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(54) **Pyrazoloquinoline compounds**

Pyrazolochinolinverbindungen

Composés pyrazoloquinoliniques

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Description

Technical Field

[0001] The present invention relates to a pyrazoloquinoline compound which is useful as an active ingredient for a pharmaceutical composition, in particular, a pharmaceutical composition for treating storage dysfunction, voiding dysfunction, bladder/urethral diseases, and the like.

Background Art

[0002] The important roles of voiding function are urine storage and voiding, which are regulated by a coordinated action of the bladder and the urethra. That is, during the urine storage, the bladder smooth muscle is relaxed and the urethra sphincter is contracted, whereby a state in which urethral resistance is high is maintained, and urinary continence is also maintained. On the other hand, during the voiding, the bladder smooth muscle is contracted while the urethra smooth muscle is relaxed, and the contraction of the external urethral sphincter is also inhibited. Examples of voiding dysfunction include a storage dysfunction such as overactive bladder and the like in which urine cannot be retained during urine storage and a voiding dysfunction in which urine cannot be drained sufficiently due to increase in the urethral resistance and decrease in the bladder contractile force. These two dysfunctions may be expressed simultaneously.

[0003] In treatment of a storage dysfunction such as overactive bladder and the like, anticholinergic agents have been used frequently. However, these agents cannot provide a sufficient therapeutic effect, and further, side effects based on the anticholinergic action (dry mouth, gastrointestinal symptoms, eye symptoms, arrhythmias, or the like) appear, and accordingly, administration of the agents may be often interrupted. Further, the anticholinergic agents reduce the bladder contractile force, and are therefore contraindicated for urinary frequency/incontinence accompanying urethral obstruction such as benign prostatic hyperplasia and the like.

[0004] Voiding dysfunction is caused by an increase in urethral resistance during the voiding or a decrease in the bladder contractile force. As a disease causing an increase in urethral resistance, voiding dysfunction accompanying benign prostatic hyperplasia is well known, which is characterized by urethral obstruction due to nodular hypertrophy of the prostate tissues. An α_1 receptor antagonist has now been used for the purpose of treating voiding dysfunction accompanying benign prostatic hyperplasia (see, for example, Non-Patent Document 1). Other causes of the increase in urethral resistance include functional obstructions such as urethra relaxation failure during voiding or detrusor-external urethral sphincter dyssynergia and the like due to neurological disorders such as diabetes, aging, bone marrow damage, pelvic surgery, and the like,. With patients with these diseases, there exists many cases in which the α_1 receptor antagonist is ineffective. On the other hand, a decrease in the bladder contractile force during the voiding, referred to as underactive bladder, acontractile bladder, neurogenic bladder, or the like, also causes voiding dysfunction. Known factors for decreasing the bladder contractile force include aging, neurological diseases such as diabetes, Parkinson's disease, multiple sclerosis and the like, bone marrow damage, and neurological disorders due to pelvic surgery. Examples of an agent for treating a decrease in the bladder contractile force during voiding include bethanechol chloride which is a muscarinic receptor agonist and distigmine bromide which is a cholinesterase inhibitor. Both of these drugs have side effects, and thus, their satisfactoriness is low (see, for example, Non-Patent Documents 2 and 3). In voiding dysfunction caused by an increase in the urethral resistance or a decrease in the bladder contractile force as described above, residual urine after voiding is observed. Increased residual urine may cause a decrease in effective bladder capacity, and thus, cause overactive bladder symptoms such as urinary frequency and the like, or severe symptoms, such as hydronephrosis in some cases, and in this regard, there is a demand for a therapeutic agent which is more effective than a current therapeutic agent.

[0005] It is known that a relaxation system due to nitric oxide (NO) is present in the smooth muscle, and NO produced in the nerve terminals or locally activates soluble guanylate cyclase present in the smooth muscle cells. The activated guanylate cyclase increases cyclic guanosine monophosphate (cGMP) in the cells. On the other hand, the cGMP is degraded into 5'-GMP by phosphodiesterase (PDE) which is an enzyme degrading the cGMP. An increase in the intracellular cGMP concentration is considered to contribute significantly to the smooth muscle relaxation. Therefore, the decrease of the NO-cGMP system causes relaxation failure of the smooth muscle. For example, in patients showing urethral obstruction in benign prostatic hyperplasia or in the elderly as described above, it is reported that NO production is significantly decreased (Non-Patent Documents 4 and 5).

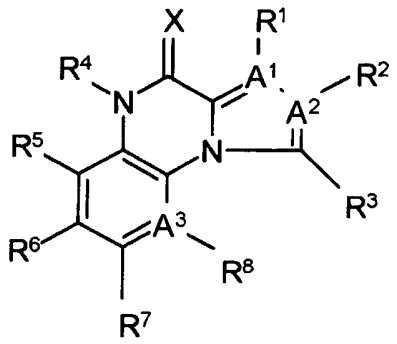
[0006] As a subtype of PDE which specifically degrades cGMP, PDE5, PDE6 and PDE9 are known, and among these, PDE9 has a higher substrate affinity than PDE5 and PDE6 (Non-Patent Document 6). Further, from the viewpoint that in the distribution of expression in various tissues, PDE9 is observed at its highest expression in the human prostate (Non-Patent Document 7), it plays an important role in smooth muscle relaxation in lower urethra smooth muscle and a PDE9 inhibitor enhances the relaxation of the urethra via cGMP in the tissue. Therefore, it is considered that the PDE9 inhibitor exhibits an effect against voiding dysfunction due to an increase in the urethral resistance. Since the PDE9

inhibitor decreases the urethral resistance, an effect against voiding dysfunction in which the bladder contractile forces are decreased can be expected. In addition, the decrease in residual urine due to an improvement of the voiding dysfunction will lead to the improvement of overactive bladder symptoms such as urinary frequency and the like or avoidance of renal disorders. Therefore, it is considered that the PDE9 inhibitor is useful as an agent for preventing and/or treating storage dysfunction, voiding dysfunction, and bladder/urethral diseases.

[0007] For example, as a compound having a PDE5- and/or PDE9-inhibitory action(s), in Patent Documents 1 and 2, there are disclosed quinoxaline derivatives represented by the following formulae (A) and (B), respectively. Further, in Patent Documents 3 and 4, there are disclosed a thienopyrimidine derivative and a quinazoline derivative as compounds having a PDE5- and/or PDE9-inhibitory action(s), respectively. In addition, in Patent Documents 5 to 12, there is disclosed a pyrazolopyridine derivative which has a PDE9-inhibitory action.

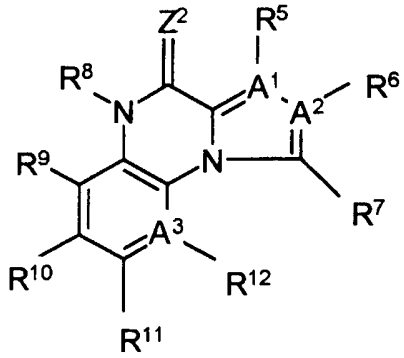
[0008] Furthermore, in Patent Documents 13 to 17, there are disclosed compounds represented by the following formulae (C) to (G), but there is no specific disclosure of the compounds of the present invention. In addition, there is no description that the compound has a PDE9-inhibitory action and can be used for treating disorders in voiding function.

[Chem. 1]



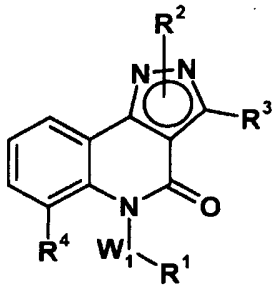
(A)

[Chem. 2]



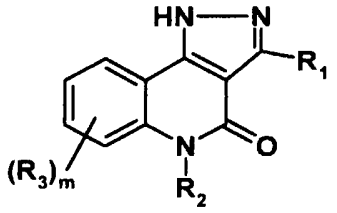
(B)

[Chem. 3]



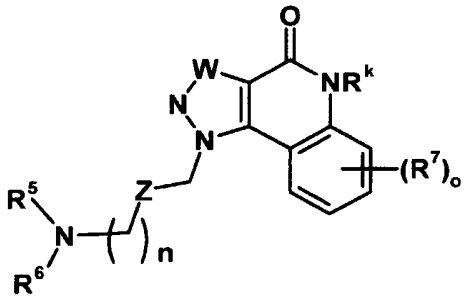
(C)

[Chem. 4]



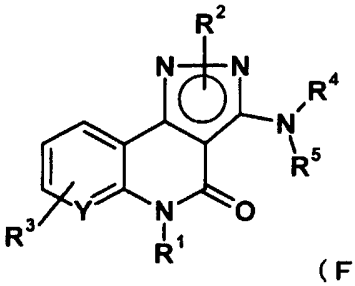
(D)

[Chem. 5]



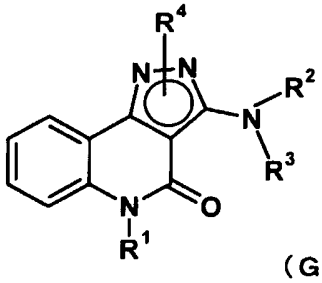
(E)

[Chem. 6]



(F)

[Chem. 7]



(G)

[0009] (For the symbols in the formulae, refer to each of the corresponding patent publications.)

Related Art

Patent Document

[0010]

[Patent Document 1] Pamphlet of International Publication WO 2008/072779
[Patent Document 2] Pamphlet of International Publication WO 2008/072778
[Patent Document 3] Pamphlet of International Publication WO 2006/135080

[Patent Document 4] Pamphlet of International Publication WO 2008/018306
[Patent Document 5] Pamphlet of International Publication WO 2010/026214
[Patent Document 6] Pamphlet of International Publication WO 2010/084438
[Patent Document 7] Pamphlet of International Publication WO 2009/068617
[Patent Document 8] Pamphlet of International Publication WO 2009/121919
[Patent Document 9] Pamphlet of International Publication WO 2008/139293
[Patent Document 10] Pamphlet of International Publication WO 2004/018474
[Patent Document 11] Pamphlet of International Publication WO 2003/037432
[Patent Document 12] Pamphlet of International Publication WO 2003/037899
[Patent Document 13] Pamphlet of International Publication WO 2005/028474
[Patent Document 14] JP-A-2006-45118
[Patent Document 15] Pamphlet of International Publication WO 2007/115232
[Patent Document 16] JP-A-5-132484
[Patent Document 17] European Patent Publication No. 476544

Non-Patent Document

[0011]

[Non-Patent Document 1] Thiyagarajan, M., Pharmacology, 65:pp. 119-128 (2002)
[Non-Patent Document 2] Shah, P. J. R., et al., Br. J. Urol., 55:pp. 229-232 (1983)
[Non-Patent Document 3] Finkbeiner, A.E., J. Urol., 134:pp. 443-449 (1985)
[Non-Patent Document 4] Bloch, W., et al., Prostate, 33:pp. 1-8 (1997)
[Non-Patent Document 5] Toprakqi, M., et al., Int. J. Clin. Lab. Res., 30:pp. 83-85 (2000)
[Non-Patent Document 6] Fisher, D.A., et al., J. Biol. Chem., 273:pp. 15559-15564(1998)
[Non-Patent Document 7] Rentero, C., et al., Biochem. Biophys. Res. Commun., 301 :pp. 686-692 (2003)

Summary of Invention

Problems to Be Solved by the Invention

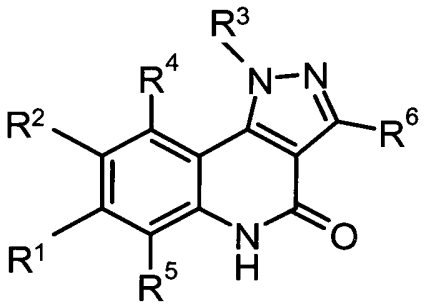
[0012] The present inventors aim to provide a compound which has a PDE9-inhibitory action and is useful as an active ingredient for a pharmaceutical composition for preventing and treating storage dysfunction, voiding dysfunction, bladder/urethral diseases, and the like.

Means for Solving the Problems

[0013] The present inventors have extensively investigated a compound which has a PDE9-inhibitory action, and as a result, they have found that a compound of the formula (I) is useful as a compound having a PDE9-inhibitory action, thereby completing the present invention.

[0014] That is, the present invention relates to a compound of the formula (I) or a salt thereof, and a pharmaceutical composition including the compound of the formula (I) or a salt thereof, and an excipient.

[Chem. 8]

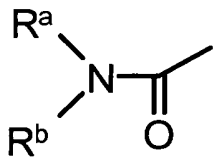


(I)

wherein

R^1 is hydrogen, halogeno-C_{1-6} alkyl, C_{1-6} alkyl, or -O-C_{1-6} alkyl,
R^2 is a group of the formula (II):

[Chem. 17]



(II)

R^3 is C_{1-6} alkylene-(cycloalkyl which may be substituted with halogen or -O-C_{1-6} alkyl); C_{1-6} alkylene-oxygen-containing saturated hetero ring; cycloalkyl which may be substituted with halogen or -O-C_{1-6} alkyl; an oxygen-containing saturated hetero ring; or a monocyclic nitrogen-containing saturated hetero ring which may be substituted with C_{1-6} alkyl, C_{1-6} alkylene-aryl, or -CO-C_{1-6} alkylene-O-C_{1-6} alkyl,
R^4, R^5 and R^6 are hydrogen,
R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring, which may be substituted with a group selected from:

-OH; halogeno-C_{1-6} alkyl; -O-C_{1-6} alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; C_{1-6} alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl, -O-cycloalkyl, -O-C_{1-6} alkyl, and -O-halogeno-C_{1-6} alkyl; and C_{1-6} alkylene-O-C_{1-6} alkyl which maybe substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl,
the group G_1 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-hetero ring, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-hetero ring, aryl which may be substituted with C_{1-6} alkyl, a hetero ring which may be substituted with C_{1-6} alkyl, -COOH, -CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, - CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, - CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CO-N(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring, and
the group G_2 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno- C_{1-6} alkyl, cyano, -N(C_{1-6} alkyl)$_2$, -NH-CO-C_{1-6} alkyl, C_{1-6} alkylene-O-C_{1-6} alkyl, C_{1-6} alkylene-hetero ring, aryl, a hetero ring which may be substituted with C_{1-6} alkyl-, COOH, -CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, -CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CON(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring
wherein "aryl" refers to a C_{6-14} monocyclic to tricyclic aromatic hydrocarbon ring group and the term "hetero ring" refers to a ring group containing (i) a monocyclic 3- to 8-membered ring containing 1 to 4 hetero atoms selected from oxygen, sulfur and nitrogen, or (ii) a bi- to tricyclic ring containing 1 to 5 hetero atoms selected from oxygen, sulfur and nitrogen, formed by ring fusion of a monocyclic hetero ring with one or two rings selected from the group consisting of a monocyclic hetero ring, a benzene ring, C_{5-8} cycloalkane, and C_{5-8} cycloalkene.

[0015] Furthermore, unless specifically described otherwise, in the case where the symbols in any of the formulae in the present specification are also used in other formulae, the same symbols denote the same meanings.

[0016] Furthermore, the present invention relates to a pharmaceutical composition for preventing or treating storage dysfunction, voiding dysfunction, and bladder/urethral diseases, and the like, which includes a compound of the formula (I) or a salt thereof. Further, the pharmaceutical composition includes an agent for preventing or treating storage dysfunction, voiding dysfunction, and bladder/urethral diseases, and the like, which includes a compound of the formula (I) or a salt thereof.

[0017] The present invention further relates to use of the compound of the formula (I) or a salt thereof for the manufacture

of a pharmaceutical composition for preventing or treating storage dysfunction, voiding dysfunction, bladder/urethral diseases, and the like; and the compound of the formula (I) or a salt thereof for use in a method of preventing or treating storage dysfunction, voiding dysfunction, bladder/urethral diseases, and the like, in which the method includes administering to a subject an effective amount of the compound of the formula (I) or a salt thereof. Further, the "subject" is a human or another animal in need of such prevention or treatment, and in a certain embodiment, a human in need of such prevention or treatment.

[0018] In the present specification, the "storage dysfunction" refers to "storage function disorder (storage dysfunction)" with which urine cannot be held during storage, and the "voiding dysfunction" refers to "voiding function disorder (voiding dysfunction)" with which urine cannot be discharged sufficiently during voiding due to increased urethral resistance and decreased bladder contraction (Neurourol Urodynam, 21: pp. 167-178 (2002)).

[0019] As used in the present specification, the "bladder/urethral diseases" include "lower urinary tract dysfunction", and "lower urinary tract symptoms (LUTS)" (Neurourol Urodynam, 21: pp. 167-178 (2002)), which are symptoms derived from the lower urinary tract dysfunction. Accordingly, "bladder/urethral diseases" as used herein include "storage dysfunction" and "voiding dysfunction".

[0020] In the present invention, examples of the bladder/urethral diseases include, in a certain embodiment, underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, overactive bladder, and lower urinary tract symptoms thereof, and benign prostatic hyperplasia, interstitial cystitis, chronic prostatitis, urethra calculus, and lower urinary tract symptoms accompanying them, and the like.

[0021] In another embodiment, examples of the bladder/urethral diseases include underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, and lower urinary tract symptoms thereof, and benign prostatic hyperplasia, interstitial cystitis, chronic prostatitis, urethra calculus, and lower urinary tract symptoms accompanying them, and the like.

[0022] In a further embodiment, examples of the bladder/urethral diseases include underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, and lower urinary tract symptoms thereof, benign prostatic hyperplasia and lower urinary tract symptoms accompanying them, and the like.

[0023] In a still further embodiment, examples of the bladder/urethral diseases include underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, lower urinary tract symptoms thereof, benign prostatic hyperplasia and lower urinary tract symptoms accompanying them, and the like.

[0024] In the present invention, specific examples of the storage dysfunction include overactive bladder, and overactive bladder symptoms such as urinary urgency, urinary frequency, urge incontinence, nocturia, and the like.

[0025] In the present invention, examples of the voiding dysfunction include voiding dysfunction due to an increase in urethral resistance and voiding dysfunction due to a decrease in the bladder contractile force. In a certain embodiment, specific examples thereof include voiding dysfunction in the underactive bladder, voiding dysfunction in the hypotonic bladder, voiding dysfunction in the acontractile bladder, voiding dysfunction in the neurogenic bladder, voiding dysfunction in the detrusor underactivity, voiding dysfunction in the urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, voiding dysfunction accompanying benign prostatic hyperplasia, voiding dysfunction accompanying chronic prostatitis, voiding dysfunction accompanying urethra calculus, voiding dysfunction accompanying interstitial cystitis, voiding dysfunction accompanying detrusor underactivity, and the like.

[0026] In a further embodiment, examples of the voiding dysfunction include voiding dysfunction in the underactive bladder, voiding dysfunction in the hypotonic bladder, voiding dysfunction in the acontractile bladder, voiding dysfunction in the detrusor underactivity, voiding dysfunction in the urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, voiding dysfunction accompanying benign prostatic hyperplasia, and the like.

Effect of the Invention

[0027] The compound of the formula (I) or a salt thereof has a PDE9-inhibitory action, and can be used as an agent for preventing and/or treating diseases related to degradation of cGMP by PDE9, for example, storage dysfunction, voiding dysfunction, and bladder/urethral diseases, in another embodiment, diseases such as underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, overactive bladder, and lower urinary tract symptoms thereof, and benign prostatic hyperplasia, interstitial cystitis, chronic prostatitis, urethra calculus, and lower urinary tract symptoms accompanying them, and the like, and in a further embodiment, diseases such as underactive bladder, hypotonic bladder, acontractile bladder, neurogenic bladder, detrusor underactivity, overactive bladder, urinary frequency, nocturia, incontinence, benign prostatic hyperplasia, lower urinary tract symptoms, voiding dysfunction accompanying urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, interstitial cystitis, chronic prostatitis, urethra calculus, and the like.

Embodiments for Carrying Out the Invention

[0028] The "lower alkyl" as used herein is straight or branched chain alkyl having 1 to 6 carbon atoms (hereinafter simply referred to as C_{1-6}), for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, sec-pentyl, n-hexyl, or the like, and in another embodiment, C_{1-4} alkyl, and in a further embodiment, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl or tert-butyl.

[0029] The "lower alkylene" as used herein is linear or branched chain C_{1-6} alkylene, for example, methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, propylene, methylmethylene, ethylethylene, 1,2-dimethylethylene or 1,1,2,2-tetramethylethylene.

[0030] The "halogen" means F, Cl, Br or I.

[0031] The "halogeno-lower alkyl" is C_{1-6} alkyl substituted with one or more halogen atoms, in another embodiment, lower alkyl substituted with 1 to 5 halogen atoms, and in a further embodiment, trifluoromethyl.

[0032] The "cycloalkyl" is a C_{3-10} saturated hydrocarbon ring group, which may have a bridge. It is, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, adamantyl, or the like, in another embodiment, C_{3-8} cycloalkyl, in a further embodiment, C_{3-6} cycloalkyl, and in a still further embodiment, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

[0033] Unless otherwise indicated, the "aryl" refers to a C_{6-14} monocyclic to tricyclic aromatic hydrocarbon ring group, and includes a ring group fused with C_{5-8} cycloalkene at its double bond site. It is, for example, phenyl, naphthyl, 5-tetrahydronaphthyl, 1-tetrahydronaphthyl, 4-indenyl, 1-fluorenyl, or the like. In another embodiment, it is phenyl or 1-tetrahydronaphthyl.

[0034] Unless otherwise indicated, the "hetero ring" means a ring group containing i) a monocyclic 3- to 8-membered hetero ring, and in another embodiment, 5- to 7-membered hetero ring, each containing 1 to 4 hetero atoms selected from oxygen, sulfur and nitrogen, and ii) a bi- to tricyclic hetero ring containing 1 to 5 hetero atoms selected from oxygen, sulfur and nitrogen, formed by ring fusion of monocyclic hetero ring with one or two rings selected from the group consisting of a monocyclic hetero ring, a benzene ring, C_{5-8} cycloalkane, and C_{5-8} cycloalkene, and it includes a spiro ring group. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide.

[0035] Examples of the "hetero ring" include the following embodiments:

(1) Monocyclic saturated hetero rings

[0036]

(a) those containing 1 to 4 nitrogen atoms, for example, azepanyl, diazepanyl, aziridinyl, azetidinyl, pyrrolidinyl, imidazolidinyl, piperidyl, pyrazolidinyl, piperazinyl, azocanyl, and the like;
(b) those containing 1 to 3 nitrogen atoms and 1 to 2 sulfur atoms and/or 1 to 2 oxygen atoms, for example, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, morpholinyl, and the like;
(c) those containing 1 to 2 sulfur atoms, for example, tetrahydrothiopyranyl, tetrahydrothiophenyl, and the like;
(d) those containing 1 to 2 sulfur atoms and 1 to 2 oxygen atoms, for example, oxathiolanyl and the like;
(e) those containing 1 to 2 oxygen atoms, for example, oxiranyl, oxetanyl, dioxiranyl, tetrahydrofuranyl, tetrahydropyranyl, 1,4-dioxanyl, and the like;

(2) Monocyclic unsaturated hetero ring groups

[0037]

(a) those containing 1 to 4 nitrogen atoms, for example, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, tetrahydropyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl, tetrazolyl, triazinyl, dihydrotriazinyl, azepinyl, and the like;
(b) those containing 1 to 3 nitrogen atoms and 1 to 2 sulfur atoms and/or 1 to 2 oxygen atoms, for example, thiazolyl, isothiazolyl, thiadiazolyl, dihydrothiazinyl, oxazolyl, isoxazolyl, oxadiazolyl, oxazinyl, and the like;
(c) those containing 1 to 2 sulfur atoms, for example, thienyl, thiepinyl, dihydrodithiopyranyl, dihydrodithionyl, and the like;
(d) those containing 1 to 2 sulfur atoms and 1 to 2 oxygen atoms, for example, dihydroxathiopyranyl and the like;
(e) those containing 1 to 2 oxygen atoms, for example, furyl, pyranyl, oxepinyl, dioxolyl, and the like;

(3) Fused polycyclic saturated hetero ring groups

[0038]

(a) those containing 1 to 5 nitrogen atoms, for example, quinuclidinyl, azabicyclo[2.2.1]heptyl, diazabicyclo[2.2.1]heptyl, azabicyclo[3.2.1]octyl, diazabicyclo[3.2.1]octyl, diazabicyclo[3.3.1]nonyl, octahydropyrrolopyrazinyl, octahydropyrrolopyrrolyl, and the like;
(b) those containing 1 to 4 nitrogen atoms and 1 to 3 sulfur atoms and/or 1 to 3 oxygen atoms, for example, trithiadiazaindenyl, dioxoloimidazolidinyl, 2-oxa-5-azabicyclo[2.2.1]heptyl, and the like;
(c) those containing 1 to 3 sulfur atoms and/or 1 to 3 oxygen atoms, for example, 2,6-dioxabicyclo[3.2.2]oct-7-yl and the like;

(4) Fused polycyclic unsaturated hetero ring groups

[0039]

(a) those containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolinyl(2,3-dihydroindolyl), isoindolinyl(1,3-dihydroisoindolyl), indolidinyl, benzoimidazolyl, dihydrobenzoimidazolyl, tetrahydrobenzoimidazolyl, dihydropyrrolopyridyl, dihydropyrrolopyrimidinyl, quinolyl, dihydroquinolyl, tetrahydroquinolyl, isoquinolyl, tetrahydroisoquinolyl, indazolyl, imidazopyridyl, benzotriazolyl, tetrazolopyridazinyl, carbazolyl, acridinyl, quinoxalinyl, dihydroquinoxalinyl, tetrahydroquinoxalinyl, phthalazinyl, dihydroindazolyl, benzopyrimidinyl, naphthyridinyl, quinazolinyl, cinnolinyl, tetrahydronaphthyridinyl, tetrahydropyridopyrimidinyl, tetrahydropyrazolopyridyl, tetrahydropyrrolopyrazinyl, hexahydropyrrolopyrazinyl, tetrahydroimidazopyrazinyl, tetrahydrobenzoazepinyl, tetrahydropyridonaphthyridinyl, tetrahydropyridoindolyl, hexahydropyridoindolyl, tetrahydropyrrolopyridyl, tetrahydroimidazopyridyl, tetrahydrocarbolinyl, tetrahydrotriazolopyrazinyl, and the like;
(b) those containing 1 to 4 nitrogen atoms and 1 to 3 sulfur atoms and/or 1 to 3 oxygen atoms, for example, benzothiazolyl, dihydrobenzothiazolyl, benzothiadiazolyl, imidazothiazolyl, imidazothiadiazolyl, benzoxazolyl, dihydrobenzoxazolyl, dihydrobenzoxazinyl, dihydropyridoxazinyl, benzoxadiazolyl, benzoisothiazolyl, benzoisoxazolyl, tetrahydrothienopyridyl, tetrahydroxazolopyridyl, tetrahydrothiazolopyridyl, tetrahydroisoquixazolopyridyl, and the like;
(c) those containing 1 to 3 sulfur atoms, for example, benzothienyl, benzodithiopyranyl, dibenzothienyl, and the like;
(d) those containing 1 to 3 sulfur atoms and 1 to 3 oxygen atoms, for example, benzoxathiopyranyl, phenoxazinyl, and the like;
(e) those containing 1 to 3 oxygen atoms, for example, benzodioxolyl, benzofuranyl, dihydrobenzofuranyl, isobenzofuranyl, chromanyl, chromenyl, dibenzofuranyl, methylenedioxyphenyl, ethylenedioxyphenyl, and the like; and

(5) Spiro ring groups

[0040]

(a) those containing only a saturated bond, for example, azaspiro[4,4]nonyl, azaspiro[4,5]decyl, diazaspiro[4,5]decyl, triazaspiro[4,5]decyl, azaspiro[5,5]undecyl, diazaspiro[5,5]undecyl, oxazaspiro[4,5]decyl, and the like; and
(b) those containing an unsaturated bond, for example, 3H-spiro[2-benzofuran-1,4'-piperidyl], spiro[1-benzofuran-3,4'-piperidyl], 2,3-dihydrospiro[indene-1,4'-piperidyl], 3,4-dihydro-2H-spiro[naphthalene-1,3'-piperidyl], 1,2-dihydrospiro[indole-3,4'-piperidyl], and the like.

[0041] Specific examples of the "hetero ring" in the substituent for the polycyclic nitrogen-containing hetero ring formed by R^a and R^b which are combined with the adjacent nitrogen atom, or the "hetero ring" in the "hetero ring which may be substituted" in R^a and R^b include pyridyl, azethidinyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, and the like.
[0042] Specific examples of the "hetero ring" in the substituent for the monocyclic nitrogen-containing hetero ring formed by R^a and R^b which are combined with the adjacent nitrogen atom include azethidinyl, pyrrolidinyl, piperidyl, piperazinyl, azepanyl, morpholinyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, thiazolyl, thiadiazolyl, oxazolyl, isooxazolyl, furanyl, thienyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiophenyl, indolinyl(2,3-dihydroindolyl), dihydroquinolyl, and the like, and in another embodiment, pyridyl.
[0043] The "saturated hetero ring" in R^3 means a group described in (1) Monocyclic saturated hetero rings and (3) Fused polycyclic saturated hetero rings of the "hetero ring" above. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide. In another embodiment, the saturated hetero ring is a monocyclic saturated hetero ring, and in another embodiment, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl or piperidyl.
[0044] Specific examples of the "saturated hetero ring" in R^3 include "oxygen-containing saturated hetero rings", and "monocyclic nitrogen-containing saturated hetero rings".
[0045] The "oxygen-containing saturated hetero ring" as an example of the "saturated hetero ring" in R^3 means a saturated hetero ring which contains at least one oxygen atom, among (1)(b), (1)(d), (1)(e), (3)(b), (3)(c), and the like of

the "hetero ring" above, and in another embodiment, the oxygen-containing saturated hetero ring is a monocyclic saturated hetero ring containing 1 to 2 oxygen atoms, for example, oxiranyl, oxetanyl, dioxolanyl, tetrahydrofuranyl, tetrahydropyranyl, 1,4-dioxanyl, and the like.

[0046] Specific examples of the "oxygen-containing saturated hetero ring" as an example of the "saturated hetero ring" in R^3 include tetrahydropyranyl and tetrahydrofuranyl, in another embodiment, tetrahydropyranyl, and in a further embodiment, tetrahydrofuranyl.

[0047] The "monocyclic nitrogen-containing saturated hetero ring" as an example of the "saturated hetero ring" in R^3 means a monocyclic saturated hetero ring which contains at least one nitrogen atom and may further contain a heteroatom selected from oxygen and sulfur, as the group described in (1)(a), (1)(b), and the like of the "hetero ring" above. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide. In another embodiment, the monocyclic nitrogen-containing saturated hetero ring is azethidinyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, azepanyl, or diazepanyl.

[0048] Specific examples of the "monocyclic nitrogen-containing saturated hetero ring" as an example of the "saturated hetero ring" in R^3 include azethidinyl, pyrrolidinyl, piperidyl and piperazinyl, and in another embodiment, pyrrolidinyl and piperidyl.

[0049] The "monocyclic nitrogen-containing hetero ring" formed by R^a and R^b which are combined with the adjacent nitrogen atom means a monocyclic saturated hetero ring or a monocyclic unsaturated hetero ring, which contains at least one nitrogen atom and may further contain a heteroatom selected from oxygen and sulfur, as the group described in (1)(a), (1)(b), (2)(a), (2)(b), and the like of the "hetero ring" above, which is a group having a binding arm on a nitrogen atom. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide. In another embodiment, the monocyclic nitrogen-containing hetero ring is azethidinyl, pyrrolidinyl, piperidyl, piperazinyl, morpholinyl, thiomorpholinyl, azepanyl or diazepanyl.

[0050] Specific examples of the "monocyclic nitrogen-containing hetero ring" formed by R^a and R^b which are combined with the adjacent nitrogen atom include azethidinyl, pyrrolidinyl, piperidyl, piperazinyl and morpholinyl, in another embodiment, piperidyl and piperazinyl, in a further embodiment, piperidyl, and in a still further embodiment, piperazinyl.

[0051] The "polycyclic nitrogen-containing hetero ring" formed by R^a and R^b which are combined with the adjacent nitrogen atom means a bi- to tricyclic fused polycyclic saturated hetero ring or a bi- to tricyclic fused polycyclic unsaturated hetero ring, which contains at least one nitrogen atom and may further contain a heteroatom selected from oxygen and sulfur, as the group described in (3)(a), (3)(b), (4)(a), (4)(b), and the like of the "hetero ring" above, which is a group having a binding arm on a nitrogen atom. Further, the polycyclic nitrogen-containing hetero ring also includes groups having one or more nitrogen atoms among the groups described in (5) Spiro ring groups of the "hetero rings" above. The ring atom, sulfur or nitrogen, may be oxidized to form an oxide or a dioxide. In another embodiment, the polycyclic nitrogen-containing hetero ring is indolinyl, isoindolinyl, dihydropyrrolopyridyl, dihydropyrrolopyrimidinyl, tetrahydroquinolyl, tetrahydroisoquinolyl, dihydrobenzoxadinyl, dihydropyridoxadinyl, tetrahydronaphthyridinyl, tetrahydropyridopyrimidinyl, tetrahydrothienopyridyl, tetrahydroxazolopyridyl, tetrahydropyrazolopyridyl, tetrahydropyrrolopyrazinyl, hexahydropyrrolopyrazinyl, hexahydropyrrolopyrrolyl, octahydropyrrolopyrrolyl, octahydropyrrolopyrazinyl, tetrahydroimidazopyrazinyl, tetrahydrothiazolopyridyl, tetrahydrobenzoazepinyl, tetrahydropyridonaphthyridinyl, hexahydropyridoindolyl, tetrahydroisoquixazolopyridyl, tetrahydropyrrolopyridyl, tetrahydroimidazopyridyl, tetrahydropyridoindolyl, tetrahydrotriazolopyrazinyl, diazabicyclo[2.2.1]heptyl, diazabicyclo[3.2.1]octyl, 3H-spiro[2-benzofuran-1,4'-piperidyl], 1H-spiro[1-benzofuran-3,4'-piperidyl], 2,3-dihydrospiro[indene-1,4'-piperidyl], diazaspiro[4,5]decyl, and diazaspiro[5,5]undecyl.

[0052] Specific examples of the "polycyclic hetero ring" formed by R^a and R^b which are combined with the adjacent nitrogen atom include indolinyl(2,3-dihydroindolyl), isoindolinyl(1,3-dihydroisoindolyl), dihydropyrrolopyridyl, hexahydropyrrolopyrazinyl, octahydropyrrolopyrazinyl, diazabicyclo[2.2.1]heptyl, diazabicyclo[3.2.1]octyl, 3H-spiro[2-benzofuran-1,4'-piperidyl], spiro[1-benzofuran-3,4'-piperidyl], diazaspiro[4,5]decyl, diazaspiro[5,5]undecyl, oxazaspiro[4,5]decyl and octahydropyrrolopyrrolyl;
in another embodiment, indolinyl(2,3-dihydroindolyl), isoindolinyl(1,3-dihydroisoindolyl), dihydropyrrolopyridyl, diazabicyclo[2.2.1]heptyl, diazaspiro[5,5]undecyl, 3H-spiro[2-benzofuran-1,4'-piperidyl], spiro[1-benzofuran-3,4'-piperidyl], oxazaspiro[4,5]decyl, octahydropyrrolopyrazinyl and octahydropyrrolopyrrolyl; and
in a further embodiment, diazabicyclo[2.2.1]heptyl.

[0053] The "protected carboxyl" group as used herein refers to the following groups.

(1) Ester groups: -CO-O-lower alkyl, -CO-O-lower alkylene-O-lower alkyl, -COO-lower alkylene-aryl, and -CO-O-lower alkylene-O-aryl;
(2) Carbamoyl groups: -CO-NH_2, -CO-NH-lower alkyl, -CO-N(lower alkyl)$_2$,-CO-N(lower alkyl)-aryl, -CO-N(lower alkyl)-hetero ring, -CO-N(lower alkyl)-(lower alkylene-aryl), -CO-NH-lower alkylene-OH, and -CO-NH-hetero ring.

[0054] In the present specification, the expression "which may be substituted" represents "which is not substituted" or "which is substituted with 1 to 5 substituents". Further, if it has a plurality of substituents, the substituents may be the

same as or different from each other.

[0055] Examples of the substituent for "lower alkyl, -O-lower alkyl or cycloalkyl, each of which may be substituted" in R^1 and R^2 include -OH, -O-lower alkyl, $-NH_2$, -NH-lower alkyl, $-N(\text{lower alkyl})_2$, and a monocyclic nitrogen-containing hetero ring which may be substituted with lower alkyl. The substituent for the "lower alkyl which may be substituted" is, in another embodiment, -O-lower alkyl.

[0056] Examples of the substituent for the "lower alkyl, cycloalkyl or a saturated hetero ring, each of which may be substituted" in R^3 include cycloalkyl which may be substituted with halogen or -O-lower alkyl, halogen, lower alkyl, an oxygen-containing saturated hetero ring, -OH, oxo(=O), -O-lower alkyl, lower alkylene-aryl, and -CO-lower alkylene-O-lower alkyl.

[0057] Examples of the substituent for the "lower alkyl which may be substituted" in R^3 include, in another embodiment, cycloalkyl which may be substituted with halogen or -O-lower alkyl, and an oxygen-containing saturated hetero ring, in a further embodiment, cyclopropyl and cyclobutyl, in a still further embodiment, cycloalkyl substituted with halogen, in a still further embodiment, cyclobutyl substituted with halogen, and in a still further embodiment, tetrahydropyranyl.

[0058] Examples of the substituent for the "cycloalkyl which may be substituted" in R^3 include, in another embodiment, halogen and -O-lower alkyl,
in a further embodiment, halogen, and
in a still further embodiment, -O-lower alkyl.

[0059] Examples of the substituent for the "saturated hetero ring which may be substituted" in R^3 include, in another embodiment, lower alkyl, lower alkylene-aryl, and - CO-lower alkylene-O-lower alkyl, and in a further embodiment, lower alkyl.

[0060] Examples of the substituent for the "lower alkyl, cycloalkyl, aryl or a hetero ring, each of which may be substituted" in R^a and R^b include halogen; -OH; lower alkyl; -O-lower alkyl; halogeno-lower alkyl; cycloalkyl which may be substituted with a group selected from the group consisting of a hetero ring which may be substituted with -O-lower alkyl, and $-N(\text{lower alkyl})_2$; $-NH_2$; -NH-lower alkyl; $-N(\text{lower alkyl})_2$; -N(lower alkyl)(cycloalkyl); -N(lower alkyl)(aryl); aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); -CO-(aryl which may be substituted with a group selected from a group G_1); -CO-(hetero ring which may be substituted with a group selected from a group G_2); and -CO-N(lower alkyl)(hetero ring).

[0061] Examples of the substituent for the "lower alkyl which may be substituted" in R^a and R^b include, in another embodiment, -OH; -O-lower alkyl; cycloalkyl which may be substituted with a group selected from the group consisting of a hetero ring which may be substituted with -O-lower alkyl, and $-N(\text{lower alkyl})_2$; $-NH_2$; -NH-lower alkyl; $-N(\text{lower alkyl})_2$; -N(lower alkyl)(cycloalkyl); -N(lower alkyl)(aryl); aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; -CO-(hetero ring which may be substituted with a group selected from a group G_2); and -CO-N(lower alkyl)(hetero ring).

[0062] Examples of the substituent for the "cycloalkyl which may be substituted" in R^a and R^b include, in another embodiment, a hetero ring which may be substituted with a group selected from a group G_2, and in a further embodiment, a hetero ring.

[0063] Examples of the substituent for the "hetero ring which may be substituted" in R^a and R^b include, in another embodiment, lower alkylene-(aryl which may be substituted with a group selected from a group G_1), and in a substituent embodiment, lower alkylene-aryl.

[0064] Examples of the substituent for the "the monocyclic nitrogen-containing hetero ring or the polycyclic nitrogen-containing hetero ring, each of which may be substituted", formed by R^a and R^b which are each combined with the adjacent nitrogen atom, include halogen; -OH; oxo(=O); -O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-lower alkyl, cycloalkyl and aryl; cyano; halogeno-lower alkyl; cycloalkyl which may be substituted with a substituent selected from the group consisting of halogen, -OH, lower alkyl, -O-lower alkyl and lower alkylene-O-lower alkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-$N(\text{lower alkyl})_2$; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-(cycloalkyl which may be substituted with a group selected from a group G_1); lower alkylene-O-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-O-(hetero ring which may be substituted with a group selected from a group G_2) ; lower alkylene-O-(cycloalkyl which may be substituted with a group selected from a group G_1); lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -OH, -COOH, protected carboxy, cyano, aryl, hetero ring, - O-aryl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl and cycloalkyl; -COOH; protected carboxy;$-NH_2$; -NH-lower alkyl; -N(lower alkyl which may be substituted with halogeno-lower alkyl or $-\text{O-lower alkyl})_2$; -O-(aryl which may be substituted with a group selected

from a group G_1); -O-(hetero ring which may be substituted with a group selected from a group G_2); -O-cycloalkyl; -CO-lower alkyl; -CO-(aryl which may be substituted with a group selected from a group G_1); -CO-(hetero ring which may be substituted with a group selected from a group G_2); and -CO-NH-hetero ring.

[0065] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, -OH; oxo(=O); -O-lower alkyl; cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); and lower alkyl which may be substituted with -OH, -O-lower alkyl or cyano.

[0066] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, halogen; -OH; oxo(=O); halogeno-lower alkyl; -O-lower alkyl which may be substituted with a group selected from the group consisting of halogen, halogeno-lower alkyl, -O-lower alkyl, cycloalkyl and aryl; cycloalkyl which may be substituted with a group selected from the group consisting of halogen, -OH, lower alkyl, -O-lower alkyl, and lower alkylene-O-lower alkyl; -COOH; protected carboxy; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-N(lower alkyl)$_2$; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-(cycloalkyl which may be substituted with a group selected from a group G_1); lower alkylene-O-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-O-(cycloalkyl which may be substituted with a group selected from a group G_1); -N(lower alkyl which may be substituted with halogeno-lower alkyl or -O-lower alkyl)$_2$; -O-(aryl which may be substituted with a group selected from a group G_1); -O-(hetero ring which may be substituted with a group selected from a group G_2); -O-cycloalkyl; -CO-(hetero ring which may be substituted with a group selected from a group G_2); -CO-NH-hetero ring; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -OH, -COOH, protected carboxy, cyano, aryl, hetero ring, -O-aryl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl. Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are combined with the adjacent nitrogen atom include, in another embodiment, halogen; -OH; oxo(=O); halogeno-lower alkyl; -O-lower alkyl which may be substituted with a group selected from the group consisting of halogen, halogeno-lower alkyl, -O-lower alkyl, cycloalkyl and aryl; cycloalkyl which may be substituted with a group selected from the group consisting of halogen, -OH, lower alkyl, -O-lower alkyl, and lower alkylene-O-lower alkyl; -COOH; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-N(lower alkyl)$_2$; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-(cycloalkyl which may be substituted with lower alkylene-O-lower alkyl); lower alkylene-O-(aryl); lower alkylene-O-(hetero ring); lower alkylene-O-(cycloalkyl); -N(lower alkyl which may be substituted with halogeno-lower alkyl or -O-lower alkyl)$_2$; -O-(aryl which may be substituted with -COOH); -O-(hetero ring which may be substituted with halogen or lower alkyl); -O-cycloalkyl; -CO-(hetero ring which may be substituted with lower alkyl); -CO-NH-hetero ring; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -OH, -COOH, cyano, aryl, a hetero ring, -O-aryl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0067] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, -OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0068] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, -OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; aryl; pyridyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen and lower alkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(pyridyl which may be substituted with lower alkyl); lower alkyl which may be substituted with one or more groups selected from the group

consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0069] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, -O-lower alkyl which may be substituted with 1 to 3 groups selected from halogen and cycloalkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0070] Examples of the substituent for the "monocyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, -O-lower alkyl which may be substituted with 1 to 3 halogen atoms; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0071] Examples of the substituent for the "polycyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, halogen; -OH; oxo(=O); -O-lower alkyl; cyano; halogeno-lower alkyl; cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; and lower alkyl which may be substituted with -OH, -O-lower alkyl, or cyano, in a further embodiment, halogen; -OH; oxo(=O); -O-lower alkyl; cyano; halogeno-lower alkyl; cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-cycloalkyl; and lower alkyl which may be substituted with -OH, -O-lower alkyl, or cyano.

[0072] Examples of the substituent for the "polycyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); and lower alkylene-O-lower alkyl.

[0073] Examples of the substituent for the "polycyclic nitrogen-containing hetero ring which may be substituted" formed by R^a and R^b which are each combined with the adjacent nitrogen atom include, in another embodiment, halogen, lower alkyl, and -O-lower alkyl.

[0074] The group G_1 consists of halogen, lower alkyl, halogeno-lower alkyl, -OH, -O-lower alkyl, -O-hetero ring, -O-lower alkylene-aryl, -O-lower alkylene-hetero ring, -O-halogeno-lower alkyl, -N(lower alkyl)$_2$, lower alkylene-N(lower alkyl)$_2$, lower alkylene-hetero ring, aryl which may be substituted with lower alkyl, a hetero ring which may be substituted with lower alkyl, -COOH, and protected carboxy.

[0075] In another embodiment, the group G_1 consists of -O-hetero ring, -O-lower alkylene-hetero ring, -N(lower alkyl)$_2$, lower alkylene-N(lower alkyl)$_2$, lower alkylene-hetero ring, lower alkylene-N(lower alkyl)$_2$, and a hetero ring.

[0076] In a further embodiment, the group G_1 consists of halogen, lower alkyl, -O-lower alkyl, -COOH, and protected carboxy.

[0077] The group G_2 consists of halogen, lower alkyl, halogeno-lower alkyl, -OH, -O-lower alkyl, -O-lower alkylene-aryl, -O-lower alkylene-hetero ring, -O-halogeno-lower alkyl, cyano, -N(lower alkyl)$_2$, -NH-CO-lower alkyl, lower alkylene-O-lower alkyl, lower alkylene-hetero ring, aryl, a hetero ring which may be substituted with lower alkyl,-COOH, and protected carboxy.

[0078] In another embodiment, the group G_2 consists of lower alkyl, -O-lower alkyl, aryl, and a hetero ring.

[0079] In a further embodiment, the group G_2 consists of halogen, lower alkyl, halogeno-lower alkyl, -OH, -O-lower alkyl, cyano, -N(lower alkyl)$_2$, -NH-CO-lower alkyl, lower alkylene-O-lower alkyl, lower alkylene-hetero ring, and a hetero ring, and in a still further embodiment, halogen and lower alkyl.

[0080] Certain embodiments of the compound of the formula (I) or a salt thereof are presented below.

[0081] (1)

The compound or a salt thereof, wherein R^1 is lower alkyl; and

in a still further embodiment, the compound or a salt thereof, wherein R^1 is methyl.

[0082] (3)

(3-1) The compound or a salt thereof, wherein R^3 is lower alkylene-(cycloalkyl which may be substituted with halogen or -O-lower alkyl), or lower alkylene-oxygen-containing saturated hetero ring;

in a further embodiment, the compound or a salt thereof, wherein R^3 is lower alkylene-cyclopropyl or lower alkylene-cyclobutyl;

in a still further embodiment, the compound or a salt thereof, wherein R^3 is lower alkylene-(cyclobutyl substituted with two halogen atoms); and

in a still further embodiment, the compound or a salt thereof, wherein R^3 is lower alkylene-tetrahydropyranyl.

(3-2) The compound or a salt thereof, wherein R^3 is cycloalkyl which may be substituted;

in another embodiment, the compound or a salt thereof, wherein R^3 is cycloalkyl which may be substituted with halogen or -O-lower alkyl;
in a further embodiment, the compound or a salt thereof, wherein R^3 is cyclobutyl or cyclopentyl; and
in a still further embodiment, the compound or a salt thereof, wherein R^3 is cyclohexyl substituted with two halogen atoms.
(3-3) The compound or a salt thereof, wherein R^3 is an oxygen-containing saturated hetero ring, or a monocyclic nitrogen-containing saturated hetero ring substituted with lower alkyl;
in a still further embodiment, the compound or a salt thereof, wherein R^3 is piperidyl substituted with lower alkyl or pyrrolidinyl substituted with lower alkyl; and
in a still further embodiment, the compound or a salt thereof, wherein R^3 is tetrahydrofuranyl or tetrahydropyranyl.
(3-4) The compound or a salt thereof, wherein R^3 is lower alkylene-(cycloalkyl), lower alkylene-(cycloalkyl substituted with two halogen atoms), cycloalkyl, cycloalkyl substituted with two halogen atoms, an oxygen-containing saturated hetero ring, or a monocyclic nitrogen-containing saturated hetero ring substituted with lower alkyl;
in another embodiment, the compound or a salt thereof, wherein R^3 is cyclopropylmethyl, cyclobutylmethyl, difluorocyclobutylmethyl, cyclobutyl, cyclopentyl, cyclohexyl substituted with difluoro, tetrahydro-2H-pyran-4-yl, tetrahydrofuran-3-yl, piperidyl substituted with methyl, or pyrrolidinyl substituted with methyl;
in a further embodiment, the compound or a salt thereof, wherein R^3 is cycloalkyl or oxygen-containing saturated hetero ring;
in a still further embodiment, the compound or a salt thereof, wherein R^3 is cyclobutyl, cyclopentyl, tetrahydrofuran-3-yl, or tetrahydro-2H-pyran-4-yl; and
in a still further embodiment, the compound or a salt thereof, wherein R^3 is tetrahydro-2H-pyran-4-yl or cyclobutyl.

[0083] (9) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring which may be substituted;
in another embodiment, the compound or a salt thereof, wherein R^a and R^b each combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring which may be substituted, which may be substituted with a group selected from the group consisting of halogen; -OH; oxo(=O); halogeno-lower alkyl; -O-lower alkyl which may be substituted with a group selected from the group consisting of halogen, halogeno-lower alkyl, -O-lower alkyl, cycloalkyl and aryl; cycloalkyl which may be substituted with a group selected from the group consisting of halogen, -OH, lower alkyl, -O-lower alkyl, and lower alkylene-O-lower alkyl; -COOH; protected carboxy; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-N(lower alkyl)$_2$; lower alkylene-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-(cycloalkyl which may be substituted with a group selected from a group G_1); lower alkylene-O-(aryl which may be substituted with a group selected from a group G_1); lower alkylene-O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-O-(cycloalkyl which may be substituted with a group selected from a group G_1); -N(lower alkyl which may be substituted with halogeno-lower alkyl or - O-lower alkyl)$_2$; -O-(aryl which may be substituted with a group selected from a group G_1); -O-(hetero ring which may be substituted with a group selected from a group G_2); -O-cycloalkyl; -CO-(hetero ring which may be substituted with a group selected from a group G_2); -CO-NH-hetero ring; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -OH, -COOH, protected carboxy, cyano, aryl, hetero ring, -O-aryl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; and
in a further embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring which may be substituted, which may be substituted with a group selected from the group consisting of -OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0084] (10-1) The compound or a salt thereof, wherein R^a and R^b are each combined with the adjacent nitrogen atom to form azethidinyl which may be substituted; and
in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form azethidinyl which may be substituted, which may be substituted with a group selected from the group consisting of -O-lower alkyl; a hetero ring which may be substituted with a group selected from halogen and lower alkyl; -N(lower alkyl which may be substituted with halogeno-lower alkyl or -O-lower alkyl)$_2$-O-(aryl); lower alkyl; and lower alkylene-O-lower alkyl.

(10-2) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form morpholinyl which may be substituted; and

in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form morpholinyl which may be substituted, which may be substituted with a group selected from the group consisting of aryl which may be substituted with -O-lower alkyl; a hetero ring; and lower alkylene-N(lower alkyl)$_2$.

(10-3) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form pyrrolidinyl which may be substituted; and

in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form pyrrolidinyl which may be substituted, which may be substituted with a group selected from the group consisting of -OH; -O-lower alkyl which may be substituted with aryl; -O-aryl; a hetero ring which may be substituted with halogen or lower alkyl; and lower alkylene-O-lower alkyl.

[0085] (10-4) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl which may be substituted;

in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl which may be substituted, which may be substituted with a group selected from the group consisting of halogen; -OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with a group selected from the group consisting of halogen, halogeno-lower alkyl, -O-lower alkyl, cycloalkyl and aryl; -COOH; protected carboxy; aryl which may be substituted with -COOH or protected carboxy; a hetero ring which may be substituted with halogen, lower alkyl, or lower alkylene-O-lower alkyl; lower alkylene-(aryl which maybe substituted with -COOH); lower alkylene-hetero ring; lower alkylene-O-hetero ring; lower alkylene-O-cycloalkyl; - N(lower alkyl)$_2$; -O-(aryl which may be substituted with -COOH); -O-(hetero ring which may be substituted with halogen or lower alkyl); -O-cycloalkyl; -CO-(hetero ring which may be substituted with lower alkyl); -CO-NH-hetero ring; lower alkyl which may be substituted with one or more groups selected from the group consisting of -OH, -COOH, protected carboxy, -O-cycloalkyl, and a hetero ring; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; and

in a further embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl which may be substituted, which may be substituted with a group selected from the group consisting of -OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with lower alkyl); and lower alkylene-O-lower alkyl.

[0086] (10-5) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperazinyl which may be substituted;

in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperazinyl which may be substituted, which may be substituted with a group selected from the group consisting of oxo(=O); cycloalkyl which may be substituted with a group selected from the group consisting of halogen, -OH, lower alkyl, -O-lower alkyl, and lower alkylene-O-lower alkyl; aryl which may be substituted with halogen or -COOH; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-(aryl which may be substituted with halogen or -O-lower alkyl); lower alkylene-(hetero ring which may be substituted with a group selected from a group G_2); lower alkylene-(cycloalkyl which may be substituted with lower alkylene-O-lower alkyl); lower alkylene-O-aryl; lower alkylene-O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -OH, -COOH, protected carboxy, cyano, aryl, hetero ring, -O-aryl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; and

in a further embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperazinyl which may be substituted, which may be substituted with a group selected from the group consisting of aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from lower alkyl and halogen; lower alkylene-O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0087] (10-6) The compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl or piperazinyl, each of which may be substituted; and

in another embodiment, the compound or a salt thereof, wherein R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl or piperazinyl, which may be substituted, which may be substituted with a group selected from the group consisting of - O-lower alkyl which may be substituted with 1 to 3 groups selected from halogen and cycloalkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0088] (13) The compound or a salt thereof, which is a combination of two or more groups of the groups described in

(1) to (12) above.

[0089] The compound of the formula (I) or a salt thereof includes a compound or a salt thereof formed by one or a combination of two or more groups of the groups described in (1) to (12) above as described in (13) above, but also includes the following embodiments including specific examples thereof.

[0090] (21) The compound or a salt thereof, wherein
R^1 is lower alkyl,
R^2 is a group of the formula (II),
R^3 is tetrahydropyranyl,
R^4, R^5 and R^6 are hydrogen, and
R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring selected from azethidinyl, piperidyl, piperazinyl and morpholinyl, and the monocyclic nitrogen-containing hetero ring which may be substituted with 1 to 3 substituents selected from -O-lower alkyl, cycloalkyl, aryl, a hetero ring which may be substituted with lower alkyl, lower alkylene-(aryl which may be substituted with halogen), lower alkylene-hetero ring, lower alkylene-cycloalkyl, lower alkylene-O-lower alkyl, lower alkylene-N(lower alkyl)$_2$, -O-lower alkyl, -O-hetero ring, -N(lower alkyl)$_2$,-CO-(hetero ring which may be substituted with lower alkyl), and lower alkyl which may be substituted with -O-lower alkyl.

[0091]

(23) The compound or a salt thereof, wherein
R^1 is hydrogen, halogeno-lower alkyl, lower alkyl, or -O-lower alkyl,
R^2 is a group of the formula (II),
R^3 is lower alkylene-(cycloalkyl which may be substituted with halogen or -O-lower alkyl); lower alkylene-oxygen-containing saturated hetero ring; cycloalkyl which may be substituted with halogen or -O-lower alkyl; an oxygen-containing saturated hetero ring; or a monocyclic nitrogen-containing saturated hetero ring which may be substituted with lower alkyl, lower alkylene-aryl, or -CO-lower alkylene-O-lower alkyl,
R^4, R^5 and R^6 are hydrogen, and
R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring, each of which may be substituted.

(24) The compound or a salt thereof according to (23) above, wherein the monocyclic nitrogen-containing hetero ring formed by R^a and R^b which are combined with the adjacent nitrogen atom is piperidyl or piperazinyl.

(25) The compound or a salt thereof according to (24) above, wherein piperidyl or piperazinyl, each of which may be substituted, formed by R^a and R^b which are combined with the adjacent nitrogen atom, may be substituted with 1 to 3 substituents selected from:

- OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

(26) The compound or a salt thereof according to (25) above, wherein piperidyl or piperazinyl, each of which may be substituted, formed by R^a and R^b which are combined with the adjacent nitrogen atom, may be substituted with 1 to 3 groups selected from the group consisting of:

- O-lower alkyl which may be substituted with 1 to 3 groups selected from halogen and cycloalkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0092] (27) The compound or a salt thereof, wherein
R^1 is lower alkyl,
R^2 is a group of the formula (II),
R^3 is lower alkylene-(cycloalkyl), lower alkylene-(cycloalkyl substituted with two halogen atoms), cycloalkyl, cycloalkyl substituted with two halogen atoms, an oxygen-containing saturated hetero ring, or a monocyclic nitrogen-containing saturated hetero ring substituted with lower alkyl,
R^4, R^5 and R^6 are hydrogen, and

R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl or piperazinyl, each of which may be substituted, which may be substituted with 1 to 3 groups selected from the group consisting of:

- OH; halogeno-lower alkyl; -O-lower alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; lower alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, -O-cycloalkyl, -O-lower alkyl, and -O-halogeno-lower alkyl; and lower alkylene-O-lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and cycloalkyl.

[0093] (28) The compound or a salt thereof, wherein
R^1 is lower alkyl,
R^2 is a group of the formula (II),
R^3 is cycloalkyl or oxygen-containing saturated hetero ring,
R^4, R^5 and R^6 are hydrogen, and
R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl or piperazinyl, each of which may be substituted, which may be substituted with 1 to 3 groups selected from the group consisting of:

- O-lower alkyl which may be substituted with 1 to 3 groups selected from halogen and cycloalkyl; lower alkylene-O-cycloalkyl; -O-cycloalkyl; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0094]

(29) The compound or a salt thereof according to (27) above, wherein R^3 is cyclopropylmethyl, cyclobutylmethyl, difluorocyclobutylmethyl, cyclobutyl, cyclopentyl, cyclohexyl substituted with difluoro, tetrahydro-2H-pyran-4-yl, tetrahydrofuran-3-yl, piperidyl substituted with methyl, or pyrrolidinyl substituted with methyl.
(30) The compound or a salt thereof according to (28) above, wherein R^3 is cyclobutyl, cyclopentyl, tetrahydrofuran-3-yl or tetrahydro-2H-pyran-4-yl.

[0095] (31) The compound or a salt thereof, wherein
R^1 is lower alkyl,
R^2 is a group of the formula (II),
R^3 is tetrahydro-2H-pyran-4-yl or cyclobutyl,
R^4, R^5 and R^6 are hydrogen, and
R^a and R^b are combined with the adjacent nitrogen atom to form piperidyl or piperazinyl, each of which may be substituted, which may be substituted with 1 to 3 groups selected from the group consisting of:

- O-lower alkyl which may be substituted with 1 to 3 halogen atoms; lower alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-lower alkyl, and -O-lower alkyl; and lower alkylene-O-lower alkyl.

[0096] Examples of the specific compounds included in the present invention include the following compounds:

7-methyl-8-[(4-propoxypiperidin-1-yl)carbonyl]-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-[(4-{[(2S)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1 -(tetrahydro-2H-pyran-4-yl)-8- {[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(4,4,4-trifluorobutyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2,2-difluoro-3-methoxypropyl)piperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclobutyl-8-{[(3S)-4-(4-methoxybutyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,

and salts thereof.

[0097] In another embodiment, examples of the specific compounds included in the present invention include the following compounds:

8-[(4-ethoxypiperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclopropylmethoxy)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(4-ethoxybutyl)piperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclobutyloxy)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-[(4-{[(2R)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-[(4-{[(2S)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclobutyl-8-{[(3S)-4-(3-methoxypropyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(4,4,4-trifluorobutyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-[(4-{[(2R)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[(cyclopropyloxy)methyl]piperidin-1-yl}carbonyl)-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclopentyl-8- {[(3S)-4-(3-methoxypropyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
and salts thereof.

[0098] In a further embodiment, examples of the specific compounds included in the present invention include the following compounds:

8- {[4-(methoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(3-ethoxypropyl)piperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2-methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclobutyl-8-{[4-(3-ethoxypropyl)piperazin-1-yl]carbonyl}-7-methyl,-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclobutyl-8-{[4-(4-methoxybutyl)piperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(4-methoxybutyl)piperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2,2-difluoroethoxy)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-8-{[4-(4-methoxybutyl)piperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclobutyl-7-methyl-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2,2-difluoro-3-methoxypropyl)piperazin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2-ethoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1, 5-dihydro-4H-pyrazolo [4,3-c]quinolin-4-one,

7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-({4-[3-(trifluoromethoxy)propyl]piperazin-1-yl}carbonyl)-1,5-dihydro-4H-pyrazolo[4,3-c] quinolin-4-one,
8-{[4-(2,2-difluoropropoxy)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[(3S)-4-(5-fluoro-6-methylpyridin-2-yl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1-[(3S)-1-methylpyrrolidin-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one, 8-{[(3R)-4-(5-fluoro-6-methylpyridin-2-yl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1-[(3S)-1-methylpyrrolidin-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[(2S,5R)-4-(4-methoxybutyl)-2,5-dimethylpiperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[(2S,5R)-2,5-dimethyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-cyclopentyl-8-{[(3S)-4-(4-methoxybutyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-8-{[(2S,5R)-4-(4-methoxybutyl)-2,5-dimethylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-8-{[(2S,5R)-2,5-dimethyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl] carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c] quinolin-4-one,
1-(cyclobutylmethyl)-8-{[(2S,5R)-4-(4-methoxybutyl)-2,5-dimethylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclobutylmethyl)-8-{[(2S,5R)-2,5-dimethyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2,2-difluoropropoxy)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(4,4-difluorocyclohexyl)-8-{[(3S)-4-(4-methoxybutyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-8-{[(3S)-4-(4-methoxybutyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(trifluoromethyl)piperidin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclopropylmethoxy)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-8-[(4-propoxypiperidin-1-yl)carbonyl]-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2-ethoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclobutyloxy)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluoroethoxy)piperidin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(4,4-difluorocyclohexyl)-8-{[(3S)-4-(3-methoxypropyl)-3-methylpiperazin-1-yl]carbonyl}}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-8-{[(3S)-4-(3-methoxypropyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclobutylmethyl)-8-{[(3S)-4-(3-methoxypropyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(4-ethoxybutyl)piperazin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2-methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(4,4-difluorocyclohexyl)-7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclopropylmethyl)-7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclobutylmethyl)-7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-

pyrazolo[4,3-c]quinolin-4-one,
1-cyclopentyl-7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-(1-methylpiperidin-4-yl)-8-({4-[(5-methylpyridin-2-yl)oxy]piperidin-1-yl}carbonyl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[(3S)-4-ethyl-3-phenylpiperazin-1-yl]carbonyl}-7-methyl-1-(1-methylpiperidin-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclopropyloxy)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-({4-[3-(trifluoromethoxy)propyl]piperazin-1-yl}carbonyl)-1,5-dihydro-4H-pyrazolo[4,3-c] quinolin-4-one,
1-cyclobutyl-7-methyl-8-{[(3S)-3-methyl-4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-(cyclobutylmethyl)-8-({(3S)-4-[2-(cyclopropylmethoxy)ethyl]-3-methylpiperazin-1-yl}carbonyl)-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[2-(cyclopropylmethoxy)ethyl]piperazin-1-yl}carbonyl)-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[2-(cyclopropylmethoxy)ethyl]piperazin-1-yl}carbonyl)-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({(3S)-4-[2-(cyclopropylmethoxy)ethyl]-3-methylpiperazin-1-yl}carbonyl)-1-(cyclopropylmethyl)-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(cyclopropyloxy)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[3-(cyclopropyloxy)propyl]piperazin-1-y}carbonyl)-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[3-(cyclopropyloxy)propyl]piperazin-1-yl}carbonyl)-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-({4-[(cyclopropyloxy)methyl]piperidin-1-yl}carbonyl)-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-hydroxy-4-(trifluoromethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
1-[(3,3-difluorocyclobutyl)methyl]-8-{[(3S)-4-(4-methoxybutyl)-3-methylpiperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
and salts thereof.

[0099] The compound of the formula (I) may exist in the form of tautomers or geometrical isomers depending on the kind of substituents. In the present specification, the compound of the formula (I) shall be described in only one form of isomer, yet the present invention includes other isomers, isolated forms of the isomers, or a mixture thereof.

[0100] In addition, the compound of the formula (I) may have asymmetric carbon atoms or axial asymmetry in some cases, and correspondingly, it may exist in the form of optical isomers. The present invention includes both an isolated form of the optical isomers of the compound of the formula (I) or a mixture thereof.

[0101] Furthermore, the present invention also includes a pharmaceutically acceptable prodrug of the compound represented by the formula (I). The pharmaceutically acceptable prodrug is a compound having a group that can be converted into an amino group, a hydroxyl group, a carboxyl group, or the like through solvolysis or under physiological conditions. Examples of the group forming the prodrug include the groups described in Prog. Med., 5, 2157-2161 (1985) and Pharmaceutical Research and Development, Drug Design, Hirokawa Publishing Company (1990), Vol. 7, 163-198.

[0102] Moreover, the salt of the compound of the formula (I) is a pharmaceutically acceptable salt of the compound of the formula (I) and may form an acid addition salt or a salt with a base depending on the kind of substituents. Specific examples thereof include acid addition salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid, and the like, and with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, mandelic acid, tartaric acid, dibenzoyltartaric acid, ditolyltartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, aspartic acid, glutamic acid, and the like, and salts with inorganic bases such as sodium, potassium, magnesium, calcium, aluminum, and the like or organic bases such as methylamine, ethylamine, ethanolamine, lysine, arginine, tromethamine, ornithine, and the like, salts with various amino acids or amino acid derivatives such as acetylleucine and the like, ammonium salts, etc.

[0103] In addition, the present invention also includes various hydrates or solvates, and polymorphic crystal substances of the compound of the formula (I) and a salt thereof. In addition, the present invention also includes compounds labeled

with various radioactive or non-radioactive isotopes.

(Preparation Methods)

[0104] The compound of the formula (I) and a salt thereof can be prepared using the characteristics based on the basic structure or the type of substituent and by applying various known synthesis methods. During the preparation replacement of the relevant functional group with a suitable protective group (a group that can be easily converted into the relevant functional group) at the stage from starting material to an intermediate may be effective depending on the type of the functional group in the production technology in some cases. The protective group for such a functional group may include, for example, the protective groups described in "Greene's Protective Groups in Organic Synthesis (4th edition, 2006)" written by P. G. M. Wuts and T. W. Greene, and one of these should only be selected and used as necessary depending on reaction conditions. In this kind of method, a desired compound can be obtained by introducing the protective group, by carrying out a reaction and by eliminating the protective group as necessary.

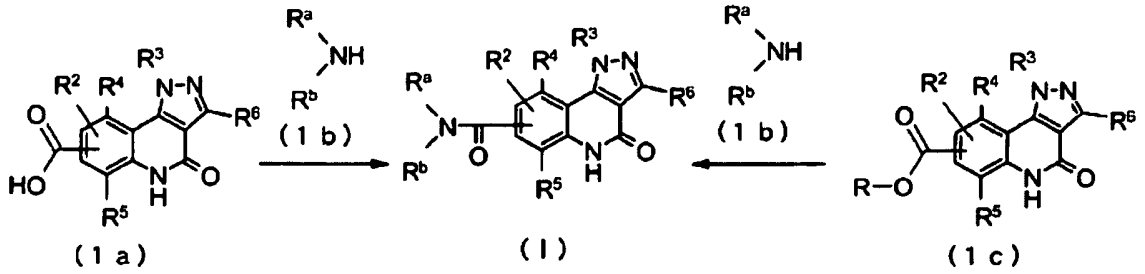
[0105] In addition, the prodrug of the compound of the formula (I) can be produced by introducing a specific group or by carrying out the reaction using the obtained compound of the formula (I) at the stage from a starting material to an intermediate, just as in the case of the above-mentioned protective group. The reaction can be carried out using methods known to those skilled in the art, such as ordinary esterification, amidation, dehydration, and the like.

[0106] Hereinbelow, the representative preparation methods for the compound of the formula (I) will be described. Each of the production processes may also be carried out with reference to the References appended in the present description. Further, the preparation methods of the present invention are not limited to the examples as shown below.

(Production Process 1)

[0107]

[Chem. 12]



(wherein R^a, R^b, R^2, R^3, R^4, R^5 and R^6 represent the same meanings as defined above. R represents lower alkyl. The same shall apply hereinafter.)

[0108] The compound (I) of the present invention can be obtained by the reaction of a compound (1a) with a compound (1b).

[0109] In this reaction, the compound (1a) and the compound (1b) in equivalent amounts, or with either thereof in an excess amount are used, and a mixture thereof is stirred under any temperature condition from cooling to heating, preferably at -20°C to 120°C, usually for 0.1 hours to 5 days, in a solvent which is inert to the reaction, in the presence of a fusing agent. The solvent as used herein is not particularly limited, but examples thereof include aromatic hydrocarbons such as benzene, toluene, xylene, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, ethers such as diethyl ether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, N,N-dimethylformamide (DMF), N-methylpyrrolidone, dimethylsulfoxide, ethyl acetate, acetonitrile or water and a mixture thereof. Examples of the condensation agent include 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, 1,3-dicyclohexylcarbodiimide, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluroniumtetrafluoroborate (TBTU), bromo(tripyrrolidin-1-yl)phosphonium hexafluorophosphate, 1, 1'-carbonyldiimidazole (CDI), diphenylphosphoryl azide and phosphoryl chloride, but are not limited to these. Further, a condensation agent-supported polystyrene resin, for example, PS-Carbodiimide (Biotage AB, Sweden) can also be used. It may be preferable for the reaction in some cases to use an additive (for example, 1-hydroxybenzotriazole). It may be advantageous in some cases for the smooth progress of the reaction to carry out the reaction in the presence of an organic base such as triethylamine, N,N-diisopropylethylamine (DIPEA), N-methylmor-

pholine, and the like, or an inorganic base such as potassium carbonate, sodium carbonate, potassium hydroxide, and the like. Further, use of a microwave reactor (Biotage AB) may allow the smooth progress of the reaction in some cases. Depending on the case, an isocyanate-supported polystyrene resin, for example, PS-Isocyanate (Biotage AB, Sweden) and the like can also be used in order to remove an excess amount of amine after completion of the reaction, and also, a quaternary ammonium salt-supported polystyrene resin, for example, MP-Carbonate (Biotage AB, Sweden) and the like can also be used in order to remove an excess amount of the additives after completion of the reaction.

[0110] Moreover, a method in which a carboxylic acid (1a) is converted to its reactive derivative and then reacted with an amine (1b) can also be used. Examples of the reactive derivative of the carboxylic acid include acid halides that can be obtained by the reaction of a halogenating agent such as phosphoryl chloride, thionyl chloride, and the like, mixed acid anhydrides that can be obtained by the reaction of isobutyl chloroformate or the like, active esters obtained by fusion with 1-hydroxybenzotriazole or the like, etc. The reaction of the reactive derivative and the compound (1b) can be carried out under any temperature condition from cooling to heating, preferably at -20°C to 60°C, in a solvent which is inert to the reaction, such as halogenated hydrocarbons, aromatic hydrocarbons, ethers, and the like.

[0111] In addition, a method in which an aluminum amide reagent obtained by reacting an ester (1c) with trimethylaluminum and the amine (1b) is allowed to undergo a reaction can also be used.

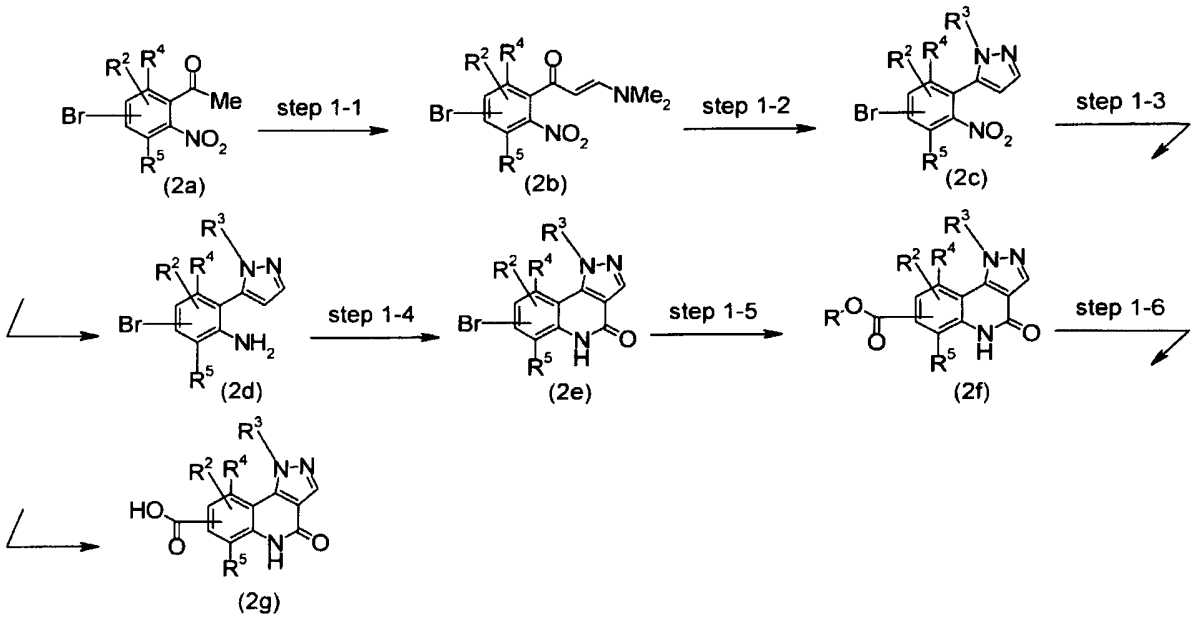
[0112] For these steps, reference may be made to the methods described in "Organic Functional Group Preparations", written by S. R. Sandler and W. Karo, 2nd edition, Vol. 1, Academic Press Inc., 1991, and "Courses in Experimental Chemistry (5th edition)", edited by The Chemical Society of Japan, Vol. 16 (2005) (Maruzen).

[0113] In addition, some of the compounds represented by the formula (I) can also be produced from the compound according 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 the like (see, for example, "Courses in Experimental Chemistry" (5th edition), edited by The Chemical Society of Japan, (2005) (Maruzen)). Furthermore, a process which can be usually used by those skilled in the art can also be used for intermediates for preparation.

(Starting Material Synthesis 1)

[0114]

[Chem. 13]



[0115] The step represented by Step 1-1 is a reaction for obtaining a compound (2b) by a reaction of a compound (2a) with (dimethoxymethyl)dimethylamine or an equivalent form thereof. In this reaction, the compound (2a) and (dimethoxymethyl)dimethylamine or an equivalent form thereof in equivalent amounts, or with either thereof in an excess amount are used, and a mixture thereof is stirred under any temperature condition from cooling to heating, preferably at 20°C

to 200°C, usually for 0.1 hours to 5 days, in a solvent which is inert to the reaction or without a solvent. As an example of the equivalent form used herein, methoxybis(dimethylamino)methane, (bisethylsulfanylmethyl)dimethylamine, bis(dimethylamino)monomethinium perchloride, N,N-dimethylformamide diethylacetal, 3-(dimethylamino)-2-azaprop-2-en-1-ylidene dimethylammonium chloride, 2-aza-1,3-bis(dimethylamino)-3-methoxy-1-propene, and the like are known. The solvent as used herein is not particularly limited, but examples thereof include aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, N,N-dimethylformamide, N,N-dimethylacetamide, dimethylsulfoxide, ethyl acetate, acetonitrile, N-ethylpyrrolidone and a mixture thereof.

[0116] For such a step, reference may be made to the methods described in Bredereck, H. et al., Chemische Berichte, 97, 3397 (1964), Ivanova, I.A. et al., Bulletin of the Academy of Sciences of the USSR, Division of Chemical Science, 1965, 2143, Arnold, Z., Zemlicka, J., Collection of Czechoslovak Chemical Communications, 25, 1302 (1960), Meerwein, H. et al., Justus Liebigs Annalen der Chemie, 641, 1 (1961), Lin, Yang-i, Lang, Stanley, A., Journal of Organic Chemistry, 45(24), 4857 (1980), Cherif, Souheir El, Rene, Loic, Synthesis (1988)2, 138, Gupton, John T., Colon, Cesar et al., Journal of Organic Chemistry, 45(22), 4522 (1980), Kantlehner, Willi, Hauber, Michael, Bulletin des Societes Chimiques Belges, 103(12), 697 (1994), Gorobets, Nikolay Yu. et al., Tetrahedron, 60(39), 8633 (2004), and the like.

[0117] Step 1-2 is a step for obtaining a compound (2c) using the compound (2b) and alkylhydrazine or a salt thereof. The mixture thereof is stirred under any temperature condition from cooling to heating, preferably at 20°C to 120°C, usually for 0.1 hours to 5 days, in a solvent which is inert to the reaction. This reaction may be carried out under any condition of an acidic condition, a neutral condition, and a basic condition. The solvent as used herein is not particularly limited, but examples thereof include aromatic hydrocarbons such as benzene, toluene, xylene, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, N,N-dimethylformamide, N,N-dimethylacetamide, dimethylsulfoxide, acetic acid, ethyl acetate, acetonitrile, N-ethylpyrrolidone and a mixture thereof. Although not always clarified, position isomers are generated during the synthesis in the reaction in some cases. However, such a mixture of the position isomers can be isolated by, for example, preparative HPLC, silica gel column chromatography, recrystallization, or the like. For this step, reference may be made to the methods described in Tanaka, Akira et al., Journal of Medicinal Chemistry, 41(13), 2390 (1998), Hernandez, Susana et al., Journal of Organic Chemistry, 75(2), 434 (2010), Adams, Nicholas D. et al., Journal of Medicinal Chemistry, 53(10), 3973 (2010), Speake, Jason D. et al., Bioorganic Medicinal Chemistry Letters, 13(6), 1183 (2006), and the like.

[0118] The step represented by Step 1-3 is a step for obtaining a compound (2d) by a reduction reaction of the compound (2c). In this reaction, the compound (2c) is stirred in the presence of a metal catalyst, usually for 1 hour to 5 days, in a solvent which is inert to the reaction. As the metal, iron, zinc, tin, or the like is suitably used. This reaction is carried out under any temperature condition from cooling to heating, preferably at 40°C to 100°C. This reaction is usually carried out under an acidic condition, but the reduction may also be carried out under a neutral or basic condition in a case of using zinc powder. This reaction can also be carried out using hydrazine monohydrate in an equivalent amount or an excess amount, relative to the compound (2c). In this reaction, stirring is performed in the presence of an iron catalyst such as activated carbon/iron (III) chloride, and the like, usually for 0.5 hours to 5 days, in a solvent inert to the reaction. The solvent as used herein is not particularly limited, but examples thereof include alcohols such as methanol, ethanol, 2-propanol, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, water, acetic acid, ethyl acetate, N,N-dimethylformamide, dimethylsulfoxide and a mixture thereof. For these steps, reference may be made to the methods described in "Courses in Experimental Chemistry" (4th edition), edited by The Chemical Society of Japan, Vol. 20 (1992) (Maruzen), and the like.

[0119] Step 1-4 is a step for obtaining a compound (2e) by a cyclization reaction of the compound (2d) with 1,1'-carbonyldiimidazole or triphosgene. The mixture thereof is stirred in the presence of an amine or a base, under any temperature condition from cooling to heating, preferably at 80°C to 200°C, in a solvent which is inert to the reaction, usually for 0.1 hours to 5 days, more preferably using a microwave reactor.

[0120] Further, this reaction may also be carried out in the absence of an amine or a base. Examples of the amine or the base as used herein include triethylamine, diisopropylethylamine, tributylamine, 1,8-diazabicyclo[5.4.0]undecene, 1,5-diazabicyclo[4.3.0]non-5-ene, imidazole, and the like. The solvent as used herein is not particularly limited, but examples thereof include aromatic hydrocarbons such as benzene, toluene, xylene, 1,2-dichlorobenzene, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform, and the like, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, N-ethylpyrrolidone, dimethylsulfoxide, sulfolane, acetic acid, ethyl acetate, acetonitrile, and a the mixture thereof. For this step, reference may be made to the method described in J. Med. Chem., 34(9), 2671 (1991).

[0121] The step represented by Step 1-5 is a reaction for obtaining a compound (2f) by a reaction of the compound (2e) with carbon monoxide and alcohol in the presence of a palladium catalyst. For this step, reference may be made to the method described in Nicolaou, K. C. et al., Angew. Chem. Int. Ed., 44, 4442 (2005), "Topics in Organometallic

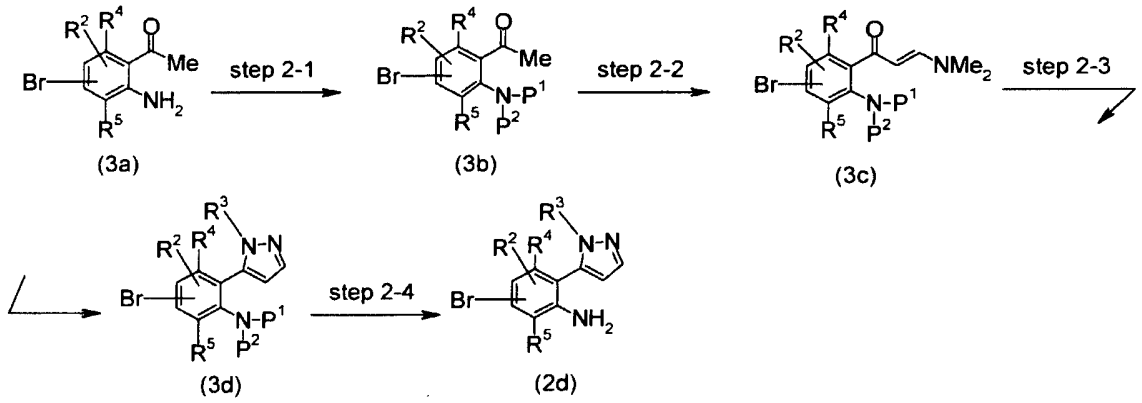
Chemistry, Vol. 14, Palladium in Organic Synthesis (2005)".

[0122] The step represented by Step 1-6 is a reaction for obtaining a compound (2g) by a hydrolysis reaction of the compound (2f). Here, the hydrolysis reaction can be carried out with reference to the method described in "Greene's Protective Groups in Organic Synthesis (4th edition, 2006)".

(Starting Material Synthesis 2)

[0123]

[Chem. 14]



(wherein at least one of P^1 and P^2 represents a protective group).

[0124] The step represented by Step 2-1 is a reaction for obtaining a compound (3b) by introducing a protective group into an amino group of a compound (3 a). As the protective group used for protection of the amino group, carbamate, urea, amide, sulfonamide, or the like can be used, and preferably acetyl, methanesulfonyl or p-toluenesulfonyl is used. This reaction can be carried out with reference to the method described in "Greene's Protective Groups in Organic Synthesis (4th edition, 2006)".

[0125] The step represented by Step 2-2 is a reaction for obtaining a compound (3c) by a reaction of the compound (3b) with (dimethoxymethyl)dimethylamine or an equivalent form thereof. For this step, the method used in Step 1-1 of (Starting Material Synthesis 1) can be incorporated.

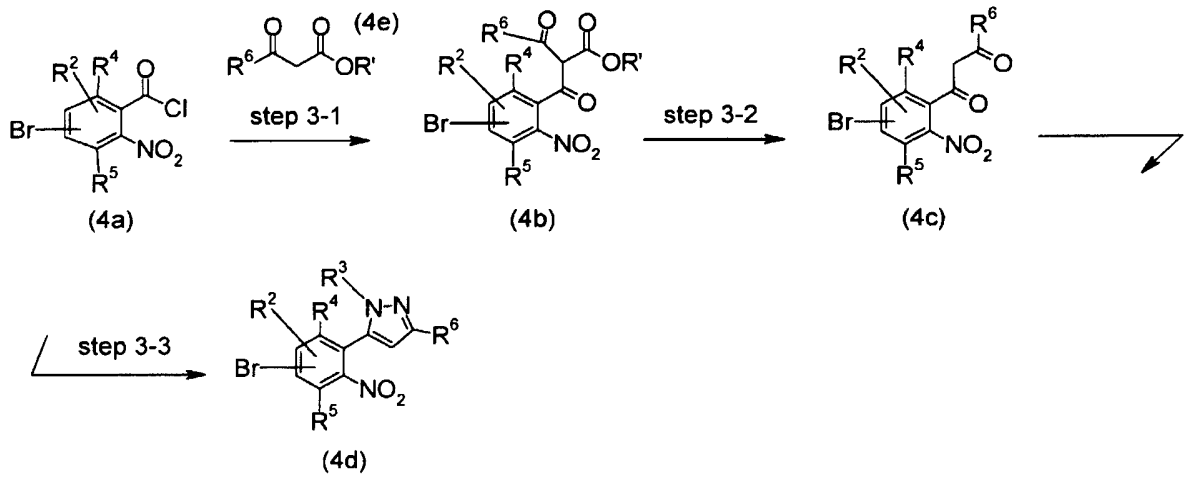
[0126] The step represented by Step 2-3 is a reaction for obtaining a compound (3d) by a cyclization reaction using the compound (3c) and alkylhydrazine or a salt thereof. For this step, the method used in Step 1-2 of (Starting Material Synthesis 1) can be incorporated.

[0127] The step represented by Step 2-4 is a reaction for obtaining a compound (2d) by a deprotection reaction of the protective group of the compound (3d). This reaction can be carried out with reference to the method described in "Greene's Protective Groups in Organic Synthesis (4th edition, 2006)".

(Starting Material Synthesis 3)

[0128]

[Chem. 15]



(wherein R' represents lower alkyl).

[0129] Step 3-1 is a step for obtaining a compound (4b) by condensation of a compound (4a) with a compound (4e).

[0130] In this reaction, the compound (4a) and the compound (4e) are stirred in the presence of a metal or a metal salt, and an equivalent amount or an excess amount of an amine or a base, in a solvent which is inert to the reaction, usually for 1 hour to 5 days, under a nitrogen atmosphere. This reaction is carried out under any temperature condition from cooling to heating, preferably at -20°C to room temperature. The metal or a metal salt used herein is not particularly limited, but examples thereof include magnesium, magnesium ethoxide, magnesium chloride, samarium chloride, and the like. The amine or the base used herein is not particularly limited, but examples thereof include triethylamine, N-ethyl-N-isopropylpropan-2-amine, tributylamine, 1,8-diazabicyclo[5.4.0]undecene, 1,5-diazabicyclo[4.3.0]non-5-ene, imidazole, pyridine, 2,6-lutidine, quinoline, N,N-dimethylaniline, sodium hydride, sodium hydroxide, potassium hydroxide, sodium methoxide, sodium ethoxide, potassium t-butoxide, sodium carbonate, potassium carbonate, cesium carbonate, and the like. The solvent as used herein is not particularly limited, but examples thereof include alcohols such as methanol, ethanol, 2-propanol, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, benzene, toluene, dichloromethane, chloroform, dichloroethane, carbon tetrachloride, and a the mixture thereof. For this step, reference may be made to the methods described in Arnould, J. C. et al., Journal of Medicinal Chemistry, 35(14), 2631 (1992), Sato, Masayuki et al., Chemical Pharmaceutical Bulletin, 31(6) 1896 (1983).

[0131] Step 3-2 is a step for obtaining a compound (4c) by the decarboxylation of the compound (4b). In this reaction, the compounds are stirred using an acid in an amount ranging from a catalytic amount to an excess amount, usually for 1 hours to 5 days, in a solvent which is inert to the reaction under a nitrogen atmosphere. This reaction is usually carried out under any temperature condition from cooling to heating. The acid as used herein is not particularly limited, but examples thereof include hydrochloric acid, hydrobromide, sulfuric acid, methanesulfonic acid, 4-toluenesulfonic acid, D-camphorsulfonic acid, trifluoroacetic acid, and the like. The solvent as used herein is not particularly limited, but examples thereof include alcohols such as methanol, ethanol, 2-propanol, and the like, ethers such as diethylether, tetrahydrofuran, 1,4-dioxane, dimethoxyethane, and the like, benzene, toluene, dichloromethane, chloroform, dichloroethane, acetonitrile, water, acetic acid, and a mixture thereof. Further, a method for obtaining the compound (4c) from the compound (4b) using sodium chloride in dimethylsulfoxide can also be obtained. Such step can be carried out with reference to the method described in WO2004/63197 A1, Cegne-Laage, Emmanuelle et al., Chemistry-A European Journal, 10(6), 1445 (2004).

[0132] Step 3-3 is a step for obtaining a compound (4d) by a reaction using the compound (4c) with alkylhydrazine or a salt thereof. For this step, the method used in Step 1-2 of (Starting Material Synthesis 1) can be incorporated.

[0133] The compounds of the formula (I) can be isolated and purified as their free compounds, salts, hydrates, solvates, or polymorphic crystal substances thereof. The salts of the compound of the formula (I) can also be prepared by carrying out the treatment of a conventional salt forming reaction.

[0134] Isolation and purification are carried out by employing ordinary chemical operations such as extraction, fractional crystallization, various types of fractional chromatography, and the like.

[0135] Various isomers can be prepared by selecting an appropriate starting compound or separated by using the difference in the physicochemical properties between the isomers. For example, the optical isomers can be obtained by means of a general method for designing optical resolution of racemic products (for example, fractional crystallization for inducing diastereomer salts with optically active bases or acids, chromatography using a chiral column or the like,

and others), and further, the isomers can also be prepared from an appropriate optically active starting material.

[0136] The pharmacological activity of the compound of the formula (I) was confirmed by the tests shown below.

Test Example 1: PDE9-Inhibiting Activity

(1) Acquisition of PDE9

[0137] The PDE9 used in the present experiment was expressed/purified by the method as in, for example, Guipponi et al., and Fisher et al. (Fisher, D.A., et al., J. Biol. Chem., 273: pp. 15559-15564 (1998), Guipponi, M., et al., Hum. Genet., 103: pp. 386-392 (1998)).

(2) Evaluation of PDE9-Inhibiting Activity

[0138] The PDE9-inhibiting activity was measured by the following method. That is, to a buffer solution containing tris(hydroxymethyl)aminomethane-hydrochloric acid (40 mM, pH 8.0), magnesium chloride (5 mM), and 2-mercaptoethanol (4 mM) were added cGMP (1μM) and ^{3}H-cGMP (0.33 μCi/ml) to give a substrate buffer solution.

[0139] A test substance solution and an enzyme solution which had been adjusted to an optimal concentration were added thereto to perform a reaction at 30°C. The enzyme reaction was stopped by the addition of Scintillation Proximity Assay (SPA) Beads (Perkin Elmer, USA) containing 5 mM 3-isobutyl-1-methylxanthine (IBMX). For the enzyme activity, the amount of 5'-GMP, which is a reaction degradation product bound to SPA beads, was measured with a TopCount microplate reader (Hewlett Packard, USA).

[0140] The inhibitory rate was calculated by taking the radioactivity of the control containing no test substance as (A), taking the radioactivity of the blank containing no enzyme as (B), and taking the radioactivity of the test substance as (C), and using the following equation.

$$\text{Inhibitory rate}=100-\{(C)-(B)/(A)-(B)\}\times 100\ (\%)$$

[0141] In addition, the IC_{50} value was calculated as a compound concentration which inhibits the results obtained by 50% by a Logistic regression method.

(3) Other Evaluation of PDE-Inhibiting Activity

[0142] For the PDE1, a recombinant enzyme was purchased (BPS Bioscience Inc., USA). The PDE2 was expressed/purified by a method of Yang et al. (Yang, Q., et al., Biochem. Biophys. Res. Commun., 205: pp. 1850-1858 (1994)), and the PDE4 was expressed/purified by a method of Nemoz et al. (Nemoz, G., et al., FEBS Lett., 384: pp. 97-102 (1996)). The PDE3, PDE5 and PDE6 were isolated from rabbit myocardium, rabbit prostate, and rat retina. That is, desired tissues were selected from each of the animals, and chipped in a buffer solution containing bis(2-hydroxyethyl)iminotris(hydroxymethyl)aminomethane (20 mM), dithiothreitol (5 mM), glycol ether diamine tetraacetic acid (2 mM), and sodium acetate (50 mM). Then, the cells were crushed using a Poritoron homogenizer. Each tissue homogenates were ultracentrifuged (100,000xg, 4°C, 60 minutes), and then, the supernatant was added to a Q Sepharose column. By the concentration gradient of a buffer solution containing 0.05 to 1.2 M sodium acetate, sodium chloride (140 mM), potassium chloride (5 mM), glucose (5 mM), and 2-[4-(2-hydroxyethyl)-1-piperazinyl]ethanesulfonic acid (10 mM), elution was performed by ion exchange to obtain a fraction as a source of enzymes. For each of the eluate fractions, PDE subtypes were identified by enzymatic properties and selective inhibitor susceptibility.

[0143] For the PDE enzyme activity, the degradability for cAMP or cGMP was measured by the amount of 5'-AMP or 5'-GMP, which is a reaction degradation product bound to SPA beads, by the method as in PDE9 above.

[0144] For the compound of the formula (I), the PDE9-inhibiting activity action was confirmed by the test method above. The PDE9-inhibiting activity actions (IC_{50} values: nM) of some compounds are shown in Table 1, in which Ex denotes Example Nos. as described later (the same shall apply hereinafter).

[Table 1]

Ex	PDE9 inhibition (nM)
1	18
2	12
6	7.6
12	8.6
13	85
14	81

Ex	PDE9 inhibition (nM)
16	9.1
17	2.1
22	2.2
23	0.4
28	9.1
40	8.9

Ex	PDE9 inhibition (nM)
41	5.7
49	3.9
50	7.5
53	3.9
55	15
56	4.4

Ex	PDE9 inhibition (nM)
63	8.4
66	4.3
70	17
74	12
79	23
84	9.3

Ex	PDE9 inhibition (nM)
86	3.3
87	12
92	6.1
94	1.7
95	14
103	13
107	15
109	5.8
119	8.9
123	18
127	5.0
128	5.2
129	1.1
133	8.3
139	3.0
145	8.3
146	5.2
148	5.1

Ex	PDE9 inhibition (nM)
150	8.0
152	53
154	32
161	31
162	7.0
166	10
168	4.3
169	2.5
173	6.3
176	8.4
177	9.7
178	4.4
179	6.8
181	4.4
182	5.5
183	3.5
184	4.7
185	19

Ex	PDE9 inhibition (nM)
186	3.8
187	8.4
188	14
189	6.9
190	7.5
191	9.5
192	11
193	5.7
195	4.4
198	3.2
199	4.7
200	9.0
201	6.6
202	3.7
203	2.8
204	6.2
207	1.7
208	1.7

Ex	PDE9 inhibition (nM)
210	1.3
211	1.2
212	2.4
213	11
214	16
217	4.4
218	17
219	15
220	16
221	24
283	5.9
427	20
624	10
640	3.3
648	2.0
655	4.7
660	28
668	9.8

[0145] Furthermore, it was confirmed that a majority of the Example compounds included in the compound of the formula (I), in particular, "the compound, wherein R^2 is a group of the formula (II), and R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring which may be substituted" have a selective PDE9 inhibitory activity. The selective PDE9-inhibiting activity refers to a more potent inhibiting activity than the inhibiting activity particularly on PDE1, PDE3 and PDE6, and it is, for example, a case where the IC_{50} value (nM) is 1/10 or less, as compared with any of PDE1, PDE3 and PDE6, preferably a case where the IC_{50} value (nM) is 1/50 or less, as compared with 1, 2, or all of PDE1, PDE3 and PDE6, and more preferably a case where the IC_{50} value (nM) is 1/100 or less, as compared with 1, 2, or all of PDE1, PDE3, and PDE6.

Test Example 2: Evaluation of PDE9-Inhibiting Activity in Cells

[0146] A CRE-luc gene in which a luciferase (luc) gene was linked to the PDE9 gene and the cyclic AMP response element (CRE) gene in the HEK293 cell was transiently introduced to prepare a PDE9 and CRE-luc co-expressing cell.

The next day, a 0.5 mM IBMX and a test substance solution were added to the cells and cultured at 37°C for 6 hours, and then the culture supernatant was removed. 0.2% Triton X-100-containing phosphate buffer solution was added thereto to crush the cells. The PDE9-inhibiting activity in the cell was evaluated by adding a luciferin substrate liquid to the cell solution obtained by crushing the cells and measuring the luciferase activity in a fluorescence/luminescence plate reader.

[0147] As a result, it was confirmed that there are some compounds exhibiting the effective activity among the compounds of the formula (I).

Test Example 3: Action in Simultaneous Measurement Model for Rat Bladder Contraction/Urethra Relaxation Responses

[0148] Simultaneous measurement of the bladder contraction and urethra relaxation responses using a rat was carried out with a partial modification of a method in Wibberley et al. (Wibberley, A., et al., Br. J. Pharmacol., 136: pp. 399-414 (2002)). That is, a female Sprague-Dawley (SD) rat (Charles River Laboratories Japan, Inc.) was anesthetized with urethane, and the bladder was exposed by a midline incision in the lower abdomen. A double lumen cannula (a cannula having a dual structure by PE190 and PE50) from the bladder apex was inserted into the bladder, and the bladder apex and the cannula were fixed by sutures at a point where the tip reached the proximal urethra. While infusing physiological saline into the urethra through the outer cannula, the urethral inner pressure was measured by a pressure transducer through the inner cannula with a saline solution infused into the urethra through the outer cannula. On the other hand, a single cannula (PE50) was inserted into the bladder from the bladder apex and placed therein. The inner pressure of the bladder was measured through this cannula. After a postoperative stabilization period had passed, physiological saline was infused into the bladder through the cannula of the bladder apex to cause a bladder contraction reaction, and thus cause a urethra relaxation response accompanying the bladder contraction reflex. The test substance was administered intravenously or intraduodenally.

[0149] As a result, it was confirmed that there are some compounds exhibiting the effective activity among the compounds of the formula (I). For some of the compounds of the formula (I), the ratio with increased urethra relaxation time during voiding at 1 mg/kg (increase relative to the solvent administration group (vs vehicle) (%)) is shown in Table 2.

[Table 2]

Ex	Ratio with increased urethra relaxation time during voiding (vs vehicle) (%)
22	142
23	168
40	138
41	159
53	145
55	166
56	158
79	139
84	154
95	166
109	158
128	136

Test Example 4: Action in Rat Drug-Induced Voiding Dysfunction Model

[0150] A male SD rat (Japan SLC, Inc.) was put under anesthesia with isoflurane to place a cannula in the bladder and the jugular vein and was later aroused in a Ballman cage. After a postoperative stabilization period, physiological saline was infused into the bladder to cause voiding. Infusion of the physiological saline was stopped immediately after voiding, and the amount of the drained urine was measured using a pan balance placed under a Ballman cage. After completion of voiding, the residual urine was collected by gravity through a cannula placed in the bladder, and the weight was measured. Further, the inner pressure of the bladder was measured by a pressure transducer through the bladder cannula. Voiding dysfunction was caused by intravenous administration of one or a combination of an anticholinergic

agent, an α_1 receptor agonist, and an NO production inhibitor, and the voiding dynamics were observed after the drug administration. The test substance was administered intravenously, orally or gastrically.

[0151] As a result, it was confirmed that there are some compounds exhibiting the effective activity among the compounds of the formula (I).

[0152] As a result of the test above, it was confirmed that some of the compound of the formula (I) has a PDE9-inhibitory action and it was confirmed that some of the compounds of the formula (I) have a urethra relaxation action during voiding in the animal models as well. Accordingly, the compound of the formula (I) can be used for preventing or treating diseases related to degradation of cGMP by PDE9, for example, diseases such as storage dysfunction, voiding dysfunction, bladder/urethral diseases, in another embodiment, underactive bladder, hypotonic bladder, acontractile bladder, detrusor underactivity, neurogenic bladder, urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, overactive bladder, and lower urinary tract symptoms thereof, and benign prostatic hyperplasia, interstitial cystitis, chronic prostatitis, urethra calculus, and lower urinary tract symptoms accompanying them, and the like, and in a further embodiment, underactive bladder, hypotonic bladder, acontractile bladder, neurogenic bladder, detrusor underactivity, overactive bladder, urinary frequency, nocturia, incontinence, benign prostatic hyperplasia, lower urinary tract symptoms, voiding dysfunction accompanying urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, interstitial cystitis, chronic prostatitis, urethra calculus, and the like.

[0153] Furthermore, some compounds, wherein R^2 is a group of the formula (II), R^4 to R^6 are hydrogen, R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring which may be substituted, among the compounds of the formula (I), have a selective PDE9 inhibitory activity and as a result, the side effects derived from the action of other PDE subtypes can be avoided, whereby the compounds can be excellent therapeutic agents having higher safety. For example, cardiovascular risk derived from the PDE3 inhibitory action or the risk of blindness derived from the PDE6 inhibitory action can be avoided (A. M. Laties Drug Safety 2009; 32, 1-18/J. B. Shipley et al., Am. J. Med. Sci., 1996; 311, 286-291/T. M. Vinogradova et al., Circ. Res., 2008; 102, 761-769).

[0154] A pharmaceutical composition containing one or two or more kinds of the compound of the formula (I) or a salt thereof as an active ingredient can be prepared using excipients that are usually used in the art, that is, excipients for pharmaceutical preparation, carriers for pharmaceutical preparation, and the like according to the methods usually used.

[0155] Administration can be accomplished either by oral administration via tablets, pills, capsules, granules, powders, solutions, and the like, or parenteral administration injections, such as intraarticular, intravenous, or intramuscular injections, and the like, suppositories, ophthalmic solutions, eye ointments, transdermal liquid preparations, ointments, transdermal patches, transmucosal liquid preparations, transmucosal patches, inhalers, and the like.

[0156] The solid composition for use in the oral administration according to the present invention is used in the form of tablets, powders, granules, or the like. In such a solid composition, one or two or more active ingredient(s) are mixed with at least one inactive excipient. In a conventional method, the composition may contain inactive additives, such as a lubricant, a disintegrating agent, a stabilizer, or a solubilization assisting agent. If necessary, tablets or pills may be coated with sugar or a film of a gastric or enteric coating substance.

[0157] The liquid composition for oral administration contains pharmaceutically acceptable emulsions, solutions, suspensions, syrups, elixirs, or the like, and also contains generally used inert diluents, for example, purified water or ethanol. In addition to the inert diluent, the liquid composition may also contain auxiliary agents, such as a solubilization assisting agent, a moistening agent, and a suspending agent, sweeteners, flavors, aromatics and antiseptics.

[0158] The injections for parenteral administration include sterile aqueous or non-aqueous solution preparations, suspensions and emulsions. The aqueous solvent includes, for example, distilled water for injection and physiological saline. Examples of the non-aqueous solvent include propylene glycol, polyethylene glycol, plant oils such as olive oil, alcohols such as ethanol, Polysorbate 80 (Japanese Pharmacopeia), and the like. Such a composition may further contain a tonicity agent, an antiseptic, a moistening agent, an emulsifying agent, a dispersing agent, a stabilizing agent, or a solubilizing assisting agent. These are sterilized, for example, by filtration through a bacteria retaining filter, blending of a bactericide, or irradiation. In addition, these can also be used by preparing a sterile solid composition, and dissolving or suspending it in sterile water or a sterile solvent for injection prior to its use.

[0159] The agent for external use includes ointments, plasters, creams, jellies, patches, sprays, lotions, eye drops, eye ointments, and the like. The agents contain generally used ointment bases, lotion bases, aqueous or non-aqueous liquid preparations, suspensions, emulsions, and the like.

[0160] As the transmucosal agents such as an inhaler, a transnasal agent, and the like, those in the form of a solid, liquid or semi-solid state are used, and can be prepared in accordance with a conventionally known method. For example, a known excipient, and also a pH adjusting agent, an antiseptic, a surfactant, a lubricant, a stabilizing agent, a thickening agent, or the like may be appropriately added thereto. For their administration, an appropriate device for inhalation or blowing can be used. For example, a compound may be administered alone or as a powder of formulated mixture, or as a solution or suspension in combination with a pharmaceutically acceptable carrier, using a conventionally known device or sprayer, such as a measured administration inhalation device, and the like. A dry powder inhaler or the like may be for single or multiple administration use, and a dry powder or a powder-containing capsule may be used.

Alternatively, this may be in a form such as a pressurized aerosol spray which uses an appropriate ejection agent, for example, a suitable gas such as chlorofluoroalkane, carbon dioxide, and the like, or other forms.

[0161] In oral administration, the daily dose is generally from about 0.001 to 100 mg/kg, preferably from 0.1 to 30 mg/kg, and more preferably from 0.1 to 10 mg/kg, per body weight, administered in one portion or in 2 to 4 divided portions. In the case of intravenous administration, the daily dose is suitably administered from about 0.0001 to 10 mg/kg per body weight, once a day or two or more times a day. In addition, a transmucosal agent is administered at a dose from about 0.001 to 100 mg/kg per body weight, once a day or two or more times a day. The dose is appropriately decided in response to the individual case by taking the symptoms, the age and the gender, and the like into consideration.

[0162] Although varying depending on administration routes, dosage forms, administration sites, or the types of excipients and additives, the pharmaceutical composition of the present invention contains 0.01 to 100% by weight, and in a certain embodiment, 0.01 to 50% by weight of one or more kinds of the compound of the formula (I) or a salt thereof, which is an active ingredient.

[0163] The compound of the formula (I) can be used in combination with various agents for treating or preventing diseases for which the compound of the formula (I) is considered to be effective. The combined preparation may be administered simultaneously, or separately and continuously, or at a desired time interval. The preparations to be co-administered may be a blend, or may be prepared individually.

Examples

[0164] It is to be understood that the compounds of the present invention are those defined by claim 1. All other compounds are included for reference purposes. For instance, in Tables 35 to 104 the following compounds are included for reference purposes: 1, 11, 12-16, 18-20, 23, 25, 26, 29, 36, 37, 74, 87, 118-120, 145, 151, 244-251, 253, 263-265, 282-332, 351-369, 382-385, 389, 408, 451-454 and 472. In Tables 143 to 146 the following compounds are included for reference purposes: 1-40.

[0165] Hereinbelow, the preparation methods for the compound of the formula (I) and other reference compounds will be described in more detail with reference to Examples. Furthermore, each of the production processes for the starting compounds will be described in Preparation Examples. Further, the preparation methods for the compound of the formula (I) are not limited to the preparation methods of the specific Examples as below, but the compound of the formula (I) can be prepared by any combination of the preparation methods or the methods that are apparent to a person skilled in the art.

[0166] In addition, for salt forming reactions that are apparent to a person skilled in the art, there are cases where addition or omission to or of the specific preparation methods of Examples or Preparation Examples. Further, there are cases where the reaction temperatures vary within a range apparent to a person skilled in the art, considering the production of the reaction rate of the compound, the production of by-products, and the like.

[0167] The following abbreviations may be used in some cases in the Examples, Preparation Examples and Tables below. tert-: Tertiary, Pr: Preparation Example No., Ex: Example No., No: Compound No., Structure: Structural formula, Syn: Preparation method (the numeral shows that the Example compound was prepared in the same manner as a compound having its number as the Example No.), Data: Physicochemical data, ESI+: m/z values in mass spectroscopy (Ionization ESI, representing $(M+H)^+$ unless otherwise specified), ESI-: m/z values in mass spectroscopy (Ionization ESI, representing $(M-H)^-$ unless otherwise specified), EI+: m/z values in mass spectroscopy (Ionization EI, representing $(M)^+$ unless otherwise specified), FAB+: m/z values in mass spectroscopy (Ionization FAB, representing $(M+H)^+$ unless otherwise specified), FAB-: m/z values in mass spectroscopy (Ionization FAB, representing $(M-H)^-$ unless otherwise specified), APCI+: m/z values in mass spectroscopy (Ionization APCI, representing $(M+H)^+$ unless otherwise specified), APCI/ESI+: m/z values in mass spectroscopy (Ionization APCI and ESI simultaneously performed, representing $(M+H)^+$ unless otherwise specified), APCI/ESI-: m/z values in mass spectroscopy (Ionization APCI and ESI simultaneously performed, representing $(M-H)^-$ unless otherwise specified), mp.: Melting point, dec.: decomposition, NMR: δ (ppm) of peak in ^1H NMR, s: singlet (spectrum), d: doublet (spectrum), t: triplet (spectrum), q: quartet (spectrum), and br: broad line (spectrum) (example: br s). Further, HCl in the structural formula represents hydrochloride (the numeral prefixed to HCl denotes a molar ratio). In addition, [M] of the concentration represents [mol/L]. A case where there is a description of "Chiral" in the structural formula indicates that the Example compound is an optically active form, but there are some cases where the stereochemistry is not determined. A case where there is no description of "Chiral" in the structural formula indicates that the Example compound is a mixture of geometrical isomers, or a racemate. Accordingly, a case where there is a description of stereochemistry but there is no description of "Chiral" indicates a racemic mixture of diastereomers having relative configurations, and a case where there is neither a description of stereochemistry nor a description of "Chiral" indicates a mixture of geometrical isomers, or a mixture of optical isomers.

Preparation Example 1

[0168] To a mixed liquid of 980 mg of 5-(4-bromo-2-nitrophenyl)-1-cyclopentyl-1H-pyrazole in 9.8 mL of tetrahydrofuran, 19.6 mL of ethanol, and 2.9 mL of water was added 102 mg of ammonium chloride, followed by heating at 70°C. 1.03 g of reduced iron was added thereto, followed by heating to reflux for 4 hours, and cooling to room temperature. The insoluble material was separated by celite filtration, the filtrate was concentrated, and a mixed liquid of chloroform/water was added thereto. The aqueous layer was separated, and then the organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 815 mg of 5-bromo-2-(1-cyclopentyl-1H-pyrazol-5-yl)aniline.

Preparation Example 2

[0169] Under a nitrogen atmosphere, to a solution of 1.15 g of (2E)-1-(4-bromo-2-nitrophenyl)-3-(dimethylamino)prop-2-en-1-one in 9.2 mL of acetic acid was added 1.05 g of cyclopentylhydrazine hydrochloride, followed by stirring at room temperature for 60 hours. The reaction liquid was poured into a mixed liquid of water/ethyl acetate, followed by adjusting to pH 10 with a 6 M aqueous sodium hydroxide solution. The aqueous layer was separated, and then the organic layer was washed with water and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure, and then the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 940 mg of 5-(4-bromo-2-nitrophenyl)-1-cyclopentyl-1H-pyrazole.

Preparation Example 3

[0170] To a solution of 100 mg of 5-bromo-2-(1-cyclopentyl-1H-pyrazol-5-yl)aniline in 2.5 mL of N-methylpyrrolidone was added 105 mg of CDI, followed by stirring at 150°C for 2 hours using a microwave reactor, and cooling to room temperature. The precipitated solid was collected by filtration, washed with ethyl acetate, and then dried under reduced pressure to obtain 73 mg of 7-bromo-1-cyclopentyl-1,5-dihydro-4H-pyrazolo[4,3-c] quinolin-4-one.

Preparation Example 4

[0171] Under a nitrogen atmosphere, a mixture of 3.62 g of 1-(4-bromo-2-nitrophenyl)ethanone and 5.3 g of (dimethoxymethyl)dimethylamine was stirred at 90°C for 4 hours. The reaction mixture was cooled to room temperature and the precipitated solid was collected by filtration. The obtained solid was washed with diisopropyl ether and dried under reduced pressure to obtain 3.93 g of (2E)-1-(4-bromo-2-nitrophenyl)-3-(dimethylamino)prop-2-en-1-one.

Preparation Example 5

[0172] To a solution of 735 mg of 7-bromo-1-cyclopentyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one in 6 mL of dimethylsulfoxide were sequentially added 49 mg of palladium acetate, 91 mg of 1,3-bis(diphenylphosphino)propane, 0.62 mL of triethylamine, and 3 mL of methanol, and the atmosphere in the reaction container was replaced with carbon monoxide. The mixture was stirred at 70°C for 7 hours, cooled to room temperature, and then poured into a mixed liquid of water and ethyl acetate. The aqueous layer was separated, the organic layer was washed with diluted hydrochloric acid and saturated brine, and then dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 551 mg of methyl 1-cyclopentyl-4-oxo-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-7-carboxylate.

Preparation Example 6

[0173] Under a nitrogen atmosphere, to a solution of 6.95 g of 1-(2-amino-5-bromo-4-methylphenyl)ethanone and 8.5 mL of triethylamine in 104 mL of tetrahydrofuran was slowly added 3.25 mL of acetyl chloride. After stirring at room temperature for 2 hours, the reaction liquid was poured into a mixed liquid of water/ethyl acetate, followed by stirring for 30 minutes and adjusting to pH 3 with 6 M hydrochloric acid, and the aqueous layer was separated. The organic layer was washed with water and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and then the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 6.33 g of N-(2-acetyl-4-bromo-5-methylphenyl)acetamide.

Preparation Example 7

[0174] Under a nitrogen atmosphere, 6.33 g of N-(2-acetyl-4-bromo-5-methylphenyl)acetamide was added to a mixed liquid of 3.3 g of (dimethoxymethyl)dimethylamine and 19 mL of toluene, followed by stirring at 120°C for 16 hours. The mixture was cooled to room temperature, then solution was concentrated, and diisopropyl ether was added thereto and triturated. The powder was collected by filtration, washed with diisopropyl ether, and then dried under reduced pressure to obtain 6.92 g of N-{4-bromo-2-[(2E)-3-(dimethylamino)prop-2-enoyl]-5-methylphenyl} acetamide.

Preparation Example 8

[0175] To a solution of 3.37 g of tetrahydro-2H-pyran-4-ylhydrazine hydrochloride in 120 mL of ethanol was added 3.82 g of powdery potassium carbonate, followed by stirring at room temperature for 30 minutes. To a mixture was added 6 g of N-{4-bromo-2-[(2E)-3-(dimethylamino)prop-2-enoyl]-5-methylphenyl}acetamide, followed by stirring at 80°C for 16 hours and cooling to room temperature. The mixture was poured into a mixed liquid of water/ethyl acetate, and the aqueous layer was separated. The organic layer was washed with water and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 3.96 g of N-{4-bromo-5-methyl-2-[1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-5-yl]phenyl} acetamide.

Preparation Example 9

[0176] 3.96 g of N-{4-bromo-5-methyl-2-[1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-5-yl]phenyl}acetamide was suspended in 18 mL of 12 M hydrochloric acid, followed by stirring at 120°C for 40 minutes. The reaction liquid was cooled to room temperature, then poured into a mixed liquid of a saturated aqueous sodium hydrogen carbonate solution/ethyl acetate, and adjusted to pH 10 with a 6 M aqueous sodium hydroxide solution. The aqueous layer was separated, and then the organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and then the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 3.36 g of 4-bromo-5-methyl-2-[1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-5-yl] aniline.

Preparation Example 10

[0177] To a mixture of 2.63 g of methyl 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylate in 52 mL of methanol was added 10.2 mL of a 3 M aqueous sodium hydroxide solution, followed by stirring at 60°C for 20 hours. The insoluble material was filtered, and the filtrate was adjusted to pH 2 with concentrated hydrochloric acid, and stirred for 1 hour as it was. The precipitated powder was collected by filtration and dried under reduced pressure to obtain 2.49 g of 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid as powder.

Preparation Example 11

[0178] Under a nitrogen atmosphere, to a solution of 1.0 g of 1-(4-bromo-2-nitrophenyl)butane-1,3-dione in 10 ml of acetic acid was added 501 mg of cyclopentylhydrazine hydrochloride, followed by stirring at 100°C for 1 hour and 30 minutes. The reaction liquid was concentrated, and to the obtained residue was added ethyl acetate. The solution was washed with a saturated aqueous sodium hydrogen carbonate solution and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and then the residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 770 mg of 5-(4-bromo-2-nitrophenyl)-1-cyclopentyl-3-methyl-1H-pyrazole.

Preparation Example 12

[0179] Under a nitrogen atmosphere, to a solution of 4.95 g of tert-butyl 2-(4-bromo-2-nitrobenzoyl)-3-oxobutanoate in 30 mL of dichloromethane was added 20 mL of trifluoroacetic acid under ice-cooling. The mixture was warmed to room temperature and stirred for 2.5 hours, and then the solvent was evaporated under reduced pressure. To the residue was added ethyl acetate, and the solution was washed with a saturated aqueous sodium hydrogen carbonate solution and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 2.7 g of 1-(4-bromo-2-nitrophenyl)butane-1,3-dione.

Preparation Example 13

[0180] Under a nitrogen atmosphere, to a suspension of 2.28 g of magnesium chloride in 50 mL of tetrahydrofuran was added 3.80 g of tert-butyl 3-oxobutanoate at room temperature. The mixture was cooled to -8°C, and 3.9 mL of pyridine was added thereto, followed by stirring at the same temperature for 30 minutes, warming to room temperature, and further stirring for 30 minutes. The mixture was cooled to -8°C, and a solution of 5.3 g of 4-bromo-2-nitrobenzoyl chloride in 20 mL of tetrahydrofuran was added thereto, followed by stirring at the same temperature for 1 hour, warming to room temperature, and further stirring for 1.5 hours. The mixture was poured into a mixed liquid of water and ethyl acetate, and adjusted to pH 3 with concentrated hydrochloric acid. The aqueous layer was separated, and then the organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to obtain 4.95 g of tert-butyl 2-(4-bromo-2-nitrobenzoyl)-3-oxobutanoate.

Preparation Example 14

[0181] To a mixture of 1.60 g of 1-(benzylpyrrolidin-3-yl)-8-bromo-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one in 80 mL of dimethylsulfoxide were added 1.27 g of tetrakis(triphenylphosphine) palladium (0), 2.04 mL of triethylamine, and 3 mL of methanol. The atmosphere in the reaction container was replaced with carbon monoxide, followed by stirring at 70°C for 10 hours. The reaction mixture was left to be cooled, and then water was added thereto, followed by extraction with chloroform/methanol. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the obtained solid was heated and washed with ethyl acetate, and then stirred at room temperature for 10 minutes. The solid was collected by filtration and dried under reduced pressure to obtain 1.33 g of methyl 1-(1-benzylpyrrolidin-3-yl)-7-methyl-4-oxo-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylate.

Preparation Example 15

[0182] 4.3 g of tert-butyl 4-(hydroxymethyl)piperidine-1-carboxylate, 66 mg of 4,7-diphenyl-1,10-phenanthroline, and 45 mg of palladium acetate were added to 50 mL of butylvinyl ether, followed by stirring at room temperature for 15 minutes, and stirring at 75°C for 2 days. The reaction mixture was filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 4.4 g of tert-butyl 4-[(vinyloxy)methyl]piperidine-1-carboxylate.

Preparation Example 16

[0183] To a mixture of 3.23 g of 4-bromo-2-[1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-5-yl]-5-(trifluoromethyl)aniline in 32 mL of N-methylpyrrolidone were added 2.6 mL of DIPEA and 1.8 g of CDI, followed by stirring at 150°C for 1.5 hours. After ice-cooling, diisopropyl ether/ethyl acetate (4/1) and ice were added thereto, followed by stirring. The precipitated solid was collected by filtration, and washed with water and diisopropyl ether/ethyl acetate (4/1). The obtained solid was heated and washed with diisopropyl ether/ethyl acetate (4/1), followed by stirring at room temperature for 10 minutes, and the solid was collected by filtration, washed with diethyl ether, and then dried under reduced pressure to obtain 2.95 g of 8-bromo-1-(tetrahydro-2H-pyran-4-yl)-7-(trifluoromethyl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one.

Preparation Example 17

[0184] To a mixture of 11.6 g of 1-[2-amino-4-(trifluoromethyl)phenyl]ethanone, 60 mL of acetonitrile, and 230 mL of diethyl ether was added 2.85 g of Amberlyst (registered trademark) 15, and 10.1 g of N-bromosuccinimide was portionwise added thereto three times in an ice bath. After stirring for 30 minutes in an ice bath, the mixture was stirred at room temperature overnight. The insoluble material was filtered and washed with ethyl acetate. The filtrate was separated by the addition of water and ethyl acetate. The organic layer was washed with a 10% aqueous sodium thiosulfate solution and saturated brine, and dried over anhydrous magnesium sulfate, and then solvent was evaporated. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 10.36 g of 1-[2-amino-5-bromo-4-(trifluoromethyl)phenyl]ethanone.

Preparation Example 18

[0185] To a mixture of 6.0 g of tetrahydro-2H-pyran-4-ylhydrazine dihydrochloride in 175 mL of N-methylpyrrolidone was added 11 mL of DIPEA, followed by stirring at room temperature for 20 minutes. To the reaction mixture was added

8.86 g of N-{4-bromo-2-[(2E)-3-(dimethylamino)prop-2-enoyl]-5-(trifluoromethyl)phenyl}-2,2,2-trifluoroacetamide, followed by stirring at 110°C for 1 hour. To the reaction liquid was added water, followed by extraction with isopropyl acetate, and the organic layer was washed with saturated brine. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol). The obtained oily substance was triturated with diethyl ether/n-hexane to obtain 4.19 g of N-{4-bromo-2-[1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-5-yl]-5-(trifluoromethyl)phenyl}-2,2,2-trifluoroacetamide.

Preparation Example 19

[0186] Under a nitrogen atmosphere, to a solution of 330 mg of tert-butyl (3S)-3-phenylpiperazine-1-carboxylate in 3.5 mL of DMF was added 75.4 mg of sodium hydride (including 40% mineral oil) under ice-cooling, followed by stirring for 30 minutes. To the mixture was added 0.27 mL of 2-bromoethyl methyl ether, followed by stirring at room temperature for 16 hours. To the mixture were added 75.4 mg of sodium hydride (including 40% mineral oil) and 0.6 mL of 2-bromoethyl methyl ether, followed by further stirring for 8 hours. The mixture was poured into a mixed liquid of water and ethyl acetate, and the aqueous layer was separated. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 330 mg of tert-butyl (3S)-4-(2-methoxyethyl)-3-phenylpiperazine-1-carboxylate.

Preparation Example 20

[0187] A mixture of 3 g of 4-ethoxybutyl p-toluenesulfonate, 2.65 g of tert-butyl (3R)-3-methylpiperazine-1-carboxylate, 3.07 mL of triethylamine, and 30 mL of acetonitrile was stirred at 90°C for 3 hours. The reaction liquid was poured into a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 3.1 g of tert-butyl (3 R)-4-(4-ethoxybutyl)-3 -methylpiperazine-1-carboxylate.

Preparation Example 21

[0188] To a solution of 420 mg of tert-butyl 4-[3-(pyridin-3-yl)propyl]piperazine-1-carboxylate in 6 mL of methanol was added 2 mL of a 4 M hydrogen chloride-dioxane solution, followed by stirring at room temperature for 16 hours. The solvent was evaporated under reduced pressure to obtain 395 mg of 1-[3-(pyridin-3-yl)propyl]piperazine trihydrochloride.

Preparation Example 22

[0189] To a solution of 2.0 g of tert-butyl 4-[(cyclopropyloxy)methyl]piperidine-1-carboxylate in 20 mL of dichloromethane was added 3.0 mL of trifluoroacetic acid, followed by stirring at room temperature for 2 hours. The reaction liquid was concentrated under reduced pressure, and to the residue were added a saturated aqueous sodium hydrogen carbonate solution and ethyl acetate. The organic layer was separated, then washed with saturated brine, and dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by basic silica gel column chromatography (chloroform/methanol) to obtain 756 mg of 4-[(cyclopropyloxy)methyl]piperidine.

Preparation Example 23

[0190] Under a nitrogen atmosphere, to a mixture of 693 mg of lithium aluminum hydride and 30 mL of tetrahydrofuran was added dropwise a solution of 1.0 g of 1-(piperidin-1-yl)cyclobutanecarbonitrile in 18 mL of tetrahydrofuran under ice-cooling. The reaction liquid was stirred at room temperature for 3 hours. Under ice-cooling, 1.5 mL of water and 1.5 mL of a 15% aqueous sodium hydroxide solution were added dropwise thereto. The mixture was diluted with ethyl acetate and the reaction liquid was filtered. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 932 mg of 1-[1-(piperidin-1-yl)cyclobutyl]methanamine.

Preparation Example 24

[0191] Under a nitrogen atmosphere, to a solution of 1.5 g of tert-butyl 4-[3-(pyridin-3-yl)propanoyl]piperazine-1-carboxylate in 25 mL of tetrahydrofuran was added 7 mL of a 1 M borane/tetrahydrofuran solution under ice-cooling. The

mixture was heated to reflux for 6 hours, and then cooled to room temperature, and 10 mL of methanol was added thereto, followed by further heating to reflux for 16 hours. After cooling to room temperature, the mixture was concentrated under reduced pressure, and a mixed liquid of a saturated aqueous sodium hydrogen carbonate solution and ethyl acetate was added thereto. The aqueous layer was separated, and then the organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 1.43 g of tert-butyl 4-[3-(pyridin-3-yl)propyl]piperazine-1-carboxylate.

Preparation Example 25

[0192] To 3.9 g of (4,4-difluorocyclohexyl)methanol was added 40 mL of toluene. 10.2 g of triphenylphosphine was added thereto at room temperature, followed by stirring for a while. The mixture was ice-cooled, and 7.2 g of di-tert-butyl azodicarboxylate was portionwise added thereto while maintaining the internal temperature at about 10 to 15°C. The reaction mixture was stirred at room temperature for 20 hours. The solvent was evaporated and the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 10.7 g of di-tert-butyl 1-[(4,4-difluorocyclohexyl)methyl]hydrazine-1,2-dicarboxylate.

Preparation Example 26

[0193] A solution of 1.5 g of 4-hydroxypyridine, 7.6 g of cyanomethylenetributylphosphorane, and 1.4 g of (2S)-2-fluoro-1-propanol in 20 mL of toluene was stirred at 105°C overnight. To the residue were added 1 M hydrochloric acid and ethyl acetate, and the aqueous layer was separated. The aqueous layer was adjusted to pH 11 by the addition of a 1 M aqueous sodium hydroxide solution, and the organic layer was separated by the addition of ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (chloroform/methanol) to obtain 2.2 g of 4-{[(2S)-2-fluoropropyl]oxy}pyridine.

Preparation Example 27

[0194] To a mixture of (3R)-1-methylpyrrolidin-3-ol in 35 mL of tetrahydrofuran was added 18.2 g of triphenylphosphine, and a solution of 13.2 g of di-tert-butyl azodicarboxylate in 10 mL of tetrahydrofuran was added dropwise thereto under ice-cooling, followed by stirring for 1 hour, and further stirring at room temperature for 1 hour. To the reaction mixture was added 40 mL of a 6 M hydrochloric acid, followed by stirring at room temperature overnight. To the reaction liquid was added 40 mL of water, tetrahydrofuran was evaporated under reduced pressure, and then 20 mL of dichloromethane was added thereto to carry out liquid separation. To the obtained aqueous layer was added 20 mL of dichloromethane to carry out liquid separation twice, and the aqueous layer was separated. Water was evaporated from the aqueous layer under reduced pressure, and then coevaporated with isopropanol. The obtained solid was collected by filtration and dried under reduced pressure to obtain 7.92 g of (3S)-3-hydrazino-1-methylpyrrolidine dihydrochloride.

Preparation Example 28

[0195] To a solution of 357 mg of methyl 2,2-difluoro-3-methoxypropionate in 7 mL of tetrahydrofuran was added 2.7 mL of a 1M aqueous sodium hydroxide solution, followed by stirring at room temperature for 3 hours. The reaction liquid was acidified by the addition of 3.0 mL of 1 M hydrochloric acid and then extracted with ethyl acetate, the organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solvent was concentrated under reduced pressure. To the reside were added 7 mL of 1,2-dichloroethane and 25 μL of DMF, and 219 μL of oxalyl chloride was added thereto under ice-cooling, followed by stirring at room temperature for 1 hour.

[0196] The reaction liquid was ice-cooled, and 1.9 mL of triethylamine and 560 mg of tert-butyl piperazine-1-carboxylate were added thereto, followed by stirring at room temperature overnight. To the reaction mixture were added chloroform and water, followed by extraction with chloroform. The mixture was washed with saturated brine and dried over anhydrous magnesium sulfate, and the solvent was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 500 mg of tert-butyl 4-(2,2-difluoro-3-methoxypropanoyl)piperazine-1-carboxylate.

Preparation Example 29

[0197] Under a nitrogen atmosphere, 63 mL of diethylzinc (1.0 M hexane solution) was added to 92 mL of 1,2-dichloroethane at -40°C, and subsequently a solution of 2.5 g of tert-butyl 4-[(vinyloxy)methyl]piperidine-1-carboxylate in 134

mL of 1,2-dichloroethane was added thereto, followed by stirring at -40°C for 30 minutes. 7.5 mL of chloroiodomethane was added thereto, followed by stirring for 4 hours while elevating the temperature from -40°C to -15°C. To the reaction mixture was added portionwise a saturated aqueous ammonium chloride solution, followed by extraction with chloroform. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 2.0 g of tert-butyl 4-[(cyclopropyloxy)methyl]piperidine-1-carboxylate.

Preparation Example 30

[0198] 2.2 g of 4-{[(2S)-2-fluoropropyl]oxy}pyridine was added to a solution of 22 mL of acetic acid in 22 mL of methanol, and 500 mg of 10% palladium on carbon (wettype) was added thereto under an argon atmosphere. The reaction liquid was stirred at room temperature overnight under a hydrogen atmosphere of 3 atm. The reaction liquid was filtered through celite and the filtrate was concentrated under reduced pressure. The residue was purified by basic silica gel column chromatography (chloroform/methanol) to obtain 988 mg of 4-{[(2S)-2-fluoropropyl]oxy}piperidine.

Preparation Example 31

[0199] To a mixture of 500 mg of 6-bromo-3-fluoro-2-methylpyridine, 580 mg of tert-butyl (3R)-3-methylpiperazine-1-carboxylate, 506 mg of sodium tert-butoxide, and 61 mg of 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene in toluene was added 48 mg of tris(dibenzylidenacetone)dipalladium (0), followed by stirring at 110°C for 3 hours. After cooling to room temperature, the reaction liquid was poured into water and extracted with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 780 mg of tert-butyl (3R)-4-(5-fluoro-6-methylpyridin-2-yl)-3-methylpiperazine-1-carboxylate.

Preparation Example 32

[0200] To a mixture of 500 mg of 3-(cyclopropyloxy)propanol in 5 mL of dichloromethane were added 1.2 mL of triethylamine and 1.3 g of p-toluenesulfonic acid chloride under ice-cooling, followed by stirring for 4 hours. The reaction liquid was diluted with chloroform, washed with 1 M hydrochloric acid, a saturated aqueous sodium hydrogen carbonate solution, and saturated brine, dried over anhydrous magnesium sulfate, and then concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to obtain 522 mg of 3-(cyclopropyloxy)propyl p-toluenesulfonate.

Preparation Example 33

[0201] To a solution of 12.8 g of 1-[2-amino-5-bromo-4-(trifluoromethyl)phenyl]ethanone of 190 mL of dichloromethane was added 8.82 mL of triethylamine, and a solution of 7.66 mL of trifluoroacetic anhydride in 5 mL of dichloromethane was added dropwise thereto over 10 minutes under ice-cooling, followed by stirring for 30 minutes. Furthermore, 2.65 mL of triethylamine in 2.3 mL of trifluoroacetic anhydride was added dropwise thereto under ice-cooling, followed by stirring for 30 minutes. To the reaction liquid was added water, followed by extraction with chloroform, and the organic layer was washed with a saturated aqueous sodium hydrogen carbonate solution/ice (1/1) and saturated brine, and dried over anhydrous magnesium sulfate. The insoluble material was separated by filtration, and then the solvent was evaporated under reduced pressure to obtain 18 g of N-[2-acetyl-4-bromo-5-(trifluoromethyl)phenyl]-2,2,2-trifluoroacetamide.

[0202] In the same manner as the method of Preparation Example 1, the compounds of Preparation Examples 1-1 to 1-2 were prepared; in the same manner as the method of Preparation Example 2, the compound of Preparation Example 2-1 was prepared; in the same manner as the method of Preparation Example 3, the compounds of Preparation Examples 3-1 to 3-13 were prepared; in the same manner as the method of Preparation Example 5, the compounds of Preparation Examples 5-1 to 5-19 were prepared; in the same manner as the method of Preparation Example 6, the compounds of Preparation Examples 6-1 to 6-2 were prepared; in the same manner as the method of Preparation Example 7, the compounds of Preparation Examples 7-1 to 7-3 were prepared; in the same manner as the method of Preparation Example 8, the compounds of Preparation Examples 8-1 to 8-18 were prepared; in the same manner as the method of Preparation Example 9, the compounds of Preparation Examples 9-1 to 9-17 were prepared; in the same manner as the method of Preparation Example 10, the compounds of Preparation Examples 10-1 to 10-21 were prepared; in the same manner as the method of Preparation Example 14, the compounds of Preparation Examples 14-1 to 14-2 were prepared; in the same manner as the method of Preparation Example 16, the compounds of Preparation Examples 16-1 to 16-8 were prepared; in the same manner as the method of Preparation Example 17, the compounds of Preparation

Examples 17-1 to 17-2 were prepared; in the same manner as the method of Preparation Example 19, the compounds of Preparation Examples 19-1 to 19-16 were prepared; in the same manner as the method of Preparation Example 20, the compounds of Preparation Examples 20-1 to 20-3 were prepared; in the same manner as the method of Preparation Example 21, the compounds of Preparation Examples 21-1 to 21-39 were prepared; in the same manner as the method of Preparation Example 24, the compounds of Preparation Examples 24-1 to 24-2 were prepared; in the same manner as the method of Preparation Example 25, the compounds of Preparation Examples 25-1 to 25-4 were prepared; in the same manner as the method of Preparation Example 26, the compounds of Preparation Examples 26-1 to 26-2 were prepared; in the same manner as the method of Preparation Example 28, the compound of Preparation Example 28-1 was prepared; in the same manner as the method of Preparation Example 30, the compounds of Preparation Examples 30-1 to 30-2 were prepared; in the same manner as the method of Preparation Example 31, the compounds of Preparation Examples 31-1 to 31-2 were prepared; in the same manner as the method of Example 7 below, the compounds of Preparation Examples 34-1 to 34-14 were prepared; in the same manner as the method of Example 4 below, the compounds of Preparation Examples 35-1 to 35-6 were prepared; in the same manner as the method of Example 2 below, the compound of Preparation Example 36 was prepared; and in the same manner as the method of Example 5 below, the compounds of Preparation Examples 37-1 to 37-2 were prepared; each using the corresponding starting materials.

[0203] The structures of Preparation Example compounds are shown in Tables 3 to 26, and the physicochemical data of Preparation Example compounds are shown in Tables 27 to 34 below.

Example 1

[0204] Under a nitrogen atmosphere, to a solution of 148 mg of 5-chloroindoline in 1 mL of toluene was added 0.54 mL of a 1.8 M trimethylaluminum solution in toluene at 0°C, followed by stirring at room temperature for 2 hours (solution A). Under a nitrogen atmosphere, to a mixture of 100 mg of methyl 1-cyclopentyl-4-oxo-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-7-carboxylate in 3 mL of toluene was added the solution A, followed by stirring at 70°C for 8 hours. After cooling to room temperature, to the reaction mixture was added diluted hydrochloric acid, and the mixture was poured into a mixed liquid of water and ethyl acetate. The pH was adjusted to 10 with 28% aqueous ammonia. The insoluble material was separated by filtration. The aqueous layer was separated, the organic layer was washed with saturated brine and then dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The obtained residue was purified by silica gel column chromatography (chloroform/methanol=100/0-92/8) to obtain 65 mg of 7-[(5-chloro-2,3-dihydro-1H-indol-1-yl)carbonyl]-1-cyclopentyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one as white powder.

Example 2

[0205] To a mixture of 120 mg of 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid in 2.4 mL of DMF were added 130 mg of 1-(pyridin-3-ylmethyl)piperazine, 0.19 mL of DIPEA, and 177 mg of TBTU, followed by stirring at room temperature overnight. The reaction liquid was ice-cooled and poured into a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with ethyl acetate. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol=100/0-92/8) to obtain white powder. The powder was suspended in 1 mL of methanol, and 0.37 mL of a 4 M hydrogen chloride-ethyl acetate solution was added thereto, followed by stirring for 30 minutes. The obtained powder was collected by filtration, washed with methanol, and then dried under reduced pressure to obtain 82 mg of 7-methyl-8-{[4-(pyridin-3-ylmethyl)piperazin-1-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one dihydrochloride as a white solid.

Example 3

[0206] To a mixture of 8.2 mg of 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid, 3.8 mg of 1-(2-aminoethyl)piperidine, 13.1 μL of DIPEA, and 0.4 mL of DMF was added a mixture of 9.8 mg of HATU and 0.1 mL of DMF, followed by stirring at room temperature overnight. The reaction liquid was purified by preparative HPLC (methanol/0.1% aqueous formic acid solution) to obtain 3.6 mg of 7-methyl-4-oxo-N-[2-(piperidin-1-yl)ethyl]-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxamide.

Example 4

[0207] To a mixture of 224 mg of 1-(1-benzylpyrrolidin-3-yl)-8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1,5-

dihydro-4H-pyrazolo [4,3-c]quinolin-4-one hydrochloride in methanol was added 23 mg of a 10% palladium hydroxide/carbon powder, followed by stirring at room temperature for 20 hours under a hydrogen atmosphere of 3 atm. After returning to normal pressure and replacing with argon, the insoluble material was removed by filtration, and the solvent was evaporated under reduced pressure. The residue was purified by reverse phase silica column chromatography (acetonitrile/water=0/100-35/65). The obtained compound was dissolved in 4 mL of methanol, and 1 mL of a 4 M hydrogen chloride-ethyl acetate solution was added thereto, followed by stirring for 1 hour. Then, the solvent was evaporated under reduced pressure and the solid was collected by filtration, washed with diethyl ether, and then dried under reduced pressure to obtain 180 mg of 8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-pyrrolidin-3-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one hydrochloride as a white solid.

Example 5

[0208] To a mixture of 110 mg of 1-cyclopentyl-7-methyl-4-oxo-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid in 4.4 mL of DMF were added 73 mg of 1-(2-isopropoxyethyl)piperazine, 121 μL of DIPEA, and 202 mg of HATU, followed by stirring at room temperature overnight. To the reaction mixture were added a saturated aqueous sodium hydrogen carbonate solution and water, followed by extraction with ethyl acetate. The organic layer was washed with water and saturated brine, and dried over anhydrous magnesium sulfate, and then solvent was evaporated. The obtained residue was purified by silica gel column chromatography (chloroform/methanol=100/0-95/5). To the obtained oily substance were added 2 mL of methanol and 265 μL of a 4 M hydrogen chloride-ethyl acetate solution, followed by stirring at room temperature for 30 minutes. The solvent was evaporated under reduced pressure, and 0.5 mL of methanol and 3 mL of diethyl ether were added thereto, followed by stirring at room temperature to give powder, which was collected by filtration and dried under reduced pressure to obtain 140 mg of 1-cyclopentyl-8-{[4-(2-isopropoxyethyl)piperazin-1-yl]carbonyl}-7-methyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one hydrochloride as white powder.

Example 6

[0209] To 95 mg of ethyl (3R)-1-{[7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinolin-8-yl]carbonyl}piperidine-3-carboxylate were added 5 mL of ethanol and 200 μL of a 3 M aqueous sodium hydroxide solution, followed by stirring at 70°C for 9 hours. The reaction mixture was left to be cooled, and water and ethyl acetate were added thereto to carry out liquid separation. The aqueous layer was adjusted to about pH 4 with 1 mL of 1 M hydrochloric acid, then the solution was coevaporated with toluene, and the precipitated powder was collected by filtration. The obtained powder was dried under reduced pressure to obtain 71 mg of (3R)-1-{[7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinolin-8-yl]carbonyl}piperidine-3-carboxylic acid as white powder.

Example 7

[0210] To a mixture of 33 mg of 8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-pyrrolidin-3-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one hydrochloride in 0.66 mL of 1,2-dichloroethane and 0.26 mL of acetic acid were added 210 μL of a 37% aqueous formaldehyde solution and 44 mg of sodium triacetoxyborohydride, followed by stirring at room temperature for 2 hours. The reaction liquid was poured into a 1 M aqueous sodium hydroxide solution, followed by extraction with chloroform. The organic layer was washed with saturated brine and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (chloroform/methanol=100/0-90/10). The obtained compound was dissolved in 1 mL of dichloromethane, and 20 μL of a 4 M hydrogen chloride-ethyl acetate solution was added thereto, followed by stirring for 15 minutes. Then, the solvent was evaporated under reduced pressure, and the solid was collected by filtration, washed with diethyl ether, and then dried under reduced pressure to obtain 24 mg of 8-{[4-(ethoxymethyl)piperidin-1-yl]carbonyl}-7-methyl-1-(1-methylpyrrolidin-3-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one hydrochloride as a white solid.

Example 8

[0211] To a mixture of 8.2 mg of 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinoline-8-carboxylic acid, 7.7 mg of methyl 3-piperidin-4-yl-benzoate monohydrochloride, 3.4 mg of 1-hydroxybenzotriazole, 7.0 μL of triethylamine, and 1.0 mL of DMF was added 100 mg of PS-Carbodiimide (Biotage), followed by stirring at room temperature overnight. To the reaction mixture were added 75 mg of MP-Carbonate (Biotage), 50 mg of PS-Isocyanate (Biotage), and 0.5 mL of DMF at room temperature, followed by stirring for 2 hours. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure. To the obtained residue were added 0.5 mL of methanol, 0.5 mL of tetrahydrofuran, and 0.5 mL of a 1M aqueous sodium hydroxide solution, followed by stirring at room temperature overnight. To the reaction liquid was added 0.5 mL of 1 M hydrochloric acid and the solvent was

evaporated under reduced pressure. The obtained residue was purified by preparative LC-MS (methanol/0.1% aqueous formic acid solution) to obtain 5.8 mg of 3-(1-{[7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4,5-dihydro-1H-pyrazolo[4,3-c]quinolin-8-yl]carbonyl}piperidin-4-yl)benzoic acid.

Example 9

[0212] To a mixture of 11.9 mg of 7-methyl-8-(piperazin-1-ylcarbonyl)-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one, 15.9 mg of 6-(1-pyrrolidinyl)nicotinaldehyde, 0.3 mL of 1,2-dichloroethane, and 30 μL of acetic acid was added 19.1 mg of sodium triacetoxyborohydride, followed by stirring at room temperature overnight. To the reaction liquid was added a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with chloroform. The solvent of the organic layer was evaporated under reduced pressure. The obtained residue was purified by preparative HPLC (methanol/0. 1% aqueous formic acid solution) to obtain 9.7 mg of 7-methyl-8-[(4- {[6-(pyrrolidin-1-yl)pyridin-3-]methyl}piperazin-1-yl)carbonyl]-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one.

Example 10

[0213] To a mixture of 6.0 mg of tert-butyl (3S)-3-methylpiperazine-1-carboxylate, 17.3 mg of 6-morpholinopyridine-2-carbaldehyde, 0.3 mL of 1,2-dichloroethane, and 5.2 μL of acetic acid was added 19.1 mg of sodium triacetoxyborohydride, followed by stirring at room temperature overnight. To the reaction liquid was added a saturated aqueous sodium hydrogen carbonate solution, followed by extraction with chloroform. The solvent of the organic layer was evaporated under reduced pressure. To the obtained residue were added 300 μL of methanol and 100 μL of a 4 M hydrogen chloride-ethyl acetate solution, followed by stirring at room temperature overnight. The solvent was evaporated under reduced pressure, and to the obtained residue were added 8.2 mg of 7-methyl-4-oxo-1-(tetrahydro-2H-pyran-4-yl)-4, 5-dihydro-1H-pyrazolo [4, 3-c]quinoline-8-carboxylic acid, 26.1 μL of DIPEA, and 0.4 mL of DMF. Then, a mixture of 9.5 mg of HATU and 0.1 mL of DMF was added thereto, followed by stirring at room temperature overnight. The reaction liquid was purified by preparative HPLC (methanol/0. 1% aqueous formic acid solution) to obtain 11 mg of 7-methyl-8-{[(3S)-3-methyl-4-{[6-(morpholin-4-yl)pyridin-2-yl]methyl}piperazin-1-yl]carbonyl}-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one.

[0214] In the same manner as in the methods of Examples 1 to 10, the compounds of Examples 11 to 677 shown in Tables below were prepared. The structures of the Example compounds are shown in Tables 35 to 104, and the preparation methods and the physicochemical data of the Example compounds are shown in Tables 105 to 142.

[0215] In addition, the structures of other compounds of the compounds of the formula (I) are shown in Tables 143 to 146. These can be easily prepared by any of the preparation methods above, the methods described in Examples, the methods apparent to those skilled in the art, or modified methods thereof.

[Table 3]

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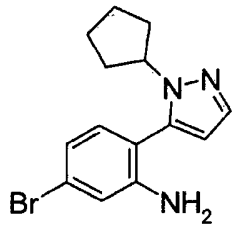
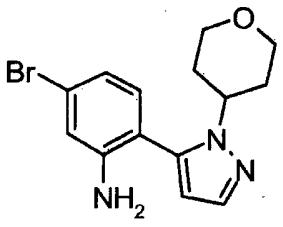
1	
1-1	

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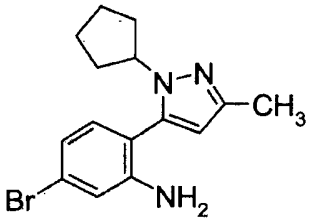
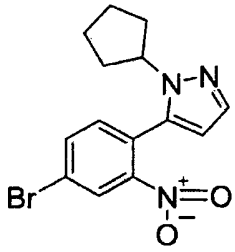
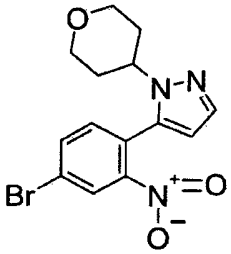
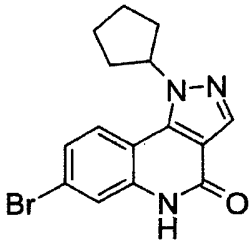
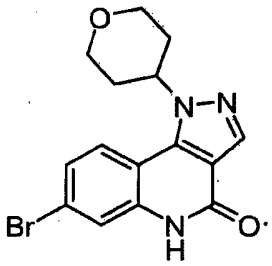
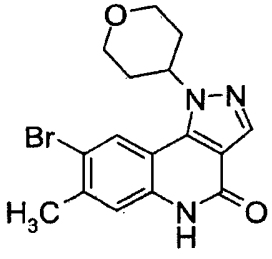
1-2	
2	
2-1	
3	
3-1	
3-2	

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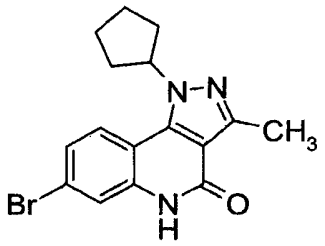
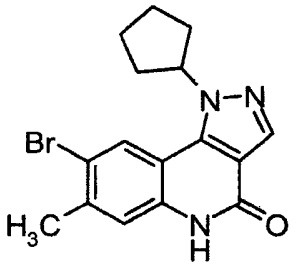
3-3	
3-4	

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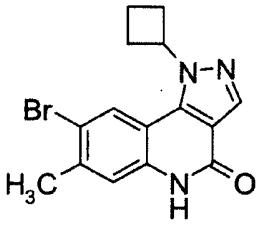
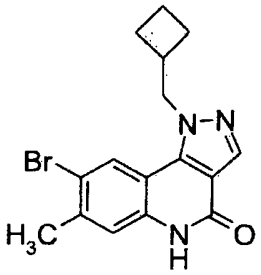
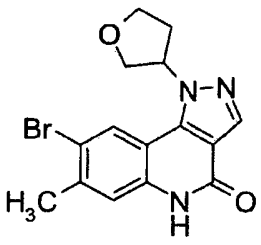
3-5	
3-6	
3-7	

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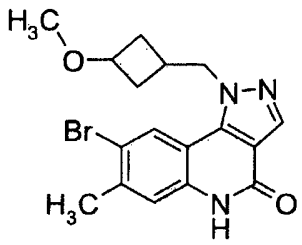
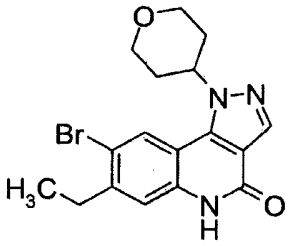
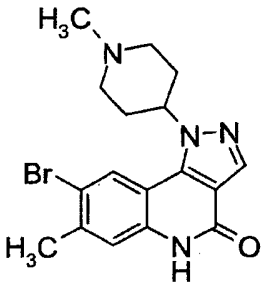
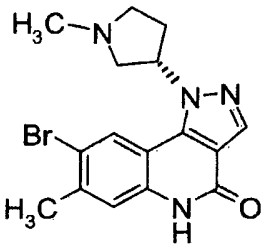
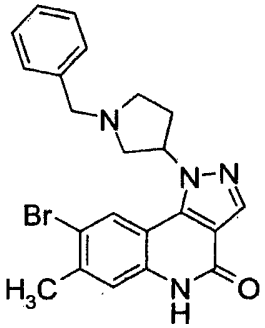
3-8	
3-9	
3-10	
3-11	Chiral 
3-12	

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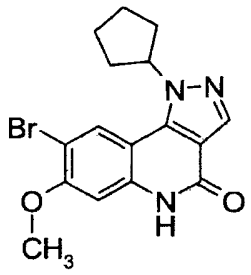
3-13	

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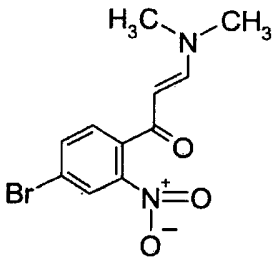
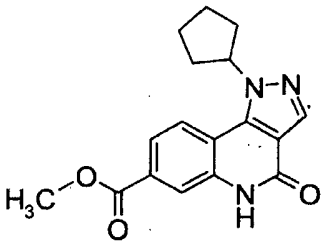
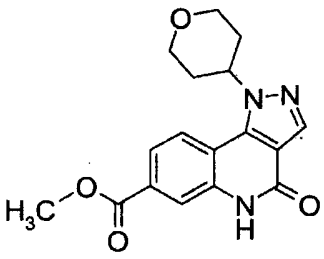
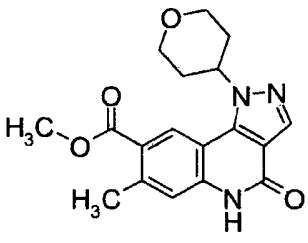
4	
5	
5-1	
5-2	

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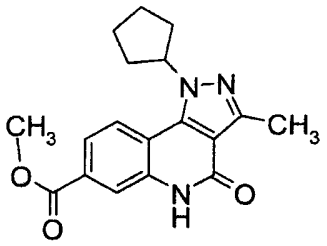
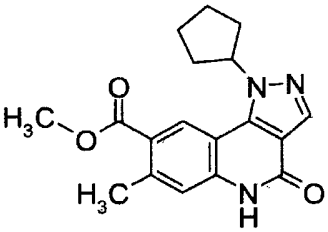
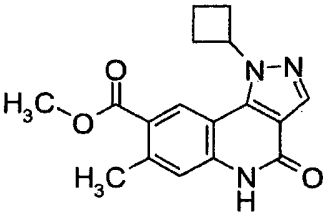
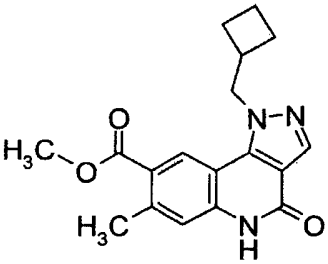
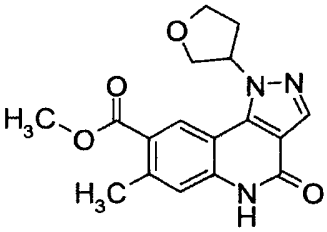
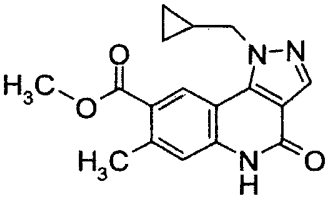
5-3	
5-4	
5-5	
5-6	
5-7	
5-8	

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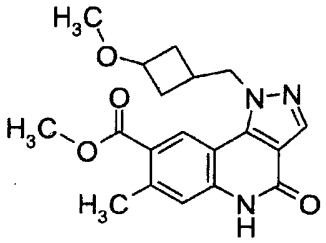
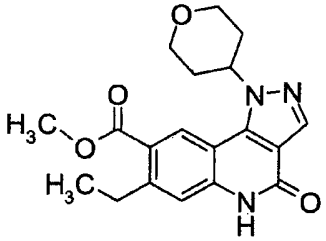
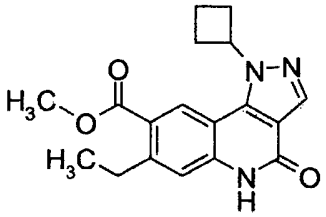
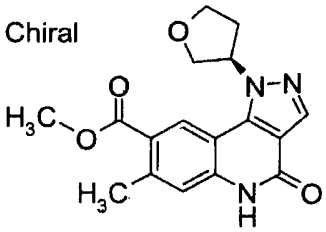
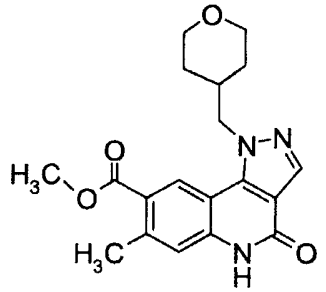
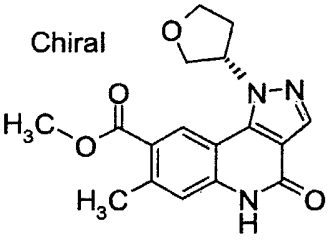
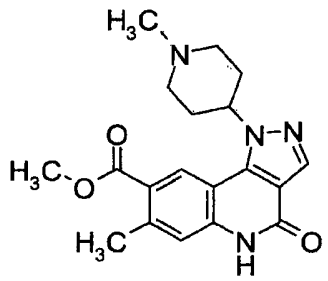
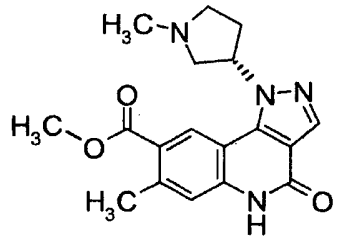
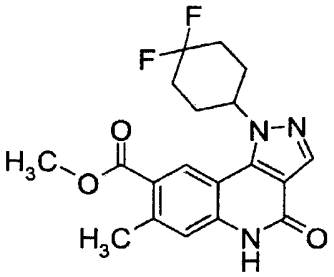
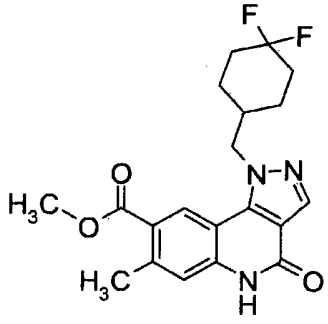
5-9	
5-10	
5-11	
5-12	
5-13	
5-14	

(continued)

Pr	Structure
5-15	
5-16	Chiral 
5-17	

[Table 7]

Pr	Structure
5-18	

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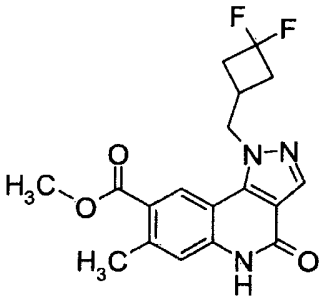
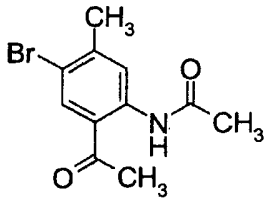
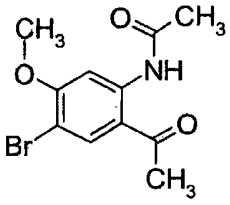
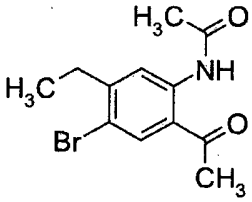
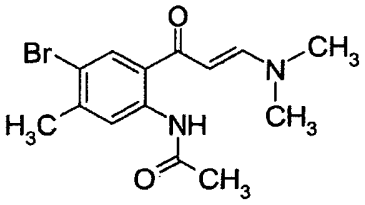
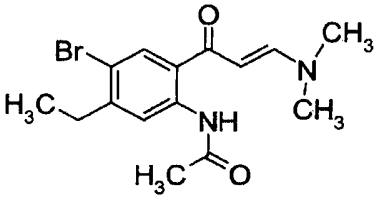
Pr	Structure
5-19	
6	
6-1	
6-2	
7	
7-1	

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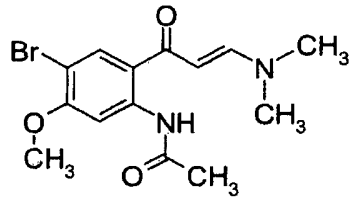
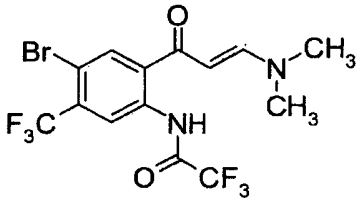
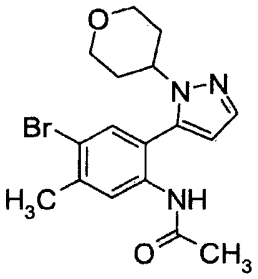
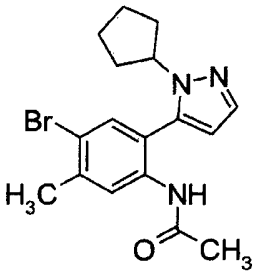
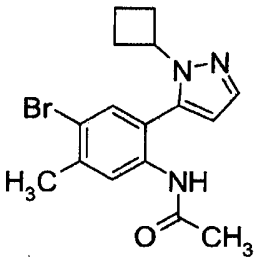
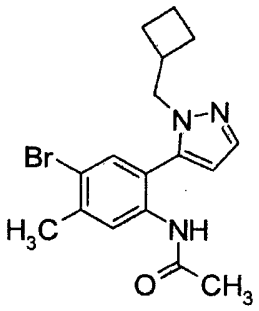
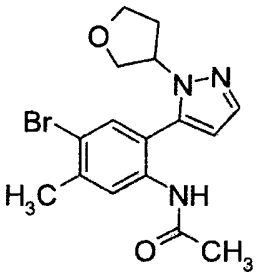
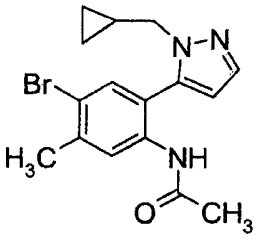
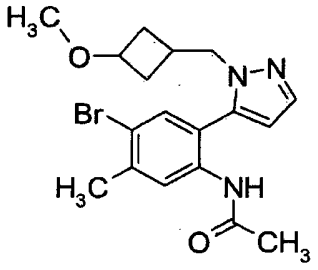
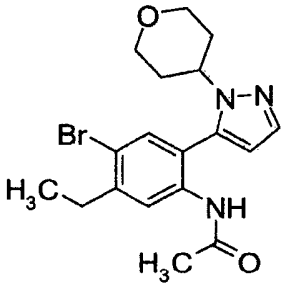
Pr	Structure
7-2	
7-3	
8	

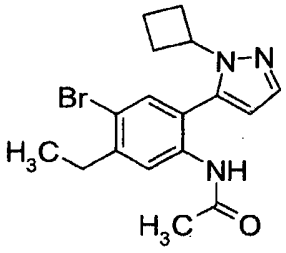
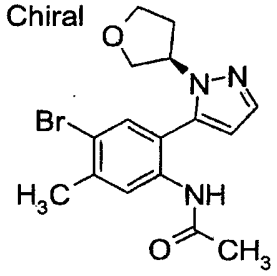
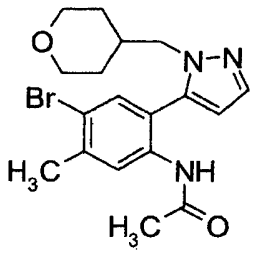
[Table 8]

Pr	Structure
8-1	
8-2	

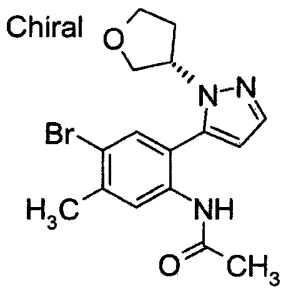
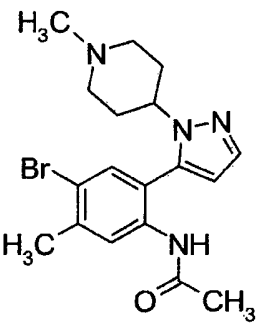
(continued)

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

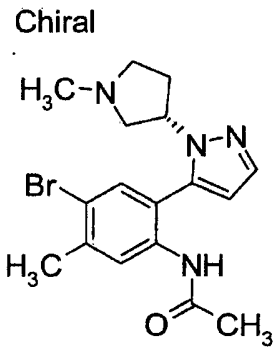
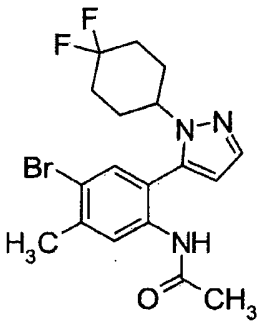
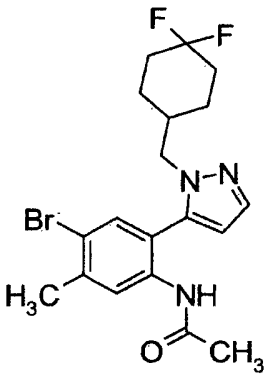
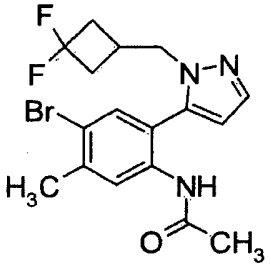
(continued)

Pr	Structure
8-8	
8-9	
8-10	

[Table 9]

Pr	Structure
8-11	
8-12	

(continued)

Pr	Structure
8-13	
8-14	
8-15	
8-16	

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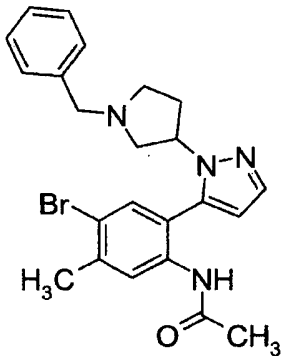
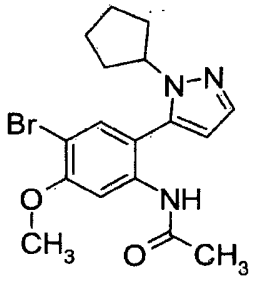
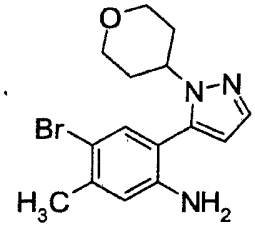
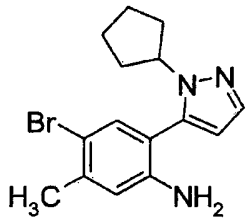
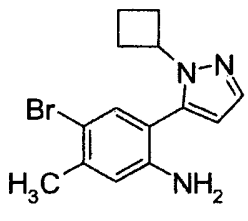
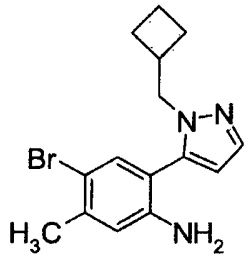
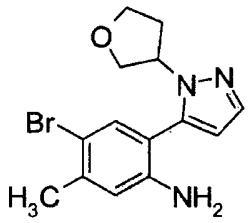
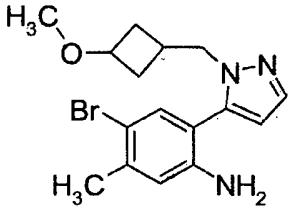
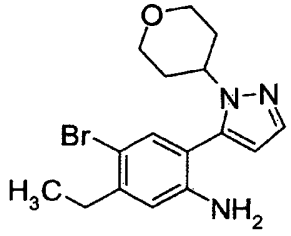
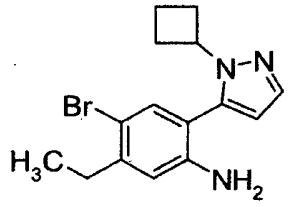
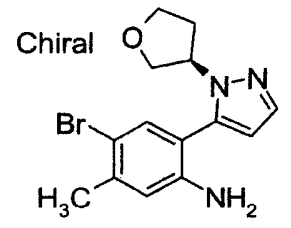
Pr	Structure
8-17	
8-18	

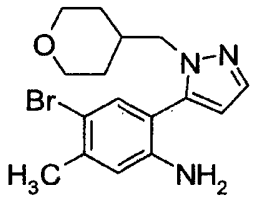
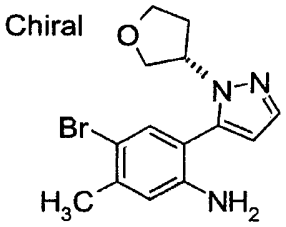
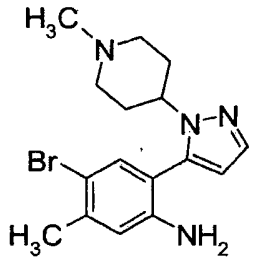
[Table 10]

Pr	Structure
9	
9-1	
9-2	

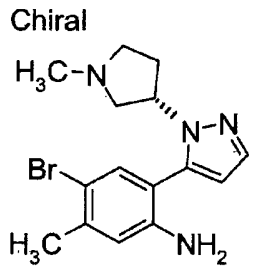
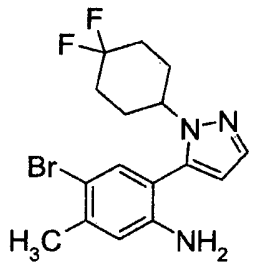
(continued)

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

(continued)

Pr	Structure
9-8	
9-10	
9-11	

[Table 11]

Pr	Structure
9-12	
9-13	

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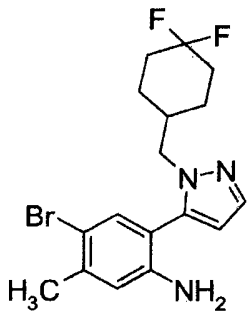
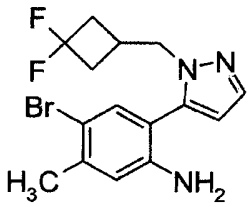
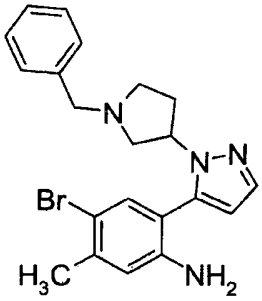
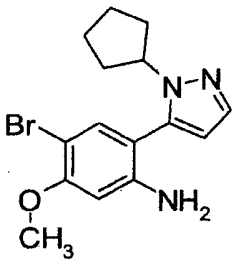
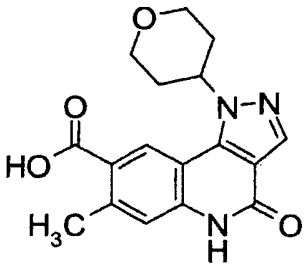
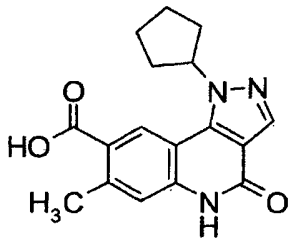
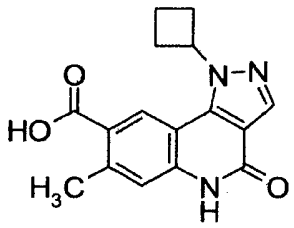
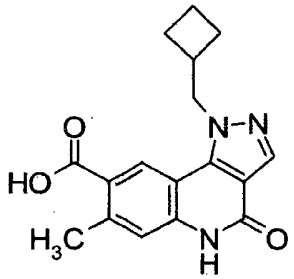
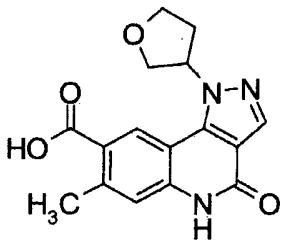
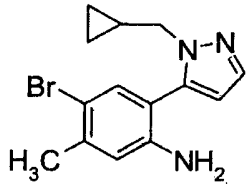
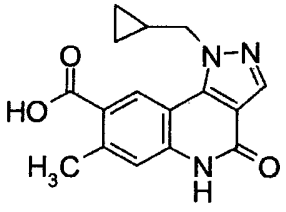
Pr	Structure
9-14	
9-15	
9-16	
9-17	
10	

(continued)

Pr	Structure
10-1	
10-2	
10-3	

[Table 12]

Pr	Structure
10-4	
10-5	
10-6	

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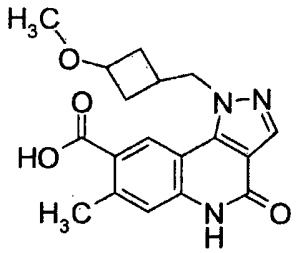
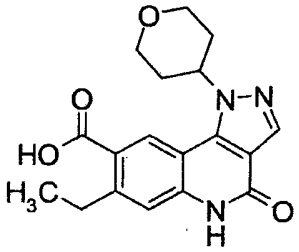
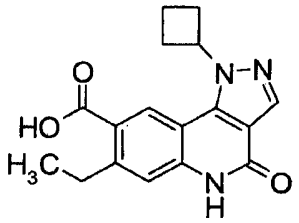
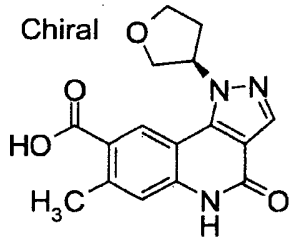
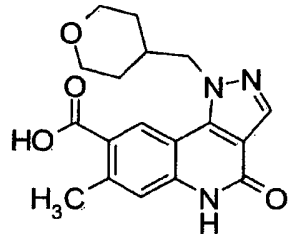
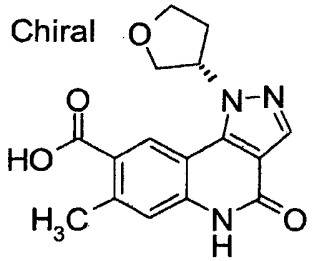
Pr	Structure
10-7	
10-8	
10-9	
10-10	
10-11	
10-12	

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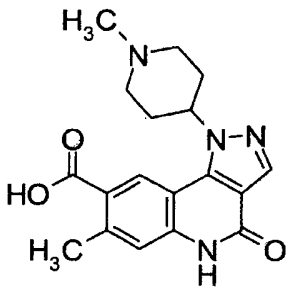
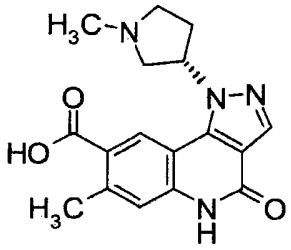
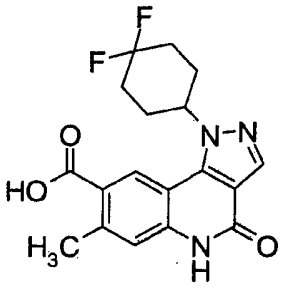
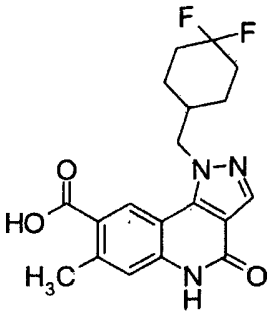
Pr	Structure
10-13	
10-14	Chiral 

[Table 13]

Pr	Structure
10-15	
10-16	

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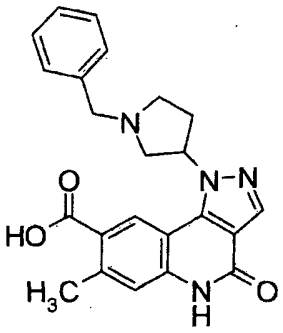
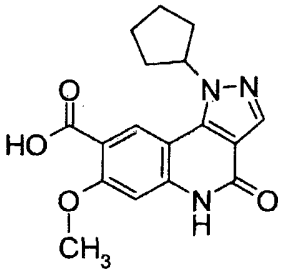
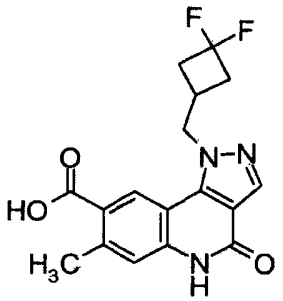
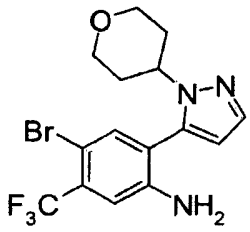
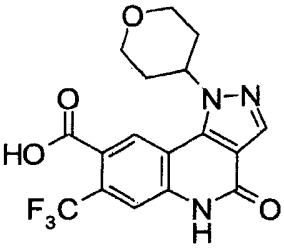
Pr	Structure
10-17	
10-18	
10-19	
10-20	
10-21	

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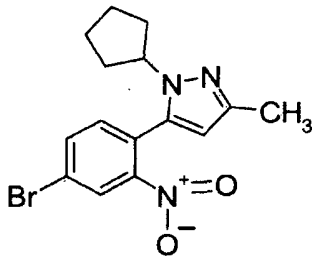
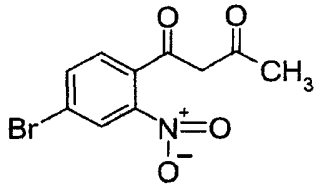
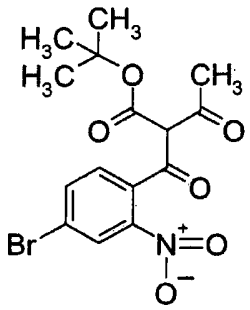
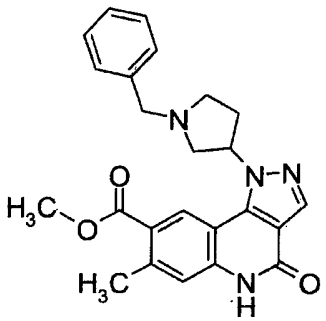
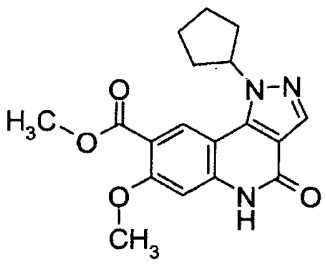
Pr	Structure
11	
12	

[Table 14]

Pr	Structure
13	
14	
14-1	

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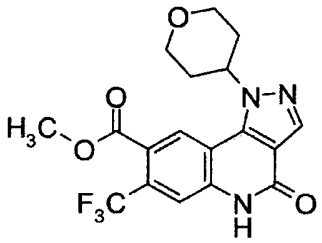
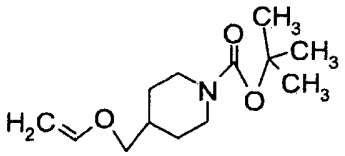
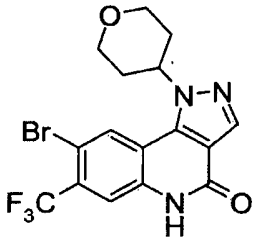
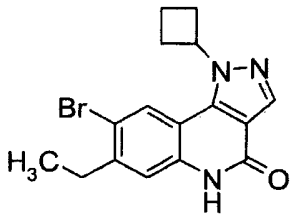
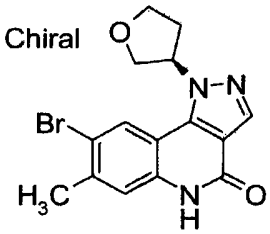
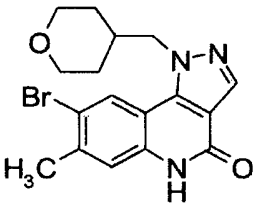
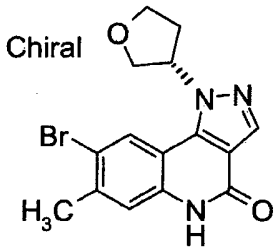
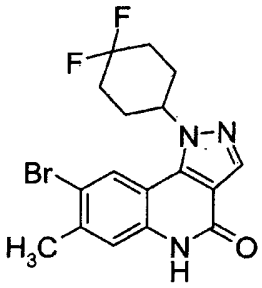
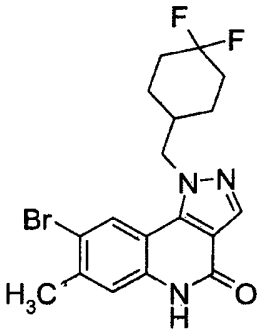
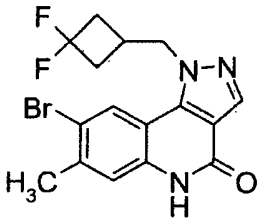
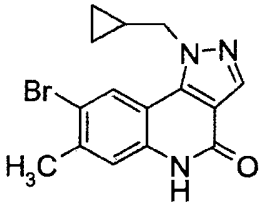
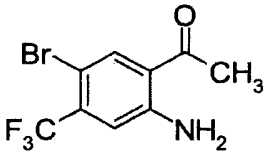
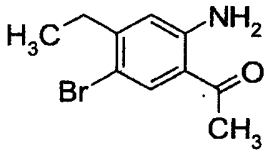
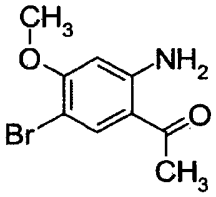
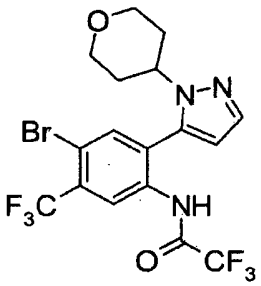
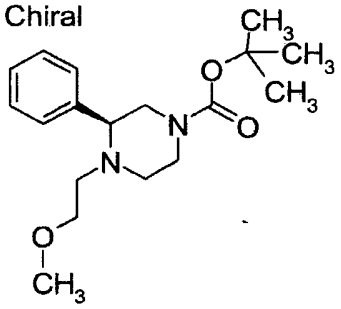
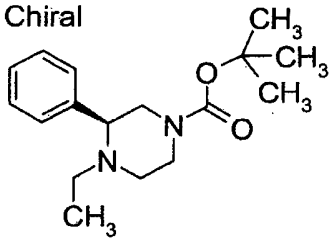
Pr	Structure
14-2	
15	
16	
16-1	
16-2	
16-3	

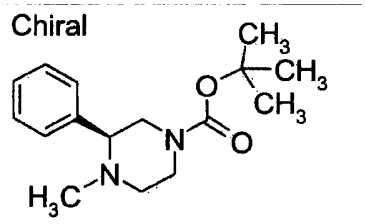
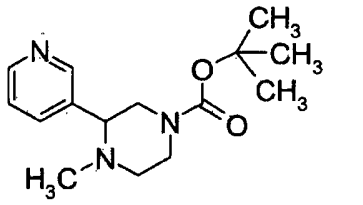
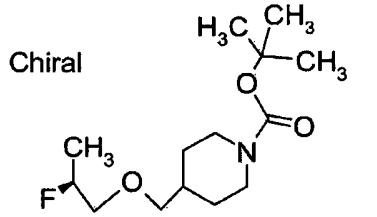
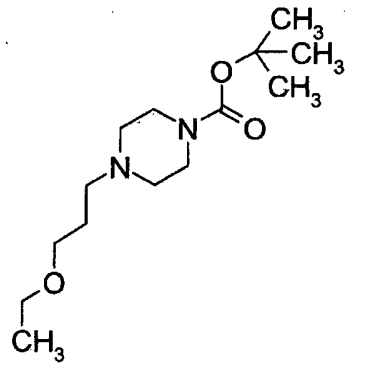
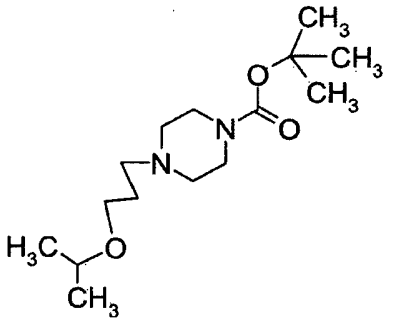
[Table 15]

Pr	Structure
16-4	
16-5	
16-6	
16-7	
16-8	
17	

(continued)

Pr	Structure
17-1	
17-2	
18	
19	
19-1	

[Table 16]

Pr	Structure
19-2	
19-3	
19-4	
19-5	
19-6	

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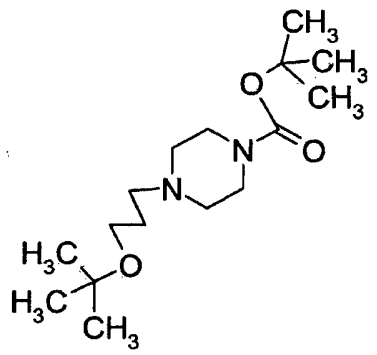
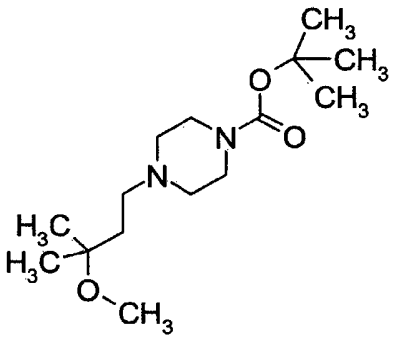
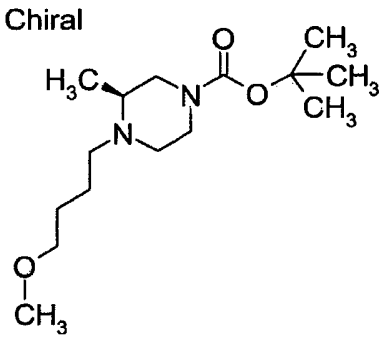
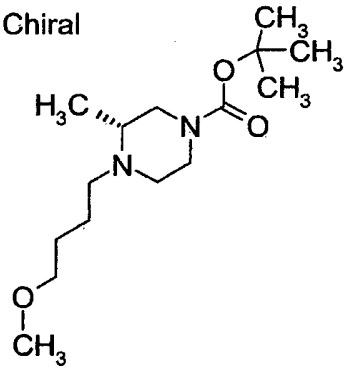
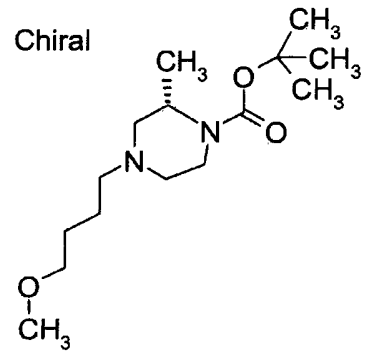
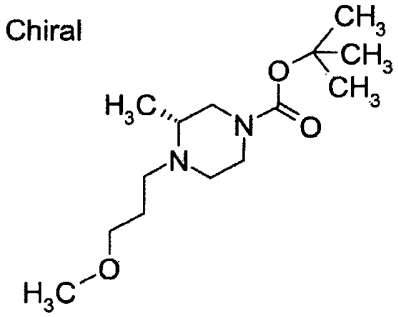
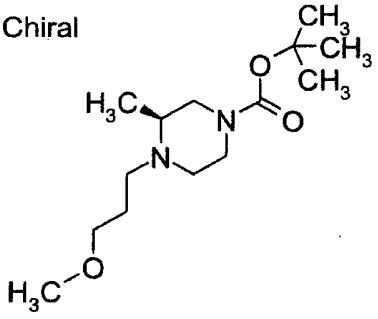
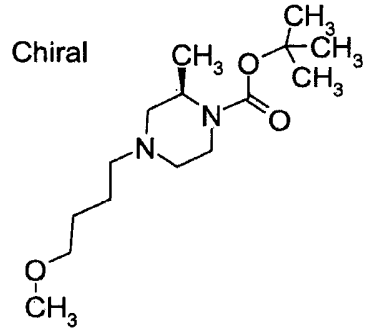
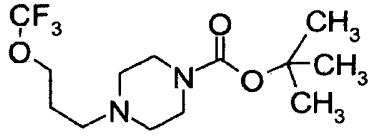
Pr	Structure
19-7	
19-8	
19-9	
19-10	

[Table 17]

Pr	Structure
19-11	
19-12	
19-13	
19-14	
19-15	

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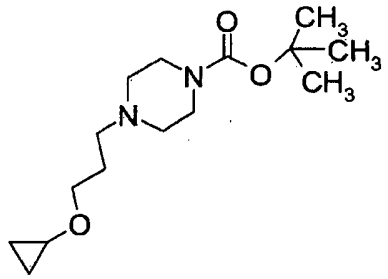
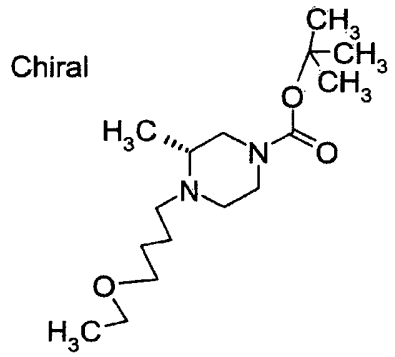
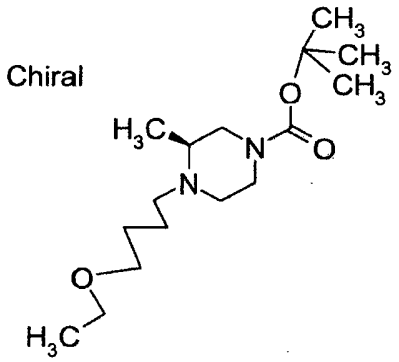
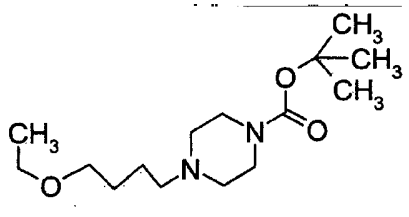
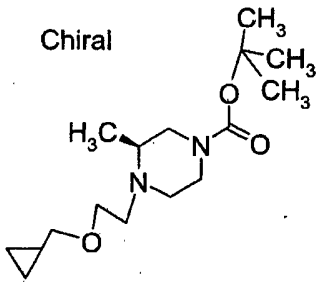
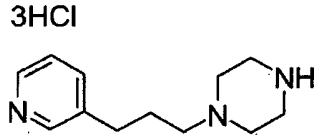
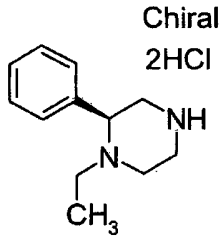
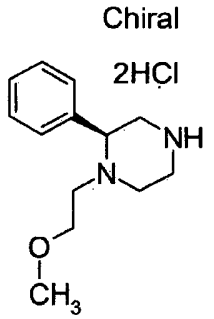
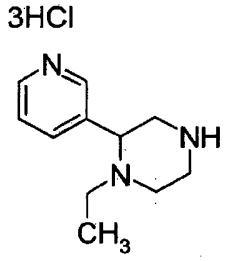
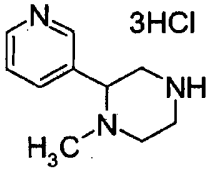
Pr	Structure
19-16	
20	
20-1	

[Table 18]

Pr	Structure
20-2	

(continued)

Pr	Structure
20-3	
21	
21-1	
21-2	
21-3	
21-4	

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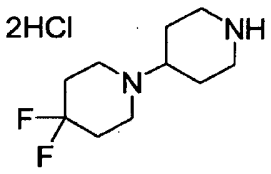
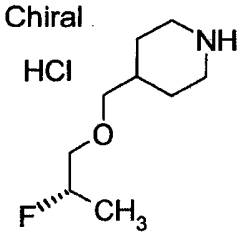
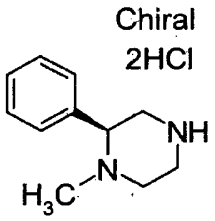
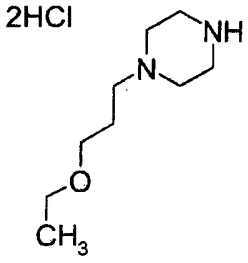
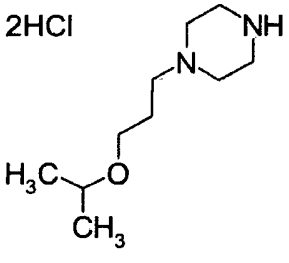
Pr	Structure
21-5	
21-6	
21-7	
21-8	

[Table 19]

Pr	Structure
21-9	
21-10	

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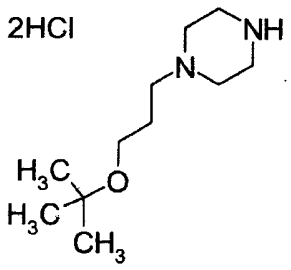
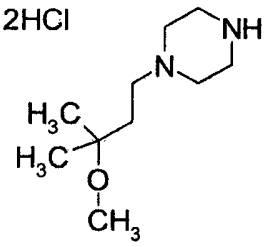
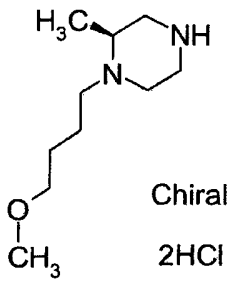
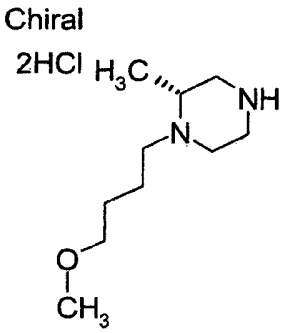
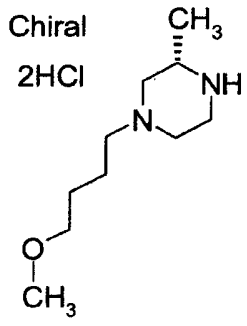
Pr	Structure
21-11	
21-12	
21-13	
21-14	
21-15	

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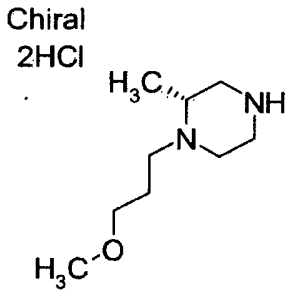
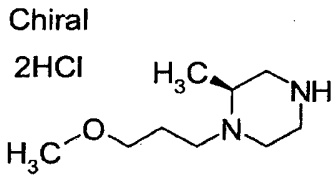
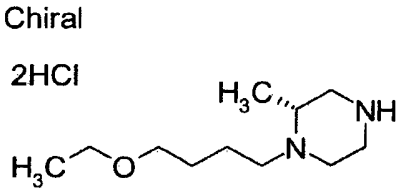
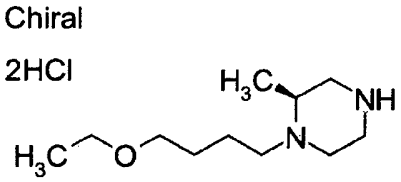
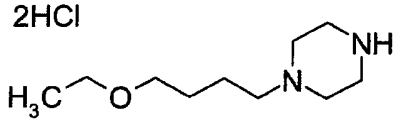
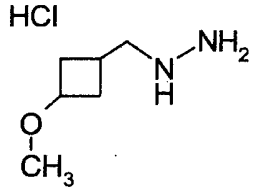
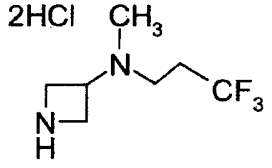
Pr	Structure
21-16	
21-17	
21-18	

[Table 20]

Pr	Structure
21-19	
21-20	
21-21	
21-22	

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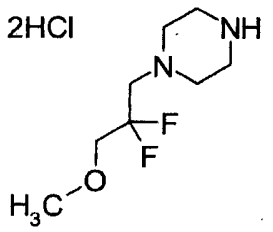
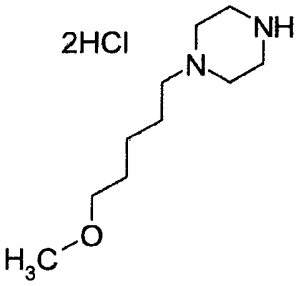
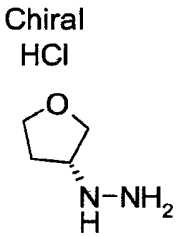
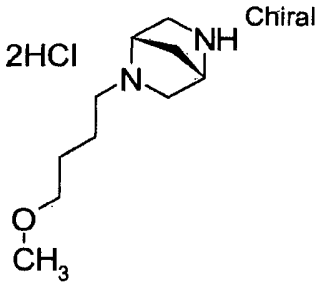
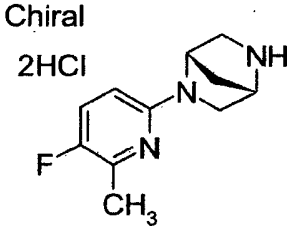
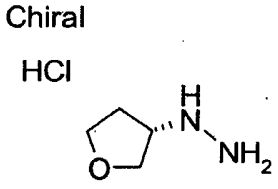
Pr	Structure
21-23	
21-24	
21-25	
21-26	
21-27	
21-28	

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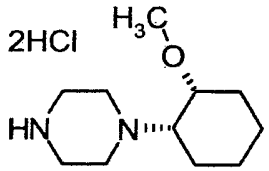
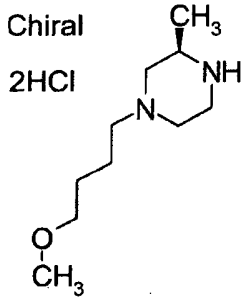
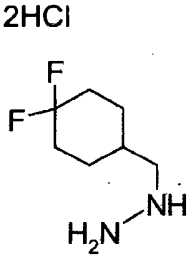
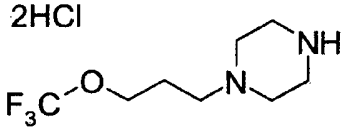
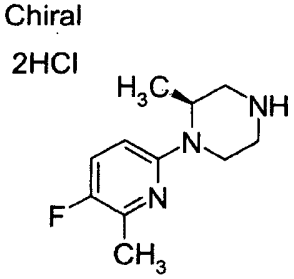
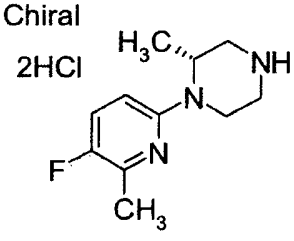
Pr	Structure
21-29	

[Table 21]

Pr	Structure
21-30	
21-31	
21-32	
21-33	
21-34	

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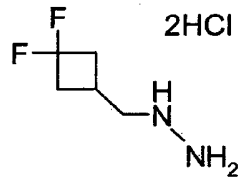
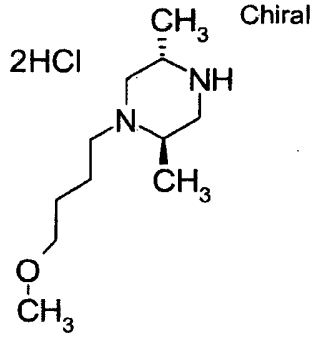
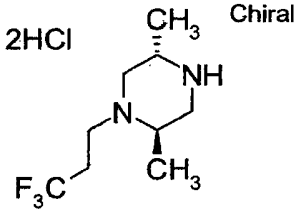
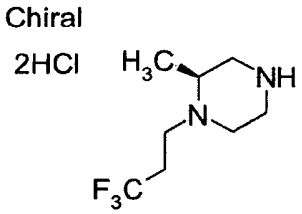
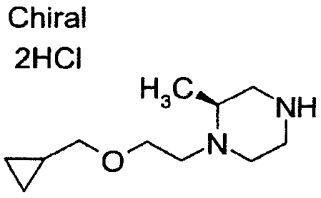
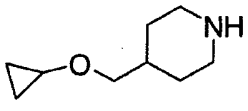
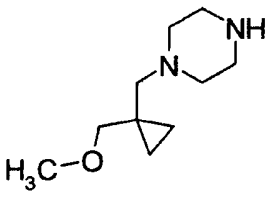
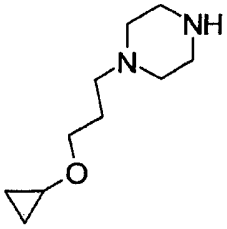
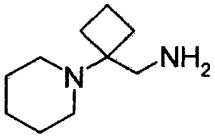
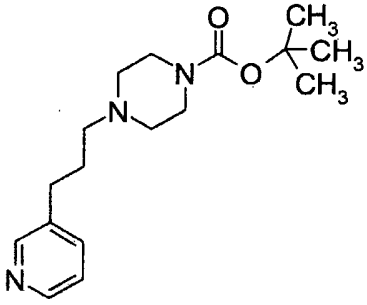
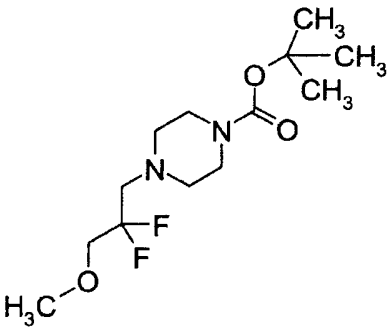
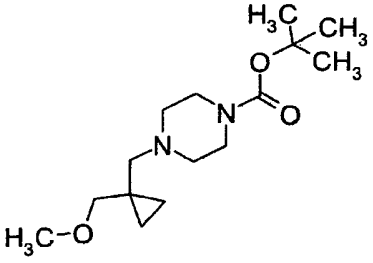
Pr	Structure
21-35	
21-36	
21-37	
21-38	
21-39	

[Table 22]

Pr	Structure
22	

(continued)

Pr	Structure
22-1	
22-2	
23	
24	
24-1	
24-2	

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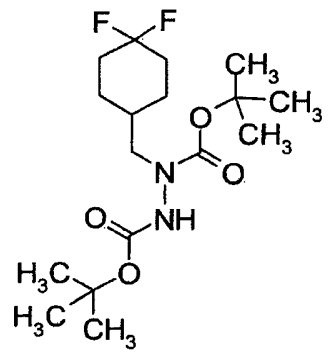
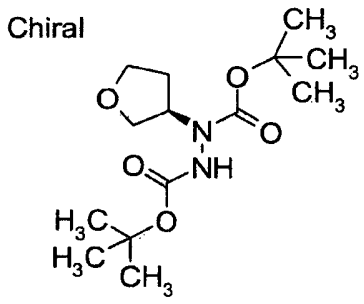
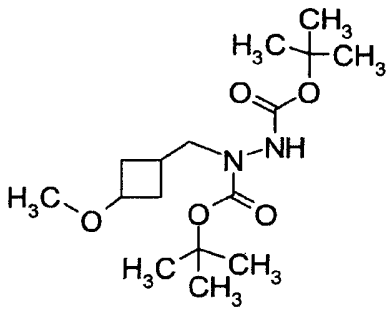
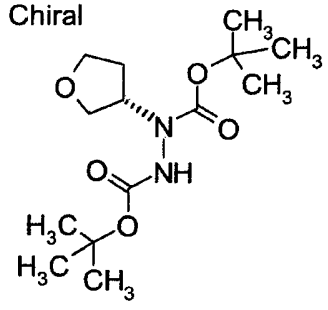
Pr	Structure
25	
25-1	
25-2	

[Table 23]

Pr	Structure
25-3	

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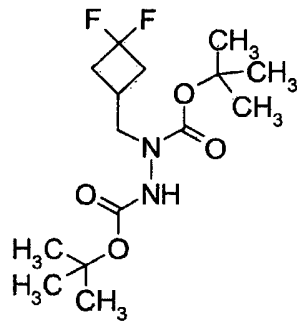
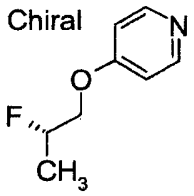
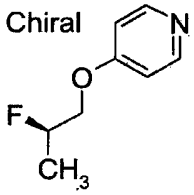
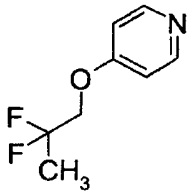
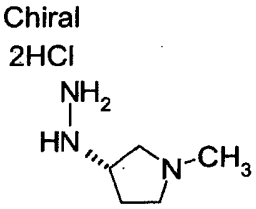
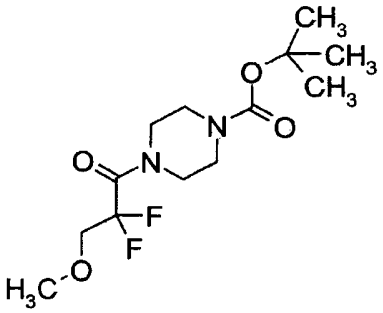
Pr	Structure
25-4	
26	
26-1	
26-2	
27	
28	

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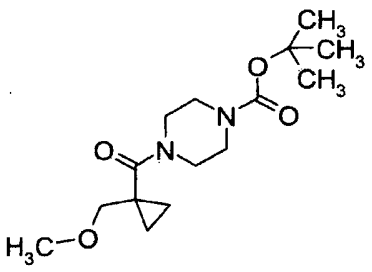
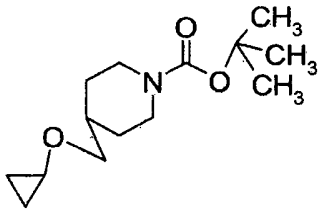
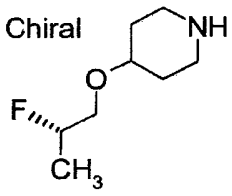
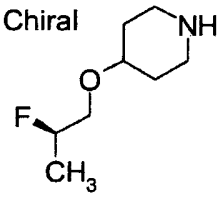
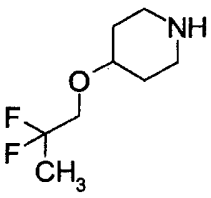
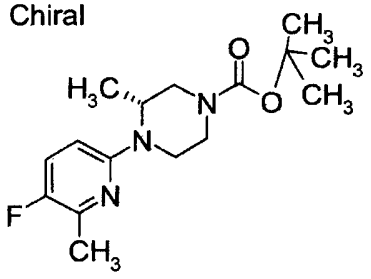
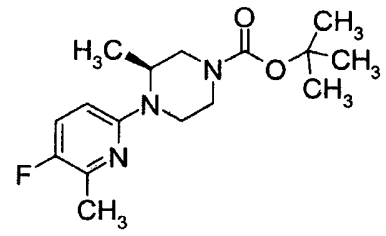
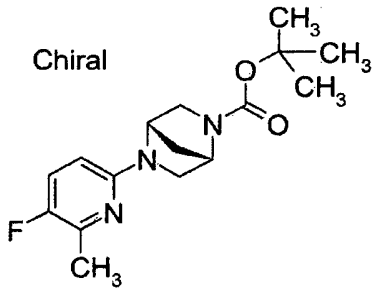
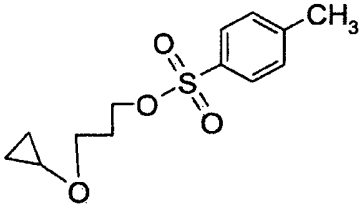
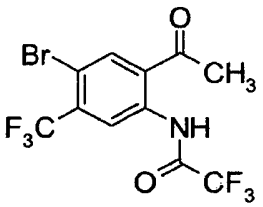
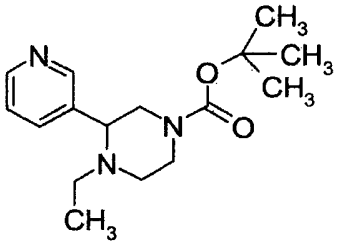
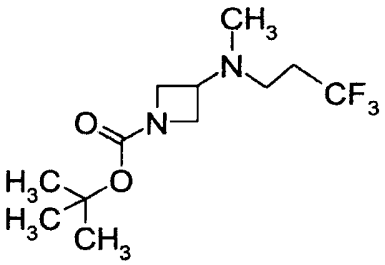
Pr	Structure
28-1	
29	
30	

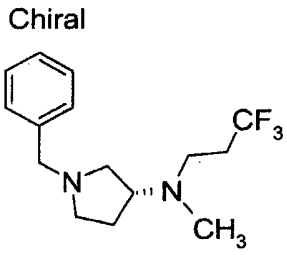
[Table 24]

Pr	Structure
30-1	
30-2	
31	

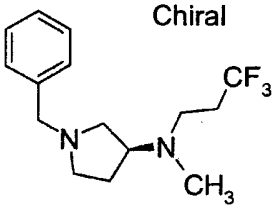
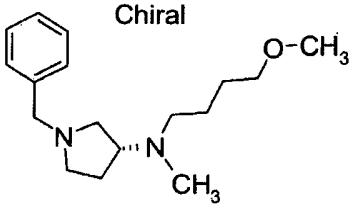
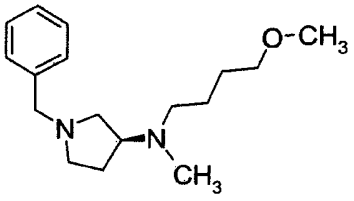
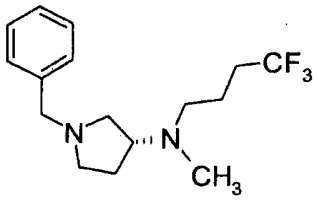
(continued)

Pr	Structure
31-1	Chiral 
31-2	Chiral 
32	
33	
34-1	
34-2	

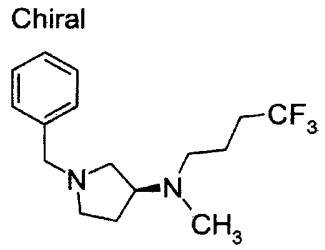
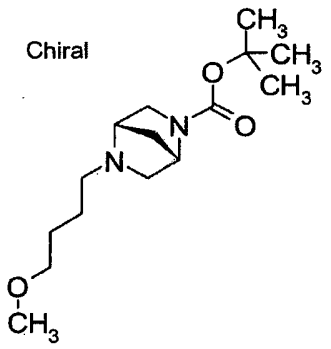
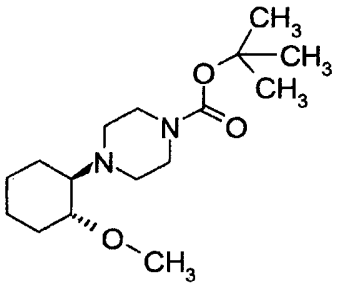
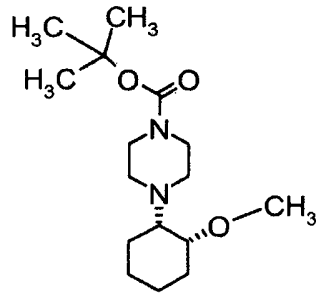
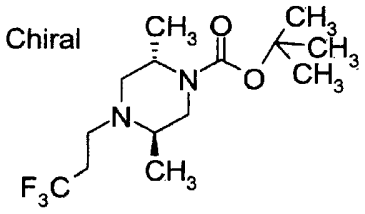
(continued)

Pr	Structure
34-3	

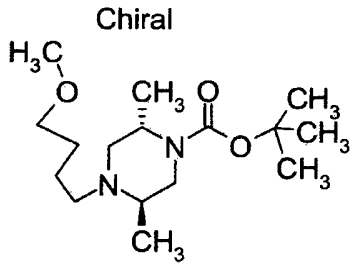
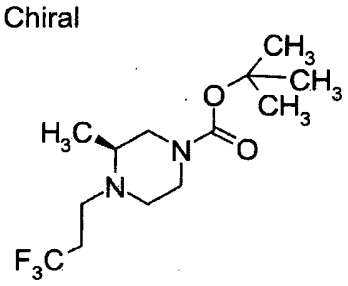
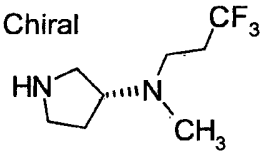
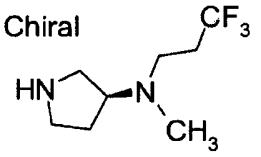
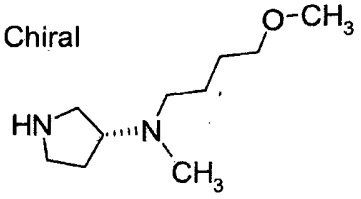
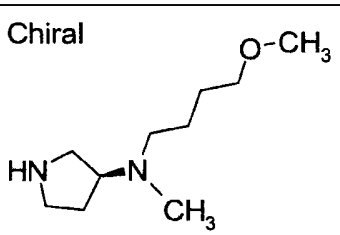
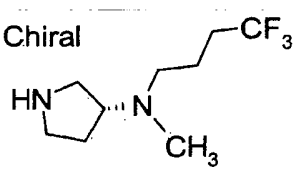
[Table 25]

Pr	Structure
34-4	
34-5	
34-6	
34-7	

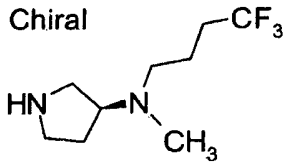
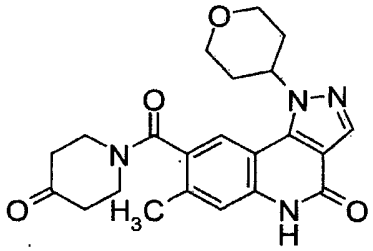
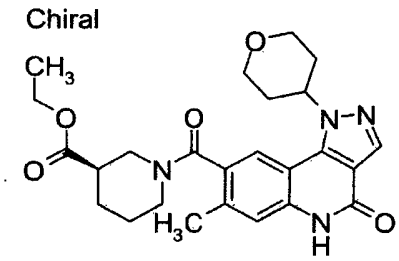
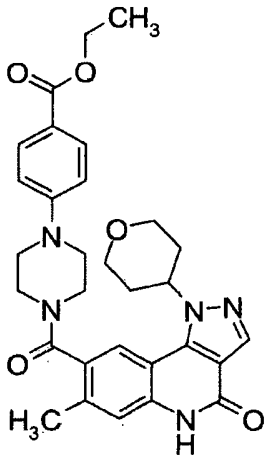
(continued)

Pr	Structure
34-8	
34-9	
34-10	
34-11	
34-12	

[Table 26]

Pr	Structure
34-13	
34-14	
35-1	
35-2	
35-3	
35-4	
35-5	

(continued)

Pr	Structure
35-6	
36	
37-1	
37-2	

[Table 27]

Pr	Data
1	ESI+: 306.0, 308.0
1-1	ESI+: 322.1, 324.1
1-2	ESI+: 320.1, 322.1
2	ESI+: 336.0, 338.0
2-1	ESI+: 352.0, 354.0
3	ESI+: 332.0, 334.0

(continued)

Pr	Data
3-1	ESI+: 348.0, 350.0
3-2	ESI+: 362.2, 364.2
3-3	ESI+: 346.2, 348.2
3-4	ESI+: 346.1, 348.1
3-5	ESI+: 332.0
3-6	ESI+: 346.0, 348.0
3-7	ESI-: 346.1, 348.1
3-8	ESI+: 376.0, 378.0
3-9	ESI+: 376.0, 378.0
3-10	ESI+: 375.2, 377.2
3-11	ESI+: 361.1, 363.1
3-12	ESI+: 437.3, 439.1
3-13	ESI+: 362.0, 364.0
4	ESI+: 299.0, 301.0
5	ESI+: 312.1
5-1	ESI+: 328.1
5-2	ESI+: 342.3
5-3	ESI+: 326.2
5-4	ESI+: 326.3
5-5	ESI+: 312.0
5-6	ESI+: 326.2
5-7	ESI+: 328.0
5-8	APCI/ESI+: 312.1
5-9	ESI+: 356.1
5-10	ESI+: 356.1
5-11	ESI+: 326.1
5-12	ESI+: 328.1

[Table 28]

Pr	Data
5-13	ESI-: 354.3
5-14	ESI+: 328.2
5-15	ESI+: 355.2
5-16	APCI+: 341.1
5-17	ESI+: 376.1
5-18	ESI-: 388.3
5-19	ESI+: 362.1

(continued)

Pr	Data
6	ESI+: 269.9, 271.9
6-1	ESI+: 286.0, 288.0
6-2	ESI+: 2.84.0, 286.0
7	ESI+: 324.9, 326.9
7-1	ESI+: 339.0, 341.1
7-2	ESI+: 341.0, 343.0
7-3	ESI+: 433.1, 435.1
8	ESI-: 376.1, 378.1
8-1	ESI+: 362.2, 364.2
8-2	ESI+: 348.0, 350.0
8-3	ESI+: 362.2, 364.2
8-4	ESI+: 364.0, 366.0
8-5	ESI-: 346.2, 348.1
8-6	ESI+: 392.0, 394.0
8-7	ESI+: 392.0, 394.0
8-8	ESI+: 362.0, 364.1
8-9	ESI+: 364.1, 366.0
8-10	ESI+: 392.0, 394.0
8-11	ESI+: 364.1, 366.1
8-12	ESI+: 391.1, 393.1
8-13	ESI+: 377.3, 379.2
8-14	ESI+: 412.0, 414.0
8-15	ESI+: 426.0, 428.0
8-16	ESI+: 398.0, 400.0
8-17	ESI+: 453.2, 455.2
8-18	ESI+: 378.2, 380.2

[Table 29]

Pr	Data
9	ESI+: 336.0, 338.0
9-1	ESI+: 320.1, 322.1
9-2	ESI+: 306.1, 308.1
9-3	ESI+: 320.2, 322.2
9-4	ESI+: 322.0, 324.0
9-5	ESI+: 350.0, 352.0
9-6	ESI+: 350.0, 352.0
9-7	ESI+: 320.0, 322.0

(continued)

Pr	Data
9-8	ESI+: 322.0, 324.0
9-9	ESI+: 350.1, 352.0
9-10	ESI+: 322.1, 324.1
9-11	ESI+: 349.1, 351.1
9-12	ESI+: 335.2, 337.2
9-13	ESI+: 370.1, 372.0
9-14	ESI+: 384.1, 386.1
9-15	ESI+: 356.1, 358.1
9-16	ESI+: 411.2, 413.1
9-17	ESI+: 336.1, 338.1
10	ESI+: 328.2.
10-1	ESI+: 312.2
10-2	ESI+: 298.0
10-3	ESI+: 312.2
10-4	ESI+: 314.1
10-5	ESI+: 306.0, 308.0
10-6	ESI-: 296.2
10-7	ESI+: 342.1
10-8	ESI+: 342.1
10-9	ESI-: 310.2
10-10	ESI-: 312.3
10-11	ESI-: 340.3
10-12	ESI-: 312.2
10-13	ESI+: 341.2
10-14	ESI+: 327.1

[Table 30]

Pr	Data
10-15	ESI-: 360.2
10-16	ESI-: 374.2
10-17	ESI+: 403.2
10-18	ESI+: 328.1
10-19	ESI-: 346.2
10-20	ESI+: 390.1, 392.1
10-21	ESI+: 382.2
11	APCI/ESI+: 350.1, 352.1
12	APCI/ESI+: 287.0

(continued)

Pr	Data
13	APCI/ESI-: 384.0, 386.0
14	APCI+:417.2
14-1	ESI+: 342.1
14-2	ESI+: 396.1
15	ESI+$(M+Na)^+$: 264.2
16	ESI+: 416.0, 418.0
16-1	ESI+: 346.0, 348.0
16-2	ESI+: 348.0, 350.0
16-3	ESI+: 376.0, 378.0
16-4	ESI+: 348.0,350.0
16-5	ESI+: 396.0,398.0
16-6	ESI-: 408.2,410.2
16-7	ESI-: 380.0,382.0
16-8	ESI+: 332.1,334.2
17	ESI+: 281.9, 284.0
17-1	ESI+: 242.0, 244.0
17-2	ESI+: 244.1, 246.1
18	ESI+: 485.9, 487.9
19	NMR-CDCl3: 1.46 (9H, s), 2.10-2.18 (2H, m), 2.25-2.33 (2H, m), 2.66-2.76 (2H, m), 3.11-3.20 (2H, m), 3.30-3.46 (3H, m), 7.22-7.43 (5H, m)
19-1	ESI+: 291.2
19-2	ESI+: 277.2
19-3	ESI+: 278.3
19-4	ESI+$(M+Na)^+$: 298.1

[Table 31]

Pr	Data
19-5	ESI+: 273.2
19-6	ESI+: 287.2
19-7	ESI+: 301.3
19-8	ESI+: 287.2
19-9	ESI+: 287.2
19-10	ESI+: 287.3
19-11	ESI+: 287.2
19-12	ESI+: 273.2
19-13	ESI+: 273.2
19-14	ESI+: 287.2
19-15	ESI+: 313.2

(continued)

Pr	Data
19-16	ESI+: 285.2
20	ESI+:301.3
20-1	ESI+:301.1
20-2	ESI+:287.1
20-3	ESI+: 299.2
21	ESI+: 206.1
21-1	ESI+: 191.2
21-2	ESI+: 221.3
21-3	ESI+: 192.2
21-4	ESI+: 178.1
21-5	ESI+: 205.2
21-6	ESI+: 199.1
21-7	ESI+: 176.2
21-8	
21-9	ESI+: 173.1
21-10	ESI+: 187.2
21-11	ESI+: 201.2
21-12	ESI+: 187.2
21-13	ESI+: 187.3
21-14	ESI+: 187.2
21-15	ESI+: 187.2
21-16	APCI+: 173.1

[Table 32]

Pr	Data
21-17	APCI+: 173.0
21-18	ESI+: 201.2
21-19	ESI+: 201.2
21-20	ESI+: 187.2
21-21	ESI+: 131.1
21-22	ESI+: 183.2
21-23	ESI+: 195.1
21-24	ESI+: 187.0
21-25	ESI+: 103.0
21-26	ESI+:185.1
21-27	ESI+: 208.2
21-28	ESI+: 103.0

(continued)

Pr	Data
21-29	ESI+: 199.1
21-30	ESI+: 187.2
21-31	ESI+: 165.2
21-32	ESI+: 213.1
21-33	ESI+: 210.1
21-34	ESI+: 210.1
21-35	ESI+: 137.2
21-36	ESI-: 201.1
21-37	ESI+: 211.1
21-38	ESI+: 197.1
21-39	ESI+: 199.2
22	ESI+: 156.2
22-1	ESI+: 185.2
22-2	ESI+: 185.3
23	ESI+: 169.2
24	ESI+: 306.1
24-1	ESI+: 295.2
24-2	ESI+: 285.2
25	ESI-: 363.2
25-1	ESI+$(M+Na)^+$: 325.1
25-2	ESI+$(M+Na)^+$: 353.1

[Table 33]

Pr	Data
25-3	ESI+$(M+Na)^+$: 325.2
25-4	ESI+$(M+Na)^+$: 359.1
26	ESI+: 156.1
26-1	ESI+: 156.1
26-2	ESI+: 174.1
27	ESI+: 116.0
28	ESI+$(M+Na)^+$: 331.1
28-1	ESI+$(M+Na)^+$: 321.1
29	ESI+$(M+Na)^+$: 278.2
30	ESI+: 162.2
30-1	ESI+: 162.2
30-2	ESI+: 180.1
31	ESI+: 310.2

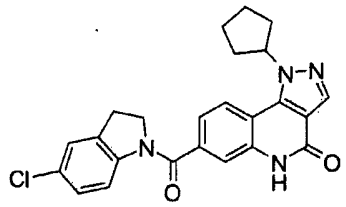
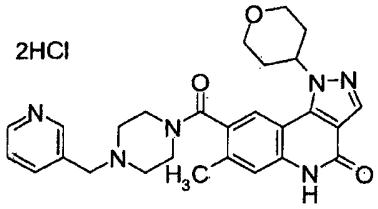
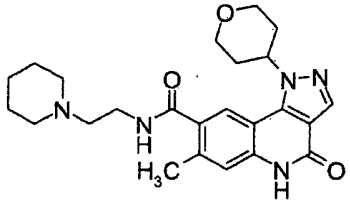
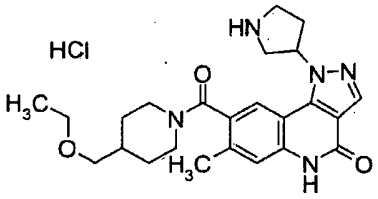
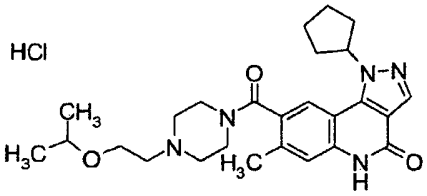
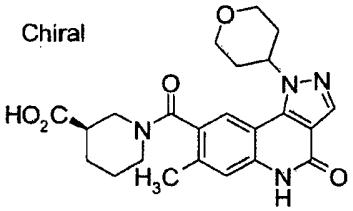
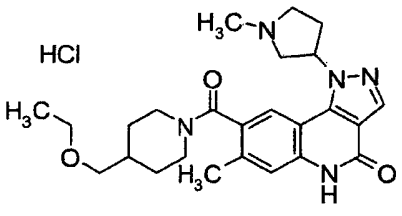
(continued)

Pr	Data
31-1	ESI+: 310.2
31-2	ESI+: 308.2
32	ESI+(M+Na)$^+$: 293.1
33	ESI-: 376.0, 378.0
34-1	ESI+: 292.2
34-2	ESI+: 283.3
34-3	ESI+: 287.2
34-4	ESI+: 287.2
34-5	ESI+: 277.3
34-6	ESI+: 277.3
34-7	ESI+: 301.3
34-8	ESI+: 301.2
34-9	ESI+: 285.2
34-10	ESI+: 299.2
34-11	ESI+: 299.2
34-12	APCI+: 311.2
34-13	ESI+: 301.3
34-14	ESI+: 297.2
35-1	ESI+: 197.1
35-2	ESI+:197.1

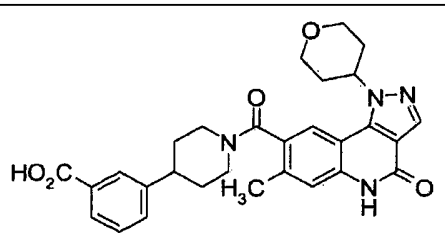
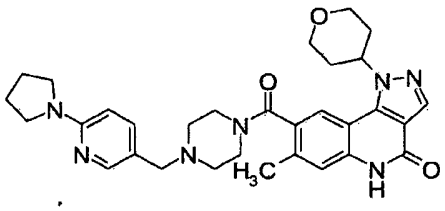
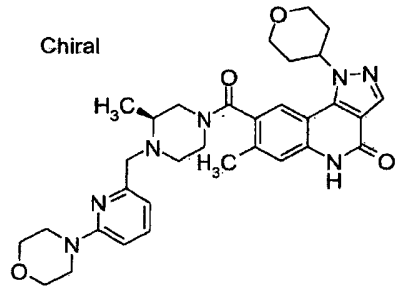
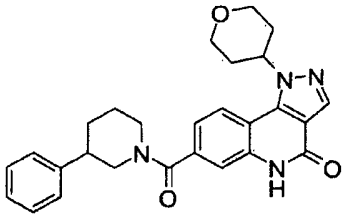
[Table 34]

Pr	Data
35-3	ESI+:187.2
35-4	ESI+:187.2
35-5	ESI+:211.1
35-6	ESI+:211.1
36	ESI+:409.3
37-1	ESI+: 467.1
37-2	ESI+: 544.1

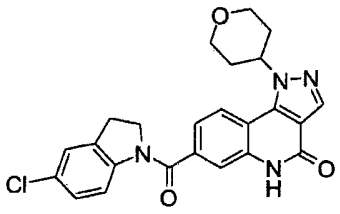
[Table 35]

Ex	Structure
1	
2	
3	
4	
5	
6	
7	

(continued)

Ex	Structure
8	
9	
10	
11	

[Table 36]

Ex	Structure
12	

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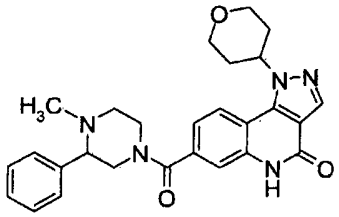
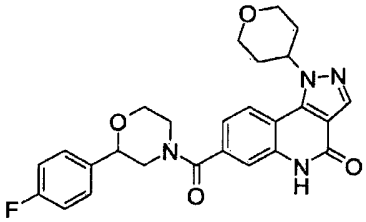
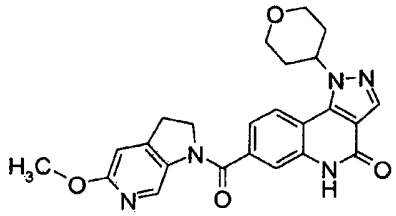
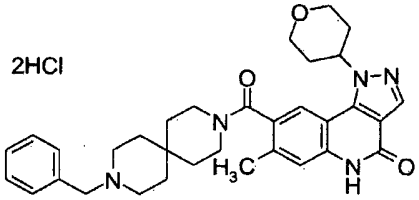
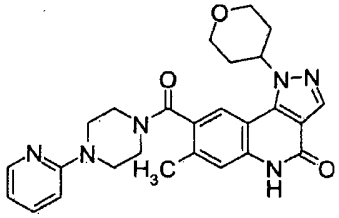
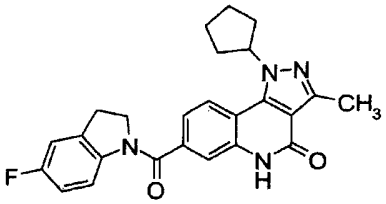
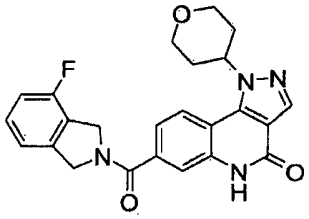
Ex	Structure
13	
14	
15	
16	
17	
18	
19	

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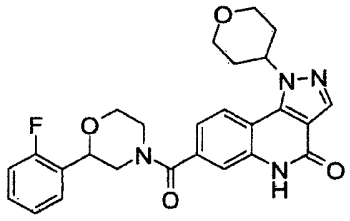
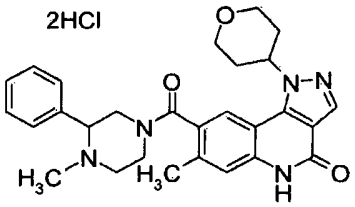
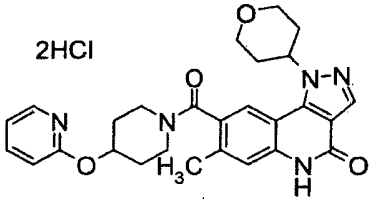
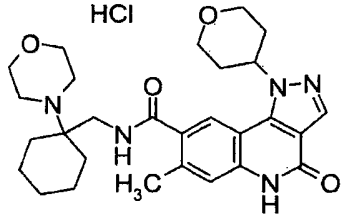
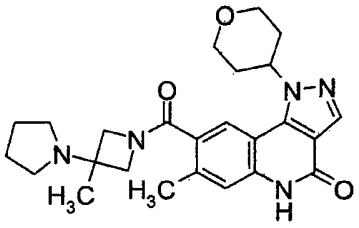
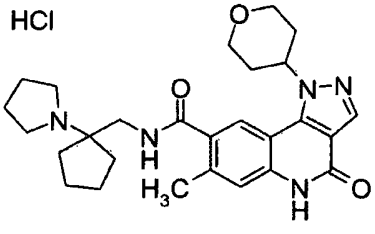
Ex	Structure
20	
21	
22	
23	

[Table 37]

Ex	Structure
24	
25	

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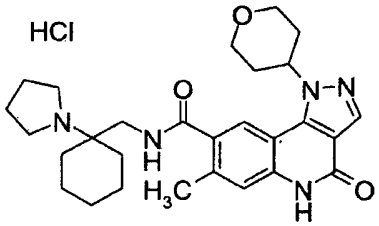
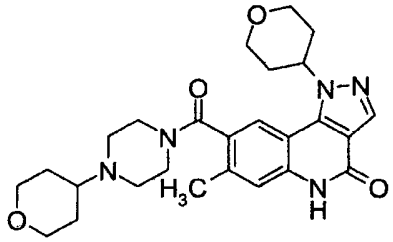
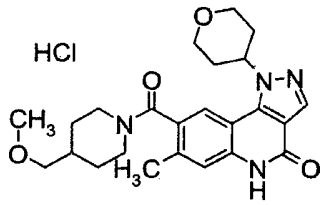
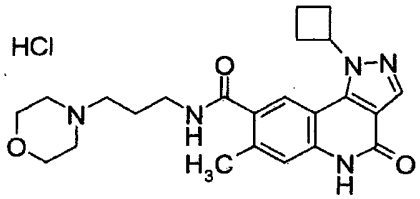
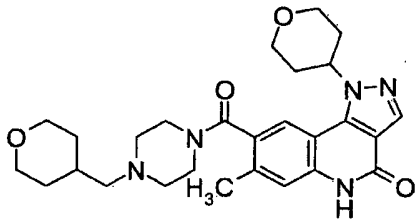
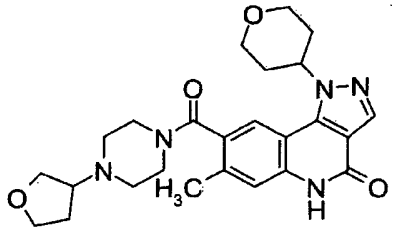
Ex	Structure
26	
27	
28	
29	
30	
31	

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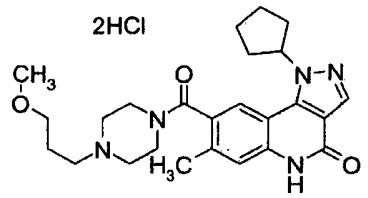
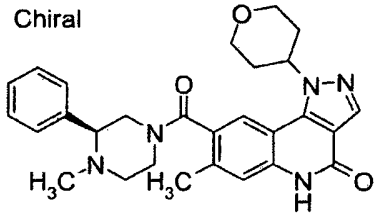
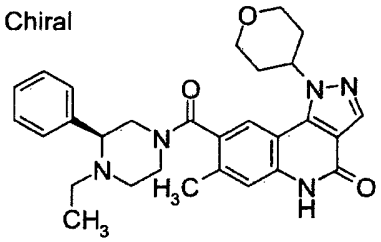
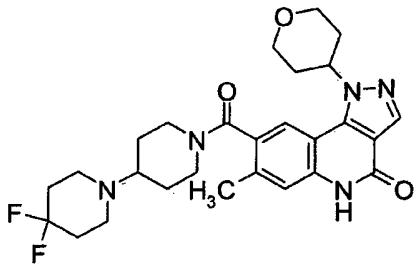
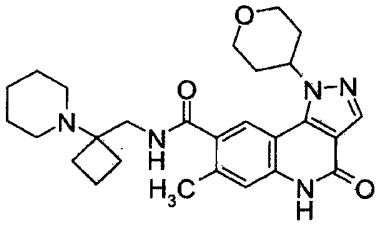
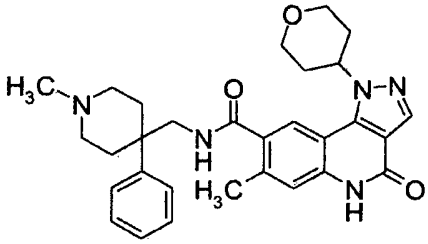
Ex	Structure
32	
33	

[Table 38]

Ex	Structure
34	
35	
36	
37	

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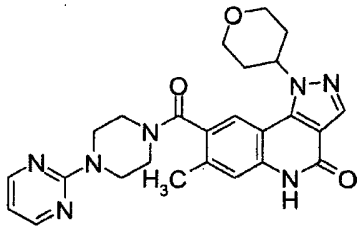
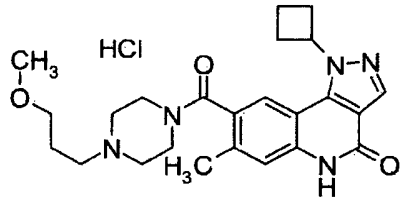
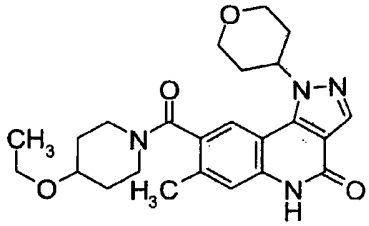
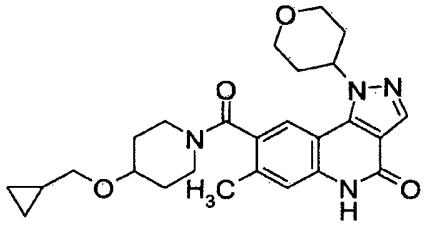
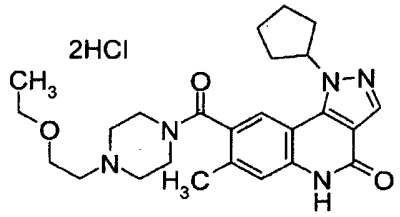
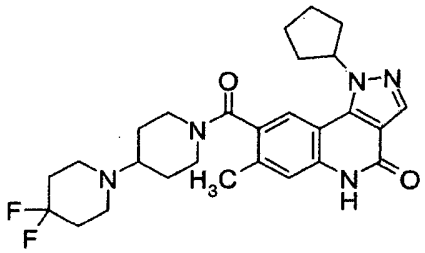
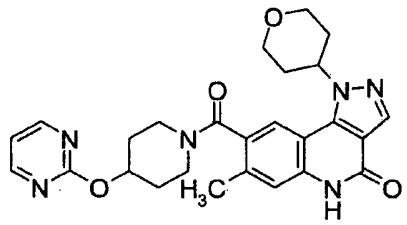
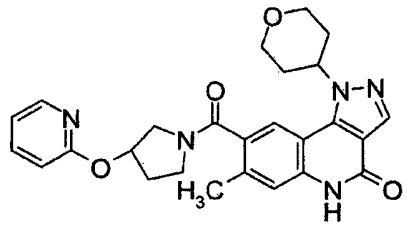
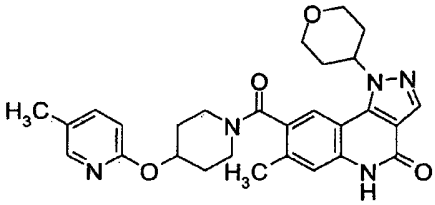
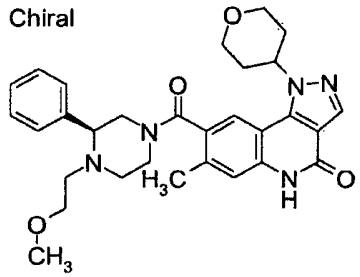
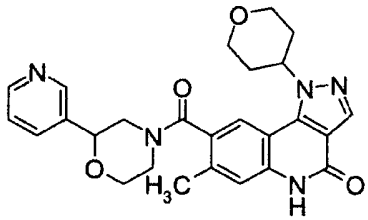
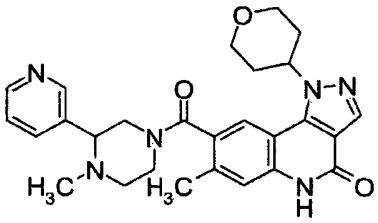
Ex	Structure
38	
39	
40	
41	
42	
43	

[Table 39]

Ex	Structure
44	
45	
46	
47	
48	
49	

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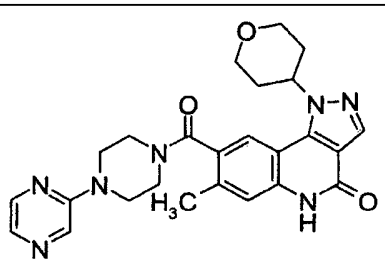
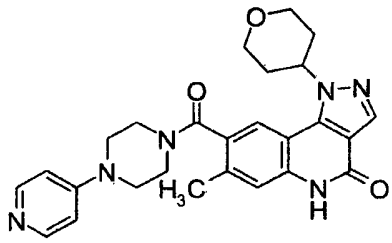
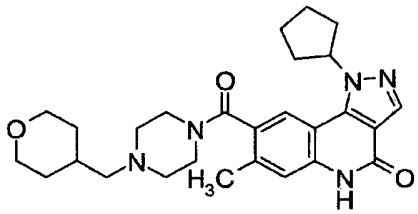
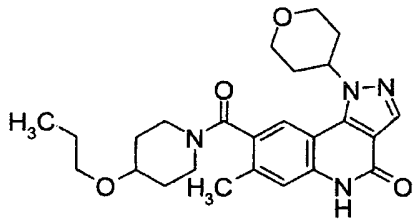
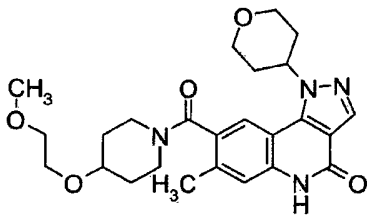
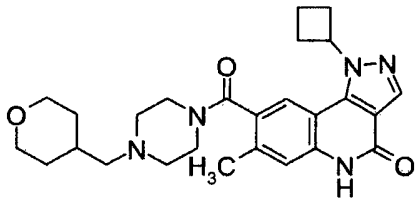
Ex	Structure
50	
51	
52	
53	

[Table 40]

Ex	Structure
54	
55	

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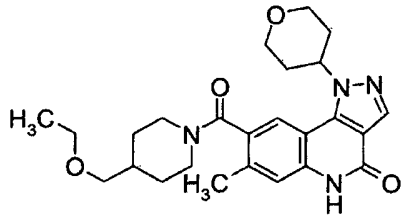
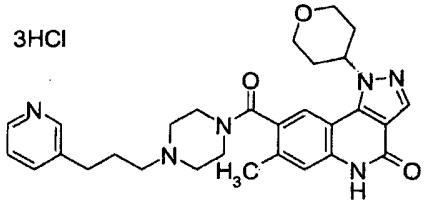
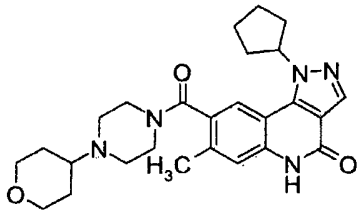
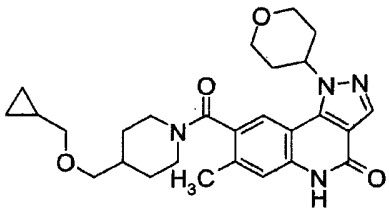
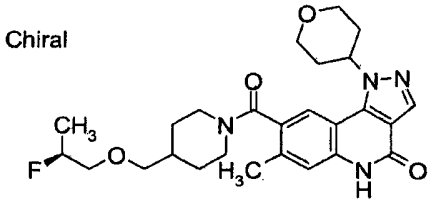
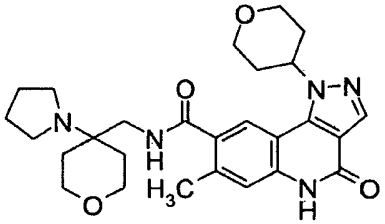
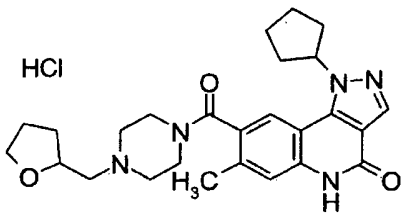
Ex	Structure
56	
57	3HCl 
58	
59	
60	Chiral 
61	
62	HCl 

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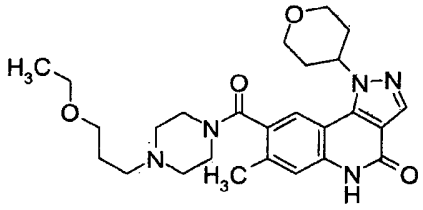
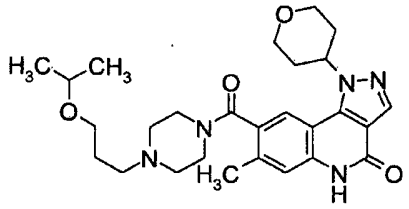
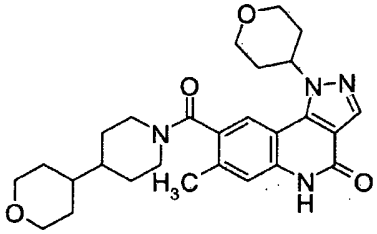
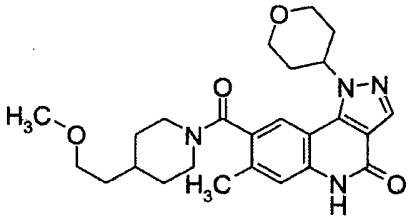
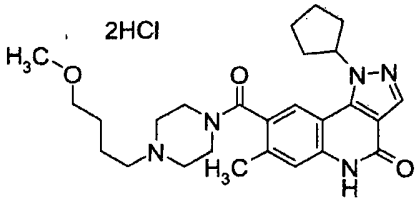
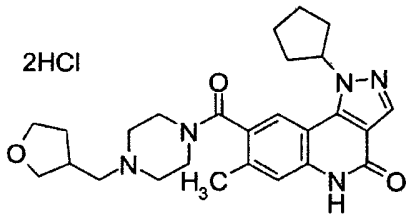
Ex	Structure
63	

[Table 41]

Ex	Structure
64	
65	
66	
67	
68	

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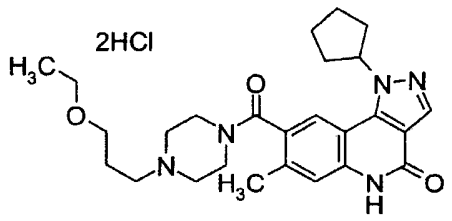
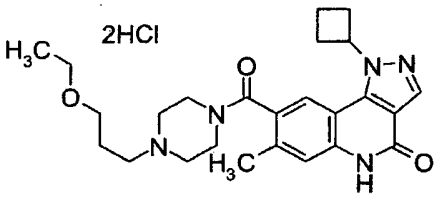
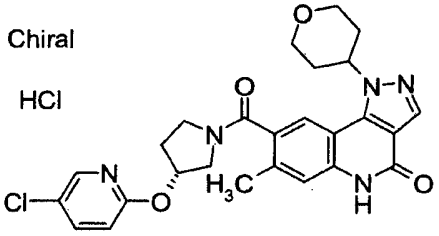
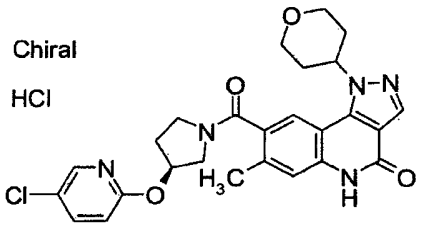
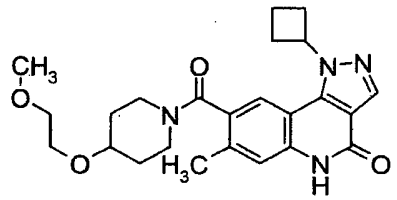
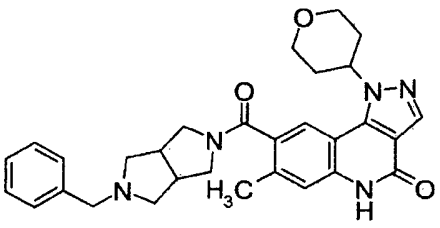
Ex	Structure
69	
70	
71	
72	
73	
74	

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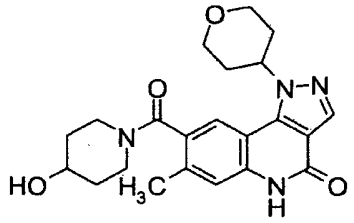
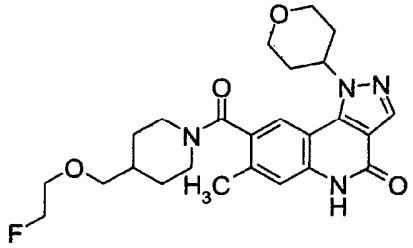
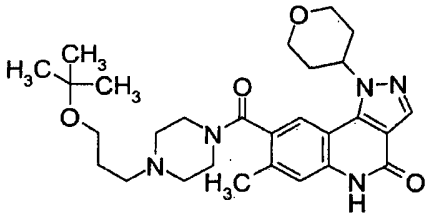
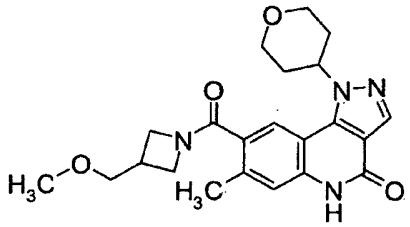
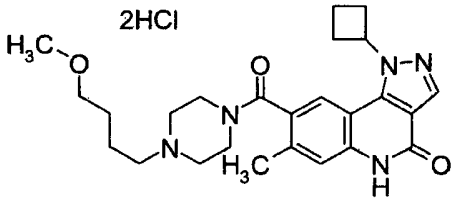
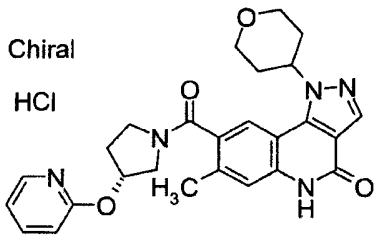
Ex	Structure
75	

[Table 42]

Ex	Structure
76	
77	
78	
79	
80	

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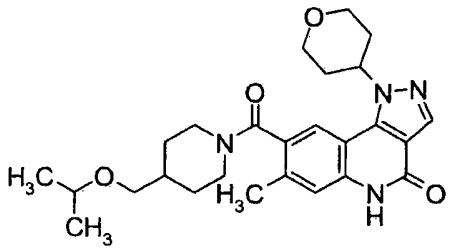
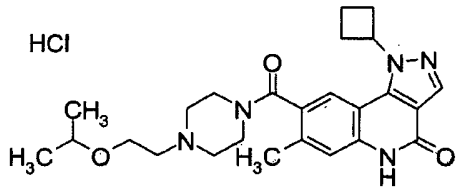
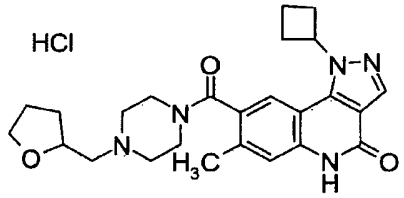
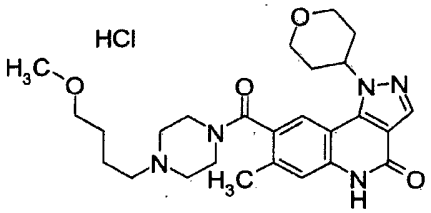
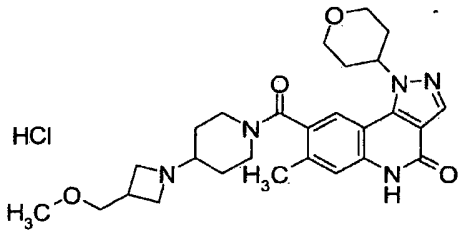
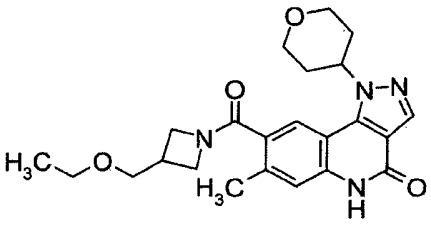
Ex	Structure
81	
82	
83	
84	
85	
86	

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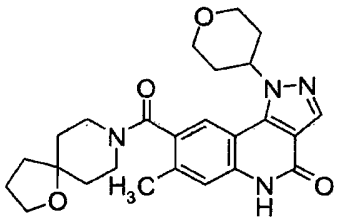
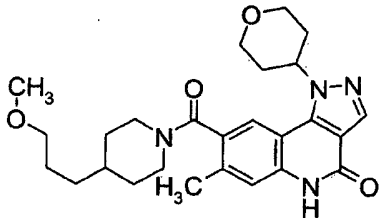
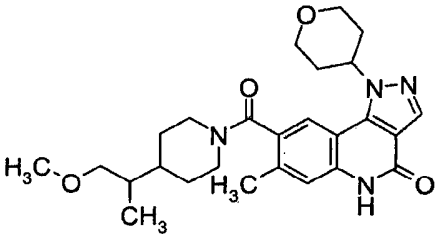
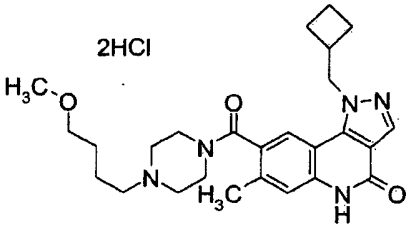
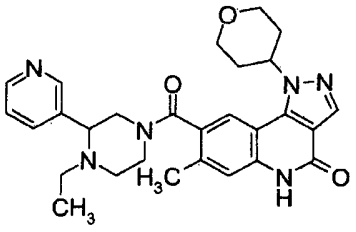
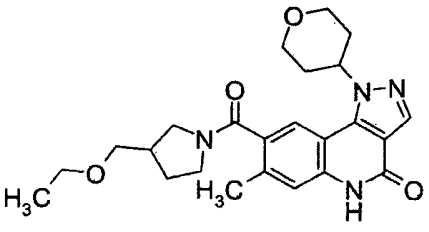
Ex	Structure
87	

[Table 43]

Ex	Structure
88	
89	
90	
91	
92	

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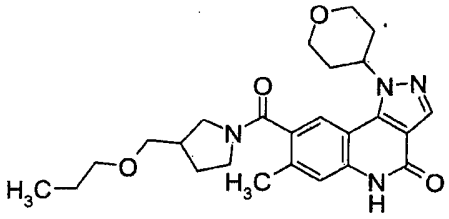
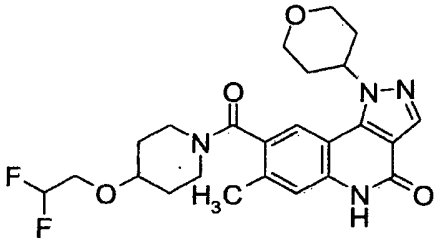
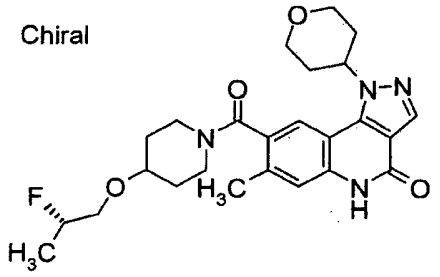
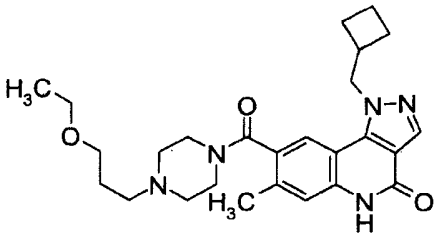
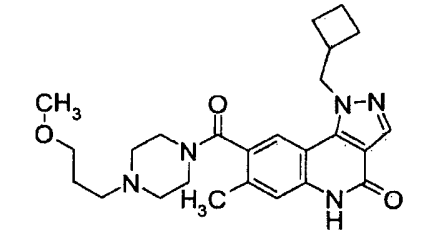
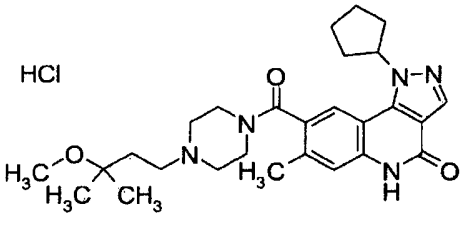
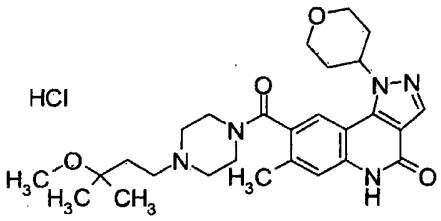
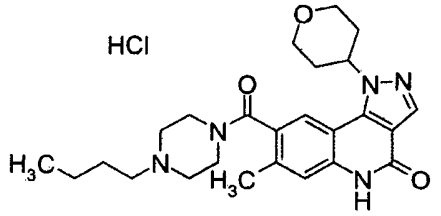
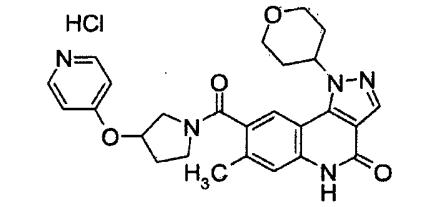
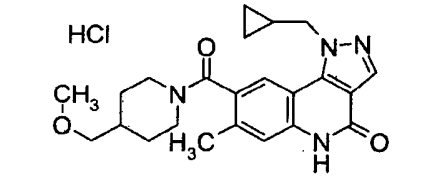
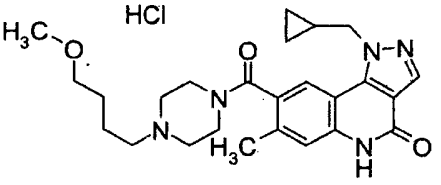
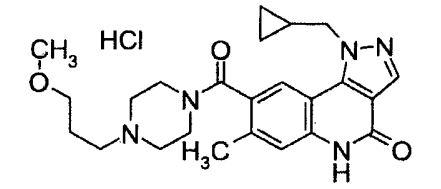
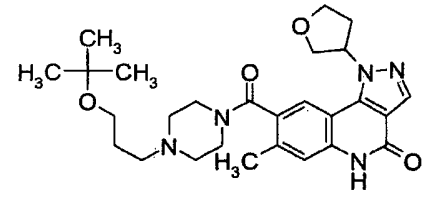
Ex	Structure
93	
94	
95	
96	
97	
98	

[Table 44]

Ex	Structure
99	
100	
101	
102	
103	
104	
105	

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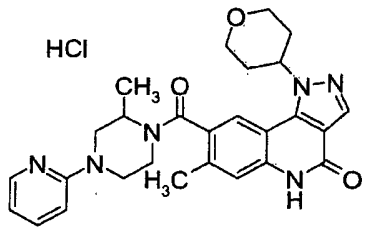
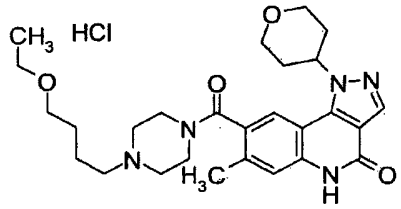
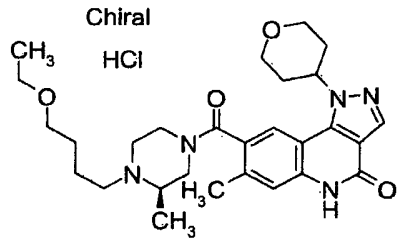
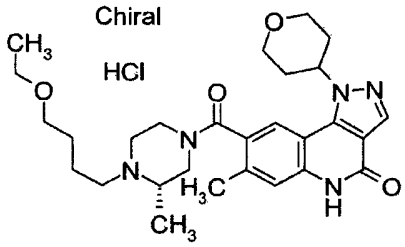
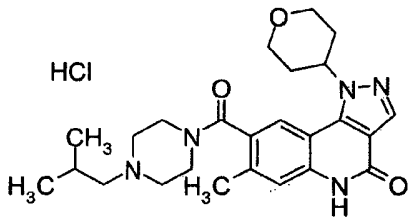
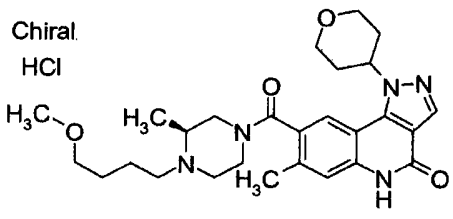
Ex	Structure
106	
107	
108	
109	

[Table 45]

Ex	Structure
110	
111	

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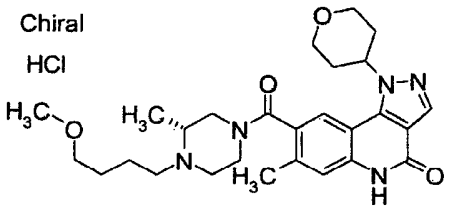
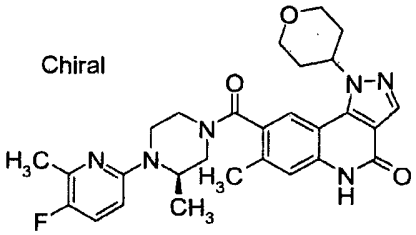
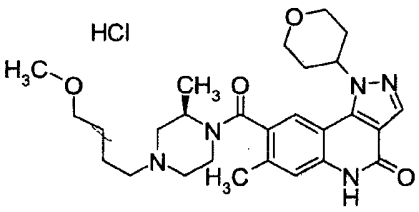
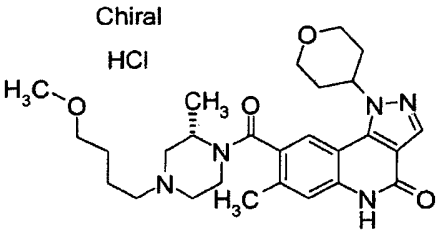
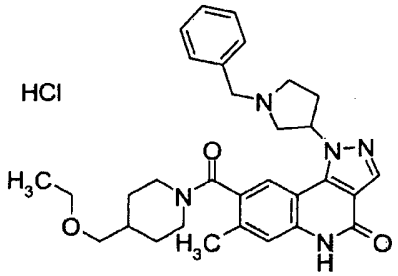
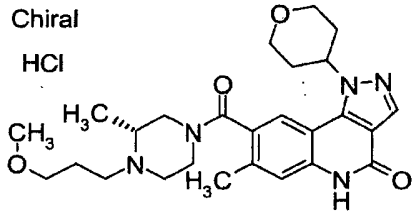
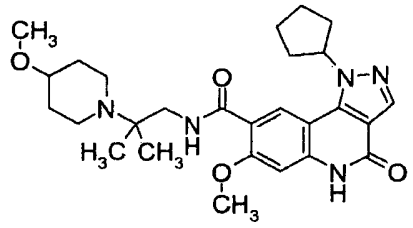
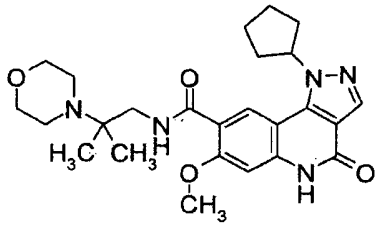
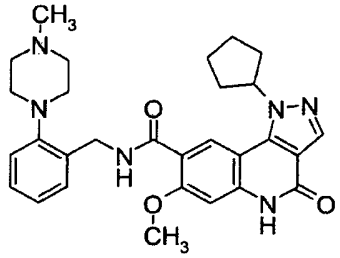
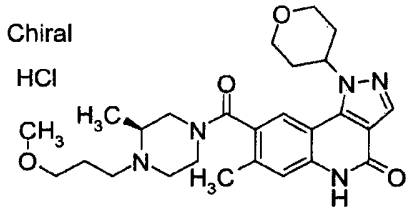
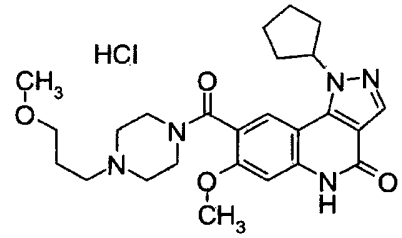
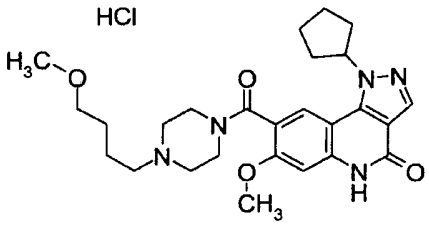
Ex	Structure
112	
113	
114	
115	
116	
117	

(continued)

Ex	Structure
118	
119	

[Table 46]

Ex	Structure
120	
121	
122	
123	

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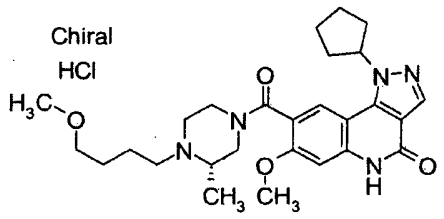
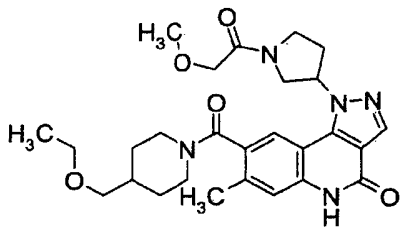
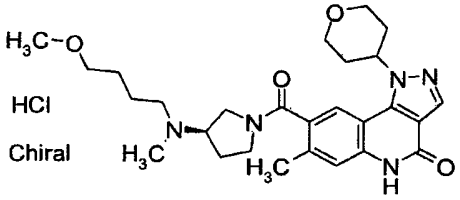
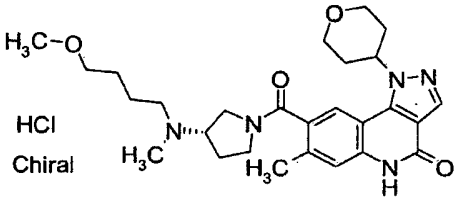
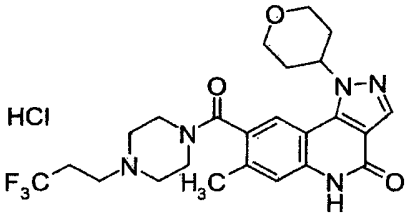
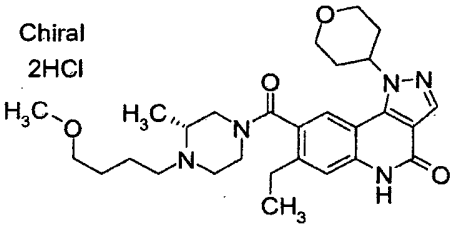
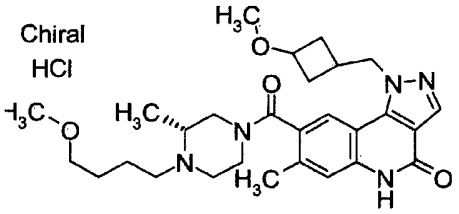
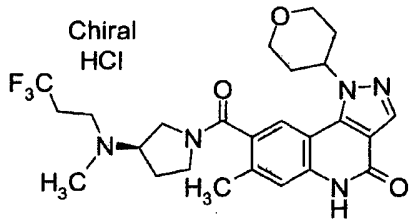
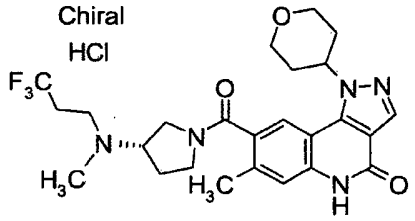
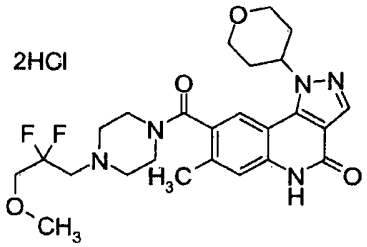
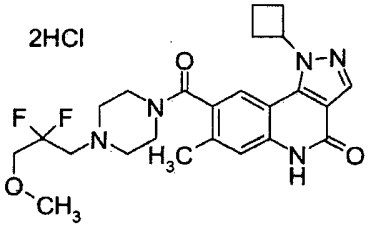
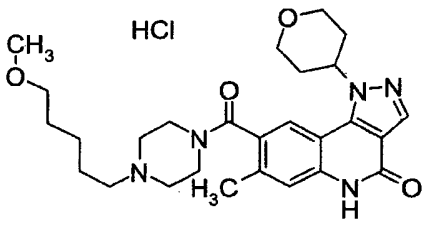
Ex	Structure
124	
125	
126	
127	
128	
129	

[Table 47]

Ex	Structure
130	
131	
132	
133	
134	
135	

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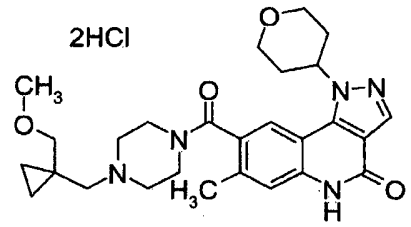
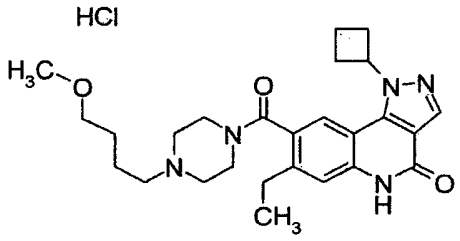
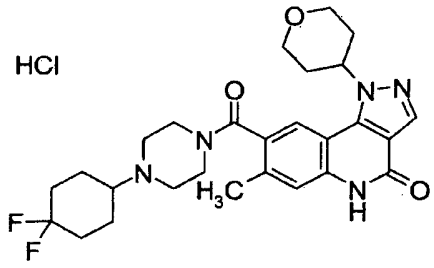
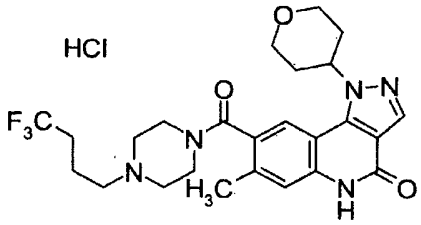
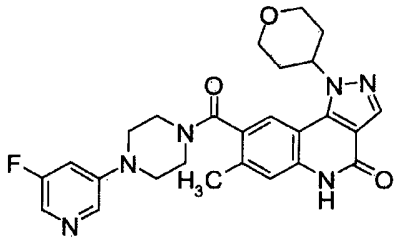
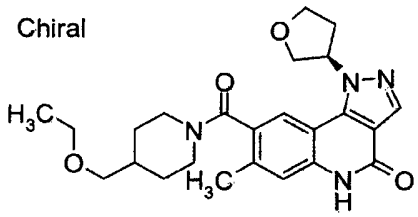
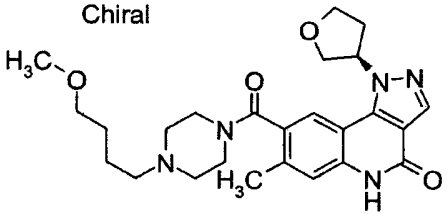
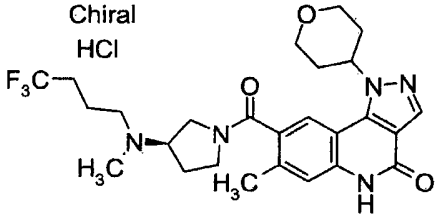
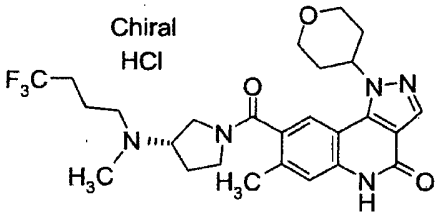
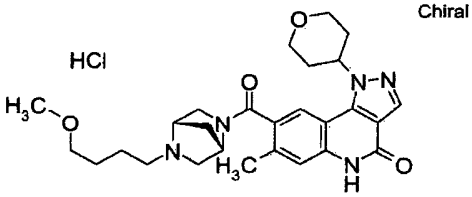
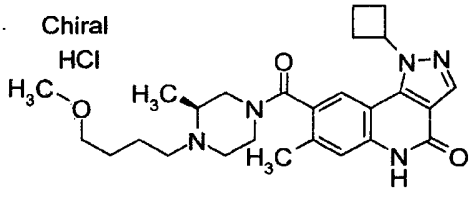
Ex	Structure
136	
137	
138	
139	

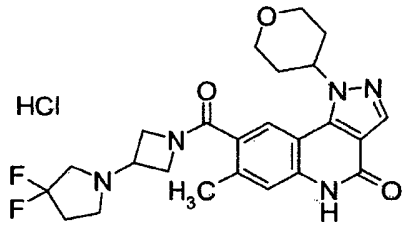
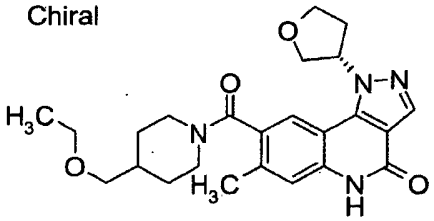
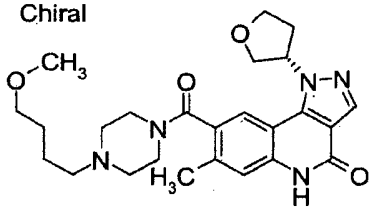
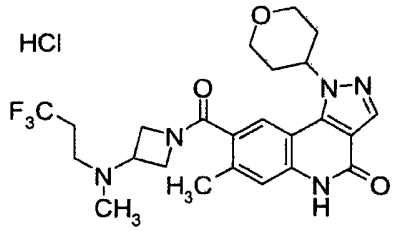
[Table 48]

Ex	Structure
140	

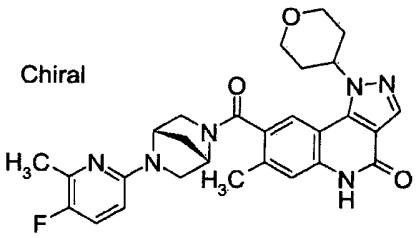
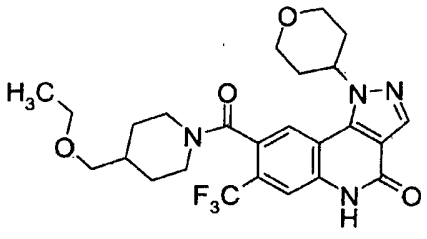
(continued)

Ex	Structure
141	
142	
143	
144	
145	
146	

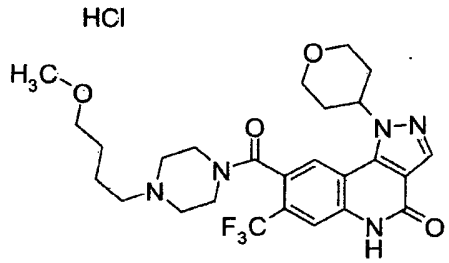
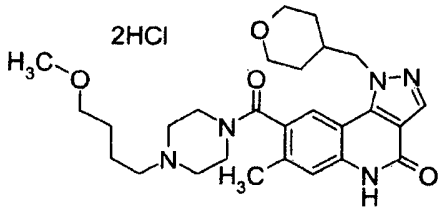
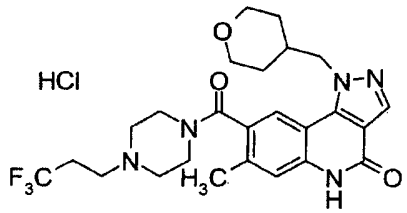
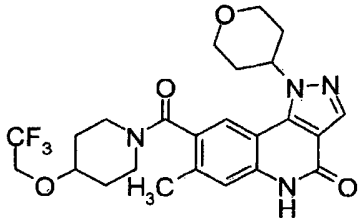
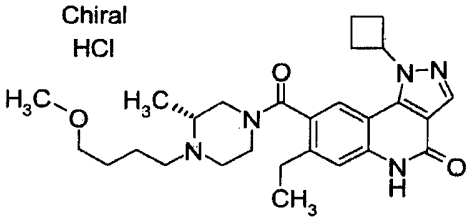
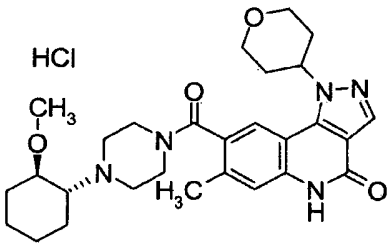
(continued)

Ex	Structure
147	
148	
149	
150	

[Table 49]

Ex	Structure
151	
152	

(continued)

Ex	Structure
153	
154	
155	
156	
157	
158	

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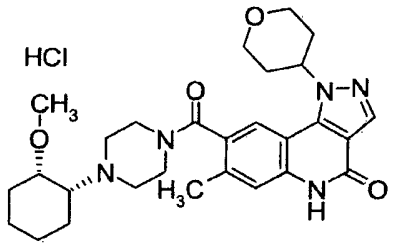
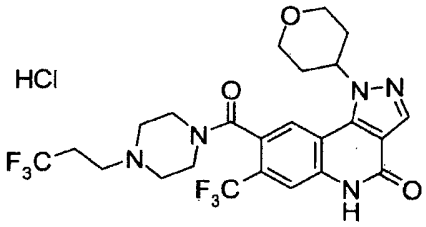
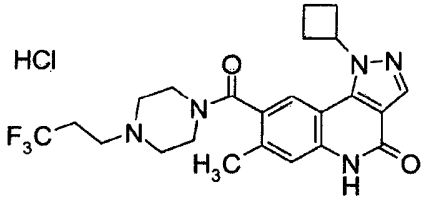
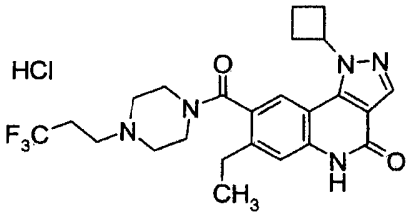
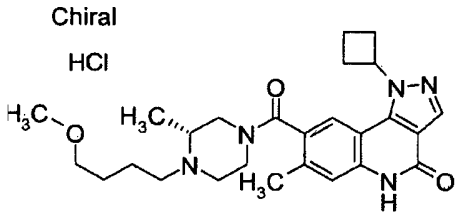
Ex	Structure
159	
160	

[Table 50]

Ex	Structure
161	
162	
163	

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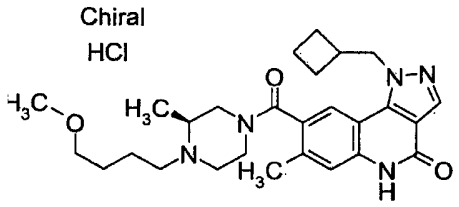
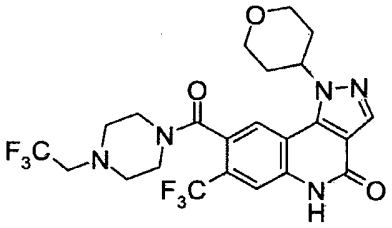
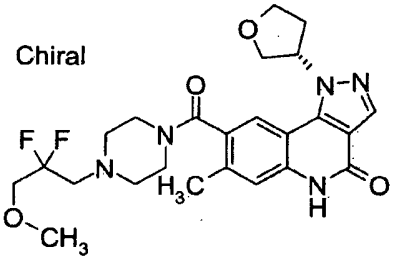
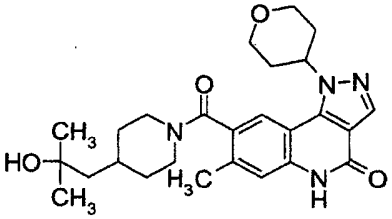
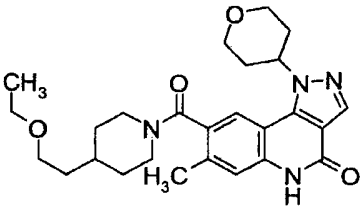
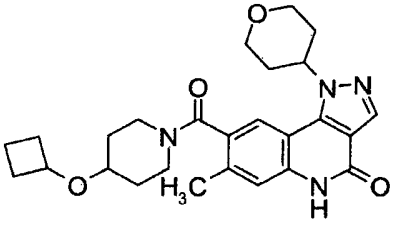
Ex	Structure
164	
165	
166	
167	
168	
169	

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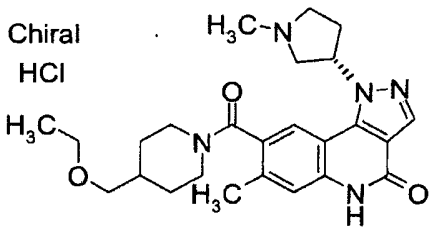
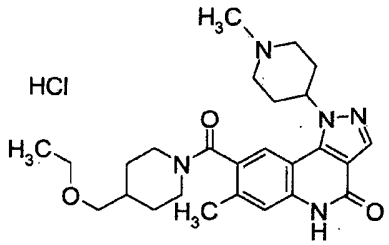
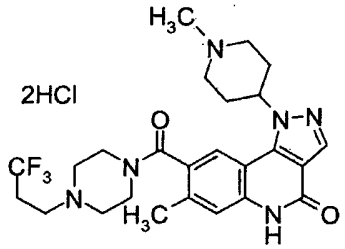
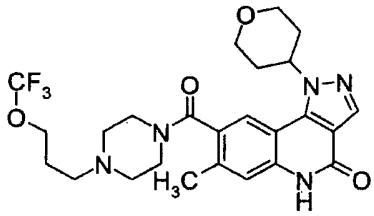
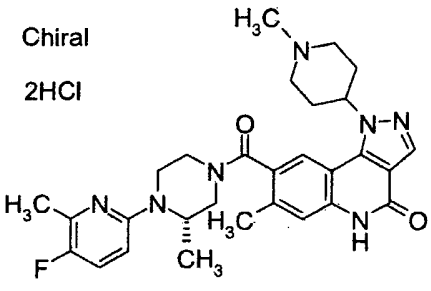
Ex	Structure
170	

[Table 51]

Ex	Structure
171	
172	
173	
174	

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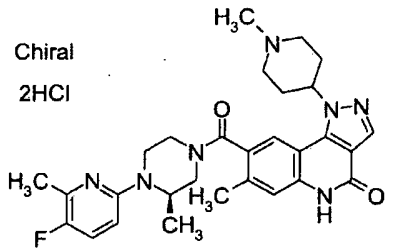
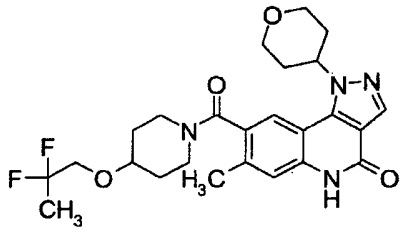
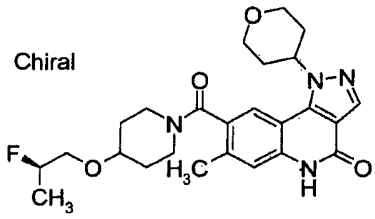
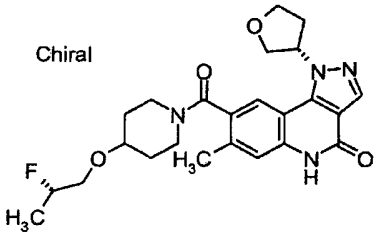
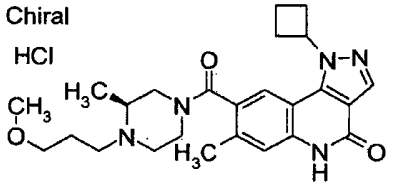
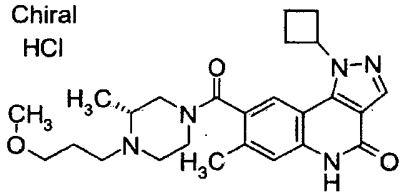
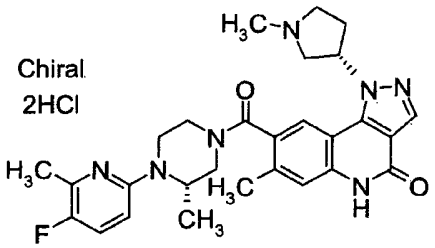
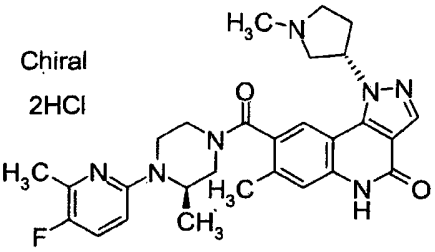
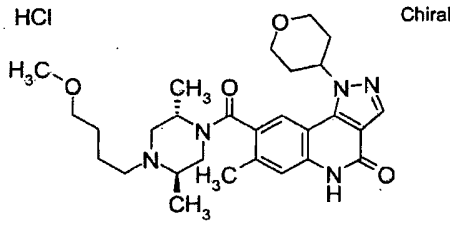
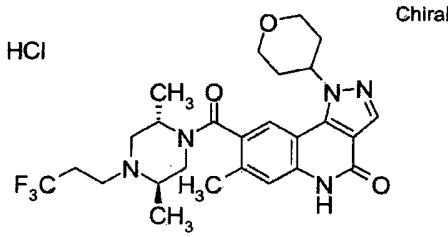
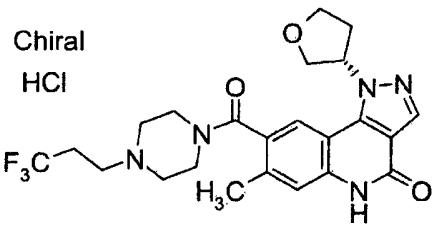
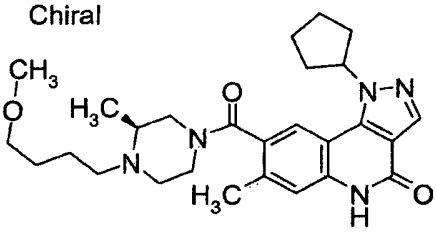
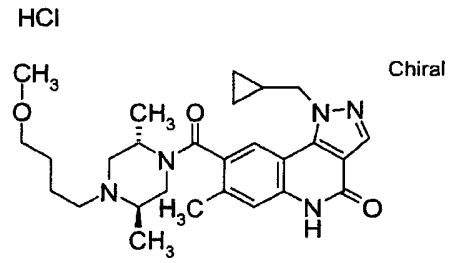
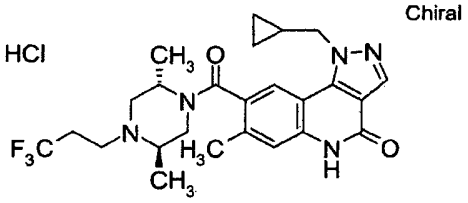
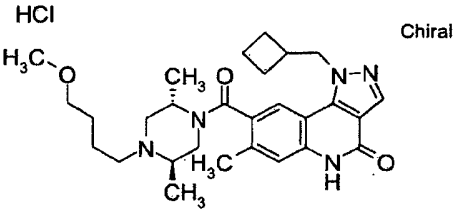
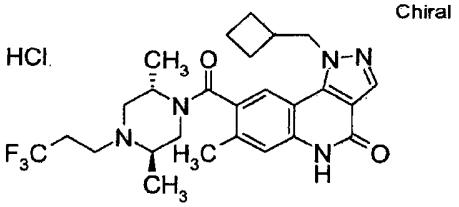
Ex	Structure
175	 Chiral 2HCl
176	
177	 Chiral
178	 Chiral
179	 Chiral HCl
180	 Chiral HCl

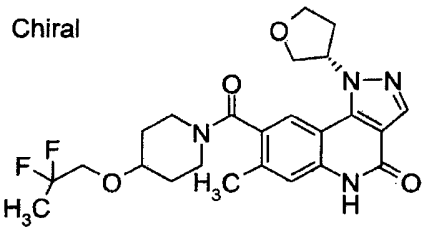
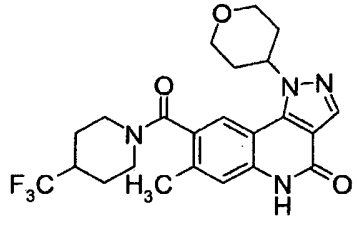
[Table 52]

Ex	Structure
181	
182	
183	
184	
185	
186	

(continued)

Ex	Structure
187	
188	
189	
190	

[Table 53]

Ex	Structure
191	
192	

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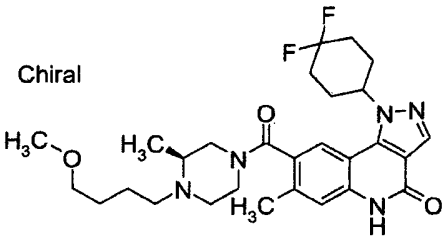
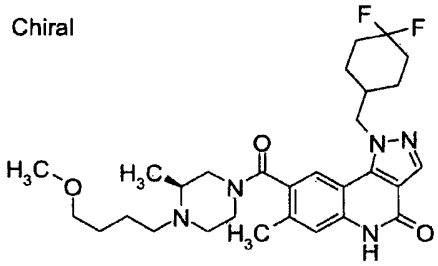
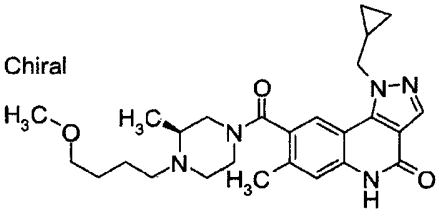
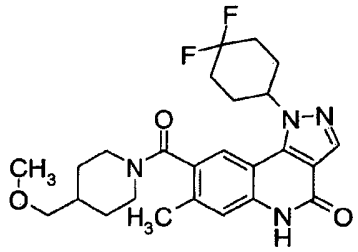
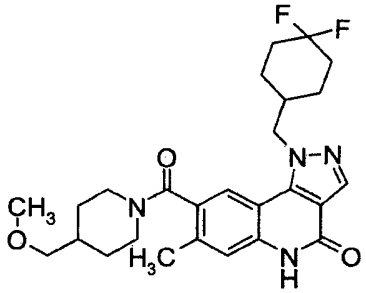
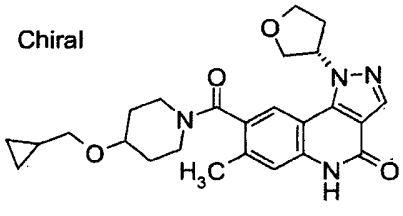
Ex	Structure
193	
194	
195	
196	
197	
198	

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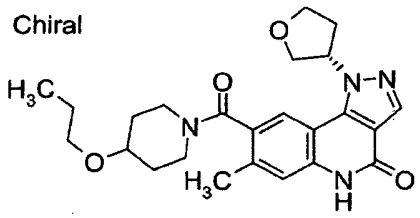
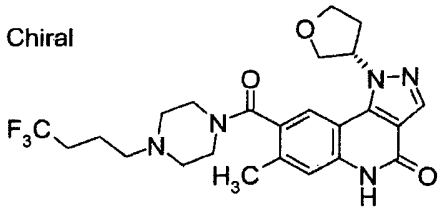
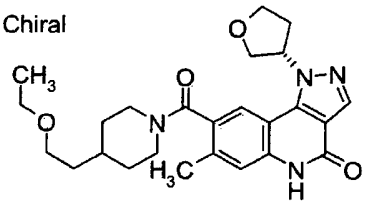
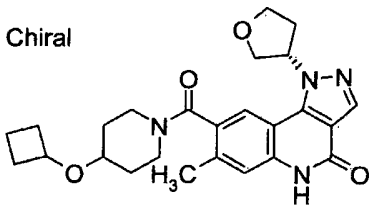
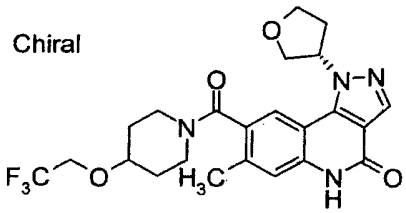
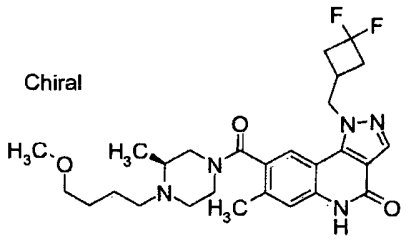
Ex	Structure
199	
200	

[Table 54]

Ex	Structure
201	
202	
203	
204	

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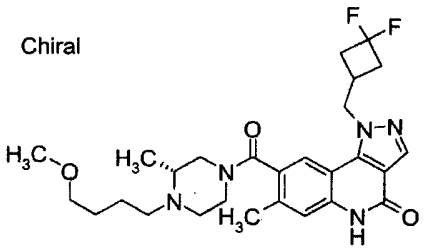
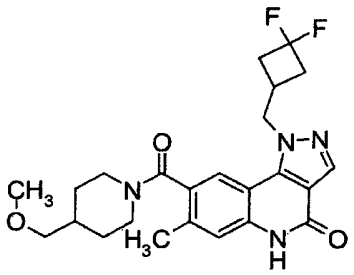
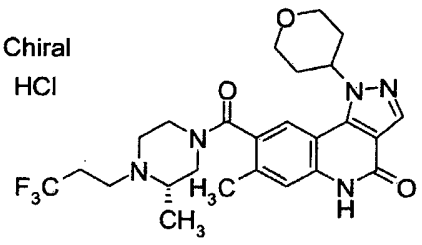
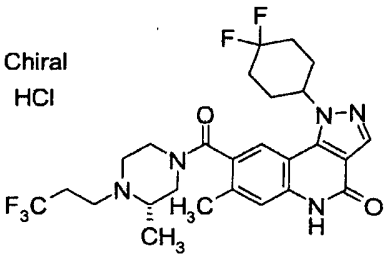
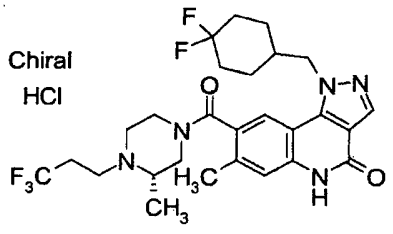
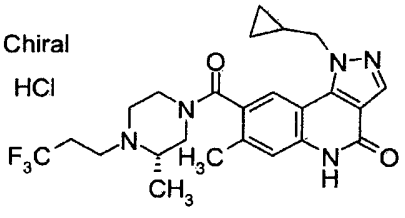
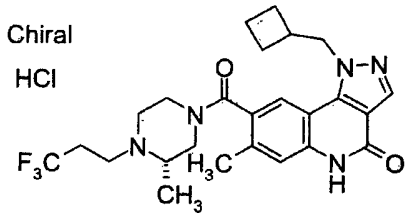
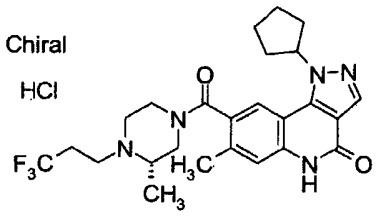
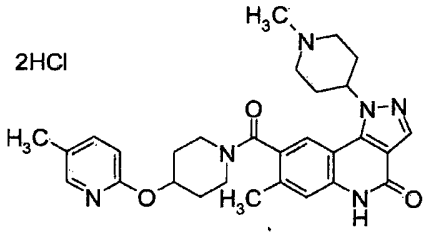
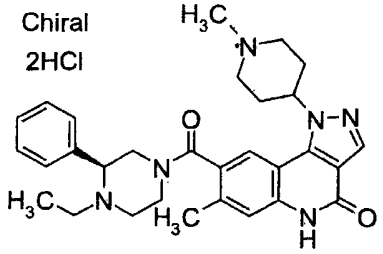
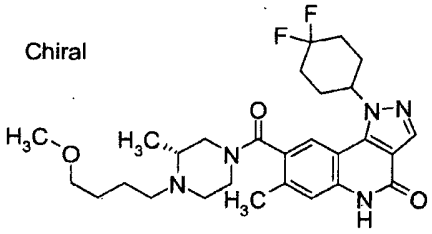
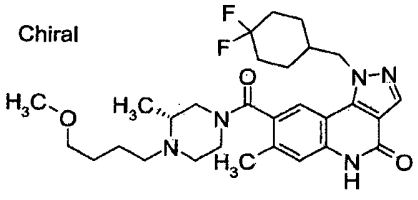
Ex	Structure
205	
206	
207	
208	
209	
210	

[Table 55]

Ex	Structure
211	
212	
213	
214	
215	
216	

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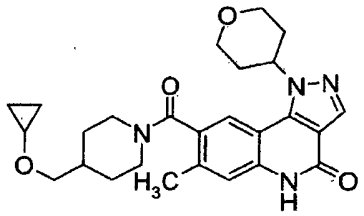
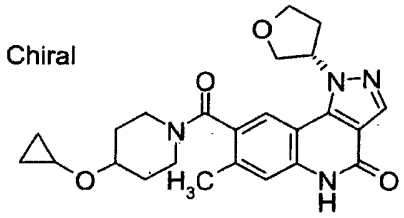
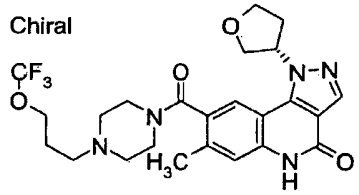
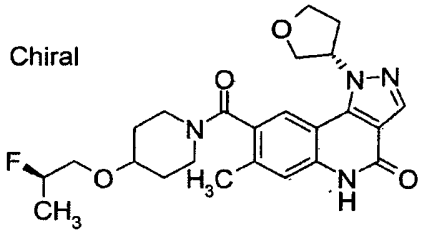
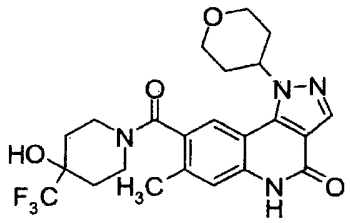
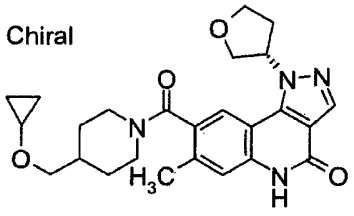
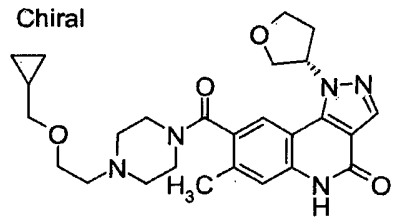
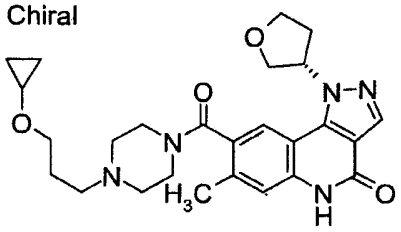
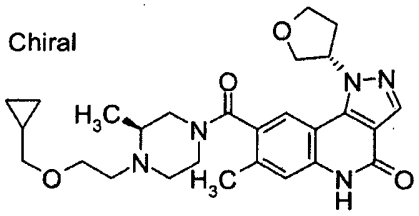
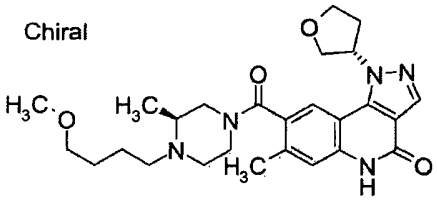
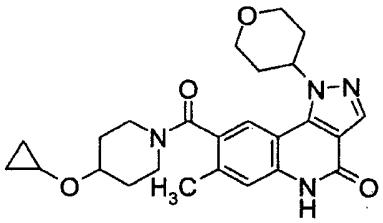
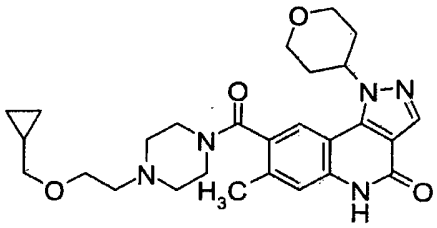
Ex	Structure
217	
218	
219	
220	
221	

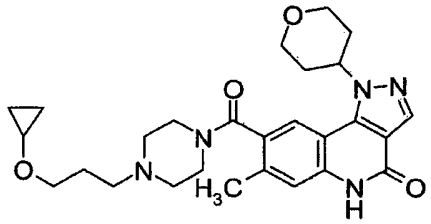
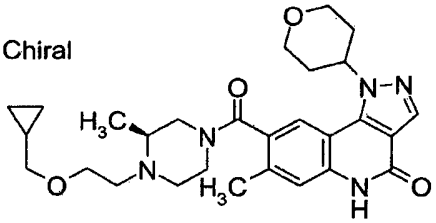
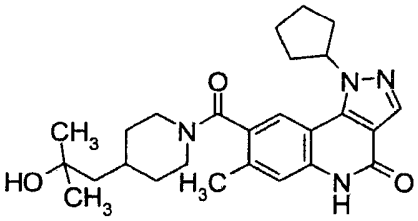
[Table 56]

Ex	Structure
222	

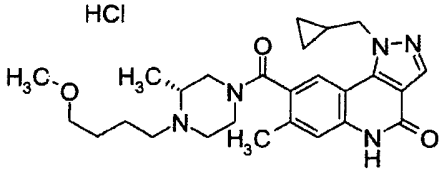
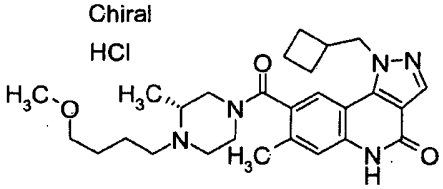
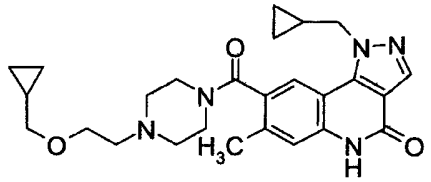
(continued)

Ex	Structure
223	
224	
225	
226	
227	
228	

(continued)

Ex	Structure
229	
230	Chiral 
231	

[Table 57]

Ex	Structure
232	Chiral HCl 
233	Chiral HCl 
234	

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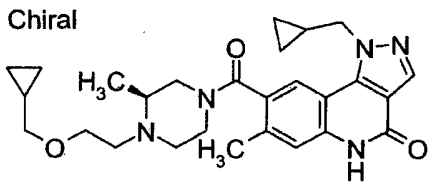
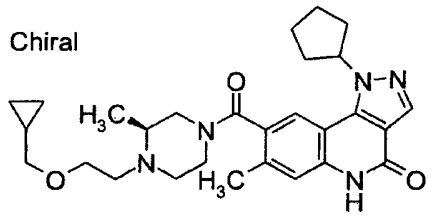
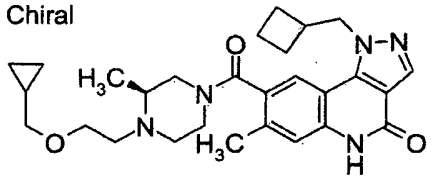
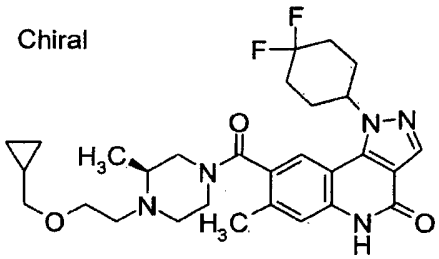
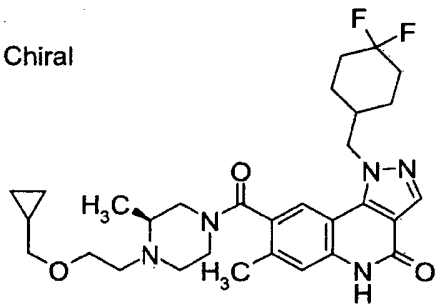
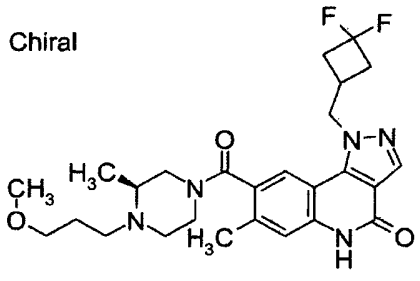
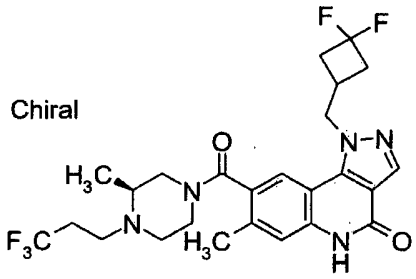
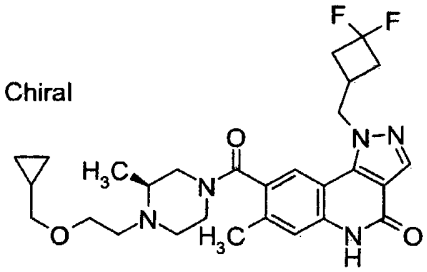
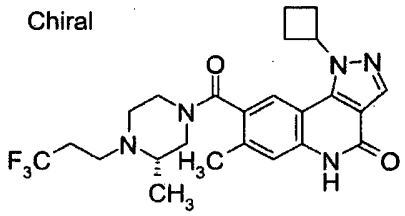
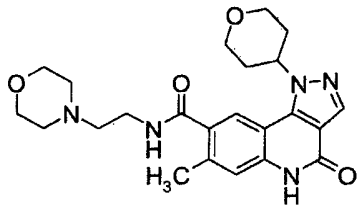
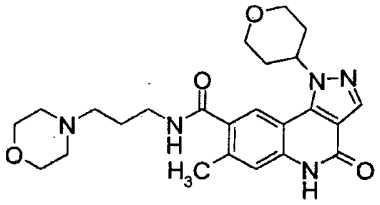
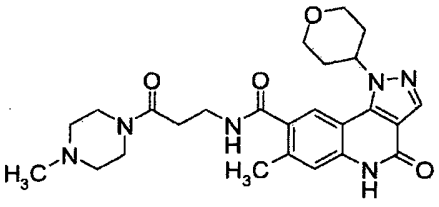
235	
236	
237	
238	
239	
240	

[Table 58]

Ex	Structure
241	
242	
243	
244	
245	
246	

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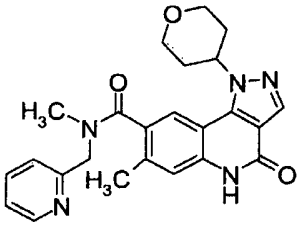
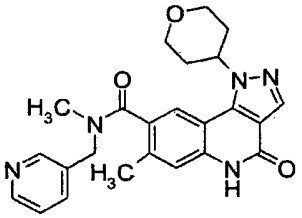
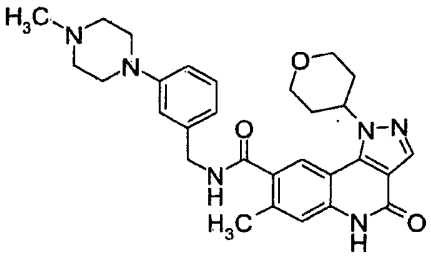
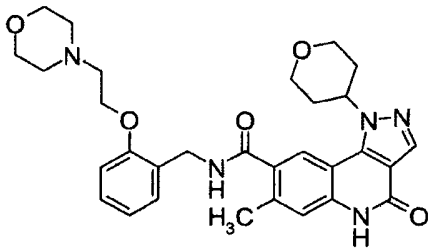
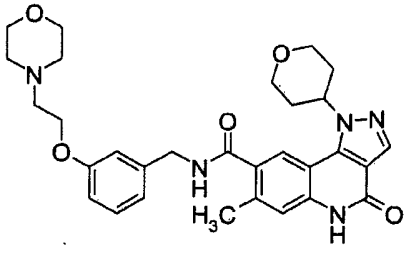
247	
248	
249	
250	

[Table 59]

Ex	Structure
251	

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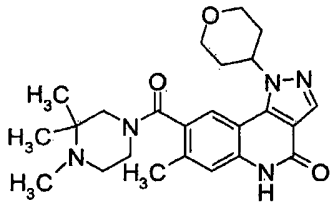
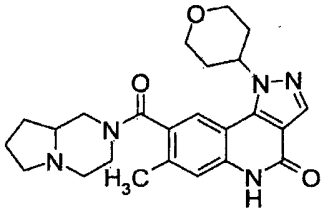
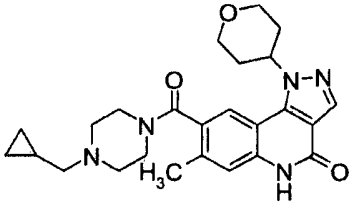
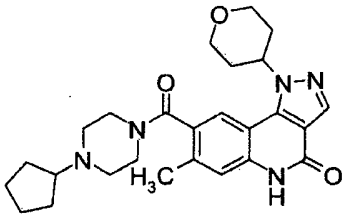
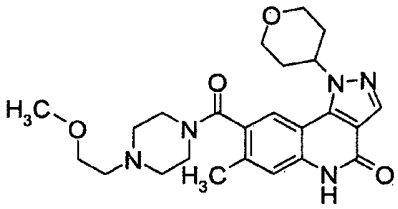
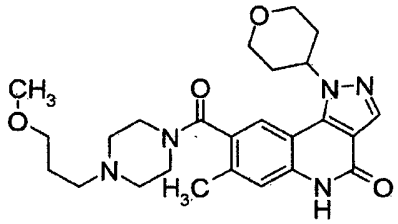
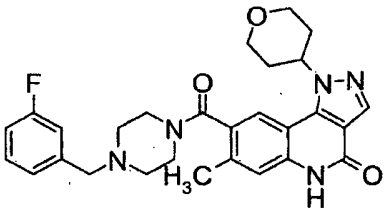
Ex	Structure
252	
253	
254	
255	
256	
257	
258	

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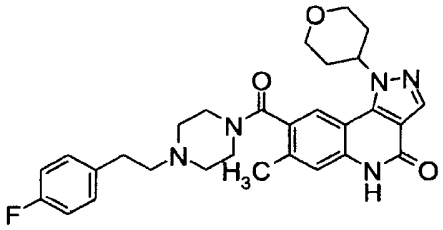
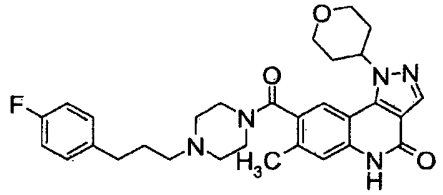
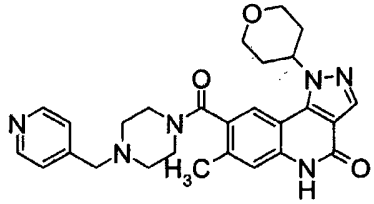
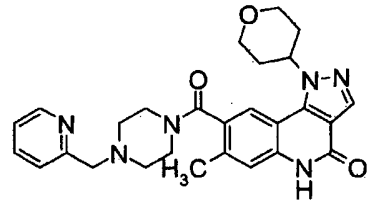
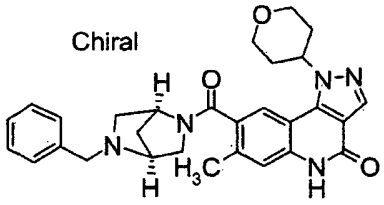
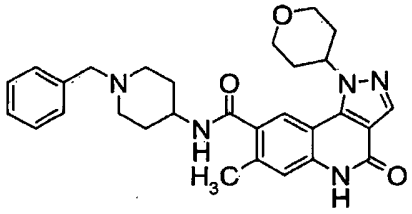
Ex	Structure
259	
260	

[Table 60]

Ex	Structure
261	
262	
263	
264	

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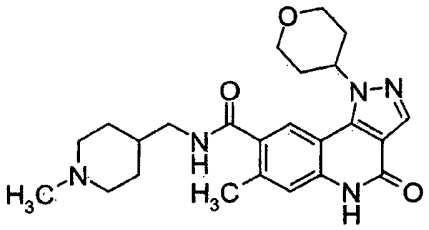
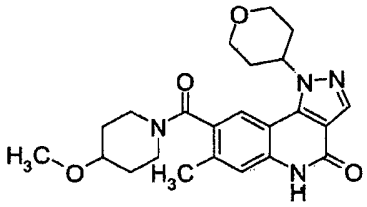
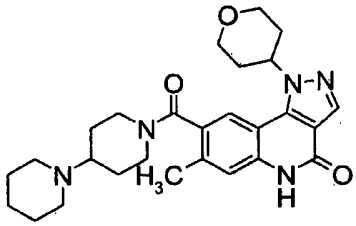
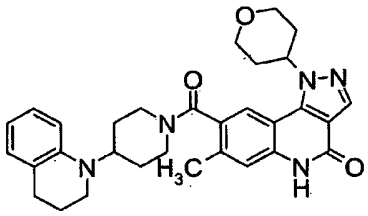
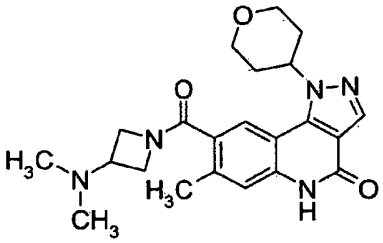
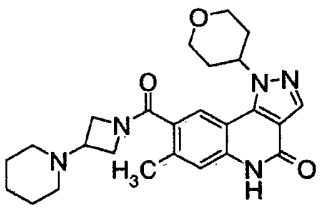
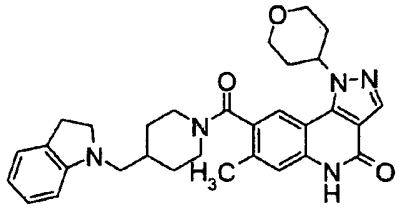
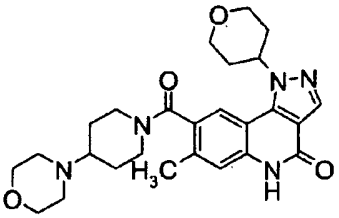
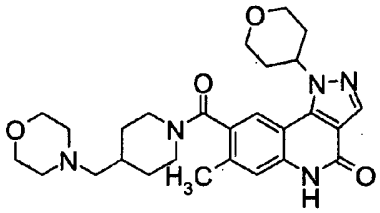
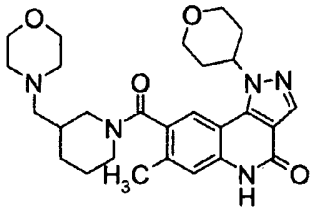
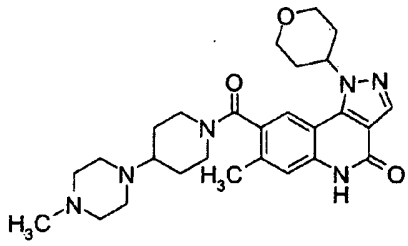
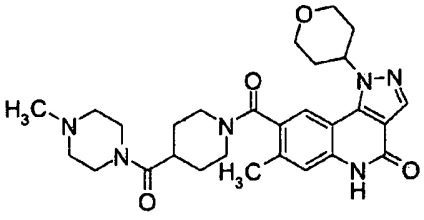
Ex	Structure
265	
266	
267	
268	
269	
270	

[Table 61]

Ex	Structure
271	
272	
273	
274	
275	
276	

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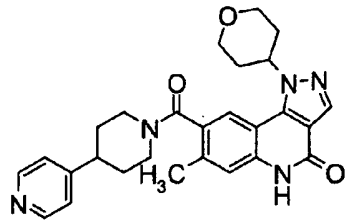
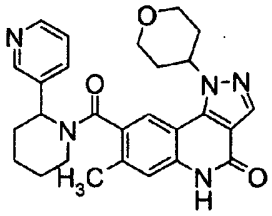
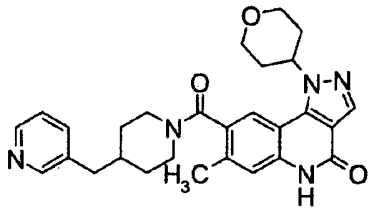
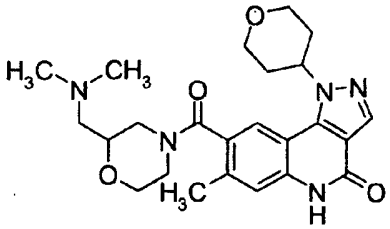
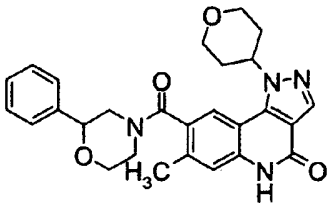
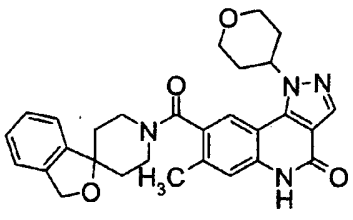
277	
278	
279	
280	

[Table 62]

Ex	Structure
281	
282	

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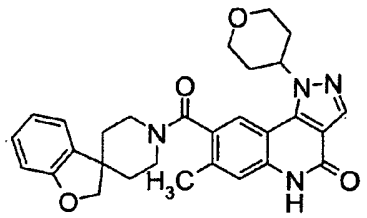
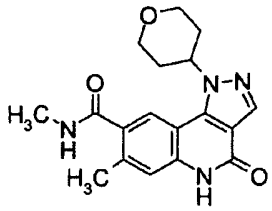
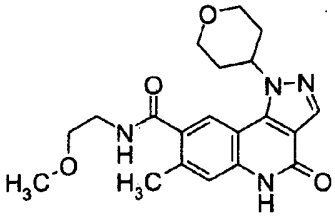
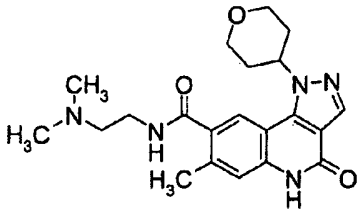
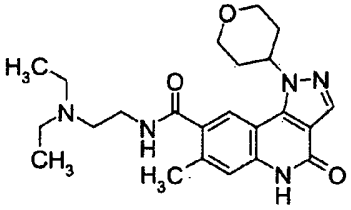
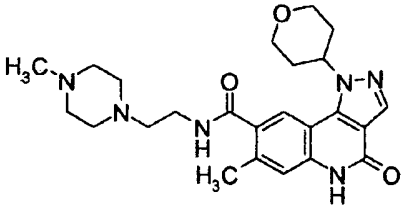
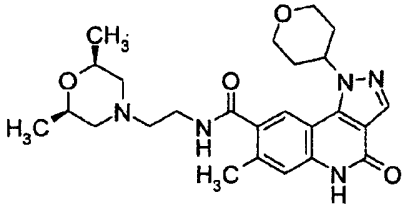
Ex	Structure
283	
284	
285	
286	
287	
288	
289	

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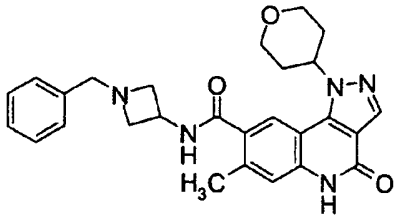
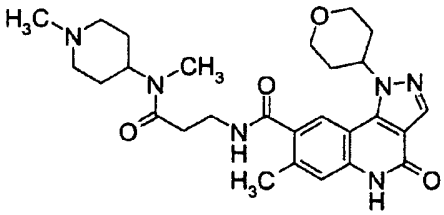
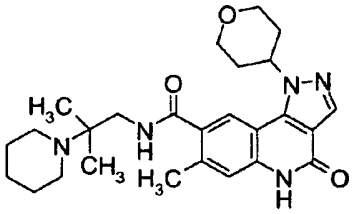
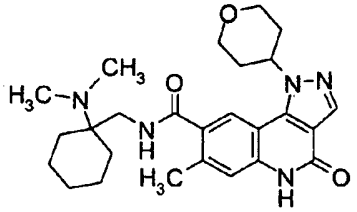
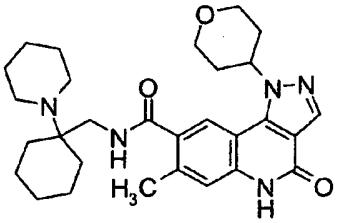
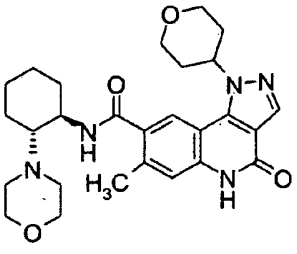
290	

[Table 63]

Ex	Structure
291	
292	
293	
294	
295	

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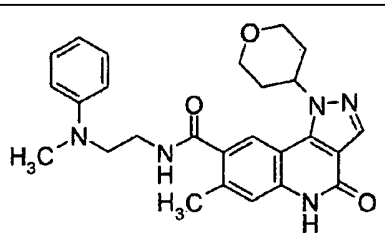
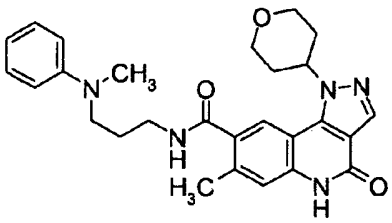
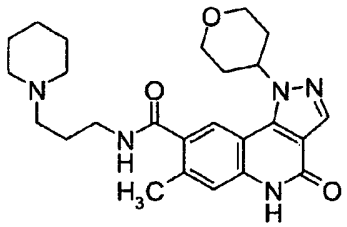
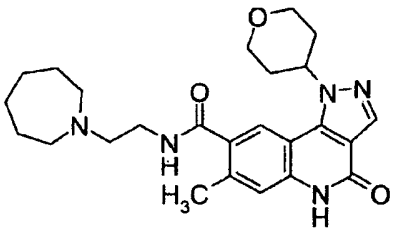
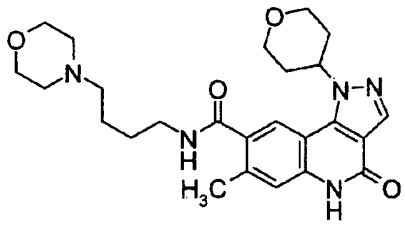
296	
297	
298	
299	
300	

[Table 64]

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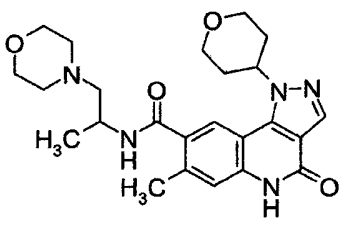
301	

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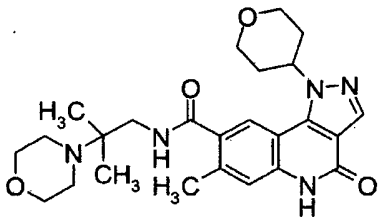
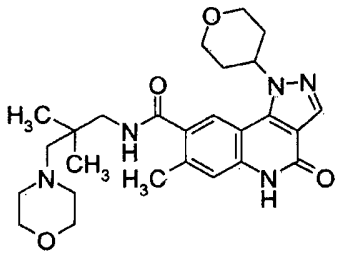
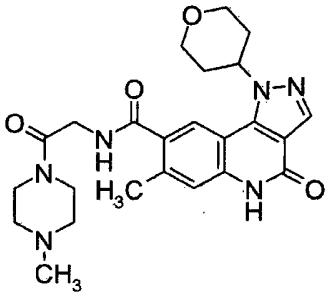
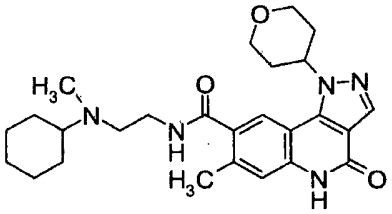
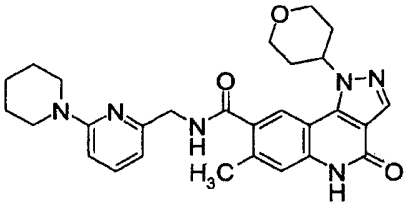
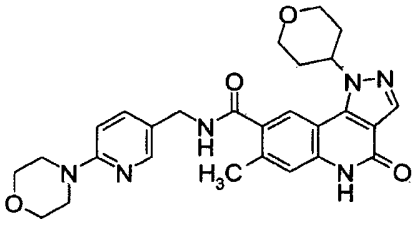
Ex	Structure
302	
303	
304	
305	
306	
307	

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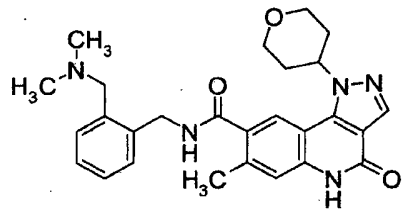
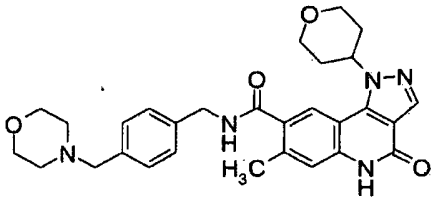
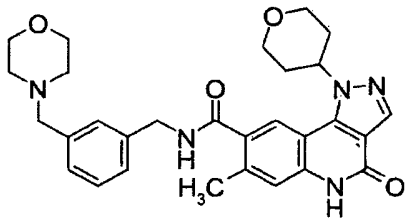
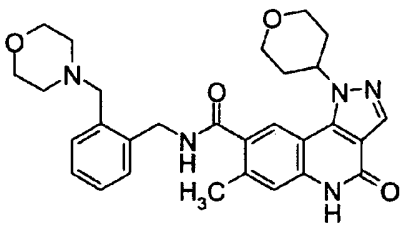
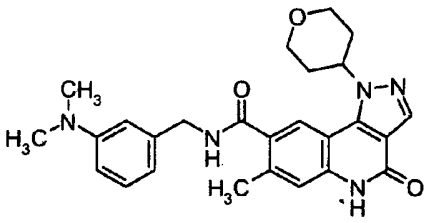
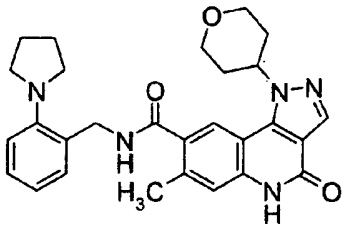
Ex	Structure
308	
309	
310	

[Table 65]

Ex	Structure
311	
312	
313	

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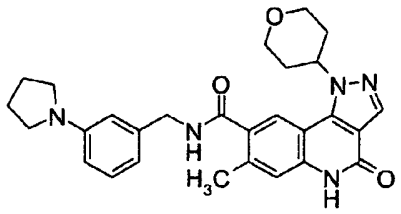
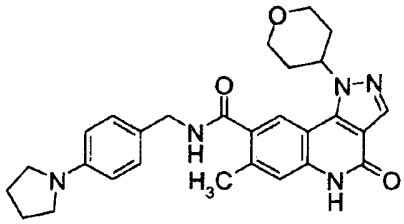
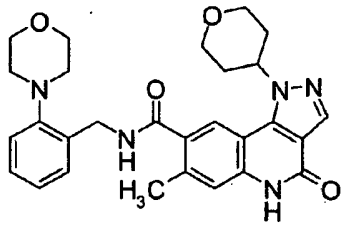
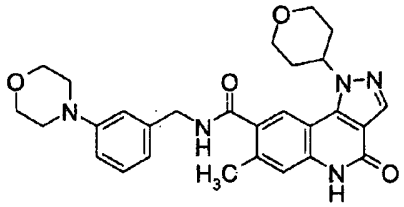
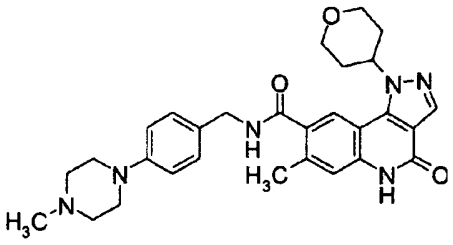
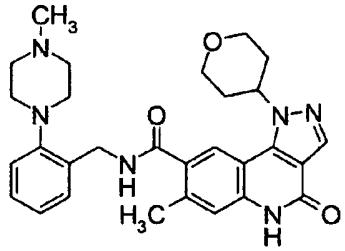
Ex	Structure
314	
315	
316	
317	
318	
319	

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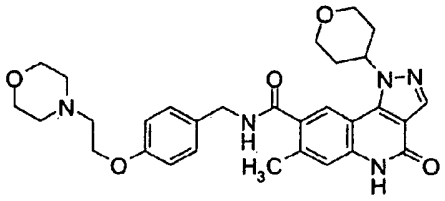
320	

[Table 66]

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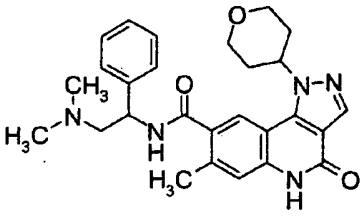
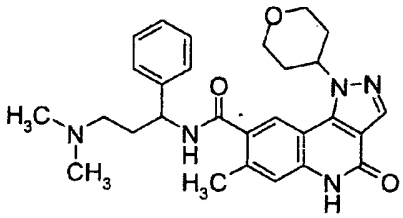
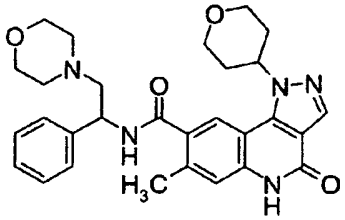
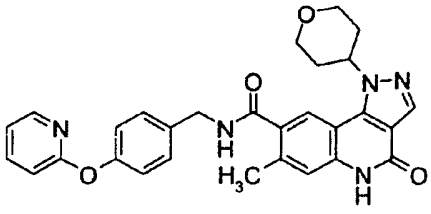
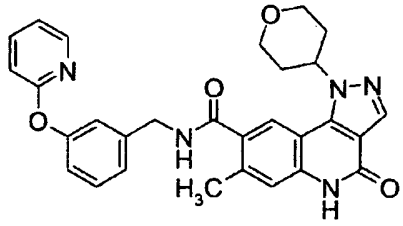
321	
322	
323	
324	
325	

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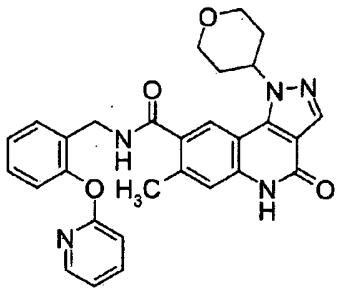
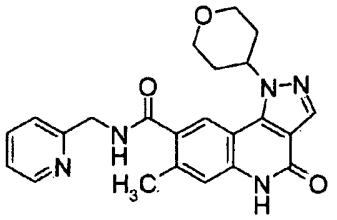
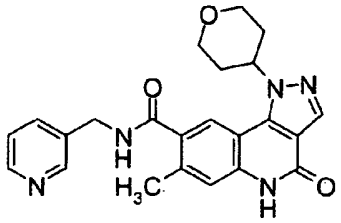
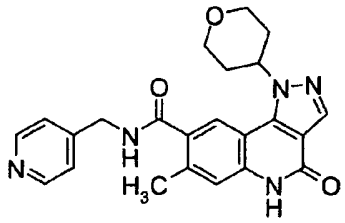
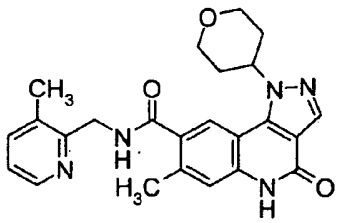
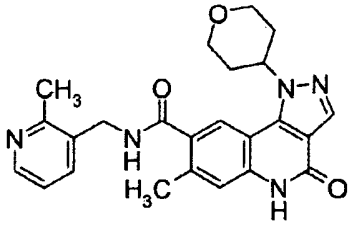
Ex	Structure
326	
327	
328	
329	
330	

[Table 67]

Ex	Structure
331	

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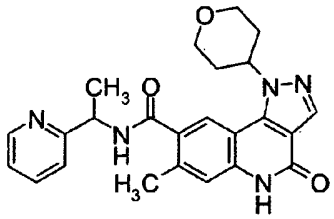
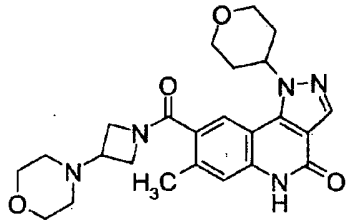
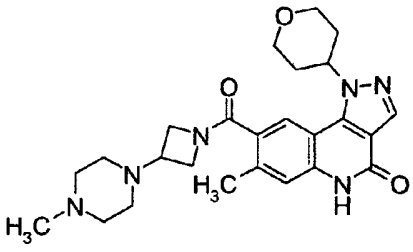
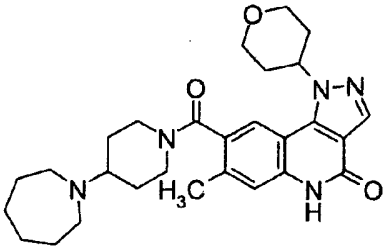
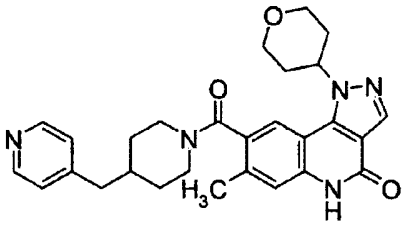
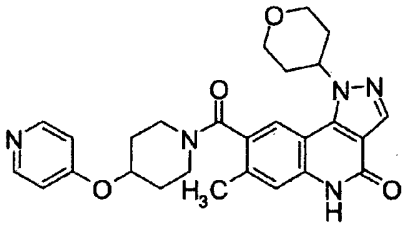
332	
333	
334	
335	
336	
337	

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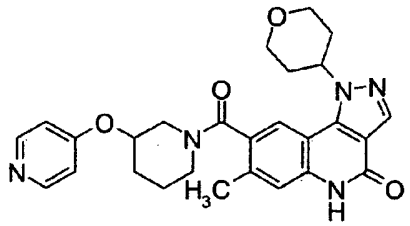
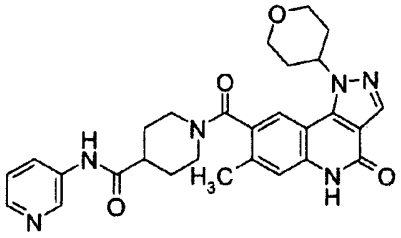
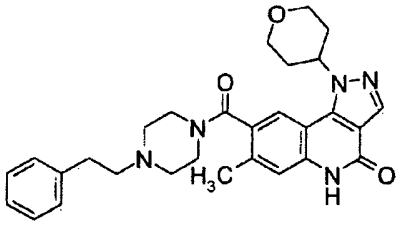
Ex	Structure
338	
339	
340	

[Table 68]

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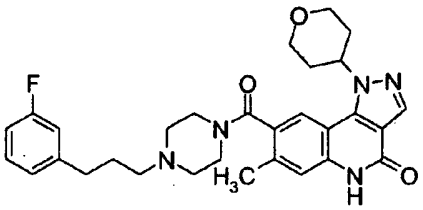
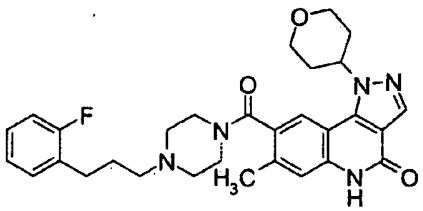
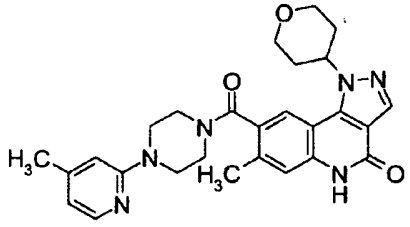
341	
342	
343	

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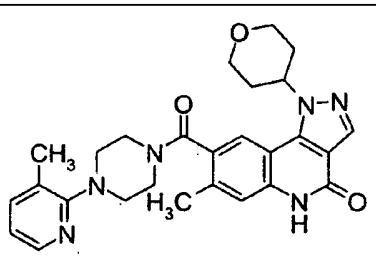
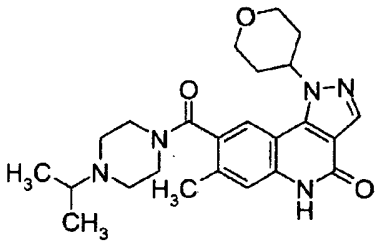
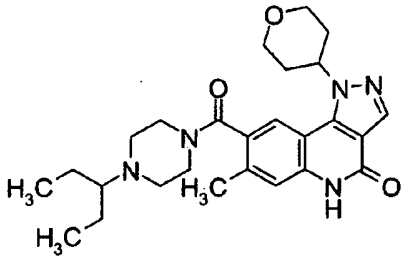
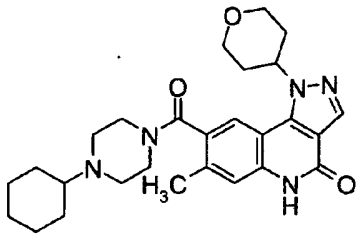
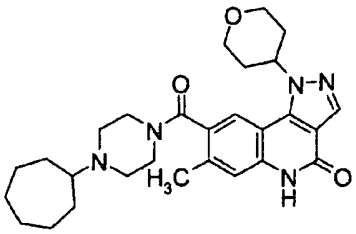
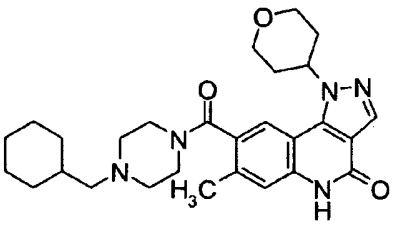
Ex	Structure
344	
345	
346	
347	
348	
349	

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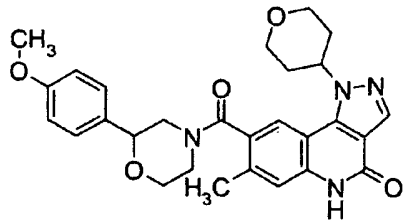
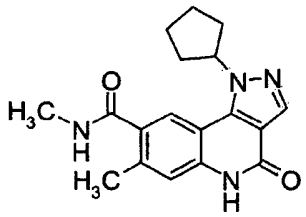
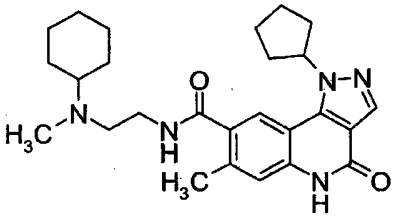
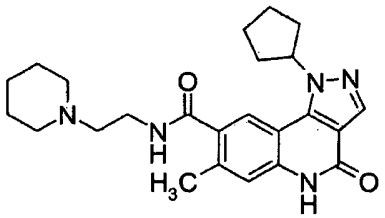
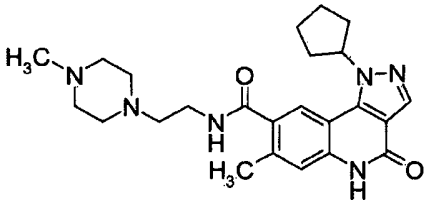
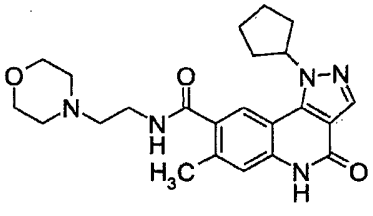
Ex	Structure
350	

[Table 69]

Ex	Structure
351	
352	
353	
354	
355	

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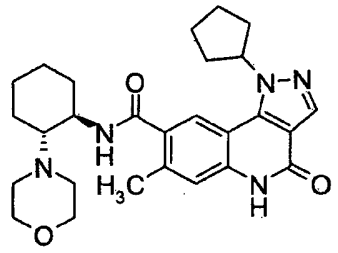
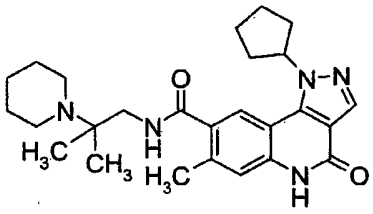
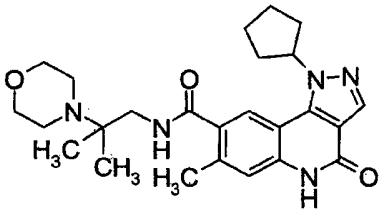
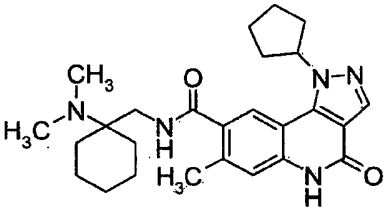
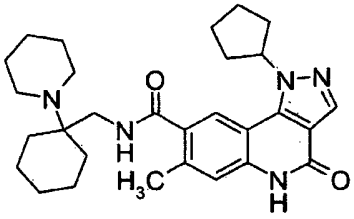
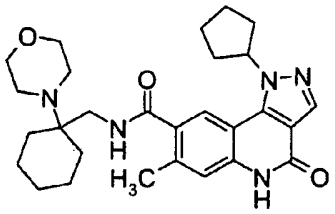
Ex	Structure
356	
357	
358	
359	
360	

[Table 70]

Ex	Structure
361	

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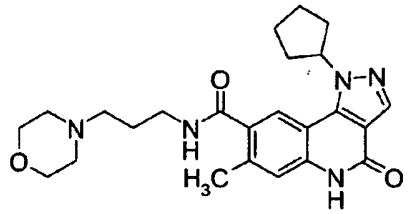
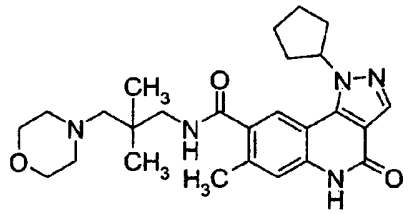
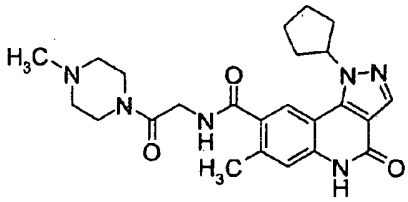
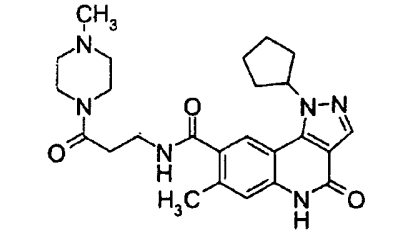
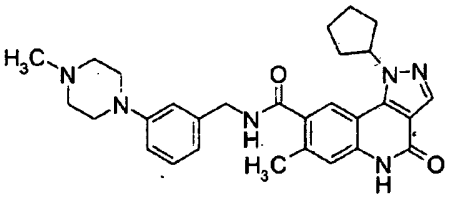
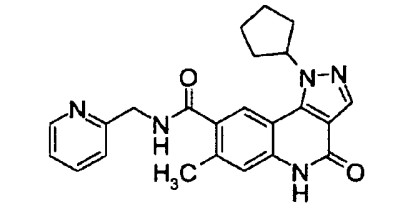
Ex	Structure
362	
363	
364	
365	
366	
367	

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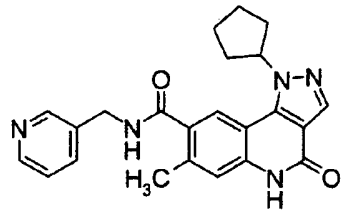
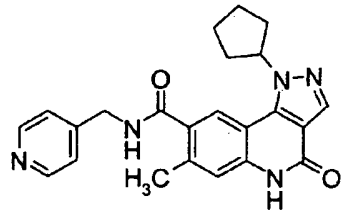
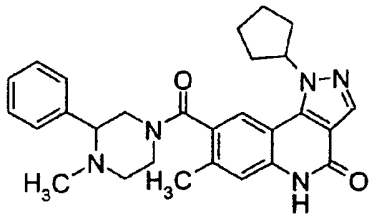
368	
369	
370	

[Table 71]

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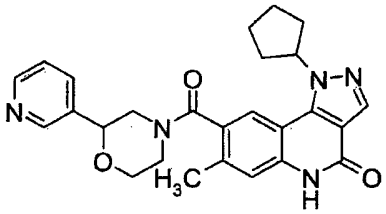
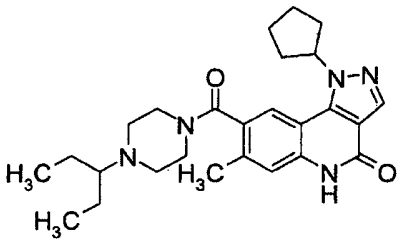
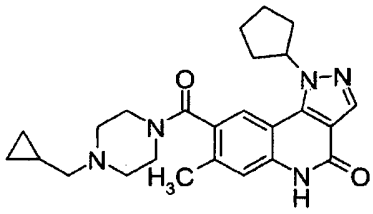
371	
372	
373	

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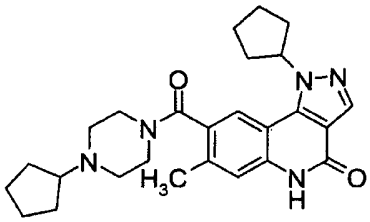
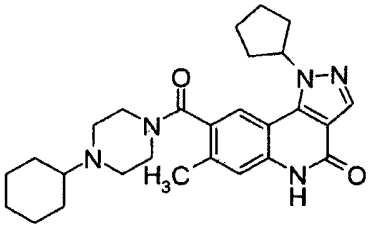
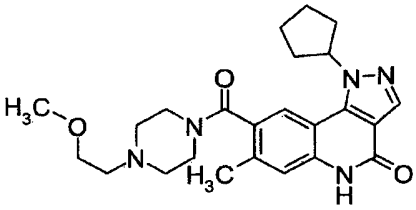
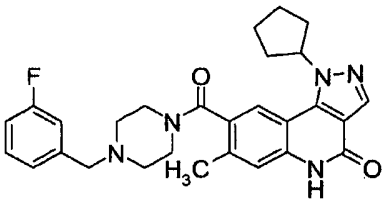
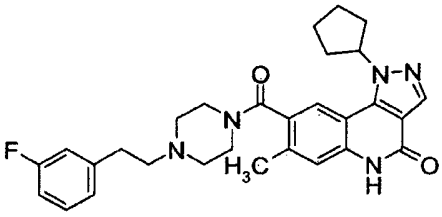
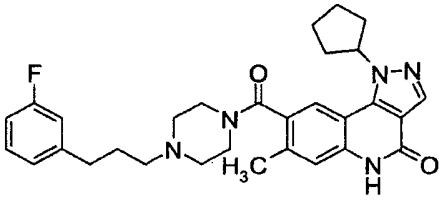
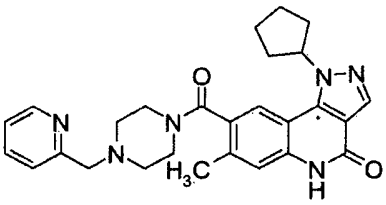
374	
375	
376	
377	
378	
379	
380	

[Table 72]

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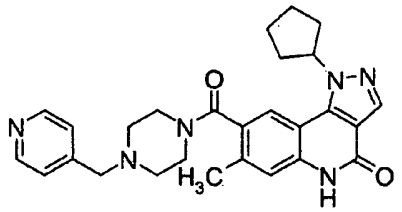
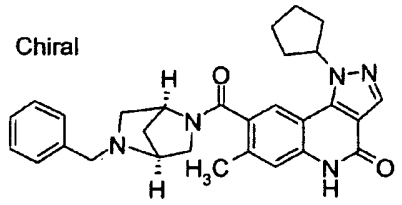
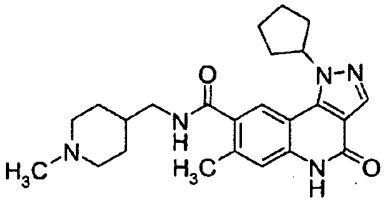
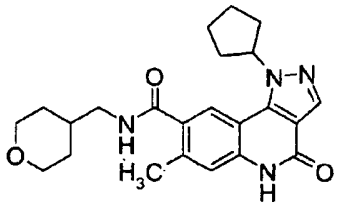
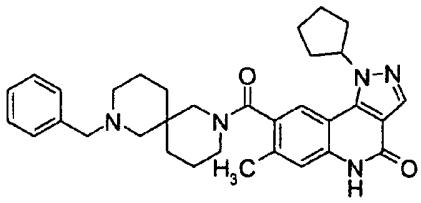
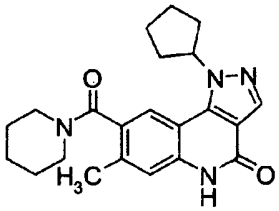
381	
382	
383	
384	
385	
386	

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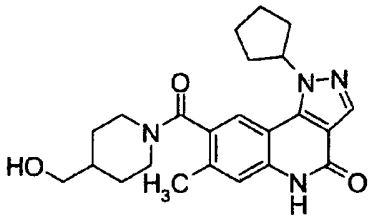
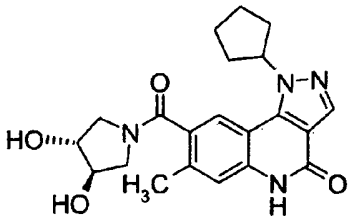
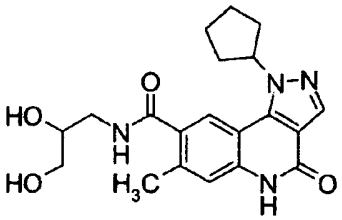
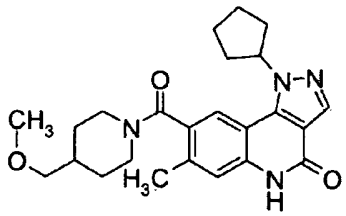
Ex	Structure
387	
388	
389	
390	

[Table 73]

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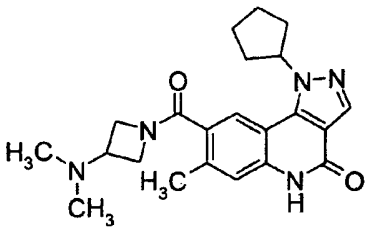
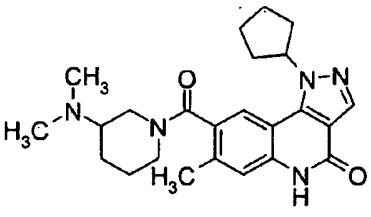
391	
392	

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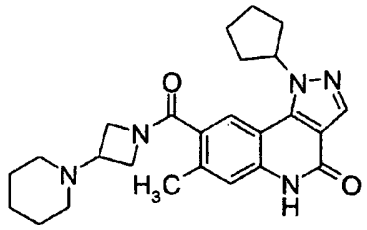
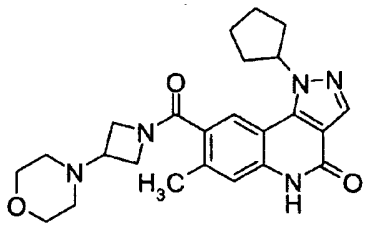
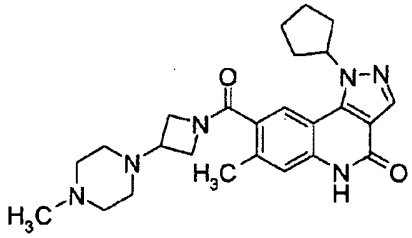
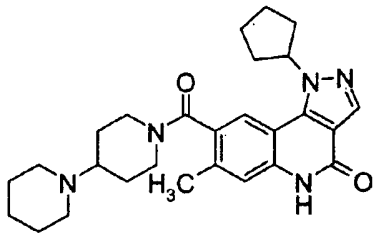
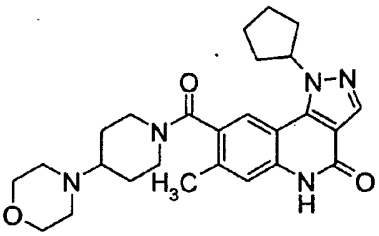
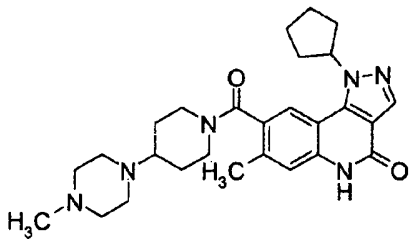
393	
394	
395	
396	
397	
398	

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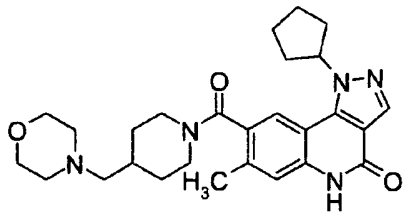
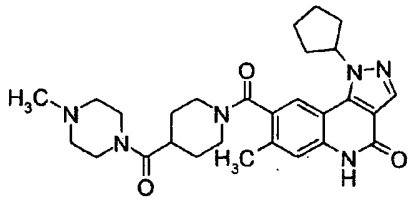
399	
400	

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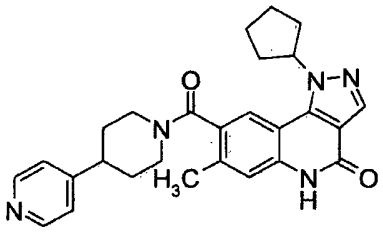
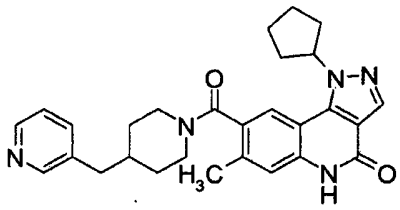
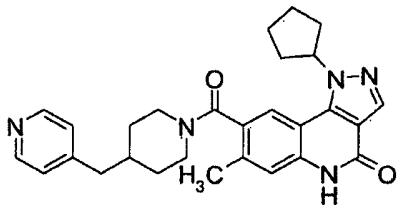
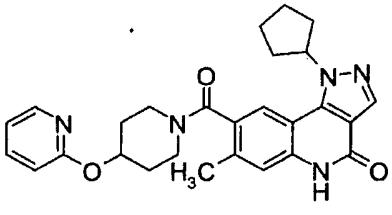
401	
402	
403	
404	

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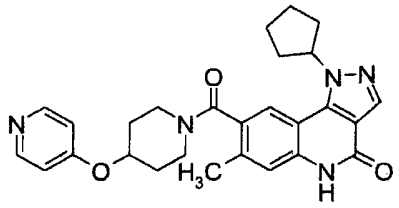
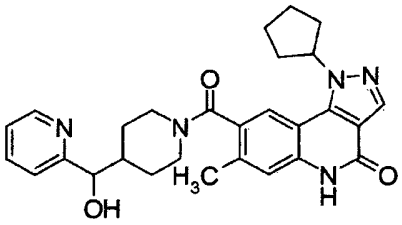
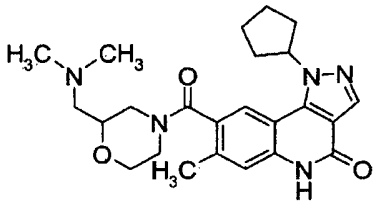
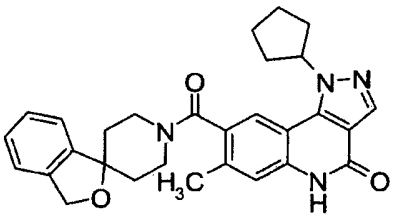
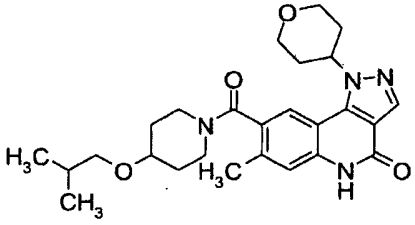
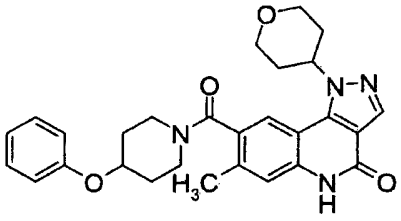
405	
406	
407	
408	
409	
410	

[Table 75]

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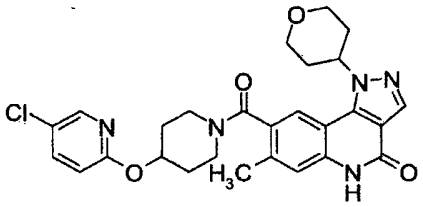
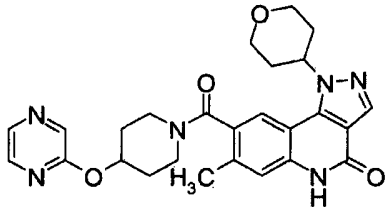
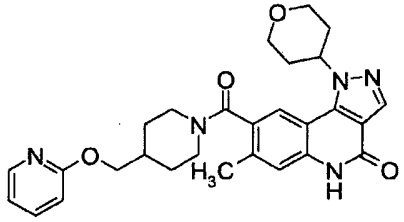
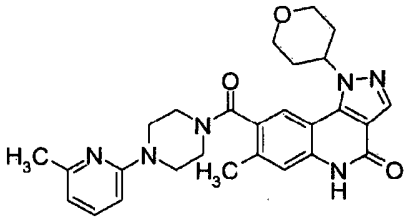
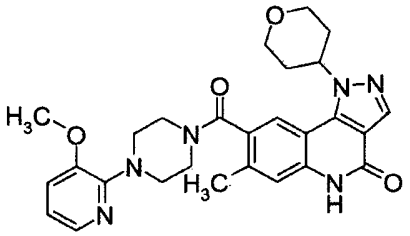
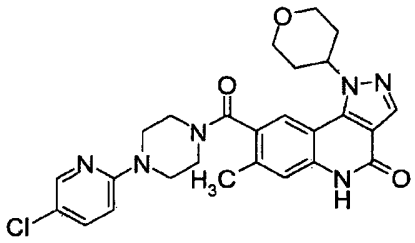
411	
412	
413	
414	
415	
416	

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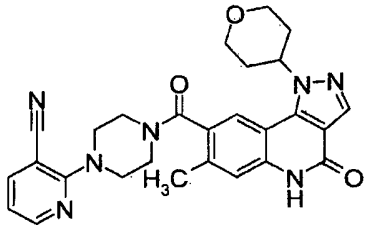
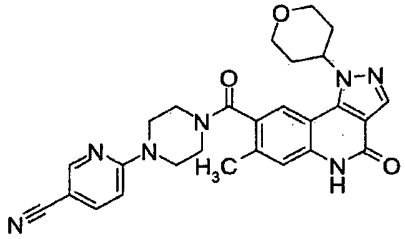
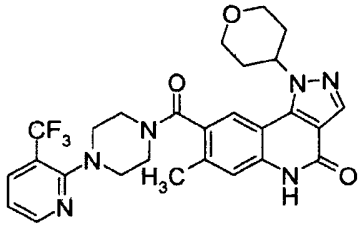
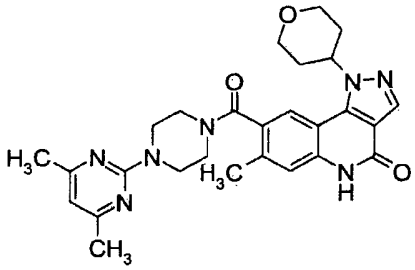
417	
418	
419	
420	

[Table 76]

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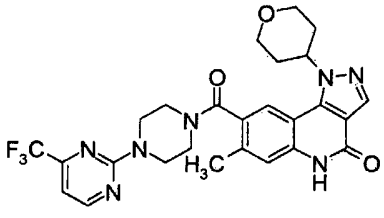
421	

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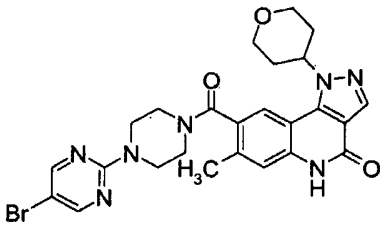
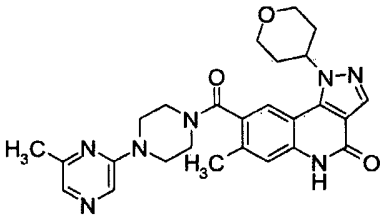
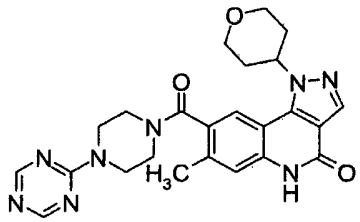
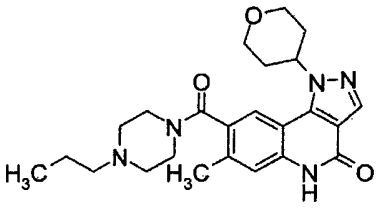
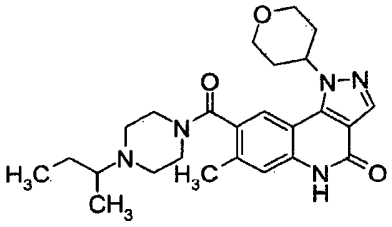
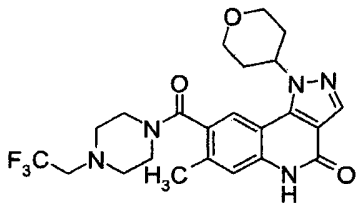
Ex	Structure
422	
423	
424	
425	
426	
427	

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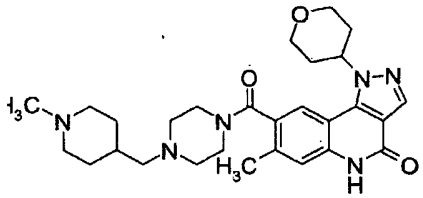
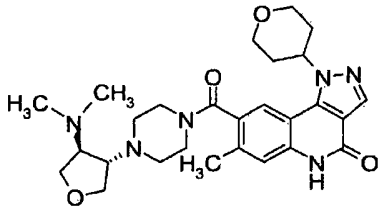
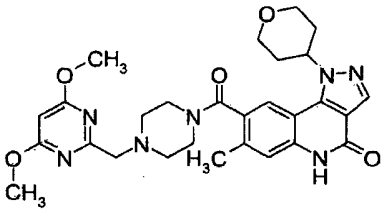
428	
429	
430	

[Table 77]

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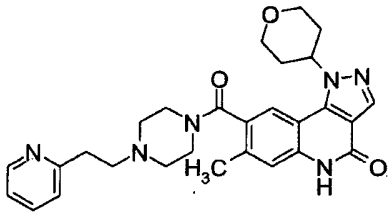
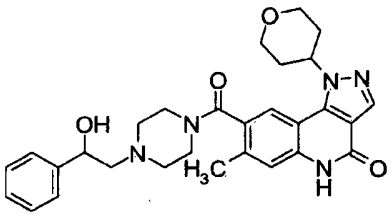
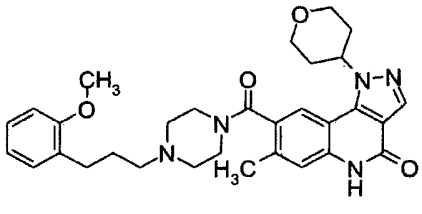
431	
432	
433	

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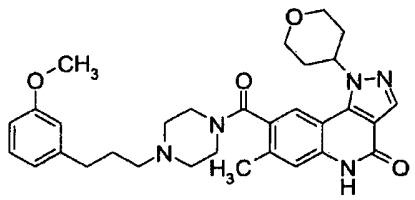
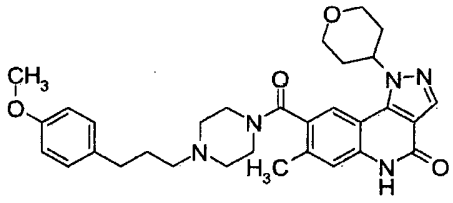
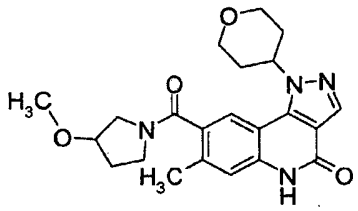
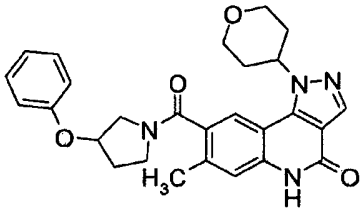
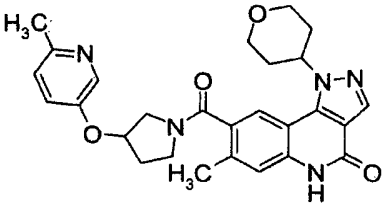
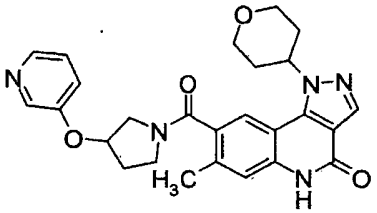
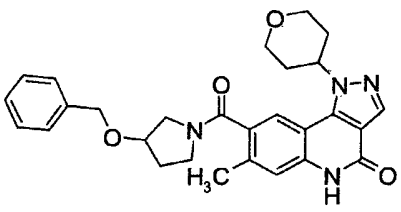
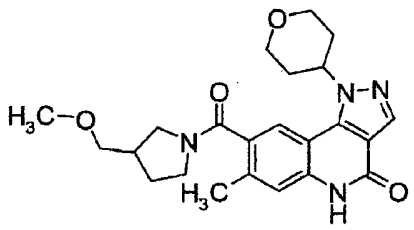
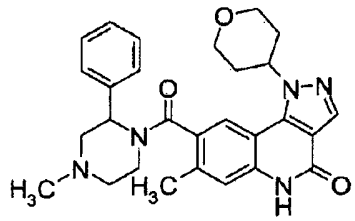
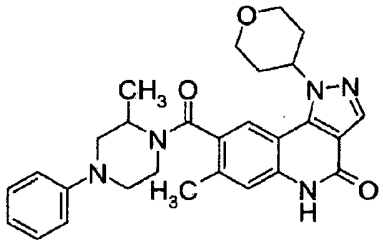
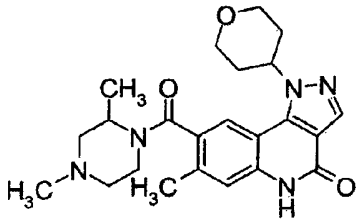
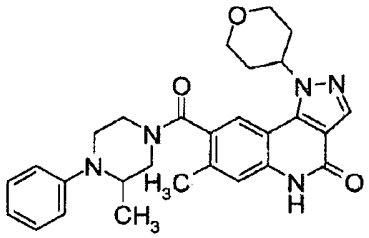
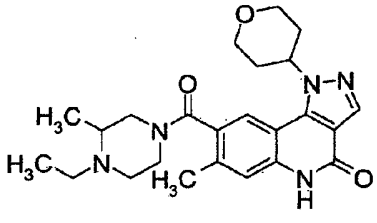
Ex	Structure
434	
435	
436	
437	
438	
439	
440	

[Table 78]

Ex	Structure
441	
442	
443	
444	
445	
446	

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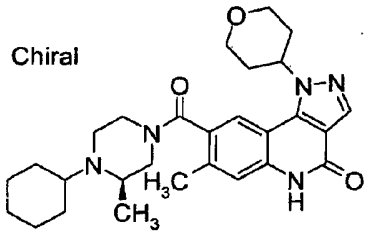
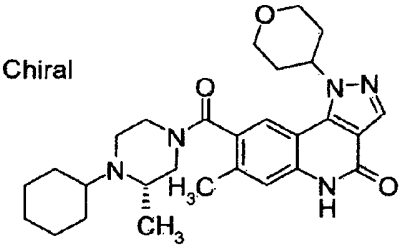
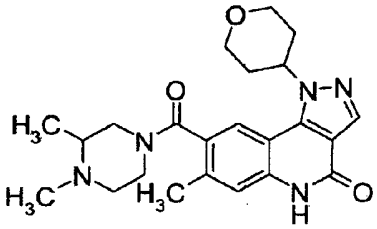
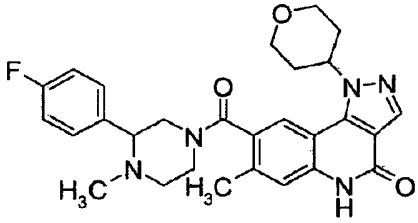
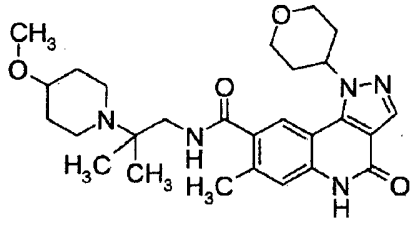
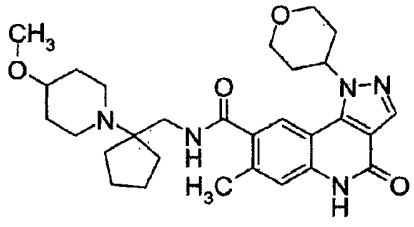
447	
448	
449	
450	

[Table 79]

Ex	Structure
451	
452	

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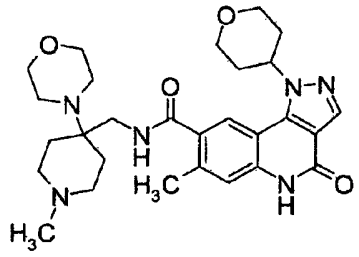
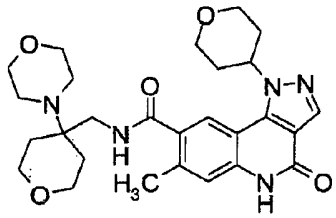
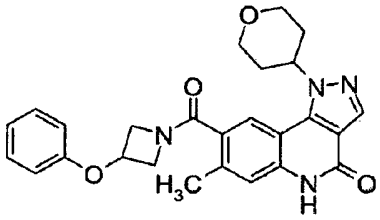
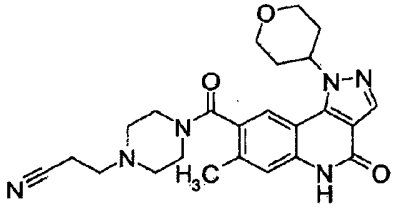
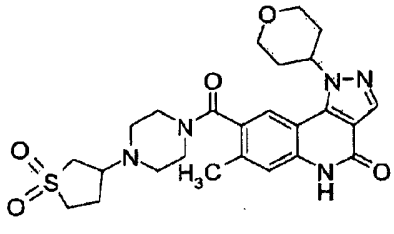
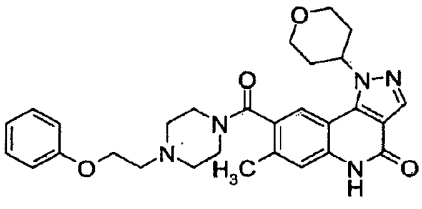
453	
454	
455	
456	
457	
458	

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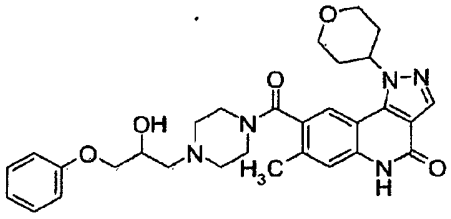
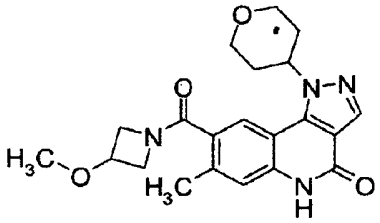
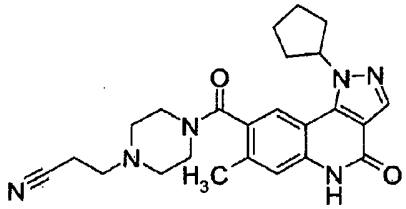
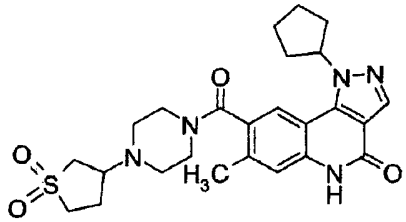
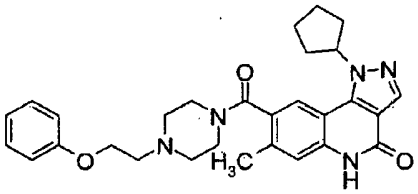
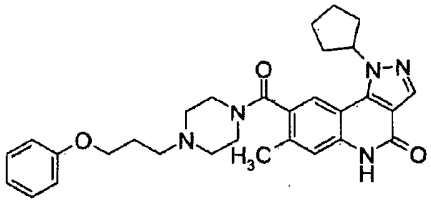
Ex	Structure
459	
460	

[Table 80]

Ex	Structure
461	
462	
463	
464	

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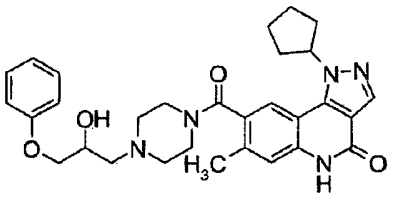
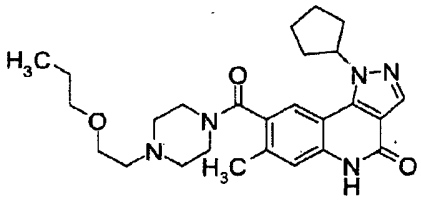
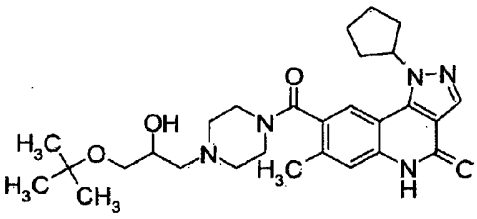
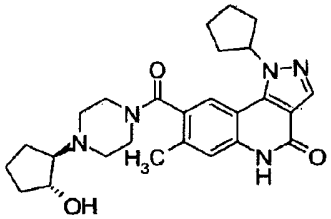
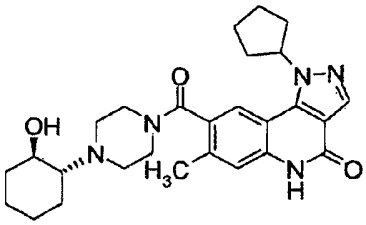
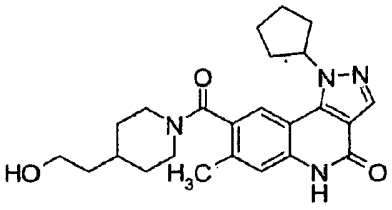
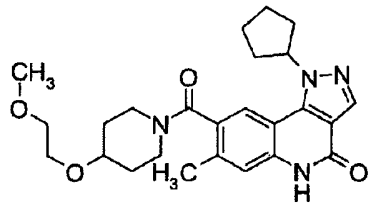
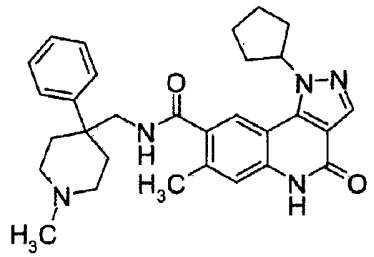
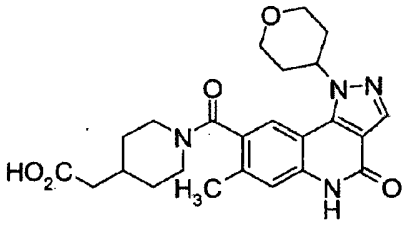
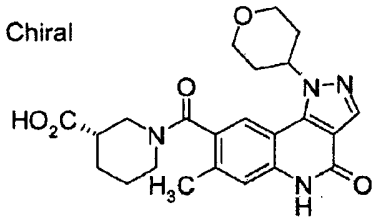
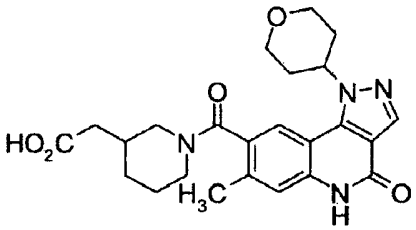
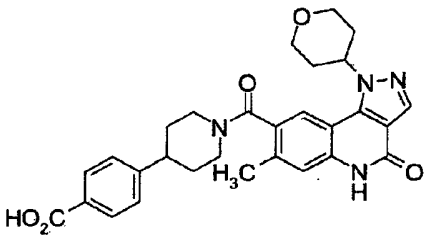
465	
466	
467	
468	
469	
470	

[Table 81]

Ex	Structure
471	
472	
473	
474	Chiral 
475	
476	

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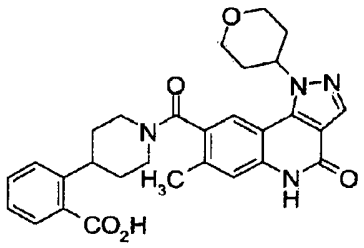
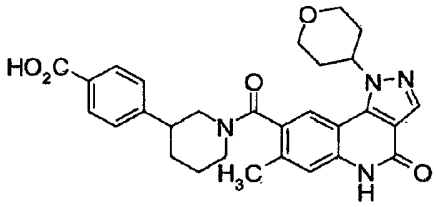
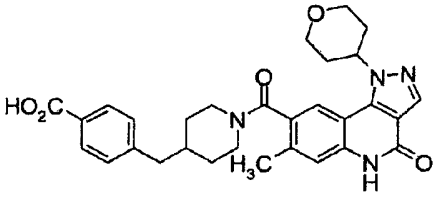
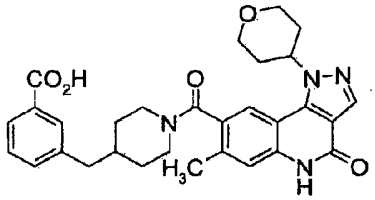
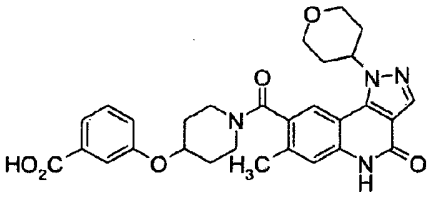
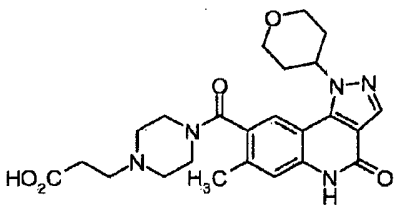
Ex	Structure
477	
478	
479	
480	

[Table 82]

Ex	Structure
481	
482	

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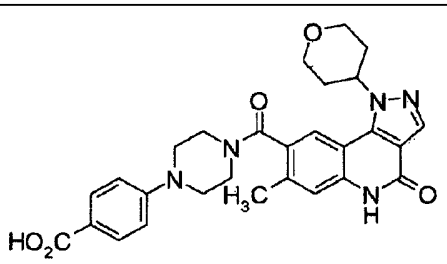
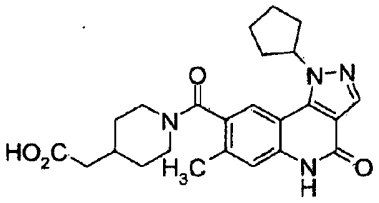
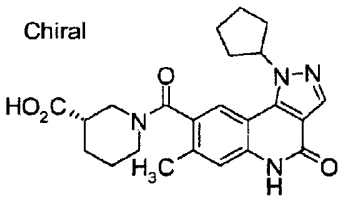
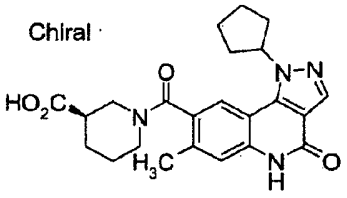
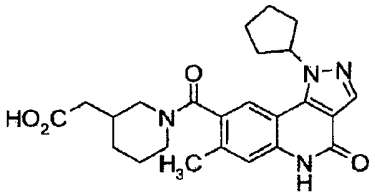
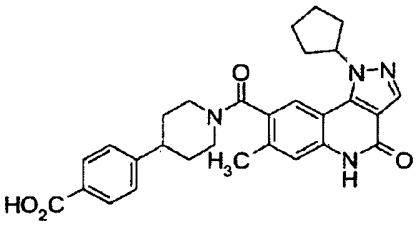
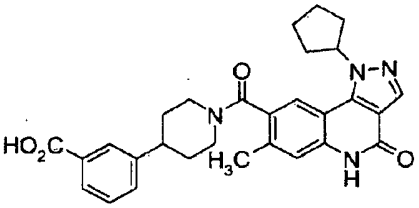
Ex	Structure
483	
484	
485	Chiral 
486	Chiral 
487	
488	
489	

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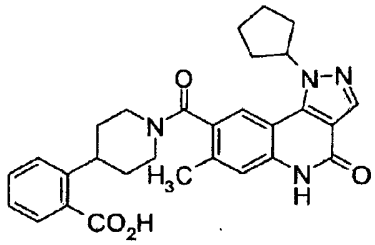
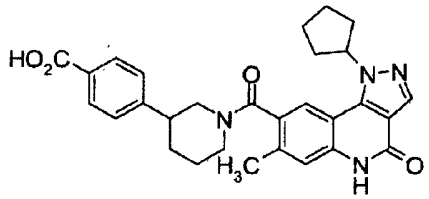
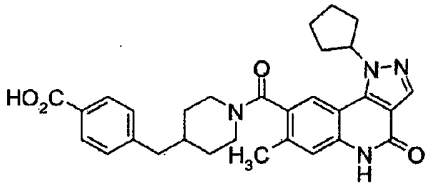
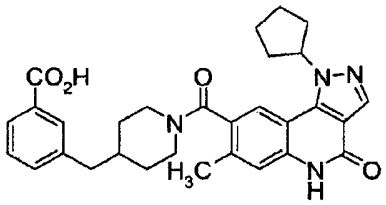
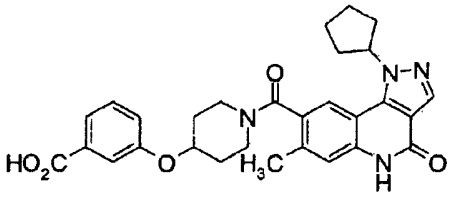
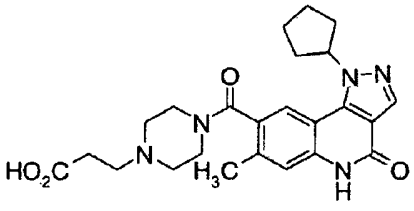
Ex	Structure
490	

[Table 83]

Ex	Structure
491	
492	
493	
494	
495	

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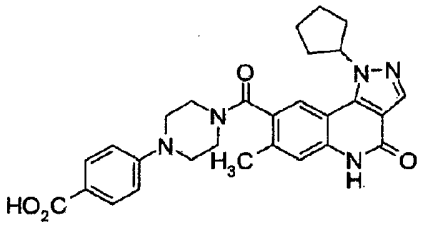
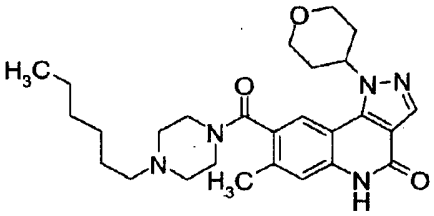
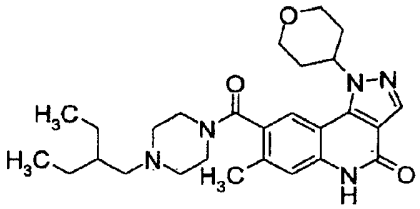
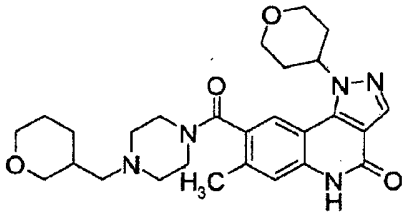
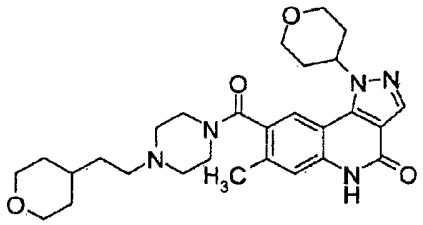
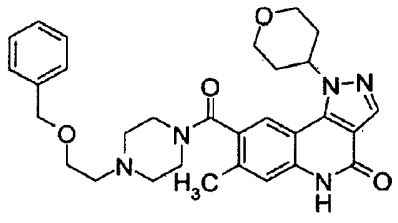
Ex	Structure
496	
497	
498	
499	
500	

[Table 84]

Ex	Structure
501	

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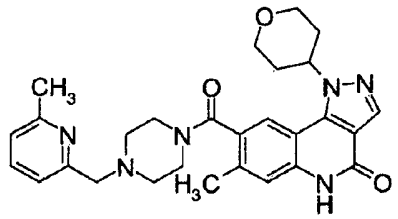
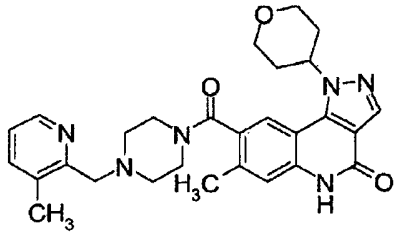
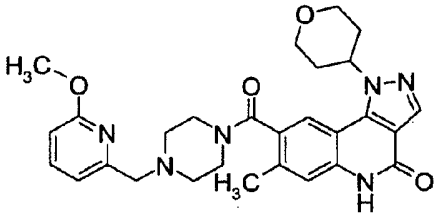
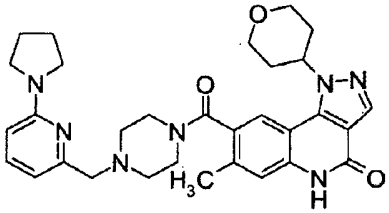
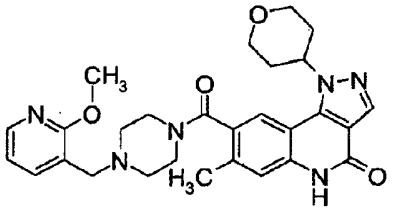
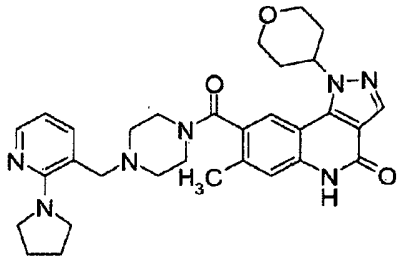
Ex	Structure
502	
503	
504	
505	
506	
507	

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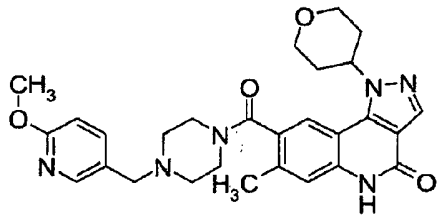
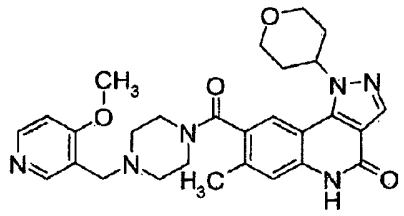
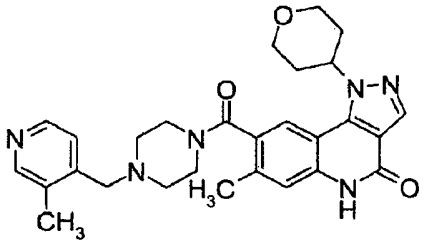
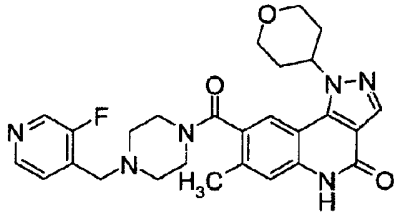
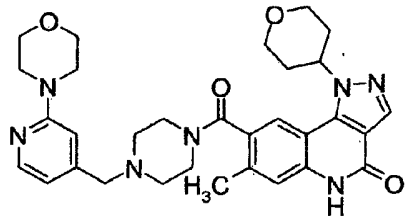
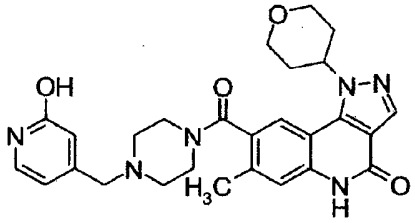
Ex	Structure
508	
509	
510	

[Table 85]

Ex	Structure
511	
512	
513	

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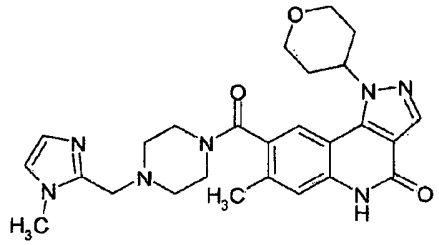
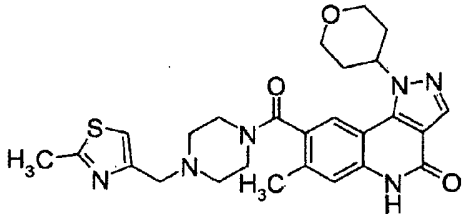
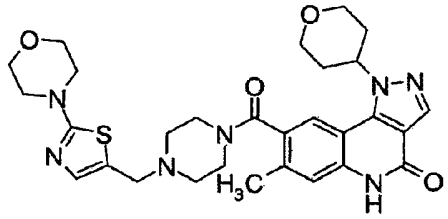
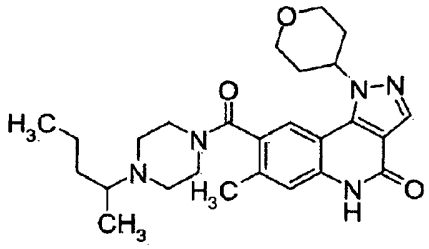
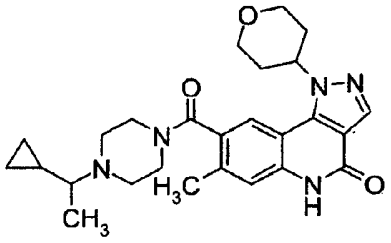
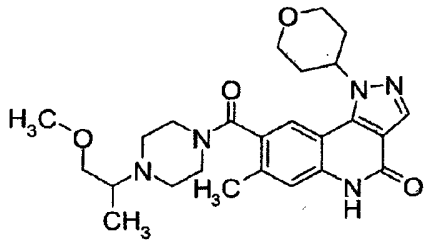
Ex	Structure
514	
515	
516	
517	
518	
519	

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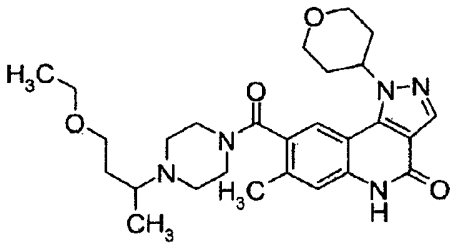
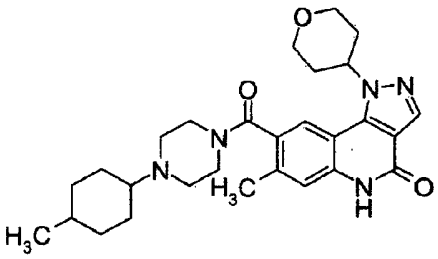
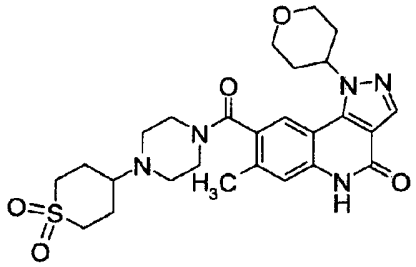
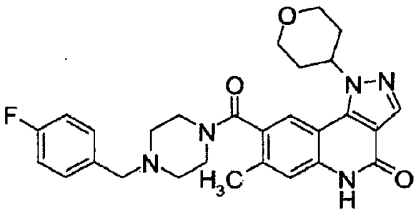
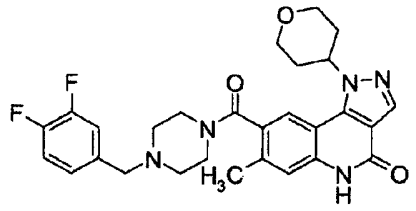
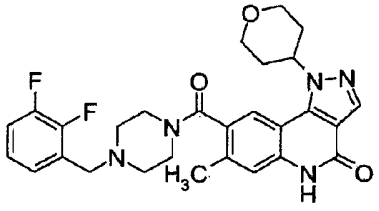
Ex	Structure
520	

[Table 86]

Ex	Structure
521	
522	
523	
524	
525	

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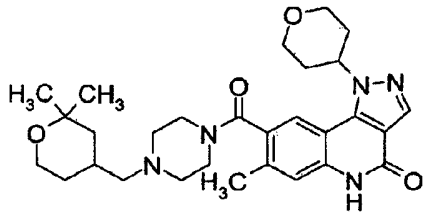
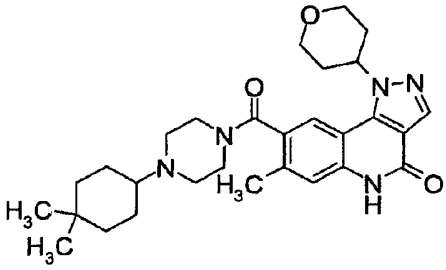
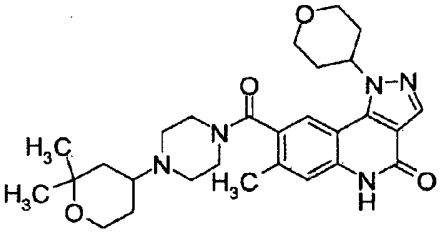
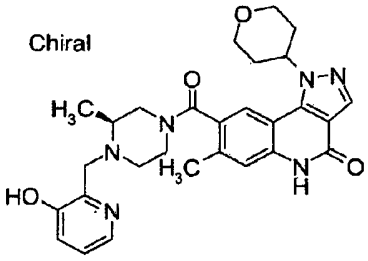
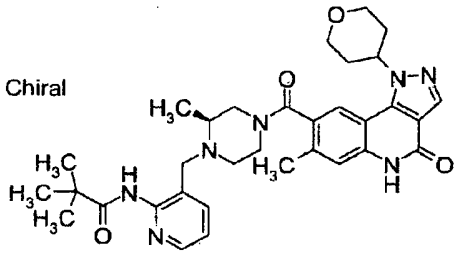
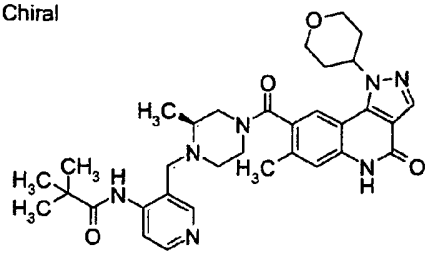
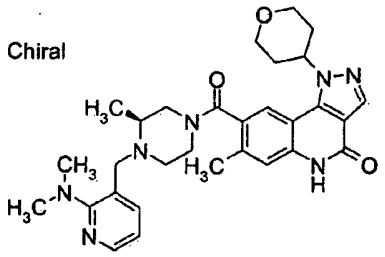
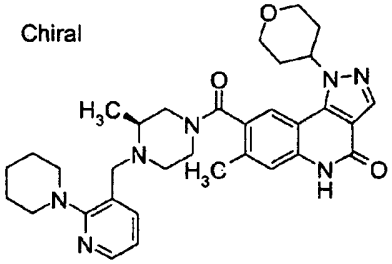
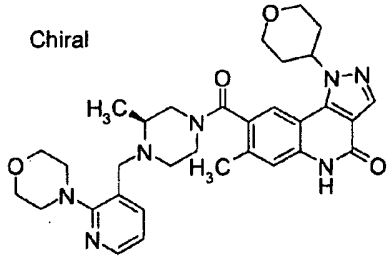
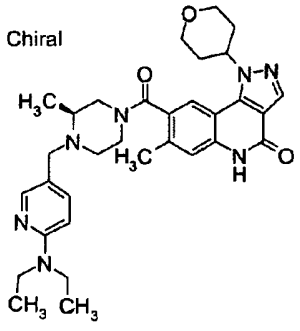
526	
527	
528	
529	
530	

[Table 87]

Ex	Structure
531	Chiral 
532	Chiral 
533	Chiral 
534	Chiral 
535	Chiral 

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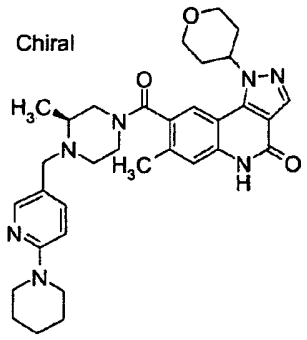
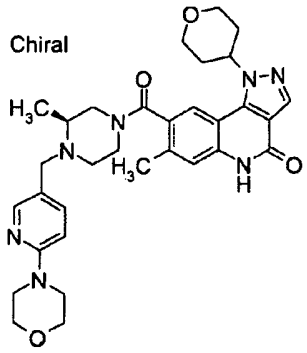
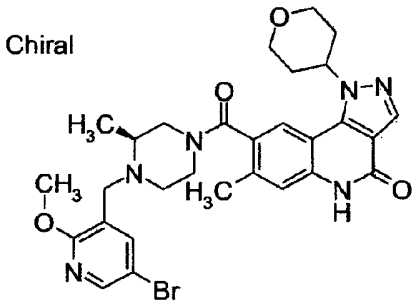
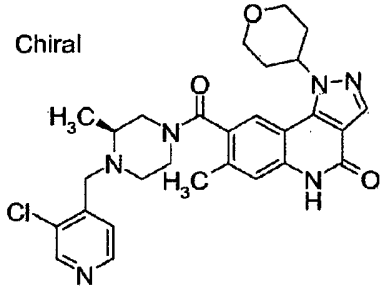
536	
537	

[Table 88]

Ex	Structure
538	
539	

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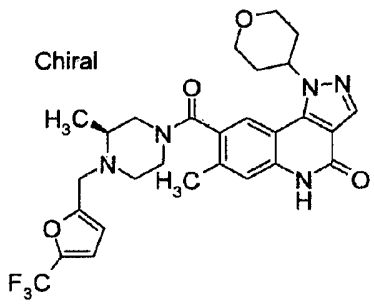
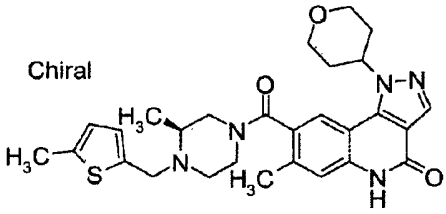
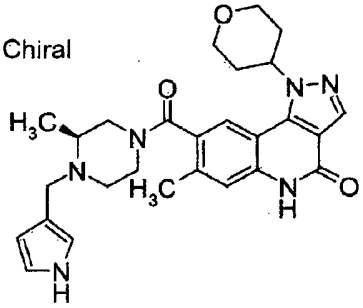
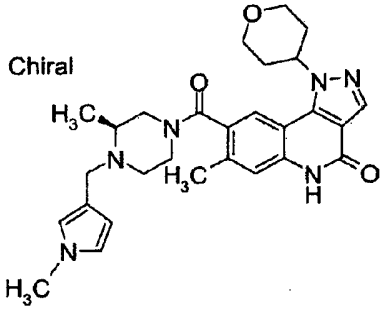
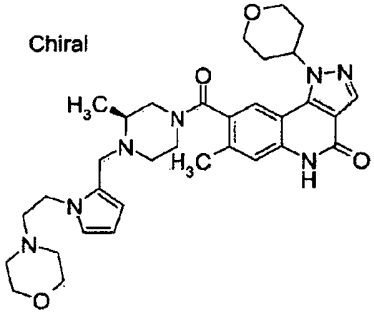
540	
541	
542	
543	
544	

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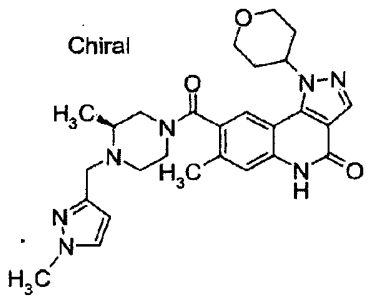
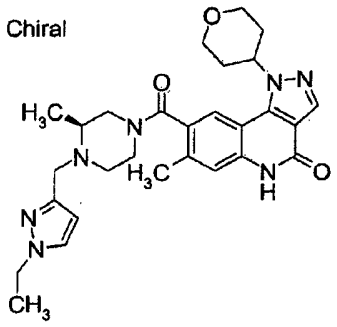
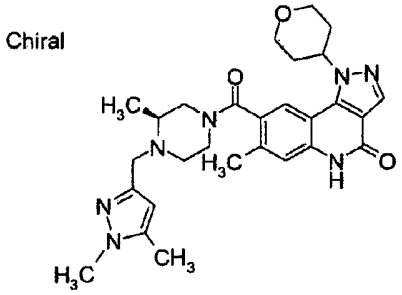
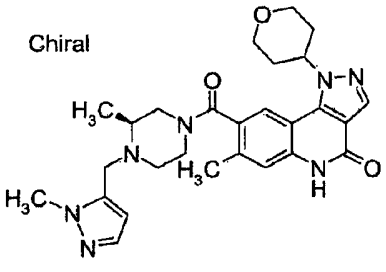
545	

[Table 89]

Ex	Structure
546	
547	
548	

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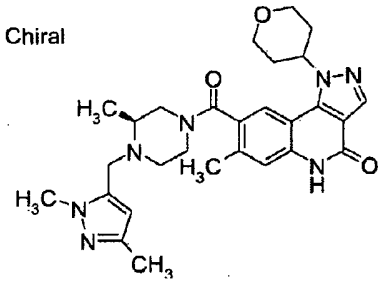
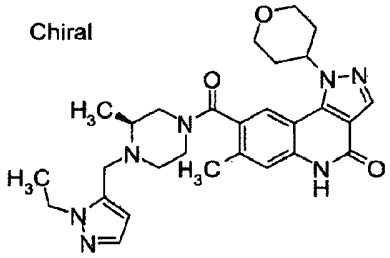
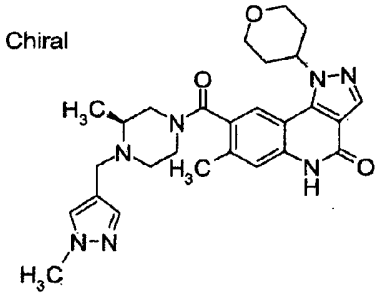
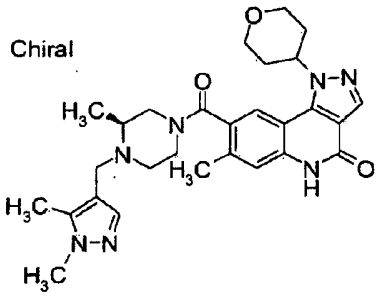
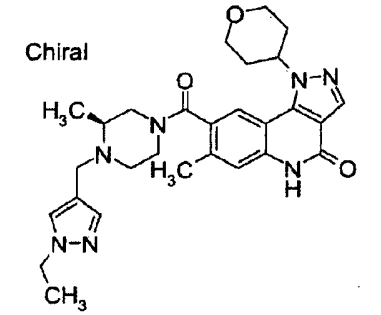
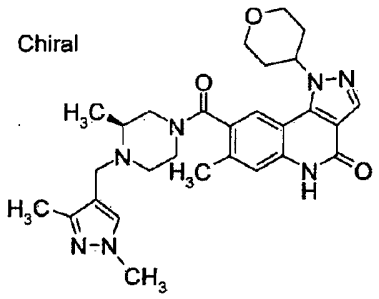
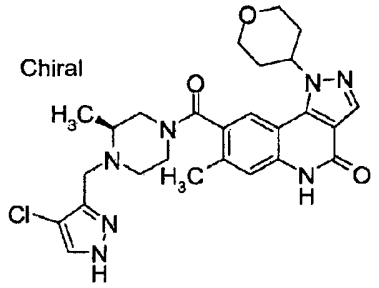
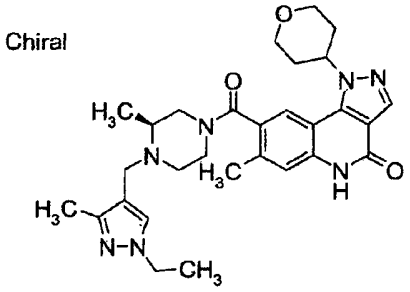
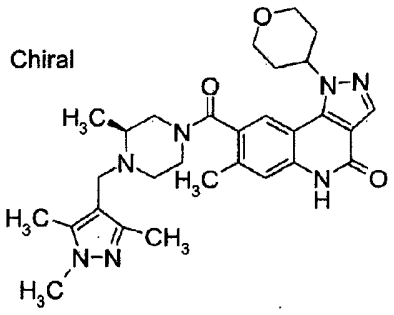
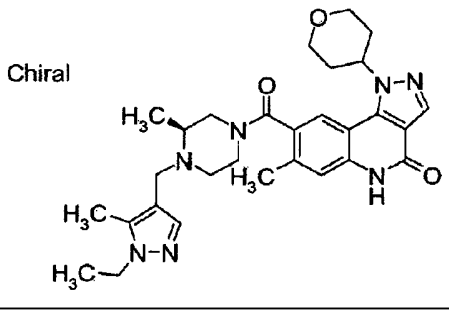
549	
550	
551	
552	
553	

[Table 90]

Ex	Structure
554	
555	
556	
557	
558	

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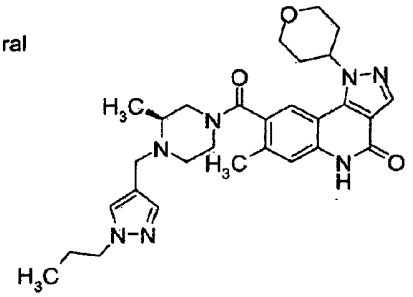
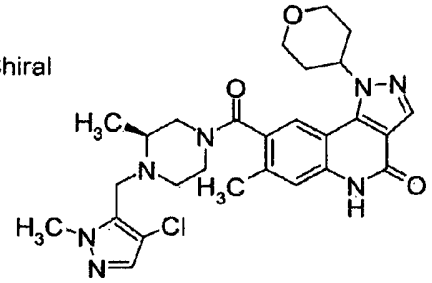
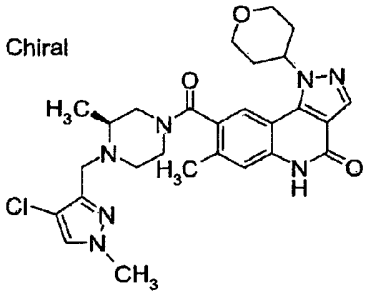
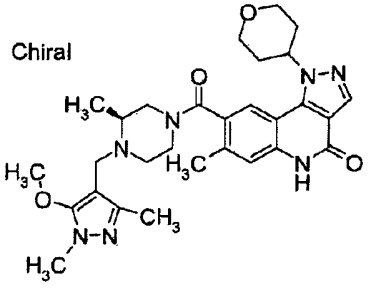
Ex	Structure
559	Chiral 
560	Chiral 
561	Chiral 

[Table 91]

Ex	Structure
562	Chiral 

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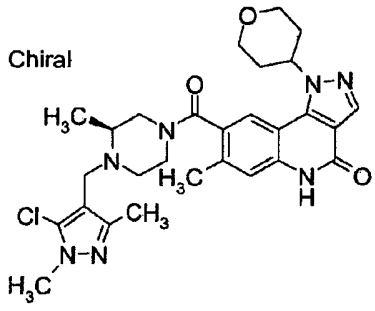
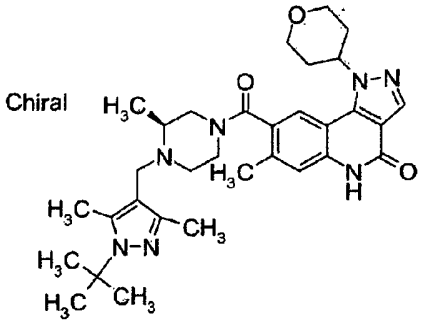
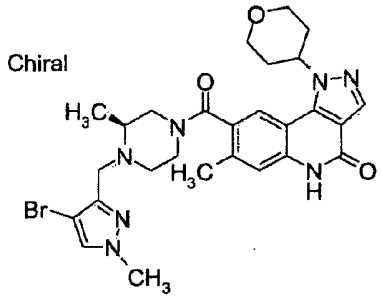
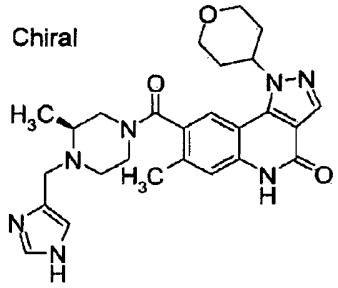
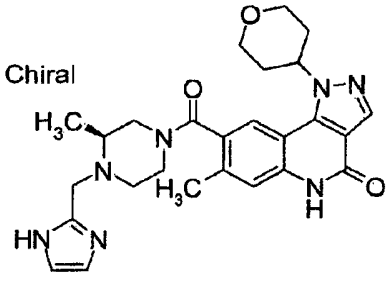
Ex	Structure
563	
564	
565	
566	
567	

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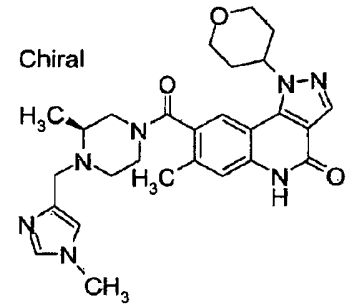
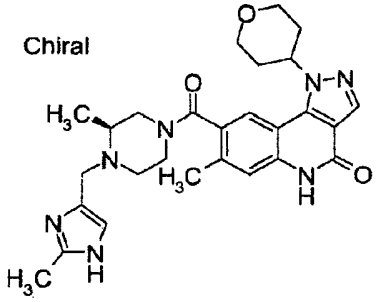
568	
569	

[Table 92]

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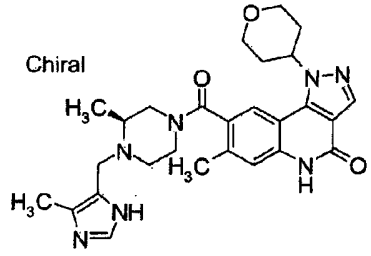
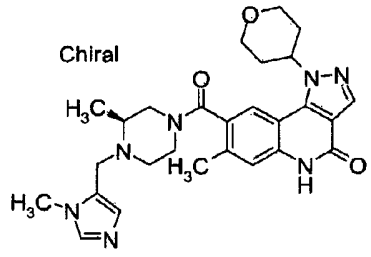
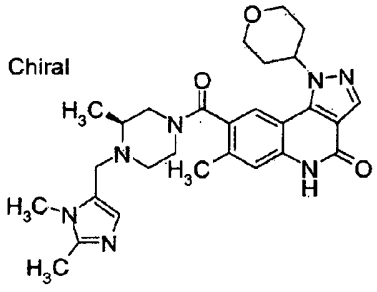
570	
571	
572	

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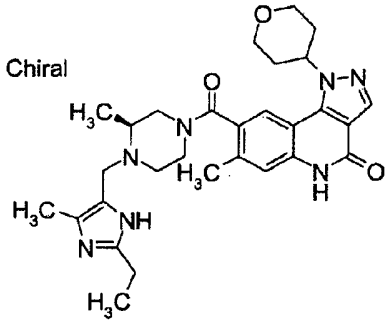
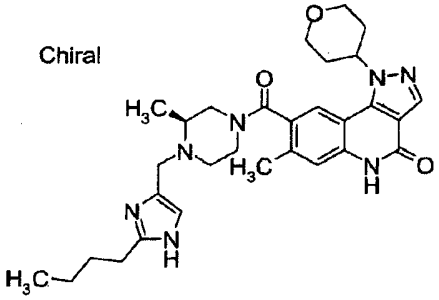
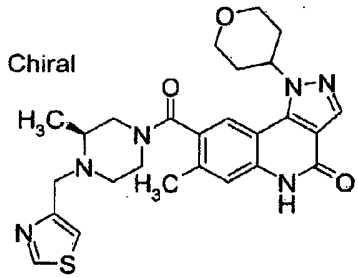
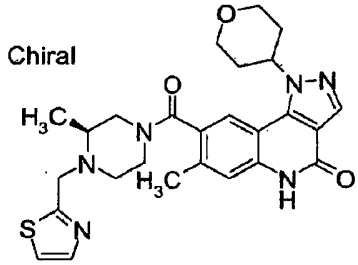
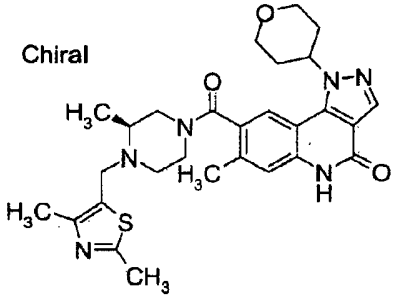
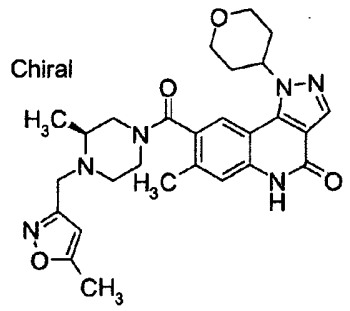
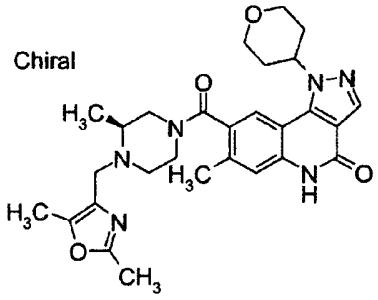
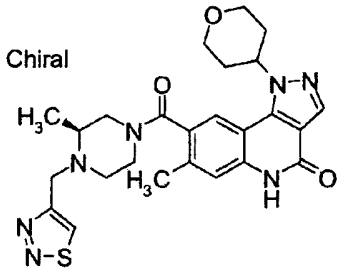
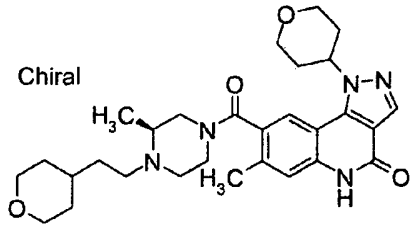
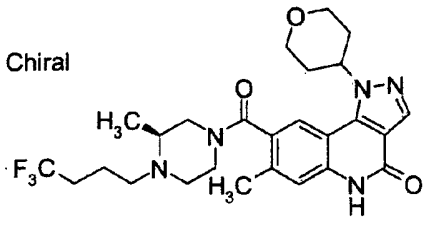
573	
574	
575	
576	
577	

[Table 93]

Ex	Structure
578	
579	
580	
581	
582	

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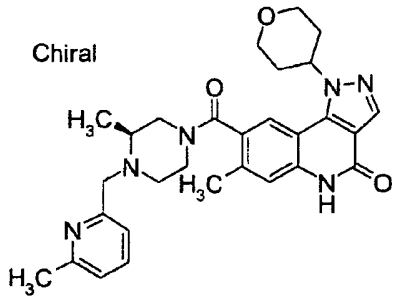
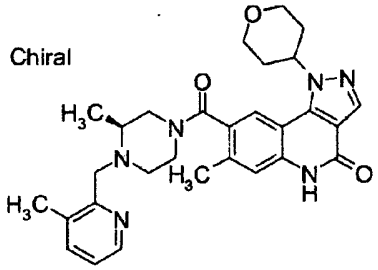
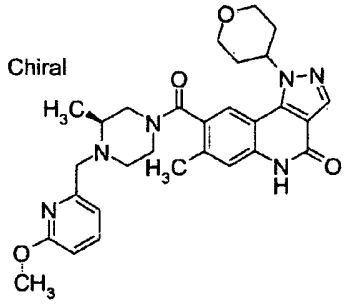
583	
584	
585	

[Table 94]

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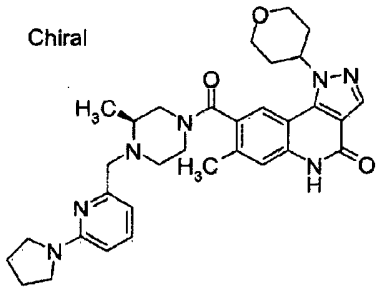
586	

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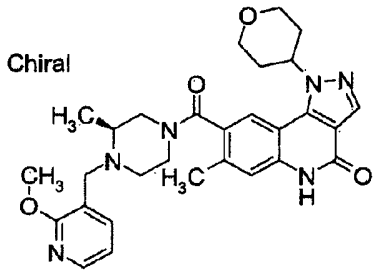
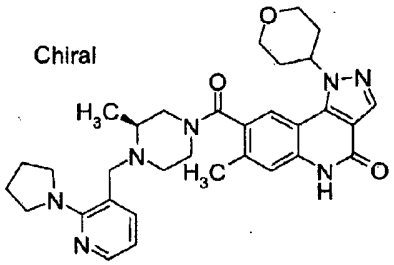
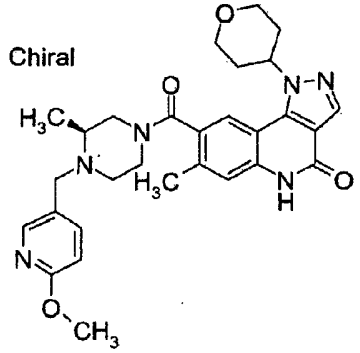
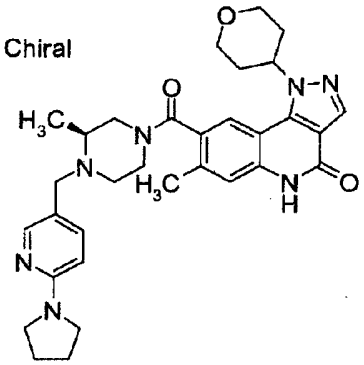
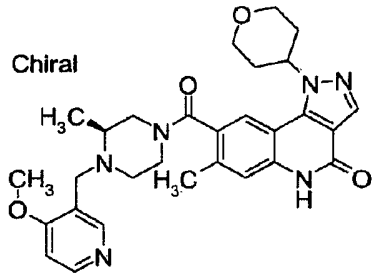
587	
588	
589	
590	
591	

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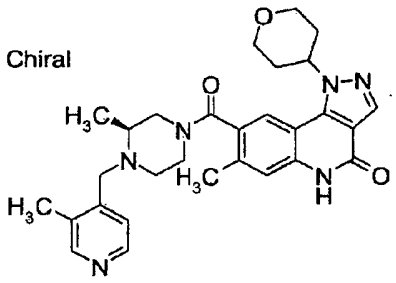
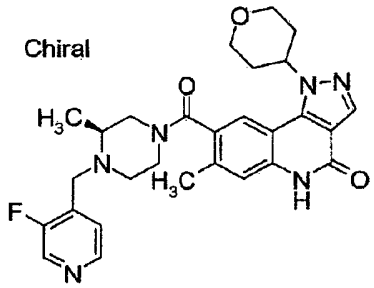
592	
593	

[Table 95]

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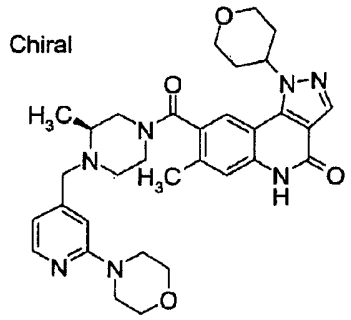
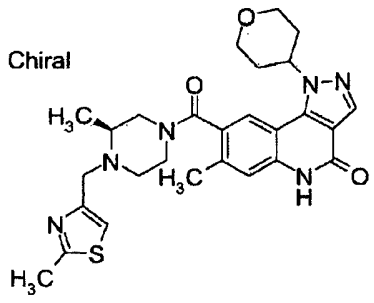
594	
595	

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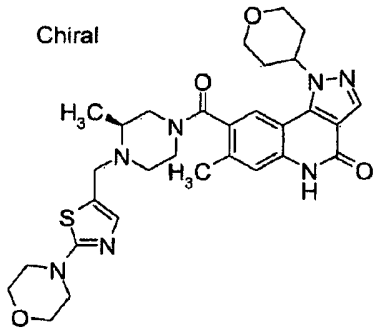
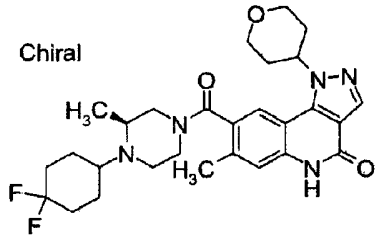
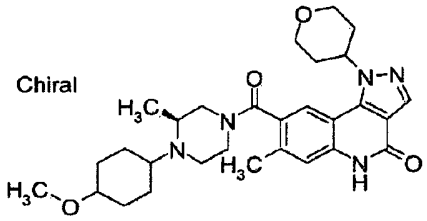
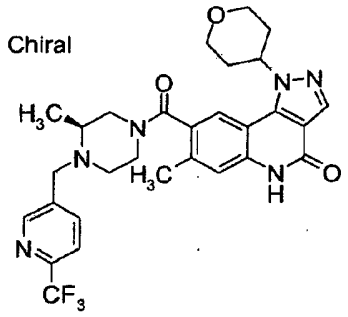
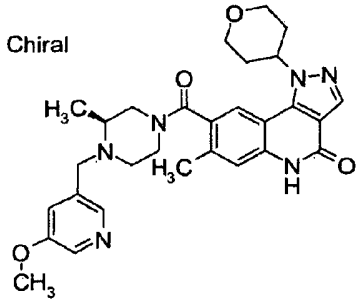
596	
597	
598	
599	
600	

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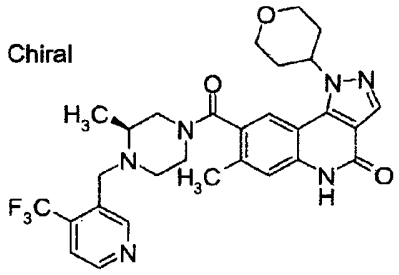
601	

[Table 96]

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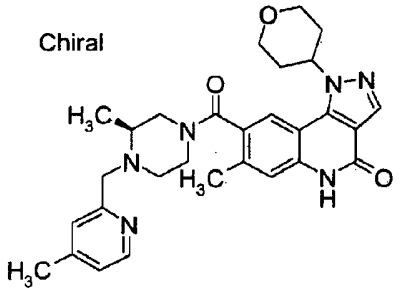
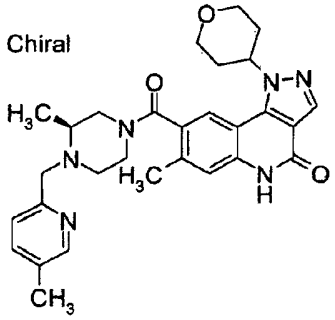
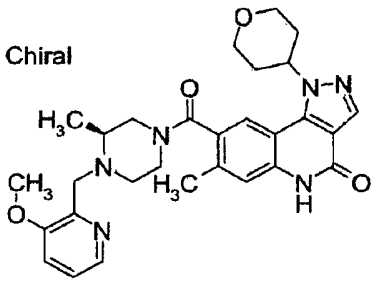
602	
603	
604	

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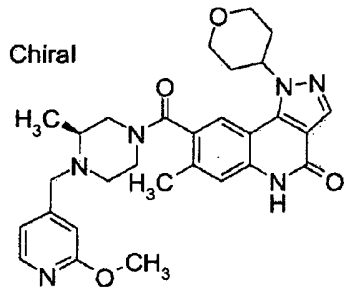
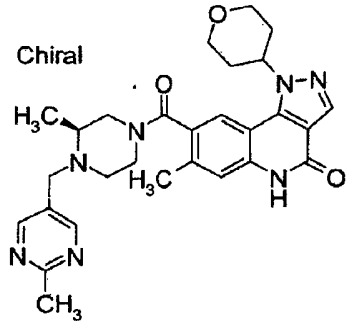
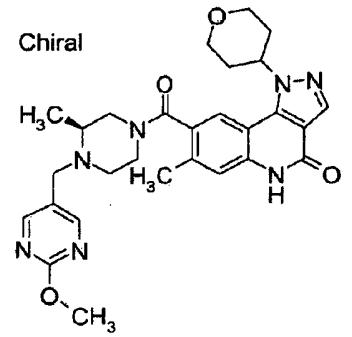
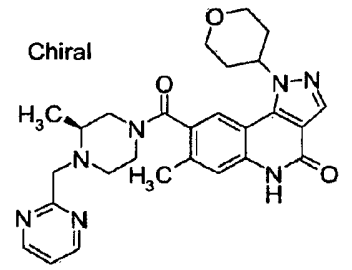
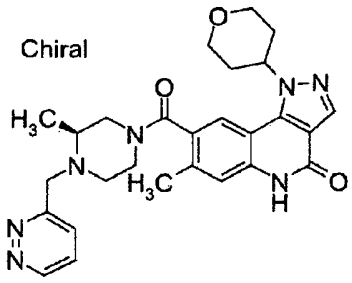
605	
606	
607	
608	
609	

[Table 97]

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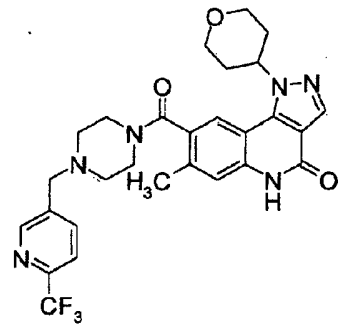
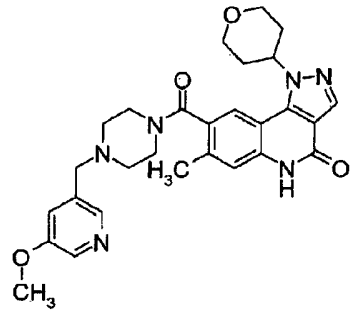
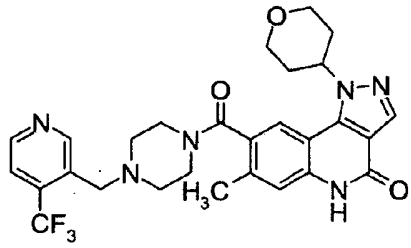
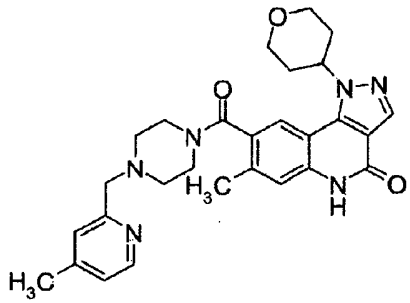
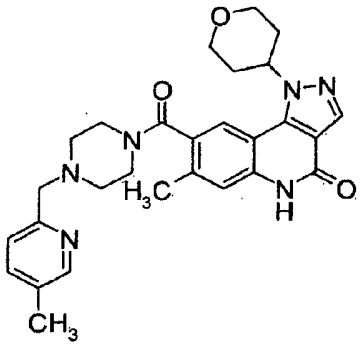
610	
611	
612	
613	
614	

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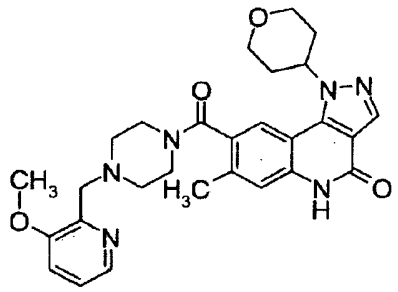
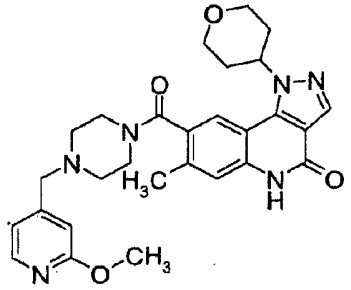
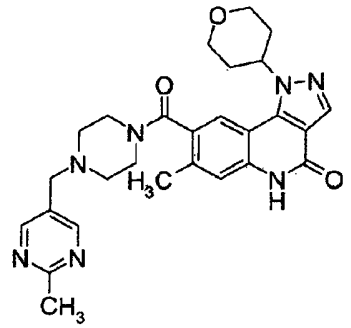
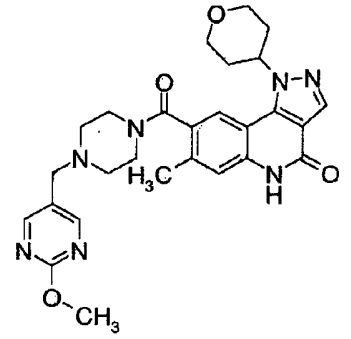
615	
616	

[Table 98]

Ex	Structure
617	
618	

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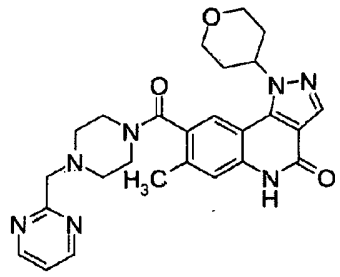
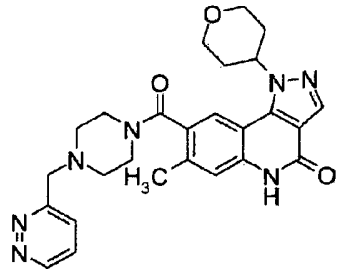
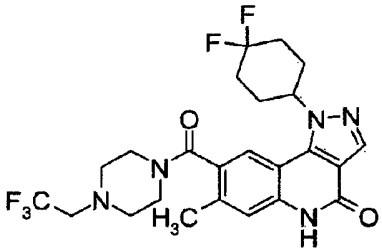
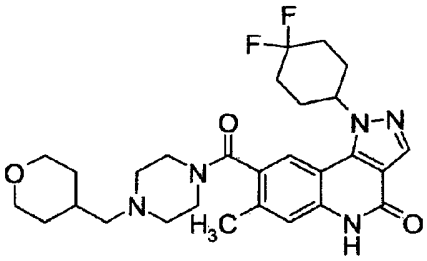
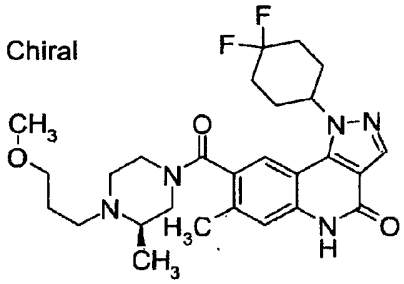
619	
620	
621	
622	
623	Chiral 

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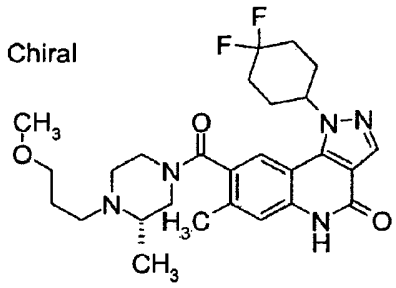
624	

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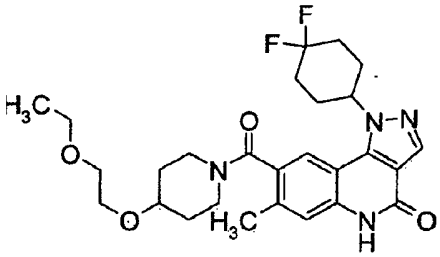
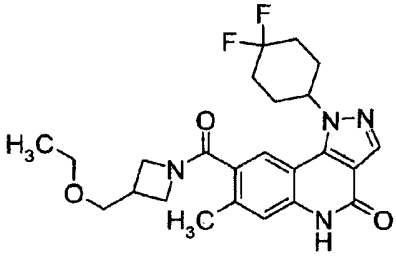
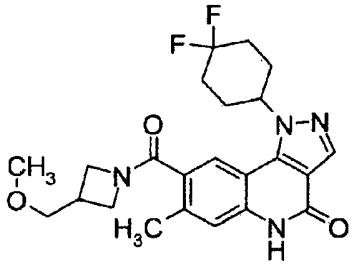
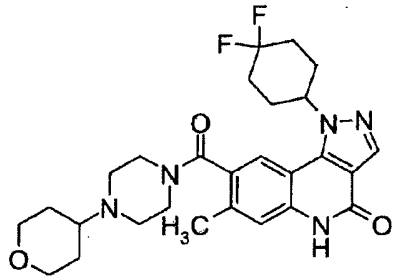
625	
626	
627	
628	

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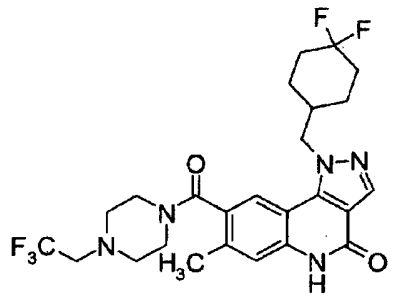
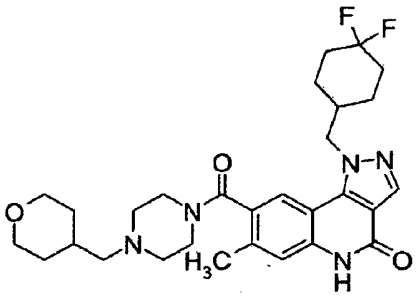
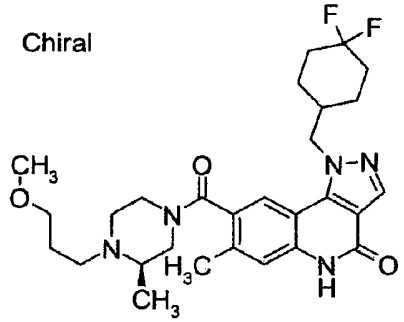
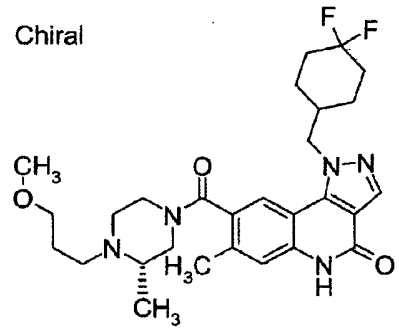
629	
630	
631	Chiral 
632	Chiral 

[Table 100]

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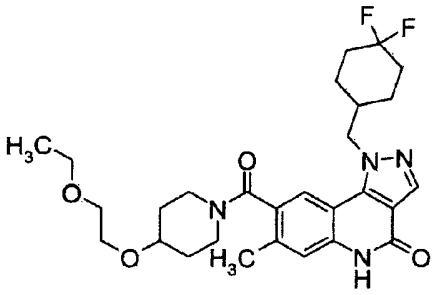
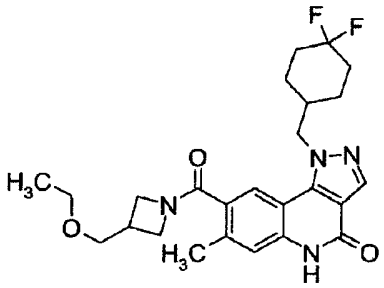
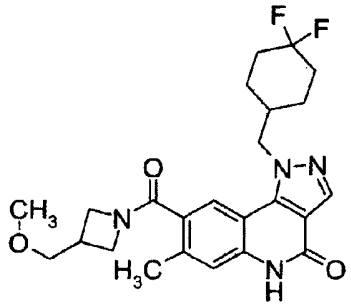
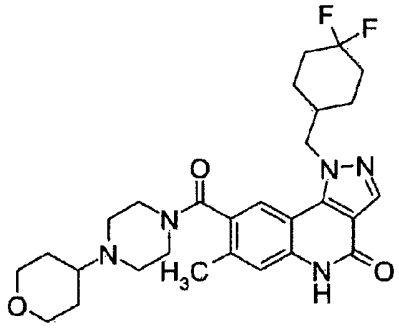
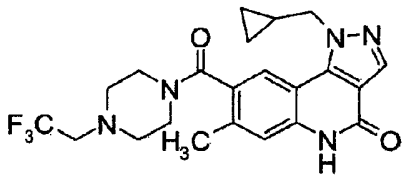
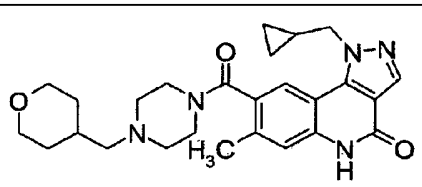
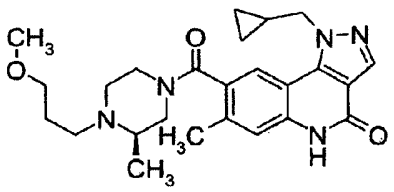
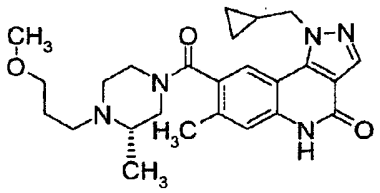
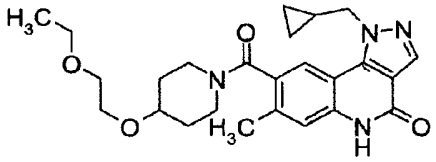
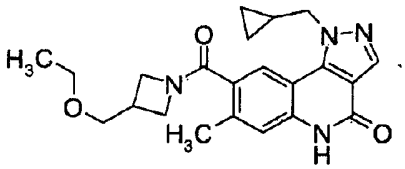
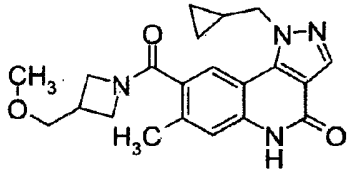
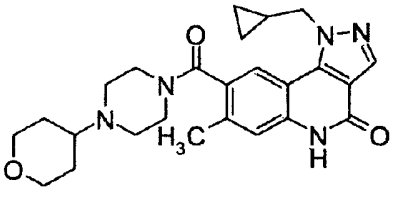
633	
634	
635	
636	
637	

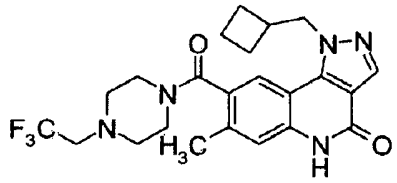
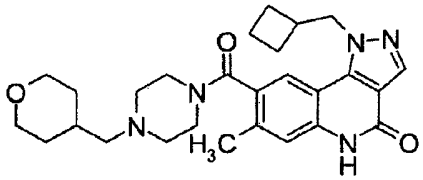
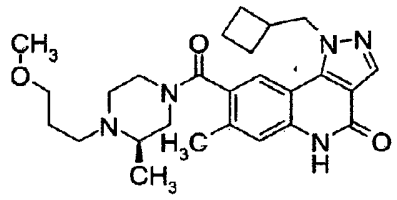
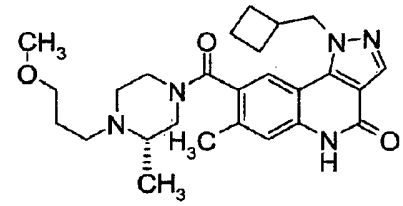
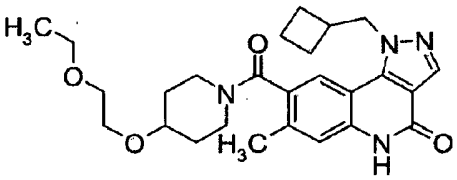
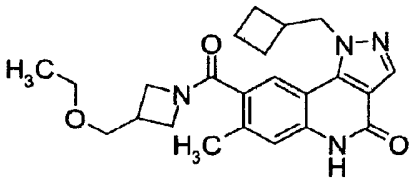
(continued)

Ex	Structure
638	
639	Chiral 
640	Chiral 
641	

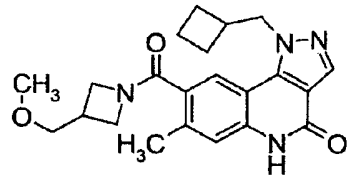
[Table 101]

Ex	Structure
642	
643	
644	

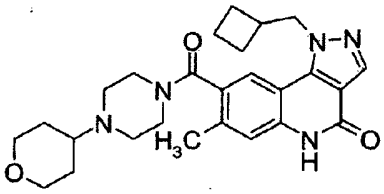
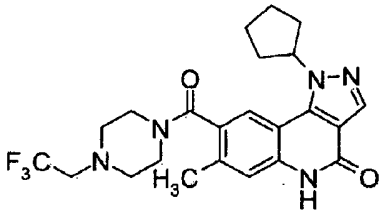
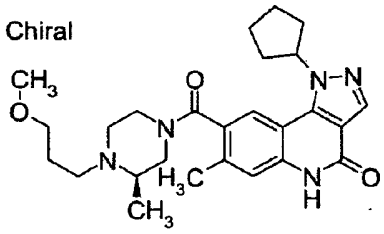
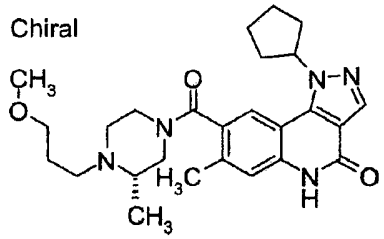
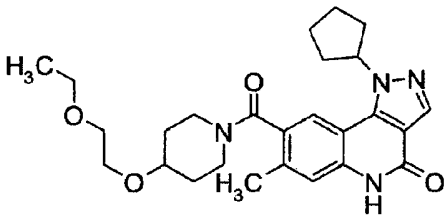
(continued)

Ex	Structure
645	
646	
647	Chiral 
648	Chiral 
649	
650	

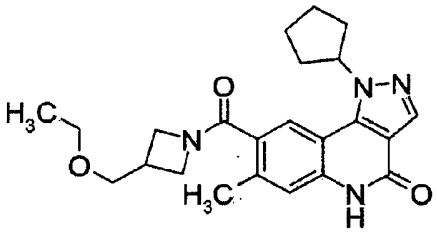
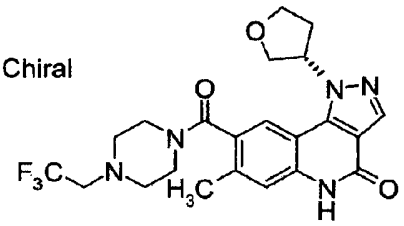
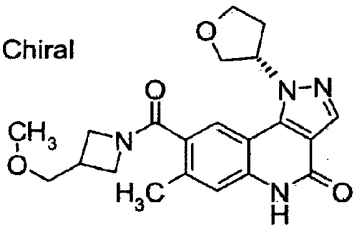
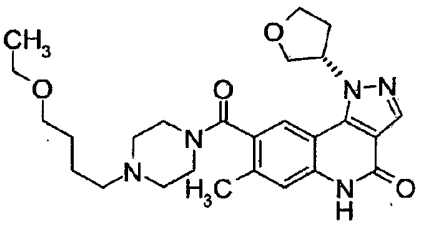
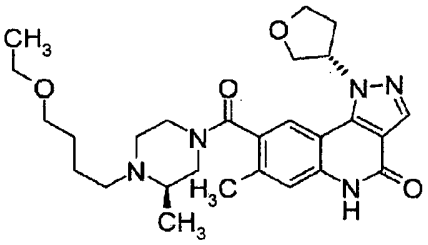
(continued)

Ex	Structure
651	

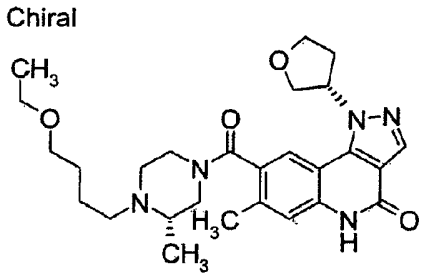
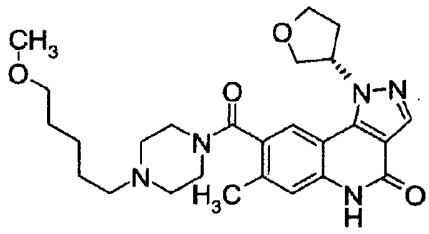
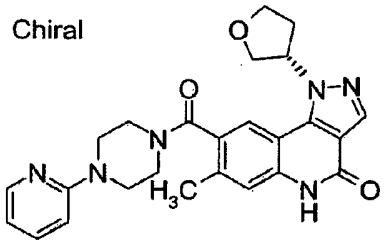
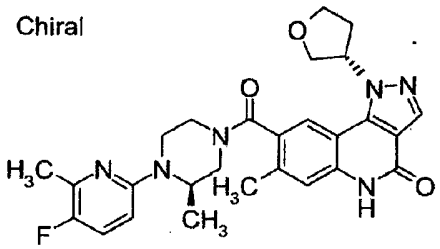
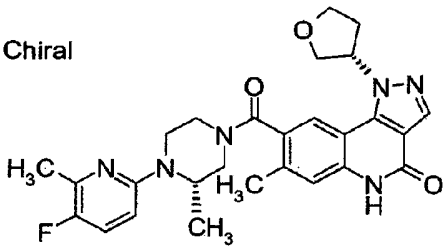
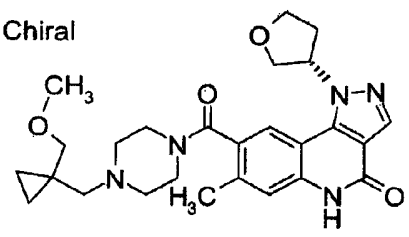
[Table 102]

Ex	Structure
652	
653	
654	
655	
656	

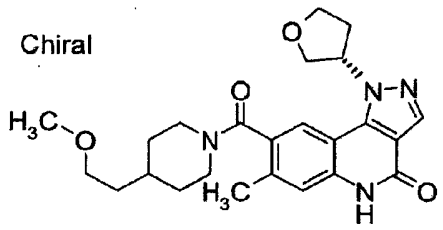
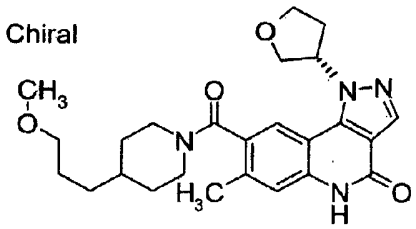
(continued)

Ex	Structure
657	
658	Chiral 
659	Chiral 
660	Chiral 
661	Chiral 

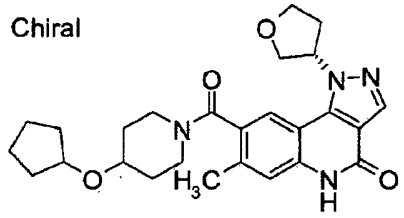
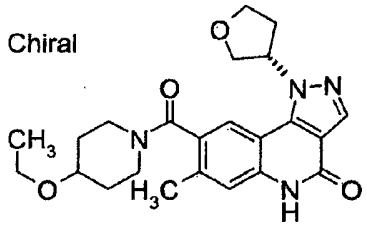
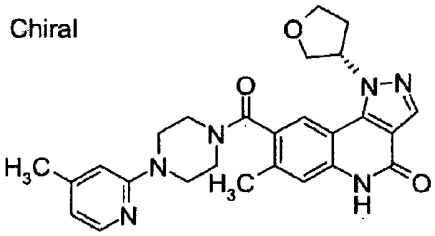
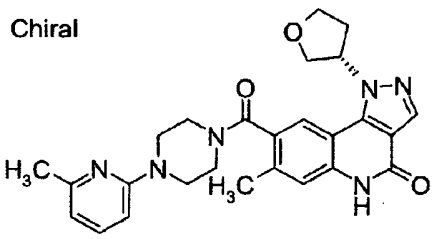
[Table 103]

Ex	Structure
662	
663	
664	
665	
666	
667	

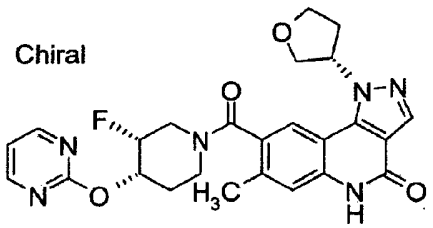
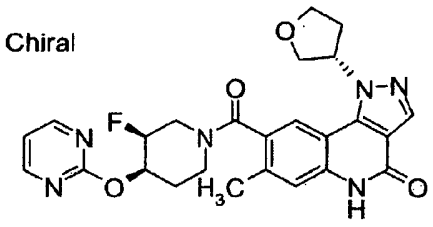
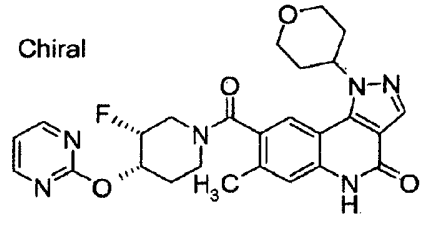
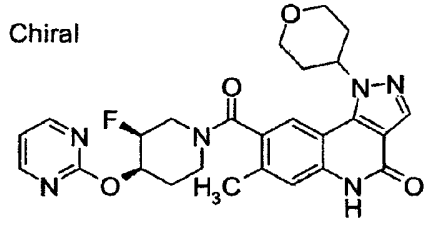
(continued)

Ex	Structure
668	
669	

[Table 104]

Ex	Structure
670	
671	
672	
673	

(continued)

Ex	Structure
674	
675	
676	
677	

[Table 105]

Ex	Syn	Data
1	1	ESI+: 433.2, 435.2 NMR-DMSO-d6: 1.65-1.95 (4H, m), 2.10-2.30 (4H, m), 3.12 (2H, t, J = 8.0 Hz), 4.07 (2H, t, J = 8.0 Hz), 5.5-5.6 (1H, m), 7.36 (1H, s), 7.51 (1H, d, J = 9.0 Hz), 7.64 (1H, s), 8.18 (1H, s), 8.37 (1H, d, J = 9.0 Hz), 11.58 (1H, s) mp: 291-294
2	2	ESI+: 487.4 NMR-DMSO-d6: 1.82-2.43 (4H, m), 2.50 (3H, s), 2.83-3.86 (10H, m), 3.86-4.12 (2H, m), 4.29-4.56 (2H, m), 5.16-5.33 (1H, m), 7.35 (1H, s), 7.64-7.71 (1H, m), 7.98 (1H, s), 8.18 (1H, s), 8.25 (1H, d, J = 6.9 Hz), 8.74 (1H, d, J = 5.2 Hz), 8.85 (1H, s), 11.54 (1H, s) mp: 259-263
3	3	ESI+: 438.1
4	4	ESI+:438.4 NMR-DMSO-d6: 0.89-1.92 (8H, m), 2.19-2.36 (3H, m), 2.54-2.58 (2H, m), 2.71-2.90 (1H, m), 2.90-3.09 (1H, m), 3.14-4.24 (9H, m), 4.50-4.64 (1H, m), 5.93-6.01 (1H, m), 7.36 (1H, s), 7.91 (1H, s), 8.24 (1H, s), 9.14-9.32 (1H, br s), 9.50-9.66 (1H, br s), 11.57 (1H, s)

(continued)

Ex	Syn	Data
5	5	ESI+: 466.3 NMR-DMSO-d6: 1.11 (6H, d, J = 6.1 Hz), 1.70-1.91 (4H, m), 2.02-2.40 (7H, m), 2.89-3.20 (1H, m), 3.24-3.44 (5H, m), 3.48-3.65 (4H, m), 3.76 (2H, m), 4.63 (1H, br.), 5.52 (1H, m), 7.35 (1H, s), 8.07 (1H, s), 8.13 (1H, s), 10.79-11.08 (1H, br.), 11.51 (1H, s)
6	6	ESI+: 439.3 NMR-DMSO-d6: 1.20-2.77 (8H, m), 2.29 (3H, s), 2.90-4.62 (9H, m), 5.13-5.35 (1H, m), 7.33 (1H, s), 7.82-7.99 (1H, br.), 8.17 (1H, s), 11.50 (1H, s), 12.23-12.53 (1H, br.)
7	7	ESI+:452.3 NMR-DMSO-d6: 0.81-1.94 (8H, m), 2.16-4.39 (19H, m), 4.48-4.72 (1H, m), 5.95-6.13 (1H, m), 7.36 (1H, s), 7.91 (1H, s), 8.26 (1H, s), 11.58 (1H, s) mp: 195
8	8	ESI+:515.0
9	9	ESI+: 556.2
10	10	ESI+: 586.2
11	1	ESI+: 457.3 NMR-DMSO-d6: 1.5-2.3 (8H, m), 3.6-3.8 (2H, m), 3.94-4.06 (2H, m), 4.45-4.65 (1H, m), 5.18-5.34 (1H, m), 7.08-7.40 (6H, m), 7.50 (1H, s), 8.16-8.33 (2H, m), 11.59 (1H, s) mp: 298-301

[Table 106]

Ex	Syn	.Data
12	1	ESI+: 449.2, 451.2 NMR-DMSO-d6: 2.03-2.28 (4H, m), 3.12 (2H, t, J = 7.8 Hz), 3.66-3.76 (2H, m), 3.97-4.13 (4H, m), 5.24-5.36 (1H, m), 7.15-7.6 (4H, m), 7.64 (1H, s), 8.23 (1H, s), 8.31 (1H, d, J = 8.3 Hz), 11.61 (1H, s) mp: 341-343
13	1	ESI+: 472.2 NMR-DMSO-d6: 1.97 (3H, s), 2.0-2.35 (8H, m), 2.9-3.1 (2H, m), 3.6-3.8 (2H, m), 3.95-4.05 (2H, m), 4.3-4.5 (1H, m), 5.15-5.35 (1H, m), 7.16-7.49 (6H, m), 7.52 (1H, s), 8.13-8.33 (2H, m), 11.58 (1H, s) mp: 183-186
14	1	ESI+: 477.2 NMR-DMSO-d6: 1.97-2.29 (4H, m), 3.45-4.63 (11H, m), 5.19-5.36 (1H, m), 7.05-7.65 (6H, m), 8.14-8.40 (2H, m), 11.60 (1H, s) mp: 293-296
15	1	ESI+: 446.3 NMR-DMSO-d6: 2.04-2.27 (4H, m), 3.09-3.16 (2H, m), 3.66-3.75 (2H, m), 3.84 (3H, s), 3.97-4.11 (4H, m), 5.24-5.34 (1H, m), 6.80 (1H, s), 7.54 (1H, d, J = 7.4 Hz), 7.65 (1H, s), 8.23 (1H, s), 8.31 (1H, d, J = 8.3 Hz), 8.79 (1H, s), 11.62 (1H, s) mp: 337-340
16	2	ESI+: 554.5 NMR-DMSO-d6: 1.13-2.15 (10H, m), 2.29 (3H, s), 2.89-4.09 (10H, m), 4.22-4.34 (2H, m), 5.17-5.33 (1H, m), 7.34 (1H, s), 7.40-7.50 (3H, m), 7.53-7.65 (2H, m), 7.87-7.94 (1H, m), 8.17 (1H, s), 11.50 (1H, s) mp: 221-224

(continued)

Ex	Syn	.Data
17	2	ESI+: 473.2 NMR-DMSO-d6: 1.50-2.60 (4H, m), 2.33 (3H, s), 3.28-4.00 (12H, m), 5.20-5.30 (1H, m), 6.68 (1H, dd, J = 4.8, 7.1 Hz), 6.84 (1H, d, J = 8.7 Hz), 7.35 (1H, s), 7.53-7.59 (1H, m), 7.96 (1H, s), 8.10-8.14 (1H, m), 8.18 (1H, s), 11.52 (1H, s) mp: 272-275
18	1	ESI+: 431.1 NMR-DMSO-d6: 1.68-1.93 (4H, m), 2.10-2.27 (4H, m), 2.53 (3H, s), 3.12 (2H, t, J = 8.2 Hz), 4.07 (2H, t, J = 8.2 Hz), 5.41-5.50 (1H, m), 7.04 (1H, br s), 7.17 (1H, dd, J = 2.7, 8.5 Hz), 7.46 (1H, d, J = 7.8 Hz), 7.59 (1H, s), 8.05 (1H, br), 8.32 (1H, d, J = 8.5 Hz), 11.45 (1H, s) mp: 321-323
19	1	ESI+: 433.3 NMR-DMSO-d6: 2.04-2.14 (2H, m), 2.14-2.29 (2H, m), 3.66-3.77 (2H, m), 3.99-4.06 (2H, m), 4.89 (2H, d, J = 11.3 Hz), 4.96 (2H, s), 5.25-5.35 (1H, m), 7.09-7.19 (1.5H, m), 7.25-7.30 (0.5H, m), 7.32-7.43 (1H, m), 7.53-7.61 (1H, m), 7.66-7.71 (1H, m), 8.23 (1H, s), 8.29-8.34 (1 H, d, J = 8.4 Hz), 11.59 (1H, s) mp 312-318 (dec.)

[Table 107]

Ex	Syn	Data
20	1	ESI+: 477.4 NMR-DMSO-d6: 1.95-2.29 (4H, m), 2.84-4.92 (11H, m), 5.20-5.35 (1H, m), 7.01-7.64 (6H, m), 8.22-8.37 (2H, m), 11.60 (1H, s) mp: 174-176
21	2	ESI+: 486.4 NMR-DMSO-d6: 1.83-2.38 (4H, m), 2.44 (3H, s), 3.00-4.94 (11H, m), 4.16 (3H, s), 5.17-5.43 (1H, m), 7.17-8.26 (8H, m), 11.50, 11.57 (total 1H, both s) mp: 253-256
22	2	ESI+: 488.3 NMR-DMSO-d6: 1.46-2.20 (8H, m), 2.32 (3H, s), 3.15-4.35 (9H, m), 5.21-5.34 (1H, m), 6.77-6.87 (1H, m), 6.98 (1H, t, J = 5.4 Hz), 7.35 (1H, s), 7.73 (1H, dt, J = 2.0, 7.1 Hz), 7.95 (1H, s), 8.13-8.19 (1H, m), 8.17 (1H, s), 11.52 (1H, s) mp:250-253
23	2	ESI+: 508.3 NMR-DMSO-d6: 1.11-2.34 (14H, m), 2.45 (3H, s), 3.21-3.74 (6H, m), 3.80-4.12 (8H, m), 5.37-5.49 (1H, m), 7.31 (1H, s), 8.17 (1H, m), 9.04-9.13 (1H, m), 10.23-10.40 (1H, m), 11.56 (1H, s) mp: 281-283
24	2	ESI+: 450.4 NMR-DMSO-d6: 1.37 (3H, s), 1.63-1.73 (4H, m), 2.00-2.30 (4H, m), 2.39 (3H, s), 2.50-2.64 (4H, m), 3.51-3.76 (4H, m), 3.93-4.14 (4H, m), 5.21-5.31 (1H, m), 7.33 (1H, s), 8.01 (1H, s), 8.17 (1H, s), 11.51 (1H, s)
25	2	ESI+: 478.4 NMR-DMSO-d6: 1.59-2.75 (19H, m), 3.02-4.21 (10H, m), 5.39-5.53 (1H, m), 7.31 (1H, s), 8.19 (1H, s), 8.25 (1H, s), 8.90-9.00 (1H, m), 10.29-10.42 (1H, m), 11.55 (1H, s)
26	2	ESI+: 492.4 NMR-DMSO-d6: 1.18-1.33 (2H, m), 1.44-1.76 (6H, m), 1.84-2.04 (6H, m), 2.08-2.29 (4H, m), 2.45 (3H, s), 3.19-3.51 (4H, m), 3.58-3.70 (2H, m), 3.79-3.89 (2H, m), 3.97-4.09 (2H, m), 5.44-5.58 (1H, m), 7.31 (1H, s), 8.19 (1H, s), 8.28 (1H, s), 8.86-8.99 (1H, m), 10.13-10.30 (1H, m), 11.55 (1H, s)

(continued)

Ex	Syn	Data
27	2	ESI+: 480.3 NMR-DMSO-d6: 1.32-1.46 (2H, m), 1.62-1.73 (2H, m), 1.91-2.12 (2H, m), 2.27-2.64 (6H, m), 2.29 (3H, s), 3.13-3.37 (5H, m), 3.56-4.10 (8H, m), 5.17-5.27 (1H, m), 7.33 (1H, s), 7.86 (1H, s), 8.17 (1H, s), 11.50 (1H, s)
28	2	APCI/ESI+: 439.2 NMR-DMSO-d6: 0.89-2.16 (8H, m), 2.27 (3H, s), 2.69-4.24 (10H, m), 3.23 (3H, s), 4.51-4.66 (1H, m), 5.16-5.29 (1H, m), 7.34 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 253-255

[Table 108]

Ex	Syn	Data
29	2	ESI+: 424.2 NMR-DMSO-d6: 1.77-2.08 (4H, m), 2.42-279 (7H, m), 2.95-3.22 (4H, m), 3,27-3.49 (4H, m), 3.64-4.03 (4H, m), 5.54-5.69 (1H, m), 7.26 (1H, s), 8.06 (1H, s), 8.15 (1H, s), 8.57-8.67 (1H, m), 10.84 (1H, br s), 11.48 (1H, s)
30	2	ESI+: 494.4 NMR-DMSO-d6: 0.97-1.28 (2H, m), 1.51-2.90 (16H, m), 3.09-4.38 (12H, m), 5.07-5.39 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8.17 (1H, s), 11.5 (1H, s)
31	2	ESI+: 466.4 NMR-DMSO-d6: 1.65-1.80 (1H, m), 1.89-4.21 (25H, m), 5.18-5.32 (1H, m), 7.33 (1H, s), 7.89 (1H, s), 8.17 (1H, s), 11.50 (1H, s)
32	2	ESI+: 452.4 NMR-DMSO-d6: 1.68-2.44 (13H, m), 2.83-4.13 (14H, m), 4.54-4.74 (1H, m), 5.47-5.60 (1H, m), 7.35 (1H, s), 8.08 (1H, s), 8.13 (1H, s), 10.80-11.30 (1H, m), 11.51 (1H, s) mp: 245 (dec.)
33	2	ESI+: 486.4 NMR-DMSO-d6: 1.62-2.55 (4H, m), 2.43 (3H, s), 2.69-4.17 (13H, m), 4.33-4.68 (1H, m), 5.09-5.42 (1H, m), 6.98-7.40 (6H, m), 7.79-8.23 (2H, m), 11.44-11.56 (1H, m)
34	2	ESI+: 500.4 NMR-DMSO-d6: 0.73-0.97 (3H, m), 1.88-2.57 (10H, m), 2.42 (3H, s), 2.72-4.73 (7H, m), 5.07-5.41 (1H, m), 6.99-8.25 (8H, m), 11.48, 11.52 (total 1H, both s)
35	2	ESI+: 514.4 NMR-DMSO-d6: 1.50-2.45 (12H, m), 2.54-3.06 (6H, m), 2.60 (3H, s), 3.12-3.76 (4H, m), 3.87-4.11 (2H, m), 4.53-4.68 (1H, m), 5.17-5.31 (1H, m), 7.33 (1H, s), 7.84-7.95 (1H, m), 8.17 (1H, s), 11.49 (1H, s)
36	5	ESI+: 478.4 NMR-DMSO-d6: 1.24-.278 (19H, m), 2.99-4.17 (10H, m), 5.09-5.42 (1H, m), 7.32 (1H, s), 7.92-8.14 (1H, m), 8.20 (1H, s), 9.09 (0.5H, br s), 9.80 (0.5H, br s), 11.57 (1H, br s)
37	5	ESI+: 514.4 NMR-DMSO-d6: 1.85-2.70 (18H, m), 3.14-3.46 (2H, m), 3.58-3.77 (2H, m), 3.94-4.14 (2H, m), 5.08-5.28 (1H, m), 7.16-7.23 (1H, m), 7.26 (1H, s), 7.35 (2H, dd, J = 7.4, 7.4 Hz), 7.40-7.47 (2H, m), 8.00 (1H, s), 8.18 (1H, s), 8.25-8.36 (1H, m), 11.50 (1H, s)
38	2	ESI+: 474.3 NMR-DMSO-d6: 2.0-2.1 (4H, m), 2.33 (3H, s), 3.28-3.38 (2H, m), 3.55-4.00 (10H, m), 5.20-5.30 (1H, m), 6.67 (1H, t, J = 4.8 Hz), 7.35 (1H, s), 7.96 (1H, s), 8.18 (1H, s), 8.38 (2H, d, J = 4.8 Hz), 11.52 (1H, s)

[Table 109]

Ex	Syn	Data
39	2	ESI+: 438.1 NMR-DMSO-d6: 1.73-2.05 (4H, m), 2.18-3.94 (20H, m), 4.56-4.77 (1H, m), 5.42-5.63 (1H, m), 7.31 (1H, s), 7.98 (1H, s), 8.18 (1H, s), 9.88-10.40 (1H, m), 11.50 (1H, s)
40	2	ESI+: 439.0 NMR-DMSO-d6: 1.08-2.54 (14H, m), 2.89-4.35 (11H, m), 5.12-5.34 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.49 (1H, br s)
41	2	ESI+: 465.3 NMR-DMSO-d6: 0.09-0.21 (2H, m), 0.38-0.48 (2H, m), 0.89-1.04 (1H, m), 1.19-2.59 (11H, m), 2.89-4.35 (11H, m), 5.15-5.31 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 206-208
42	2	ESI+: 452.4
43	2	ESI+: 498.4 mp: 274 (dec.)
44	2	ESI+: 489.3 NMR-DMSO-d6: 1.36-2.71 (11H, m), 3.00-4.40 (9H, m), 5.16-5.39 (1H, m), 7.12-7.14 (1H, m), 7.35 (1H, s), 7.89-8.04 (1H, m), 8.18 (1H, s), 8.60-8.61 (2H, m), 11.5 (1H, s)
45	2	ESI+: 474.3 NMR-DMSO-d6: 1.80-2.52 (9H, m), 3.13-4.17 (8H, m), 5.16-5.35 (1H, m), 5.39-5.47 (0.5H, m), 5.54-5.67 (0.5H, m), 6.75-6.84 (1 H, m), 6.90-6.98 (0.5H, m), 6.99-7.07 (0.5H, m), 7.26-7.38 (1H, m), 7.65-7.81 (1H, m), 7.92-8.08 (1.5H, m), 8.11-8.27 (1.5H, m), 11.43-11.56 (1H, m)
46	2	ESI+: 502.4 NMR-DMSO-d6: 1.37-2.53 (14H, m), 3.02-4.40 (8H, m), 5.13-5.38 (2H, m), 6.19-5.76 (1H, m), 7.34 (1H, s), 7.47-7.58 (1H, m), 7.89-8.00 (2H, m), 8.17 (1H, s), 11.50 (1H, s)
47	2	ESI+: 530.3 NMR-DMSO-d6: 1.60-2.64 (4H, m), 2.42 (3H, s), 2.76-4.14 (14H, m), 3.11 (3H, s), 4.34-4.66 (1H, m), 5.11-5.39 (1H, m), 7.00-7.52 (6H, m), 7.80-8.02 (1H, m), 8.08-8.23 (1H, m), 11.44-11.56 (1H, m) mp: 218-220
48	2	ESI+: 474.2 NMR-DMSO-d6: 1.68-2.50 (6H, m), 3,00-4.20 (6H, m), 3.16 (3H, s), 4.36-4.84 (2H, m), 5.10-5.35 (2H, m), 7.25-7.50 (2H, m), 7.83-8.11 (1H, m), 8.18 (1H, s), 8.45 (1H, s), 8.57 (1H, s), 8.68 (1H, s), 11.52 (1H, s) mp: 266-268

[Table 110]

Ex	Syn	Data
49	2	ESI+: 487.2 NMR-DMSO-d6: 1.89-2.53 (7H, m), 1.95 (3H, s), 2.79-4.15 (10H, m), 4.34-4.68 (1H, m), 5.07-5.37 (1H, m), 7.19-7.69 (2H, m), 7.77-8.00 (2H, m), 8.07-8.21 (1H, m), 8.37-8.68 (2H, m), 11.42-11.55 (1H, m) mp: 255-257
50	2	ESI+: 474.3 NMR-DMSO-d6 (measured at 60°C): 2.01-2.31 (4H, m), 2.34 (3H, s), 3.22-4.10 (12H, m), 5.16-5.25 (1H, m), 7.37 (1H, s), 7.85-7.89 (1H, m), 7.92 (1H, s), 8.07-8.11 (1H, m), 8.15 (1H, s), 8.29-8.33 (1H, m), 11.34 (1H, s)
51	2	ESI+: 473.3 NMR-DMSO-d6: 1.48-2.62 (7H, m), 3.00-4.31 (12H, m), 5.19-5.31 (1H, m), 6.79-6.86 (2H, m), 7.36 (1H, s), 7.97 (1H, s), 8.13-8.23 (3H, m), 11.53 (1H, s)

(continued)

Ex	Syn	Data
52	2	ESI+: 478.4 NMR-DMSO-d6: 1.01-1.29 (2H, m), 1.48-2.71 (16H, m), 3.07-4.04 (12H, m), 5.43-5.56 (1H, m), 7.32 (1H, s), 7.96 (1H, s), 8.12 (1H, s), 11.46 (1H, s)
53	2	ESI+: 453.4 NMR-DMSO-d6: 0.87 (3H, t, J = 7.4 Hz), 0.98-2.60 (13H, m), 2.87-4.39 (11H, m), 5.14-5.33 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 216-218
54	2	ESI+: 469.4 NMR-DMSO-d6: 1.11-2.55 (11H, m), 2.93-4.24 (16H, m), 5.17-5.31 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8.17 (1H, s), 11.50 (1H, s)
55	2	ESI+: 464.4 NMR-DMSO-d6: 1.01-4.14 (28H, m), 5.47-5.58 (1H, m), 7.31 (1H, s), 7.86 (1H, s), 8.17 (1H, s), 11.5 (1H, s)
56	2	ESI+: 453.4 NMR-DMSO-d6: 0.74-1.40 (5H, m), 1.46-2.55 (10H, m), 2.61-3.75 (9H, m), 3.80-4.12 (2H, m), 4.43-4.75 (1H, m), 5.12-5.35 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.49 (1H, s) mp: 243
57	2	ESI+: 515.4 NMR-DMSO-d6: 1.84-2.43 (6H, m), 2.51 (3H, s), 2.80-4.07 (16H, m), 5.22-5.34 (1H, m), 7.36 (1H, s), 7.95-8.06 (2H, m), 8.18 (1H, s), 8.53 (1H, d, J = 8.3 Hz), 8.82 (1H, d, J = 6.1 Hz), 8.91 (1H, s), 11.55 (1H, s) mp: 254-256
58	2	ESI+: 464.4 NMR-DMSO-d6: 1.27-1.48 (2H, m), 1.58-1.94 (6H, m), 1.94-2.76 (10H, m), 2.30 (3H, s), 3.07-3.38 (3H, m), 3.54-3.95 (4H, m), 5.40-5.57 (1H, m), 7.32 (1H, s), 7.96 (1H, s), 8.11 (1H, s), 11.46 (1H, s) mp: 263-265

[Table 111]

Ex	Syn	Data
59	2	ESI+: 479.4 NMR-DMSO-d6: 0.05-0.21 (2H, m), 0.31-0.52 (2H, m), 0.78-4.18 (24H, m), 4.45-4.58 (1H, m), 5.11-5.33 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s)
60	2	ESI+: 485.4 NMR-DMSO-d6: 0.82-1.43 (5H, m), 1.48-3.78 (19H, m), 3.81-4.20 (2H, m), 4.48-4.90 (2H, m), 5.16-5.31 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
61	5	ESI+: 494.3 NMR-DMSO-d6: 1.62-1.74 (8H, m), 2.06-2.27 (4H, m), 2.43 (3H, s), 2.74 (2H, m), 3.37 (2H, m), 3.45 (2H, d, J = 6.2 Hz), 3.55-3.71 (6H, m), 4.04 (2H, m), 5.20 (1H, m), 7.30 (1H, s), 8.02 (1H, s), 8.19 (1H, s), 8.33 (1H, t, J = 6.2 Hz), 11.52 (1H, s)
62	5	ESI+: 464.4 NMR-DMSO-d6: 1.53 (1H, m), 1.70-1.93 (6H, m), 1.99-2.41 (10H, m), 2.89-3.23 (2H, m), 3.40-3.67 (7H, m), 4.29 (1H, m), 4.62 (1H, m), 5.53 (1H, m), 7.35 (1H, s), 8.07 (1H, s), 8.13 (1H, s), 10.60-10.86 (1H, br), 11.51 (1H, s)
63	2	ESI+: 482.2 NMR-DMSO-d6: 1.08 (3H, t, J = 7.0 Hz), 1.56-1.90 (2H, m), 1.92-2.10 (4H, m), 2.26-2.38 (6H, m), 2.29 (3H, s), 3.00-4.07 (12H, m), 5.18-5.28 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 217-219

(continued)

Ex	Syn	Data
64	2	ESI+: 496.3 NMR-DMSO-d6: 1.05 (6H, d, J = 6.0 Hz), 1.19-1.34 (2H, m), 1.54-1.66 (2H, m), 1.90-2.39 (4H, m), 2.29 (3H, s), 3.02-4.07 (15H, m), 5.16-5.28 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 122-124
65	2	ESI+: 479.2 NMR-DMSO-d6: 0.77-1.68 (10H, m), 1.71-4.11 (18H, m), 4.54-4.70 (1H, m), 5.15-5.31 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
66	2	ESI+: 453.2 NMR-DMSO-d6: 0.69-3.56 (22H, m), 3.56-3.80 (2H, m), 3.83-4.18 (2H, m), 4.43-4.70 (1H, m), 5.11-5.35 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8.17 (1H, s), 11.49 (1H, s) mp: 241-242
67	2	ESI+: 466.2 mp: 234-236
68	2	ESI+: 464.2

[Table 112]

Ex	Syn	Data
69	2	ESI+: 466.2 NMR-DMSO-d6: 1.10 (3H, t, J = 7.0 Hz), 1.69-2.78 (10H, m), 2.58 (3H, s), 3.07-3.80 (14H, m), 5.49-5.57 (1H, m), 7.35 (1H, s), 8.07 (1H, s), 8.12 (1H, s), 11.50 (1H, s)
70	2	ESI+: 452.4 NMR-DMSO-d6: 1.10 (3H, t, J = 6.9 Hz), 1.83-2.06 (4H, m), 2.23-2.62 (7H, m), 3.10-3.68 (14H, m), 5.51-5.61 (1H, m), 7.33 (1H, s), 7.98 (1H, s), 8.18 (1H, s), 11.51 (1H, s)
71	2	ESI+: 508.3 NMR-DMSO-d6: 1.80-2.63 (9H, m), 3.12-3.46 (2H, m), 3.50-4.11 (6H, m), 5.14-5.34 (1H, m), 5.36-5.47 (0.5H, m), 5.50-5.68 (0.5H, m), 6.80-6.91 (1H, m), 7.25-7.38 (1H, m), 7.75-9.37 (4H, m), 11.42-11.59 (1H, m)
72	2	ESI+: 508.3 NMR-DMSO-d6: 1.85-2.64 (9H, m), 3.20-4.10 (8H, m), 5.18-5.34 (1H, m), 5.36-5.44 (0.5H, m), 5.50-5.61 (0.5H, m), 6.80-6.91 (1H, m), 6.97-7.38 (2H, m), 7.77-8.30 (3H, m), 11.45-11.56 (1H, m)
73	2	ESI+: 439.3
74	2	ESI+: 512.4 NMR-DMSO-d6: 1.96-3.78 (21H, m), 3.89-4.05 (2H, m), 5.17-5.31 (1H, m), 7.17-7.37 (6H, m), 7.95 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
75	2	ESI+: 411.3
76	2	ESI+: 471.4
77	2	ESI+: 510.2 NMR-DMSO-d6: 1.10 (9H, s), 1.52-1.62 (2H, m), 1.89-2.54 (10H, m), 2.30 (3H, s), 3.10-3.36 (2H, m), 3.51-4.08 (8H, m), 5.18-5.28 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 238-240
78	2	ESI+: 411.2 NMR-DMSO-d6: 1.97-2.15 (4H, m), 2.39 (3H, s), 2.76-2.87 (1H, m), 3.29 (3H, s), 3.52 (2H, d, J = 6.3 Hz), 3.65-3.83 (4H, m), 3.96-4.17 (4H, m), 5.20-5.30 (1H, m), 7.32 (1H, s), 8.00 (1H, s), 8.17 (1H, s), 11.51 (1H, s)

(continued)

Ex	Syn	Data
79	2	ESI+: 452.4 NMR-DMSO-d6: 1.37-1.60 (2H, m), 1.61-1.81 (2H, m), 1.81-2.05 (2H, m), 2.06-4.15 (21H, m), 4.47-4.76 (1H, m), 5.49-5.64 (1H, m), 7.33 (1H, s), 7.99 (1H, s), 8.19 (1H, s), 10.71-11.15 (1H, m), 11.51 (1H, s) mp: 161-163
80	2	ESI+: 474.2
81	2	ESI+: 467.4

[Table 113]

Ex	Syn	Data
82	5	ESI+: 452.3 NMR-DMSO-d6: 1.10 (6H, d, J = 6.1 Hz), 1.85-2.05 (2H, m), 2.24-2.39 (4H, m), 2.51-2.62 (4H, m), 2.69-3.21 (2H, m), 3.30-3.65 (7H, m), 3.74 (2H, m), 4.65 (1H, m), 5.56 (1H, m), 7.33 (1H, s), 7.97 (1H, s), 8.19 (1H, s), 10.45-10.75 (1H, br.), 11.52 (1H, s)
83	5	ESI+: 450.2 NMR-DMSO-d6: 1.45-1.59 (1H, m), 1.73-2.10 (5H, m), 2.25-2.40 (4H, m), 2.49-2.63 (4H, m), 2.67-3.23 (4H, m), 3.28-3.65 (4H, m), 3.72 (1H, m), 3.82 (1H, m), 4.31 (1H, m), 4.63 (1H, m), 5.57 (1H, m), 7.33 (1H, s), 7.98 (1H, s), 8.19 (1H, s), 10.61-10.92 (1H, br.), 11.52 (1H, s)
84	2	ESI+: 482.2 NMR-DMSO-d6: 1.46-2.56 (11H, m), 2.73-4.09 (15H, m), 3.23 (3H, s), 4.56-4.72 (1H, m), 5.21-5.32 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.18 (1H, s), 11.55 (1H, s) mp:240-242
85	7	ESI+: 494.3 NMR-DMSO-d6: 1.88-2.43 (8H, m), 2.50 (3H, s), 2.69-4.22 (15H, m), 3.57 (3H, s), 4.51-4.71 (1H, m), 5.17-5.30 (1H, m), 7.35 (1H, s), 7.89 (1H, s), 8.17 (1H, s), 11.52 (1H, s)
86	2	ESI+: 425.3 NMR-DMSO-d6: 1.12 (3H, t, J = 7.2 Hz), 1.97-2.34 (4H, m), 2.39 (3H, s), 2.76-2.87 (1H, m), 3.47 (2H, q, J = 7.2 Hz), 3.55 (2H, d, J = 6.4 Hz), 3.60-3.80 (4H, m), 3.96-4.17 (4H, m), 5.21-5.31 (1H, m), 7.32 (1H, s), 8.00 (1H, s), 8.17 (1H, s), 11.51 (1H, s) mp: 226-228
87	2	ESI+: 451.3 NMR-DMSO-d6: 1.27-2.19 (11H, m), 2.22-2.58 (4H, m), 3.06-3.48 (3H, m), 3.53-4.28 (7H, m), 5.14-5.38 (1H, m), 7.33 (1H, s), 7.83-8.00 (1H, m), 8.17 (1H, s), 11.49 (1H, s)
88	2	ESI+: 467.4 NMR-DMSO-d6: 0.72-1.37 (4H, m), 1.38-1.69 (4H, m), 1.70-1.87 (1H, m), 1.87-2.16 (3H, m), 2.18-2.56 (4H, m), 2.62-3.02 (2H, m), 3.10-3.53 (6H, m), 3.56-3.79 (2H, m), 3.82-4.14 (2H, m), 4.38-4.72 (1H, m), 5.08-5.36 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8.17 (1H, s), 11.50 (1H, s)
89	2	ESI+: 467.3
90	2	ESI+: 466.2 NMR-DMSO-d6: 1.48-1.59 (2H, m), 1.69-2.02 (8H, m), 2.23-2.40 (2H, m), 2.50 (3H, s), 2.80-3.68 (11H, m), 3.23 (3H, s), 4.68-4.81 (2H, s), 7.34 (1H, s), 7.92 (1H, s), 8.12 (1H, s), 11.52 (1H, s) mp: 178-180

[Table 114]

Ex	Syn	Data
91	2	ESI+: 501.2 NMR-DMSO-d6: 0.75-1.06 (3H, m), 1.57-2.66 (10H, m), 2.42 (3H, s), 2.78-4.78 (7H, m), 5.05-5.44 (1H, m), 7.18-7.76 (2H, m), 7.76-8.05 (2H, m), 8.05-8.78 (3H, m), 11.45-11.55 (1H, m) mp: 272-274
92	2	ESI+: 439.2
93	2	ESI+: 453.2
94	2	ESI+:475.0 NMR-DMSO-d6: 1.12-1.83 (2H, m), 1.88-2.61 (9H, m), 2.92-4.31 (11H, m), 5.11-5.36 (1H, m), 5.93-6.31 (1H, m), 7.33 (1H, s), 7.91 (1H, s), 8.17 (1H, s), 11.5 (1H, br s)
95	2	ESI+: 471.3 NMR-DMSO-d6: 1.10-2.55 (14H, m), 2.84-4.32 (11H, m), 4.64-4.75 (0.5H, m), 4.76-4.88 (0.5H, m), 5.16-5.33 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 209-210
96	2	APCI/ESI+: 466.3 NMR-DMSO-d6: 1.10 (3H, t, J = 7.2 Hz), 1.76-2.02 (8H, m), 2.25-2.38 (3H, m), 2.50 (3H, s), 2.80-2.95 (1H, m), 3.08-3.65 (4H, m), 3.78-3.92 (6H, m), 4.65-4.85 (3H, s), 7.34 (1H, s), 7.91 (1H, s), 8.12 (1H, s), 11.51 (1H, s)
97	2	ESI+: 452.2 NMR-DMSO-d6: 1.60-1.70 (2H, m), 1.76-2.03 (6H, m), 2.25-2.48 (4H, m), 2.29 (3H, s), 2.80-2.92 (1H, m), 3.12-3.39 (6H, m), 3.20 (3H, s), 3.56-3.80 (2H, m), 4.57-4.95 (2H, m), 7.31 (1H, s), 7.77 (1H, s), 8.10 (1H, s), 11.47 (1H, s) mp: 186-188
98	5	ESI+: 480.2 NMR-DMSO-d6: 1.12 (6H, s), 1.70-1.96 (6H, m), 2.01-2.43 (7H, m), 2.84-2.91 (1H, m), 3.04-3.16 (5H, m), 3.35-3.46 (3H, m), 3.48-3.70 (3H, m), 4.59-4.72 (1H, m), 5.53 (1H, m), 7.35 (1H, s), 8.08 (1H, s), 8.13 (1H, s), 11.03-11.34 (1H, br.), 11.51 (1H, s)
99	5	ESI+: 496.2 NMR-DMSO-d6: 1.13 (6H, s), 1.81-2.13 (4H, m), 2.24-2.44 (3H, m), 2.77-2.96 (1H, m), 3.00-3.15 (5H, m), 3.35-3.80 (10H, m), 3.90-4.09 (2H, m), 4.59-4.60 (1H, m), 5.27 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.19 (1H, s), 10.89-11.31 (1H, br.), 11.55 (1H, s)
100	5	ESI+: 452.2 NMR-DMSO-d6: 0.91 (3H, t, J = 7.3 Hz), 1.30 (2H, m), 1.58-1.74 (2H, m), 1.88-2.17 (3H, m), 2.22-2.45 (4H, m), 2.78-2.94 (1H, m), 2.98-3.14 (3H, m), 3.28-3.80 (7H, m), 3.91-4.08 (2H, m), 4.59-4.72 (1H, m), 5.27 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.19 (1H, s), 10.85-11.27 (1H, br.), 11.55 (1H, s)

[Table 115]

Ex	Syn	Data
101	2	ESI+: 474.2
102	2	ESI+: 409.3
103	2	ESI+: 452.4 NMR-DMSO-d6: 0..31-0.61 (4H, m), 1.20-1.36 (1H, m), 1.41-1.61 (2H, m), 1.64-1.85 (2H, m), 2.21-2.44 (3H, m), 2.76-3.90 (14H, m), 4.41-4.94 (3H, m), 7.35 (1H, s), 8.02 (1H, s), 8.12 (1H, s), 10.51-1098 (1H, m), 11.52 (1H, s) mp: 207-208

(continued)

Ex	Syn	Data
104	2	ESI+: 438.2 NMR-DMSO-d6: 0.32-0.60 (4H, m), 1.22-1.38 (1H, m), 1.86-2.07 (2H, m), 2.20-2.44 (3H, m), 2.76-2.87 (14H, m), 4.41-4.97 (3H, m), 7.35 (1H, s), 8.02 (1H, s), 8.13 (1H, s), 10.72-11.20 (1H, m), 11.53 (1H, s)
105	5	ESI+: 496.2 ESI+: 496.2 NMR-DMSO-d6: 1.11 (9H, s), 1.56 (2H, m), 2.06-2.23 (1H, br.), 2.30 (3H, s), 2.30-2.42 (5H, m), 2.46-2.71 (4H, m), 3.12-3.25 (2H, m), 3.88-4.29 (4H, m), 5.81 (1H, m), 7.33 (1H, s), 7.87-7.99 (1H, br.), 8.15 (1H, s), 11.50 (1H, s)
106	5	ESI+: 487.2 NMR-DMSO-d6: 1.00-1.39 (4H, m), 1.87-4.96 (14H, m), 2.33 (3H, s), 5.25 (1H, m), 6.91 (1H, m), 7.25 (1H, m), 7.37 (1H, s), 7.86-8.03 (2H, m), 8.05 (1H, d, J = 3.2 Hz), 8.19 (1H, s), 11.55 (1H, s)
107	2	ESI+:496.2 NMR-DMSO-d6: 1.11 (3H, t, J = 12.8 Hz), 1.46-2.47 (14H, m), 2.78-3.81 (12H, m), 3.92-4.07 (2H, m), 4.66 (1H, d, J = 12.0 Hz), 5.26-5.31 (1H, m), 7.36 (1H, s), 8.01 (1H, s), 8.19 (1H, s), 11.55 (1H, s)
108	2	ESI+:510.3 NMR-DMSO-d6: 1.10-2.41 (20H, m), 2.96-4.14 (13H, m), 4.62 (1H, d, J = 12.0 Hz), 5.21-5.38 (1H, m), 7.35 (1H, s), 8.00 (1H, s), 8.18 (1H, s), 11.54 (1H, s)
109	2	ESI+:510.3 NMR-DMSO-d6: 1.11-2.40 (20H, m), 2.85-4.70 (14H, m), 5.27 (1H, s), 7.36 (1H, s), 7.98 (1H, m), 8.19 (1H, s), 11.55 (1H, s)
110	2	ESI+: 452.2 NMR-DMSO-d6: 0.99 (6H, d, J = 8.0 Hz), 1.74-3.81 (19H, m), 3.84-4.20 (2H, m), 4.45-4.77 (1H, m), 5.1.6-5.38 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.19 (1H, s), 9.91-10.65 (1H, m), 11.55 (1H, s)
111	2	ESI+:496.3 NMR-DMSO-d6: 0.95-2.54 (14H, m), 2.70-4.20 (17H, m), 4.31-4.77 (1H, m), 5.04-5.40 (1H, m), 7.36 (1H, s), 7.88-8.09 (1H, m), 8.19 (1H, s), 10.33-11.10 (1H, m), 11.45-11.67 (1H, m)

[Table 116]

Ex	Syn	Data
112	2	ESI+:496.3 NMR-DMSO-d6: 0.94-2.59 (14H, m), 2.74-4.15 (17H, m), 4.34-4.79 (1H, m), 5.07-5.39 (1H, m), 7.36 (1H, s), 7.90-8.08 (1H, m), 8.19 (1H, s), 10.36-11.07 (1H, m), 11.50-11.60 (1H, m)
113	2	ESI+:519.4 NMR-DMSO-d6: 0.81-2.60 (13H, m), 2.62-4.14 (9H, m), 4.23-4.72 (2H, m), 5.22 (1H, m), 6.65-6.57 (1H, m), 7.45 (2H, m), 7.85-7.99 (1H, m), 8.18 (1H, s), 11.52 (1H, m) mp:168
114	2	ESI+: 496.4 NMR-DMSO-d6: 1.08-5.40 (33H, m), 7.36 (1H, s), 7.91-8.10 (1H, m), 8.19 (1H, s), 10.30-10.72 (1H, m), 11.55 (1H, s)
115	2	ESI+: 496.3 NMR-DMSO-d6: 1.05-4.32 (31H, m), 4.51-4.78 (0.5H, m), 4.91-5.40 (1.5H, m), 7.36 (1H, s), 7.92-8.11 (1H, m), 8.19 (1H, s), 10.41-10.87 (1H, m), 11.55 (1H, s)
116	2	ESI+:528.3 NMR-DMSO-d6: 1.01-1.98 (8H, m), 2.16-3.07 (7H, m), 3.16-4.12 (2H, m), 4.40-4.08 (7H, m), 4.33-4.69 (3H, m), 5.90-6.08 (1H, m), 7.34 (1H, s), 7.42-7.51 (3H, m), 7.56-7.67 (2H, m), 7.80-7.89 (1H, m), 8.22-8.33 (1H, m), 11.55 (1H, s)

(continued)

Ex	Syn	Data
117	2	ESI+: 482.4 NMR-DMSO-d6: 0.79-4.18 (29H, m), 4.26-4.70 (1H, m), 5.00-5.44 (1H, m), 7.36 (1H, s), 7.89-8.06 (1H, m), 8.19 (1H, s), 10.53-11.16 (1H, m), 11.50-11.60 (1H, m)
118	2	ESI+:496.4 NMR-DMSO-d6: 1.04 (6H, s), 1.37-1.48 (2H, m), 1.71-1.79 (2H, m), 1.83-1.94 (4H, m), 2.22 (4H, q, J = 6.8 Hz), 2.49-2.51 (2H, m), 2.77-2.84 (2H, m), 3.17-3.21 (1H, m), 3.24 (3H, s), 3.24-3.33 (2H, m), 4.03 (3H, s), 5.33-5.41 (1H, m), 7.19 (1H, s), 8.10 (1H, s), 8.38 (1H, m), 8.86 (1H, s), 11.48 (1H, s)
119	2	ESI+:468.4 NMR-DMSO-d6: 1.04 (6H, s), 1.71-1.82 (2H, m), 1.82-1.95 (2H, m), 2.19-2.27 (4H, q, J = 5.6 Hz), 2.52-2.54 (4H, m), 3.40-3.44 (2H, m), 3.63 (4H, m), 4.05 (3H, s), 5.34-5.42 (1H, m), 7.18 (1H, s), 8.10 (1H, s), 8.38 (1H, m), 8.84 (1H, s), 11.48 (1H, s) mp: 279
120	2	ESI+:515.4 NMR-DMSO-d6: 1.67-1.80 (2H, m), 1.80-1.92 (2H, m), 2.18-2.24 (4H, m), 2.25 (3H, s), 2.52-2.56 (4H, m), 2.88 (4H, t, J = 4.8 Hz), 3.96 (3H, s), 4.61 (2H, d, J = 6.4 Hz), 5.34-5.43 (1H, m), 7.07 (1H, t, J = 6.4 Hz), 7.13-7.16 (2H, m), 7.24 (1H, t, J = 7.2 Hz), 7.31 (1H, d, J = 8.0 Hz), 8.10 (1H, s), 8.64 (1H, m), 8.70 (1H, s), 11.47(1H,s) mp: 210

[Table 117]

Ex	Syn	Data
121	2	ESI+: 482.4 NMR-DMSO-d6: 0.86-4.16 (29H, m), 4.30-4.78 (1H, m), 4.98-5.42 (1H, m), 7.35 (1H, s), 7.89-8.06 (1H, m), 8..18-(1H, s), 10.33-11.11 (1H, m), 11.0-11.57 (1H, m)
122	2	ESI+:468.3 NMR-DMSO-d6: 1.67-2.27 (10H, m), 2.78-3.71 (13H, m), 3.82-3.93 (3H, m), 4.61 (2H, d, J = 13.6 Hz), 5.40-5.47 (1H, m), 7.13 (1H, s), 8.07 (1H, s), 8.10 (1H, s), 10.94 (1H, br s), 11.46 (1H, s)
123	2	ESI+:482.3 NMR-DMSO-d6: 1.49-1.59 (2H, m), 1.65-1.90 (6H, m), 2.06-2.24 (4H, m), 2.41-2.56 (6H, m), 2.79-2.97 (1H, m), 3.02-3.19 (2H, m), 3.27 (3H, s), 3.34 (2H, t, J = 6.4 Hz), 3.83-3.92 (3H, s), 4.55-4.65 (1H, m), 5.40-5.48 (1H, m), 7.13 (1H, s), 8.07 (1H, s), 8.10 (1H, s), 10.85 (1H, br s), 11.46 (1H, s)
124	2	ESI+:496.4 NMR-DMSO-d6: 1.07-2.27 (15H, m), 2.97-3.81 (12H, m), 3.81-3.98 (3H, m), 4.37-4.61 (1H, m), 5.38-5.53 (1H, m), 7.14 (1H, s), 8.05-8.09 (1H, m), 8.11 (1H, s), 10.68-11.02 (1H,m), 11.46 (1H, s)
125	2	ESI+:510.3 NMR-DMSO-d6: 1.09-1.85 (8H, m), 2.06-2.61 (5H, m), 2.65-2.75 (1H, m), 2.75-2.85 (1H, m), 3.00-3.10 (1H, m), 3.23-3.30 (5H, m), 3.39 (2H, q, J = 6.8 Hz), 3.62-3.76 (2H, m), 3.73-4.21 (4H, m), 4.56-4.60 (1H, m), 5.71-5.83 (1H, m), 7.34 (1H, s), 7.84 (1H, s), 8.15 (1H, s), 11.55 (1H, s)
126	2	ESI+:496.4 NMR-DMSO-d6: 1.31-4.10 (32H, m), 5.22-5.35 (1H, m), 7.34 (1H, s), 7.97-8.06 (1H, m), 8.18 (1H, s), 10.90-11.14 (1H, m), 11.53 (1H, s)
127	2	ESI+:496.4 NMR-DMSO-d6: 1.31-4.10 (32H, m), 5.23-5.34 (1H, m), 7.34 (1H, s), 7.96-8.06 (1H, m), 8.18 (1H, s), 10.74-10.96 (1H, m), 11.52 (1H, s)

(continued)

Ex	Syn	Data
128	2	ESI+:492.3 NMR-DMSO-d6: 1.80-2.65 (7H, m), 2.80-4.29 (15H, m), 4.52-4.82 (1H, m), 5.21-5.35 (1H, m), 7.36 (1H, s), 7.98 (1H, s), 8.19 (1H, s), 11.33-11.80 (2H, m) mp: 174-176
129	2	ESI+: 510.4 NMR-DMSO-d6: 0.91-4.11 (33H, m), 4.28-4.79 (1H, m), 5.01-5.38 (1H, m), 7.43 (1H, s), 7.90-8.10 (1H, m), 8.14-8.30 (1H, m), 10.92-11.79 (2H, m)
130	2	ESI+: 510.4 NMR-DMSO-d6: 0.77-5.15 (35H, m), 7.35 (1H, s), 7.80-8.07 (1H, m), 8.10-8.20 (1H, m), 11.22-11.97 (2H, m)
131	2	ESI+:506.4 NMR-DMSO-d6: 1.90-4.20 (25H, m), 5.23-5.35 (1H, m), 7.34 (1H, s), 7.96-8.08 (1H, m), 8.18 (1H, s), 11.52 (1H, s), 11.55-11.67 (1H, m)

[Table 118]

Ex	Syn	Data
132	2	ESI+:506.4 NMR-DMSO-d6: 1.91-4.18 (25H, m), 5.24-5.38 (1H, m), 7.34 (1H, s), 7.97-8.08 (1H, m), 8.18 (1H, s), 11.52 (1H, s), 11.71-11.89 (1H, m)
133	2	ESI+: 504.2 NMR-DMSO-d6: 1.86-5.70 (27H, m), 7.36 (1H, s), 7.96 (1H, s), 8.19 (1H, s), 11.54(1H,s) mp: 212-213
134	2	ESI+; 474.2 NMR-DMSO-d6: 1.76-4.51 (24H, m), 5.46-5.63 (1H, m), 7.33 (1H, s), 7.94 (1H, s), 8.18 (1H, s), 11.05 (1H, s)
135	2	ESI+: 496.3 NMR-DMSO-d6: 1.10-2.57 (13H, m), 2.4-4.20 (18H, m), 4.46-4.87 (1H, m), 5.11-5.42 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.19 (1H, s), 10.36-10.91 (1H, s), 11.54 (1H, s)v
136	2	ESI+: 494.3 NMR-DMSO-d6: 0.50-0.84 (4H, m), 1.93-2.46 (7H, m), 2.80-5.40 (10H, m), 7.36 (1H, s), 7.98 (1H, s), 8.18 (1H, s), 10.35-10.82 (1H, m), 11.55 (1H, s)
137	2	ESI+: 466.3 NMR-DMSO-d6: 0.92-2.15 (28H, m), 4.41-4.82 (1H, m), 5.45-5.73 (1H, m), 7.42 (1H, s), 7.99 (1H, s), 8.20 (1H, s), 10.83-11.03 (0.5H, m), 11.10-11.36 (0.5H, m), 11.52 (1H, s)
138	2	ESI+:514.4 NMR-DMSO-d6: 1.02-1.35 (1H, m), 1.59-2.57 (14H, m), 2.80-3.82 (10H, m), 3.88-4.13 (2H, m), 4.50-4.84 (1H, m), 5.14-5.38 (1H, m), 7.36 (1H, s), 8.01 (1H, s), 8.19 (1H, s), 11.54 (1H, s) mp: 210
139	2	ESI+:506.4 NMR-DMSO-d6: 1.24-1.30 (1H, m), 1.88-2.60 (10H, m), 2.75-3.81 (11H, m), 3.91-4.10 (2H, m), 4.59-4.73 (1H, m), 5.18-5.33 (1H, m), 7.36 (1H, s), 8.00 (1H, s), 8.19 (1H, s), 11.04-11.44 (1H, m), 11.55 (1H, s) mp:192
140	2	ESI+: 491.2

(continued)

Ex	Syn	Data
141	5	ESI+: 439.1 NMR-DMSO-d6: 0.90-1.20 (2H, m), 1.09 (6H, t, J = 7.0 Hz), 1.50-1.87 (4H, m), 2.23-2.36 (6H, m), 2.56-3.09 (4H, m), 3.20-3.27 (2H, m), 3.40 (2H, q, J = 7.0 Hz), 3.86-4.36 (4H, m), 4.59 (1H, m), 5.82 (1H, m), 7.33 (1H, s), 7.86-8.00 (1H, br.), 8.15 (1H, s), 11.51 (1H, s)

[Table 119]

Ex	Syn	Data
142	5	ESI,+: 468.1 NMR-DMSO-d6: 0.70-1.20 (2H, m), 1.47 (4H, m), 2.29 (3H, s), 2.08-2.70 (10H, m), 3.20 (3H, s), 3.30 (2H, m), 3.50-4.26 (4H, m), 5.81 (1H, m), 7.33 (1H, s), 7.87-7.98 (1H, br.), 8.15 (1H, s), 11.52 (1H, s)
143	2	ESI+:520.4 NMR-DMSO-d6: 1.76-4.21 (27H, m), 5.23-5.38 (1H, m), 7.34 (1H, s), 7.97-8.09 (1H, m), 8.18 (1H, s), 11.52 (1H, s)
144	2	ESI+:520.4 NMR-DMSO-d6: 1.78-4.11 (27H, m), 5.23-5.38 (1H, m), 7.34 (1H, s), 7.98-8.07 (1H, m), 8.18 (1H, s), 11.52 (1H, s)
145	2	ESI+:494.4 NMR-DMSO-d6: 1.45-2.54 (15H, m), 2.95-3.41 (9H, m), 3.45-4.08 (4H, m), 4.17-5.00 (2H, m), 5.13-5.63 (1H, m), 7.29-7.39 (1H, m), 7.94-8.01 (1H, m), 8.15-8.24 (1H, m), 11.49-11.57 (1H, m) mp:203
146	2	ESI+:466.4 NMR-DMSO-d6: 0.96-2.10 (10H, m), 2.19-3.95 (19H, m), 4.33-4.78 (1H, m), 5.34-5.68 (1H, m), 7.33 (1H, s), 7.89-8.10 (1H, m), 8.19 (1H, s), 10.50-11.00 (1H, br s), 11.51 (1H, s)
147	2	ESI+:472.2 NMR-DMSO-d6: 1.98-2.38 (4H, m), 2.49 (3H, s), 3.10-4.41 (15H, m), 5.27-5.41 (1H, m), 7.32 (1H, s), 8.08 (1H, s), 8.18 (1H, s), 11.51 (1H,s)
148	5	ESI+: 439.4 0.90-1.20 (2H, m), 1.09 (3H, t, J = 7.0 Hz), 1.50-1.87 (4H, m), 2.23-2.36 (3H, m), 2.56-3.09 (4H, m), 3.20-3.27 (2H, m), 3.40 (2H, q, J = 7.0 Hz), 3.86-4.36 (4H, m), 4.59 (1H, m), 5.81 (1H,m), 7.33 (1H, s), 7.85-7.98 (1H, br.), 8.15 (1H, s), 11.49 (1H, s)
149	5	ESI+: 468.1 0.70-1.20 (2H, m), 1.47 (4H, m), 2.29 (3H, s), 2.08-2.70 (10H, m), 3.20 (3H, s), 3.30 (2H, m), 3.50-4.26 (4H, m), 5.81 (1H, m), 7.33 (1H, s), 7.87-7.98 (1H, br.), 8.15 (1H, s), 11.51 (1H, s)
150	2	ESI+:492.2 NMR-DMSO-d6: 0.79-4.73 (23H, m), 5.11-5.48 (1H, m), 7.33 (1H, s), 7.86-8.10 (1H, m), 8.19 (1H, s), 11.48-11.56 (1H, m)
151	2	ESI+: 517.2 NMR-DMSO-d6: 1.74-2.51 (12H, m), 2.95-4.31 (9H, m), 4.72-7.82 (1H, m), 5.04-5.36 (1H, m), 6.27-6.51 (1H, m), 7.22-7.47 (2H, m), 7.85-8.08 (1H, m), 8.13-8.20 (1H, m), 11.47-11.55 (1H, m) mp: 224

[Table 120]

Ex	Syn	Data
152	2	ESI+: 507.2 NMR-DMSO-d6: 0.80-1.42 (5H, m), 1.48-2.56 (7H, m), 2.60-3.10 (2H, m), 3.14-3.51 (5H, m), 3.60-3.78 (2H, m), 3.86-4.12 (2H, m), 4.49-4.61 (1H, m), 5.30-5.41 (1H, m), 7.88 (1H, s), 8.08-8.17 (1H, m), 8.26-8.30 (1H, m), 11.80 (1H, s)
153	2	ESI+:536.3
154	2	ESI+: 496.4 NMR-DMSO-d6: 1.07-1.88 (10H, m), 1.97-4.94 (22H, m), 7.35 (1H, s), 7.88-8.08 (1H, m), 8.14 (1H, s), 10.83-11.34 (1H, m), 11.55 (1H, s)
155	2	ESI+: 506.4 NMR-DMSO-d6: 1.18-5.00 (26H, m), 7.35 (1H, s), 7.97 (1H, s), 8.13 (1H, s), 11.54 (1H, s)
156	2	ESI+: 493.3, NMR-DMSO-d6: 1.25-2.63 (11H, m), 2.97-4.37 (11H, m), 5.15-5.33 (1H, m), 7.33 (1H, s), 7.91 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
157	2	ESI+:480.4 NMR-DMSO-d6: 0.93-2.13 (12H, m), 2.28-3.97 (19H, m), 4.20-4.80 (1H, m), 5.28-5.77 (1H, m), 7.40 (1H, s), 7.80-8.10 (1H, m), 8.19 (1H, s), 10,45-11.12 (1H, m), 11.49 (1H, s)
158	2	ESI+:508.4
159	2	ESI+: 508.4
160	2	ESI+: 546.4
161	2	ESI+: 462.4 NMR-DMSO-d6: 1.76-2.07 (2H, m), 2.13-3.79 (18H, m), 4.44-4.82 (1H, m), 5.44-5.63 (1H, m), 7.33 (1H, s), 7.97 (1H, s), 8.18 (1H, s), 11.51 (1H, s)
162	2	ESI+: 476.4 NMR-DMSO-d6: 1.06-1.26 (3H, m), 1.80-2.06 (2H, m), 2.26-3.82 (17H, m), 4.44-4.82 (1H, m), 5.47-5.62 (1H, m), 7.40 (1H, s), 7.96 (1H, s), 8.19 (1H, s), 11.20-11.71 (2H, m)
163	2	ESI+: 466.4 NMR-DMSO-d6: 1.00-2.11 (10H, m), 2.18-4.05 (19H, m), 4.26-4.78 (1H, m), 5.38-5.71 (1H, m), 7.32 (1H, s), 7.87-8.08 (1H, m), 8.19 (1H, s), 11.51 (1H, s)
164	2	ESI+: 480.4 NMR-DMSO-d6: 1.00-2.50 (16H, m), 2.78-4.05 (14H, m), 4.23-5.00 (3H, m), 7.33 (1H, s), 7.78-8.04 (1H, m), 8.12 (1H, s), 11.52 (1H, s)
165	2	ESI+: 532.2
166	5	ESI+:490.4 NMR-DMSO-d6: 2.30 (3H, s), 2.32-2.63 (6H, m), 2.81 (2H, t, J = 14.2 Hz), 3.35 (3H, s), 3.16-4.26 (8H, m), 3.66 (2H, t, J = 13.5 Hz), 5.81 (1H, m), 7.33 (1H, s), 7.89-7.98 (1H, br.), 8.15 (1H, s), 11.50 (1H, s)

[Table 121]

Ex	Syn	Data
167	2	ESI+: 467.3 NMR-DMSO-d6: 0.76-1.38 (10H, m), 1.49-2.57 (10H, m), 2.59-3.47 (3H, m), 3.55-3.76 (2H, m), 3.84-4.16 (3H, m), 4.37-4.59 (1H, m), 5.15-5.32 (1H, m), 7.33 (1H, s), 7.86 (1H, s), 8.17 (1H, s), 11.49 (1H, s)

(continued)

Ex	Syn	Data
168	2	ESI+: 467.3 NMR-DMSO-d6: 0.79-1.34 (5H, m), 1.36-2.58 (12H, m), 2.64-3.09 (2H, m), 3.19-3.52 (5H, m), 3.55-3.78 (2H, m), 3.85-4.13 (2H, m), 4.44-4.65 (1H, m), 5.13-5.31 (1H, m), 7.33 (1H, s), 7.89 (1H, br), 8.17 (1H, s), 11.49 (1H, s)
169	2	ESI+: 465.3 NMR-DMSO-d6: 1.13-2.62 (17H, m), 2.80-4.30 (10H, m), 5.16-5.31 (1H, m), 7.33 (1H, s), 7.89 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
170	2	ESI+:452.3 NMR-DMSO-d6: 0.76-4.41 (27H, m), 4.49-4.72 (1H, m), 5.96-6.12 (1H, m), 7.35 (1H, s), 7.89 (1H, s), 8.27 (1H, s), 11.58 (1H, s)
171	2	ESI+: 466.3 NMR-DMSO-d6: 0.88-1.95 (8H, m), 2.14-3.07 (11H, m), 3.15-4.26 (10H, m), 4.54-4.69 (1H, m), 5.16-5.57 (1H, m), 7.35 (1H, s), 7.88 (1H, s), 8.20 (1H, s), 10.39-10.74 (1H, m), 11.55 (1H, s)
172	2	ESI+: 505.3 NMR-DMSO-d6: 2.14-4.83 (26H, m), 5.22-5.79 (1H, m), 7.37 (1H, s), 7.89-8.25 (2H, m), 11.59 (1H, s) mp: 218
173	2	ESI+: 522.3 NMR-DMSO-d6: 1.62-2.64 (9H, m), 2.73-4.38 (15H, m), 4.44-4.85 (1H, m), 5.08-5.38 (1H, m), 7.29-7.41 (1H, m), 7.87-8.05 (1H, m), 8.13-8.24 (1H, m), 11.47-11.60 (1H, m)
174	2	ESI+: 532.3 NMR-DMSO-d6: 0.76-1.31 (3H, m), 2.00-4.80 (23H, m), 5.14-5.60 (2H, m), 6.54-6.70 (1H, m), 7.30-7.51 (2H, m), 7.82-8.07 (1H, m), 8.21 (1H, s), 11.58 (1H, s)
175	2	ESI+: 532.3 NMR-DMSO-d6: 0.82-1.30 (3H, m), 2.02-5.08 (24H, m), 5.16-5.58 (1H, m), 6.53-6.64 (1H, m), 7.28-7.57 (2H, m), 7.83-8.05 (1H, m), 8.21 (1H, s), 11.59 (1H, s) mp: 233
176	2	ESI+ 489.3 NMR-DMSO-d6: 1.17-2.60 (14H, m), 2.89-4.50 (11H, m), 5.11-5.41 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.16 (1H, s), 11.49 (1H, s) mp: 210-211

[Table 122]

Ex	Syn	Data
177	2	ESI+:471.3 NMR-DMSO-d6: 0.99-2.57 (15H, m), 2.79-4.29 (10H, m), 4.64-4.75 (0.5H, m), 4.77-4.90 (0.5H, m), 5.14-5.32 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.49 (1H, s) mp: 205-206
178	2	ESI+: 457.2 NMR-DMSO-d6: 1.09-2.73 (13H, m), 3.00-3.69 (5H, m), 3.85-4.30 (5H, m), 4.65-4.89 (1H, m), 5.74-5.91 (1H, m), 7.34 (1H, s), 7.88-8.03 (1H, m), 8.16 (1H, s), 11.50 (1H, s)
179	2	ESI+: 452.3 NMR-DMSO-d6: 0.94-1.51 (3H, m), 1.75-2.03 (4H, m), 2.18-2.40 (3H, m), 2.41-3.78 (18H, m), 5.43-5.66 (1H, m), 7.33 (1H, s), 7.93-8.03 (1H, br s), 8.19 (1H, s), 11.51 (1H, s) mp: 183

(continued)

Ex	Syn	Data
180	2	ESI+: 452.3 NMR-DMSO-d6: 0.96-1.52 (3H, m), 1.79-2.09 (4H, m), 2.19-2.41 (3H, m), 2.42-3.95 (18H, m), 5.37-5.63 (1H, m), 7.33 (1H, s), 7.87-8.06 (1H, br s), 8.18 (1H, s), 11.51 (1H, s) mp: 186
181	2	ESI+: 518.3 NMR-DMSO-d6: 0.82-1.28 (3H, m), 2.20-2.68 (8H, m), 2.76-4.70 (14H, m), 5.88-6.14 (1H, m), 6.55-6.68 (1H, m), 7.30-7.51 (2H, m), 7.84-8.08 (1H, m), 8.29 (1H, s), 11.62 (1H, s)
182	2	ESI+: 518.3 NMR-DMSO-d6: 0.84-1.31 (3H, m), 2.20-4.77 (22H, m), 5.94-6.11 (1H, m), 6.53-6.69 (1H, m), 7.33-7.50 (2H, m), 7.85-8.11 (1H, m), 8.28 (1H, s), 11.61 (1H, s) mp: 212
183	2	ESI+: 510.3 NMR-DMSO-d6: 0.98-2.54 (14H, m), 2.83-4.12 (20H, m), 4.95-5.30 (1H, m), 7.23-7.42 (1H, m), 7.67-8.11 (1H, m), 8.20 (1H, s), 11.56 (1H, s) mp:187
184	2	ESI+: 520.3 NMR-DMSO-d6: 0.85-1.70 (6H, m), 1.84-2.78 (9H, m), 2.85-4.16 (12H, m), 4.93-5.35 (1H, m), 7.28-7.40 (1H, m), 7.45-8.08 (1H, m), 8.19 (1H, s), 11.55 (1H, s) mp: 193
185	2	ESI+: 478.3 NMR-DMSO-d6: 2.06-2.74 (5H, m), 2.77-4.33 (15H, m), 4.41-4.88 (1H, m), 5.71-5.91 (1H, m), 7.36 (1H, s), 8.03 (1H, br s), 8.17 (1H, s), 11.41-11.98 (2H, m)

[Table 123]

Ex	Syn	Data
186	2	ESI+:480.3 NMR-DMSO-d6: 0.70-1.17 (3H, m), 1.29-1.63 (4H, m), 1.64-3.67 (24H, m), 3.85-4.20 (1H, m), 5.41-5.53 (1H, m), 7.32 (1H, s), 7.95 (1H, s), 8.12 (1H, s), 11.46 (111, s)
187	2	ESI+:480.3 NMR-DMSO-d6: 0.27-0.70 (4H, m), 1.04-1.90 (12N, m), 2.14-2.62 (4H, m), 2.88-4.00 (11H, m), 4.27-4.81 (2H, m), 7.29-7.44 (1H, m), 7.44-8.06 (1H, m), 8.12 (1H, s), 11.56 (1H, s) mp:162
188	2	ESI+: 490.2 NMR-DMSO-d6: 0.34-0.64 (4H, m), 1.03-1.69 (7H, m), 2.19-2.44 (3H, m), 2.48-4.00 (10H, m), 4.25-4.83 (2H, m), 7.31-7.39 (1H, m), 7.75-8.05 (1H, m), 8.13 (1H, s), 11.54 (1H, s)
189	2	ESI+: 494.3 NMR-DMSO-d6: 0.88-2.08 (17H, m), 2.13-2.43 (3H, m), 2.58-4.01 (13H, m), 4.31-4.88 (2H, m), 7.27-7.39 (1H, m), 7.54-8.01 (1H, m), 8.12 (1H,s), 11.53 (1H, s) mp: 166
190	2	ESI+: 504.3 NMR-DMSO-d6: 1.00-1.61 (6H, m), 1.72-2.12 (7H, m), 2.14-2.42 (3H, m), 2.49-4.00 (10H, m), 4.42-4.88 (2H, m), 7.28-7.41 (1H, m), 7.47-8.02 (1H, m), 8.12 (1H, s), 11.53 (1H, s)
191	2	ESI+: 475.2 NMR-DMSO-d6: 1.14-2.10 (7H, m), 2.19-1.73 (5H, m), 2.95-3.80 (6H, m), 3.83-4.42 (5H, m), 5.73-5.98 (1H, m), 7.33 (1H, s), 7.88-8.03 (1H, m), 8.15 (1H, s), 11,49 (1H, s)

(continued)

Ex	Syn	Data
192	2	ESI+:463.2 NMR-DMSO-d6: 1.05-3.75 (17H, m), 3.78-4.24 (2H, m), 4.53-4.81 (1H, m), 5.15-5.36 (1H, m), 7.34 (1H, s), 7.85-8.02 (1H, m), 8.17 (1H, s), 11.50 (1H, s)
193	5	ESI+:530.3 NMR-DMSO-d6: 0.75-1.12 (3H, m), 1.33-1.57 (4H, m), 2.29 (3H, s), 1.86-3.51 (21H, m), 3.92-4.18 (1H, m), 5.24 (1H, m), 7.33 (1H, s), 7.90-7.99 (1H, m), 8.16 (1H,s), 11.50 (1H, s)
194	5	ESI+:544.3
195	5	ESI+: 466.3 NMR-DMSO-d6: 0.36-0.55 (4H, m), 0.74-1.11 (3H, m), 1.29 (1H, m), 1.34-1.58 (4H, m), 2.02-3.42 (10H, m), 2.30 (3H, s), 3.21 (3H, s), 93-4.15 (1H, m), 4.41-4.79 (2H, m), 7.32 (1H, s), 7.88 (1H, s), 8.12 (1H, s), 11.50 (1H, s)
196	5	ESI+: 473.3
197	5	ESI+: 487.3

[Table 124]

Ex	Syn	Data
198	2	ESI+: 451.3 NMR-DMSO-d6: 0.07-0.22 (2H, m), 0.37-0.51 (2H, m), 0.90-1.04 (1H, m), 1.14-2.05 (4H, m), 2.71-2.74 (5H, m), 2.94-3.63 (6H, m), 3.84-4.28 (5H, m), 5.75-5.88 (1H, m), 7.33 (1H, s), 7.88-8.01 (1H, in), 8.15 (1H, s), 11.49 (1H, s)
199	2	ESI+: 439.3 NMR-DMSO-d6: 0.87 (3H, t, J = 7.2 Hz), 1.13-2.06 (6H, m), 2.08-2.71 (5H, m), 2.96-3.59 (6H, m), 3.82-4.29 (5H, m), 5.74-5.88 (1H, m), 7.33 (1H, s), 7.85-8.03 (1H, m), 8.15 (1H, s), 11.49 (1H, s)
200	2	ESI+: 492.3 NMR-DMSO-d6: 1.56-1.72 (2H, m), 2.02-2.84 (13H, m), 3.02-3.42 (2H, m), 3.47-4.31 (6H, m), 5.76-5.87 (1H, m), 7.33 (1H, s), 7.85-8.02 (1H, m), 8.15 (1H, s), 11.50 (1H, s)
201	2	ESI+: 453.3 NMR-DMSO-d6: 0.80-1.89 (10H, m), 2.08-3.10 (7H, m), 3.19-3.52 (5H, m), 3.81-4.35 (4H, m), 4.42-4.66 (1H, m), 5.73-5.90 (1H, m), 7.33 (1H, s), 7.82-8.01 (1H, m), 8.15 (1H, s), 11.49(1H,s)
202	2	ESI+: 451.2 NMR-DMSO-d6: 1.13-2.02 (8H, m), 2.03-2.73 (7H, m), 2.94-3.62 (4H, m), 3.80-4.32 (6H, m), 5.73-5.89 (1H, m), 7.32 (1H, s), 7.84-8.03 (1H, m), 8.15 (1H, s), 11.49 (1H, s)
203	2	ESI+:479.2 NMR-DMSO-d6: 0.87-2.73 (9H, m), 2.94-3.49 (3H, m), 3.65-3.82 (1H, m), 3.83-4.39 (7H, m), 5.68-5.93 (1H, m), 7.33 (1H, s), 7.80-8.06 (1H, m), 8.15 (1H, s), 11.49 (1H, s)
204	5	ESI+: 516.3 NMR-DMSO-d6: 0.76-1.12 (3H, m), 1.32-1.60 (4H, m), 1.99-3.44 (15H, m), 2.29 (3H, s), 3.20 (3H, s), 3.90-4.18 (1H, m), 4.66-5.02 (2H, m), 7.32 (1H, s), 7.85 (1H, s), 8.15 (1H, s), 11.50 (1H, s)
205	5	ESI+:516.3
206	5	ESI+:459.2
207	2	ESI+:506.3 NMR-DMSO-d6: 1.01-1.57 (3H, m), 1.82-2.65 (7H, m), 2.79-3.84 (13H, m), 3.86-4.18 (2H, m), 5.09-5.35 (1H, m), 7.36 (1H, s), 7.98 (1H, s), 8.19 (1H, s), 11.54(1H,s) mp:186

(continued)

Ex	Syn	Data
208	2	ESI+:540.3 NMR-DMSO-d6: 1.00-1.58 (3H, m), 1.83-3.10 (13H, m), 3.17-4.13 (9H, m), 5.12-5.36 (1H, m), 7.37 (1H, s), 8.02 (1H, s), 8.18 (1H, s), 11.55 (1H, s) mp:190

[Table 125]

Ex	Syn	Data
209	2	ESI+:554.3 NMR-DMSO-d6: 1.02-2.55 (17H, m), 2.81-3.99 (9H, m), 4.43-4.80 (2H, m), 7.34 (1H, s), 7.87-8.03 (1H, m), 8.15 (1H, s), 11.55 (1H, s)
210	2	ESI+:476.2 NMR-DMSO-d6: 0.36-0.60 (4H, m), 1.02-1.57 (4H, m), 2.31-4.00 (14H, m), 4.44-4.74 (2H, m), 7.35 (1H, s), 7.9.1-8.03 (1H, br s), 8.13 (1H, s), 11.52 (1H, s) mp: 187
211	2	ESI+: 490.2 NMR-DMSO-d6: 0.96-1.58 (3H, m), 1.73-2.45 (12H, m), 2.50-3.96 (9H, m), 4.49-4.86 (2H, m), 7.33 (1H, s), 7.81-7.95 (1H, br s), 8.12 (1H, s), 11.52 (1H, s) mp:171
212	2	ESI+:490.3 NMR-DMSO-d6: 0.98-1.57 (3H, m), 1.65-4.00 (22H, m), 5.45-5.58 (1H, m), 7.34 (1H, s), 8.02-8.09 (1H, br s), 8.13 (1H, s), 11.51 (1H, s) mp: 176
213	2	ESI+:515.3 NMR-DMSO-d6: 1.40-2.42 (10H, m), 2.77-2.89 (3H, m), 3.14-3.72 (6H, m), 4.09-4.26 (1H, m), 4.91-5.57 (7H, m), 6.71-6.83 (1H, m), 7.36 (1H, s), 7.50-7.62 (1H, m), 7.88-8.02 (2H, m), 8.20 (1H, s), 11.56 (1H, s)
214	2	ESI+: 513.3 NMR-DMSO-d6: 1.01-1.22 (3H, m), 1.96-4.97 (23H, m), 5.21-5.72 (1H, m), 7.22-8.37 (7H, m), 10.08-10.26 (1H, br s), 11.45-11.67 (1H, m) mp: 221
215	2	ESI+:530.3 NMR-DMSO-d6: 0.73-1.16 (4H, m), 1.28-1.57 (4H, m), 1.81-3.69 (23H, m), 3.88-4.12 (1H, m), 5.12-5.33 (1H, m), 7.33 (1H, s), 7.85-7.99 (1H, m), 8.16 (1H, s), 11.50(1H,s)
216	2	ESI+: 544.3 NMR-DMSO-d6: 0.72-1.13 (3H, m), 1.25-1.87 (10H, m), 1.92-3.43 (19H, m), 3.91-4.17 (1H, m), 4.34-4.86 (2H, m), 7.32 (1H, s), 7.79-7.89 (1H, m), 8.14 (1H, s), 11.49 (1H, s)
217	2	ESI+: 465.2 NMR-DMSO-d6: 0.22-0.49 (4H, m), 0.65-3.77 (20H, m), 3.78-4.15 (2H, m), 4.39-4.76 (1H, m), 4.99-5.40 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.49 (1H, s) mp: 210-211
218	2	ESI+:437.3 NMR-DMSO-d6: 0.29-0.53 (4H, m), 0.97-2.69 (9H, m), 2.94-4.31 (10H, m), 5.71-5.91 (1H, m), 7.32 (1H, s), 7.85-8.01 (1H, m), 8.15 (1H, s), 11.49 (1H, s) mp: 197-198

[Table 126]

Ex	Syn	Data
219	2	ESI+:508.3 NMR-DMSO-d6: 1.75-1.88 (2H, m), 2.10-2.72 (7H, m), 3.11-4.42 (14H, m), 5.73-5.98 (1H, m), 7.33 (1H, s), 7.84-8.03 (1H, m), 8.15 (1H, s), 11.50 (1H, s)
220	2	ESI+:457.3 NMR-DMSO-d6: 1.59-2.72 (12H, m), 2.89-3.68 (6H, m), 3.71-4.32 (5H, m), 4.64-4.74 (0.5H, m), 4.77-4.90 (0.5H, m), 5.70-5.91 (1H, m), 7.3.3 (1H, s), 7.83-8.04 (1H, m), 8.15 (1H, s), 11.49 (1H, s) mp:194
221	2	ESI+:479.2 NMR-DMSO-d6: 1.31-2.54 (11H, m), 2.89-3.50 (3H, m), 3.53-3.76 (2H, m), 3.78-4.12 (2H, m), 4.46-4.68 (1H, m), 5.13-5.35 (1H, m), 6.15 (1H, s), 7.34 (1H, s), 7.88-8.03 (1H, m), 8.17 (1H, s), 11.50 (1H, s)
222	2	ESI+:451.2 NMR-DMSO-d6: 0.18-0.51 (4H, m), 0.74-1.86 (6H, m), 1.95-3.46 (10H, m), 3.63-4.38 (4H, m), 4.40-4.72 (1H, m), 5.69-5.87 (1H, m), 7.32 (1H, s), 7.79-8.02 (1H, m), 8.15 (1H, s), 11.48 (1H, s)
223	2	ESI+:480.3 NMR-DMSO-d6: 0.07-0.17 (2H, m), 0.37-0.47 (2H, m), 0.87-1.02 (1H, m), 2.02-2.73 (11H, m), 3.00-4.28 (12H, m), 5.74-5.87 (1H, m), 7.33 (1H, s), 7.84-8.02 (1H, m), 8.15 (1H, s), 11.49 (1H, s)
224	2	ESI+: 480.1
225	2	ESI+: 494.1 NMR-DMSO-d6: 0.08-0.29 (2H, m), 0.38-0.55 (2H, m), 0.74-1.36 (4H, m), 2.10-3.63 (17H, m), 3.81-4.48 (5H, m), 5.72-5.91 (1H, m), 7.32 (1H, s), 7.92 (1H, br s), 8.15 (1H, s), 11.50 (1H, s)
226	5	ESI+: 482.3 NMR-DMSO-d6: 0.73-1.12 (3H, m), 131-1.57 (4H, m), 1.94-3.44 (12H, m), 2.29 (3H, s), 3.20 (3H, s), 3.81-4.41 (5H, m), 5.80 (1H, m), 7.33 (1H, s), 7.93 (1H, s), 8.15 (1H, s), 11.50 (1H, s)
227	2	ESI+: 451.2 NMR-DMSO-d6: 0.35-0.55 (4H, m), 1.02-2.67 (11H, m), 2.87-4.34 (10H, m), 5.14-5.34 (1H, m), 7.33 (1H, s), 7.90 (1H, s), 8.17 (1H, s), 11.49 (1H, s)
228	2	ESI+: 494.3 NMR-DMSO-d6: 0.10-0.21 (2H, m), 0.39-0.52 (2H, m), 0.89-1.04 (1H, m), 1.86-2.75 (13H, m), 3.09-4.13 (12H, m), 5.16-5.31 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H,s), 11.49 (1H, s)

[Table 127]

Ex	Syn	Data
229	2	E5I+: 494.3 NMR-DMSO-d6: 0.36-0.55 (4H, m), 1.72-2.61 (9H, m), 2.69-3.83 (14H, m), 3.84-4.18 (2H, m), 4.50-4.81 (1H, m), 5.12-5.37 (1H, m), 7.35 (1H, s), 7.99 (1H, s), 8.18 (1H, s), 11.54 (1H, m)
230	2	ESI+: 508. 1 NMR-DMSO-d6: 0.07-0.28 (2H, m), 0.38-0.61 (2H, m), 0.75-1.44 (4H, m), 1.82-3.57 (19H, m), 3.59-3.85 (2H, m), 3.89-4.44 (3H, m), 5.14-5.42 (1H, m), 7.33(1H, s), 7.78-7.99 (1H, m), 8.17(1H, s), 11.50 (1H, s)
231	2	ESI+: 451.1 NMR-DMSO-d6: 0.84-1.42 (10H, m), 1.53-2.44 (14H, m), 2.70-3.14 (2H, m), 3.24-3.44 (1H, m), 4.08 (1H, s), 4.35-4.61 (1H, m), 5.39-5.57 (1H, m), 7.32 (1H, s), 7.94(1H, s), 8.11 (1H, s), 11.44 (1H, s)

(continued)

Ex	Syn	Data
232	2	ESI+:466.3 NMR-DMSO-d6: 0.24-0.55 (4H, m), 0.93-1.85 (8H, m), 2.00-2.55 (3H, m), 2.67-3.97 (14H, m), 4.10-5.04 (2H, m), 7.34 (1H, s), 7.80-8.08 (1H, m), 8.14 (1H, s), 10.04-10.63 (1H, m), 11.51 (1H, m)
233	2	ESI+: 480.3 NMR-DMSO-d6: 1.00-2.43 (17H, m), 2.77-4.12 (13H, m), 4.36-4.98 (3H, m), 7.33 (1H, s), 7.80-8.07 (1H, m), 8.07-8.13 (1H, m), 10.58-11.18 (1H, m), 11.51 (1H, s)
234	2	ESI+: 464.3 NMR-DMSO-d6: 0.07-0.21 (2H, m), 0.34-0.57 (6H, m), 0.90-1.02 (1H, m), 1.23-1.36 (1H, m), 2.13-2.72 (9H, m), 3.00-3.41 (4H, m), 3.43-3.56 (2H, m), 3.57-3.84 (2H, m), 4.44-4.81 (2H, m), 7.32 (1H, s), 7.89 (1H, s), 8.11 (1H, s), 11.48 (1H, s)
235	2	ESI+:478.2 NMR-DMSO-d6: 0.07-0.26 (2H, m), 0.35-0.63 (6H, m), 0.73-1.19 (4H, m), 1.22-1.38 (1H, m), 2.18-3.67 (15H, m), 3.92-4.23 (1H, m), 4.35-4.84 (2H, m), 7.32 (1H, s), 7.88 (1H, s), 8.11 (1H, s), 11.48 (1H, s)
236	2	ESI+: 492.3 NMR-DMSO-d6: 0.09-0.23 (2H, m), 0.38-0.52 (2H, m), 0.78-1.17 (4H, m), 1.64-3.01 (12H, m), 3.10-3.55 (11H, m), 3.85-4.24 (1H, m), 5.40-5.53 (1H, m), 7.32 (1H, s), 7.95 (1H, s), 8.12 (1H, s), 11.46 (1H, s)
237	2	ESI+:492.3 NMR-DMSO-d6: 0.08-0.2.3 (2H, m), 0.35-0.51 (2H, m), 0.78-1.15 (4H, m), 1.76-2.06 (6H, m), 2.21-3.66 (16H, m), 3.92-4.20 (1H, m), 4.48-4.96 (2H, m), 7.31 (1H, s), 7.74-7.80 (1H, br s), 8.11 (1H, s), 11.47 (1H, s)

[Table 128]

Ex	Syn	Data
238	2	ESI+:542.3 NMR-DMSO-d6: 0.05-0.19 (2H, m), 0.35-0.53 (2H, m), 0.73-1.20 (6H, m), 1.82-3.70 (21H, m), 3.90-4.26 (1H, m), 5.17-5.31 (1H, m), 7.34 (1H, s), 7.87-8.00 (1H, m), 8.16 (1H,s), 11.50 (1H, s)
239	2	ESI+:556.3
240	5	ESI+:502.3 NMR-DMSO-d6: 0.72-1.10 (3H, m), 1.62 (2H, m), 1.97-3.40 (15H, m), 2.29 (3H, s), 3.20 (3H, s), 3.90-4.16 (1H, m), 4.66-5.01 (2H, m), 7.32 (1H, s), 7.88 (1H, br.), 8.15 (1H,s), 11.50 (1H, s)
241	5	ESI+: 526.2 NMR-DMSO-d6: 0.76-1.12 (3H, m), 2.09-3.35 (15H, m), 2.30 (3H, s), 3.94-4.18 (1H, m), 4.67-4.99 (2H, m), 7.33 (1H, s), 7.87 (1H, s), 8.15 (1H, s), 11.50 (1H, s)
242	5	ESI+:528.3 NMR-DMSO-d6: 0.13 (2H, m), 0.43 (2H, m), 0.75-1.12 (4H, m), 2.07-3.33 (15H, m), 2.29 (3H, s), 3.47 (2H, m), 3.93-4.17 (1H, m), 4.61-5.02 (2H, m), 7.32 (1H, s), 7.82-7.90 (1H, br.), 8.15 (1H, s), 11.50 (1H, s)
243	2	ESI+: 476.1
244	3	ES1+: 440.1
245	3	ESI+: 454.1
246	3	ESI+: 481.1
247	3	ESI+: 432.1
248	3	ESI+: 432.1

(continued)

Ex	Syn	Data
249	3	ESI+: 515.2
250	3	ESI+: 546.1
251	3	ESI+: 546.2
252	3	ESI+: 438.1
253	3	ESI+: 436.1
254	3	ESI+: 450.1
255	3	ESI+: 464.4 NMR-DMSO-d6: 1.25-1.83 (8H, m), 1.92-2.58 (5H, m), 2.31 (3H, s), 3.10-4.09 (12H, m), 5.18-5.28 (1H, m), 7.33 (1H, s), 7.87 (1H, s), 8.17 (1H, s), 11.50 (1H, s) mp: 228-230
256	3	ESI+: 454.1
257	3	ESI+: 468.1
258	3	ESI+: 504.1
259	3	ESI+: 518.1

[Table 129]

Ex	Syn	Data
260	3	ESI+: 532.1
261	3	ESI+: 487.1
262	3	ESI+: 487.1
263	3	ESI+: 498.1
264	3	ESI+: 500.1
265	3	ESI+: 438.1
266	3	ESI+: 425.1
267	3	ESI+: 478.1
268	3	ESI+: 526.2
269	3	ESI+: 410.1
270	3	ESI+: 450.1
271	3	ESI+: 526.2
272	3	ESI+: 480.1
273	3	ESI+: 494.2
274	3	ESI+: 494.1
275	3	ESI+: 493.1
276	3	ESI+: 521.2
277	3	ESI+: 472.1
278	3	ESI+: 472.1
279	3	ESI+: 486.1
280	3	ESI+: 454.1

(continued)

Ex	Syn	Data
281	3	ESI+: 473.1
282	3	ESI+: 499.1
283	3	ESI+: 499.1
284	3	ESI+: 341.0
285	3	ESI+: 385.0
286	3	ESI+: 398.1
287	3	ESI+: 426.1
288	3	ESI+: 453.1
289	3	ESI+: 468.1
290	3	ESI+: 472.1

[Table 130]

Ex	Syn	Data
291	3	ESI+: 509.1
292	3	ESI+: 466.1
293	3	ESI+: 466.1
294	3	ESI+: 506.1
295	3	ESI+: 494.1
296	3	ESI+: 460.1
297	3	ESI+: 474.1
298	3	ESI+: 452.1
299	3	ESI+: 452.1
300	3	ESI+: 468.1
301	3	ESI+: 454.1
302	3	ESI+: 468.1
303	3.	ESI+: 482.1
304	3	ESI+: 467.1
305	3	ESI+: 466.1
306	3	ESI+: 501.1
307	3	ESI+: 503.1
308	3	ESI+: 474.1
309	3	ESI+: 516.1
310	3	ESI+: 516.1
311	3	ESI+: 516.1
312	3	ESI+: 460.1
313	3	ESI+: 486.0
314	3	ESI+: 486.1

(continued)

Ex	Syn	Data
315	3	ESI+: 486.1
316	3	ESI+: 502.1
317	3	ESI+: 502.1
318	3	ESI+: 515.1
319	3	ESI+: 515.1
320	3	ESI+: 546.1
321	3	ESI+: 474.1

[Table 131]

Ex	Syn	Data
322	3	ESI+: 488.1
323	3	ESI+: 516.1
324	3	ESI+: 10.0
325	3	ESI+: 510.0
326	3	ESI±: 510.0
327	3	ESI+: 418.0
328	3	ES1+: 418.0
329	3	ESI+: 418.0
330	3	ESI+: 432.1
331	3	ESI+: 432.1
332	3	ESI+: 432.1
333	3	ESI+: 452.1
334	3	ESI+: 465.1
335	3	ESI+: 492.1
336	3	ESI+: 486.0
337	3	ESI+: 488.1
338	3	ESI+: 488.1
339	3	ESI+: 515.1
340	3	ESI+: 500.1
341	3	ESI+: 532.1
342	3	ESI+: 532.0
343	3	ESI+: 487.1
344	3	ESI+: 487.1
345	3	ESI+: 438.1
346	3	ESI+: 466.1
347	3	ESI±: 478.1
348	3	ESI+: 492.1

(continued)

Ex	Syn	Data
349	3	ESI+: 492.1
350	3	ESI+: 503.1
351	3	ESI+: 325.1
352	3	ESI+: 450.1

[Table 132]

Ex	Syn	Data
353	3	ESI+: 422.1
354	3	ESI+: 437.1
355	3	ESI+: 424.1
356	3	ESI+: 478.1
357	3	ESI+: 450.1
358	3	ESI+: 452.1
359	3	ESI+: 450.1
360	3	ESI+: 490.1
361	3	ESI+: 492.1
362	3	ESI+: 438.1
363	3	ESI+: 466.1
364	3	ESI+: 451.1
365	3	ESI+: 465.1
366	3	ESI+: 499.1
367	3	ESI+: 402.0
368	3	ESI+: 402.0
369	3	ESI+: 402.0
370	3	ESI+: 470.1
371	3	ESI+: 458.0
372	3	ESI+: 450.1
373	3	ESI+: 434.1
374	3	ESI+: 448.1
375	3	ESI+: 462.1
376	3	ESI+: 438.1
377	3	ESI+: 488.1
378	3	ESI+: 502.1
379	3	ESI+: 516.1
380	3	ESI+: 471.1
381	3	ESI+: 471.1
382	3	ESI+: 482.1

(continued)

Ex	Syn	Data
383	3	ESI+: 422.1

[Table 133]

Ex	Syn	Data
384	3	ESI+: 409.1
385	3	ESI+: 538.2
386	3	ESI+: 379.1
387	3	ESI+: 409.1
388	3	ESI+: 397.0
389	3	ESI+: 385.1
390	3	ESI+: 423.1
391	3	ESI+: 394.1
392	3	ESI+: 422.1
393	3	ESI+: 434.1
394	3	ESI+: 436.1
395	3	ESI+: 449.1
396	3	ESI+: 462.1
397	3	ESI+: 464.1
398	3	ESI+: 477.1
399	3	ESI+: 478.1
400	3	ESI+: 505.1
401	3	ESI+: 456.1
402	3	ESI+: 470.1
403	3	ESI+: 470.1
404	3	ESI+: 472.1
405	3	ESI+: 472.1
406	3	ESI+: 486.1
407	3	ESI+: 438.1
408	3	ESI+: 483.1
409	3	ESI+: 467.1
410	3	ESI+: 487.0
411	3	ESI+: 522.0, 524.0
412	3	ESI+: 489.0
413	3	ESI+: 502.0
414	3	ESI+: 487.0

[Table 134]

Ex	Syn	Data
415	3	ESI+: 503.0
416	3	ESI+: 507.0, 509.0
417	3	ESI+: 498.0
418	3	ESI+: 498.0
419	3	ESI+: 541.0
420	3	ESI+: 502.0
421	3	ESI+: 542.0
422	3	ESI+: 551.9,553.9
423	3	ESI+: 488.1
424	3	ESI+: 475.0
425	3	ESI+: 438.1
426	3	ESI+: 452.1
427	2	ESI+: 478.3 NMR-DMSO-d6: 1.86-2.88 (11H, m), 3.12-4.18 (10H, m), 5.16-5.31 (1H, m), 7.33 (1H, s), 7.88 (1H, s), 8,17 (1H, s),11.50 (1H, s)
428	3	ESI+: 507.1
429	3	ESI+: 509.1
430	3	ESI+: 548.0
431	3	ESI+: 501.1
432	3	ESI+: 516.1
433	3	ESI+: 544.1
434	3	ESI+: 544.1
435	3	ESI+: 544.1
436	3	ESI+: 411.1
437	3	ESI+: 473.0
438	3	ESI+: 488.1
439	3	ESI+: 474.0
440	3	ESI+: 487.0
441	3	ESI+: 425.0
442	3	ESI+: 486.0
443	3	ESI+: 486.0
444	3	ESI+: 424.1

[Table 135]

Ex	Syn	Data
445	3	ESI+: 486.0
446	3	ESI+: 438.1
447	3	ESI+: 492.1

(continued)

Ex	Syn	Data
448	3	ESI+: 492.1
449	3	ESI+: 424.1
450	3	ESI+: 504.0
451	3	ESI+: 496.1
452	3	ESI+: 522.1
453	3	ESI+: 523.1
454	3	ESI+: 510.1
455	3	ESI+: 459.0
456	3	ESI+: 449.0
457	3	ESI+: 514.0
458	3	ESI+: 516.1
459	3	ESI+: 546.0
460	3	ESI+: 397.0
461	3	ESI+: 433.1
462	3	ESI+: 498.1
463	3	ESI+: 500.1
464	3	ESI+: 514.1
465	3	ESI+: 530.1
466	3	ESI+: 466.1
467	3	ESI+: 510.1
468	3	ESI+: 464.1
469	3	ESI+: 478.1
470	3	ESI+: 423.1
471	3	ESI+: 453.0
472	3	ESI+: 498.1
473	8	ESI+: 453.0
474	8	ESI+: 439.0
475	8	ESI+: 453.0

[Table 136]

Ex	Syn	Data
476	8	ESI+: 515.0
477	8	ESI+: 515.0
478	8	ESI+: 515.0
479	8	ESI+: 529.0
480	8	ESI+: 529.0
481	8	ESI+: 531.0

(continued)

Ex	Syn	Data
482	8	ESI+: 468.0
483	6	ESI+: 516.0
484	8	ESI+: 437.0
485	8	ESI+: 423.0
486	8	ESI+: 423.0
487	8	ESI+: 437.0
488	8	ESI+: 499.0
489	8	ESI+: 499.0
490	8	ESI+: 499.0
491	8	ESI+: 499.0
492	8	ESI+: 513.1
493	8	ESI+: 513.1
494	8	ESI+: 515.1
495	8	ESI+: 452.1
496	8	ESI+: 500.1
497	9	ESI+: 480.1
498	9	ESI+: 480.1
499	9	ESI+: 494.1
500	9	ESI+: 508.1
501	9	ESI+: 530.1
502	9	ESI+: 501.1
503	9	ESI+: 501.1
504	9	ESI+: 517.1
505	9	ESI+: 556.2
506	9	ESI+: 517.1

[Table 137]

Ex	Syn	Data
507	9	ESI+: 556.2
508	9	ESI+: 517.1
509	9	ESI+: 517.1
510	9	ESI+: 501.1
511	9	ESI+: 505.1
512	9	ESI+: 572.1
513	9	ESI+: 503.1
514	9	ESI+: 490.1
515	9	ESI+: 507.0

(continued)

Ex	Syn	Data
516	9	ESI+: 578.1
517	9	ESI+: 466.1
518	9	ESI+: 464.1
519	9	ESI+: 468.1
520	9	ESI+: 496.1
521	9	ESI+: 492.1
522	9	ESI+: 528.1
523	9	ESI+: 504.1
524	9	ESI+: 522.0
525	9	ESI+: 522.1
526	9	ESI+: 522.2
527	9	ESI+: 506.1
528	9	ESI+: 508.1
529	10	ESI+: 517.1
530	10	ESI+: 600.2
531	10	ESI+: 600.2
532	10	ESI+: 544.1
533	10	ESI+: 584.2
534	10	ESI+: 586.2
535	10	ESI+: 572.2
536	10	ESI+: 584.2
537	10	ESI+: 586.2

[Table 138]

Ex	Syn	Data
538	10	ESI+: 609.0, 611.0
539	10	ESI+: 535.1, 537.1
540	10	ESI+: 558.1
541	10	ESI+: 520.1
542	10	ESI+: 489.1
543	10	ESI+: 503.1
544	10	ESI+: 602.2
545	10	ESI+: 504.1
546	10	ESI+: 518.1
547	10	ESI+: 518.1
548	10	ESI+: 504.1
549	10	ESI+: 518.1

(continued)

Ex	Syn	Data
550	10	ESI+: 518.1
551	10	ESI+: 504.1
552	10	ESI±: 518.1
553	10	ESI+: 518.1
554	10	ES1+: 518.1
555	10	ESI+: 524.1, 526.1
556	10	ES1+: 532.2
557	10	ES1+: 532.2
558	10	ESI+: 532.2
559	10	ESI+: 532.2
560	10	ESI+: 538.1, 540.1
561	10	ESI+: 538.1, 540.1
562	10	ESI+: 548.2
563	10	ESI+: 552.1, 554.1
564	10	ESI+: 574.2
565	10	ESI+: 582.0, 584.0
566	10	ESI+: 490.1
567	10	ESI+: 490.1
568	10	ESI+: 504.1

[Table 139]

Ex	Syn	Data
569	10	ESI+: 504.1
570	10	ESI+: 504.1
571	10	ESI+: 504.1
572	10	ESI+: 518.1
573	10	ESI+: 532.2
574	10	ESI+: 546.2
575	10	ESI+: 507.1
576	10	ESI+: 507.1
577	10	ESI+: 535.1
578	10	ESI+: 505.1
579	10	ESI+: 519.1
580	10	ESI+: 508.1
581	10	ESI+: 522.2
582	10	ESI+: 520.1
583	10	ESI+: 515.2

(continued)

Ex	Syn	Data
584	10	ESI+: 515.2
585	10	ESI+: 531.1
586	10	ESI+: 570.2
587	10	ESI+: 531.1
588	10	ESI+: 570.2
589	10	ESI+: 531.1
590	10	ESI+: 570.2
591	10	ESI+: 531.1
592	10	ESI+: 515.2
593	10	ESI+: 519.1
594	10	ESI+: 586.2
595	10	ESI+: 521.1
596	10	ESI+: 592.1
597	10	ESI+: 528.2
598	10	ESI+: 522.2
599	10	ESI+: 569.1

[Table 140]

Ex	Syn	Data
600	10	ESI+: 531.1
601	10	ESI+: 569.2
602	10	ESI+: 515.2
603	10	ESI+: 515.2
604	10	ESI+: 531.1
605	10	ESI+: 531.1
606	10	ESI+: 516.2
607	10	ESI+: 532.1
608	10	ESI+: 502.1
609	10	ESI+: 502.1
610	10	ESI+: 555.1
611	10	ESI+: 517.1
612	10	ESI+: 555.1
613	10	ESI+: 501.1
614	10	ESI+: 501.1
615	10	ESI+: 517.1
616	10	ESI+: 517.1
617	10	ESI+: 502.2

(continued)

Ex	Syn	Data
618	10	ESI+: 518.1
619	10	ESI+: 488.1
620	10	ESI+: 488.1
621	3	ESI+: 512.1
622	3	ESI+: 528.2
623	3	ESI+: 516.2
624	3	ESI+: 516.2
625	3	ESI+: 517.2
626	3	ESI+: 459.1
627	3	ESI+: 445.1
628	3	ESI+: 514.2
629	3	ESI+: 526.1
630	3	ESI+: 542.2

[Table 141]

Ex	Syn	Data
631	3	ESI+: 530.2
632	3	ESI+: 530.2
633	3	ESI+: 531.2
634	3	ESI+: 473.1
635	3	ESI+: 459.1
636	3	ESI+: 528.2
637	3	ESI+: 448.1
638	3	ESI+: 464.2
639	3	ESI+: 452.2
640	3	ESI+: 452.2
641	3	ESI+: 453.2
642	3	ESI+: 395.1
643	3	ESI+: 381.1
644	3	ESI+: 450.2
645	3	ESI+: 462.1
646	3	ESI+: 478.2
647	3	ESI+: 466.2
648	3	ESI+: 466.2
649	3	ESI+: 467.2
650	3	ESI+: 409.2
651	3	ES1+: 395.1

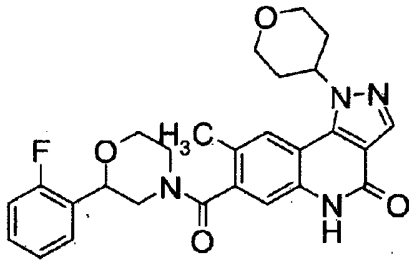
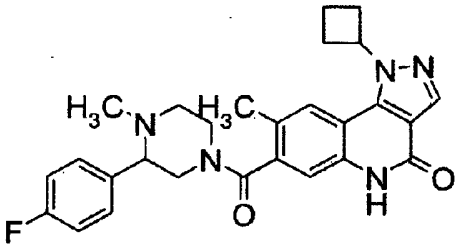
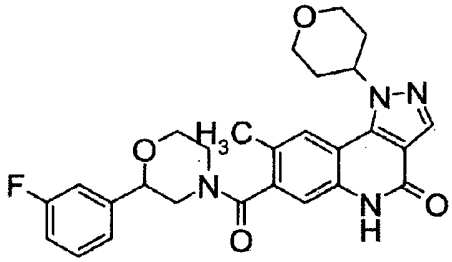
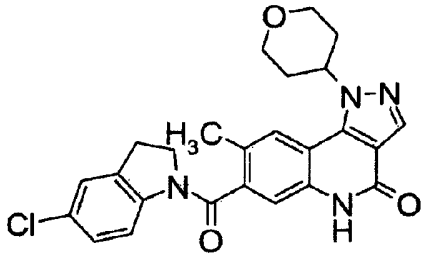
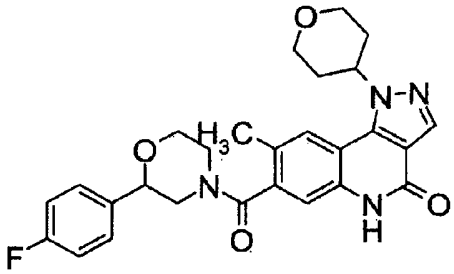
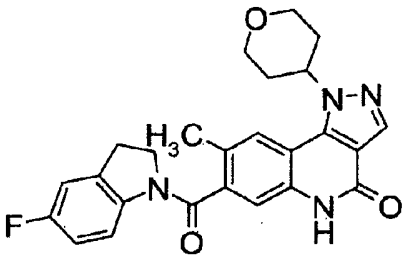
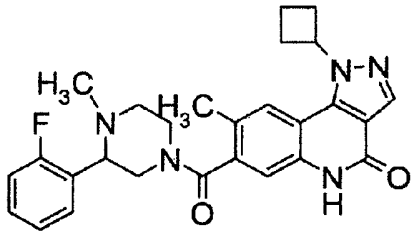
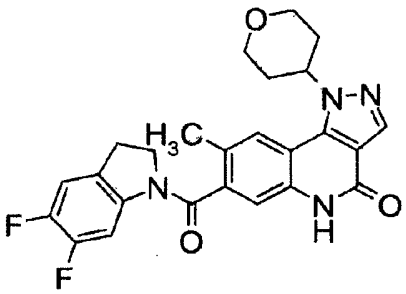
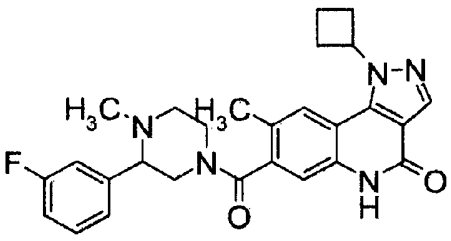
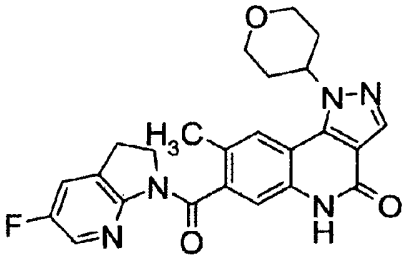
(continued)

Ex	Syn	Data
652	3	ESI+: 464.1
653	3	ESI+: 462.1
654	3	ESI+: 466.2
655	3	ESI+: 466.2
656	3	ESI+: 467.2
657	3	ESI+: 409.2
658	3	ESI+: 464.1
659	3	ESI+: 397.1
660	3	ESI+: 482.2
661	3	ESI+: 496.2

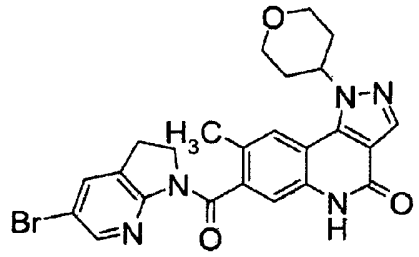
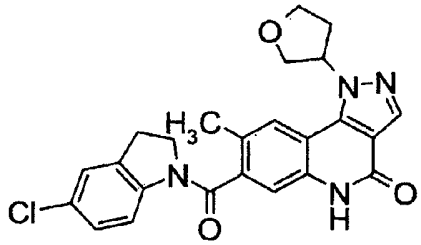
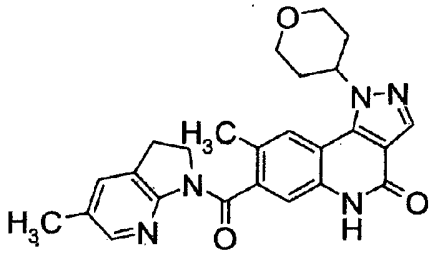
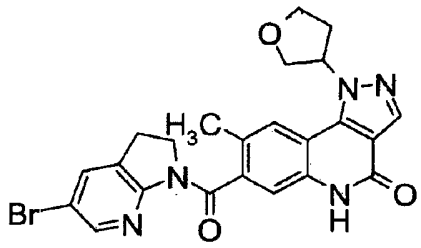
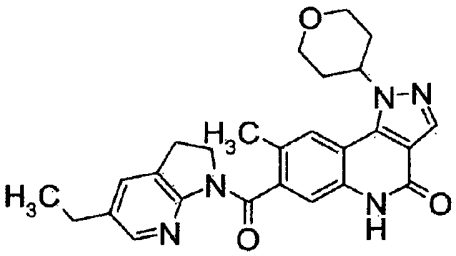
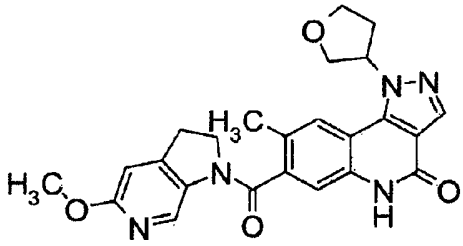
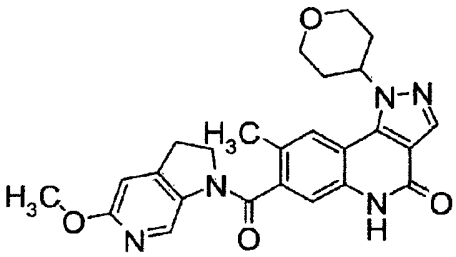
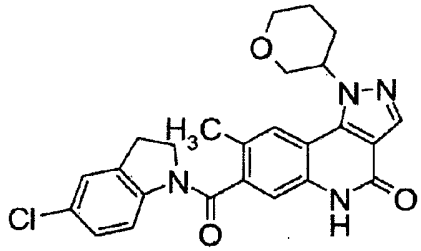
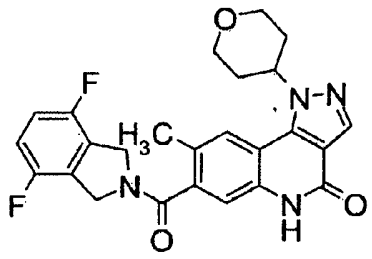
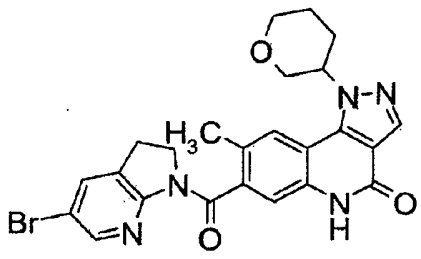
[Table 142]

Ex	Syn	Data
662	3	ESI+: 496.2
663	3	ESI+: 482.2
664	3	ESI+: 459.1
665	3	ESI+: 505.1
666	3	ESI+: 505.1
667	3	ESI+: 480.1
668	3	ESI+: 439.1
669	3	ESI+: 453.2
670	3	ESI+: 465.2
671	3	ESI+: 425.2
672	3	ESI+: 473.1
673	3	ESI+: 473.1
674	3	ESI+: 493.1
675	3	ESI+: 493.1
676	3	ESI+: 507.1
677	3	CSI+: 507.1

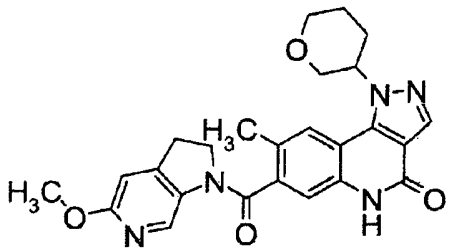
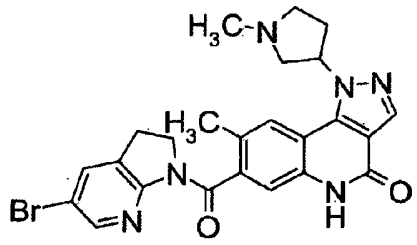
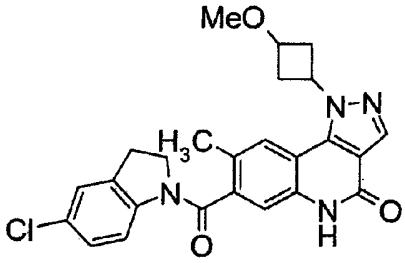
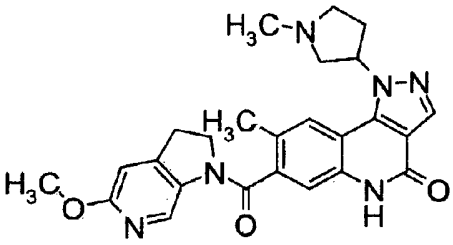
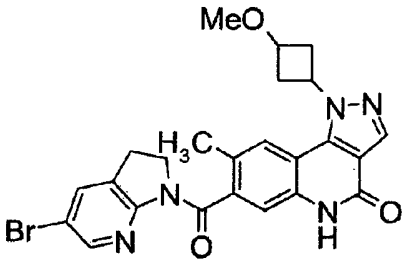
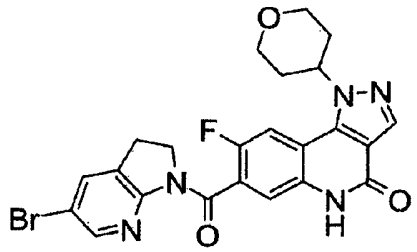
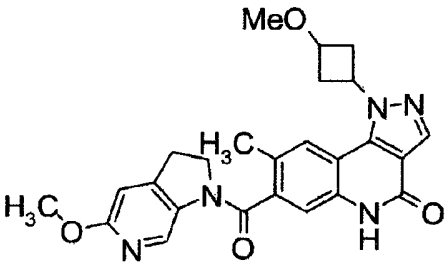
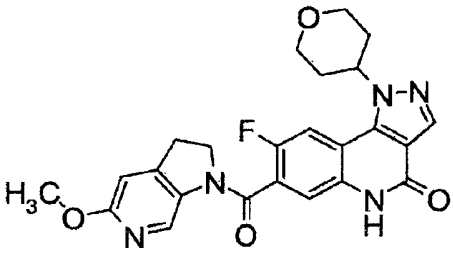
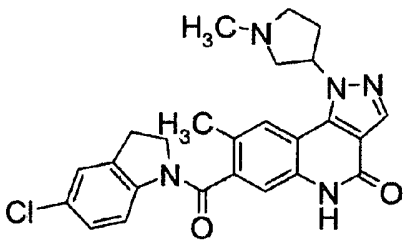
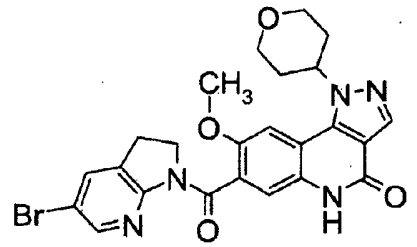
[Table 143]

No	Structure	No	Structure
1		6	
2		7	
3		8	
4		9	
5		10	

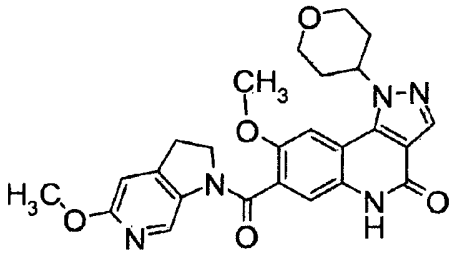
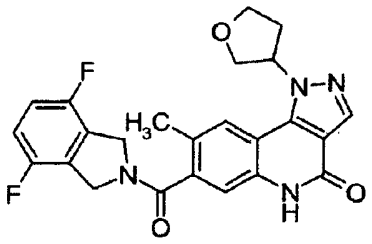
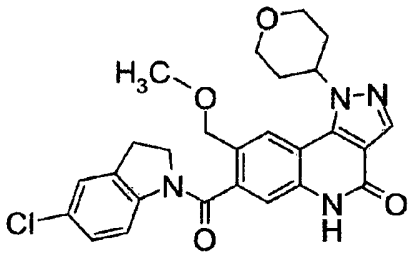
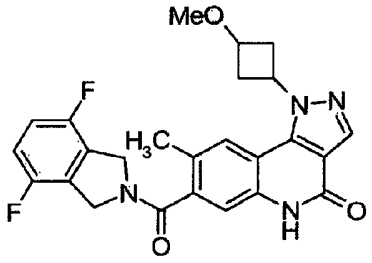
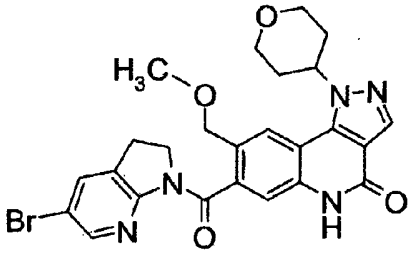
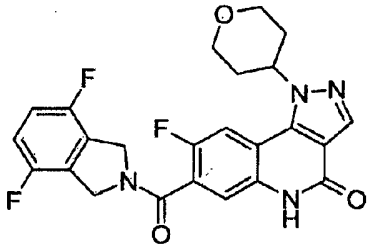
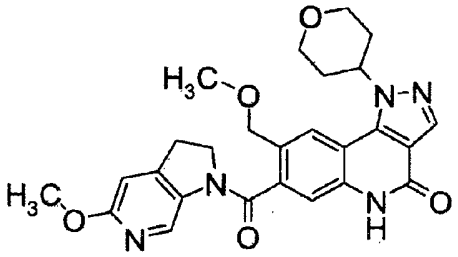
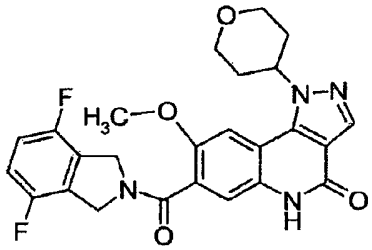
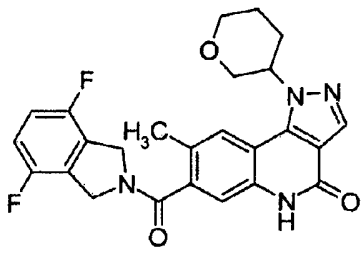
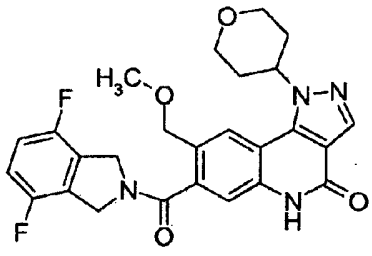
[Table 144]

No	Structure	No	Structure
11		16	
12		17	
13		18	
14		19	
15		20	

[Table 145]

No	Structure	No	Structure
21		26	
22		27	
23		28	
24		29	
25		30	

[Table 146]

No	Structure	No	Structure
31		35	
32		37	
33		38	
34		39	
35		40	

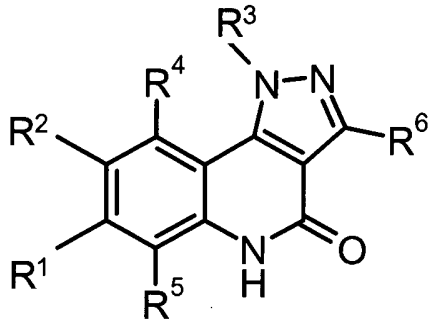
Industrial Applicability

[0216] The compound of the formula (I) or a salt thereof has a PDE9 inhibitory action, and can be used as an agent for preventing and/or treating diseases related to degradation of cGMP by PDE9, for example, underactive bladder, hypotonic bladder, acontractile bladder, neurogenic bladder, detrusor underactivity, overactive bladder, urinary frequency, nocturia, incontinence, benign prostatic hyperplasia, lower urinary tract symptoms, voiding dysfunction accompanying

urethra relaxation failure or detrusor-external urethral sphincter dyssynergia, interstitial cystitis, chronic prostatitis, or urethra calculus.

Claims

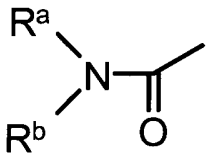
1. A compound of the formula (I) or a salt thereof:



(I)

wherein

R^1 is hydrogen, halogeno-C_{1-6} alkyl, C_{1-6} alkyl, or -O-C_{1-6} alkyl,
R^2 is a group of the formula (II):



(II)

R^3 is C_{1-6} alkylene-(cycloalkyl which may be substituted with halogen or -O-C_{1-6} alkyl); C_{1-6} alkylene-oxygen-containing saturated hetero ring; cycloalkyl which may be substituted with halogen or -O-C_{1-6} alkyl; an oxygen-containing saturated hetero ring; or a monocyclic nitrogen-containing saturated hetero ring which may be substituted with C_{1-6} alkyl, C_{1-6} alkylene-aryl, or -CO-C_{1-6} alkylene-O-C_{1-6} alkyl,
R^4, R^5 and R^6 are hydrogen,
R^a and R^b are combined with the adjacent nitrogen atom to form a monocyclic nitrogen-containing hetero ring, which may be substituted with a group selected from:

-OH; halogeno-C_{1-6} alkyl; -O-C_{1-6} alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; C_{1-6} alkylene-O-cycloalkyl; -O-cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl, -O-cycloalkyl, -O-C_{1-6} alkyl, and -O-halogeno-C_{1-6} alkyl; and C_{1-6} alkylene-O-C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl,
the group G_1 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-hetero ring, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-hetero ring, aryl which may be substituted with C_{1-6} alkyl, a hetero ring which may be substituted with C_{1-6} alkyl, -COOH, -CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, - CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, - CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CO-N(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring, and
the group G_2 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno- C_{1-6} alkyl, cyano, -N(C_{1-6} alkyl)$_2$, -NH-CO-C_{1-6} alkyl, C_{1-6}

alkylene-O-C_{1-6} alkyl, C_{1-6} alkylene-hetero ring, aryl, a hetero ring which may be substituted with C_{1-6} alkyl, -COOH, -CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, -CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CON(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring

wherein "aryl" refers to a C_{6-14} monocyclic to tricyclic aromatic hydrocarbon ring group and the term "hetero ring" refers to a ring group containing (i) a monocyclic 3- to 8-membered ring containing 1 to 4 hetero atoms selected from oxygen, sulfur and nitrogen, or (ii) a bi- to tricyclic ring containing 1 to 5 hetero atoms selected from oxygen, sulfur and nitrogen, formed by ring fusion of a monocyclic hetero ring with one or two rings selected from the group consisting of a monocyclic hetero ring, a benzene ring, C_{5-8} cycloalkane, and C_{5-8} cycloalkene.

2. The compound or a salt thereof as set forth in claim 1, wherein the monocyclic nitrogen-containing hetero ring which may be substituted, formed by R^a and R^b which are combined with the adjacent nitrogen atom, is piperidyl or piperazinyl, each of which may be substituted with 1 to 3 groups selected from:

-OH; halogeno-C_{1-6} alkyl; -O-C_{1-6} alkyl which may be substituted with 1 to 3 groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl; aryl which may be substituted with a group selected from a group G_1; a hetero ring which may be substituted with a group selected from a group G_2; C_{1-6} alkylene-O-cycloalkyl; -O- cycloalkyl; -O-(hetero ring which may be substituted with a group selected from a group G_2); C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl, -O-cycloalkyl, -O-C_{1-6}alkyl, and -O-halogeno-C_{1-6} alkyl; and C_{1-6} alkylene-O-C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl and cycloalkyl,
the group G_1 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-hetero ring, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno-C_{1-6} alkyl, -N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-N(C_{1-6} alkyl)$_2$, C_{1-6} alkylene-hetero ring, aryl which may be substituted with C_{1-6} alkyl, a hetero ring which may be substituted with C_{1-6} alkyl, -COOH, -CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, - CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, - CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CO-N(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring, and
the group G_2 consists of halogen, C_{1-6} alkyl, halogeno-C_{1-6} alkyl, -OH, -O-C_{1-6} alkyl, -O-C_{1-6} alkylene-aryl, -O-C_{1-6} alkylene-hetero ring, -O-halogeno- C_{1-6} alkyl, cyano, -N(C_{1-6} alkyl)$_2$, -NH-CO-C_{1-6} alkyl, C_{1-6} alkylene-O-C_{1-6} alkyl, C_{1-6} alkylene-hetero ring, aryl, a hetero ring which may be substituted with C_{1-6} alkyl, -COOH,-CO-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-O-C_{1-6} alkyl, -CO-O-C_{1-6} alkylene-aryl, -CO-O-C_{1-6} alkylene-O-aryl, -CO-NH_2, -CO-NH-C_{1-6} alkyl, -CO-N(C_{1-6} alkyl)$_2$, -CO-N(C_{1-6} alkyl)-aryl, -CON(C_{1-6} alkyl)-hetero ring, -CO-N(C_{1-6} alkyl)-(C_{1-6} alkylene-aryl), -CO-NH-C_{1-6} alkylene-OH, and -CO-NH-hetero ring.

3. The compound or a salt thereof as set forth in claim 2, wherein
piperidyl or piperazinyl, each of which may be substituted, formed by R^a and R^b which are combined with the adjacent nitrogen atom, may be substituted with 1 to 3 groups selected from the group consisting of:

- O-C_{1-6} alkyl which may be substituted with 1 to 3 groups selected from halogen and cycloalkyl; C_{1-6} alkylene-O-cycloalkyl; -O-cycloalkyl; C_{1-6} alkyl which may be substituted with one or more groups selected from the group consisting of halogen, halogeno-C_{1-6} alkyl, and -O-C_{1-6} alkyl; or C_{1-6} alkylene-O-C_{1-6} alkyl.

4. The compound or a salt thereof as set forth in any one of claims 1 to 3, wherein
R^1 is C_{1-6} alkyl, and
R^3 is C_{1-6} alkylene-(cycloalkyl), C_{1-6} alkylene-(cycloalkyl substituted with two halogen atoms), cycloalkyl, cycloalkyl substituted with two halogen atoms, an oxygen-containing saturated hetero ring, or a monocyclic nitrogen-containing saturated hetero ring substituted with C_{1-6} alkyl.

5. The compound or a salt thereof as set forth in any one of claims 1 to 3, wherein
R^1 is C_{1-6} alkyl, and
R^3 is cycloalkyl or an oxygen-containing saturated hetero ring.

6. The compound or a salt thereof as set forth in claim 1, which is
8-[(4-{[(2S)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-l-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyra-

zolo[4,3-c]quinolin-4-one,
7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-[(4-{[(2R)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
8-{[4-(2-methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluoroethyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

7. The compound or a salt thereof as set forth in claim 1, which is
7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluoroethyl)piperazin-1-yl]carbonyl-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

8. The compound or a salt thereof as set forth in claim 1, which is
8-[(4-{[(2S)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

9. The compound or a salt thereof as set forth in claim 1, which is
7-methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

10. The compound or a salt thereof as set forth in claim 1, which is
8-[(4-{[(2R)-2-fluoropropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

11. The compound or a salt thereof as set forth in claim 1, which is
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

12. The compound or a salt thereof as set forth in claim 1, which is
8-{[4-(2-methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

13. The compound or a salt thereof as set forth in claim 1, which is
7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluoroethyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinolin-4-one,
or a salt thereof.

14. A pharmaceutical composition comprising the compound or a salt thereof as set forth in any one of claims 1 to 13, and a pharmaceutically acceptable excipient.

15. Use of the compound or a salt thereof as set forth in any one of claims 1 to 13 for the manufacture of the pharmaceutical composition for preventing or treating underactive bladder.

16. Use of the compound or a salt thereof as set forth in any one of claims 1 to 13 for the manufacture of the pharmaceutical composition for preventing or treating voiding dysfunction in the underactive bladder.

17. Use of the compound or a salt thereof as set forth in any one of claims 1 to 13 for the manufacture of the pharmaceutical composition for preventing or treating benign prostatic hyperplasia.

18. Use of the compound or a salt thereof as set forth in any one of claims 1 to 13 for the manufacture of the pharmaceutical composition for preventing or treating voiding dysfunction accompanying benign prostatic hyperplasia.

19. The compound or a salt thereof as set forth in any one of claims 1 to 13, for use in a method of preventing or treating underactive bladder.

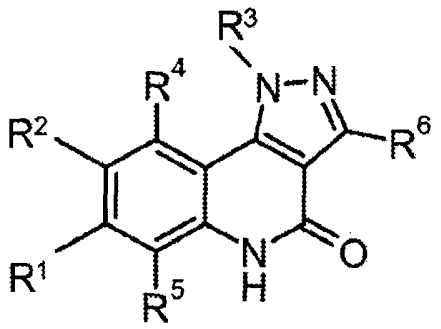
20. The compound or a salt thereof as set forth in any one of claims 1 to 13, for use in a method of preventing or treating voiding dysfunction in the underactive bladder.

21. The compound or a salt thereof as set forth in any one of claims 1 to 13, for use in a method of preventing or treating benign prostatic hyperplasia.

22. The compound or a salt thereof as set forth in any one of claims 1 to 13, for use in a method of preventing or treating voiding dysfunction accompanying benign prostatic hyperplasia.

Patentansprüche

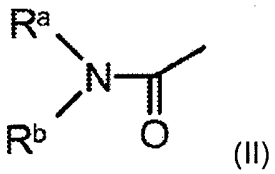
1. Verbindung der Formel (I) oder ein Salz davon:



(I)

worin:

R^1 Wasserstoff, Halogen-C_{1-6}-alkyl, C_{1-6}-Alkyl oder -O-C_{1-6}-Alkyl ist,
R^2 eine Gruppe der Formel (II):



(II)

ist,
R^3 C_{1-6}-Alkylen-(cycloalkyl, das mit Halogen oder -O-C_{1-6}-Alkyl substituiert sein kann); ein C_{1-6}-Alkylen-sauerstoffhaltiger gesättigter Heteroring; Cycloalkyl, das mit Halogen oder -O-C_{1-6}-Alkyl substituiert sein kann; ein sauerstoffhaltiger gesättigter Heteroring oder ein monocyclischer stickstoffhaltiger gesättigter Heteroring, der mit C_{1-6}-Alkyl, C_{1-6}-Alkylen-aryl oder -O-C_{1-6}-Alkylen-O-C_{1-6}-alkyl substituiert sein kann, ist,
R^4, R^5 und R^6 Wasserstoff sind,
R^a und R^b mit dem benachbarten Stickstoffatom verbunden sind, um einen monocyclischen stickstoffhaltigen

Heteroring zu bilden, der mit einer Gruppe, ausgewählt aus:
-OH; Halogen-C_{1-6}-alkyl; -O-C_{1-6}-Alkyl, das mit 1 bis 3 Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl und Cycloalkyl, substituiert sein kann; Aryl, das mit einer Gruppe, ausgewählt aus der Gruppe G_1, substituiert sein kann; einem Heteroring, der mit einer Gruppe, ausgewählt aus der Gruppe G_2, substituiert sein kann; C_{1-6}-Alkylen-O-cycloalkyl; -O-Cycloalkyl; -O-(Heteroring, der mit einer Gruppe, ausgewählt aus der Gruppe G_2, substituiert sein kann); C_{1-6}-Alkyl, das mit einer oder mehreren Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl, -O-Cycloalkyl, -O-C_{1-6}-Alkyl und -O-Halogen-C_{1-6}-alkyl, substituiert sein kann; und C_{1-6} Alkylen-O-C_{1-6}-alkyl, das mit einer oder mehreren Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl und Cycloalkyl, substituiert sein kann, substituiert sein kann,
die Gruppe G_1 aus Halogen, C_{1-6}-Alkyl, Halogen-C_{1-6}-alkyl, -OH, -O-C_{1-6}-Alkyl, -O-Heteroring, -O-C_{1-6}-Alkylen-aryl, -O-C_{1-6}-Alkylen-Heteroring, -O-Halogen-C_{1-6}-alkyl, -N(C_{1-6}-Alkyl)$_2$, C_{1-6}-Alkylen-N(C_{1-6}-alkyl)$_2$, C_{1-6}-Alkylen-Heteroring, Aryl, das mit C_{1-6}-Alkyl substituiert sein kann, Heteroring, der mit C_{1-6}-Alkyl substituiert sein kann, -COOH, -CO-O-C_{1-6}-Alkyl, -CO-O-C_{1-6}-Alkylen-O-C_{1-6}-alkyl, -CO-O-C_{1-6}-Alkylen-aryl, -CO-O-C_{1-6}-Alkylen-O-aryl, -CO-NH_2, -CO-NH-C_{1-6}-Alkyl, -CO-N(C_{1-6}-Alkyl)$_2$, -CO-N(C_{1-6}-Alkyl)-aryl, -CO-N(C_{1-6}-Alkyl)-Heteroring, -CO-N(C_{1-6}-Alkyl)-(C_{1-6}-alkylen-aryl), -CO-NH-C_{1-6}-Alkylen-OH und - CO-NH-Heteroring besteht und
die Gruppe G_2 aus Halogen, C_{1-6}-Alkyl, Halogen-C_{1-6}-alkyl, -OH, -O-C_{1-6}-Alkyl, -O-C_{1-6}-Alkylen-aryl, -O-C_{1-6}-Alkylen-Heteroring, -O-Halogen-C_{1-6}-alkyl, Cyano, -N(C_{1-6}-Alkyl)$_2$, -NH-CO-C_{1-6}-Alkyl, C_{1-6}-Alkylen-O-C_{1-6}-alkyl, C_{1-6}-Alkylen-Heteroring, Aryl, Heteroring, der mit C_{1-6}-Alkyl substituiert sein kann, -COOH, -CO-O-C_{1-6}-Alkyl, -CO-O-C_{1-6}-Alkylen-O-C_{1-6}-alkyl, -CO-O-C_{1-6}-Alkylen-aryl, -CO-O-C_{1-6}-Alkylen-O-aryl, -CO-NH_2, -CO-NH-C_{1-6}-Alkyl, -CO-N(C_{1-6}-Alkyl)$_2$, -CO-N(C_{1-6}-Alkyl)-aryl, -CO-N(C_{1-6}-Alkyl)-Heteroring, -CO-N(C_{1-6}-Alkyl)-(C_{1-6}-alkylen-aryl), -CO-NH-C_{1-6}-Alkylen-OH und -CO-NH-Heteroring besteht,

wobei sich "Aryl" auf eine monocyclische bis tricyclische aromatische C_{6-14}-Kohlenwasserstoffringgruppe bezieht und der Ausdruck "Heteroring" sich auf eine Ringgruppe bezieht, die (i) einen monocyclischen 3- bis 8-gliedrigen Ring mit 1 bis 4 Heteroatom(en), ausgewählt aus Sauerstoff, Schwefel und Stickstoff, oder (ii) einen bi- bis tricyclischen Ring mit 1 bis 5 Heteroatom(en), ausgewählt aus Sauerstoff, Schwefel und Stickstoff, der durch Ringkondensation eines monocyclischen Heterorings mit einem oder zwei Ring(en), ausgewählt aus der Gruppe bestehend aus einem monocyclischen Heteroring, einem Benzolring, C_{5-8}-Cycloalkan und C_{5-8}-Cycloalken, gebildet ist, enthält.

2. Verbindung oder ein Salz davon gemäss Anspruch 1, wobei der monocyclische stickstoffhaltige Heteroring, der substituiert sein kann, der durch R^a und R^b, die mit dem benachbarten Stickstoffatom verbunden sind, gebildet ist, Piperidyl oder Piperazinyl ist, die jeweils mit 1 bis 3 Gruppe(n), ausgewählt aus:

-OH; Halogen-C_{1-6}-alkyl; -O-C_{1-6}-Alkyl, das mit 1 bis 3 Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl und Cycloalkyl, substituiert sein kann; Aryl, das mit einer Gruppe, ausgewählt aus der Gruppe G_1, substituiert sein kann; einem Heteroring, der mit einer Gruppe, ausgewählt aus der Gruppe G_2, substituiert sein kann; C_{1-6}-Alkylen-O-cycloalkyl; -O-Cycloalkyl; -O-(Heteroring, der mit einer Gruppe, ausgewählt aus der Gruppe G_2, substituiert sein kann); C_{1-6}-Alkyl, das mit einer oder mehreren Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl, -O-Cycloalkyl, -O-C_{1-6}-Alkyl und -O-Halogen-C_{1-6}-alkyl, substituiert sein kann; und C_{1-6}-Alkylen-O-C_{1-6}-alkyl, das mit einer oder mehreren Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl und Cycloalkyl, substituiert sein können,
die Gruppe G_1 aus Halogen, C_{1-6}-Alkyl, Halogen-C_{1-6}-alkyl, -OH, -O-C_{1-6}-Alkyl, -O-Heteroring, -O-C_{1-6}-Alkylen-aryl, -O-C_{1-6}-Alkylen-Heteroring, -O-Halogen-C_{1-6}-alkyl, -N(C_{1-6}-Alkyl)$_2$, C_{1-6}-Alkylen-N(C_{1-6}-alkyl)$_2$, C_{1-6}-Alkylen-Heteroring, Aryl, das mit C_{1-6}-Alkyl substituiert sein kann, Heteroring, der mit C_{1-6}-Alkyl, -COOH, -CO-O-C_{1-6}-Alkyl, -CO-O-C_{1-6}-Alkylen-O-C_{1-6}-alkyl, -CO-O-C_{1-6}-Alkylen-aryl, -CO-O-C_{1-6}-Alkylen-O-aryl, -CO-NH_2, -CO-NH-C_{1-6}-Alkyl, -CO-N(C_{1-6}-Alkyl)$_2$, -CO-N(C_{1-6}-Alkyl)-aryl, -CO-N(C_{1-6}-Alkyl)-Heteroring, -CO-N(C_{1-6}-Alkyl)-(C_{1-6}-alkylen-aryl), -CO-NH-C_{1-6}-Alkylen-OH und -CO-NH-Heteroring besteht, und die Gruppe G_2 aus Halogen, C_{1-6}-Alkyl, Halogen-C_{1-6}-alkyl, -OH, -O-C_{1-6}-Alkyl, -O-C_{1-6}-Alkylen-aryl, -O-C_{1-6}-Alkylen-Heteroring, -O-Halogen-C_{1-6}-alkyl, Cyano, -N(C_{1-6}-Alkyl)$_2$, -NH-CO-C_{1-6}-Alkyl, C_{1-6}-Alkylen-O-C_{1-6}-alkyl, C_{1-6}-Alkylen-Heteroring, Aryl, Heteroring, der mit C_{1-6}-Alkyl substituiert sein kann, -COOH, -CO-O-C_{1-6}-Alkyl, -CO-O-C_{1-6}-Alkylen-O-C_{1-6}-alkyl, -CO-O-C_{1-6}-Alkylen-aryl, -CO-O-C_{1-6}-Alkylen-O-aryl, -CO-NH_2, -CO-NH-C_{1-6}-Alkyl, -CO-N(C_{1-6}-Alkyl)$_2$, -CO-N(C_{1-6}-Alkyl)-aryl, -CO-N(C_{1-6}-Alkyl)-Heteroring, -CO-N(C_{1-6}-Alkyl)-(C_{1-6}-alkylen-aryl), -CO-NH-C_{1-6}-Alkylen-OH und -CO-NH-Heteroring besteht.

3. Verbindung oder ein Salz davon gemäss Anspruch 2, wobei das Piperidyl oder Piperazinyl, die jeweils substituiert sein können, und durch R^a und R^b, die mit dem benachbarten Stickstoffatom verbunden sind, gebildet sind, mit 1

bis 3 Gruppe(n), ausgewählt aus der Gruppe bestehend aus:

-O-C_{1-6}-Alkyl, das mit 1 bis 3 Gruppe(n), ausgewählt aus Halogen und Cycloalkyl, substituiert sein kann; C_{1-6}-Alkylen-O-cycloalkyl; -O-Cycloalkyl; C_{1-6}-Alkyl, das mit einer oder mehreren Gruppe(n), ausgewählt aus der Gruppe bestehend aus Halogen, Halogen-C_{1-6}-alkyl und -O-C_{1-6}-Alkyl, substituiert sein kann; oder C_{1-6}-Alkylen-O-C_{1-6}-alkyl,
substituiert sein können.

4. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 3, worin:

R^1 C_{1-6}-Alkyl ist und
R^3 C_{1-6}-Alkylen-(cycloalkyl), C_{1-6}-Alkylen-(cycloalkyl, substituiert mit zwei Halogenatomen), Cycloalkyl, Cycloalkyl, substituiert mit zwei Halogenatomen, ein sauerstoffhaltiger gesättigter Heteroring oder ein monocyclischer stickstoffhaltiger gesättigter Heteroring, substituiert mit C_{1-6}-Alkyl, ist.

5. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 3, worin
R^1 C_{1-6}-Alkyl ist und
R^3 Cycloalkyl oder ein sauerstoffhaltiger gesättigter Heteroring ist.

6. Verbindung oder ein Salz davon gemäss Anspruch 1, die
8-[(4-{[(2S)-2-Fluorpropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
7-Methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
8-[(4-{[(2R)-2-Fluorpropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
8-{[4-(2-Methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo-[4,3-c]chinolin-4-on,
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluorethyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

7. Verbindung oder ein Salz davon gemäss Anspruch 1, die
7-Methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on,
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluorethyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

8. Verbindung oder ein Salz davon gemäss Anspruch 1, die
8-[(4-{[(2S)-2-Fluorpropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

9. Verbindung oder ein Salz davon gemäss Anspruch 1, die
7-Methyl-1-(tetrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

10. Verbindung oder ein Salz davon gemäss Anspruch 1, die
8-[(4-{[(2R)-2-Fluorpropyl]oxy}piperidin-1-yl)carbonyl]-7-methyl-1-(tetrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

11. Verbindung oder ein Salz davon gemäss Anspruch 1, die
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluorpropyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

12. Verbindung oder ein Salz davon gemäss Anspruch 1, die
8-{[4-(2-Methoxyethyl)piperidin-1-yl]carbonyl}-7-methyl-1-[(3S)-tetrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo-[4,3-c]chinolin-4-on
oder ein Salz davon ist.

13. Verbindung oder ein Salz davon gemäss Anspruch 1, die
7-Methyl-1-[(3S)-tetrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluorethyl)piperazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]chinolin-4-on
oder ein Salz davon ist.

14. Pharmazeutische Zusammensetzung, umfassend eine Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 13 und einen pharmazeutisch annehmbaren Hilfsstoff.

15. Verwendung einer Verbindung oder eines Salzes davon gemäss irgendeinem der Ansprüche 1 bis 13 bei der Herstellung einer pharmazeutischen Zusammensetzung zur Prävention oder Behandlung einer Unterfunktion der Blase.

16. Verwendung einer Verbindung oder eines Salzes davon gemäss irgendeinem der Ansprüche 1 bis 13 bei der Herstellung einer pharmazeutischen Zusammensetzung zur Prävention oder Behandlung einer Entleerungsstörung bei einer Unterfunktion der Blase.

17. Verwendung einer Verbindung oder eines Salzes davon gemäss irgendeinem der Ansprüche 1 bis 13 bei der Herstellung einer pharmazeutischen Zusammensetzung zur Prävention oder Behandlung von benigner Prostatahyperplasie.

18. Verwendung einer Verbindung oder eines Salzes davon gemäss irgendeinem der Ansprüche 1 bis 13 bei der Herstellung einer pharmazeutischen Zusammensetzung zur Prävention oder Behandlung einer Entleerungsstörung bei benigner Prostatahyperplasie.

19. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 13 zur Verwendung in einem Verfahren zur Prävention oder Behandlung einer Unterfunktion der Blase.

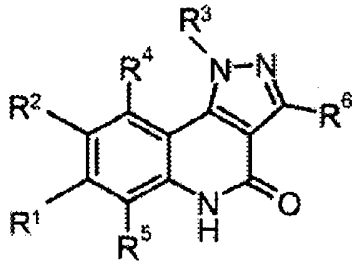
20. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 13 zur Verwendung in einem Verfahren zur Prävention oder Behandlung einer Entleerungsstörung bei einer Unterfunktion der Blase.

21. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 13 zur Verwendung in einem Verfahren zur Prävention oder Behandlung von benigner Prostatahyperplasie.

22. Verbindung oder ein Salz davon gemäss irgendeinem der Ansprüche 1 bis 13 zur Verwendung in einem Verfahren zur Prävention oder Behandlung einer Entleerungsstörung bei benigner Prostatahyperplasie.

Revendications

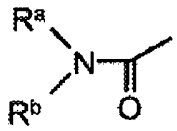
1. Composé de la formule (I) ou sel de celui-ci :



(I)

où

R^1 est l'hydrogène, un groupe halogéno-alkyle en C_{1-6}, alkyle en C_{1-6}, ou -O-alkyle en C_{1-6},
R^2 est un groupe de la formule (II) :



(II)

R^3 est un groupe alkylène en C_{1-6}-(cycloalkyle qui peut être substitué avec un halogène ou -O-alkyle en C_{1-6}) ; alkylène en C_{1-6}-hétérocycle saturé contenant de l'oxygène ; cycloalkyle qui peut être substitué avec un halogène ou -O-alkyle en C_{1-6} ; un hétérocycle saturé contenant de l'oxygène ; ou un hétérocycle saturé contenant de l'azote monocyclique qui peut être substitué avec un groupe alkyle en C_{1-6}, alkylène en C_{1-6}-aryle, ou -CO-alkylène en C_{1-6}-O-alkyle en C_{1-6},
R^4, R^5 et R^6 sont l'hydrogène,
R^a et R^b sont combinés avec l'atome d'azote adjacent pour former un hétérocyclique contenant de l'azote monocyclique, qui peut être substitué avec un groupe choisi parmi :

-OH ; un groupe halogéno-alkyle en C_{1-6} ; -O-alkyle en C_{1-6} qui peut être substitué avec de 1 à 3 groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6} et cycloalkyle ; aryle qui peut être substitué avec un groupe choisi dans un groupe G_1 ; un hétérocyclique qui peut être substitué avec un groupe choisi dans un groupe G_2 ; alkylène en C_{1-6}-O-cycloalkyle ; -O-cycloalkyle ; -0-(hétérocycle qui peut être substitué avec un groupe choisi dans un groupe G_2) ; alkyle en C_{1-6} qui peut être substitué avec un ou plusieurs groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6}, -O-cycloalkyle, -O-alkyle en C_{1-6}, et -O-halogéno-alkyle en C_{1-6} ; et alkylène en C_{1-6}-O-alkyle en C_{1-6} qui peut être substitué avec un ou plusieurs groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6} et cycloalkyle,
le groupe G_1 est constitué d'un halogène, d'un groupe alkyle en C_{1-6}, halogéno-alkyle en C_{1-6}, -OH, -O-alkyle en C_{1-6}, -O-hétérocycle, -0-alkylène en C_{1-6}-aryle, -O-alkylène en C_{1-6}-hétérocycle, -O-halogéno-alkyle en C_{1-6}, -N(alkyle en C_{1-6})$_2$, alkylène en C_{1-6}-N(alkyle en C_{1-6})$_2$, alkylène en C_{1-6}-hétérocycle, aryle qui peut être substitué avec un groupe alkyle en C_{1-6}, un hétérocycle qui peut être substitué avec un groupe alkyle en C_{1-6}, -COOH, -CO-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-aryle, -CO-O-alkylène en C_{1-6}-O-aryle, -CO-NH_2, -CO-NH-alkyle en C_{1-6}, -CO-N-(alkyle en C_{1-6})$_2$, -CO-N-(alkyle en C_{1-6})-aryle, -CO-N(alkyle en C_{1-6})-hétérocycle, -CO-N(alkyle en C_{1-6})-(alkylène en C_{1-6}-aryle), -CO-NH-alkylène en C_{1-6}-OH, et -CO-NH-hétérocycle, et
le groupe G_2 est constitué d'un halogène, d'un groupe alkyle en C_{1-6}, halogéno-alkyle en C_{1-6}, -OH, -O-alkyle en C_{1-6}, -O-alkylène en C_{1-6}-aryle, -O-alkylène en C_{1-6}-hétérocycle, -O-halogéno-alkyle en C_{1-6}, cyano, -N(alkyle en C_{1-6})$_2$, -NH-CO-alkyle en C_{1-6}, alkylène en C_{1-6}-O-alkyle en C_{1-6}, alkylène en C_{1-6}-hétérocycle, aryle, un hétérocycle qui peut être substitué avec un groupe alkyle en C_{1-6}, -COOH, -CO-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-aryle, -CO-O-alkylène en C_{1-6}-O-aryle, -CO-NH_2, -CO-NH-alkyle en C_{1-6}, -CO-N(alkyle en C_{1-6})$_2$, -CO-N(alkyle en C_{1-6})-aryle, -CO-N(alkyle en C_{1-6})-hétérocycle, -CON(alkyle en C_{1-6})-(alkylène en C_{1-6}-aryle), -CO-NH-alkylène en C_{1-6}-OH, et -CO-NH-hétérocycle
où "aryle" fait référence à un groupe cyclique hydrocarboné aromatique monocyclique à tricyclique en C_{6-14} et le terme "hétérocycle" fait référence à un groupe cyclique contenant (i) un cycle à de 3 à 8 éléments

monocycliques contenant de 1 à 4 hétéroatomes choisis parmi l'oxygène, le soufre et l'azote, ou (ii) un cycle bi- à tricyclique contenant de 1 à 5 hétéroatomes choisis parmi l'oxygène, le soufre et l'azote, formé par condensation de cycle d'un hétérocycle monocyclique avec un ou deux cycles choisis dans le groupe constitué d'un hétérocycle monocyclique, d'un cycle benzène, d'un cycloalcane en C_{5-8} et d'un cycloalcène en C_{5-8}.

2. Composé ou sel de celui-ci selon la revendication 1, dans lequel l'hétérocycle contenant de l'azote monocyclique qui peut être substitué, formé par R^a et R^b qui sont combinés avec l'atome d'azote adjacent, est le groupe pipéridine ou pipérazinyle, dont chacun peut être substitué avec de 1 à 3 groupes choisis parmi :

-OH ; un groupe halogéno-alkyle en C_{1-6} ; -O-alkyle en C_{1-6} qui peut être substitué avec de 1 à 3 groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6} et cycloalkyle ; aryle qui peut être substitué avec un groupe choisi dans un groupe G_1 ; un hétérocyclique qui peut être substitué avec un groupe choisi dans un groupe G_2 ; alkylène en C_{1-6}-O-cycloalkyle ; -O-cycloalkyle ; -O-(hétérocycle qui peut être substitué avec un groupe choisi dans un groupe G_2) ; alkyle en C_{1-6} qui peut être substitué avec un ou plusieurs groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6}, -O-cycloalkyle, -O-alkyle en C_{1-6}, et -O-halogéno-alkyle en C_{1-6} ; et alkylène en C_{1-6}-O-alkyle en C_{1-6} qui peut être substitué avec un ou plusieurs groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6} et cycloalkyle,
le groupe G_1 est constitué d'un halogène, d'un groupe alkyle en C_{1-6}, halogéno-alkyle en C_{1-6}, -OH, -O-alkyle en C_{1-6}, -O-hétérocycle, -O-alkylène en C_{1-6}-aryle, -O-alkylène en C_{1-6}-hétérocycle, -O-halogéno-alkyle en C_{1-6}, -N(alkyle en $C_{1-6})_2$, alkylène en C_{1-6}-N(alkyle en $C_{1-6})_2$, alkylène en C_{1-6}-hétérocycle, aryle qui peut être substitué avec un groupe alkyle en C_{1-6}, un hétérocycle qui peut être substitué avec un groupe alkyle en C_{1-6}, -COOH, -CO-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-aryle, -CO-O-alkylène en C_{1-6}-O-aryle, -CO-NH_2, -CO-NH-alkyle en C_{1-6}, -CO-N-(alkyle en $C_{1-6})_2$, -CO-N-(alkyle en C_{1-6})-aryle, -CO-N(alkyle en C_{1-6})-hétérocycle, -CO-N(alkyle en C_{1-6})-(alkylène en C_{1-6}-aryle), -CO-NH-alkylène en C_{1-6}-OH, et -CO-NH-hétérocycle, et
le groupe G_2 est constitué d'un halogène, d'un groupe alkyle en C_{1-6}, halogéno-alkyle en C_{1-6}, -OH, -O-alkyleen C_{1-6}, -O-alkylène en C_{1-6}-aryle, -O-alkylène en C_{1-6}-hétérocycle, -O-halogéno-alkyle en C_{1-6}, cyano, -N(alkyle en $C_{1-6})_2$, -NH-CO-alkyle en C_{1-6}, alkylène en C_{1-6}-O-alkyle en C_{1-6}, alkylène en C_{1-6}-hétérocycle, aryle, un hétérocycle qui peut être substitué avec un groupe alkyle en C_{1-6}, -COOH, -CO-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-O-alkyle en C_{1-6}, -CO-O-alkylène en C_{1-6}-aryle, -CO-O-alkylène en C_{1-6}-O-aryle, -CO-NH_2, -CO-NH-alkyle en C_{1-6}, -CO-N(alkyle en $C_{1-6})_2$, -CO-N(alkyle en C_{1-6})-aryle, -CO-N(alkyle en C_{1-6})-hétérocycle, -CO-N(alkyle en C_{1-6})-(alkylène en C_{1-6}-aryle), -CO-NH-alkylène en C_{1-6}-OH, et -CO-NH-hétérocycle.

3. Composé ou sel de celui-ci selon la revendication 2, dans lequel le groupe pipéridyle ou pipérazinyle, dont chacun peut être substitué, formé par R^a et R^b qui sont combinés avec l'atome d'azote adjacent, peut être substitué avec de 1 à 3 groupes choisis dans le groupe constitué de :

- O-alkyle en C_{1-6} qui peut être substitué avec de 1 à 3 groupes choisis parmi un halogène et un groupe cycloalkyle ; alkylène en C_{1-6}-O-cycloalkyle ; -O-cycloalkyle ; alkyle en C_{1-6} qui peut être substitué avec un ou plusieurs groupes choisis dans le groupe constitué d'un halogène, d'un groupe halogéno-alkyle en C_{1-6}, et -O-alkyle en C_{1-6} ; ou alkylène en C_{1-6}-O-alkyle en C_{1-6}.

4. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 3, dans lequel
R^1 est un groupe alkyle en C_{1-6}, et
R^3 est un groupe alkylène en C_{1-6}-(cycloalkyle), alkylène en C_{1-6}-(cycloalkyle substitué avec deux atomes d'halogène), cycloalkyle, cycloalkyle substitué avec deux atomes d'halogène, un hétérocycle saturé contenant de l'oxygène, ou un hétérocycle saturé contenant de l'azote monocyclique substitué avec un groupe alkyle en C_{1-6}.

5. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 3, dans lequel
R^1 est un groupe alkyle en C_{1-6}, et
R^3 est un groupe cycloalkyle ou un hétérocycle saturé contenant de l'oxygène.

6. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 8-[(4-{[(2S)-2-fluoropropyl]oxy}pipéridin-1-yl)carbonyl]-7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]quinoléin-4-one,
la 7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluoro-propyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyra-

zolo[4,3-c]quinoléin-4-one,
la 8-[(4-{[(2R)-2-fluoropropyl]oxy}pipéridin1-yl)carbonyl]-7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
la 7-méthyl-1[(3S)-tétrahydrofuran-3yl]-8-{[4-(3,3,3-trifluoropropyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
la 8-{[4-(2-méthoxyéthyl)pipéridin-1-yl]carbonyl}-7-méthyl-1-[(3S)-tétrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinoléin-4-one,
la 7-méthyl-1[(3S)-tétrahydrofuran-3yl]-8-{[4-(2,2,2-trifluoroéthyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
ou un sel de celles-ci.

7. Composé ou sel de celui-ci selon la revendication 1, lequel est la
la 7-méthyl-1(tétrahydro-2H-pyran-4-yl]-8-{[4-(3,3,3-trifluoropropyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
la 7-méthyl-1-[(3S)-tétrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
la 7-méthyl-1[(3S)-tétrahydrofuran-3yl]-8-{[4-(2,2,2-trifluoroéthyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
ou un sel de celles-ci.

8. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 8-[(4-{[(2S)-2-fluoropropyl]oxy}pipéridin-1-yl)carbonyl]-7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
ou un sel de celle-ci.

9. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-8-{[4-(3,3,3-trifluoropropyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
ou un sel de celle-ci.

10. Composé ou sel de celui-ci selon la revendication 1, lequel est la
la 8-[(4-{[(2R)-2-fluoropropyl]oxy}pipéridin-1-yl)carbonyl]-7-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one
ou un sel de celle-ci.

11. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 7-méthyl-1-[(3S)-tétrahydrofuran-3-yl]-8-{[4-(3,3,3-trifluoropropyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]-quinoléin-4-one,
ou un sel de celle-ci.

12. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 8-{[4-(2-méthoxyéthyl)pipéridin-l-yl]carbonyl}-7-méthyl-[(3S)-(tétrahydrofuran-3-yl]-1,5-dihydro-4H-pyrazolo[4,3-c]quinoléin-4-one
ou un sel de celle-ci.

13. Composé ou sel de celui-ci selon la revendication 1, lequel est
la 7-méthyl-1-[(3S)-tétrahydrofuran-3-yl]-8-{[4-(2,2,2-trifluoro-éthyl)pipérazin-1-yl]carbonyl}-1,5-dihydro-4H-pyrazolo[4,3-c]quinoléin-4-one,
ou un sel de celle-ci.

14. Composition pharmaceutique comprenant le composé ou un sel de celui-ci selon l'une quelconque des revendications 1 à 13, et un excipient pharmaceutiquement acceptable.

15. Utilisation du composé ou d'un sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour la fabrication de la composition pharmaceutique pour la prévention ou le traitement de vessie sous active.

16. Utilisation du composé ou d'un sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour la fabrication de la composition pharmaceutique pour la prévention ou le traitement de dysfonctionnement d'élimination dans la

vessie sous active.

17. Utilisation du composé ou d'un sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour la fabrication de la composition pharmaceutique pour la prévention ou le traitement d'hyperplasie prostatique bégnine.

18. Utilisation du composé ou d'un sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour la fabrication de la composition pharmaceutique pour la prévention ou le traitement de dysfonctionnement d'élimination accompagnant une hyperplasie prostatique bégnine.

19. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour une utilisation dans un procédé de prévention ou de traitement de vessie sous active.

20. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour une utilisation dans un procédé de prévention ou de traitement de dysfonctionnement d'élimination dans la vessie sous active.

21. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour une utilisation dans un procédé de prévention ou de traitement d'hyperplasie prostatique bénigne.

22. Composé ou sel de celui-ci selon l'une quelconque des revendications 1 à 13 pour une utilisation dans un procédé de prévention ou de traitement de dysfonctionnement d'élimination accompagnant une hyperplasie prostatique bénigne.

REFERENCES CITED IN THE DESCRIPTION

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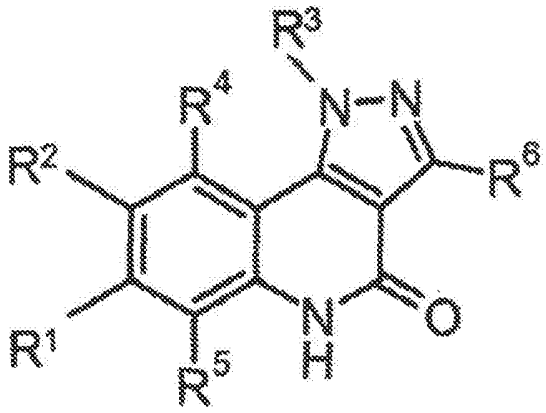
Pirazolokinolin vegyületek

Szabadalmi igénypontok

1. Egy (I):

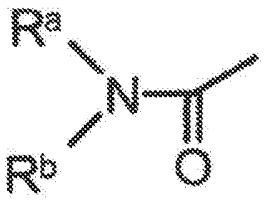


(I)

képletű vegyület vagy sója, ahol

R^1 hidrogénatom, halogén-(1-6 szénatomos)-alkil, (1-6 szénatomos)-alkil, vagy -O-(1-6 szénatomos)-alkilcsoport,

R^2 egy (II):



(II)

képletű csoport,

R^3 (1-6 szénatomos)-alkilén-(cikloalkil mely halogénatommal vagy -O-(1-6 szénatomos)-alkilcsoporttal lehet szubsztituált); (1-6 szénatomos)-alkilén-oxigén-tartalmú telített heterogyűrű; cikloalkilcsoport, mely halogénatommal vagy -O-(1-6 szénatomos)-alkilcsoporttal lehet szubsztituált; egy oxigén-tartalmú telített heterogyűrű; vagy egy monociklusos nitrogén-tartalmú telített heterogyűrű, mely (1-6 szénatomos)-alkil, (1-6 szénatomos)-alkilén-aril, vagy -CO-(1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkilcsoporttal lehet szubsztituált,

R^4, R^5 és R^6 hidrogénatom,

R^a és R^b a szomszédos nitrogénatommal egy monociklusos nitrogén-tartalmú heterogyűrűt alkot, mely a következő csoportok közül választott szubsztituenst tartalmazhat: -OH; halogén-(1-6 szénatomos)-alkil; -O-(1-6 szénatomos)-alkilcsoport, mely 1-3, halogénatom, halogén-(1-6 szénatomos)-alkil és cikloalkilcsoportok közül választott szubsztituenst tartalmazhat; arilcsoport, mely a G_1 csoportok közül választott szubsztituenst tartalmazhat; egy heterogyűrű, mely a G_2 csoportok közül választott szubsztituenst tartalmazhat; (1-6 szénatomos)-alkilén-O-cikloalkil; -O-cikloalkil; -O-(heterogyűrű mely a G_2 csoportok közül választott szubsztituenst tartalmazhat); (1-6 szénatomos)-alkilcsoport, mely egy vagy több, halogénatom, halogén-(1-6 szénatomos)-alkil, -O-cikloalkil, -O-(1-6 szénatomos)-alkil, és -O-halogén-(1-6 szénatomos)-alkilcsoportok közül választott szubsztituenst tartalmazhat; és (1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkilcsoport, mely egy vagy több, halogénatom, halogén-(1-6 szénatomos)-alkil és cikloalkilcsoportok közül választott szubsztituenst tartalmazhat,

G_1 halogénatom, (1-6 szénatomos)-alkil, halogén-(1-6 szénatomos)-alkil, -OH, -O-(1-6 szénatomos)-alkil, -O-heterogyűrű, -O-(1-6 szénatomos)-alkilén-aril, -O-(1-6 szénatomos)-alkilén-heterogyűrű, -O-halogén-(1-6 szénatomos)-alkil, $-N((1\text{-}6\ szénatomos)\text{-}alkil)_2$, (1-6 szénatomos)-alkilén-$N((1\text{-}6\ szénatomos)\text{-}alkil)_2$, (1-6 szénatomos)-alkilén-heterogyűrű, arilcsoport, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált, egy heterogyűrű, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált, -COOH, -CO-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkil, - CO-O-(1-6 szénatomos)-alkilén-aril, -CO-O-(1-6 szénatomos)-alkilén-O-aril, $-CO\text{-}NH_2$, -CO-NH-(1-6 szénatomos)-alkil, - $CO\text{-}N((1\text{-}6\ szénatomos)\text{-}alkil)_2$, -CO-N((1-6 szénatomos)-alkil)-aril, -CO-N((1-6 szénatomos)-alkil)-heterogyűrű, -CO-N((1-6 szénatomos)-alkil)-((1-6 szénatomos)-alkilén-aril), -CO-NH-(1-6 szénatomos)-alkilén-OH, és -CO-NH-heterogyűrű, és

G_2 halogénatom, (1-6 szénatomos)-alkil, halogén-(1-6 szénatomos)-alkil, -OH, -O-(1-6 szénatomos)-alkil, -O-(1-6 szénatomos)-alkilén-aril, -O-(1-6 szénatomos)-alkilén-heterogyűrű, -O-halogén- (1-6 szénatomos)-alkil, ciano, $-N((1\text{-}6\ szénatomos)\text{-}alkil)_2$, -NH-CO-(1-6 szénatomos)-alkil, (1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkil, (1-6 szénatomos)-alkilén-heterogyűrű, arilcsoport, egy heterogyűrű, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált, -COOH, -CO-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-aril, -CO-O-(1-6 szénatomos)-alkilén-O-aril, $-CO\text{-}NH_2$, -CO-NH-(1-6 szénatomos)-alkil, $-CO\text{-}N((1\text{-}6\ szénatomos)\text{-}alkil)_2$, -CO-N((1-6 szénatomos)-alkil)-aril, -CON((1-6 szénatomos)-alkil)-heterogyűrű,

-CO-N((1-6 szénatomos)-alkil)-((1-6 szénatomos)-alkilén-aril), -CO-NH-(1-6 szénatomos)-alkilén-OH, és -CO-NH-heterogyűrű,
ahol az "aril" kifejezés 6-14 szénatomos monociklusostól triciklusosig terjedő aromás gyűrűs szénhidrogéncsoportot jelent, és a "heterogyűrű" kifejezés olyan gyűrűs csoportot jelent, mely (i) egy monociklusos 3-8-tagú, 1-4, oxigén, kén és nitrogén közül választott heteroatomot tartalmazó gyűrű, vagy (ii) egy bi- vagy triciklusos gyűrű, mely 1-5, oxigén, kén és nitrogén közül választott heteroatomot tartalmaz, és egy monociklusos heterogyűrű és egy vagy két, egy monociklusos heterogyűrű, egy benzolgyűrű, 5-8 szénatomos cikloalkán, és cikloalkén közül választott gyűrű fúziójával jön létre.

2. Az 1. igénypont szerinti vegyület vagy sója, ahol az R^a és R^b által a szomszédos nitrogénatommal egy monociklusos nitrogén-tartalmú heterogyűrűt alkotó, monociklusos nitrogén-tartalmú heterogyűrű, mely szubsztituált lehet, piperidil vagy piperazinilcsoport, mely 1-3, alábbiak közül választott szubsztituenst tartalmazhat:
-OH; halogén-(1-6 szénatomos)-alkil; -O-(1-6 szénatomos)-alkilcsoport, mely 1-3, halogénatom, halogén-(1-6 szénatomos)-alkil és cikloalkilcsoportok közül választott csoporttal lehet szubsztituált; arilcsoport, mely a G_1 csoportok közül választott szubsztituenst tartalmazhat; a heterogyűrű, mely a G_2 csoportok közül választott szubsztituenst tartalmazhat; (1-6 szénatomos)-alkilén-O-cikloalkil; -O- cikloalkil; -O-(heterogyűrű mely a G_2 csoportok közül választott szubsztituenst tartalmazhat); (1-6 szénatomos)-alkilcsoport, mely egy vagy több, halogénatom, halogén-(1-6 szénatomos)-alkil, -O-cikloalkil, -O-(1-6 szénatomos)-alkil, és -O-halogén-(1-6 szénatomos)-alkilcsoportok közül választott szubsztituenst tartalmazhat; és (1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkilcsoport, mely egy vagy több, halogénatom, halogén-(1-6 szénatomos)-alkil és cikloalkilcsoportok közül választott szubsztituenst tartalmazhat,
G_1 halogénatom, (1-6 szénatomos)-alkil, halogén-(1-6 szénatomos)-alkil, -OH,
-O-(1-6 szénatomos)-alkil, -O-heterogyűrű, -O-(1-6 szénatomos)-alkilén-aril,
-O-(1-6 szénatomos)-alkilén-heterogyűrű, -O-halogén-(1-6 szénatomos)-alkil,
-N((1-6 szénatomos)-alkil)$_2$, (1-6 szénatomos)-alkilén-N((1-6 szénatomos)-alkil)$_2$, (1-6 szénatomos)-alkilén-heterogyűrű, arilcsoport, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált, egy heterogyűrű, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált,
-COOH, -CO-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkil, - CO-O-(1-6 szénatomos)-alkilén-aril, -COO-(1-6 szénatomos)-alkilén-O-aril,
-CO-NH$_2$, -CO-NH-(1-6 szénatomos)-alkil, - CO-N((1-6 szénatomos)-alkil)$_2$, -CO-N((1-6

szénatomos)-alkil)-aril, -CO-N((1-6 szénatomos)-alkil)-heterogyűrű, -CO-N((1-6 szénatomos)-alkil)-((1-6 szénatomos)-alkilén-aril), -CO-NH-(1-6 szénatomos)-alkilén-OH, és -CO-NH-heterogyűrű, és

G_2 halogénatom, (1-6 szénatomos)-alkil, halogén-(1-6 szénatomos)-alkil, -OH, -O-(1-6 szénatomos)-alkil, -O-(1-6 szénatomos)-alkilén-aril, -O(1-6 szénatomos)-alkilén-heterogyűrű, -O-halogén- (1-6 szénatomos)-alkil, ciano, -N((1-6 szénatomos)-alkil)$_2$, -NH-CO-(1-6 szénatomos)-alkil, (1-6 szénatomos)-alkilén-O(1-6 szénatomos)-alkil, (1-6 szénatomos)-alkilén-heterogyűrű, arilcsoport, egy heterogyűrű, mely (1-6 szénatomos)-alkilcsoporttal lehet szubsztituált, -COOH, -CO-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkil, -CO-O-(1-6 szénatomos)-alkilén-aril, -CO-O-(1-6 szénatomos)-alkilén-O-aril, -CO-NH$_2$, -CO-NH-(1-6 szénatomos)-alkil, -CO-N((1-6 szénatomos)-alkil)$_2$, -CO-N((1-6 szénatomos)-alkil)-aril, -CON((1-6 szénatomos)-alkil)-heterogyűrű, -CO-N((1-6 szénatomos)-alkil)-((1-6 szénatomos)-alkilén-aril), -CO-NH-(1-6 szénatomos)-alkilén-OH, és -CO-NH-heterogyűrű.

3. A 2. igénypont szerinti vegyület vagy sója, ahol az R^a és R^b által a szomszédos nitrogénatommal egy monociklusos nitrogén-tartalmú heterogyűrűt alkotó, monociklusos nitrogén-tartalmú heterogyűrű, mely szubsztituált lehet, piperidil vagy piperazinilcsoport, mely 1-3, alábbiak közül választott szubsztituenst tartalmazhat:

- O-(1-6 szénatomos)-alkilcsoport, mely 1-3, halogénatom és cikloalkilcsoport közül választott szubsztituenst tartalmazhat; (1-6 szénatomos)-alkilén-O-cikloalkil; -O-cikloalkil; (1-6 szénatomos)-alkilcsoport, mely egy vagy több, halogénatom, halogén-(1-6 szénatomos)-alkil, és -O-(1-6 szénatomos)-alkilcsoport közül választott szubsztituenst tartalmazhat; vagy (1-6 szénatomos)-alkilén-O-(1-6 szénatomos)-alkilcsoport.

4. Az 1-3. igénypontok bármelyike szerinti vegyület vagy sója, ahol

R^1 jelentése (1-6 szénatomos)-alkilcsoport, és

R^3 jelentése (1-6 szénatomos)-alkilén-(cikloalkil), (1-6 szénatomos)-alkilén-(két halogénatommal szubsztituált cikloalkil), cikloalkil, két halogénatommal szubsztituált cikloalkilcsoport, egy oxigén-tartalmú telített heterogyűrű, vagy egy (1-6 szénatomos)-alkilcsoporttal szubsztituált monociklusos nitrogén-tartalmú telített heterogyűrű.

5. Az 1-3. igénypontok bármelyike szerinti vegyület vagy sója, ahol

R^1 jelentése (1-6 szénatomos)-alkilcsoport, és

R^3 jelentése cikloalkilcsoport vagy egy oxigén-tartalmú telített heterogyűrű.

6. Az 1. igénypont szerinti vegyület vagy sója, mely
8-{(4-{[(2S)-2-fluorpropil]oxi}piperidin-1-il)karbonil]-7-metil-1-(tetrahidro-2H-piran-4-il)-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
7-metil-1-(tetrahidro-2H-piran-4-il)-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
8-[(4- {[(2R)-2-fluorpropil]oxi}piperidin-1-il)karbonil]-7-metil-1-(tetrahidro-2H-piran-4-il)-1,5-dihidro-4Hpirazolo[4,3-c]kinolin-4-on,
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
8-{[4-(2-metoxietil)piperidin-1-il]karbonil}-7-metil-1-[(3S)-tetrahidrofuran-3-il]-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(2,2,2-trifluoretil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
vagy sója.

7. Az 1. igénypont szerinti vegyület vagy sója, mely
7-metil-1-(tetrahidro-2H-piran-4-il)-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(2,2,2-trifluoretil)piperazin-1-il]karbonil-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
vagy sója.

8. Az 1. igénypont szerinti vegyület vagy sója, mely
8-{(4- {[(2S)-2-fluorpropil]oxi}piperidin-1-il)karbonil]-7-metil-1-(tetrahidro-2H-piran-4-il)-1,5-dihidro-4Hpirazolo[4,3-c]kinolin-4-on,
vagy sója.

9. Az 1. igénypont szerinti vegyület vagy sója, mely
7-metil-1-(tetrahidro-2H-piran-4-il)-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,

vagy sója.

10. Az 1. igénypont szerinti vegyület vagy sója, mely
8-[(4-{[(2R)-2-fluorpropil]oxi}piperidin-1-il)karbonil]-7-metil-1-(tetrahidro-2H-piran-4-il)-1,5-dihidro-4Hpirazolo[4,3-c]kinolin-4-on,
vagy sója.

11. Az 1. igénypont szerinti vegyület vagy sója, mely
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(3,3,3-trifluorpropil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
vagy sója.

12. Az 1. igénypont szerinti vegyület vagy sója, mely
8-{[4-(2-metoxietil)piperidin-1-il]karbonil}-7-metil-1-[(3S)-tetrahidrofuran-3-il]-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
vagy sója.

13. Az 1. igénypont szerinti vegyület vagy sója, mely
7-metil-1-[(3S)-tetrahidrofuran-3-il]-8-{[4-(2,2,2-trifluoretil)piperazin-1-il]karbonil}-1,5-dihidro-4H-pirazolo[4,3-c]kinolin-4-on,
vagy sója.

14. Gyógyászati készítmény, mely az 1-13. igénypontok bármelyike szerinti vegyületet vagy sóját és egy gyógyászatilag elfogadható kötőanyagot tartalmaz.

15. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója alkalmazása csökkent húgyhólyag aktivitás megelőzésére vagy kezelésére szolgáló gyógyászati készítmény előállítására.

16. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója alkalmazása csökkent aktivitású húgyhólyagban ürítési diszfunkció megelőzésére vagy kezelésére szolgáló gyógyászati készítmény előállítására.

17. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója alkalmazása jóindulatú prosztata hyperplasia megelőzésére vagy kezelésére szolgáló gyógyászati készítmény előállítására.

18. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója alkalmazása jóindulatú prosztata hyperplasiával összefüggő ürítési diszfunkció megelőzésére vagy kezelésére szolgáló gyógyászati készítmény előállítására.

19. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója csökkent húgyhólyag aktivitás megelőzésében és kezelésében történő alkalmazásra.

20. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója csökkent aktivitású húgyhólyagban ürítési diszfunkció megelőzésében vagy kezelésében történő alkalmazásra.

21. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója jóindulatú prosztata hyperplasia megelőzésében vagy kezelésében történő alkalmazásra.

22. Az 1-13. igénypontok bármelyike szerinti vegyület vagy sója jóindulatú prosztata hyperplasiával összefüggő ürítési diszfunkció megelőzésében vagy kezelésében történő alkalmazásra.

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