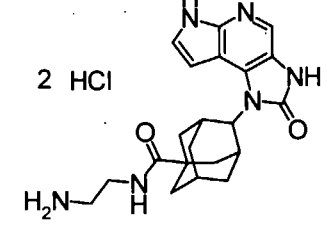
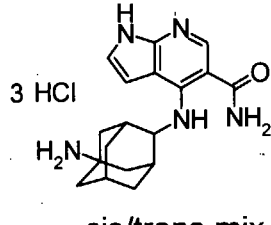
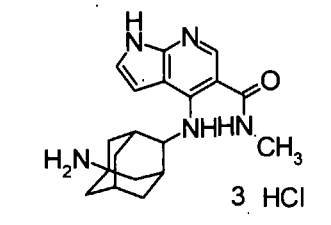
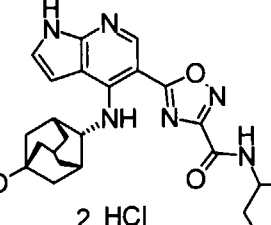
Ex	Structure	Ex	Structure
361	 cis	362	 cis
363	 cis	364	 cis/trans mix
365	 diastereomer of 16 cis or trans unknown	366	 cis
367	 2 HCl cis/trans mix	368	 3 HCl cis/trans mix
369	 3 HCl cis/trans mix	370	 2 HCl cis

Table 71 (contd.)

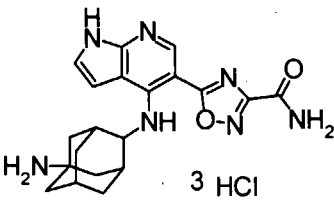
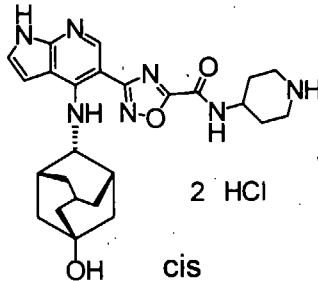
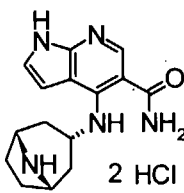
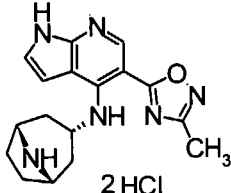
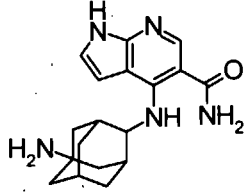
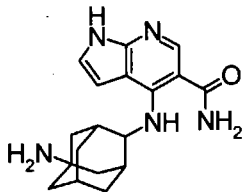
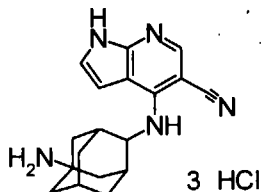
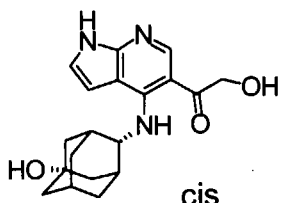
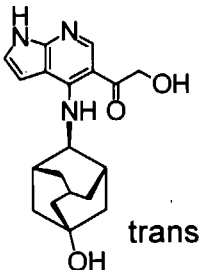
Ex	Structure	Ex	Structure
371	 3 HCl cis/trans mix	372	 2 HCl cis
373	 2 HCl	374	 2 HCl
375	 diastereomer of 376 cis or trans unknown	376	 diastereomer of 375 cis or trans unknown
377	 3 HCl cis/trans mix	378	 cis or trans unknown
379	 cis	380	 trans

Table 71 (contd.)

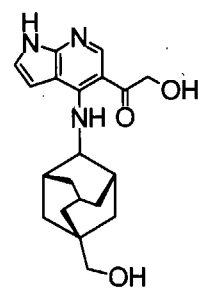
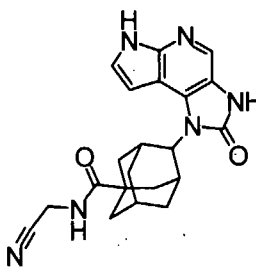
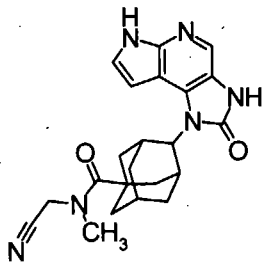
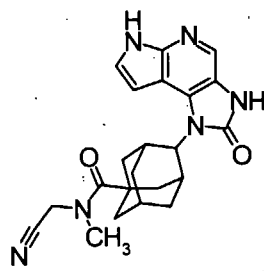
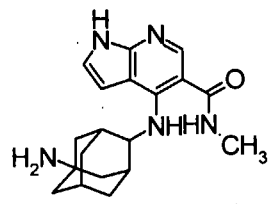
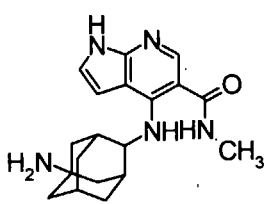
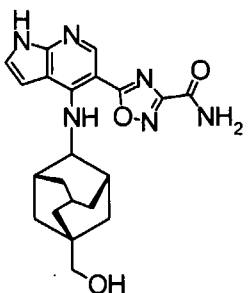
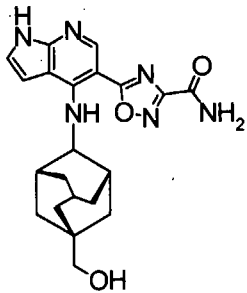
Ex	Structure	Ex	Structure
381	 cis/trans mix	382	 diastereomer of 22 cis or trans unknown
383	 diastereomer of 384 cis or trans unknown	384	 diastereomer of 383 cis or trans unknown
385	 diastereomer of 386 cis or trans unknown	386	 diastereomer of 385 cis or trans unknown
387	 diastereomer of 388 cis or trans unknown	388	 diastereomer of 387 cis or trans unknown

Table 71 (contd.)

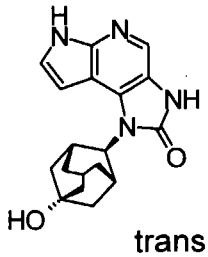
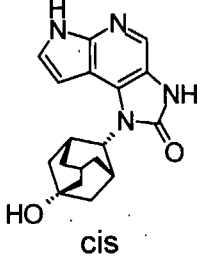
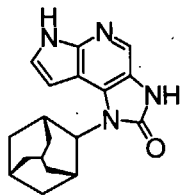
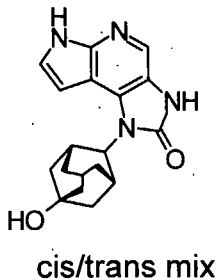
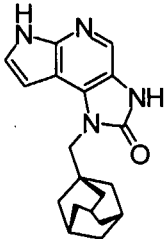
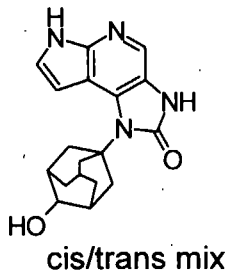
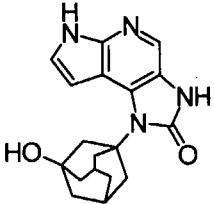
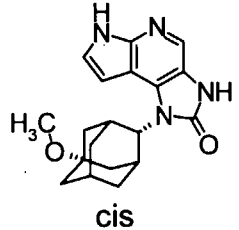
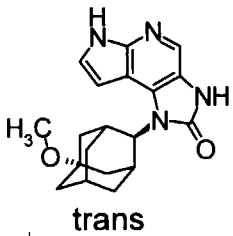
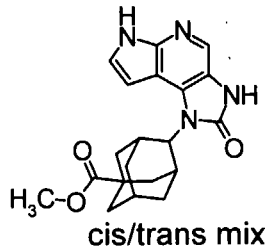
Ex	Structure	Ex	Structure
389	 trans	390	 cis
391		392	 cis/trans mix
393		394	 cis/trans mix
395		396	 cis
397	 trans	398	 cis/trans mix

Table 71 (contd.)

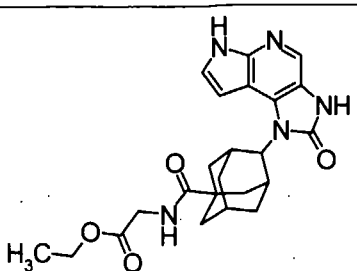
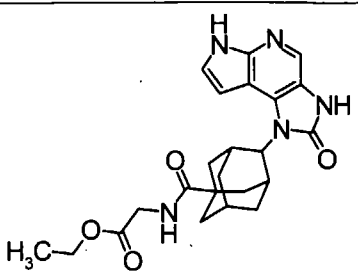
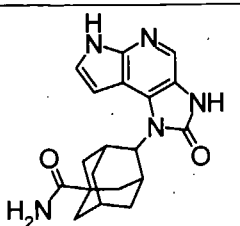
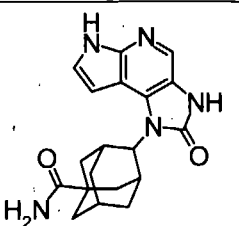
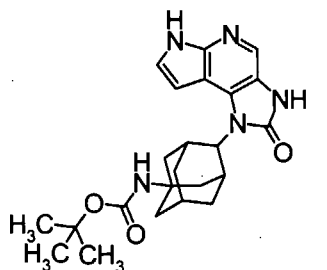
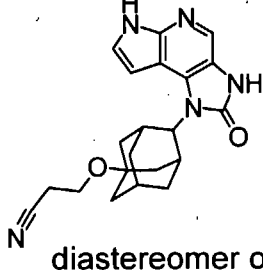
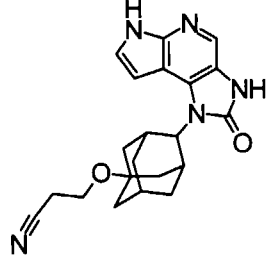
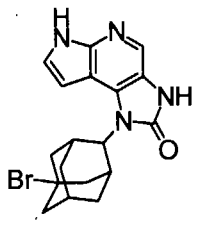
Ex	Structure	Ex	Structure
399	 diastereomer of 400 cis or trans unknown	400	 diastereomer of 399 cis or trans unknown
401	 diastereomer of 402 cis or trans unknown	402	 diastereomer of 401 cis or trans unknown
403	 cis/trans mix	404	 diastereomer of 405 cis or trans unknown
405	 diastereomer of 404 cis or trans unknown	406	 cis or trans unknown

Table 71 (contd.)

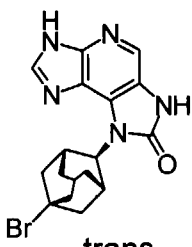
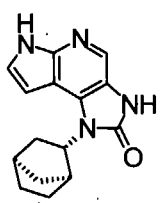
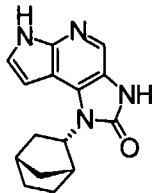
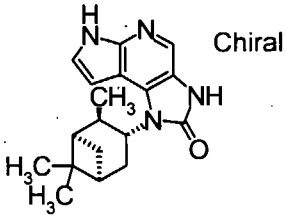
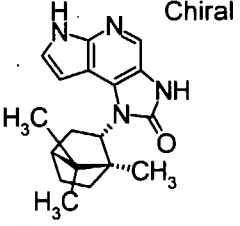
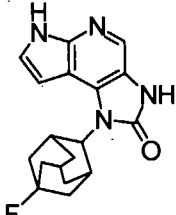
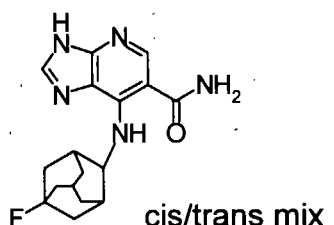
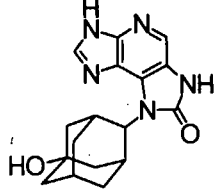
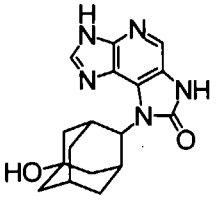
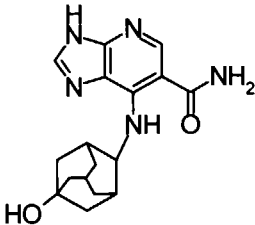
Ex	Structure	Ex	Structure
407	 trans	408	
409		410	 Chiral
411	 Chiral	412	 cis/trans mix
413	 cis/trans mix	414	 diastereomer of 415 cis or trans unknown
415	 diastereomer of 414 cis or trans unknown	416	 cis/trans mix

Table 71 (contd.)

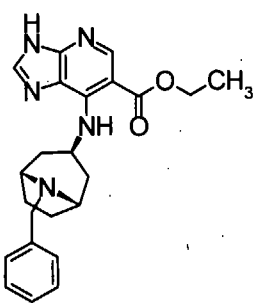
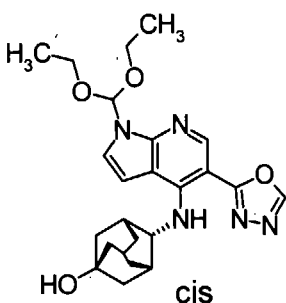
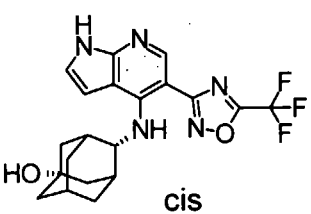
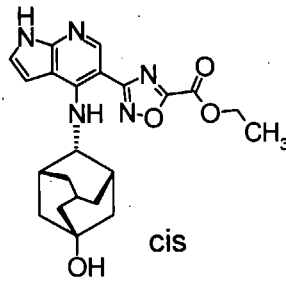
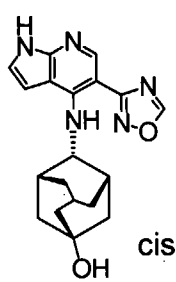
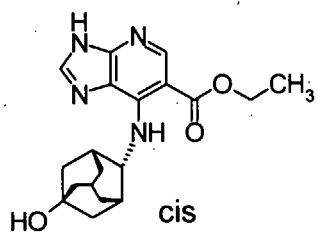
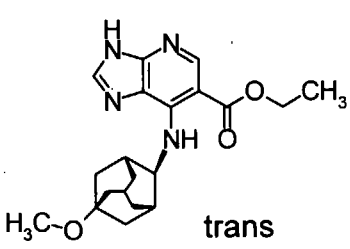
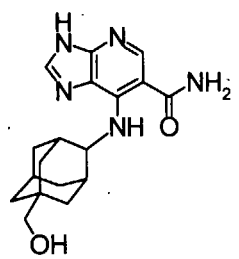
Ex	Structure	Ex	Structure
417		418	
419		420	
421		422	
423		424	

Table 71 (contd.)

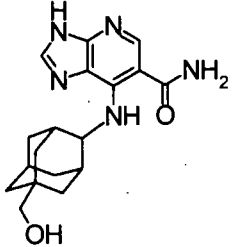
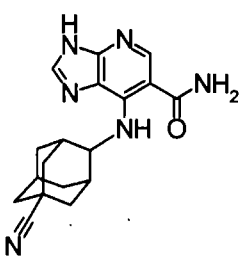
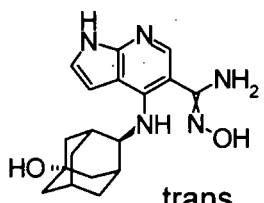
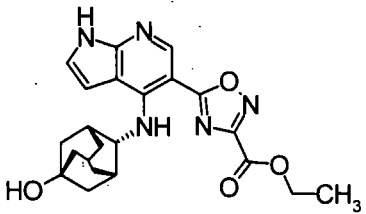
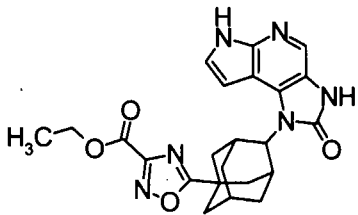
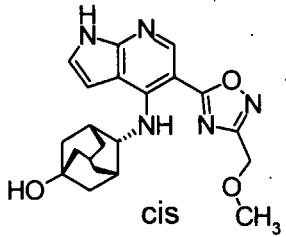
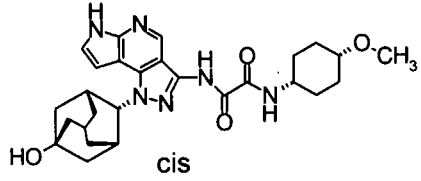
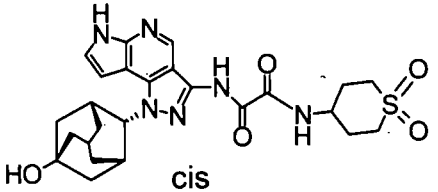
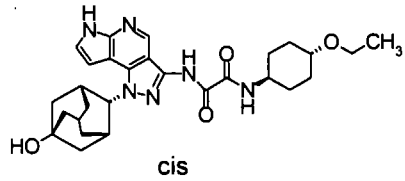
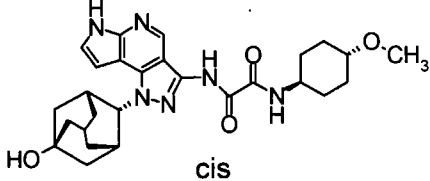
Ex	Structure	Ex	Structure
425	 diastereomer of 424 cis or trans unknown	426	 cis or trans unknown
427	 trans	428	 cis
429	 cis/trans mix	430	 cis
431	 cis	432	 cis
433	 cis	434	 cis

Table 71 (contd.)

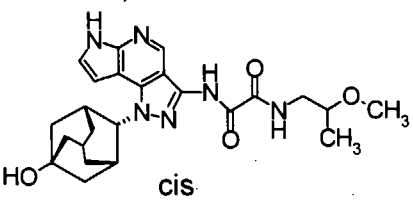
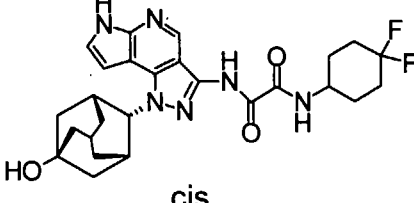
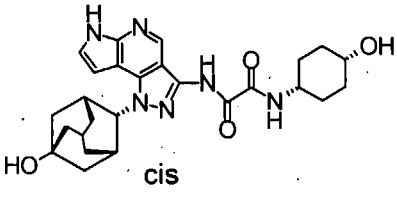
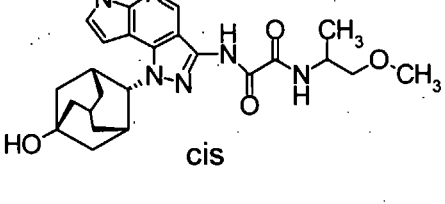
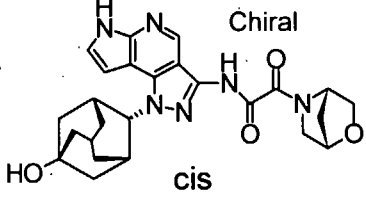
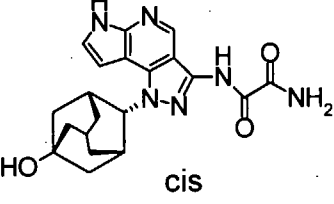
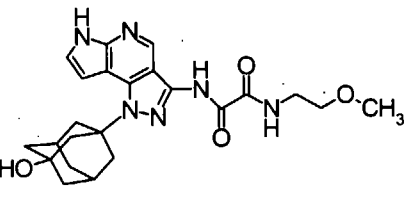
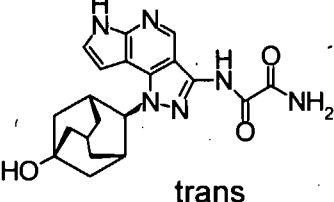
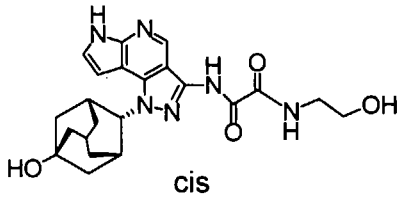
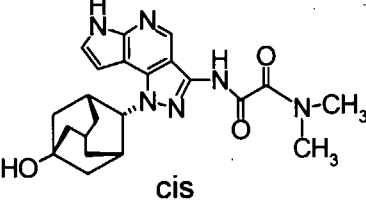
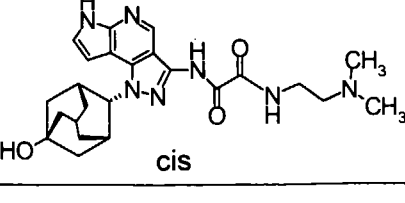
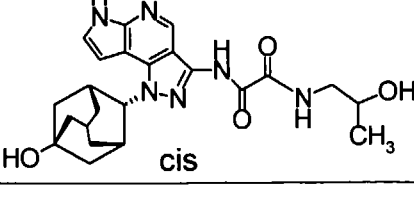
Ex	Structure	Ex	Structure
435	 cis	436	 cis
437	 cis	438	 cis
439	 cis	440	 cis
441		442	 trans
443	 cis	444	 cis
445	 cis	446	 cis

Table 71 (contd.)

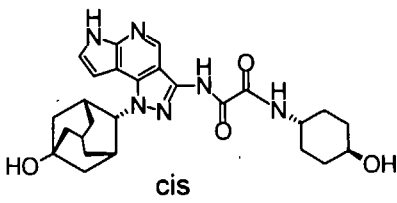
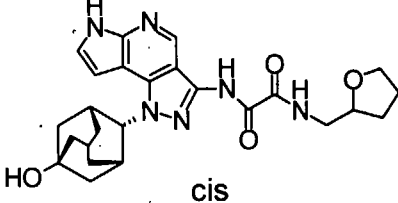
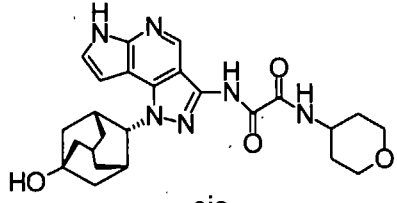
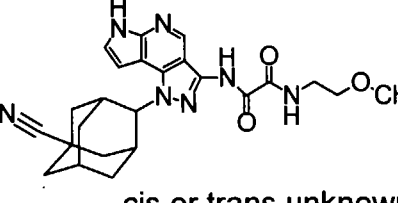
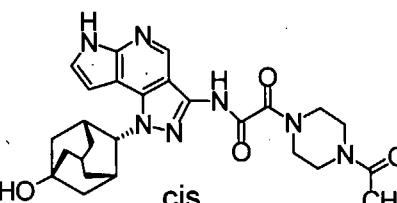
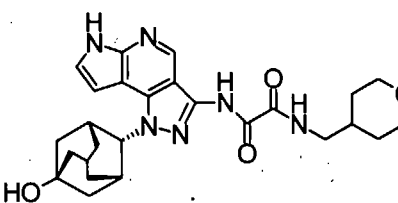
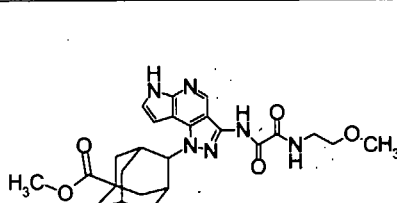
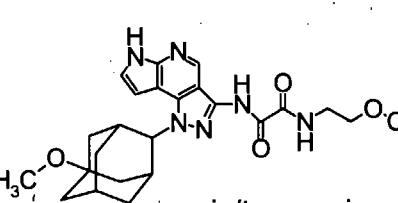
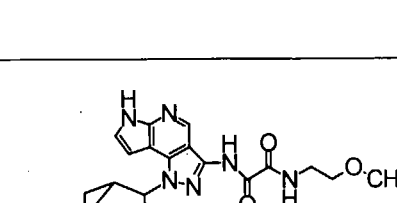
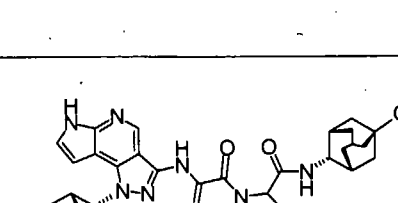
Ex	Structure	Ex	Structure
447	 cis	448	 cis
449	 cis	450	 cis or trans unknown
451	 cis	452	 cis
453	 cis/trans mix	454	 cis/trans mix
455	 cis/trans mix	456	 cis

Table 71 (contd.)

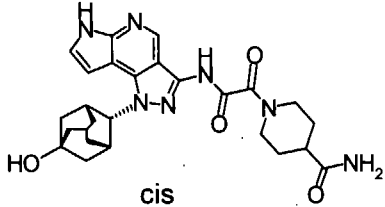
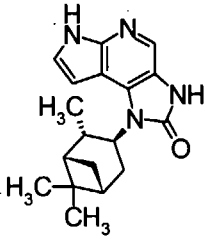
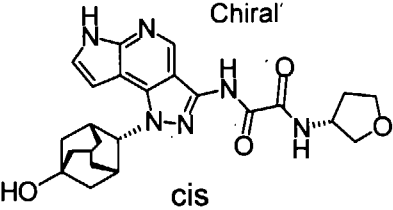
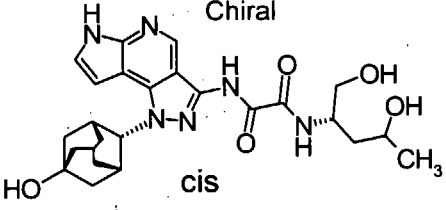
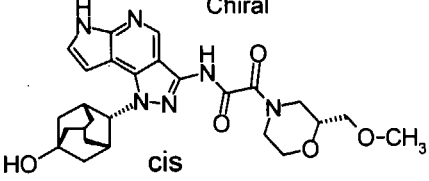
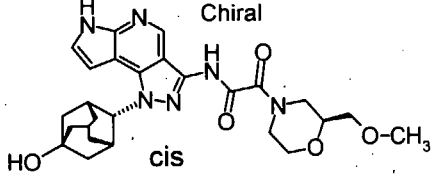
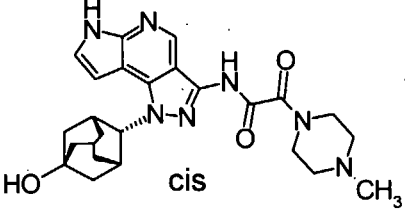
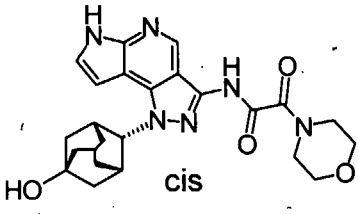
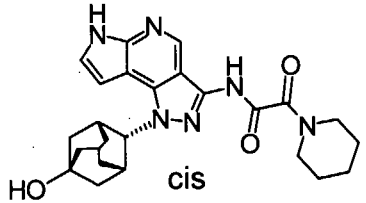
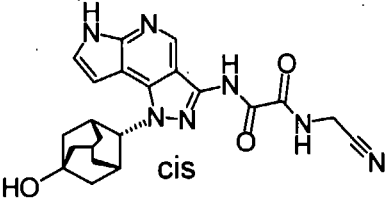
Ex	Structure	Ex	Structure
457	 cis	458	Chiral  cis
459	Chiral  cis	460	Chiral  cis
461	Chiral  cis	462	Chiral  cis
463	 cis	464	 cis
465	 cis	466	 cis

Table 71 (contd.)

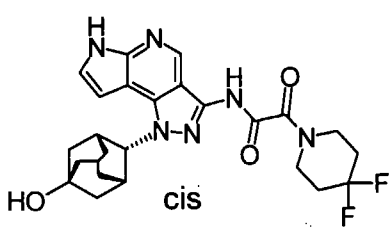
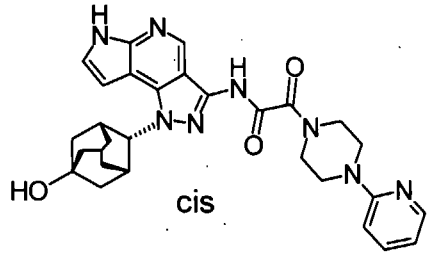
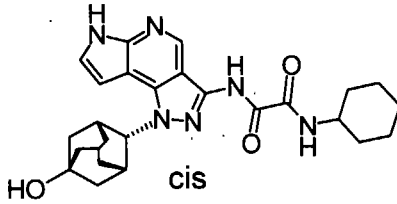
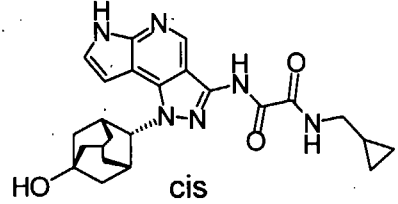
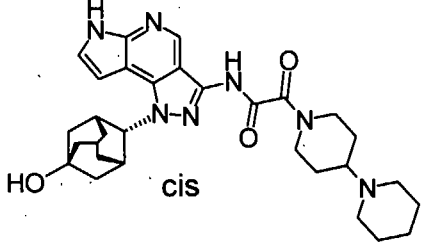
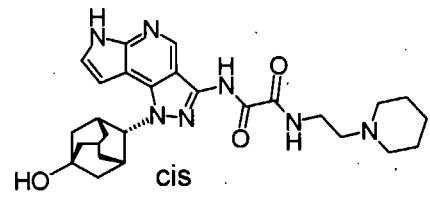
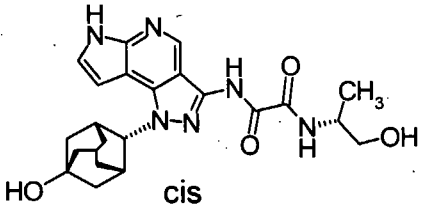
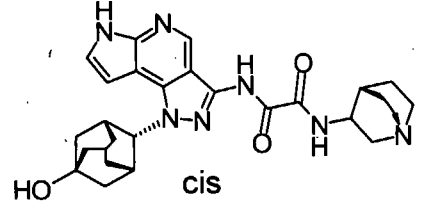
Ex	Structure	Ex	Structure
467	 cis	468	 cis
469	 cis	470	 cis
471	 cis	472	 cis
473	Chiral  cis	474	 cis

Table 71 (contd.)

Ex	Structure	Ex	Structure
475	Chiral cis	476	cis
477	cis	478	cis
479	cis	480	cis
481	cis	482	cis
483	cis	484	cis

Table 71(contd.)

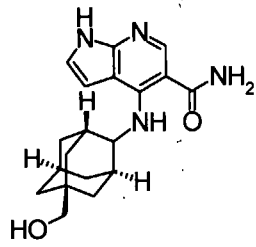
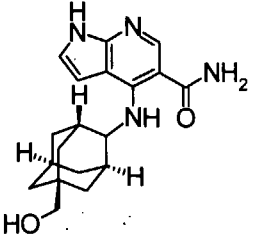
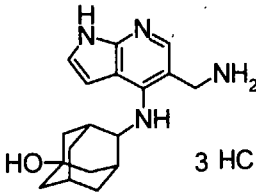
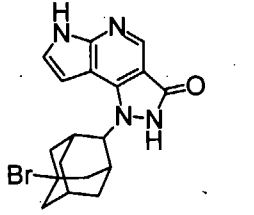
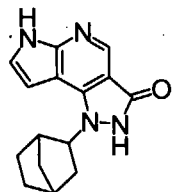
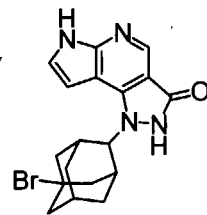
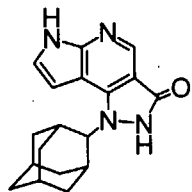
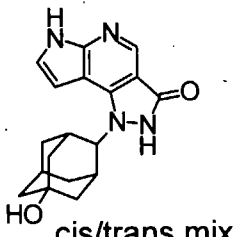
Ex	Structure	Ex	Structure
485	 diastereomer of 486 cis or trans unknown	486	 diastereomer of 485 cis or trans unknown
487	 3 HCl cis/trans mix	488	 diastereomer of 490 cis or trans unknown
489		490	 diastereomer of 488 cis or trans unknown
491		492	 cis/trans mix

Table 71(contd.)

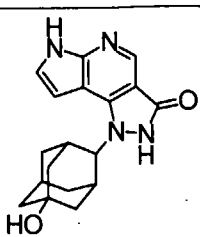
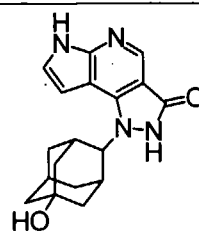
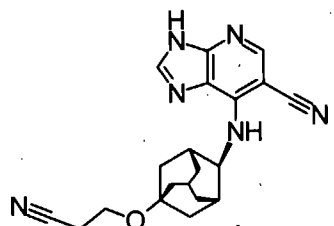
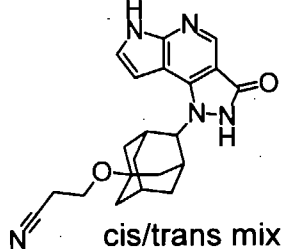
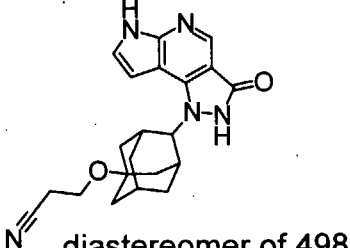
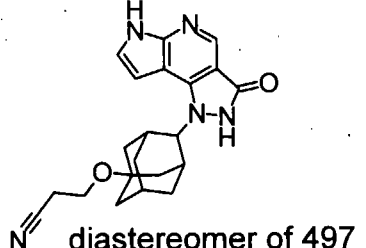
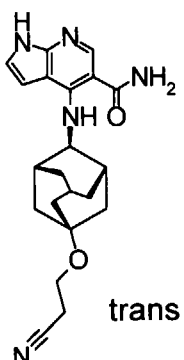
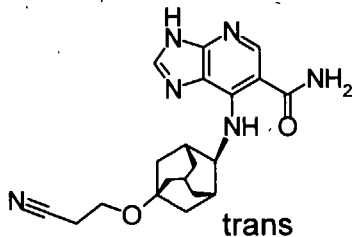
Ex	Structure	Ex	Structure
493	 diastereomer of 494 cis or trans unknowr	494	 diastereomer of 493 cis or trans unknowr
495	 trans	496	 cis/trans mix
497	 diastereomer of 498 cis or trans unknowr	498	 diastereomer of 497 cis or trans unknowr
499	 trans	500	 trans

Table 71(contd.)

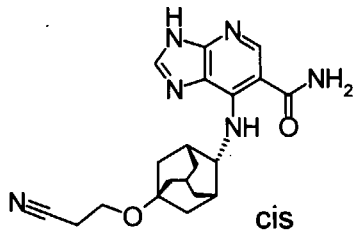
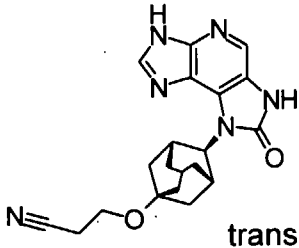
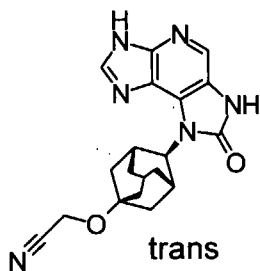
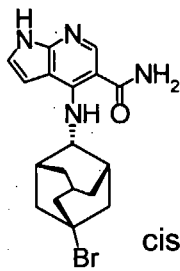
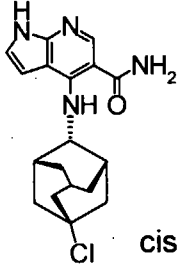
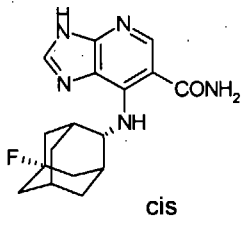
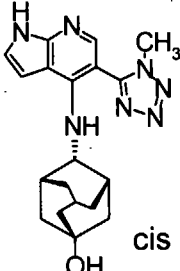
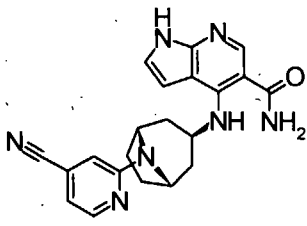
Ex	Structure	Ex	Structure
501	 cis	502	 trans
503	 trans	504	 cis
505	 cis	506	 cis
507	 cis	508	

Table 71 (contd.)

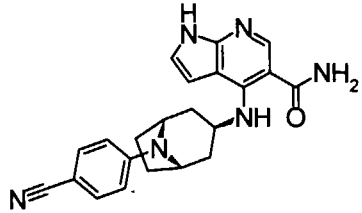
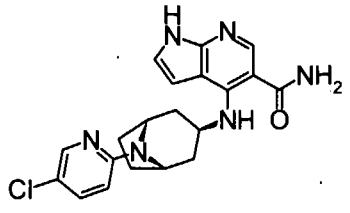
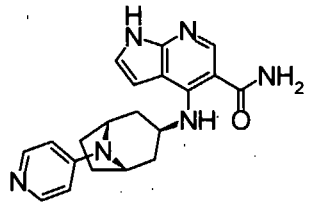
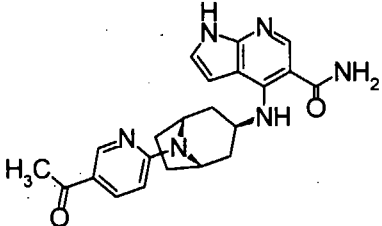
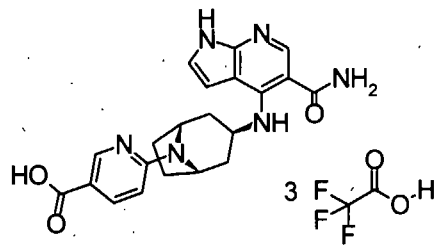
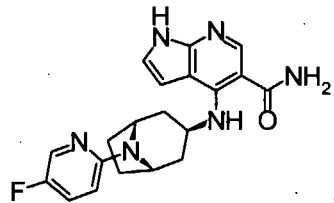
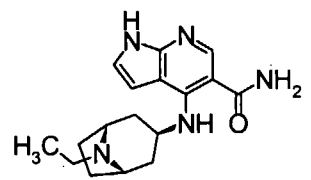
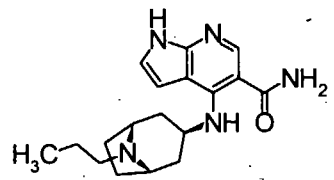
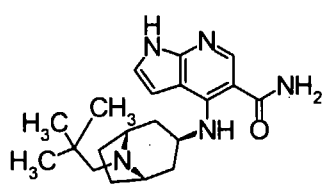
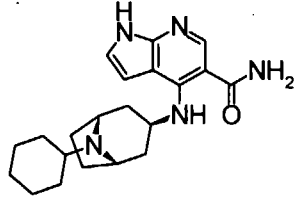
Ex	Structure	Ex	Structure
509		510	
511		512	
513		514	
515		516	
517		518	

Table 71 (contd.)

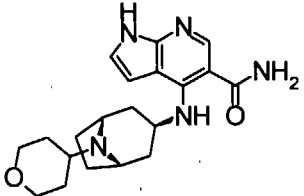
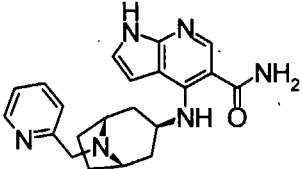
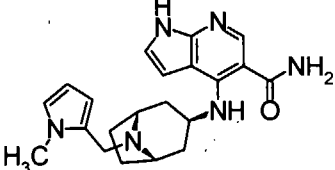
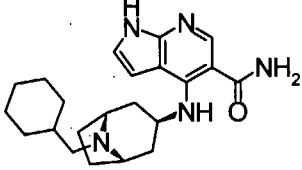
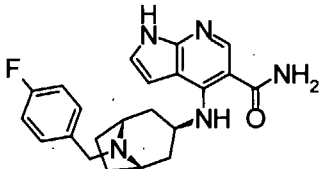
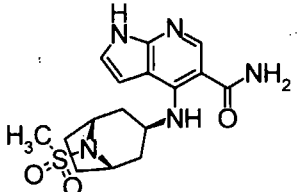
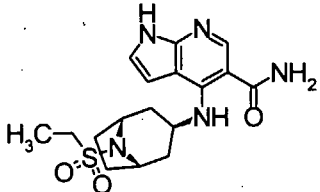
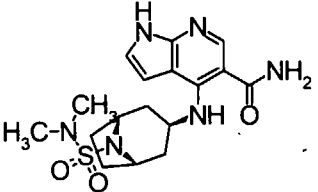
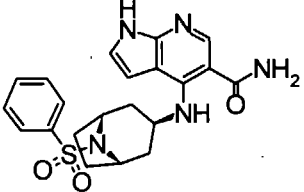
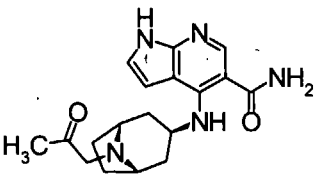
Ex	Structure	Ex	Structure
519		520	
521		522	
523		524	
525		526	
527		528	

Table 71 (contd.)

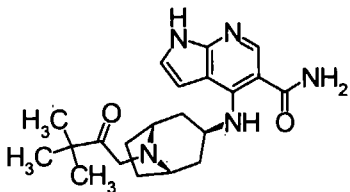
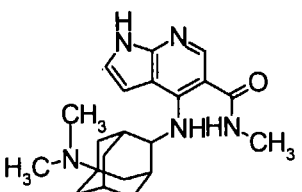
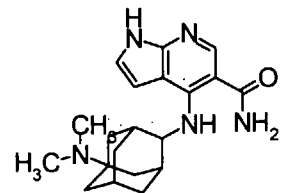
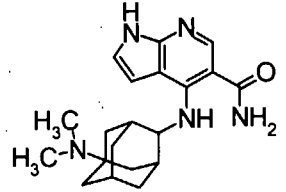
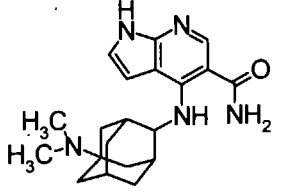
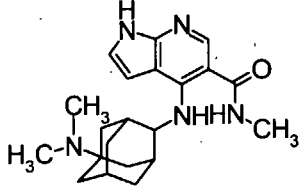
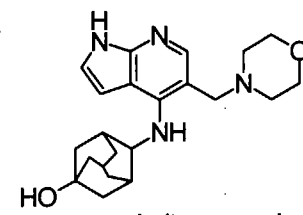
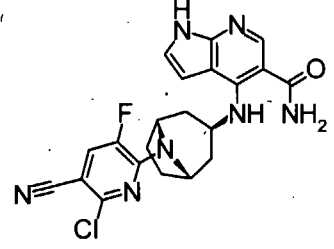
Ex	Structure	Ex	Structure
529		530	 diastereomer of 534 cis or trans unknown
531	 cis/trans mix	532	 diastereomer of 533 cis or trans unknown
533	 diastereomer of 532 cis or trans unknown	534	 diastereomer of 530 cis or trans unknown.
535	 cis/trans mix	536	

Table 71 (contd.)

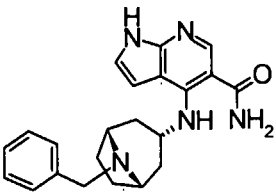
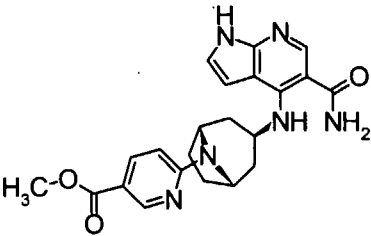
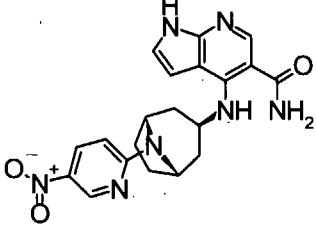
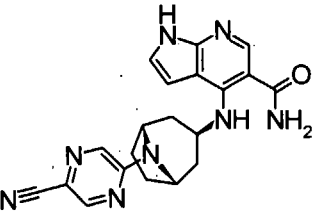
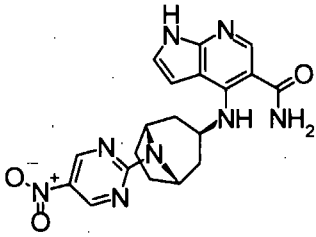
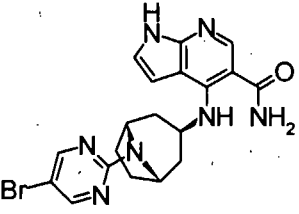
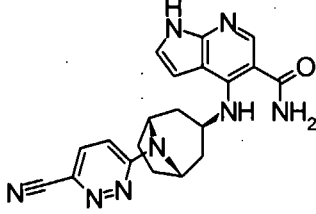
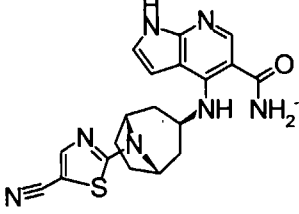
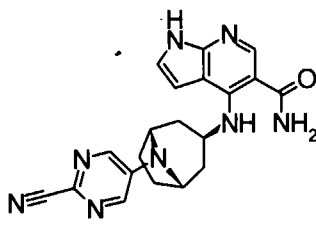
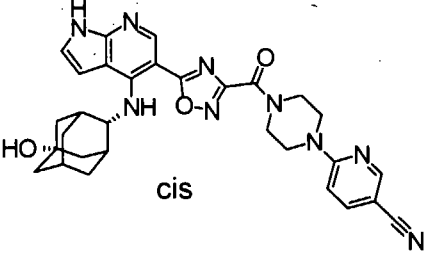
Ex	Structure	Ex	Structure
537		538	
539		540	
541		542	
543		544	
545		546	

Table 71 (contd.)

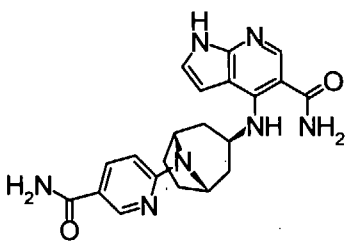
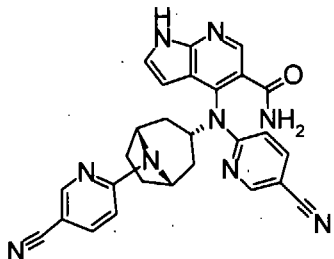
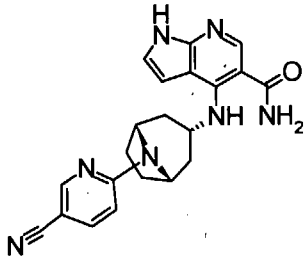
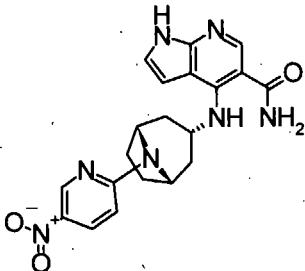
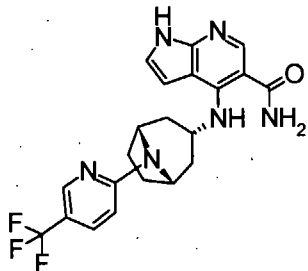
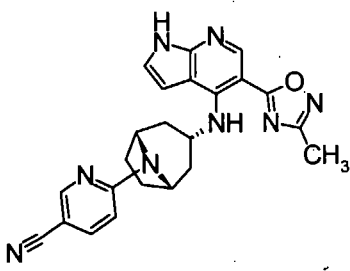
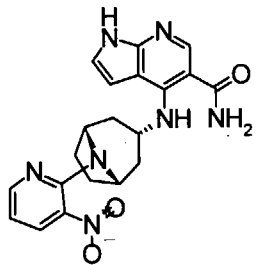
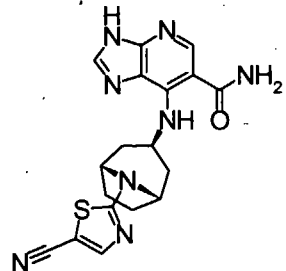
Ex	Structure	Ex	Structure
547		548	
549		550	
551		552	
553		554	

Table 71 (contd.)

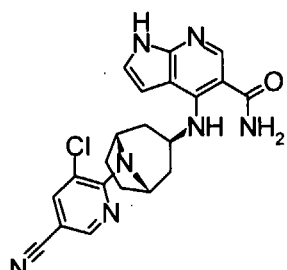
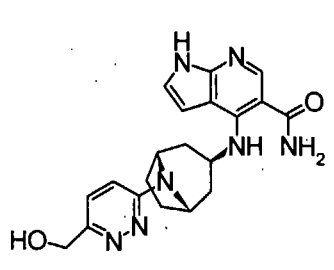
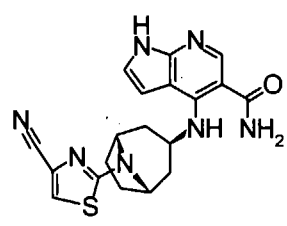
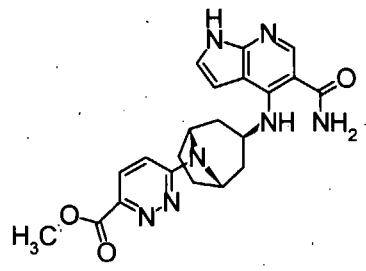
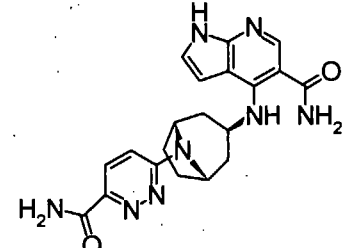
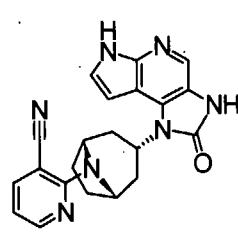
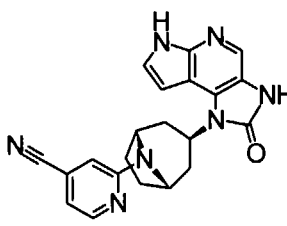
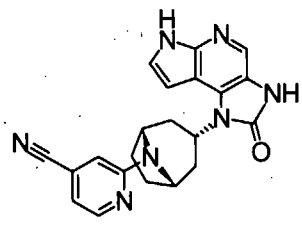
Ex	Structure	Ex	Structure
555		556	
557		558	
559		560	
561		562	

Table 71(contd.)

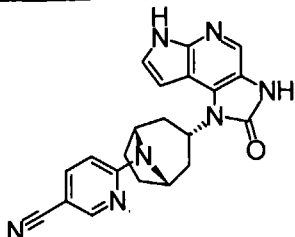
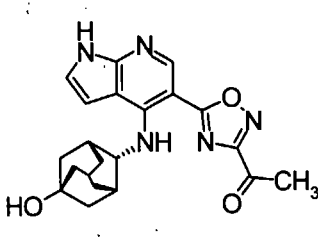
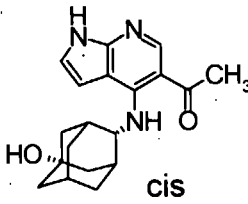
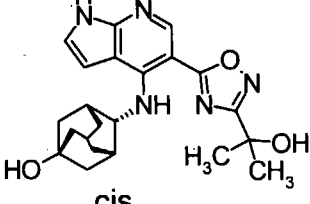
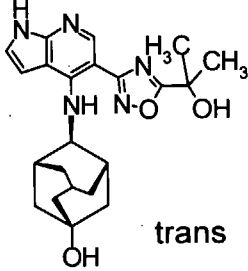
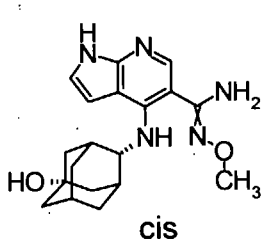
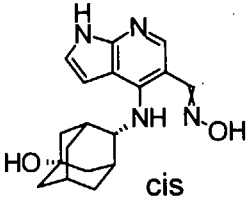
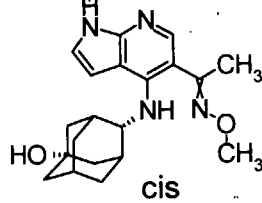
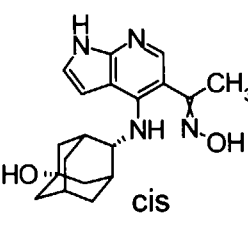
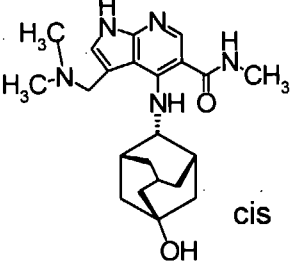
Ex	Structure	Ex	Structure
563		564	
565	 cis	566	 cis
567	 trans	568	 cis
569	 cis	570	 cis
571	 cis	572	 cis

Table 71(contd.)

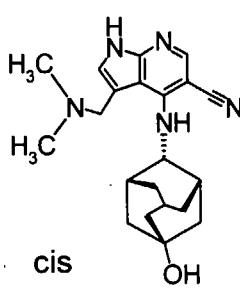
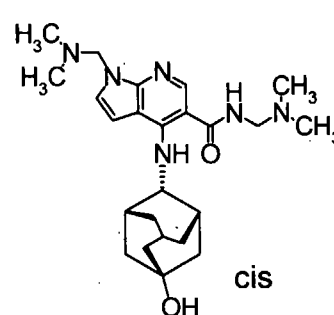
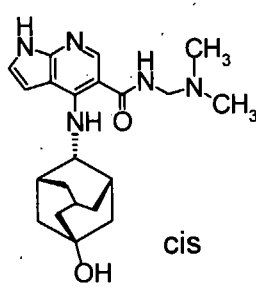
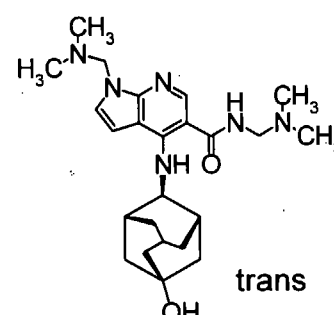
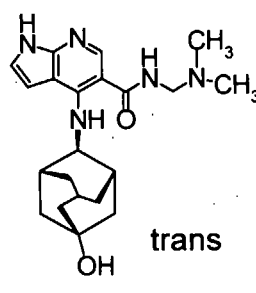
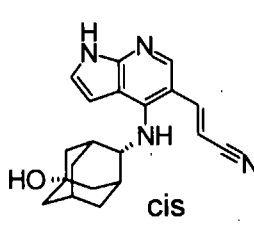
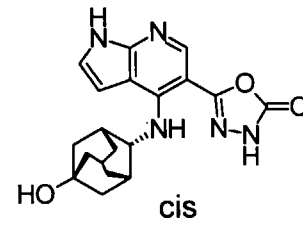
Ex	Structure	Ex	Structure
573	 cis	574	 cis
575	 cis	576	 trans
577	 trans	578	 cis
579	 cis		

Table 72

Ex	Ref -Ex	Data
1	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.44-2.38 (10H, m), 2.85 (3H, d, J=4.8Hz), 4.23 (1H, m), 4.53 (1H, s), 6.58 (1H, m), 7.27 (1H, m), 8.58 (1H, s), 8.78 (1H, m), 9.25 (1H, m), 11.79 (1H, s). MS: 409 (M+H) +
2	—	MS: 313 (M+H) +
3	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.52-2.46 (11H, m), 2.63-2.72 (2H, m), 4.49-4.53 (1H, m), 6.31-6.35 (1H, m), 7.42-7.45 (1H, m), 7.89-7.90 (1H, m), 10.75-10.77 (1H, m), 11.55-11.58 (1H, m), 12.10 (1H, br). MS: 353 (M+H) +
4	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.51-2.13 (8H, m), 2.18-2.47 (3H, m), 2.65-2.76 (2H, m), 4.02-4.13 (2H, m), 4.50-4.55 (1H, m), 6.34-6.39 (1H, m), 7.44-7.46 (1H, m), 7.90 (1H, s), 8.14-8.39 (1H, m), 10.77-10.78 (1H, m), 11.58 (1H, s). MS: 391 (M+H) +
5	—	MS: 404 (M+H) +
6	—	MS: 371 (M+H) +
7	—	MS: 508 (M+H) +
8	—	MS: 409 (M+H) +
9	—	MS: 542 (M+Na) +
10	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.38-2.77 (18H, m), 4.38-4.54 (1H, m), 6.29-6.35 (1H, m), 7.25-7.37 (1H, m), 7.42-7.45 (1H, m), 7.89-7.90 (1H, m), 10.75 (1H, br), 11.57 (1H, s). MS: 380 (M+H) +
11	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.46-2.29 (9H, m), 3.83 (3H, s), 4.10 (1H, m), 4.56 (1H, s), 6.50 (1H, m), 7.18 (1H, m), 8.55 (1H, s), 9.27 (1H, m), 11.68 (1H, s). MS: 342 (M+H) +
12	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.43-1.54 (2H, m), 1.58-1.73 (4H, m), 1.73-1.86 (4H, m), 2.05-2.12 (1H, m), 2.17 (3H, s), 2.21-2.29 (2H, m), 4.08-4.16 (1H, m), 4.56 (1H, s), 4.99 (2H, s), 6.48-6.55 (1H, m), 7.18-7.24 (1H, m), 8.63 (1H, s), 9.12 (1H, d, J=7.8Hz), 11.74 (1H, s). MS: 384 (M+H) +
13	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.43-1.53 (2H, m), 1.57-1.74 (4H, m), 1.74-1.90 (4H, m), 1.80 (3H, s), 2.04-2.12 (1H, m), 2.20-2.29 (2H, m), 4.06-4.14 (1H, m), 4.56 (1H, s), 6.45 (2H, brs), 6.47-6.52 (1H, m), 7.14-7.19 (1H, m), 8.76 (1H, s), 9.41 (1H, d, J=8.0Hz), 11.64 (1H, s). MS: 384 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
14	-	MS:369 (M+H) +
15	-	MS:383 (M-H) -
16	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.57-1.63 (2H, m), 1.95-2.09 (3H, m), 2.17-2.24 (2H, m), 3.31-3.71 (6H, m), 4.62 (1H, s), 6.38-6.40 (1H, m), 7.44 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.80 (1H, s), 11.58 (1H, s). MS:334 (M+H) +
17	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-1.56 (2H, m), 1.63-1.74 (4H, m), 1.83-1.91 (4H, m), 2.09-2.13 (1H, m), 2.30-2.34 (2H, m), 4.22-4.25 (1H, m), 4.58 (1H, s), 6.62 (1H, d, J=3.6Hz), 7.31 (1H, d, J=3.6Hz), 8.50 (1H, d, J=7.6Hz), 8.66 (1H, s), 12.00 (1H, brs). MS:399 (M+Na) +
18	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.48 (10H, m), 2.72-2.85 (2H, m), 4.61 (1H, s), 6.44-6.61 (1H, m), 7.64-7.71 (1H, m), 8.02-8.35 (4H, m), 11.59-11.64 (1H, m), 12.51-12.53 (1H, m). MS:324 (M+H) +
19	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.48 (2H, m), 1.59-1.74 (6H, m), 1.79-1.85 (2H, m), 2.02-2.07 (1H, m), 2.16-2.20 (2H, m), 4.45-4.48 (3H, m), 4.97 (1H, d, J=7.4Hz), 7.13-7.19 (2H, m), 7.36-7.40 (2H, m), 8.06 (1H, s), 8.48 (1H, s), 8.89 (1H, t, J=5.9Hz), 9.62. MS:436 (M+H) +
20	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.50-1.56 (2H, m), 1.62-1.72 (4H, m), 1.77-1.88 (4H, m), 2.08-2.11 (1H, m), 2.24-2.28 (2H, m), 3.56 (1H, m), 4.15-4.20 (1H, m), 6.67-6.69 (1H, m), 7.36-7.38 (1H, m), 8.28 (1H, s), 9.40 (1H, br), 10.36-10.41 (1H, m), 11.55 (1H, s), 12.53 (1H, brs), 14.29 (1H, br). MS:343 (M-HCl+H) +
21	-	¹ H-NMR (400MHz, d6-DMSO) δ : 0.86-1.37 (3H, m), 1.58-1.69 (2H, m), 2.20-2.24 (1H, m), 2.41-2.51 (2H, m), 2.77-2.80 (1H, m), 2.90 (1H, s), 3.03-3.05 (1H, m), 4.29-4.35 (2H, m), 6.63 (1H, s), 7.43 (1H, s), 7.87 (1H, s), 10.7 (1H, s), 11.6 (1H, s). MS:299 (M+H) +
22	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.68-1.93 (6H, m), 2.02-2.13 (3H, m), 2.40-2.47 (2H, m), 2.71-2.75 (2H, m), 4.04 (2H, d, J=5.5Hz), 4.50 (1H, s), 6.34-6.36 (1H, m), 7.45 (1H, t, J=3.0Hz), 7.90 (1H, s), 8.16 (1H, t, J=5.6Hz), 10.77 (1H, s), 11.59 (1H, s). MS:391 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
23	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.71-1.89 (6H, m), 2.21-2.25 (3H, m), 2.53-2.56 (6H, m), 6.63 (1H, s), 7.46 (1H, t, J=3.2Hz), 7.90 (1H, s), 10.77 (1H, s), 11.61 (1H, s). MS: 309 (M+H) +
24	-	MS: 342 (M+H) +
25	-	MS: 312 (M+H) +
26	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.33 (6H, d, J=6.2Hz), 1.46-1.86 (10H, m), 2.06 (1H, brs), 2.22 (2H, brs), 4.54 (1H, s), 5.05 (1H, d, J=8.8Hz), 5.18-5.15 (1H, m), 8.12 (1H, s), 8.63 (1H, s), 9.16 (1H, d, J=8.8Hz), 13.0 (1H, brs). MS: 371 (M+H) +
27	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.45 (2H, m), 1.59-1.62 (2H, m), 1.65-1.70 (2H, m), 1.74-1.79 (2H, m), 1.88-1.92 (2H, m), 2.05-2.09 (1H, m), 2.18-2.21 (2H, m), 4.02-4.05 (1H, m), 4.32 (1H, s), 5.82 (2H, brs), 6.41-6.42 (1H, m), 7.09-7.11 (1H, m), 8.13 (1H, s), 8.96 (1H, d, J=8.1Hz), 9.50 (1H, s), 11.23 (1H, brs). MS: 342 (M+H) +
28	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.57 (2H, m), 1.57-1.78 (4H, m), 1.78-1.97 (4H, m), 2.05-2.14 (1H, m), 2.26-2.34 (2H, m), 2.44 (3H, s), 4.17-4.24 (1H, m), 4.53 (1H, s), 6.56-6.61 (1H, m), 7.24-7.28 (1H, m), 8.58 (1H, s), 9.10 (1H, d, J=7.8Hz), 11.82 (1H, brs). MS: 366 (M+H) +
29	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.32 (13H, m), 4.20-4.22 (1H, m), 4.55 (1H, s), 6.55-6.57 (1H, m), 7.25-7.27 (1H, m), 8.49 (1H, s), 8.79 (1H, d, J=8.0Hz), 9.27 (1H, s), 11.73 (1H, brs). MS: 374 (M+Na) +
30	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.52 (2H, m), 1.62-1.64 (2H, m), 1.68-1.73 (2H, m), 1.81-1.91 (4H, m), 2.09-2.11 (1H, m), 2.28-2.31 (2H, m), 2.67 (3H, s), 4.19-4.22 (1H, m), 4.53 (1H, s), 6.53-6.54 (1H, m), 7.22-7.24 (1H, m), 7.88 (1H, d, J=7.8Hz), 8.69 (1H, s), 11.61 (1H, brs). MS: 366 (M+H) +
31	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.49 (2H, m), 1.62-1.64 (2H, m), 1.74-1.79 (2H, m), 1.98-2.03 (4H, m), 2.15-2.18 (1H, m), 3.00-3.03 (2H, m), 4.45 (1H, brs), 4.61 (1H, brs), 5.77 (2H, s), 6.35-6.37 (1H, m), 7.33-7.35 (1H, m), 8.14 (1H, s), 11.44 (1H, brs). MS: 324 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
32	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.60 (13H, m), 3.27 (3H, s), 3.37-3.49 (4H, m), 4.44 (1H, m), 4.77 (1H, s), 6.66 (1H, m), 7.46 (1H, m), 8.71 (1H, s), 8.98 (1H, m), 10.92 (1H, s), 12.08 (1H, s). MS: 453 (M+H) +
33	-	MS: 409 (M+H) +
34	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42-1.51 (2H, m), 1.58-1.75 (4H, m), 1.76-1.95 (4H, m), 2.05-2.13 (1H, m), 2.25-2.32 (2H, m), 4.11-4.19 (1H, m), 4.50 (1H, brs), 6.49-6.54 (1H, m), 7.17-7.22 (1H, m), 7.24 (2H, s), 8.06 (1H, s), 9.70 (1H, d, J=7.6Hz), 11.57 (1H, s). MS: 383 (M+H) +
35	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.49 (10H, m), 2.72-2.80 (2H, m), 4.49-4.56 (2H, m), 4.60-4.67 (1H, m), 5.64-5.71 (1H, m), 6.34-6.39 (1H, m), 7.42-7.47 (1H, m), 7.89-7.92 (1H, m), 8.62 (1H, s), 10.77-10.83 (1H, m), 11.55-11.61 (1H, m). MS: 407 (M+H) +
36	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32-1.87 (12H, m), 2.09 (1H, m), 2.08 (2H, m), 4.18-4.22 (1H, m), 4.68 (1H, m), 6.70-6.71 (1H, m), 7.09 (1H, s), 7.25 (1H, s), 7.37-7.39 (1H, m), 8.32 (1H, s), 10.32 (1H, m), 12.68 (1H, brs). MS: 313 (M-3HCl+H) +
37	-	MS: 328 (M+H) +
38	-	MS: 378 (M+H) +
39	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.63 (2H, m), 1.86-2.56 (10H, m), 2.77-2.85 (1H, m), 4.91 (1H, s), 6.64-6.66 (1H, m), 7.36-7.38 (1H, m), 8.50 (1H, s), 10.82 (1H, s), 11.93-11.95 (1H, m). MS: 387, 389 (M+H) +
40	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.50-1.53 (2H, m), 1.64-2.01 (8H, m), 2.11 (1H, s), 2.32 (2H, s), 4.21 (1H, d, J=7.5Hz), 4.56 (2H, s), 6.58 (1H, s), 7.26 (1H, s), 8.61 (1H, s), 9.86 (1H, brs), 11.77 (1H, s). MS: 350 (M-H) -
41	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.60 (2H, m), 1.68-1.77 (4H, m), 1.78-1.86 (2H, m), 1.90-1.98 (2H, m), 2.12-2.16 (1H, m), 2.25-2.30 (2H, m), 2.68 (2H, t, J=6.0Hz), 3.57 (2H, t, J=6.0Hz), 4.08 (1H, d, J=7.8Hz), 6.46 (1H, dd, J=2.0, 3.6Hz), 7.04 (1H, br), 7.13 (1H, dd, J=2.6, 3.6Hz), 7.80 (1H, br), 8.38 (1H, s), 10.17 (1H, d, J=8.2Hz), 11.47 (1H, s). MS: 380 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
42	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.21 (3H, t, J=7.2Hz), 1.41-2.34 (13H, m), 3.33-3.42 (2H, m), 4.12-4.18 (1H, m), 4.50 (1H, s), 6.48-6.51 (1H, m), 7.17-7.21 (1H, m), 8.02 (1H, brd, J=7.6Hz), 8.42 (1H, brt, J=5.6Hz), 8.58 (1H, s), 11.51 (1H, brs). MS: 395 (M+H) +
43	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.58-1.69 (2H, m), 1.86-1.96 (2H, m), 2.04-2.11 (1H, m), 2.14-2.23 (2H, m), 2.34-2.44 (4H, m), 2.61-2.71 (2H, m), 4.38-4.42 (1H, m), 6.63-6.67 (1H, m), 7.25 (1H, s), 7.35 (1H, br), 8.05 (1H, br), 10.58 (1H, s), 10.58 (1H, s), 11.94 (1H, s). MS: 389, 391 (M+H) +
44	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.72-2.04 (9H, m), 2.29-2.91 (4H, m), 4.42-4.45 (1H, m), 6.37 (1H, d, J=3.5Hz), 7.44 (1H, d, J=3.5Hz), 7.90 (1H, s), 10.80 (1H, br, s), 11.58 (1H, s). MS: 327 (M+H) +
45	—	MS: 366 (M+H) +
46	—	MS: 388 (M+H) +
47	—	MS: 406 (M+H) +
48	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.84-1.97 (2H, m), 1.97-2.17 (4H, m), 2.19-2.34 (2H, m), 2.96 (3H, s), 4.12-4.24 (2H, m), 4.30-4.40 (1H, m), 6.44-6.51 (1H, m), 7.04 (1H, br), 7.08-7.15 (1H, m), 7.81 (1H, br), 8.38 (1H, s), 10.22 (1H, d, J=7.6Hz), 11.47 (1H, s). MS: 364 (M+H) +
49	—	MS: 386 (M+H) +
50	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.48-1.53 (2H, m), 1.62-1.65 (2H, m), 1.64 (6H, s), 1.69-1.74 (2H, m), 1.81-1.93 (4H, m), 2.08-2.12 (1H, m), 2.29-2.32 (2H, m), 4.19-4.23 (1H, m), 4.53 (1H, s), 6.07 (1H, s), 6.53-6.55 (1H, m), 7.22-7.24 (1H, m), 7.87-7.90 (1H, m), 8.72 (1H, s), 11.62 (1H, brs). MS: 410 (M+H) +
51	—	MS: 389 (M+H) +
52	—	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-2.47 (9H, m), 3.17 (1H, m), 4.10 (1H, m), 4.58 (1H, s), 6.51 (1H, m), 7.21 (1H, m), 8.22 (1H, s), 9.79 (1H, s), 9.90 (1H, m), 11.84 (1H, s). MS: 312 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
53	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-2.33 (8H, m), 3.90 (3H, s), 4.15 (1H, m), 4.51 (1H, s), 6.48 (1H, m), 7.17 (1H, m), 7.90 (1H, s), 8.43 (1H, s), 8.46 (1H, m), 11.50 (1H, s). MS: 341 (M+H) +
54	-	MS: 410 (M+H) +
55	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.37-1.48 (2H, m), 1.57-1.91 (8H, m), 2.04-2.08 (1H, m), 2.24-2.33 (2H, m), 3.71 (3H, s), 3.99-4.02 (1H, m), 4.50 (1H, s), 5.85-5.87 (1H, m), 6.34-6.38 (1H, m), 6.43-6.46 (1H, m), 7.14-7.17 (1H, m), 7.93-7.98 (1H, m), 8.20 (1H, s), 11.49 (1H, brs). MS: 368 (M+H) +
56	-	MS: 361 (M+H) +
57	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.45 (2H, m), 1.59-1.61 (2H, m), 1.64-1.70 (2H, m), 1.73-1.79 (2H, m), 1.85-1.91 (5H, m), 2.05-2.08 (1H, m), 2.20-2.23 (2H, m), 4.01-4.04 (1H, m), 4.42-4.52 (1H, m), 6.44 (1H, d, J=3.6Hz), 7.12 (1H, d, J=3.6Hz), 8.15 (1H, s), 10.05 (1H, br), 11.38 (1H, brs). MS: 326 (M-AcOH+H) +
58	-	MS: 284 (M+H) +
59	-	MS: 427 (M+Na) +, 403 (M-H) -
60	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.27 (7H, m), 3.12 (3H, s), 3.18 (3H, s), 4.07 (1H, m), 4.46 (1H, s), 6.44 (1H, m), 7.09 (1H, m), 8.58 (1H, s), 9.08 (1H, s), 10.56 (1H, m), 11.45 (1H, s). MS: 382.3 (M+H) +
61	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.69 (13H, m), 4.19 (1H, m), 4.53 (1H, s), 6.54 (1H, m), 7.25 (1H, m), 8.43 (1H, s), 8.75 (1H, m), 11.68 (1H, s). MS: 367.3 (M+H), 365.0 (M-H) -
62	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.45 (2H, m), 1.59-1.70 (4H, m), 1.75-1.81 (2H, m), 1.90-1.95 (2H, m), 2.06-2.09 (1H, m), 2.20-2.23 (2H, m), 3.35 (2H, m), 3.89 (2H, t, J=9.6Hz), 4.04-4.08 (1H, m), 4.43 (1H, br), 6.44 (1H, d, J=3.6Hz), 6.87 (1H, brs), 7.10 (1H, d, J=3.5Hz), 8.21 (1H, s), 10.97 (1H, d, J=7.8Hz), 11.34 (1H, brs). MS: 352 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
63	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.48 (2H, m), 1.60-1.63 (2H, m), 1.66-1.72 (2H, m), 1.77-1.83 (2H, m), 1.87-1.92 (2H, m), 2.06-2.10 (1H, m), 2.22-2.26 (2H, m), 4.05 (2H, t, J=9.0Hz), 4.09-4.13 (1H, m), 4.32 (2H, t, J=9.0Hz), 4.47 (1H, s), 6.47-6.49 (1H, m), 7.15-7.17 (1H, m), 8.34 (1H, s), 9.98 (1H, d, J=7.8Hz), 11.49 (1H, brs). MS: 353 (M+H) +
64	-	¹ H-NMR (400MHz, d6-DMSO) δ : 1.02-1.05 (4H, m), 1.37-1.41 (9H, m), 1.53-1.67 (5H, m), 1.74-1.85 (2H, m), 2.01-2.23 (5H, m), 4.11-4.18 (2H, m), 6.29-6.36 (1H, m), 7.09-7.13 (1H, m), 7.28-7.32 (1H, m), 7.64-7.65 (1H, m), 11.11 (1H, brs). MS: 413 (M+H) +
65	1	MS: 431 (M+H) +
66	1	MS: 341 (M+H) +
67	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.81-2.02 (8H, m), 2.09-2.62 (5H, m), 4.15-4.20 (1H, m), 6.43-6.46 (1H, m), 7.09 (1H, br), 7.14-7.16 (1H, m), 7.86 (1H, br), 8.40 (1H, s), 10.25 (1H, d, J=8.2Hz), 11.50 (1H, s). MS: 336 (M+H) +
68	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.60 (2H, m), 1.86-1.97 (3H, m), 1.99-2.03 (2H, m), 2.08-2.15 (4H, m), 2.27-2.35 (2H, m), 4.27 (1H, d, J=7.6Hz), 6.50-6.52 (1H, m), 6.99 (1H, br), 7.14 (1H, t), 7.81 (1H, s), 8.38 (1H, s), 10.17 (1H, d, J=8.3Hz), 11.48 (1H, s). MS: 336 (M+H) +
69	1	MS: 534 (M+H) +, 532 (M-H) -
70	1	MS: 376 (M+H) +
71	1	MS: 402 (M+H) +
72	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.43 (2H, m), 1.62-1.72 (4H, m), 1.79-1.89 (4H, m), 2.02-2.09 (1H, m), 2.11-2.17 (2H, m), 2.75 (3H, d, J=4.3Hz), 4.09-4.16 (1H, m), 4.49 (1H, brs), 6.39-6.41 (1H, m), 7.11-7.15 (1H, m), 8.18-8.25 (1H, m), 8.30 (1H, s), 9.87 (1H, d, J=8.3Hz), 11.42 (1H, brs). MS: 341 (M+H) +
73	1	MS: 341 (M+H) +
74	1	MS: 355 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
75	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-2.27 (9H, m), 2.76 (3H, d, J=4.4Hz), 4.23 (1H, m), 6.48 (1H, m), 7.14 (1H, m), 8.25 (1H, m), 8.32 (1H, s), 9.87 (1H, m), 11.45 (1H, s). MS: 343 (M+H) +
76	1	MS: 355 (M+H) +
77	1	MS: 440 (M+H) +
78	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-2.36 (8H, m), 1.63 (6H, s), 4.22 (1H, m), 4.54 (1H, s), 5.90 (1H, s), 6.55 (1H, m), 7.25 (1H, m), 8.50 (1H, s), 8.80 (1H, m), 11.72 (1H, s). MS: 410 (M+H) +
79	1	MS: 382 (M+H) +, 380 (M-H) -
80	1	MS: 417 (M+Na) +, 395 (M+H) +
81	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.48 (2H, m), 1.60-1.68 (4H, m), 1.76-1.85 (4H, m), 2.06-2.08 (1H, m), 2.29-2.31 (2H, m), 4.13-4.15 (1H, m), 4.53-4.54 (1H, m), 5.99 (1H, d, J=7.0Hz), 6.68 (1H, d, J=3.6Hz), 7.28 (1H, d, J=3.6Hz), 8.11 (1H, s), 11.86 (1H, brs). MS: 331 (M+Na) +
82	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-1.43 (2H, m), 1.64-1.69 (4H, m), 1.83-1.88 (4H, m), 2.05-2.07 (1H, m), 2.21-2.23 (2H, m), 4.25-4.27 (1H, m), 4.52 (1H, brs), 6.04 (1H, d, J=7.2Hz), 6.68 (1H, d, J=3.5Hz), 7.28 (1H, d, J=3.4Hz), 8.10 (1H, s), 11.85 (1H, brs). MS: 309 (M+H) +
83	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.50-1.55 (2H, m), 1.62-1.73 (4H, m), 1.79-1.89 (4H, m), 2.08-2.12 (1H, m), 2.28-2.32 (2H, m), 4.24-4.28 (1H, m), 6.68-6.71 (1H, m), 7.39-7.41 (1H, m), 8.42 (1H, s), 8.44-8.48 (1H, m), 12.48 (1H, brs). MS: 368 (M+H) +
84	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.50-1.57 (2H, m), 1.81-1.87 (2H, m), 1.92-2.00 (5H, m), 2.04-2.09 (2H, m), 2.18-2.24 (2H, m), 3.62 (3H, s), 4.30-4.33 (1H, m), 6.16 (1H, d, J=7.1Hz), 6.72 (1H, d, J=3.4Hz), 7.28 (1H, d, J=3.3Hz), 8.11 (1H, s), 11.85 (1H, brs). MS: 373 (M+Na) +
85	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.70-1.75 (2H, m), 1.78-1.91 (5H, m), 1.94-2.02 (2H, m), 2.04-2.12 (2H, m), 2.19-2.26 (2H, m), 3.60 (3H, s), 4.25-4.28 (1H, m), 6.19 (1H, d, J=7.1Hz), 6.70-6.72 (1H, m), 7.27-7.29 (1H, m), 8.10 (1H, s), 11.85 (1H, brs). MS: 373 (M+Na) +
86	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.53 (2H, m), 1.63-1.74 (4H, m), 1.81-1.91 (4H, m), 2.08-2.11 (1H, m), 2.21 (3H, s), 2.29-2.36 (4H, m), 2.39-2.42 (2H, m), 3.49-3.53 (2H, m), 3.66-3.70 (2H, m), 4.19-4.23 (1H, m), 4.49 (1H, s), 6.57-6.59 (1H, m), 7.27-7.29 (1H, m), 8.64 (1H, s), 8.83-8.86 (1H, m), 11.86 (1H, brs). MS: 478 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
87	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.46-1.52 (2H, m), 1.61-1.81 (8H, m), 2.05-2.08 (1H, m), 2.20-2.24 (2H, m), 4.09-4.12 (1H, m), 4.53 (1H, s), 6.63-6.65 (1H, m), 6.82-6.86 (1H, m), 7.30-7.32 (1H, m), 8.65 (1H, s), 10.52-10.56 (1H, m), 11.80 (1H, brs). MS: 352 (M+H) +
88	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 0.85-0.93 (1H, m), 1.34, 1.40 (9H, s), 1.47-1.53 (1H, m), 1.67-1.79 (1H, m), 1.85-1.92 (3H, m), 1.99-2.06 (3H, m), 2.13-2.34 (4H, m), 4.21-4.25, 4.30-4.34 (1H, m), 6.37-6.41, 6.54-6.56 (1H, m), 6.51-6.63, 6.57-6.59 (1H, m), 7.28-7.29 (1H, m), 8.06-8.32 (2H, m), 8.63, 8.64 (1H, s), 8.87-8.89, 8.99-9.01 (1H, m), 11.88 (1H, brs). MS: 516 (M+Na) +
89	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.31-1.36 (1H, m), 1.47-1.53 (3H, m), 1.59-1.64 (1H, m), 1.67-1.80 (2H, m), 1.89-2.00 (3H, m), 2.06-2.11 (1H, m), 2.16-2.20 (2H, m), 3.02-3.09 (2H, m), 4.27-4.44 (2H, m), 6.52-6.54, 6.61-6.63 (1H, m), 7.26-7.29 (1H, m), 8.10-8.31 (2H, m), 8.63 (1H, s), 8.92-8.95, 9.04-9.07 (1H, m), 11.86 (1H, brs). MS: 431 (M+Na) +
90	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.48-1.53 (2H, m), 1.62-1.73 (4H, m), 1.81-1.92 (4H, m), 2.09-2.12 (1H, m), 2.29-2.32 (2H, m), 3.46 (3H, s), 4.20-4.24 (1H, m), 4.54 (1H, s), 4.86 (2H, s), 6.54-6.56 (1H, m), 7.24-7.25 (1H, m), 7.84-7.86 (1H, m), 8.72 (1H, s), 11.65 (1H, s). MS: 396 (M+H) +
91	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 0.74-0.88 (1H, m), 1.13-1.75 (7H, m), 2.10-2.30 (2H, m), 4.27-4.44 (1H, m), 6.55 (1H, brs), 6.56 (1H, d, J=3.4Hz), 7.11 (1H, m), 7.65 (1H, d, J=3.4Hz), 8.35 (1H, s), 9.86 (1H, d, J=7.9Hz), 11.43 (1H, brs). MS: 271 (M+H) +
92	1	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.75-2.33 (5H, m), 2.97-3.36 (5H, m), 3.73-3.88 (1H, m), 4.38-4.64 (1H, m), 6.63 (1H, d, J=3.4Hz), 7.17 (1H, brs), 7.23 (1H, d, J=3.4Hz), 7.92 (1H, brs), 8.44 (1H, s), 10.25 (1H, d, J=7.8Hz), 11.68 (1H, s). MS: 286 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
93	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.29-2.02 (5H, m), 2.41 (1H, dd, J=3.8, 13.8Hz), 2.65-2.83 (4H, m), 4.05-4.20 (1H, m), 4.36 (1H, t, J=5.1Hz), 6.51-6.58 (1H, m), 6.88-7.94 (3H, m), 8.37 (1H, s), 9.99 (1H, d, J=7.9Hz), 11.46 (1H, brs). MS: 286 (M+H) +
94	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.12-1.65 (7H, m), 1.82-1.97 (1H, m), 2.25-2.34 (2H, m), 3.85-3.96 (1H, m), 6.57 (1H, d, J=3.3Hz), 7.12 (1H, d, J=2.4Hz), 6.78-7.92 (2H, brs), 8.35 (1H, s), 9.57 (1H, d, J=7.1Hz), 11.5 (1H, brs). MS: 271 (M+H) +
95	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.17-1.64 (10H, m), 2.0-2.07 (1H, m), 2.18-2.22 (1H, m), 2.38-2.40 (1H, m), 3.18-3.23 (1H, m), 4.14 (1H, t, J=7.8Hz), 4.25 (2H, q, J=7.0Hz), 4.46 (1H, t, J=4.8Hz), 7.17 (1H, s), 6.70 (1H, s), 8.51 (1H, s), 8.78 (1H, d, J=8.0Hz), 11.7 (1H, s). MS: 330 (M+H) +
96	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-1.86 (10H, m), 2.07 (1H, brs), 2.19 (2H, brs), 2.29 (3H, s), 3.97 (1H, d, J=8.0Hz), 4.49 (1H, s), 6.14 (1H, s), 6.98 (1H, brs), 7.78 (1H, brs), 8.28 (1H, s), 9.99 (1H, d, J=8.0Hz), 11.3 (1H, s). MS: 341 (M+H) +
97	1	¹ H-NMR (400MHz, CDCl ₃) δ : 1.35-2.67 (13H, m), 3.75 (1H, brs), 4.05-4.20 (1H, m), 5.00-5.12 (1H, brs), 6.45-6.48 (1H, m), 7.15-7.16 (1H, m), 7.95 (1H, d, J=4.7Hz), 10.0 (1H, brs). MS: 302 (M+H) +
98	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-2.30 (13H, m), 3.92-3.96 (1H, m), 4.44 (1H, s), 5.27-5.29 (1H, m), 6.51 (1H, dd, J=2.0, 3.2Hz), 7.21 (1H, dd, J=2.8, 3.2Hz), 7.88 (1H, d, J=4.8Hz), 11.3 (1H, s). MS: 302 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
99	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.13-1.40 (3H, m), 1.48-1.63 (3H, m), 1.93-2.00 (1H, m), 2.14-2.18 (1H, m), 2.35-2.38 (1H, m), 3.12-3.20 (1H, m), 3.41-3.47 (1H, m), 4.04-4.10 (1H, m), 4.38-4.41 (1H, m), 6.61-6.65 (1H, m), 6.81-7.03 (1H, br), 7.09-7.13 (1H, m), 7.61-7.86 (1H, br), 8.33 (1H, s), 9.64 (1H, d, J=8.0Hz), 11.45 (1H, brs). MS: 301 (M+H)+.
100	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-2.28 (12H, m), 2.87-2.98 (1H, m), 3.63 (3H, s), 4.45-4.57 (1H, m), 6.42-6.45 (1H, m), 6.80-7.13 (1H, br), 7.18-7.22 (1H, m), 7.51-7.93 (1H, br), 8.34 (1H, s), 9.44 (1H, d, J=8.0Hz), 11.49 (1H, brs). MS: 357 (M+H)+.
101	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.33 (3H, t, J=8.0Hz), 1.47-1.51 (2H, m), 1.61-1.72 (4H, m), 1.78-1.85 (4H, m), 2.07-2.10 (1H, m), 2.23-2.27 (2H, m), 4.09-4.12 (1H, m), 4.30 (2H, q, J=8.0Hz), 4.56 (1H, brs), 6.48-6.50 (1H, m), 7.17-7.19 (1H, m), 8.56 (1H, s), 9.28 (1H, d, J=7.6Hz), 11.69 (1H, brs). MS: 356 (M+H)+.
102	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32 (3H, t, J=6.8Hz), 1.43-1.50 (2H, m), 1.65-1.73 (4H, m), 1.78-1.90 (4H, m), 2.06-2.10 (1H, m), 2.16-2.21 (2H, m), 4.19-4.23 (1H, m), 4.29 (2H, q, J=6.8Hz), 4.54 (1H, brs), 6.45-6.46 (1H, m), 7.18-7.20 (1H, m), 8.56 (1H, s), 9.26 (1H, d, J=8.0Hz), 11.68 (1H, brs). MS: 356 (M+H)+.
103	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-1.48 (2H, m), 1.59-1.70 (4H, m), 1.73-1.86 (4H, m), 2.03-2.09 (1H, m), 2.11-2.16 (1H, m), 2.18-2.23 (1H, m), 3.258 (1.5H, s), 3.263 (1.5H, s), 3.53 (1.5H, s), 3.54 (1.5H, s), 4.00-4.05 (0.5H, m), 4.10-4.15 (0.5H, m), 4.50 (0.5H, brs), 4.52 (0.5H, brs), 6.42-6.45 (0.5H, m), 6.46-6.48 (0.5H, m), 7.16-7.19 (1H, m), 7.89 (0.5H, d, J=8.4Hz), 7.94 (0.5H, d, J=8.4Hz), 8.15-8.16 (1H, m), 11.52 (1H, brs). MS: 371 (M+H)+.
104	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.24 (13H, m), 4.31-4.33 (1H, m), 4.52 (1H, s), 6.52-6.53 (1H, m), 7.25-7.27 (1H, m), 8.49 (1H, s), 8.76 (1H, d, J=8.0Hz), 9.25 (1H, s), 11.72 (1H, s). MS: 352 (M+H)+.

Table 72 (contd.)

Ex	Ref -Ex	Data
105	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-2.17 (13H, m), 3.07-3.08 (2H, m), 4.31-4.32 (1H, m), 4.40-4.42 (1H, m), 6.50-6.51 (1H, m), 7.24-7.25 (1H, m), 8.49 (1H, s), 8.84 (1H, d, J=8.0Hz), 9.25 (1H, s), 11.71 (1H, s). MS: 366.3 (M+H) +
106	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.13-2.19 (13H, m), 2.97-3.00 (2H, m), 3.82-3.83 (1H, m), 4.31-4.40 (1H, m), 6.57-6.58 (1H, m), 7.26-7.27 (1H, m), 8.48 (1H, s), 8.78 (1H, d, J=8.0Hz), 9.24-9.25 (1H, m), 11.70 (1H, s). MS: 366 (M+H) +
107	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-2.31 (13H, m), 4.17-4.18 (1H, m), 4.58 (1H, brs), 6.56 (1H, d, J=3.4Hz), 7.22 (1H, d, J=2.7Hz), 7.50-7.57 (5H, m), 8.06 (1H, s), 10.58 (1H, d, J=7.9Hz), 11.82 (1H, brs). MS: 388 (M+H) +.
108	1	¹ H-NMR (400MHz, d6-DMSO) δ : 0.88-2.26 (13H, m), 4.10-4.11 (1H, m), 4.58 (1H, brs), 4.60 (2H, s), 4.82 (2H, s), 6.51-6.52 (1H, s), 7.17-7.18 (1H, s), 7.30-7.38 (5H, m), 10.52 (1H, d, J=7.9Hz), 11.76 (1H, brs). MS: 432 (M+H) +
109	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-2.25 (13H, m), 3.36 (3H, s), 4.10-4.12 (1H, m), 4.57 (1H, s), 4.69 (2H, s), 6.51-6.52 (1H, m), 7.16-7.18 (1H, m), 8.49 (1H, s), 10.51 (1H, d, J=8.0Hz), 11.76 (1H, brs). MS: 356 (M+H) +
110	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.25 (14H, m), 4.10 (1H, d, J=7.9Hz), 5.48 (2H, s), 6.51-6.53 (1H, m), 6.92-6.99 (3H, m), 7.18 (1H, brs), 7.28-7.30 (2H, m), 8.65 (1H, s), 10.44 (1H, d, J=7.9Hz), 11.8 (1H, s). MS: 418 (M+H) +
111	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.19 (13H, m), 4.21-4.23 (1H, m), 4.51 (1H, s), 4.59 (2H, s), 4.80 (2H, s), 6.46-6.48 (1H, m), 7.17-7.18 (1H, m), 7.29-7.37 (6H, m), 10.45 (1H, d, J=8.0Hz), 11.73 (1H, s). MS: 432 (M+H) +
112	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.23-2.33 (13H, m), 2.99-3.11 (2H, m), 4.21 (1H, brs), 4.40-4.41 (1H, m), 4.59 (2H, s), 4.79 (2H, s), 6.51 (1H, brs), 7.16-7.37 (6H, m), 8.51 (1H, s), 10.50 (1H, d, J=8.0Hz), 11.72 (1H, s). MS: 446 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
113	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-2.33 (13H, m), 3.53-3.75 (2H, m), 4.16-4.17 (1H, m), 4.40 (1H, s), 4.87 (1H, s), 6.19-6.20 (1H, m), 6.82 (1H, s), 7.21-7.22 (1H, m), 9.80 (1H, d, J=8.0Hz), 11.64 (1H, s). MS: 398 (M+H) +
114	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-1.52 (2H, m), 1.62 (6H, s), 1.64-2.31 (11H, m), 4.19-4.20 (1H, m), 4.54 (1H, s), 6.27 (1H, s), 6.53 (1H, brs), 7.20-7.22 (1H, m), 8.30 (1H, s), 9.80 (1H, d, J=8.0Hz), 11.64 (1H, brs). MS: 426 (M+H) +
115	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.32 (13H, m), 2.82 (3H, d, J=4.8Hz), 4.27-4.28 (1H, m), 4.52 (1H, s), 6.55-6.57 (1H, m), 7.22-7.23 (1H, m), 8.83 (1H, m), 9.31-9.32 (1H, m), 9.82-9.83 (1H, m), 11.76 (1H, s). MS: 424.9 (M-H) -
116	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.27-2.77 (24H, m), 3.75-3.77 (1H, m), 4.24-4.25 (1H, m), 4.53 (1H, s), 6.55-6.56 (1H, m), 7.23-7.24 (1H, m), 8.38 (1H, s), 9.24 (1H, d, J=8.0Hz), 9.80 (1H, d, J=7.6Hz), 11.77 (1H, brs). MS: 508 (M+H) +
117	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.55-1.61 (2H, m), 1.71-1.75 (2H, m), 1.81-2.05 (10H, m), 4.16-4.21 (1H, m), 6.40-6.43 (1H, m), 6.81-7.06 (1H, br), 7.10-7.13 (1H, m), 7.53-7.91 (1H, br), 8.37 (1H, s), 10.17 (1H, d, J=8.0Hz), 11.44 (1H, brs). MS: 311 (M+H) +.
118	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.64-1.74 (6H, m), 2.02-2.15 (9H, m), 6.66-6.69 (1H, m), 6.96-7.13 (1H, br), 7.15-7.18 (1H, m), 7.66-7.93 (1H, br), 8.33 (1H, s), 9.70 (1H, brs), 11.45 (1H, brs). MS: 311 (M+H) +.
119	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.37-1.43 (2H, m), 1.91-2.10 (11H, m), 3.77-3.81 (1H, m), 4.68-4.70 (1H, m), 6.67-6.70 (1H, m), 6.92-7.14 (1H, br), 7.16-7.19 (1H, m), 7.66-7.91 (1H, br), 8.33 (1H, s), 9.68 (1H, brs), 11.45 (1H, brs). MS: 349 (M+Na) +.

Table 72 (contd.)

Ex	Ref -Ex	Data
120	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.66 (6H, m), 1.88-1.95 (6H, m), 2.21-2.26 (2H, m), 4.63 (1H, brs), 6.63-6.66 (1H, m), 6.93-7.15 (1H, br), 7.17-7.20 (1H, m), 7.70-7.91 (1H, br), 8.34 (1H, s), 9.70 (1H, brs), 11.46 (1H, brs). MS: 349 (M+Na)+.
121	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-1.44 (2H, m), 1.63-1.71 (4H, m), 1.80-1.87 (4H, m), 2.02-2.07 (1H, m), 2.12-2.16 (2H, m), 4.11-4.15 (1H, m), 4.50 (1H, brs), 6.39-6.41 (1H, m), 6.90-7.05 (1H, br), 7.11-7.14 (1H, m), 7.70-7.83 (1H, br), 8.37 (1H, s), 10.09 (1H, d, J=8.0Hz), 11.45 (1H, brs). MS: 327 (M+H)+.
122	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.50 (2H, m), 1.58-1.71 (4H, m), 1.76-1.86 (4H, m), 2.06-2.10 (1H, m), 2.21-2.25 (2H, m), 4.05-4.10 (1H, m), 4.54 (1H, brs), 6.51-6.53 (1H, m), 7.08-7.26 (2H, m), 7.88-8.03 (1H, br), 8.42 (1H, s), 10.43-10.51 (1H, m), 11.80 (1H, s). MS: 327 (M+H)+.
123	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.48 (0.8H, m), 1.49-1.56 (1.2H, m), 1.65-1.97 (8H, m), 2.08-2.16 (1H, m), 2.17-2.23 (0.8H, m), 2.23-2.28 (1.2H, m), 4.05-4.11 (0.6H, m), 4.15-4.20 (0.4H, m), 6.44-6.48 (1H, m), 6.87-7.11 (1H, br), 7.11-7.15 (1H, m), 7.66-7.91 (1H, br), 8.37 (0.4H, s), 8.38 (0.6H, s), 10.12 (0.4H, d, J=8.4Hz), 10.14 (0.6H, d, J=8.4Hz), 11.45 (1H, brs). MS: 341 (M+H)+.
124	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.51 (1H, m), 1.68-1.96 (8H, m), 2.01-2.31 (3H, m), 2.33-2.40 (1H, m), 4.06-4.12 (0.5H, m), 4.21-4.28 (0.5H, m), 6.45-6.53 (1H, m), 6.88-7.20 (2H, m), 7.65-7.95 (1H, br), 8.38 (0.5H, s), 8.39 (0.5H, s), 10.10 (0.5H, d, J=8.4Hz), 10.18 (0.5H, d, J=8.4Hz), 11.48 (1H, brs). MS: 329 (M+H)+.
125	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.48 (2H, m), 1.69-1.78 (4H, m), 1.82-1.98 (4H, m), 2.08-2.13 (1H, m), 2.17-2.23 (2H, m), 3.15 (3H, s), 4.15-4.20 (1H, m), 6.44-6.47 (1H, m), 6.86-7.10 (1H, br), 7.11-7.15 (1H, m), 7.62-7.91 (1H, br), 8.37 (1H, s), 10.12 (1H, d, J=8.4Hz), 11.45 (1H, brs). MS: 341 (M+H)+.

Table 72 (contd.)

Ex	Ref -Ex	Data
126	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-1.56 (2H, m), 1.64-1.75 (4H, m), 1.77-1.95 (4H, m), 2.10-2.15 (1H, m), 2.23-2.28 (2H, m), 3.12 (3H, s), 4.05-4.11 (1H, m), 6.44-6.48 (1H, m), 6.89-7.10 (1H, br), 7.11-7.15 (1H, m), 7.61-7.93 (1H, br), 8.38 (1H, s), 10.14 (1H, d), 11.45 (1H, brs). MS: 341 (M+H)+.
127	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.68-1.76 (4H, m), 1.79-1.89 (4H, m), 2.01-2.09 (2H, m), 2.19-2.25 (1H, m), 2.32-2.38 (2H, m), 4.06-4.12 (1H, m), 6.45-6.49 (1H, m), 6.91-7.18 (2H, m), 7.65-7.92 (1H, br), 8.39 (1H, s), 10.18 (1H, d, J=8.4Hz), 11.48 (1H, brs). MS: 351 (M+Na)+.
128	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.06 (3H, t, J=8.0Hz), 1.53-1.59 (2H, m), 1.68-1.75 (4H, m), 1.80-1.94 (4H, m), 2.10-2.14 (1H, m), 2.24-2.28 (2H, m), 3.42 (2H, q, J=8.0Hz), 4.08-4.13 (1H, m), 6.51-6.53 (1H, m), 7.12-7.31 (2H, m), 7.83-8.03 (1H, br), 8.42 (1H, s), 10.43 (1H, d, J=8.0Hz), 11.74 (1H, brs). MS: 355 (M+H)+.
129	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.53-2.20 (13H, m), 3.58-3.64 (3H, m), 4.19-4.29 (1H, m), 6.54-6.58 (1H, m), 7.19-7.47 (2H, m), 7.96-8.16 (1H, br), 8.46 (1H, s), 10.65-10.72 (1H, m), 11.98 (1H, brs). MS: 369 (M+H)+.
130	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.49 (2H, m), 1.82-1.94 (6H, m), 2.12-2.29 (5H, m), 4.22-4.26 (1H, m), 6.47-6.50 (1H, m), 6.86-7.17 (2H, m), 7.66-7.93 (1H, br), 8.38 (1H, s), 10.10 (1H, d, J=8.0Hz), 11.47 (1H, brs). MS: 329 (M+H)+.
131	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32-1.39 (1H, m), 1.63-1.90 (8H, m), 1.98-2.14 (2H, m), 2.30-2.37 (1H, m), 3.76-3.80 (1H, m), 4.18-4.23 (1H, m), 4.96-5.00 (1H, m), 6.34-6.38 (1H, m), 6.61-7.09 (2H, m), 7.21-7.72 (1H, br), 8.23 (1H, s), 10.03 (1H, d, J=8.0Hz), 11.33 (1H, brs). MS: 327 (M+H)+.

Table 72 (contd.)

Ex	Ref -Ex	Data
132	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.83 (7H, m), 1.87-2.09 (4H, m), 2.19-2.25 (1H, m), 3.88-3.92 (1H, m), 4.53-4.58 (1H, m), 4.97-5.00 (1H, m), 6.75-6.78 (1H, m), 6.80-7.14 (2H, m), 7.59-7.89 (1H, br), 8.35 (1H, s), 10.17 (1H, d, J=8.0Hz), 11.39 (1H, brs). MS: 327 (M+H)+.
133	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.17-1.57 (7H, m), 1.87-1.91 (1H, m), 2.27-2.30 (2H, m), 3.90 (1H, m), 6.57-6.58 (1H, m), 6.88-7.15 (1H, brs), 7.11-7.13 (1H, m), 7.60-7.90 (1H, brs), 8.35 (1H, s), 9.57 (1H, d, J=3.6Hz), 11.45 (1H, s). MS: 271 (M+H)+
134	1	¹ H-NMR (400MHz, d6-DMSO) δ : 0.12-0.15 (2H, m), 0.40-0.44 (2H, m), 0.89-0.92 (2H, m), 1.49-1.72 (8H, m), 1.81-1.91 (4H, m), 2.10 (1H, s), 2.30 (1H, s), 4.12 (1H, s), 4.21 (1H, d, J=7.5Hz), 4.54 (1H, s), 6.53-6.57 (2H, brs), 6.55 (1H, s), 7.24 (1H, m), 7.89 (1H, d, J=7.7Hz), 8.72 (1H, s), 11.63 (1H, s). MS: 435 (M+H)+
135	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.91 (15H, m), 2.10 (1H, s), 2.30 (2H, s), 2.70 (2H, d, J=5.7Hz), 3.58-3.63 (1H, m), 3.72-3.77 (1H, m), 3.88-3.91 (1H, m), 4.12 (2H, s), 4.21 (1H, d, J=7.6Hz), 4.54 (1H, s), 6.54 (1H, d, J=1.7Hz), 7.23-7.24 (1H, m), 7.89 (1H, d, J=7.6Hz), 8.72 (1H, s), 11.62 (1H, s). MS: 465 (M+H)+, 487 (M+Na)+
136	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.24-1.33 (2H, m), 1.48-1.51 (2H, m), 1.64-1.72 (4H, m), 1.79-1.91 (6H, m), 2.10 (1H, s), 2.30 (2H, s), 2.66 (1H, brs), 2.72-2.77 (1H, m), 3.26-3.33 (2H, m), 3.81-3.85 (2H, m), 4.13 (2H, s), 4.21 (1H, d, J=7.5Hz), 4.54 (1H, s), 6.54-6.55 (1H, m), 7.23-7.24 (1H, m), 7.90 (1H, d, J=7.8Hz), 8.71 (1H, s), 11.63 (1H, s). MS: 465 (M+H)+
137	1	¹ H-NMR (400MHz, d6-DMSO) δ : 0.90 (1H, m), 1.48-1.51 (2H, m), 1.63 (2H, s), 1.69-1.72 (2H, m), 1.82-1.91 (4H, m), 2.10 (1H, s), 2.30 (2H, s), 2.79-2.82 (2H, m), 3.25 (3H, s), 3.41-3.44 (2H, m), 4.11 (2H, s), 4.20 (1H, d, J=7.5Hz), 4.54 (1H, s), 6.54 (1H, m), 7.23-7.24 (1H, m), 7.89 (1H, d, J=7.8Hz), 8.71 (1H, s), 11.63 (1H, s). MS: 439 (M+H)+, 461 (M+Na)+

Table 72 (contd.)

Ex	Ref -Ex	Data
138	1	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.52 (2H, m), 1.63 (2H, s), 1.69-1.72 (2H, m), 1.82-1.92 (4H, m), 2.10 (1H, s), 2.30 (2H, s), 2.70-2.73 (2H, m), 3.49-3.50 (2H, m), 4.12 (2H, s), 4.22 (1H, d, J=7.5Hz), 4.55 (2H, s), 6.55 (1H, s), 7.24 (1H, s), 7.89 (2H, d, J=7.8Hz), 8.72 (1H, s), 11.63 (1H, s). MS: 425 (M+H) ⁺ , 447 (M+Na) ⁺
139	2	MS: 343 (M+H) ⁺
140	2	MS: 343 (M+H) ⁺
141	2	MS: 364 (M+H) ⁺
142	2	MS: 300 (M+H) ⁺
143	2	MS: 388 (M+H) ⁺
144	3	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-2.46 (11H, m), 2.64-2.82 (2H, m), 4.47-4.69 (1H, m), 6.33-6.39 (1H, m), 7.41-7.50 (1H, m), 7.89-7.94 (1H, m), 10.77-10.83 (1H, m), 11.59 (1H, s). MS: 421 (M+H) ⁺
145	3	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-1.46 (2H, m), 1.58-1.68 (4H, m), 1.72-1.78 (2H, m), 1.83-1.89 (2H, m), 2.04-2.09 (1H, m), 2.29-2.33 (2H, m), 3.99-4.03 (1H, m), 4.52 (1H, brs), 5.74-5.77 (1H, m), 6.26 (1H, d, J=15.7Hz), 6.43-6.45 (1H, m), 7.16-7.18 (1H, m), 7.87 (1H, d, J=15.7Hz), 8.16 (1H, s), 11.47 (1H, brs), 12.12 (1H, br). MS: 354 (M+H) ⁺
146	3	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.62 (4H, m), 1.69-1.78 (2H, m), 1.90-1.99 (2H, m), 2.09-2.14 (2H, m), 2.19-2.26 (2H, m), 2.77-2.88 (1H, m), 4.47-4.59 (1H, m), 6.43-6.47 (1H, m), 6.85-7.10 (1H, br), 7.20-7.23 (1H, m), 7.57-7.90 (1H, br), 8.34 (1H, s), 9.45 (1H, d, J=8.0Hz), 11.49 (1H, brs), 12.12 (1H, brs). MS: 343 (M+H) ⁺
147	3	MS: 328 (M+H) ⁺
148	3	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.55 (2H, m), 1.58-1.75 (4H, m), 1.77-1.93 (4H, m), 2.05-2.13 (1H, m), 2.22-2.29 (2H, m), 4.09-4.16 (1H, m), 4.60 (1H, s), 6.61 (1H, d, J=3.5Hz), 7.27 (1H, d, J=3.5Hz), 8.63 (1H, s), 11.83-12.00 (1H, m), 12.08 (1H, brs), 13.43 (1H, br). MS: 396 (M+H) ⁺

Table 72 (contd.)

Ex	Ref -Ex	Data
149	3	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-1.50 (2H, m), 1.61-1.71 (4H, m), 1.77-1.86 (4H, m), 2.06-2.10 (1H, m), 2.23-2.27 (2H, m), 4.06-4.11 (1H, m), 4.54 (1H, brs), 6.46-6.50 (1H, m), 7.15-7.18 (1H, m), 8.52 (1H, s), 9.50 (1H, brs), 11.61 (1H, brs), 12.36 (1H, brs). MS: 350 (M+Na)+.
150	3	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.43-1.49 (2H, m), 1.65-1.73 (4H, m), 1.78-1.91 (4H, m), 2.05-2.10 (1H, m), 2.16-2.21 (2H, m), 4.18-4.24 (1H, m), 4.54 (1H, brs), 6.47-6.50 (1H, m), 7.20-7.22 (1H, m), 8.54 (1H, s), 9.65 (1H, d, J=8.0Hz), 11.76 (1H, brs), 12.69 (1H, brs). MS: 328 (M+H)+.
151	3	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.49-2.15 (13H, m), 4.12-4.20 (1H, m), 6.42-6.46 (1H, m), 6.87-7.15 (2H, m), 7.63-7.91 (1H, br), 8.37 (1H, s), 10.14-10.23 (1H, m), 11.45 (1H, brs), 12.13 (1H, brs). MS: 355 (M+H)+.
152	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.50-2.75 (15H, m), 3.21-3.72 (2H, m), 4.48-4.54 (1H, m), 6.33-6.39 (1H, m), 7.43-7.46 (1H, m), 7.75-8.01 (2H, m), 10.76-10.78 (1H, m), 11.58 (1H, s). MS: 405 (M+H)+.
153	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.69-1.77 (2H, m), 1.83-1.92 (4H, m), 2.03-2.12 (3H, m), 2.39-2.48 (2H, m), 2.70-2.75 (2H, m), 3.59 (2H, d, J=5.6Hz), 4.49 (1H, s), 6.34-6.36 (1H, m), 6.99 (1H, s), 7.12 (1H, s), 7.42-7.45 (2H, m), 7.90 (1H, s), 10.76 (1H, s), 11.57 (1H, s). MS: 409 (M+H)+.
154	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.50-1.57 (2H, m), 1.83-1.89 (2H, m), 1.95-2.03 (3H, m), 2.20-2.28 (2H, m), 2.38-2.46 (2H, m), 2.63-2.70 (2H, m), 3.63 (2H, d, J=5.8Hz), 4.54 (1H, s), 6.39-6.40 (1H, m), 6.95-7.25 (3H, m), 7.45 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.77 (1H, br), 11.57 (1H, s). MS: 409 (M+H)+.
155	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.57-2.73 (13H, m), 3.20-3.28 (3H, m), 4.36-4.39 (2H, m), 4.51-4.59 (1H, m), 6.30-6.38 (1H, m), 7.41-7.46 (1H, m), 7.89-7.90 (1H, m), 10.72-10.87 (1H, m), 11.53-11.61 (1H, m). MS: 405 (M+H)+.
156	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.20-1.56 (2H, m), 1.80-2.16 (7H, m), 2.31-2.45 (2H, m), 2.65-2.78 (2H, m), 3.54-3.60 (2H, m), 4.45-4.54 (1H, m), 6.27-6.37 (1H, m), 7.43-7.46 (1H, m), 7.83-7.94 (2H, m), 10.78 (1H, s), 11.58 (1H, s). MS: 391 (M+H)+.

Table 72 (contd.)

Ex	Ref -Ex	Data
157	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-2.70 (17H, m), 3.71-3.84 (1H, m), 4.46-4.56 (1H, m), 6.29-6.39 (1H, m), 7.42-7.44 (1H, m), 7.89-7.91 (1H, m), 10.77-10.81 (1H, m), 11.55-11.59 (1H, m). MS: 417 (M+H) +
158	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-2.87 (13H, m), 4.41-4.72 (1H, m), 6.28-6.42 (1H, m), 7.40-7.48 (1H, m), 7.86-7.93 (1H, m), 8.01-8.11 (1H, m), 8.20-8.32 (1H, m), 10.71-10.82 (1H, m), 11.54-11.63 (1H, m). MS: 420 (M+H) +
159	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.22 (9H, m), 2.36-2.44 (2H, m), 2.63-2.74 (2H, m), 3.06-3.18 (2H, m), 3.36-3.44 (2H, m), 4.46-4.54 (1H, m), 4.61-4.68 (1H, m), 6.35-6.38 (1H, m), 7.24-7.55 (2H, m), 7.90 (1H, s), 10.74-10.76 (1H, m), 11.57 (1H, s). MS: 396 (M+H) +
160	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.35-1.99 (9H, m), 1.50-2.45 (11H, m), 2.63-2.74 (2H, m), 2.92-3.14 (4H, m), 4.46-4.53 (1H, m), 6.32-6.39 (1H, m), 6.78-9.86 (1H, m), 7.32-7.60 (2H, m), 7.90 (1H, s), 10.73-10.79 (1H, m), 11.57 (1H, s). MS: 495 (M+H) +
161	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.59-1.65 (2H, m), 1.85-1.95 (2H, m), 2.05-2.11 (1H, m), 2.13-2.21 (2H, m), 2.35-2.47 (6H, m), 5.16 (1H, d, J=8.7Hz), 7.13 (1H, br), 7.91 (1H, br), 8.08 (1H, s), 8.47 (1H, s), 9.98 (1H, d, J=8.7Hz), 12.81 (1H, br). MS: 390, 392 (M+H) +
162	4	MS: 479 (M+H) +
163	4	MS: 465 (M+H) +
164	4	MS: 508 (M+H) +
165	4	MS: 492 (M+H) +
166	4	MS: 508 (M+H) +
167	4	MS: 488 (M+H) +
168	4	MS: 513 (M+H) +
169	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.78-1.89 (4H, m), 2.04-2.11 (1H, m), 2.22-2.25 (4H, m), 2.30-2.35 (2H, m), 2.51-2.56 (2H, m), 5.05 (1H, d, J=8.7Hz), 7.20 (1H, br), 7.95 (1H, br), 8.07 (1H, s), 8.49 (1H, s), 10.17 (1H, d, J=8.7Hz), 12.81 (1H, br). MS: 390, 392 (M+H) +
170	4	MS: 353 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
171	4	MS: 390 (M+H) +
172	4	MS: 434 (M+H) +
173	4	MS: 417 (M+H) +
174	4	MS: 369 (M+H) +
175	4	MS: 369 (M+H) +
176	4	MS: 355 (M+H) +
177	4	MS: 433 (M+H) +
178	4	MS: 423 (M+H) +
179	4	MS: 433 (M+H) +
180	4	MS: 419 (M+H) +
181	4	MS: 558 (M+Na) +
182	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-2.34 (12H, m), 3.09 (3H, s), 4.08 (2H, s), 4.44 (1H, s), 4.50 (1H, m), 5.00 (1H, m), 8.04 (1H, s), 9.11 (1H, s), 10.18 (1H, m), 11.11 (1H, m), 12.80 (1H, s). MS: 424 (M+H) +
183	4	MS: 434 (M+H) +. MS: 432 (M-H) -
184	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43 (9H, s), 1.68-1.84 (2H, m), 1.84-2.13 (4H, m), 2.13-2.31 (2H, m), 4.04-4.17 (2H, m), 4.30-4.39 (1H, m), 6.44-6.49 (1H, m), 7.01 (1H, br), 7.06-7.12 (1H, m), 7.77 (1H, br), 8.37 (1H, s), 10.24 (1H, d, J=7.6Hz), 11.43 (1H, s). MS: 386 (M+H) +
185	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.76-2.40 (8H, m), 3.95 (1H, d, J=18.8Hz), 4.05 (1H, d, J=18.8Hz), 4.13-4.24 (1H, m), 4.29-4.41 (1H, m), 4.44-4.55 (1H, m), 6.39-6.47 (1H, m), 7.04 (1H, br), 7.08-7.15 (1H, m), 7.80 (1H, br), 8.38 (1H, s), 10.28 (1H, d, J=7.6Hz), 11.46 (1H, s). MS: 353 (M+H) +
186	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.72-2.52 (8H, m), 3.94-4.09 (1H, m), 4.37-4.48 (1H, m), 4.58-4.73 (1H, m), 6.45-6.51 (1H, m), 7.02 (1H, br), 7.07-7.14 (1H, m), 7.42-7.56 (5H, m), 7.79 (1H, br), 8.37 (1H, s), 10.29 (1H, d, J=7.7Hz), 11.45 (1H, s). MS: 390 (M+H) +
187	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.30-1.50 (11H, m), 1.67-2.22 (6H, m), 4.12 (2H, brs), 5.40-5.55 (1H, m), 7.10 (1H, brs), 7.82 (1H, brs), 8.10 (1H, s), 8.43 (1H, s), 9.28 (1H, d, J=8.6Hz), 12.8 (1H, brs). MS: 387 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
188	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 0.96-2.19 (13H, m), 4.09-4.19 (1H, m), 6.42-6.43 (1H, m), 6.55-6.57 (1H, m), 7.11-7.14 (1H, m), 7.63-7.65 (1H, m), 7.86-7.89 (1H, m), 7.86-7.89 (1H, m), 8.20 (1H, s), 8.37 (1H, d, J=2.8Hz), 10.11-10.23 (1H, m), 11.47 (1H, s), 12.16 (1H, s) ..MS: 393 (M+H) +
189	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.42-1.60 (4H, m), 1.70-1.83 (4H, m), 2.05-2.11 (2H, m), 2.19-2.26 (2H, m), 2.76-2.87 (1H, m), 4.54-4.66 (1H, m), 6.53-6.56 (1H, m), 6.71 (1H, brs), 6.88-7.10 (1H, br), 7.19-7.22 (1H, m), 7.35 (1H, brs), 7.60-7.85 (1H, br), 8.34 (1H, s), 9.45 (1H, d, J=8.0Hz), 11.46 (1H, brs) .MS: 364 (M+Na) +.
190	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.49-2.13 (13H, m), 4.10-4.21 (1H, m), 6.43-6.46 (1H, m), 6.73-6.78 (1H, m), 6.92-7.14 (3H, m), 7.61-7.95 (1H, br), 8.37-8.39 (1H, m), 10.11-10.18 (1H, m), 11.46 (1H, brs) .MS: 354 (M+H) +
191	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.47-1.53 (2H, m), 1.78-1.96 (7H, m), 2.00-2.10 (4H, m), 4.16-4.21 (1H, m), 6.44-6.46 (1H, m), 6.76 (1H, brs), 6.88-7.13 (3H, m), 7.62-7.90 (1H, br), 8.37 (1H, s), 10.17 (1H, d, J=8.0Hz), 11.45 (1H, brs) .MS: 376 (M+Na) +.
192	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.69-1.98 (11H, m), 2.10-2.15 (2H, m), 4.10-4.15 (1H, m), 6.43-6.46 (1H, m), 6.75 (1H, brs), 6.90-7.09 (2H, m), 7.11-7.15 (1H, m), 7.66-7.93 (1H, br), 8.37 (1H, s), 10.13 (1H, d, J=8.0Hz), 11.46 (1H, brs) .MS: 354.2 (M+H) +.
193	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.40-1.86 (10H, m), 2.05 (1H, brs), 2.19 (2H, brs), 4.48 (1H, s), 4.94 (1H, d, J=8.7Hz), 7.09 (1H, brs), 7.83 (1H, brs), 8.04 (1H, s), 8.45 (1H, s), 9.97 (1H, d, J=8.7Hz), 12.8 (1H, brs) .MS: 328 (M+H) +
194	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.40-1.89 (10H, m), 2.11 (1H, brs), 2.18 (2H, brs), 3.15 (3H, s), 5.04 (1H, d, J=8.8Hz), 7.10 (1H, brs), 7.82 (1H, brs), 8.06 (1H, s), 8.46 (1H, s), 9.98 (1H, d, J=8.8Hz), 12.7 (1H, brs) .MS: 342 (M+H) +
195	4	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.40-1.65 (2H, m), 1.80-2.15 (6H, m), 3.90-4.10 (2H, m), 4.20 (1H, brs), 4.55 (1H, brs), 5.45-5.55 (1H, m), 7.18 (1H, brs), 7.81 (1H, brs), 8.11 (1H, s), 8.25 (1H, s), 9.25 (1H, d, J=9.1Hz), 12.8 (1H, brs) .MS: 376 (M+Na) +

Table 72 (contd.)

Ex	Ref -Ex	Data
196	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.2-2.1 (14H, m), 2.73 (1H, s), 2.89 (1H, s), 3.7-4.6 (4H, m), 6.4-6.5 (1H, m), 7.1-7.5 (1H, m), 7.9-8.0 (1H, m), 8.3-8.4 (1H, m), 10.1-10.2 (1H, m), 11.46 (1H, s). MS: 497.2 (M+H) +.
197	4	MS: 385 (M+H) +
198	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.52-2.23 (13H, m), 3.23-3.34 (3H, m), 4.12-4.47 (3H, m), 6.47-6.58 (1H, m), 6.94-7.14 (2H, m), 7.81 (1H, brs), 8.34-8.47 (1H, m), 10.12-10.27 (1H, m, J=11.44Hz), 11.44 (1H, s). MS: 393 (M+H) +.
199	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.56-2.31 (14H, m), 2.77 (3H, d, J=4.4Hz), 4.16-4.18 (1H, m), 6.43 (1H, s), 7.14-7.16 (1H, s), 8.31-8.40 (1H, s), 9.96-9.98 (1H, s), 11.48 (1H, s). MS: 350 (M+H) +
200	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-2.34 (14H, m), 2.74 (3H, d, J=4.0Hz), 4.2-4.3 (1H, m), 6.50-6.52 (1H, m), 7.13-7.15 (1H, m), 8.25-8.26 (1H, m), 9.92-9.95 (1H, m), 11.46 (1H, s). MS: 350 (M+H) +
201	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.54 (2H, m), 1.62-1.74 (4H, m), 1.81-1.92 (4H, m), 2.08-2.11 (1H, m), 2.28-2.31 (2H, m), 3.36-3.44 (2H, m), 3.48-3.76 (6H, m), 4.04, 4.12 (2H, s), 4.20-4.24 (1H, m), 4.40, 4.50 (1H, s), 6.58-6.61 (1H, m), 7.27-7.30 (1H, m), 8.65 (1H, s), 8.83-8.86 (1H, m), 11.90 (1H, brs). MS: 531 (M+H) +
202	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.57-2.20 (8H, m), 2.42 (3H, s), 4.05-4.06 (2H, m), 4.26-4.27 (1H, m), 4.58 (2H, s), 6.66-6.67 (1H, m), 7.31-7.32 (1H, m), 8.43 (1H, d, J=8.0 Hz), 8.57 (1H, s), 11.88 (1H, brs). MS: 392.2 (M+H) +
203	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.31-1.50 (4H, m), 1.54-1.72 (8H, m), 1.72-1.89 (4H, m), 2.03-2.11 (1H, m), 2.16-2.25 (2H, m), 2.75-2.87 (4H, m), 3.98-4.06 (1H, m), 4.53 (1H, s), 6.41-6.47 (1H, m), 7.10-7.15 (1H, m), 8.27 (1H, s), 9.09 (1H, brs), 9.52 (1H, d, J=6.8Hz), 11.46 (1H, brs). MS: 410 (M+H) +
204	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-1.81 (16H, m), 2.02-2.10 (1H, m), 2.14-2.22 (2H, m), 3.45-3.56 (4H, m), 3.93-4.01 (1H, m), 4.50 (1H, s), 6.44-6.48 (1H, m), 6.97 (1H, d, J=8.4Hz), 7.16-7.21 (1H, m), 7.80 (1H, s), 11.46 (1H, brs). MS: 395 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
205	4	¹ H-NMR (400MHz, d6-DMSO) δ : 0.93-1.88 (20H, m), 2.01-2.09 (1H, m), 2.12-2.22 (2H, m), 3.85-4.03 (2H, m), 4.48 (1H, s), 4.59 (2H, s), 6.42-6.47 (1H, m), 7.11 (1H, d, J=8.0Hz), 7.13-7.18 (1H, m), 7.94 (1H, s), 11.40 (1H, brs). MS: 424 (M+H) +
206	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.04-1.92 (20H, m), 2.03-2.12 (1H, m), 2.15-2.27 (2H, m), 2.65-2.77 (1H, m), 3.98-4.08 (1H, m), 4.51 (1H, s), 4.90-5.01 (1H, m), 6.40-6.47 (1H, m), 7.10-7.16 (1H, m), 8.27 (1H, s), 9.47 (1H, d, J=8.1Hz), 9.66-9.74 (1H, m), 11.47 (1H, s). MS: 424 (M+H) +
207	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42-1.49 (2H, m), 1.58-1.72 (4H, m), 1.75-1.88 (4H, m), 1.92 (3H, s), 2.04-2.10 (1H, m), 2.18-2.25 (2H, m), 4.03-4.08 (1H, m), 4.52 (1H, s), 6.44-6.48 (1H, m), 7.14-7.17 (1H, m), 8.42 (1H, s), 9.65 (1H, d, J=8.0Hz), 9.76 (1H, s), 9.99 (1H, brs), 11.52 (1H, brs). MS: 384 (M+H) +
208	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.88-2.47 (8H, m), 2.42 (3H, s), 3.98 (1H, d, J=18.9Hz), 4.08 (1H, d, J=18.9Hz), 4.20-4.26 (1H, m), 4.48-4.57 (2H, m), 6.56-6.61 (1H, m), 7.23-7.28 (1H, m), 8.58 (1H, s), 9.17 (1H, d, J=7.6Hz), 11.83 (1H, s). MS: 392 (M+H) +
209	4	¹ H-NMR (400MHz, d6-DMSO) δ : 1.81-1.94 (4H, m), 2.11 (1H, m), 2.46-2.51 (3H, m), 4.13 (2H, s), 4.39 (1H, s), 4.71 (1H, s), 4.97 (1H, m), 6.26 (1H, s), 7.36-7.44 (1H, m), 7.94 (1H, s), 11.02 (1H, brs), 11.65 (1H, s). MS: 373 (M+Na) +
210	4	MS: 439 (M+H) +
211	4	MS: 493 (M+H) +
212	4	MS: 404 (M+H) +
213	4	MS: 404 (M+H) +
214	4	MS: 415 (M+H) +
215	4	MS: 415 (M+H) +
216	4	MS: 415 (M+H) +
217	4	MS: 408 (M+H) +
218	4	MS: 420 (M+H) +
219	4	MS: 420 (M+H) +
220	4	MS: 432 (M+H) +
221	4	MS: 448 (M+H) +
222	4	MS: 328 (M+H) +
223	4	MS: 342 (M+H) +
224	4	MS: 344 (M+H) +
225	4	MS: 354 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
226	4	MS: 356 (M+H) +
227	4	MS: 358 (M+H) +
228	4	MS: 370 (M+H) +
229	4	MS: 371 (M+H) +
230	4	MS: 391 (M+H) +
231	4	MS: 391 (M+H) +
232	4	MS: 391 (M+H) +
233	4	MS: 396 (M+H) +
234	4	MS: 397 (M+H) +
235	4	MS: 405 (M+H) +
236	4	MS: 422 (M+H) +
237	4	MS: 434 (M+H) +
238	4	MS: 468 (M+H) +
239	4	MS: 483 (M+H) +
240	4	MS: 385 (M+H) +
241	4	MS: 398 (M+H) +
242	4	MS: 413 (M+H) +
243	4	MS: 384 (M+H) +
244	4	MS: 399 (M+H) +
245	4	MS: 425 (M+H) +
246	4	MS: 424 (M+H) +
247	4	MS: 450 (M+H) +
248	4	MS: 411 (M+H) +
249	4	MS: 415 (M+H) +
250	4	MS: 425 (M+H) +
251	4	MS: 411 (M+H) +
252	4	MS: 438 (M+H) +
253	4	¹ H-NMR (400MHz, d6-DMSO) δ : 0.81 (3H, s), 0.91 (3H, s), 0.99 (3H, s), 0.87-1.31 (3H, m), 1.34-1.52 (3H, m), 2.33-2.49 (1H, m), 4.13-4.28 (1H, m), 6.42 (1H, d, J=2.6Hz), 6.72-7.94 (3H, m), 8.36 (1H, s), 10.09 (1H, d, J=8.4Hz), 11.46 (1H, brs). MS: 313 (M+H) +
254	4	MS: 440 (M+H) +
255	4	MS: 398 (M+H) +
256	4	MS: 435 (M+H) +
257	4	MS: 435 (M+H) +
258	4	MS: 435 (M+H) +
259	4	MS: 442 (M+H) +
260	4	MS: 407 (M+H) +
261	4	MS: 403 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
262	4	MS: 410 (M+H) +
263	4	MS: 411 (M+H) +
264	4	MS: 447 (M+H) +
265	4	MS: 432 (M+H) +
266	4	MS: 447 (M+H) +
267	4	MS: 432 (M+H) +
268	7	MS: 469 (M+H) +
269	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.35 (10H, m), 3.39 (2H, m), 3.76-4.13 (5H, m), 4.23 (1H, m), 4.54 (1H, s), 6.56 (1H, m), 7.26 (1H, m), 7.74 (1H, m), 8.80 (1H, s), 9.41 (1H, m), 11.69 (1H, s). MS: 479 (M+H) +
270	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.48 (14H, m), 3.41 (2H, m), 4.23 (1H, m), 4.55 (1H, s), 6.57 (1H, m), 7.26 (1H, m), 7.72 (1H, m), 8.78 (1H, s), 9.30 (1H, m), 11.69 (1H, s). MS: 466 (M+H) +
271	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-2.32 (12H, m), 3.45 (2H, m), 3.85 (2H, m), 4.01 (1H, m), 4.23 (1H, m), 4.56 (1H, s), 4.87 (1H, m), 6.56 (1H, m), 7.26 (1H, m), 7.72 (1H, m), 8.71 (1H, s), 11.71 (1H, s). MS: 479 (M+H) +
272	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.47 (14H, m), 3.67-3.78 (4H, m), 4.24 (1H, m), 4.56 (1H, s), 6.56 (1H, m), 7.25 (1H, m), 7.71 (1H, m), 8.71 (1H, s), 11.71 (1H, s). MS: 478 (M+H) +
273	7	MS: 550 (M+H) +
274	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.38 (13H, m), 3.55 (4H, m), 3.99 (1H, m), 4.23 (1H, m), 4.51 (1H, s), 4.82 (2H, m), 6.60 (1H, m), 7.27 (1H, m), 8.17 (1H, m), 8.65 (1H, m), 8.84 (1H, m), 11.88 (1H, s). MS: 469 (M+H) +
275	7	MS: 469 (M+H) +
276	7	MS: 556 (M+H) +
277	7	MS: 505 (M+Na) +
278	7	MS: 491 (M+Na) +
279	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42 (9H, s), 1.44-2.38 (7H, m), 2.85 (2H, m), 3.89-4.05 (4H, m), 4.22 (1H, m), 4.38 (1H, s), 6.60 (1H, m), 7.27 (1H, m), 8.31 (1H, m), 8.73 (1H, m), 8.89 (1H, m), 11.87 (1H, s). MS: 600 (M+Na) +

Table 72 (contd.)

Ex	Ref -Ex	Data
280	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.51 (2H, m), 1.61-1.64 (2H, m), 1.67-1.73 (2H, m), 1.81-1.87 (2H, m), 1.93-1.99 (2H, m), 2.08-2.12 (1H, m), 2.32-2.36 (2H, m), 4.19-4.23 (1H, m), 4.46 (1H, s), 6.60 (1H, d, J=3.6Hz), 7.28 (1H, d, J=3.6Hz), 8.17-8.21 (2H, m), 8.64 (1H, s), 8.88 (1H, d, J=7.5Hz), 11.88 (1H, brs). MS: 395 (M+H) +
281	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.53 (2H, m), 1.62-1.65 (2H, m), 1.67-1.74 (2H, m), 1.81-1.92 (4H, m), 2.08-2.12 (1H, m), 2.28-2.32 (2H, m), 3.06 (3H, s), 3.11 (3H, s), 4.19-4.23 (1H, m), 4.50 (1H, s), 6.59 (1H, d, J=3.6Hz), 7.28 (1H, d, J=3.6Hz), 8.65 (1H, s), 8.88 (1H, d, J=7.6Hz), 11.89 (1H, brs). MS: 423 (M+H) +
282	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.5-2.2 (14H, m), 2.98 (3H, s), 3.00 (3H, s), 4.11-4.18 (1H, m), 6.44-6.48 (1H, m), 7.11-7.12 (1H, m), 7.39-7.56 (1H, m), 7.70-7.73 (1H, m), 8.31 (1H, s), 8.37-8.38 (1H, m), 10.16-10.18 (1H, m), 11.46 (1H, brs). MS: 382.3 (M+H) +.
283	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.54 (2H, m), 1.61-1.65 (2H, m), 1.68-1.74 (2H, m), 1.82-1.93 (4H, m), 2.08-2.12 (1H, m), 2.29-2.33 (2H, m), 3.56-3.63 (4H, m), 3.68-3.70 (4H, m), 4.20-4.24 (1H, m), 4.52 (1H, s), 6.59 (1H, d, J=3.6Hz), 7.29 (1H, d, J=3.6Hz), 8.64 (1H, s), 8.84 (1H, d, J=7.8Hz), 11.89 (1H, brs). MS: 487 (M+Na) +
284	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.53 (2H, m), 1.62-1.65 (2H, m), 1.68-1.73 (2H, m), 1.81-1.92 (4H, m), 2.08-2.12 (1H, m), 2.28-2.33 (2H, m), 2.68-2.72 (2H, m), 2.75-2.79 (2H, m), 3.40-3.43 (2H, m), 3.59-3.62 (2H, m), 4.19-4.22 (1H, m), 4.51 (1H, brs), 6.57-6.60 (1H, m), 7.27-7.29 (1H, m), 8.64 (1H, s), 8.83-8.86 (1H, m), 11.89 (1H, brs). MS: 464 (M+H) +
285	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.54 (2H, m), 1.63-1.65 (2H, m), 1.69-1.74 (2H, m), 1.82-1.92 (4H, m), 2.09-2.12 (1H, m), 2.30-2.33 (2H, m), 2.86 (3H, s), 4.22-4.25 (1H, m), 4.55 (1H, brs), 6.57 (1H, d, J=3.6Hz), 7.27 (1H, d, J=3.6Hz), 7.71-7.74 (1H, m), 8.78 (1H, s), 9.38 (1H, brs), 11.68 (1H, brs). MS: 409 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
286	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.51 (2H, m), 1.61-1.64 (2H, m), 1.67-1.73 (2H, m), 1.81-1.87 (2H, m), 1.93-1.99 (2H, m), 2.08-2.12 (1H, m), 2.32-2.36 (2H, m), 4.19-4.23 (1H, m), 4.46 (1H, s), 6.60 (1H, d, J=3.6Hz), 7.28 (1H, d, J=3.6Hz), 8.17-8.21 (2H, m), 8.64 (1H, s), 8.88 (1H, d, J=7.5Hz), 11.88 (1H, brs). MS: 395 (M+H) +
287	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.53 (2H, m), 1.63-1.80 (8H, m), 1.82-1.99 (6H, m), 2.09-2.12 (1H, m), 2.17 (3H, s), 2.30-2.33 (2H, m), 2.76-2.81 (2H, m), 3.73-3.79 (1H, m), 4.22-4.25 (1H, m), 4.53 (1H, s), 6.56-6.57 (1H, m), 7.25-7.27 (1H, m), 7.74-7.76 (1H, m), 8.80 (1H, s), 9.33-9.36 (1H, m), 11.68 (1H, brs). MS: 492 (M+H) +
288	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-1.55 (2H, m), 1.63-1.66 (2H, m), 1.69-1.75 (2H, m), 1.82-1.93 (4H, m), 2.09-2.12 (1H, m), 2.30-2.33 (2H, m), 3.67-3.73 (6H, m), 3.83-3.86 (2H, m), 4.22-4.26 (1H, m), 4.52 (1H, s), 6.55-6.57 (1H, m), 7.24-7.26 (1H, m), 7.70-7.73 (1H, m), 8.72 (1H, s), 11.68 (1H, brs). MS: 465 (M+H) +
289	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-1.54 (2H, m), 1.63-1.65 (2H, m), 1.69-1.75 (2H, m), 1.82-1.93 (4H, m), 2.09-2.12 (1H, m), 2.30-2.33 (2H, m), 3.10 (3H, s), 3.25 (3H, s), 4.22-4.26 (1H, m), 4.52 (1H, s), 6.55-6.57 (1H, m), 7.24-7.26 (1H, m), 7.71-7.73 (1H, m), 8.72 (1H, s), 11.67 (1H, brs). MS: 423 (M+H) +
290	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.42 (9H, m), 1.48-1.57 (4H, m), 1.63-1.74 (4H, m), 1.78-1.92 (6H, m), 2.09-2.12 (1H, m), 2.30-2.32 (2H, m), 2.79-2.90 (1H, m), 3.33-3.39 (2H, m), 3.93-4.02 (2H, m), 4.22-4.26 (1H, m), 4.53 (1H, s), 6.56-6.58 (1H, m), 7.25-7.27 (1H, m), 7.73-7.76 (1H, m), 8.79 (1H, s), 9.37-9.40 (1H, m), 11.68 (1H, brs). MS: 578 (M+H) +
291	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.54 (2H, m), 1.63-1.65 (2H, m), 1.69-1.74 (2H, m), 1.82-2.00 (6H, m), 2.09-2.12 (1H, m), 2.30-2.33 (2H, m), 3.33-3.62 (2H, m), 3.79-4.01 (2H, m), 4.22-4.25 (1H, m), 4.54, 4.55 (1H, m), 4.72-4.73 (1H, m), 5.00-5.01, 5.55-5.56 (1H, m), 6.55-6.57 (1H, m), 7.25-7.26 (1H, m), 7.71-7.74 (1H, m), 8.73, 8.74 (1H, s), 11.72 (1H, m). MS: 477 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
292	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.52 (2H, m), 1.67-1.75 (4H, m), 1.87-1.93 (4H, m), 2.08-2.12 (1H, m), 2.23-2.26 (2H, m), 2.85 (3H, d, J=4.7Hz), 3.17 (1H, s), 4.33-4.37 (1H, m), 6.53-6.55 (1H, m), 7.27-7.29 (1H, m), 7.74-7.77 (1H, m), 8.78 (1H, s), 9.37-9.41 (1H, m), 11.72 (1H, brs). MS: 409 (M+H) +
293	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.31 (13H, m), 3.28 (3H, s), 3.47-3.52 (4H, m), 4.22-4.23 (1H, m), 4.52 (1H, brs), 6.55-6.57 (1H, m), 7.25-7.26 (1H, m), 7.71-7.73 (1H, m), 8.78 (1H, s), 9.42 (1H, brs), 11.66 (1H, brs). MS: 453 (M+H) +
294	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.08 (3H, d, J=6.0Hz), 1.49-2.32 (13H, m), 3.16-3.27 (2H, m), 3.84-3.86 (1H, m), 4.23-4.24 (1H, m), 4.52 (1H, s), 4.82 (1H, d, J=4.8Hz), 6.55-6.57 (1H, m), 7.25-7.27 (1H, m), 7.72-7.74 (1H, m), 8.78 (1H, s), 9.26-9.27 (1H, m), 11.66 (1H, brs). MS: 453 (M+H) +
295	7	¹ H-NMR (400MHz, d6-DMSO) δ : 1.02-2.31 (18H, m), 3.20-3.24 (4H, m), 3.83-3.84 (2H, m), 4.23-4.24 (1H, m), 4.52 (1H, brs), 6.56-6.57 (1H, m), 7.24-7.26 (1H, m), 7.72-7.74 (1H, m), 8.78 (1H, s), 9.45-9.46 (1H, m), 11.66 (1H, brs). MS: 493 (M+H) +
296	8	MS: 439 (M+H) +
297	8	MS: 453 (M+H) +
298	8	MS: 453 (M+H) +
299	8	MS: 466 (M+H) +
300	8	MS: 452 (M+H) +
301	8	MS: 463 (M+H) +
302	8	MS: 479 (M+H) +
303	8	MS: 488 (M+H) +
304	8	MS: 460 (M+H) +
305	8	MS: 465 (M+H) +
306	8	MS: 479 (M+H) +
307	8	MS: 506 (M+H) +
308	8	MS: 506 (M+H) +
309	8	MS: 478 (M+H) +
310	8	MS: 477 (M+H) +
311	8	MS: 493 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
312	8	MS: 479 (M+H) +
313	8	MS: 492 (M+H) +
314	8	MS: 479 (M+H) +
315	8	MS: 493 (M+H) +
316	8	MS: 506 (M+H) +
317	8	MS: 508 (M+H) +
318	8	MS: 541 (M+H) +
319	8	MS: 546 (M+H) +
320	8	MS: 434 (M+H) +
321	8	MS: 499 (M+H) +
322	8	MS: 423 (M+H) +
323	8	MS: 352 (M+H) +
324	8	MS: 452 (M+H) +
325	8	MS: 467 (M+H) +
326	8	MS: 483 (M+H) +
327	8	MS: 475 (M+H) +
328	8	MS: 486 (M+H) +
329	8	MS: 486 (M+H) +
330	8	MS: 486 (M+H) +
331	8	MS: 492 (M+H) +
332	8	MS: 493 (M+H) +
333	8	MS: 506 (M+H) +
334	8	MS: 509 (M+H) +
335	8	MS: 477 (M+H) +
336	8	MS: 556 (M+H) +
337	8	MS: 513 (M+H) +
338	8	MS: 527 (M+H) +
339	8	MS: 508 (M+H) +
340	8	MS: 479 (M+H) +
341	8	MS: 504 (M+H) +
342	8	MS: 449 (M+H) +
343	8	¹ H-NMR (400MHz, d6-DMSO) δ : 1.92-2.32 (8H, m), 2.49 (3H, s), 3.58-4.57 (5H, m), 6.76-6.77 (1H, m), 7.39-7.40 (1H, m), 8.69 (1H, s), 8.79-9.05 (3H, m), 12.20 (1H, brs). MS: 325 (M+H) +
344	10	MS: 542 (M+H) +
345	10	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-2.39 (9H, m), 2.79 (6H, s), 2.81 (2H, m), 3.57 (2H, m), 3.99 (1H, m), 4.21 (1H, m), 4.40 (1H, s), 6.59 (1H, m), 7.27 (1H, m), 8.64 (1H, s), 8.76 (1H, m), 8.90 (1H, m), 11.89 (1H, s). MS: 571 (M+Na) +

Table 72 (contd.)

Ex	Ref -Ex	Data
346	10	MS: 585 (M+H) +
347	10	MS: 535 (M+H) +
348	13	¹ H-NMR (400MHz, d6-DMSO) δ : 1.30 (3H, t, J=7.1Hz), 1.45-1.54 (2H, m), 1.58-1.75 (4H, m), 1.77-1.89 (4H, m), 2.06-2.12 (1H, m), 2.23-2.29 (2H, m), 4.09-4.15 (1H, m), 4.30 (2H, q, J=7.1Hz), 4.58 (1H, s), 6.49-9.53 (1H, m), 7.10 (2H, brs), 7.17-7.21 (1H, m), 8.90 (1H, s), 9.33 (1H, d, J=7.8Hz), 11.72 (1H, brs). MS: 442 (M+H) +
349	13	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43 (9H, s), 1.71-1.85 (2H, m), 1.80 (3H, s), 1.90-2.09 (4H, m), 2.17-2.32 (2H, m), 4.08-4.17 (2H, m), 4.38-4.46 (1H, m), 6.45 (2H, brs), 6.50-6.56 (1H, m), 7.12-7.17 (1H, m), 8.77 (1H, s), 9.51 (1H, d, J=7.6Hz), 11.64 (1H, s). MS: 443 (M+H) +
350	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.55 (2H, m), 1.79-1.82 (2H, m), 1.86-1.99 (5H, m), 2.02-3.15 (4H, m), 4.09 (2H, d, J=5.5Hz), 4.17-4.23 (1H, m), 6.44-6.47 (1H, m), 7.00 (1H, br), 7.11-7.14 (1H, m), 7.78 (1H, br), 8.28 (1H, t, J=5.4Hz), 8.38 (1H, s), 10.18 (1H, d, J=8.2Hz), 11.46 (1H, s). MS: 393 (M+H) +
351	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.71-2.03 (11H, m), 2.13-2.17 (2H, m), 4.06 (2H, d, J=5.5Hz), 4.12-4.16 (1H, m), 6.43-6.46 (1H, m), 6.99 (1H, br), 7.11-7.15 (1H, m), 7.77 (1H, br), 8.21 (1H, d, J=5.5Hz), 8.37 (1H, s), 10.18 (1H, d), 11.46 (1H, s). MS: 393 (M+H) +
352	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.37-1.39 (9H, m), 1.43-1.48 (2H, m), 1.68-2.03 (8H, m), 2.05-2.19 (3H, m), 4.04-4.17 (1H, m), 6.36-6.56 (2H, m), 6.87-7.16 (2H, m), 7.76 (1H, br), 8.36-8.38 (1H, m), 10.11-10.15 (1H, m), 11.44 (1H, m). MS: 426 (M+H) +
353	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.14-2.21 (13H, m), 4.02-4.04 (1H, m), 4.36 (2H, brs), 4.48 (1H, s), 6.43-6.33 (1H, m), 7.12-7.13 (1H, m), 8.28 (1H, s), 9.48 (1H, s), 9.67 (1H, d, J=8.0Hz), 11.42 (1H, brs). MS: 342 (M+H) +
354	14	MS: 366 (M+H) +
355	14	MS: 418 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
356	14	MS: 418 (M+H) +
357	14	MS: 418 (M+H) +
358	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.22 (8H, m), 3.70 (3H, s), 4.04 (1H, m), 4.53 (1H, s), 6.45 (1H, m), 7.15 (1H, m), 8.16 (1H, s), 9.41 (1H, s), 11.41 (1H, s), 11.51 (1H, s). MS: 357 (M+H) +
359	14	MS: 355 (M+H) +, 353 (M-H) -
360	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.09-2.23 (16H, m), 3.28 (2H, m), 4.48 (1H, s), 4.96 (1H, m), 8.05 (1H, s), 8.31 (1H, m), 8.40 (1H, s), 9.73 (1H, m), 12.73 (1H, s). MS: 356 (M+H) +
361	14	¹ H-NMR (400MHz, d6-DMSO) δ : 1.22-2.34 (13H, m), 4.29 (2H, m), 4.51 (1H, s), 5.01 (1H, m), 8.08 (1H, s), 8.43 (1H, s), 8.99 (1H, m), 9.65 (1H, m), 12.86 (1H, s). MS: 367 (M+H) +
362	14	MS: 377 (M-H) -
363	15	MS: 408 (M+Na) +, 384 (M-H) -
364	16	¹ H-NMR (400MHz, d6-DMSO) δ : 0.80-2.84 (13H, m), 4.60-4.69 (1H, m), 7.43-7.47 (1H, m), 7.90-7.92 (1H, m), 8.91-8.94 (1H, m), 10.78-10.85 (1H, m), 11.55-11.65 (1H, m). MS: 402 (M+H) +
365	16	¹ H-NMR (400MHz, d6-DMSO) δ : 1.90-1.97 (4H, m), 2.03-2.12 (5H, m), 2.62-2.67 (2H, m), 2.74-2.79 (2H, m), 4.54 (1H, s), 6.34-6.35 (1H, m), 7.45 (1H, t, J=3.1Hz), 7.91 (1H, s), 10.86 (1H, s), 11.61 (1H, s). MS: 334 (M+H) +
366	17	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-1.83 (10H, m), 2.07 (1H, brs), 2.29 (2H, brs), 4.57 (1H, s), 4.67-4.77 (1H, m), 5.95-6.02 (1H, m), 8.245 (1H, s), 8.249 (1H, s), 13.1 (1H, brs). MS: 332 (M+Na) +
367	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.52-1.61 (2H, m), 1.72-1.92 (3H, m), 1.99-2.13 (4H, m), 2.22-2.41 (3H, m), 2.64-2.74 (2H, m), 2.80-2.93 (2H, m), 3.26-3.38 (2H, m), 4.57-4.64 (1H, m), 6.52-6.59 (1H, m), 7.58-7.63 (1H, m), 7.82-7.91 (2H, m), 7.96. MS: 395 (M+H) +
368	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.50-1.59 (2H, m), 1.72-1.99 (6H, m), 2.05-2.17 (2H, m), 2.24-2.36 (2H, m), 4.21-4.30 (1H, m), 6.52-6.66 (1H, m), 7.31-7.39 (1H, m), 7.62 (1H, br), 7.70-7.71 (1H, m), 8.00-8.39 (4H, m), 8.53-8.56 (1H, m), 9.10 (1H, s), 11.08 (1H, br), 12.44 (1H, br), 14.38 (1H, br). MS: 326 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
369	18	MS: 340 (M+H) +
370	18	MS: 478 (M+H) +
371	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-1.57 (1H, m), 1.71-1.79 (2H, m), 1.83-1.90 (2H, m), 1.96-2.02 (2H, m), 2.06-2.20 (4H, m), 2.33-2.46 (2H, m), 4.38-4.42 (1H, m), 6.60-6.62, 6.73-6.75 (1H, m), 7.41-7.45 (1H, m), 8.11-8.29 (3H, m), 8.44, 8.56 (1H, brs), 8.80 (1H, s), 9.31-9.34, 9.45-9.50 (1H, m), 12.45 (1H, brs). MS: 394 (M-3HCl+H) +
372	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.52-1.57 (2H, m), 1.65-1.75 (4H, m), 1.84-1.92 (6H, m), 1.97-2.02 (2H, m), 2.10-2.14 (1H, m), 2.32-2.36 (2H, m), 2.99-3.09 (2H, m), 3.30-3.36 (2H, m), 4.09-4.16 (1H, m), 4.32-4.35 (1H, m), 6.72-6.75 (1H, m), 7.40-7.42 (1H, m), 8.29-8.41 (1H, m), 8.56-8.65 (1H, m), 8.74-8.79 (1H, m), 8.82 (1H, s), 9.66-9.68 (1H, m), 12.37 (1H, brs). MS: 478 (M-2HCl+H) +
373	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.93-2.24 (6H, m), 2.46-2.61 (2H, m), 3.95-4.09 (2H, m), 4.42-4.54 (1H, m), 6.68-6.76 (1H, m), 7.34-7.41 (1H, m), 7.78 (1H, brs), 8.51 (1H, brs), 8.63 (1H, s), 9.11-9.51 (2H, m), 11.25 (1H, d, J=7.3Hz), 12.69 (1H, s), 14.76 (1H, br). MS: 286 (M+H-2HCl) +
374	18	¹ H-NMR (400MHz, d6-DMSO) δ : 2.02-2.20 (4H, m), 2.24-2.36 (2H, m), 2.43-2.61 (2H, m), 2.47 (3H, s), 4.01-4.11 (2H, m), 4.53-4.62 (1H, m), 6.67-6.73 (1H, m), 7.37-7.42 (1H, m), 8.74 (1H, s), 9.00-9.10 (1H, m), 9.18-9.29 (1H, m), 9.45 (1H, d, J=7.6Hz), 12.34 (1H, brs). MS: 325 (M+H-2HCl) +
375	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.34-2.15 (15H, m), 4.02-4.11 (1H, m), 6.43 (1H, d, J=2.9Hz), 6.56 (1H, d, J=2.9Hz), 7.11-7.12 (1H, m), 7.63-7.65 (1H, m), 8.37 (1H, s), 10.11 (1H, d, J=8.0Hz), 11.43 (1H, brs). MS: 326 (M+H) +.
376	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-2.08 (15H, m), 4.09-4.11 (1H, m), 6.39 (1H, d, J=3.5Hz), 6.56 (1H, d, J=3.5Hz), 7.11-7.12 (1H, m), 7.64-7.65 (1H, m), 8.35 (1H, s), 10.09 (1H, d, J=8.2Hz), 11.44 (1H, brs). MS: 326 (M+H) +.
377	18	¹ H-NMR (400MHz, d6-DMSO) δ : 1.15-2.51 (15H, m), 4.28-4.33 (1H, m), 6.53-6.59 (1H, m), 6.75-6.79 (1H, m), 7.32-7.34 (1H, m), 8.06-8.12 (3H, m), 8.24-8.25 (1H, m), 12.09-12.14 (1H, m). MS: 308 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
378	19	MS:286 (M+H) +
379	19	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.51 (2H, m), 1.63 (1H, brs), 1.68-1.71 (2H, m), 1.80-1.89 (4H, m), 2.09 (1H, brs), 2.25 (1H, brs), 4.10-4.13 (1H, m), 4.56 (1H, m), 4.75 (2H, d, J=5.6Hz), 4.87 (1H, t, J=5.6Hz), 6.50-6.52 (1H, m), 7.11-7.18 (1H, m), 8.47 (1H, s), 10.50 (1H, d, J=8.0Hz), 11.77 (1H, brs). MS:342 (M+H) +
380	19	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.19 (13H, m), 4.21-4.23 (1H, m), 4.51 (1H, s), 4.74-4.76 (2H, d, J=6.0Hz), 4.83 (1H, t, J=6.9Hz), 6.46-6.48 (1H, m), 7.17-7.19 (1H, m), 8.47 (1H, s), 10.46 (1H, d, J=8.0Hz), 11.74 (1H, s). MS:342 (M+H) +
381	19	¹ H-NMR (400MHz, d6-DMSO) δ : 1.23-2.32 (13H, m), 3.00-3.07 (2H, m), 4.21 (1H, brs), 4.43 (1H, brs), 4.75 (2H, brs), 6.46-6.49 (1H, m), 6.55 (1H, s), 7.16-7.17 (1H, m), 8.46 (1H, s), 10.54 (1H, d, J=8.0Hz), 11.75 (1H, brs). MS:356 (M+H) +
382	22	MS:391 (M+H) +
383	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.77-1.87 (2H, m), 1.92-2.08 (6H, m), 2.10-2.15 (1H, m), 2.65-2.73 (4H, m), 3.21 (3H, s), 4.36 (2H, s), 4.51 (1H, s), 6.35-6.38 (1H, m), 7.45 (1H, t, J=2.9Hz), 7.91 (1H, s), 10.84 (1H, s), 11.60 (1H, s). MS:405 (M+H) +
384	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.59-1.67 (2H, m), 1.82-2.07 (3H, m), 2.16-2.30 (4H, m), 2.35-2.43 (2H, m), 2.69-2.73 (2H, m), 3.28 (3H, s), 4.39 (2H, s), 4.59 (1H, s), 6.31-6.35 (1H, m), 7.43 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.77 (1H, br), 11.56 (1H, s). MS:406 (M+H) +
385	22	MS:340 (M+H) +
386	22	MS:340 (M+H) +
387	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-1.53 (4H, m), 1.58-1.64 (2H, m), 1.70-1.75 (2H, m), 1.93-1.96 (1H, m), 2.05-2.11 (2H, m), 2.16-2.20 (2H, m), 3.06-3.08 (2H, m), 4.27-4.30 (1H, m), 4.41-4.45 (1H, m), 6.52-6.54 (1H, m), 7.26-7.28 (1H, m), 8.11-8.12 (1H, m), 8.29-8.31 (1H, m), 8.63 (1H, s), 9.03-9.06 (1H, m), 11.86 (1H, brs). MS:409 (M+H) +
388	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.31-1.35 (2H, m), 1.47-1.49 (2H, m), 1.75-1.80 (2H, m), 1.85-2.00 (5H, m), 2.16-2.19 (2H, m), 3.01-3.03 (2H, m), 4.33-4.41 (2H, m), 6.61-6.63 (1H, m), 7.27-7.28 (1H, m), 8.14-8.16 (1H, m), 8.19-8.20 (1H, m), 8.63 (1H, s), 8.92-8.95 (1H, m), 11.87 (1H, brs). MS:409 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
389	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.46 (2H, m), 1.69-1.79 (4H, m), 1.96-2.08 (3H, m), 2.31-2.37 (2H, m), 2.67-2.70 (2H, m), 4.48 (1H, s), 4.57 (1H, s), 6.3 (1H, d, J=3.4 Hz), 7.45-7.45 (1H, m), 7.89 (1H, s), 10.75 (1H, s), 11.57 (1H, s). MS: 325 (M+H) +
390	22	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.49 (2H, m), 1.63-1.79 (4H, m), 1.92-1.98 (2H, m), 2.14-2.34 (3H, m), 2.78-2.81 (1H, m), 4.37 (1H, s), 4.39 (1H, s), 6.33-6.35 (1H, m), 6.55 (1H, s), 7.43 (1H, t, J=2.9 Hz), 7.89 (1H, s), 10.75 (1H, s), 11.56 (1H, s). MS: 325 (M+H) +
391	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.57-1.63 (2H, m), 1.75-2.11 (8H, m), 2.44-2.59 (4H, m), 4.55 (1H, s), 6.34 (1H, dd, J=1.4 Hz, 3.3 Hz), 7.43 (1H, t, J=2.9 Hz), 7.89 (1H, s), 10.74 (1H, s), 11.56 (1H, s). MS: 309 (M+H) +
392	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42-3.57 (13H, m), 4.37-4.61 (2H, m), 3.29-3.36 (1H, m), 7.42-7.46 (1H, m), 7.90 (1H, s), 10.75-10.77 (1H, m), 11.56 (1H, s). MS: 325 (M+H) +
393	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.68 (12H, m), 1.86-1.91 (3H, m), 3.71 (2H, s), 6.65 (1H, dd, J=1.8 Hz, 3.5 Hz), 7.39 (1H, t, J=3.1 Hz), 7.91 (1H, s), 10.86 (1H, s), 11.52 (1H, s). MS: 323 (M+H) +
394	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-1.59 (2H, m), 2.03-2.14 (5H, m), 2.33-2.52 (4H, m), 2.63-2.68 (2H, m), 3.90 (1H, s), 4.76 (1H, d, J=3.1 Hz), 6.64-6.65 (1H, m), 7.47 (1H, t, J=3.1 Hz), 7.90 (1H, s), 10.78 (1H, s), 11.61 (1H, s). MS: 325 (M+H) +
395	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.56-1.79 (5H, m), 2.31-2.55 (9H, m), 4.75 (1H, s), 6.61 (1H, s), 7.48 (1H, t, J=3.1 Hz), 7.91 (1H, s), 10.78 (1H, s), 11.61 (1H, s). MS: 325 (M+H) +
396	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.51-1.60 (2H, m), 1.71-1.84 (4H, m), 1.95-2.02 (2H, m), 2.20-2.25 (1H, m), 2.39-2.45 (2H, m), 2.79-2.84 (2H, m), 3.11 (3H, s), 4.42 (1H, s), 6.35-6.38 (1H, m), 7.44 (1H, t, J=3.1 Hz), 7.90 (1H, s), 10.76 (1H, s), 11.57 (1H, s). MS: 338 (M+H) +
397	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.50 (2H, m), 1.74-1.77 (2H, m), 1.83-1.88 (2H, m), 2.02-2.15 (3H, m), 2.72-2.37 (2H, m), 2.75-2.79 (2H, m), 3.19 (3H, s), 4.50 (1H, s), 6.34 (1H, dd, J=1.7 Hz, 3.6 Hz), 7.44 (1H, t, J=3.0 Hz), 7.90 (1H, s), 10.77 (1H, s), 11.56 (1H, s). MS: 339 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
398	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.53-1.60 (2H, m), 1.85-1.92 (2H, m), 1.97-2.09 (3H, m), 2.18-2.26 (2H, m), 2.38-2.45 (2H, m), 2.65-2.71 (2H, m), 3.64 (3H, s), 4.54 (1H, s), 6.30-6.31 (1H, m), 7.43 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.78 (1H, s), 11.57 (1H, s). MS: 367 (M+H) +
399	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.17 (3H, t, J=7.1Hz), 1.69-1.93 (6H, m), 2.03-2.11 (2H, m), 2.37-2.47 (2H, m), 2.71-2.75 (2H, m), 3.73 (2H, d, J=5.8Hz), 4.06 (2H, q, J=7.1Hz), 4.49 (1H, s), 6.34-6.36 (1H, m), 7.44 (1H, t, J=3.0Hz), 7.81 (1H, t, J=5.8Hz), 7.90 (1H, s), 10.75 (1H, s), 11.57 (1H, s). MS: 438 (M+H) +
400	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.2 (3H, t, J=7.1Hz), 1.50-1.58 (2H, m), 1.84-1.88 (2H, m), 1.95-2.03 (3H, m), 2.18-2.26 (2H, m), 2.38-2.46 (2H, m), 2.63-2.70 (2H, m), 3.8 (2H, d, J=5.8Hz), 4.09 (2H, q, J=7.1Hz), 4.55 (1H, s), 6.36-6.38 (1H, m), 7.45 (1H, t, J=3.0Hz), 7.90 (1H, s), 8.07 (1H, t, J=6.1Hz), 10.78 (1H, s), 11.58 (1H, s). MS: 438 (M+H) +
401	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.67-1.73 (2H, m), 1.78-1.82 (2H, m), 1.84-1.91 (2H, m), 2.00-2.10 (3H, m), 2.37-2.44 (2H, m), 2.68-2.72 (2H, m), 4.48 (1H, s), 6.34-6.35 (1H, m), 6.70 (1H, s), 6.91 (1H, s), 7.44 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.75 (1H, s), 11.56 (1H, s). MS: 352 (M+H) +
402	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.55 (2H, m), 1.81-1.85 (2H, m), 1.93-2.00 (3H, m), 2.16-2.21 (2H, m), 2.38-2.45 (2H, m), 2.61-2.66 (2H, m), 4.53 (1H, s), 6.38-6.39 (1H, m), 6.80 (1H, s), 7.15 (1H, s), 7.44 (1H, t, J=3.0Hz), 7.90 (1H, s), 10.76 (1H, s), 11.56 (1H, s). MS: 352 (M+H) +
403	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.35-1.40 (9H, m), 1.45-2.13 (7H, m), 2.25-2.40 (4H, m), 2.64-2.77 (2H, m), 4.41-4.49 (1H, m), 6.27-6.34 (1H, m), 6.39-6.58 (1H, m), 7.42-7.47 (1H, m), 7.89 (1H, s), 10.75-10.76 (1H, m), 11.54-11.59 (1H, m). MS: 424 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
404	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.57-1.63 (2H, m), 1.74-1.85 (4H, m), 1.95-2.02 (2H, m), 2.21-2.26 (1H, m), 2.42-2.48 (2H, m), 2.65 (2H, t, J=6.0Hz), 2.79-2.83 (2H, m), 3.55 (2H, t, J=6.0Hz), 4.44 (1H, s), 6.38-6.40 (1H, m), 7.46 (1H, t, J=3.0Hz), 7.92 (1H, s), 10.83 (1H, s), 11.65 (1H, s). MS: 378 (M+H) +
405	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.52 (2H, m), 1.75-1.81 (2H, m), 1.86-1.92 (2H, m), 2.08-2.17 (3H, m), 2.31-2.37 (2H, m), 2.71 (2H, t, J=6.0Hz), 2.75-2.79 (2H, m), 3.65 (2H, t, J=6.0Hz), 4.53 (1H, s), 6.38 (1H, s), 7.45 (1H, t, J=3.0Hz), 7.91 (1H, s), 10.82 (1H, s), 11.62 (1H, s). MS: 378 (M+H) +
406	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.58-1.67 (2H, m), 2.06-2.11 (1H, m), 2.30-2.59 (6H, m), 2.66-2.78 (4H, m), 4.68 (1H, s), 6.34-6.36 (1H, m), 7.44 (1H, t, J=3.1Hz), 7.90 (1H, s), 10.79 (1H, s), 11.58 (1H, s). MS: 387, 389 (M+H) +
407	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.59-1.69 (2H, m), 2.07-2.14 (1H, m), 2.36-2.47 (6H, m), 2.65-2.72 (2H, m), 2.86-2.92 (2H, m), 4.98 (1H, s), 7.99 (1H, s), 8.35 (1H, s), 10.98 (1H, s), 13.00 (1H, s). MS: 388, 390 (M+H) +
408	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.17-2.47 (9H, m), 2.93-3.00 (1H, m), 4.36-4.42 (1H, m), 6.54-6.57 (1H, m), 7.42-7.44 (1H, m), 7.88 (1H, s), 10.77 (1H, brs), 11.58 (1H, brs). MS: 269 (M+H) +
409	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.20-1.86 (7H, m), 2.32-2.42 (1H, m), 3.05-3.17 (1H, m), 4.71-4.84 (1H, m), 6.49-6.55 (1H, m), 6.91 (1H, s), 7.40-7.46 (1H, m), 7.90 (1H, s), 10.77 (1H, brs), 11.56 (1H, brs). MS: 269 (M+H) +
410	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.01 (3H, d, J=7.2Hz), 1.24 (3H, s), 1.30 (3H, s), 1.88-2.09 (3H, m), 2.29-2.52 (4H, m), 4.81-4.92 (1H, m), 6.44-6.49 (1H, m), 7.43-7.47 (1H, m), 7.92 (1H, s), 10.92 (1H, brs), 11.64 (1H, brs). MS: 311 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
411	23	¹ H-NMR (400MHz, d6-DMSO) δ : 0.78 (3H, s), 0.91 (3H, s), 1.14 (3H, s), 1.21-1.31 (1H, m), 1.63-1.73 (1H, m), 1.80-1.88 (2H, m), 1.97-2.11 (2H, m), 2.75 (1H, dd, J=5.3, 12.5Hz), 4.80 (1H, ddd, J=2.4, 5.3, 12.0Hz), 6.45 (1H, dd, J=1.7, 3.6Hz), 7.40-7.43 (1H, m), 7.91 (1H, s), 10.89 (1H, brs), 11.58 (1H, brs). MS: 311 (M+H) +
412	23	¹ H-NMR (400MHz, d6-DMSO) δ : 1.15-3.14 (13H, m), 4.41-4.60 (1H, m), 6.35-6.40 (1H, m), 7.43-7.47 (1H, m), 7.90-7.92 (1H, m), 10.80-10.87 (1H, m), 11.62 (1H, brs). MS: 327 (M+H) +
413	24	MS: 330 (M+H) +
414	24	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46 (2H, d, J=12.3Hz), 1.63 (2H, s), 1.72 (2H, d, J=12.1Hz), 1.92 (2H, d, J=12.1Hz), 1.99 (1H, s), 2.39 (2H, d, J=12.3Hz), 2.96 (2H, s), 4.34 (1H, s), 4.67 (1H, s), 7.97 (1H, s), 8.31 (1H, s), 10.9 (1H, s), 13.0 (1H, s). MS: 348 (M+Na) +
415	24	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42 (2H, d, J=12.5Hz), 1.68 (2H, s), 1.72 (2H, d, J=12.0Hz), 2.00 (2H, d, J=12.0Hz), 2.08 (1H, s), 2.39 (2H, d, J=12.5Hz), 2.79 (2H, s), 4.49 (1H, s), 4.88 (1H, s), 7.97 (1H, s), 8.32 (1H, s), 10.9 (1H, brs), 13.0 (1H, brs). MS: 348 (M+Na) +
416	25	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-2.18 (11H, m), 3.33-3.40 (1H, m), 4.47 (1H, s), 4.92-5.05 (1H, m), 7.05 (1H, br), 7.82 (1H, br), 8.05 (1H, s), 8.45 (1H, s), 9.97 (1H, d, J=9.2Hz), 11.5 (1H, s), 12.8 (1H, br). MS: 328 (M+H) +
417	25	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32 (3H, t, J=7.1Hz), 1.56 (2H, t, J=10.7Hz), 1.80-1.83 (2H, m), 1.92-2.08 (4H, m), 3.20 (2H, brs), 3.57 (2H, s), 4.28 (2H, q, J=7.1Hz), 5.30-5.45 (1H, brs), 7.20-7.24 (1H, m), 7.32 (2H, dd, J=7.2, 7.8Hz), 7.39 (2H, d, J=7.2Hz), 8.14 (1H, s), 8.48 (1H, d, J=8.8Hz), 8.60 (1H, s), 13.0 (1H, brs). MS: 406 (M+H) +
418	25	¹ H-NMR (400MHz, d6-DMSO) δ : 1.11 (6H, t, J=6.8Hz), 1.50-2.31 (13H, m), 3.46-3.68 (4H, m), 4.11-4.12 (1H, m), 4.57 (1H, s), 6.65-6.66 (1H, m), 6.74 (1H, s), 7.38-7.39 (1H, m), 8.54 (1H, s), 8.88 (1H, d, J=8.0Hz), 9.30 (1H, s). MS: 454 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
419	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-1.52 (2H, m), 1.64-1.66 (2H, m), 1.78-1.84 (2H, m), 2.01-2.06 (2H, m), 2.18-2.27 (3H, m), 3.10-3.12 (2H, m), 4.40 (1H, s), 4.76 (1H, br), 6.53-6.55 (1H, m), 7.61-7.63 (1H, m), 8.56-8.59 (1H, s), 12.09 (1H, brs), 13.14 (1H, brs). MS: 442 (M+Na) +
420	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39 (3H, t, J=7.1Hz), 1.48-1.53 (2H, m), 1.62-1.65 (2H, m), 1.69-1.74 (2H, m), 1.81-1.93 (4H, m), 2.09-2.12 (1H, m), 2.29-2.33 (2H, m), 4.22-4.26 (1H, m), 4.47 (2H, q, J=7.1Hz), 4.54 (1H, brs), 6.56-6.58 (1H, m), 7.26-7.27 (1H, m), 7.80-7.83 (1H, m), 8.71 (1H, s), 11.71 (1H, brs). MS: 424 (M+H) +
421	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.48-2.31 (13H, m), 4.24 (1H, m), 4.52 (1H, s), 6.55 (1H, m), 7.23 (1H, m), 7.86 (1H, m), 8.75 (1H, s), 9.67 (1H, s), 11.63 (1H, s). MS: 352 (M+H) +
422	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.34 (3H, t, J=7.1Hz), 1.45-1.84 (10H, m), 2.06 (1H, brs), 2.22 (2H, brs), 4.31 (2H, q, J=7.1Hz), 4.53 (1H, s), 5.04 (1H, d, J=8.7Hz), 8.12 (1H, s), 8.64 (1H, s), 9.16 (1H, d, J=8.7Hz), 12.8 (1H, brs). MS: 357 (M+H) +
423	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.32 (3H, t, J=7.1Hz), 1.42-1.90 (10H, m), 2.15 (1H, brs), 2.22 (2H, brs), 3.15 (3H, s), 4.31 (2H, q, J=7.1Hz), 5.12 (1H, d, J=8.7Hz), 8.14 (1H, s), 8.64 (1H, s), 9.14 (1H, d, J=8.7Hz), 13.0 (1H, brs). MS: 371 (M+H) +
424	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-1.67 (10H, m), 1.88-1.94 (1H, m), 2.02 (2H, brs), 3.03 (2H, d, J=5.5Hz), 4.37 (1H, t, J=5.5Hz), 5.05 (1H, d, J=8.9Hz), 7.04 (1H, brs), 7.82 (1H, brs), 8.03 (1H, s), 8.45 (1H, s), 10.0 (1H, d, J=8.9Hz), 12.7 (1H, brs). MS: 342 (M+H) +
425	26	¹ H-NMR (400MHz, d6-DMSO) δ : 1.22-1.84 (10H, m), 1.94 (1H, brs), 2.06 (2H, brs), 2.98 (2H, d, J=5.7Hz), 4.36 (1H, t, J=5.7Hz), 5.06 (1H, d, J=8.7Hz), 7.10 (1H, brs), 7.82 (1H, brs), 8.04 (1H, s), 8.45 (1H, s), 10.0 (1H, d, J=8.7Hz), 12.7 (1H, brs). MS: 342 (M+H) +
426	26	MS: 337 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
427	27	¹ H-NMR (400MHz, d6-DMSO) δ : 1.36-1.41 (2H, m), 1.64-1.70 (4H, m), 1.80-1.93 (4H, m), 2.04-2.07 (1H, m), 2.11-2.14 (2H, m), 4.13-4.16 (1H, m), 4.44 (1H, s), 5.82 (2H, br s), 6.37-6.38 (1H, m), 7.09-7.11 (1H, m), 8.13 (1H, s), 8.97 (1H, d, J=8.2Hz), 9.54 (1H, s), 11.23 (1H, brs). MS: 342 (M+H) +
428	28	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39 (3H, t, J=7.2Hz), 1.46-1.54 (2H, m), 1.58-1.77 (4H, m), 1.80-1.90 (2H, m), 1.97-2.14 (3H, m), 2.28-2.35 (2H, m), 4.18-4.25 (1H, m), 4.42 (1H, s), 4.43 (2H, q, J=7.2Hz), 6.60 (1H, d, J=3.5Hz), 7.29 (1H, d, J=3.5Hz), 8.65 (1H, s), 9.04 (1H, d, J=7.7Hz), 11.91 (1H, brs). MS: 424 (M+H) +
429	28	¹ H-NMR (400MHz, d6-DMSO) δ : 1.30-1.36 (3H, m), 1.63-1.72 (2H, m), 1.93-2.04 (2H, m), 2.07-2.49 (6H, m), 2.75-2.84 (3H, m), 4.37-4.45 (2H, m), 4.61-4.68 (1H, m), 6.36-6.41 (1H, m), 7.43-7.47 (1H, m), 7.91 (1H, s), 10.82 (1H, s), 11.58-11.61 (1H, m). MS: 449 (M+H) +
430	28	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.29 (13H, m), 3.42 (3H, s), 4.21-4.22 (1H, m), 4.46 (1H, s), 4.65 (2H, s), 6.58-6.59 (1H, m), 7.26-7.27 (1H, m), 8.60 (1H, s), 9.04 (1H, d, J=8.0Hz), 11.84 (1H, s). MS: 396.3 (M+H) +
431	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.39 (20H, m), 2.60 (1H, s), 2.69 (1H, m), 3.22 (3H, s), 3.69 (1H, m), 4.44 (1H, m), 4.77 (1H, s), 6.64 (1H, m), 7.45 (1H, m), 8.74 (1H, m), 8.78 (1H, m), 10.83 (1H, s), 12.05 (1H, s). MS: 507 (M+H) +
432	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.67 (18H, m), 3.12 (2H, m), 4.02 (2H, m), 4.44 (1H, m), 4.77 (1H, s), 6.66 (1H, m), 7.46 (1H, m), 8.73 (1H, s), 9.21 (1H, m), 10.94 (1H, m), 12.07 (1H, m). MS: 549 (M+Na) +
433	32	MS: 543 (M+Na) +
434	32	MS: 505 (M-H) -
435	32	MS: 467 (M+H) +
436	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.69 (21H, m), 3.89 (1H, m), 4.42 (1H, m), 4.76 (1H, s), 6.65 (1H, m), 7.45 (1H, m), 8.74 (1H, s), 9.02 (1H, m), 10.88 (1H, s), 12.05 (1H, s). MS: 513 (M+H) +
437	32	¹ H-NMR (400MHz, d6-DMSO) δ : 0.85-2.61 (21H, m), 3.63-3.79 (2H, m), 4.35 (1H, m), 4.44 (1H, m), 4.76 (1H, s), 6.65 (1H, m), 7.46 (1H, m), 8.72 (1H, s), 8.74 (1H, s), 10.86 (1H, s), 12.07 (1H, s). MS: 493 (M+H) +
438	32	MS: 464 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
439	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.50 (2H, m), 1.65-1.68 (2H, m), 1.77-2.04 (6H, m), 2.17-2.21 (1H, m), 2.33-2.40 (2H, m), 2.59-2.64 (2H, m), 3.35-3.48 (1H, m), 3.77-3.88 (3H, m), 4.46-4.48 (1H, m), 4.67-4.69 (1H, m), 4.75-4.77 (1H, m), 4.89, 5.18 (1H, m), 6.64-6.65 (1H, m), 7.44-7.46 (1H, m), 8.74, 8.78 (1H, m), 11.03-11.19 (1H, m), 12.10 (1H, brs). MS: 499 (M+N) +
440	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.44-1.49 (2H, m), 1.65-1.68 (2H, m), 1.77-1.83 (2H, m), 1.99-2.05 (2H, m), 2.17-2.21 (1H, m), 2.35-2.40 (2H, m), 2.58-2.62 (2H, m), 4.45 (1H, s), 4.75-4.77 (1H, m), 6.65-6.67 (1H, m), 7.45-7.47 (1H, m), 8.03 (1H, brs), 8.39 (1H, brs), 8.74 (1H, s), 10.82 (1H, brs), 12.08 (1H, brs). MS: 417 (M+Na) +
441	32	¹ H-NMR (400MHz, d6-DMSO) δ : 0.77-3.54 (22H, m), 4.84 (1H, brs), 6.82-6.86 (1H, m), 7.49-7.53 (1H, m), 8.64 (1H, s), 8.87-8.93 (1H, m), 12.12 (1H, brs). MS: 453 (M+H) +
442	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.44 (2H, m), 1.71-1.73 (2H, m), 1.78-1.83 (2H, m), 2.04-2.09 (2H, m), 2.11-2.15 (1H, m), 2.38-2.44 (2H, m), 2.49-2.51 (2H, m), 4.56 (1H, s), 4.88-4.89 (1H, m), 6.60-6.62 (1H, m), 7.45-7.47 (1H, m), 8.01 (1H, brs), 8.36 (1H, brs), 8.74 (1H, s), 10.85-10.90 (1H, m), 12.07 (1H, brs). MS: 417 (M+Na) +
443	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.39 (13H, m), 3.16 (2H, d, J=5.2Hz), 3.50 (2H, q, J=5.6Hz), 4.07 (1H, q, J=5.6Hz), 4.76 (1H, brs), 4.78 (1H, t, J=5.2Hz), 6.65-6.66 (1H, m), 7.45-7.47 (1H, m), 8.71 (1H, s), 8.88-8.90 (1H, m), 10.89 (1H, s), 12.07 (1H, brs). MS: 439 (M+H) +
444	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.37 (13H, m), 2.94 (3H, s), 3.12 (3H, s), 4.46-4.47 (1H, m), 4.75 (1H, brs), 6.63-6.64 (1H, m), 7.45-7.46 (1H, m), 8.78 (1H, s), 11.36 (1H, s), 12.16 (1H, s). MS: 423.3 (M+H) +
445	32	¹ H-NMR (400MHz, d6-DMSO) δ : 1.15-2.45 (13H, m), 2.49-2.51 (6H, m), 4.21 (4H, brs), 4.76 (1H, brs), 6.55-6.55 (1H, m), 7.45-7.46 (1H, m), 8.56 (1H, s), 8.72 (1H, s), 8.83-8.87 (1H, m), 11.44 (1H, s), 12.07 (1H, brs). MS: 466.3 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
446	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-2.39 (11H, m), 2.49-2.45 (m, 3H), 2.60 (2H, brs), 3.16-3.20 (2H, m), 3.81-3.82 (1H, m), 4.45 (1H, s), 4.76 (1H, brs), 4.85 (1H, d, J=4.8 Hz), 6.65-6.67 (1H, m), 7.45-7.46 (1H, m), 8.72 (1H, s), 8.82-8.82 (1H, m), 10.90 (1H, s), 12.07 (1H, brs). MS: 453 (M+Na) +
447	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.04-2.38 (17H, m), 3.46-3.70 (5H, m), 4.35-4.36 (1H, m), 4.45 (1H, q), 4.57-4.59 (1H, m), 4.76 (1H, brs), 6.65-6.66 (1H, m), 7.45-7.46 (1H, m), 8.72 (1H, s), 8.82 (1H, d, J=8.0Hz), 10.88 (1H, s), 12.06 (1H, brs). MS: 515 (M+H) +
448	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-2.60 (17H, m), 3.45-4.00 (6H, m), 4.47 (1H, s), 4.76 (1H, brs), 6.56-6.57 (1H, m), 7.45-7.46 (1H, m), 8.71 (1H, s), 10.93 (1H, brs), 12.07 (1H, brs). MS: 477 (M-H) -
449	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-2.39 (17H, m), 3.43-3.99 (5H, m), 4.34-4.54 (1H, m), 4.76 (1H, brs), 6.65-6.66 (1H, m), 7.45-7.46 (1H, m), 8.73 (1H, s), 9.02 (1H, d, J=8.0Hz), 10.91 (1H, brs), 12.07 (1H, brs). MS: 477 (M-H) -
450	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.56-1.59 (2H, m), 2.03-2.08 (3H, m), 2.22-2.25 (2H, m), 2.46-2.57 (6H, m), 3.28 (3H, s), 3.39-3.40 (2H, m), 3.48-3.49 (2H, m), 5.04 (1H, s), 6.78 (1H, s), 7.46 (1H, s), 8.73 (1H, s), 8.95 (1H, m), 10.99 (1H, s), 12.05 (1H, s). MS: 462 (M+H) +, 484 (M+Na) +
451	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.36-2.37 (17H, m), 3.43-3.60 (7H, m), 4.48 (1H, brs), 4.75 (1H, brs), 6.64 (1H, brs), 7.45 (1H, brs), 8.81-8.83 (1H, m), 11.45 (1H, brs), 12.11 (1H, brs). MS: 506 (M+H) +
452	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ : 1.45-2.39 (18H, m), 3.42-4.01 (6H, m), 4.47 (1H, s), 4.76 (1H, brs), 6.56-6.57 (1H, m), 7.45-7.46 (1H, m), 8.71 (1H, s), 8.95-8.96 (1H, m), 10.93 (1H, brs), 12.07 (1H, brs). MS: 515 (M+Na) +

Table 72 (contd.)

Ex	Ref -Ex	Data
453	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 1.56 (2H, m), 1.75-1.77 (1H, m), 1.88-1.95 (4H, m), 2.04-2.12 (4H, m), 2.29-2.33 (2H, m), 3.28 (3H, s), 3.38-3.42 (2H, m), 3.47-3.49 (2H, m), 3.59 and 3.65 (total 3H, eachs), 4.90 and 4.96 (total 1H, eachs), 6.66-6.77 (1H, m), 7.44-7.47 (1H, m), 8.71 and 8.72 (total 1H, eachs), 8.97 (1H, m), 11.00 (1H, s), 12.07 (1H, s). MS: 517 (M+Na) +
454	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 52-1.55 (3H, m), 1.74-1.84 (5H, m), 2.04-2.07 (2H, m), 2.25 (1H, s), 2.64 (2H, s), 3.13 (3H, s), 3.28 (3H, s), 3.39-3.42 (2H, m), 3.47-3.50 (2H, m), 4.81 (1H, s), 6.68 (1H, dd, J=1.9, 3.3Hz), 7.40 (1H, t, J=3.0Hz), 8.71 (1H, s), 8.94 (1H, t, J=5.8Hz), 11.02 (1H, s), 12.06 (1H, s). MS: 467 (M+H) +, 489 (M+Na) +
455	32	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 1.27-1.32 (2H, m), 1.45-1.55 (4H, m), 1.68-1.71 (2H, m), 1.84-1.91 (2H, m), 2.00 (1H, s), 2.09-2.17 (2H, m), 3.03 and 3.13 (total 2H, eachd, J=5.5 and 5.5Hz), 3.28 (3H, s), 3.39-3.42 (2H, m), 3.47-3.50 (2H, m), 4.30 and 4.47 (total 1H, eacht, J=5.5 and 5.5Hz), 4.85 and 4.87 (total 1H, eachs), 6.60 and 6.65 (total 1H, eachm), 7.46 (1H, t, J=3.0Hz), 8.71 and 8.72 (total 1H, s), 8.97 (1H, m), 10.96 and 10.97 (total 1H, s), 12.07 (1H, s). MS: 467 (M+H) +, 489 (M+Na) +
456	33	MS: 646 (M+H) +
457	33	MS: 506 (M+H) +
458	33	¹ H-NMR (400MHz, d ₆ -DMSO) δ: 1.01 (3H, d, J=7.6Hz), 1.24 (3H, s), 1.30 (3H, s), 1.88-2.83 (7H, m), 4.80-4.90 (1H, m), 6.45-6.48 (1H, m), 7.43-7.46 (1H, m), 7.92 (1H, s), 10.91 (1H, brs), 11.63 (1H, brs). MS: 311 (M+H) +
459	33	MS: 465 (M+H) +
460	33	MS: 497 (M+H) +
461	33	MS: 509 (M+H) +
462	33	MS: 509 (M+H) +
463	33	MS: 478 (M+H) +
464	33	MS: 465 (M+H) +
465	33	MS: 463 (M+H) +
466	33	MS: 434 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
467	33	MS: 499 (M+H) +
468	33	MS: 541 (M+H) +
469	33	MS: 477 (M+H) +
470	33	MS: 449 (M+H) +
471	33	MS: 546 (M+H) +
472	33	MS: 506 (M+H) +
473	33	MS: 453 (M+H) +
474	33	MS: 504 (M+H) +
475	33	MS: 453 (M+H) +
476	34	¹ H-NMR (400MHz, d6-DMSO) δ : 1.75-1.90 (4H, m), 2.00-2.10 (2H, m), 2.14-2.28 (3H, m), 2.37-2.54 (4H, m), 4.21-4.27 (1H, m), 6.36 (1H, d, J=6.8Hz), 6.73-6.78 (1H, m), 7.27-7.31 (1H, m), 8.11 (1H, s), 11.86 (1H, brs). MS: 427 (M+Na) +
477	35	MS: 314 (M+H) +
478	35	MS: 393 (M+H) +
479	35	MS: 382 (M+H) +
480	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.39-1.46 (2H, m), 1.56-1.87 (8H, m), 2.07 (1H, m), 2.18 (3H, s), 2.25 (2H, m), 4.03 (1H, m), 4.47 (1H, s), 4.77 (1H, d, J=7.2Hz), 6.38 (1H, d, J=3.6Hz), 7.13 (1H, d, J=3.6Hz), 7.71 (1H, s), 8.32 (1H, s), 11.156 (1H, s). MS: 298 (M+H) +
481	35	MS: 378 (M+Na) +
482	35	MS: 420 (M+Na) +
483	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.22-2.24 (13H, m), 3.20-3.40 (2H, m), 4.42-4.65 (2H, m), 6.44-6.48 (1H, m), 6.82-7.09 (1H, br), 7.16-7.19 (1H, m), 7.56-7.84 (1H, br), 8.34 (1H, s), 9.45 (1H, d, J=8.0Hz), 11.48 (1H, brs). MS: 329 (M+H) +.
484	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-1.51 (2H, m), 1.61-1.63 (2H, m), 1.68-1.73 (2H, m), 1.81-1.87 (2H, m), 1.91-1.96 (2H, m), 2.08-2.12 (1H, m), 2.28-2.31 (2H, m), 4.19-4.23 (1H, m), 4.46 (1H, brs), 4.66-4.68 (2H, m), 5.68-5.71 (1H, m), 6.58-6.60 (1H, m), 7.25-7.26 (1H, m), 8.60 (1H, s), 9.07 (1H, d, J=7.8Hz), 11.83 (1H, brs). MS: 382 (M+H) +
485	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.31-1.35 (2H, m), 1.47-1.50 (2H, m), 1.61-1.98 (7H, m), 2.07-2.12 (2H, m), 2.96-2.99 (2H, m), 4.11-4.16 (1H, m), 4.35-4.39 (1H, m), 6.42-6.46 (1H, m), 6.80-7.09 (1H, br), 7.10-7.13 (1H, m), 7.52-7.88 (1H, br), 8.36 (1H, s), 10.13 (1H, d, J=8.0Hz), 11.43 (1H, brs). MS: (M+H) +.

Table 72 (contd.)

Ex	Ref -Ex	Data
486	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.70 (8H, m), 1.89-1.96 (3H, m), 2.05-2.10 (2H, m), 3.03-3.08 (2H, m), 4.08-4.15 (1H, m), 4.39-4.44 (1H, m), 6.40-6.44 (1H, m), 6.95-7.19 (2H, m), 7.68-7.96 (1H, br), 8.38 (1H, s), 10.27 (1H, d, J=8.0Hz), 11.55 (1H, brs). MS: 341 (M+H)+.
487	35	¹ H-NMR (400MHz, d6-DMSO) δ : 1.34-1.44 (2H, m), 1.58-1.72 (4H, m), 1.80-1.90 (2H, m), 2.00-2.11 (3H, m), 2.33-2.44 (2H, m), 4.18-4.28 (3H, m), 6.59-6.60, (1H, m), 6.90-6.98 (1H, m), 7.20 (1H, brs), 7.33 (1H, brs), 7.38-7.39 (1H, m), 7.46 (1H, brs), 8.19 (1H, s), 8.61 (3H, br), 12.63 (1H, brs). MS: 313 (M-3HCl+H)+
488	39	¹ H-NMR (400MHz, d6-DMSO) δ : 1.85-2.25 (8H, m), 2.37-2.41 (1H, m), 2.53-2.57 (2H, m), 2.91-2.96 (1H, m), 3.11-3.18 (1H, m), 4.74 (1H, s), 6.55-6.59 (1H, m), 7.37 (1H, t, J=2.7Hz), 8.51-8.52 (1H, m), 10.89 (1H, s), 11.94 (1H, s). MS: 387, 389 (M+H)+
489	39	¹ H-NMR (400MHz, d6-DMSO) δ : 1.10-1.28 (2H, m), 1.36-2.38 (7H, m), 2.54 (1H, brs), 5.02-5.08 (1H, m), 6.72-6.74 (1H, m), 7.35-7.37 (1H, m), 8.47 (1H, s), 10.9 (1H, brs), 12.0 (1H, s). MS: 269 (M+H)+
490	39	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.64 (2H, m), 2.10-2.63 (9H, m), 2.75-2.83 (2H, m), 4.91 (1H, s), 6.64-6.66 (1H, m), 7.37 (1H, t, J=3.0Hz), 8.50 (1H, s), 10.81 (1H, s), 11.93 (1H, s). MS: 387, 389 (M+H)+
491	39	¹ H-NMR (400MHz, d6-DMSO) δ : 1.55-1.60 (2H, m), 1.77-1.80 (2H, m), 1.90-2.02 (4H, m), 2.06-2.13 (2H, m), 2.32-2.36 (2H, m), 2.52-2.57 (2H, m), 4.75-4.77 (1H, m), 6.53-6.56 (1H, m), 7.35-7.38 (1H, m), 8.50 (1H, s), 10.78 (1H, brs), 11.92 (1H, brs). MS: 309 (M+H)+.
492	40	¹ H-NMR (400MHz, d6-DMSO) δ : 1.38-1.48 (2H, m), 1.64-1.81 (4H, m), 1.93-2.05 (2H, m), 2.11-2.19 (1H, m), 2.37-2.57 (4H, m), 4.44 (0.34H, brs), 4.56-4.59 (1H, m), 4.70 (0.66H, brs), 6.50-6.52 (0.66H, m), 6.54-6.56 (0.34H, m), 7.36-7.38 (1H, m), 8.50 (0.66H, s), 8.51 (0.34H, s), 10.78 (1H, brs), 11.92 (1H, brs). MS: 325 (M+H)+.
493	40	MS: 325 (M+H)+.

Table 72 (contd.)

Ex	Ref -Ex	Data
494	40	¹ H-NMR (400MHz, d6-DMSO) δ : 0.88 (3H, d, J=6.9Hz), 1.72-1.92 (2H, m), 2.15-2.26 (1H, m), 3.55-3.70 (4H, m), 5.30-5.40 (1H, m), 7.01 (1H, d, J=9.2Hz), 7.15 (1H, brs), 7.76 (1H, d, J=9.2Hz), 7.90 (1H, brs), 8.09 (1H, s), 8.39 (1H, s), 8.48 (1H, s), 9.89 (1H, d, J=9.0Hz), 12.9 (1H, brs). MS: 420 (M+H) +
495	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.52 (2H, m), 1.76-1.91 (6H, m), 2.10-2.16 (1H, m), 2.27-2.33 (3H, m), 2.68 (2H, t, J=6Hz), 3.59 (2H, t, J=6Hz), 4.76-4.85 (1H, m), 6.09 (1H, d, J=7.3Hz), 8.25-8.27 (3H, m), 13.21 (1H, br). MS: 363 (M+H) +
496	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.00-1.59 (13H, m), 2.64-2.75 (2H, m), 3.54-3.69 (2H, m), 4.63-4.76 (1H, m), 6.55-6.64 (1H, m), 7.35-7.39 (1H, m), 8.50 (1H, s), 10.79-10.83 (1H, m), 11.91 (1H, s). MS: 378 (M+H) +
497	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.54-1.62 (2H, m), 1.73-1.86 (4H, m), 1.96-2.27 (4H, m), 2.54-2.61 (3H, m), 2.67 (2H, t, J=6.0Hz), 3.57 (2H, t, J=6.0Hz), 4.63 (1H, s), 6.56-6.59 (1H, m), 7.36-7.39 (1H, m), 8.49-8.51 (1H, m), 10.83 (1H, s), 11.93 (1H, s). MS: 378 (M+H) +
498	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-1.49 (2H, m), 1.77-1.82 (2H, m), 1.84-1.89 (2H, m), 2.15-2.22 (4H, m), 2.41-2.48 (3H, m), 2.71 (2H, t, J=6.0Hz), 3.66 (2H, t, J=6.0Hz), 4.76 (1H, s), 6.61-6.63 (1H, m), 7.36-7.37 (1H, m), 8.50 (1H, s), 10.79 (1H, s), 11.92 (1H, s). MS: 378 (M+H) +
499	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42-1.49 (2H, m), 1.73-1.80 (4H, m), 1.83-1.89 (2H, m), 1.97-2.03 (2H, m), 2.09-2.13 (1H, m), 2.18-2.23 (2H, m), 2.68 (2H, t, J=6.0Hz), 3.61 (2H, t, J=6.0Hz), 4.17-4.21 (1H, m), 6.48 (1H, dd, J=1.9, 3.5Hz), 6.99 (1H, br), 7.12 (1H, dd, J=2.5, 3.5Hz), 7.79 (1H, br), 8.37 (1H, s), 10.11 (1H, d, J=8.3Hz), 11.46 (1H, s). MS: 390 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
500	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.42-1.48 (2H, m), 1.71-1.90 (7H, m), 2.10-2.20 (4H, m), 2.68 (2H, t, J=5.9Hz), 3.59 (2H, t, J=5.9Hz), 5.07 (1H, d, J=8.7Hz), 7.12 (1H, br), 7.86 (1H, br), 8.05 (1H, s), 8.45 (1H, s), 9.97 (1H, d, J=8.7Hz), 12.78 (1H, br). MS: 381 (M+H) +
501	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.53-1.60 (2H, m), 1.70-1.79 (6H, m), 1.87-1.95 (2H, m), 2.08-2.15 (1H, m), 2.21-2.27 (2H, m), 2.69 (2H, t, J=6Hz), 3.58 (2H, t, J=6Hz), 4.99 (1H, d, J=8.6Hz), 7.18 (1H, br), 7.89 (1H, br), 8.06 (1H, s), 8.46 (1H, s), 10.05 (1H, d, J=8.6Hz), 12.79 (1H, br). MS: 381 (M+H) +
502	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.51 (2H, m), 1.77-1.80 (2H, m), 1.83-1.90 (2H, m), 2.03-2.09 (2H, m), 2.12-2.17 (1H, m), 2.33-2.40 (3H, m), 2.70 (2H, t, J=6.0Hz), 2.89-2.93 (2H, m), 3.61 (2H, t, J=6.0Hz), 4.87 (1H, s), 7.98 (1H, s), 10.94 (1H, s), 12.95 (1H, br). MS: 379 (M+H) +
503	41	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.52 (2H, m), 1.79-1.84 (2H, m), 1.87-1.95 (2H, m), 2.06-2.10 (2H, m), 2.14-2.19 (1H, m), 2.28-2.38 (2H, m), 2.95-3.02 (2H, m), 4.48 (2H, s), 4.82 (1H, s), 7.98 (1H, s), 8.33 (1H, s), 10.95 (1H, s), 12.99 (1H, br). MS: 356 (M+H) +
504	43	¹ H-NMR (400MHz, d6-DMSO) δ : 1.83-1.90 (2H, m), 1.93-1.99 (2H, m), 2.08-2.13 (1H, m), 2.23-2.29 (5H, m), 2.32-2.36 (3H, m), 4.27 (1H, d, J=7.8Hz), 6.6 (1H, d, J=1.9Hz), 7.3 (1H, t, J=2.3Hz), 7.53 (1H, br), 8.16 (1H, br), 8.47 (1H, s), 10.94 (1H, s), 12.11 (1H, s). MS: 389, 391 (M+H) +
505	43	¹ H-NMR (400MHz, d6-DMSO) δ : 1.22-2.33 (10H, m), 4.12 (1H, m), 6.44 (1H, m), 7.03 (1H, m), 7.14 (1H, m), 7.64 (1H, m), 8.39 (1H, s), 10.25 (1H, m), 11.48 (1H, s). MS: 345 (M+H) +
506	43	¹ H-NMR (400MHz, d6-DMSO) δ : 1.68-2.38 (13H, m), 4.98-5.02 (1H, m), 7.08 (1H, brs), 7.90 (1H, brs), 8.06 (1H, s), 8.47 (1H, s), 10.4 (1H, d, J=8.6Hz), 12.7 (1H, brs). MS: 330 (M+H) +
507	45	MS: 366 (M+H) +
508	46	MS: 388 (M+H) +
509	46	MS: 387 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
510	46	MS:397 (M+H) +
511	46	MS:363 (M+H) +
512	46	MS:405 (M+H) +
513	46	MS:749 (M+H) +
514	46	MS:381 (M+H) +
515	46	MS:314 (M+H) +
516	46	MS:328 (M+H) +
517	46	MS:356 (M+H) +
518	46	MS:368 (M+H) +
519	46	MS:370 (M+H) +
520	46	MS:377 (M+H) +
521	46	MS:379 (M+H) +
522	46	MS:382 (M+H) +
523	46	MS:394 (M+H) +
524	46	MS:378 (M+H) +
525	46	MS:378 (M+H) +
526	46	MS:393 (M+H) +
527	46	MS:426 (M+H) +
528	46	MS:342 (M+H) +
529	46	MS:384 (M+H) +
530	47	MS:368 (M+H) +
531	47	MS:354 (M+H) +
532	47	MS:354 (M+H) +
533	47	MS:354 (M+H) +
534	47	MS:368 (M+H) +
535	47	¹ H-NMR (400MHz, d6-DMSO) δ :1.13-1.27 (1H, m), 1.43-1.52 (2H, m), 1.62-1.73 (4H, m), 1.78-1.91 (5H, m), 2.07-2.42 (6H, m), 3.54-3.67 (5H, m), 4.00-4.13 (1H, m), 4.53 (1H, brs), 6.35-6.43 (1H, m), 7.18-7.20 (1H, m), 7.70 (1H, s), 7.82 (1H, m), 11.64 (1H, brs). MS:383 (M+H) +
536	49	MS:440 (M+H) +
537	47	¹ H-NMR (400MHz, d6-DMSO) δ :1.58-2.42 (8H, m), 3.04-3.66 (4H, m), 4.19-4.38 (1H, m), 6.37-6.54 (1H, m), 6.87-7.96 (8H, m), 8.36 (1H, s), 10.08-10.26 (1H, m), 11.42 (1H, brs). MS:376 (M+H) +
538	49	MS:421 (M+H) +
539	49	MS:408 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
540	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-2.22 (9H, m), 4.59 (1H, m), 4.83 (2H, m), 6.59 (1H, m), 6.98 (1H, m), 7.20 (1H, m), 7.73 (1H, m), 8.33 (1H, m), 8.37 (1H, m), 9.34 (1H, m), 11.53 (1H, s). MS: 389 (M+H) +
541	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.49-2.36 (7H, m), 4.63 (1H, m), 4.91 (2H, m), 6.61 (1H, m), 6.98 (1H, m), 7.21 (1H, m), 7.77 (1H, m), 8.32 (1H, m), 9.15 (2H, m), 9.39 (1H, m), 11.54 (1H, s). MS: 409 (M+H) +
542	49	MS: 442, 444
543	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.41-2.33 (8H, m), 4.61 (1H, m), 4.86 (2H, m), 6.60 (1H, m), 6.95 (1H, m), 7.21 (1H, m), 7.32 (1H, m), 7.74 (1H, m), 7.88 (1H, m), 8.32 (1H, m), 9.34 (1H, m), 11.53 (1H, s). MS: 389 (M+H) +
544	49	MS: 394 (M+H) +
545	49	MS: 389 (M+H) +
546	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-1.51 (2H, m), 1.59-1.62 (2H, m), 1.66-1.71 (2H, m), 1.81-1.92 (4H, m), 2.07-2.10 (1H, m), 2.28-2.31 (2H, m), 3.69-3.87 (8H, m), 4.20-4.24 (1H, m), 4.47 (1H, s), 6.59-6.61 (1H, m), 6.96 (1H, d, J=9.0Hz), 7.28-7.29 (1H, m), 7.91 (1H, dd, J=2.4, 9.1Hz), 8.52-8.53 (1H, m), 8.66 (1H, s), 8.86-8.89 (1H, m), 11.90 (1H, brs). MS: 566 (M+H) +
547	49	MS: 405 (M+H) +
548	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.75-1.87 (2H, m), 1.98-2.14 (2H, m), 2.14-2.33 (4H, m), 4.25-4.35 (1H, m), 4.50-4.83 (2H, m), 6.38-6.45 (1H, m), 6.85 (1H, d, J=9.0Hz), 7.03-7.10 (1H, m), 7.05 (1H, br), 7.83 (1H, br), 7.85 (1H, dd, J=9.0, 2.2Hz), 8.38 (1H, s), 8.51 (1H, d, J=2.2Hz), 10.36 (1H, d, J=7.7Hz), 11.43 (1H, s). MS: 388 (M+H) +
549	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.75-1.87 (2H, m), 1.98-2.14 (2H, m), 2.14-2.33 (4H, m), 4.25-4.35 (1H, m), 4.50-4.83 (2H, m), 6.38-6.45 (1H, m), 6.85 (1H, d, J=9.0Hz), 7.03-7.10 (1H, m), 7.05 (1H, br), 7.83 (1H, br), 7.85 (1H, dd, J=9.0, 2.2Hz), 8.38 (1H, s), 8.51 (1H, d, J=2.2Hz), 10.36 (1H, d, J=7.7Hz), 11.43 (1H, s). MS: 388 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
550	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.83-1.94 (2H, m), 2.01-2.18 (2H, m), 2.18-2.36 (4H, m), 4.27-4.38 (1H, m), 4.46-5.09 (2H, m), 6.38-6.45 (1H, m), 6.87 (1H, d, J=9.5Hz), 7.04-7.11 (1H, m), 7.05 (1H, br), 7.83 (1H, br), 8.24 (1H, d, J=9.5, 2.8Hz), 8.39 (1H, s), 9.01 (1H, d, J=2.8Hz), 10.38 (1H, d, J=7.7Hz), 11.45 (1H, s). MS: 408 (M+H) +
551	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.69-1.84 (2H, m), 1.99-2.14 (2H, m), 2.14-2.36 (4H, m), 4.24-4.34 (1H, m), 4.54-4.75 (2H, m), 6.38-6.44 (1H, m), 6.88 (1H, d, J=8.9Hz), 7.02-7.07 (1H, m), 7.06 (1H, br), 7.79 (1H, dd, J=8.9, 2.5Hz), 7.80 (1H, br), 8.38 (1H, s), 8.42-8.45 (1H, m), 10.35 (1H, d, J=7.7Hz), 11.42 (1H, s). MS: 431 (M+H) +
552	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.83-1.95 (2H, m), 2.05-2.21 (2H, m), 2.21-2.41 (4H, m), 2.45 (3H, s), 4.42-4.52 (1H, m), 4.58-4.85 (2H, m), 6.54-6.60 (1H, m), 6.89 (1H, d, J=8.9Hz), 7.17-7.22 (1H, m), 7.87 (1H, dd, J=8.9, 2.4Hz), 8.53 (1H, dd, J=2.4, 0.4Hz), 8.59 (1H, s), 9.26 (1H, d, J=7.6Hz), 11.79 (1H, s). MS: 427 (M+H) +
553	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.80-2.00 (4H, m), 2.11-2.22 (2H, m), 2.29-2.42 (2H, m), 4.28-4.40 (3H, m), 6.42-6.48 (1H, m), 6.89 (1H, dd, J=8.0, 4.6Hz), 7.04 (1H, br), 7.05-7.10 (1H, m), 7.74 (1H, br), 8.21 (1H, dd, J=8.0, 1.7Hz), 8.37 (1H, s), 8.42 (1H, dd, J=4.6, 1.7Hz), 10.27 (1H, d, J=7.7Hz), 11.41 (1H, s). MS: 408 (M+H) +
554	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.55-1.65 (2H, m), 2.02-2.25 (6H, m), 4.38-4.44 (2H, m), 5.55-5.65 (1H, m), 7.10 (1H, brs), 7.82 (1H, brs), 8.05 (1H, s), 8.11 (1H, s), 8.42 (1H, s), 9.18 (1H, d, J=8.5Hz), 12.9 (1H, brs). MS: 395 (M+H) +
555	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.60-1.67 (2H, m), 1.96-2.06 (4H, m), 2.16-2.21 (2H, m), 4.50-4.60 (2H, m), 4.99 (1H, brs), 6.59 (1H, s), 7.00 (1H, brs), 7.20 (1H, s), 7.80 (1H, brs), 8.22 (1H, d, J=1.9Hz), 8.34 (1H, s), 8.55 (1H, d, J=1.9Hz), 9.43 (1H, d, J=8.5Hz), 11.5 (1H, s). MS: 422 (M+H) +

Table 72 (contd.)

Ex	Ref-Ex	Data
556	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.22-2.03 (8H, m), 4.58-4.67 (5H, m), 5.38 (1H, brs), 6.58-6.59 (1H, m), 6.97 (1H, brs), 7.19-7.25 (2H, m), 7.44-7.46 (1H, m), 7.75 (1H, brs), 8.31 (1H, s), 9.30 (1H, d, J=8.0Hz), 11.54 (1H, s). MS: 394 (M+H) +
557	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.30-2.15 (8H, m), 4.34 (2H, brs), 4.55-4.56 (1H, m), 6.57-6.58 (1H, m), 6.95 (1H, brs), 7.18-7.20 (1H, m), 7.86 (1H, brs), 8.00 (1H, s), 8.34 (1H, s), 9.39 (1H, d, J=8.0Hz), 11.55 (1H, brs). MS: 394 (M+H) +
558	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.56-2.56 (8H, m), 3.69 (3H, s), 4.66-4.85 (3H, m), 6.66 (1H, s), 7.25-7.35 (2H, m), 7.85-7.94 (1H, m), 8.35-8.43 (1H, m), 9.33-9.45 (1H, m), 11.53 (1H, m). MS: 422 (M+H) +
559	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.23-2.32 (8H, m), 4.60-4.80 (3H, m), 6.61 (1H, s), 7.24-7.36 (2H, m), 7.85-8.40 (6H, m), 9.27-9.37 (1H, m), 11.53 (1H, brs). MS: 405 (M-H) -
560	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.96-1.98 (2H, m), 2.15-2.20 (2H, m), 2.31-2.37 (2H, m), 2.51-2.58 (2H, m), 4.33 (1H, m), 5.00 (2H, s), 5.96 (1H, s), 6.94-6.97 (1H, m), 7.37 (1H, t, J=3.0Hz), 7.90 (1H, s), 8.14 (1H, dd, J=1.8, 7.7Hz), 8.47 (1H, dd, J=2.0, 4.8Hz), 10.95 (1H, s), 11.60 (1H, s). MS: 386 (M+H) +
561	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.71-1.73 (2H, m), 1.98-1.99 (2H, m), 2.13 (2H, m), 2.43-2.54 (4H, m), 4.81 (2H, s), 5.10 (1H, brs), 7.07 (1H, d, J=4.9Hz), 7.44 (1H, s), 7.90 (1H, s), 8.41 (1H, d, J=5.1Hz), 10.97 (1H, s), 11.52 (1H, s). MS: 386 (M+H) +, 408 (M+Na) +
562	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.94-1.96 (2H, m), 2.15 (2H, m), 2.26-2.32 (2H, m), 2.47-2.54 (2H, m), 4.04 (1H, m), 4.77 (1H, s), 5.59 (1H, brs), 7.06 (1H, d, J=5.2Hz), 7.32 (1H, brs), 7.48 (1H, s), 7.88 (1H, s), 8.39 (1H, d, J=5.0Hz), 10.92 (1H, s), 11.58 (1H, s). MS: 386 (M+H) +

Table 72 (contd.)

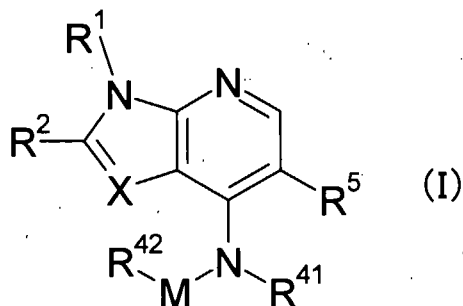
Ex	Ref -Ex	Data
563	49	¹ H-NMR (400MHz, d6-DMSO) δ : 1.97-1.99 (2H, m), 2.16 (2H, brs), 2.28-2.35 (2H, m), 2.46-2.54 (2H, m), 4.03 (1H, m), 4.83 (2H, s), 5.70 (1H, s), 7.70 (1H, d, J=9.0Hz), 7.33 (1H, s), 7.88 (1H, s), 7.98 (1H, dd, J=2.4, 9.0Hz), 8.60 (1H, d, J=2.4Hz), 10.94 (1H, s), 11.60 (1H, s). MS: 386 (M+H) +
564	50	MS: 394 (M+H) -
565	50	¹ H-NMR (400MHz, d6-DMSO) δ : 1.46-2.22 (13H, m), 2.59 (3H, s), 4.09 (1H, m), 4.55 (1H, s), 6.49 (1H, m), 7.16 (1H, m), 8.58 (1H, s), 10.67 (1H, m), 11.71 (1H, s). MS: 326.2 (M+H) +
566	50	MS: 410 (M+H) +
567	50	¹ H-NMR (400MHz, d6-DMSO) δ : 1.43-1.50 (4H, m), 1.63 (6H, s), 1.65-1.74 (3H, m), 1.87-1.94 (3H, m), 2.03-2.11 (1H, m), 2.21-2.24 (2H, m), 4.30-4.34 (1H, m), 4.53 (1H, s), 6.06 (1H, s), 6.49-6.51 (1H, m), 7.23-7.25 (1H, m), 7.84-7.87 (1H, m), 8.71 (1H, s), 11.63 (1H, brs). MS: 410 (M+H) +
568	53	¹ H-NMR (400MHz, d6-DMSO) δ : 1.45-2.33 (7H, m), 3.80 (3H, s), 4.07 (1H, m), 4.46 (1H, m), 6.07 (2H, s), 6.43 (1H, m), 7.11 (1H, m), 8.13 (1H, s), 8.84 (1H, m), 11.31 (1H, s). MS: 356 (M+H) +
569	53	¹ H-NMR (400MHz, d6-DMSO) δ : 1.40-2.45 (13H, m), 4.11 (1H, m), 4.44 (1H, s), 6.45 (1H, m), 7.14 (1H, m), 7.86 (1H, s), 8.32 (1H, s), 8.60 (1H, m), 10.77 (1H, s), 11.41 (1H, s). MS: 327 (M+H) +
570	53	¹ H-NMR (400MHz, d6-DMSO) δ : 1.47-2.25 (7H, m), 2.31 (3H, s), 3.96 (3H, s), 4.10 (1H, m), 4.50 (1H, s), 6.46 (1H, m), 7.13 (1H, m), 8.16 (1H, s), 9.12 (1H, m), 11.39 (1H, s). MS: 328 (M+H) +
571	53	¹ H-NMR (400MHz, d6-DMSO) δ : 1.29-2.27 (12H, m), 2.31 (3H, s), 4.09 (1H, m), 4.32-4.37 (2H, m), 6.44 (1H, m), 7.12 (1H, m), 8.11 (1H, s), 9.33 (1H, m), 10.88 (1H, s), 11.32 (1H, s). MS: 341 (M+H) +
572	54	MS: 398 (M+H) +
573	54	MS: 366 (M+H) +
574	54	MS: 439 (M-H) +
575	54	MS: 384 (M+H) +

Table 72 (contd.)

Ex	Ref -Ex	Data
576	54	MS: 440 (M-H) -
577	54	MS: 384 (M+H) +
578	55	$^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$) δ : 1.36-1.42 (2H, m), 1.57-1.69 (4H, m), 1.73-1.79 (2H, m), 1.93-1.99 (2H, m), 2.05-2.09 (1H, m), 2.27-2.31 (2H, m), 4.00-4.04 (1H, m), 4.48 (1H, s), 6.11 (1H, d, $J=16.1\text{Hz}$), 6.10-6.13 (1H, m), 6.42-6.44 (1H, m), 7.16-7.18 (1H, m), 7.91 (1H, d, $J=16.1\text{Hz}$), 8.21 (1H, s), 11.53 (1H, brs). MS: 335 (M+H) +
579	61	$^1\text{H-NMR}$ (400MHz, $\text{d}_6\text{-DMSO}$) δ : 1.45-2.69 (13H, m), 4.19 (1H, m), 4.53 (1H, s), 6.54 (1H, m), 7.25 (1H, m), 8.43 (1H, s), 8.75 (1H, m), 11.68 (1H, s), MS: 367 (M+H) +, 365 (M-H) -

CLAIMS

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



5

wherein

X is N or CR³,

M is (CH₂)_m; m is 0 or 1,

R¹ is -H or lower alkyl which may be substituted,

10 R² is -H or lower alkyl which may be substituted,

R³ is -H, halogen, or lower alkyl which may be

substituted,

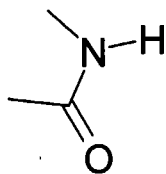
R⁴¹ is -H or heteroaryl which may be substituted,

R⁴² is a bridged ring group which may be substituted,

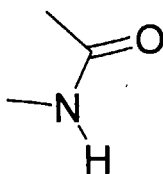
15 R⁵ is a group selected from the group consisting of
halogen, cyano, acyl, acylamino, lower alkyl, lower alkenyl,
-O-lower alkyl, 5- or 6-membered heterocycloalkyl, 5- or
6-membered heterocycloalkenyl, and 5-membered heteroaryl,
each of which may be substituted,

20 provided that when R⁵ is 5-membered heteroaryl, X is -CR³,
or R⁴¹ and R⁵ may be linked via a specific functional group

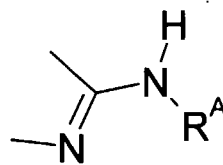
to form bivalent groups shown below:



(I-A)



(I-B)



(I-C)

wherein R^A is -H or acyl which may be substituted,
or pharmaceutically acceptable salts thereof.

5

2. The compound according to claim 1, wherein

R^1 is -H or lower alkyl which may be substituted with
a group selected from the group consisting of mono- or di-lower
alkylamino and -O-lower alkyl,

10

R^2 is -H or lower alkyl,

R^3 is -H or lower alkyl substituted with a group selected
from the group consisting of halogen, mono- or di-lower
alkylamino, and cyclic amino,

15

R^{41} is -H or heteroaryl which may be substituted with
cyano,

R^{42} is bridged cyclic hydrocarbon or aza-bridged cyclic
hydrocarbon, each of which may be substituted,

20

R^5 is a group selected from the group consisting of
halogen, cyano, loweralkylcarbonyl, lower alkyloxycarbonyl,
hydroxycarbonyl, formyl, amidinooxycarbonyl,
guanidinooxycarbonyl, guanidino, carbamoyl, -C(=O) -5- or

-6-membered heterocycloalkyl, -C(=O)-5- or -6-membered heteroaryl, lower alkyl, lower alkenyl, -O-lower alkyl, 5- or 6-membered heterocycloalkyl, and 5-membered heteroaryl, each of which may be substituted,

5 provided that when R^5 is 5-membered heteroaryl, X is $-CR^3$.

3. The compound according to claim 1 or 2, wherein R^{42} is adamantyl, bicyclo[2.2.1]heptyl or tropanyl, each of which may be substituted.

10

4. The compound according to claim 1, 2 or 3, wherein R^5 is carbamoyl, 5-membered heteroaryl, lower alkylcarbonyl, each of which may be substituted with NH_2 , hydroxymethyl or OH.

15

or R^{41} and R^5 may be linked via a specific functional group to form (I-A).

or R^{41} and R^5 may be linked via a specific functional group to form (I-B).

20

or R^{41} and R^5 may be linked via a specific functional group to form (I-C) wherein R^A is $-C(=O)-C(=O)NH$ -loweralkyl which may be substituted with lower alkyloxy.

25

5. The compound according to claim 1, 2 or 3, wherein R^5 is oxadiazole or thiadiazole, each of which may be substituted.

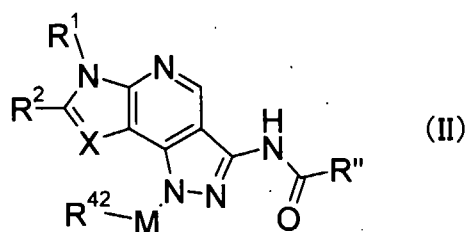
6. A compound selected from those described below:

- 1) 4-[(1R,2R,4S)-Bicyclo[2.2.1]hept-2-ylamino]-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 5 2) 4-{[(3-exo)-8-(5-Cyanopyridin-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 3) rel-4-{[(1R,2S,3S,5s)-5-Hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 4) rel-4-{[(1R,2R,3S,5s)-5-Hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 10 5) 4-{[(3-exo)-8-(5-Nitropyridin-2-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 6) rel-(1s,3R,4R,5S)-4-{[5-(5-Amino-1,3,4-thiadiazol-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino}adamantan-1-ol
- 15 7) 4-{[(3-exo)-8-(6-Cyanopyridazin-3-yl)-8-azabicyclo[3.2.1]oct-3-yl]amino}-1H-pyrrolo[2,3-b]pyridine-5-carboxamide
- 8) rel-(1s,3R,4R,5S)-4-({5-[3-(Hydroxymethyl)-1,2,4-oxadiazol-5-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl}amino)adamantan-1-ol
- 20 9) N-(Cyanomethyl)-N-methyl-4-(2-oxo-3,6-dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridin-1(2H)-yl)adamantane-1-carboxamide
- 10) 7-[(5-Cyanoadamantan-2-yl)amino]-3H-imidazo[4,5-b]pyridine-6-carboxamide
- 25

- 11) rel-(1s,3R,4R,5S)-4-{[5-(1,3,4-Oxadiazol-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino}adamantan-1-ol
- 12) 2-Hydroxy-1-(rel-4-{[(1R,2R,3S,5s)-5-hydroxyadamantan-2-yl]amino}-1H-pyrrolo[2,3-b]pyridin-5-yl)ethanone
- 5 13) 3-{[4-(3-oxo-3,6-Dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridin-1(2H)-yl)adamantan-1-yl]oxy}propanenitrile
- 14) rel-N-{1-[(1R,2R,3S,5s)-5-Hydroxyadamantan-2-yl]-1,6-dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridin-3-yl}-N'-(2-methoxyethyl)ethanediamide
- 10 15) rel-N-{1-[(1R,2R,3S,5s)-5-Hydroxyadamantan-2-yl]-1,6-dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridin-3-yl}-N'-methylethanediamide
- 16) rel-N-{1-[(1R,2R,3S,5s)-5-Hydroxyadamantan-2-yl]-1,6-dihydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridin-3-yl}-N'-(trans-4-methoxycyclohexyl)ethanediamide
- 15 17) 3-{[4-(2-oxo-3,6-Dihydroimidazo[4,5-d]pyrrolo[2,3-b]pyridin-1(2H)-yl)adamantan-1-yl]oxy}propanenitrile

7. The compound according to any one of claims 1 to 6,
20 said compound being an optically-active substance and/or endo-exo isomer.

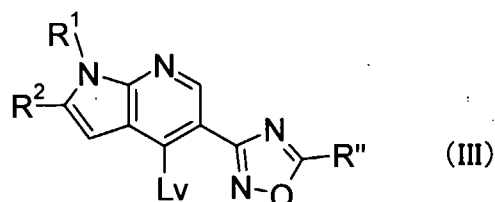
8. A process for preparing the compound represented by the following formula (II) or salts thereof:



wherein R^1 , R^2 , R^{42} , X and M are as defined in claim 1; R'' is suitable substituent.

by reacting the compound represented by the following formula

5 (III):



wherein R^1 , R^2 , R'' and Lv are as defined above;

with a primary amine represented by $R^{42}-M-NH_2$.

10 9. The compound according to any one of claims 1 to 7, said compound being used as a medicament.

10. The compound according to any one of claims 1 to 7, said compound being used to treat and/or prevent diseases
 15 including rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopy, Alzheimer's disease, tumors, plasmacytic myeloma and leukemia in human beings or animals.

11. A medicament containing the compound according to any one of claims 1 to 7 as an active ingredient.

12. A medicament containing the compound according to any one of claims 1 to 7 as an active ingredient, with a pharmaceutically acceptable carrier or excipient.

13. A janus kinase 3 (JAK3) inhibitor comprising the compound according to any one of claims 1 to 7.

10

14. A method for treating and/or preventing diseases including rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopy, Alzheimer's disease, tumors, plasmacytic myeloma and leukemia in human beings or animals, said method comprising administration of the compound according to any one of claims 1 to 7 to human beings or animals.

15. A use of the compound according to any one of claims 1 to 7 to treat and/or prevent diseases including rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopy, Alzheimer's disease, tumors, plasmacytic myeloma and leukemia in human beings or animals.

25

16. A product comprising a pharmaceutical composition containing the compound according to any one of claims 1 to 7 and a written notice regarding the pharmaceutical composition, said written notice stating that the compound (I) can be or should be used to treat and/or prevent diseases including rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, atopy, Alzheimer's disease, tumors, plasmacytic myeloma and leukemia in human beings or animals.