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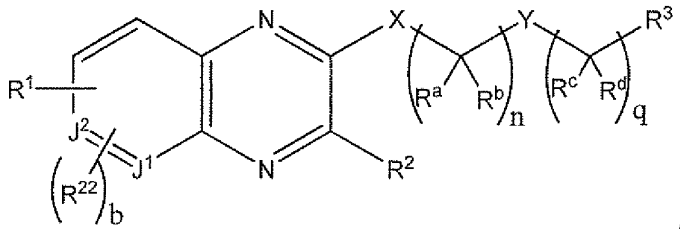
(54) Title: QUINOXALINES AND AZA-QUINOXALINES AS CRTH2 RECEPTOR MODULATORS



(I)

(57) Abstract: The invention provides certain quinoxalines and aza-quinoxalines of the Formula (I), and their pharmaceutically acceptable salts, wherein J^1, J^2, R^1, R^2, R^3, R^{22}, R^a, R^b, R^c, R^d, X, Y, b, n, and q are as defined herein. The invention also provides pharmaceutical compositions comprising such compounds, and methods of using the compounds for treating diseases or conditions associated with with uncontrolled or inappropriate stimulation of $CRTH_2$ function.

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QUINOXALINES AND AZA-QUINOXALINES AS $CRTH_2$ RECEPTOR MODULATORS

FIELD OF THE INVENTION

[0001] The present invention relates to certain quinoxalines and aza-quinoxalines of the Formula (I) (also referred to herein as the "compounds of the Formula (I)"), compositions comprising such compounds, and methods of using such compounds for treating an inflammatory disease, or other disorder mediated by the the chemoattractant receptor-homologous molecule expressed on T-helper-type-2 cells ($CRTH_2$).

BACKGROUND OF THE INVENTION

[0002] Prostaglandin D_2 (PGD_2) belongs to a class of chemical mediators which cells synthesize in response to stimuli, such as local tissue damage or hormonal stimuli, or by cellular activation pathways. Cells synthesize PGD_2 from arachidonic acid by cyclooxygenase and other specific synthases in the pathway.

[0003] Upon stimulation, mast cells release PGD_2 in major amounts and this release plays a major role in the etiology of respiratory disease, such as asthma and congestion. PGD_2 achieves this effect by binding with either of two G-protein coupled receptors, which are the D-prostanoid (DP) receptor and the $CRTH_2$ receptor. TH-2 cells, eosinophils, and basophils express the $CRTH_2$ receptor, which mediates the chemoattractant effect of PGD_2.

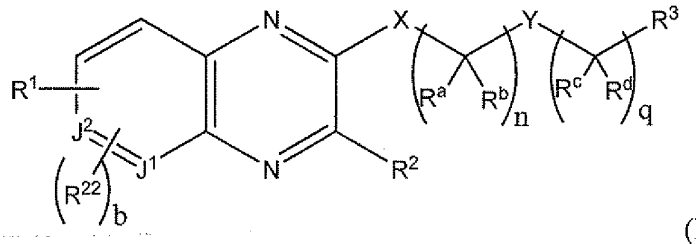
[0004] Scientific studies support a clear role for PGD_2 in an allergic inflammatory response. PGD_2 is found at high levels in the bronchoalveolar lavage of asthmatics. Inhalation of PGD_2 enhances eosinophilic and lymphocytic airway inflammation in allergic animal models. Evidence obtained by studying $CRTH_2$ knockout mice demonstrates that PGD_2 achieves this enhancement by binding to the $CRTH_2$ receptor. Hence, $CRTH_2$ receptor antagonists would be expected to reduce the allergic inflammatory response caused by PGD_2, and these compounds would be useful in the treatment or prevention of allergic/immune disorders.

[0005] Current drugs of choice for the treatment of chronic inflammatory airway disease, such as asthma or COPD, are synthetic glucocorticoids; examples of these compounds currently indicated for treating these disorders include fluticasone and mometasone. The difficulty with treating patients with this class of compounds is that the compounds possess a number of systemic side-effects; these include adrenal suppression, altered bone metabolism and growth suppression in children. These side effects limit the dose that can be administered on a daily basis to the patient. While a non-steroidal class of therapeutics that inhibit bronchoconstriction

exists ($CysLT_1$ antagonists), this class of compounds has limited efficacy in achieving the endpoints of reducing inflammatory and improving in lung function when compared to the glucocorticoids. Therefore, a therapeutic that combines the efficacy of inhaled glucocorticoids without the side effects would be advantageous.

SUMMARY OF THE INVENTION

[0006] In one aspect, the present invention provides a compound of the Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

J^1 and J^2 are independently C(H), C(R^1), C(R^{22}), or N wherein the following provisos apply:

(i) no more than one of J^1 and J^2 is N,

(ii) no more than one of J^1 and J^2 is C(R^{22}); and

(iii) only one R^1 is substituted on the illustrated ring containing J^1 and J^2;

R^1 is selected from the group consisting of:

(i) –C(O)-N(R^{6a})(R^{6b}),

(ii) –$S(O)_2$-N(R^{6a})(R^{6b}),

(iii) –C(O)-C(R^{7a})(R^{7b})(R^{7c}),

(iv) –N(H)-C(O)-C(R^{7a})(R^{7b})(R^{7c}),

(v) –C(O)-O-C(R^{7a})(R^{7b})(R^{7c}), and

(vi) –N(H)-$S(O)_2$-C(R^{7a})(R^{7b})(R^{7c});

R^{6a} and R^{6b} are independently:

a. H,

b. C_1-C_6 alkyl,

c. C_3-C_6 alkenyl,

d. C_3-C_6 alkynyl,

e. –O-(C_1-C_3 alkyl),

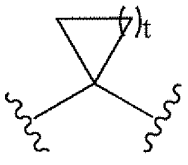
f. –Q-R^{AH}, wherein R^{AH} is phenyl or 5- to 6-membered heteroaryl containing 1 to 2 heteroatoms independently selected from the group consisting of N, O, and S,

and wherein R^{AH} is unsubstituted or substituted with 1 to 5 R^8 moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -O-(C_1-C_3 fluoroalkyl), hydroxyl, phenyl, and –CN;

Q is selected from the group consisting of a

(a) a bond;

(b) C_1-C_6 alkylene, wherein said C_1-C_6 alkylene is unsubstituted or substituted by 1 to 2 fluoro, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, or C_1-C_3 fluoroalkyl; and

(c)  wherein t is 1, 2, 3, or 4;

g. –Q-R^{HC}, wherein R^{HC} is

(i) 5- to 7-membered heterocyclyl containing 1 heteroatom selected from the group consisting of N, O, S, S(O), and $S(O)_2$, wherein said heterocyclyl of R^{HC} is optionally fused to a benzene, pyridyl ring; or

(ii) C_3-C_7 cycloalkyl, wherein said cycloalkyl of R^{HC} is optionally fused to a benzene or pyridyl ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 5 R^{12} moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -O-(C_1-C_3 fluoroalkyl), hydroxyl, –CN, and -$S(O)_2$-(C_1-C_3 alkyl), or wherein when two R^{12} moieties are geminally substituted on the same carbon atom, the two geminally substituted R^{12} moieties, together with the carbon atom on which they are attached form –C(O)-;

h. or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is independently selected from the group consisting of:

(i) a 4- to 9-membered heterocyclyl, optionally containing one additional nitrogen atom, wherein said heterocyclyl of R^{6H} is optionally fused to phenyl, C_3-C_6 cycloalkyl, or a 5-membered heteroaryl containing 1 to 3 N atoms;

(ii) a 4- to 7-membered heterocyclenyl, optionally containing one additional nitrogen atom, wherein said heterocyclenyl of R^{6H} is optionally fused to phenyl; and

(iii) a 6- to 8-membered aza- or a diazabicycloheterocycloalkyl ring;

wherein R^{6H} is unsubstituted or substituted by 1 to 5 R^9 moieties wherein each R^9 moiety is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 fluoroalkyl, fluoro, hydroxyl, -CN, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), or

R^9 is -Z-R^{CY} wherein

Z is

(i) a bond,

(ii) -C(O)-,

(iii) -C(=N-OH)-,

(iv) $-S(O)_2-$,

(v) C_1-C_3 alkylene, wherein said C_1-C_3 alkylene of Z is optionally substituted by 1 to 2 fluoro or C_1-C_3 alkyl;

(vi) –O-;

(vii) –O-(C_1-C_3 alkylene)-;or

(viii) –C(O)-O-CH_2-

R^{CY} is selected from the group consisting of:

(i) phenyl

(ii) 5- to 10-membered mono or bicyclic heteroaryl containing 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S; or

(iii) 5- to 6-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{CY} is optionally fused to phenyl;

wherein R^{CY} is unsubstituted or substituted by 1 to 4 R^{10} moieties;

each R^{10} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), -CN, ~~or~~ pyridyl, or cyclopropyl or, wherein when two R^{10} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

or, optionally, where two R^9 moieties are geminally substituted on a common ring carbon of R^{6H}, the two R^9 moieties, together with the ring carbon on which they are substituted, form R^{YC}, wherein R^{YC} is

(i) a 4- to 7-membered cycloalkyl, wherein said cycloalkyl of R^{YC} is optionally fused to phenyl or pyridyl; or

(ii) a 4- to 7-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{YC} is optionally fused to phenyl;

wherein R^{YC} is unsubstituted or substituted by 1 to 4 R^{11} moieties;

each R^{11} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), phenyl, or pyridyl, or, wherein when two R^{11} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

R^{7a} and R^{7b} are independently

a) H,

b) C_1-C_6 alkyl,

c) R^{7a} and R^{7b} together with the carbon atom on which they are substituted, form R^{PC}, wherein R^{PC} is

(i) C_3-C_7 cycloalkyl, or

(ii) phenyl, wherein said phenyl of R^{PC} is unsubstituted or substituted by 1 to 5 moieties independently selected from the group consisting of halo, trifluoromethyl, and trifluoromethoxy;

R^{7c} is

a) H, or

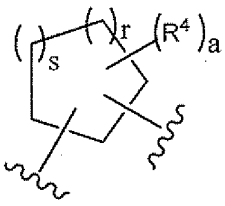
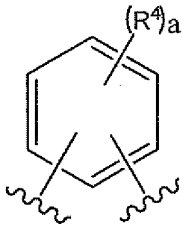
b) absent, when R^{7a} and R^{7b} together with the carbon atom on which they are substituted form phenyl;

R^{22} is halo, C_1-C_3 alkyl, or C_1-C_3 fluoroalkyl;

b is 0 or 1;

X is a bond, –O-, -S-, -S(O)-, –$S(O)_2$-, or N(H);

Y is selected from the group consisting of

(i) a bond, (ii)  , (iii)  , (iv) –O-, (v) –S-, (vi) –S(O)-, and (vii) $–S(O)_2$-;

wherein

a is 0, 1, 2, or 3;

r is 0, 1, or 2;

s is 0, 1, or 2;

each occurrence of R^4 is independently halo, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

R^a, R^b, R^c, and R^d are independently H, fluoro, hydroxyl, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, or C_1-C_6 alkoxy;

R^2 is selected from the group consisting of:

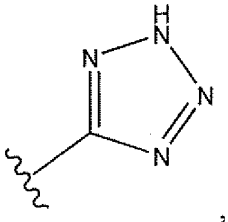
(i) phenyl;

(ii) 5- to 6-membered heteroaryl containing from 1 to 3 heteroatoms selected from the group consisting of N, O, and S;

(iii) 5- to 6-membered heterocyclenyl, containing from 1 to 2 heteroatoms selected from the group consisting of N, O, and S; and

(iv) 5- to 6-membered heterocyclyl containing from 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein R^2 is unsubstituted or substituted by 1 to 5 R^5 groups independently selected from the group consisting of halo, C_1-C_3 fluoroalkyl, C_1-C_3 alkyl, C_1-C_3 alkoxy, -CN, $-OCF_3$, -C(O)-(C_1-C_3 alkyl), and $-S(O)_2$-(C_1-C_3 alkyl);

R^3 is –C(O)OH,  , or $–N(H)-SO_2-R^e$,

wherein R^e is C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 alkoxy, and phenyl;

n is 1, 2, 3, 4, or 5; and

q is 0, 1, or 2.

[0007] In another aspect, the present invention provides a compound of the Formula (I) or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of:

(i) $-C(O)-N(R^{6a})(R^{6b})$,

(ii) $-S(O)_2-N(R^{6a})(R^{6b})$,

(iii) $-C(O)-C(R^{7a})(R^{7b})(R^{7c})$,

(iv) $-N(H)-C(O)-C(R^{7a})(R^{7b})(R^{7c})$,

(v) $-C(O)-O-C(R^{7a})(R^{7b})(R^{7c})$, and

(vi) $-N(H)-S(O)_2-C(R^{7a})(R^{7b})(R^{7c})$;

R^{6a} and R^{6b} are independently:

a. H,

b. C_1-C_6 alkyl,

c. C_3-C_6 alkenyl,

d. C_3-C_6 alkynyl,

e. $-O-(C_1$-C_3 alkyl),

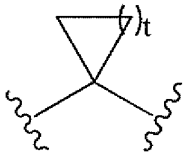
f. $-Q-R^{AH}$, wherein R^{AH} is phenyl or 5- to 6-membered heteroaryl containing 1 to 2 heteroatoms independently selected from the group consisting of N, O, and S,

and wherein R^{AH} is unsubstituted or substituted with 1 to 5 R^8 moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, $-O-(C_1$-C_3 fluoroalkyl), hydroxyl, phenyl, and –CN;

Q is selected from the group consisting of a

(a) a bond;

(b) C_1-C_6 alkylene, wherein said C_1-C_6 alkylene is unsubstituted or substituted by 1 to 2 fluoro, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, or C_1-C_3 fluoroalkyl; and

(c)  wherein t is 1, 2, 3, or 4;

g. $-Q-R^{HC}$, wherein R^{HC} is

(i) 5- to 6-membered heterocyclyl containing 1 heteroatom selected from the group consisting of N and O, wherein said heterocyclyl of R^{HC} is optionally fused to a benzene ring; or

(ii) C_5-C_7 cycloalkyl, wherein said cycloalkyl of R^{HC} is optionally fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 5 R^{12} moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -O-(C_1-C_3 fluoroalkyl), hydroxyl, and –CN, or wherein when two R^{12} moieties are geminally substituted on the same carbon atom, the two geminally substituted R^{12} moieties, together with the carbon atom on which they are attached form –C(O)-;

h. or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is independently selected from the group consisting of:

(i) a 4- to 7-membered heterocyclyl, optionally containing one additional nitrogen atom, wherein said heterocyclyl of R^{6H} is optionally fused to phenyl; and

(ii) a 4- to 7-membered heterocyclenyl, optionally containing one additional nitrogen atom, wherein said heterocyclenyl of R^{6H} is optionally fused to phenyl;

wherein R^{6H} is unsubstituted or substituted by 1 to 5 R^9 moieties wherein each R^9 moiety is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, fluoro, hydroxyl, -CN, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), or

R^9 is -Z-R^{CY} wherein

Z is

(i) a bond,

(ii) -C(O)-,

(iii) -C(=N-OH)-,

(iv) –$S(O)_2$-, or

(v) C_1-C_3 alkylene, wherein said C_1-C_3 alkylene of Z is optionally substituted by 1 to 2 fluoro or C_1-C_3 alkyl;

R^{CY} is selected from the group consisting of:

(i) phenyl

(ii) 5- to 10-membered mono or bicyclic heteroaryl containing 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S; or

(iii) 5- to 6-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{CY} is optionally fused to phenyl;

wherein R^{CY} is unsubstituted or substituted by 1 to 4 R^{10} moieties;

each R^{10} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), -CN, or pyridyl, or, wherein when two R^{10} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

or, optionally, where two R^9 moieties are geminally substituted on a common ring carbon of R^{6H}, the two R^9 moieties, together with the ring carbon on which they are substituted, form R^{YC}, wherein R^{YC} is

(i) a 4- to 7-membered cycloalkyl, wherein said cycloalkyl of R^{YC} is optionally fused to phenyl; or

(ii) a 4- to 7-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{YC} is optionally fused to phenyl;

wherein R^{YC} is unsubstituted or substituted by 1 to 4 R^{11} moieties;

each R^{11} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), phenyl, or pyridyl, or, wherein when two R^{11} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

R^{7a} and R^{7b} are independently

a) H,

b) C_1-C_6 alkyl,

c) R^{7a} and R^{7b} together with the carbon atom on which they are substituted, form R^{PC}, wherein R^{PC} is

(i) C_3-C_7 cycloalkyl, or

(ii) phenyl, wherein said phenyl of R^{PC} is unsubstituted or substituted by 1 to 5 moieties independently selected from the group consisting of halo, trifluoromethyl, and trifluoromethoxy;

R^{7c} is

a) H, or

b) absent, when R^{7a} and R^{7b} together with the carbon atom on which they are substituted form phenyl; and

J^1, J^2, Y, R^a, R^b, R^c, R^d, R^2, R^3, R^{22}, b, n, and q are as specified in claim 1.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0008] The terms used herein have their ordinary meaning and the meaning of such terms is independent at each occurrence thereof. That notwithstanding and except where stated otherwise, the following definitions apply throughout the specification and claims. Chemical names, common names, and chemical structures may be used interchangeably to describe the same structure. If a chemical compound is referred to using both a chemical structure and a chemical name, and an ambiguity exists between the structure and the name, the structure predominates. These definitions apply regardless of whether a term is used by itself or in combination with other terms, unless otherwise indicated. Hence, the definition of "alkyl" applies to "alkyl" as well as the "alkyl" portions of "hydroxyalkyl," "fluoroalkyl," "-O-alkyl," etc.

[0009] As used herein, and throughout this disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings:

[0010] A "patient" is a human or non-human mammal. In one embodiment, a patient is a human. In another embodiment, a patient is a chimpanzee.

[0011] The term "therapeutically effective amount" as used herein, refers to an amount of the compound of Formula (I) and/or an additional therapeutic agent, or a composition thereof that is effective in producing the desired therapeutic, ameliorative, inhibitory or preventative effect when administered to a patient suffering from pain or an inflammatory disease or disorder. In the combination therapies of the present invention, a therapeutically effective amount can refer to each individual agent or to the combination as a whole, wherein the amounts of all agents administered are together effective, but wherein the component agent of the combination may not be present individually in an effective amount.

[0012] The term "preventing," as used herein with respect to pain or an inflammatory disease or disorder, refers to reducing the likelihood of pain or an inflammatory disease or disorder.

[0013] The term "alkyl," as used herein, refers to an aliphatic hydrocarbon group having one of its hydrogen atoms replaced with a bond. An alkyl group may be straight or branched and contain from about 1 to about 20 carbon atoms. In one embodiment, an alkyl group contains from about 1 to about 12 carbon atoms. In different embodiments, an alkyl group contains from 1 to 6 carbon atoms (C_1-C_6 alkyl) or from 1 to 3 carbon atoms (C_1-C_3 alkyl). Non-limiting examples of alkyl groups include methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, n-pentyl, neopentyl, isopentyl, n-hexyl, isohexyl and neohexyl. In one embodiment, an alkyl group is linear. In another embodiment, an alkyl group is branched. Unless otherwise indicated, an alkyl group is unsubstituted.

[0014] The term "alkylene," as used herein, refers to an alkyl group, as defined above, wherein one of the alkyl group's hydrogen atoms has been replaced with a bond. Non-limiting examples of alkylene groups include $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH(CH_3)CH_2CH_2-$, $-CH(CH_3)-$ and $-CH_2CH(CH_3)CH_2-$. In one embodiment, an alkylene group has from 1 to about 6 carbon atoms. In another embodiment, an alkylene group has from 1 to 3 carbon atoms. In another embodiment, an alkylene group is branched. In another embodiment, an alkylene group is linear. In one embodiment, an alkylene group is $-CH_2-$. The term "C_1-C_3 alkylene" refers to an alkylene group having from 1 to 3 carbon atoms. Unless otherwise indicated, an alkylene group is unsubstituted.

[0015] The term "alkenyl," as used herein, refers to an aliphatic hydrocarbon group containing at least one carbon-carbon double bond and having one of its hydrogen atoms replaced with a bond. An alkenyl group may be straight or branched and contain from about 2 to about 15 carbon atoms. In one embodiment, an alkenyl group contains from about 3 to 6 carbon atoms. Non-limiting examples of alkenyl groups include ethenyl, propenyl, n-butenyl, 3-methylbut-2-enyl, n-pentenyl, octenyl and decenyl. The term "C_2-C_6 alkenyl" refers to an alkenyl group having from 2 to 6 carbon atoms. Unless otherwise indicated, an alkenyl group is unsubstituted.

[0016] The term "alkenylene," as used herein, refers to an alkenyl group, as defined above, wherein one of the alkenyl group's hydrogen atoms has been replaced with a bond. Non-limiting examples of alkenylene groups include $-CH_2CH=CH-$, $-CH_2CH=CHCH_2-$, and $-CH(CH_3)CH=CH-$. In one embodiment, an alkenylene group has from 3 to 6 carbon atoms. In another embodiment, an alkenylene group is branched. In another embodiment, an alkenylene

group is linear. The term "C_3-C_6 alkenylene" refers to an alkenylene group having from 3 to 6 carbon atoms. Unless otherwise indicated, an alkenylene group is unsubstituted.

[0017] The term "alkynyl," as used herein, refers to an aliphatic hydrocarbon group containing at least one carbon-carbon triple bond and having one of its hydrogen atoms replaced with a bond. An alkynyl group may be straight or branched and contain from about 2 to about 15 carbon atoms. In one embodiment, an alkynyl group contains from about 3 to about 6 carbon atoms. Non-limiting examples of alkynyl groups include ethynyl, propynyl, 2-butynyl and 3-methylbutynyl. Unless otherwise indicated, an alkynyl group is unsubstituted.

[0018] The term "alkynylene," as used herein, refers to an alkynyl group, as defined above, wherein one of the alkynyl group's hydrogen atoms has been replaced with a bond. Non-limiting examples of alkynylene groups include $-CH_2C{\equiv}C-$, $-CH_2C{\equiv}CCH_2-$, and $-CH(CH_3)C{\equiv}C-$. In one embodiment, an alkynylene group has from 3 to 6 carbon atoms. In another embodiment, an alkynylene group is branched. In another embodiment, an alkynylene group is linear. The term "C_3-C_6 alkynylene" refers to an alkynylene group having from 3 to 6 carbon atoms. Unless otherwise indicated, an alkenylene group is unsubstituted.

[0019] The term "alkoxy" as used herein, refers to an –O-alkyl group, wherein an alkyl group is as defined above. Non-limiting examples of alkoxy groups include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy and t-butoxy. An alkoxy group is bonded via its oxygen atom.

[0020] The term "aryl," as used herein, refers to an aromatic monocyclic or multicyclic ring system comprising from about 6 to about 14 carbon atoms. In one embodiment, an aryl group contains from about 6 to 10 carbon atoms (C_6-C_{10} aryl). In another embodiment an aryl group is phenyl. An aryl group can be optionally substituted with one or more "ring system substituents" which may be the same or different, and are as defined herein below. In one embodiment, an aryl group can be optionally fused to a cycloalkyl or cycloalkanoyl group. Non-limiting examples of aryl groups include phenyl and naphthyl. Unless otherwise indicated, an aryl group is unsubstituted.

[0021] The terms " aza- or diazabicycloheterocycloalkyl" refer to saturated or mono-unsaturated cyclic systems having a first ring which is a 5, 6, or 7-membered ring having one or two nitrogen ring atoms with the remainder of the ring atoms being carbon atoms and a second ring formed from an alkylene bridge having 1 or 2 carbon atoms which is joined to two non-adjacent ring carbon atoms of the first ring. In one embodiment, an aza- or diabicycloheterocycloalkyl is a group selected from 2,5-diazabicyclo[2.2.1]heptane and 2,5-diazabicyclo[2.2.2]octane, 3,8-diazabicyclo[3.2.1]octane, and 8-azabyciyclo[3.2.1]oct-2-ene.

[0022] The term "carbamyl," as used herein, refers to the moiety $-C(O)NH_2$ wherein the point of attachment is through the carbonyl carbon atom.

[0023] The term "cycloalkyl," as used herein, refers to a non-aromatic mono- or multicyclic ring system comprising from about 3 to about 10 ring carbon atoms. In one embodiment, a cycloalkyl contains from about 5 to 10 ring carbon atoms. In another embodiment, a cycloalkyl contains from about 3 to about 7 ring atoms. In another embodiment, a cycloalkyl contains from about 5 to about 6 ring atoms. Non-limiting examples of monocyclic cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl. Non-limiting examples of multicyclic cycloalkyls include 1-decalinyl, norbornyl and adamantyl. The term "C_3-C_7 cycloalkyl" refers to a cycloalkyl group having from 3 to 7 ring carbon atoms. Unless otherwise indicated, a cycloalkyl group is unsubstituted.

[0024] The term "halo," as used herein, means –F, -Cl, -Br or -I. In one embodiment, a halo group is –F or –Cl. In another embodiment, a halo group is –F.

[0025] The term "fluoroalkyl," as used herein, refers to an alkyl group as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with a fluorine. In one embodiment, a fluoroalkyl group has from 1 to 6 carbon atoms. In another embodiment, a fluoroalkyl group is substituted with from 1 to 3 F atoms. Non-limiting examples of fluoroalkyl groups include $-CH_2F$, $-CHF_2$, and $-CF_3$. The term "C_1-C_3 fluoroalkyl" refers to a fluoroalkyl group having from 1 to 3 carbon atoms.

[0026] The term "hydroxyalkyl," as used herein, refers to an alkyl group as defined above, wherein one of the alkyl group's hydrogen atoms has been replaced with a hydroxyl moiety. In one embodiment, a hydroxyalkyl group has from 1 to 3 carbon atoms. Non-limiting examples of hydroxyalkyl groups include $-CH_2OH$, $-CH_2CH_2OH$, and $-CH_2CH(CH_3)CH_2OH$, and $-CH(CH_3)CH_2OH$. The term "C_1-C_3 hydroxyalkyl" refers to a hydroxyalkyl group having from 1 to 3 carbon atoms.

[0027] The term "heteroaryl," as used herein, refers to an aromatic monocyclic or multicyclic ring system comprising about 5 to about 14 ring atoms, wherein from 1 to 4 of the ring atoms is independently O, N or S and the remaining ring atoms are carbon atoms. In one embodiment, a heteroaryl group has 5 to 10 ring atoms. In another embodiment, a heteroaryl group is monocyclic and has 5 or 6 ring atoms. In another embodiment, a heteroaryl group is bicyclic. A heteroaryl group is joined via a ring carbon atom, and any nitrogen atom of a heteroaryl can be optionally oxidized to the corresponding N-oxide. The term "heteroaryl" also encompasses a heteroaryl group, as defined above, which is fused to a benzene ring. Non-limiting examples of heteroaryls include pyridyl, pyrazinyl, furanyl, thienyl, pyrimidinyl,

pyridone (including N-substituted pyridones), isoxazolyl, isothiazolyl, oxazolyl, oxadiazolyl, thiazolyl, pyrazolyl, furazanyl, pyrrolyl, triazolyl, 1,2,4-thiadiazolyl, pyrazinyl, pyridazinyl, quinoxalinyl, phthalazinyl, oxindolyl, imidazo[1,2-a]pyridinyl, imidazo[2,1-b]thiazolyl, benzofurazanyl, indolyl, azaindolyl, benzimidazolyl, benzothienyl, quinolinyl, imidazolyl, benzimidazolyl, thienopyridyl, quinazolinyl, thienopyrimidyl, pyrrolopyridyl, imidazopyridyl, isoquinolinyl, benzoazaindolyl, 1,2,4-triazinyl, benzothiazolyl and the like. In one embodiment, a heteroaryl group is a 5-membered heteroaryl. In another embodiment, a heteroaryl group is a 6-membered heteroaryl. In another embodiment, a heteroaryl group comprises a 5- to 6-membered heteroaryl group fused to a benzene ring. Unless otherwise indicated, a heteroaryl group is unsubstituted.

[0028] The term "heterocyclyl," as used herein, refers to a non-aromatic saturated monocyclic or multicyclic ring system comprising 3 to about 11 ring atoms, wherein from 1 to 4 of the ring atoms are independently O, S, or N, and the remainder of the ring atoms are carbon atoms. A heterocyclyl group can be joined via a ring carbon or ring nitrogen atom. In one embodiment, a heterocyclyl group is monocyclic and has from about 3 to about 7 ring atoms. In another embodiment, a heterocyclyl group is monocyclic has from about 4 to about 7 ring atoms. In another embodiment, a heterocyclyl group is bicyclic and has from about 7 to about 11 ring atoms. In still another embodiment, a heterocyclyl group is monocyclic and has 5 or 6 ring atoms. In one embodiment, a heterocyclyl group is monocyclic. In another embodiment, a heterocyclyl group is bicyclic. The term "heterocyclyl" also encompasses a heterocyclyl group, as defined above, which is fused to an aryl (*e.g.*, benzene) or heteroaryl ring. The nitrogen or sulfur atom of the heterocyclyl can be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Non-limiting examples of monocyclic heterocyclyl rings include oxetanyl, piperidyl, pyrrolidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, 1,4-dioxanyl, tetrahydrofuranyl, tetrahydrothiophenyl, delta-lactam, delta-lactone, and the like.

[0029] In one embodiment, a heterocyclyl group is a 5- to 6-membered monocyclic heterocyclyl. In another embodiment, a heterocyclyl group is a 5-membered monocyclic heterocyclyl. In another embodiment, a heterocyclyl group is a 6-membered monocyclic heterocyclyl. The term "5- to 6-membered heterocyclyl" refers to a monocyclic heterocyclyl group having from 5 to 6 ring atoms. Unless otherwise indicated, a heterocyclyl group is unsubstituted.

[0030] "Heterocyclenyl" means a non-aromatic monocyclic or multicyclic ring system comprising about 3 to about 10 ring atoms, preferably about 5 to about 10 ring atoms, in which one or more of the atoms in the ring system is an element other than carbon, for example

nitrogen, oxygen or sulfur atom, alone or in combination, and which contains at least one carbon-carbon double bond or carbon-nitrogen double bond. In specific embodiments of the ring system, from 1 to 4 of the ring atoms are independently O, S, or N, and the remainder of the ring atoms are carbon atoms. There are no adjacent oxygen and/or sulfur atoms present in the ring system. Preferred heterocyclenyl rings contain about 5 to about 6 ring atoms. The prefix aza, oxa or thia before the heterocyclenyl root name means that at least a nitrogen, oxygen or sulfur atom respectively is present as a ring atom. Unless otherwise indicated, a heterocyclenyl group is unsubstituted. The nitrogen or sulfur atom of the heterocyclenyl can be optionally oxidized to the corresponding N-oxide, S-oxide or S,S-dioxide. Non-limiting examples of suitable heterocyclenyl groups include 1,2,3,4- tetrahydropyridinyl, 1,2-dihydropyridinyl, 1,4-dihydropyridinyl, 1,2,3,6-tetrahydropyridinyl, 1,4,5,6-tetrahydropyrimidinyl, 2-pyrrolinyl, 3-pyrrolinyl, 2-imidazolinyl, 2-pyrazolinyl, dihydroimidazolyl, dihydrooxazolyl, dihydrooxadiazolyl, dihydrothiazolyl, 3,4-dihydro-2H-pyranyl, dihydrofuranyl, fluorodihydrofuranyl, 7-oxabicyclo[2.2.1]heptenyl, dihydrothiophenyl, dihydrothiopyranyl, and the like. "

[0031] The term "substituted" means that one or more hydrogens on the atoms of the designated are replaced with a selection from the indicated group, provided that the atoms' normal valencies under the existing circumstances are not exceeded, and that the substitution results in a stable compound. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. By "stable compound' or "stable structure" is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

[0032] When any substituent or variable occurs more than one time in any constituent or the compound of Formula (I), its definition on each occurrence is independent of its definition at every other occurrence, unless otherwise indicated.

[0033] The term "in purified form," as used herein, refers to the physical state of a compound after the compound is isolated from a synthetic process (*e.g.*, from a reaction mixture), a natural source, or a combination thereof. The term "in purified form," also refers to the physical state of a compound after the compound is obtained from a purification process or processes described herein or well-known to the skilled artisan (*e.g.*, chromatography, recrystallization and the like), in sufficient purity to be characterizable by standard analytical techniques described herein or well-known to the skilled artisan.

[0034] It should also be noted that any carbon as well as heteroatom with unsatisfied valences in the text, schemes, examples and tables herein is assumed to have the sufficient number of hydrogen atom(s) to satisfy the valences.

[0035] One or more compounds of the invention may exist in unsolvated as well as solvated forms with pharmaceutically acceptable solvents such as water, ethanol, and the like, and it is intended that the invention embrace both solvated and unsolvated forms. "Solvate" means a physical association of a compound of this invention with one or more solvent molecules. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. "Solvate" encompasses both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include ethanolates, methanolates, and the like. "Hydrate" is a solvate wherein the solvent molecule is H_2O.

[0036] The compounds of Formula (I) may contain asymmetric or chiral centers, and, therefore, exist in different stereoisomeric forms. It is intended that all stereoisomeric forms of the compounds of Formula (I) as well as mixtures thereof, including racemic mixtures, form part of the present invention.

[0037] Diastereomeric mixtures can be separated into their individual diastereomers on the basis of their physical chemical differences by methods well known to those skilled in the art, such as, for example, by chromatography and/or fractional crystallization. Enantiomers can be separated by converting the enantiomeric mixture into a diastereomeric mixture by reaction with an appropriate optically active compound (*e.g.*, chiral auxiliary such as a chiral alcohol or Mosher's acid chloride), separating the diastereomers and converting (*e.g.*, hydrolyzing) the individual diastereomers to the corresponding pure enantiomers. Also, some of the compounds of Formula (I) may be atropisomers (*e.g.*, substituted biaryls) and are considered as part of this invention. Enantiomers can also be separated by use of chiral HPLC column.

[0038] It is also possible that the compounds of Formula (I) may exist in different tautomeric forms, and all such forms are embraced within the scope of the invention.

[0039] All stereoisomers (for example, geometric isomers, optical isomers and the like) of the present compounds (including those of the salts and solvates of the compounds as well as the salts, solvates and esters of the prodrugs), such as those which may exist due to asymmetric carbons on various substituents, including enantiomeric forms (which may exist even in the absence of asymmetric carbons), rotameric forms, atropisomers, and diastereomeric forms, are contemplated within the scope of this invention. Individual stereoisomers of the compounds of

the invention may, for example, be substantially free of other isomers, or may be admixed, for example, as racemates or with all other, or other selected, stereoisomers. The chiral centers of the present invention can have the S or R configuration as defined by the *IUPAC* 1974 Recommendations.

[0040] The compounds of Formula (I) can form salts which are also within the scope of this invention. Reference to a compound of Formula (I) herein is understood to include reference to salts thereof, unless otherwise indicated. The term "salt(s)", as employed herein, denotes acidic salts formed with inorganic and/or organic acids, as well as basic salts formed with inorganic and/or organic bases. In addition, when a compound of Formula (I) contains both a basic moiety, such as, but not limited to a pyridine or imidazole, and an acidic moiety, such as, but not limited to a carboxylic acid, zwitterions ("inner salts") may be formed and are included within the term "salt(s)" as used herein. Such acidic and basic salts used within the scope of the invention are pharmaceutically acceptable (*i.e.*, non-toxic, physiologically acceptable) salts. Salts of the compounds of Formula (I) may be formed, for example, by reacting a compound of Formula (I) with an amount of acid or base, such as an equivalent amount, in a medium such as one in which the salt precipitates or in an aqueous medium followed by lyophilization.

[0041] Exemplary acid addition salts include acetates, ascorbates, benzoates, benzenesulfonates, bisulfates, borates, butyrates, citrates, camphorates, camphorsulfonates, fumarates, hydrochlorides, hydrobromides, hydroiodides, lactates, maleates, methanesulfonates, naphthalenesulfonates, nitrates, oxalates, phosphates, propionates, salicylates, succinates, sulfates, tartarates, thiocyanates, toluenesulfonates (also known as tosylates,) and the like. Additionally, acids which are generally considered suitable for the formation of pharmaceutically useful salts from basic pharmaceutical compounds are discussed, for example, by P. Stahl *et al*, Camille G. (eds.) *Handbook of Pharmaceutical Salts. Properties, Selection and Use.* (2002) Zurich: Wiley-VCH; S. Berge *et al*, *Journal of Pharmaceutical Sciences* (1977) 66(1) 1-19; P. Gould, *International J. of Pharmaceutics* (1986) 33 201-217; Anderson *et al*, *The Practice of Medicinal Chemistry* (1996), Academic Press, New York; and in *The Orange Book* (Food & Drug Administration, Washington, D.C. on their website). These disclosures are incorporated herein by reference.

[0042] Exemplary basic salts include ammonium salts, alkali metal salts such as sodium, lithium, and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases (for example, organic amines) such as dicyclohexylamines, t-butyl amines, and salts with amino acids such as arginine, lysine and the like. Basic nitrogen-containing groups may be quarternized with agents such as lower alkyl halides (*e.g.*, methyl,

ethyl, and butyl chlorides, bromides and iodides), dialkyl sulfates (*e.g.*, dimethyl, diethyl, and dibutyl sulfates), long chain halides (*e.g.*, decyl, lauryl, and stearyl chlorides, bromides and iodides), aralkyl halides (*e.g.*, benzyl and phenethyl bromides), and others.

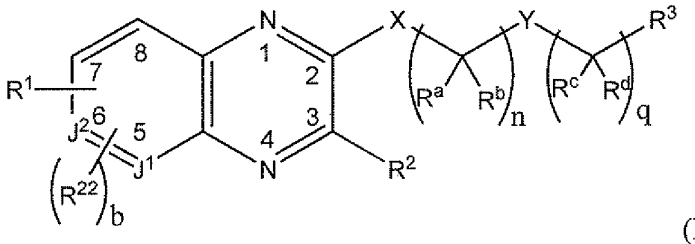
[0043] The present invention further includes the compounds of Formula (I) in all their isolated forms. For example, the above-identified compounds are intended to encompass all forms of the compounds such as, any solvates, hydrates, stereoisomers, and tautomers thereof.

[0044] As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts.

[0045] In the compounds of generic Formula (I), the atoms may exhibit their natural isotopic abundances, or one or more of the atoms may be artificially enriched in a particular isotope having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number predominantly found in nature. The present invention is meant to include all suitable isotopic variations of the compounds of generic Formula (I). For example, different isotopic forms of hydrogen (H) include protium (^{1}H) and deuterium (^{2}H). Protium is the predominant hydrogen isotope found in nature. Enriching for deuterium may afford certain therapeutic advantages, such as increasing *in vivo* half-life or reducing dosage requirements, or may provide a compound useful as a standard for characterization of biological samples. Isotopically-enriched compounds within generic Formula (I) can be prepared without undue experimentation by conventional techniques well known to those skilled in the art or by processes analogous to those described in the Schemes and Examples herein using appropriate isotopically-enriched reagents and/or intermediates.

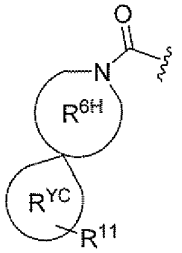
Compounds of the Invention

[0046] The present invention provides compound of Formula (I) or pharmaceutically acceptable salts thereof, wherein J^1, J^2, R^1, R^2, R^3, R^{22}, R^a, R^b, R^c, R^d, X, Y, b, n, and q are as defined above for the compound of Formula (I). The compounds of Formulas (IA), (IB), and (IC) as are described in detail below, are embodiments of the compound of Formula (I). The structural formula illustrated below indicates the peripheral numbering of the ring system.



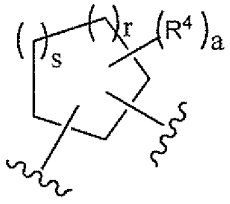
(I)

[0047] In specific embodiments of the compound of Formula (I), wherein R^1 is $-C(O)-N(R^{6a})(R^{6b})$ or $-S(O)_2-N(R^{6a})(R^{6b})$; and R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, it is be understood that two R^9 moieties can be geminally substituted on a common ring carbon of R^{6H} to form R^{YC}, such that R^1 forms the group:

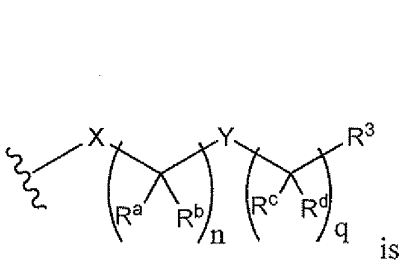


wherein R^{6H} and R^{YC} are as described above, and R^{11} is either absent or present.

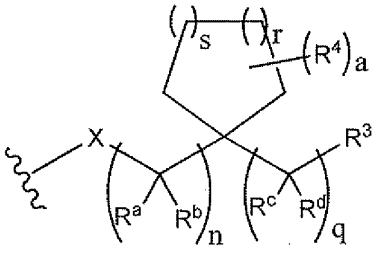
[0048] In certain embodiments of the compound of the Formula (I), wherein Y is



, it is to be understood that the bonds joining the illustrated cycloalkyl ring to the chain can either be attached on different ring carbon atoms, *e.g.*, on vicinal ring carbon atoms, or on the same ring carbon atom. For example, in some embodiments, the group



is



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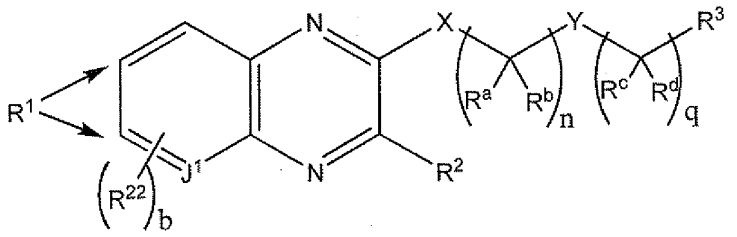
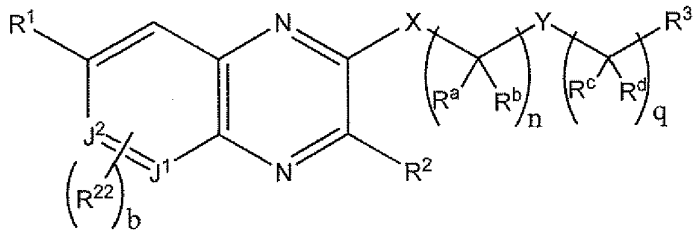
[0049] In embodiment no. 1 of the compound of Formula (I), R^1 is substituted on the 6 or 7 position of the illustrated bicyclic ring of Formula 1.

[0050] In embodiment no. 2, R^1 is substituted on the 7 or 8 position of the illustrated bicyclic ring of Formula (I), and J^2 is C(H), $C(R^1)$, or $C(R^{22})$. In other words, R^1 is substituted

on a ring carbon atom that is beta to the ring fusion of the illustrated bicyclic ring as shown below.



[0051] In embodiment no. 3, the compound has the formula (IA)



(IA)

wherein J^1 and J^2 are independently C(H) or C(R^{22}), or N wherein the following provisos apply:

(i) no more than one of J^1 and J^2 is N, and

(ii) no more than one of J^1 and J^2 is C(R^{22}).

[0052] In embodiment no. 4, R^1 is selected from the group consisting of:

(i) –C(O)-N(R^{6a})(R^{6b}), and

(ii) –$S(O)_2$-N(R^{6a})(R^{6b}).

[0053] In embodiment no. 5, R^1 is as described above in embodiment no. 4, and

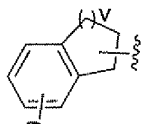
(i) R^{6a} is H and

R^{6b} is –Q-R^{AH} or -Q-R^{HC}; or

(ii) R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}.

[0054] In embodiment no. 6, R^1 is–C(O)-N(R^{6a})(R^{6b}).

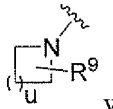
[0055] In embodiment no. 7, R^1 is–C(O)-N(R^{6a})(R^{6b}), wherein R^{6a} is H, and R^{6b} is –Q-R^{AH} or -Q-R^{HC}. In specific instances of embodiment no. 7, R^{6b} is

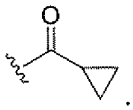


-Q-R^{HC}, wherein Q is absent and R^{HC} is , wherein v is 1 or 2, and R^{12} is present or absent.

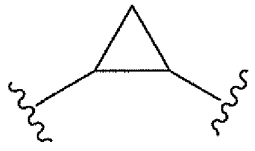
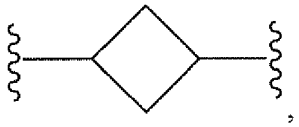
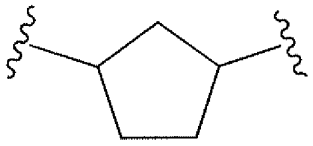
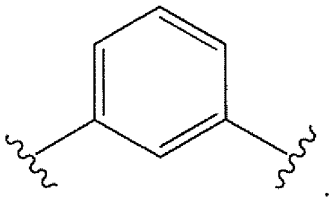
[0056] In embodiment no. 8, R^1 is

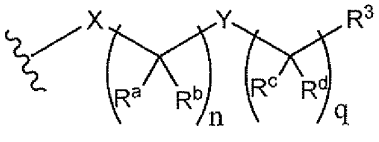
–C(O)-N(R^{6a})(R^{6b}), wherein R^{6a} and R^{6b} together with the N atom to which they are attached

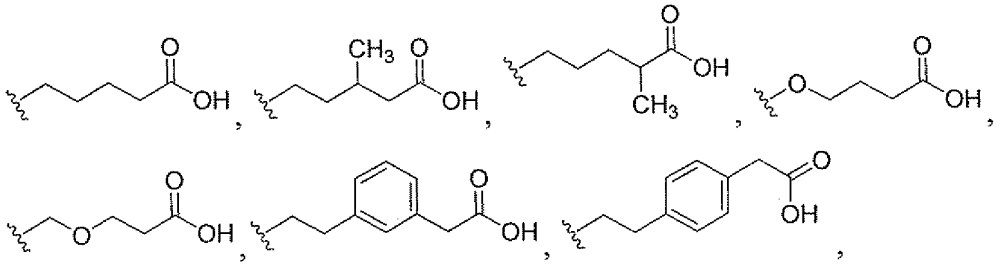
form R^{6H}. In specific instances of embodiment no. 8, R^{6H} is  wherein u is 1, 2, or 3, and R^9 is present or absent.

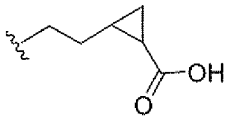
[0057] In embodiment no. 9 of the compound of Formula (I), R^1 is $-C(O)C(R^{7a})(R^{7b})(R^{7c})$. In specific instances of embodiment no. 9, R^1 is $-C(O)C(H)(R^{7a})(R^{7b})$, wherein R^{7a} and R^{7b} together with the carbon atom to which they are attached form R^{PC}, wherein R^{PC} is C_3-C_7 cycloalkyl. For example, in one instance of embodiment no. 9, R^1 is  .

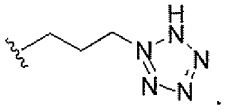
[0058] In embodiment no. 10 of the compound of Formula (I), R^1 is $-C(O)-O-C(R^{7a})(R^{7b})(R^{7c})$. For example, in one instance of embodiment no. 10, R^1 is $-C(O)-O-CH_3$.

[0059] In embodiment no. 11, Y is selected from the group consisting of (i) a bond, (ii)  , (iii)  , (iv)  , and (v)  .

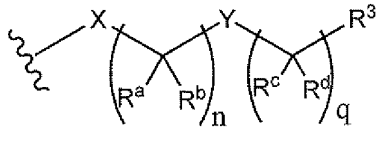
[0060] In embodiment no. 12, the group  is selected from the group consisting of:





, and 

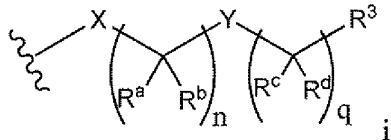
.

[0061] In embodiment no. 13, the compound has the Formula (IA) as described above in embodiment no. 3; and the group 

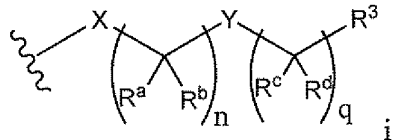
is as described above in embodiment no. 12.

[0062] In embodiment no. 14, R^2 is phenyl, pyridyl, or thienyl; wherein R^2 is unsubstituted or substituted by 1 to 2 R^5 groups independently selected from the group consisting of fluoro, chloro, trifluoromethyl, C_1-C_3 alkoxy, -CN, and -OCF_3;

[0063] In embodiment no. 15, b is 0, such that R^{22} is absent.

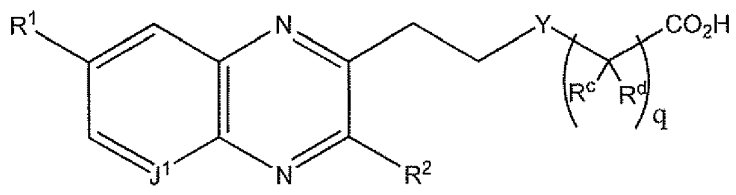
[0064] In embodiment no. 16, the compound has the Formula (IA) as described above in embodiment no. 3, R^1 is as described above in embodiment no. 4, the group 

is as described above in embodiment no. 12, R^2 is as described in embodiment no. 14, and b is 0.

[0065] In embodiment no. 17, the compound has the Formula (IA) as described above in embodiment no. 3, R^1 is as described above in embodiment no. 5, the group 

is as described above in embodiment no. 12, R^2 is as described in embodiment no. 14, and b is 0.

[0066] In embodiment no. 18, the compound of the Formula (I) has the Formula (IB)



(IB)

wherein

J^1 is C(H) or N;

R^1 is –C(O)-N(R^{6a})(R^{6b});

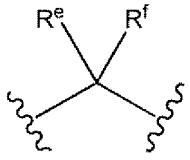
I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl or pyridyl,

and wherein R^{AH} is unsubstituted or substituted with 1 to 2 R^8 moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, trifluoromethyl, trifluoromethoxy, and –CN;

Q is selected from the group consisting of:

(i) a bond;

(ii) 

wherein R^e and R^f are independently H, C_1-C_3 alkyl, or trifluoromethyl;

(iii) C_2-C_4 alkylene, wherein said C_2-C_6 alkylene is unsubstituted;

b) –Q-R^{HC}, wherein R^{HC} is

(i) 5- to 6-membered heterocyclyl containing 1 heteroatom selected from the group consisting of N and O; or

(ii) C_5-C_7 cycloalkyl, wherein said C_5-C_7 cycloalkyl is optionally fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of C_1-C_3 alkyl, halo, and hydroxyl, or wherein when two R^{12} moieties are geminally substituted on the same carbon atom, the two geminally substituted R^{12} moieties, together with the carbon atom on which they are attached form –C(O)-;

II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is independently selected from the group consisting of:

a) a 4- to 6-membered heterocyclyl, optionally containing one additional nitrogen atom, wherein said 4- to 6-membered heterocyclyl is optionally fused to phenyl; and

b) a 5- to 6-membered heterocyclenyl, optionally containing one additional nitrogen atom, wherein said 4- to 6-membered heterocyclyl is optionally fused to phenyl;

wherein R^{6H} is unsubstituted or substituted by 1 to 2 R^9 moieties wherein each R^9 moiety is independently C_1-C_3 alkyl,, F, Cl, -CN, or

R^9 is -Z-R^{CY} wherein

Z is a bond or $-CH_2-$;

R^{CY} is selected from the group consisting of:

(i) phenyl;

(ii) 5- to 6-membered heteroaryl containing 1 to 3 N atoms; or

(iii) 5- to 6-membered heterocyclyl containing 2 N atoms, wherein said 5- to 6-membered heterocyclyl of R^{CY} is fused to phenyl;

wherein R^{CY} is unsubstituted or substituted by 1 to 2 R^{10} moieties;

each R^{10} moiety is independently C_1-C_3 alkyl, halo, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), or -CN, or, wherein two R^{10} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form–C(O)-;

or, optionally, where two R^9 moieties are geminally substituted on a common ring carbon of R^{6H}, the two R^9 moieties, together with the ring carbon on which they are substituted, form R^{YC}, wherein R^{YC} is

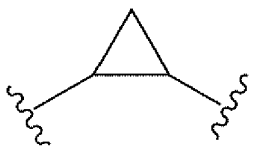
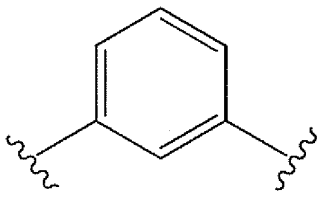
(i) a 5- to 6-membered cycloalkyl, wherein said or 5- to 6-membered cycloalkyl is fused to phenyl; or

(ii) a 4- to 6-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said or 4- to 6-membered heterocyclyl is optionally fused to phenyl;

wherein R^{YC} is unsubstituted or substituted by 1 to 3 R^{11} moieties;

each R^{11} moiety is independently C_1-C_3 alkyl, -C(O)-(C_1-C_3 alkyl), or phenyl, or, wherein two R^{11} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

Y is selected from the group consisting of

(i) a bond, (ii)  , and (iii)  ;

R^c is H or methyl;

R^d is H;

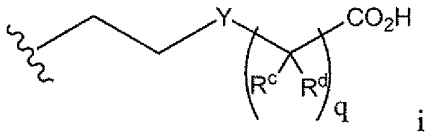
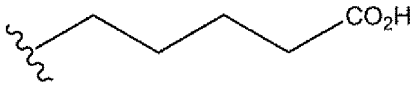
R^2 is phenyl, pyridyl, or thienyl;

wherein R^2 is unsubstituted or substituted by 1 to 2 R^5 groups independently selected from the group consisting of fluoro, chloro, trifluoromethyl, C_1-C_3 alkoxy, -CN, and -OCF_3;

q is 0, 1, or 2.

[0067] In embodiment no. 19, J^1 is CH, and the structural formula and the remaining variables are as described above in embodiment no. 18.

[0068] In embodiment no. 20, R^2 is unsubstituted or substituted phenyl, and the structural formula and the remaining variables are as described above in embodiment no. 18.

[0069] In embodiment no. 21, the group  is  , and the structural formula and the remaining variables are as described above in embodiment no. 18.

[0070] In embodiment no. 22, the compound of the Formula (I) has the Formula (IB)

J^1 is C(H);

R^1 is –C(O)-N(R^{6a})(R^{6b});

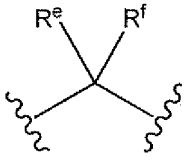
I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl,

and wherein R^{AH} is unsubstituted or substituted with 1 R^8 moiety selected from the group consisting of fluoro and chloro;

Q is selected from the group consisting of:

(i) a bond;

(ii)  wherein R^e is H, and R^f is H or methyl;

b) –Q-R^{HC}, wherein R^{HC} is C_5-C_6 cycloalkyl, wherein said C_5-C_6 cycloalkyl is fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of fluoro and chloro;

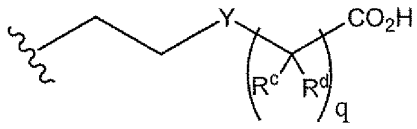
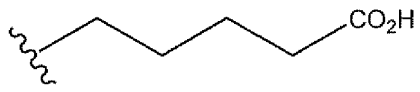
II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is azetidinyl, pyrrolidinyl, piperidinyl, or piperazinyl:

wherein R^{6H} is substituted by -Z-R^{CY};

wherein

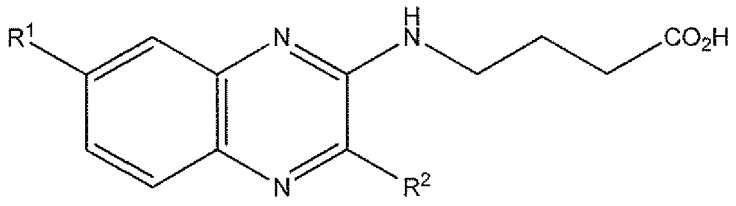
Z is a bond;

R^{CY} is unsubstituted phenyl or phenyl substituted by 1 to 2 R^{10} moieties selected from the group consisting of fluoro and chloro;

the group  is  ;

R^2 is unsubstituted phenyl or phenyl substituted by 1 to 2 fluoro or chloro.

[0071] In embodiment no. 23, the compound of the Formula (I) has the Formula (IC)



(IC)

wherein

R^1 is –C(O)-N(R^{6a})(R^{6b});

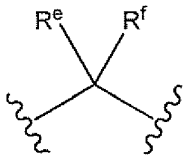
I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl,

and wherein R^{AH} is unsubstituted or substituted with 1 R^8 moiety selected from the group consisting of halo and -CN;

Q is selected from the group consisting of:

(i) a bond;

(ii)  wherein R^e is H, and R^f is H or methyl;

b) –Q-R^{HC}, wherein R^{HC} is C_5-C_6 cycloalkyl, wherein said C_5-C_6 cycloalkyl is fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of halo and -CN;

II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is azetidinyl, pyrrolidinyl, piperidinyl, or piperazinyl;

wherein R^{6H} is substituted with -Z-R^{CY} wherein

Z is a bond; and

R^{CY} is unsubstituted phenyl or phenyl substituted by 1 to 2 R^{10} moieties selected from the group consisting of halo and -CN;

R^{6H} is optionally substituted by 1 to 2 R^9 moieties wherein each R^9 moiety is independently C_1-C_3 alkyl, halo or -CN, and

R^2 is unsubstituted or substituted by 1 to 2 R^5 groups independently selected from the group consisting of fluoro, chloro, C_1-C_3 alkyl, trifluoromethyl, C_1-C_3 alkoxy, -CN, and -OCF_3.

[0072] In embodiment no. 24, the compound of the Formula (I) has the Formula (IC) wherein

R^1 is –C(O)-N(R^{6a})(R^{6b});

I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl,

and wherein R^{AH} is unsubstituted or substituted with 1 R^8 moiety selected from the group consisting of fluoro and -CN;

b) –Q-R^{HC}, wherein R^{HC} is C_5-C_6 cycloalkyl, wherein said C_5-C_6 cycloalkyl is fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of halo and -CN;

II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is pyrrolidinyl, piperidinyl, or piperazinyl;

wherein R^{6H} is substituted with -Z-R^{CY} wherein

R^{CY} is unsubstituted phenyl or phenyl substituted by 1 to 2 R^{10} moieties selected from the group consisting of halo and -CN;

R^{6H} is optionally substituted by 1 to 2 R^9 moieties wherein each R^9 moiety is independently C_1-C_3 alkyl, halo or -CN,

R^2 is unsubstituted phenyl; and

Q and Z are as described above in embodiment no. 23.

[0073] In embodiment no. 25, R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is piperazinyl, and the structural formula and the remaining variables are as described above in embodiment no. 24.

[0074] The invention also provides any one of the compounds specified in **Tables A** and **B** in the Examples section below, which tables include compounds **3**, **3T**, **3U**, **3V**, **3W**, **3X**, **3Y**, **3Z**, **3AA**, **3AB**, **3AC**, **3AD**, **3AE**, **3AF**, **3AG**, **4**, **4D**, **4E**, **4F**, **4G**, **5**, **5G**, **5N**, **5o**, **5P**, **5Q**, **5R**, **5S**,

6, 6F, 6G, 7, 7C, 8, 8G, 9, 10, 10C, 10D, 10E, 10F, 11, 11D, 11E, 11F, 12, 13, 14, 14C, 14D, 14E, 14F, 14G, 14H, 15A, 15B, 15C, 15D, 15E, 15F, 15G, 15H, 15i, 15J, 15K, 15L, 15M, 15N, 15o, 15P, 15Q, 15R, 15S, 15T, 15U, 15V, 15X, 15Y, 15Z, 15AA, 15AB, 15AC, 15AD, 15AE, 15AF, 15AG, 15AH, 15Ai, 15AJ, 15AK, 15AL, 15AM, 15AN, 15Ao, 15AP, 15AQ, 15AR, 15AS, 15AT, 15AU, 15AV, 15AW, 15AX, 15AY, 15AZ, 15BA, 15BB, 15BC, 15BD, 15BE, 15BF, 15BG, 15BH, 15Bi, 15BJ, 15BK, 15BL, 15BM, 15BN, 15Bo, 15BQ, 15BR, 15BS, 15BT, 15BU, 16, 16F, 16G, 16H, 16i, 16J, 16K, 16L, 16M, 16N, 16o, 16P, 16Q, 16R, 16S, 16T, 16U, 16V, 16W, 16X, 16Y, 16Z, 16AA, 16AB, 16AC, 16AD, 16AE, 16AF, 16AG, 16AH, 16Ai, 16AJ, 16AK, 16AL, 16AM, 16AN, 16Ao, 16AP, 16AQ, 16AR, 16AS, 17, 17D, 17E, 17F, 17G, 17H, 17i, 17J, 17K, 17L, 17M, 17N, 17o, 17P, 17Q, 17R, 17S, 17T, 17U, 17V, 17V, 17W, 17X, 17Y, 17Z, 18, 18D, 18E, 18F, 18G, 18H, 19, 19F, 19G, 19H, 19i, 19J, 19K, 20, 20F, 20G, 20H, 21, 22, 22D, 23, 24, 24H, 24i, 25, 26, 26E, 26F, 26G, 26H, 26i, 26J, 26K, 26L, 26M, 26N, 26o, 26P, 26Q, 26R, 26S, 26T, 26U, 26V, 26W, 26X, 26Y, 26Z, 26AA, 26AB, 28, 29, 30, 30E, 31, 31C, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 44, 44D, 44E, 44F, 44G, 44H, 44i, 44J, 44K, 44L, 44M, 44N,and **100-728**, or a pharmaceutically acceptable salt thereof. The structural formulas and names of these compounds are as set forth in the Examples section below.

[0075] In another embodiment, the invention also provides any one of the compounds specified in **Table A** in the Examples section below, which table includes compounds **3, 3T, 3U, 3V, 3W, 3X, 3Y, 3Z, 3AA, 3AB, 3AC, 3AD, 3AE, 3AF, 3AG, 4, 4D, 4E, 4F, 4G, 5, 5G, 5N, 5o, 5P, 5Q, 5R, 5S, 6, 6F, 6G, 7, 7C, 8, 8G, 9, 10, 10C, 10D, 10E, 10F, 11, 11D, 11E, 11F, 12, 13, 14, 14C, 14D, 14E, 14F, 14G, 14H, 15A, 15B, 15C, 15D, 15E, 15F, 15G, 15H, 15i, 15J, 15K, 15L, 15M, 15N, 15o, 15P, 15Q, 15R, 15S, 15T, 15U, 15V, 15X, 15Y, 15Z, 15AA, 15AB, 15AC, 15AD, 15AE, 15AF, 15AG, 15AH, 15Ai, 15AJ, 15AK, 15AL, 15AM, 15AN, 15Ao, 15AP, 15AQ, 15AR, 15AS, 15AT, 15AU, 15AV, 15AW, 15AX, 15AY, 15AZ, 15BA, 15BB, 15BC, 15BD, 15BE, 15BF, 15BG, 15BH, 15Bi, 15BJ, 15BK, 15BL, 15BM, 15BN, 15Bo, 15BQ, 15BR, 15BS, 15BT, 15BU, 16, 16F, 16G, 16H, 16i, 16J, 16K, 16L, 16M, 16N, 16o, 16P, 16Q, 16R, 16S, 16T, 16U, 16V, 16W, 16X, 16Y, 16Z, 16AA, 16AB, 16AC, 16AD, 16AE, 16AF, 16AG, 16AH, 16Ai, 16AJ, 16AK, 16AL, 16AM, 16AN, 16Ao, 16AP, 16AQ, 16AR, 16AS, 17, 17D, 17E, 17F, 17G, 17H, 17i, 17J, 17K, 17L, 17M, 17N, 17o, 17P, 17Q, 17R, 17S, 17T, 17U, 17V, 17V, 17W, 17X, 17Y, 17Z, 18, 18D, 18E, 18F, 18G, 18H, 19, 19F, 19G, 19H, 19i, 19J, 19K, 20, 20F, 20G, 20H, 21, 22, 22D, 23, 24, 24H, 24i, 25, 26, 26E, 26F, 26G, 26H, 26i, 26J, 26K, 26L, 26M, 26N, 26o, 26P, 26Q, 26R, 26S, 26T, 26U, 26V, 26W, 26X, 26Y,**

26Z, **26AA**, **26AB**, **28**, **29**, **30**, **30E**, **31**, **31C**, and **100-253**, or a pharmaceutically acceptable salt thereof.

[0076] In another specific embodiment, the invention provides any one of the compounds selected from the group consisting of **14**, **14D**, **14G**, **15A**, **15B**, **15C**, **15D**, **15E**, **15K**, **15N**, **15P**, **15Q**, **15R**, **15S**, **15T**, **15X**, **15Z**, **15AB**, **15AC**, **15AD**, **15AF**, **15Ai**, **15AJ**, **15AK**, **15AL**, **15AN**, **15Ao**, **15AP**, **15AR**, **15AU**, **15AV**, **15AW**, **15AX**, **15AY**, **15AZ**, **15BA**, **15BB**, **15BC**, **15BD**, **15BF**, **15BH**, **15BK**, **15BM**, **15BN**, **15BQ**, **15BR**, **15BS**, **15BT**, **15BU**, **16**, **16F**, **16H**, **16i**, **16J**, **16K**, **16L**, **16N**, **16P**, **16R**, **16S**, **16T**, **16U**, **16V**, **16Y**, **16AB**, **16AC**, **16AE**, **16AG**, **16AH**, **16AK**, **16AQ**, **17**, **17D**, **17M**, **17S**, **18**, **19**, **19G**, **20**, **24i**, **26E**, **26J**, **26K**, **26L**, **26N**, **26o**, **26P**, **26S**, **26Y**, **39**, **40**, **41**, **44H**, **44i**, **100**, **102-107**, **109-113**, **117**, **119-132**, **135**, **136**, **142**, **143**, **145**, **147**, **148**, **162**, **163**, **164**, **166**, **167**, **172**, **174**, **217**, **231**, **251**, **254**, **255**, **256**, **375**, **412**, **426**, **457**, **491**, **507**, **512**, **585**, and **628** or a pharmaceutically acceptable salt thereof.

[0077] In another specific embodiment, the invention provides any one of the compounds selected from the group consisting of **14**, **14D**, **14G**, **15A**, **15B**, **15C**, **15D**, **15E**, **15K**, **15N**, **15P**, **15Q**, **15R**, **15S**, **15T**, **15X**, **15Z**, **15AB**, **15AC**, **15AD**, **15AF**, **15Ai**, **15AJ**, **15AK**, **15AL**, **15AN**, **15Ao**, **15AP**, **15AR**, **15AU**, **15AV**, **15AW**, **15AX**, **15AY**, **15AZ**, **15BA**, **15BB**, **15BC**, **15BD**, **15BF**, **15BH**, **15BK**, **15BM**, **15BN**, **15BQ**, **15BR**, **15BS**, **15BT**, **15BU**, **16**, **16F**, **16H**, **16i**, **16J**, **16K**, **16L**, **16N**, **16P**, **16R**, **16S**, **16T**, **16U**, **16V**, **16Y**, **16AB**, **16AC**, **16AE**, **16AG**, **16AH**, **16AK**, **16AQ**, **17**, **17D**, **17M**, **17S**, **18**, **19**, **19G**, **20**, **24i**, **26E**, **26J**, **26K**, **26L**, **26N**, **26o**, **26P**, **26S**, **26Y**, **100**, **102-107**, **109-113**, **117**, **119-132**, **135**, **136**, **142**, **143**, **145**, **147**, **148**, **162**, **163**, **164**, **166**, **167**, **172**, **174**, **217**, **231**, **251**, **254**, and **255**, or a pharmaceutically acceptable salt thereof.

[0078] The invention also provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof in purified form.

Compositions and Administration

[0079] This invention is also directed to pharmaceutical compositions which comprise a compound of Formula (I), or a pharmaceutically acceptable salt of said compound and a pharmaceutically acceptable carrier.

[0080] A preferred dosage is about 0.001 to 100 mg/kg of body weight/day of the compound of Formula (I). An especially preferred dosage is about 0.01 to 10 mg/kg of body weight/day of a compound of Formula (I), or a pharmaceutically acceptable salt of said compound.

[0081] The term "pharmaceutical composition" is also intended to encompass both the bulk composition and individual dosage units comprised of more than one (*e.g.*, two) pharmaceutically active agents such as, for example, a compound of the present invention and an additional therapeutic agent selected from the lists of the additional agents described herein below, along with any pharmaceutically inactive excipients. The bulk composition and each individual dosage unit can contain fixed amounts of the afore-said "more than one pharmaceutically active agents". The bulk composition is material that has not yet been formed into individual dosage units. An illustrative dosage unit is an oral dosage unit such as a tablet, a pill and the like. Similarly, the herein-described method of treating a patient by administering a pharmaceutical composition of the present invention is also intended to encompass the administration of the afore-said bulk composition and individual dosage units.

[0082] For preparing pharmaceutical compositions from the compounds described by this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets and suppositories. The powders and tablets may be comprised of from about 5 to about 95 percent active ingredient. Suitable solid carriers are known in the art, *e.g.*, magnesium carbonate, magnesium stearate, talc, sugar or lactose. Tablets, powders, cachets and capsules can be used as solid dosage forms suitable for oral administration. Examples of pharmaceutically acceptable carriers and methods of manufacture for various compositions may be found in A. Gennaro (ed.), *Remington's Pharmaceutical Sciences,* 18th Edition, (1990), Mack Publishing Co., Easton, Pennsylvania.

[0083] Liquid form preparations include solutions, suspensions and emulsions. Examples of materials useful for forming such liquid form preparations include water or water-propylene glycol solutions for parenteral injection, or sweeteners and opacifiers for oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions or suspensions for intranasal administration.

[0084] Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be in combination with a pharmaceutically acceptable carrier, such as an inert compressed gas, *e.g.*, nitrogen.

[0085] Also included are solid form preparations that are intended to be converted, shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

[0086] The compounds of the invention can also be deliverable transdermally. The transdermal compositions can take the form of creams, lotions, aerosols and/or emulsions and

can be included in a transdermal patch of the matrix or reservoir type as are conventional in the art for this purpose.

[0087] The compounds of this invention may also be delivered subcutaneously.

[0088] Preferably the compound is administered orally.

[0089] Preferably, the pharmaceutical preparation is in a unit dosage form. In such form, the preparation is subdivided into suitably sized unit doses containing appropriate quantities of the active component, *e.g.*, an effective amount to achieve the desired purpose.

[0090] The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 0.001 mg to about 100 mg per kg body weight of a mammal, preferably from about 0.01 mg to about 10 mg per kg. The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage regimen for a particular situation is within the skill of the art. For convenience, the total daily dosage may be divided and administered in portions during the day as required.

[0091] The compositions of the invention can further comprise one or more additional therapeutic agents, as discussed in further detail below. Accordingly, in one embodiment, the present invention provides compositions comprising: (i) a compound of Formula (I) or a pharmaceutically acceptable salt thereof; (ii) one or more additional therapeutic agents, that are not compounds of Formula (I); and (iii) a pharmaceutically acceptable carrier, wherein the amounts in the composition are together effective to treat one of the disease or conditions discussed above.

Uses of the Compounds

[0092] The compounds of Formula (I) bind to $CRTH_2$ and, therefore, are useful in characterizing tissues containing $CRTH_2$, and in identifying further compounds which bind to $CRTH_2$. The general value of the compounds of the invention in binding the $CRTH_2$ receptor can be determined, for example, using the radioligand binding assay described below in the Examples section.

[0093] The compounds of Formula (I) can also be useful as modulators of $CRTH_2$ receptor function. In some embodiments, compounds of Formula (I) are antagonists of the $CRTH_2$ receptor. The general value of the compounds of the invention in antagonizing $CRTH_2$ receptor function can be determined, for example, using the chemiluminescent-based cAMP assay, the β-Arrestin assay, or the eosinophil shape change assay described below in the Examples section.

[0094] While not being bound by any specific theory, Applicants believe that the compounds of Formula (I) are useful in treating the symptoms of diseases or conditions associated with uncontrolled or inappropriate stimulation of $CRTH_2$ function because of their ability to antagonize the $CRTH_2$ receptor. Accordingly, in one embodiment, the invention provides a method for treating a disease or conditions associated with uncontrolled or inappropriate stimulation of $CRTH_2$ function, comprising administering a therapeutically effective amount of a compound of Formula (I) to a patient in need of such treatment. In certain embodiments, the compound of Formula (I) used in the method is selected from one of the representative compounds listed in Table A as set forth in the Examples section.

[0095] Diseases or conditions associated with uncontrolled or inappropriate stimulation of $CRTH_2$ function include (but not limited to) asthma, congestion, allergic rhinitis, atopic dermatitis, chronic obstructive pulmonary disease ("COPD"), dermatitis, inflammatory bowel disease, rheumatoid arthritis, allergic nephritis, conjunctivitis, bronchial asthma, fold allergy, systemic mast cell disorder, anaphylactic shock, urticaria, eczema, itching, inflammation, ischemia-reperfusion injury, cerebrovascular disorders, pleuritis, ulcerative colitis, eosinophil-related diseases, such as Churg-Strauss syndrome and sinusitis, and basophile-related diseases, such as basophilic leukemia and basophilic leukocytosis, in humans and other mammals. Examples of cerebrovascular disorders include stroke.

[0096] In certain embodiments, the present invention provides a method for treating asthma, congestion, allergic rhinitis or COPD which comprises administering a therapeutically effective dose of a compound of Formula (I) or a pharmaceutically acceptable salt thereof to a patient in need of such treatment. In a specific embodiment, the disease or condition being treated is asthma. In another embodiment, the disease or condition being treated is COPD.

[0097] In addition, compounds of the Formula (I) which act as $CRTH_2$ receptor antagonists can inhibit prostanoid-induced smooth muscle contraction by antagonizing contractile prostanoids or mimicking relaxing prostanoids and hence may be used in the treatment of dysmenorrhea, premature labor and eosinophil related disorders.

[0098] In another embodiment, the present invention provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for treating a disease or condition selected from the group consisting of asthma, congestion, allergic rhinitis, atopic dermatitis, COPD, dermatitis, inflammatory bowel disease, rheumatoid arthritis, allergic nephritis, conjunctivitis, bronchial asthma, food allergy, systemic mast cell disorder, anaphylactic shock, urticaria, eczema, itching, inflammation, ischemia-reperfusion injury, cerebrovascular disorders, pleuritis, ulcerative colitis, eosinophil-related diseases, such as Churg-

Strauss syndrome and sinusitis, and basophile-related diseases, such as basophilic leukemia and basophilic leukocytosis. In certain embodiments of the use, the compound of Formula (I) is selected from one of the representative compounds listed in Table A as set forth in the Examples section.

[0099] In another embodiment, the present invention provides a compound of Formula (I) or a pharmaceutically acceptable salt thereof for use in treating a disease or condition from the group consisting of asthma, congestion, allergic rhinitis, atopic dermatitis, COPD, dermatitis, inflammatory bowel disease, rheumatoid arthritis, allergic nephritis, conjunctivitis, bronchial asthma, food allergy, systemic mast cell disorder, anaphylactic shock, urticaria, eczema, itching, inflammation, ischemia-reperfusion injury, cerebrovascular disorders, pleuritis, ulcerative colitis, eosinophil-related diseases, such as Churg-Strauss syndrome and sinusitis, and basophile-related diseases, such as basophilic leukemia and basophilic leukocytosis. In certain embodiments of the use, the compound of Formula (I) is selected from one of the representative compounds listed in Table A as set forth in the Examples section.

[00100] In specific embodiments of the methods and uses described above, the compound used in the method or use described above is selected one of the compounds **3T, 3U, 3V, 3W, 3X, 3Y, 3AA, 3AB, 3AC, 3AD, 3AE, 3AF, 4, 4D, 4E, 4F, 5N, 5P, 5R, 5S, 6F, 7C, 8, 8G, 10, 10C, 10D, 10F, 11, 11D, 11E, 11F, 12, 14, 14C, 14D, 14E, 14F, 14G, 14H, 15A, 15B, 15C, 15D, 15E, 15F, 15H, 15i, 15J, 15K, 15L, 15M, 15N, 15o, 15P, 15Q, 15R, 15S, 15T, 15X, 15Z, 15AA, 15AB, 15AC, 15AD, 15AE, 15AF, 15AG, 15AH, 15Ai, 15AJ, 15AK, 15AL, 15AM, 15AN, 15AP, 15AR, 15AU, 15AV, 15AW, 15AX, 15AY, 15AZ, 15BA, 15BB, 15BC, 15BD, 15BE, 15BF, 15BH, 15BJ, 15BK, 15BL, 15BM, 15BN, 15Bo, 15BQ, 15BR, 15BS, 15BT, 15BU, 16, 16F, 16H, 16i, 16J, 16K, 16L, 16N, 16P, 16S, 16T, 16U, 16V, 16W, 16X, 16Y, 16AB, 16AC, 16AD, 16AE, 16AG, 16AH, 16AJ, 16AK, 16AQ, 16AR, 17, 17D, 17E, 17G, 17M, 17S, 17Y, 17Z, 18, 19, 19F, 19G, 19J, 20, 20F, 20G, 20H, 22, 22D, 23, 24H, 24i, 25, 26E, 26F, 26G, 26H, 26i, 26J, 26K, 26L, 26M, 26N, 26o, 26P, 26Q, 26R, 26S, 26T, 26U, 26V, 26W, 26X, 26Y, 26AA, 26AB, 28, 29, 30, 31, 31C, 100, 102, 104-128, 130-136, 143, 145, 148, 155, 156, 160, 162-164, 166, 167, 169, 170, 172, 174-176, 180, 182-191, 198, 199, 204-212, 215, 217-222, 224-229, 231, 232, 234-243, 245-249,** and **251-255** or a pharmaceutically acceptable salt thereof.

Combination Therapy

[00101] The compounds of Formula (I) or their pharmaceutically acceptable salts may be used in combination, either in a single formulation or co-administered as separate formulations

with at least one additional therapeutic agent to treat or prevent the diseases and conditions described herein. These additional therapeutic agents include, but are not limited to: (1) a DP receptor antagonist, such as S-5751 and laropiprant; (2) a corticosteroid, such as triamcinolone acetonide, budesonide, beclomethasone, fluticasone and mometasone; (3) a β2-adrenergic agonist, such as salmeterol, formoterol, arformoterol, terbutaline, metaproterenol, albuterol and the like; (4) a leukotriene modifier, including a leukotriene receptor antagonist, such as montelukast, zafirlukast, pranlukast, or a lipooxygenase inhibitor including 5-lipooxygenase inhibitors and FLAP (5-lipooxygenase activating protein) inhibitors, such as zileuton; (5) an antihistamine such as bromopheniramine, chlorpheniramine, dexchlorpheniramine, triprolidine, clemastine, diphenhydramine, diphenylpyraline, tripelennamine, hydroxyzine, methdilazine, promethazine, trimeprazine, azatadine, cyproheptadine, antazoline, pheniramine pyrilamine, astemizole, terfenadine, loratadine, cetirizine, fexofenadine, descarboethoxyloratadine, and the like; (6) a decongestant, including phenylephrine, phenylpropanolamine, pseudophedrine, oxymetazoline, ephinephrine, naphazoline, xylometazoline, propylhexedrine, or levo-desoxyephedrine; (7) an antiitussive, including codeine, hydrocodone, caramiphen, carbetapentane, or dextramethorphan; (8) another prostaglandin ligand, including prostaglandin F agonist such as latanoprost; misoprostol, enprostil, rioprostil, ornoprostol or rosaprostol; (9) a diuretic; (10) non-steroidal antiinflammatory agents (NSAIDs), such as propionic acid derivatives (alminoprofen, benoxaprofen, bucloxic acid, carprofen, fenbufen, fenoprofen, fluprofen, flurbiprofen, ibuprofen, indoprofen, ketoprofen, miroprofen, naproxen, oxaprozin, pirprofen, pranoprofen, suprofen, tiaprofenic acid, and tioxaprofen), acetic acid derivatives (indomethacin, acemetacin, alclofenac, clidanac, diclofenac, fenclofenac, fenclozic acid, fentiazac, furofenac, ibufenac, isoxepac, oxpinac, sulindac, tiopinac, tolmetin, zidometacin, and zomepirac), fenamic acid derivatives (flufenamic acid, meclofenamic acid, mefenamic acid, niflumic acid and tolfenamic acid), biphenylcarboxylic acid derivatives (diflunisal and flufenisal), oxicams (isoxicam, piroxicam, sudoxicam and tenoxican), salicylates (acetyl salicylic acid, sulfasalazine) and the pyrazolones (apazone, bezpiperylon, feprazone, mofebutazone, oxyphenbutazone, phenylbutazone); (11) cyclooxygenase-2 (COX-2) inhibitors, such as celecoxib and rofecoxib; (12) inhibitors of phosphodiesterase type IV (PDE-IV) *e.g.,* Ariflo, roflumilast; (13) antagonists of the chemokine receptors, especially CCR-1, CCR-2, and CCR-3; (14) cholesterol lowering agents such as HMG-CoA reductase inhibitors (lovastatin, simvastatin and pravastatin, fluvastatin, atorvastatin, and other statins), sequestrants (cholestyramine and colestipol), nicotinic acid, fenofibric acid derivatives (gemfibrozil, clofibrat, fenofibrate and benzafibrate), and probucol; (15) anti-diabetic agents such as insulin, sulfonylureas, biguanides

(metformin), α-glucosidase inhibitors (acarbose) and glitazones (troglitazone, pioglitazone, englitazone, rosiglitazone and the like); (16) preparations of interferon beta (interferon beta-1a, interferon beta-1b); (17) anticholinergic agents, such as muscarinic antagonists (ipratropium bromide and tiotropium bromide), as well as selective muscarinic M3 antagonists; (18) steroids such as beclomethasone, methylprednisolone, betamethasone, prednisone, dexamethasone, and hydrocortisone; (19) triptans commonly used for the treatment of migraine such as sumitriptan and rizatriptan; (20) alendronate and other treatments for osteoporosis; (21) other compounds such as 5-aminosalicylic acid and prodrugs thereof, antimetabolites such as azathioprine and 6-mercaptopurine, cytotoxic cancer chemotherapeutic agents, bradykinin (BK2) antagonists such as FK-3657, TP receptor antagonists such as seratrodast, neurokinin antagonists (NK1/NK2), VLA-4 antagonists, such as those described in US 5,510,332, WO97/03094, WO97/02289, WO96/40781, WO96/22966, WO96/20216, WO96/01644, WO96/06108, WO95/15973 and WO96/31206. In addition, the invention encompasses a method of treating prostaglandin D2 mediated diseases comprising: administration to a patient in need of such treatment a non-toxic therapeutically effective amount of a compound of Formula (I), optionally co-administered with one or more of such ingredients as listed immediately above.

[00102] When administering a combination therapy to a patient in need of such administration, the therapeutic agents in the combination, or a pharmaceutical composition or compositions comprising the therapeutic agents, may be administered in any order such as, for example, sequentially, concurrently, together, simultaneously and the like.

[00103] In one embodiment, the compound of Formula (I) is administered during a time when the additional therapeutic agent(s) exert their prophylactic or therapeutic effect, or *vice versa*.

[00104] In another embodiment, the compound of Formula (I) and the additional therapeutic agent(s) are administered in doses commonly employed when such agents are used as monotherapy for treating the disorder.

[00105] In another embodiment, the compound of Formula (I) and the additional therapeutic agent(s) are administered in doses lower than the doses commonly employed when such agents are used as monotherapy for treating the disorder.

[00106] In one embodiment, the compound of Formula (I) and the additional therapeutic agent(s) are present in the same composition, which is suitable for oral administration.

[00107] The compound of Formula (I) and the additional therapeutic agent(s) can act additively or synergistically. A synergistic combination may allow the use of lower dosages of one or more agents and/or less frequent administration of one or more agents of a combination

therapy. A lower dosage or less frequent administration of one or more agents may lower toxicity of the therapy without reducing the efficacy of the therapy.

[00108] The doses and dosage regimen of the additional therapeutic agent(s) used in the combination therapies of the present invention for the treatment or prevention of a disease or disorder can be determined by the attending clinician, taking into consideration the approved doses and dosage regimen in the package insert; the age, sex and general health of the patient; and the type and severity of the viral infection or related disease or disorder.

[00109] Another aspect of this invention is a kit comprising a therapeutically effective amount of the compound of Formula (I) or a pharmaceutically acceptable salt of said compound, optionally at least one additional therapeutic agent listed above and a pharmaceutically acceptable carrier, vehicle or diluent.

Methods of Preparing the Compounds of Formula (I)

[00110] In general, the compounds in the invention may be produced by a variety of processes known to those skilled in the art and by know, processes analogous thereto. The invention disclosed herein is exemplified by the following preparations and examples which should not be construed to limit the scope of the disclosure. Alternative mechanistic pathways and analogous structures will be apparent to those skilled in the art. The practitioner is not limited to these methods.

[00111] One skilled in the art will recognize that one route will be optimized depending on the choice of appendage substituents. Additionally, one skilled in the art will recognize that in some cases the order of steps has to be controlled to avoid functional group incompatability.

[00112] The prepared compounds may be analyzed for their composition and purity as well as characterized by standard analytical techniques such as, for example, elemental analysis, NMR, mass spectroscopy and IR spectra.

[00113] One skilled in the art will recognize that reagents and solvents actually used may be selected from several reagents and solvents well known in the art to be effective equivalents. Hence, when a specific solvent or reagent is mentioned, it is meant to be an illustrative example of the conditions desirable for that particular reaction scheme or for the preparation described below.

[00114] Where NMR data are presented, ^{1}H spectra were obtained on either a Varian VXR-400 (400 MHz, 1H), Varian Gemini-300 (300 MHz), Varian Mercury VX-400 (400 MHz), Bruker-Biospin AV-500 (500 MHz) or Bruker Avance DRX-500 (500 MHz), and chemical shifts are reported as ppm with number of protons and multiplicities indicated parenthetically.

Where LC/MS data are presented, analyses was performed using a 1200 series Agilent 6140 Quadrupole LCMS with a 1.8 μM Zorbax SB-C18 column (10-95% of MeCN-H_2O with 0.1% TFA over 2.7 min, 1 mL/min) or with an Applied Biosystems API-150 mass spectrometer and Gemini C18 column (50 x 4.6 mm, 10-95% CH_3CN-H_2O with 0.05% TFA over 5 min, 1 mL/min).

[00115] The following solvents and reagents may be referred to by their abbreviations in parenthesis:

[00116] Me = methyl; Et = ethyl; Pr = propyl; Bu = butyl; t-Bu = *tert*-butyl; Ph = phenyl, and Ac = acetyl

[00117] μl = microliters

[00118] Acac = acetylacetone

[00119] AcOEt or EtOAc = ethyl acetate

[00120] AcOH or HOAc = acetic acid

[00121] ACN = acetonitrile

[00122] aq = aqueous

[00123] Ar = aryl

[00124] atm = atmosphere

[00125] 9-BBN = 9-borabicyclo[3.3.1]nonane

[00126] Bn = benzyl

[00127] Boc or BOC = tert-butoxycarbonyl

[00128] Bz = benzoyl

[00129] Boc = *tert*-butoxycarbonyl

[00130] BINAP = 2,2'-bis(diphenylphosphino)-1,1'-bisnaphthyl

[00131] cat = catalyst or catalytic

[00132] Cbz = benyzloxycarbonyl

[00133] DAST = diethylaminosulfur trifluoride

[00134] DBU = 1,8-Diaza-7-bicyclo[5.4.0]undecene

[00135] DCM or CH_2Cl_2: dichloromethane:

[00136] DMAP = 4-Dimethylaminopyridine

[00137] DIBAL = diisobutylaluminum hydride

[00138] DIPEA or Hünig's Base = N,N-diisopropylethylamine

[00139] DME = 1,2-dimethoxyethane

[00140] DMF = dimethylformamide

[00141] DMS = dimethylsulfide

[00142] DMSO = dimethyl sulfoxide

[00143] Dppf = 1,1'-bis(diphenylphosphino)ferrocene

[00144] EDCI or DEC = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide

[00145] g = grams

[00146] h = hour

[00147] HetAr = heteroaryl

[00148] HMDS = 1,1,1,3,3,3-hexamethyldisilazane

[00149] HATU = N,N,N',N'-tetramethyl-O-(7-azabenzotriazol-1-yl)uranium

[00150] hexafluorophosphate

[00151] HOBt = 1-hydroxybenzotriazole

[00152] Im = imidazole

[00153] LAH = lithium aluminum hydride

[00154] LDA = lithium diisopropylamide

[00155] LCMS = liquid chromatography mass spectrometry

[00156] LG = leaving group

[00157] min = minute

[00158] mg = milligrams

[00159] mL = milliliters

[00160] mmol = millimoles

[00161] MeOH: methanol

[00162] MS = mass spectrometry

[00163] NBS = N-bromosuccimide

[00164] NMR = nuclear magnetic resonance spectroscopy

[00165] PG = protecting group

[00166] Pyr = pyridine

[00167] *rac* or (±) = racemic mixture or enantiomers

[00168] RT or rt = room temperature (ambient, about 25 °C)

[00169] sat = saturated

[00170] SM = starting material

[00171] TBSCl = t-butyldimethylsilyl chloride

[00172] TBS = t-butyldimethyl silyl

[00173] TEA = triethylamine (Et_3N)

[00174] TFA = trifluoroacetic acid

[00175] TFAA = trifluoroacetic anhydride

[00176] THF = tetrahydrofuran

[00177] TLC = thin layer chromatography

[00178] TMS = trimethylsilyl

[00179] Tos or Ts = p-toluenesulfonyl (tosyl)

[00180] Tol = toluene

[00181] IBMX = = 3-Isobutyl-1-methylxanthine

[00182] HBSS = Hank's balanced salt solution

[00183] HEPES = 1-[4-(2-Hydroxyethyl)-1-piperazinyl]ethane-2-sulfonic acid

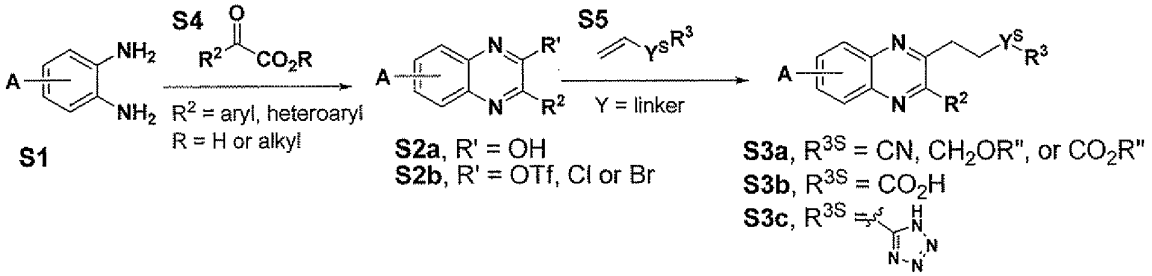
[00184] The compounds of this invention can be prepared through the general approach outlined in the following schemes. These schemes are being provided to illustrate the present invention. To assist one in this endeavor, the ordinary practitioner would have full knowledge of literature sources such as *Chemical Abstracts; Beilstein, Protective Groups in Organic Synthesis 2nd Edition T.W. Greene, P.G.M. Wuts 1991, Wiley and Sons; Comprehensive Organic Transformations, Advanced Organic Chemistry* etc.

[00185] Scheme 1 shows an approach in which an aminoaniline **S1** is treated with a substituted oxoacetic acid (R^2 = aryl or heteroaryl; R = H; preactivated by a chloroformate, oxalyl chloride or the like) or oxoacetic ester **S4** (R^2 = aryl or heteroaryl; R = alkyl) to provide the quinoxaline **S2a** (R' = OH). This intermediate is then converted to **S2b** (wherein R' = OTf, Cl, Br or other suitable group by treatment with $POCl_3$, $SOCl_2$, P_2O_5/Bu_4NCl, P_2O_5/Bu_4NBr, Tf_2O, $PhNTf_2$ etc.) and coupled with **S5** (which has been preactivated via a hydroboration reaction with 9-BBN or similar boron-based reagent; Y^S = a suitable alkyl, cycloalkyl, aryl or heterocylic linker; R^{3S} = ester or other appropriate group, such a as nitrile or alcohol) to provide **S3a**. Final conversion to **S3b** is then achieved by one of many appropriate synthetic methods known to practitioners in the art (such as acid- or base-hydrolysis when R^{3S} = ester, oxidation when R^{3S} = alcohol, hydrolysis when R^{3S} = nitrile etc.). Additionally, when R^{3S} is a nitrile, conversion to a carbon linked tetrazole may be achieved by reaction with an appropriate azide.

[00186] Left side transformation, in which A is a functional group such as an ester, nitrile, halogen, optionally functionalized alcohol, sulfonic acid or other group, to A = one of the various definitions of R^1, such as amide, ketone, or sulfonamide) occurs by a process known to a practitioner in then art. For example, an activated alcohol or halogen may be carbonylated by a metal catalyzed or metal-facilitated process to provide an ester or acid, which may be further transformed to an amide or ketone. When converting an acid to an amide, an appropriate amine

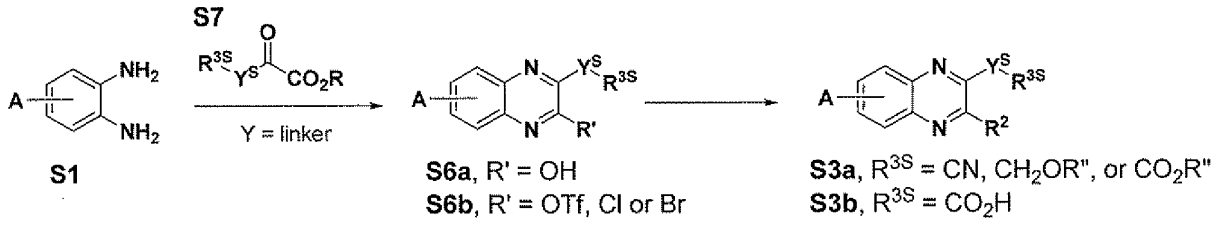
and coupling agent (as EDCI, HOBt, PyBop, HATU etc.) or activation method (oxalyl chloride, thionyl chloride etc.) may be used.

Scheme 1



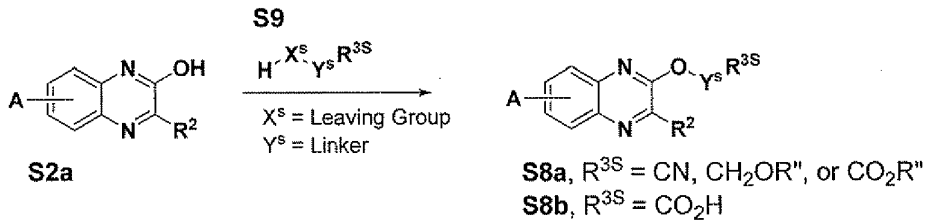
[00187] Scheme 2 shows an approach in which **S1** is treated with an optionally substituted oxoacetic acid or oxoacetic ester **S7** (Y = a suitable alkyl, cycloalkyl, aryl or heterocyclic linker). The resulting product **S6a** is then converted to **S6b** (wherein R' = OTf, Cl, Br or other suitable group) and coupled with an appropriately activated, and optionally substituted, partner by a metal catalyzed or metal-facilitated process (such as Stille coupling, Suzuki coupling, Negishi coupling) to provide **S3a**.

Scheme 2



[00188] Scheme 3 shows an approach in which **S2a** is reacted with **S9** (in which X^S is a leaving group, such as halogen, activated alcohol etc.) and appropriate base (such as LiOtBu, Cs_2CO_3 DIPEA, LDA, NaH, or other appropriate reagent) to provide **S8a**.

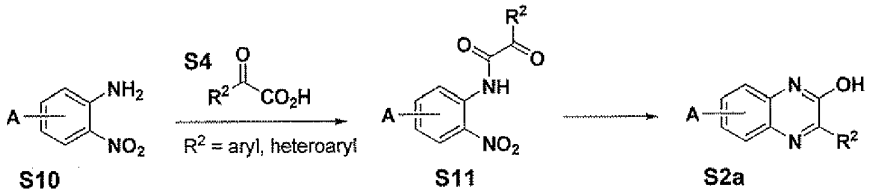
Scheme 3



[00189] Scheme 4 shows an alternative sequence in which the quinoxaline synthesis occurs in a stepwise fashion. The nitroaniline **S10** is reacted with **S4** (R^2 = aryl or heteroaryl; preactivated by a chloroformate, oxalyl chloride or the like or the like). The resulting ketamide

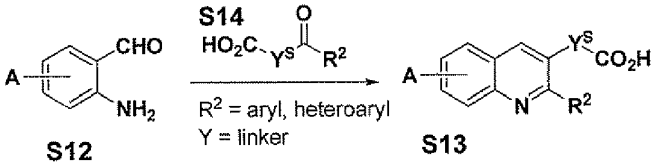
S11 is subjected to nitro reduction (by hydrogenation, or treatment with $SnCl_2$, or other method) and concomitant cyclization to provide **S2a**.

Scheme 4



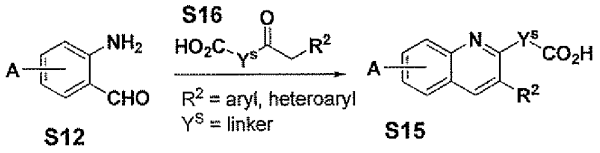
[00190] Scheme 5 shows an approach in which a substituted aminobenzaldehyde **S12** is subjected to a Friedlander quinoline synthesis with ketone **S14** (in which R^2 is aryl or heteroaryl and Y is a linker) and hydroxide base to provide **S13**.

Scheme 5



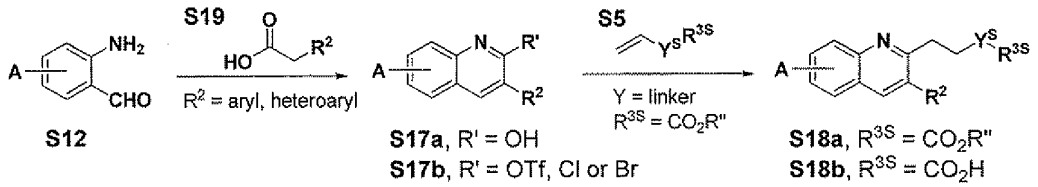
[00191] Scheme 6 shows an approach in which a substituted aminobenzaldehyde **S12** is treated with the ketone **S16** (in which R^2 is aryl or heteroaryl and Y^S is an alkyl linker) and hydroxide base to provide **S15**.

Scheme 6



[00192] Scheme 7 shows an approach in which a substituted aminobenzaldehyde **S12** is treated with the substituted acetic acid **S19** (in which R^2 is aryl or heteroaryl; activated with acetic anhydride or the like) to provide **S17a** (R' = OH). This intermediate is then converted to **S17b** (wherein R' = OTf, Cl, Br), coupled with **S5** (Y^S = a suitable linker; R^{3S} = ester) and hydrolyzed to provide the acid **S18** as described for Scheme 1.

Scheme 7

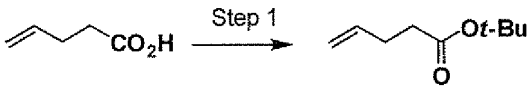


[00193] The starting materials (such as **S1**, **S4**, **S5**, **S7**, **S9**, **S10**, **S12**, **S14**, **S16**, and **S19**) and reagents used in preparing compounds described are either available from commercial suppliers such as Aldrich Chemical Co. (Wisconsin, USA) and Acros Organics Co. (New Jersey, USA) or were prepared by literature methods known to those skilled in the art.

[00194] Compounds, such as those described by formulae **S3b**, **S3c**, **S8b**, **S13**, **S15**, and **S18b**, can be prepared by the general methods outlined above. Exemplary compounds were prepared as described in the examples below or from starting materials known in the art. When unavailable from commercial suppliers, starting materials are synthesized according to methods known in the literature. These examples are being provided to further illustrate the present invention. They are for illustrative purposes only; the scope of the invention is not to be considered limited in any way thereby.

EXAMPLES

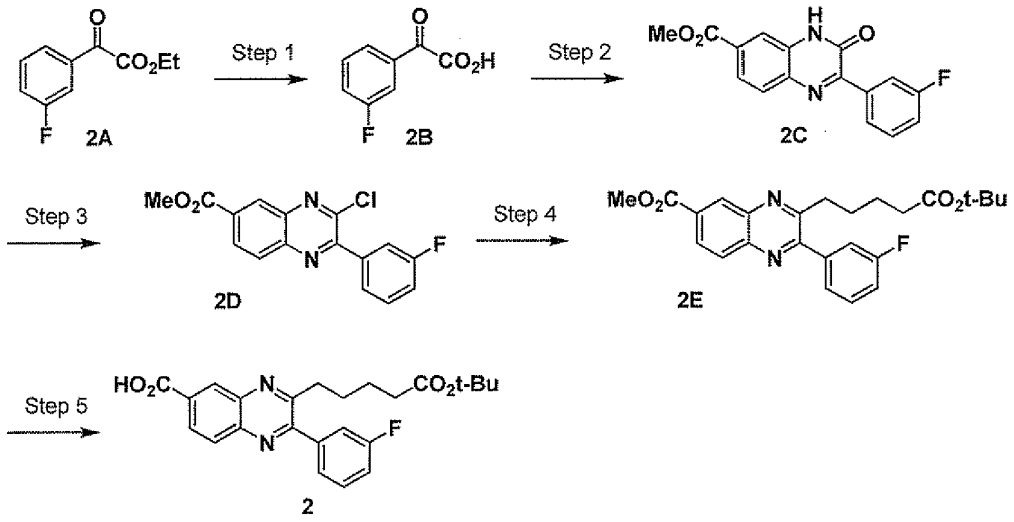
Example 1



1A 1

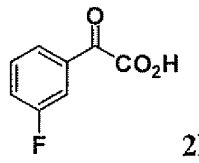
[00195] A solution of pent-4-enoic acid **1A** (8.00 g, 80.0 mmol) in DCM (50 mL) was cooled to 0 °C under nitrogen. TFAA (25 mL, 180 mmol) was added and the reaction was stirred for 40 min at 0 °C. *tert*-Butanol (86 mL, 896 mmol) was added and the reaction was warmed to RT and stirred for 16 h. After this time, the reaction was quenched with saturated aqueous $NaHCO_3$ and diluted with Et_2O. The aqueous layer was separated and extracted with Et_2O. The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography (0% to 20% Et_2O/pentane) to yield **1** (4.47 g, yield = 18%): ^1H NMR (500 MHz, $CDCl_3$) δ 5.92–5.76 (m, 1H), 5.12–4.96 (m, 2H), 2.49–2.43 (m, 1H), 2.42–2.36 (m, 1H), 2.36–2.27 (m, 2H), 1.44 (s, 9H).

Example 2



Step 1

2-(3-Fluorophenyl)-2-oxoacetic Acid.

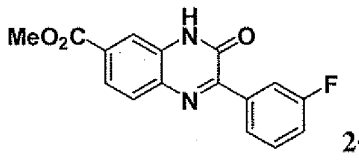


2B

[00196] To a stirred solution of ethyl 2-(3-fluorophenyl)-2-oxoacetate (**2A**) (3.14 g, 16.0 mmol) in THF (120 mL) was added LiOH (1.64 g, 31.9 mmol) in water (40 mL). The reaction was stirred at RT for 1 h. After this time, the reaction was diluted with water and heptane. The aqueous layer was separated, cooled to 0 °C, acidified with 1 N HCl to pH 3, and extracted with EtOAc. The combined organics were washed with water, dried (Na_2SO_4), filtered, and concentrated to yield **2B** (2.32 g, yield = 86%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (br s, 1H), 8.18–8.12 (m, 1H), 8.05–7.96 (m, 1H), 7.60–7.51 (m, 1H), 7.45–7.39 (m, 1H).

Step 2

Methyl 2-(3-Fluorophenyl)-3-oxo-3,4-dihydroquinoxaline-6-carboxylate.



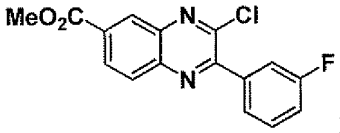
2C

[00197] To a stirred solution of **2B** (1.65 g, 9.81 mmol) and triethylamine (1.37 mL, 9.82 mmol) in THF (3 mL) was added ethyl chloroformate (0.93 mL, 9.76 mmol) at 0 °C under nitrogen. The resulting mixture was stirred at 0 °C for 20 min and a solution of methyl 3,4-diaminobenzoate (1.79 g, 10.8 mmol) in THF (27 mL) was slowly added over 50 min. The

reaction was stirred at 0 °C for 1 h, then warmed to RT and stirred for 3 days. After this time, the reaction was concentrated, and the residue was triturated with Et_2O and water. The solids were collected by vacuum filtration and the filter cake was washed with Et_2O and dried under vacuum to yield **2C** (2.56 g, yield = 87%): ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.82 (s, 1H), 8.26–8.05 (m, 2H), 8.01–7.91 (m, 2H), 7.90–7.80 (m, 1H), 7.64–7.51 (m, 1H), 7.46–7.36 (m, 1H), 3.91 (s, 3H).

Step 3

Methyl 3-Chloro-2-(3-fluorophenyl)quinoxaline-6-carboxylate.

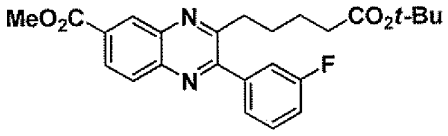


2D

[00198] A suspension of **2C** (2.56 g, 8.58 mmol) and $POCl_3$ (23 mL) was stirred at 110 °C under nitrogen for 24 h. The reaction was cooled to RT and concentrated. The residue was dissolved in DCM and ice was slowly added. The mixture was stirred at 0 °C for 1 h. The aqueous layer was separated and extracted with DCM. The combined organics were dried (Na_2SO_4), filtered, and concentrated to yield **2D** (2.00 g, yield = 74%): MS (M+H) = 317.

Step 4

Methyl 3-(5-*tert*-Butoxy-5-oxopentyl)-2-(3-fluorophenyl)quinoxaline-6-carboxylate.

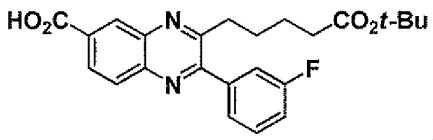


2E

[00199] To a solution of **1** (1.14 g, 7.30 mmol) in anhydrous THF (10 mL) was added 9-BBN (0.5 M in THF, 14.6 mL, 7.30 mmol) at 0 °C under nitrogen. The reaction was stirred at 0 °C for 30 min and warmed to RT for 3 h. **2D** (1.00 g, 3.16 mmol), Pd(dppf)Cl_2•CH_2Cl_2 (310 mg, 0.380 mmol), and K_3PO_4 (1.88 g, 8.86 mmol) were added. The suspension was degassed (3 × vacuum/nitrogen) and heated at 60 °C for 18 h. After this time, the reaction was cooled to RT and filtered. The filtrate was diluted with DCM and water. The aqueous layer was separated and extracted with DCM. The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (10% EtOAc/heptane) to yield **2E** (1.43 g, yield = >99%): MS (M+H) = 439.

Step 5

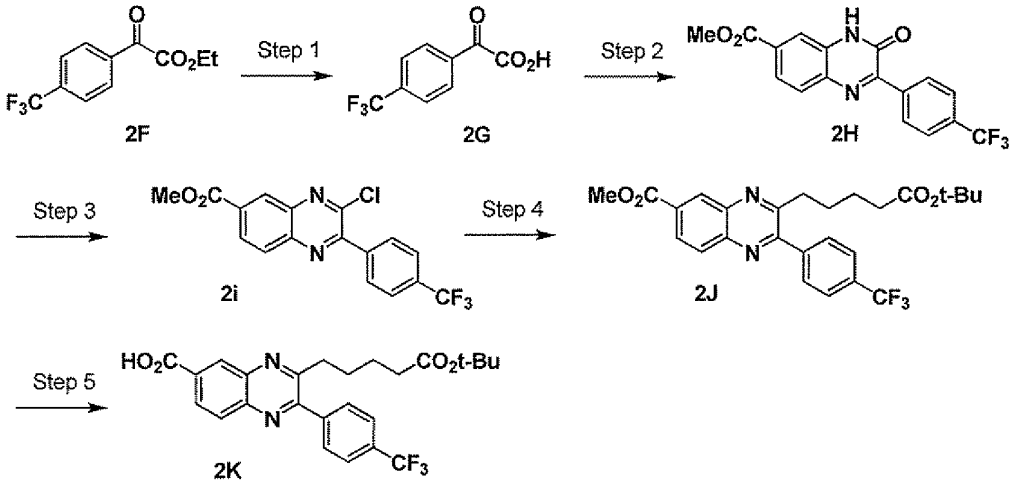
3-(5-*tert*-Butoxy-5-oxopentyl)-2-(3-fluorophenyl)quinoxaline-6-carboxylic Acid



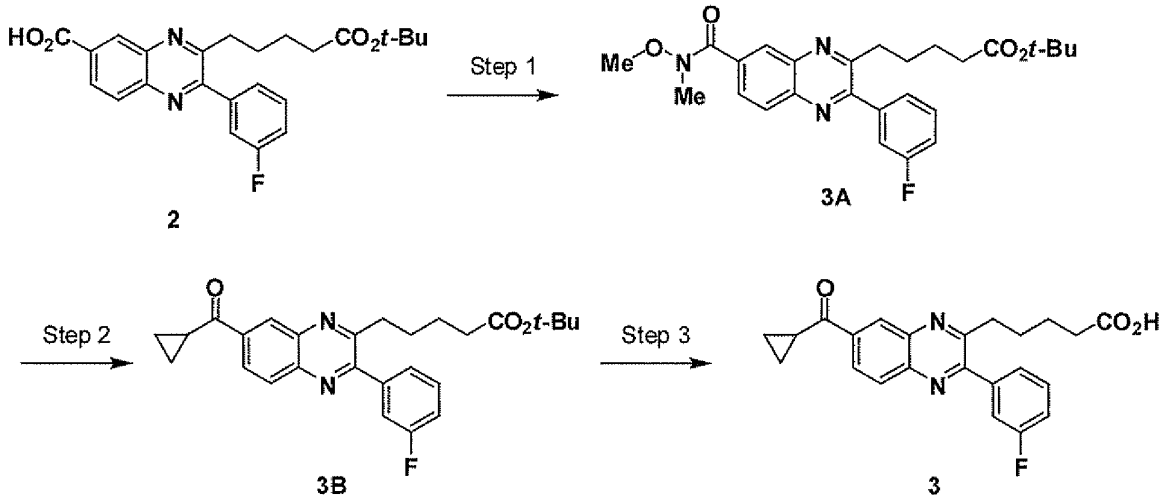
2

[00200] A solution of **2E** (1.43 g, 3.16 mmol) and LiOH (265 mg, 6.32 mmol) in THF (20 mL) and water (10 mL) was stirred at RT for 1 h. After this time, the reaction was diluted with water and extracted with heptane. The aqueous layer was acidified with 1 N HCl, then extracted with DCM. The combined organics were washed with water, dried (Na_2SO_4), filtered, and concentrated to yield **2** (1.13 g, yield = 84%): MS (M+H) = 425.

[00201] In a manner similar to that described above, compound **2F** was treated with LiOH to provide **2G** (^{1}H NMR, 300 MHz, $CDCl_3$ δ 8.48 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.3 Hz, 2H)) and then reacted with methyl 3,4-diaminobenzoate. The resulting 3-oxo-quinoxaline **2H** (MS: M+H = 349) was sequentially reacted with $POCl_3$ (to provide **2i**, MS: M+H = 367), coupled with compound **1** (to provide **2J**, MS: M+H = 489), and hydrolyzed with LiOH to provide **2K** (MS: M+H = 475)

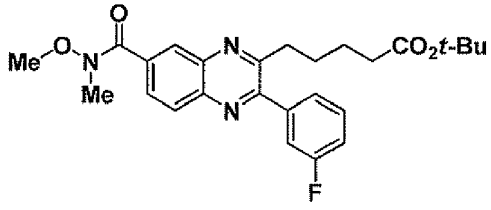


Example 3



Step 1

***tert*-Butyl 5-{3-(3-Fluorophenyl)-7-[methoxy(methyl)carbamoyl]quinoxalin-2-yl}pentanoate.**

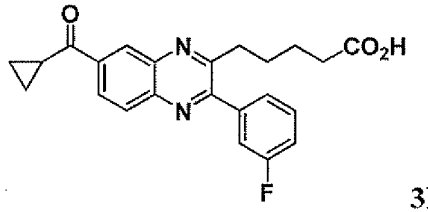


3A

[00202] A solution of **2** (304 mg, 0.716 mmol), *O*,*N*-dimethylhydroxylamine hydrochloride (175 mg, 1.79 mmol), diisopropylethylamine (0.62 mL, 3.56 mmol), and BOP-Cl (547 mg, 2.15 mmol) in anhydrous THF (10 mL) was stirred at RT for 18 h under nitrogen. After this time, the reaction was diluted with EtOAc and washed with water. The organic layer was separated, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (30% to 50% EtOAc/heptane) to yield **3A** (308 mg, yield = 92%): MS (M+H) = 468.

Step 2

***tert*-Butyl 5-[7-(Cyclopropanecarbonyl)-3-(3-fluorophenyl)quinoxalin-2-yl]pentanoate.**

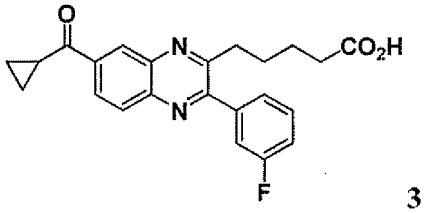


3B

[00203] To a stirred solution of **3A** (150 mg, 0.321 mmol) in anhydrous THF (1 mL) was added cyclopropylmagnesium bromide (0.5 M in THF, 1.93 mL, 0.965 mmol) at –40 °C under nitrogen. After the addition, the reaction was warmed to 10 °C over 1 h. After this time, the reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (30% EtOAc/heptane) to yield **3B** (102 mg, yield = 71%): MS (M+H) = 449.

Step 3

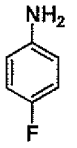
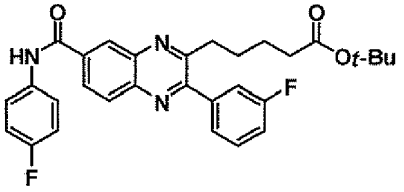
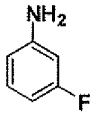
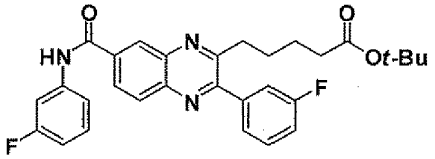
5-[7-(Cyclopropanecarbonyl)-3-(3-fluorophenyl)quinoxalin-2-yl]pentanoic Acid.

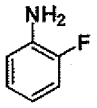
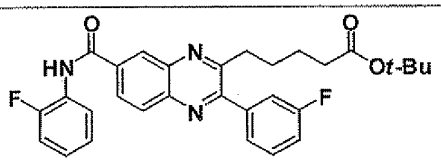


3

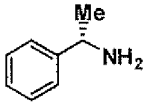
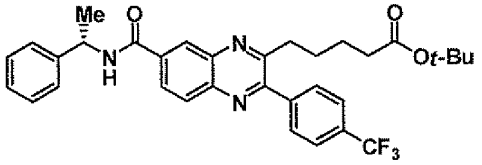
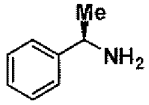
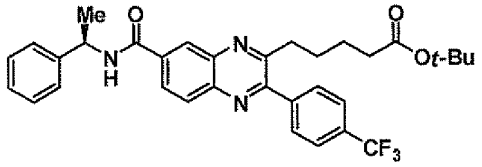
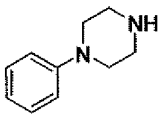
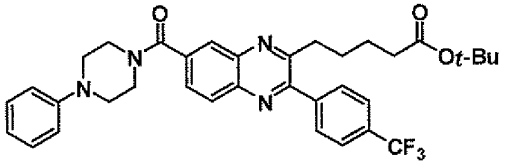
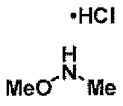
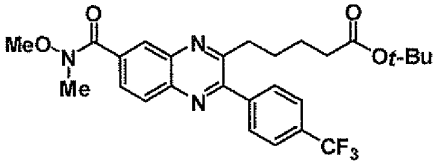
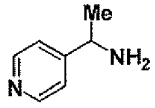
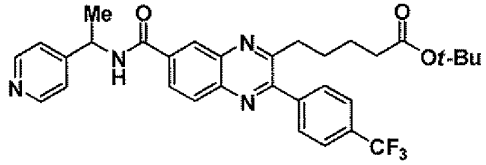
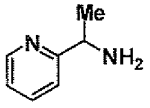
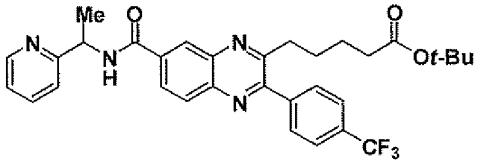
[00204] To a solution of **3B** (102 mg, 0.227 mmol) in DCM (2 mL) was added TFA (1 mL) and the solution stirred for 1.5 h at RT. After this time, the reaction was concentrated and the residue was triturated with a mixture of water (0.1 mL), DCM (3 mL), and heptane (20 mL). The solids were collected by vacuum filtration and the filter cake was dissolved in 2:2:0.2 CH_3CN/H_2O/1 M NH_4OH (2.2 mL), and lyophilized to yield **3** (70 mg, yield = 75%): MS (M+H) = 393.

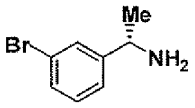
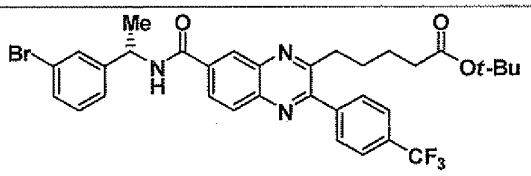
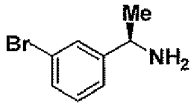
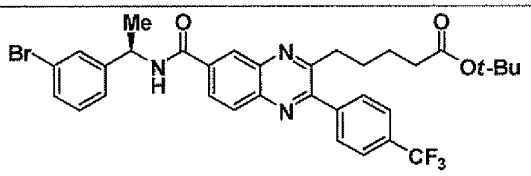
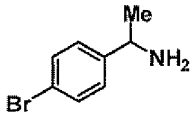
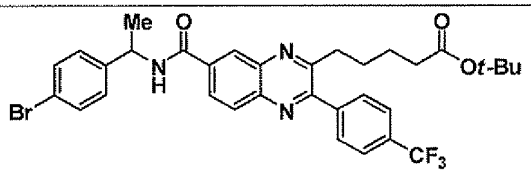
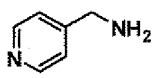
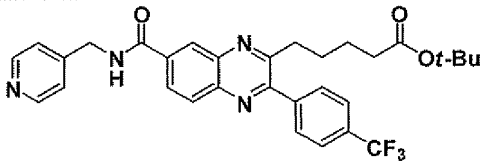
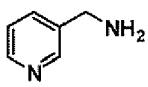
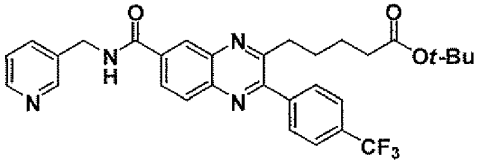
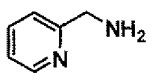
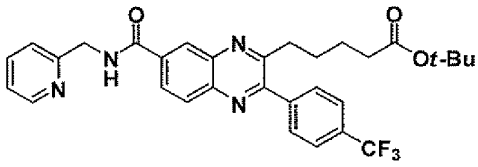
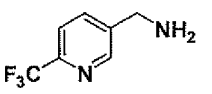
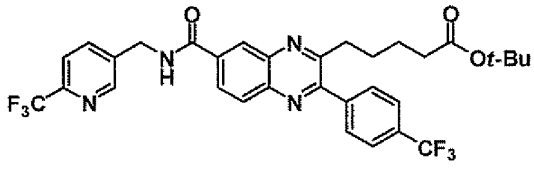
[00205] In a manner similar to that described for 3A above, compound 2 was coupled with the appropriate amine to provide the following compounds:

Compound Number	Coupling Partner	Compound	M+H
3C			518
3D			518

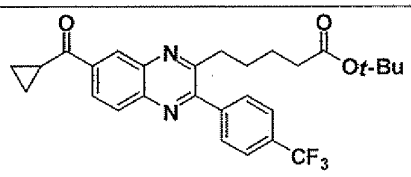
3E			518

[00206] In a manner similar to that described for **3A** above, compound **2K** was coupled with the appropriate amine to provide the following compounds:

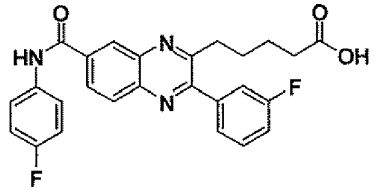
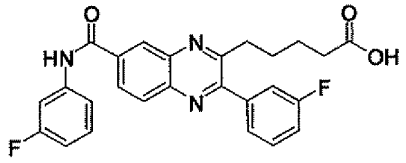
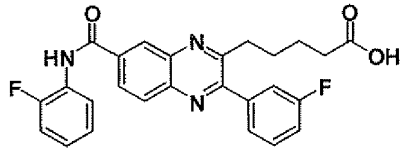
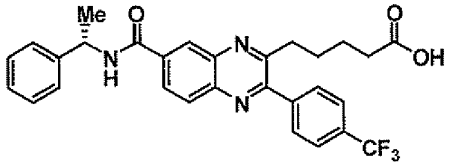
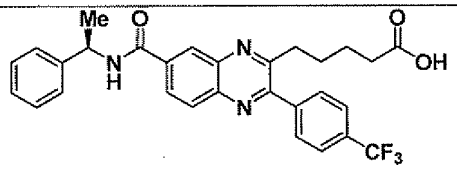
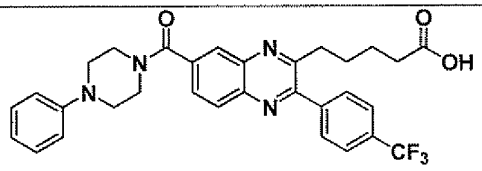
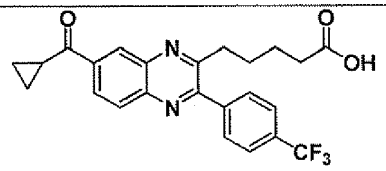
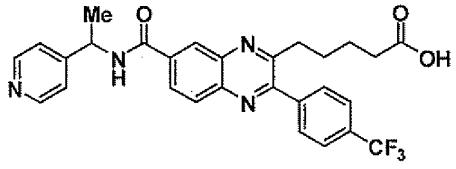
Compound Number	Coupling Partner	Compound	M+H
3F			578
3G			578
3H			619
3i			518
3J			579
3K			579

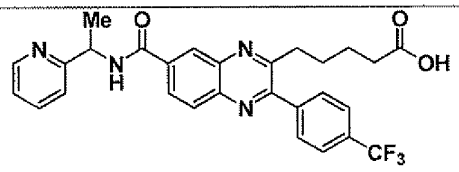
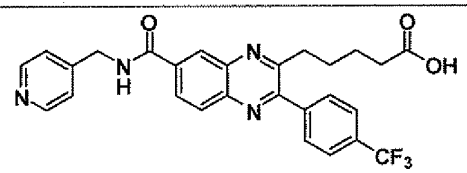
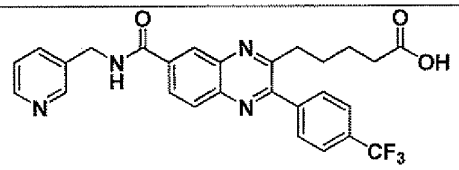
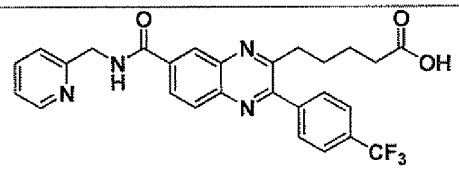
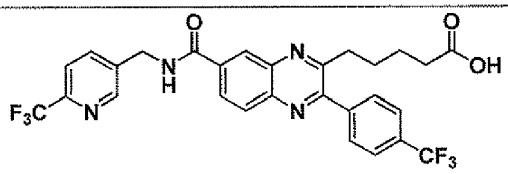
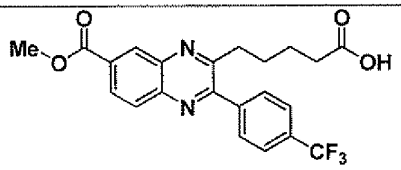
3L			656
3M			656
3N			656
3o			565
3P			565
3Q			565
3R			633

[00207] In a manner similar to that described for **3B** above, compound **3i** was reacted with cyclopropylmagnesium bromide to provide the following compound:

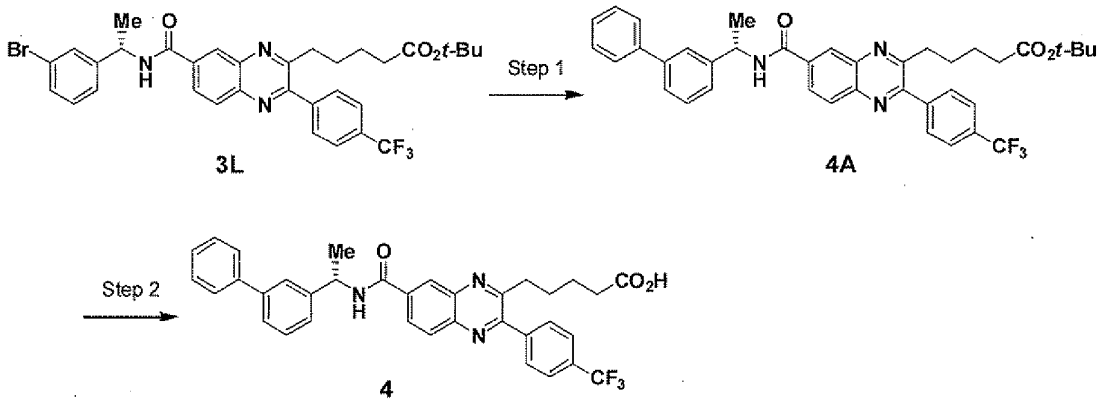
Compound Number	Starting Material	Compound	M+H
3S	3i		499

[00208] In a manner similar to that described above for compound **3**, the following compounds were prepared from the TFA deprotection of the indicated starting materials (SM):

No.	SM	Compound		M+H
3T	**3C**		3-(3-fluorophenyl)-7-[[(4-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
3U	**3D**		3-(3-fluorophenyl)-7-[[(3-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
3V	**3E**		3-(3-fluorophenyl)-7-[[(2-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
3W	**3F**		7-[[(1(S)-phenylethyl)amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	522
3X	**3G**		7-[[(1(R)-phenylethyl)amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	522
3Y	**3H**		7-[(4-phenyl-1-piperazinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	563
3Z	**3S**		7-(cyclopropylcarbonyl)-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	443
3AA	**3J**		7-[[[1-(4-pyridinyl)ethyl]-amino]carbonyl]-3-[4-(trifluoromethyl)-phenyl]-2-quinoxaline-pentanoic acid	523

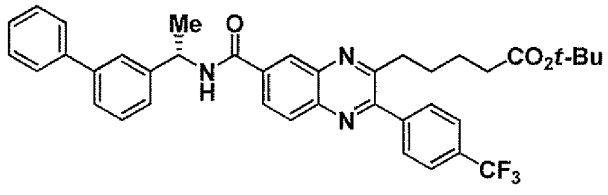
3AB	3K		7-[[[1-(2-pyridinyl)ethyl]-amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	523
3AC	3o		7-[[(4-pyridinylmethyl)-amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	509
3AD	3P		5-(7-(pyridin-3-ylmethylcarbamoyl)-3-(4-(trifluoromethyl)phenyl)quinoxalin-2-yl)pentanoic acid	509
3AE	3Q		7-[[(2-pyridinylmethyl)-amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	509
3AF	3R		3-[4-(trifluoromethyl)phenyl]-7-[[[[6-(trifluoromethyl)-3-pyridinyl]methyl]amino]-carbonyl]-2-quinoxaline-pentanoic acid	577
3AG	2J		7-(methoxycarbonyl)-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	433

Example 4



Step 1

(*S*)-*tert*-Butyl 5-{7-[1-(biphenyl-3-yl)ethylcarbamoyl]-3-[4-(trifluoromethyl)-phenyl]quinoxalin-2-yl}pentanoate.

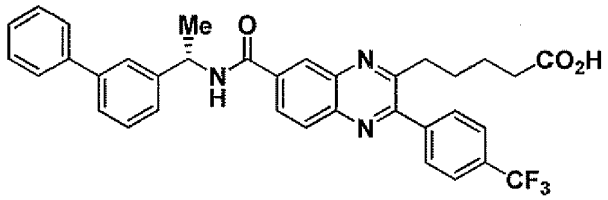


4A

[00209] A stirred solution of **3L** (59 mg, 0.090 mmol), phenylboronic acid (11 mg, 0.090 mmol), $Pd(PPh_3)_4$ (0.46 mg, 0.005 mmol), and sodium carbonate (25 mg, 0.225 mmol) in toluene (2 mL) and water (0.1 mL) was heated at reflux for 16 h. After this time, the reaction was cooled to RT, filtered through a short pad of CELITE, and the filter cake was washed with EtOAc. The filtrate was diluted with EtOAc, washed with water, dried (Na_2SO_4), filtered, and concentrated to yield **4A** (47 mg, yield = 79%): MS (M+H) = 654.

Step 2

(*S*)-5-{7-[1-(biphenyl-3-yl)ethylcarbamoyl]-3-[4-(trifluoromethyl)phenyl]quinoxalin-2-yl}pentanoic Acid.

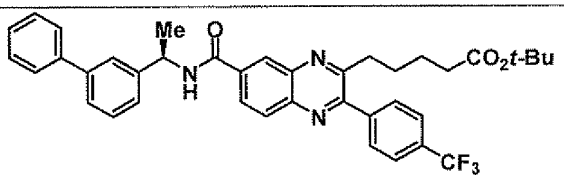
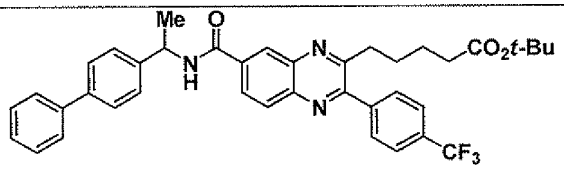


4

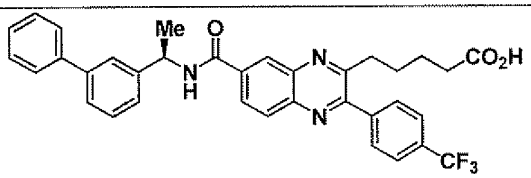
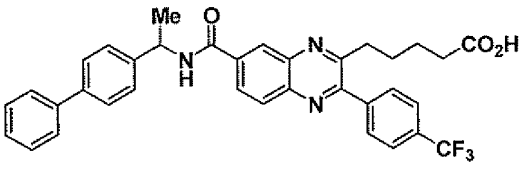
[00210] To a stirred solution of **4A** (47 mg, 0.071 mmol) in DCM (2 mL) was added TFA (1 mL) and the solution stirred for 1.5 h at RT. After this time, the reaction was concentrated and the residue was triturated with a mixture of water (0.1 mL), DCM (3 mL) and heptane (20

mL). The solids collected by vacuum filtration and the filter cake was dissolved in 2:2:0.2 CH_3CN/H_2O/1 M NH_4OH (2.2 mL) and lyophilized to yield **4** (21 mg, yield = 47%): MS (M+H) = 598.

[00211] In a manner similar to that described above for **4A**, the following compounds were prepared:

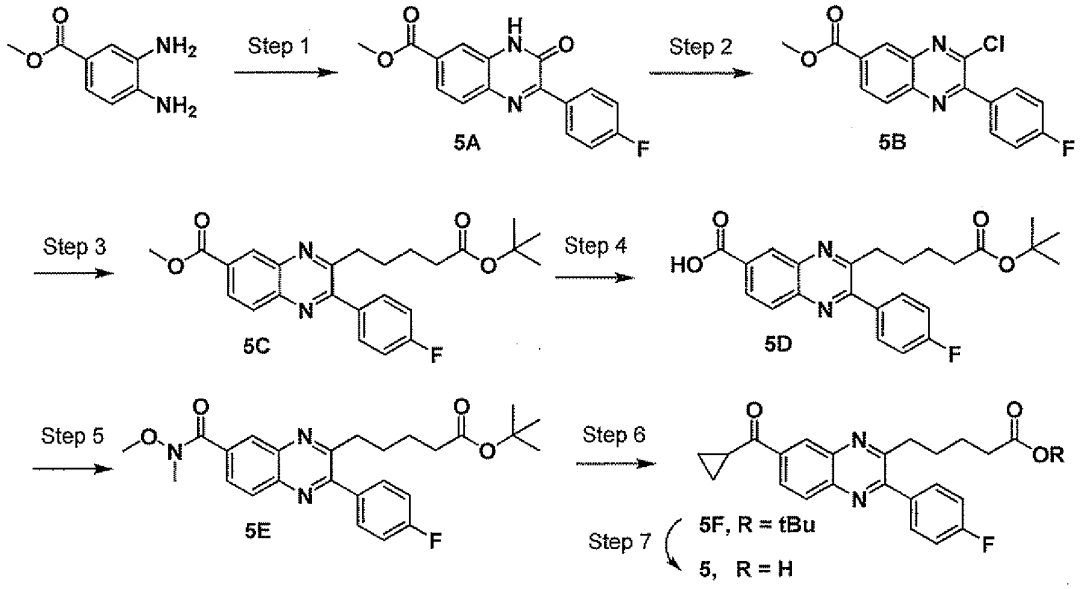
Compound Number	Starting Material	Compound	M+H
4B	**3M**		654
4C	**3N**		654

[00212] In a manner similar to that described above for compound **4**, the following compounds were prepared via a TFA deprotection of the indicated starting materials (SM):

No.	SM	Compound	Name	M+H
4D	**4B**		7-[[[1(R)-[1,1'-biphenyl]-3-ylethyl]amino]carbonyl]-3-[4-(trifluoromethyl)-phenyl]-2-quinoxaline-pentanoic acid	598
4E	**4C**		7-[[(1-[1,1'-biphenyl]-4-ylethyl)amino]carbonyl]-3-[4-(trifluoromethyl)-phenyl]-2-quinoxaline-pentanoic acid	598

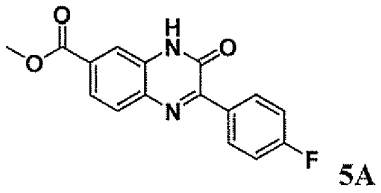
[00213] The racemic mixture **4E** was separated on a semi-preparative Chiralpak IC column (15% ethanol-hexanes-0.1% diethylamine) to provide the pure enantiomers **4F** (Enantiomer 1, > 99% ee, LCMS: M+H = 598) and **4G** (Enantiomer 2, > 99% ee, LCMS: M+H = 598).

Example 5



Step 1

Methyl 2-(4-fluorophenyl)-3-oxo-3,4-dihydroquinoxaline-6-carboxylate.

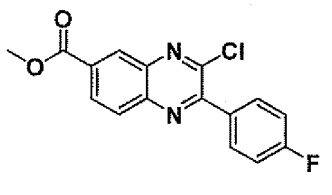


5A

[00214] To a solution of 2-(4-fluorophenyl)-2-oxoacetic acid (507 mg, 3.02 mmol, prepared from ethyl 2-(4-fluorophenyl)-2-oxoacetate as described in Example 2) and triethylamine (0.42 mL, 3.0 mmol) cooled to 0 °C was added ethyl chloroformate (0.29 mL, 3.0 mmol). The resulting mixture was stirred at 0 °C for 20 minutes and methyl 3,4-diaminobenzoate (551 mg, 3.32 mmol) was added slowly over 50 minutes as a solution in THF (10 mL). The reaction was stirred at 0 °C for 1 h and at RT for 72 h. The reaction was concentrated to remove most of the THF. The solid was diluted with Et_2O and water and cooled to 0 °C. The solid was filtered and washed with Et_2O (1 x 20 mL) and DCM (1 x 20 mL) to yield methyl 2-(4-fluorophenyl)-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**5A**, 665 mg; Yield = 73.9%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.77 (s, 1H), 8.50–8.38 (m, 2H), 7.98–7.89 (m, 2H), 7.84 (dd, J = 8.5, 1.8 Hz, 1H), 7.41–7.29 (m, 2H), 3.91 (s, 3H).

Step 2

Methyl 3-chloro-2-(4-fluorophenyl)quinoxaline-6-carboxylate

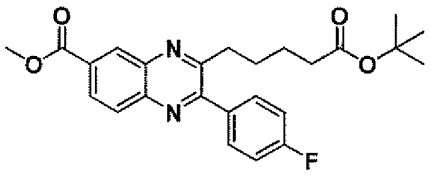


5B

[00215] A suspension of methyl 2-(4-fluorophenyl)-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**5A**, 2.20 g, 7.38 mmol), phosphoryl chloride (20 mL, 200 mmol), and was degassed and stirred at 110 °C for 40 h. The reaction was cooled to RT, some of the excess $POCl_3$ was concentrated, and then cooled to at 0 °C. The mixture was diluted with DCM and ice was added slowly. This mixture was stirred at 0 °C for 1 h. The organic layer was removed and the aqueous phase was extracted with DCM (3x). The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography (0% to 50% EtOAc/hexanes) to yield methyl 3-chloro-2-(4-fluorophenyl)quinoxaline-6-carboxylate (**5B**, 2.1 g; Yield = 90%), MS (M+H) = 317.

Step 3

Methyl 3-(5-tert-butoxy-5-oxopentyl)-2-(4-fluorophenyl)quinoxaline-6-carboxylate.

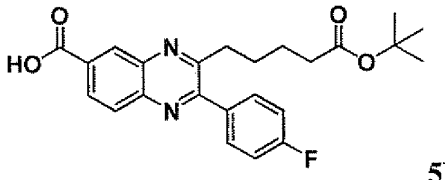


5C

[00216] To a solution of tert-butyl pent-4-enoate (**1**, 1.5 g, 9.8 mmol) in THF (10 mL, 100 mmol) cooled to 0 °C was added 0.5 M of 9-Borabicyclo[3.3.1]nonane in THF (19.6 mL). The reaction was stirred at 0 °C for 30 minutes and at RT for 3 h. To this solution was added methyl 3-chloro-2-(4-fluorophenyl)quinoxaline-6-carboxylate (**5B**, 1.33 g, 4.20 mmol), [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)-complex with dichloromethane (1:1) (0.423 g, 0.518 mmol), and potassium phosphate (2.5 g, 12 mmol). The resulting solution was degassed and stirred at 60 °C for 16 h. The filtrate was diluted with DCM and water. The organic layer was removed and the aqueous phase was extracted with DCM (2x). The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography (0% to 60% EtOAc/hexanes) to yield methyl 3-(5-tert-butoxy-5-oxopentyl)-2-(4-fluorophenyl)quinoxaline-6-carboxylate (**5C**, 1.82 g; Yield = 98%), MS (M+H) = 439.

Step 4

3-(5-tert-butoxy-5-oxopentyl)-2-(4-fluorophenyl)quinoxaline-6-carboxylic acid.

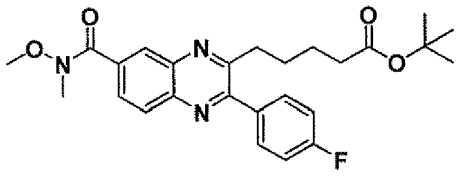


5D

[00217] To a solution of methyl 3-(5-tert-butoxy-5-oxopentyl)-2-(4-fluorophenyl)quinoxaline-6-carboxylate (**5C**, 1.82 g, 4.15 mmol) in THF (30 mL, 400 mmol) and water (15 mL, 830 mmol) was added lithium hydroxide monohydrate (352 mg, 8.39 mmol). The reaction was stirred at RT for 1 h and quenched with 0.1N HCl. The reaction was diluted with EtOAc and the organic layer was removed. The aqueous phase was extracted with EtOAc (3x) and the combined organics were dried (Na_2SO_4), filtered, and concentrated to yield **5D** (1.67 g; Yield = 94.8%, MS: M+H = 425). The material was used without purification.

Step 5

tert-butyl 5-(3-(4-fluorophenyl)-7-(methoxy(methyl)carbamoyl)quinoxalin-2-yl)pentanoate.

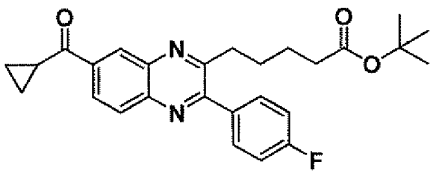


5E

[00218] To a solution of crude 3-(5-tert-butoxy-5-oxopentyl)-2-(4-fluorophenyl)quinoxaline-6-carboxylic acid (**5D**, 1.67 g, 3.93 mmol), N,O-dimethylhydroxylamine hydrochloride (534 mg, 5.47 mmol), and N,N-diisopropylethylamine (2.40 mL, 13.8 mmol) in DCM (40 mL, 600 mmol) was added 1-hydroxybenzotriazole (0.802 g, 5.94 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (1.53 g, 7.98 mmol). The reaction was stirred at RT for 18 h. The reaction was diluted with 0.3N HCl. The organic layer was removed and the aqueous phase was extracted with DCM (3x). The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography (0% to 100% EtOAc/hexanes) to yield tert-butyl 5-(3-(4-fluorophenyl)-7-(methoxy(methyl)carbamoyl)quinoxalin-2-yl)pentanoate (**5E**, 1.50 g; Yield = 81.5%), MS (M+H) = 468.

Step 6

tert-butyl 5-(7-(cyclopropanecarbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoate.

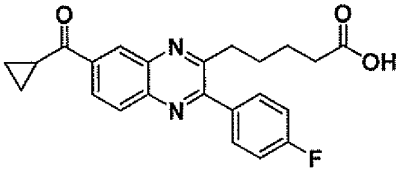


5F

[00219] To a solution of tert-butyl 5-(3-(4-fluorophenyl)-7-(methoxy(methyl)carbamoyl)quinoxalin-2-yl)pentanoate (**5E**, 80 mg, 0.2 mmol) in THF (2 mL, 20 mmol) cooled to -40 °C was added 0.5 M of cyclopropylmagnesium bromide in THF (0.530 mL). The reaction was stirred for 45 minutes gradually warming to 10 °C. The reaction was quenched with dilute HCl and diluted with DCM. The organic layer was removed and the aqueous phase was extracted with DCM (3x). The combined organics were concentrated. The residue was purified by flash chromatography (0% to 70% EtOAc/hexanes) to yield tert-butyl 5-(7-(cyclopropanecarbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoate (**5F**, 58 mg; Yield = 80%), MS (M+H) = 449.

Step 7

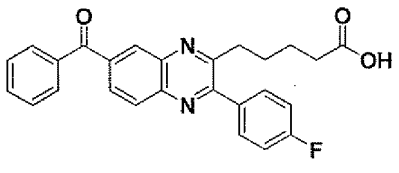
5-(7-(cyclopropanecarbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid.



5

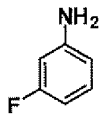
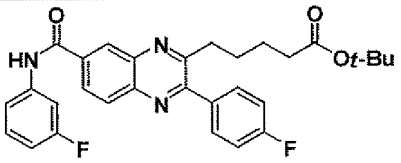
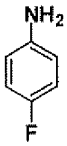
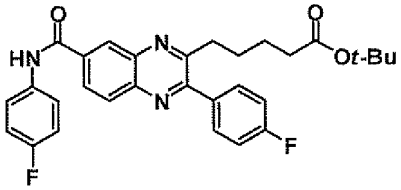
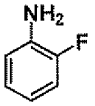
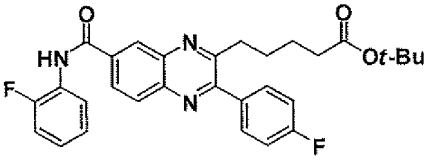
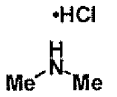
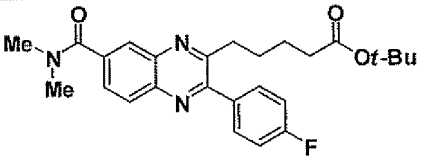
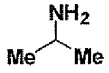
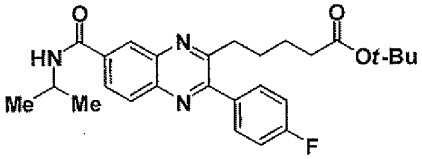
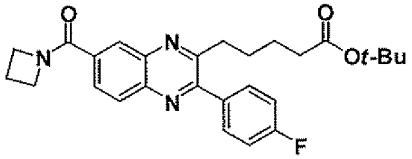
[00220] A solution of tert-butyl 5-(7-(cyclopropanecarbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoate (**5F**, 57 mg, 0.13 mmol) and TFA (0.4 mL, 5 mmol) in DCM (1.6 mL, 25 mmol) was stirred for 2 h. The residue was purified by reverse phase chromatography (10:90 to 100:00 CH_3CN/H_2O (0.1% TFA)) to yield 5-(7-(cyclopropanecarbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid (**5**). MS (M+H) = 393.

[00221] In a manner similar to that described above, the compound **5G** (MS, M+H = 429) was prepared from **5E**:

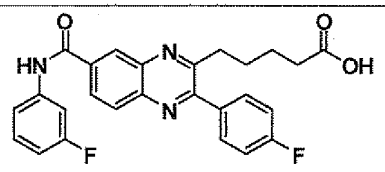
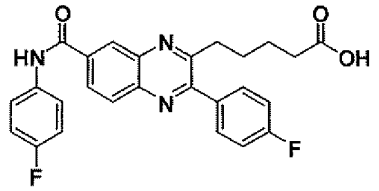
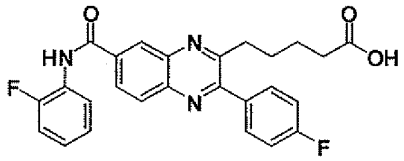
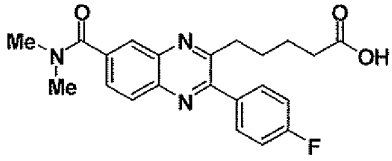
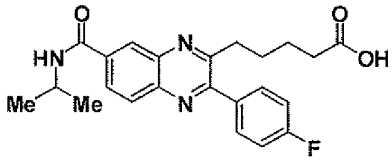
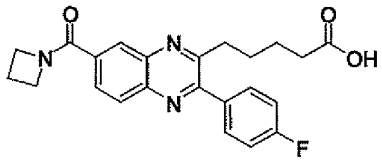


5G

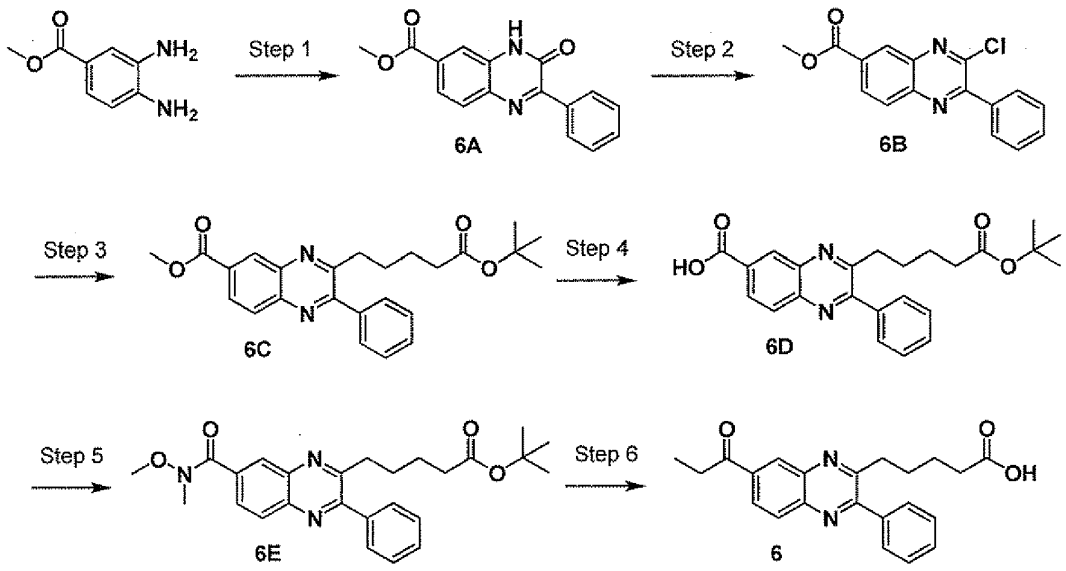
[00222] In a manner similar to that described for **3A** above, compound **5D** was coupled with the appropriate amine to provide the following compounds:

Compound Number	Coupling Partner	Compound	M+H
5H			518
5i			518
5J			518
5K			452
5L			466
5M			464

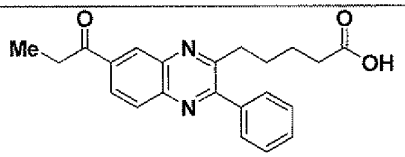
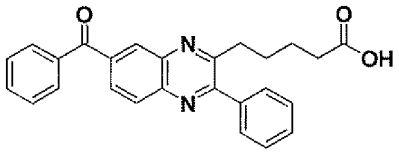
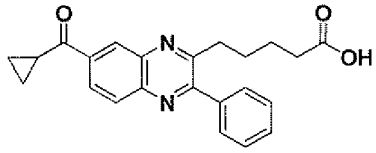
[00223] In a manner similar to that described above, the following compounds were prepared from the TFA deprotection of the indicated starting materials (SM):

No.	SM	Compound	Name	M+H
5N	5H		3-(4-fluorophenyl)-7-[[(3-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
5o	5i		3-(4-fluorophenyl)-7-[[(4-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
5P	5J		3-(4-fluorophenyl)-7-[[(2-fluorophenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	462
5Q	5K		7-[(dimethylamino)carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	396
5R	5L		3-(4-fluorophenyl)-7-[[(1-methylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	410
5S	5M		7-(1-azetidinylcarbonyl)-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	408

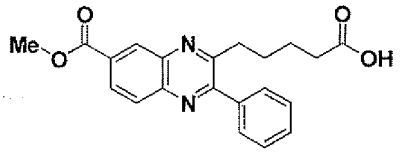
Example 6



[00224] In a manner similar to that described in Example 5, methyl 3,4-diaminobenzoate was reacted with 2-oxo-2-phenylacetic acid. The resulting product **6A** was then advanced to compound to **6E**, which was used to prepare the following compounds:

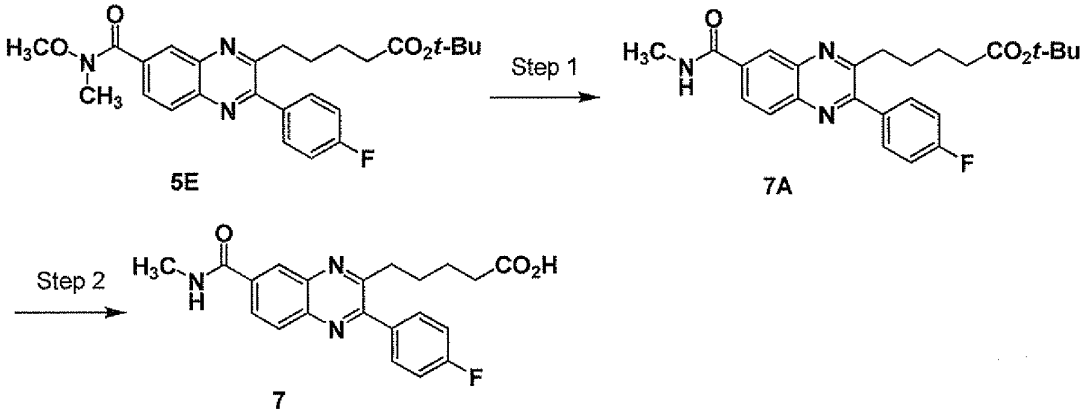
No.	Compound	Name	M+H
6		7-(1-oxopropyl)-3-phenyl-2-quinoxalinepentanoic acid	363
6F		7-benzoyl-3-phenyl-2-quinoxalinepentanoic acid	411
6G		7-(cyclopropylcarbonyl)-3-phenyl-2-quinoxalinepentanoic acid	375

[00225] In a manner similar to that previously described, **6C** was deprotected with TFA to provide 7-(methoxycarbonyl)-3-phenyl-2-quinoxalinepentanoic acid **6H** (MS, M+H = 365).



6H

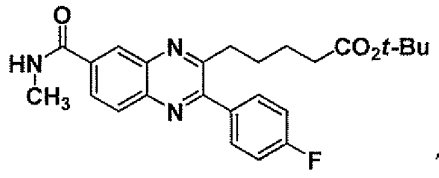
Example 7



5E 7A 7

Step 1

***tert*-Butyl 5-[3-(4-Fluorophenyl)-7-(methylcarbamoyl)quinoxalin-2-yl]pentanoate.**

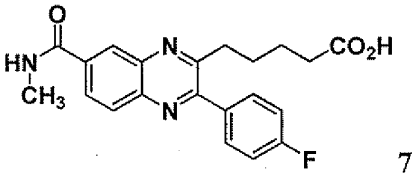


7A

[00226] To a stirred solution of **5E** (154 mg, 0.329 mmol) in anhydrous THF (5 mL) was added *tert*-butylmagnesium chloride (2 M in THF, 0.330 mL, 0.660 mmol) at –20 °C under nitrogen. The reaction mixture was slowly warmed to 10 °C over 40 min and then quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with DCM. The combined extracts were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (50% to 70% EtOAc/heptane) to yield **7A** (58 mg, yield = 40%): MS (M+H) = 438.

Step 2

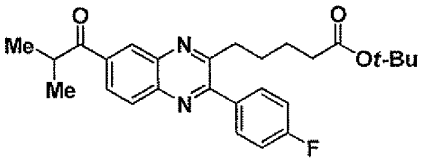
5-[3-(4-Fluorophenyl)-7-(methylcarbamoyl)quinoxalin-2-yl]pentanoic Acid



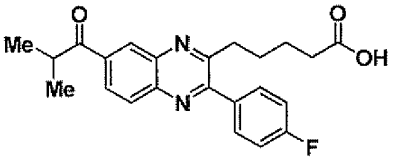
7

[00227] A solution of **7A** (58 mg, 0.133 mmol) and TFA (1 mL) in DCM (2 mL) was stirred at RT for 2 h. After this time, the reaction mixture was concentrated and the resulting residue was purified by column chromatography (2% to 10% MeOH/DCM) and lyophilized from CH_3CN (2 mL), H_2O (1 mL), and 1 M NH_4OH (0.2 mL) to yield 3-(4-fluorophenyl)-7-[(methylamino)carbonyl]-2-quinoxalinepentanoic acid **7** (43 mg, yield = 81%): MS (M+H) = 382.

[00228] In a manner similar to that described above, compound **5E** was reacted with isopropylmagnesium bromide to provide **7B** (MS, M+H = 451) and then deprotected with TFA to provide 3-(4-fluorophenyl)-7-(2-methyl-1-oxopropyl)-2-quinoxalinepentanoic acid **7C** (MS, M+H = 395):

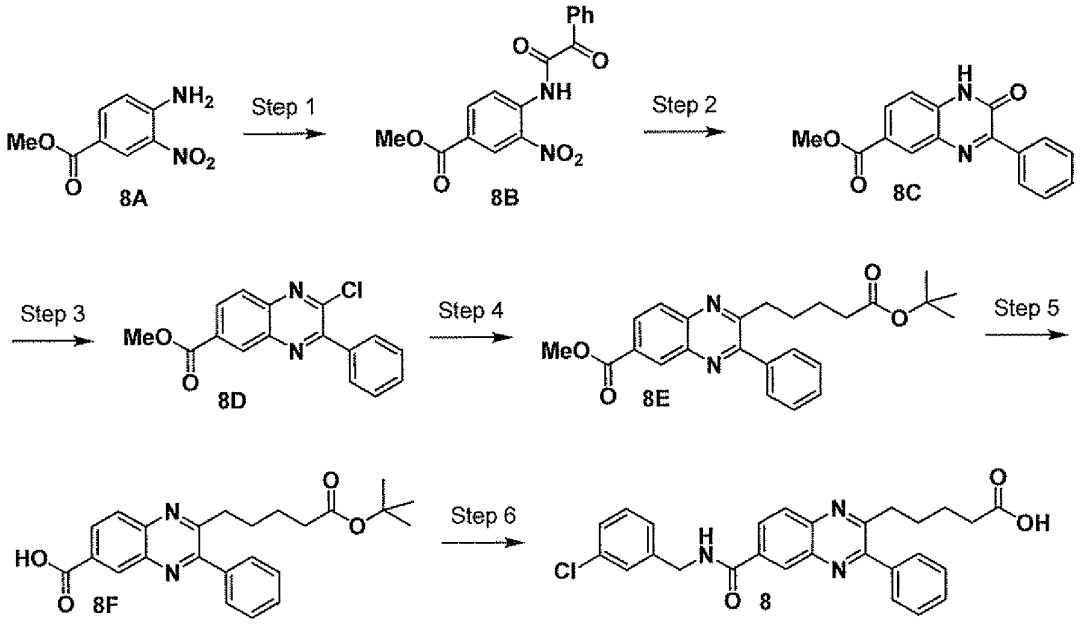


7B



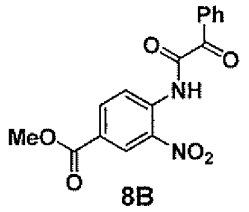
7C

Example 8



Step 1

Methyl 3-Nitro-4-{[oxo(phenyl)acetyl]amino}benzoate

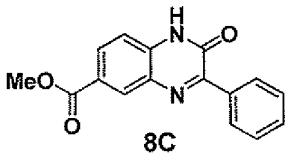


8B

[00229] Following the addition of DMF (0.030 mL, 0.382 mmol) to a chilled solution of benzoylformic acid (1.26 g, 8.41 mmol) in THF (19 mL) at 0 °C, oxalyl chloride (0.74 mL, 8.4 mmol) was added dropwise (to give vigorous bubbling) and the reaction mixture was stirred at 0 °C for 30 min, then allowed to warm to RT over 2 h. The reaction solution was then added dropwise to a chilled solution of methyl 4-amino-3-nitrobenzoate (**8A**, 1.5 g, 7.7 mmol) and triethylamine (2.1 mL, 15 mmol) in THF (57 mL) at 0 °C and allowed to warm to RT overnight. The reaction was partitioned between EtOAc and aqueous $NaHCO_3$ (sat'd). The organics were then washed with brine, dried over Na_2SO_4, and concentrated to give a yellow solid **8B**.

Step 2

Methyl 2-Oxo-3-phenyl-1,2-dihydroquinoxaline-6-carboxylate.

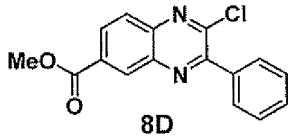


8C

[00230] A solution of the yellow solid **8B** (2.45 g, 7.46 mmol) and Pt/V (0.73 g, 0.037 mmol) in THF (50 mL) and MeOH (50 mL) was stirred under an atmosphere of hydrogen (balloon) at RT for 30 min. The reaction was filtered through CELITE and concentrated to a yellow solid. Purification by chromatography on SiO_2 (0-20% EtOAc/DCM) gave **8C**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.85 (s, 1 H), 8.33 (s, 1 H), 8.29 (d, J = 8.1 Hz, 2 H), 8.06 (d, J = 8.6 Hz, 1 H), 7.48-7.52 (m, 3 H), 7.39 (d, J = 8.6 Hz, 1 H), 3.88 (s, 3 H); MS (M+H) = 281.

Step 3

Methyl 2-Chloro-3-phenylquinoxaline-6-carboxylate.



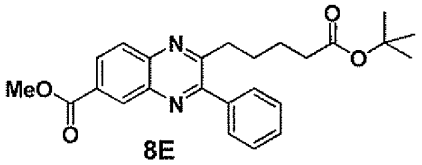
8D

[00231] A suspension of **8C** (300 mg, 1.1 mmol) in $POCl_3$ (3 mL) was stirred overnight at 110 °C and concentrated to dryness. The residue was dissolved in DCM and extracted with 1 N

NaOH, water, dried (Na_2SO_4), and concentrated. Purification by chromatography on SiO_2 (0-50% EtOAc/DCM) gave **8D**. ^1H NMR (500 MHz, $CDCl_3$) δ 8.87 (s, 1 H), 8.39 (d, J = 8.8 Hz, 1 H), 8.11 (d, J = 8.6 Hz, 1 H), 7.87-7.89 (m, 2 H), 7.55-7.56 (m, 3 H), 4.02 (s, 3 H); MS (M+H) = 299.

Step 4

Methyl 2-(5-*tert*-Butoxy-5-oxopentyl)-3-phenylquinoxaline-6-carboxylate.

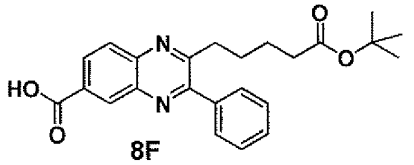


8E

[00232] A chilled solution of *tert*-butyl pent-4-enoate (**1**, 230 mg, 1.47 mmol) in THF (2 mL) at 0 °C was charged with a 0.5 M solution of 9-BBN in THF (3.0 mL, 1.47 mmol) and stirred at 0 °C for 30 min. The reaction was allowed to warm to RT over 2.5 h, then added to a flask containing **8D** (110 mg, 0.368 mmol), $PdCl_2$(dppf)-CH_2Cl_2 (39 mg, 0.048 mmol), and K_3PO_4 (190 mg, 0.88 mmol). The new solution was degassed for 15 min by bubbling nitrogen gas, heated to 60 °C, and stirred overnight. The reaction was diluted with DCM and water and the layers were then separated. The aqueous layer was then extracted with DCM. Organics were combined, dried (Na_2SO_4), and concentrated. Chromatography on SiO_2 (0-50% EtOAc/hexanes) provided **8E**. MS (M+H) = 421.

Step 5

2-(5-*tert*-Butoxy-5-oxopentyl)-3-phenylquinoxaline-6-carboxylic Acid.

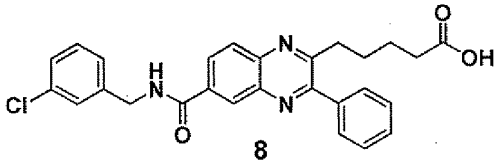


8F

[00233] A solution of the methyl ester **8E** (85 mg, 0.20 mmol) in 1 mL of THF was charged with a 1 M solution of LiOH in water (1 mL). After stirring for 2 hours, the reaction mixture was diluted with EtOAc, extracted with 1 N HCl, water, dried (Na_2SO_4) and concentrated to give **8F**. MS (M+H) = 407.

Step 6

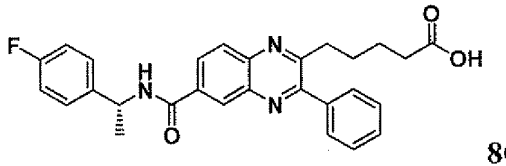
5-(6-{[(3-Chlorobenzyl)oxy]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic Acid.



8

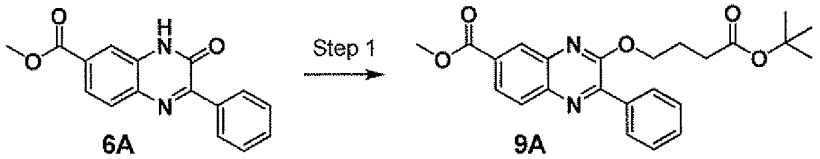
[00234] A solution of the acid **8F** (20 mg, 0.049 mmol), 3-chlorobenzylamine (9 μL, 0.07 mmol), HOBT (11 mg, 0.074 mmol), and EDC (19 mg, 0.098 mmol) in DCM (1 mL) was stirred at RT overnight. The reaction was charged with TFA (160 μL) and stirred for 2 h and concentrated. Reverse phase chromatography (MeCN/water) provided the desired final product **8**. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.44 (t, J = 5.9 Hz, 1 H), 8.62 (s, 1 H), 8.25 (d, J = 8.8 Hz, 1 H), 8.14 (d, J = 8.8 Hz, 1 H), 7.69 (m, 2 H), 7.55 (m, 3 H), 7.30-7.40 (m, 3 H), 4.53 (d, J = 6.1 Hz, 2 H), 3.02 (t, J = 7.4 Hz, 2 H), 2.14 (t, J = 7.5 Hz, 2 H), 1.71 (t, J = 7.5 Hz, 2 H), 1.46 (m, 2 H); MS (M+H) = 474.

[00235] In a manner similar to that described for the synthesis of **8**, compound **8G** (MS, M+H = 472) was prepared by coupling acid **8F** to (R)-1-(4-fluorophenyl)-ethanamine followed by a TFA deprotection

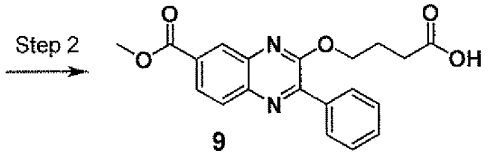


8G

Example 9



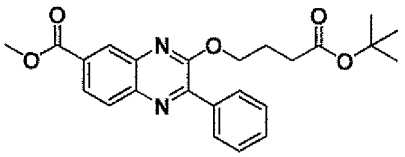
6A 9A



9

Step 1

Methyl 3-(4-*tert*-Butoxy-4-oxobutoxy)-2-phenylquinoxaline-6-carboxylate.

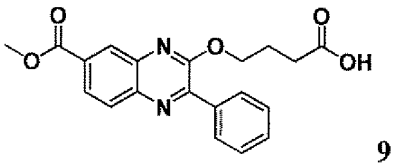


9A

[00236] A suspension of **6A** (300 mg, 1.1 mmol) and Cs_2CO_3 (500 mg, 1.5 mmol) in 5 mL of DMF was treated with *tert*-butyl 4-bromobutanoate (300 mg, 1.3 mmol) and stirred for 3 hours at 100 °C. Diluted with DCM, extracted with 2 N HCl, water, dried, conc. Chromatography on SiO_2 (0-100% EtOAc/hexanes) gave the desired *O*-alkylation product **9A** along with a small amount of undesired *N*-alkylated product. MS (M+H) = 423.

Step 2

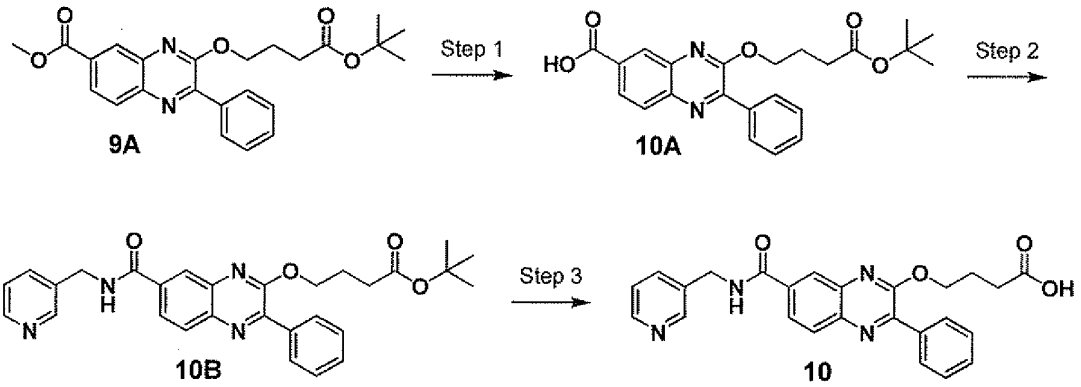
4-{[7-(Methoxycarbonyl)-3-phenylquinoxalin-2-yl]oxy}butanoic Acid.



9

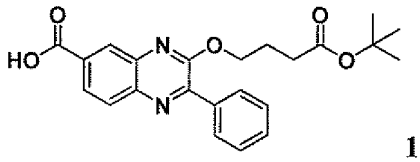
[00237] The *tert*-butyl ester **9A** (100 mg) was dissolved in 1 mL of DCM and 1 mL of TFA, stirred 1 hour and concentrated. Reverse-phase chromatography (MeCN/water) provided the desired title product **9**. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.2 (s, 1 H), 8.36 (s, 1 H), 8.06-8.14 (m, 4 H), 7.54 (m, 3 H), 4.53 (t, J = 6.3 Hz Hz, 2 H), 3.92 (s, 3 H), 2.41 (t, J = 7.3 Hz, 2 H); 2.04 (m, 2 H); MS (M+H) = 367.

Example 10



Step 1

3-(4-*tert*-Butoxy-4-oxobutoxy)-2-phenylquinoxaline-6-carboxylic Acid

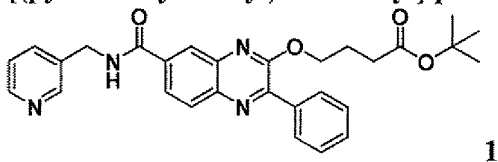


10A

[00238] A solution of the methyl ester **9A** (200 mg, 0.47 mmol) in 3 mL of THF and 1 mL of water was treated with LiOH (20 mg, 0.84 mmol) and stirred overnight. The reaction mixture was diluted with DCM and extracted with 1 N HCl, water, dried (Na_2SO_4), and concentrated to provide the intermediate acid **10A**.

Step 2

***tert*-Butyl 4-({3-Phenyl-7-[(pyridin-3-ylmethyl)carbamoyl]quinoxalin-2-yl}oxy)butanoate.**

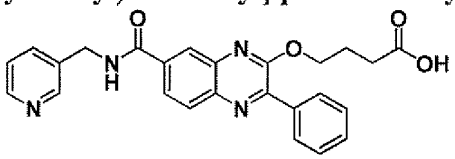


10B

[00239] A solution of the acid **10A** (20 mg, 0.05 mmol), 1-(pyridin-3-yl)methanamine (15 mg, 0.14 mmol), EDC (20 mg, 0.10 mmol) and HOBt (10 mg, 0.065 mmol) in 1 mL of DCM was stirred overnight. The reaction mixture was diluted with EtOAc, washed with 2 N HCl, 2 N NaOH, and water, dried (Na_2SO_4), and concentrated to provide **10B**.

Step 3

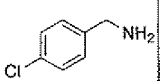
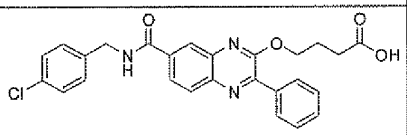
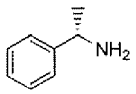
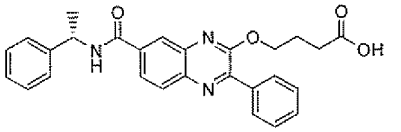
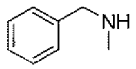
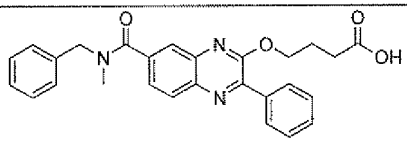
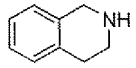
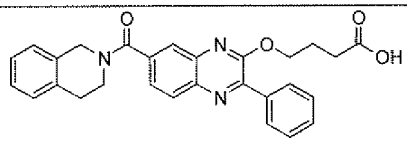
4-({3-Phenyl-7-[(pyridin-3-ylmethyl)carbamoyl]quinoxalin-2-yl}oxy)butanoic Acid.



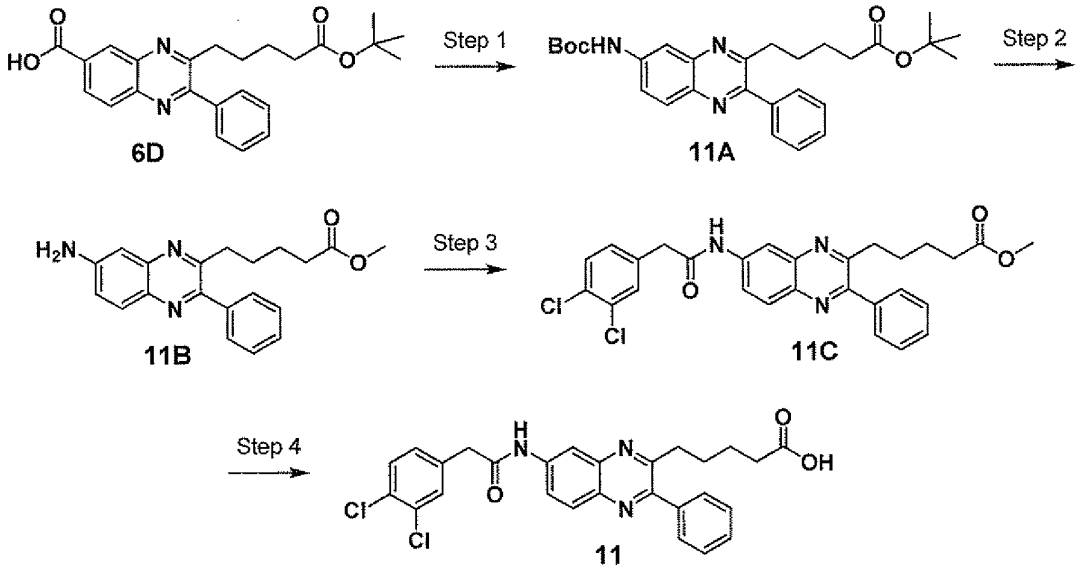
10

[00240] A solution of the intermediate tert-butyl ester **10B** (24 mg) in 1 mL of DCM and 1 mL of TFA was stirred for 1 hour and concentrated. The residue was purified by reverse phase chromatography (MeCN/water) to provide the final acid **10**. MS (M+H) = 443.

[00241] In a manner similar to that described for the synthesis of **10**, the following compounds were prepared by coupling acid **10A** to the appropriate amine reagent followed by a TFA deprotection:

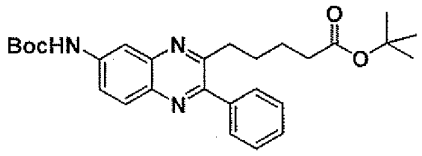
No.	Reagent	Compound Structure	Name	M+H
10C			4-({7-[(4-chlorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}oxy)butanoic acid	476
10D			4-[(3-phenyl-7-{[(1S)-1-phenylethyl]carbamoyl}quinoxalin-2-yl)oxy]butanoic acid	456
10E			4-({7-[benzyl(methyl)carbamoyl]-3-phenylquinoxalin-2-yl}oxy)butanoic acid	456
10F			4-{[7-(3,4-dihydroisoquinolin-2(1H)-ylcarbonyl)-3-phenylquinoxalin-2-yl]oxy}butanoic acid	468

Example 11



Step 1

***tert*-Butyl 5-{7-[(*tert*-Butoxycarbonyl)amino]-3-phenylquinoxalin-2-yl}pentanoate.**

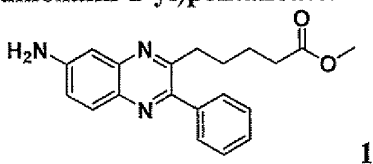


11A

[00242] To a flask containing 3-(5-*tert*-butoxy-5-oxopentyl)-2-phenylquinoxaline-6-carboxylic acid **6D** (0.8 g, 1.97 mmol) was added tBuOH (13 mL,), Et_3N (6.0 eq), and diphenylphosphoryl azide (2.0 eq). The mixture was heated at reflux for 20h. The mixture was cooled to RT, and concentrated to remove most of tBuOH, then diluted with EtOAc and sat. $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$. Concentration and flash chromatography (0-15% EtOAc/CH_2Cl_2) gave **11A**. MS (M+H) = 478.

Step 2

Methyl 5-(7-amino-3-phenylquinoxalin-2-yl)pentanoate.

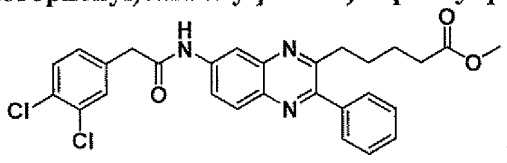


11B

[00243] To a solution *tert*-butyl 5-{7-[(*tert*-butoxycarbonyl)amino]-3-phenylquinoxalin-2-yl}pentanoate **11A** (0.5 g, 1.1 mmol) in DCM (6 mL) at RT was added TFA (2 mL), and the mixture was stirred at RT for 4h. The mixture was concentrated under reduced pressure and the crude residue was taken up in MeOH (0.15M). Then $SOCl_2$ (3 eq) was added at 0 °C and the reaction mixture was stirred at the same temperature for 1.5h. The mixture was then diluted with EtOAc, and quenched slowly with sat. $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organics were washed with H_2O, brine, and dried over $MgSO_4$. Concentration afforded the title compound, which was contaminated by some minor impurities. This material **11B** was used for next step without purification. MS (M+H) = 336.

Step 3

Methyl 5-(7-{[(3,4-Dichlorophenyl)carbonyl]amino}-3-phenylquinoxalin-2-yl) pentanoate.



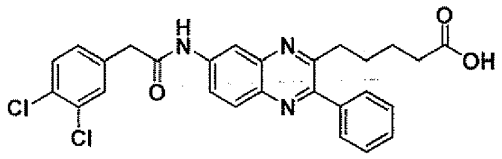
11C

[00244] To a solution of methyl 5-(7-amino-3-phenylquinoxalin-2-yl)pentanoate **11B** (50 mg, 0.15 mmol) in CH_2Cl_2 (2 mL) was added 3,4-dichlorophenylacetic acid (1.0 eq), Hunig's Base (3.0 eq), HOBt (1.2 eq), and EDC (1.4 eq). The mixture was stirred at ambient temperature

overnight, and purified without workup by flash chromatography to afford **11C**. MS (M+H) = 522.

Step 4

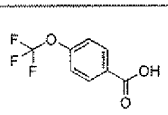
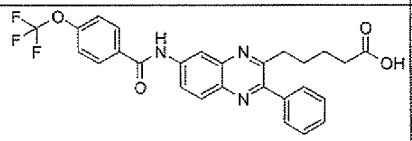
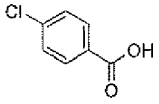
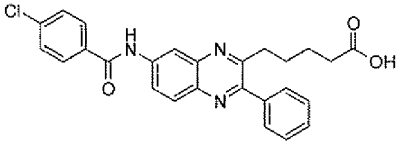
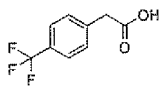
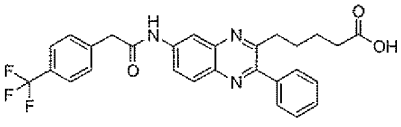
5-(7-{[(3,4-Dichlorophenyl)carbonyl]amino}-3-phenylquinoxalin-2-yl)pentanoic Acid



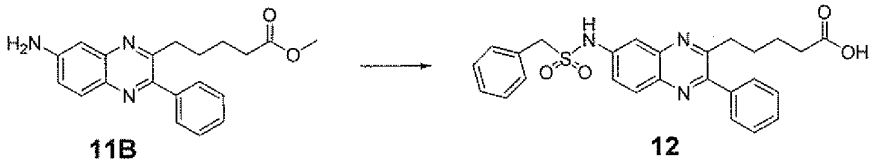
11

[00245] To a solution of methyl 5-(7-{[(3,4-dichlorophenyl)carbonyl]amino}-3-phenylquinoxalin-2-yl)pentanoate **11C** (68 mg, 0.13 mmol) in a mixture of THF (1.5 mL) and MeOH (0.7 mL) was added 1N NaOH (3 eq). The mixture was stirred at RT for 4h, and then acidified with 1N HCl. The mixture was purified by reverse chromatography (MeCN/water) to provide the desired acid **11**. ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.0 (brs, 1 H), 10.72 (s, 1H), 8.52 (s, 1H), 8.03 (d, J = 9.0 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.62-7.70 (m, 4H), 7.52-7.60 (m, 3H), 7.40 (d, J= 8.4Hz, 1H), 3.85 (s, 2H), 2.99 (t, J = 7.2 Hz, 2H), 2.17 (t, J = 7.2 Hz, 2H), 1.69-1.74 (m, 2H), 1.45-1.51 (m, 2H). MS (M+H) = 508.

[00246] In a manner similar to that described for the synthesis of **11**, the following compounds were prepared by coupling aniline **11B** to the appropriate acid reagent followed by ester hydrolysis:

No.	Reagent	Compound Structure	Name	M+H
11D			5-[3-phenyl-7-({[4-(trifluoro-methoxy)phenyl]carbonyl-amino)quinoxalin-2-yl]-pentanoic acid	510
11E			5-(7-{[(4-chlorophenyl)-carbonyl]amino}-3-phenyl-quinoxalin-2-yl)pentanoic acid	460
11F			5-[3-phenyl-7-({[4-(trifluoromethyl)phenyl]acetyl}amino)quinoxalin-2-yl]pentanoic acid	508

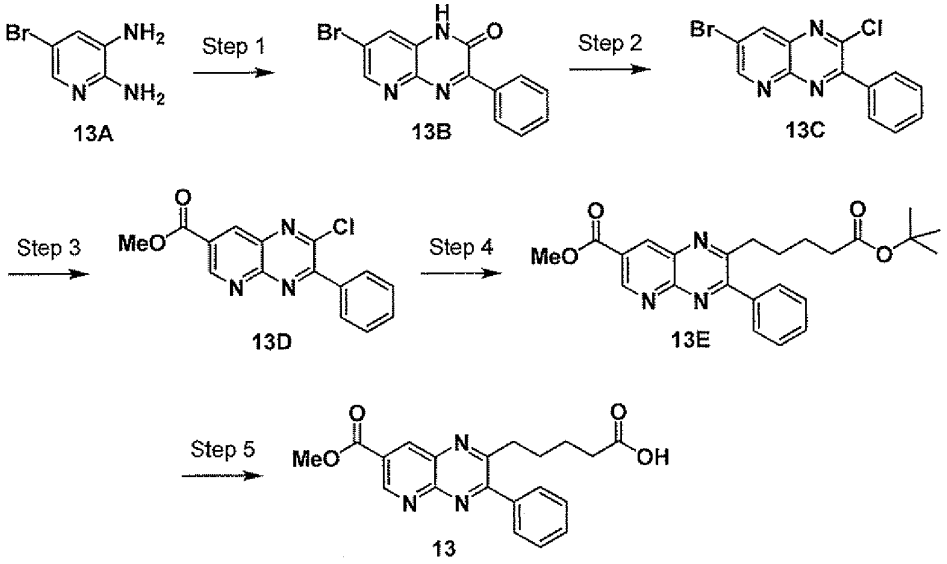
Example 12



11B 12

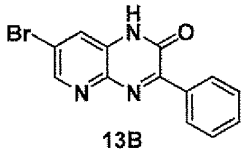
[00247] Triethylamine (0.083 mL, 0.596 mmol) and alpha-toluenesulfonyl chloride (56.8 mg, 0.298 mmol) were added to methyl 5-(7-amino-3-phenylquinoxalin-2-yl)pentanoate (**11B**, 50 mg, 0.149 mmol) stirred in CH_2Cl_2 (1 mL) and the mixture was stirred at RT for 1 h. The reaction was then concentrated. The residue was then diluted with THF and NaOH (0.5 mL, 0.500 mmol) along with MeOH (0.05) were then added. The mixture was stirred at RT for overnight. The next day the reaction was concentrated in vacuo and then 1N HCl (0.5mL) was added before the reaction was concentrated again. The residue was then diluted with MeOH and purified (reversed phase C18 HPLC eluting with 1% TFA acetonitrile/water gradient and then column chromatography on silica gel Biotage SNAP KP-Sil 10g, eluting with EtOAc/hexanes and flushed with 5% MeOH/ethyl acetate) to provide 5-{7-[(benzylsulfonyl)amino]-3-phenylquinoxalin-2-yl}pentanoic Acid (**12**). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, J = 8.9 Hz, 1 H), 7.83 (d, J = 2.4 Hz, 1 H), 7.56 (d, J = 6.9 Hz, 2 H), 7.44-7.50 (m, 3 H), 7.42 (dd, J = 9.0, 2.4 Hz, 1 H), 7.20-7.36 (m, 6 H), 4.44 (s, 2 H), 3.02 (dd, J = 17.3, 9.5 Hz, 2 H), 2.22-2.35 (m, 2 H), 1.72–1.83 (m, 2 H), 1.56–1.67 (m, 2 H). MS (M+H) = 476.

Example 13



Step 1

7-Bromo-3-phenylpyrido[2,3-*b*]pyrazin-2(1*H*)-one

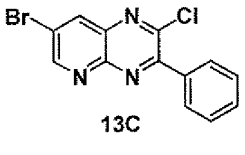


13B

[00248] To a solution of benzoylformic acid (4.0 g, 27 mmol) in CH_2Cl_2 was added catalytic DMF (0.05 eq), followed by the addition of oxalyl chloride (1.0 eq) slowly. The reaction mixture was stirred for 4h, and then concentrated under reduced pressure. The residue was taken up in in THF (20 mL) and the resulting solution was added slowly to a mixture of 5-bromopyridine-2,3-diamine (**13A**, 1.0 eq) and Et_3N (1.0 eq) in THF (100 mL) at 0 °C. The reaction mixture was kept stirring at 0 °C for 30 min, then RT for 2h, then heated at reflux overnight. The reaction mixture was cooled to RT, diluted with aqueous $NaHCO_3$ and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organics were washed with H_2O, brine, dried over $MgSO_4$, and concentrated. To the resultant viscous dark oil was added CH_2Cl_2 (~80 mL), stirred vigorously for 15 min. The mixture was filtered and the brown solid obtained was washed with CH_2Cl_2 to give **13B**, which was contaminated by some minor impurities. This material was used for next step without purification. ^{1}H-NMR (600 MHz, DMSO-d_6) δ 12.7 (s, 1H), 8.58 (s, 1H), 8.28-8.30 (m, 2H), 7.83 (s, 1H), 7.45-7.55 (m, 3H). MS (M+H) = 302.

Step 2

7-Bromo-2-chloro-3-phenylpyrido[2,3-*b*]pyrazine.

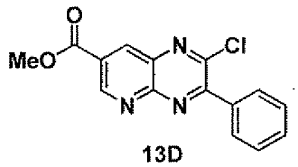


13C

[00249] To a flask containing 7-bromo-3-phenylpyrido[2,3-*b*]pyrazin-2(1*H*)-one (**13B**, 1.2 g, 4.0 mmol) was added phosphorus oxychloride (20 eq), and the mixture was heated at reflux for 2h. The reaction mixture was then cooled to RT, slowly poured a beaker containing aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined organics were washed with H_2O, brine, dried over $MgSO_4$. Concentration and purification by flash chromatography **13C** which was contaminated by some minor impurities. The pure title compound was obtained through recrystalization from EtOAc. MS (M+H) = 320.

Step 3

Methyl 2-Chloro-3-phenylpyrido[2,3-*b*]pyrazine-7-carboxylate.

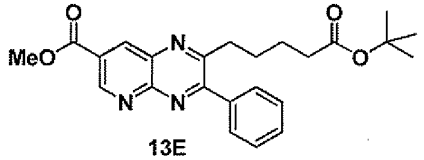


13D

[00250] To a flask containing a solution of 7-bromo-2-chloro-3-phenylpyrido[2,3-*b*]pyrazine (**13C**, 1 g, 3.1 mmol) in dioxane (20 mL) was added Et_3N (10 mL) and MeOH (10 eq). The mixture was degassed by bubbling N_2 for 10 min. Then $Pd(OAc)_2$ (0.1 eq) and xanphos (0.2 eq) were added, and a balloon filled with CO (g) was connected to the reaction flask via three-way adapter. The mixture was vacuumed and back-filled with CO(g) three times from CO(g) balloon. The mixture was then heated at 70°C overnight. The reaction mixture was cooled to RT, diluted with CH_2Cl_2, and aqueous $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organics were washed with brine, dried over $MgSO_4$. Concentration and flash chromatography afforded **13D**. ^{1}H-NMR (600 MHz, $CDCl_3$) δ 9.70 (d, J = 2.4 Hz, 1H), 9.15 (d, J = 2.4 Hz, 1H), 8.01-8.03 (m, 2H), 7.54-7.60 (m, 3H), 4.07 (s, 3H). MS (M+H) = 300.

Step 4

Methyl 2-(5-*tert*-Butoxy-5-oxopentyl)-3-phenylpyrido[2,3-*b*] pyrazine-7-carboxylate.



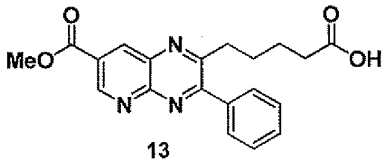
13E

[00251] To a solution of *tert*-butyl pent-4-enoate (0.47 g, 3.0 mmol) in 3 mL THF at 0 °C was added 0.5 M 9-BBN in THF (1.05 eq) dropwise, and the reaction mixture was stirred at 0 °C for 30 min, then RT for 3h.

[00252] To a microwave reaction vessel containing ethyl 2-chloro-3-phenylpyrido[2,3-*b*]pyrazine-7-carboxylate (**13D**, 0.28 g, 0.95 mmol) in THF (0.3 M) was added $K_3PO_4.H_2O$ (2.5 eq), and a solution of alkyl 9-BBN reagent from pot above (1.8 eq). The mixture was degassed by bubbling argon for 10 min. Then $Pd(OAc)_2$ (0.08 eq) and S-Phos (0.16 eq) was added, and the mixture was heated at 70 °C for 1.5h. The reaction mixture was cooled to RT, diluted with aq. $NaHCO_3$, and extracted with EtOAc. The combined organics were washed with brine, dried over $MgSO_4$. Concentration and flash chromatography gave **13E**. MS (M+H) = 422.

Step 5

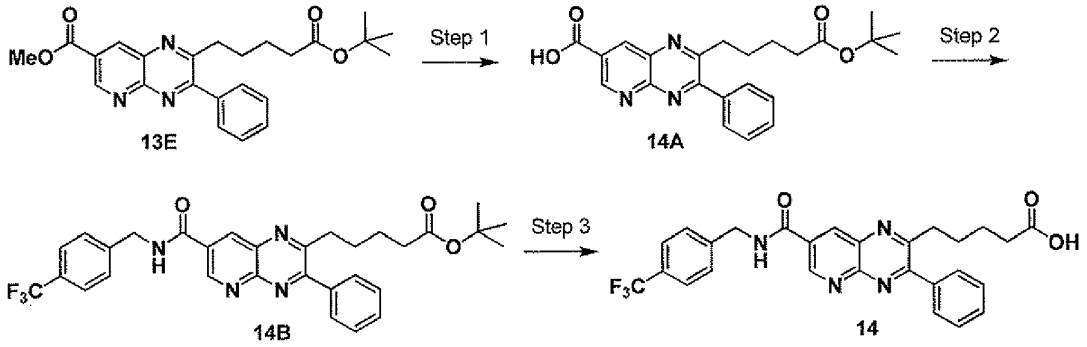
5-[7-(Methoxycarbonyl)-3-phenylpyrido[2,3-*b*]pyrazin-2-yl]pentanoic Acid



13

[00253] To a solution of methyl 2-(5-*tert*-butoxy-5-oxopentyl)-3-phenylpyrido[2,3-*b*] pyrazine-7-carboxylate (**13E**, 35 mg, 0.08 mmol) in CH_2Cl_2 (2.0 mL) was added TFA (0.5 mL). The reaction mixture was stirred at RT for 4h. The mixture was concentrated, and minimal amount of THF was added. The title compound precipitated **13** and was collected through filtration. MS (M+H) = 366.

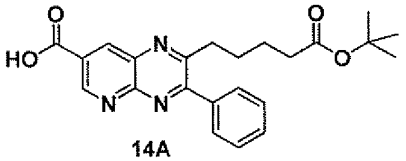
Example 14



13E 14A 14B 14

Step 1

Methyl 2-(5-*tert*-Butoxy-5-oxopentyl)-3-phenylpyrido[2,3-*b*]pyrazine-7-carboxylate.

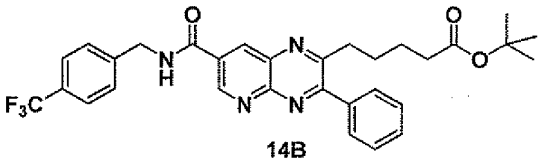


14A

[00254] To a solution of methyl 2-(5-*tert*-butoxy-5-oxopentyl)-3-phenylpyrido[2,3-*b*] pyrazine-7-carboxylate (**13E**, 0.25 g, 0.60 mmol) in a mixture of THF/H_2O (3.0 mL/1.5 mL) was added LiOH (2.0 eq), and the mixture was stirred at RT for 3 h. The mixture was then diluted with EtOAc and H_2O, and acidified with 1N HCl to pH = 3~4. The organic layer was separated, washed with brine, dried over $MgSO_4$. Concentration afforded the desired carboxylic acid **14A**, which was used for next step without purification.

Step 2

***tert*-Butyl 5-(3-Phenyl-7-{[4-(trifluoromethyl)benzyl]carbamoyl}pyrido[2,3-*b*]pyrazi n -2-yl)pentanoate.**

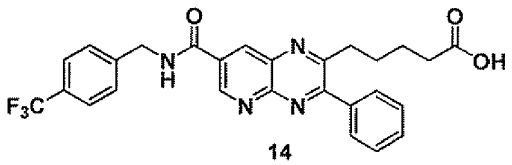


14B

[00255] To a flask containing the carboxylic acid **14A** (40 mg, 0.1 mmol) in DMF (0.05) was added amine (1.5 eq), Hunig's Base (3.0 eq), HOBT (1.7 eq), and EDC (1.3eq). The mixture was stirred at ambient temperature overnight. The mixture was purified by flash chromatography to afford **14B**. ^{1}H-NMR (600 MHz, $CDCl_3$) δ 9.49 (s, 1H), 8.75 (d, J = 2.0 Hz, 1H), 7.46-7.63 (m, 10H), 7.24 (d, J= 2.0 Hz, 1H), 4.74 (d, J = 5.4Hz, 2H), 3.08 (t, J = 7.2 Hz, 2H), 2.15 (t, J = 7.2 Hz, 2H), 1.75-1.80 (m, 2H), 1.54-1.58 (m, 2H). MS (M+H) = 565.

Step 3

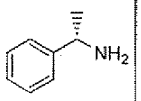
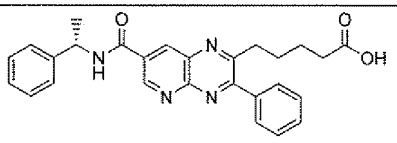
5-(3-Phenyl-7-{[4-(trifluoromethyl)benzyl]carbamoyl}pyrido[2,3-*b*]pyrazin-2-yl)pentanoic Acid

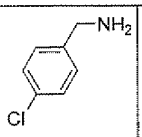
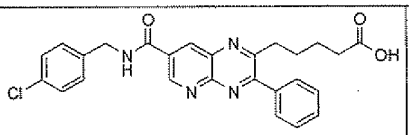
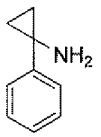
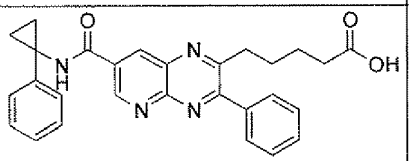
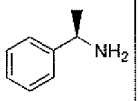
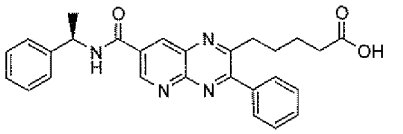
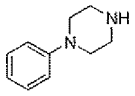
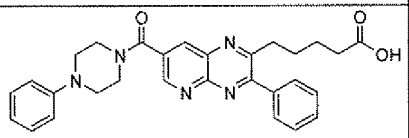
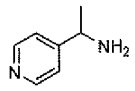
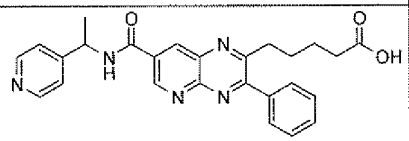


14

[00256] To a solution of [*tert*-butyl 5-(3-phenyl-7-{[4-(trifluoromethyl)benzyl]-carbamoyl}pyrido[2,3-*b*]pyrazin-2-yl)pentanoate (**14B**, 41mg, 0.07 mmol) in DCM (2 mL) at RT was added TFA (0.5 mL), and the mixture was stirred at RT for 3h. The mixture was concentrated, and the title compound **14** precipitated out after the addition of minimal amount of Et_2O, which was collected by filtration. MS (M+H) = 509.

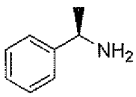
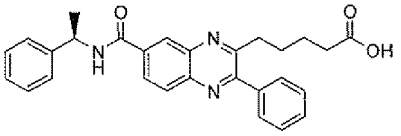
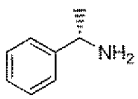
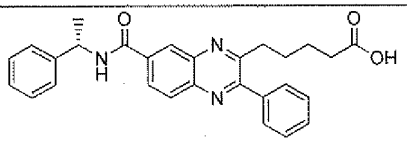
[00257] In a manner similar to that described for the synthesis of **14**, the following compounds were prepared by coupling acid **14A** to the appropriate amine reagent followed by a TFA deprotection:

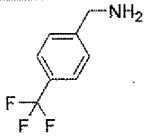
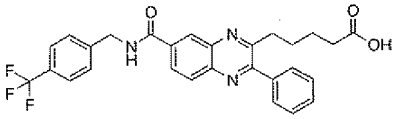
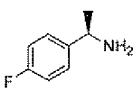
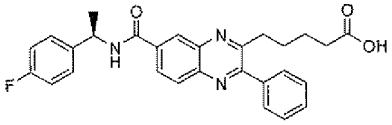
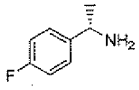
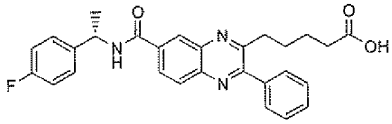
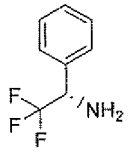
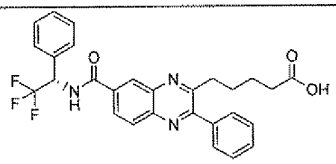
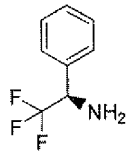
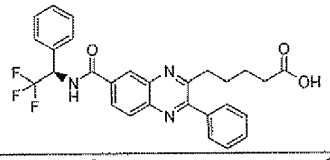
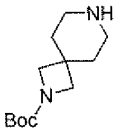
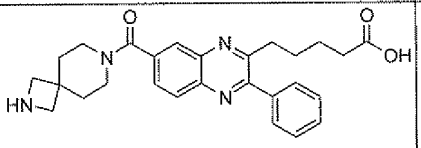
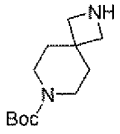
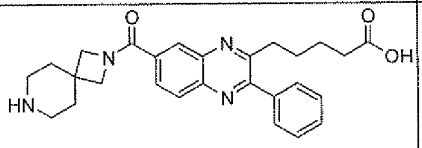
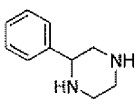
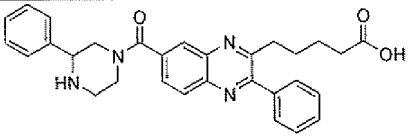
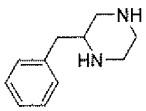
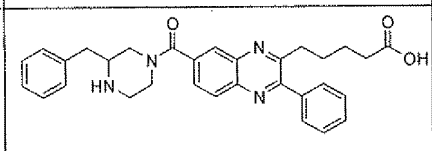
No.	Reagent	Compound Structure	Name	M+H
14C			5-(3-phenyl-7-{[(1S)-1-phenylethyl]carbamoyl}pyrido[2,3-b]pyrazin-2-yl)pentanoic acid	455

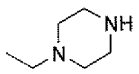
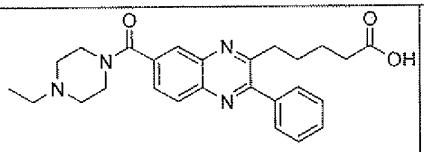
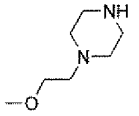
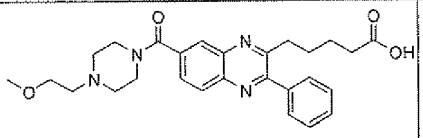
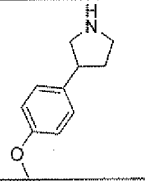
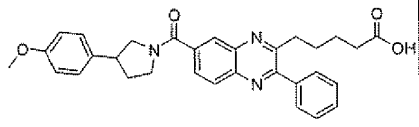
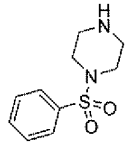
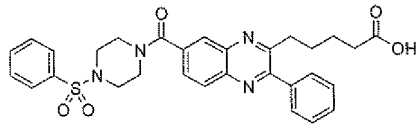
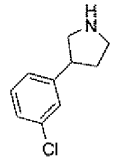
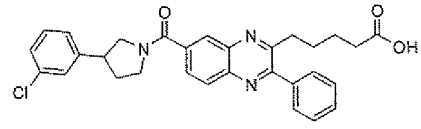
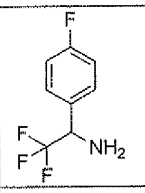
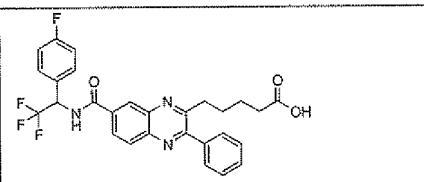
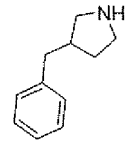
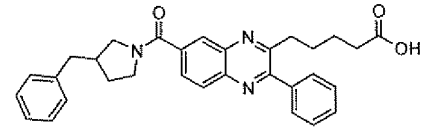
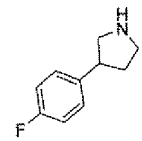
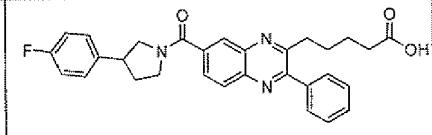
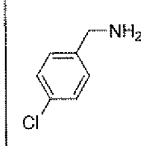
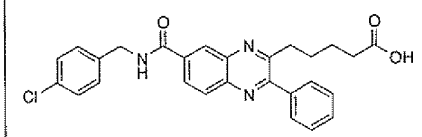
14D			5-{7-[(4-chlorobenzyl)-carbamoyl]-3-phenylpyrido[2,3-b]pyrazin-2-yl}pentanoic acid	475
14E			5-{3-phenyl-7-[(1-phenylcyclopropyl)carbamoyl]-pyrido[2,3-b]pyrazin-2-yl}pentanoic acid	467
14F			5-(3-phenyl-7-{[(1R)-1-phenylethyl]carbamoyl}pyrido[2,3-b]pyrazin-2-yl)pentanoic acid	455
14G			5-{3-phenyl-7-[(4-phenylpiperazin-1-yl)carbonyl]pyrido[2,3-b]pyrazin-2-yl}pentanoic acid	496
14H			5-{3-phenyl-7-[(1-pyridin-4-ylethyl)carbamoyl]pyrido[2,3-b]pyrazin-2-yl}pentanoic acid	456

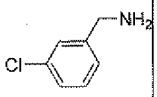
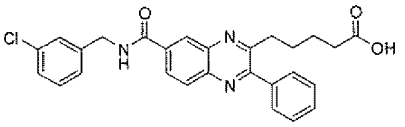
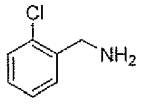
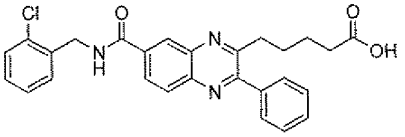
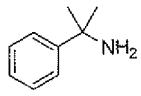
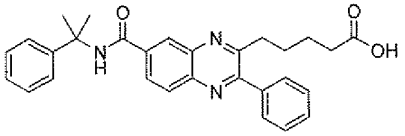
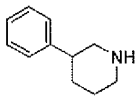
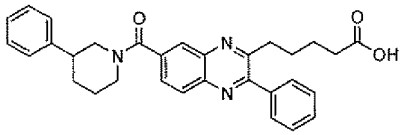
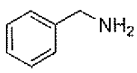
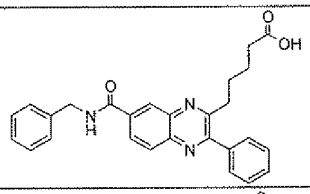
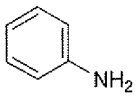
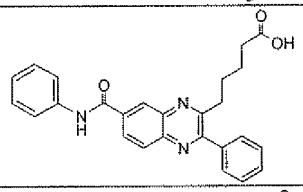
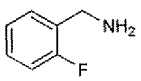
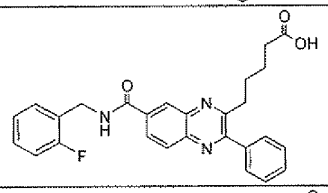
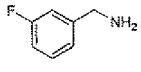
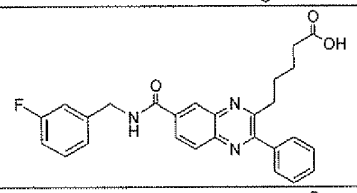
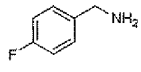
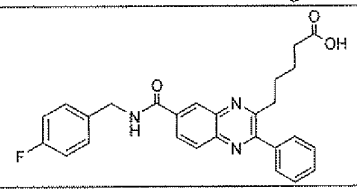
Example 15

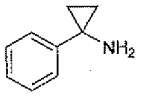
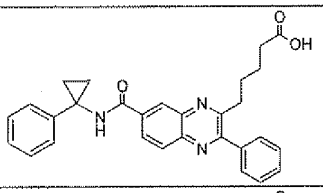
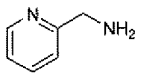
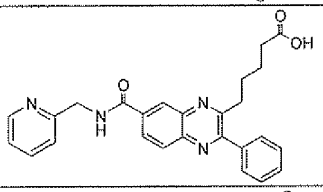
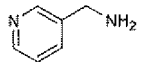
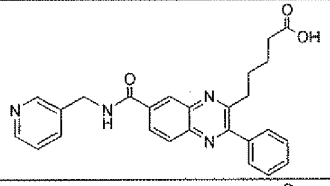
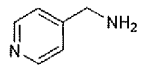
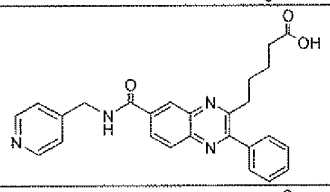
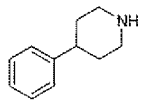
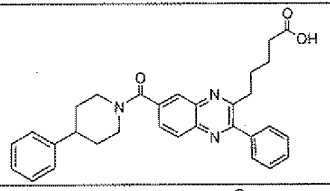
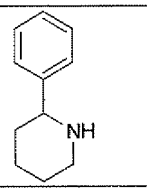
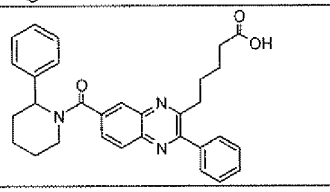
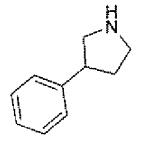
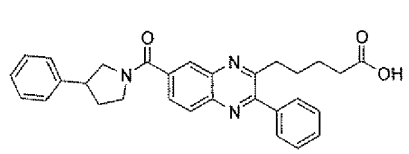
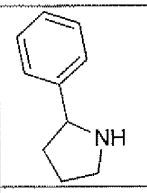
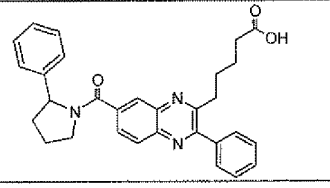
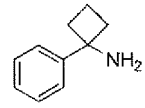
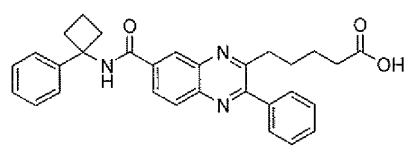
[00258] In a manner similar to that described for the synthesis of **3A**, the following compounds were prepared by coupling acid **6D** to the appropriate amine reagent followed by a TFA deprotection:

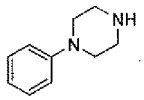
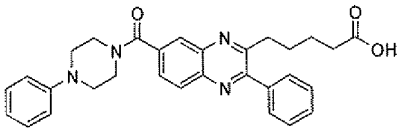
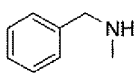
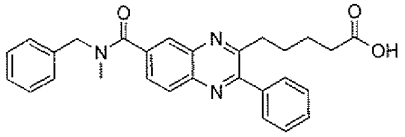
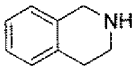
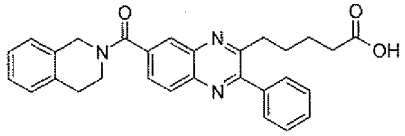
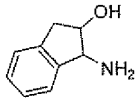
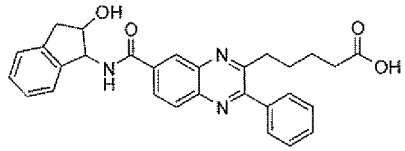
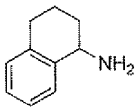
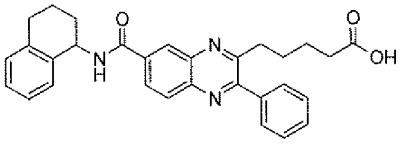
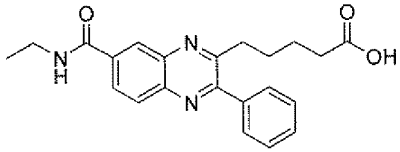
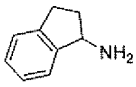
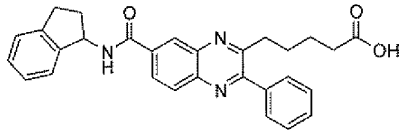
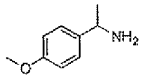
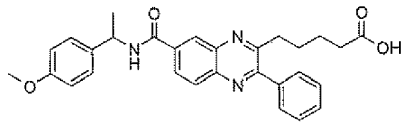
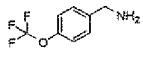
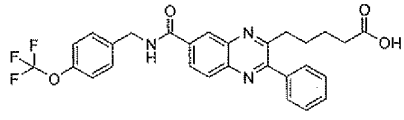
No.	Reagent	Compound Structure	Name	M+H
15A			5-(3-phenyl-7-{[(1R)-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	454
15B			5-(3-phenyl-7-{[(1S)-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	454

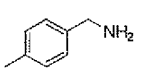
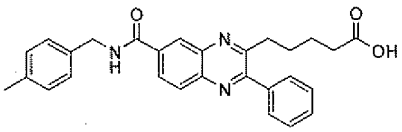
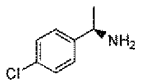
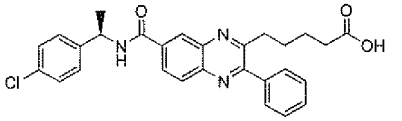
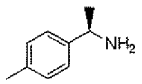
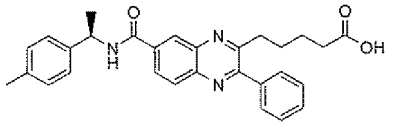
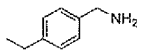
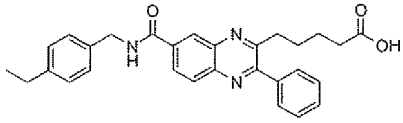
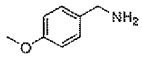
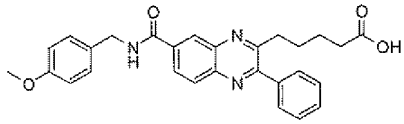
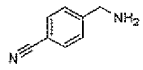
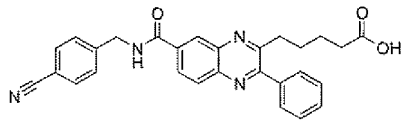
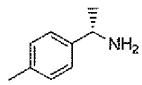
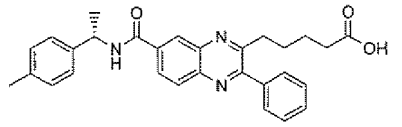
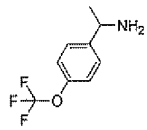
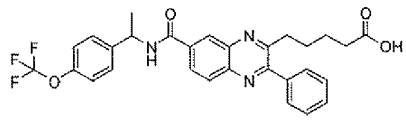
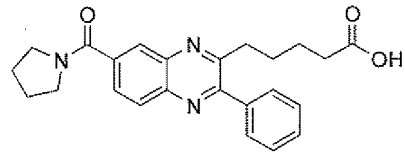
15C			5-(3-phenyl-7-{[4-(trifluoromethyl)benzyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	508
15D			5-(7-{[(1R)-1-(4-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	472
15E			5-(7-{[(1S)-1-(4-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	472
15F			5-(3-phenyl-7-{[(1S)-2,2,2-trifluoro-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	508
15G			5-(3-phenyl-7-{[(1R)-2,2,2-trifluoro-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	508
15H			5-[7-(2,7-diazaspiro-[3.5]non-7-ylcarbonyl)-3-phenylquinoxalin-2-yl]pentanoic acid	459
15i			5-[7-(2,7-diazaspiro-[3.5]non-2-ylcarbonyl)-3-phenylquinoxalin-2-yl]pentanoic acid	459
15J			5-{3-phenyl-7-[(3-phenylpiperazin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	495
15K			5-{7-[(3-benzylpiperazin-1-yl)carbonyl]-3-phenylquinoxalin-2-yl}pentanoic acid	509

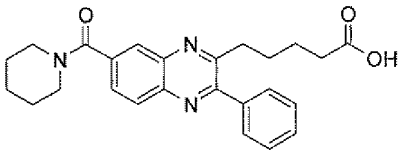
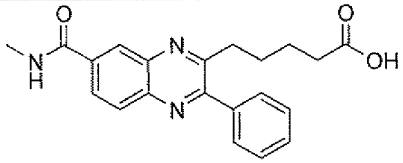
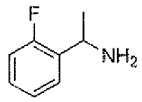
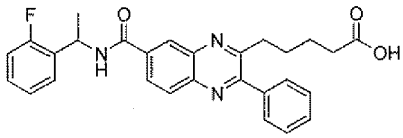
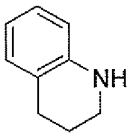
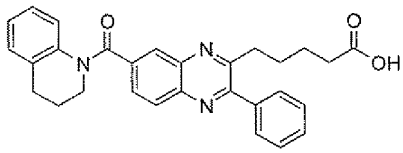
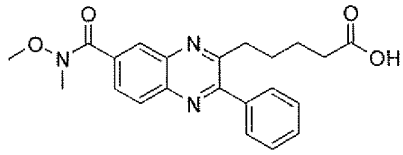
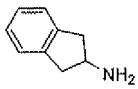
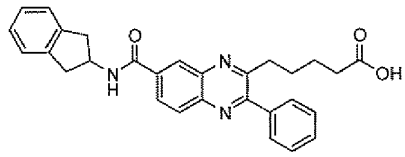
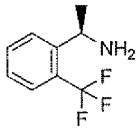
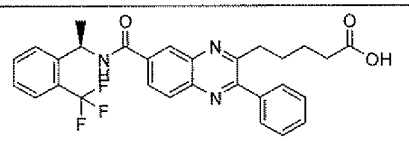
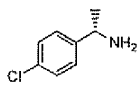
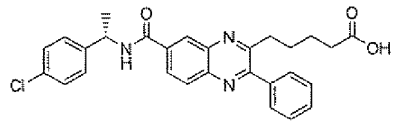
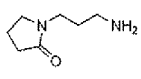
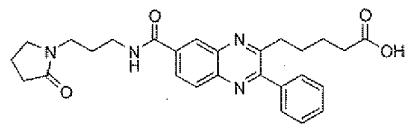
15L			5-{7-[(4-ethylpiperazin-1-yl)carbonyl]-3-phenylquinoxalin-2-yl}pentanoic acid	447
15M			5-(7-{[4-(2-methoxyethyl)piperazin-1-yl]-carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid	477
15N			5-(7-{[3-(4-methoxyphenyl)pyrrolidin-1-yl]-carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid	510
15o			5-(3-phenyl-7-{[4-(phenylsulfonyl)piperazin-1-yl]carbonyl}quinoxalin-2-yl)pentanoic acid	559
15P			5-(7-{[3-(3-chlorophenyl)pyrrolidin-1-yl]-carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid	514
15Q			5-(3-phenyl-7-{[2,2,2-trifluoro-1-(4-fluorophenyl)ethyl]carbamoyl}-quinoxalin-2-yl)pentanoic acid	526
15R			5-{7-[(3-benzylpyrrolidin-1-yl)carbonyl]-3-phenylquinoxalin-2-yl}pentanoic acid	494
15S			5-(7-{[3-(4-fluorophenyl)-pyrrolidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)-pentanoic acid	498
15T			5-{7-[(4-chlorobenzyl)-carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	474

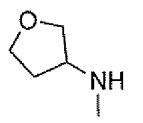
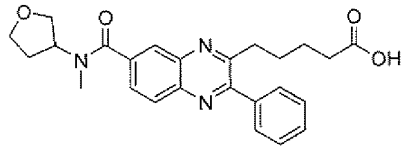
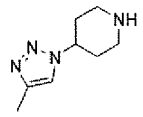
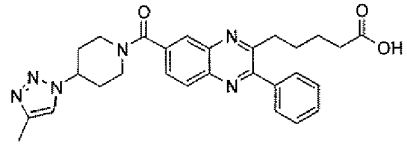
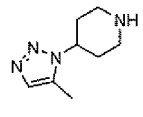
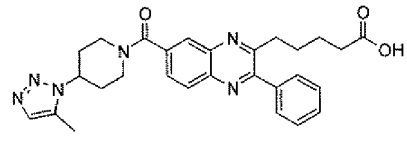
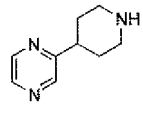
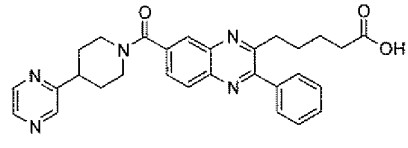
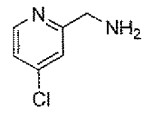
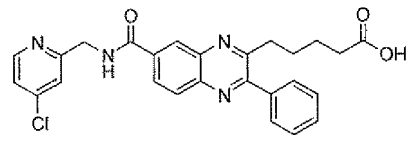
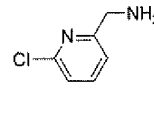
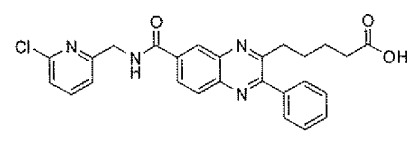
15U			5-{7-[(3-chlorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	474
15V			5-{7-[(2-chlorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	474
15X			5-{7-[(1-methyl-1-phenylethyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	468
15Y			5-{3-phenyl-7-[(3-phenylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	494
15Z			5-[7-(benzylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid	440
15AA			5-[3-phenyl-7-(phenylcarbamoyl)quinoxalin-2-yl]pentanoic acid	426
15AB			5-{7-[(2-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	458
15AC			5-{7-[(3-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	458
15AD			5-{7-[(4-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	458

15AE			5-{3-phenyl-7-[(1-phenylcyclopropyl)carbamoyl]quinoxalin-2-yl}pentanoic acid	466
15AF			5-{3-phenyl-7-[(pyridin-2-ylmethyl)carbamoyl]quinoxalin-2-yl}pentanoic acid	441
15AG			5-{3-phenyl-7-[(pyridin-3-ylmethyl)carbamoyl]quinoxalin-2-yl}pentanoic acid	441
15AH			5-{3-phenyl-7-[(pyridin-4-ylmethyl)carbamoyl]quinoxalin-2-yl}pentanoic acid	441
15Ai			5-{3-phenyl-7-[(4-phenylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	494
15AJ			5-{3-phenyl-7-[(2-phenylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	494
15AK			5-{3-phenyl-7-[(3-phenylpyrrolidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	480
15AL			5-{3-phenyl-7-[(2-phenylpyrrolidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	480
15AM			5-{3-phenyl-7-[(1-phenylcyclobutyl)carbamoyl]quinoxalin-2-yl}pentanoic acid	480

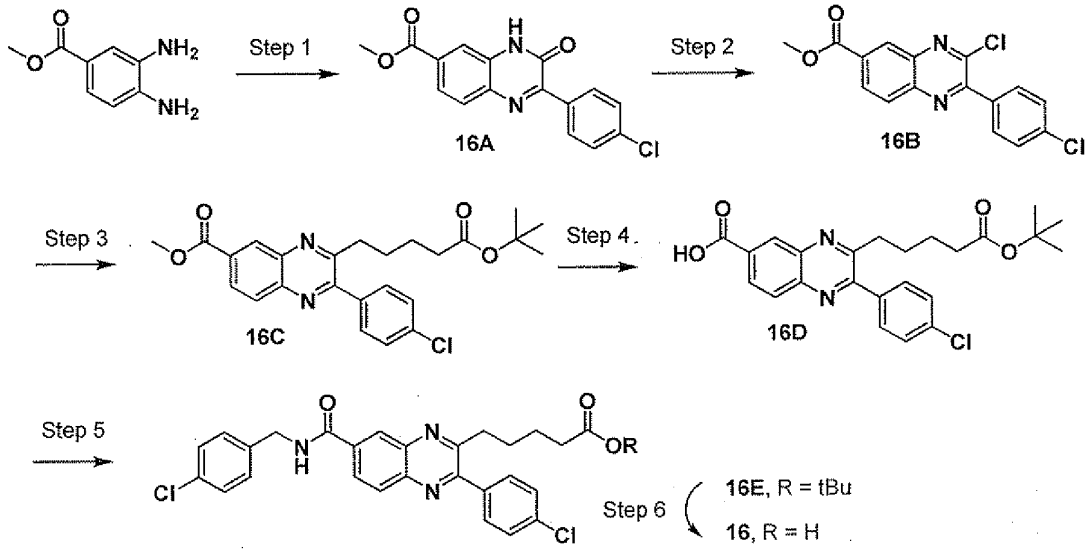
15AN			5-{3-phenyl-7-[(4-phenylpiperazin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	495
15Ao			5-{7-[benzyl(methyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	454
15AP			5-[7-(3,4-dihydroisoquinolin-2(1H)-ylcarbonyl)-3-phenylquinoxalin-2-yl]pentanoic acid	466
15AQ			5-{7-[(2-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	482
15AR			5-[3-phenyl-7-(1,2,3,4-tetrahydronaphthalen-1-ylcarbamoyl)quinoxalin-2-yl]pentanoic acid	480
15AS			5-[7-(ethylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid	378
15AT			5-[7-(2,3-dihydro-1H-inden-1-ylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid	466
15AU			5-(7-{[1-(4-methoxyphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	484
15AV			5-(3-phenyl-7-{[4-(trifluoromethoxy)benzyl]carbamoyl}quinoxalin-2-yl)pentanoic acid	524

15AW			5-{7-[(4-methylbenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	454
15AX			5-(7-{[(1R)-1-(4-chlorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	488
15AY			5-(7-{[(1R)-1-(4-methylphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	468
15AZ			5-{7-[(4-ethylbenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	468
15BA			5-{7-[(4-methoxybenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	470
15BB			5-{7-[(4-cyanobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	465
15BC			5-(7-{[(1S)-1-(4-methylphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	468
15BD			5-[3-phenyl-7-({1-[4-(trifluoromethoxy)phenyl]ethyl}carbamoyl)quinoxalin-2-yl]pentanoic acid	538
15BE			5-[3-phenyl-7-(pyrrolidin-1-ylcarbonyl)quinoxalin-2-yl]pentanoic acid	404

15BF			5-[3-phenyl-7-(piperidin-1-ylcarbonyl)quinoxalin-2-yl]pentanoic acid	418
15BG			5-[7-(methylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid	364
15BH			5-(7-{[1-(2-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	472
15Bi			5-[7-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)-3-phenylquinoxalin-2-yl]pentanoic acid	466
15BJ			5-{7-[methoxy(methyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid	394
15BK			5-[7-(2,3-dihydro-1H-inden-2-ylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid	466
15BL			5-[3-phenyl-7-({(1R)-1-[2-(trifluoromethyl)phenyl]ethyl}carbamoyl)quinoxalin-2-yl]pentanoic acid	522
15BM			5-(7-{[(1S)-1-(4-chlorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	488
15BN			5-(7-{[3-(2-oxopyrrolidin-1-yl)propyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	475

15Bo			5-{7-[methyl (tetrahydrofuran-3-yl) carbamoyl]-3-phenyl quinoxalin-2-yl}pentanoic acid	434
15BQ			5-(7-{[4-(4-methyl-1H-1,2, 3-triazol-1-yl)piperidin-1-yl]carbonyl}-3-phenyl quinoxalin-2-yl)pentanoic acid	499
15BR			5-(7-{[4-(5-methyl-1H-1,2,3-triazol-1-yl)piperidin-1-yl]carbonyl}-3-phenyl quinoxalin-2-yl)pentanoic acid	499
15BS			5-{3-phenyl-7-[(4-pyrazin-2-ylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid	496
15BT			5-(7-{[(4-chloropyridin-2-yl)methyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	475
15BU			5-(7-{[(6-chloropyridin-2-yl)methyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid	475

Preparative Example 16

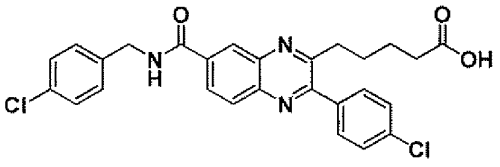


[00259] In a manner similar to that previously, methyl 3,4-diaminobenzoate was 2-(4-fluorophenyl)-2-oxoacetic acid (prepared from ethyl 2-(4-chlorophenyl)-2-oxoacetate as described in Example 2) to provide **16A** (MS: M+H = 315).

[00260] A mixture of **16A** (13.43 g, 42.67 mmol), $SOCl_2$ (70 mL, 1000 mmol), and DMF (0.4 mL, 5 mmol) was stirred at 80 °C for 4h and then at 40 °C overnight.

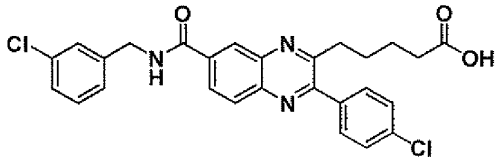
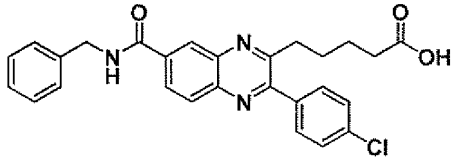
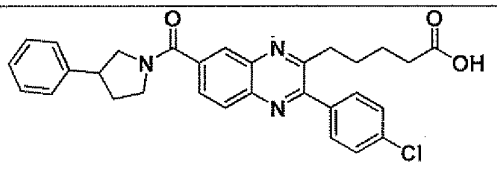
[00261] The excess $SOCl_2$ was removed. The resulting residue was stirred with cold water for 2h. The solid was then filtered and dried overnight in vacuo to give methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate (**16B**, 12.94 g; Yield = 91.04%). LCMS (M+H) = 333.

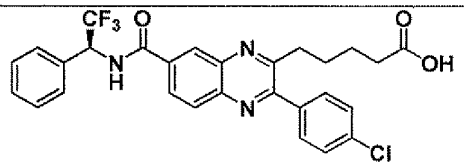
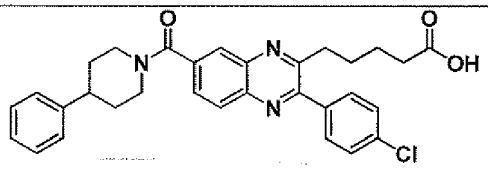
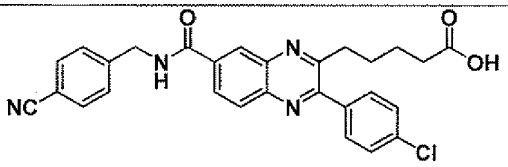
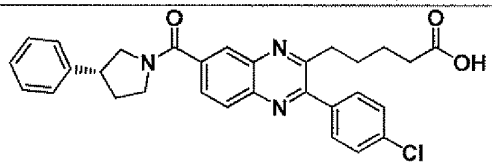
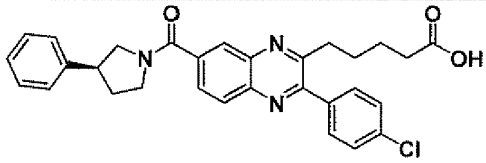
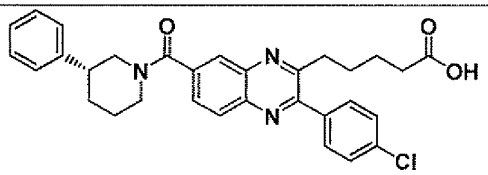
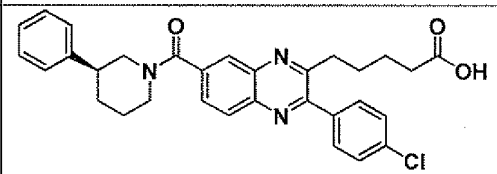
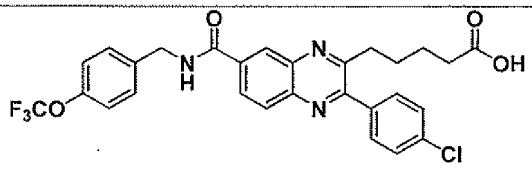
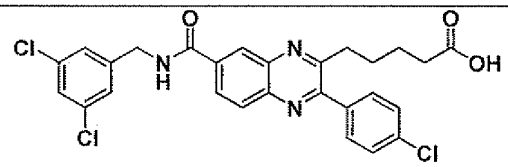
[00262] In a manner similar to that previously described, **16B** was sequentially coupled with compound **1**, hydrolyzed with LiOH (to afford **16D**), coupled with 4-chlorobenzylamine, and deprotected with TFA to provide the title compound **16**. LCMS (M+H) = 508

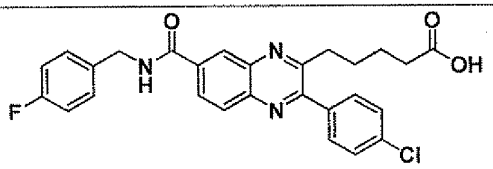
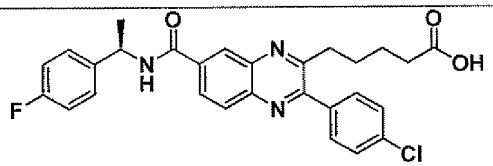
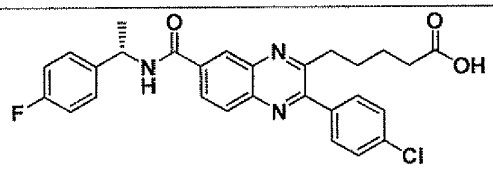
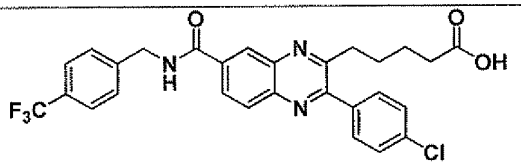
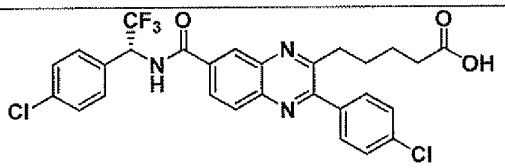
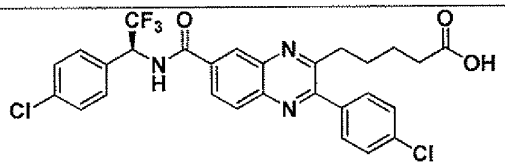
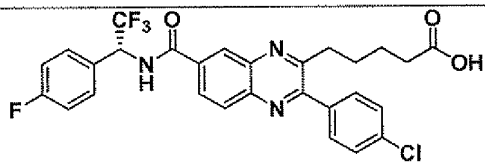
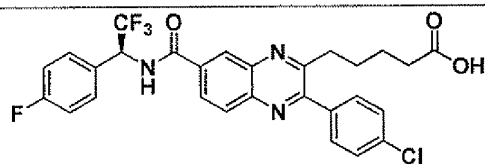
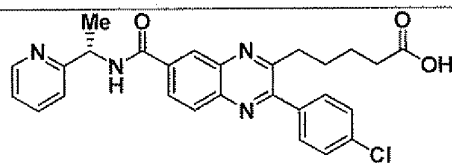


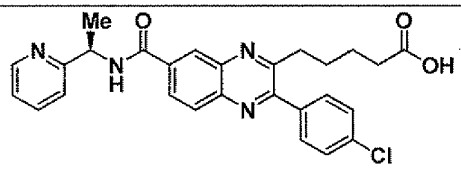
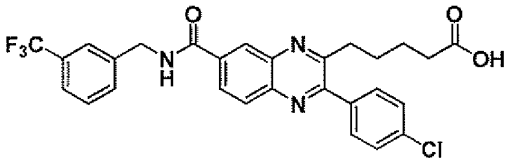
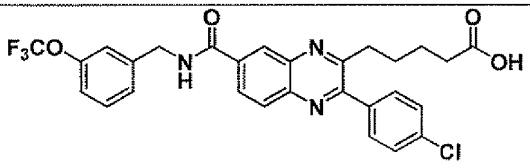
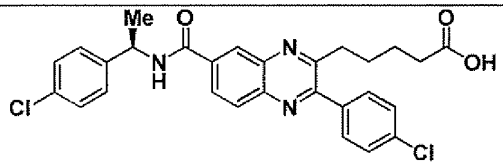
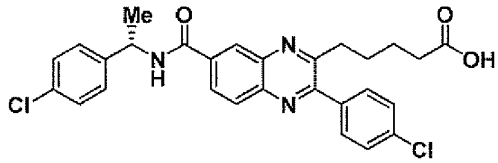
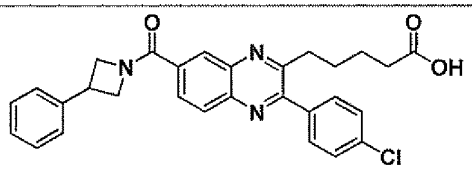
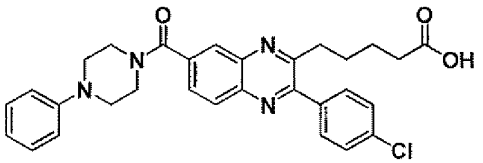
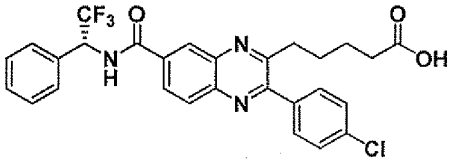
16

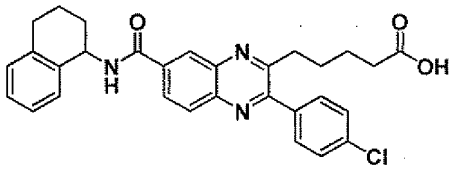
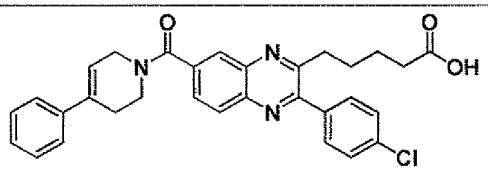
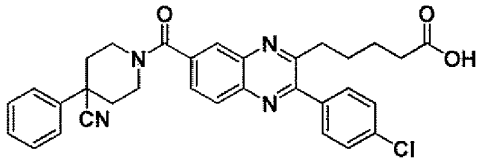
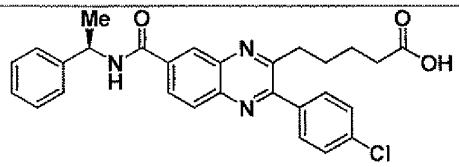
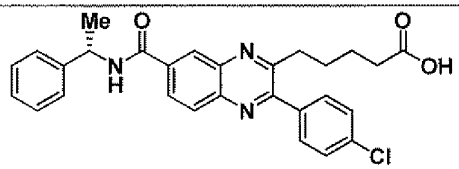
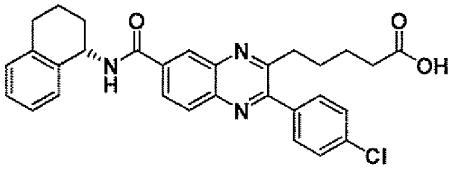
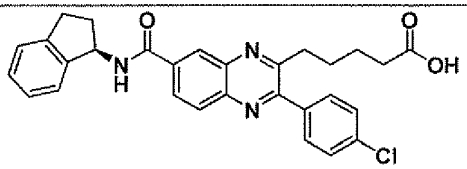
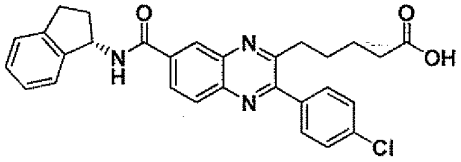
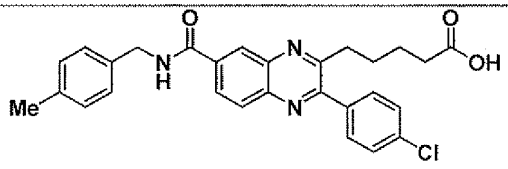
[00263] In a similar manner, the following compounds were prepared by coupling acid **16D** to the appropriate amine reagent followed by a TFA deprotection:

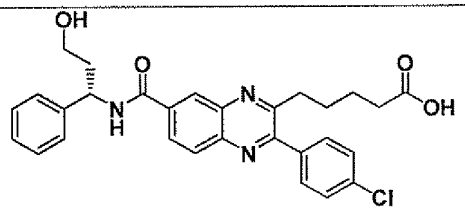
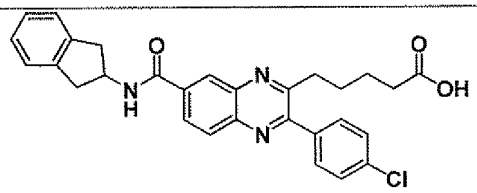
No.	Compound	Name	M+H
16F		3-(4-chlorophenyl)-7-[[[(3-chlorophenyl)methyl]amino] carbonyl]-2-quinoxalinepentanoic acid	508
16G		3-(4-chlorophenyl)-7-[[(phenylmethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	474
16H		3-(4-chlorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	514

16i		3-(4-chlorophenyl)-7-[[(2,2,2-trifluoro-1(s)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	542
16J		3-(4-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
16K		3-(4-chlorophenyl)-7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	499
16L		3-(4-chlorophenyl)-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	514
16M		3-(4-chlorophenyl)-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	514
16N		3-(4-chlorophenyl)-7-[(3(R)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
16o		3-(4-chlorophenyl)-7-[(3(S)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
16P		3-(4-chlorophenyl)-7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	558
16Q		3-(4-chlorophenyl)-7-[[[(3,5-dichlorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	542

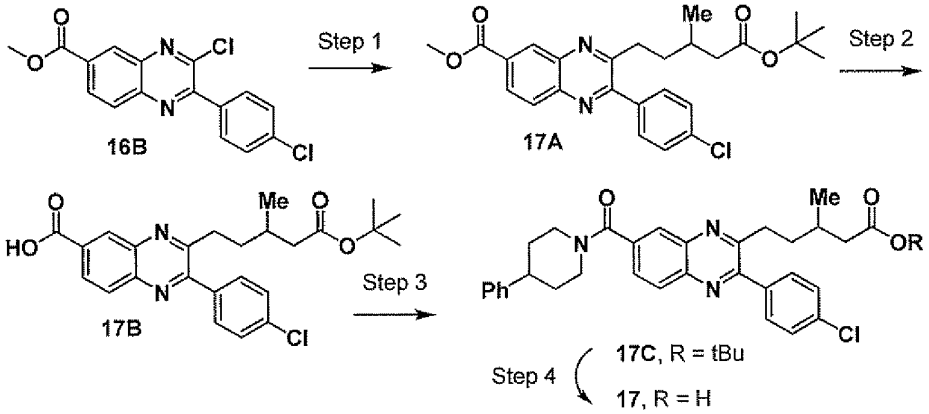
16R		3-(4-chlorophenyl)-7-[[[(4-fluorophenyl)methyl]amino] carbonyl]-2-quinoxalinepentanoic acid	492
16S		3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl) ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	506
16T		3-(4-chlorophenyl)-7-[[[1(S)-(4-fluorophenyl) ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	506
16U		3-(4-chlorophenyl)-7-[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	542
16V		3-(4-chlorophenyl)-7-[[[1(R)-(4-chlorophenyl)-2,2,2-trifluoroethyl] amino]carbonyl]-2-quinoxalinepentanoic acid	576
16W		3-(4-chlorophenyl)-7-[[[(1(S)-(4-chlorophenyl)-2,2,2-trifluoroethyl] amino]carbonyl]-2-quinoxalinepentanoic acid	576
16X		3-(4-chlorophenyl)-7-[[[2,2,2-trifluoro-1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	560
16Y		3-(4-chlorophenyl)-7-[[[2,2,2-trifluoro-1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	560
16Z		3-(4-chlorophenyl)-7-[[[1(S)-(2-pyridinyl)ethyl] amino]carbonyl]-2-quinoxalinepentanoic acid	489

16AA		3-(4-chlorophenyl)-7-[[[1(S)-(2-pyridinyl)ethyl] amino] carbonyl]-2-quinoxalinepentanoic acid	489
16AB		3-(4-chlorophenyl)-7-[[[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	542
16AC		3-(4-chlorophenyl)-7-[[[[3-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	558
16AD		3-(4-chlorophenyl)-7-[[[1(R)-(4-chlorophenyl)ethyl]amino] carbonyl]-2-quinoxalinepentanoic acid	522
16AE		3-(4-chlorophenyl)-7-[[[1(S)-(4-chlorophenyl)ethyl]amino] carbonyl]-2-quinoxalinepentanoic acid	522
16AF		3-(4-chlorophenyl)-7-[(3-phenyl-1-azetidinyl)carbonyl]- 2-quinoxalinepentanoic acid	500
16AG		3-(4-chlorophenyl)-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid	529
16AH		3-(4-chlorophenyl)-7-[[(2,2,2-trifluoro-1(R)-phenylethyl)amino]carbonyl] -2-quinoxalinepentanoic acid	542

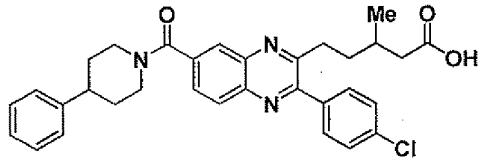
16Ai		3-(4-chlorophenyl)-7-[[(1,2,3,4-tetrahydro-1-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	514
16AJ		3-(4-chlorophenyl)-7-[(3,6-dihydro-4-phenyl-1(2H)-pyridinyl)carbonyl]-2-quinoxalinepentanoic acid	526
16AK		3-(4-chlorophenyl)-7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	553
16AL		3-(4-chlorophenyl)-7-[[(1(R)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	488
16AM		3-(4-chlorophenyl)-7-[[(1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	488
16AN		3-(4-chlorophenyl)-7-[[(1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	514
16Ao		3-(4-chlorophenyl)-7-[[(2,3-dihydro-1H-inden-1(R)-yl)amino]carbonyl]-2-quinoxalinepentanoic acid	500
16AP		3-(4-chlorophenyl)-7-[[(2,3-dihydro-1H-inden-1(S)-yl)amino]carbonyl]-2-quinoxalinepentanoic acid	500
16AQ		3-(4-chlorophenyl)-7-[[[(4-methylphenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	488

16AR		3-(4-chlorophenyl)-7-[[(3-hydroxy-1(S)-phenylpropyl)amino]carbonyl]-2-quinoxalinepentanoic acid	518
16AS		3-(4-chlorophenyl)-7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-2-quinoxalinepentanoic acid	500

Example 17

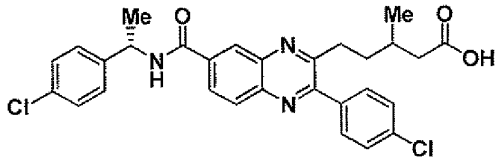
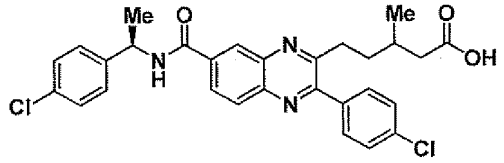
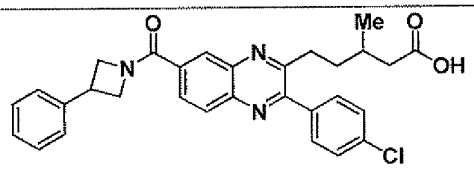
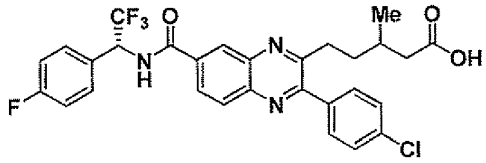
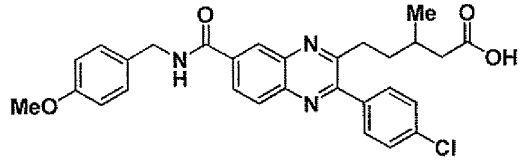
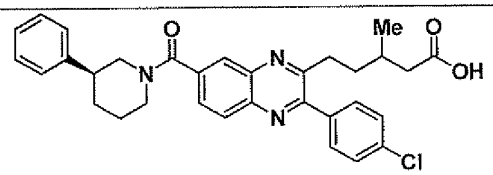
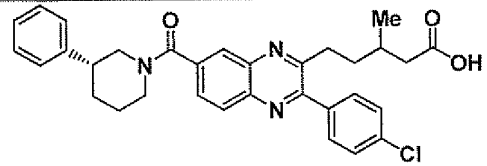
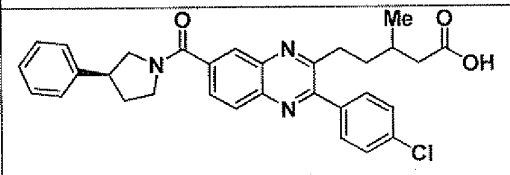


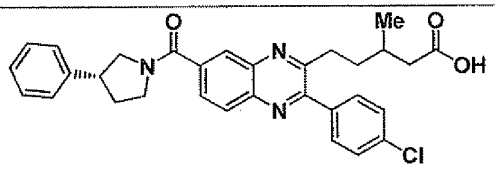
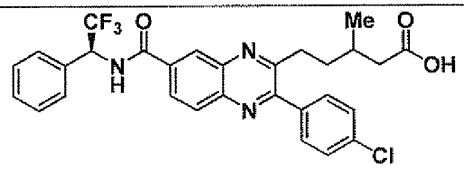
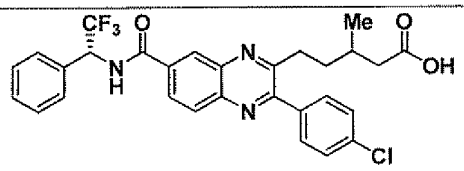
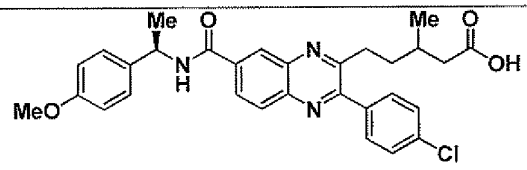
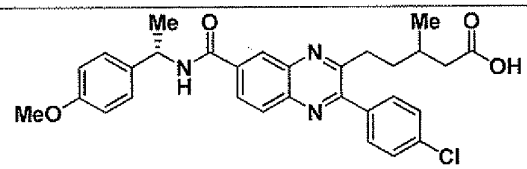
[00264] In a manner similar to that previously, methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate (**16B**) was coupled with tert-butyl 3-methylpent-4-enoate (prepared from 3-methyl-4-pentenoic acid, TFAA, and tBuOH in a manner similar to that described for compound **1**) to provide **17A** (LCMS: M+H = 469), which was subsequently hydrolyzed with LiOH (to afford **17B**, LCMS: M+H = 455), coupled with 4-phenylpiperidine and deprotected with TFA to provide 3-(4-chlorophenyl)-beta-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid **17**. LCMS (M+H) = 542.



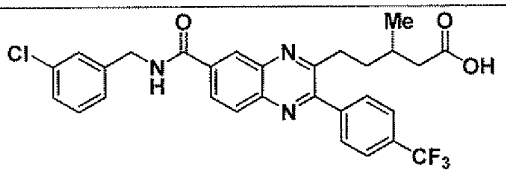
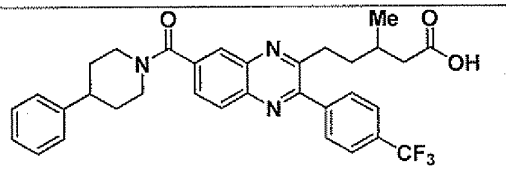
17

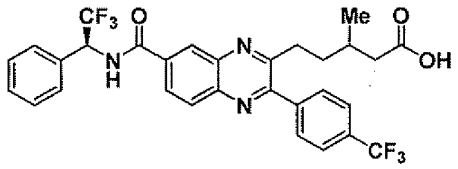
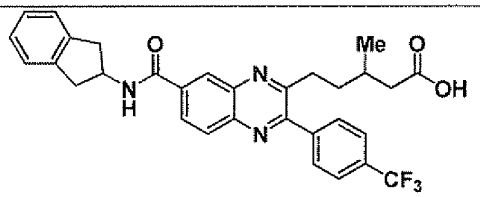
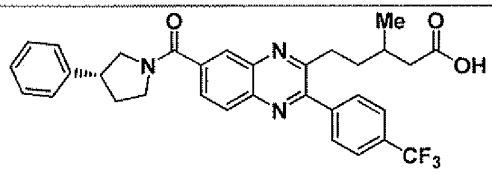
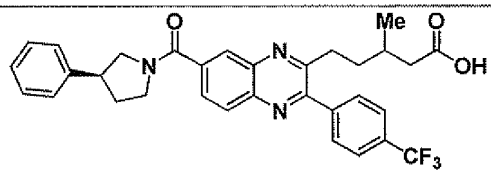
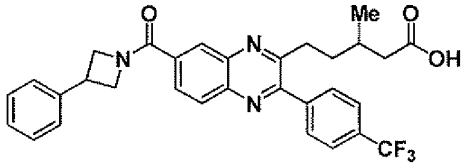
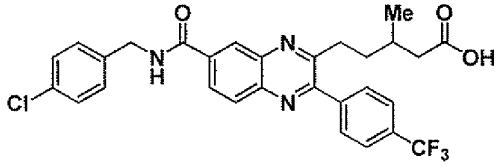
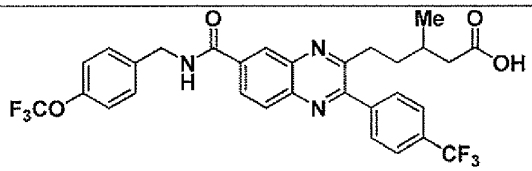
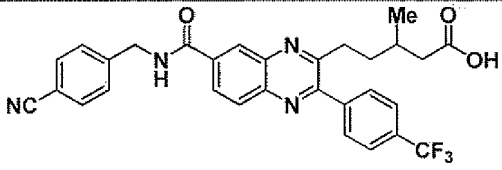
[00265] In a similar manner, the following compounds were prepared by coupling acid **17B** to the appropriate amine reagent followed by a TFA deprotection:

No.	Compound	Name	M+H
17D		3-(4-chlorophenyl)-7-[[[1(S)-(4-chlorophenyl)ethyl] amino]carbonyl]-beta-methyl- 2-quinoxaline pentanoic acid	536
17E		3-(4-chlorophenyl)-7-[[[1(R)-(4-chlorophenyl)ethyl]amino]carbonyl]-beta-methyl-2-quinoxalinepentanoic acid	536
17F		3-(4-chlorophenyl)-beta-methyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid	514
17G		3-(4-chlorophenyl)-beta-methyl-7-[[[2,2,2-trifluoro-1(R)-(4-fluorophenyl)ethyl] amino]carbonyl]-2-quinoxalinepentanoic acid	574
17H		3-(4-chlorophenyl)-7-[[[(4-methoxyphenyl)methyl] amino]carbonyl]-beta-methyl-2-quinoxaline pentanoic acid	518
17i		3-(4-chlorophenyl)-beta-methyl-7-[(3(S)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	542
17J		3-(4-chlorophenyl)-beta-methyl-7-[(3(R)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	542
17K		3-(4-chlorophenyl)-beta-methyl-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	528

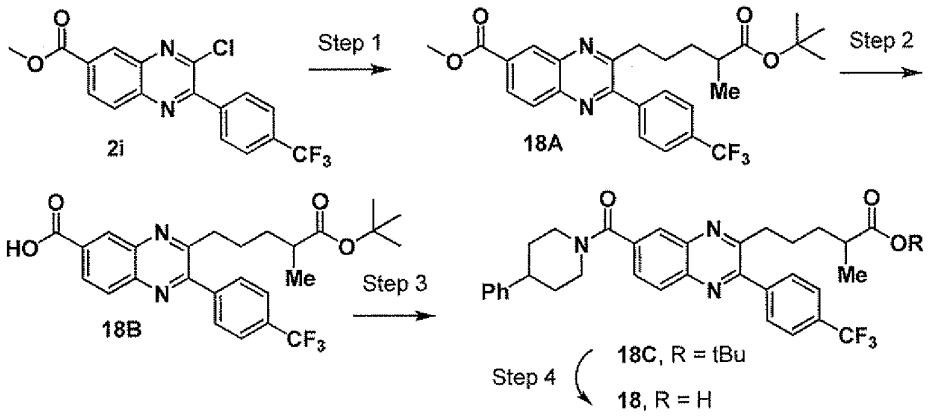
17L		3-(4-chlorophenyl)-beta-methyl-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
17M		3-(4-chlorophenyl)-beta-methyl-7-[[[2,2,2-trifluoro-(1S)-phenylethyl]amino] carbonyl]-2-quinoxaline pentanoic acid	556
17N		3-(4-chlorophenyl)-beta-methyl-7-[[(2,2,2-trifluoro-1(R)-phenylethyl)amino]carbonyl] -2-quinoxalinepentanoic acid	556
17o		3-(4-chlorophenyl)-7-[[[1(R)-(4-methoxyphenyl) ethyl]amino]carbonyl]-beta-methyl-2-quinoxaline pentanoic acid	532
17P		3-(4-chlorophenyl)-7-[[[1(S)-(4-methoxyphenyl)ethyl] amino]carbonyl]-beta-methyl-2-quinoxaline pentanoic acid	532

[00266] In a similar manner to that described above, the following compounds were prepared from methyl 3-chloro-2-(4-(trifluoromethyl)phenyl)quinoxaline-6-carboxylate (**2i**) and tert-butyl 3-methylpent-4-enoate, followed by sequential hydrolysis with LiOH, coupling with an appropriate amine and deprotection with TFA.

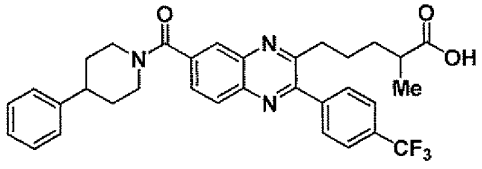
No.	Compound	Name	M+H
17Q		7-[[[(3-chlorophenyl)methyl] amino]carbonyl]-beta-methyl-3-[4-(trifluoro methyl)phenyl]-2-quinoxalinepentanoic acid	556
17R		beta-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	576

17S		beta-methyl-3-[4-(trifluoromethyl)phenyl]-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	590
17T		7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-beta-methyl-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	548
17U		beta-methyl-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	562
17V		beta-methyl-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	562
17W		beta-methyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	548
17X		7-[[[(4-chlorophenyl)methyl]amino]carbonyl]-beta-methyl-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	556
17Y		beta-methyl-7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	606
17Z		7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-beta-methyl-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	547

Example 18

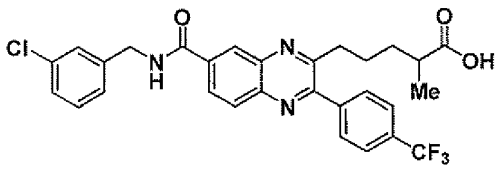
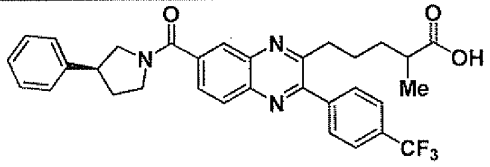


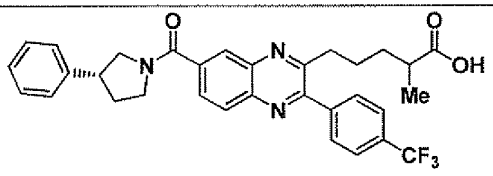
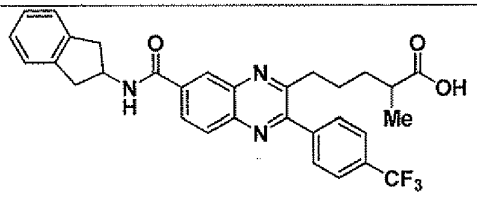
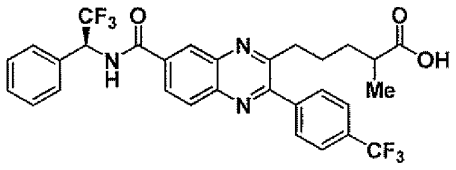
[00267] In a manner similar to that previously, methyl 3-chloro-2-(4-(trifluoromethyl)phenyl)quinoxaline-6-carboxylate (**2i**) was coupled tert-butyl 2-methylpent-4-enoate (prepared from 2-methylpent-4-enoic acid, TFAA, and tBuOH in a manner similar to that described for compound **1**) to provide **18A**, which was subsequently hydrolyzed with LiOH, coupled with 4-phenylpiperidine and deprotected with TFA to provide alpha-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid **18**. LCMS (M+H) = 576.



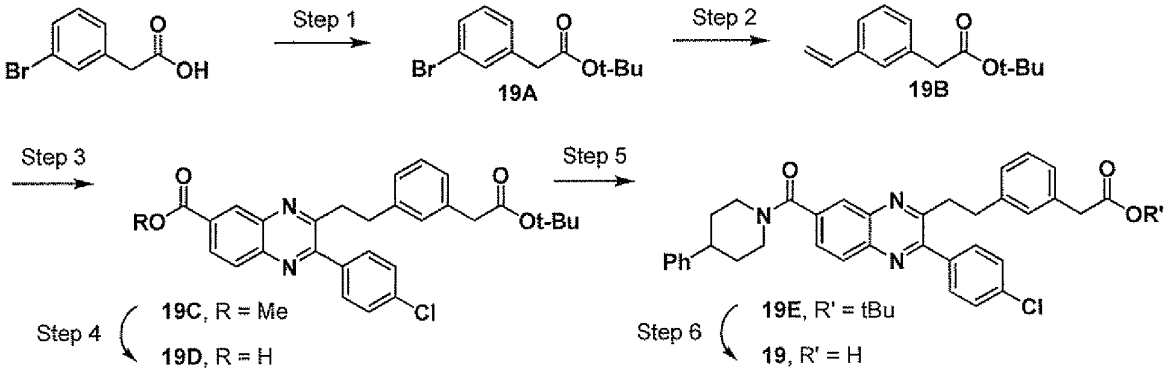
18

[00268] In a similar manner, the following compounds were prepared by coupling acid **18B** to the appropriate amine reagent followed by a TFA deprotection:

No.	Compound	Name	M+H
18D		7-[[[(3-chlorophenyl) methyl]amino]carbonyl]-alpha-methyl-3-[4-(trifluoro methyl)phenyl]-2-quinoxalinepentanoic acid	556
18E		alpha-methyl-7-[(3(S)-phenyl-1-pyrrolidinyl) carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	562

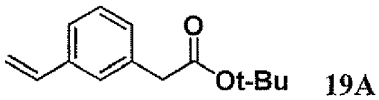
18F		alpha-methyl-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	562
18G		7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-alpha-methyl-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	548
18H		alpha-methyl-3-[4-(trifluoromethyl)phenyl]-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	590

Example 19



Steps 1-2

***tert*-Butyl 2-(3-Vinylphenyl)acetate.**



19A

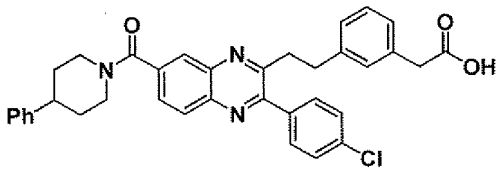
[00269] In a manner similar to that described for compound **1,** 2-(3-bromophenyl)acetic acid was reacted with TFAA and tBuOH to provide tert-butyl 2-(3-bromophenyl)acetate (**19A**).

[00270] A solution of **19A** (600 mg, 2.21 mmol), potassium vinyltrifluoroborate (296 mg, 2.21 mmol), $Pd(dppf)_2Cl_2 \cdot CH_2Cl_2$ (180 mg, 0.221 mmol), and cesium carbonate (2.16 g, 6.63 mmol) in water (1 mL) and 1,4-dioxane (9 mL) under nitrogen was stirred at 90 °C for 18 h. After this time, the reaction was cooled to RT and diluted with water and DCM. The aqueous

layer was separated and extracted with DCM. The combined organics were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography (0% to 20% EtOAc/heptane) to yield **19B** (268 mg, yield = 56%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.24 (m, 3H), 7.18–7.15 (m, 1H), 6.70 (dd, J = 23.5, 14.5 Hz, 1H), 5.75 (d, J = 23.5 Hz, 1H), 5.24 (d, J = 14.5 Hz, 1H), 3.52 (s, 2H), 1.44 (s, 9H).

Steps 3-6

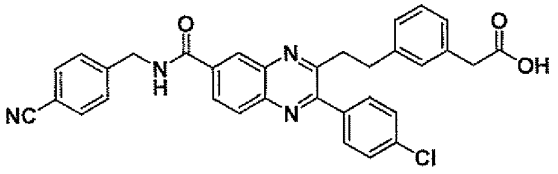
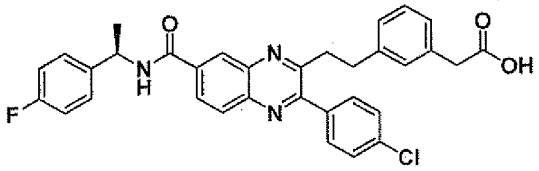
2-(3-(2-(3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)ethyl)phenyl)acetic acid

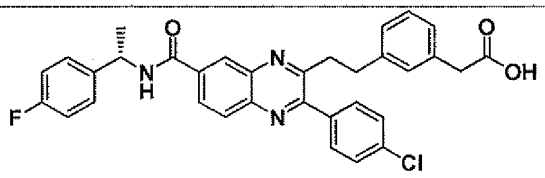
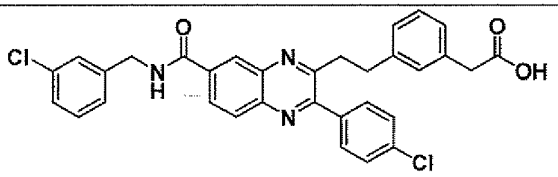
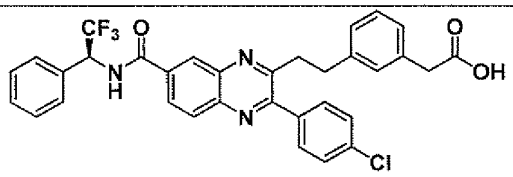
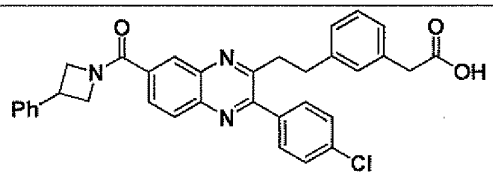


19

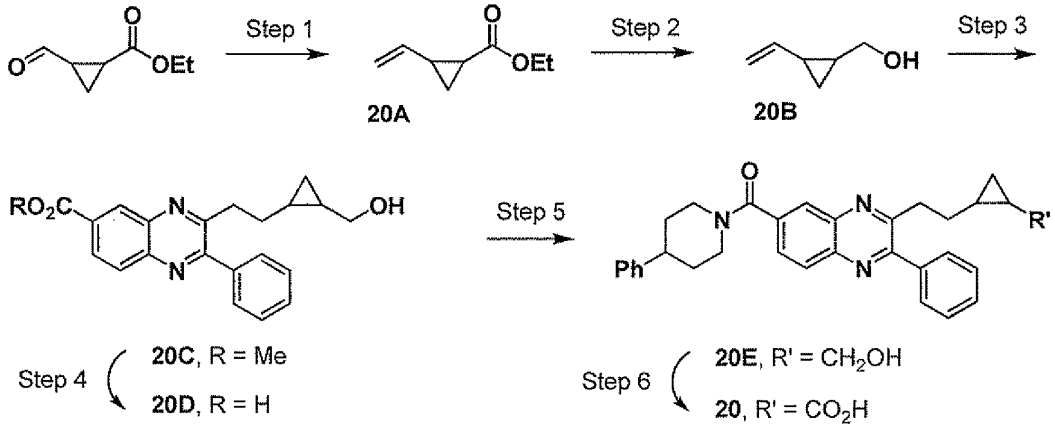
[00271] In a manner similar to that previously, *tert*-butyl 2-(3-vinylphenyl)acetate (**19B**) was sequentially coupled with methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate (**16B**) and hydrolyzed with LiOH. The resulting acid **19C** (3-(3-(2-tert-butoxy-2-oxoethyl)phenethyl)-2-(4-chlorophenyl)quinoxaline-6-carboxylic acid) was coupled with 4-phenylpiperidine and deprotected with TFA to provide -[2-[3-(4-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid **19**. LCMS (M+H) = 590.

[00272] In a similar manner, the following compounds were prepared by coupling acid **19C** to the appropriate amine reagent followed by a TFA deprotection:

No.	Compound	Name	M+H
19F		3-[2-[3-(4-chlorophenyl)-7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	561
19G		3-[2-[3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	568

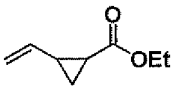
19H		3-[2-[3-(4-chlorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	568
19i		3-[2-[3-(4-chlorophenyl)-7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	570
19J		3-[2-[3-(4-chlorophenyl)-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	604
19K		3-[2-[3-(4-chlorophenyl)-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	562

Example 20



Step 1

Ethyl 2-vinylcyclopropanecarboxylate.



20A

[00273] A mixture of methyltriphenyl-phosphonium bromide (60.3 g, 168.8 mmol, 2.4 eq) in 500 mL of THF was cooled down to °C and treated slowly with KOtBu (18.9 g, 168.8 mmol, 2.4 eq). The reaction was stirred at °C for 30 min, treated dropwise with ethyl 2-fomyl-1-cyclopropanecarboxylate (10 g, 70.34 mmol, 1.0 eq) in 200 mL THF, and then stirred for 2 h at RT. The mixture was then cooled to °C, treated with water and extracted with ether (2x). The organic extracts were dried over Na_2SO_4, filtered and concentrated. Chromatography (*0 to 25% ether in pentane) afforded the olefin **20A** (8.15g).

Step 2

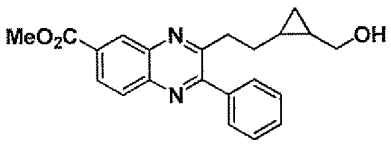
(2-Vinylcyclopropyl)methanol.

20B

[00274] A solution of ethyl 2-vinylcyclopropanecarboxylate (**20A**, 4.26 g, 30.4 mmol, 1.0 eq) in THF (100 mL, anhydrous) was cooled to °0 C and treated slowly with LAH (1.60 g, 38.0 mmol, 1.25 eq). The reaction was then slowly warmed to RT, stirred overnight, and then quenched with water. The precipitate was filtered and washed with THF. Chromatography of the filtrate (0 to 60% ether/hexanes) gave the alcohol **20B** (2.0g).

Step 3

Methyl 3-(2-(2-(hydroxymethyl)cyclopropyl)ethyl)-2-phenylquinoxaline-6-carboxylate



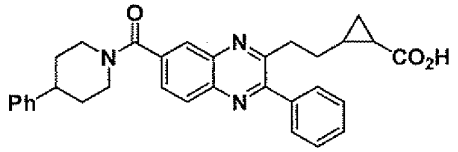
20C

[00275] To a solution of (2-vinylcyclopropyl)methanol (**20B**, 0.5 g, 5.10 mmol, 2.0 eq) in anhydrous THF (20 mL) was added 9-BBN (0.5 M in THF, 20 mL, 10.2 mmol, 4 eq) at 0 °C under nitrogen. The reaction was stirred at 0 °C for 30 min and warmed to RT for 4 h. methyl 3-chloro-2-phenylquinoxaline-6-carboxylate **6B** (0.76 g, 2.55 mmol, 1.0 eq), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (310 mg, 0.380 mmol, 0.15 eq), and K_3PO_4 (1.62 g, 7.65 mmol, 3.0 eq) were added. The suspension was degassed (3 × vacuum/nitrogen) and heated at 68 °C overnight. The reaction was then cooled to RT and filtered. The filtrate was diluted with DCM and water.

The aqueous layer was separated and extracted with DCM. The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography (20%-50% EtOAc/hexane) to yield **20C** (0.84 g). Further purification of the mixture (SFC chiral chromatography) provided the 4 stereoisomers, each in high purity.

Steps 4-6

2-(2-(3-phenyl-7-(4-phenylpiperidine-1-carbonyl)quinoxaline-2-yl)ethyl)cyclopropanecarboxylic acid



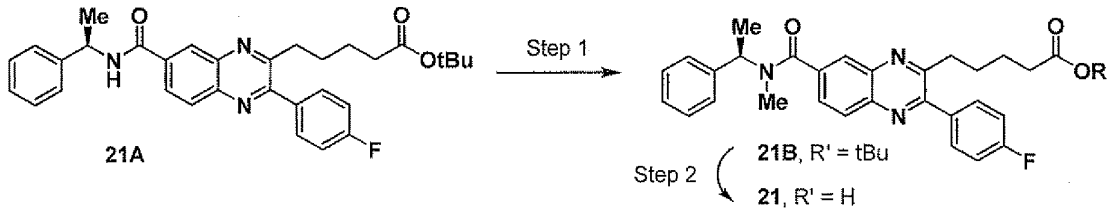
20

[00276] In a manner similar to that previously, each pure stereoisomer of **20C** was individually hydrolyzed with LiOH and coupled with 4-phenylpiperidine to provide (3-(2-(2-(hydroxymethyl)cyclopropyl)ethyl)-2-phenylquinoxalin-6-yl)(4-phenylpiperidin-1-yl)methanone (**20E**). The first stereoisomer was then subjected to the following oxidation:

[00277] A mixture of the alcohol **20E** (103 mg, 0.21mmol, 1.0 eq), sodium periodate (135 mg, 0.629 mmol, 3.0 eq) and ruthenium chloride trihydrate (3 mg, 0.011 mmol, 0.05 eq) were combined in 3 mL CCl_4-4 mL H_2O-3 mL CH_3CN. The mixture was stirred at RT overnight, quenched with 10 mL sat. aq. NH_4Cl and filtered. The precipitate was filtered and washed with EtOAc. The aqueous layer was extracted with EtOAc (1x). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Chromatography (0 to 10% MeOH/CH_2Cl_2) provided the title compound **20** (74 mg, LCMS: M+H 506).

[00278] The other three stereoisomers of **20E** were similarly subjected to this oxidation to provide **20F** (LCMS: M+H 506), **20G** (LCMS: M+H 506), and **20H** (LCMS: M+H 506).

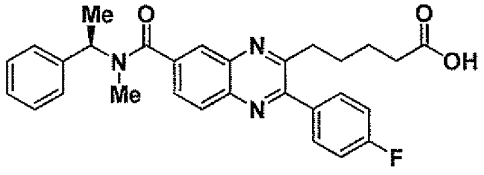
Example 21



Steps 1-2

(R)-5-(3-(4-fluorophenyl)-7-(methyl(1-phenylethyl)carbamoyl)quinoxalin-2-yl)pentanoic

acid

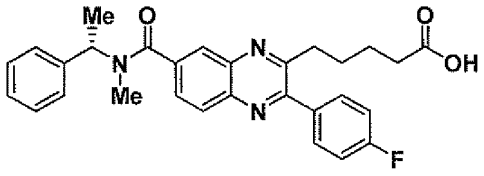


21

[00279] A solution of (R)-tert-butyl 5-(3-(4-fluorophenyl)-7-(1-phenylethyl -carbamoyl)quinoxalin-2-yl)pentanoate (**21A**, 62 mg, 0.118 mmol; derived from the coupling of **5D** and (R)-1-phenylethanamine as previously described) in 5 DMF (5 mL) was cooled to 0 °C and treated with NaH (60%, 7 mg, 0.176 mmol, 1.5 eq). After 20 min at 0 °C, MeI (15 μL) was added and the reaction was warrmed to RT for 2 h. The reaction was concentrated and then diluted with CH_2Cl_2 and H_2O. The H_2O layer was extracted with CH_2Cl_2 (1X). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Chromatography (0 to 50% EtOAc/Hexane) provided the (R)-tert-butyl 5-(3-(4-fluorophenyl)-7-(methyl(1-phenylethyl)carbamoyl)-quinoxalin-2-yl)pentanoate (**21B**, 46 mg).

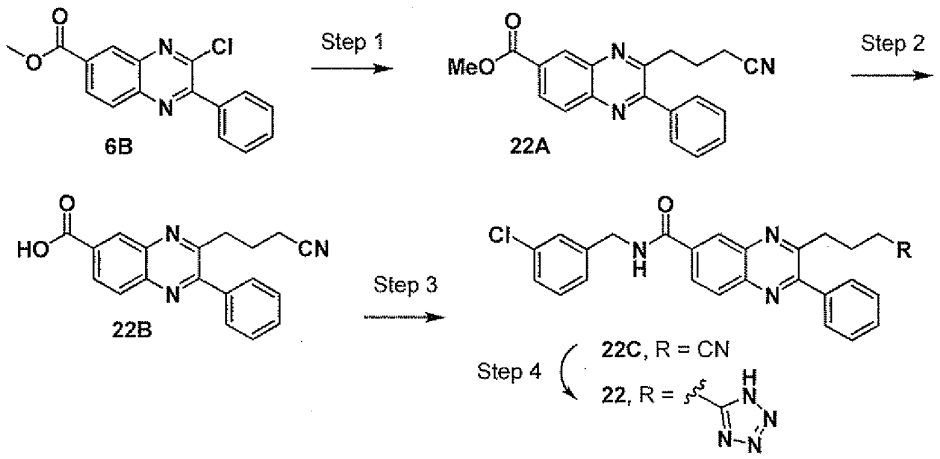
[00280] In a manner similar to that previously described, **21B** was deprotected with TFA to provide **21**. LCMS (M+H) = 486.

[00281] The enantiomer -(4-fluorophenyl)-7-[[methyl(1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid **21C** was synthesized in a similar fashion. LCMS (M+H) = 486.



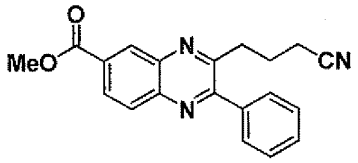
21C

Example 22



Step 1

Methyl 3-(3-cyanopropyl)-2-phenylquinoxaline-6-carboxylate.

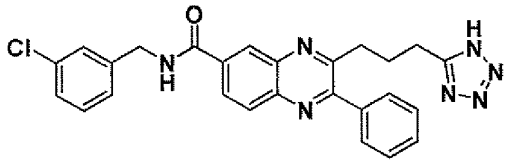


22A

[00282] In a manner similar to that described in Example 2, the following reaction was completed: To a solution of 3-butenenitrile in THF cooled to 0 °C was added 9-BBN. The reaction was stirred at 0 °C for 30 min and at RT for 3 h. To this solution was added methyl 3-chloro-2-phenylquinoxaline-6-carboxylate (**6B**), $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ and K_3PO_4 The resulting solution was degassed and stirred at 60 °C for 16 h. The filtrate was diluted with DCM and water. The organic layer was removed and the aqueous phase was extracted with DCM (2x). The combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was purified by flash chromatography to provide **22A**.

Steps 2-4

N-(3-chlorobenzyl)-3-(3-cyanopropyl)-2-phenylquinoxaline-6-carboxamide

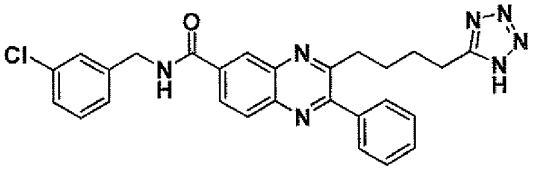


22

[00283] In a manner similar to that described previously (*e.g.*, Examples 2-3), **22A** was hydrolyzed with LiOH and then treated with 3-chlorobenzylamine, DIPEA, and Bop-Cl to provide **22C**.

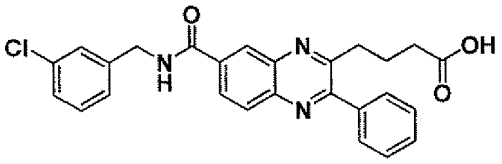
[00284] To a solution of the nitrile **22C** and trimethylsilylazide in toluene was added dibutyltinoxide, and the reaction mixture was heated at 110 degree overnight until the nitrile was consumed. The mixture was concentrated down, dissolved in methanol and reconcentrated, then partitioned between EtOAc (20 mL) and 10% $NaHCO_3$ solution (20 mL). The organic layer was extracted with an additional portion of 10% $NaHCO_3$ solution (20 mL). The combined aqueous extracts were acidified to pH 2 with 10% HCl and then extracted with EtOAc (2 x 20 mL). The combined organic extracts were dried, concentrated, and purified by reverse-phase (C18, 5-95% MeCN-H_2O with 0.1% TFA) to give the 5-substituted tetrazole **22**. LCMS (M+H) = 484.

[00285] In a similar manner, N-[(3-chlorophenyl)methyl]-2-phenyl-3-[4-(1H-tetrazol-5-yl)butyl]-6-quinoxalinecarboxamide **22D** was synthesized by using 4-pentenenitrile in Step 1, and then following the described sequence. LCMS (M+H) = 498



22D

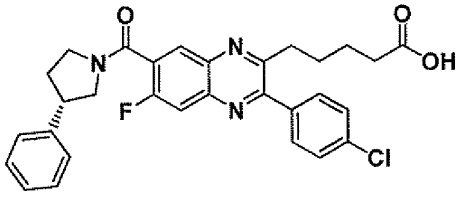
Example 23



23

[00286] In a manner similar to that previously described in Examples 6 and 10, 7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-3-phenyl-2-quinoxalinebutanoic acid **23** (LCMS, M+H = 460) was synthesized by coupling tert-butyl 3-butenoate with **6B** and then advancing the product through the described sequence.

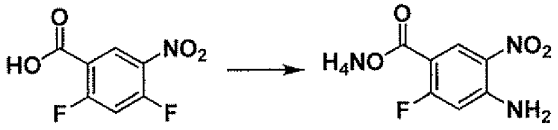
Example 24



24

Step 1

Ammonium 4-amino-2-fluoro-5-nitrobenzoate.



24A **24B**

[00287] A solution of 2,4-difluoro-5-nitrobenzoic acid (**24A**, 10.0 g, 49.2 mmol) in 250 mL 0.5 NH_3/dioxane was heated in a sealed tube at 90°C overnight. After the reaction mixture was cooled to RT, it was filtered and the solid collected was dried over the vacuum to provide the product as yellow solid **24B** (8.3 g, 77%).

Step 2

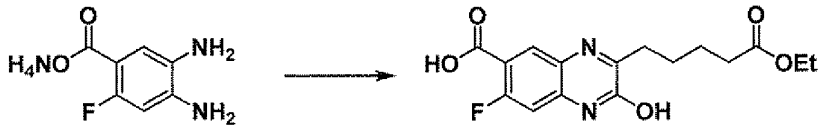
Ammonium 4,5-diamino-2-fluorobenzoate.

24B **24C**

[00288] A suspension of **24B** (3.5 g, 16.1 mmol) in MeOH/CH_2Cl_2 (4:1 v/v, 50 mL) was added with 10% Pd/C (wet, 0.88 g) and stirred under H_2 balloon overnight. The reaction mixture was then filtered and the filtrate was concentrated under vacuum to give crude product **24C** (3.3 g) which was used in the next step without purification.

Step 3

3-(5-Ethoxy-5-oxopentyl)-7-fluoro-2-hydroxyquinoxaline-6-carboxylic acid.

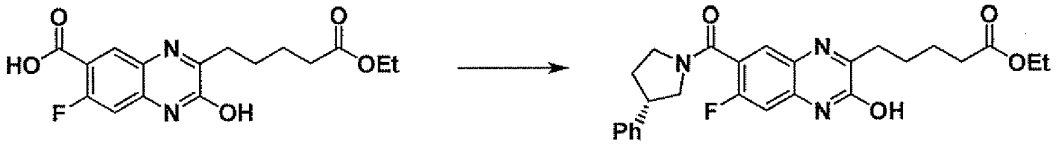


24C **24D**

[00289] To the crude product **24C** (3.3 g) in EtOH (50 mL) was added diethyl 2-oxoheptane-1,7-dicarboxylate (5.6 g, 24.2 mmol) and the mixture was heated at reflux overnight. It was then cooled to RT and acidified with 1N HCl to pH = 5 and concentrated under vacuum. The resulting residue was purified by flash chromatography (CH_2Cl_2/MeOH) to provide **24D** as gray solid (1.9 g, 35% over two steps).

Step 4

(S)-ethyl 5-(6-fluoro-3-hydroxy-7-(3-phenylpyrrolidine-1-carbonyl)-quinoxalin-2-yl)pentanoate



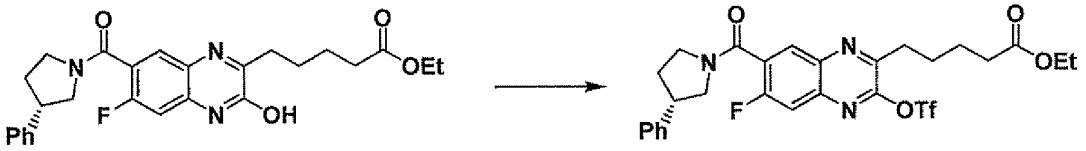
24D **24E**

[00290] To a solution of **24D** (509 mg, 1.4 mmol) in CH_2Cl_2 (10 mL) was added (S)-3-phenylpyrrolidine hydrochloride (220 mg, 1.2 mmol), HATU (912 mg, 2.4 mmol) and DIPEA (1.0 mL, 6.0 mmol) and the mixture was stirred at RT overnight. It was then diluted with CH_2Cl_2

and washed by H_2O, brine and dried over Na_2SO_4, then concentrated under vacuum. The resulting residue was purified by flash chromatography (EtOAc/hexane) to provide product **24E** as colorless oil (500 mg, 90%).

Step 5

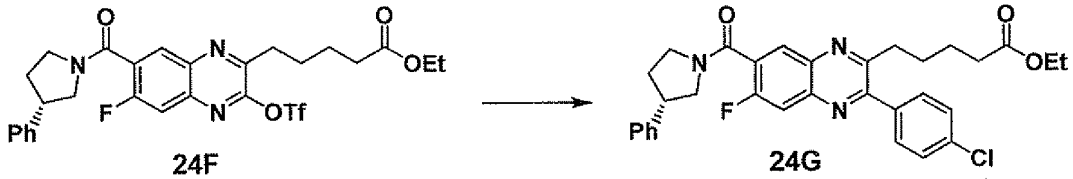
(S)-ethyl 5-(6-fluoro-7-(3-phenylpyrrolidine-1-carbonyl)-3-(trifluoromethyl-sulfonyloxy)quinoxalin-2-yl)pentanoate



[00291] To a solution of **24E** (700 mg, 1.5 mmol) in DMF (10 mL) was added $PhNTf_2$ (591 mg, 1.7 mmol) and DBU (252 mg, 1.7 mmol) and the mixture was stirred at RT overnight. Then it was diluted with EtOAc and washed by H_2O, brine and dried over Na_2SO_4, then concentrated over vacuum. The resulting residue was purified by flash chromatography (EtOAc/hexane) to provide product **24F** as colorless oil (400 mg, 45%).

Step 6

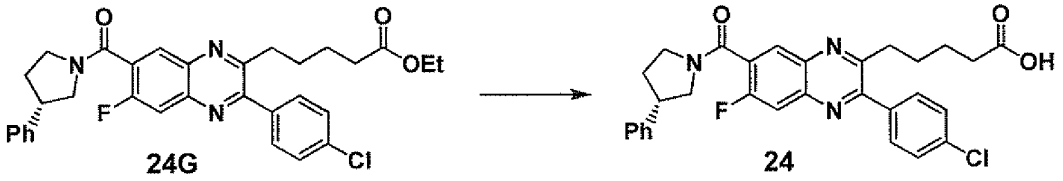
(S)-ethyl 5-(3-(4-chlorophenyl)-6-fluoro-7-(3-phenylpyrrolidine-1-carbonyl)-quinoxalin-2-yl)pentanoate



[00292] To a solution of **24F** (100 mg, 0.17 mmol) in dioxane (10 mL) in a sealed tube was added 4-chlorophenylboronic acid (52 mg, 0.33 mmol), K_3PO_4 (71 mg, 0.33 mmol) and KBr (40 mg, 0.33 mmol) and the mixture was degassed for 5 min. Then $Pd(PPh_3)_4$ (53 mg, 0.046 mmol) was added and the resulting mixture was heated at 80 °C overnight. It was then taken into EtOAc and washed by H_2O, brine and dried over Na_2SO_4, then concentrated over vacuum. The resulting residue was purified by flash chromatography (EtOAc/hexane) to provide product **24G** as colorless oil (90 mg, 95%).

Step 7

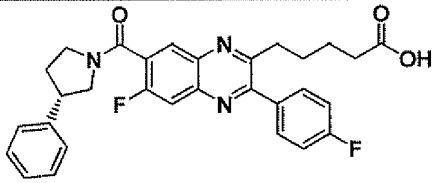
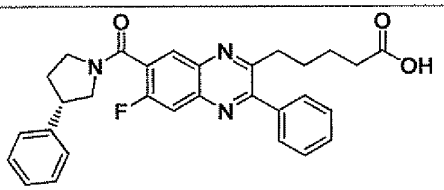
3-(4-chlorophenyl)-6-fluoro-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid



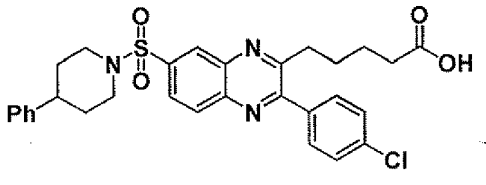
24G 24

[00293] A mixture of **24G** (90 mg, 0.16 mmol) and $LiOH \cdot H_2O$ (10 mg, 0.24 mmol) in THF/H_2O (3:1 v/v, 4 mL) was stirred at RT overnight. Then it was acidified by 1N HCl to pH = 5 and concentrated under vacuum. The resulting residue was purified by reverse phase HPLC to provide product **24** as colorless oil (50 mg, 59%). MS (M+H) = 532.0.

[00294] In a similar manner, the following compounds were prepared by coupling the appropriate boronic acid to **24F** followed by hydrolysis.

No.	Compound	Name	M+H
24H		6-fluoro-3-(4-fluorophenyl)-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	516
24i		6-fluoro-3-phenyl-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	498

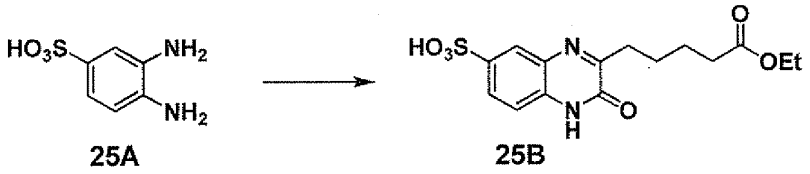
Example 25



25

Step 1

3-(5-Ethoxy-5-oxopentyl)-2-oxo-1,2-dihydroquinoxaline-6-sulfonic acid

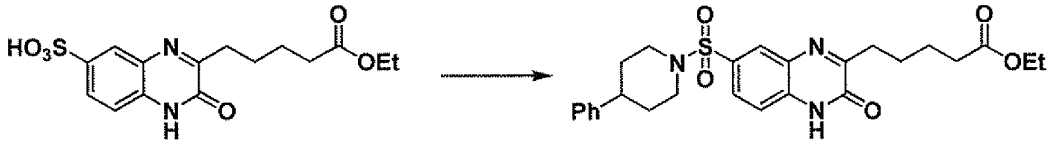


25A 25B

[00295] A mixture of 3,4-diaminobenzenesulfonic acid **25A** (4.6 g, 24.6 mmol) and diethyl 2-oxoheptane-1,7-dicarboxylate (7.4 g, 32.0 mmol) in EtOH (100 mL) was heated at reflux overnight. Then it was concentrated under vacuum and the residue was purified by flash chromatography (CH_2Cl_2/MeOH) to provide**25B** as brown solid (4.5 g, 52%).

Step 2

Ethyl 5-(3-oxo-7-(4-phenylpiperidin-1-ylsulfonyl)-3,4-dihydroquinoxalin-2-yl)pentanoate

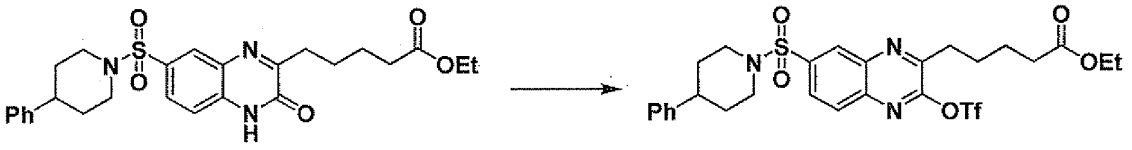


25B 25C

[00296] A solution of **25B** (1.2 g, 3.45 mmol) in pyridine (10 mL) was stirred for 30 min and then concentrated under vacuum to give pyridine salt of **25B**. In a different flask, to a solution of Ph_3PO (2.1 g, 7.6 mmol) in CH_2Cl_2 (20 mL) was added Tf_2O (0.58 mL, 3.45 mmol) and the mixture was stirred for 15 min. Then the above solution was cannulated into the pyridine salt of **25B** and the resulting mixture was stirred for 30 min. A solution of 4-phenylpiperidine (1.1 g, 6.9 mmol) and Et_3N (4.2 mL, 15.2 mmol) in CH_2Cl_2 (3 mL) was then added into the above mixture slowly at 0 °C and stirred overnight. It was then diluted with CH_2Cl_2, washed by H_2O, brine, dried over Na_2SO_4 and concentrated under vacuum. The resulting residue was purified by flash chromatography (CH_2Cl_2/MeOH) to provide **25C** as brownish oil (300 mg, 17%).

Step 3

ethyl 5-(7-(4-phenylpiperidin-1-ylsulfonyl)-3-(trifluoromethylsulfonyloxy)-quinoxalin-2-yl)pentanoate

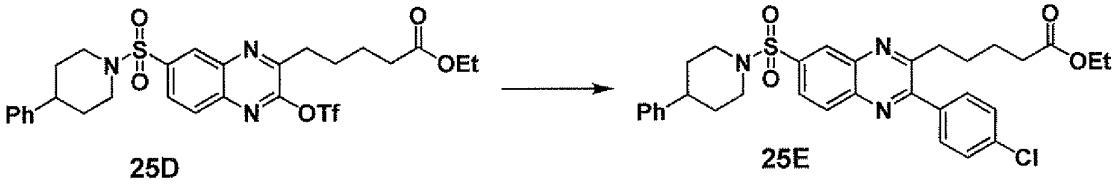


25C 25D

[00297] A mixture of **25C** (300 mg, 0.6 mmol), $PhNTf_2$ (268 mg, 0.75 mmol) and DBU (114 mg, 0.75 mmol) in DMF (6 mL) was stirred overnight. Then it was diluted with EtOAc, washed by H_2O, brine, dried over Na_2SO_4 and concentrated under vacuum. The resulting residue was purified by flash chromatography (EtOAc/hexane) to provide **25D** as colorless oil (170 mg, 45%).

Step 4

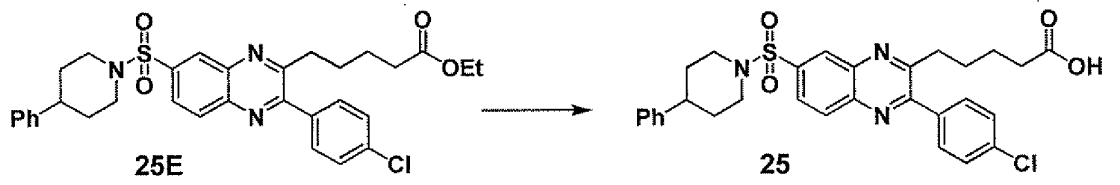
ethyl 5-(3-(4-chlorophenyl)-7-(4-phenylpiperidin-1-ylsulfonyl)quinoxalin-2-yl)pentanoate



[00298] To a solution of **25D** (170 mg, 0.27 mmol) in dioxane (6 mL) in a sealed tube was added 4-chlorophenylboronic acid (84 mg, 0.54 mmol), K_3PO_4 (115 mg, 0.54 mmol), and KBr (64 mg, 0.54 mmol) and the mixture was degassed for 5 min. Then $Pd(PPh_3)_4$ (94 mg, 0.08 mmol) was added and the mixture was heated at 80 °C overnight. It was then taken into EtOAc and washed by H_2O, brine and dried over Na_2SO_4, concentrated over vacuum. The resulting residue was purified by flash chromatography (EtOAc/hexane) to provide product **25E** as colorless oil (40 mg, 25%).

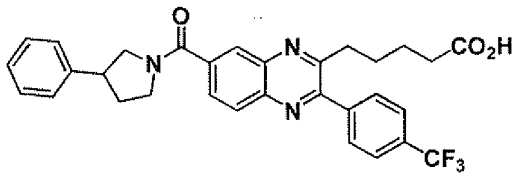
Step 5

5-(3-(4-chlorophenyl)-7-(4-phenylpiperidin-1-ylsulfonyl)quinoxalin-2-yl)pentanoic acid



[00299] A mixture of **25E** (34 mg, 0.057 mmol) and $LiOH{\cdot}H_2O$ (3.6 mg, 0.086 mmol) in THF/H_2O (3:1 v/v, 2.7 mL) was stirred at RT overnight. Then it was acidified by 1N HCl to PH = 5 and concentrated under vacuum. The resulting residue was purified by reverse phase HPLC to provide product **25** as white solid (10 mg). MS (M+H) = 564.

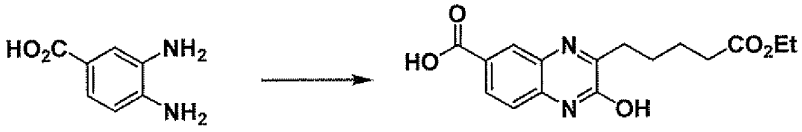
Example 26



26

Step 1

3-(5-Ethoxy-5-oxopentyl)-2-hydroxyquinoxaline-6-carboxylic acid.

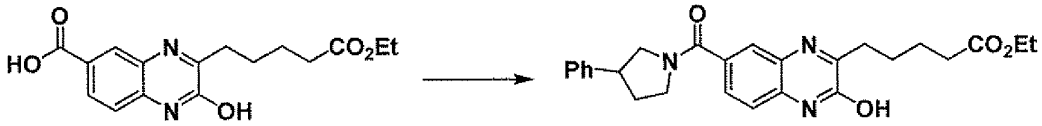


26A

[00300] A suspension of 3,4-diaminobenzoic acid (0.5 g, 3.29 mmol) and diethyl 2-oxoheptane-1,7-dicarboxylate (0.757 g, 3.29 mmol, 1.0 equiv) in 10 mL AcOH/EtOH (1:1) was heated to 100 °C. After 2 h of heating, the reaction mixture was cooled to RT upon which some precipitation occurred. The solid precipitate was filtered, triturated with cold EtOH (2 x 5 mL) and dried to afford 0.35 g of the desired compound **26A** as a brown solid.

Step 2

Ethyl 5-(3-hydroxy-7-(3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)-pentanoate.

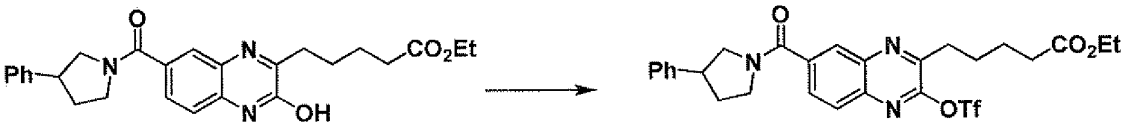


26A 26B

[00301] A mixture of **26A** (0.25 g, 0.785 mmol), 3-phenylpyrrolidine HCl (0.144 g, 0.785 mmol), HATU (0.597 g, 1.57 mmol, 2.0 equiv), and DIPEA (0.273 mL, 1.57 mmol, 2.0 equiv) in 5 mL CH_2Cl_2 was allowed to stir at RT overnight. Upon completion, water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (2 x 10 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (3% MeOH/CH_2Cl_2) to yield 0.2 g of **26B**.

Step 3

Ethyl 5-(7-(3-phenylpyrrolidine-1-carbonyl)-3-(trifluoromethylsulfonyloxy)-quinoxalin-2-yl)pentanoate.

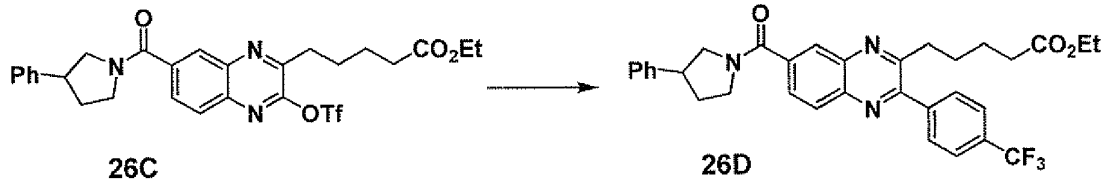


26B 26C

[00302] To a mixture of **26B** (0.1 g, 0.22 mmol) in DMF (3 mL) at 0 °C was added DBU (37 μL, 0.25 mmol, 1.1 equiv). After stirring at that temperature for 30 min was added *N*-phenyl-bis(trifluoromethanesulfonimide) (0.094 g, 0.26 mmol, 1.2 equiv). The reaction was stirred at 0 °C for 1 h after which water (10 mL) was added. The reaction mixture was extracted with EtOAc (2 x 10 mL), washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness. Purification of the crude product by flash chromatography (40% EtOAc/ hexanes) afforded 0.1 g of the desired product **26C** as a pale yellow solid.

Step 4

Ethyl 5-(7-(3-phenylpyrrolidine-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)-quinoxalin-2-yl)pentanoate.



26C 26D

[00303] A mixture of **26C** (100 mg, 0.17 mmol), 4-trifluoromethylbenzene boronic acid (49 mg, 0.26 mmol, 1.5 equiv), $Pd(PPh_3)_4$ (20 mg, 0.017 mmol, 10 mol %) and K_3PO_4 (55 mg, 0.26 mmol, 1.5 equiv) in 2.0 mL of 1,4-dioxane/ H_2O (4:1) was heated to 90 °C for 2 h. After cooling, the reaction mixture was loaded onto a flash column and purified by eluting with 40 % EtOAc/ hexanes to yield 72 mg of compound **26D**.

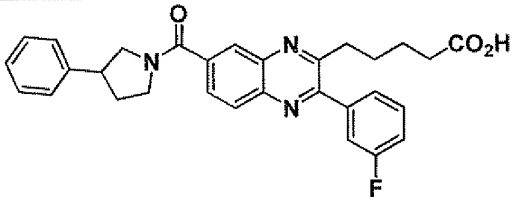
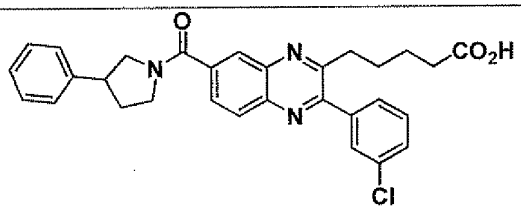
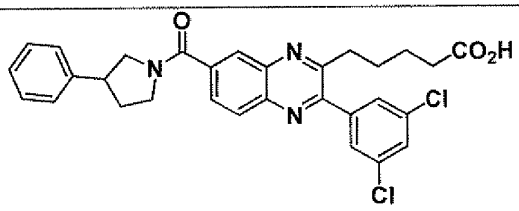
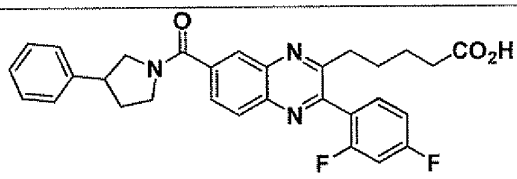
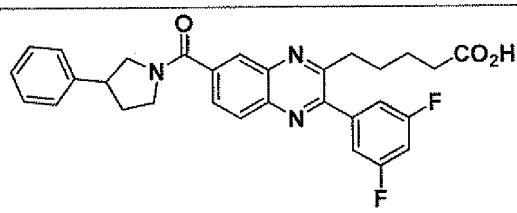
Step 5

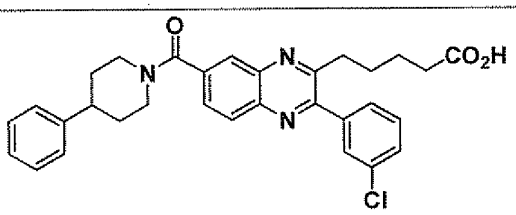
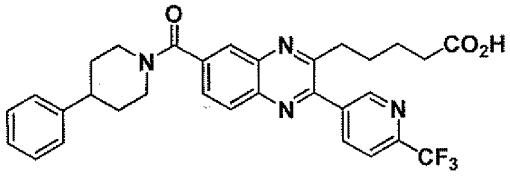
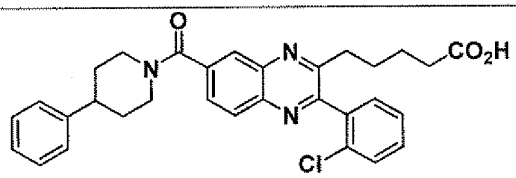
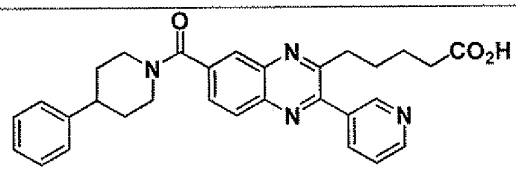
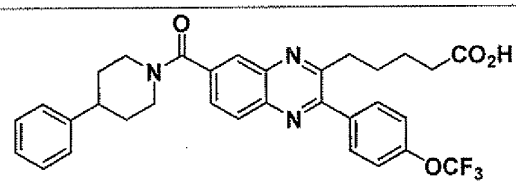
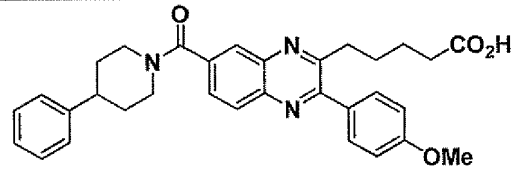
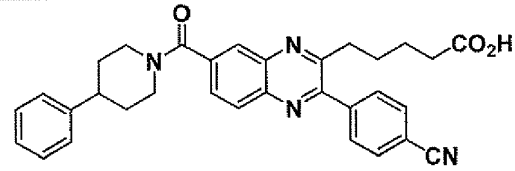
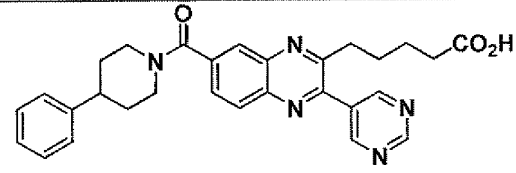
5-(7-(3-Phenylpyrrolidine-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)-quinoxalin-2-yl)pentanoic acid

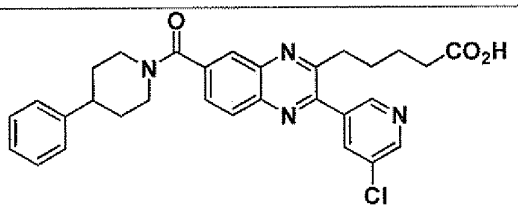
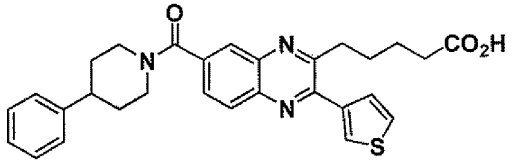
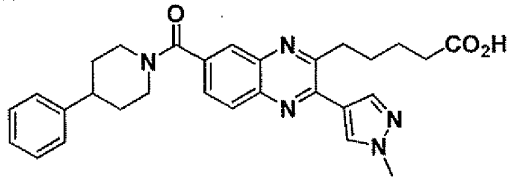
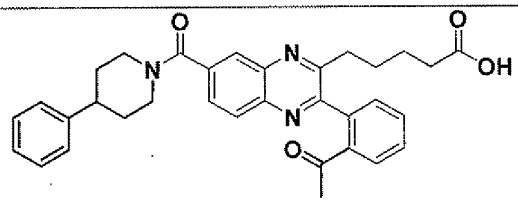
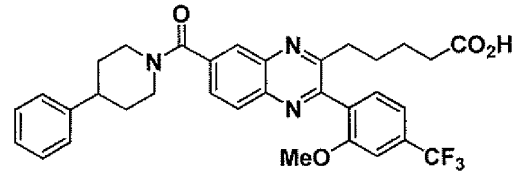
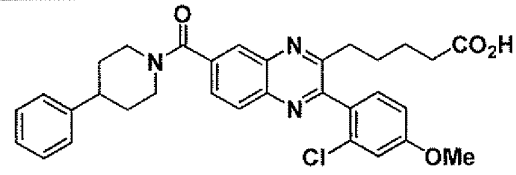
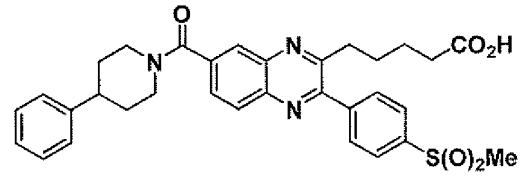
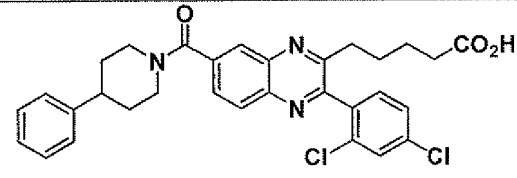
26D 26

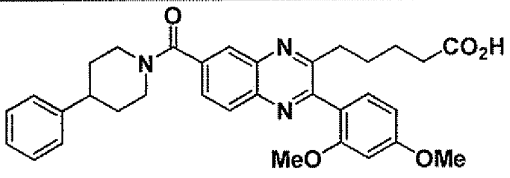
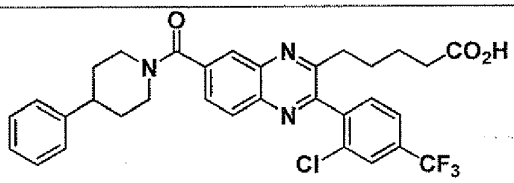
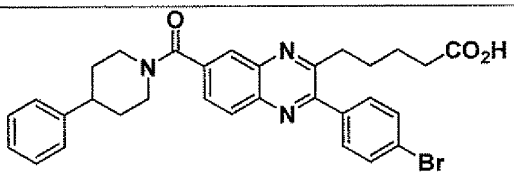
[00304] To a mixture of **26D** (72 mg, 0.13 mmol) in 3 mL THF was added LiOH (22 mg, 0.25 mmol, 4.0 equiv) in 1 mL water. The reaction mixture was heated to 50 °C for 2 h after which another 11 mg of LiOH was added and stirred an additional 30 min. Upon completion, the reaction mixture was neutralized with 4 N HCl, extracted with EtOAc, dried over Na_2SO_4, filtered and concentrated to dryness. Purification by preparative TLC (60% CH_2Cl_2/ 30% hexanes/ 9% MeOH/ 1% AcOH) yielded 25 mg of the desired product **26** as an off white solid. MS (M+H) = 548.

The following compounds were prepared in a similar manner to that described above:

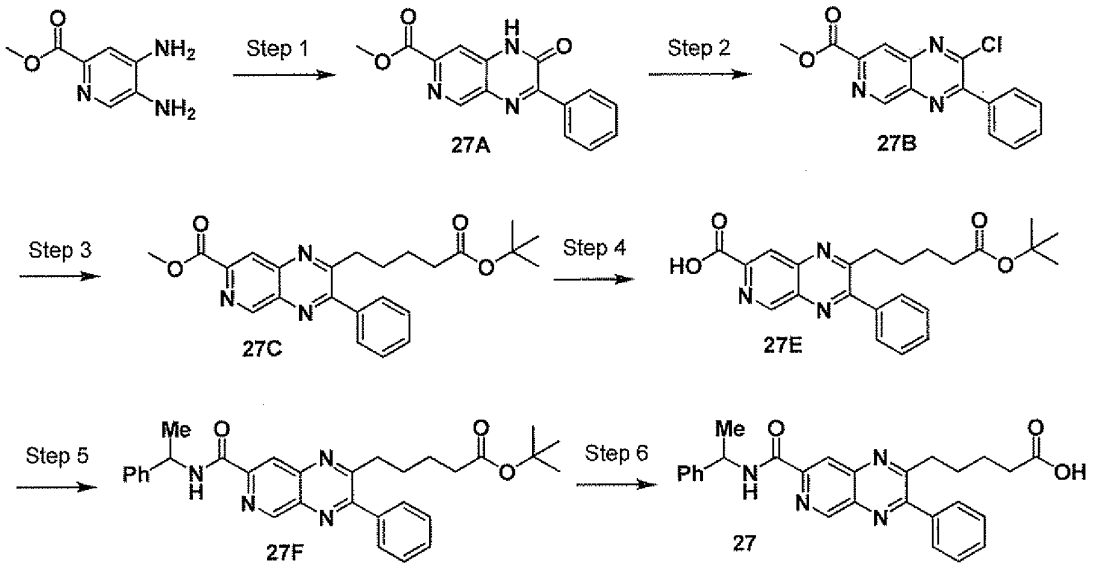
No.	Compound	Name	M+H
26E		3-(3-fluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	498
26F		3-(3-chlorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	514
26G		3-(3,5-dichlorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	548
26H		3-(2,4-difluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	516
26i		3-(3,5-difluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	516

26J		3-(3-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
26K		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[6-(trifluoromethyl)-3-pyridinyl]-2-quinoxalinepentanoic acid	563
26L		3-(2-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
26M		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-(3-pyridinyl)-2-quinoxalinepentanoic acid	495
26N		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethoxy)phenyl]-2-quinoxalinepentanoic acid	578
26o		3-(4-methoxyphenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	524
26P		3-(4-cyanophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	519
26Q		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-(5-pyrimidinyl)-2-quinoxalinepentanoic acid	496

26R		3-(5-chloro-3-pyridinyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	529
26S		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-(3-thienyl)-2-quinoxalinepentanoic acid	500
26T		3-(1-methyl-1H-pyrazol-4-yl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	498
26U		3-(2-acetylphenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	536
26V		3-[2-methoxy-4-(trifluoromethyl)phenyl]-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	592
26W		3-(2-chloro-4-methoxyphenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	558
26X		3-[4-(methylsulfonyl)phenyl]-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	572
26Y		3-(2,4-dichlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	562

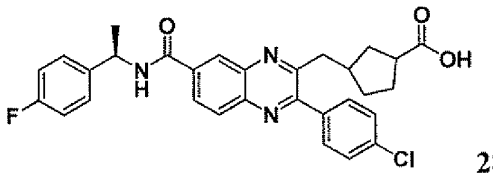
26Z		3-(2,4-dimethoxyphenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	554
26AA		3-[2-chloro-4-(trifluoromethyl)phenyl]-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	596
26AB		3-(4-bromophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	572

Example 27



[00305] In a manner similar to that previously described (*e.g.*, Example 5), 4,5-diaminopyridine-2-carboxylic acid methyl ester (available from 4-amino-5-nitropyridine-2-carboxylic acid methyl ester by hydrogenation on Pd-C) is reacted with 2-oxo-2-phenylacetic. The resulting product **27A** is advanced through the sequence previously described (chlorination with $POCl_3$, coupling with tert-butyl pent-4-enoate, hydrolysis with LiOH, amide coupling with alpha-methylbenzylamine, and deprotection with TFA) to give **27**.

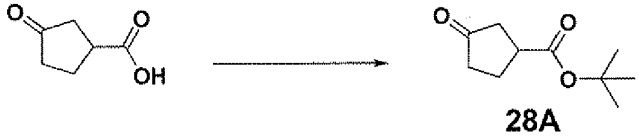
Example 28



28

Step 1

tert-butyl 3-oxocyclopentanecarboxylate

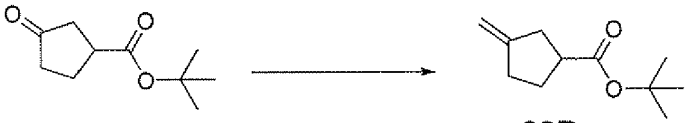


28A

[00306] To a solution of 3-oxocyclopentanecarboxylic acid (11.0 g, 85.9 mmol) in CH_2Cl_2 (200 mL) was added TFAA (23.9 mL, 171.9 mmol) and stirred at RT for 3 h. Then *t*-BuOH (64.4 mL, 687.5 mmol) was added and the reaction was stirred overnight. The mixture was then diluted with CH_2Cl_2 and washed with H_2O and brine, dried (Na_2SO_4), concentrated and purified by flash chromatography to give product **28A** as colorless liquid (10.8 g).

Step 2

tert-butyl 3-methylenecyclopentanecarboxylate

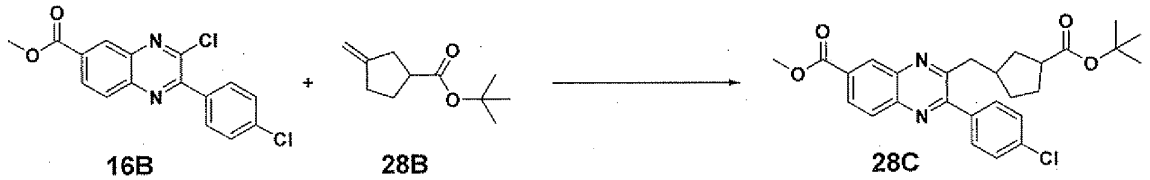


28A 28B

[00307] A mixture of Ph_3PMeBr (35.7 g, 100 mmol) and KOtBu (11.2 g, 100 mmol) in THF (200 mL) was stirred at RT for 3 h, and then was treated with **28A** (9.2 g, 50 mmol). The resulting mixture was stirred at RT overnight, then diluted with EtOAc and washed with H_2O and brine. The organic layer was dried (Na_2SO_4), concentrated and purified by flash chromatography to give product **28B** as colorless liquid (9.5 g).

Step 3

methyl 3-((3-(tert-butoxycarbonyl)cyclopentyl)methyl)-2-(4-chlorophenyl)-quinoxaline-6-carboxylate

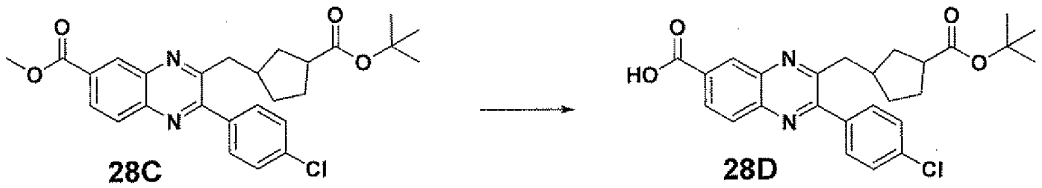


16B 28B 28C

[00308] To a solution of **28B** (2.1 g, 11.3 mmol) in THF (12 mL) was added 9-BBN (28.2 mL, 0.4 M/hexane) and stirred for 3 h at RT. Compound **16B** (1.5 g, 4.5 mmol), $Pd_2(dba)_3$ (103 mg, 0.11 mmol), cataCXium A (161 mg, 0.45 mmol), K_2CO_3 (1.24 g, 9.0 mmol) and H_2O (3 mL) were then added into the above mixture and heated at 80 °C overnight. The reaction was diluted with EtOAc, washed with H_2O, brine, dried (Na_2SO_4), concentrated and purified by flash chromatography to give product **28C** as colorless oil (2.0 g, cis/trans = 3:1).

Step 4

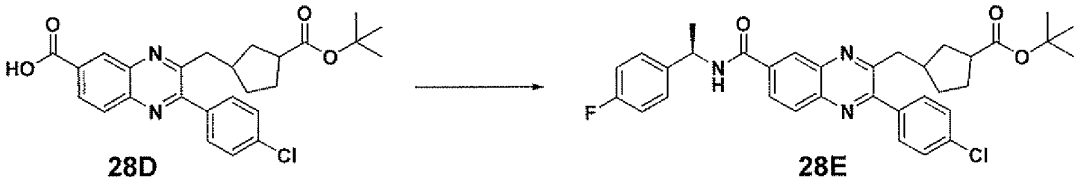
3-((3-(tert-butoxycarbonyl)cyclopentyl)methyl)-2-(4-chlorophenyl)-quinoxaline-6-carboxylic acid



[00309] A mixture of **28C** (440 mg, 0.92 mmol) and LiOH-$_2$O (46 mg, 1.10 mmol) was stirred at RT overnight. Then the reaction was acidified with 1N HCl to pH = 5 and concentrated under reduced pressure to give crude residue, which was purified by HPLC to give product **28D** as colorless oil (429 mg, cis/trans = 3:1).

Step 5

tert-butyl 3-((3-(4-chlorophenyl)-7-((R)-1-(4-fluorophenyl)ethylcarbamoyl)-quinoxalin-2-yl)methyl)cyclopentanecarboxylate

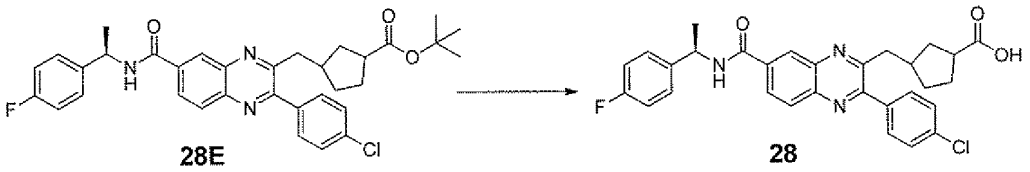


[00310] To a solution of **28D** (429 mg, 0.92 mmol) in DMF (10 mL) was added (R)-1-(4-fluorophenyl)ethanamine (258 mg, 1.84 mmol), HATU (699 mg, 1.84 mmol) and DIPEA (0.32 mL, 1.84 mmol) and the mixture was stirred at RT overnight. Then the reaction was diluted with EtOAc and washed with H_2O, brine, dried (Na_2SO_4), concentrated and purified by flash chromatography to give product **28E** as colorless oil (320 mg, cis/trans = 3:1).

Step 6

3-((3-(4-chlorophenyl)-7-((R)-1-(4-fluorophenyl)ethylcarbamoyl)quinoxalin-2-

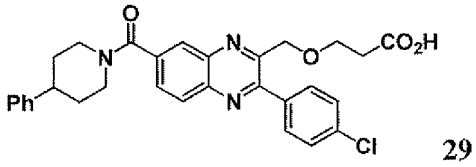
yl)methyl)cyclopentanecarboxylic acid



28E 28

[00311] To a solution of **28E** (320 mg, 0.54 mmol) in CH_2Cl_2 (10 mL) was added TFA (0.84 mL) and the mixture was stirred overnight. The reaction was concentrated under reduced pressure and the residue was purified by HPLC to give product **28** as off-white powder (170 mg, cis/trans = 3:1). LCMS (M + H) = 532.

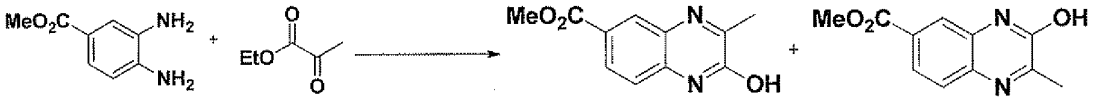
Example 29



29

Step 1

methyl 2-hydroxy-3-methylquinoxaline-6-carboxylate

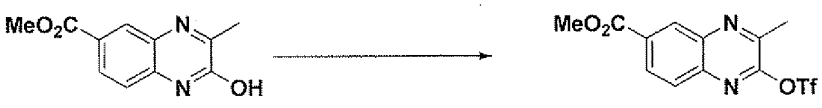


29A 29B

[00312] A suspension of methyl 3,4-diaminobenzoate (5.0 g, 30.09 mmol) and ethyl pyruvate (3.34 mL, 30.09 mmol, 1.0 equiv) in 60 mL AcOH/EtOH (1:1) was heated to 100 °C. After 2 h of heating, the reaction mixture was cooled to RT upon which some precipitation occurred. The solid precipitate was filtered, triturated with cold EtOH (2 x 10 mL) followed by Et_2O (2 x 30 mL) and dried to afford 2.42 g of compound **29B** as a brown solid. To the mother liquor was added 150 mL Et_2O upon which more precipitation occurred. The solid precipitate was filtered, triturated with Et_2O and dried to afford 1.16 g of the desired compound **29A** as a brown solid.

Step 2

methyl 3-methyl-2-(trifluoromethylsulfonyloxy)quinoxaline-6-carboxylate

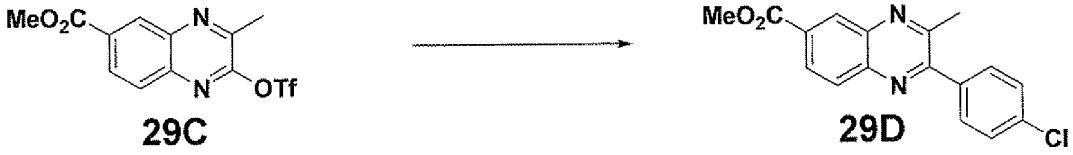


29A 29C

[00313] To a mixture of **29A** (1.81 g, 8.29 mmol) in DMF (30 mL) at 0 °C was added DBU (1.37 mL, 9.12 mmol, 1.1 equiv). After stirring at that temperature for 30 min, *N*-phenyl-bis(trifluoromethanesulfonimide) (3.56 g, 9.95 mmol, 1.2 equiv) was added. The reaction was stirred at 0 °C for 1 h after which water (50 mL) was added. The reaction mixture was extracted with EtOAc (2 x 30 mL), washed with brine, dried over Na_2SO_4, filtered and evaporated to dryness to yield 2.9 g of **29C** as a brown solid. The product was used as such without further purification.

Step 3

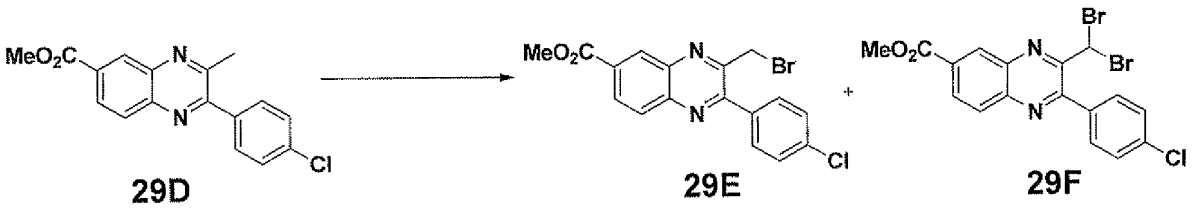
methyl 2-(4-chlorophenyl)-3-methylquinoxaline-6-carboxylate



[00314] A mixture of **29C** (2.9 g, 8.3 mmol), 4-chlorobenzeneboronic acid (1.95 g, 12.45 mmol, 1.5 equiv), $Pd(PPh_3)_4$ (958 mg, 0.83 mmol, 10 mol %) and K_3PO_4 (2.64 g, 12.45 mmol, 1.5 equiv) in 30 mL of 1,4-dioxane/ H_2O (4:1) was heated to 90 °C for 2 h. After cooling, the reaction mixture was concentrated to half its volume, loaded onto a flash column and purified by eluting with 40 % EtOAc/ hexanes to yield 1.49 g of compound **29D**.

Step 4

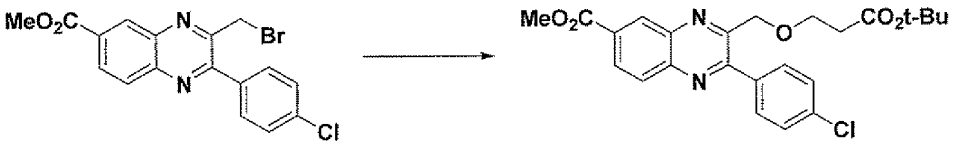
methyl 3-(bromomethyl)-2-(4-chlorophenyl)quinoxaline-6-carboxylate



[00315] To a mixture of **29D** (1.39 g, 4.44 mmol) in 25 mL AcOH was added 1 mL HBr (33% in AcOH) followed by pyridinium tribromide (1.56 g, 4.88 mmol, 1.1 equiv). After all the starting material had been consumed, H_2O (30 mL) was added. The reaction mixture was extracted with Et_2O (2 x 20 mL), dried over Na_2SO_4, filtered and evaporated to dryness to yield a mixture of products. Purification by flash chromatography (5% EtOAc/hexanes) afforded 250 mg of the desired product **29E** as a white powder and 120 mg of **29F**.

Step 5

methyl 3-((3-tert-butoxy-3-oxopropoxy)methyl)-2-(4-chlorophenyl)-quinoxaline-6-carboxylate

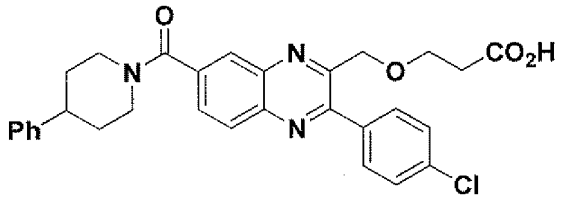


29E **29F**

[00316] To a mixture of NaH (54 mg, 1.35 mmol, 3.0 equiv) in 5 mL THF at 0 °C was added *tert*-butyl 3-hydroxypropionate (200 µL, 1.35 mmol, 3.0 equiv) dropwise. After 30 min, **29E** (175 mg, 0.45 mmol, 1.0 equiv) in THF (3 mL) was added dropwise and the reaction was gradually warmed to RT. After 3 h of stirring, 5 mL of a 0.5 N HCl solution was added. The reaction mixture was extracted with CH_2Cl_2 (2 x 5 mL), dried over Na_2SO_4, filtered and evaporated to dryness. Purification by preparative TLC (20% EtOAc/hexanes) afforded 30 mg of the desired product **29F**.

Steps 6-8

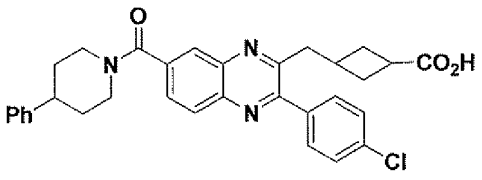
3-((3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)methoxy)propanoic acid



29

[00317] In a manner similar to that previously described, compound **29F** was sequentially treated with LiOH (2 eq., THF- H_2O, 50 °C, 2 h), coupled with 4-phenylpiperidine (HATU, DIPEA, DCM, RT overnight), and then deprotected with TFA to afford the title compound **29**. LCMS (M+H) = 530.

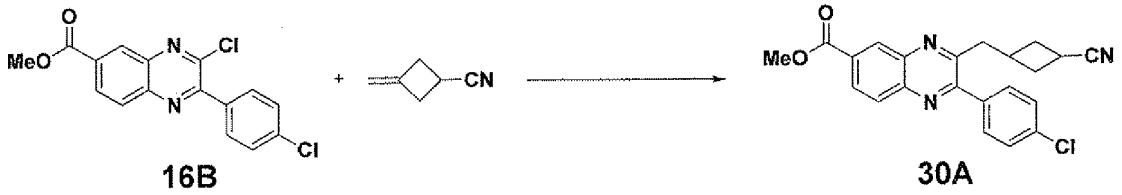
Example 30



30

Step 1

methyl 2-(4-chlorophenyl)-3-((3-cyanocyclobutyl)methyl)quinoxaline-6-carboxylate

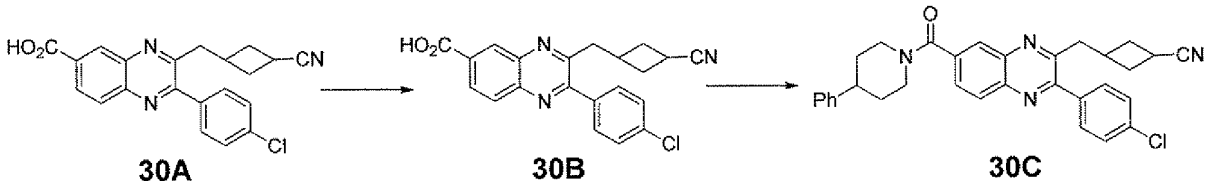


16B 30A

[00318] A stirred solution of 3-methylenecyclobutanecarbonitrile (0.218 g, 2.34 mmol, 1.5 equiv) in THF (1 mL) under nitrogen was cooled to 0 °C. 9-BBN (0.5 N in THF, 5.62 mL, 2.81 mmol, 1.8 equiv) was added and the solution was heated to 60 °C for 3 h. After this time, the reaction mixture was cooled to RT and methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate **16B** (520 mg, 1.56 mmol), $Pd(dppf)_2Cl_2.CH_2Cl_2$ (255 mg, 0.312 mmol, 20 mol %) and K_3PO_4 (993 mg, 4.68 mmol, 3.0 equiv) were added. The reaction mixture was degassed and was heated at 60 °C under nitrogen for 12 h. After this time, the reaction was cooled to room temperature and diluted with water and CH_2Cl_2. The aqueous layer was separated and extracted with CH_2Cl_2 (2 x 15 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (10-15% EtOAc/hexanes) to yield 256 mg of the desired product **30A**.

Steps 2-3

3-((3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclobutanecarbonitrile

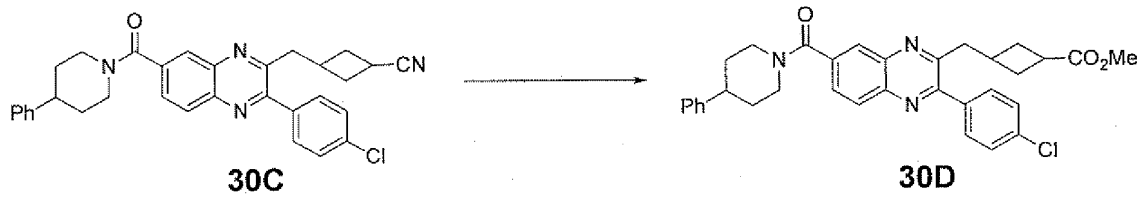


30A 30B 30C

[00319] In a manner similar to that previously described, **30A** was hydrolyzed with LiOH (2 eq, THF-H_2O, 3h, RT) and then coupled with 4-phenylpiperidine (1 eq., 2 eq. HATU, 2 eq. DIPEA, DCM, overnight, RT) to provide **30C**.

Steps 4-5

3-((3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclobutanecarboxylic acid

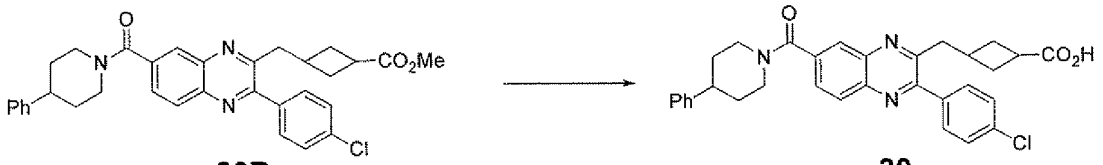


30C 30D

[00320] To a solution of **30C** (150 mg, 0.29 mmol) in 5 mL MeOH was passed HCl (g) at 0 °C. After 3 min of passing, the reaction mixture was allowed to stir at room temperature for 1 h. The excess solvent and HCl was concentrated, diluted with H_2O and extracted with CH_2Cl_2 (2 x 10 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (20-30% EtOAc/hexanes) to yield 50 mg of the desired product **30D**.

Step 6

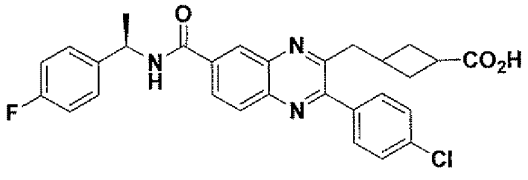
3-((3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclobutanecarboxylic acid



30D **30**

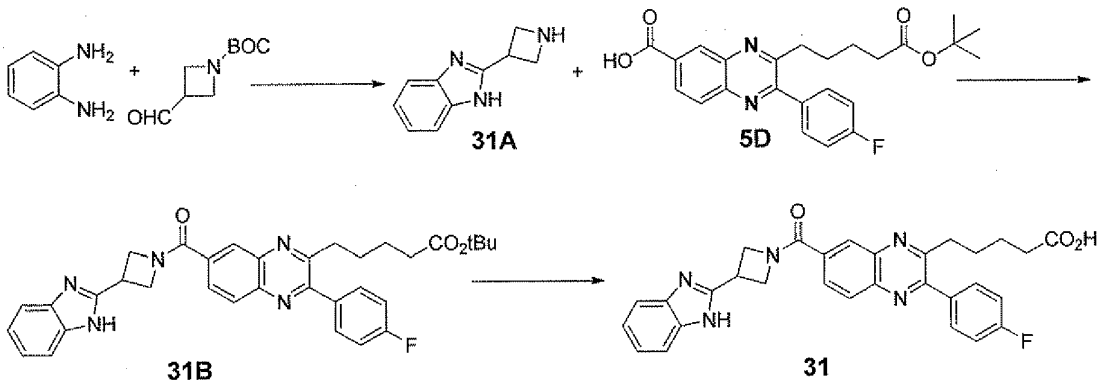
[00321] To a mixture of **30D** (50 mg, 0.09 mmol) in 2 mL THF was added $LiOH.H_2O$ (15 mg, 0.36 mmol, 4.0 equiv) in 1 mL water. The reaction mixture was heated to 50 °C for 2h. Upon completion, the reaction mixture was neutralized with 2 N HCl, extracted with CH_2Cl_2 (2 x 5 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The crude product was purified by preparative TLC (60% CH_2Cl_2/30% hexanes/9% MeOH/1% AcOH) to yield 44 mg of the desired product **30**. LCMS (M+H) = 540.

[00322] Compound **30E** was prepared analogous manner using (R)-1-(4-fluorophenyl)ethanamine in Step 3. LCMS (M+H) = 518.



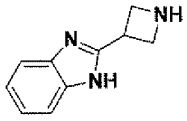
30E

Example 31



Step 1

2-(azetidin-3-yl)-1H-benzo[d]imidazole

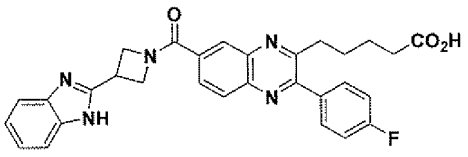


31A

[00323] To a solution of compound 1,2-phenylenediamine (1.0g, 9.25mmol) and 1-Boc-3-azetidinecarboxaldehyde (2.1g, 11.10mmol) in 60 mL of IPA was added Pd/C (10%, 0.8g). After heating at 80 °C for 2h, the mixture was cooled down to RT, filtered through the CELITE, concentrated and purified (2.1g). The product was treated with 4N HCl (8 mL) in 1,4-dioxane (20 mL) to give 2g of compound **31A** (Yield = 83%).

Step 2

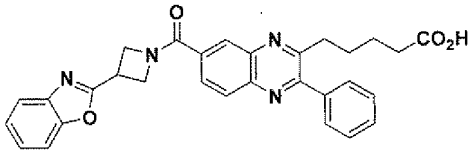
5-(7-(3-(1H-benzo[d]imidazol-2-yl)azetidine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid



31

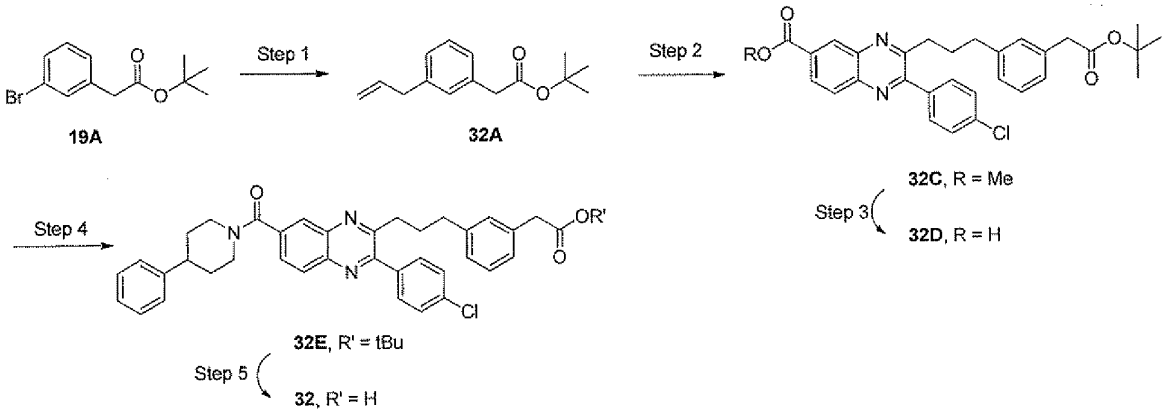
[00324] To a solution of compound **31A** (0.11g, 0.46mmol) and **5D** (0.13g, 0.31mmol) in 5mL of DCM was added DEC (0.088g, 0.46mmol), HOBT (0.062g, 0.046mmol), and DIEA (0.16 mL, 0.93mmol). After stirring at RT for 20h, the mixture was extracted with DCM and saturated $NaHCO_3$ (aq), dried over Na_2SO_4, concentrated and purified (0.063g). The product **31B** was deprotected with 0.5 mL of TFA in 5 mL of DCM to give the title compound **31** (0.051g). MS (M+H) = 524.

[00325] Compound **31C** was prepared analogous manner using 2-aminophenol in Step 1. MS (M+H) = 507.



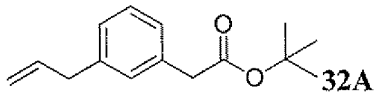
31C

Example 32



Step 1

***tert*-Butyl 2-(3-allylphenyl)acetate**

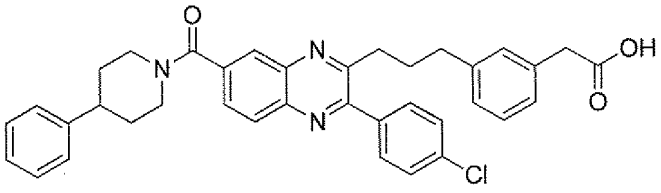


32A

[00326] To a solution of **19A** (2.0 g, 7.38 mmol) in toluene (20 mL) was added allyltri-n-butyltin (2.382 mL, 9.59 mmol), and $Pd(Ph_3P)_4$ (0.852 g, 0.738 mmol). The reaction mixture was degassed and heated at 90 °C overnight under a nitrogen atmosphere. The mixture was diluted with EtOAc and washed with H_2O. Potassium fluoride (10 g, 172 mmol) and 200 mL of H_2O was added to the organic mixture and the mixture was stirred for 1.5 h. The layers were split and filtered the solids through CELITE, dried over $MgSO_4$, filtered and concentrated. The concentrate was purified by flash chromatography (over 120 g of silica gel) in 0-10% Et_2O in hexanes to yield 1.24 g (73% yield) of **19B**.

Step 2-5

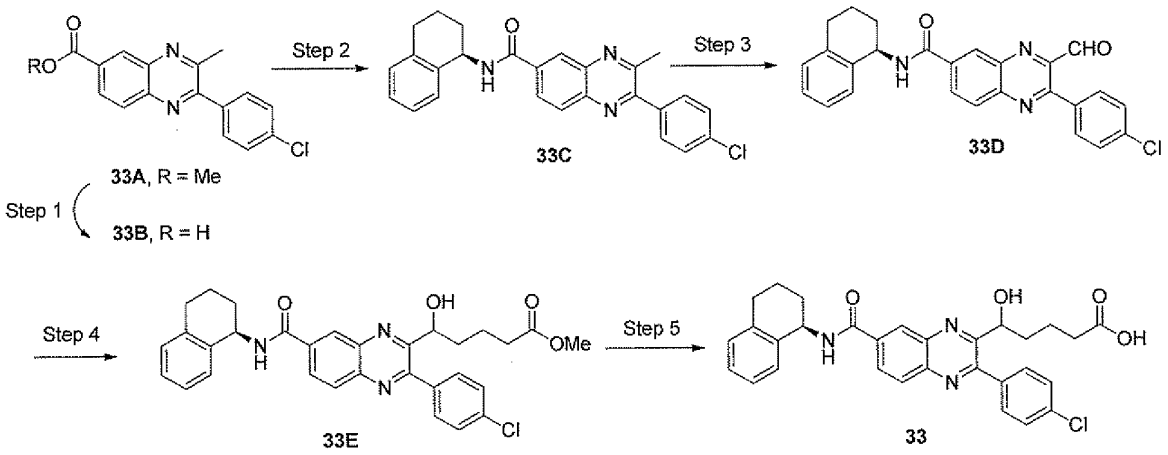
2-(3-(3-(3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)propyl)phenyl)acetic acid



32

[00327] In a manner similar to that previously described, **19B** was coupled with methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate (**16B**) and hydrolyzed with LiOH. The resulting acid **32D** was coupled with 4-phenylpiperidine and deprotected with TFA to provide **32**. MS (M+H) = 604.

Example 33



Step 1-2

(R)-2-(4-chlorophenyl)-3-methyl-N-(1,2,3,4-tetrahydronaphthalen-1-yl)quinoxaline-6-carboxamide

[00328] In a manner similar to that previously described, **33A** was hydrolyzed with LiOH and coupled with (*R*)-tetrahydronaphthalen-1-amine to provide **33C**.

Step 3

(*R*)-2-(4-chlorophenyl)-3-formyl-*N*-(1,2,3,4-tetrahydronaphthalen-1-yl)quinoxaline-6-carboxamide

[00329] To **33C** (50 mg, 0.117 mmol) in dioxane (1 mL) was added selenium dioxide (19.45 mg, 0.175 mmol) in a sealed tube. The mixture was heated at 100 °C for 12 h. After cooling, the excess solvent was concentrated and the reaction mixture was purified by preparative TLC eluting with 3:1 Hex/EtOAc, then 2:1 Hex/EtOAc to yield 49 mg of **33D**.

Step 4

methyl 5-(3-(4-chlorophenyl)-7-(((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-hydroxypentanoate

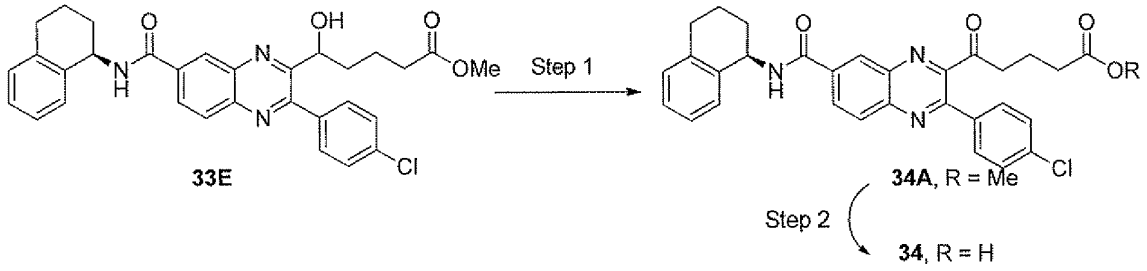
[00330] To **33D** (246 mg, 0.557 mmol) and CuCN (4.99 mg, 0.056 mmol) in DCM (5 mL) was added 4-ethoxy-4-oxobutylzinc bromide in THF (3.34 mL, 1.670 mmol). The reaction was stirred at 22 °C overnight, after which it was quenched with water and 1 N hydrochloric acid (1 mL) and extracted with ethyl acetate and with dichloromethane. The combined organics was dried over $MgSO_4$, filtered and concentrated. Purification by flash chromatography (over 80 g of silica gel) in 0-25-50 % EtOAc in hexanes afforded 59 mg (yield =19%) of **33E**.

Step 5

5-(3-(4-chlorophenyl)-7-(((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-hydroxypentanoic acid

[00331] To **33E** (10.1 mg, 0.018 mmol) in THF (0.1 mL), Water (0.100 mL), and MeOH (0.100 mL) was added LiOH (3.04 mg, 0.072 mmol). The reaction was stirred at 22 °C for 3 h. The mixture was quenched with water, acidified with 1 N HCl to pH<1 and extracted with dichloromethane. The combined organics was dried over $MgSO_4$, filtered and concentrated. The mixture was purified by preparative TLC in 10:1 DCM/MeOH to obtain 3.0 mg (yield=29%) of desired product **2**. MS (M+H) = 530.

Example 34



Step 1

(*R*)-methyl 5-(3-(4-chlorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-oxopentanoate

[00332] To **33E** (50 mg, 0.090 mmol) in DCM (1 mL) was added Dess-Martin periodinane (76 mg, 0.179 mmol). The reaction mixture was stirred at 22 °C overnight. After

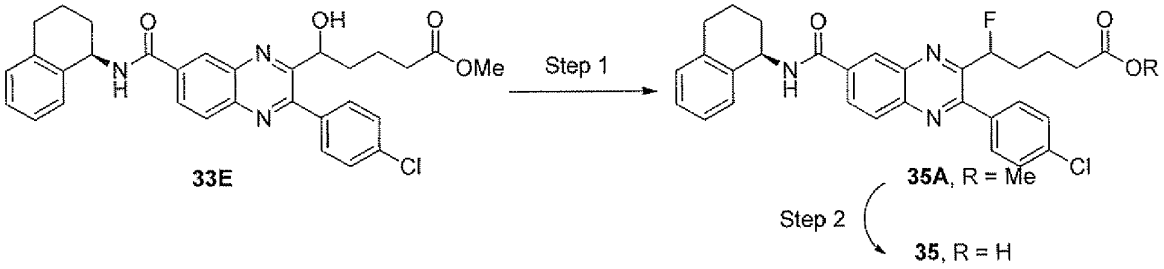
MS indicated the reaction was complete, the mixture was loaded on a 1 mm preparative TLC plate and eluted with 2:1 Hex/EtOAc twice to yield 13 mg (26% yield) of **34A**.

Step 2

(*R*)-5-(3-(4-chlorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-oxopentanoic acid

[00333] To **34A** (13.0 mg, 0.023 mmol) in THF (0.3 mL), MeOH (0.300 mL), and water (0.300 mL) was added LiOH (3.92 mg, 0.094 mmol). The reaction was stirred at 22 °C and purified by preparative TLC in 10:1 DCM/MeOH to obtain 5.0 mg (41% yield) of product **34**. MS (M+H) = 528.

Example 35



Step 1

methyl 5-(3-(4-chlorophenyl)-7-(((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-fluoropentanoate

[00334] To **33E** (40 mg, 0.072 mmol) in dichloroethane (1 mL) was added DAST (0.024 mL, 0.179 mmol). The reaction mixture was stirred at 22 °C overnight. The reaction was quenched with aqueous ammonium chloride and extracted with dichloromethane. The combined organics was dried over $MgSO_4$, filtered and concentrated. The mixture was purified on a 1 mm preparative TLC plate in 2:1 Hex/EtOAc to yield 38 mg of **35A**.

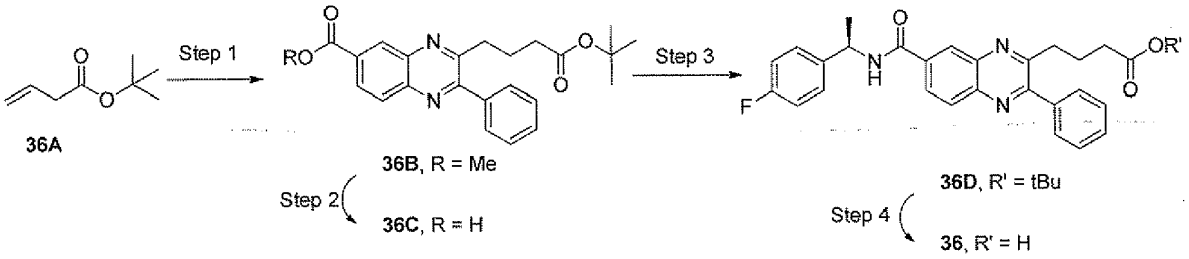
Step 2

5-(3-(4-chlorophenyl)-7-(((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-5-fluoropentanoic acid

[00335] To **35A** (38.7 mg, 0.069 mmol) in THF (0.3 mL), MeOH (0.300 mL) and water (0.300 mL) was added LiOH (11.60 mg, 0.276 mmol). The mixture was stirred at 22 °C for 2 h. The reaction was quenched with water and hydrochloric acid and extracted with dichloromethane. The combined organics were dried over $MgSO_4$, filtered and concentrated.

The mixture was purified by preparative TLC in 10:1 DCM/MeOH to yield 2.5 mg of **35**. MS (M+H) = 532.

Example 36

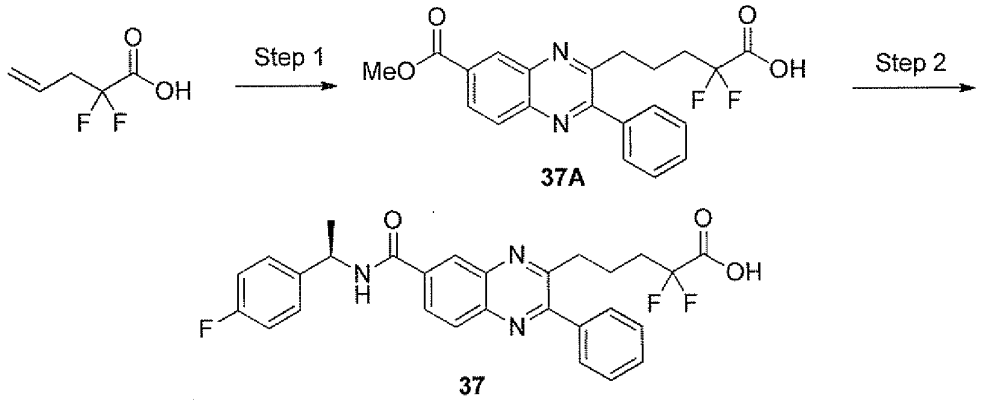


Steps 1-4

(*R*)-4-(7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)butanoic acid

[00336] In a manner similar to that previously described, **36A** was coupled with methyl 3-chloro-2-phenylquinoxaline-6-carboxylate (**6B**) and hydrolyzed with LiOH. The resulting acid **36C** was coupled with (*R*)-1-(4-fluorophenyl)ethanamine to provide **36D** which was deprotected with TFA to provide **36**.

Example 37



Step 1

2,2-difluoro-5-(7-(methoxycarbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid

[00337] 9-Borabicyclo[3.3.1]nonane (32.6 mL, 16.32 mmol) was added to a stirred, cooled 0 °C mixture of 2,2-difluoropent-4-enoic acid (1.110 g, 8.16 mmol) and the mixture was stirred at 0 °C for 30 min. before it was warmed to room temperature and stirred for overnight. Reactant **6B** (1.4 g, 4.08 mmol), butyl di-1-adamantylphosphine (0.117 g, 0.326 mmol), potassium phosphate tribasic (1.732 g, 8.16 mmol) and tris(dibenzylideneacetone)dipalladium(0) chloroform adduct (0.084 g, 0.082 mmol) were dissolved in H_2O (13.60 mL) and THF (27.2

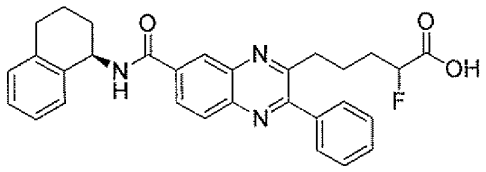
mL). The solution was added to the 9-BBN adduct and stirred at 80 °C under nitrogen for 1 h. The mixture was cooled, diluted with ethyl acetate (30 mL), washed with hydrochloric acid (1 M, 1x 20 mL), dried (Na_2SO_4), filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (50 g silica gel), eluting with EtOAc/Hexanes (10% to 80%) to give **37A** as a yellow foam. MS (M+H) = 508.

Step 2

(*R*)-2,2-difluoro-5-(7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid

[00338] Isopropylmagnesium chloride (281 µl, 0.562 mmol) was added to a stirred, cooled 0 °C mixture of (*R*)-1-(4-fluorophenyl)ethylamine (31.3 mg, 0.225 mmol) and **6A** (45 mg, 0.112 mmol) in THF (1124 µl) and the mixture was stirred at room temperature for overnight. The reaction was quenched by NH_4Cl and worked up. The residue was purified by preparative HPLC Reverse phase (C-18), eluting with Acetonitrile/Water + 0.1% TFA, to give 20 mg (34% yield) of **37** as an orange solid.

Example 38

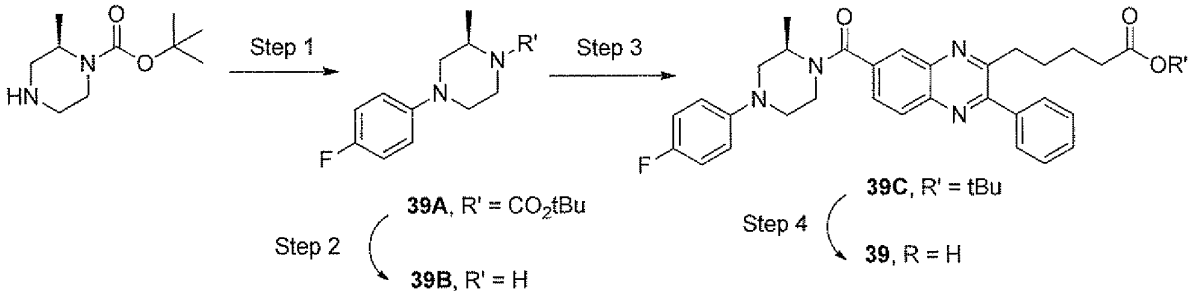


38 (racemic)
38A (1st eluting enantiomer)
38B (2nd eluting enantiomer)

[00339] In a manner similar to that described previously (Step 3), ethyl 2-fluoropent-4-enoate (prepared from allyl iodide of ethyl fluoroacetate, NaH, and allyl iodide in HMPA and benzene, 80 °C, 12 h as described in *J. Am. Chem. Soc.* **2003**, *125*, 15521, S-21) was sequentially reacted with 9-BBN and **6B** to provide the desired ethyl ester, which was subsequently treated with LiOH to afford 2-fluoro-5-(3-phenyl-7-(((*R*)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid (**38**, LCMS, M+H = 498).

[00340] The enantiomers of **38** were separated by supercritical fluid chromatography (AD column, injected in MeOH, 55%MeOH co-solvent and 45% CO_2) to provide **38A** (LCMS, M+H = 498) and **38B.** MS (M+H) = 498.

Example 39



Step 1

(*R*)-tert-butyl 4-(4-fluorophenyl)-2-methylpiperazine-1-carboxylate

[00341] A mixture of (*R*)-tert-butyl 2-methylpiperazine-1-carboxylate (1.7 g, 8.49 mmol), 1-bromo-4-fluorobenzene (1.63 g, 9.34 mmol, 1.1 eq), $Pd_2(dba)_3$ (0.78 g, 0.85 mmol, 0.1 eq), P(*t*Bu)$_3$ (0.343 g, 1.70 mmol, 0.2 eq) and *t*-BuOK (0.952 g, 8.49 mmol, 1.0 eq) in toluene (8.0 mL) under nitrogen atmosphere was heated to 110 °C for 1 h in a microwave. After the reaction was complete, the mixture was diluted with water (100 mL) and extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and evaporated to dryness. The crude reaction mixture was purified by column chromatography eluting with 10-20% EtOAc/hexanes to yield 1.9 g of **39A**.

Step 2

(*R*)-1-(4-fluorophenyl)-3-methylpiperazine

[00342] To a solution of **39A** (1.9 g, 6.45 mmol) in CH_2Cl_2 (10 mL) was added TFA (3.0 mL, 38.7 mmol, 6.0 eq) and the reaction was stirred at room temperature for 2 h. After reaction was complete, the excess TFA was concentrated to yield product **39B** which was used as such without any further purification.

Step 3

(*R*)-tert-butyl 5-(7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoate

[00343] To a flask containing the carboxylic acid **6D** (2.2 g, 5.41 mmol) in CH_2Cl_2 (40 mL) was added (*R*)-1-(4-fluorophenyl)-3-methylpiperazine (1.16 g, 5.95 mmol, 1.1 eq), Hunig's base (3.75 mL, 21.65 mmol, 4.0 eq) and HATU (4.12 g, 10.82 mmol, 2.0 eq). The mixture was stirred at ambient temperature overnight after which the mixture was concentrated and purified by flash chromatography (10-30% EtOAc/hexanes) to yield 2.3 g of **39C** (69% yield).

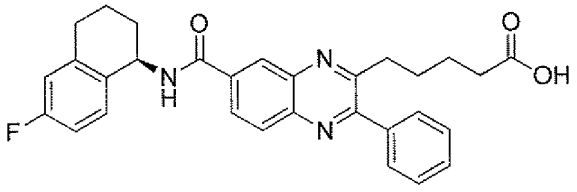
Step 4

(*R*)-5-(7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid

[00344] To a solution of **39C** (2.3 g, 3.95 mmol) in CH_2Cl_2 (10 mL) was added TFA (1.83 mL, 23.68 mmol, 6.0 eq), and the reaction was stirred at room temperature for 2 h. After the reaction was complete, the excess TFA was concentrated to yield product **39** which was purified by column chromatography eluting with 2-4% MeOH/CH_2Cl_2 to yield 1.9 g of desired product **39**. ^{1}H NMR (DMSO, 500 MHz) δ 8.16 (d, 1 H, J = 8.5 Hz), 8.08 (s, 1 H), 7.82 (dd, 1 H, J = 1.5 Hz, J = 8.5 Hz), 7.71-7.69 (m, 2 H), 7.60-7.57 (m, 3 H), 7.08 (t, 2 H, J = 9 Hz), 7.00-6.97 (m, 2 H), 3.61-3.36 (m, 3 H), 3.03 (t, 2 H, J = 7.5 Hz), 2.91 (d, 1 H, J = 9.5 Hz), 2.72 (dt, 1 H, J = 2.5 Hz, J = 11.5 Hz, J = 14.5 Hz), 2.47 (m, 2 H), 2.16 (t, 2 H, J = 7 Hz), 1.74-1.70 (m, 2 H), 1.51-1.46 (m, 2 H), 1.42-1.32 (m, 3 H). MS (M+H) = 527.

Example 40

(*R*)-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid

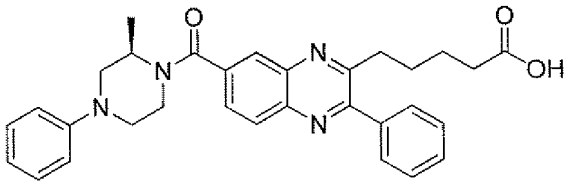


40

[00345] In a manner similar to that previously described, **6C** was hydrolyzed with LiOH. The resulting acid **6D** was coupled with (*R*)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-amine and deprotected with TFA to provide **40.** ^{1}H NMR (DMSO, 500 MHz) δ 11.97 (s, 1 H), 9.17 (d, 1 H, J = 8.5 Hz), 8.65 (d, 1 H, J = 2 Hz), 8.28 (dd, 1 H, J = 1.5 Hz, J = 8.5 Hz), 8.13 (d, 1 H, J = 9 Hz), 7.71-7.69 (m, 2 H), 7.58-7.56 (m, 2 H), 7.30 (t, 1 H, J = 7 Hz), 7.02-6.98 (m, 2 H), 5.28 (q, 1 H, J = 7 Hz, J = 12 Hz), 3.02 (t, 2 H, J = 7.5 Hz), 2.86-2.75 (m, 2 H), 2.15 (t, 2 H, J = 7 Hz), 2.03-1.97 (m, 2 H), 1.94-1.87 (m, 1 H), 1.80-1.71 (m, 3 H), 1.51-1.45 (m, 2 H). MS (M+H) = 498.

Example 41

(*R*)-5-(7-(2-methyl-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid

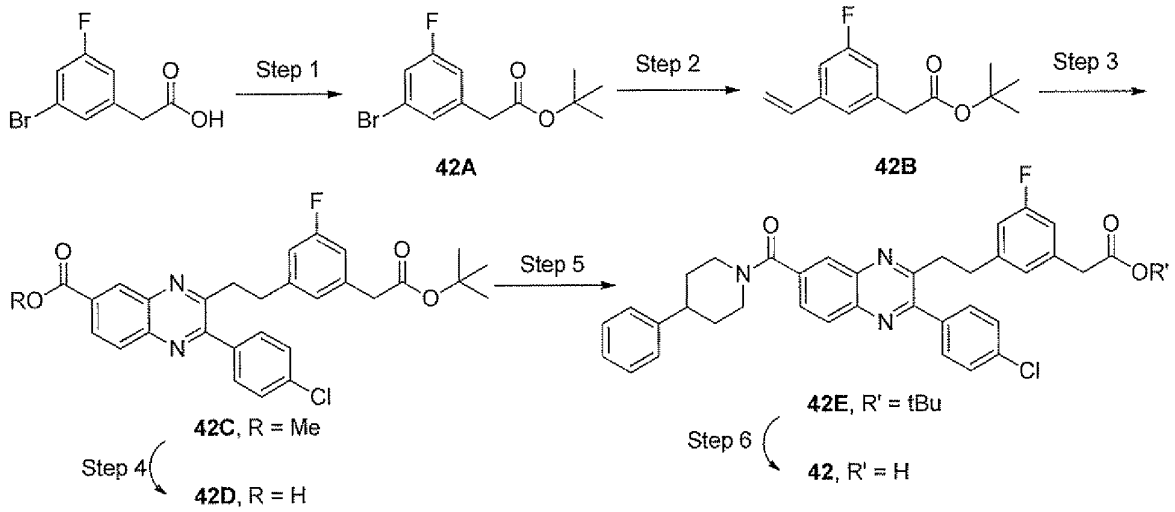


41

[00346] In a manner similar to that previously described, **6C** was hydrolyzed with LiOH. The resulting acid **6D** was coupled with (*R*)-3-methyl-1-phenylpiperazine and deprotected with TFA to provide **41**. ^{1}H NMR (DMSO, 500 MHz) δ 8.16 (d, 1 H, *J* = 8.5 Hz), 8.08 (d, 1 H, *J* = 1.5 Hz), 7.82 (dd, 1 H, *J* = 2 Hz, *J* = 8.5 Hz), 7.71-7.69 (m, 2 H), 7.59-7.57 (m, 3 H), 7.26-7.22 (m, 2 H), 6.96 (d, 2 H, *J* = 8 Hz), 6.82 (t, 1 H, *J* = 7 Hz), 3.71-3.49 (m, 3 H), 3.03 (t, 2 H, *J* = 7.5 Hz), 2.98-2.92 (m, 1 H), 2.76 (dt, 1 H, *J* = 3.5 Hz, *J* = 12 Hz, *J* = 15.5 Hz), 2.44 (m, 2 H), 2.16 (t, 2 H, *J* = 7.5 Hz), 1.76-1.70 (m, 2 H), 1.51-1.45 (m, 2 H), 1.43-1.30 (m, 3 H). MS (M+H) = 509.

Example 42

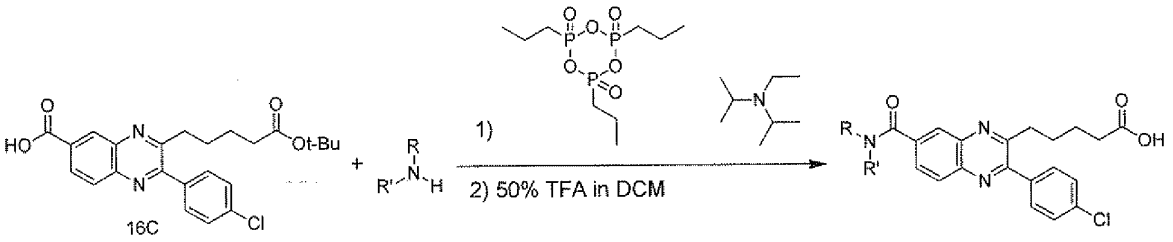
2-(3-(2-(3-(4-chlorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid



[00347] In a manner similar to that previously described for compound **19**, 3-bromo-5-fluorophenylacetic acid was reacted with TFAA and *t*-BuOH to provide *tert*-butyl 2-(3-bromo-5-fluorophenyl)acetate **42A** and coupled with potassium vinyltrifluoroborate to afford **42B**. The resulting vinyl compound **42B** was coupled with methyl 3-chloro-2-(4-chlorophenyl)quinoxaline-6-carboxylate (**16B**) and hydrolyzed with LiOH. The resulting acid **42D** was coupled with 4-phenylpiperidine and deprotected with TFA to provide **42** (LCMS, M+H = 608).

Example 43

Parallel Preparation of Compounds Bearing a 4-Chlorophenyl R^2 Substituent from Compound 16C



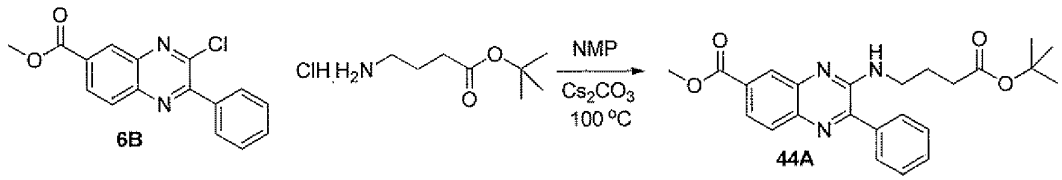
[00348] Into twenty-four 2 dram vials were added the amines (R')(R)NH (0.044 mmol), followed by a DCM (1.0 mL) solution of 3-(5-*tert*-butoxy-5-oxopentyl)-2-(4-chlorophenyl)quinoxaline-6-carboxylic acid **16C** (15.0 mg, 0.034 mmol) and DIEA (24 μL, 0.137 mmol). The mixtures shaken at room temperature for 5 min., then 1-propanephosphonic acid cyclic anhydride (50% w/w in EtOAc) (30.0 μL, 0.050 mmol) was added, and then the vials were capped and shaken at room temperature overnight.

[00349] Trifluoroacetic acid (50%) in DCM (1.0 mL, 6.49 mmol) was then added to each of the vials. The vials were then recapped and shaken at room temperature for 2 hrs. The solvent was then concentrated *in vacuo* from each vial.

[00350] DMSO (1.0 mL) was then added to each of the vials. The vials were sonicated until all were in solution, and the DMSO solutions passed through a filter plate under vacuum into a deep-well plate and purified by reverse-phase chromatography.

Example 44

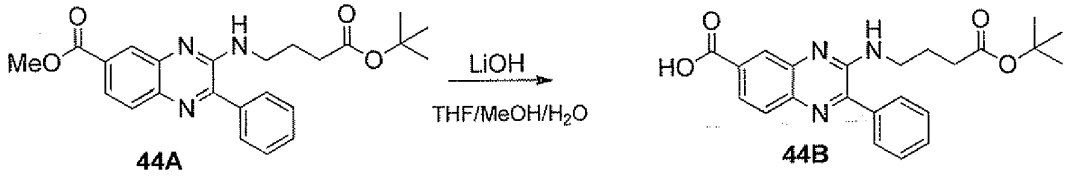
Step 1



[00351] To the mixture of compound **6B** (8.6 g, 28.8 mmol) in *N*-methyl-2-pyrrolidinone (50 mL), H-gamma-ABU-OtBu HCl salt (7.04 g, 36.0 mmol), and Cs_2CO_3 (23.45 g, 72.0 mmol) was stirred and heated to 100 °C for 16 hours. The reaction mixture was worked up with ethyl acetate (200 mL) and brine (150 mL x 3) to give a brown paste. The paste was separated by

flash chromatography (220 g silica gel) eluting with 10~20% EtOAc/Hexanes to give compound **44A** (10.5 g, 82%).

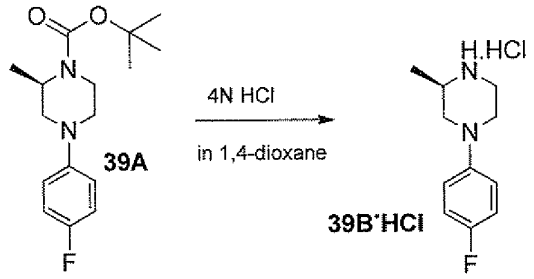
Step 2



44A 44B

[00352] The mixture of **44A** (10.3 g, 24.4 mmol) in THF/MeOH/H_2O (50 mL, 2:2:1) and LiOH-H_2O (2.05 g, 48.9 mmol) was stirred at RT for 2 hours. The reaction mixture was neutralized with 1 N HCl, extracted with CH_2Cl_2 (100 mL x 2). The organic solution was dried (Na_2SO_4) and concentrated to give compound **44B** (9.4 g, 76 %).

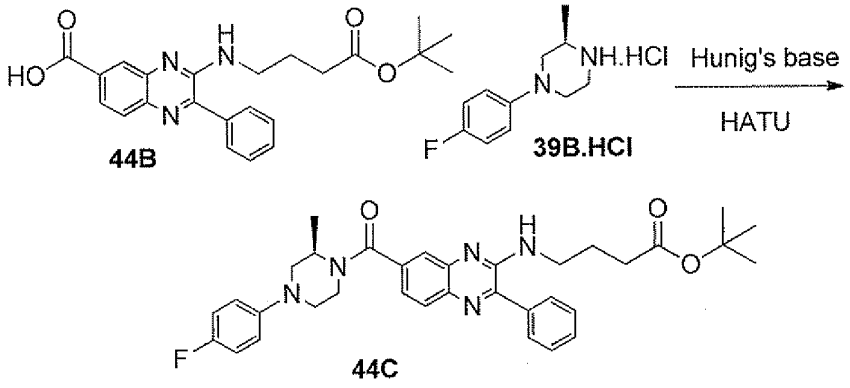
Step 3



39A 39B·HCl

[00353] A mixture of **39A** (0.95 g, 3.23 mmol) in dichloromethane (2 mL) and 4 N HCl in 1,4-dioxane (4.03 mL. 16.14 mmol) was stirred at room temperature for 2 hours. The excess HCl and solvents were removed *in vacuo* to give 0.74 g compound **39B·HCl** (0.74 g, 99%).

Step 4

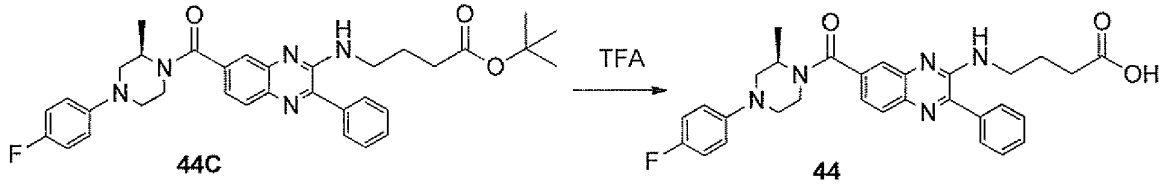


44B 39B.HCl 44C

[00354] The mixture of compound **44B** (2.0 g, 4.91 mmol) in dichloromethane (20 mL), compound **39B·HCl** (1.13 g, 4.91 mmol), Hunig's base (1.59 g, 12.27 mmol) and HATU (2.80 g, 7.36 mmol) was stirred at room temperature for 16 h. The reaction mixture was worked up with dichloromethane (100 mL)/ water (40 mL), and purified by flash chromatography (120 g silica gel) eluting with 20~30 % EtOAc/Hexanes to give compound **44C** (1.6 g, 51%).

Step 5

(*R*)-4-((7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid

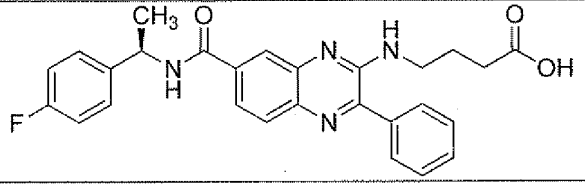


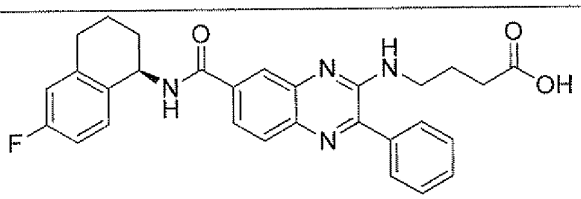
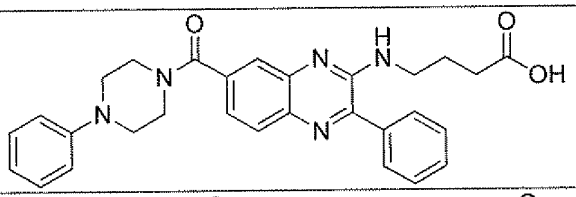
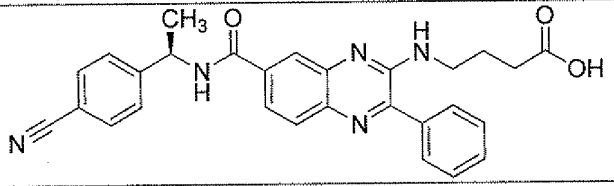
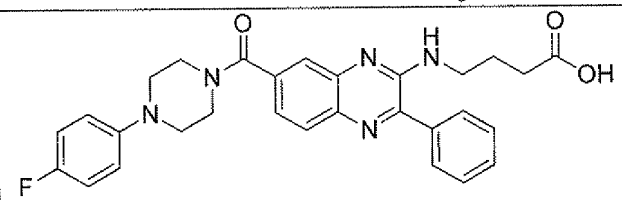
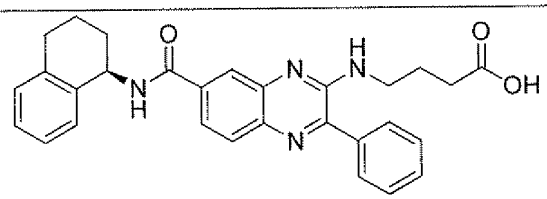
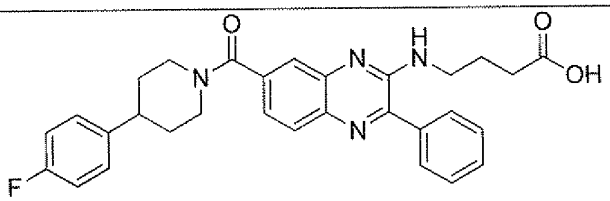
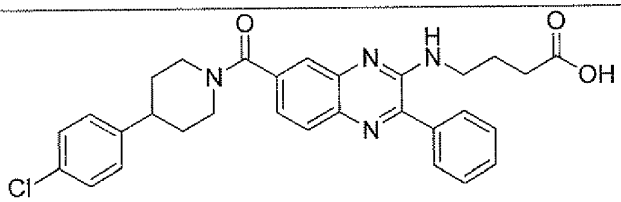
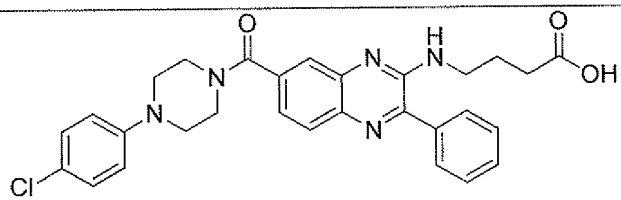
44C 44

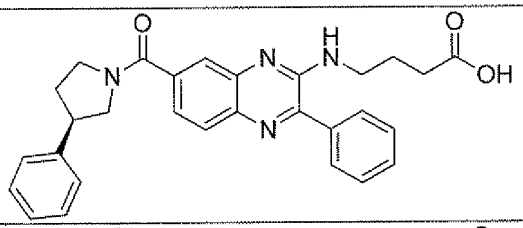
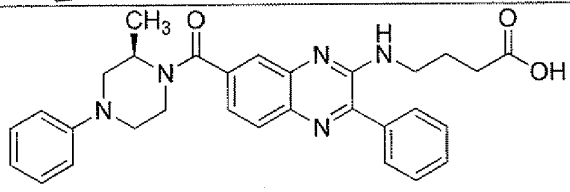
[00355] A mixture of compound **44C** (1.4 g, 2.40 mmol) in dichloromethane (2 mL) and TFA (2.73 g, 23.99 mmol) was stirred at room temperature for 2 h. The excess TFA and the solvent were removed to give a brown gum. The gum was neutralized with 2 N NaOH and purified by flash column chromatography (40 g silica gel) eluting with 40~60% EtOAc/hexanes to give compound **44** (1.15 g, 86%). MS (M+H) = 528.

[00356] Compound **44H**, shown below, was prepared in a similar manner. ^{1}H NMR (DMSO, 500 MHz) δ 7.84 (d, 1 H, J = 8.5 Hz), 7.74-7.72 (m, 2 H), 7.61(d, 1 H, J = 1.5 Hz), 7.60-7.57 (m, 2 H), 7.36 (dd, 1 H, J = 1.5 Hz, J = 8 Hz), 7.10-7.05 (m, 2 H), 7.02-6.99 (m, 2 H), 6.95-6.88 (m, 1 H), 3.88-3.74 (m, 2 H), 3.63-3.5 (m, 2 H), 3.46 (q, 2 H, J = 6.5 Hz, J = 12.5 Hz), 3.38- 3.05 (m, 4 H), 2.29 (t, 2 H, J = 7 Hz), 1.86 (t, 2 H, J = 6.5 Hz).

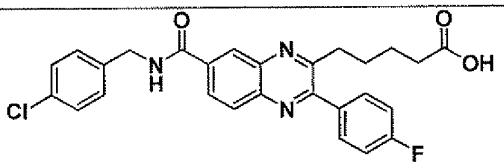
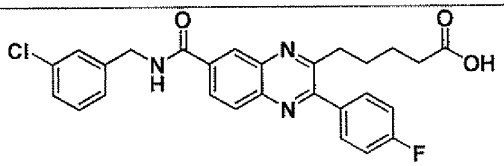
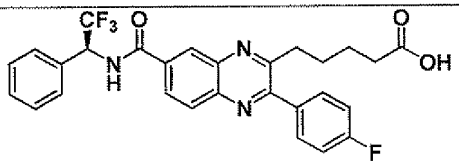
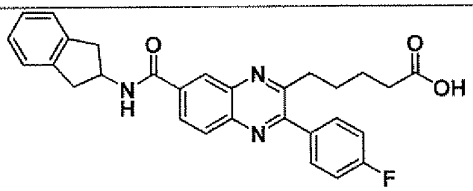
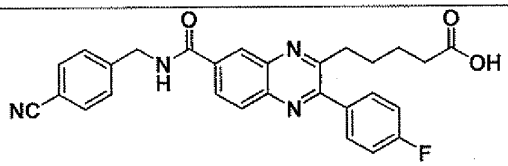
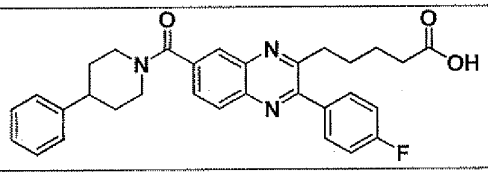
[00357] The following compounds were prepared in a similar manner to that described above in Example 44:

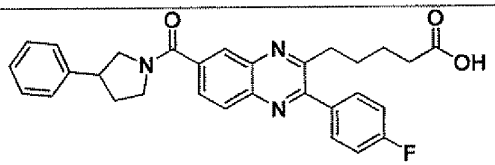
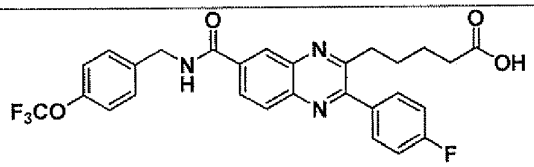
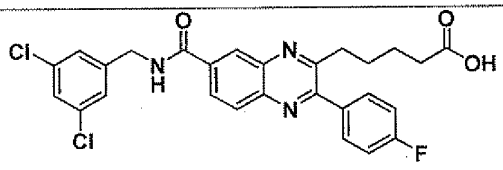
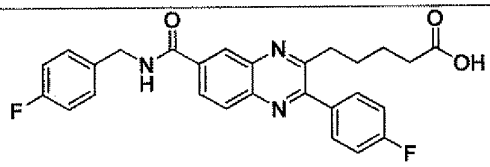
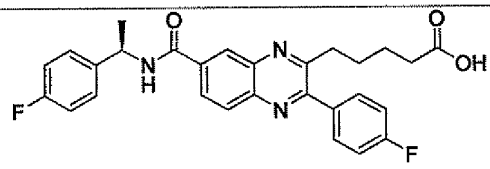
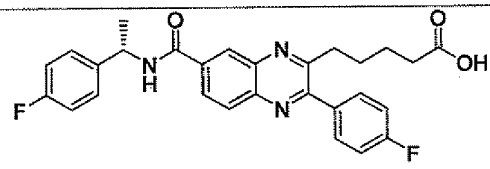
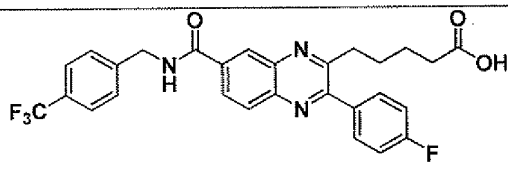
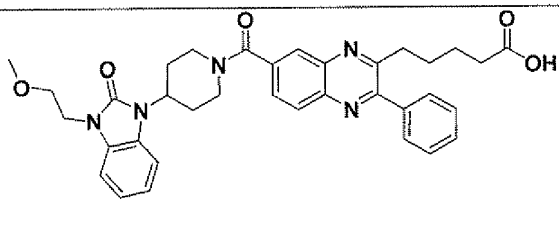
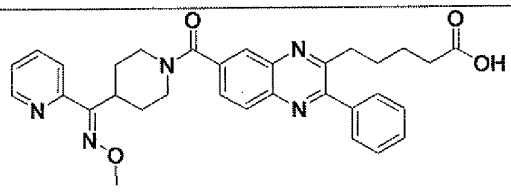
No.	Structure	Name	M+H
44D		(R)-4-((7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	473

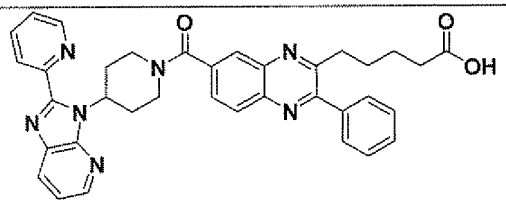
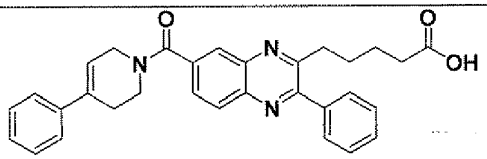
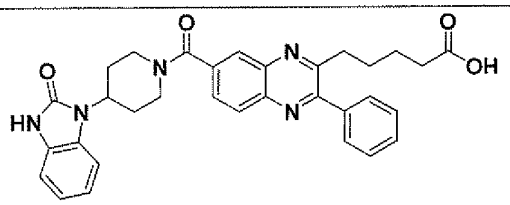
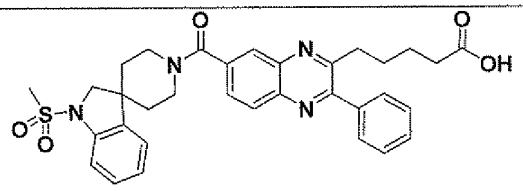
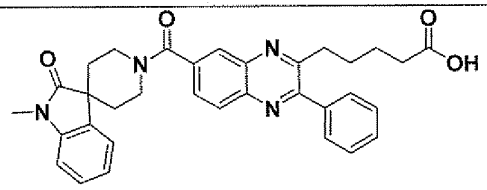
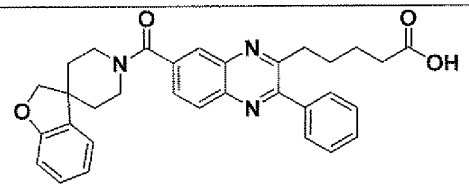
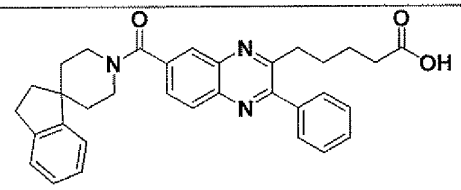
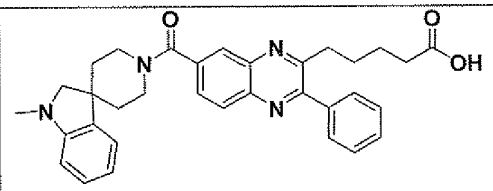
44E		(R)-4-((7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	499
44F		4-((3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)amino)butanoic acid	496
44G		(R)-4-((7-((1-(4-cyanophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	480
44H		4-((7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	514
44i		(R)-4-((3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)amino)butanoic acid	481
44J		4-((7-(4-(4-fluorophenyl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	513
44K		4-((7-(4-(4-chlorophenyl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	529
44L		4-((7-(4-(4-chlorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	530

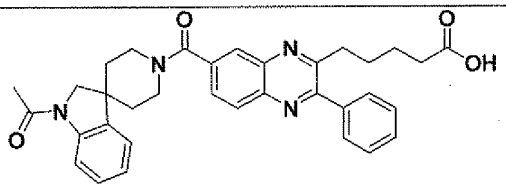
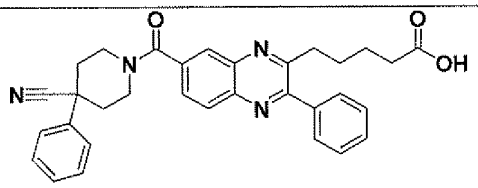
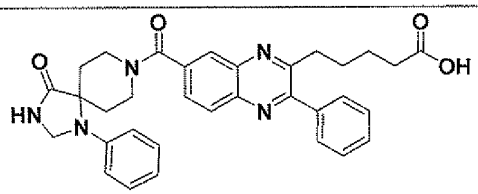
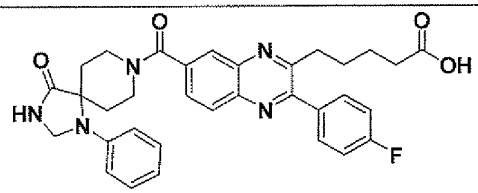
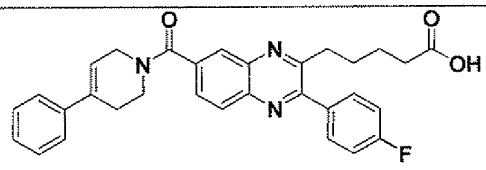
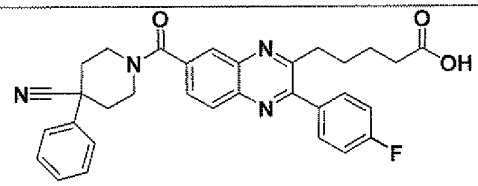
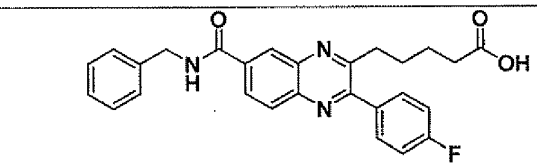
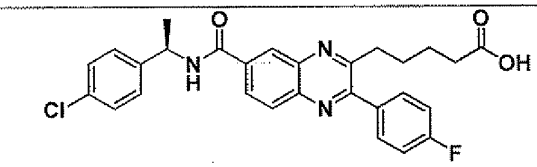
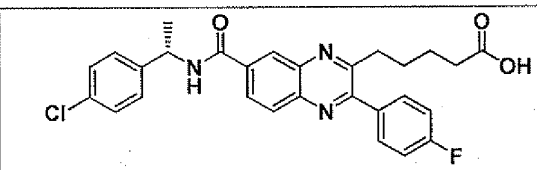
44M		(R)-4-((3-phenyl-7-(3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)amino)butanoic acid	481
44N		(R)-4-((7-(2-methyl-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid	510

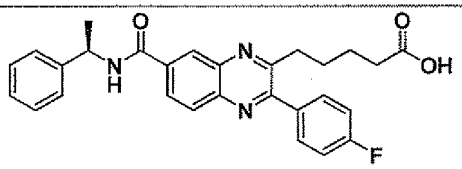
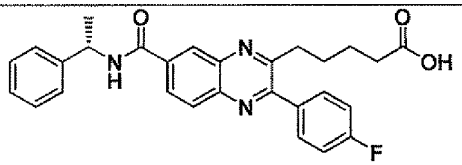
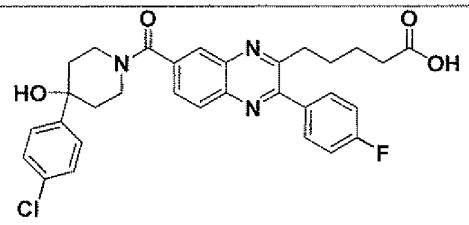
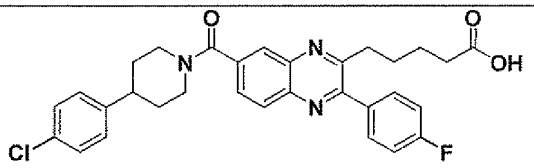
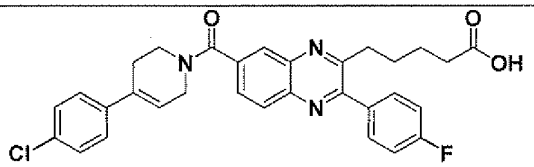
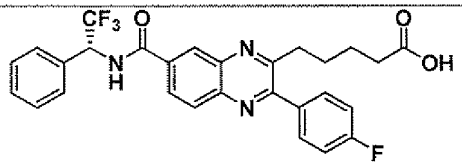
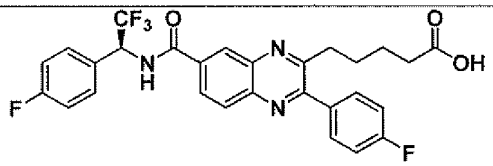
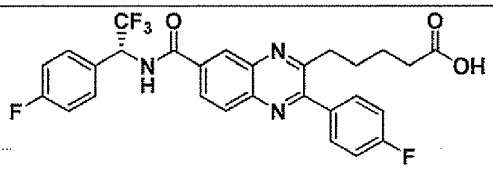
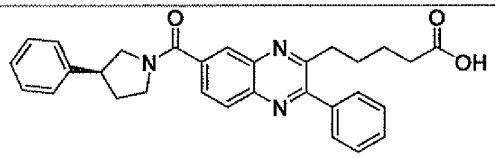
[00358] The following compounds were prepared following procedures similar to those exemplified in the examples above.

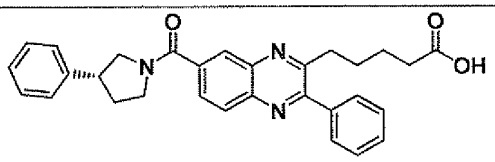
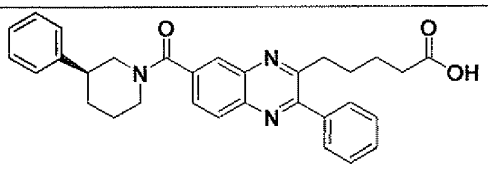
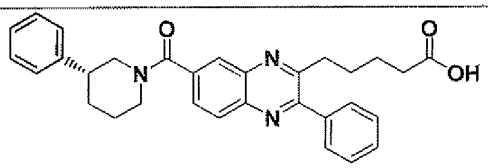
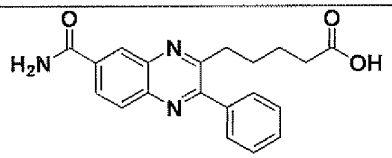
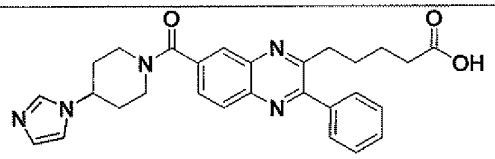
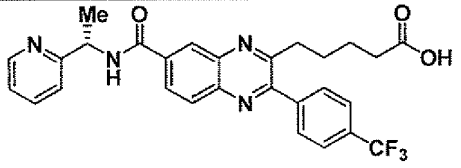
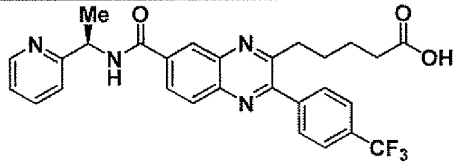
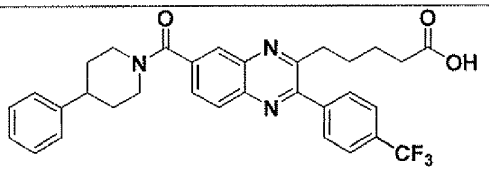
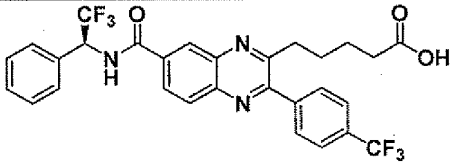
No.	Structure	Name	M+H
100		7-[[[(4-chlorophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	492
101		7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	492
102		3-(4-fluorophenyl)-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	526
103		7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	484
104		7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	483
105		3-(4-fluorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	512

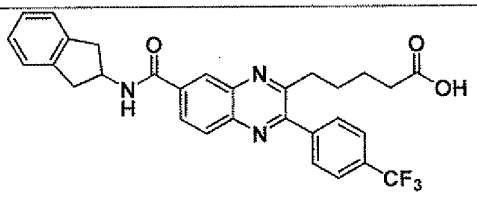
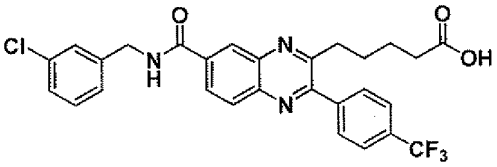
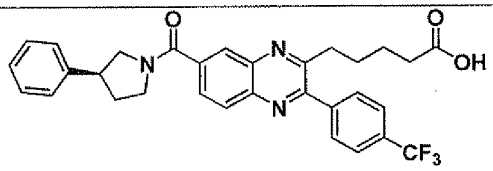
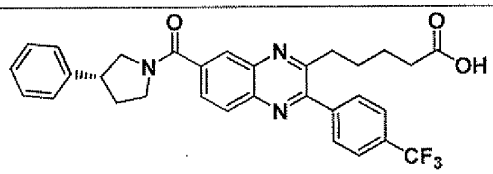
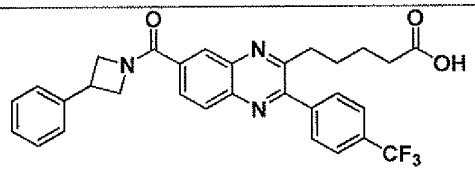
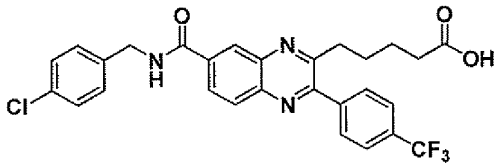
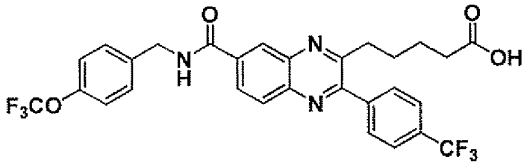
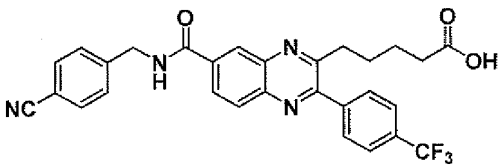
106		3-(4-fluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	498
107		3-(4-fluorophenyl)-7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	542
108		7-[[[(3,5-dichlorophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	526
109		3-(4-fluorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	476
110		3-(4-fluorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	490
111		3-(4-fluorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	490
112		3-(4-fluorophenyl)-7-[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid	526
113		7-[[4-[2,3-dihydro-3-(2-methoxyethyl)-2-oxo-1H-benzimidazol-1-yl]-1-piperidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	608
114		7-[[4-[(E)-(methoxyimino)-2-pyridinylmethyl]-1-piperidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	552

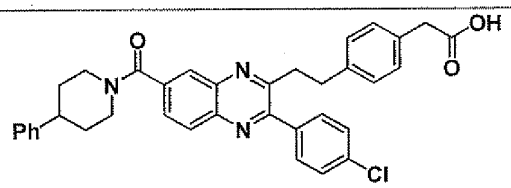
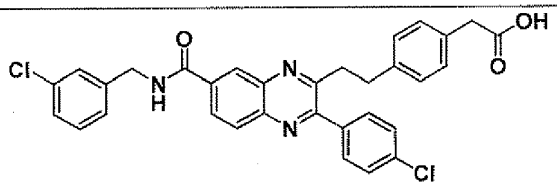
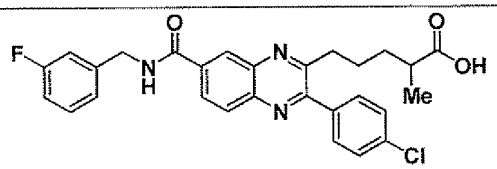
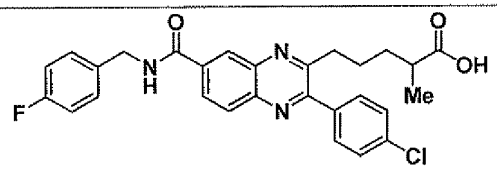
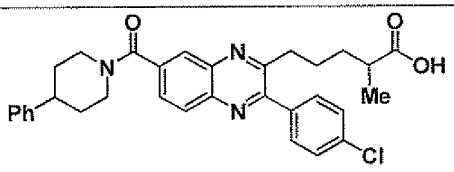
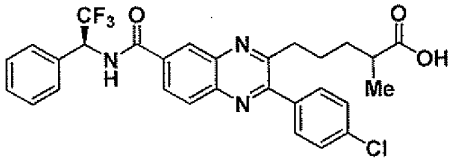
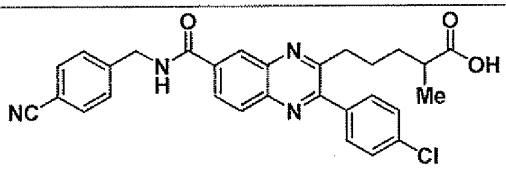
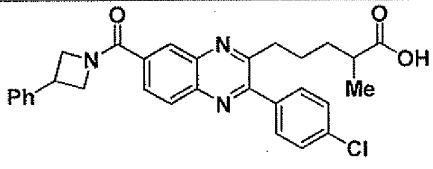
115		3-phenyl-7-[[4-[2-(2-pyridinyl)-1H-benzimidazol-1-yl]-1-piperidinyl]carbonyl]-2-quinoxalinepentanoic acid	612
116		7-(4-phenyl-1,2,3,6-tetrahydropyridine-1-carbonyl)-3-phenyl-2-quinoxalinepentanoic acid	492
117		7-[[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	550
118		7-[[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	599
119		7-[(1,2-dihydro-1-methyl-2-oxospiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	549
120		3-phenyl-7-(spiro[benzofuran-3(2H),4'-piperidin]-1'-ylcarbonyl)-2-quinoxalinepentanoic acid	522
121		7-[(2,3-dihydrospiro[1H-indene-1,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	520
122		7-[(1,2-dihydro-1-methylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	535

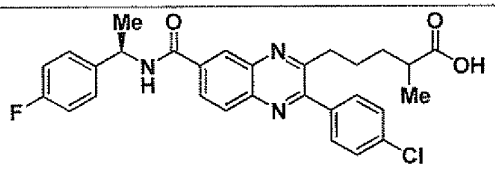
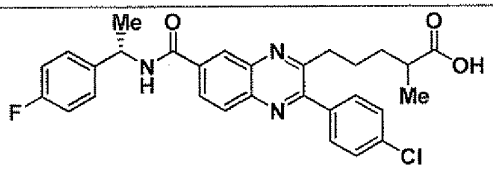
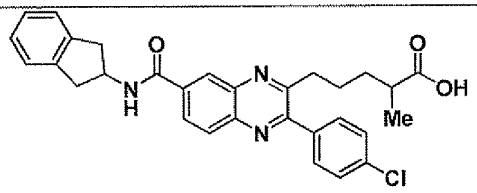
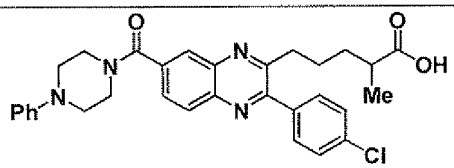
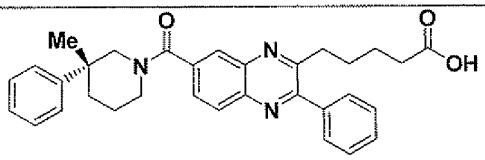
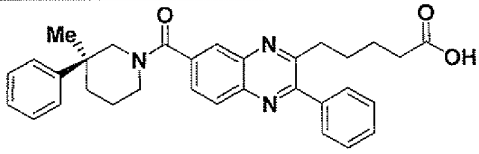
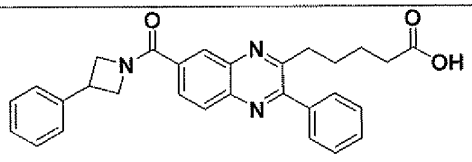
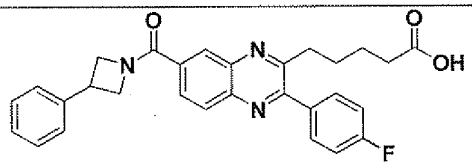
123		7-[(1-acetyl-1,2-dihydrospiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	563
124		7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	519
125		7-[(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	564
126		3-(4-fluorophenyl)-7-[(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)carbonyl]-2-quinoxalinepentanoic acid	582
127		5-(3-(4-fluorophenyl)-7-(4-phenyl-1,2,3,6-tetrahydropyridine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	510
128		7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	537
129		3-(4-fluorophenyl)-7-[[(phenylmethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	458
130		7-[[[1(R)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	506
131		7-[[[1(S)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	506

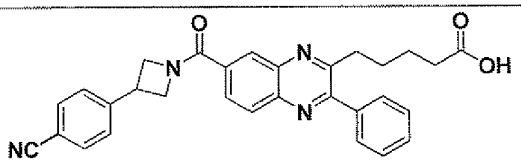
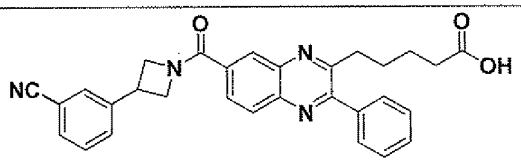
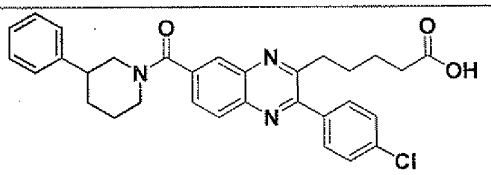
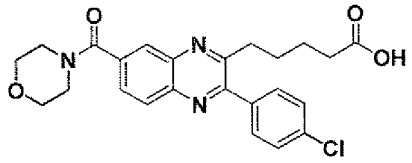
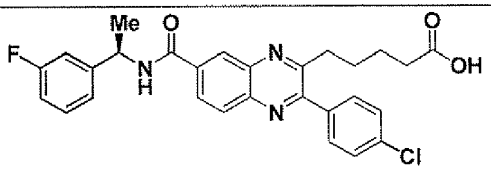
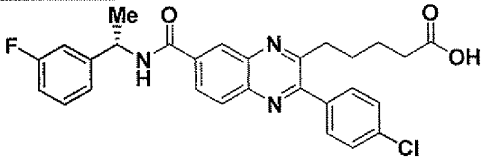
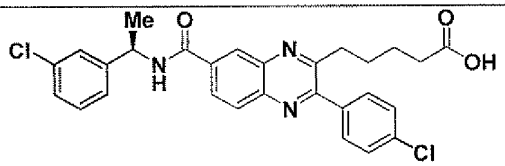
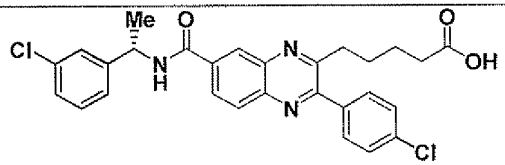
132		3-(4-fluorophenyl)-7-[[(1(R)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	472
133		3-(4-fluorophenyl)-7-[[(1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	472
134		7-[[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	562
135		7-[[4-(4-chlorophenyl)-1-piperidinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	546
136		7-[[4-(4-chlorophenyl)-3,6-dihydro-1(2H)-pyridinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	544
137		3-(4-fluorophenyl)-7-[[[2,2,2-trifluoro-1(R)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	526
138		3-(4-fluorophenyl)-7-[[[2,2,2-trifluoro-1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	544
139		3-(4-fluorophenyl)-7-[[[(1R)-2,2,2-trifluoro-1-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	544
140		3-phenyl-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	480

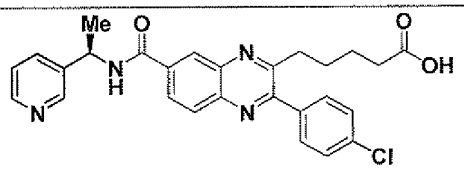
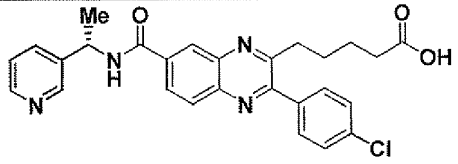
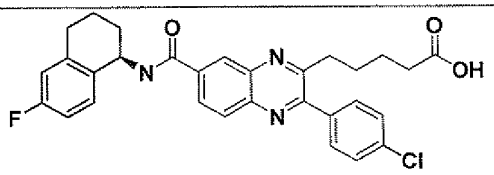
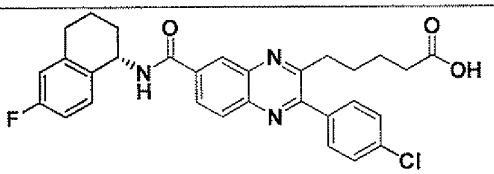
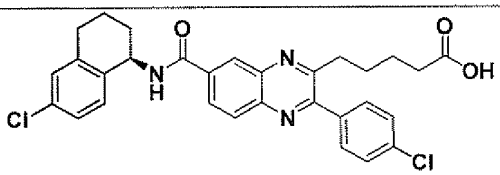
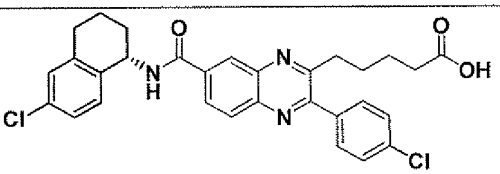
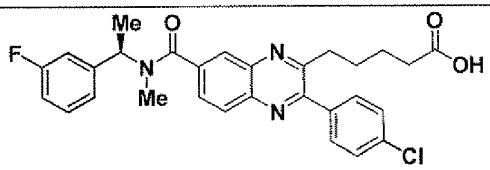
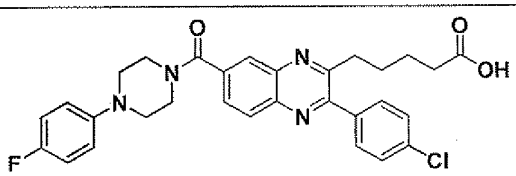
141		3-phenyl-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid	480
142		3-phenyl-7-[(3(S)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	494
143		3-phenyl-7-[(3(R)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	494
144		5-(7-carbamoyl-3-phenylquinoxalin-2-yl)pentanoic acid	350
145		5-(7-(4-(1H-imidazol-1-yl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	484
146		7-[[[1(S)-(2-pyridinyl)ethyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	523
147		7-[[[1(R)-(2-pyridinyl)ethyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	523
148		7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	562
149		3-[4-(trifluoromethyl)phenyl]-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	576

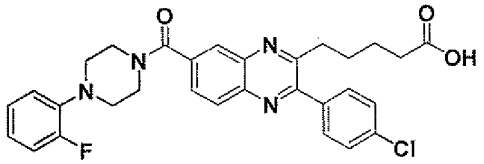
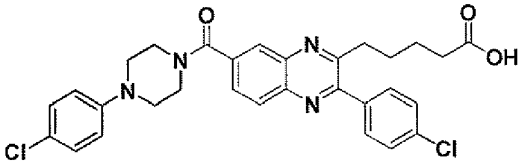
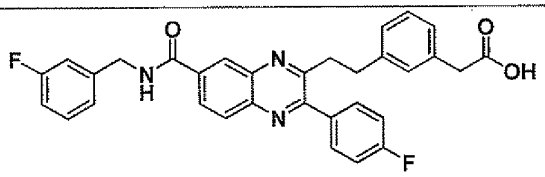
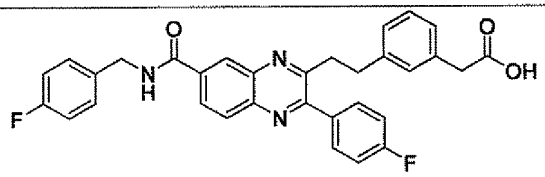
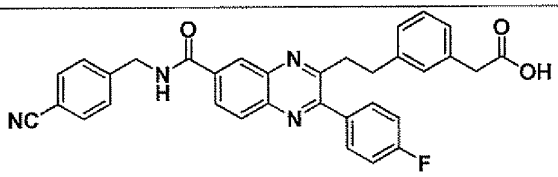
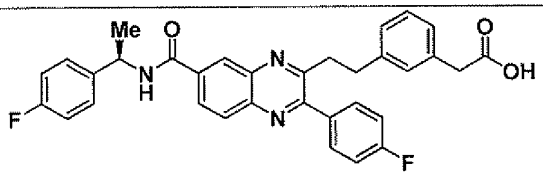
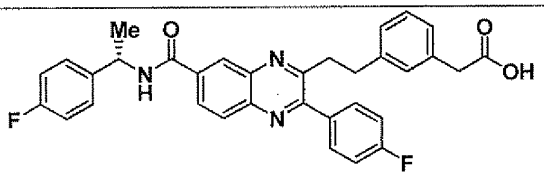
150		7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	534
151		7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	542
152		7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	548
153		7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	548
154		7-[(3-phenyl-1-azetidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	534
155		7-[[[(4-chlorophenyl)methyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	542
156		7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	592
157		7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid	533

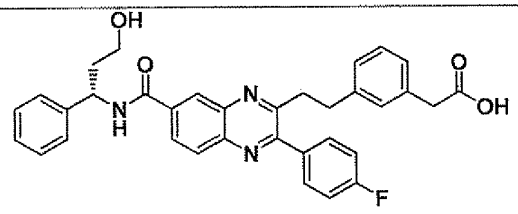
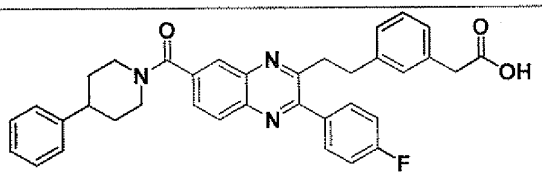
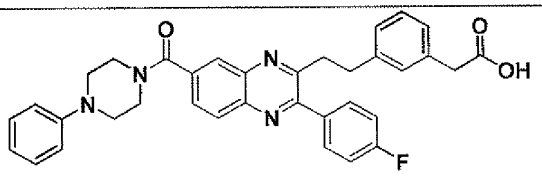
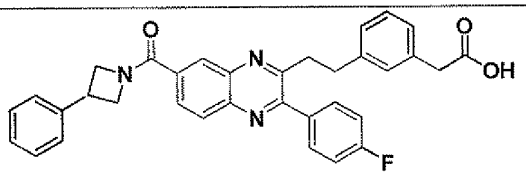
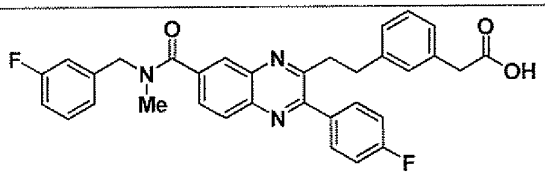
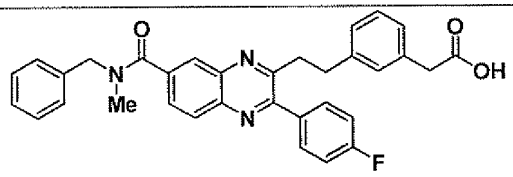
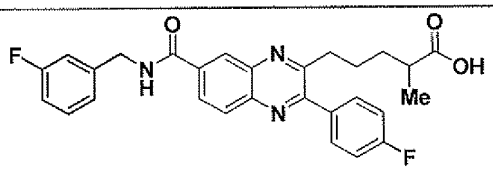
158		4-[2-[3-(4-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	590
159		4-[2-[3-(4-chlorophenyl)-7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	570
160		3-(4-chlorophenyl)-7-[[[(3-fluorophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	506
161		3-(4-chlorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	506
162		3-(4-chlorophenyl)-alpha-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	542
163		3-(4-chlorophenyl)-alpha-methyl-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	556
164		3-(4-chlorophenyl)-7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	513
165		3-(4-chlorophenyl)-alpha-methyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid	514

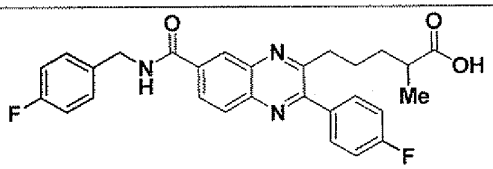
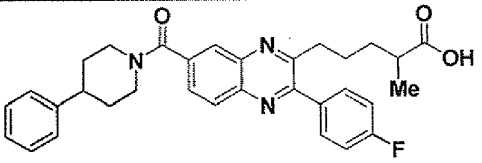
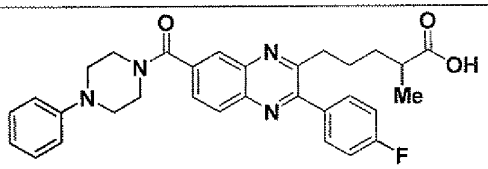
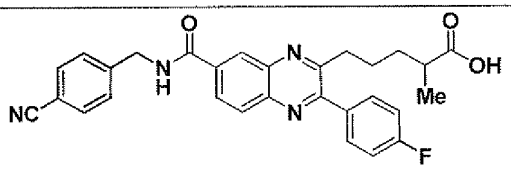
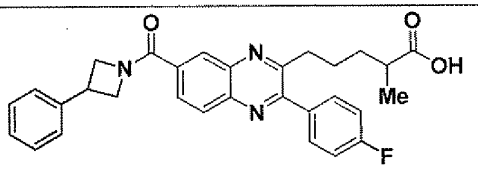
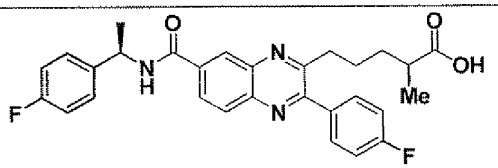
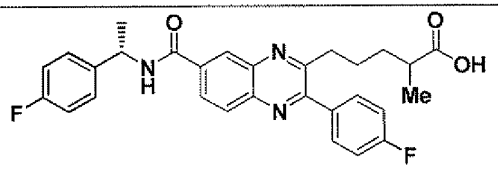
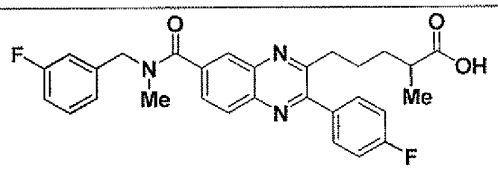
166		3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	520
167		3-(4-chlorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	520
168		3-(4-chlorophenyl)-7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	514
169		3-(4-chlorophenyl)-alpha-methyl-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid	543
170 *		7-[(3(R)-methyl-3-phenyl-1-piperidinyl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	508
171 *		7-[(3(S)-methyl-3-phenyl-1-piperidinyl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	508
172		3-phenyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid	466
173		3-(4-fluorophenyl)-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid	484

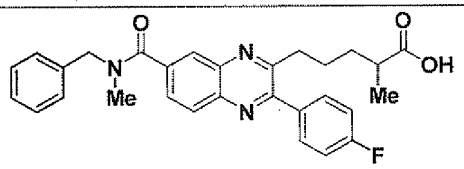
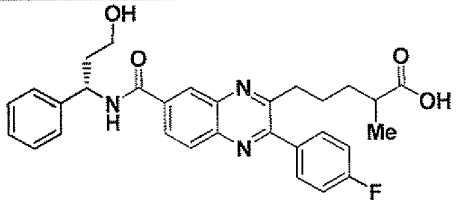
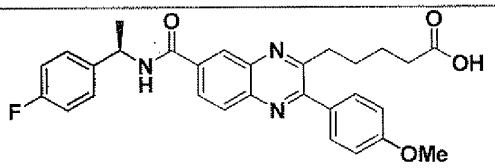
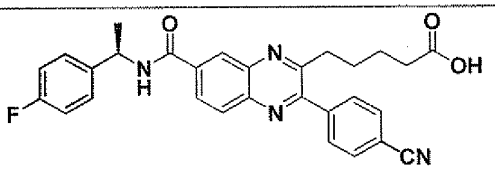
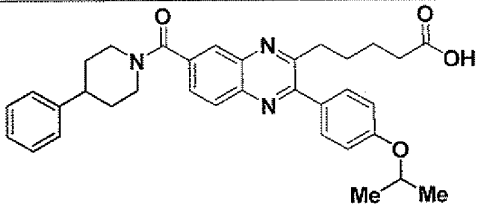
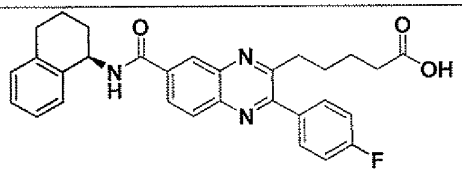
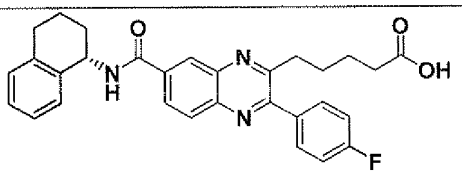
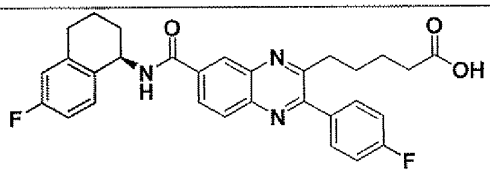
174		7-[[3-(4-cyanophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	491
175		7-[[3-(3-cyanophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	491
176		3-(4-chlorophenyl)-7-[(3-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	528
177		3-(4-chlorophenyl)-7-(4-morpholinylcarbonyl)-2-quinoxalinepentanoic acid	454
178		3-(4-chlorophenyl)-7-[[[1(R)-(3-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	506
179		3-(4-chlorophenyl)-7-[[[1(S)-(3-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	506
180		3-(4-chlorophenyl)-7-[[[1(R)-(3-chlorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	522
181		3-(4-chlorophenyl)-7-[[[1(S)-(3-chlorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	522

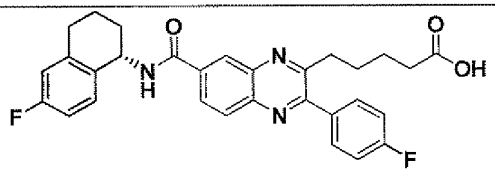
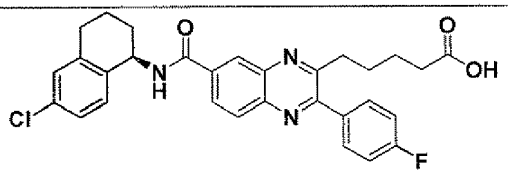
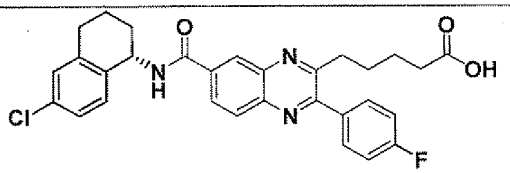
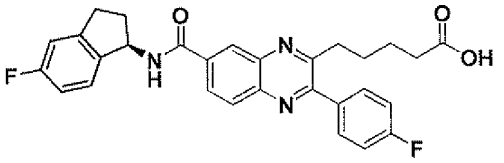
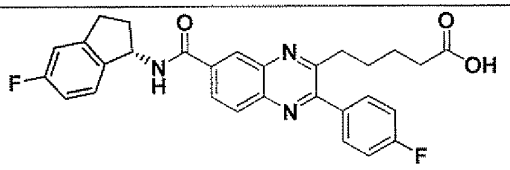
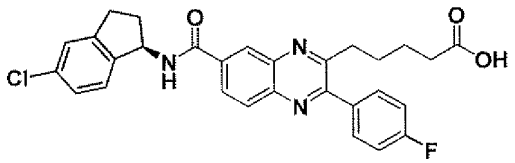
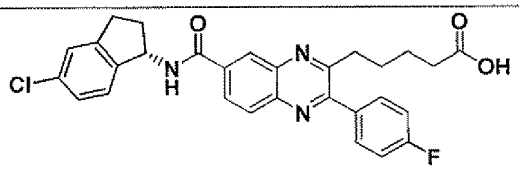
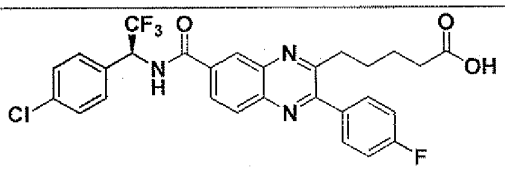
182		3-(4-chlorophenyl)-7-[[[1(R)-(3-pyridinyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	489
183		3-(4-chlorophenyl)-7-[[[1(S)-(3-pyridinyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	489
184		3-(4-chlorophenyl)-7-[[(6-fluoro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	532
185		3-(4-chlorophenyl)-7-[[(6-fluoro-1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]2-quinoxalinepentanoic acid	532
186		3-(4-chlorophenyl)-7-[[(6-chloro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	548
187		3-(4-chlorophenyl)-7-[[(6-chloro-1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	548
188		3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]methylamino]carbonyl]-2-quinoxalinepentanoic acid	520
189		3-(4-chlorophenyl)-7-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-2-quinoxalinepentanoic acid	547

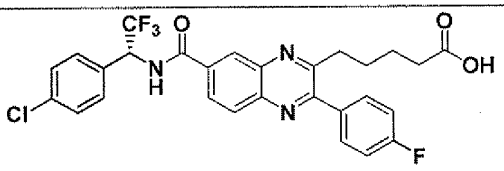
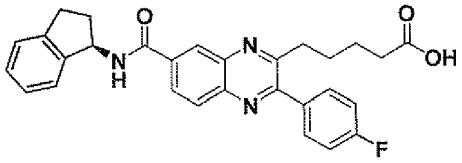
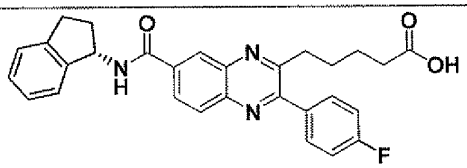
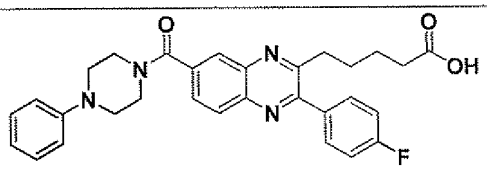
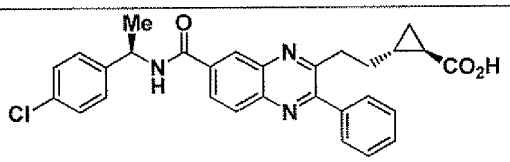
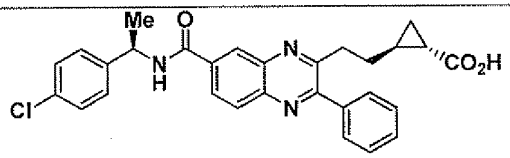
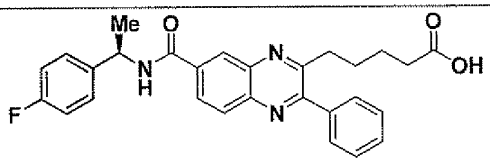
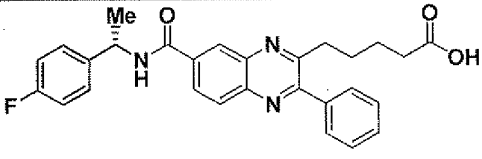
190		3-(4-chlorophenyl)-7-[[4-(2-fluorophenyl)-1-piperazinyl]carbonyl]-2-quinoxalinepentanoic acid	547
191		3-(4-chlorophenyl)-7-[[4-(4-chlorophenyl)-1-piperazinyl]carbonyl]-2-quinoxalinepentanoic acid	563
192		3-[2-[3-(4-fluorophenyl)-7-[[[(3-fluorophenyl)methyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	538
193		3-[2-[3-(4-fluorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	538
194		3-[2-[7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinyl]ethyl]benzeneacetic acid	545
195		3-[2-[3-(4-fluorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	552
196		3-[2-[3-(4-fluorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	552

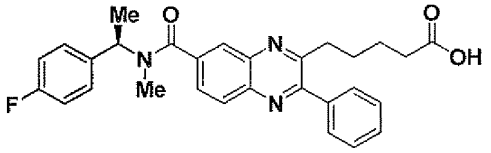
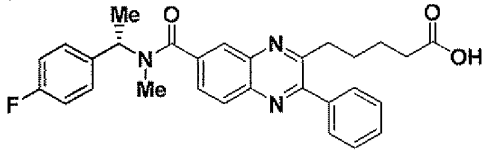
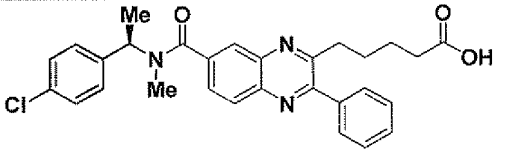
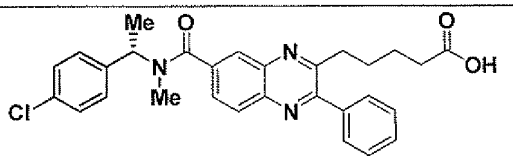
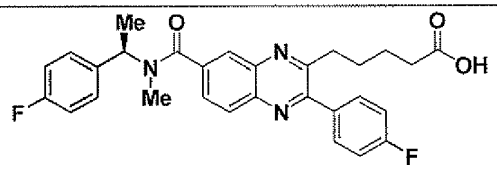
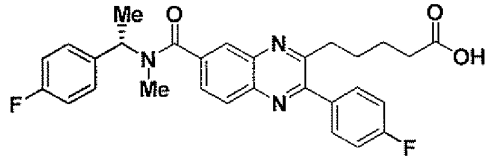
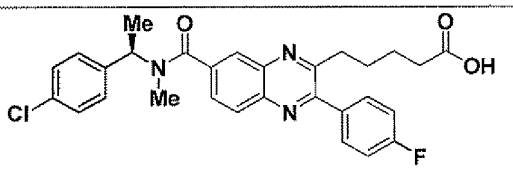
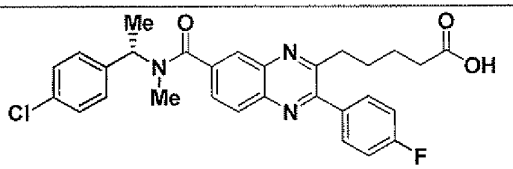
197		3-[2-[3-(4-fluorophenyl)-7-[[(3-hydroxy-1(S)-phenylpropyl)amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	564
198		3-[2-[3-(4-fluorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	574
199		3-[2-[3-(4-fluorophenyl)-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	575
200		3-[2-[3-(4-fluorophenyl)-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	546
201		3-[2-[3-(3-fluorophenyl)-7-[[[(4-fluorophenyl)methyl]methylamino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	552
202		3-[2-[3-(4-fluorophenyl)-7-[[methyl(phenylmethyl)amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid	534
203		3-(4-fluorophenyl)-7-[[[(3-fluorophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	490

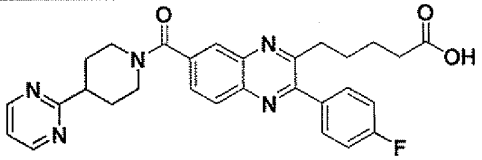
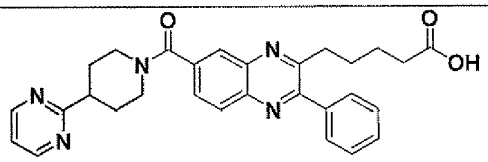
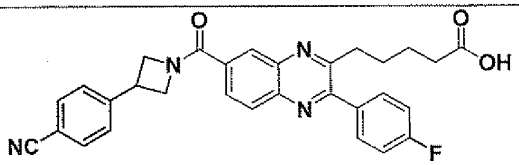
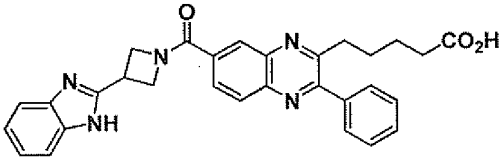
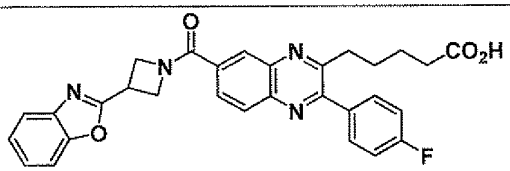
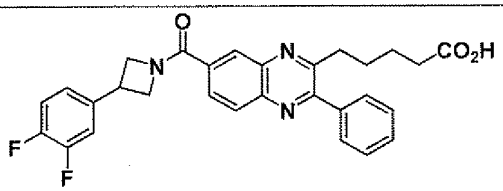
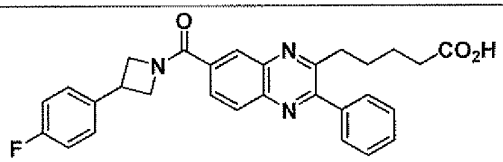
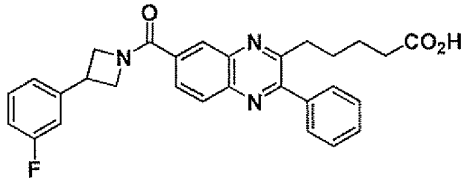
204		3-(4-fluorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	490
205		3-(4-fluorophenyl)-alpha-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	526
206		3-(4-fluorophenyl)-alpha-methyl-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid	527
207		7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-alpha-methyl-2-quinoxalinepentanoic acid	497
208		3-(4-fluorophenyl)-alpha-methyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid	498
209		3-(4-fluorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	504
210		3-(4-fluorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	504
211		3-(4-fluorophenyl)-7-[[[(3-fluorophenyl)methyl]methylamino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	504

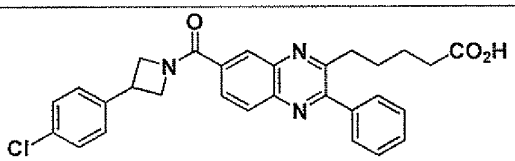
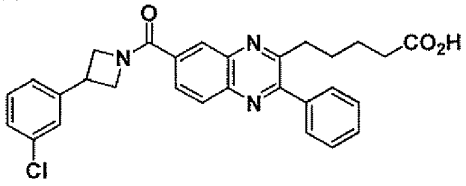
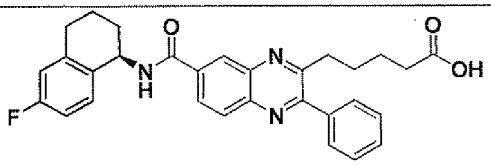
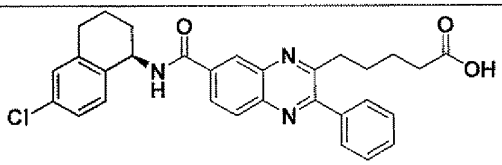
212		3-(4-fluorophenyl)-alpha-methyl-7-[[methyl(phenylmethyl)amino]carbonyl]-2-quinoxalinepentanoic acid	486
213		3-(4-fluorophenyl)-7-[[(3-hydroxy-1(S)-phenylpropyl)amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid	516
214		7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-3-(4-methoxyphenyl)-2-quinoxalinepentanoic acid	502
215		3-(4-cyanophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid	497
216		3-[4-(1-methylethoxy)phenyl]-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid	552
217		3-(4-fluorophenyl)-7-[[(1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	498
218		3-(4-fluorophenyl)-7-[[(1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	498
219		3-(4-fluorophenyl)-7-[[(6-fluoro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	516

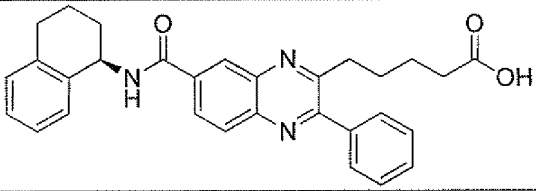
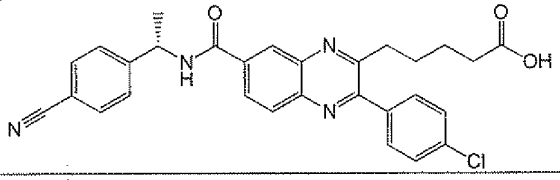
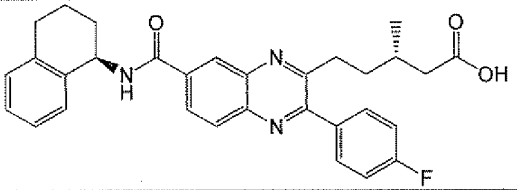
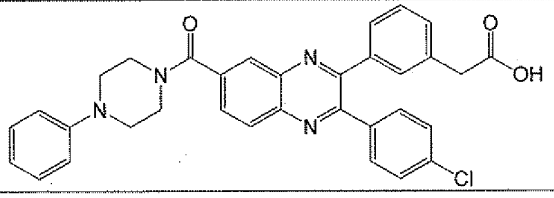
220		3-(4-fluorophenyl)-7-[[(6-fluoro-1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid	516
221		7-[[(6-chloro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	532
222		7-[[(6-chloro-1,2,3,4-tetrahydro-1(S)-naphthalenyl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	532
223		7-[[(5-fluoro-2,3-dihydro-1H-inden-1(R)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	502
224		7-[[(5-fluoro-2,3-dihydro-1H-inden-1(S)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	502
225		7-[[(5-chloro-2,3-dihydro-1H-inden-1(R)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	518
226		7-[[(5-chloro-2,3-dihydro-1H-inden-1(S)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	518
227		7-[[[1(S)-(4-chlorophenyl)-2,2,2-trifluoroethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	560

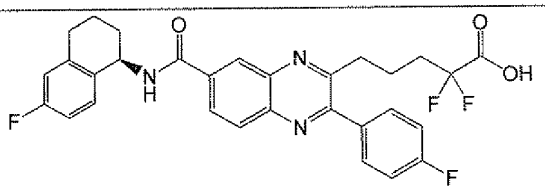
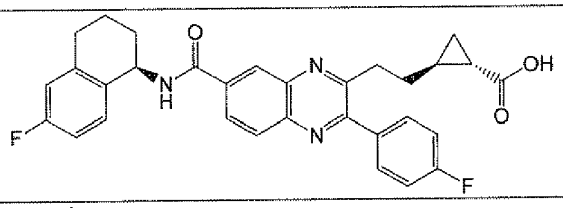
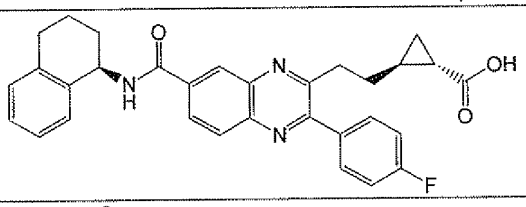
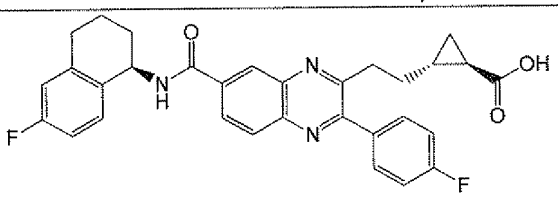
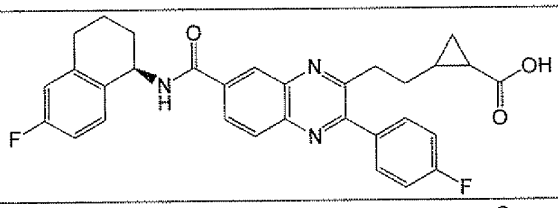
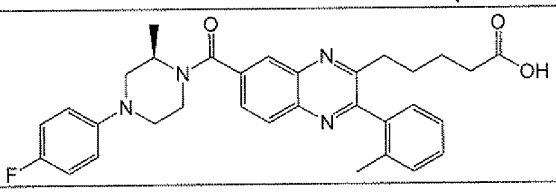
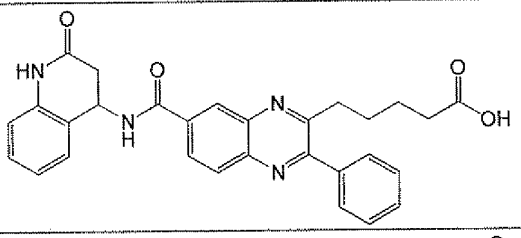
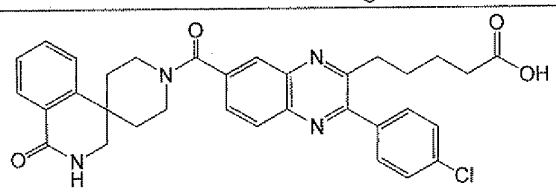
228		7-[[[1(R)-(4-chlorophenyl)-2,2,2-trifluoroethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	560
229		7-[[(2,3-dihydro-1H-inden-1(R)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	484
230		7-[[(2,3-dihydro-1H-inden-1(S)-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	484
231		3-(4-fluorophenyl)-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid	513
232		trans-2-[2-[7-[[[1(R)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-phenyl-2-quinoxalinyl]ethyl]cyclopropanecarboxylic acid	500
233		trans-2-[2-[7-[[[1(R)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-phenyl-2-quinoxalinyl]ethyl]cyclopropanecarboxylic acid	500
234		7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	472
235		7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	472

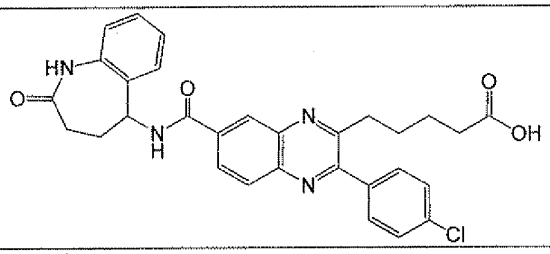
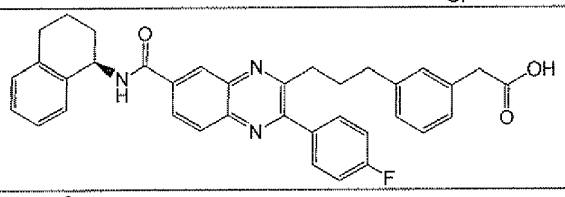
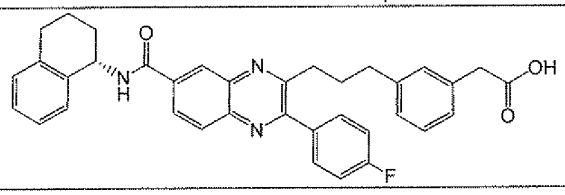
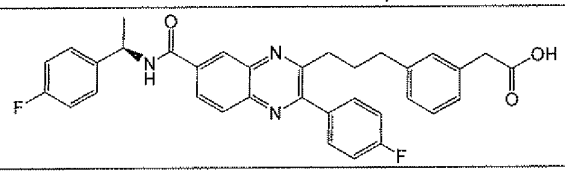
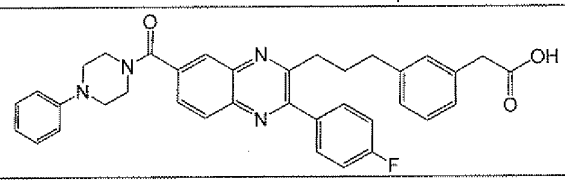
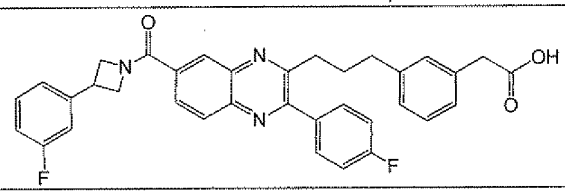
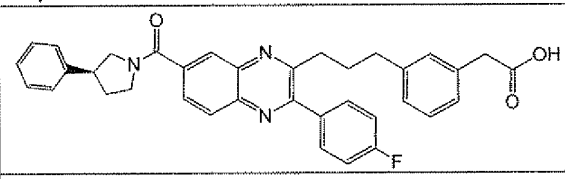
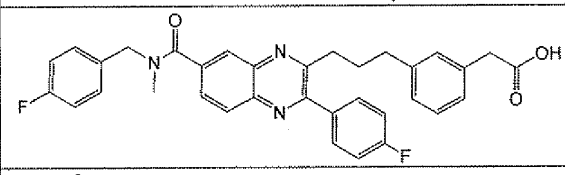
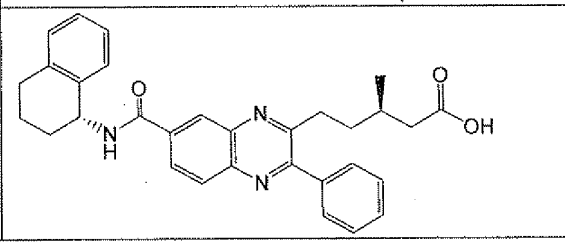
236		7-[[[1(R)-(4-fluorophenyl)ethyl]methylamino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	486
237		7-[[[1(S)-(4-fluorophenyl)ethyl]methylamino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	486
238		7-[[[1(R)-(4-chlorophenyl)ethyl]methylamino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	502
239		7-[[[1(S)-(4-chlorophenyl)ethyl]methylamino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	502
240		3-(4-fluorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]methylamino]carbonyl]-2-quinoxalinepentanoic acid	504
241		3-(4-fluorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]methylamino]carbonyl]-2-quinoxalinepentanoic acid	504
242		7-[[[1(R)-(4-chlorophenyl)ethyl]methylamino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	520
243		7-[[[1(S)-(4-chlorophenyl)ethyl]methylamino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	520

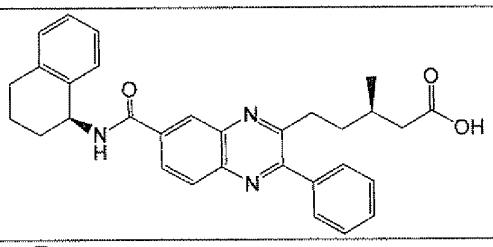
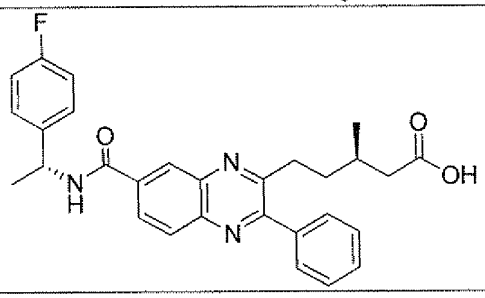
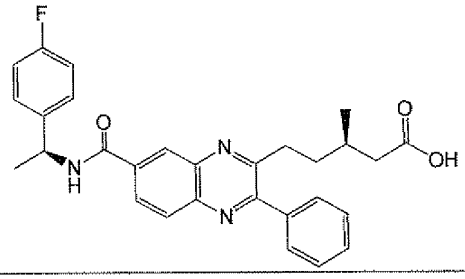
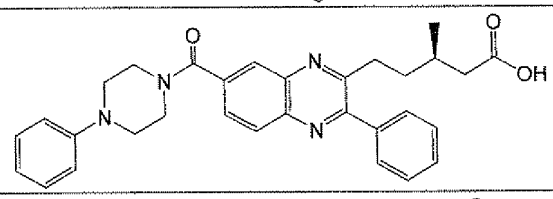
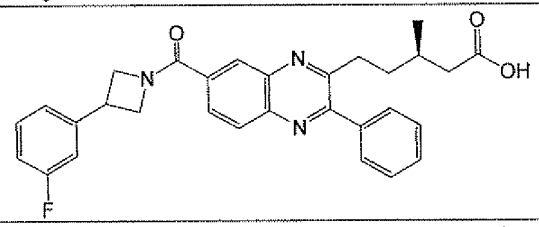
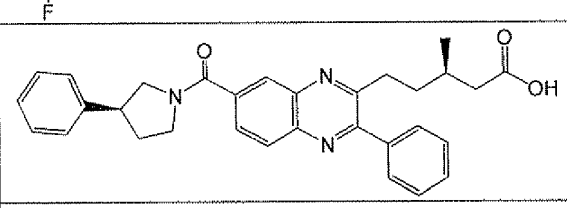
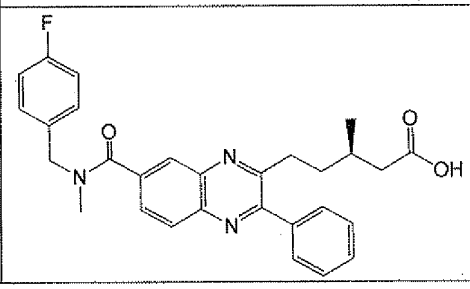
244		3-(4-fluorophenyl)-7-[[4-(2-pyrimidinyl)-1-piperidinyl]carbonyl]-2-quinoxalinepentanoic acid	514
245		3-phenyl-7-[[4-(2-pyrimidinyl)-1-piperidinyl]carbonyl]-2-quinoxalinepentanoic acid	496
246		7-[[3-(4-cyanophenyl)-1-azetidinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	509
247		7-[[3-(1H-benzimidazol-2-yl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	506
248		7-[[3-(2-benzoxazolyl)-1-azetidinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid	525
249		7-[[3-(3,4-difluorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	502
250		7-[[3-(4-fluorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	484
251		7-[[3-(3-fluorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	484

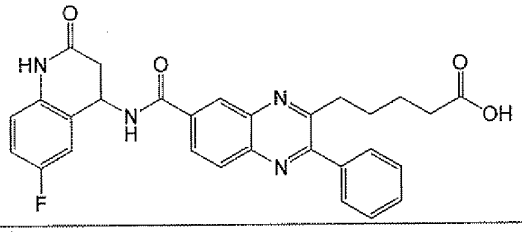
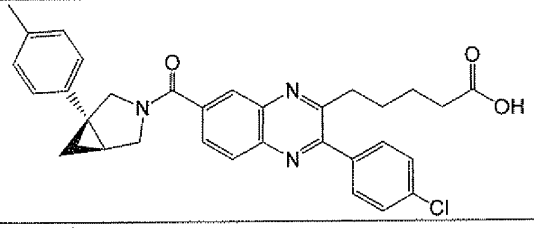
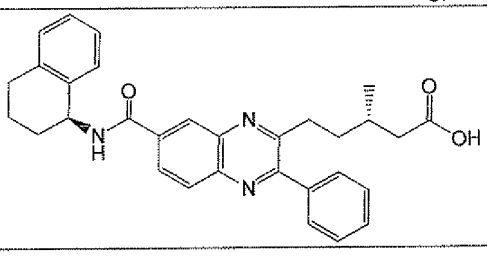
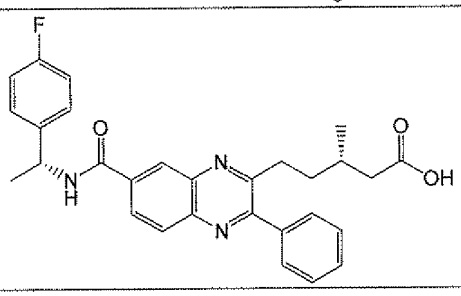
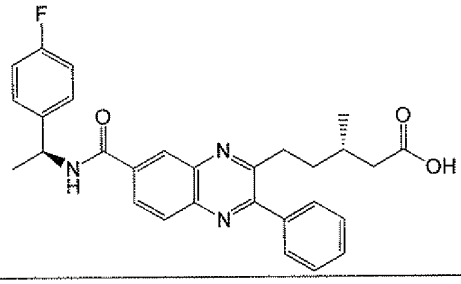
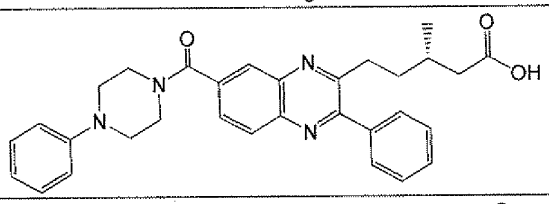
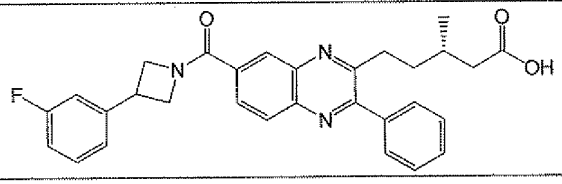
252		7-[[3-(4-chlorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	500
253		7-[[3-(3-chlorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	500
254		7-[[(6-fluoro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	498
255		7-[[(6-chloro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid	514

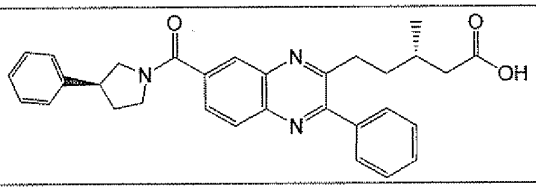
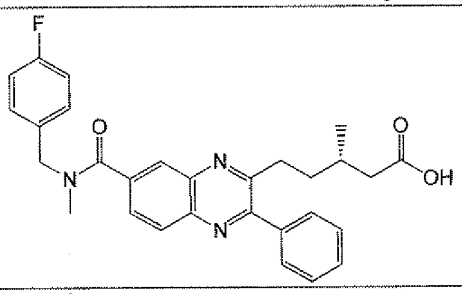
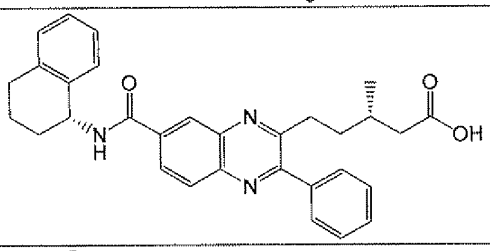
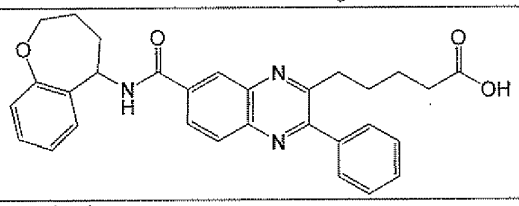
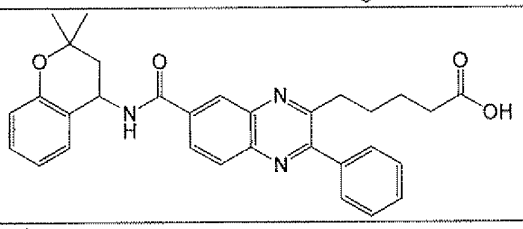
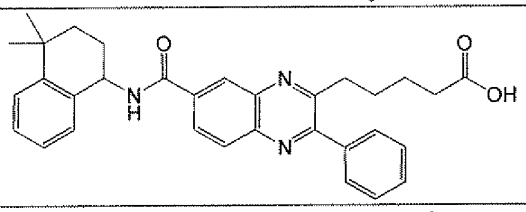
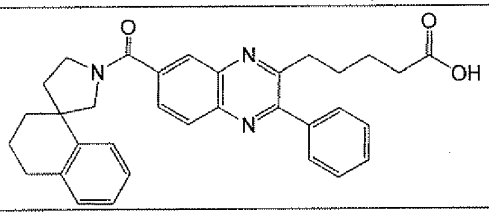
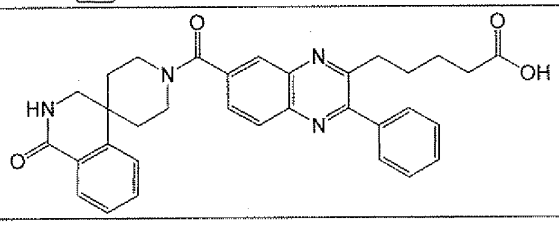
No.	Structure	Name	M+H
256		(R)-5-(3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	480
257		(S)-5-(3-(4-chlorophenyl)-7-((1-(4-cyanophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	513
258		(S)-5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	512
259		2-(3-(3-(4-chlorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)phenyl)acetic acid	563

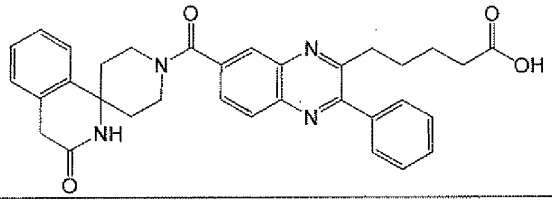
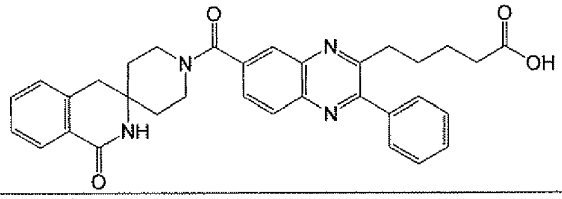
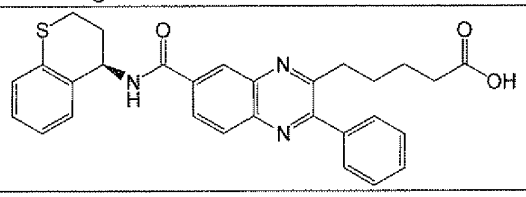
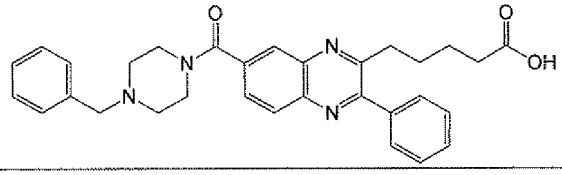
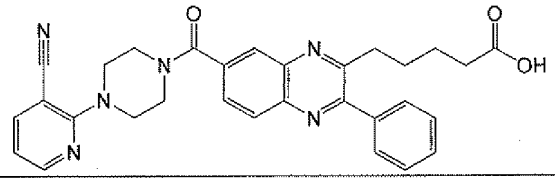
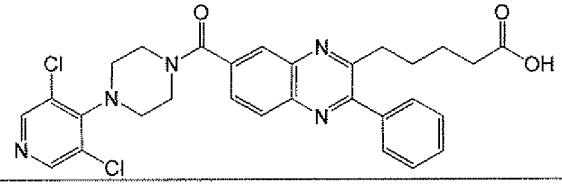
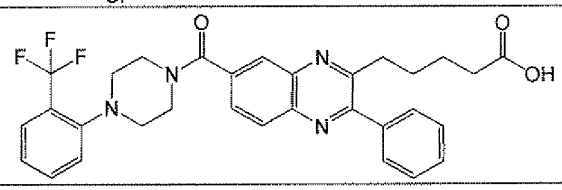
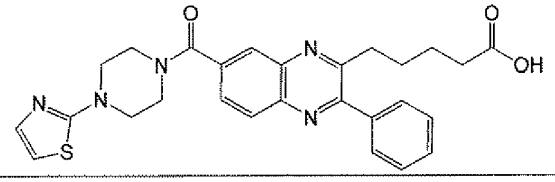
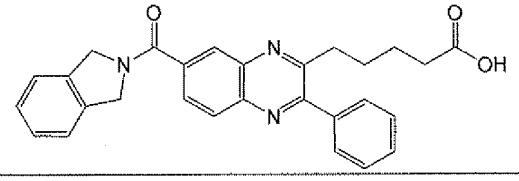
260		(R)-2,2-difluoro-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	552
261		(1S,2S)-2-(2-(7-(((R)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	528
262		(1S,2S)-2-(2-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	510
263		(1R,2R)-2-(2-(7-(((R)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	528
264		2-(2-(7-(((R)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	528
265		(R)-5-(7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	527
266		5-(7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	495
267		5-(3-(4-chlorophenyl)-7-(1-oxo-2,3-dihydro-1H-spiro[isoquinoline-4,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.3

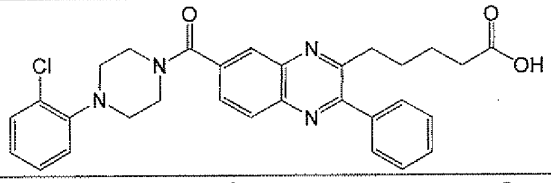
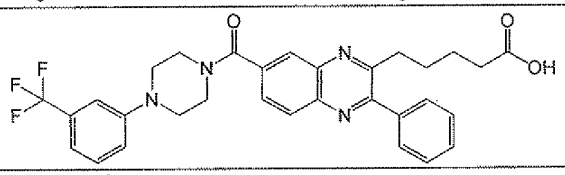
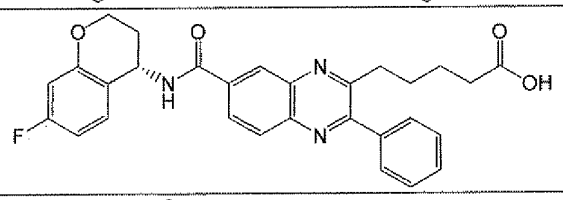
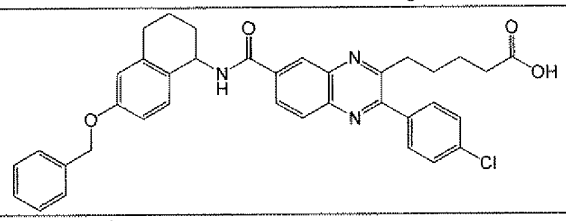
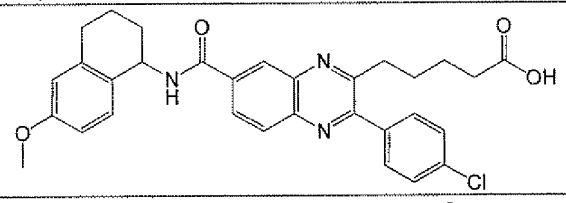
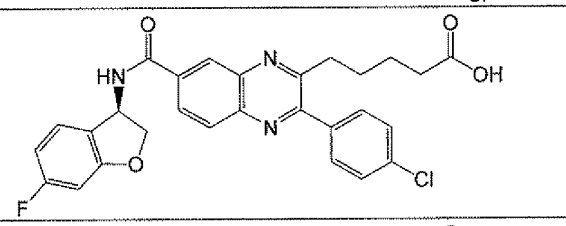
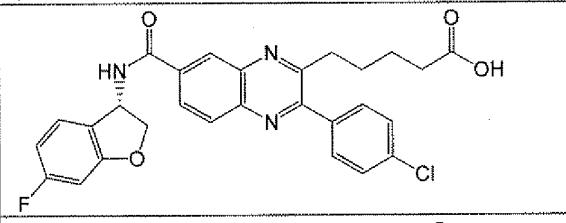
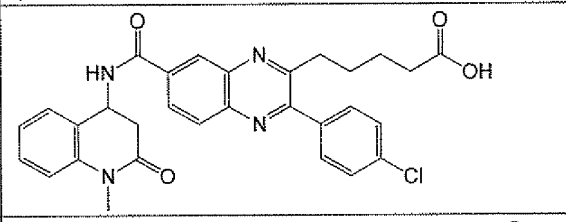
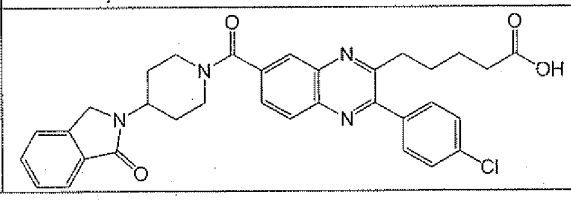
268		5-(3-(4-chlorophenyl)-7-((2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	543.3
269		(R)-2-(3-(3-(3-(4-fluorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	574.4
270-		(S)-2-(3-(3-(3-(4-fluorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	574.4
271		(R)-2-(3-(3-(3-(4-fluorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl) quinoxalin-2-yl)propyl)phenyl)acetic acid	566.3
272		2-(3-(3-(3-(4-fluorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	589.4
273		2-(3-(3-(3-(4-fluorophenyl)-7-(3-(3-fluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	578.4
274		(S)-2-(3-(3-(3-(4-fluorophenyl)-7-(3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	574.4
275		2-(3-(3-(7-((4-fluorobenzyl)(methyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	566.4
276		(R)-3-methyl-5-(3-phenyl-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494.4

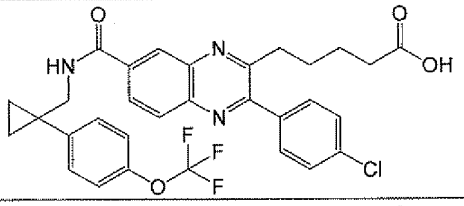
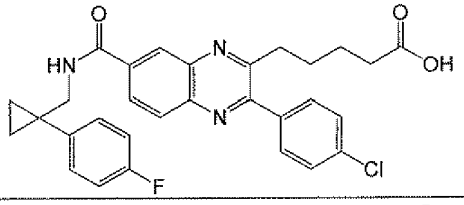
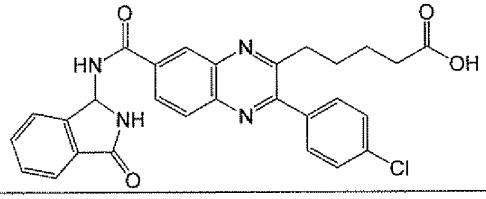
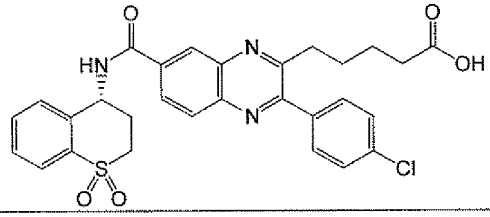
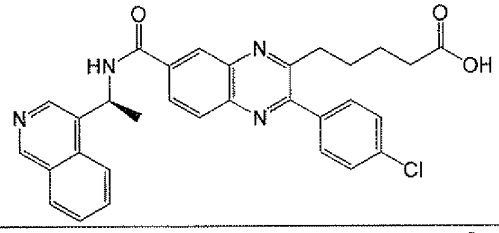
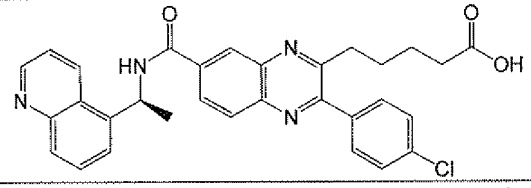
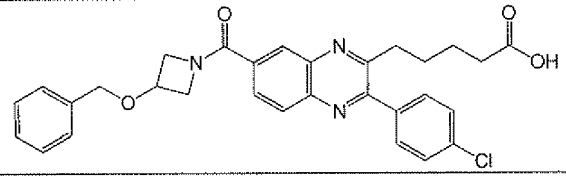
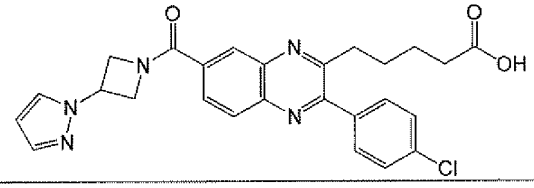
277		(R)-3-methyl-5-(3-phenyl-7-(((S)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494.4
278		(R)-5-(7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.4
279		(R)-5-(7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.4
280		(R)-3-methyl-5-(3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	509.4
281		(R)-5-(7-(3-(3-fluorophenyl)azetidine-1-carbonyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	498.4
282		(R)-3-methyl-5-(3-phenyl-7-((S)-3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	494.4
283		(R)-5-(7-((4-fluorobenzyl)(methyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.4

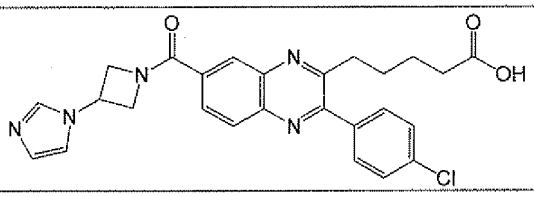
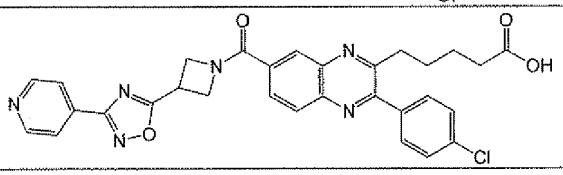
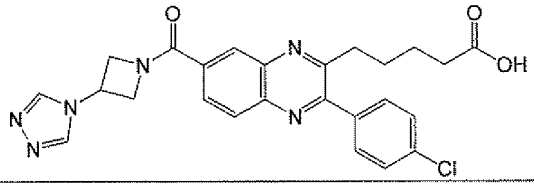
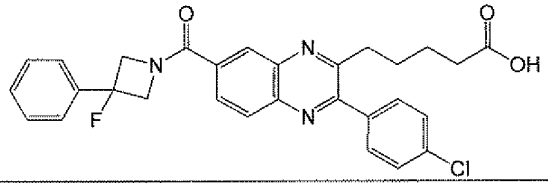
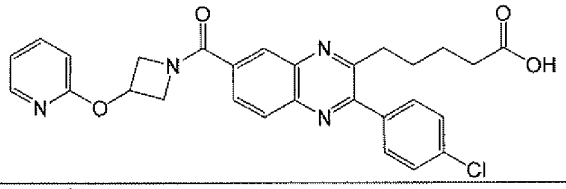
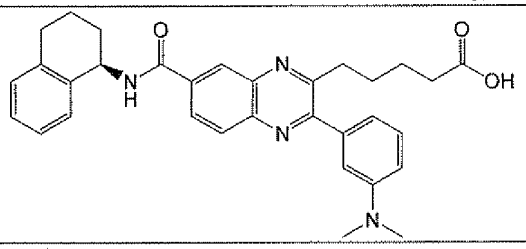
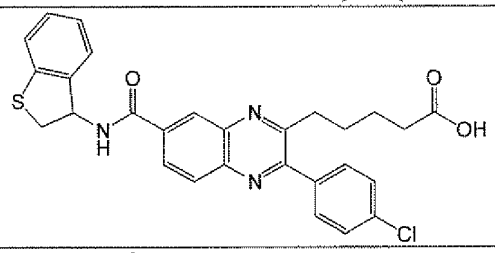
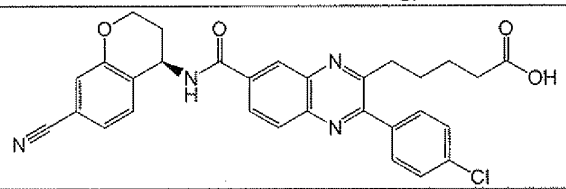
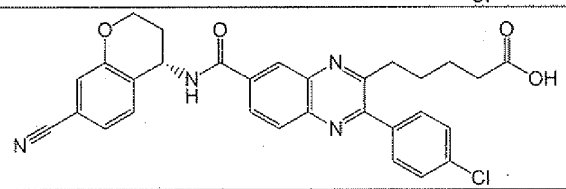
284		5-(7-((6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	513
285		5-(3-(4-chlorophenyl)-7-((1R,5S)-1-(p-tolyl)-3-azabicyclo[3.1.0]hexane-3-carbonyl)quinoxalin-2-yl)pentanoic acid	540.4
286		(S)-3-methyl-5-(3-phenyl-7-(((S)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494.4
287		(S)-5-(7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.3
288		(S)-5-(7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.3
289		(S)-3-methyl-5-(3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	509.4
290		(S)-5-(7-(3-(3-fluorophenyl)azetidine-1-carbonyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	498.4

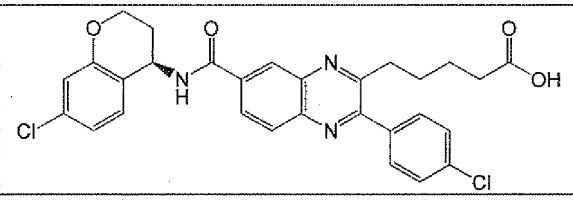
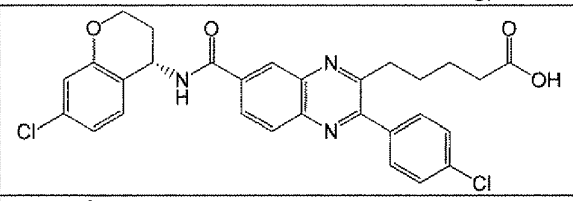
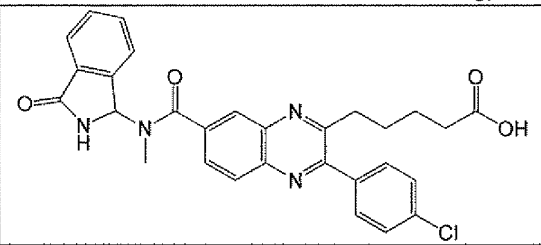
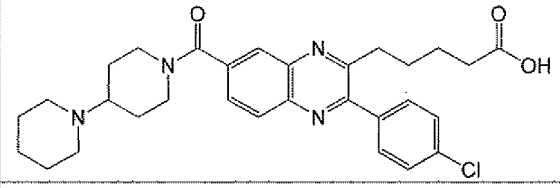
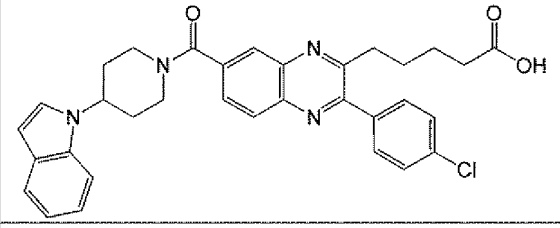
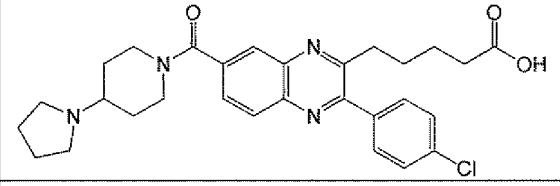
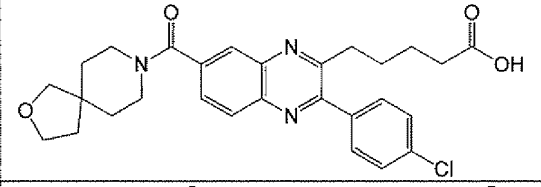
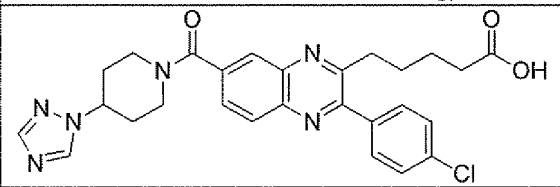
291		(S)-3-methyl-5-(3-phenyl-7-((S)-3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	494.4
292		(S)-5-(7-((4-fluorobenzyl)(methyl)carbamoyl)-3-phenylquinoxalin-2-yl)-3-methylpentanoic acid	486.3
293		(S)-3-methyl-5-(3-phenyl-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494.4
294		5-(3-phenyl-7-((2,3,4,5-tetrahydrobenzo[b]oxepin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	496.4
295		5-(7-((2,2-dimethylchroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	510.4
296		5-(7-((4,4-dimethyl-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	508.4
297		5-(7-(3,4-dihydro-2H-spiro[naphthalene-1,3'-pyrrolidin]-1'-ylcarbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	520.4
298		5-(7-(1-oxo-2,3-dihydro-1H-spiro[isoquinoline-4,4'-piperidin]-1'-ylcarbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	549.4

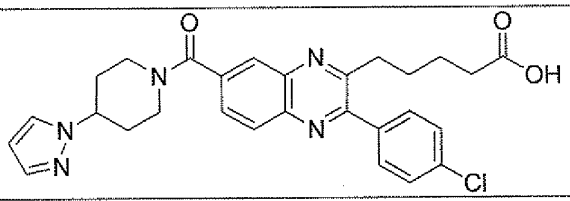
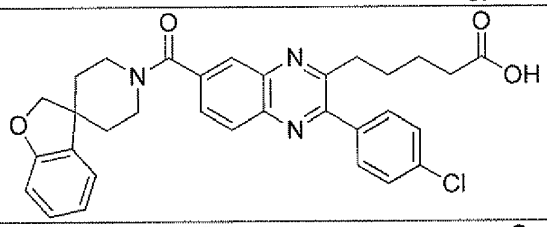
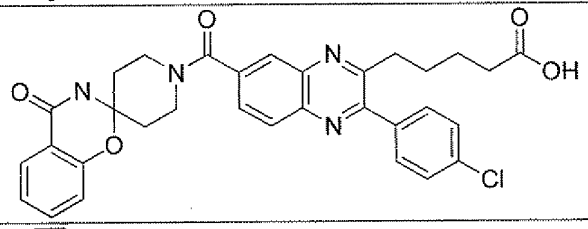
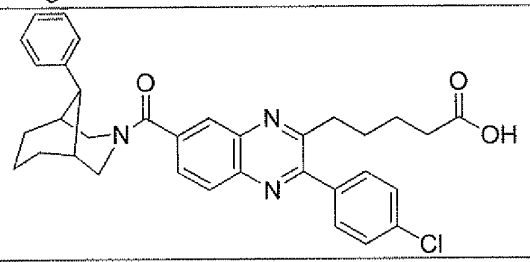
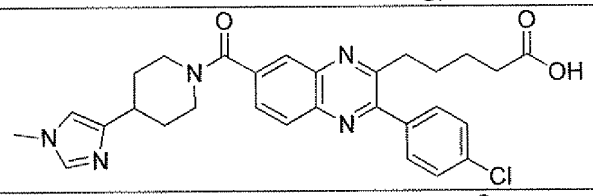
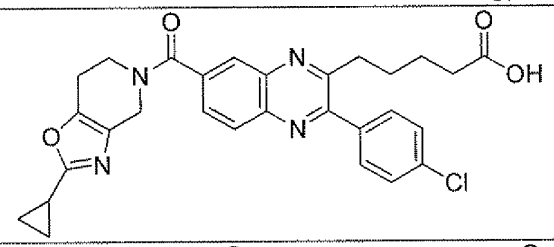
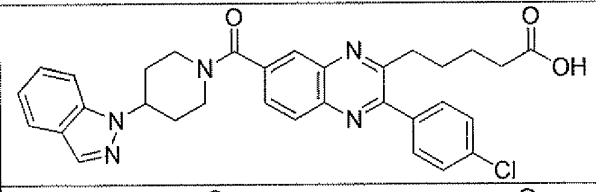
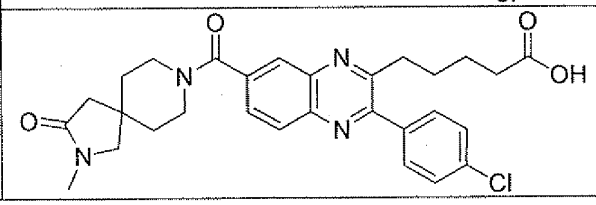
299		5-(7-(3-oxo-3,4-dihydro-2H-spiro[isoquinoline-1,4'-piperidin]-1'-ylcarbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	549.4
300		5-(7-(1-oxo-2,4-dihydro-1H-spiro[isoquinoline-3,4'-piperidin]-1'-ylcarbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	549.4
301		(R)-5-(3-phenyl-7-(thiochroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	498.3
302		5-(7-(4-benzylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	509.4
303		5-(7-(4-(3-cyanopyridin-2-yl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	521.4
304		5-(7-(4-(3,5-dichloropyridin-4-yl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	564.3
305		5-(3-phenyl-7-(4-(2-(trifluoromethyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	563.3
306		5-(3-phenyl-7-(4-(thiazol-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	502.3
307		5-(7-(isoindoline-2-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	452.3

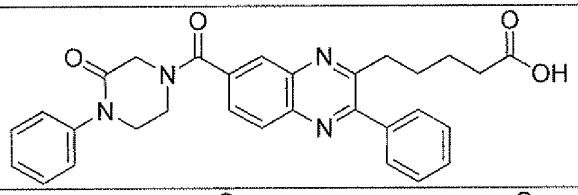
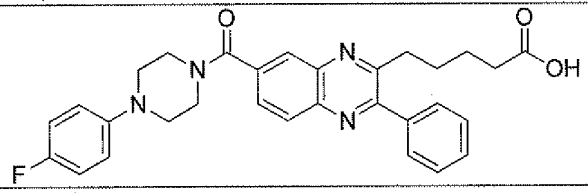
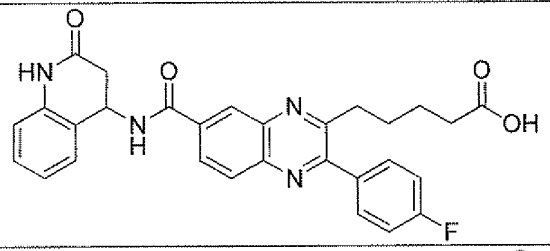
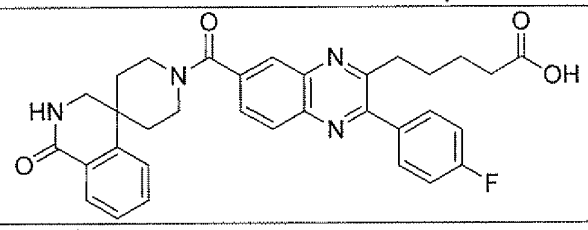
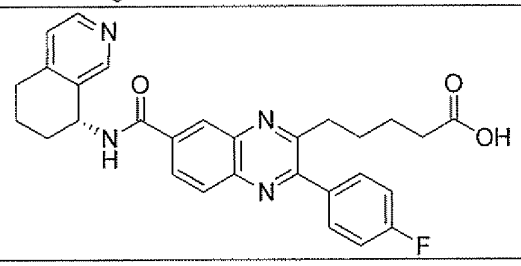
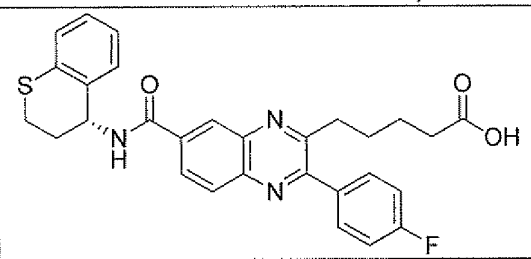
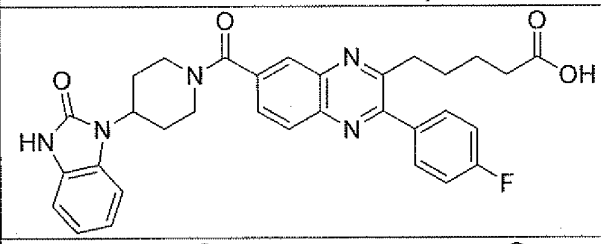
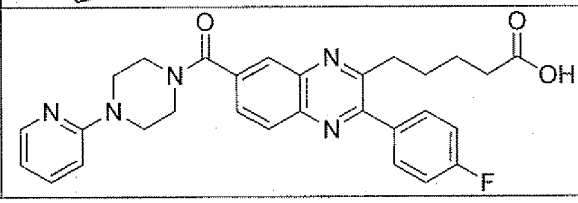
308		5-(7-(4-(2-chlorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	529.3
309		5-(3-phenyl-7-(4-(3-(trifluoromethyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	563.4
310		(S)-5-(7-((7-fluorochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	500.3
311		5-(7-((6-(benzyloxy)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	620.6
312		5-(3-(4-chlorophenyl)-7-((6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	544.5
313		(R)-5-(3-(4-chlorophenyl)-7-((6-fluoro-2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	520.4
314		(S)-5-(3-(4-chlorophenyl)-7-((6-fluoro-2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	520.4
315		5-(3-(4-chlorophenyl)-7-((1-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	543.3
316		5-(3-(4-chlorophenyl)-7-(4-(1-oxoisoindolin-2-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	583.5

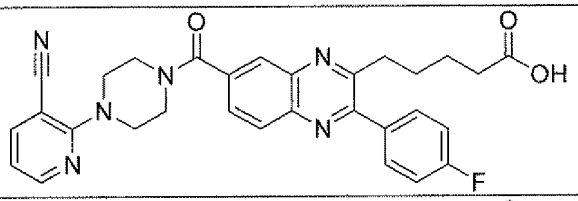
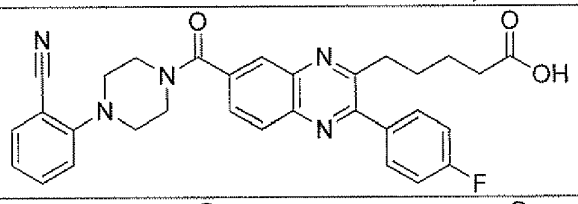
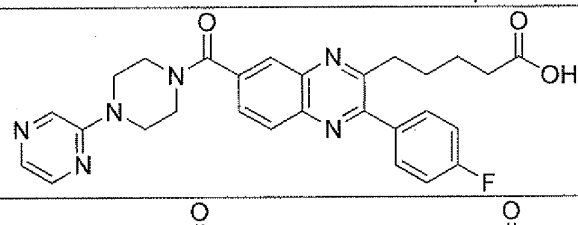
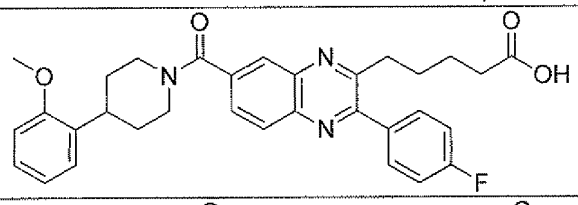
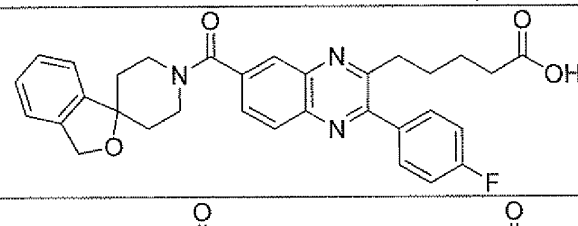
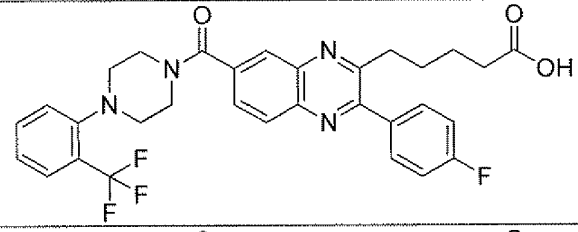
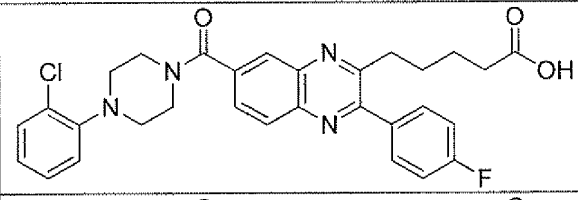
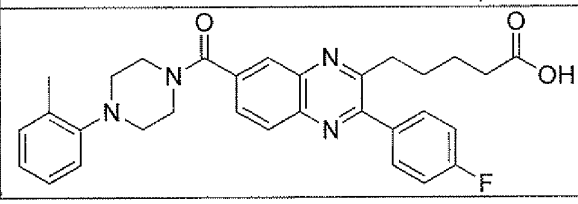
317		5-(3-(4-chlorophenyl)-7-(((1-(4-(trifluoromethoxy)phenyl)cyclopropyl)methyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	598.5
318		5-(3-(4-chlorophenyl)-7-(((1-(4-fluorophenyl)cyclopropyl)methyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	532.5
319		5-(3-(4-chlorophenyl)-7-((3-oxoisoindolin-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	515.4
320		(R)-5-(3-(4-chlorophenyl)-7-((1,1-dioxidothiochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	564.4
321		(S)-5-(3-(4-chlorophenyl)-7-((1-(isoquinolin-4-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539.5
322		(S)-5-(3-(4-chlorophenyl)-7-((1-(quinolin-5-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539.5
323		5-(7-(3-(benzyloxy)azetidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	530.5
324		5-(7-(3-(1H-pyrazol-1-yl)azetidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	490.4

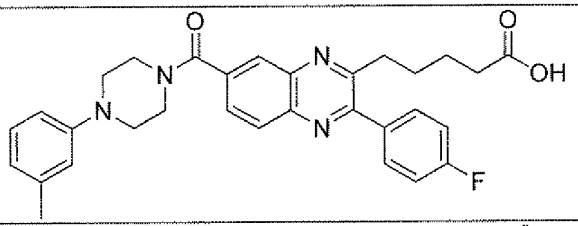
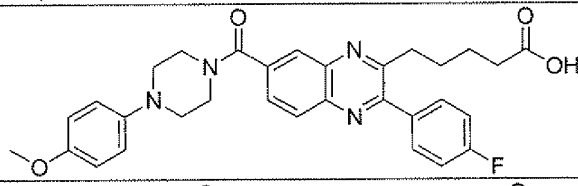
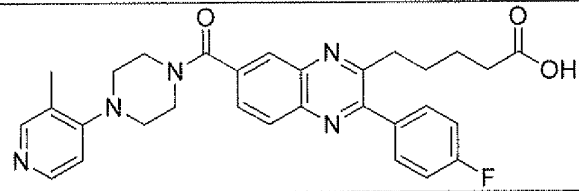
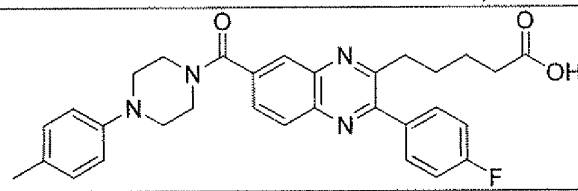
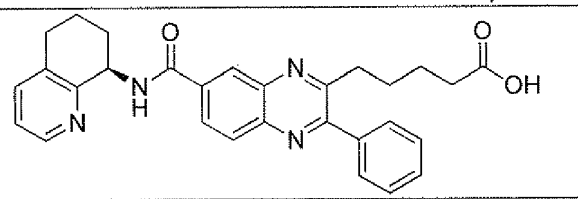
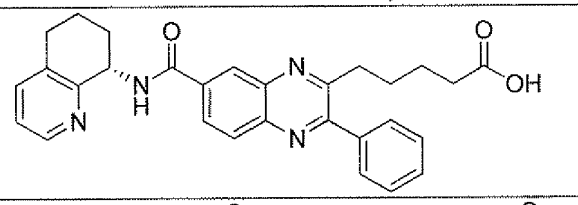
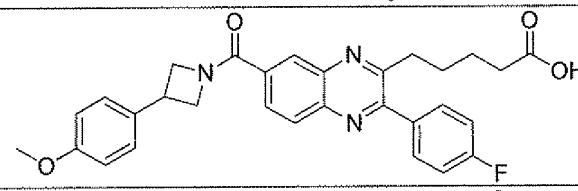
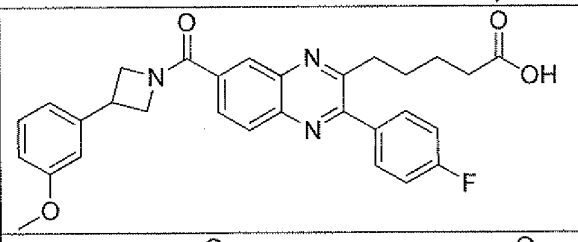
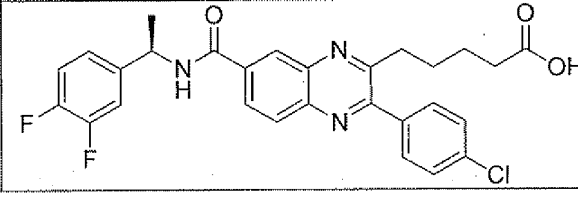
325		5-(7-(3-(1H-imidazol-1-yl)azetidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	490.4
326		5-(3-(4-chlorophenyl)-7-(3-(3-(pyridin-4-yl)-1,2,4-oxadiazol-5-yl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	569.5
327		5-(7-(3-(4H-1,2,4-triazol-4-yl)azetidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	491.4
328		5-(3-(4-chlorophenyl)-7-(3-fluoro-3-phenylazetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	518.4
329		5-(3-(4-chlorophenyl)-7-(3-(pyridin-2-yloxy)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	517.5
330		(R)-5-(3-(3-(dimethylamino)phenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	523.4
331		5-(3-(4-chlorophenyl)-7-((2,3-dihydrobenzo[b]thiophen-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	518.2
332		(R)-5-(3-(4-chlorophenyl)-7-((7-cyanochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	541.2
333		(S)-5-(3-(4-chlorophenyl)-7-((7-cyanochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	541.2

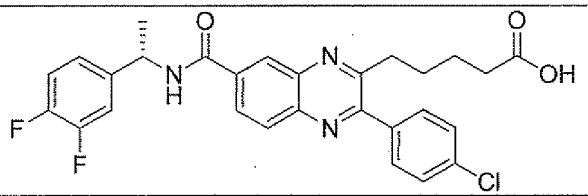
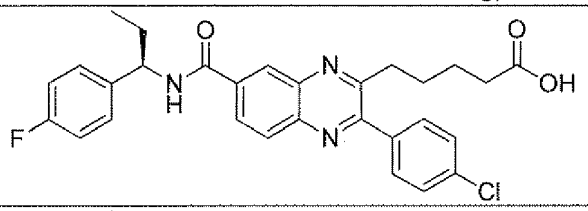
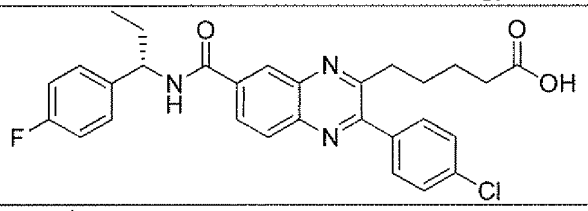
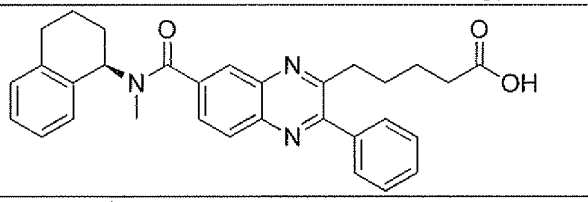
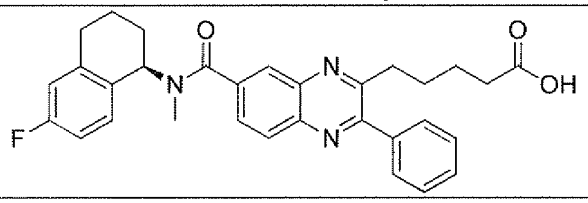
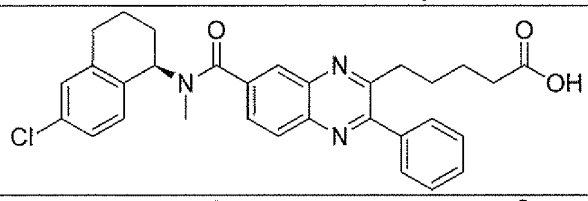
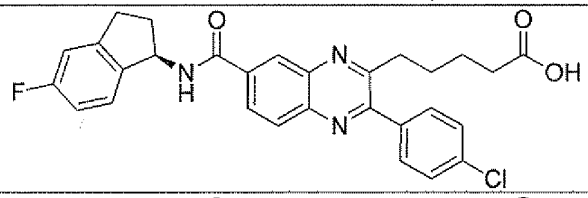
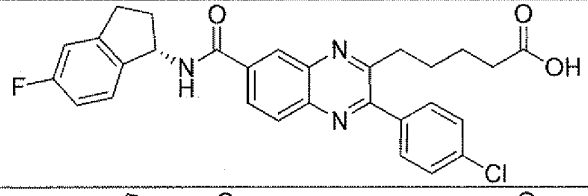
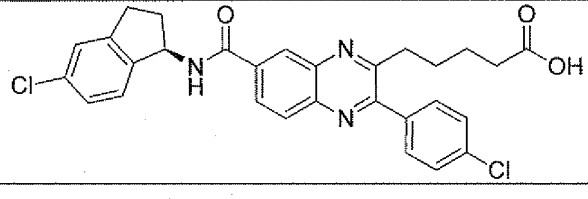
334		(R)-5-(7-((7-chlorochroman-4-yl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	550.2
335		(S)-5-(7-((7-chlorochroman-4-yl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	550.2
336		5-(3-(4-chlorophenyl)-7-(methyl(3-oxoisoindolin-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	529.2
337		5-(7-([1,4'-bipiperidine]-1'-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	535.3
338		5-(7-(4-(1H-indol-1-yl)piperidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	567.3
339		5-(3-(4-chlorophenyl)-7-(4-(pyrrolidin-1-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	521.3
340		5-(3-(4-chlorophenyl)-7-(2-oxa-8-azaspiro[4.5]decane-8-carbonyl)quinoxalin-2-yl)pentanoic acid	508.3
341		5-(7-(4-(1H-1,2,4-triazol-1-yl)piperidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	519.3

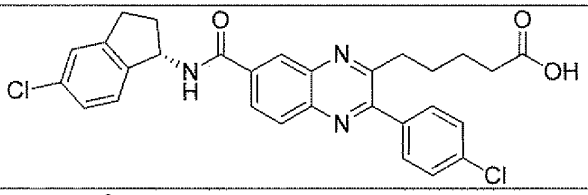
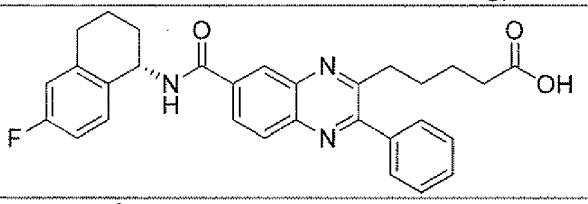
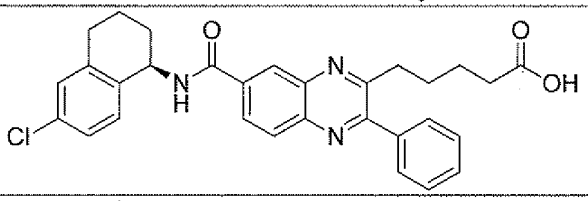
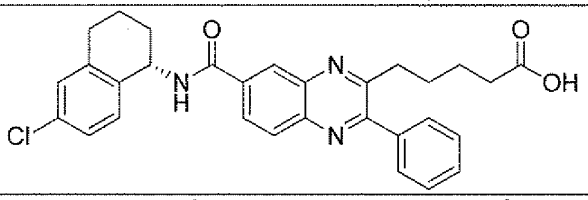
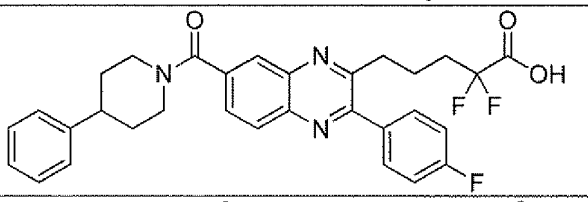
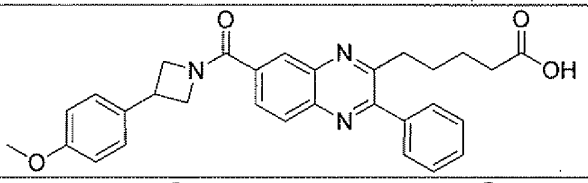
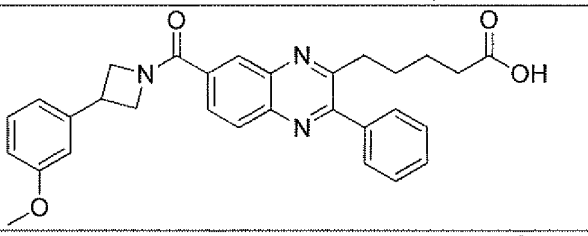
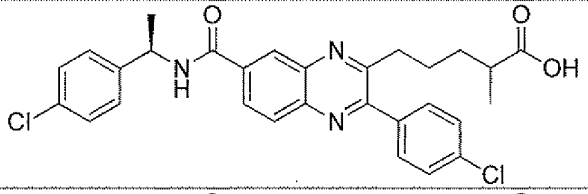
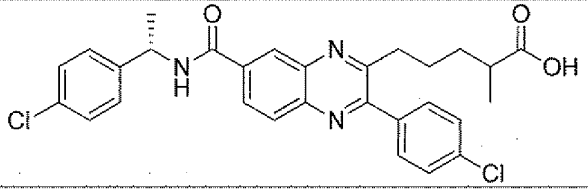
342		5-(7-(4-(1H-pyrazol-1-yl)piperidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	518.3
343		5-(3-(4-chlorophenyl)-7-(2H-spiro[benzofuran-3,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	556.3
344		5-(3-(4-chlorophenyl)-7-(4-oxo-3,4-dihydrospiro[benzo[e][1,3]oxazine-2,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	585.3
345		5-(3-(4-chlorophenyl)-7-((1R,5S,9r)-9-phenyl-3-azabicyclo[3.3.1]nonane-3-carbonyl)quinoxalin-2-yl)pentanoic acid	568.3
346		5-(3-(4-chlorophenyl)-7-(4-(1-methyl-1H-imidazol-4-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
347		5-(3-(4-chlorophenyl)-7-(2-cyclopropyl-4,5,6,7-tetrahydrooxazolo[4,5-c]pyridine-5-carbonyl)quinoxalin-2-yl)pentanoic acid	531.2
348		5-(7-(4-(1H-indazol-1-yl)piperidine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	568.3
349		5-(3-(4-chlorophenyl)-7-(2-methyl-3-oxo-2,8-diazaspiro[4.5]decane-8-carbonyl)quinoxalin-2-yl)pentanoic acid	535.3

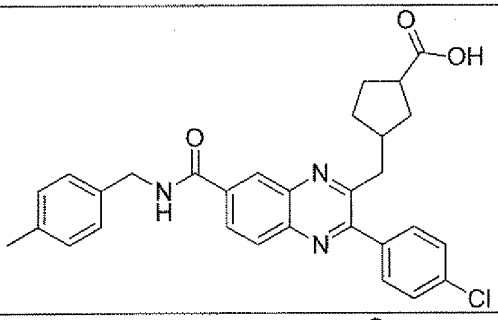
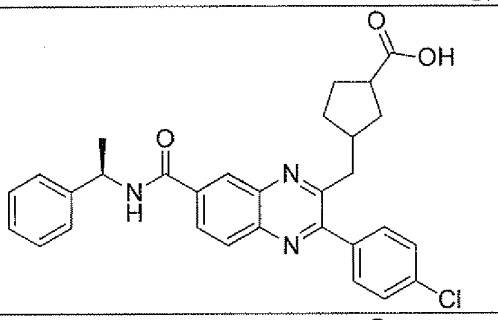
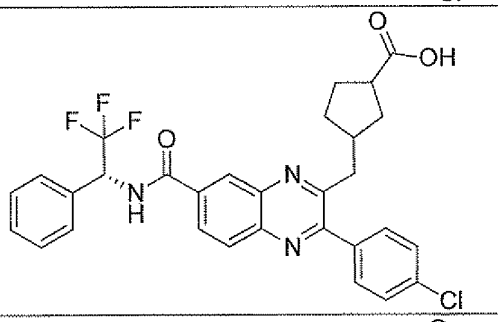
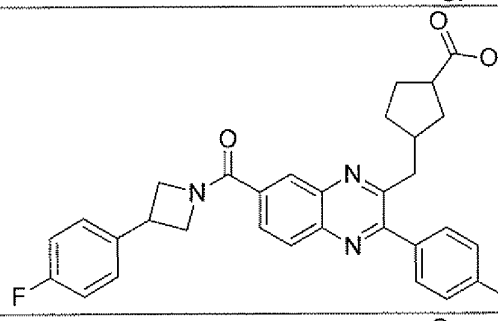
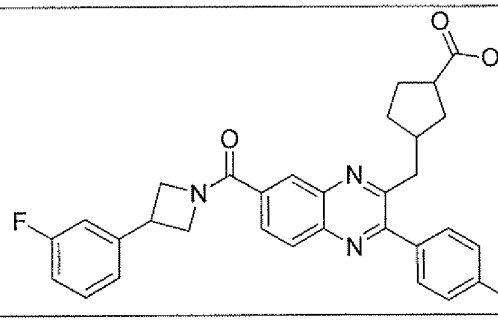
350		5-(7-(3-oxo-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	509.3
351		5-(7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	513.3
352		5-(3-(4-fluorophenyl)-7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	513.3
353		5-(3-(4-fluorophenyl)-7-(1-oxo-2,3-dihydro-1H-spiro[isoquinoline-4,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	567.3
354		(R)-5-(3-(4-fluorophenyl)-7-((5,6,7,8-tetrahydroisoquinolin-8-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	499.3
355		(R)-5-(3-(4-fluorophenyl)-7-(thiochroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	516.3
356		5-(3-(4-fluorophenyl)-7-(4-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	568.3
357		5-(3-(4-fluorophenyl)-7-(4-(pyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	514.3

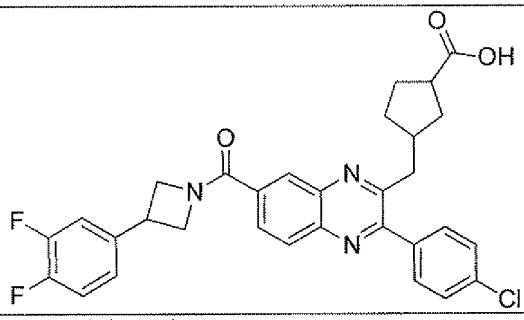
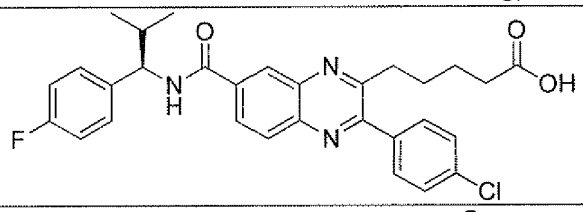
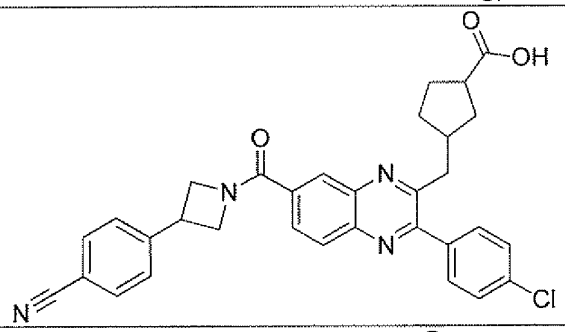
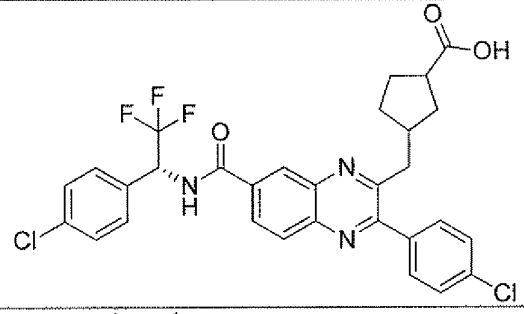
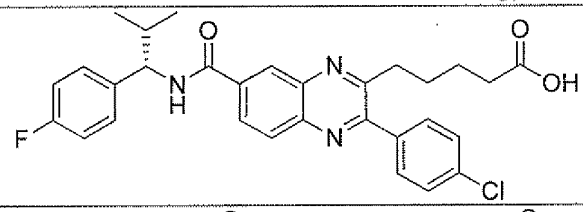
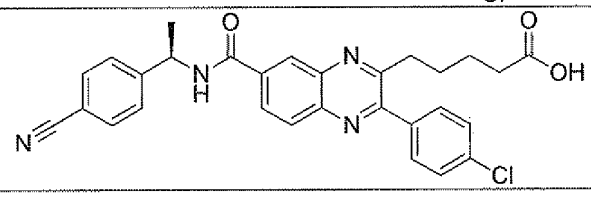
358		5-(7-(4-(3-cyanopyridin-2-yl)piperazine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	539.3
359		5-(7-(4-(2-cyanophenyl)piperazine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	538.3
360		5-(3-(4-fluorophenyl)-7-(4-(pyrazin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	515.3
361		5-(3-(4-fluorophenyl)-7-(4-(2-methoxyphenyl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	542.3
362		5-(3-(4-fluorophenyl)-7-(3H-spiro[isobenzofuran-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	540.3
363		5-(3-(4-fluorophenyl)-7-(4-(2-(trifluoromethyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	581.3
364		5-(7-(4-(2-chlorophenyl)piperazine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	547.3
365		5-(3-(4-fluorophenyl)-7-(4-(o-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	527.3

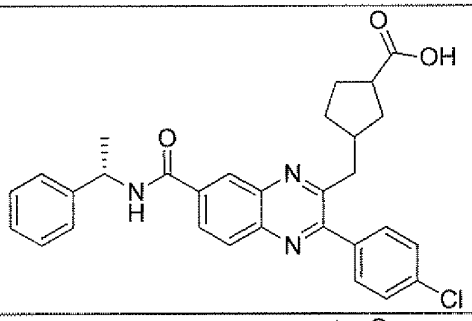
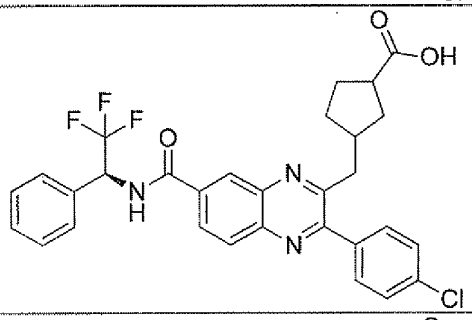
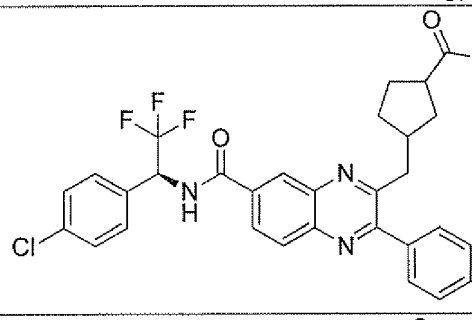
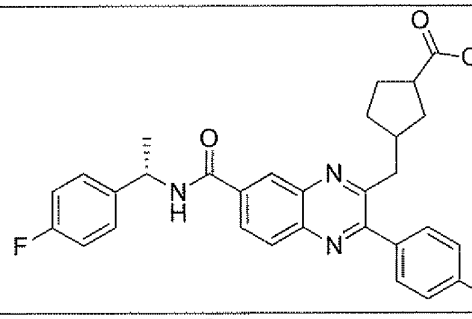
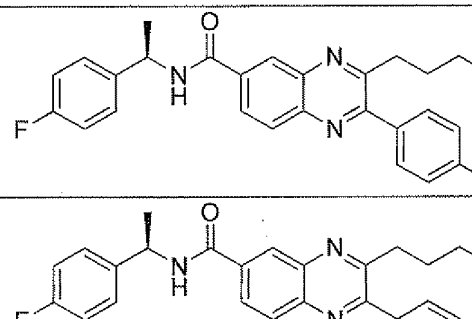
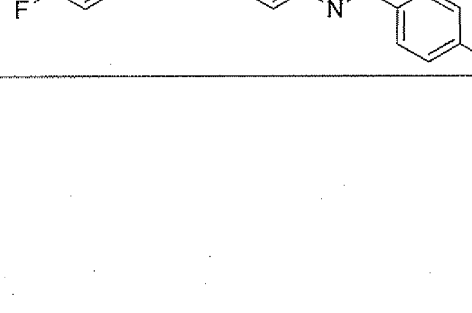
366		5-(3-(4-fluorophenyl)-7-(4-(m-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	527.3
367		5-(3-(4-fluorophenyl)-7-(4-(4-methoxyphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3
368		5-(3-(4-fluorophenyl)-7-(4-(3-methylpyridin-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	528.3
369		5-(3-(4-fluorophenyl)-7-(4-(p-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	527.3
370		(R)-8-(3-(4-carboxybutyl)-2-phenylquinoxaline-6-carboxamido)-5,6,7,8-tetrahydroquinolin-1-ium 2,2,2-trifluoroacetic acid	481
371		(S)-8-(3-(4-carboxybutyl)-2-phenylquinoxaline-6-carboxamido)-5,6,7,8-tetrahydroquinolin-1-ium 2,2,2-trifluoroacetic acid	481
372		5-(3-(4-fluorophenyl)-7-(3-(4-methoxyphenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	514
373		5-(3-(4-fluorophenyl)-7-(3-(3-methoxyphenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	514
374		(R)-5-(3-(4-chlorophenyl)-7-((1-(3,4-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	524

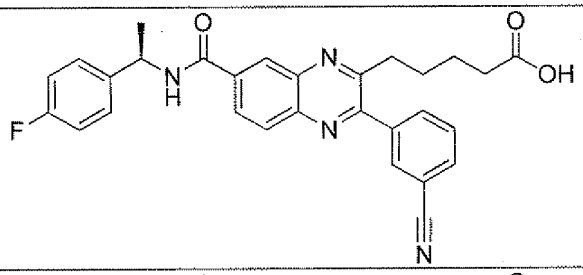
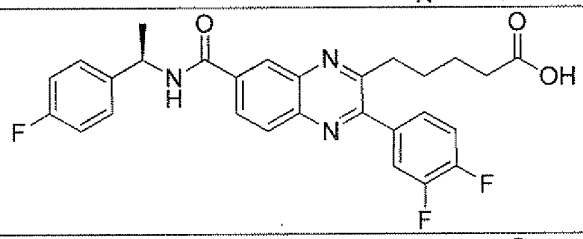
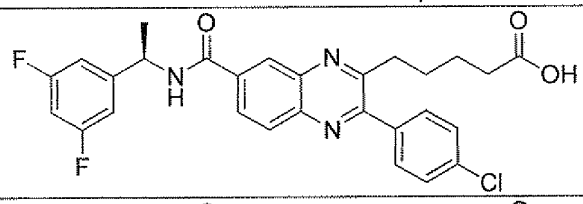
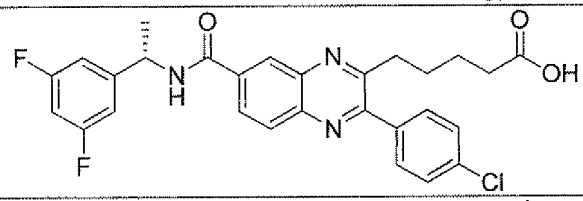
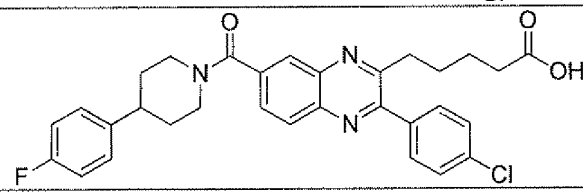
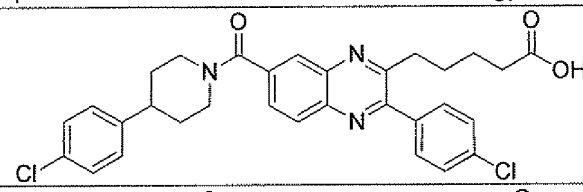
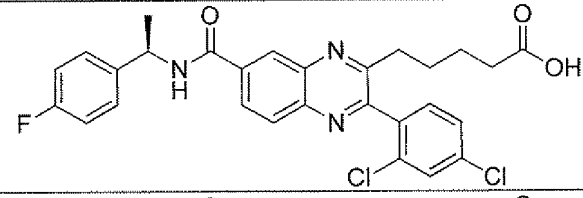
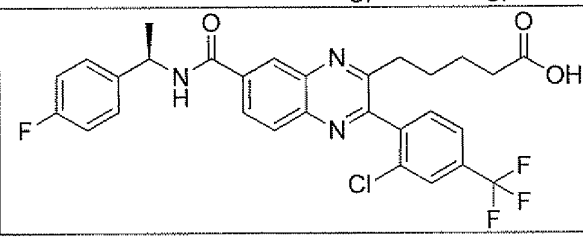
375		(S)-5-(3-(4-chlorophenyl)-7-((1-(3,4-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	524
376		(R)-5-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)propyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	522
377		(S)-5-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)propyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	522
378		(R)-5-(7-(methyl(1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	494
379		(R)-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)(methyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	512
380		(R)-5-(7-((6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)(methyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	528
381		(R)-5-(3-(4-chlorophenyl)-7-((5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	518
382		(S)-5-(3-(4-chlorophenyl)-7-((5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	518
383		(R)-5-(7-((5-chloro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	534

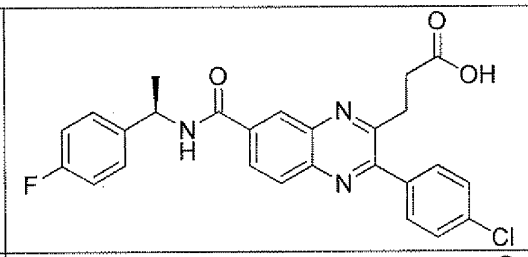
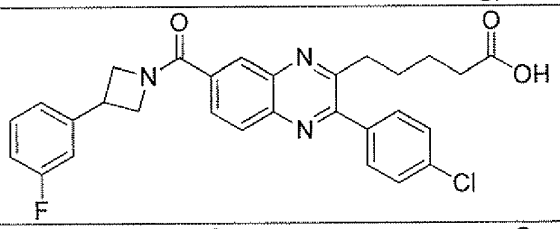
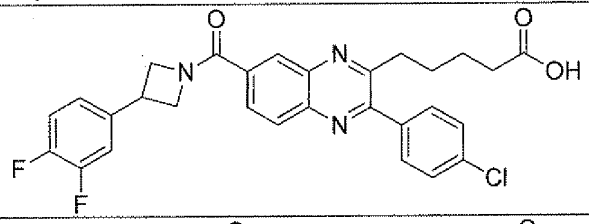
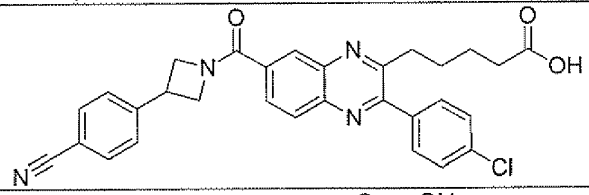
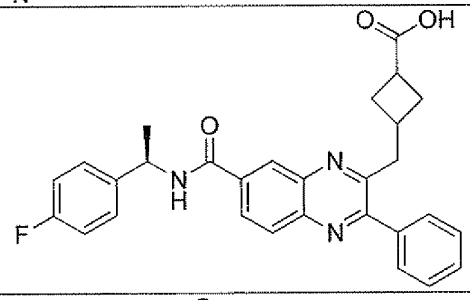
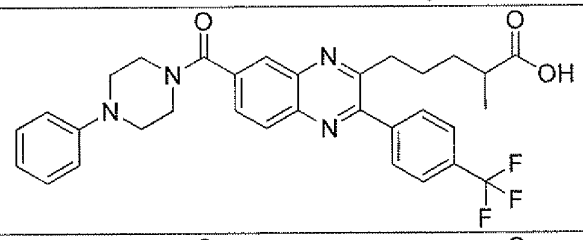
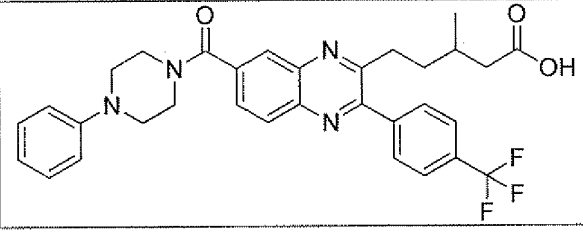
384		(S)-5-(7-((5-chloro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	534
385		(S)-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	498
386		(R)-5-(7-((6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	514
387		(S)-5-(7-((6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	514
388		(S)-5-(3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	480
389		5-(7-(3-(4-methoxyphenyl)azetidine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	496
390		5-(7-(3-(3-methoxyphenyl)azetidine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	496
391		5-(3-(4-chlorophenyl)-7-(((R)-1-(4-chlorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	536
392		5-(3-(4-chlorophenyl)-7-(((S)-1-(4-chlorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	536

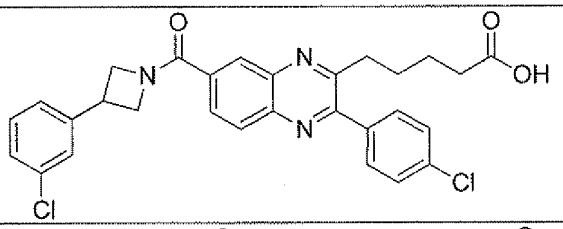
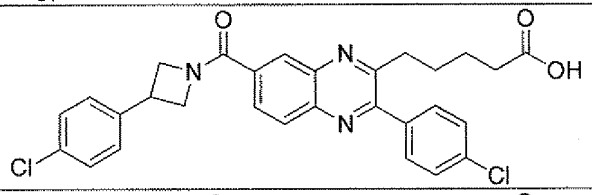
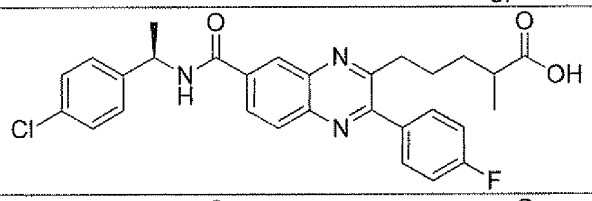
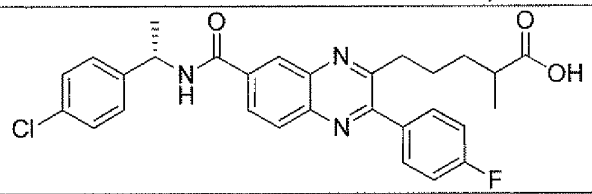
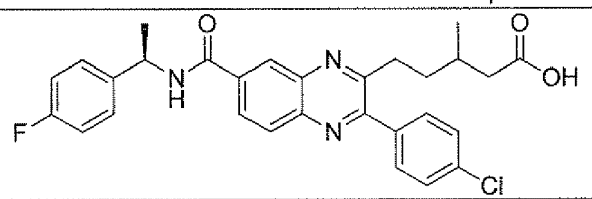
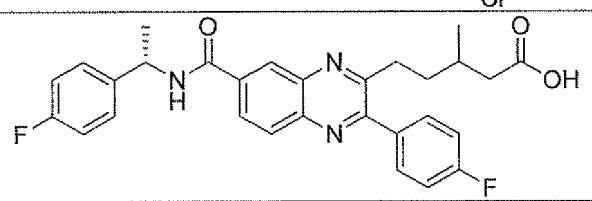
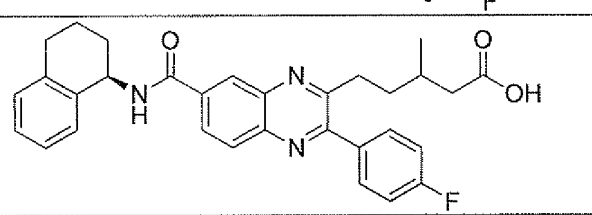
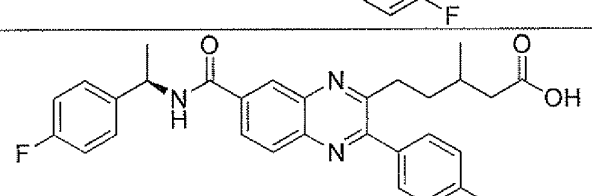
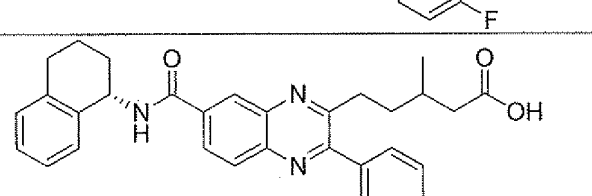
393		3-((3-(4-chlorophenyl)-7-((4-methylbenzyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	514
394		3-((3-(4-chlorophenyl)-7-(((R)-1-phenylethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	514
395		3-((3-(4-chlorophenyl)-7-(((R)-2,2,2-trifluoro-1-phenylethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	568
396		3-((3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	544
397		3-((3-(4-chlorophenyl)-7-(3-(3-fluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	544

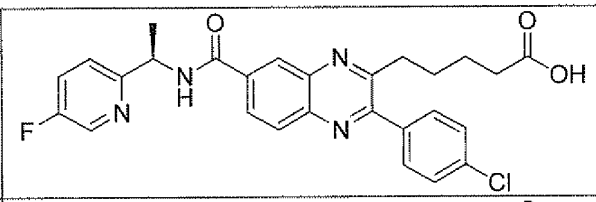
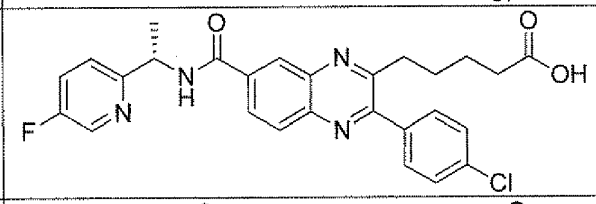
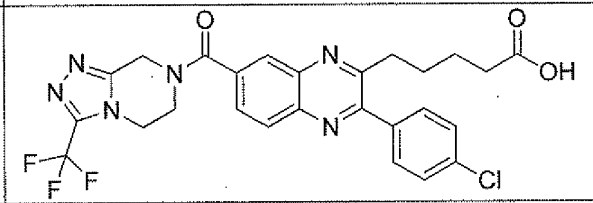
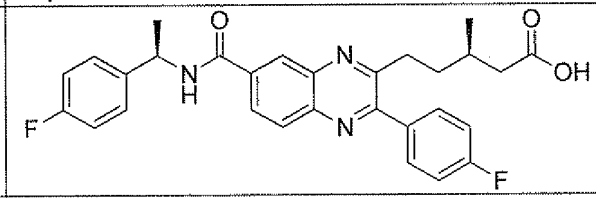
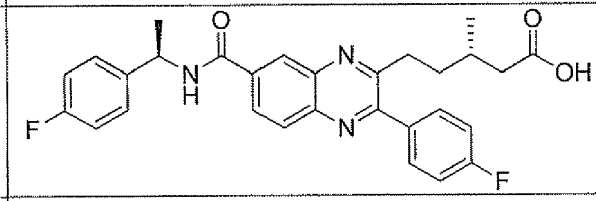
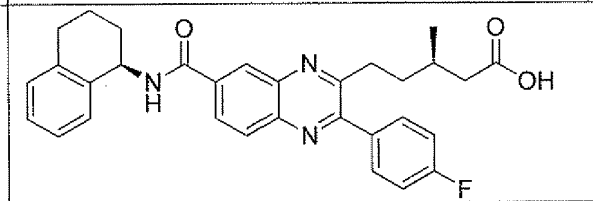
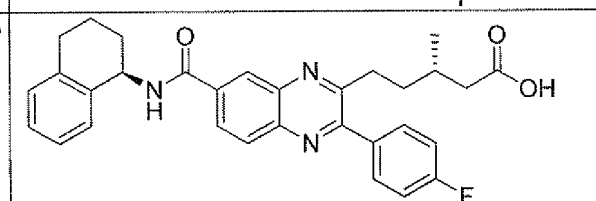
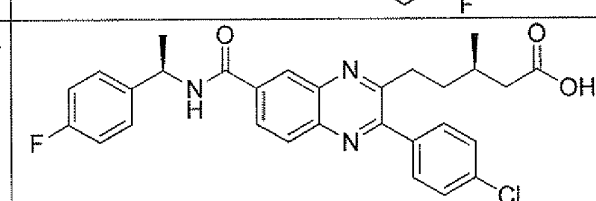
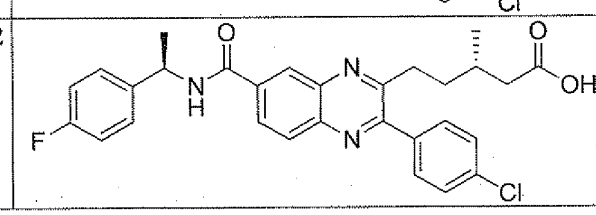
398		3-((3-(4-chlorophenyl)-7-(3-(3,4-difluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	562
399		(R)-5-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)-2-methylpropyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534
400		3-((3-(4-chlorophenyl)-7-(3-(4-cyanophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	551
401		3-((3-(4-chlorophenyl)-7-(((R)-1-(4-chlorophenyl)-2,2,2-trifluoroethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	603
402		(S)-5-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)-2-methylpropyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534
403		(R)-5-(3-(4-chlorophenyl)-7-((1-(4-cyanophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	513

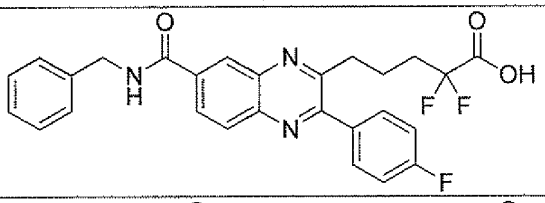
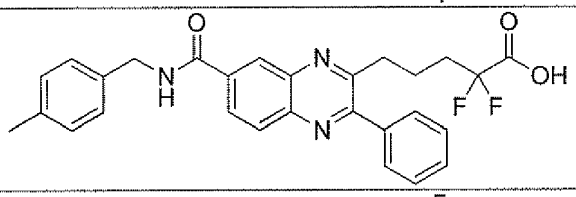
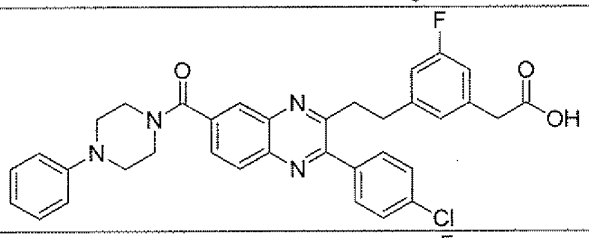
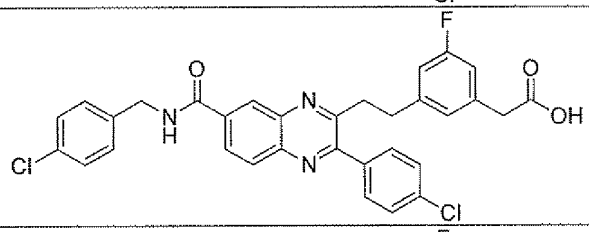
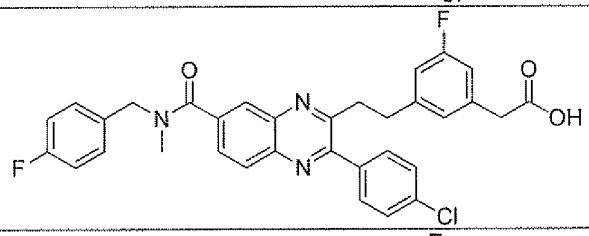
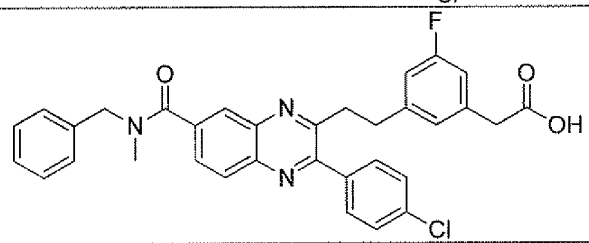
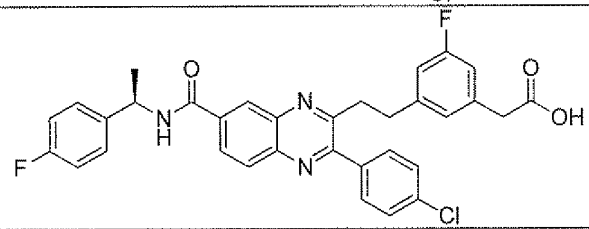
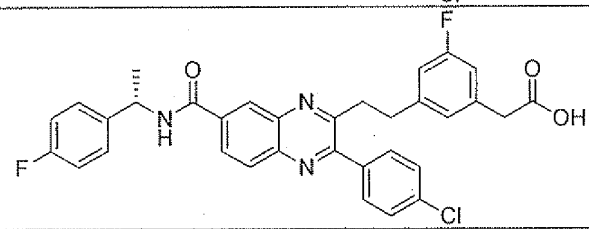
404		3-((3-(4-chlorophenyl)-7-(((S)-1-phenylethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	514
405		3-((3-(4-chlorophenyl)-7-(((S)-2,2,2-trifluoro-1-phenylethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	568
406		3-((3-(4-chlorophenyl)-7-(((S)-1-(4-chlorophenyl)-2,2,2-trifluoroethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	603
407		3-((3-(4-chlorophenyl)-7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)methyl)cyclopentanecarboxylic acid	532
408		5-(3-(4-chlorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	520
409		5-(3-(4-chlorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	520

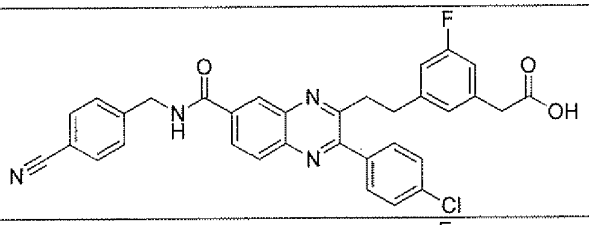
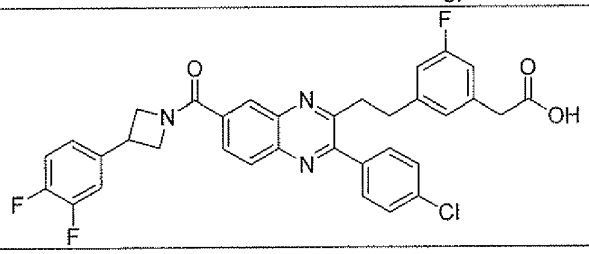
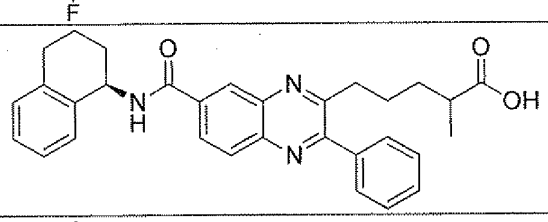
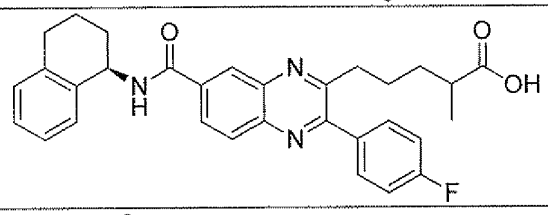
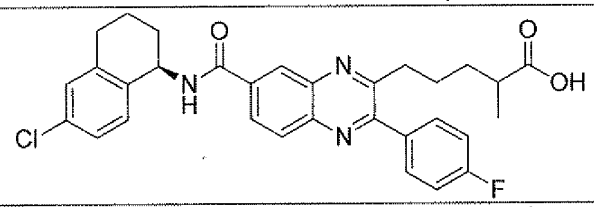
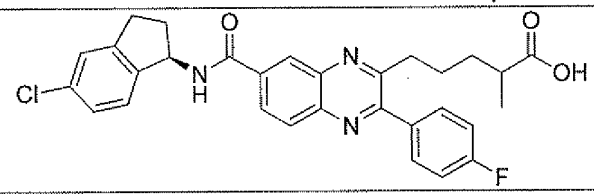
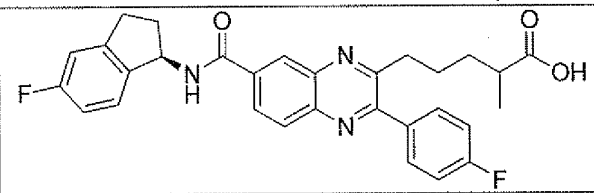
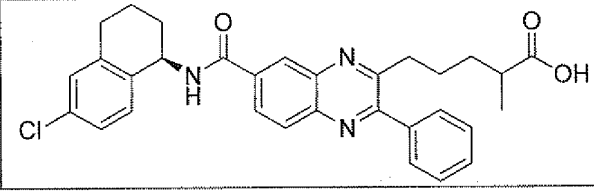
410		(R)-5-(3-(3-cyanophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	497
411		(R)-5-(3-(3,4-difluorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	508
412		(R)-5-(3-(4-chlorophenyl)-7-((1-(3,5-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	524
413		(S)-5-(3-(4-chlorophenyl)-7-((1-(3,5-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	524
414		5-(3-(4-chlorophenyl)-7-(4-(4-fluorophenyl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	546
415		5-(3-(4-chlorophenyl)-7-(4-(4-chlorophenyl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	562
416		(R)-5-(3-(2,4-dichlorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	540
417		(R)-5-(3-(2-chloro-4-(trifluoromethyl)phenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	574

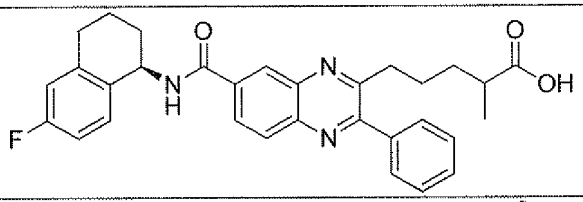
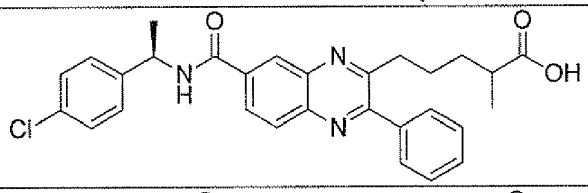
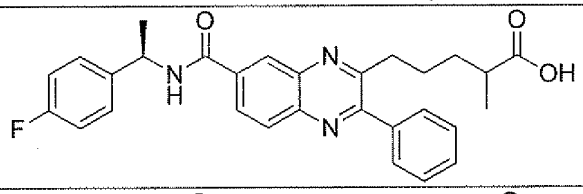
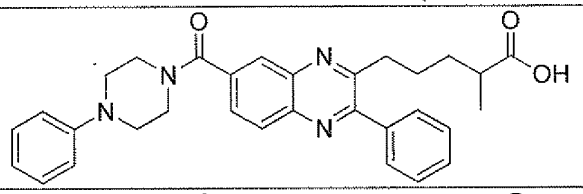
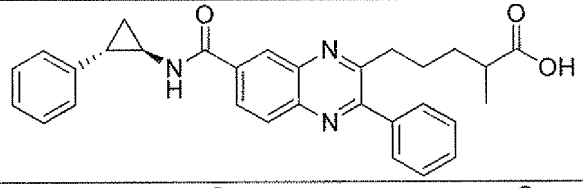
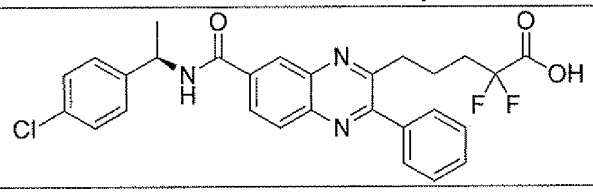
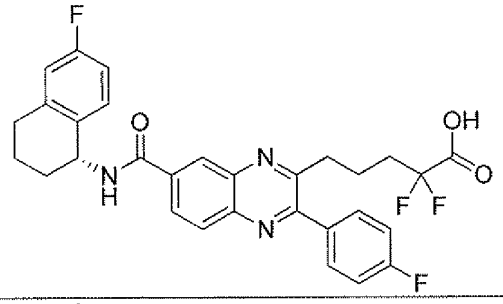
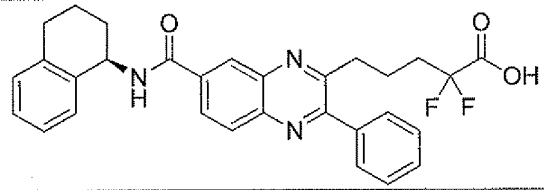
418		(R)-3-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)propanoic acid	478
419		5-(3-(4-chlorophenyl)-7-(3-(3-fluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	518
420		5-(3-(4-chlorophenyl)-7-(3-(3,4-difluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	536
421		5-(3-(4-chlorophenyl)-7-(3-(4-cyanophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	525
422		(R)-3-((7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)methyl)cyclobutanecarboxylic acid	484
423		2-methyl-5-(7-(4-phenylpiperazine-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)quinoxalin-2-yl)pentanoic acid	577
424		3-methyl-5-(7-(4-phenylpiperazine-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)quinoxalin-2-yl)pentanoic acid	577

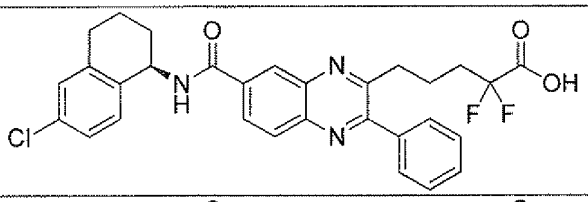
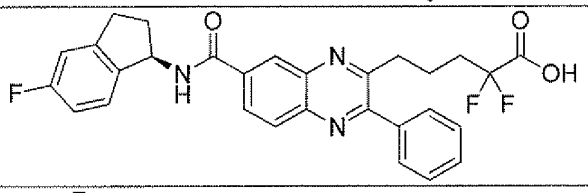
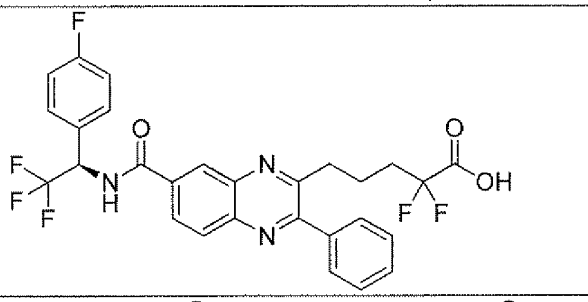
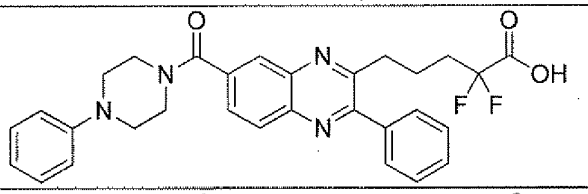
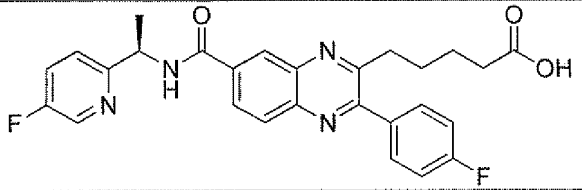
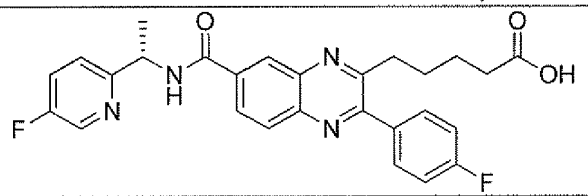
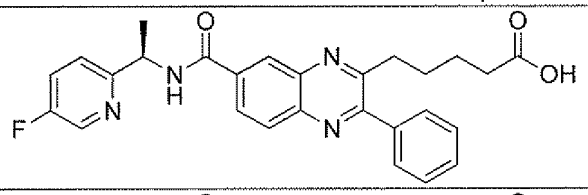
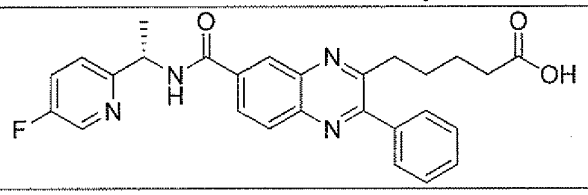
425		5-(3-(4-chlorophenyl)-7-(3-(3-chlorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	534
426		5-(3-(4-chlorophenyl)-7-(3-(4-chlorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	534
427		5-(7-(((R)-1-(4-chlorophenyl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	520
428		5-(7-(((S)-1-(4-chlorophenyl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	520
429		5-(3-(4-chlorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	520
430		5-(3-(4-fluorophenyl)-7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	504
431		5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	512
432		5-(3-(4-fluorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	504
433		5-(3-(4-fluorophenyl)-7-(((S)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	512

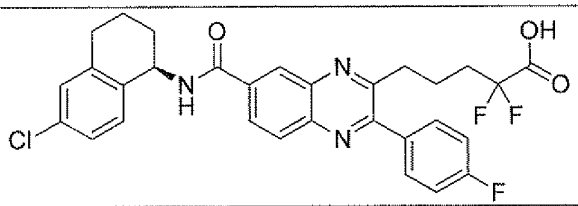
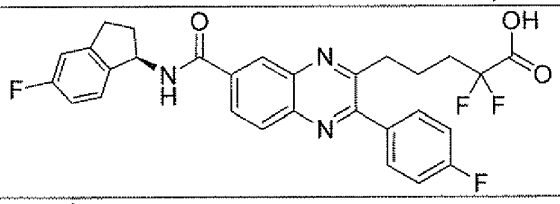
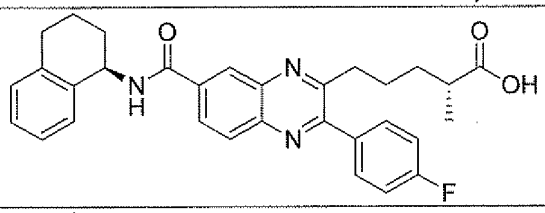
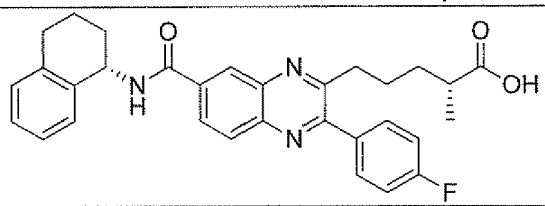
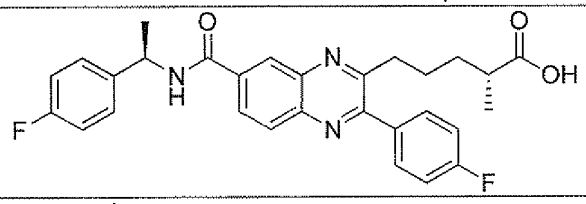
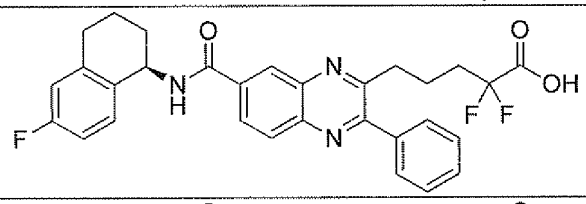
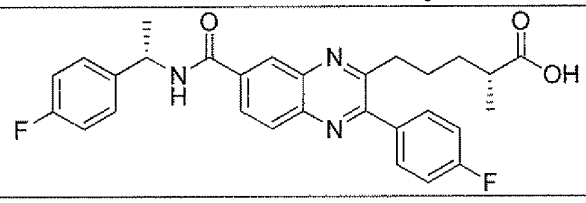
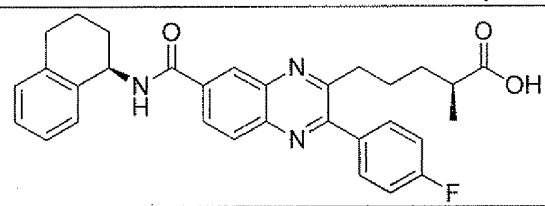
434		(R)-5-(3-(4-chlorophenyl)-7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	507
435		(S)-5-(3-(4-chlorophenyl)-7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	507
436		5-(3-(4-chlorophenyl)-7-(3-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)quinoxalin-2-yl)pentanoic acid	559
437		(R)-5-(3-(4-fluorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	504
438		(S)-5-(3-(4-fluorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	504
439		(R)-5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	512
440		(S)-5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	512
441		(R)-5-(3-(4-chlorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	520
442		(S)-5-(3-(4-chlorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-3-methylpentanoic acid	520

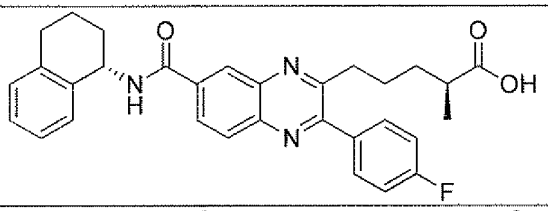
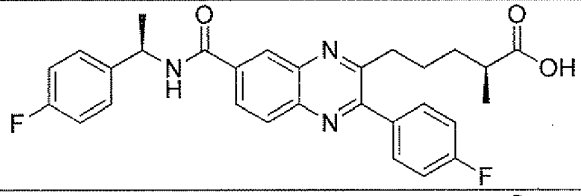
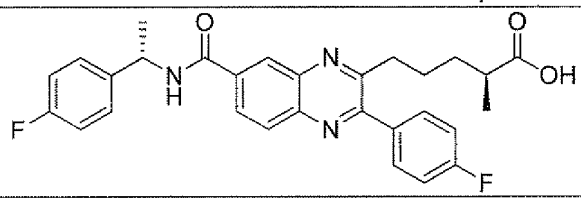
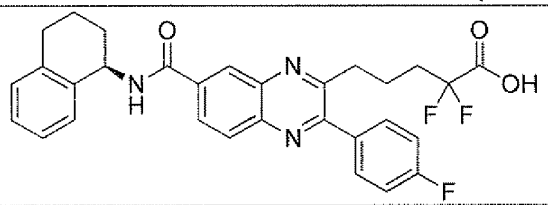
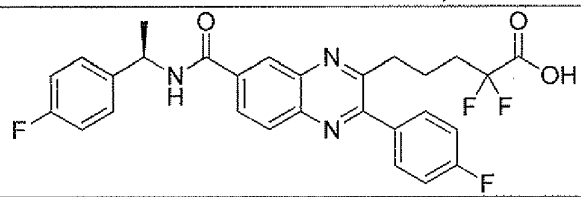
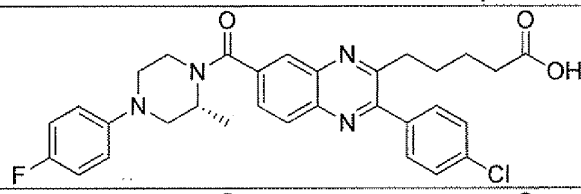
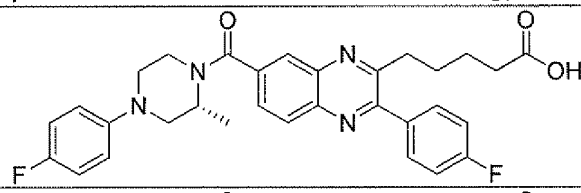
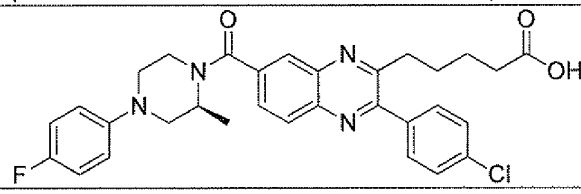
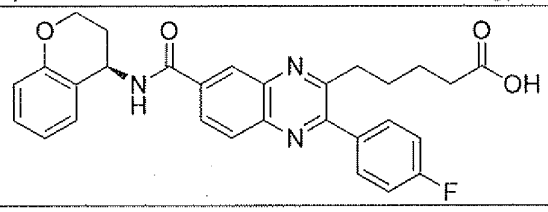
443		5-(7-(benzylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2,2-difluoropentanoic acid	494
444		2,2-difluoro-5-(7-((4-methylbenzyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	490
445		2-(3-(2-(3-(4-chlorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	610
446		2-(3-(2-(7-((4-chlorobenzyl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	589
447		2-(3-(2-(3-(4-chlorophenyl)-7-((4-fluorobenzyl)(methyl)carbamoyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	586
448		2-(3-(2-(7-(benzyl(methyl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	568
449		(R)-2-(3-(2-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	586
450		(S)-2-(3-(2-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	586

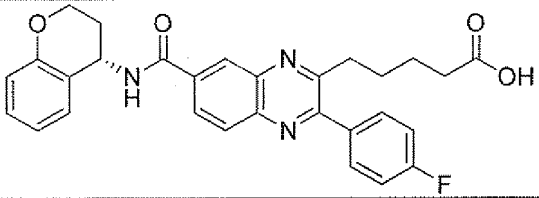
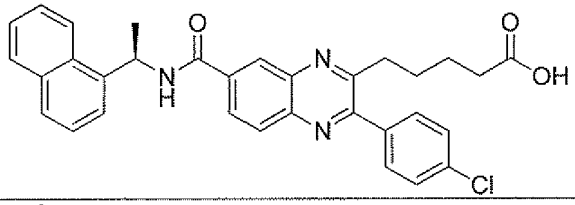
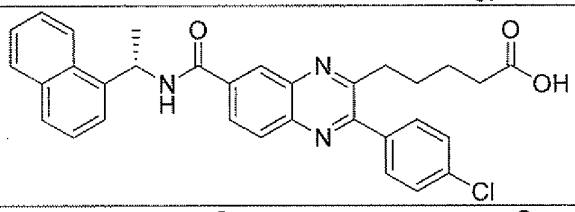
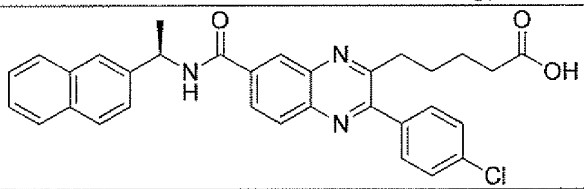
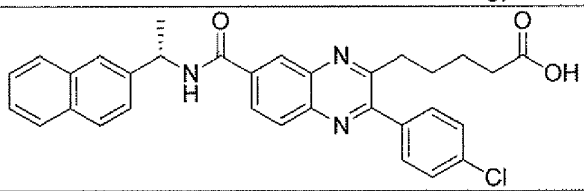
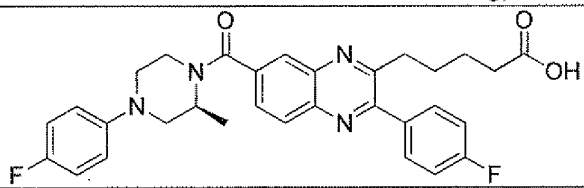
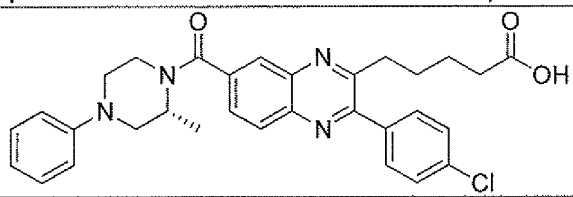
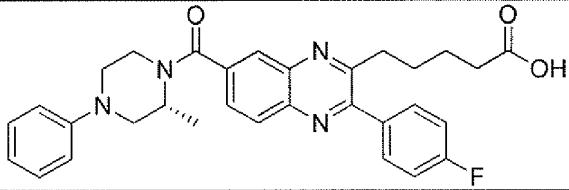
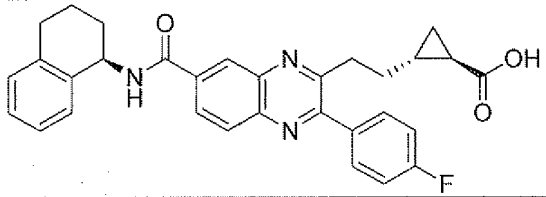
451		2-(3-(2-(3-(4-chlorophenyl)-7-((4-cyanobenzyl)carbamoyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	579
452		2-(3-(2-(3-(4-chlorophenyl)-7-(3-(3,4-difluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)ethyl)-5-fluorophenyl)acetic acid	616
453		2-methyl-5-(3-phenyl-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494
454		5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	512
455		5-(7-(((R)-6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	546
456		5-(7-(((R)-5-chloro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	532
457		5-(7-(((R)-5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	516
458		5-(7-(((R)-6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)-2-methylpentanoic acid	528

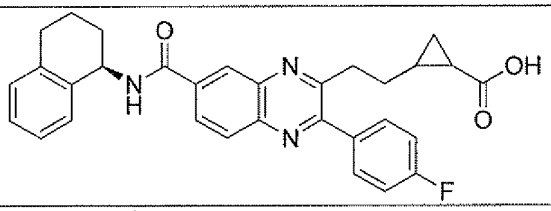
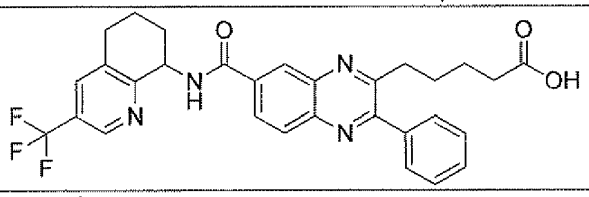
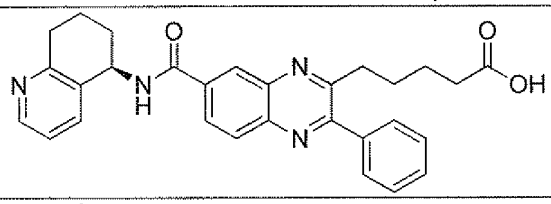
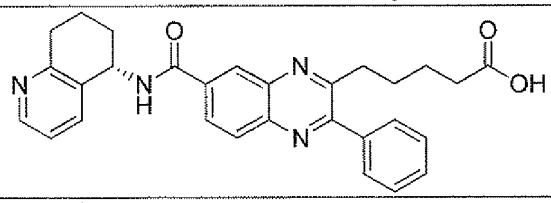
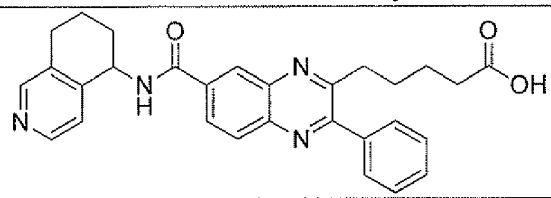
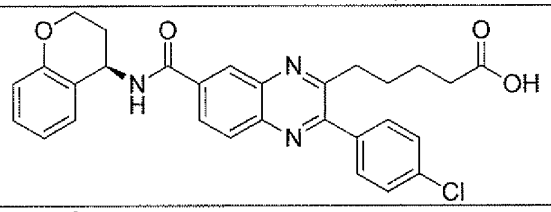
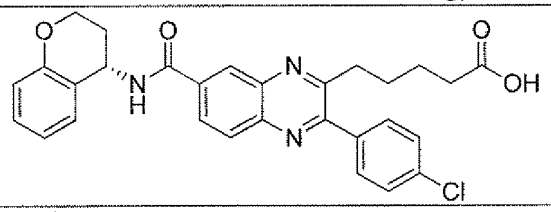
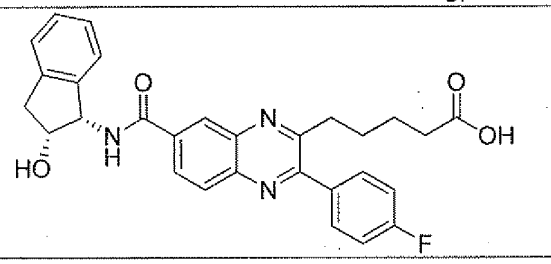
459		5-(7-(((R)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)-2-methylpentanoic acid	512
460		5-(7-(((R)-1-(4-chlorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-2-methylpentanoic acid	502
461		5-(7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-2-methylpentanoic acid	486
462		2-methyl-5-(3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	509
463		2-methyl-5-(3-phenyl-7-(((1R,2S)-2-phenylcyclopropyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	480
464		(R)-5-(7-((1-(4-chlorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)-2,2-difluoropentanoic acid	524
465		(R)-2,2-difluoro-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	552
466		(R)-2,2-difluoro-5-(3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	516

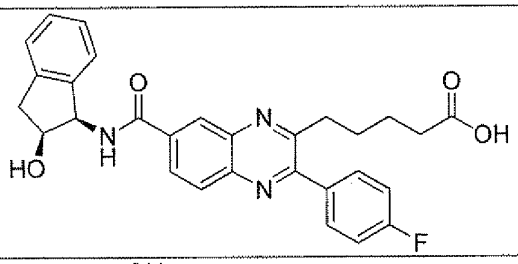
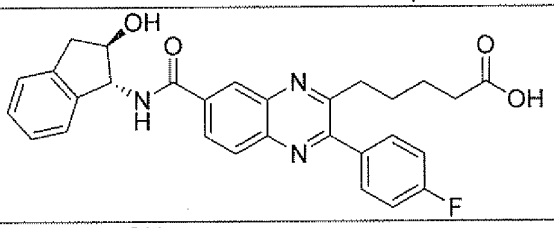
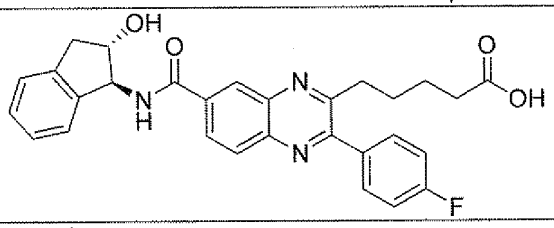
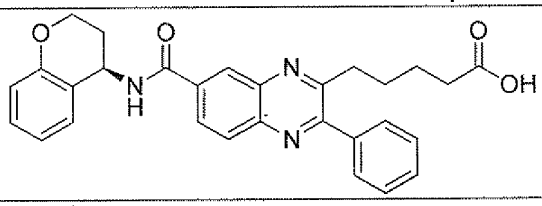
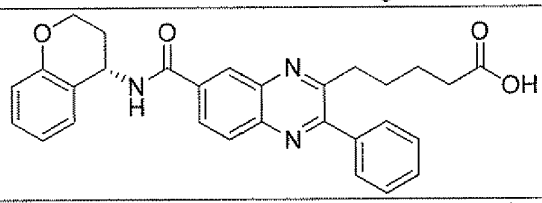
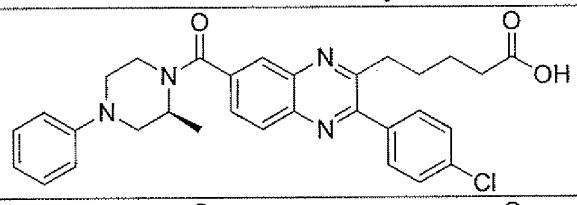
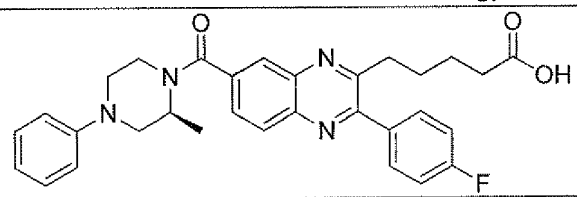
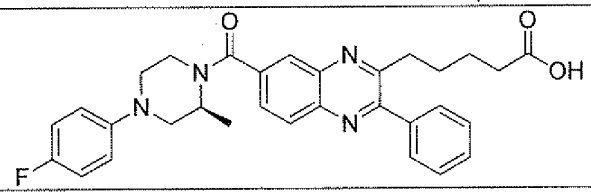
467		(R)-5-(7-((6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)-2,2-difluoropentanoic acid	550
468		(R)-2,2-difluoro-5-(7-((5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	520
469		(R)-2,2-difluoro-5-(3-phenyl-7-((2,2,2-trifluoro-1-(4-fluorophenyl)ethyl)carbamoyl) quinoxalin-2-yl)pentanoic acid	562
470		2,2-difluoro-5-(3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	531
471		(R)-5-(3-(4-fluorophenyl)-7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	491
472		(S)-5-(3-(4-fluorophenyl)-7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	491
473		(R)-5-(7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	473
474		(S)-5-(7-((1-(5-fluoropyridin-2-yl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	473

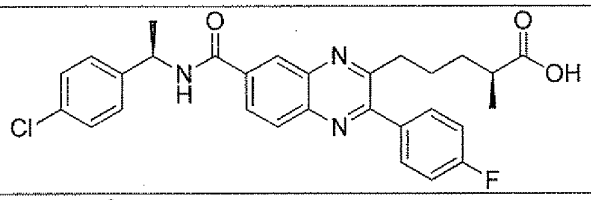
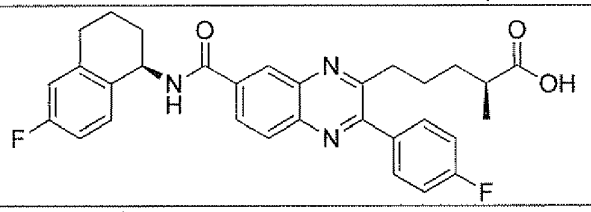
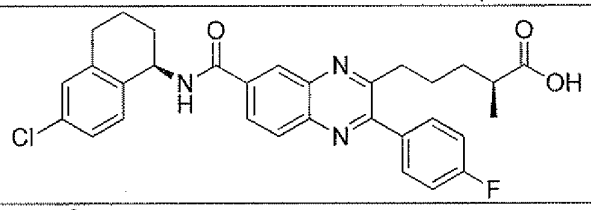
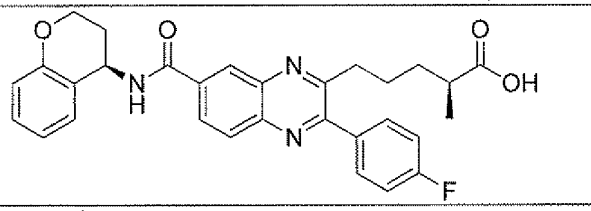
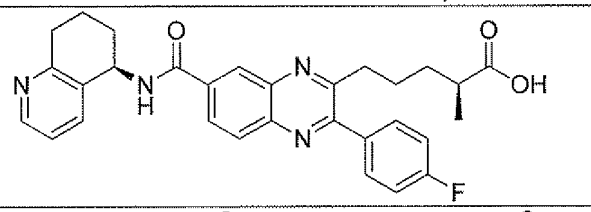
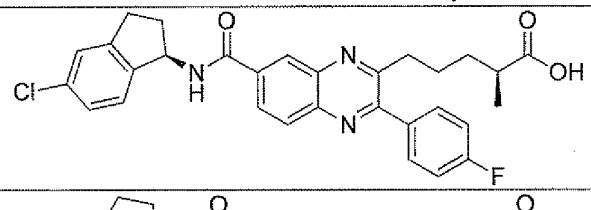
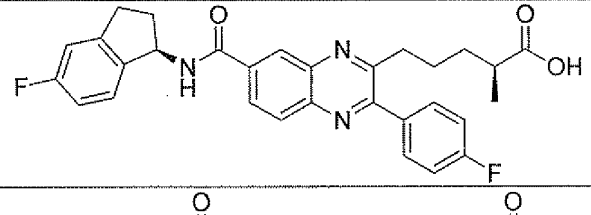
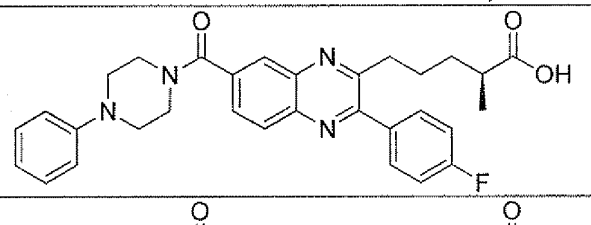
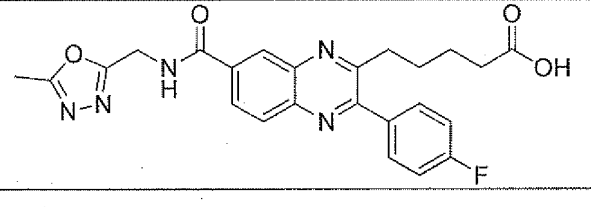
475		(R)-5-(7-((6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2,2-difluoropentanoic acid	568
476		(R)-2,2-difluoro-5-(7-((5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	538
477		(R)-5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	512
478		(R)-5-(3-(4-fluorophenyl)-7-(((S)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	512
479		(R)-5-(3-(4-fluorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	504
480		(R)-2,2-difluoro-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	534
481		(R)-5-(3-(4-fluorophenyl)-7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	504
482		(S)-5-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	512

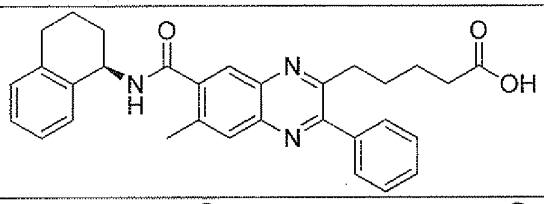
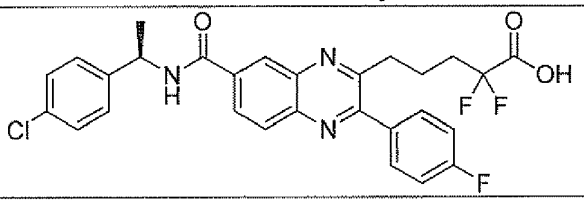
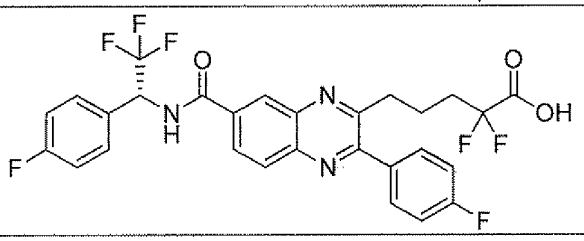
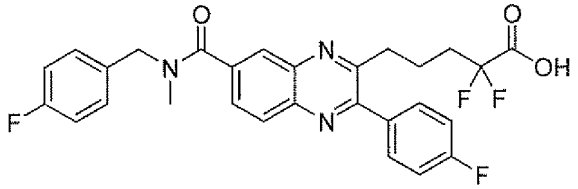
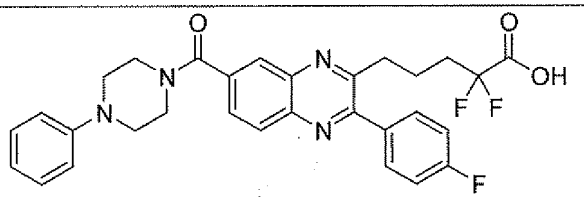
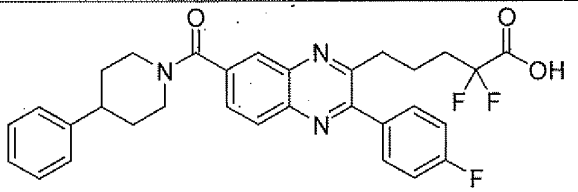
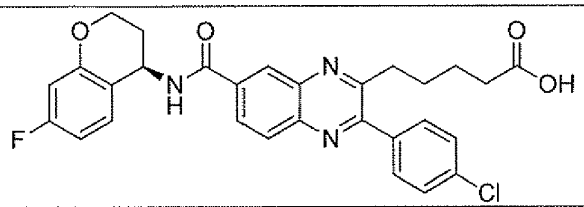
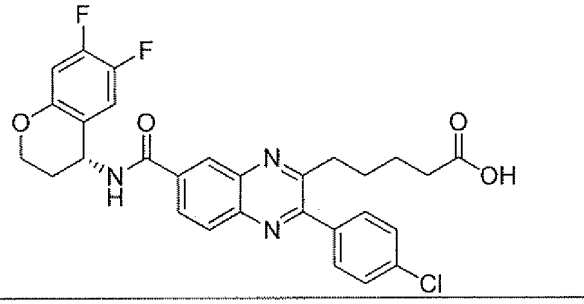
483		(S)-5-(3-(4-fluorophenyl)-7-(((S)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	512
484		(S)-5-(3-(4-fluorophenyl)-7-(((R)-1-(4-fluorophenyl)ethyl)carbamoyl) quinoxalin-2-yl)-2-methylpentanoic acid	504
485		(S)-5-(3-(4-fluorophenyl)-7-(((S)-1-(4-fluorophenyl)ethyl)carbamoyl) quinoxalin-2-yl)-2-methylpentanoic acid	504
486		(R)-2,2-difluoro-5-(3-(4-fluorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534
487		(R)-2,2-difluoro-5-(3-(4-fluorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl) quinoxalin-2-yl)pentanoic acid	526
488		(R)-5-(3-(4-chlorophenyl)-7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	561
489		(R)-5-(3-(4-fluorophenyl)-7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	545
490		(S)-5-(3-(4-chlorophenyl)-7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	561
491		(R)-5-(7-(chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	500

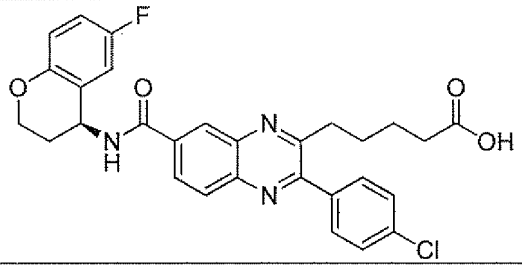
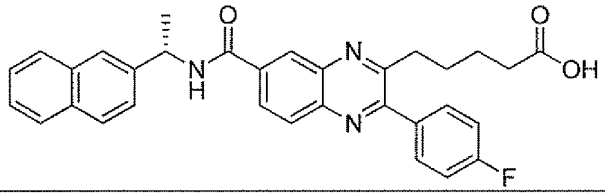
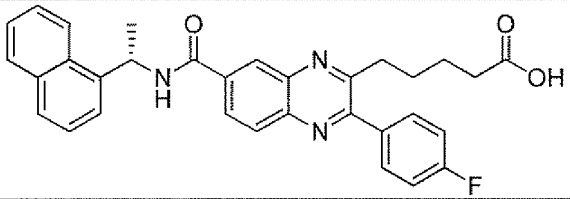
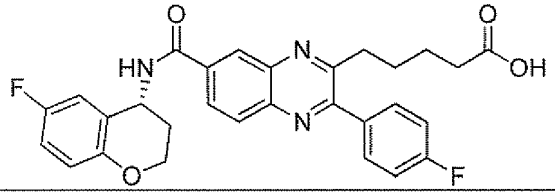
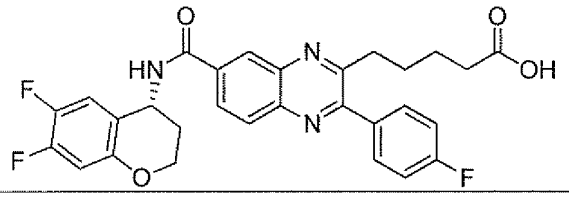
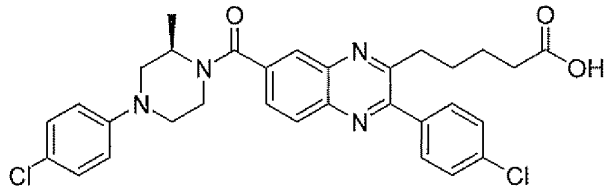
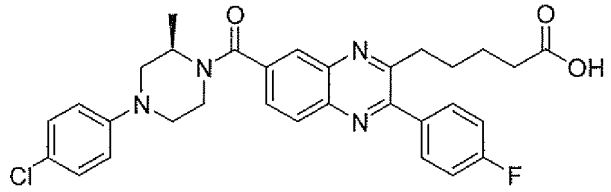
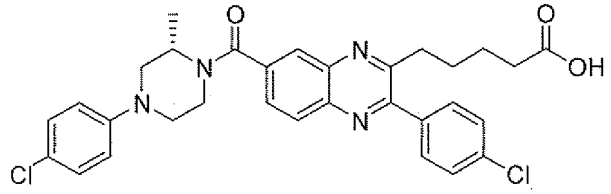
492		(S)-5-(7-(chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	500
493		(R)-5-(3-(4-chlorophenyl)-7-((1-(naphthalen-1-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539
494		(S)-5-(3-(4-chlorophenyl)-7-((1-(naphthalen-1-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539
495		(R)-5-(3-(4-chlorophenyl)-7-((1-(naphthalen-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539
496		(S)-5-(3-(4-chlorophenyl)-7-((1-(naphthalen-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539
497		(S)-5-(3-(4-fluorophenyl)-7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	545
498		(R)-5-(3-(4-chlorophenyl)-7-(2-methyl-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543
499		(R)-5-(3-(4-fluorophenyl)-7-(2-methyl-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	527
500		(1R,2R)-2-(2-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	510

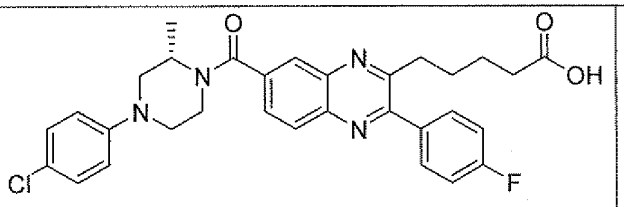
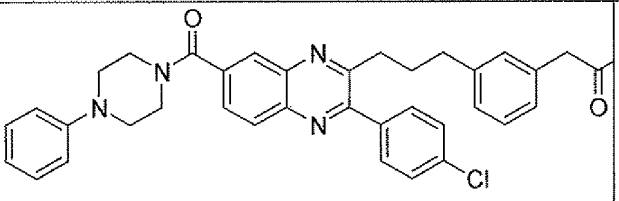
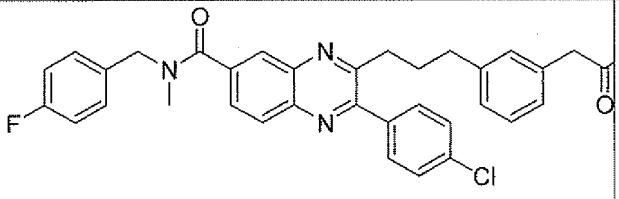
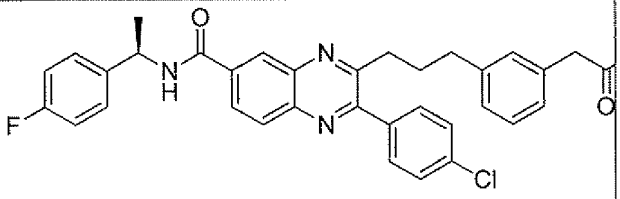
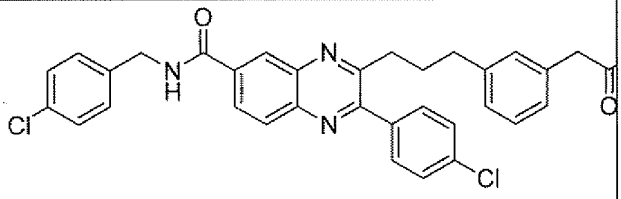
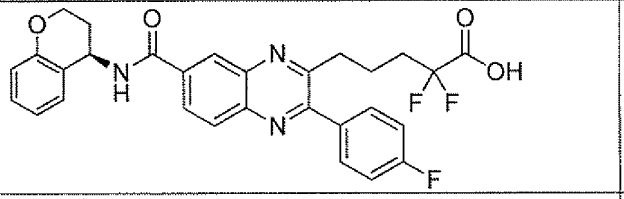
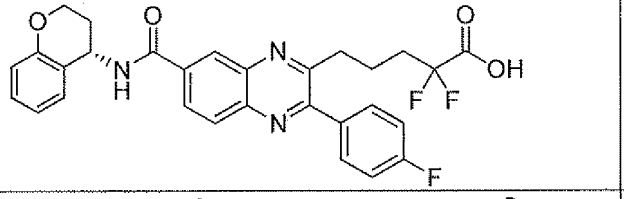
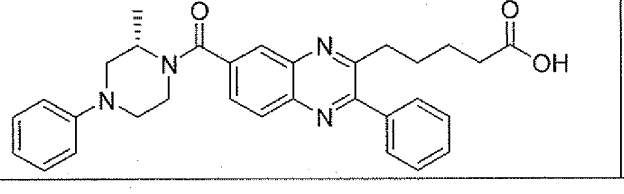
501		2-(2-(3-(4-fluorophenyl)-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)ethyl)cyclopropanecarboxylic acid	510
502		5-(3-phenyl-7-((3-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-8-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	549
503		(R)-5-(3-phenyl-7-((5,6,7,8-tetrahydroquinolin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	481
504		(S)-5-(3-phenyl-7-((5,6,7,8-tetrahydroquinolin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	481
505		5-(3-phenyl-7-((5,6,7,8-tetrahydroisoquinolin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	481
506		(R)-5-(3-(4-chlorophenyl)-7-(chroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	516
507		(S)-5-(3-(4-chlorophenyl)-7-(chroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	516.3
508		5-(3-(4-fluorophenyl)-7-(((1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	500

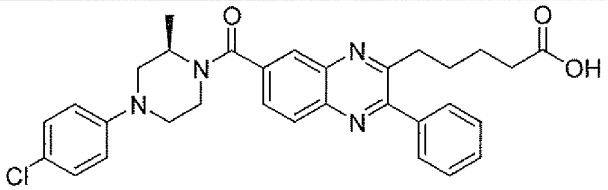
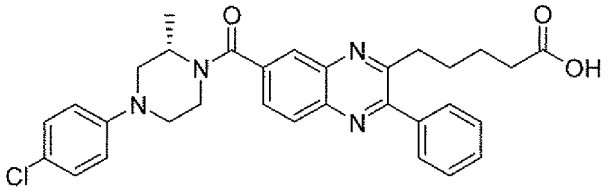
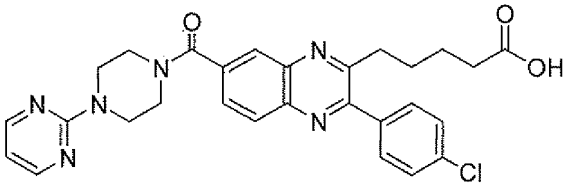
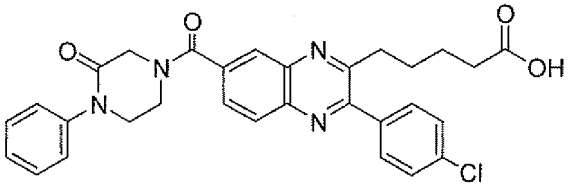
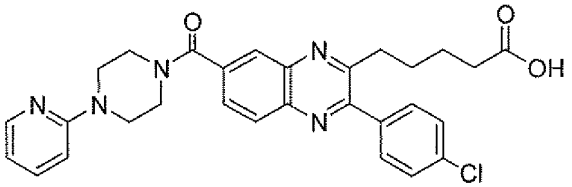
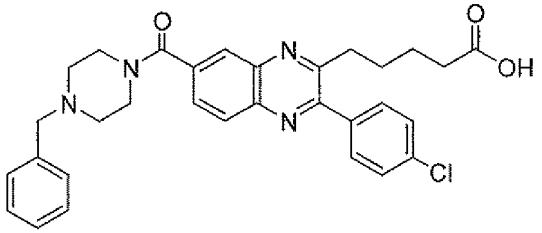
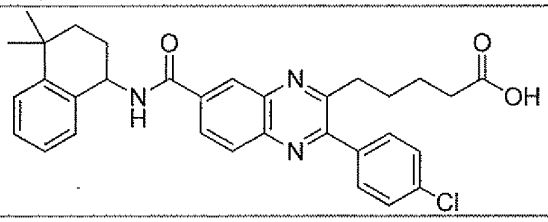
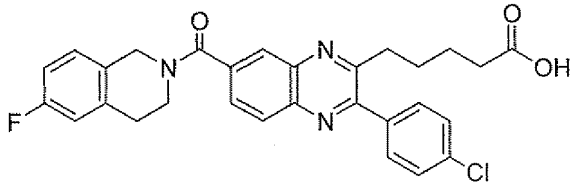
509		5-(3-(4-fluorophenyl)-7-(((1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	500
510		5-(3-(4-fluorophenyl)-7-(((1R,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	500
511		5-(3-(4-fluorophenyl)-7-(((1S,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	500
512		(R)-5-(7-(chroman-4-ylcarbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	482
513		(S)-5-(7-(chroman-4-ylcarbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	482
514		(S)-5-(3-(4-chlorophenyl)-7-(2-methyl-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543
515		(S)-5-(3-(4-fluorophenyl)-7-(2-methyl-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	527
516		(S)-5-(7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	527

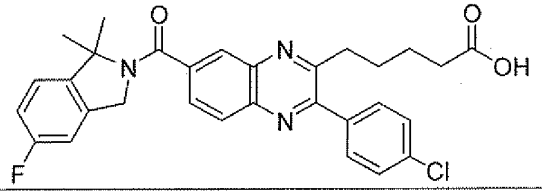
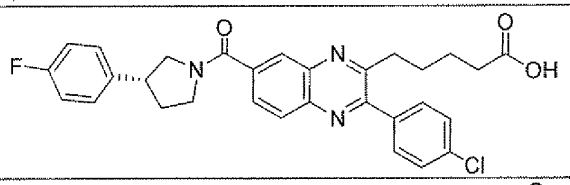
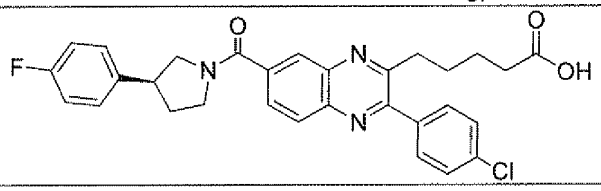
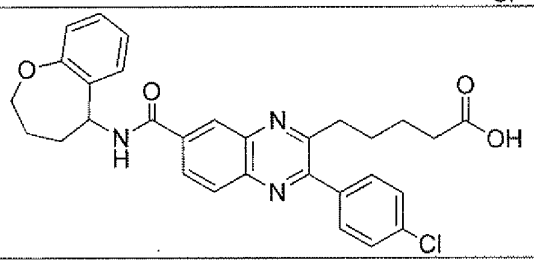
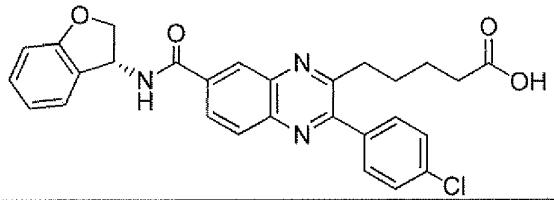
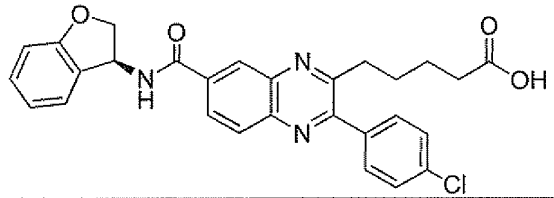
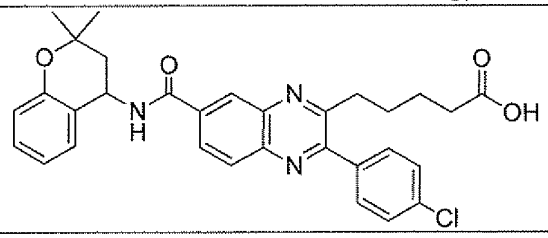
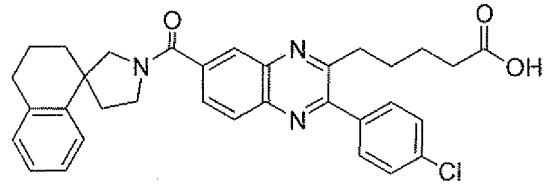
517		(S)-5-(7-(((R)-1-(4-chlorophenyl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	520
518		(S)-5-(7-(((R)-6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	530
519		(S)-5-(7-(((R)-6-chloro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	546
520		(S)-5-(7-((R)-chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	514
521		(S)-5-(3-(4-fluorophenyl)-7-(((R)-5,6,7,8-tetrahydroquinolin-5-yl)carbamoyl)quinoxalin-2-yl)-2-methylpentanoic acid	513
522		(S)-5-(7-(((R)-5-chloro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	532
523		(S)-5-(7-(((R)-5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid	516
524		(S)-5-(3-(4-fluorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)-2-methylpentanoic acid	527
525		5-(3-(4-fluorophenyl)-7-(((5-methyl-1,3,4-oxadiazol-2-yl)methyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	464

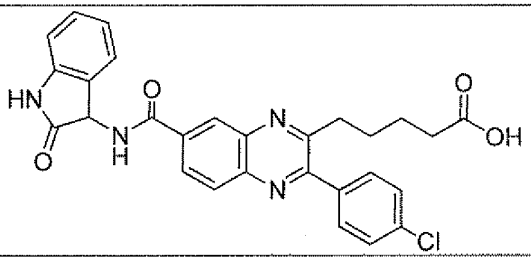
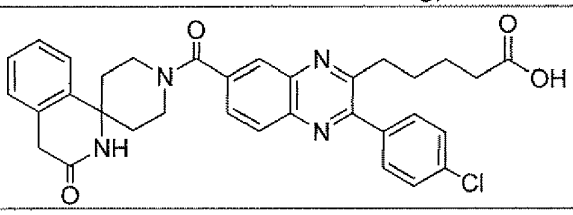
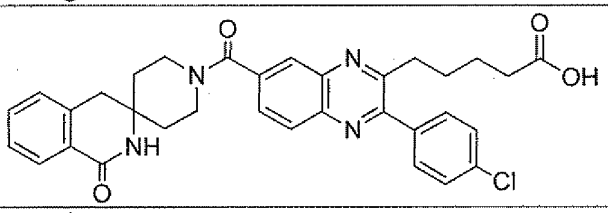
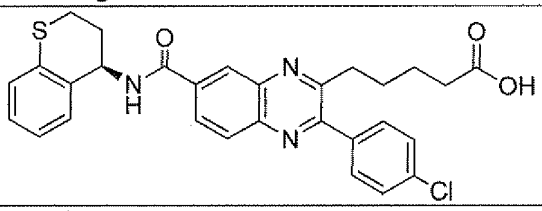
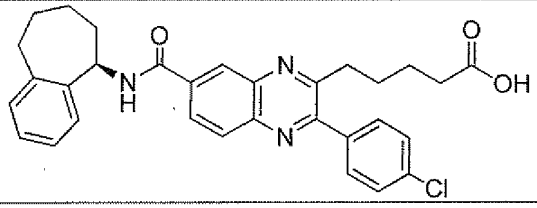
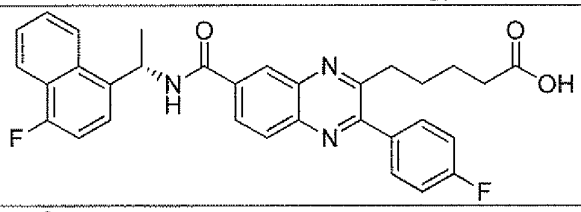
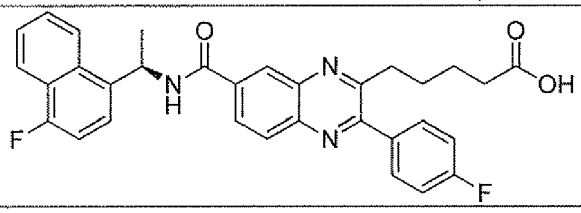
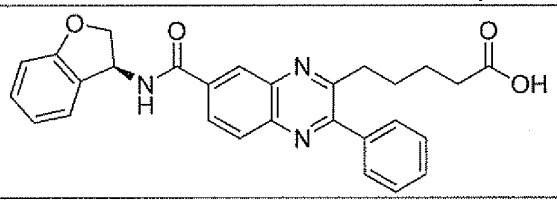
526		(R)-5-(6-methyl-3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	494
527		(R)-5-(7-((1-(4-chlorophenyl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2,2-difluoropentanoic acid	542
528		(R)-2,2-difluoro-5-(3-(4-fluorophenyl)-7-((2,2,2-trifluoro-1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	580
529		2,2-difluoro-5-(7-((4-fluorobenzyl)(methyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	526
530		2,2-difluoro-5-(3-(4-fluorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	549
531		2,2-difluoro-5-(3-(4-fluorophenyl)-7-(4-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	548
532		(R)-5-(3-(4-chlorophenyl)-7-((7-fluorochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534
533		(R)-5-(3-(4-chlorophenyl)-7-((6,7-difluorochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	552

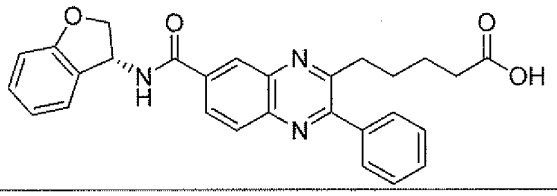
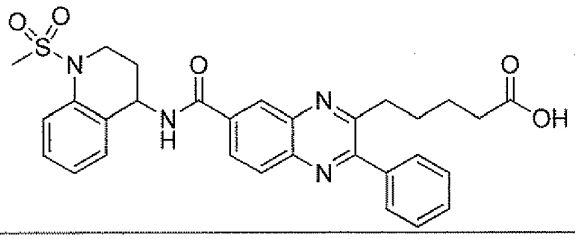
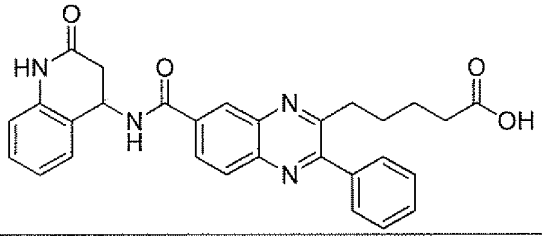
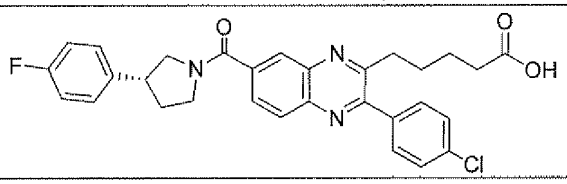
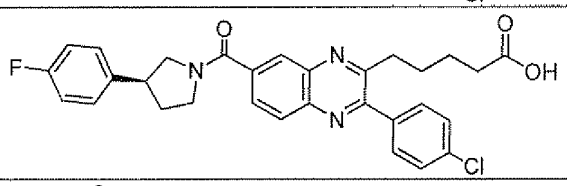
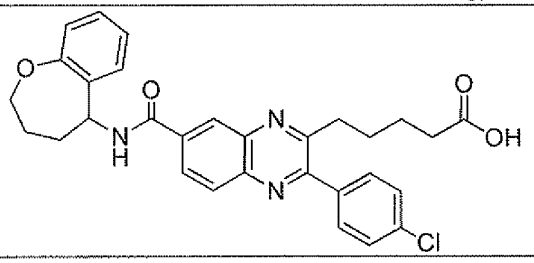
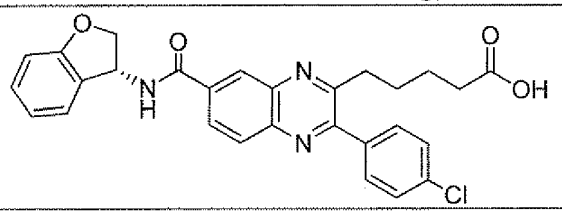
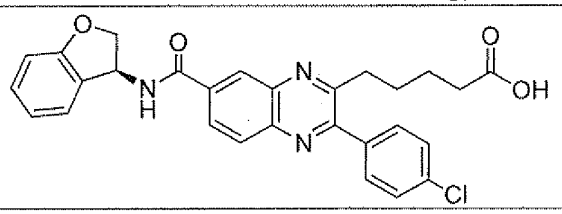
534		(S)-5-(3-(4-chlorophenyl)-7-((6-fluorochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534
535		(S)-5-(3-(4-fluorophenyl)-7-((1-(naphthalen-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	522
536		(S)-5-(3-(4-fluorophenyl)-7-((1-(naphthalen-1-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	522
537		(R)-5-(7-((6-fluorochroman-4-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	518
538		(R)-5-(7-((6,7-difluorochroman-4-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	536
539		(R)-5-(3-(4-chlorophenyl)-7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	577
540		(R)-5-(7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	561
541		(S)-5-(3-(4-chlorophenyl)-7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	577

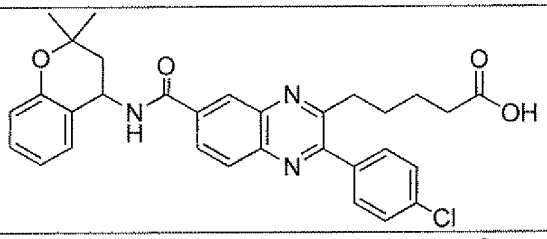
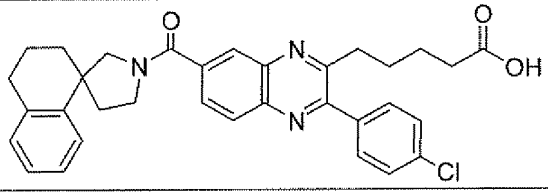
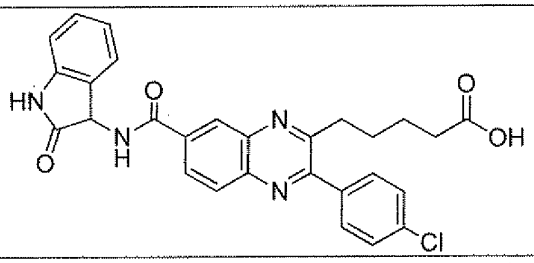
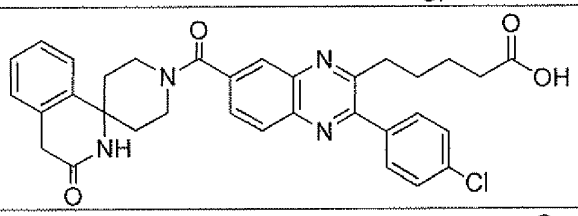
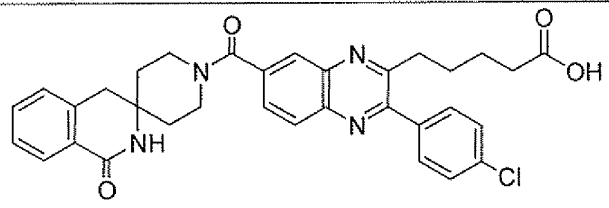
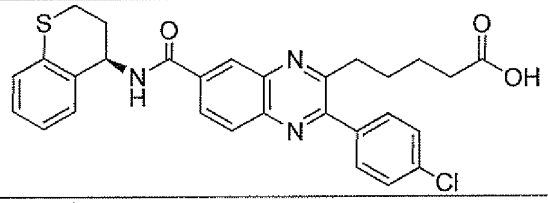
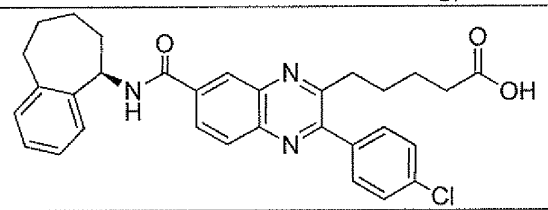
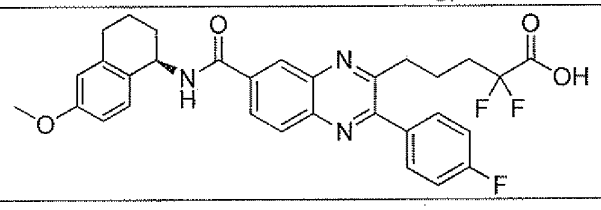
542		(S)-5-(7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	561
543		2-(3-(3-(3-(4-chlorophenyl)-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	601
544		2-(3-(3-(3-(4-chlorophenyl)-7-((4-fluorobenzyl)(methyl)carbamoyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	582
545		(R)-2-(3-(3-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	582
546		2-(3-(3-(7-((4-chlorobenzyl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)propyl)phenyl)acetic acid	586
547		(R)-5-(7-(chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2,2-difluoropentanoic acid	536
548		(S)-5-(7-(chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2,2-difluoropentanoic acid	536
549		(S)-5-(7-(2-methyl-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	509

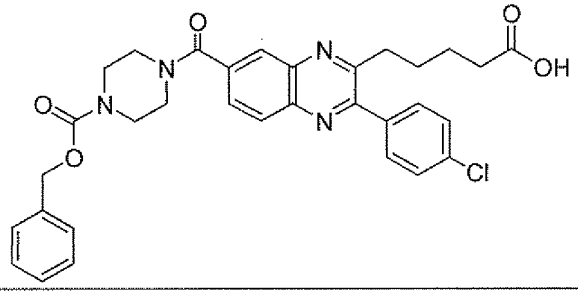
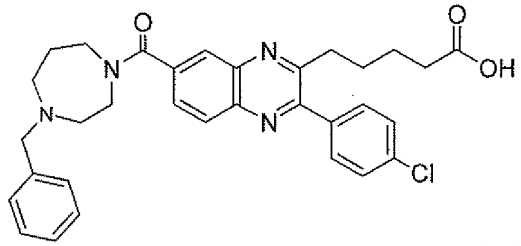
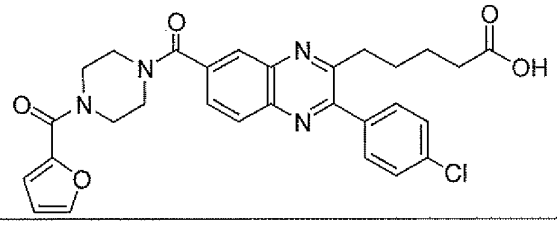
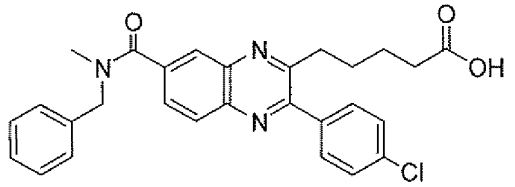
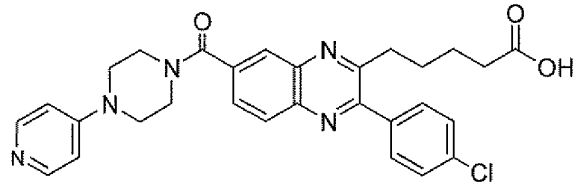
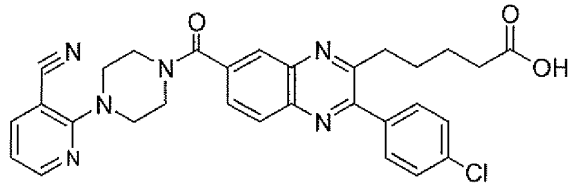
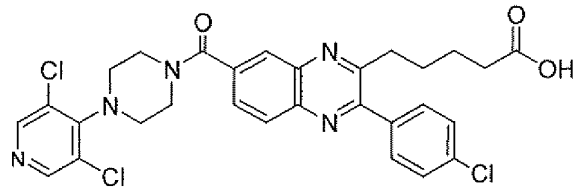
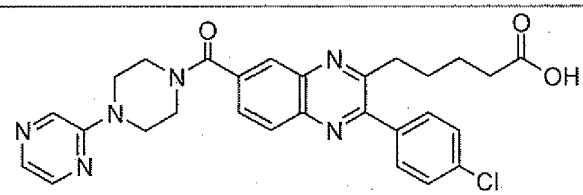
550		(R)-5-(7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	543
551		(S)-5-(7-(4-(4-chlorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid	543
552		5-(3-(4-chlorophenyl)-7-(4-(pyrimidin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	531.3
553		5-(3-(4-chlorophenyl)-7-(3-oxo-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3
554		5-(3-(4-chlorophenyl)-7-(4-(pyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	530.3
555		5-(7-(4-benzylpiperazine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	543.3
556		5-(3-(4-chlorophenyl)-7-((4,4-dimethyl-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	542.3
557		5-(3-(4-chlorophenyl)-7-(6-fluoro-1,2,3,4-tetrahydroisoquinoline-2-carbonyl)quinoxalin-2-yl)pentanoic acid	518.2

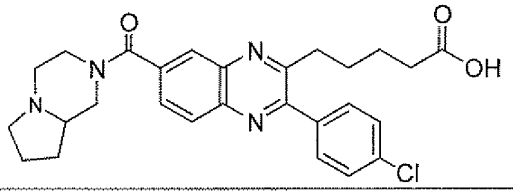
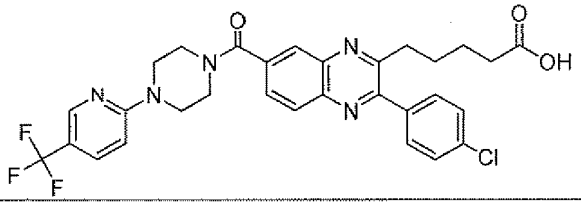
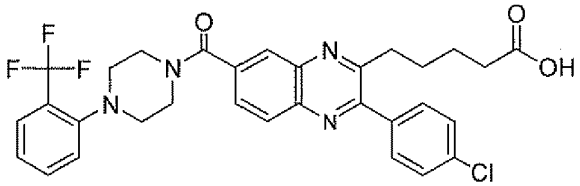
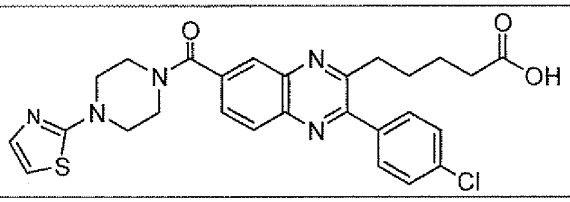
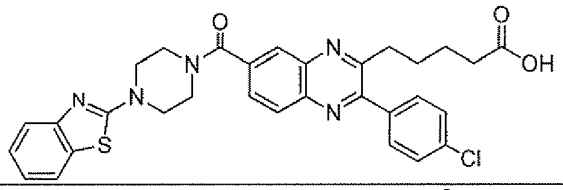
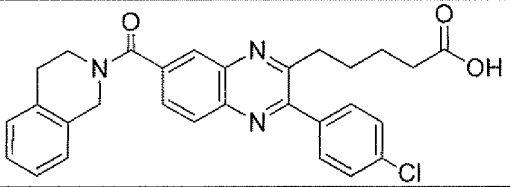
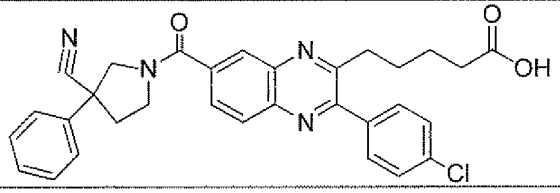
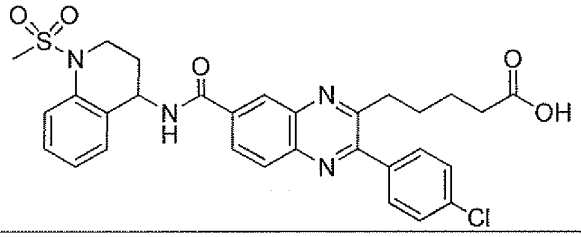
558		5-(3-(4-chlorophenyl)-7-(5-fluoro-1,1-dimethylisoindoline-2-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
559		(R)-5-(3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
560		(S)-5-(3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
561		5-(3-(4-chlorophenyl)-7-((2,3,4,5-tetrahydrobenzo[b]oxepin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	530.3
562		(R)-5-(3-(4-chlorophenyl)-7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	502.2
563		(S)-5-(3-(4-chlorophenyl)-7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	502.2
564		5-(3-(4-chlorophenyl)-7-((2,2-dimethylchroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	544.3
565		5-(3-(4-chlorophenyl)-7-(3,4-dihydro-2H-spiro[naphthalene-1,3'-pyrrolidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	554.3

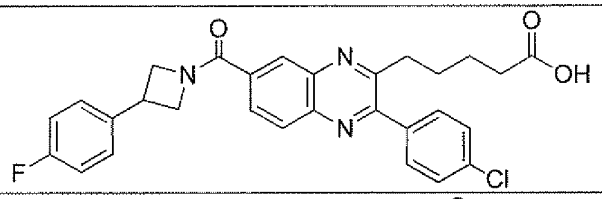
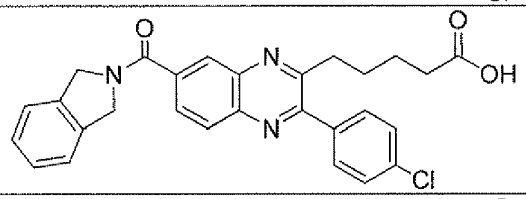
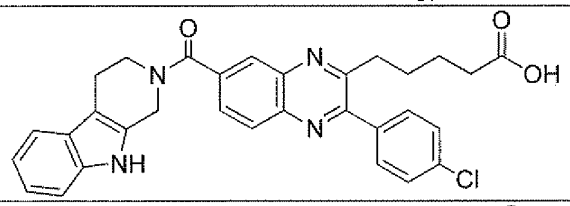
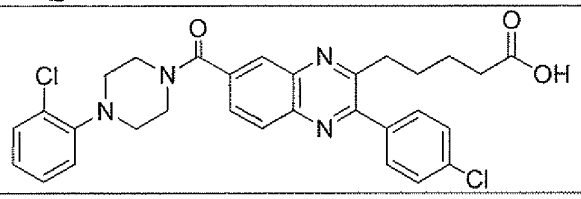
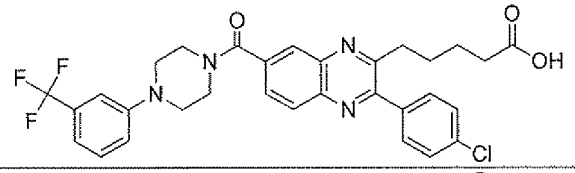
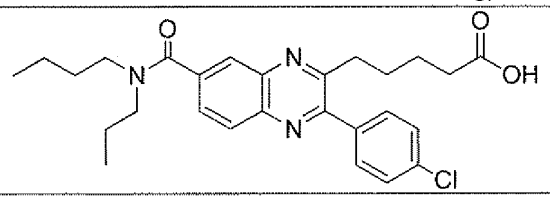
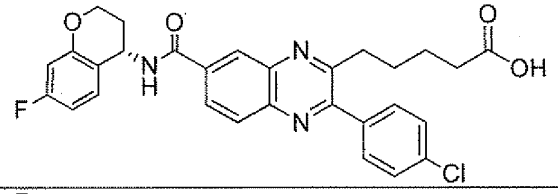
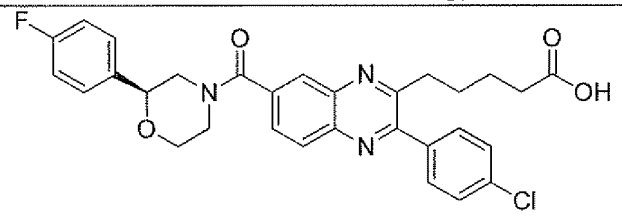
566		5-(3-(4-chlorophenyl)-7-((2-oxoindolin-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	515.2
567		5-(3-(4-chlorophenyl)-7-(3-oxo-3,4-dihydro-2H-spiro[isoquinoline-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.3
568		5-(3-(4-chlorophenyl)-7-(1-oxo-2,4-dihydro-1H-spiro[isoquinoline-3,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.3
569		(R)-5-(3-(4-chlorophenyl)-7-(thiochroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	532.3
570		(R)-5-(3-(4-chlorophenyl)-7-((6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	528.3
571		(S)-5-(7-((1-(4-fluoronaphthalen-1-yl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	540
572		(R)-5-(7-((1-(4-fluoronaphthalen-1-yl)ethyl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	540
573		(S)-5-(7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	468

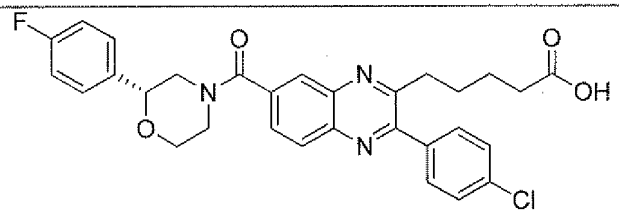
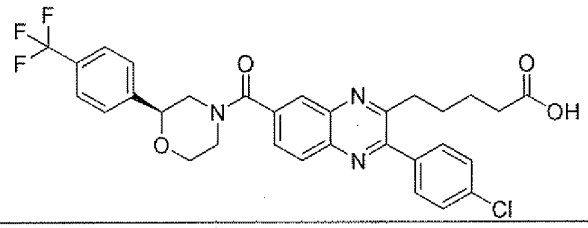
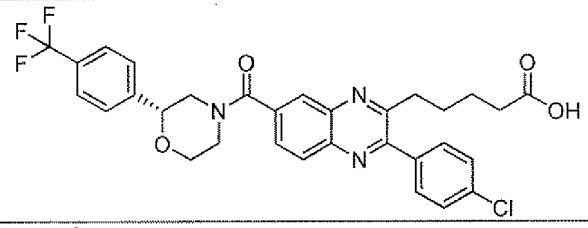
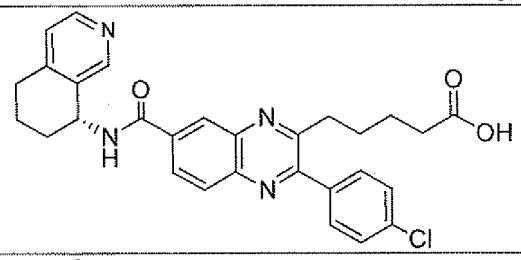
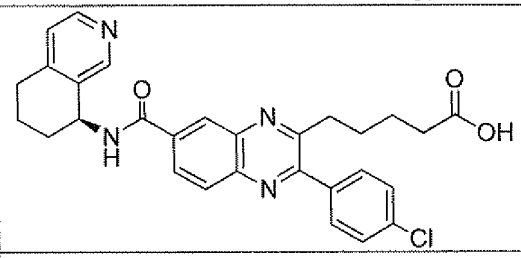
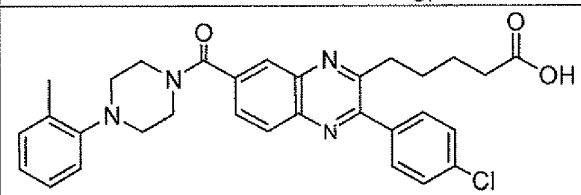
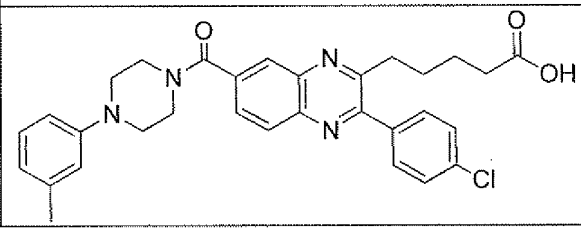
574		(R)-5-(7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	468
575		5-(7-((1-(methylsulfonyl)-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	559
576		5-(7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	495
577		(R)-5-(3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
578		(S)-5-(3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
579		5-(3-(4-chlorophenyl)-7-((2,3,4,5-tetrahydrobenzo[b]oxepin-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	530.3
580		(R)-5-(3-(4-chlorophenyl)-7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	502.2
581		(S)-5-(3-(4-chlorophenyl)-7-((2,3-dihydrobenzofuran-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	502.2

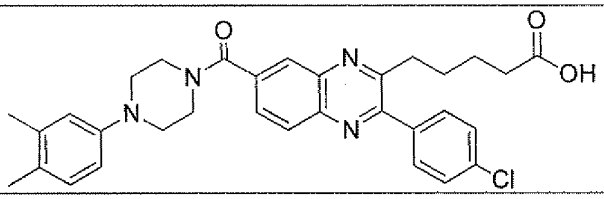
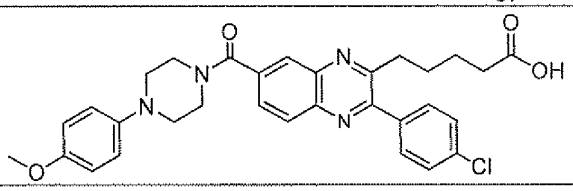
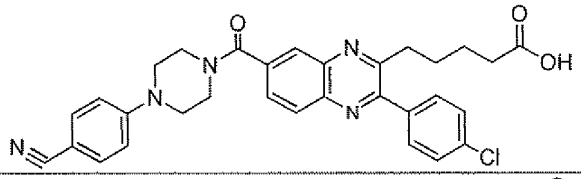
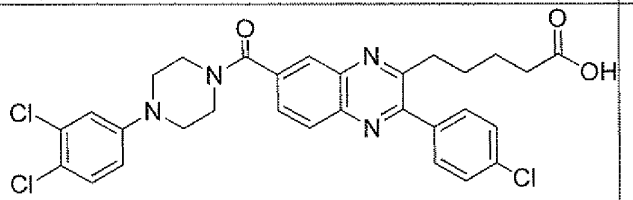
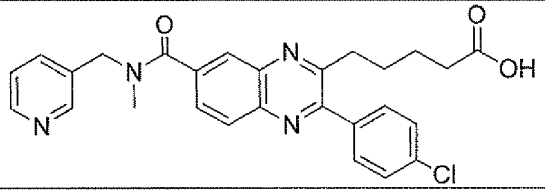
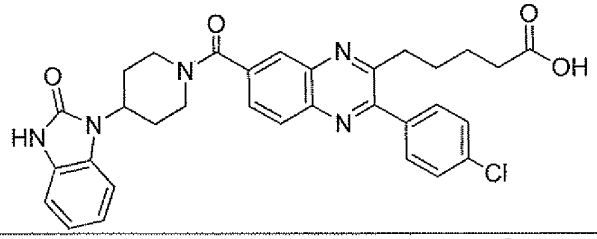
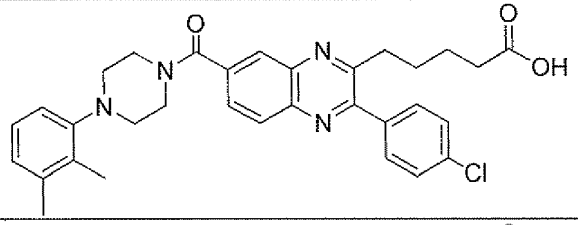
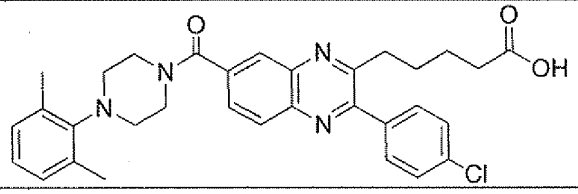
582		5-(3-(4-chlorophenyl)-7-((2,2-dimethylchroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	544.3
583		5-(3-(4-chlorophenyl)-7-(3,4-dihydro-2H-spiro[naphthalene-1,3'-pyrrolidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	554.3
584		5-(3-(4-chlorophenyl)-7-((2-oxoindolin-3-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	515.2
585		5-(3-(4-chlorophenyl)-7-(3-oxo-3,4-dihydro-2H-spiro[isoquinoline-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.3
586		5-(3-(4-chlorophenyl)-7-(1-oxo-2,4-dihydro-1H-spiro[isoquinoline-3,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.3
587		(R)-5-(3-(4-chlorophenyl)-7-(thiochroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid	532.3
588		(R)-5-(3-(4-chlorophenyl)-7-((6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	528.3
589		(R)-2,2-difluoro-5-(3-(4-fluorophenyl)-7-((6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	564

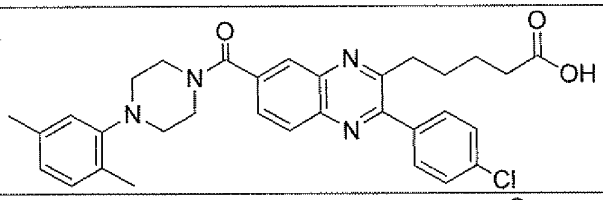
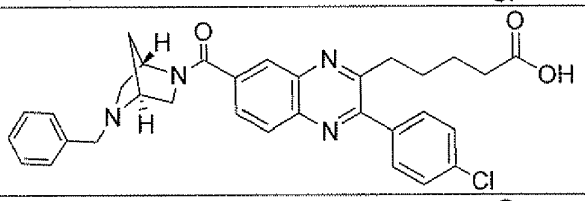
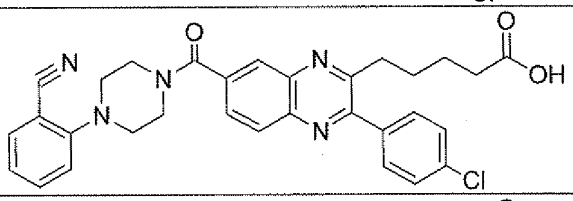
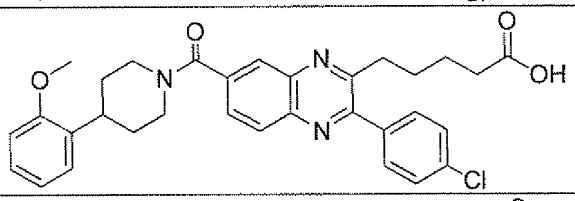
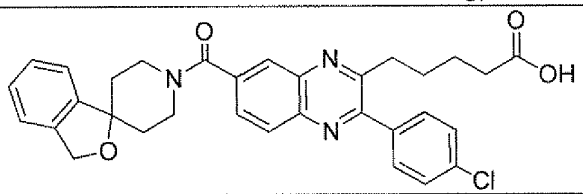
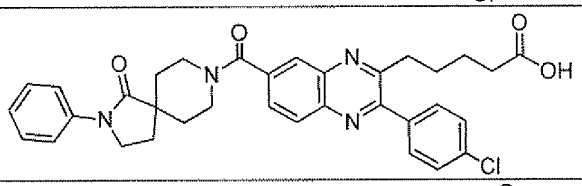
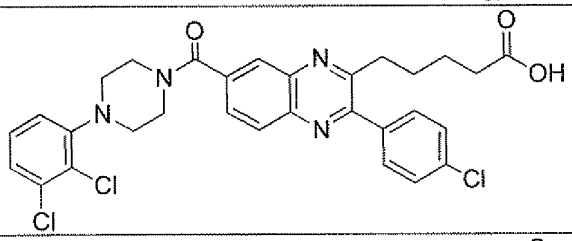
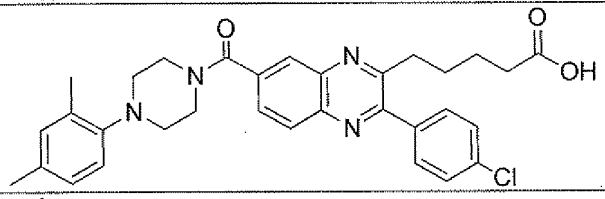
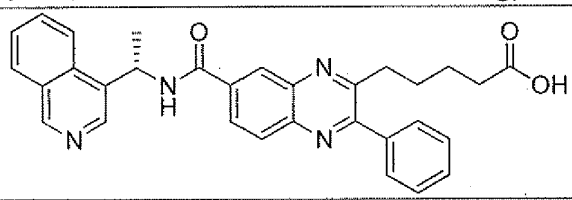
590		5-(7-(4-((benzyloxy)carbonyl)piperazine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	587.4
591		5-(7-(4-benzyl-1,4-diazepane-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	557.3
592		5-(3-(4-chlorophenyl)-7-(4-(furan-2-carbonyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	547.3
593		5-(7-(benzyl(methyl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	488.2
594		5-(3-(4-chlorophenyl)-7-(4-(pyridin-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	530.3
595		5-(3-(4-chlorophenyl)-7-(4-(3-cyanopyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	555.3
596		5-(3-(4-chlorophenyl)-7-(4-(3,5-dichloropyridin-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	600.2
597		5-(3-(4-chlorophenyl)-7-(4-(pyrazin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	531.3

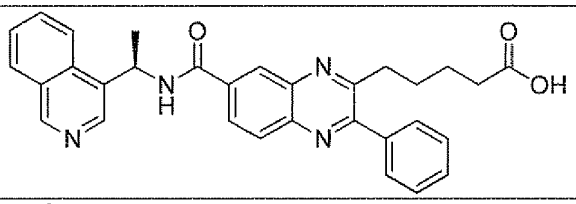
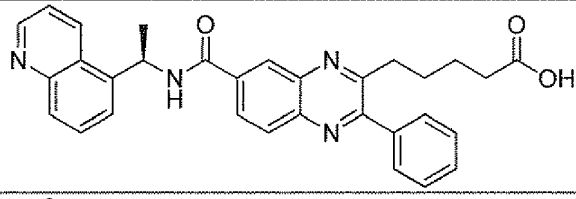
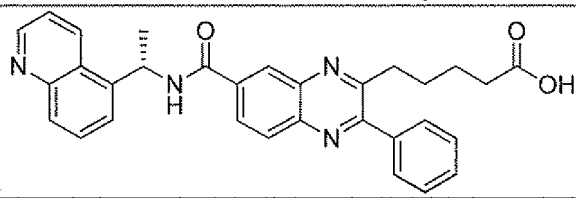
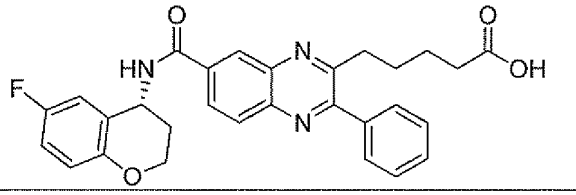
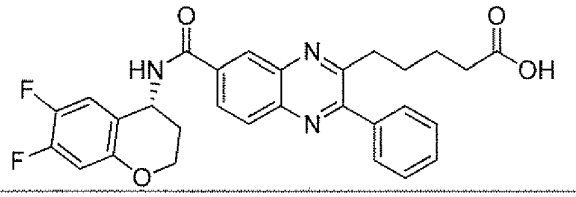
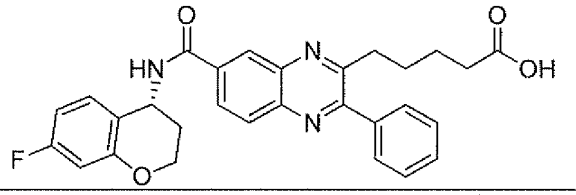
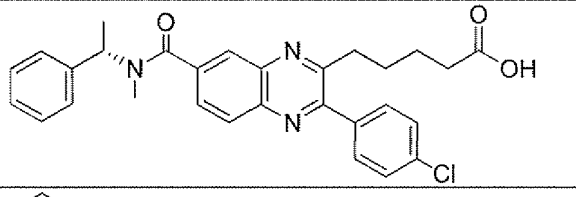
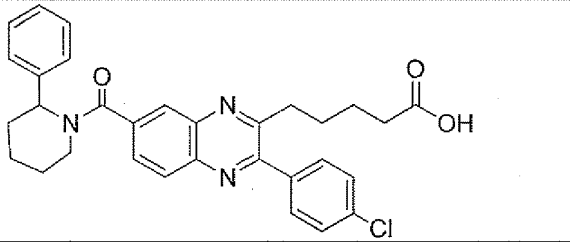
598		5-(3-(4-chlorophenyl)-7-(octahydropyrrolo[1,2-a]pyrazine-2-carbonyl)quinoxalin-2-yl)pentanoic acid	493.3
599		5-(3-(4-chlorophenyl)-7-(4-(5-(trifluoromethyl)pyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	599.3
600		5-(3-(4-chlorophenyl)-7-(4-(2-(trifluoromethyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	597.3
601		5-(3-(4-chlorophenyl)-7-(4-(thiazol-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	536.2
602		5-(7-(4-(benzo[d]thiazol-2-yl)piperazine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	586.3
603		5-(3-(4-chlorophenyl)-7-(1,2,3,4-tetrahydroisoquinoline-2-carbonyl)quinoxalin-2-yl)pentanoic acid	500.3
604		5-(3-(4-chlorophenyl)-7-(3-cyano-3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	539.3
605		5-(3-(4-chlorophenyl)-7-((1-(methylsulfonyl)-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	539.3

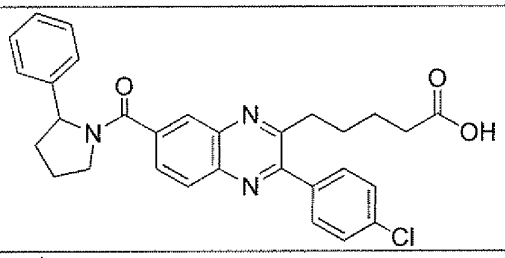
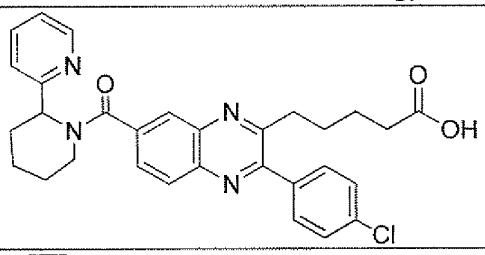
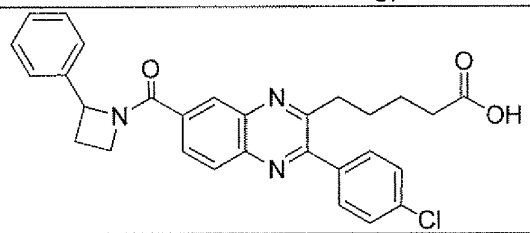
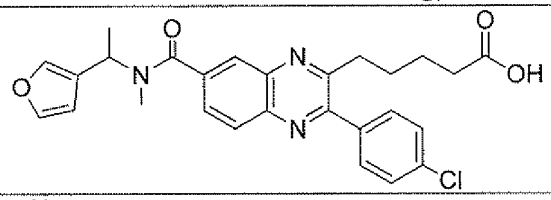
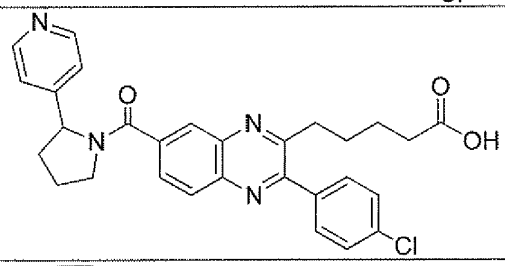
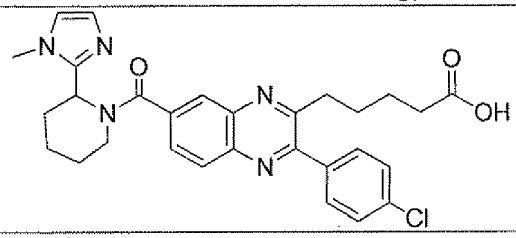
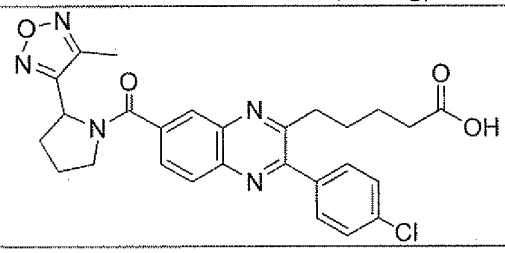
606		5-(3-(4-chlorophenyl)-7-(3-(4-fluorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	518.3
607		5-(3-(4-chlorophenyl)-7-(isoindoline-2-carbonyl)quinoxalin-2-yl)pentanoic acid	486.3
608		5-(3-(4-chlorophenyl)-7-(2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-2-carbonyl)quinoxalin-2-yl)pentanoic acid	539.3
609		5-(3-(4-chlorophenyl)-7-(4-(2-chlorophenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	563.3
610		5-(3-(4-chlorophenyl)-7-(4-(3-(trifluoromethyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	597.7
611		5-(7-(butyl(propyl)carbamoyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	492.3
612		(S)-5-(3-(4-chlorophenyl)-7-((7-fluorochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	534.3
613		(S)-5-(3-(4-chlorophenyl)-7-(2-(4-fluorophenyl)morpholine-4-carbonyl)quinoxalin-2-yl)pentanoic acid	548

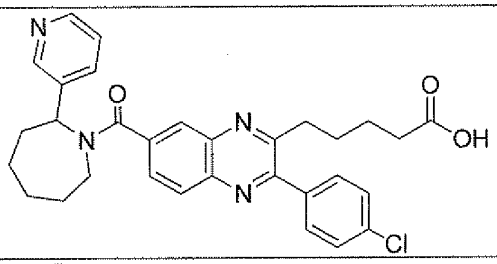
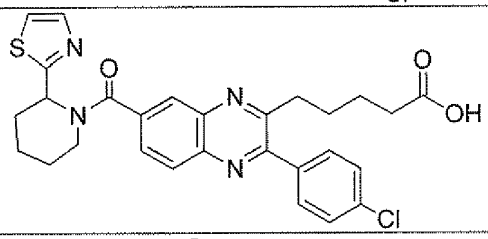
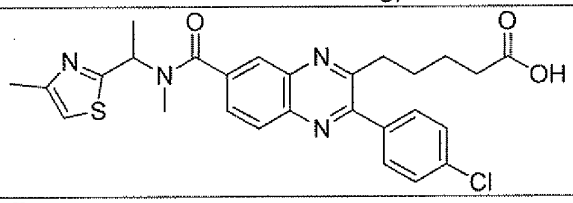
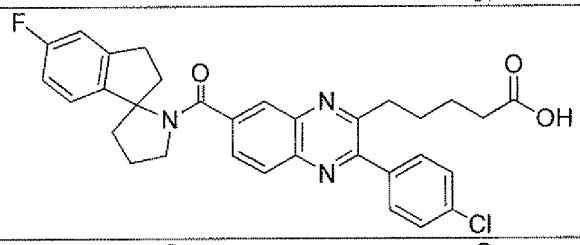
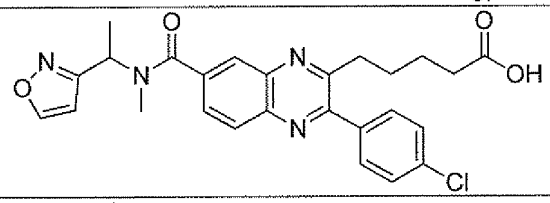
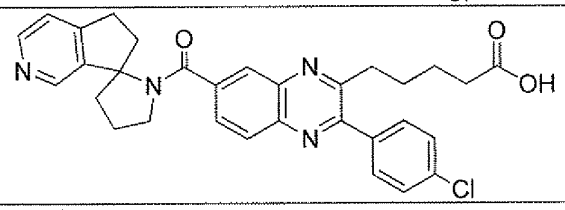
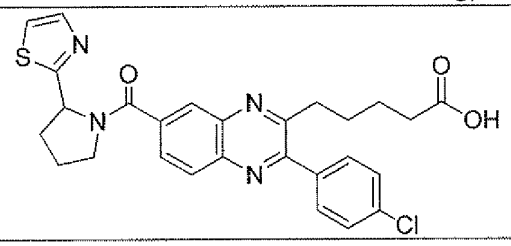
614		(R)-5-(3-(4-chlorophenyl)-7-(2-(4-fluorophenyl)morpholine-4-carbonyl)quinoxalin-2-yl)pentanoic acid	548
615		(S)-5-(3-(4-chlorophenyl)-7-(2-(4-(trifluoromethyl)phenyl)morpholine-4-carbonyl)quinoxalin-2-yl)pentanoic acid	598
616		(R)-5-(3-(4-chlorophenyl)-7-(2-(4-(trifluoromethyl)phenyl)morpholine-4-carbonyl)quinoxalin-2-yl)pentanoic acid	598
617		(R)-5-(3-(4-chlorophenyl)-7-((5,6,7,8-tetrahydroisoquinolin-8-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	515.4
618		(S)-5-(3-(4-chlorophenyl)-7-((5,6,7,8-tetrahydroisoquinolin-8-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	515.4
619		5-(3-(4-chlorophenyl)-7-(4-(o-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3
620		5-(3-(4-chlorophenyl)-7-(4-(m-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3

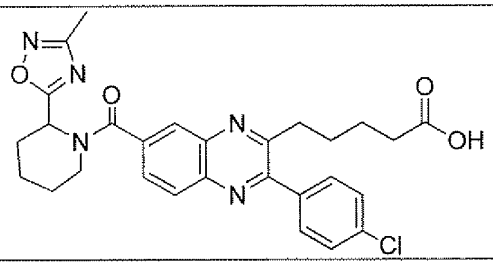
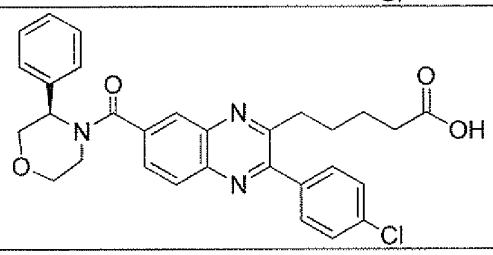
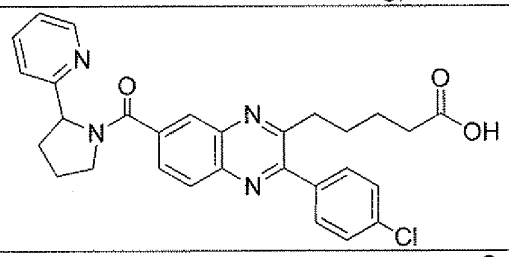
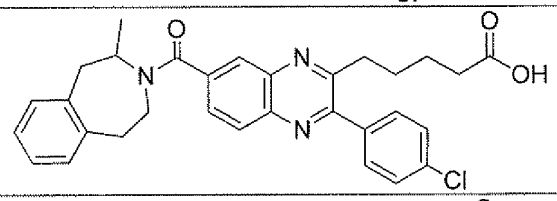
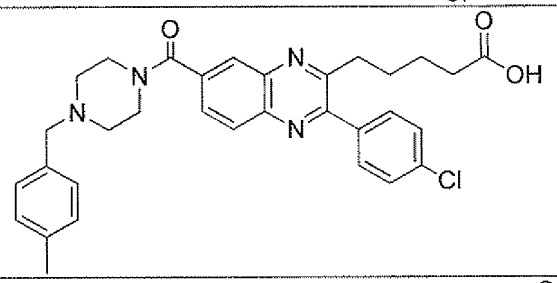
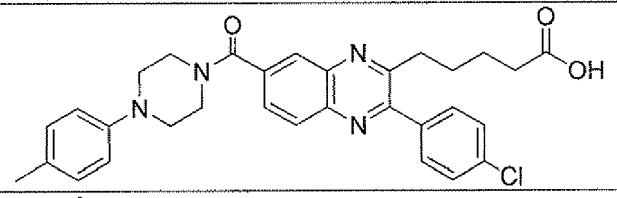
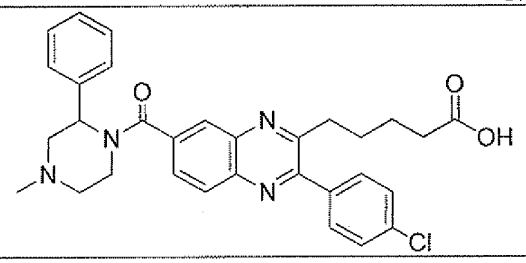
621		5-(3-(4-chlorophenyl)-7-(4-(3,4-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
622		5-(3-(4-chlorophenyl)-7-(4-(4-methoxyphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	559.4
623		5-(3-(4-chlorophenyl)-7-(4-(4-cyanophenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	554.4
624		5-(3-(4-chlorophenyl)-7-(4-(3,4-dichlorophenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	597.3
625		5-(3-(4-chlorophenyl)-7-(methyl(pyridin-3-ylmethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	489.3
626		5-(3-(4-chlorophenyl)-7-(4-(2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	584.4
627		5-(3-(4-chlorophenyl)-7-(4-(2,3-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
628		5-(3-(4-chlorophenyl)-7-(4-(2,6-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4

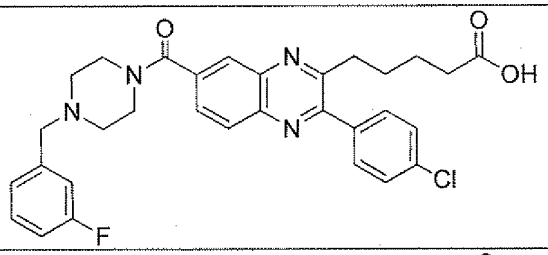
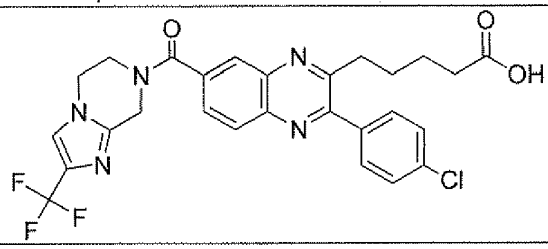
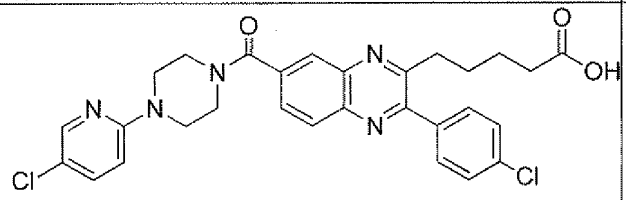
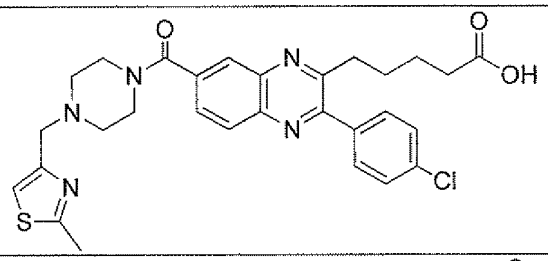
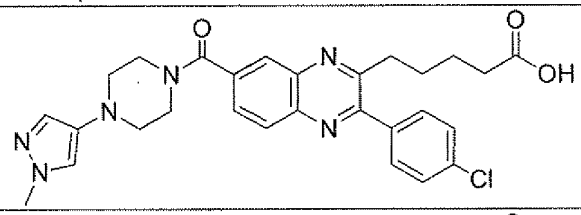
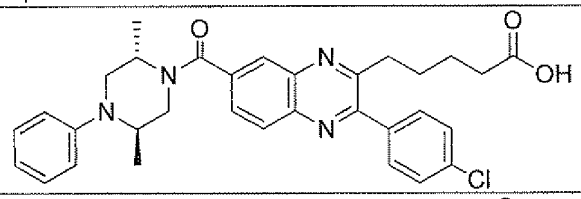
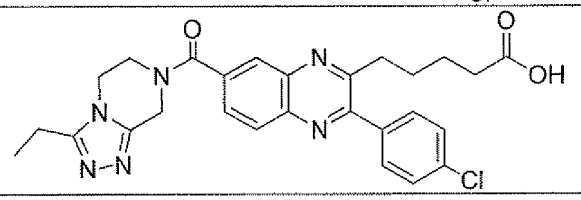
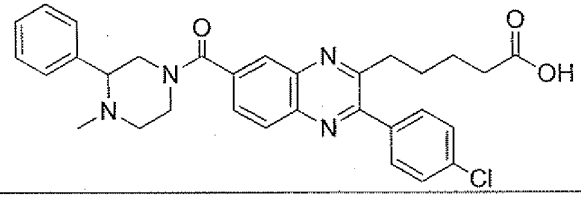
629		5-(3-(4-chlorophenyl)-7-(4-(2,5-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
630		5-(7-((1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	555.4
631		5-(3-(4-chlorophenyl)-7-(4-(2-cyanophenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	554.4
632		5-(3-(4-chlorophenyl)-7-(4-(2-methoxyphenyl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	558.4
633		5-(3-(4-chlorophenyl)-7-(3H-spiro[isobenzofuran-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	556.4
634		5-(3-(4-chlorophenyl)-7-(1-oxo-2-phenyl-2,8-diazaspiro[4.5]decane-8-carbonyl)quinoxalin-2-yl)pentanoic acid	597.5
635		5-(3-(4-chlorophenyl)-7-(4-(2,3-dichlorophenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	597.3
636		5-(3-(4-chlorophenyl)-7-(4-(2,4-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
637		(S)-5-(7-((1-(isoquinolin-4-yl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	505

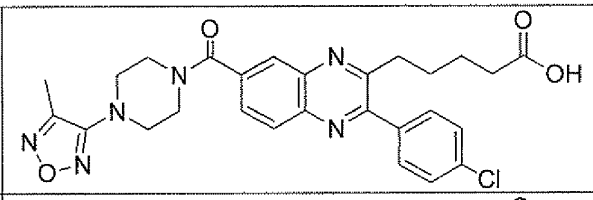
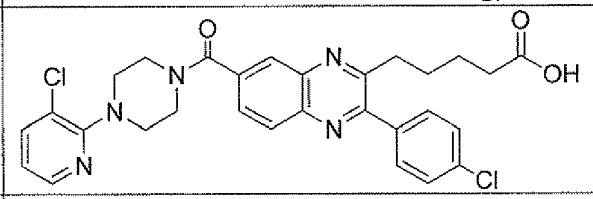
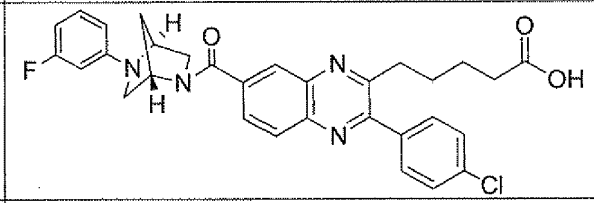
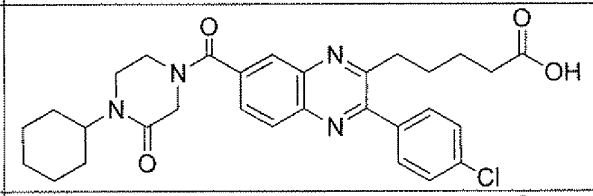
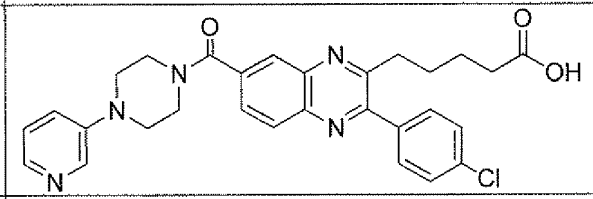
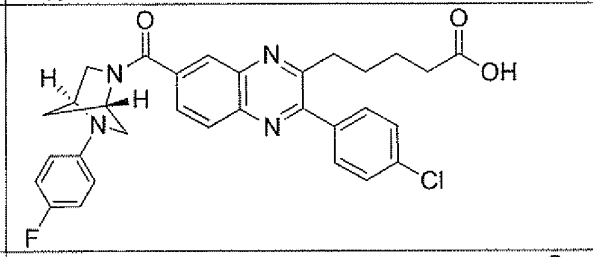
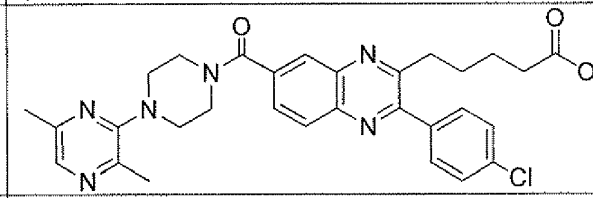
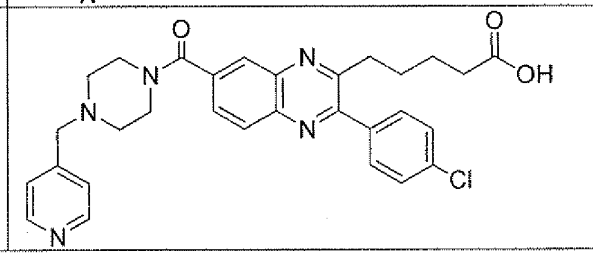
638		(R)-5-(7-((1-(isoquinolin-4-yl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	505
639		(R)-5-(3-phenyl-7-((1-(quinolin-5-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	505
640		(S)-5-(3-phenyl-7-((1-(quinolin-5-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	505
641		(R)-5-(7-((6-fluorochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	500
642		(R)-5-(7-((6,7-difluorochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	518
643		(R)-5-(7-((7-fluorochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	500
644		(S)-5-(3-(4-chlorophenyl)-7-(methyl(1-phenylethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	502.3
645		5-(3-(4-chlorophenyl)-7-(2-phenylpiperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	528.3

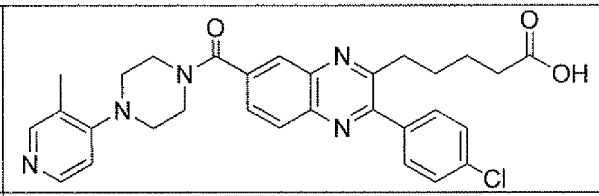
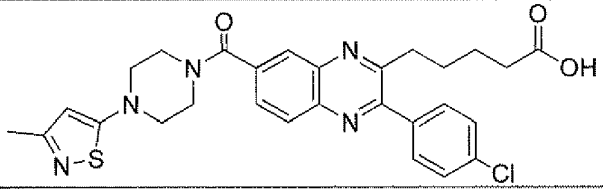
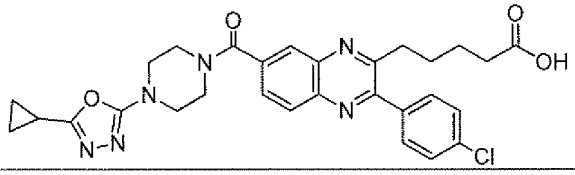
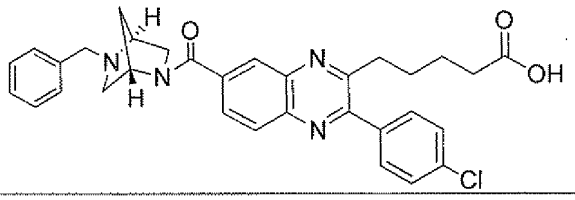
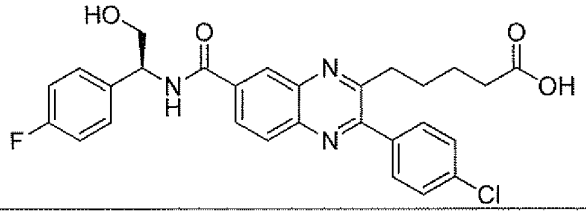
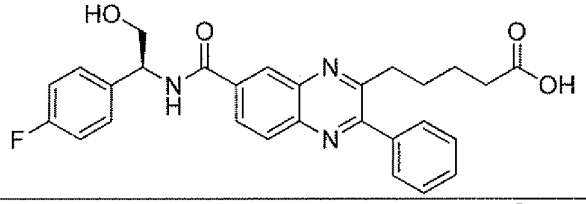
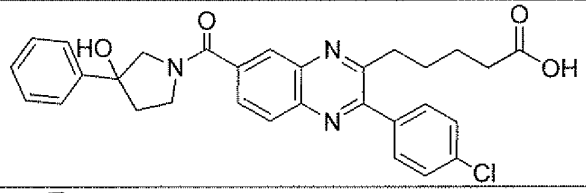
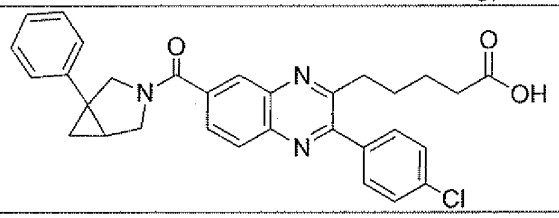
646		5-(3-(4-chlorophenyl)-7-(2-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	514.3
647		5-(3-(4-chlorophenyl)-7-(2-(pyridin-2-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	529.3
648		5-(3-(4-chlorophenyl)-7-(2-phenylazetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	500.3
649		5-(3-(4-chlorophenyl)-7-((1-(furan-3-yl)ethyl)(methyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	492.3
650		5-(3-(4-chlorophenyl)-7-(2-(pyridin-4-yl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	515.3
651		5-(3-(4-chlorophenyl)-7-(2-(1-methyl-1H-imidazol-2-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	532.3
652		5-(3-(4-chlorophenyl)-7-(2-(4-methyl-1,2,5-oxadiazol-3-yl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	520.3

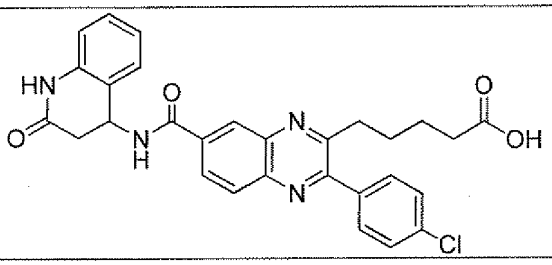
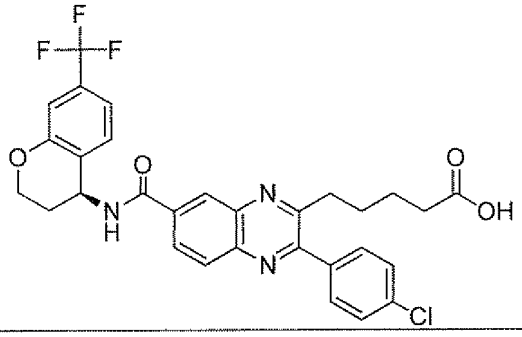
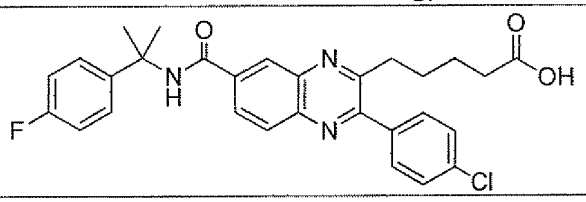
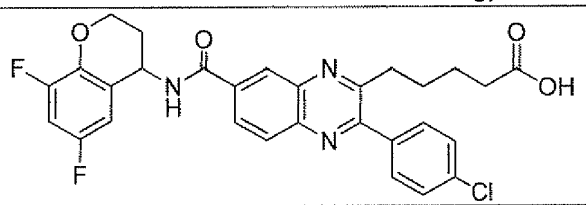
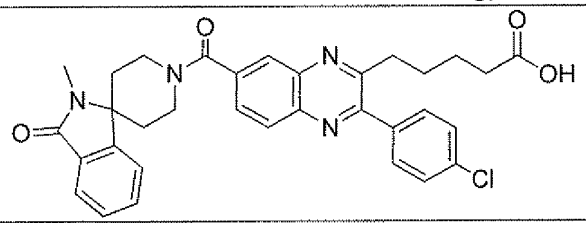
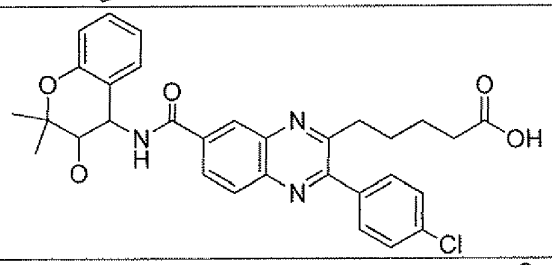
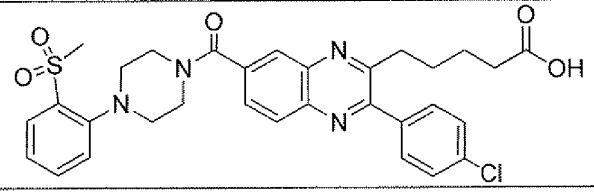
653		5-(3-(4-chlorophenyl)-7-(2-(pyridin-3-yl)azepane-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3
654		5-(3-(4-chlorophenyl)-7-(2-(thiazol-2-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	535.3
655		5-(3-(4-chlorophenyl)-7-(methyl(1-(4-methylthiazol-2-yl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	523.3
656		5-(3-(4-chlorophenyl)-7-(5-fluoro-2,3-dihydrospiro[indene-1,2'-pyrrolidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	558.3
657		5-(3-(4-chlorophenyl)-7-((1-(isoxazol-3-yl)ethyl)(methyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	493.3
658		5-(3-(4-chlorophenyl)-7-(5,6-dihydrospiro[cyclopenta[c]pyridine-7,2'-pyrrolidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	541.3
659		5-(3-(4-chlorophenyl)-7-(2-(thiazol-2-yl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	521.2

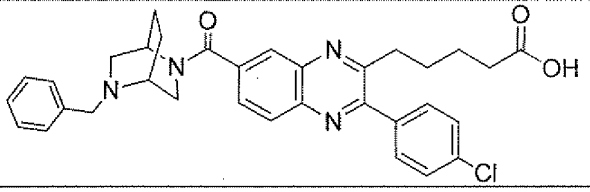
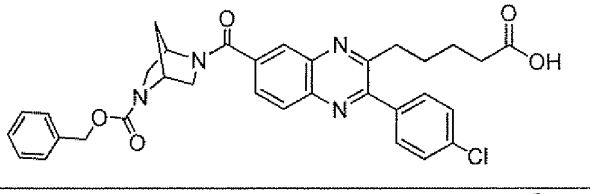
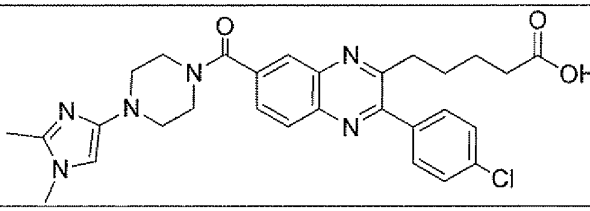
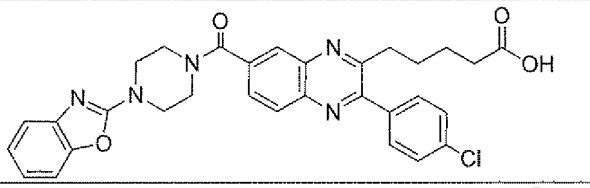
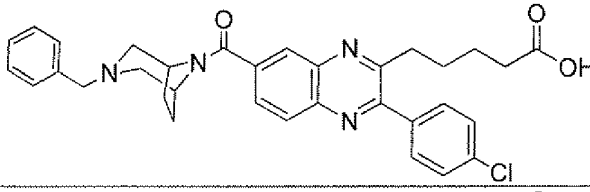
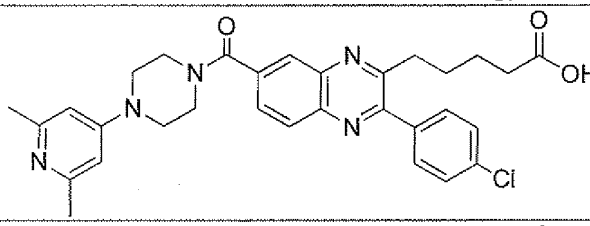
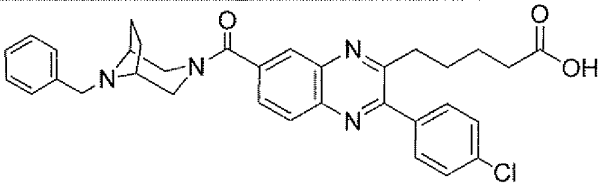
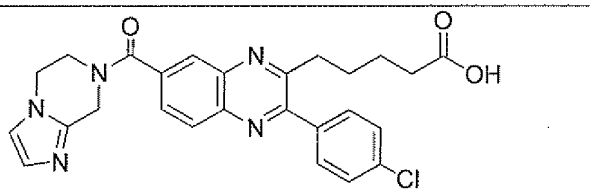
660		5-(3-(4-chlorophenyl)-7-(2-(3-methyl-1,2,4-oxadiazol-5-yl)piperidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	534.3
661		(R)-5-(3-(4-chlorophenyl)-7-(3-phenylmorpholine-4-carbonyl)quinoxalin-2-yl)pentanoic acid	530.3
662		5-(3-(4-chlorophenyl)-7-(2-(pyridin-2-yl)pyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	515.3
663		5-(3-(4-chlorophenyl)-7-(2-methyl-2,3,4,5-tetrahydro-1H-benzo[d]azepine-3-carbonyl)quinoxalin-2-yl)pentanoic acid	528.3
664		5-(3-(4-chlorophenyl)-7-(4-(4-methylbenzyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
665		5-(3-(4-chlorophenyl)-7-(4-(p-tolyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3
666		5-(3-(4-chlorophenyl)-7-(4-methyl-2-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3

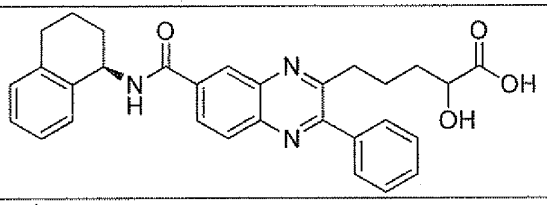
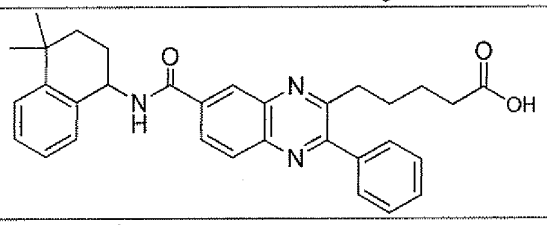
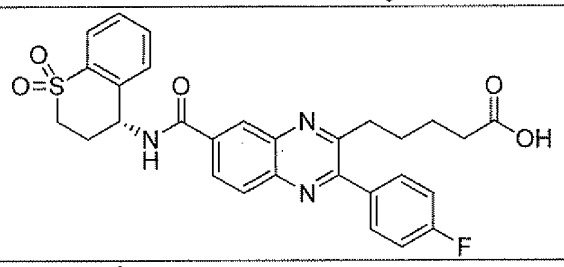
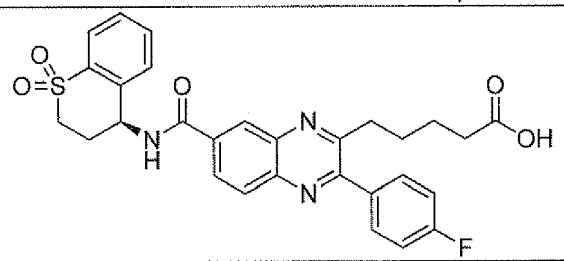
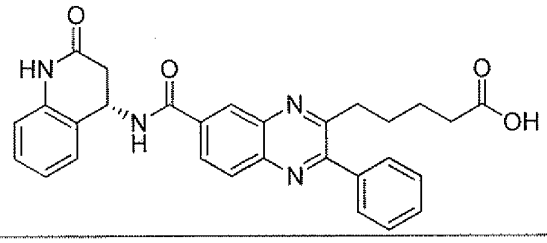
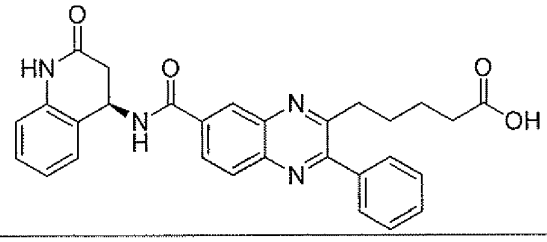
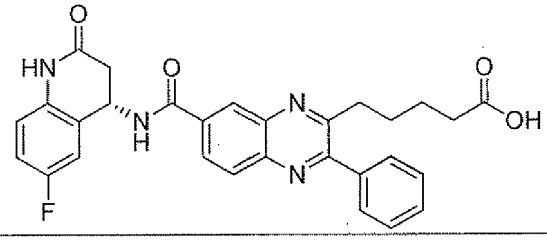
667		5-(3-(4-chlorophenyl)-7-(4-(3-fluorobenzyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	561.3
668		5-(3-(4-chlorophenyl)-7-(2-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-7-carbonyl)quinoxalin-2-yl)pentanoic acid	558.3
669		5-(3-(4-chlorophenyl)-7-(4-(5-chloropyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	564.3
670		5-(3-(4-chlorophenyl)-7-(4-((2-methylthiazol-4-yl)methyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	564.3
671		5-(3-(4-chlorophenyl)-7-(4-(1-methyl-1H-pyrazol-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	533.3
672		5-(3-(4-chlorophenyl)-7-((2S,5R)-2,5-dimethyl-4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	557.4
673		5-(3-(4-chlorophenyl)-7-(3-ethyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)quinoxalin-2-yl)pentanoic acid	519.3
674		5-(3-(4-chlorophenyl)-7-(4-methyl-3-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	543.3

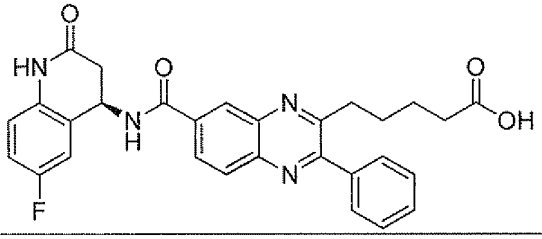
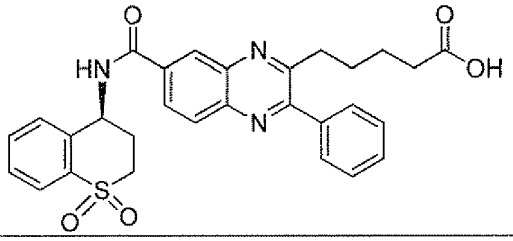
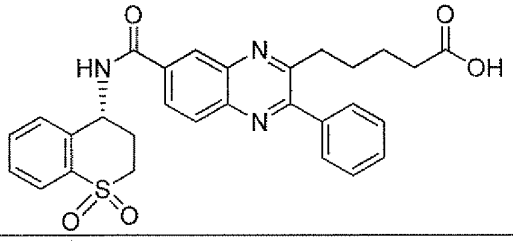
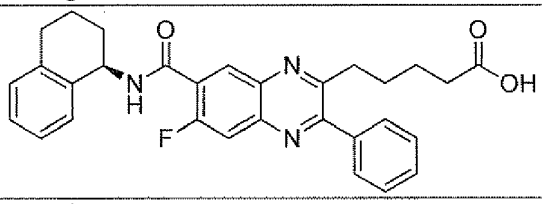
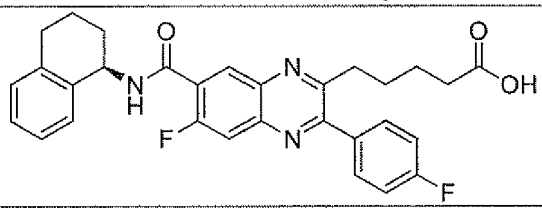
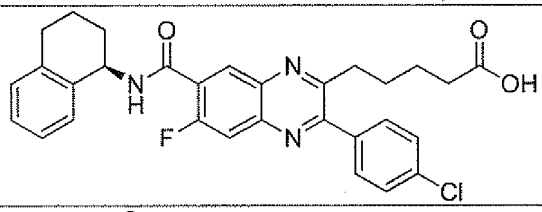
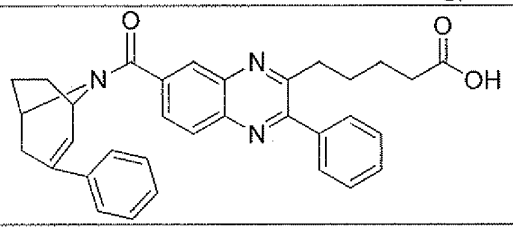
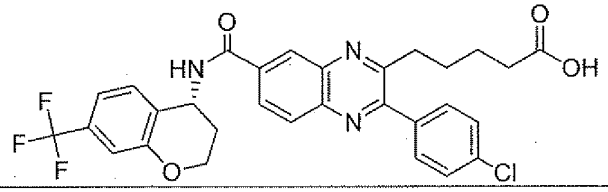
675		5-(3-(4-chlorophenyl)-7-(4-(4-methyl-1,2,5-oxadiazol-3-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	535.3
676		5-(3-(4-chlorophenyl)-7-(4-(3-chloropyridin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	564.3
677		5-(3-(4-chlorophenyl)-7-((1S,4S)-5-(3-fluorophenyl)-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)quinoxalin-2-yl)pentanoic acid	559.3
678		5-(3-(4-chlorophenyl)-7-(4-cyclohexyl-3-oxopiperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	549.4
679		5-(3-(4-chlorophenyl)-7-(4-(pyridin-3-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	530.3
680		5-(3-(4-chlorophenyl)-7-((1S,4S)-5-(4-fluorophenyl)-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)quinoxalin-2-yl)pentanoic acid	559.3
681		5-(3-(4-chlorophenyl)-7-(4-(3,6-dimethylpyrazin-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	559.4
682		5-(3-(4-chlorophenyl)-7-(4-(pyridin-4-ylmethyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	544.3

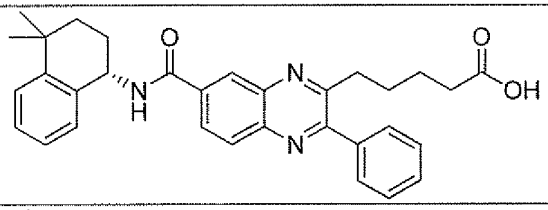
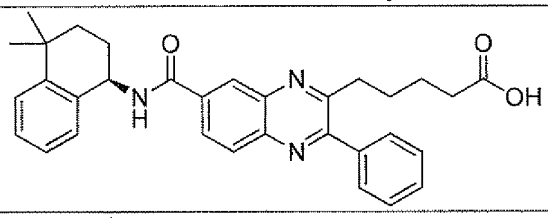
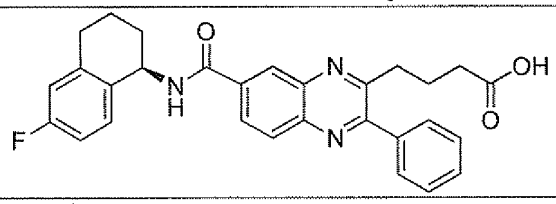
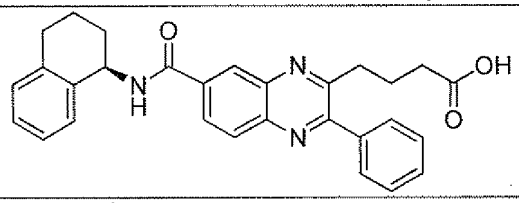
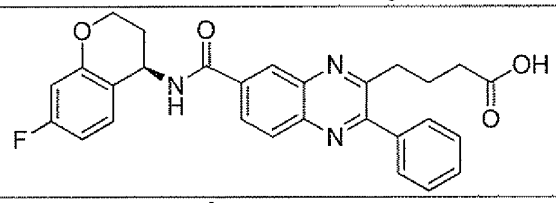
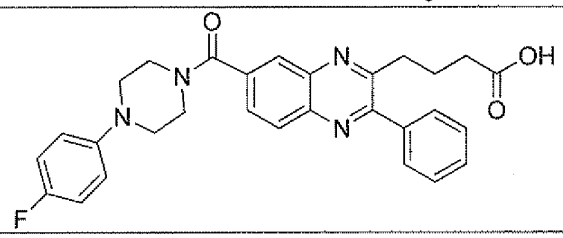
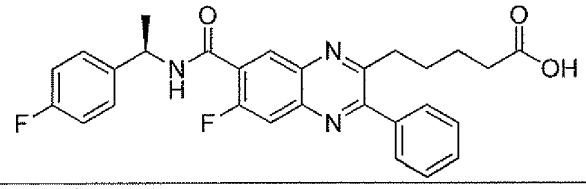
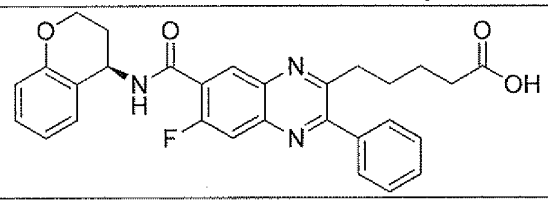
683		5-(3-(4-chlorophenyl)-7-(4-(3-methylpyridin-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	544.3
684		5-(3-(4-chlorophenyl)-7-(4-(3-methylisothiazol-5-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	550.3
685		5-(3-(4-chlorophenyl)-7-(4-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	561.4
686		5-(7-((1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	555.4
687		(S)-5-(3-(4-chlorophenyl)-7-((1-(4-fluorophenyl)-2-hydroxyethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid	522
688		(S)-5-(7-((1-(4-fluorophenyl)-2-hydroxyethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	488
689		5-(3-(4-chlorophenyl)-7-(3-hydroxy-3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	530.4
690		5-(3-(4-chlorophenyl)-7-(1-phenyl-3-azabicyclo[3.1.0]hexane-3-carbonyl)quinoxalin-2-yl)pentanoic acid	526.4

691		5-(3-(4-chlorophenyl)-7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	529.4
692		(S)-5-(3-(4-chlorophenyl)-7-((7-(trifluoromethyl)chroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	584.4
693		5-(3-(4-chlorophenyl)-7-((2-(4-fluorophenyl)propan-2-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	520.4
694		5-(3-(4-chlorophenyl)-7-((6,8-difluorochroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	552.4
695		5-(3-(4-chlorophenyl)-7-(2-methyl-3-oxospiro[isoindoline-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid	583.5
696		5-(3-(4-chlorophenyl)-7-((3-hydroxy-2,2-dimethylchroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	560.4
697		5-(3-(4-chlorophenyl)-7-(4-(2-(methylsulfonyl)phenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	607.5

698		5-(7-((1R,4R)-5-benzyl-2,5-diazabicyclo[2.2.2]octane-2-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	569.5
699		5-(7-((1R,4R)-5-((benzyloxy)carbonyl)-2,5-diazabicyclo[2.2.1]heptane-2-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	599.5
700		5-(3-(4-chlorophenyl)-7-(4-(1,2-dimethyl-1H-imidazol-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	547.5
701		5-(7-(4-(benzo[d]oxazol-2-yl)piperazine-1-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	570.5
702		5-(7-((1R,5S)-3-benzyl-3,8-diazabicyclo[3.2.1]octane-8-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	569.5
703		5-(3-(4-chlorophenyl)-7-(4-(2,6-dimethylpyridin-4-yl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid	558.5
704		5-(7-((1R,5S)-8-benzyl-3,8-diazabicyclo[3.2.1]octane-3-carbonyl)-3-(4-chlorophenyl)quinoxalin-2-yl)pentanoic acid	569.5
705		5-(3-(4-chlorophenyl)-7-(5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-7-carbonyl)quinoxalin-2-yl)pentanoic acid	490.3

706		2-hydroxy-5-(3-phenyl-7-(((R)-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	496
707		5-(7-((4,4-dimethyl-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	508
708		(R)-5-(7-((1,1-dioxidothiochroman-4-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	548
709		(S)-5-(7-((1,1-dioxidothiochroman-4-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid	548
710		(S)-5-(7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	495
711		(R)-5-(7-((2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	495
712		(S)-5-(7-((6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	513

713		(R)-5-(7-((6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	513
714		(S)-5-(7-((1,1-dioxidothiochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	530
715		(R)-5-(7-((1,1-dioxidothiochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	530
716		(R)-5-(6-fluoro-3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	498
717		(R)-5-(6-fluoro-3-(4-fluorophenyl)-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	516
718		(R)-5-(3-(4-chlorophenyl)-6-fluoro-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	532
719		5-(3-phenyl-7-(3-phenyl-8-azabicyclo[3.2.1]oct-2-ene-8-carbonyl)quinoxalin-2-yl)pentanoic acid	518.4
720		(R)-5-(3-(4-chlorophenyl)-7-((7-(trifluoromethyl)chroman-4-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid	584.5

721		(S)-5-(7-((4,4-dimethyl-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	508
722		(R)-5-(7-((4,4-dimethyl-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	508
723		(R)-4-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)butanoic acid	484
724		(R)-4-(3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)butanoic acid	466
725		(R)-4-(7-((7-fluorochroman-4-yl)carbamoyl)-3-phenylquinoxalin-2-yl)butanoic acid	486
726		4-(7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)butanoic acid	500
727		(R)-5-(6-fluoro-7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid	490
728		(R)-5-(7-(chroman-4-ylcarbamoyl)-6-fluoro-3-phenylquinoxalin-2-yl)pentanoic acid	500

*The left side 3-methyl-3-phenylpiperidine used to synthesize compounds **170** and **171** was prepared according to *J. Org. Chem.* **2007**, *72*, 4431

BIOLOGICAL ASSAYS

Radioligand binding assay.

[00359] Radioligand binding assays were performed at room temperature in 50 mM Tris-HCl pH 7.4, 1mM EDTA containing 2 mM $MnCl_2$ and 3.0 nM [^{3}H]PGD_2 (New England Nuclear, Boston, MA) (171 Ci $mmol^{-1}$), in a final volume of 0.2 mL. Competing ligands were diluted in dimethylsulfoxide (Me_2SO) that was kept constant at 1% (v/v) of the final incubation volume. The reaction was initiated by the addition of 8-20 μg of membrane protein prepared from a human embryonic kidney (HEK)-h$CRTH_2$ cell line. Total and non-specific binding were determined in the absence and the presence of 10 μM PGD_2, respectively. Under these conditions, specific binding (total minus non-specific) of the radioligand to the receptor reached equilibrium within 50 min and was stable up to 180 min. The reaction was routinely conducted for 60 min at room temperature and terminated by rapid filtration through prewetted (0.3% polyethyleneimine) 96-well printed filtermate™ (Wallac) using a Tomtec® harvester (Hamden, CT). After washing with cold buffer, the filter was dried for 2 minutes in microwave, and Meltilex Scintillator sheet (Wallac) was melted on for 2 min. The radioactivity was measured with Betaplate model 1205 (Wallac). Tables A and B below list representative compounds of the invention with binding data whereby the Ki values are rated "A", "B," "C," "D," or "E." The Ki values are rated "A" for Ki values in the range of 0.1 to 2.0 nM, "B" for Ki values in the range from 2.1-20 nM, "C" for Ki values in the range from 20.1-200 nM, "D" for Ki values in the range from 201-700 nM, and "E" for Ki values in the range from 701-2300 nM. The designation "NT" indicates that the compound in the entry was not tested in this binding assay.

Table A

No.	Ki (nM)
3	B
3T	C
3U	C
3V	D
3W	B
3X	B
3Y	A
3Z	A
3AA	B
3AB	B
3AC	B
3AD	B
3AE	B
3AF	B

No.	Ki (nM)
26Q	C
26R	C
26S	A
26T	B
26U	B
26V	A
26W	A
26X	C
26Y	A
26Z	A
26AA	A
26AB	A
28	B
29	B

3AG	B
4	B
4D	C
4E	A
4F	B
4G	B
5	A
5G	A
5N	C
5O	C
5P	D
5Q	C
5R	B
5S	B
6	A
6F	NT
6G	A
6H	B
7	B
7C	A
8	C
8G	C
9	B
10	B
10C	A
10D	B
10E	A
10F	B
11	C
11D	D
11E	D
11F	D
12	D
13	C
14	B
14C	C
14D	B
14E	C
14F	C
14G	A
14H	C
15A	B
15B	B
15C	A
15D	A
15E	A
15F	B
15G	B

30	B
30E	B
31	B
31C	B
32	B
33	C
34	D
35	C
36	E
37	C
38	C
38A	C
38B	C
39	B
40	B
41	B
42	B
44	B
44D	B
44E	B
44F	B
44G	C
44H	B
44i	A
44J	B
44K	A
44L	B
44M	B
44N	B
100	A
101	B
102	B
103	A
104	B
105	B
106	A
107	B
108	B
109	B
110	B
111	B
112	B
113	B
114	B
115	C
116	B
117	B
118	B

15H	C
15i	D
15J	B
15K	B
15L	C
15M	C
15N	B
15o	B
15P	A
15Q	A
15R	A
15S	A
15T	A
15U	B
15V	A
15X	A
15Y	A
15Z	A
15AA	C
15AB	A
15AC	A
15AD	B
15AE	B
15AF	B
15AG	B
15AH	C
15Ai	A
15AJ	B
15AK	B
15AL	A
15AM	B
15AN	B
15Ao	A
15AP	B
15AQ	B
15AR	A
15AS	B
15AT	A
15AU	B
15AV	A
15AW	A
15AX	B
15AY	B
15AZ	B
15BA	A
15BB	B
15BC	B
15BD	B

119	B
120	B
121	B
122	B
123	B
124	B
125	B
126	B
127	B
128	B
129	A
130	A
131	B
132	B
133	B
134	A
135	B
136	B
137	C
138	B
139	B
140	A
141	B
142	B
143	B
144	C
145	B
146	C
147	B
148	A
149	B
150	A
151	A
152	B
153	A
154	A
155	B
156	B
157	B
158	D
159	D
160	B
161	B
162	A
163	B
164	B
165	B
166	B

15BE	B
15BF	B
15BG	B
15BH	B
15Bi	A
15BJ	B
15BK	A
15BL	C
15BM	B
15BN	B
15Bo	C
15BQ	B
15BR	A
15BS	B
15BT	A
15BU	A
16	A
16F	A
16G	A
16H	A
16i	A
16J	B
16K	A
16L	B
16M	A
16N	A
16o	A
16P	A
16Q	A
16R	A
16S	A
16T	A
16U	A
16V	A
16W	A
16X	B
16Y	A
16Z	B
16AA	A
16AB	A
16AC	A
16AD	A
16AE	A
16AF	A
16AG	A
16AH	B
16Ai	A
16AJ	A

167	B
168	B
169	B
170	B
171	B
172	A
173	A
174	A
175	B
176	B
177	B
178	A
179	A
180	A
181	A
182	B
183	B
184	A
185	B
186	A
187	B
188	A
189	A
190	A
191	A
192	B
193	B
194	C
195	C
196	C
197	D
198	B
199	B
200	B
201	A
202	A
203	B
204	B
205	B
206	B
207	B
208	B
209	B
210	B
211	B
212	B
213	C
214	A

16AK	A
16AL	A
16AM	A
16AN	A
16Ao	A
16AP	A
16AQ	A
16AR	B
16AS	A
17	B
17D	A
17E	B
17F	A
17G	B
17H	B
17i	B
17J	B
17K	A
17L	B
17M	B
17N	B
17o	A
17P	B
17Q	B
17R	A
17S	B
17T	A
17U	B
17V	A
17W	A
17X	B
17Y	B
17Z	B
18	B
18D	B
18E	A
18F	B
18G	A
18H	B
19	B
19F	B
19G	B
19H	B
19i	B
19J	C
19K	B
20	C
20F	B

215	B
216	C
217	A
218	A
219	A
220	A
221	A
222	B
223	A
224	A
225	A
226	A
227	A
228	A
229	A
230	A
231	B
232	B
233	B
234	B
235	B
236	B
237	B
238	B
239	B
240	B
241	B
242	B
243	B
244	B
245	B
246	A
247	B
248	B
249	A
250	A
251	A
252	A
253	A
254	A
255	A

20G	B
20H	B
21	A
21C	B
22	C
22D	C
23	C
24	B
24H	B
24i	B
25	D
26	A
26E	B
26F	B
26G	B
26H	B
26i	B
26J	A
26K	B
26L	B
26M	B
26N	A
26o	A
26P	B

Table B

No.	Ki (nM)
256	A
257	B
258	B
259	D
260	B
261	B
262	B
263	B
264	B
265	B
266	B
267	B

No.	Ki (nM)
414	A
415	A
416	B
417	B
418	C
419	A
420	A
421	A
422	B
423	B
424	B
425	A

No.	Ki (nM)
572	C
573	B
574	B
575	A
576	B
577	A
578	A
579	B
580	A
581	A
582	A
583	A

268	B
269	D
270	D
271	D
272	C
273	C
274	B
275	C
276	B
277	B
278	C
279	C
280	E
281	C
282	D
283	D
284	B
285	B
286	C
287	C
288	C
289	C
290	B
291	B
292	C
293	B
294	B
295	B
296	B
297	B

426	A
427	B
428	C
429	A
430	B
431	B
432	A
433	B
434	A
435	A
436	C
437	C
438	B
439	B
440	A
441	B
442	A
443	B
444	C
445	B
446	B
447	A
448	A
449	B
450	B
451	B
452	B
453	B
454	B
455	B

584	B
585	A
586	B
587	A
588	B
589	C
590	B
591	B
592	B
593	A
594	D
595	A
596	A
597	B
598	B
599	A
600	A
601	B
602	A
603	B
604	A
605	A
606	B
607	A
608	B
609	A
610	A
611	B
612	A
613	C

298	B
299	B
300	B
301	B
302	B
303	B
304	B
305	B
306	C
307	C
308	B
309	B
310	B
311	B
312	B
313	B
314	B
315	B
316	B
317	B
318	B
319	B
320	B
321	B
322	B
323	B
324	B
325	C
326	B
327	C

456	B
457	A
458	B
459	B
460	B
461	B
462	B
463	B
464	C
465	B
466	B
467	B
468	B
469	D
470	C
471	B
472	C
473	B
474	B
475	B
476	C
477	B
478	C
479	C
480	B
481	C
482	B
483	B
484	B
485	B

614	B
615	B
616	C
617	A
618	A
619	A
620	A
621	A
622	B
623	B
624	A
625	B
626	B
627	A
628	A
629	A
630	B
631	A
632	A
633	A
634	B
635	A
636	A
637	B
638	D
639	C
640	B
641	B
642	B
643	A

328	B
329	B
330	B
331	B
332	B
333	B
334	B
335	B
336	C
337	C
338	B
339	C
340	B
341	B
342	B
343	B
344	B
345	B
346	B
347	C
348	B
349	C
350	C
351	B
352	B
353	B
354	C
355	B
356	C
357	B

486	B
487	C
488	B
489	B
490	B
491	A
492	B
493	B
494	B
495	B
496	B
497	B
498	B
499	B
500	B
501	C
502	C
503	C
504	B
505	B
506	A
507	A
508	B
509	C
510	C
511	B
512	A
513	A
514	B
515	B

644	B
645	B
646	B
647	C
648	B
649	C
650	C
651	C
652	B
653	D
654	C
655	B
656	B
657	C
658	C
659	C
660	C
661	B
662	C
663	B
664	B
665	B
666	B
667	B
668	C
669	B
670	B
671	C
672	C
673	C

358	B
359	B
360	C
361	B
362	B
363	B
364	B
365	B
366	B
367	B
368	C
369	B
370	D
371	B
372	B
373	B
374	A
375	A
376	B
377	B
378	C
379	B
380	B
381	A
382	A
383	A
384	A
385	B
386	A
387	B

516	B
517	B
518	B
519	B
520	B
521	C
522	B
523	B
524	B
525	C
526	D
527	B
528	C
529	C
530	C
531	B
532	B
533	B
534	B
535	B
536	B
537	B
538	B
539	B
540	B
541	B
542	B
543	C
544	C
545	D

674	B
675	B
676	B
677	B
678	B
679	B
680	B
681	B
682	C
683	B
684	B
685	C
686	C
687	B
688	C
689	B
690	B
691	B
692	B
693	B
694	B
695	B
696	B
697	B
698	B
699	B
700	C
701	B
702	B
703	D

388	B
389	A
390	A
391	B
392	B
393	B
394	B
395	B
396	B
397	B
398	B
399	B
400	B
401	C
402	B
403	A
404	B
405	B
406	B
407	B
408	A
409	C
410	C
411	C
412	A
413	A

546	C
547	C
548	D
549	B
550	B
551	B
552	B
553	B
554	B
555	B
556	B
557	B
558	B
559	A
560	A
561	A
562	A
563	A
564	B
565	A
566	B
567	A
568	B
569	A
570	B
571	B

704	B
705	D
706	D
707	B
708	D
709	B
710	C
711	B
712	C
713	B
714	C
715	B
716	B
717	B
718	B
719	B
720	B
721	B
722	B
723	C
724	D
725	D
726	D
727	B
728	B

[00360] Representative compounds of the invention had the Ki values specified in parentheses immediately following the compound number in the above-described assay: **3** (3.2 nM), **5P** (265.6 nM), **6G** (0.5 nM), **11F** (222.9 nM), **15H** (152.4 nM), **15i** (282.9 nM), **15o** (16.7 nM), **15Ai** (1.9 nM), **15Ao** (1.0 nM), **15AR** (1.6 nM), **15AX** (3.0 nM), **15BL** (69.9 nM), **15BR**

(0.1 nM), **16S** (0.7 nM), **16V** (2.7 nM), **16W** (0.4 nM), **16AG** (1.2 nM), **16Ao** (0.4 nM), **26o** (1.4 nM), **26Q** (96.7 nM), **36** (716.1) **39** (8.0 nM), **40** (5.7 nM), **41** (8.8 nM), **44H** (3.1 nM) **144** (117.9 nM), **146** (132.0 nM), **152** (2.9 nM), **159** (564.4 nM), **173** (1.6 nM), **180** (0.6 nM), **193** (14.6 nM), **197** (464.1 nM), **217** (1.2 nM), **231** (4.0 nM), **246** (1.9 nM), **251** (1.0 nM), **254** (1.2 nM), **255** (1.5 nM), **264** (15.4 nM), **292** (39.2 nM), **368** (21.4 nM), **438** (4.2 nM), **507** (1.3 nM), **526** (259.3 nM), **637** (4.2 nM), **657** (37.4 nM), and **709** (18.4 nM).

i[cAMP] measurements.

[00361] The ability of the compounds to antagonize the formation of cAMP can be assayed using the ELISA-based assay described in this example. HEK-hCRTH$_2$ cells are grown to 80-90% confluency. On the day of the assay, the cells are washed with phosphate buffered saline (PBS), incubated for 2 min in cell dissociation buffer, harvested by centrifugation at 300g for 7 min at room temperature and resuspended at 1.25e10^6 cells mL^{-1} in Hanks' balanced salt solution containing 20 mM HEPES pH 7.4 and 0.75 mM IBMX (HBSS/HEPES/IBMX). The assay is performed in 384-plate format with 0.01 mL HBSS/HEPES/IBMX per well containing 12 500 cells and 70 to 75 nl of the test compound and DK-PGD$_2$ at various concentrations. Following a 0 to 10 to min pre-incubation of the cells with the test compound at 37°C, 0.005 mL of 30 μM Forskolin dilute in HBSS 20 mM HEPES, is added at a final concentration of 10 uM to initiate the reaction. After 10 to 60 min incubation at room temperature or 37 °C, the cAMP content was quantified using the cAMP XS+ HitHunter chemiluminescence assay (GE Healthcare 90-0075). Percent inhibition is calculated using the Forskolin and EC85 DK-PGD$_2$ controls.

β-Arrestin assay:

[00362] CHO-K1 cells obtained from DiscoverX are stably transfected with human CRTH$_2$ (propagation medium: F-12, 10% FBS, 300 ug/mL hygB and 800 ug/mL G418). Cells are grown in T175 cm^2 flask. While in log phase, cells are collected via 0.05% trypsin treatment. Triturated cells are filtered and 40 uL (10K cells) are plated per well in a 384-well white clear bottom plate and incubated O/N. Cell plate is emptied via inversion and blotted dry. Each well is filled with 35uL of HBSS (with Ca^{++} and Mg^{++}) and incubated for 5 min. Compounds are added in volumes of 1 μL and the plate is gently shaken for 2 min., followed by incubation at 37 °C for 20 min. All compounds and controls are diluted in HBSS assay buffer (with Ca^{++} and Mg^{++}) with a final concentration range of 10^{-5} M to 3 x 10^{-11} M, 11 point Dose response curves at appropriate half-log increments. Final DMSO % is ≤ 0.3%. Agonist Assay: 1 μl/well of

compound is added into cell plate and left to incubate at 37 °C for 90 min. Antagonist Assay: 1 µl/well of compounds are added into a cell plate. Incubate 30 minutes at 37 °C. Stimulate cells with 1 ul/well of PGD_2 [100 nM] final. Incubate plate for 60 minutes at 37 °C. Resulting luminescent signal is detected via Discoverx PathHunter Detection Kit per manufacturer's instructions. A total of 12 µl/well is added to each well. The plate is covered and incubated for 60 min. with gentle shaking. Chemiluminescent detection is done by a SpectraMax plate reader.

Eosinophil shape change assay in human whole blood:

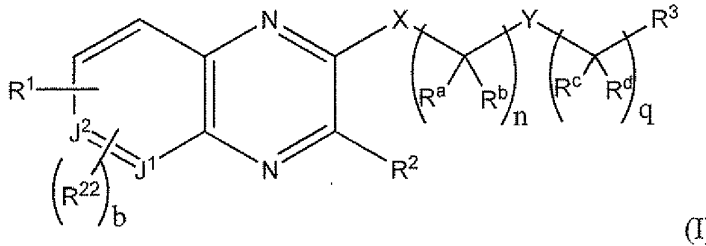
[00363] Blood is collected in vacutainers containing EDTA. The antagonist is added to blood and incubated for 10 min at room temperature. DK-PGD_2 (13,14-dihydro-15-keto prostaglandin D_2) are then added to blood for 4 min at 37° C in a running water bath. Blood cells are then fixed in presence of cold 0.25%(v/v) paraformaldehyde prepared in 75%(v/v) DPBS without Ca^{++} and Mg^{++} for 1 min on ice. 175 µL of fixed blood is transferred into 870 µL of cold 155mM NH_4Cl lysis solution and incubated at 4 °C for at least 40 min. The solution is then centrifuged at 430 g for 5 min and the supernatant is discarded. Centrifuged cells are resuspended in residual supernatant and sodium azide is added (1% final concentration). Samples are analyzed with a FACs Calibur flow cytometer (Becton Dickinson). Flow cytometry raw data is analyzed with Diva software by isolating the eosinophils from the neutrophils based on their high autofluorescence and determining the percent of total eosinophils with increased forward light scatter. Maximum (100%) and minimum (0%) shape change is determined in the presence of 10 µM DK-PGD_2 and DPBS, respectively. A dose response curve with DK-PGD_2 is performed with every assay to determine the EC_{50} for each blood donor. Compounds are tested in 11-dose titration curves in the presence of 50 nM DK-PGD_2 to determine an antagonist IC_{50}.

[00364] Compounds of the present invention are selective for the $CRTH_2$ receptor over the DP receptor. Assays on the DP, as well as other prostanoid, receptors are described in WO2003/06220.

[00365] While the present invention has been described in conjunction with the specific embodiments set forth above, many alternatives, modifications and other variations thereof will be apparent to those of ordinary skill in the art. All such alternatives, modifications and variations are intended to fall within the spirit and scope of the present invention.

WHAT IS CLAIMED IS:

1. A compound of the formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

J^1 and J^2 are independently C(H), C(R^1), C(R^{22}), or N wherein the following provisos apply:

(i) no more than one of J^1 and J^2 is N,

(ii) no more than one of J^1 and J^2 is C(R^{22}); and

(iii) only one R^1 is substituted on the illustrated ring containing J^1 and J^2;

R^1 is selected from the group consisting of:

(i) –C(O)-N(R^{6a})(R^{6b}),

(ii) –$S(O)_2$-N(R^{6a})(R^{6b}),

(iii) –C(O)-C(R^{7a})(R^{7b})(R^{7c}),

(iv) –N(H)-C(O)-C(R^{7a})(R^{7b})(R^{7c}),

(v) –C(O)-O-C(R^{7a})(R^{7b})(R^{7c}), and

(vi) –N(H)-$S(O)_2$-C(R^{7a})(R^{7b})(R^{7c});

R^{6a} and R^{6b} are independently:

a. H,

b. C_1-C_6 alkyl,

c. C_3-C_6 alkenyl,

d. C_3-C_6 alkynyl,

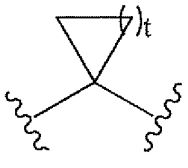
e. –O-(C_1-C_3 alkyl),

f. –Q-R^{AH}, wherein R^{AH} is phenyl or 5- to 6-membered heteroaryl containing 1 to 2 heteroatoms independently selected from the group consisting of N, O, and S, and wherein R^{AH} is unsubstituted or substituted with 1 to 5 R^8 moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -O-(C_1-C_3 fluoroalkyl), hydroxyl, phenyl, and –CN;

Q is selected from the group consisting of a

(a) a bond;

(b) C_1-C_6 alkylene, wherein said C_1-C_6 alkylene is unsubstituted or substituted by 1 to 2 fluoro, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, or C_1-C_3 fluoroalkyl; and

(c)  wherein t is 1, 2, 3, or 4;

g. –Q-R^{HC}, wherein R^{HC} is

(i) 5- to 7-membered heterocyclyl containing 1 heteroatom selected from the group consisting of N, O, S, S(O), and $S(O)_2$, wherein said heterocyclyl of R^{HC} is optionally fused to a benzene, pyridyl ring; or

(ii) C_3-C_7 cycloalkyl, wherein said cycloalkyl of R^{HC} is optionally fused to a benzene or pyridyl ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 5 R^{12} moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -O-(C_1-C_3 fluoroalkyl), hydroxyl, –CN, and -$S(O)_2$-(C_1-C_3 alkyl), or wherein when two R^{12} moieties are geminally substituted on the same carbon atom, the two geminally substituted R^{12} moieties, together with the carbon atom on which they are attached form –C(O)-;

h. or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is independently selected from the group consisting of:

(i) a 4- to 9-membered heterocyclyl, optionally containing one additional nitrogen atom, wherein said heterocyclyl of R^{6H} is optionally fused to phenyl, C_3-C_6 cycloalkyl, or a 5-membered heteroaryl containing 1 to 3 N atoms;

(ii) a 4- to 7-membered heterocyclenyl, optionally containing one additional nitrogen atom, wherein said heterocyclenyl of R^{6H} is optionally fused to phenyl; and

(iii) a 6- to 8-membered aza- or a diazabicycloheterocycloalkyl ring;

wherein R^{6H} is unsubstituted or substituted by 1 to 5 R^9 moieties wherein each R^9 moiety is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 fluoroalkyl, fluoro, hydroxyl, -CN, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), or R^9 is -Z-R^{CY} wherein

Z is

(i) a bond,

(ii) -C(O)-,

(iii) -C(=N-OH)-,

(iv) $-S(O)_2-$,

(v) C_1-C_3 alkylene, wherein said C_1-C_3 alkylene of Z is optionally substituted by 1 to 2 fluoro or C_1-C_3 alkyl;

(vi) –O-;

(vii) –O-(C_1-C_3 alkylene)-;or

(viii) –C(O)-O-CH_2-

R^{CY} is selected from the group consisting of:

(i) phenyl

(ii) 5- to 10-membered mono or bicyclic heteroaryl containing 1 to 3 heteroatoms independently selected from the group consisting of N, O, and S; or

(iii) 5- to 6-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{CY} is optionally fused to phenyl;

wherein R^{CY} is unsubstituted or substituted by 1 to 4 R^{10} moieties;

each R^{10} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, C_1-C_3 fluoroalkyl, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), -CN, ~~or~~ pyridyl, or cyclopropyl or, wherein when two R^{10} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

or, optionally, where two R^9 moieties are geminally substituted on a common ring carbon of R^{6H}, the two R^9 moieties, together with the ring carbon on which they are substituted, form R^{YC}, wherein R^{YC} is

(i) a 4- to 7-membered cycloalkyl, wherein said cycloalkyl of R^{YC} is optionally fused to phenyl or pyridyl; or

(ii) a 4- to 7-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said heterocyclyl of R^{YC} is optionally fused to phenyl;

wherein R^{YC} is unsubstituted or substituted by 1 to 4 R^{11} moieties;

each R^{11} moiety is independently C_1-C_3 alkyl, halo, hydroxyl, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), -$S(O)_2$-(C_1-C_3 alkyl), -C(O)-(C_1-C_3 alkyl), phenyl, or pyridyl, or, wherein when two R^{11} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

R^{7a} and R^{7b} are independently

a) H,

b) C_1-C_6 alkyl,

c) R^{7a} and R^{7b} together with the carbon atom on which they are substituted, form R^{PC}, wherein R^{PC} is

(i) C_3-C_7 cycloalkyl, or

(ii) phenyl, wherein said phenyl of R^{PC} is unsubstituted or substituted by 1 to 5 moieties independently selected from the group consisting of halo, trifluoromethyl, and trifluoromethoxy;

R^{7c} is

a) H, or

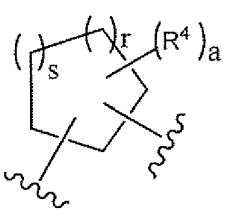
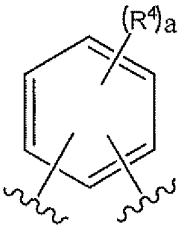
b) absent, when R^{7a} and R^{7b} together with the carbon atom on which they are substituted form phenyl;

R^{22} is halo, C_1-C_3 alkyl, or C_1-C_3 fluoroalkyl;

b is 0 or 1;

X is a bond, –O-, -S-, -S(O)-,–$S(O)_2$-, or N(H);

Y is selected from the group consisting of

(i) a bond, (ii)  , (iii)  , (iv) –O-, (v) –S-, (vi) –S(O)-, and (vii) –$S(O)_2$-;

wherein

a is 0, 1, 2, or 3;

r is 0, 1, or 2;

s is 0, 1, or 2;

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each occurrence of R^4 is independently halo, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl;

R^a, R^b, R^c, and R^d are independently H, fluoro, hydroxyl, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, or C_1-C_6 alkoxy;

R^2 is selected from the group consisting of:

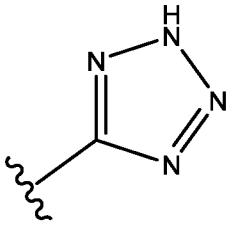
(i) phenyl;

(ii) 5- to 6-membered heteroaryl containing from 1 to 3 heteroatoms selected from the group consisting of N, O, and S;

(iii) 5- to 6-membered heterocyclenyl, containing from 1 to 2 heteroatoms selected from the group consisting of N, O, and S; and

(iv) 5- to 6-membered heterocyclyl containing from 1 to 2 heteroatoms selected from the group consisting of N, O, and S;

wherein R^2 is unsubstituted or substituted by 1 to 5 R^5 groups independently selected from the group consisting of halo, C_1-C_3 fluoroalkyl, C_1-C_3 alkyl, C_1-C_3 alkoxy, -CN, -OCF_3, -C(O)-(C_1-C_3 alkyl), and -$S(O)_2$-(C_1-C_3 alkyl);

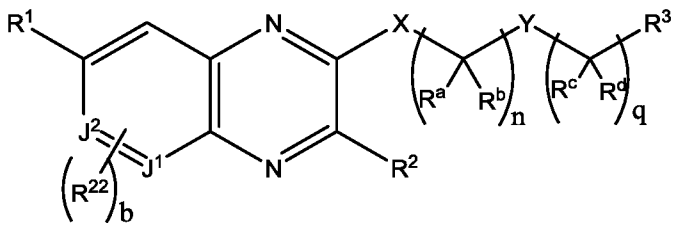
R^3 is –C(O)OH,  , or –N(H)-SO_2-R^e,

wherein R^e is C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_1-C_6 alkoxy, and phenyl;

n is 1, 2, 3, 4, or 5; and

q is 0, 1, or 2.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound has the formula (IA)



(IA)

wherein J^1 and J^2 are independently C(H) or C(R^{22}), or N wherein the following provisos apply:

(i) no more than one of J^1 and J^2 is N, and

(ii) no more than one of J^1 and J^2 is C(R^{22}).

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3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of:

(i) $-C(O)-N(R^{6a})(R^{6b})$, and

(ii) $-S(O)_2-N(R^{6a})(R^{6b})$.

4. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein R^1 is $-C(O)-N(R^{6a})(R^{6b})$.

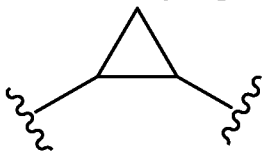
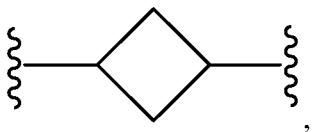
5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein

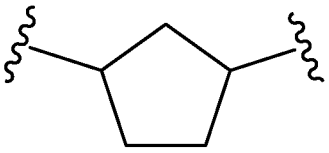
R^{6a} is H and

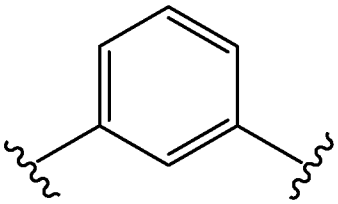
R^{6b} is $-Q-R^{AH}$ or $-Q-R^{HC}$.

6. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}.

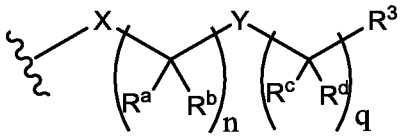
7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein Y is selected from the group consisting of:

(i) a bond, (ii)  , (iii)  ,



(iv) , and (v)  .

8. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein the group



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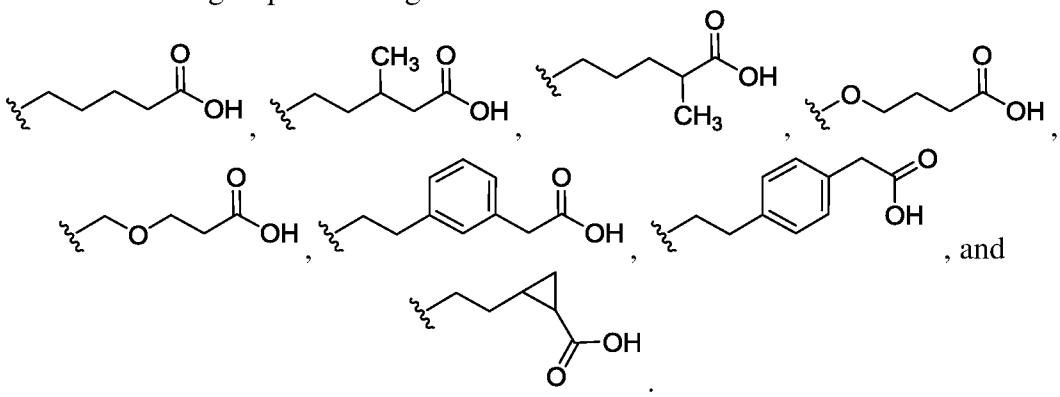
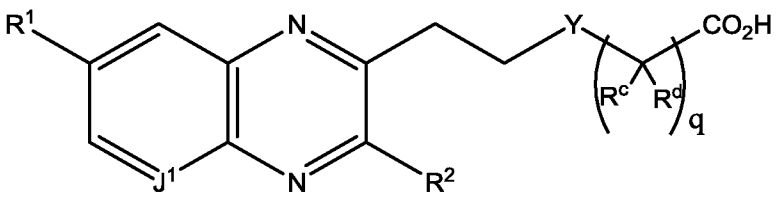
is selected from the group consisting of:



9. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound of the Formula (I) has the Formula (IB)



(IB)

wherein

J^1 is C(H) or N;

R^1 is –C(O)-N(R^{6a})(R^{6b});

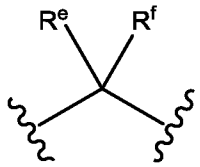
I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl or pyridyl,

and wherein R^{AH} is unsubstituted or substituted with 1 to 2 R^8 moieties independently selected from the group consisting of halo, C_1-C_3 alkyl, C_1-C_3 alkoxy, trifluoromethyl, trifluoromethoxy, and –CN;

Q is selected from the group consisting of:

(i) a bond;

(ii)  ,wherein R^e and R^f are independently H, C_1-C_3 alkyl, or trifluoromethyl;

(iii) C_2-C_4 alkylene, wherein said C_2-C_6 alkylene is unsubstituted;

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b) –Q-R^{HC}, wherein R^{HC} is

(i) 5- to 6-membered heterocyclyl containing 1 heteroatom selected from the group consisting of N and O; or

(ii) C_5-C_7 cycloalkyl, wherein said C_5-C_7 cycloalkyl is optionally fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of C_1-C_3 alkyl, halo, and hydroxyl, or wherein when two R^{12} moieties are geminally substituted on the same carbon atom, the two geminally substituted R^{12} moieties, together with the carbon atom on which they are attached form –C(O)-;

II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is independently selected from the group consisting of:

a) a 4- to 6-membered heterocyclyl, optionally containing one additional nitrogen atom, wherein said 4- to 6-membered heterocyclyl is optionally fused to phenyl; and

b) a 5- to 6-membered heterocyclenyl, optionally containing one additional nitrogen atom, wherein said 4- to 6-membered heterocyclyl is optionally fused to phenyl;

wherein R^{6H} is unsubstituted or substituted by 1 to 2 R^9 moieties wherein each R^9 moiety is independently C_1-C_3 alkyl, F, Cl, -CN, or

R^9 is -Z-R^{CY}, wherein

Z is a bond or –CH_2-;

R^{CY} is selected from the group consisting of:

(i) phenyl;

(ii) 5- to 6-membered heteroaryl containing 1 to 3 N atoms; or

(iii) 5- to 6-membered heterocyclyl containing 2 N atoms, wherein said 5- to 6-membered heterocyclyl of R^{CY} is fused to phenyl;

wherein R^{CY} is unsubstituted or substituted by 1 to 2 R^{10} moieties;

each R^{10} moiety is independently C_1-C_3 alkyl, halo, C_1-C_3 alkoxy, -(C_1-C_3 alkylene)-(C_1-C_3 alkoxy), or -CN, or, wherein two R^{10} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form–C(O)-;

or, optionally, where two R^9 moieties are geminally substituted on a common ring carbon of R^{6H}, the two R^9 moieties, together with the ring carbon on which they are substituted, form R^{YC}, wherein R^{YC} is

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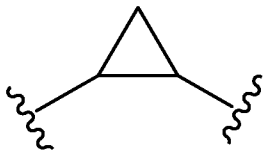
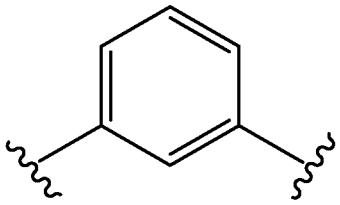
(i) a 5- to 6-membered cycloalkyl, wherein said or 5- to 6-membered cycloalkyl is fused to phenyl; or

(ii) a 4- to 6-membered heterocyclyl containing 1 to 2 N atoms or 1 O atom, wherein said or 4- to 6-membered heterocyclyl is optionally fused to phenyl;

wherein R^{YC} is unsubstituted or substituted by 1 to 3 R^{11} moieties;

each R^{11} moiety is independently C_1-C_3 alkyl, -C(O)-(C_1-C_3 alkyl), or phenyl, or, wherein two R^{11} moieties are geminally substituted on a common carbon atom, together with the carbon atom on which they are substituted, form –C(O)-;

Y is selected from the group consisting of

(i) a bond, (ii)  , and (iii)  ;

R^c is H or methyl;

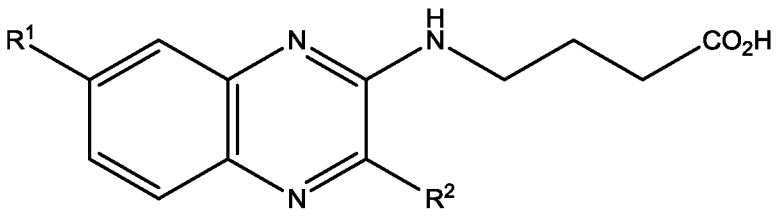
R^d is H;

R^2 is phenyl, pyridyl, or thienyl;

wherein R^2 is unsubstituted or substituted by 1 to 2 R^5 groups independently selected from the group consisting of fluoro, chloro, trifluoromethyl, C_1-C_3 alkoxy, -CN, and -OCF_3; and

q is 0, 1, or 2.

10. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound of the Formula (I) has the Formula (IC)



(IC)

wherein

R^1 is –C(O)-N(R^{6a})(R^{6b});

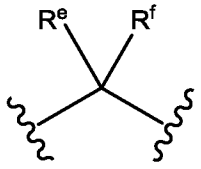
I) R^{6a} is H and R^{6b} is:

a) –Q-R^{AH}, wherein R^{AH} is phenyl,

and wherein R^{AH} is unsubstituted or substituted with one R^8 moiety selected from the group consisting of fluoro and -CN;

Q is selected from the group consisting of:

(i) a bond;

(ii) 

, wherein R^e is H, and R^f is H or methyl;

b) $-Q-R^{HC}$, wherein R^{HC} is C_5-C_6 cycloalkyl, wherein said C_5-C_6 cycloalkyl is fused to a benzene ring;

and wherein R^{HC} is unsubstituted or substituted with 1 to 2 R^{12} moieties independently selected from the group consisting of halo and -CN;

II) or R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is azetidinyl, pyrrolidinyl, piperidinyl, or piperazinyl;

wherein R^{6H} is substituted with $-Z-R^{CY}$, wherein

Z is a bond; and

R^{CY} is unsubstituted phenyl or phenyl substituted by 1 to 2 R^{10} moieties selected from the group consisting of halo and -CN;

R^{6H} is optionally substituted by 1 to 2 R^9 moieties, wherein each R^9 moiety is independently C_1-C_3 alkyl, halo or -CN, and

R^2 is unsubstituted phenyl.

11. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

(**14**) 5-(3-phenyl-7-{[4-(trifluoromethyl)benzyl]carbamoyl}pyrido[2,3-b]pyrazin-2-yl)pentanoic acid;

(**14D**) 5-{7-[(4-chlorobenzyl)carbamoyl]-3-phenylpyrido[2,3-b]pyrazin-2-yl}pentanoic acid;

(**14G**) 5-{3-phenyl-7-[(4-phenylpiperazin-1-yl)carbonyl]pyrido[2,3-b]pyrazin-2-yl}pentanoic acid;

(**15A**) 5-(3-phenyl-7-{[(1R)-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid;

(**15B**) 5-(3-phenyl-7-{[(1S)-1-phenylethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid;

(**15C**) 5-(3-phenyl-7-{[4-(trifluoromethyl)benzyl]carbamoyl}quinoxalin-2-yl)pentanoic acid;

(**15D**) 5-(7-{[(1R)-1-(4-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15E**) 5-(7-{[(1S)-1-(4-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15K**) 5-{7-[(3-benzylpiperazin-1-yl)carbonyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15N**) 5-(7-{[3-(4-methoxyphenyl)pyrrolidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15P**) 5-(7-{[3-(3-chlorophenyl)pyrrolidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15Q**) 5-(3-phenyl-7-{[2,2,2-trifluoro-1-(4-fluorophenyl)ethyl]carbamoyl}quinoxalin-2-yl)pentanoic acid;

(**15R**) 5-{7-[(3-benzylpyrrolidin-1-yl)carbonyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15S**) 5-(7-{[3-(4-fluorophenyl)pyrrolidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15T**) 5-{7-[(4-chlorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15X**) 5-{7-[(1-methyl-1-phenylethyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15Z**) 5-[7-(benzylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid;

(**15AB**) 5-{7-[(2-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15AC**) 5-{7-[(3-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15AD**) 5-{7-[(4-fluorobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15AF**) 5-{3-phenyl-7-[(pyridin-2-ylmethyl)carbamoyl]quinoxalin-2-yl}pentanoic acid;

(**15Ai**) 5-{3-phenyl-7-[(4-phenylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

(**15AJ**) 5-{3-phenyl-7-[(2-phenylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

(**15AK**) 5-{3-phenyl-7-[(3-phenylpyrrolidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

(**15AL**) 5-{3-phenyl-7-[(2-phenylpyrrolidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

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(**15AN**) 5-{3-phenyl-7-[(4-phenylpiperazin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

(**15AO**) 5-{7-[benzyl(methyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15AP**) 5-[7-(3,4-dihydroisoquinolin-2(1H)-ylcarbonyl)-3-phenylquinoxalin-2-yl]pentanoic acid;

(**15AR**) 5-[3-phenyl-7-(1,2,3,4-tetrahydronaphthalen-1-ylcarbamoyl)quinoxalin-2-yl]pentanoic acid;

(**15AU**) 5-(7-{[1-(4-methoxyphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15AV**) 5-(3-phenyl-7-{[4-(trifluoromethoxy)benzyl]carbamoyl}quinoxalin-2-yl)pentanoic acid;

(**15AW**) 5-{7-[(4-methylbenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15AX**) 5-(7-{[(1R)-1-(4-chlorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15AY**) 5-(7-{[(1R)-1-(4-methylphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15AZ**) 5-{7-[(4-ethylbenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15BA**) 5-{7-[(4-methoxybenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15BB**) 5-{7-[(4-cyanobenzyl)carbamoyl]-3-phenylquinoxalin-2-yl}pentanoic acid;

(**15BC**) 5-(7-{[(1S)-1-(4-methylphenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BD**) 5-[3-phenyl-7-({1-[4-(trifluoromethoxy)phenyl]ethyl}carbamoyl)quinoxalin-2-yl]pentanoic acid;

(**15BF**) 5-[3-phenyl-7-(piperidin-1-ylcarbonyl)quinoxalin-2-yl]pentanoic acid;

(**15BH**) 5-(7-{[1-(2-fluorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BK**) 5-[7-(2,3-dihydro-1H-inden-2-ylcarbamoyl)-3-phenylquinoxalin-2-yl]pentanoic acid;

(**15BM**) 5-(7-{[(1S)-1-(4-chlorophenyl)ethyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

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(**15BN**) 5-(7-{[3-(2-oxopyrrolidin-1-yl)propyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BQ**) 5-(7-{[4-(4-methyl-1H-1,2,3-triazol-1-yl)piperidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BR**) 5-(7-{[4-(5-methyl-1H-1,2,3-triazol-1-yl)piperidin-1-yl]carbonyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BS**) 5-{3-phenyl-7-[(4-pyrazin-2-ylpiperidin-1-yl)carbonyl]quinoxalin-2-yl}pentanoic acid;

(**15BT**) 5-(7-{[(4-chloropyridin-2-yl)methyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**15BU**) 5-(7-{[(6-chloropyridin-2-yl)methyl]carbamoyl}-3-phenylquinoxalin-2-yl)pentanoic acid;

(**16**) 3-(4-chlorophenyl)-7-[[[(4-chlorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16F**) 3-(4-chlorophenyl)-7-[[[(3-chlorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16H**) 3-(4-chlorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16i**) 3-(4-chlorophenyl)-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16J**) 3-(4-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16K**) 3-(4-chlorophenyl)-7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16L**) 3-(4-chlorophenyl)-7-[(3(R)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16N**) 3-(4-chlorophenyl)-7-[(3(R)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16P**) 3-(4-chlorophenyl)-7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16R**) 3-(4-chlorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16S**) 3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16T**) 3-(4-chlorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16U**) 3-(4-chlorophenyl)-7-[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16V**) 3-(4-chlorophenyl)-7-[[[1(R)-(4-chlorophenyl)-2,2,2-trifluoroethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16Y**) 3-(4-chlorophenyl)-7-[[[2,2,2-trifluoro-1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16AB**) 3-(4-chlorophenyl)-7-[[[[3-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16AC**) 3-(4-chlorophenyl)-7-[[[[3-(trifluoromethoxy)phenyl]methyl]-amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16AE**) 3-(4-chlorophenyl)-7-[[[1(S)-(4-chlorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16AG**) 3-(4-chlorophenyl)-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16AH**) 3-(4-chlorophenyl)-7-[[(2,2,2-trifluoro-1(R)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**16AK**) 3-(4-chlorophenyl)-7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**16AQ**) 3-(4-chlorophenyl)-7-[[[(4-methylphenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**17**) 3-(4-chlorophenyl)-beta-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**17D**) 3-(4-chlorophenyl)-7-[[[1(S)-(4-chlorophenyl)ethyl]amino]carbonyl]-beta-methyl- 2-quinoxalinepentanoic acid;

(**17M**) 3-(4-chlorophenyl)-beta-methyl-7-[[[2,2,2-trifluoro-1(S)-phenylethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**17S**) beta-methyl-3-[4-(trifluoromethyl)phenyl]-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**18**) alpha-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid;

(**19**) 3-[2-[3-(4-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid;

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(**19G**) 3-[2-[3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinyl]ethyl]benzeneacetic acid;

(**20**) 2-[2-[3-phenyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinyl]ethyl]cyclopropanecarboxylic acid;

(**24i**) 6-fluoro-3-phenyl-7-[(3(S)-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26E**) 3-(3-fluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26J**) 3-(3-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26K**) 7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[6-(trifluoromethyl)-3-pyridinyl]-2-quinoxalinepentanoic acid;

(**26L**) 3-(2-chlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26N**) 7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethoxy)phenyl]-2-quinoxalinepentanoic acid;

(**26O**) 3-(4-methoxyphenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26P**) 3-(4-cyanophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**26S**) 7-[(4-phenyl-1-piperidinyl)carbonyl]-3-(3-thienyl)-2-quinoxalinepentanoic acid;

(**26Y**) 3-(2,4-dichlorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**39**) (R)-5-(7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid;

(**40**) (R)-5-(7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid;

(**41**) (R)-5-(7-(2-methyl-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid;

(**44H**) 4-((7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

(**44i**) (R)-4-((3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)amino)butanoic acid;

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(**100**) 7-[[[(4-chlorophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**102**) 3-(4-fluorophenyl)-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**103**) 7-[[(2,3-dihydro-1H-inden-2-yl)amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**104**) 7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**105**) 3-(4-fluorophenyl)-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**106**) 3-(4-fluorophenyl)-7-[(3-phenyl-1-pyrrolidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**107**) 3-(4-fluorophenyl)-7-[[[[4-(trifluoromethoxy)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**109**) 3-(4-fluorophenyl)-7-[[[(4-fluorophenyl)methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**110**) 3-(4-fluorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**111**) 3-(4-fluorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**112**) 3-(4-fluorophenyl)-7-[[[[4-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-2-quinoxalinepentanoic acid;

(**113**) 7-[[4-[2,3-dihydro-3-(2-methoxyethyl)-2-oxo-1H-benzimidazol-1-yl]-1-piperidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**117**) 7-[[4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**119**) 7-[(1,2-dihydro-1-methyl-2-oxospiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**120**) 3-phenyl-7-(spiro[benzofuran-3(2H),4'-piperidin]-1'-ylcarbonyl)-2-quinoxalinepentanoic acid;

(**121**) 7-[(2,3-dihydrospiro[1H-indene-1,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**122**) 7-[(1,2-dihydro-1-methylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

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(**123**) 7-[(1-acetyl-1,2-dihydrospiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**124**) 7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**125**) 7-[(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**126**) 3-(4-fluorophenyl)-7-[(4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)carbonyl]-2-quinoxalinepentanoic acid;

(**127**) 5-(3-(4-fluorophenyl)-7-(4-phenyl-1,2,3,6-tetrahydropyridine-1-carbonyl)quinoxalin-2-yl)pentanoic acid;

(**128**) 7-[(4-cyano-4-phenyl-1-piperidinyl)carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**129**) 3-(4-fluorophenyl)-7-[[(phenylmethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**130**) 7-[[[1(R)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**131**) 7-[[[1(S)-(4-chlorophenyl)ethyl]amino]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**132**) 3-(4-fluorophenyl)-7-[[(1(R)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**135**) 7-[[4-(4-chlorophenyl)-1-piperidinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**136**) 7-[[4-(4-chlorophenyl)-3,6-dihydro-1(2H)-pyridinyl]carbonyl]-3-(4-fluorophenyl)-2-quinoxalinepentanoic acid;

(**142**) 3-phenyl-7-[(3(S)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**143**) 3-phenyl-7-[(3(R)-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**145**) 5-(7-(4-(1H-imidazol-1-yl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)pentanoic acid;

(**147**) 7-[[[1(R)-(2-pyridinyl)ethyl]amino]carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid;

(**148**) 7-[(4-phenyl-1-piperidinyl)carbonyl]-3-[4-(trifluoromethyl)phenyl]-2-quinoxalinepentanoic acid;

(**162**) 3-(4-chlorophenyl)-alpha-methyl-7-[(4-phenyl-1-piperidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**163**) 3-(4-chlorophenyl)-alpha-methyl-7-[[(2,2,2-trifluoro-1(S)-phenylethyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**164**) 3-(4-chlorophenyl)-7-[[[(4-cyanophenyl)methyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid;

(**166**) 3-(4-chlorophenyl)-7-[[[1(R)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid;

(**167**) 3-(4-chlorophenyl)-7-[[[1(S)-(4-fluorophenyl)ethyl]amino]carbonyl]-alpha-methyl-2-quinoxalinepentanoic acid;

(**172**) 3-phenyl-7-[(3-phenyl-1-azetidinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**174**) 7-[[3-(4-cyanophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**217**) 3-(4-fluorophenyl)-7-[[(1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-2-quinoxalinepentanoic acid;

(**231**) 3-(4-fluorophenyl)-7-[(4-phenyl-1-piperazinyl)carbonyl]-2-quinoxalinepentanoic acid;

(**251**) 7-[[3-(3-fluorophenyl)-1-azetidinyl]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**254**) 7-[[(6-fluoro-1,2,3,4-tetrahydro-1(R)-naphthalenyl)amino]carbonyl]-3-phenyl-2-quinoxalinepentanoic acid;

(**256**) (R)-5-(3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)pentanoic acid;

(**375**) (S)-5-(3-(4-chlorophenyl)-7-((1-(3,4-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid;

(**412**) (R)-5-(3-(4-chlorophenyl)-7-((1-(3,5-difluorophenyl)ethyl)carbamoyl)quinoxalin-2-yl)pentanoic acid;

(**426**) 5-(3-(4-chlorophenyl)-7-(3-(4-chlorophenyl)azetidine-1-carbonyl)quinoxalin-2-yl)pentanoic acid;

(**457**) 5-(7-(((R)-5-fluoro-2,3-dihydro-1H-inden-1-yl)carbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)-2-methylpentanoic acid;

(**491**) (R)-5-(7-(chroman-4-ylcarbamoyl)-3-(4-fluorophenyl)quinoxalin-2-yl)pentanoic acid;

(**507**) (S)-5-(3-(4-chlorophenyl)-7-(chroman-4-ylcarbamoyl)quinoxalin-2-yl)pentanoic acid;

(**512**) (R)-5-(7-(chroman-4-ylcarbamoyl)-3-phenylquinoxalin-2-yl)pentanoic acid;

(**585**) 5-(3-(4-chlorophenyl)-7-(3-oxo-3,4-dihydro-2H-spiro[isoquinoline-1,4'-piperidin]-1'-ylcarbonyl)quinoxalin-2-yl)pentanoic acid; and

(**628**) 5-(3-(4-chlorophenyl)-7-(4-(2,6-dimethylphenyl)piperazine-1-carbonyl)quinoxalin-2-yl)pentanoic acid.

12. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein R^{6a} and R^{6b} together with the N atom to which they are attached form R^{6H}, wherein R^{6H} is piperazinyl.

13. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

(R)-4-((7-(4-(4-fluorophenyl)-2-methylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

(R)-4-((7-((1-(4-fluorophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

(R)-4-((7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

4-((3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)amino)butanoic acid;

(R)-4-((7-((1-(4-cyanophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

4-((7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

(R)-4-((3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)amino)butanoic acid;

4-((7-(4-(4-fluorophenyl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

4-((7-(4-(4-chlorophenyl)piperidine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

4-((7-(4-(4-chlorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid;

(R)-4-((3-phenyl-7-(3-phenylpyrrolidine-1-carbonyl)quinoxalin-2-yl)amino)butanoic acid; and

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(R)-4-((7-(2-methyl-4-phenylpiperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid.

14. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is (R)-4-((7-((6-fluoro-1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid.

15. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is 4-((3-phenyl-7-(4-phenylpiperazine-1-carbonyl)quinoxalin-2-yl)amino)butanoic acid.

16. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is (R)-4-((7-((1-(4-cyanophenyl)ethyl)carbamoyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid.

17. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is 4-((7-(4-(4-fluorophenyl)piperazine-1-carbonyl)-3-phenylquinoxalin-2-yl)amino)butanoic acid.

18. The compound of claim 10 or a pharmaceutically acceptable salt thereof, wherein the compound is (R)-4-((3-phenyl-7-((1,2,3,4-tetrahydronaphthalen-1-yl)carbamoyl)quinoxalin-2-yl)amino)butanoic acid.

19. A pharmaceutical composition comprising an effective amount of the compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

20. A method for treating a disease or condition associated with uncontrolled or inappropriate stimulation of $CRTH_2$ function comprising administering to a patient in need of such treatment of an effective amount of a compound of any one of claims 1 to 18 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 19.

21. The method according to claim 20, wherein the disease or condition is asthma, congestion, allergic rhinitis or COPD.

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22. Use of a compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for treating a disease or condition associated with uncontrolled or inappropriate stimulation of $CRTH_2$ function.

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