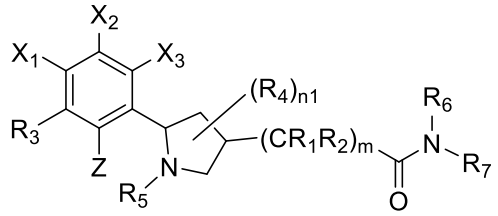
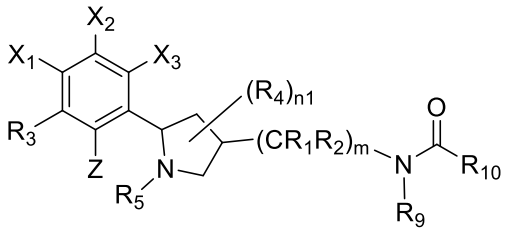
SUMMARY

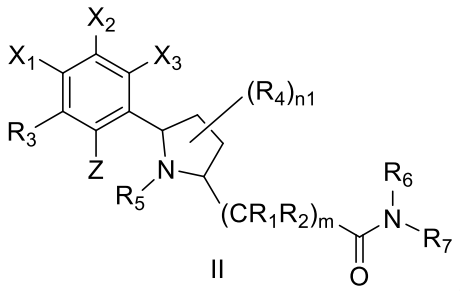
[0016a] In a first aspect of the present disclosure, there is provided a compound of Formula I, I', II, II', III, or IV, or a pharmaceutically-acceptable salt thereof,



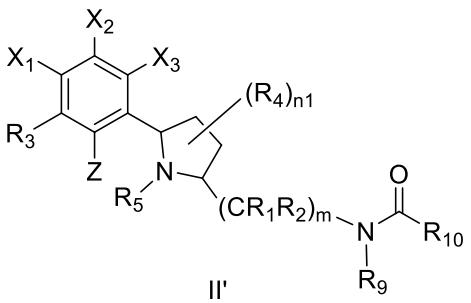
I ;



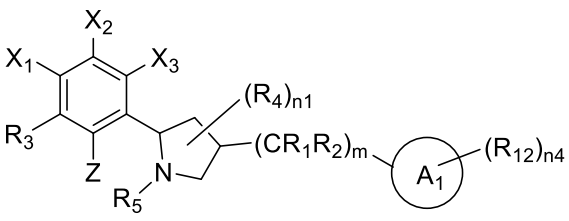
I' ;



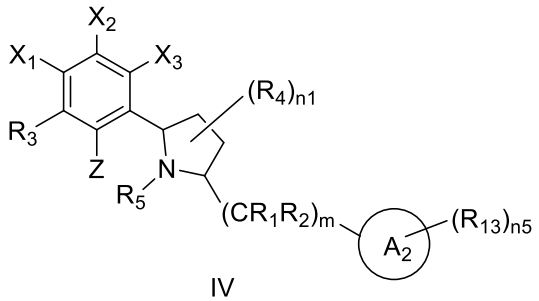
II ;



II' ;



III ;



IV ;

wherein

each occurrence of Z is independently OR_a;

each occurrence of X_1 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

each occurrence of X_2 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

each occurrence of X_3 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

or alternatively X_1 and X_2 and the carbon atoms they are connected to taken together form an optionally substituted 5- or 6-membered aryl;

or alternatively X_2 and X_3 and the carbon atoms they are connected to taken together form an optionally substituted 5- or 6-membered aryl;

each occurrence of R_1 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

each occurrence of R_2 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

or alternatively R_1 and R_2 taken together with the carbon atom they are connected to form a cycloalkyl or saturated heterocycle;

each occurrence of R_3 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

each occurrence of R_4 is independently H, alkyl, cycloalkyl, saturated heterocycle, $(CR_aR_b)_{n2}OR_a$, or $(CR_aR_b)_{n2}NR_aR_b$;

or alternatively two R_4 groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted cycloalkyl or heterocycle;

each occurrence of R_5 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, $(C=O)R_a$, $(C=O)(CR_aR_b)_{n2}OR_a$, $(C=O)(CR_aR_b)_{n2}NR_aR_b$, or SO_2R_a;

each occurrence of R_6 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

each occurrence of R_7 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

or alternatively R_6 and R_7 taken together with the nitrogen atom they are connected to form a heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S; wherein the heterocycle is optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)R_8$, $(C=O)N(R_8)_2$, $NR_8(C=O)R_8$, and oxo where valence permits;

each occurrence of R_9 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, $(C=O)R_a$, $(C=O)(CR_aR_b)_{n2}OR_a$, $(C=O)(CR_aR_b)_{n2}NR_aR_b$, or SO_2R_a;

each occurrence of R_{10} is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

A_1 is aryl or heteroaryl;

A_2 is aryl or heteroaryl;

each occurrence of R_{12} is independently H, alkyl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, $(CR_aR_b)_{n2}OR_a$, $(C=O)NR_aR_b$, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}NR_b(C=O)R_a$;

each occurrence of R_{13} is independently H, alkyl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, $(CR_aR_b)_{n2}OR_a$, $(C=O)NR_aR_b$, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}NR_b(C=O)R_a$;

each occurrence of R_a and R_b are independently H, alkyl, alkenyl, cycloalkyl, saturated heterocycle comprising 1-3 heteroatoms each selected from the group consisting of N, O, and S, aryl, or heteroaryl; or alternatively R_a and R_b together with the carbon or nitrogen atom that they are connected to form a cycloalkyl or heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

the alkyl, cycloalkyl, heterocycle, aryl, and heteroaryl in X_1, X_2, X_3, A_1, A_2, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, R_{10}, R_{12}, R_{13}, R_a, or R_b, where applicable, are optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)R_8$, $(C=O)N(R_8)_2$, $NR_8(C=O)R_8$, and oxo where valence permits;

each occurrence of R_8 is independently H, alkyl, or optionally substituted heterocycle; or alternatively the two R_8 groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of m is independently 1, 2, or 3;

each occurrence of n_1 is independently an integer from 0-3 wherein valence permits;

each occurrence of n_2 is independently an integer from 0-3; and

n_4 is an integer from 0-3;

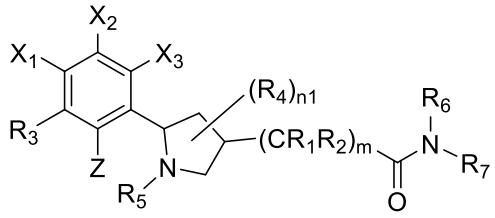
n_5 is an integer from 0-3.

[0016b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising at least one compound disclosed herein, or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable carrier or diluent.

[0016c] In yet another aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically-acceptable salt thereof, for use as a medicament.

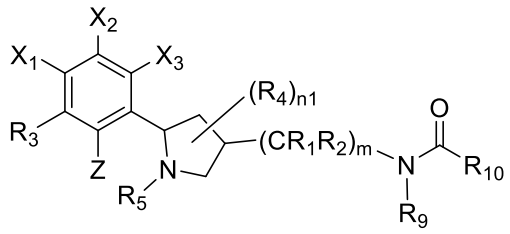
[0016d] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically-acceptable salt thereof, in the manufacture of a medicament for treating a condition in a human in need thereof, wherein the condition is selected from the group consisting of cancer, an immunological disorder, a central nervous system disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, and a kidney disease.

[0017] In one example, compounds useful as potassium channel blockers having a structure



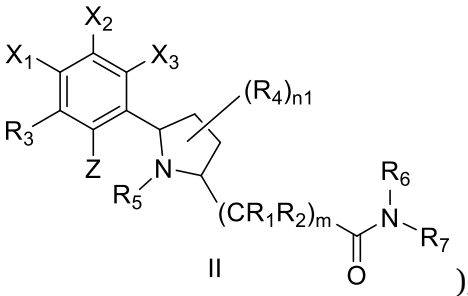
I

of Formula I ( ), Formula I'



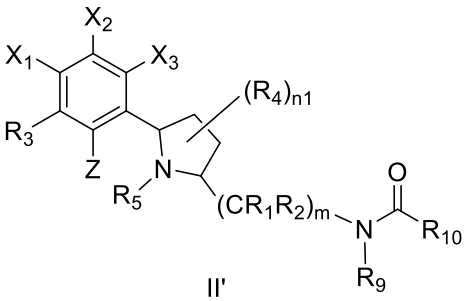
I'

( ), formula II (



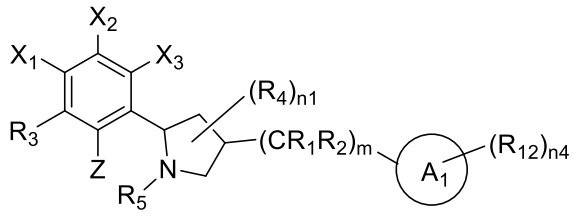
II

),



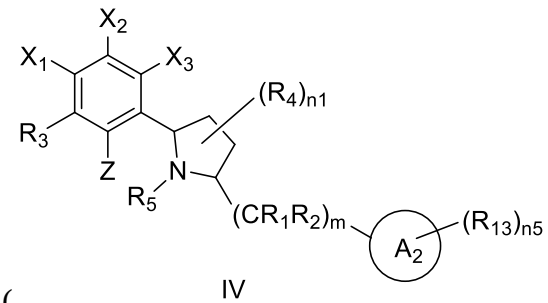
II'

formula II' ( ), formula III



III

( ), or formula IV

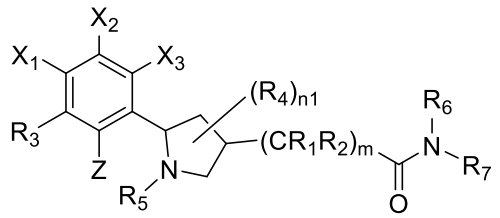


IV

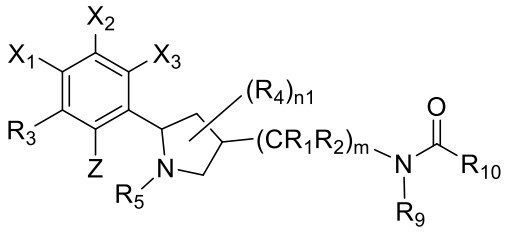
( ) are described, where the various substituents are defined herein. The compounds of Formula I, I', II, II', III, or IV described herein can block Kv1.3 potassium (K^+) channels and be used in the treatment of a variety of conditions. Methods

for synthesizing these compounds are also described herein. Pharmaceutical compositions and methods of using these compositions described herein are useful for treating conditions *in vitro* and *in vivo*. Such compounds, pharmaceutical compositions, and methods of treatment have a number of clinical applications, including as pharmaceutically active agents and methods for treating cancer, an immunological disorder, a CNS disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, a kidney disease, or a combination thereof.

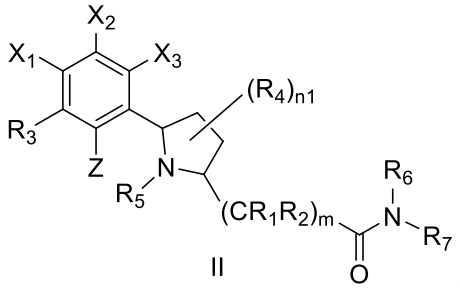
[0018] In one example, a compound of Formula I, I', II, II', III, or IV or a pharmaceutically-acceptable salt thereof is described,



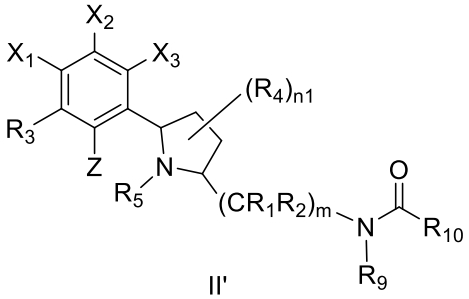
I ;



I' ;



II ;



II' ;

each occurrence of R_{13} is independently H, alkyl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, $(CR_aR_b)_{n2}OR_a$, $(C=O)NR_aR_b$, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}NR_b(C=O)R_a$;

each occurrence of R_a and R_b are independently H, alkyl, alkenyl, cycloalkyl, saturated heterocycle comprising 1-3 heteroatoms each selected from the group consisting of N, O, and S, aryl, or heteroaryl; or alternatively R_a and R_b together with the carbon or nitrogen atom that they are connected to form a cycloalkyl or heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

the alkyl, cycloalkyl, heterocycle, aryl, and heteroaryl in X_1, X_2, X_3, A_1, A_2, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, R_{10}, R_{12}, R_{13}, R_a, or R_b, where applicable, are optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)R_8$, $(C=O)N(R_8)_2$, $NR_8(C=O)R_8$, and oxo where valence permits;

each occurrence of R_8 is independently H, alkyl, or optionally substituted heterocycle; or alternatively the two R_8 groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of m is independently 1, 2, or 3;

each occurrence of n_1 is independently an integer from 0-3 wherein valence permits;

each occurrence of n_2 is independently an integer from 0-3; and

n_4 is an integer from 0-3;

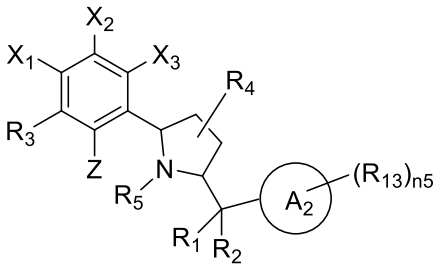
n_5 is an integer from 0-3.

[0019] In any one of the examples described herein, each occurrence of R_4 is independently H, alkyl, cycloalkyl, saturated heterocycle, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}OR_a$; and each occurrence of R_5 is independently H, alkyl, cycloalkyl, or saturated heterocycle.

[0020] In any one of the examples described herein, each occurrence of m is independently 2 or 3.

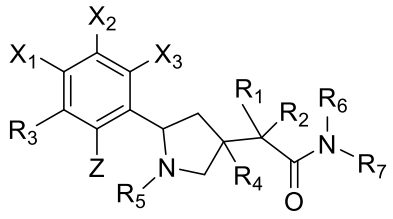
[0021] In any one of the examples described herein, one or more occurrences of m are 1.

[0022] In any one of the examples described herein, the compound has the structure of Formula Ia, Ia', IIa, IIa', IIIa, or IVa:

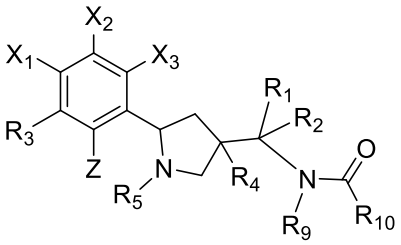


IVa .

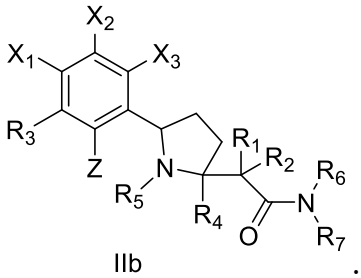
[0023] In any one of the examples described herein, the compound has the structure of Formula Ib, Ib', IIb, IIb', IIIb, or IVb:



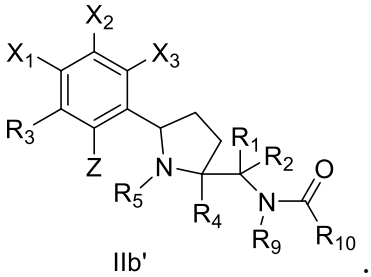
Ib ;



Ib' ;

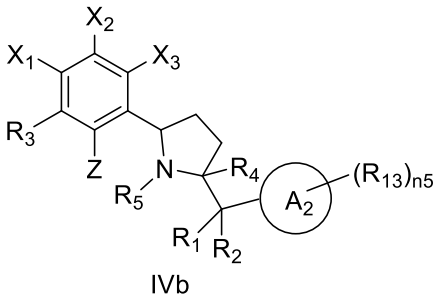


IIb ;



IIb' ;

;



IVb

.

[0024] In any one of the examples described herein, one or more occurrences of R_4 are H, alkyl, cycloalkyl, or OR_a.

[0025] In any one of the examples described herein, one or more occurrences of R_4 are H or alkyl.

[0026] In any one of the examples described herein, one or more occurrences of R_4 are H or CH_3.

[0027] In any one of the examples described herein, one or more occurrences of R_4 are saturated heterocycle, $(CR_aR_b)_{n2}OR_a$, or $(CR_aR_b)_{n2}NR_aR_b$.

[0028] In any one of the examples described herein, one or more occurrences of n_1 are 1.

[0029] In any one of the examples described herein, one or more occurrences of n_1 are 0.

[0030] In any one of the examples described herein, each occurrence of R_5 is independently H, alkyl, cycloalkyl, or saturated heterocycle.

[0031] In any one of the examples described herein, each occurrence of R_5 is independently cycloalkyl or saturated heterocycle.

[0032] In any one of the examples described herein, each occurrence of R_5 is independently H or alkyl.

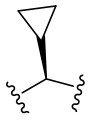
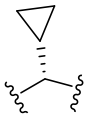
[0033] In any one of the examples described herein, each occurrence of R_5 is independently H or CH_3.

[0034] In any one of the examples described herein, each occurrence of R_1 and R_2 is independently cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$.

[0035] In any one of the examples described herein, each occurrence of R_1 and R_2 is independently H, alkyl optionally substituted with OR_8, halogen, cycloalkyl, or fluorinated alkyl.

[0036] In any one of the examples described herein, each occurrence of R_1 and R_2 is independently H, CH_3, CH_2CH_3, CH_2OH, CH_2CH_2OH, CH_2OCH_3, $CH_2CH_2OCH_3$, or .

[0037] In any one of the examples described herein, R_1 and R_2 are H and H, H and Me, Me and Me, H and Et, Me and Et, or Et and Et, H and CH_2OH, H and CH_2CH_2OH, H and CH_2OCH_3, H and $CH_2CH_2OCH_3$, or H and .

[0038] In any one of the examples described herein, each occurrence of the structural moiety $–(CR_1R_2)_m–$ is independently selected from the group consisting of $–CH_2–$, $–CH(CH_3)–$, $–C(CH_3)_2–$, $–CH(CH_2CH_3)–$, $–CH(CH_2OH)–$, $–CH(CH_2OCH_3)–$, $–CH_2–CH_2–$, $–CH(CH_3)–CH_2–$, $–CH_2–C(CH_3)_2–$, , and .

[0039] In any one of the examples described herein, each occurrence of R_6 and R_7 is - independently H, alkyl, cycloalkyl, or heterocycle; wherein the alkyl, cycloalkyl, heterocycle is optionally substituted by 1-2 substituents each independently selected from the group consisting of halogen, CN, OH, OMe, $-(CH_2)_{1-2}OMe$ and $-(CH_2)_{1-2}OH$.

[0040] In any one of the examples described herein, each occurrence of R_6 and R_7 is independently H or alkyl; wherein the alkyl is optionally substituted by 1-2 substituents each independently selected from the group consisting of halogen, CN, and OH.

[0041] In any one of the examples described herein, each occurrence of R_6 and R_7 is independently H, $-CH_3$, $-CH_2OH$, $-CH_2CH_2OH$ or $-CH_2CH_2CH_2OH$.

[0042] In any one of the examples described herein, R_6 and R_7 taken together with the nitrogen atom they are connected to form a heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S; wherein the heterocycle is optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)N(R_8)_2$, $(C=O)R_8$, $NR_8(C=O)R_8$, and oxo where valence permits.

[0043] In any one of the examples described herein, R_6 and R_7 taken together with the nitrogen atom they are connected to form a 4-, 5-, or 6-membered heterocycle; wherein the

heterocycle is optionally substituted by 1-2 substituents each independently selected from the group consisting of alkyl, halogenated alkyl, halogen, CN, OH, and -$(CH_2)_{1-2}$OH.

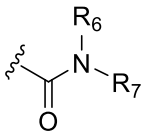
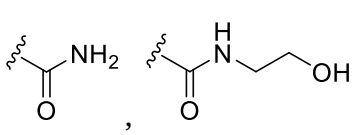
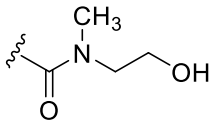
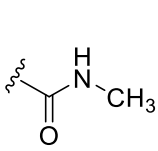
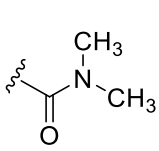
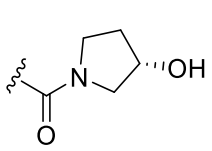
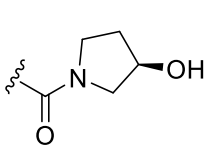
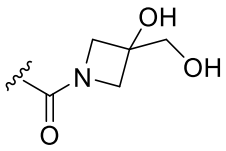
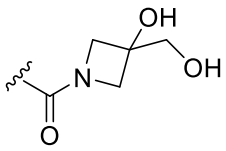
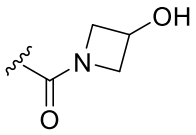
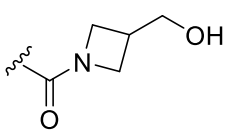
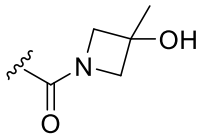
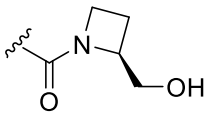
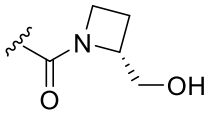
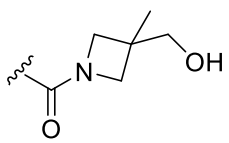
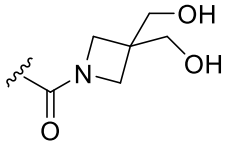
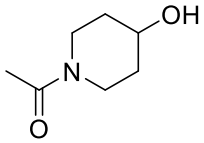
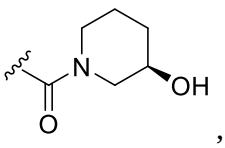
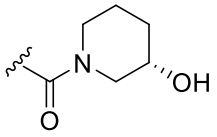
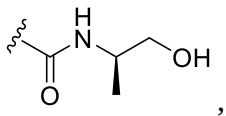
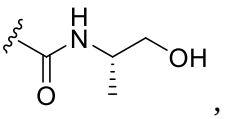
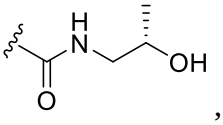
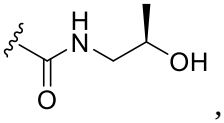
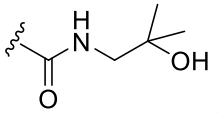
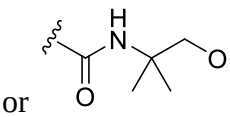
[0044] In any one of the examples described herein, the 4-, 5-, or 6-membered heterocycle is azetidine, pyrrolidine, piperidine, or piperazine.

[0045] In any one of the examples described herein, the 4-, 5-, or 6-membered heterocycle is substituted by 1-2 substituents each independently selected from the group consisting of OH and -$(CH_2)_{1-2}$OH.

[0046] In any one of the examples described herein, R_6 and R_7 taken together with the nitrogen atom they are connected to form azetidine.

[0047] In any one of the examples described herein, R_6 and R_7 taken together with the nitrogen atom they are connected to form pyrrolidine.

[0048] In any one of the examples described herein, each occurrence of R_6 and R_7 is independently alkylaryl, or alkylheteroaryl.

[0049] In any one of the examples described herein, each occurrence of the structural moiety  independently has the structure of , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , or .

[0050] In any one of the examples described herein, each occurrence of R_9 is independently cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl.

[0051] In any one of the examples described herein, each occurrence of R_9 is independently $(C=O)R_a$, $(C=O)(CR_aR_b)_{n2}OR_a$, $(C=O)(CR_aR_b)_{n2}NR_aR_b$, $(C=O)NR_aR_b$, or SO_2R_a.

[0052] In any one of the examples described herein, each occurrence of R_9 is independently H or alkyl.

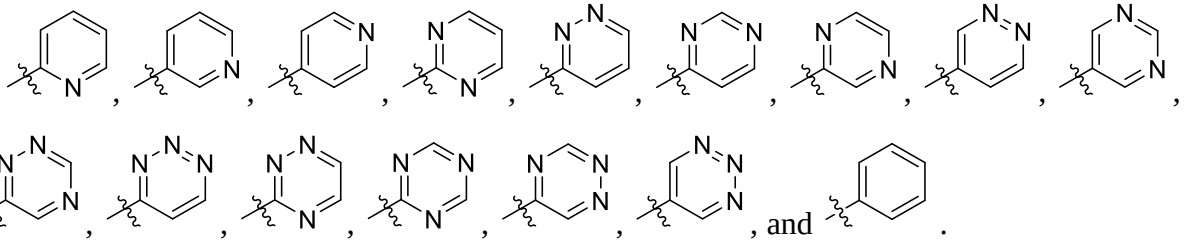
[0053] In any one of the examples described herein, each occurrence of R_9 is independently H or CH_3.

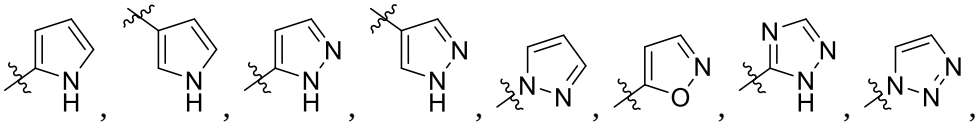
[0054] In any one of the examples described herein, each occurrence of R_{10} is independently H, alkyl, cycloalkyl, or heterocycle; wherein the alkyl, cycloalkyl, heterocycle is optionally substituted by 1-2 substituents each independently selected from the group consisting of halogen, CN, OH, OMe, $-(CH_2)_{1-2}OMe$ and $-(CH_2)_{1-2}OH$.

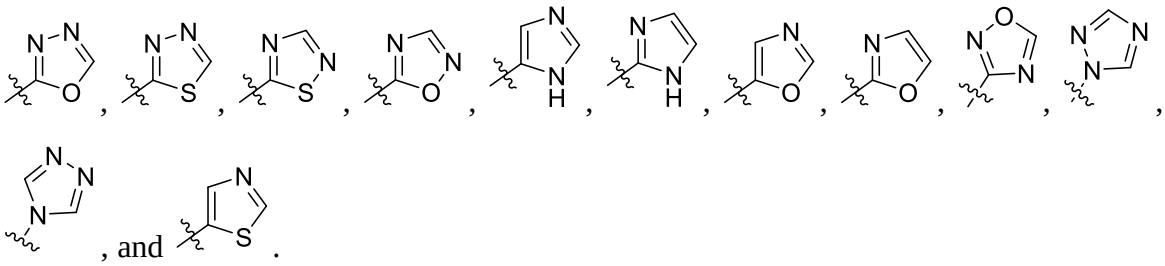
[0055] In any one of the examples described herein, one or more occurrences of R_{10} are alkyl; wherein the alkyl is optionally substituted by 1-2 substituents each independently selected from the group consisting of halogen, CN, and OH.

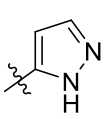
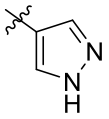
[0056] In any one of the examples described herein, each occurrence of R_{10} is independently H, $-CH_3$, $-CH_2OH$, or $-CH_2CH_2OH$.

[0057] In any one of the examples described herein, A_1 is a 5- or 6-membered aryl or heteroaryl.

[0058] In any one of the examples described herein, A_1 is selected from the group consisting of .

[0059] In any one of the examples described herein, A_1 is selected from the group consisting of .

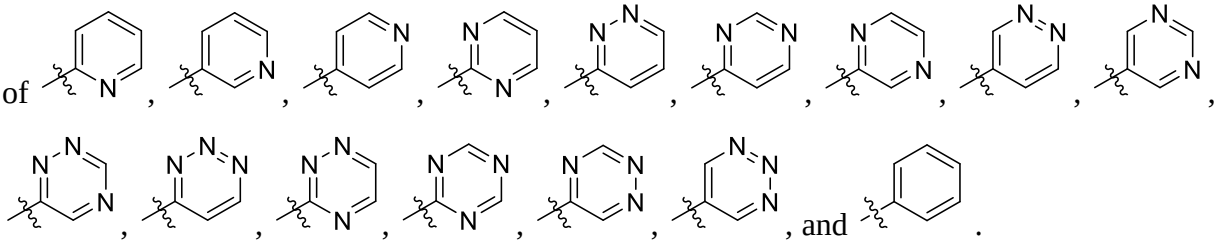


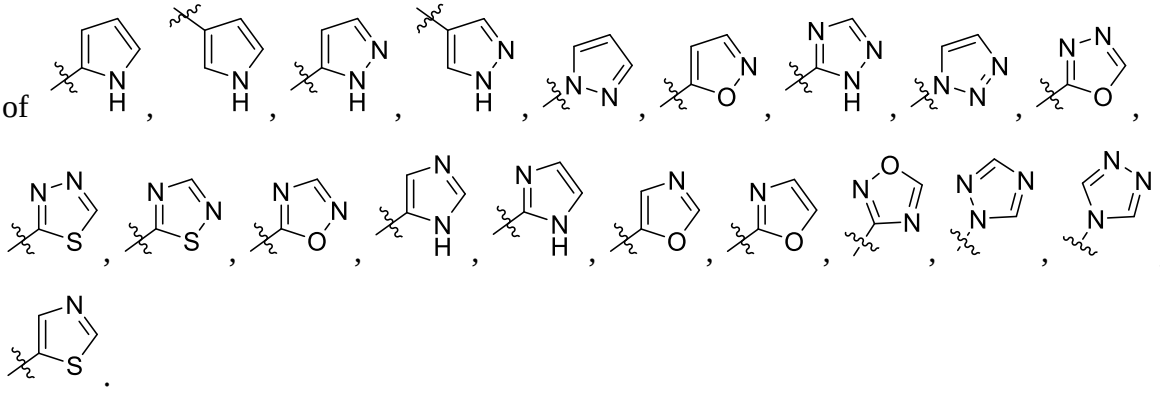
[0060] In any one of the examples described herein, A_1 is  or .

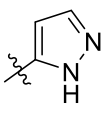
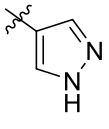
[0061] In any one of the examples described herein, each occurrence of R_{12} is independently H, halogen, fluorinated alkyl, or alkyl.

[0062] In any one of the examples described herein, one or more occurrences of R_{12} are H.

[0063] In any one of the examples described herein, A_2 is a 5- or 6-membered aryl or heteroaryl.

[0064] In any one of the examples described herein, A_2 is selected from the group consisting of .

[0065] In any one of the examples described herein, A_2 is selected from the group consisting of .

[0066] In any one of the examples described herein, A_2 is  or .

[0067] In any one of the examples described herein, each occurrence of R_{13} is independently H, halogen, fluorinated alkyl, or alkyl.

[0068] In any one of the examples described herein, one or more occurrences of R_{13} are H.

[0069] In any one of the examples described herein, each occurrence of Z is independently OH or O(C_1-C_4 alkyl).

[0070] In any one of the examples described herein, each occurrence of Z is independently OMe, OEt, or OH.

[0071] In any one of the examples described herein, one or more occurrences of Z are OH.

[0072] In any one of the examples described herein, each occurrence of X_1 is independently H, halogen, fluorinated alkyl, or alkyl.

[0073] In any one of the examples described herein, each occurrence of X_1 is independently H, F, Cl, Br, Me, CF_2H, CF_2Cl, or CF_3.

[0074] In any one of the examples described herein, one or more occurrences of X_1 are H.

[0075] In any one of the examples described herein, each occurrence of X_2 is independently H, halogen, fluorinated alkyl, or alkyl.

[0076] In any one of the examples described herein, each occurrence of X_2 is independently H, F, Cl, Br, Me, CF_2H, CF_2Cl, or CF_3.

[0077] In any one of the examples described herein, one or more occurrences of X_2 are Cl.

[0078] In any one of the examples described herein, each occurrence of X_3 is independently H, halogen, fluorinated alkyl, or alkyl.

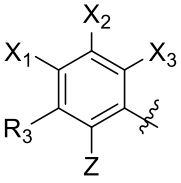
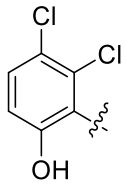
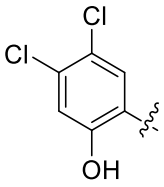
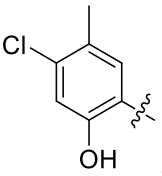
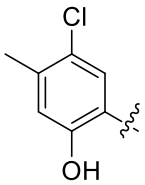
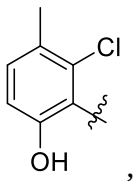
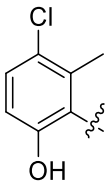
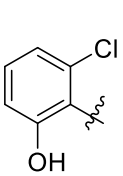
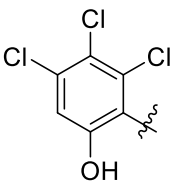
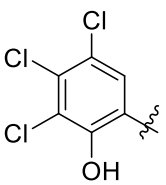
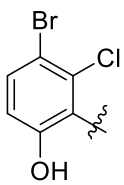
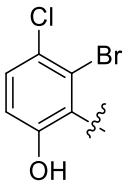
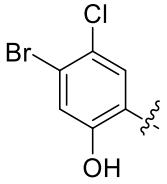
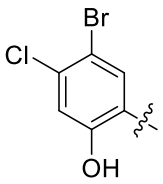
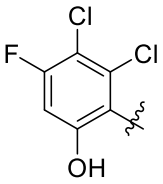
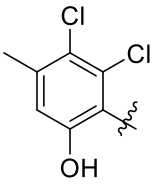
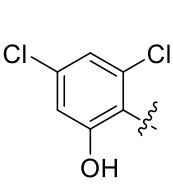
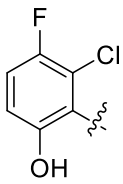
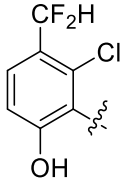
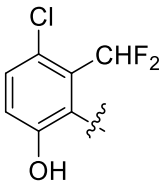
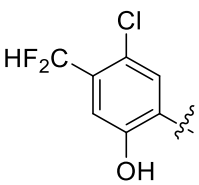
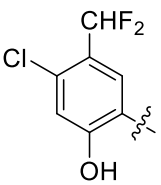
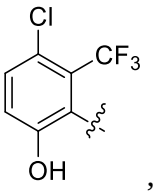
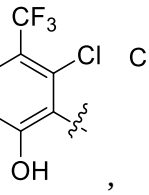
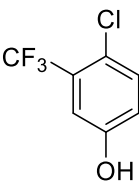
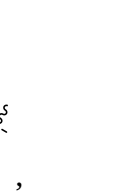
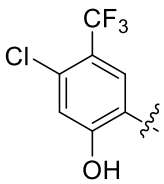
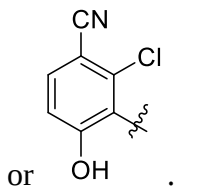
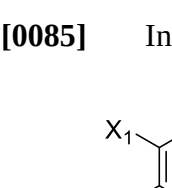
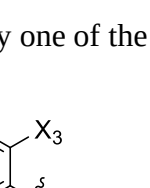
[0079] In any one of the examples described herein, each occurrence of X_3 is independently H, F, Cl, Br, Me, CF_2H, CF_2Cl, or CF_3.

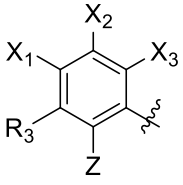
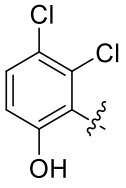
[0080] In any one of the examples described herein, one or more occurrences of X_3 are Cl.

[0081] In any one of the examples described herein, each occurrence of R_3 is independently H, alkyl, CF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$.

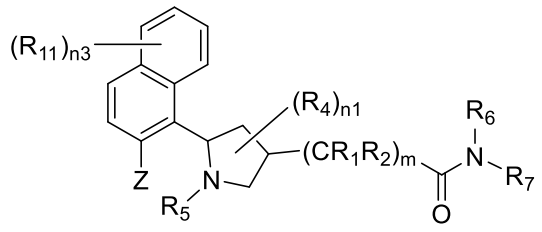
[0082] In any one of the examples described herein, each occurrence of R_3 is independently H, halogen, fluorinated alkyl, or alkyl.

[0083] In any one of the examples described herein, one or more occurrences of R_3 are H.

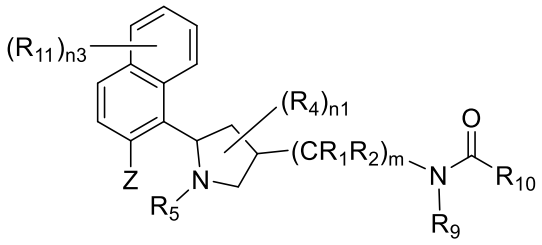
[0084] In any one of the examples described herein, each occurrence of the structural moiety  independently has the structure of , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , , or .

[0085] In any one of the examples described herein, at least one occurrence of the structural moiety  has the structure of .

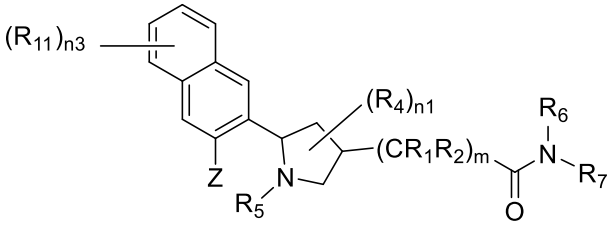
[0086] In any one of the examples described herein, the compound has a structure of Formula Ic, Ic', Id, Id', IIc, IIc', IId, IId', IIIc, IIId, IVc, or IVd:



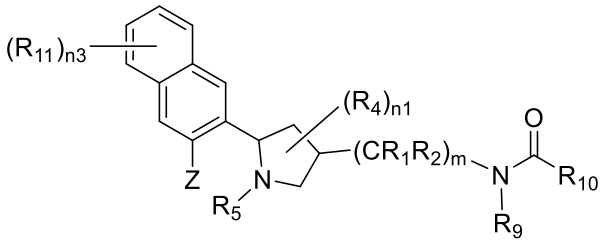
Ic ;



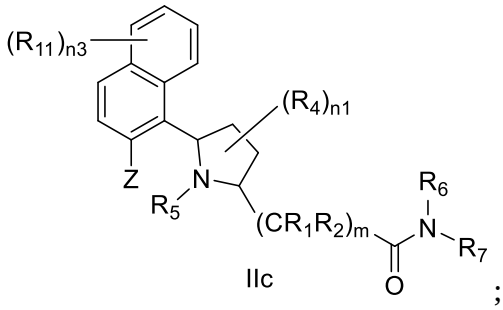
Ic' ;



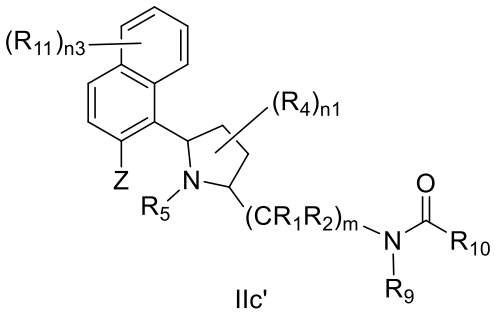
Id ;



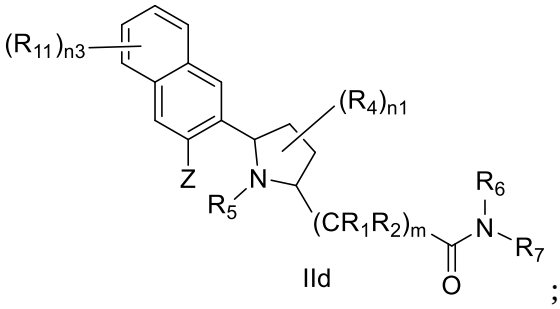
Id' ;



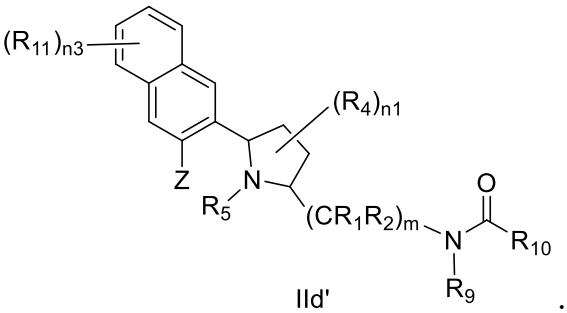
IIc ;



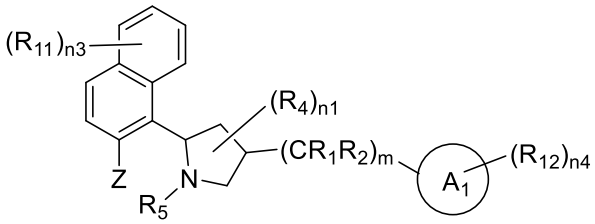
IIc' ;



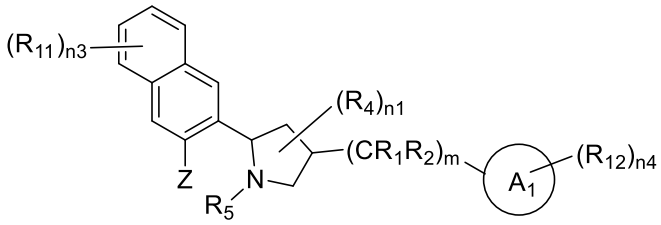
IId ;



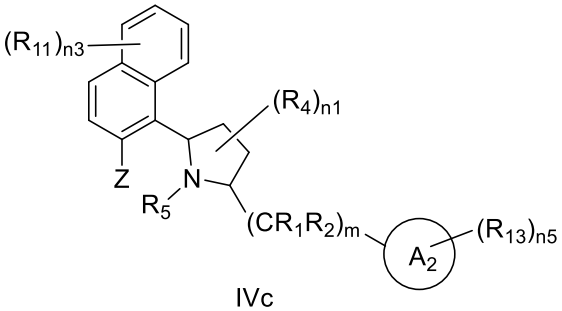
IId' ;



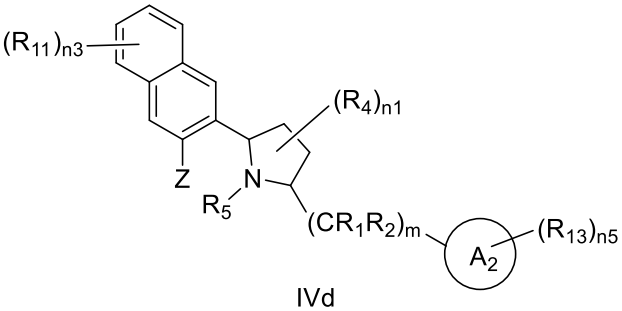
IIIc ;



IIId ;



IVc ;



IVd

wherein each occurrence of R_{11} is independently H, halogen, or alkyl; and each occurrence of n_3 is independently an integer from 0-3.

[0087] In any one of the examples described herein, each occurrence of n_3 is independently 0, 1, or 2.

[0088] In any one of the examples described herein, each occurrence of R_{11} is independently H or alkyl.

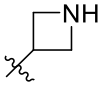
[0089] In any one of the examples described herein, at least one occurrence of R_{11} is halogen.

[0090] In any one of the examples described herein, at least one occurrence of Z is OR_a.

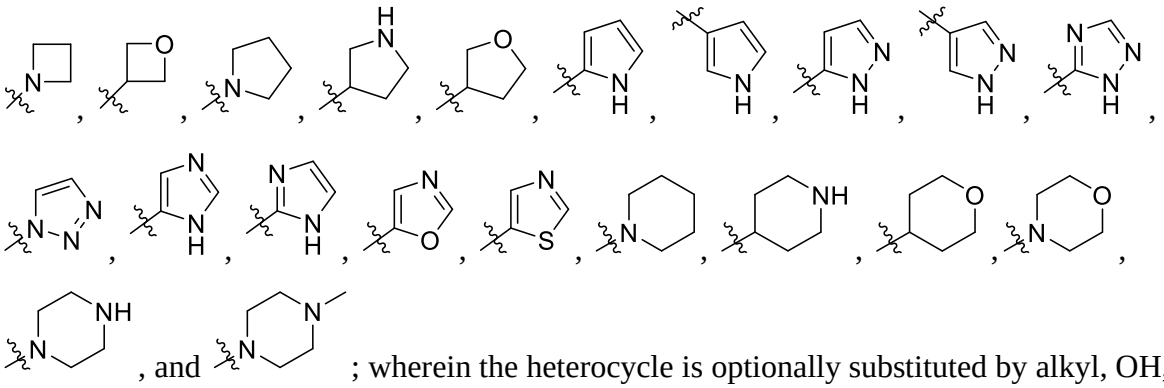
[0091] In any one of the examples described herein, at least one occurrence of Z is OH, OMe, or OEt.

[0092] In any one of the examples described herein, at least one occurrence of Z is OH.

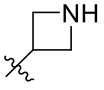
[0093] In any one of the examples described herein, at least one occurrence of R_a or R_b is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, or heteroaryl.

[0094] In any one of the examples described herein, at least one occurrence of R_a or R_b is independently H, Me, Et, Pr, or a heterocycle selected from the group consisting of 

,



; wherein the heterocycle is optionally substituted by alkyl, OH, oxo, or (C=O)C_{1-4}alkyl where valence permits.

[0095] In any one of the examples described herein, at least one occurrence of R_a or R_b is H, Me or .

[0096] In any one of the examples described herein, R_a and R_b together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S.

[0097] In any one of the examples described herein, each occurrence of R_8 is independently H, alkyl, or heterocycle optionally substituted by alkyl, halogen, or OH.

[0098] In any one of the examples described herein, each occurrence of R_8 is independently H or alkyl.

[0099] In any one of the examples described herein, each occurrence of R_8 is independently H or Me.

[0100] In any one of the examples described herein, the compound is selected from the group consisting of compounds 31-79 as shown in Table 7.

[0101] In any one of the examples described herein, the compound is selected from the group consisting of compounds 1-15 as shown in Table 1, compounds 16-20 as shown in Table 2, compounds 1a-15a as shown in Table 3, compounds 16a-30a as shown in Table 4, compounds 1b-15b as shown in Table 5, and compounds 16b-30b as shown in Table 6.

[0102] In another example, a pharmaceutical composition is described, including at least one compound according to any one of the examples described herein or a pharmaceutically-acceptable salt thereof and a pharmaceutically-acceptable carrier or diluent.

[0103] In yet another example, a method of treating a condition in a mammalian species in need thereof is described, including administering to the mammalian species a therapeutically effective amount of at least one compound according to any one of the examples described herein, or a pharmaceutically-acceptable salt thereof, or a pharmaceutical composition thereof, where the condition is selected from the group consisting of cancer, an immunological disorder, a central nervous system disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, and a kidney disease.

[0104] In any one of the examples described herein, the immunological disorder is transplant rejection or an autoimmune disease.

[0105] In any one of the examples described herein, the autoimmune disease is rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, or type I diabetes mellitus.

[0106] In any one of the examples described herein, the Central Nerve System (CNS) disorder is Alzheimer's disease.

[0107] In any one of the examples described herein, the inflammatory disorder is an inflammatory skin condition, arthritis, psoriasis, spondylitis, parodontitits, or an inflammatory neuropathy.

[0108] In any one of the examples described herein, the gastroenterological disorder is an inflammatory bowel disease.

[0109] In any one of the examples described herein, the metabolic disorder is obesity or type II diabetes mellitus.

[0110] In any one of the examples described herein, the cardiovascular disorder is an ischemic stroke.

[0111] In any one of the examples described herein, the kidney disease is chronic kidney disease, nephritis, or chronic renal failure.

[0112] In any one of the examples described herein, the condition is selected from the group consisting of cancer, transplant rejection, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, type I diabetes mellitus, Alzheimer's disease, inflammatory skin condition, inflammatory neuropathy, psoriasis, spondylitis, parodontitis, Crohn's disease, ulcerative colitis, obesity, type II diabetes mellitus, ischemic stroke, chronic kidney disease, nephritis, chronic renal failure, and a combination thereof.

[0113] In any one of the examples described herein, the mammalian species is human.

[0114] In yet another example, a method of blocking Kv1.3 potassium channel in a mammalian species in need thereof is described, including administering to the mammalian species a therapeutically effective amount of at least one compound according to any one of the examples described herein, or a pharmaceutically-acceptable salt thereof, or a pharmaceutical composition thereof.

[0115] In any one of the examples described herein, the mammalian species is human.

[0116] Any one of the examples disclosed herein may be properly combined with any other example disclosed herein. The combination of any one of the examples disclosed herein with any other examples disclosed herein is expressly contemplated. Specifically, the selection of one or more examples for one substituent group can be properly combined with the selection of one or more particular examples for any other substituent group. Such combination can be made in any one or more examples of the application described herein or any formula described herein.

DETAILED DESCRIPTION OF THE INVENTION

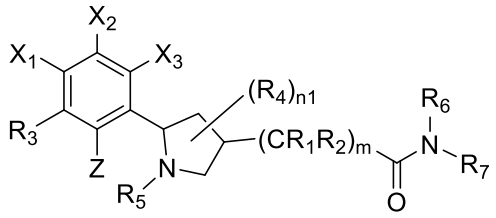
Definitions

[0117] The following are definitions of terms used in the present specification. The initial definition provided for a group or term herein applies to that group or term throughout the present specification individually or as part of another group, unless otherwise indicated. Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art.

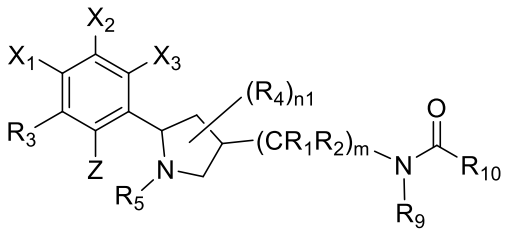
[0118] The terms "alkyl" and "alk" refer to a straight or branched chain alkane (hydrocarbon) radical containing from 1 to 12 carbon atoms, preferably 1 to 6 carbon atoms. Exemplary "alkyl" groups include methyl, ethyl, propyl, isopropyl, *n*-butyl, *t*-butyl, isobutyl pentyl, hexyl, isohexyl, heptyl, 4,4-dimethylpentyl, octyl, 2,2,4-trimethylpentyl, nonyl, decyl, undecyl, dodecyl, and the like. The term "(C_1-C_4)alkyl" refers to a straight or branched chain alkane (hydrocarbon) radical containing from 1 to 4 carbon atoms, such as methyl, ethyl, propyl, isopropyl, *n*-butyl, *t*-butyl, and isobutyl. "Substituted alkyl" refers to an alkyl group substituted with one or more substituents, preferably 1 to 4 substituents, at any available point of attachment. Exemplary substituents include, but are not limited to, one or more of the following groups: hydrogen, halogen (*e.g.*, a single halogen substituent or multiple halo substituents forming, in the latter case, groups such as CF_3 or an alkyl group bearing CCl_3), cyano, nitro, oxo

CLAIMS

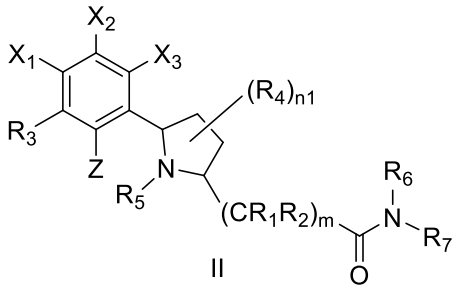
1. A compound of Formula I, I', II, II', III, or IV, or a pharmaceutically-acceptable salt thereof,



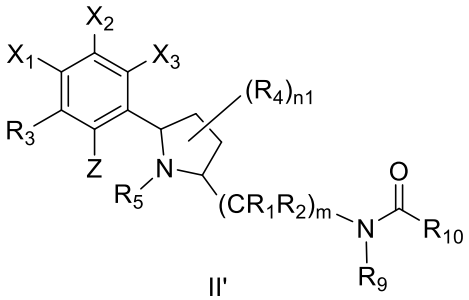
I ;



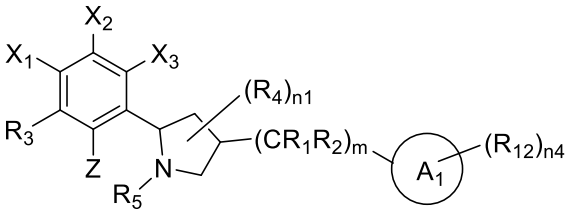
I' ;



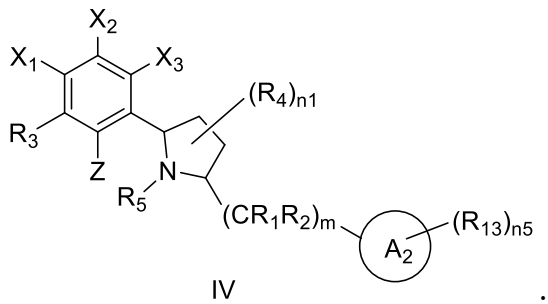
II ;



II' ;



III ;



IV ;

wherein

each occurrence of Z is independently OR_a;

each occurrence of X_1 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

each occurrence of X_2 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

each occurrence of X_3 is independently H, halogen, CN, alkyl, cycloalkyl, halogenated cycloalkyl, or halogenated alkyl;

or alternatively X_1 and X_2 and the carbon atoms they are connected to taken together form an optionally substituted 5- or 6-membered aryl;

or alternatively X_2 and X_3 and the carbon atoms they are connected to taken together form an optionally substituted 5- or 6-membered aryl;

each occurrence of R_1 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

each occurrence of R_2 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

or alternatively R_1 and R_2 taken together with the carbon atom they are connected to form a cycloalkyl or saturated heterocycle;

each occurrence of R_3 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, or $NR_b(C=O)R_a$;

each occurrence of R_4 is independently H, alkyl, cycloalkyl, saturated heterocycle, $(CR_aR_b)_{n2}OR_a$, or $(CR_aR_b)_{n2}NR_aR_b$;

or alternatively two R_4 groups taken together with the carbon atom(s) that they are connected to form a 3-7 membered optionally substituted cycloalkyl or heterocycle;

each occurrence of R_5 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, $(C=O)R_a$, $(C=O)(CR_aR_b)_{n2}OR_a$, $(C=O)(CR_aR_b)_{n2}NR_aR_b$, or SO_2R_a;

each occurrence of R_6 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

each occurrence of R_7 is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

or alternatively R_6 and R_7 taken together with the nitrogen atom they are connected to form a heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S; wherein the heterocycle is optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)R_8$, $(C=O)N(R_8)_2$, $NR_8(C=O)R_8$, and oxo where valence permits;

each occurrence of R_9 is independently H, alkyl, cycloalkyl, saturated heterocycle, aryl, heteroaryl, alkylaryl, alkylheteroaryl, $(C=O)R_a$, $(C=O)(CR_aR_b)_{n2}OR_a$, $(C=O)(CR_aR_b)_{n2}NR_aR_b$, or SO_2R_a;

each occurrence of R_{10} is independently H, alkyl, cycloalkyl, heterocycle, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

A_1 is aryl or heteroaryl;

A_2 is aryl or heteroaryl;

each occurrence of R_{12} is independently H, alkyl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, $(CR_aR_b)_{n2}OR_a$, $(C=O)NR_aR_b$, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}NR_b(C=O)R_a$;

each occurrence of R_{13} is independently H, alkyl, CN, CF_3, OCF_3, OR_a, SR_a, halogen, NR_aR_b, $(CR_aR_b)_{n2}OR_a$, $(C=O)NR_aR_b$, $(CR_aR_b)_{n2}NR_aR_b$, or $(CR_aR_b)_{n2}NR_b(C=O)R_a$;

each occurrence of R_a and R_b are independently H, alkyl, alkenyl, cycloalkyl, saturated heterocycle comprising 1-3 heteroatoms each selected from the group consisting of N, O, and S, aryl, or heteroaryl; or alternatively R_a and R_b together with the carbon or nitrogen atom that they

are connected to form a cycloalkyl or heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

the alkyl, cycloalkyl, heterocycle, aryl, and heteroaryl in X_1, X_2, X_3, A_1, A_2, R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_9, R_{10}, R_{12}, R_{13}, R_a, or R_b, where applicable, are optionally substituted by 1-4 substituents each independently selected from the group consisting of alkyl, cycloalkyl, halogenated cycloalkyl, halogenated alkyl, halogen, CN, OR_8, $-(CH_2)_{0-2}OR_8$, $N(R_8)_2$, $(C=O)R_8$, $(C=O)N(R_8)_2$, $NR_8(C=O)R_8$, and oxo where valence permits;

each occurrence of R_8 is independently H, alkyl, or optionally substituted heterocycle; or alternatively the two R_8 groups together with the nitrogen atom that they are connected to form an optionally substituted heterocycle comprising the nitrogen atom and 0-3 additional heteroatoms each selected from the group consisting of N, O, and S;

each occurrence of m is independently 1, 2, or 3;

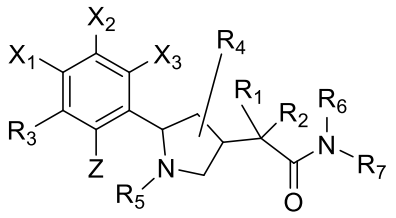
each occurrence of n_1 is independently an integer from 0-3 wherein valence permits;

each occurrence of n_2 is independently an integer from 0-3; and

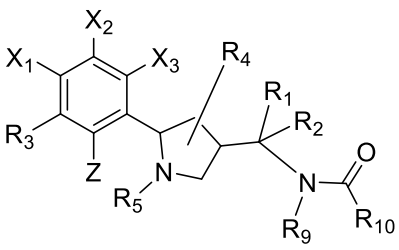
n_4 is an integer from 0-3;

n_5 is an integer from 0-3.

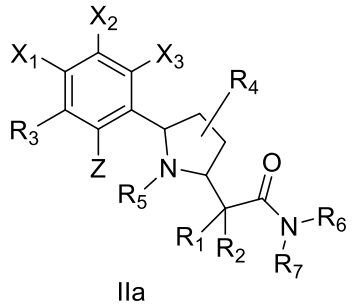
2. The compound of claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compound or pharmaceutically-acceptable salt thereof has the structure of Formula Ia, Ia', IIa, IIa', IIIa, or IVa:



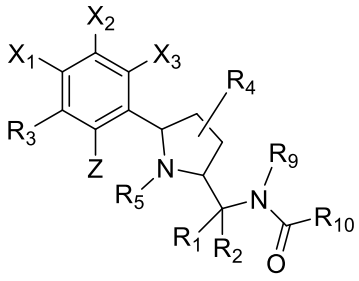
Ia ;



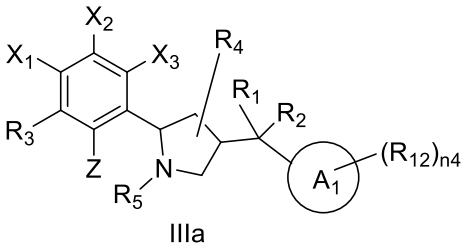
Ia' ;



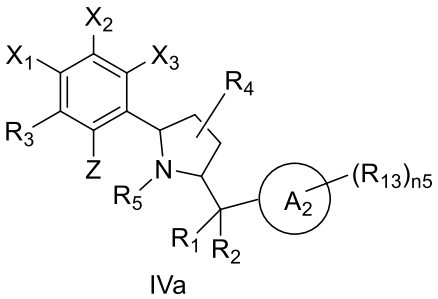
IIa ;



IIa' ;



IIIa ;



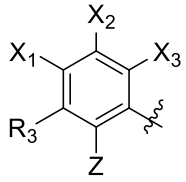
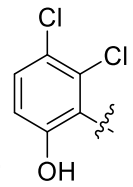
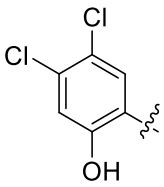
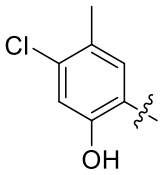
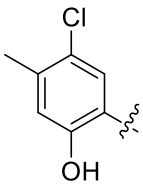
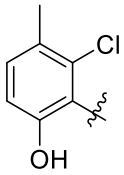
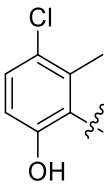
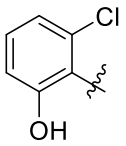
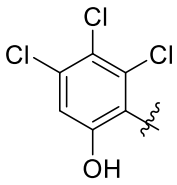
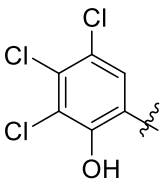
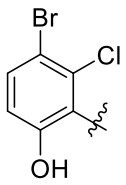
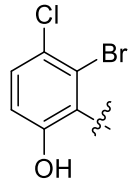
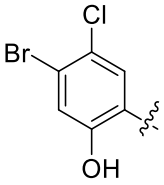
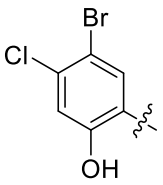
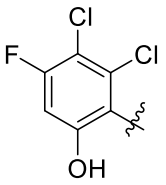
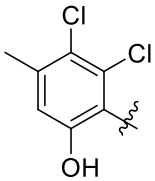
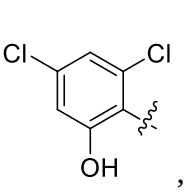
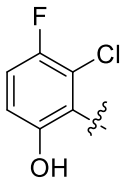
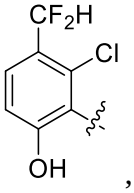
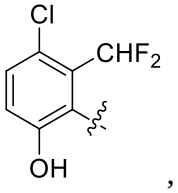
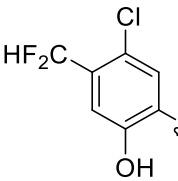
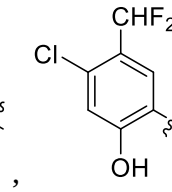
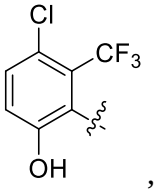
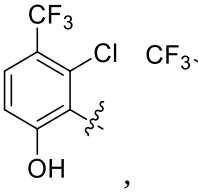
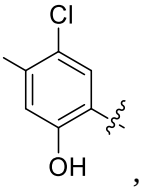
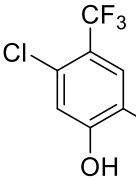
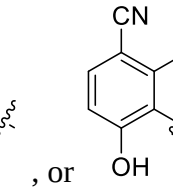
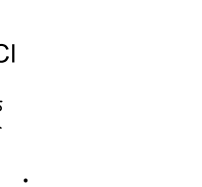
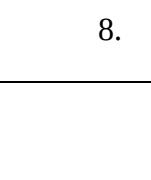
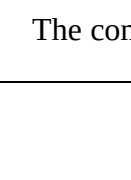
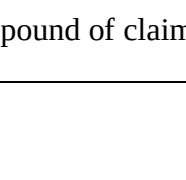
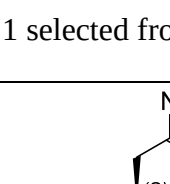
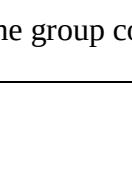
IVa .

3. The compound of claim 1 or 2, or a pharmaceutically-acceptable salt thereof, wherein one or more occurrences of R_4 are H or CH_3.

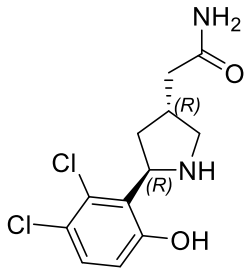
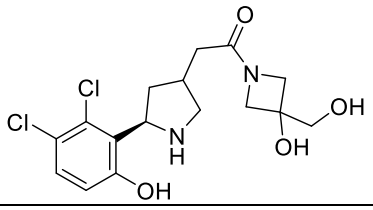
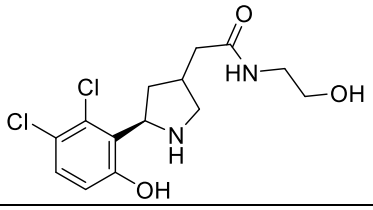
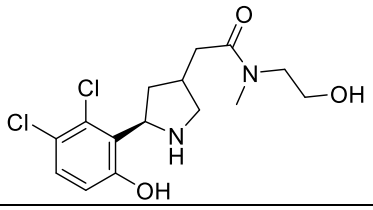
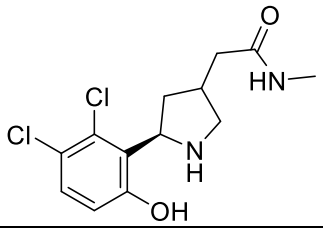
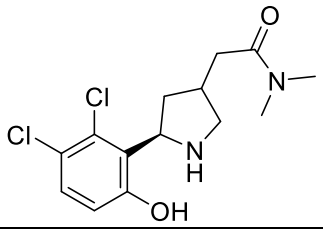
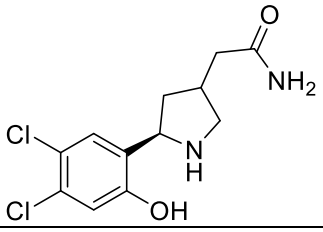
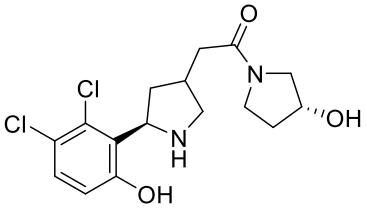
4. The compound of any one of claims 1-3, or a pharmaceutically-acceptable salt thereof, wherein each occurrence of R_5 is independently H or CH_3.

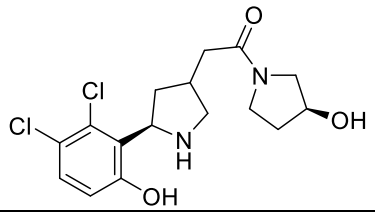
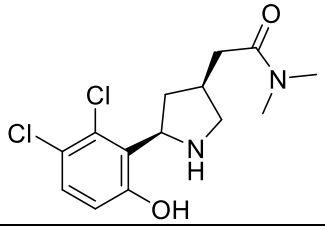
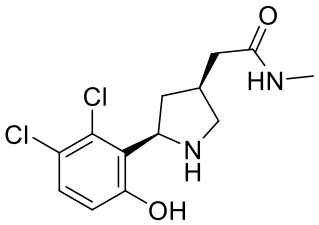
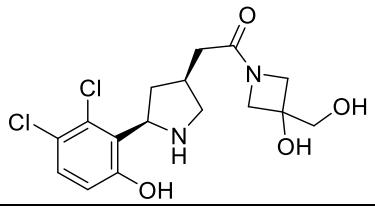
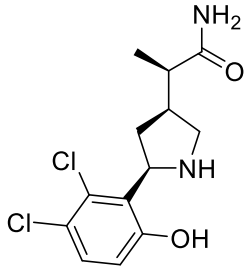
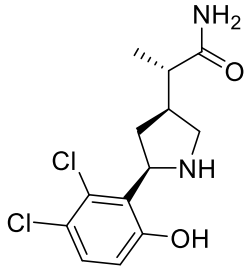
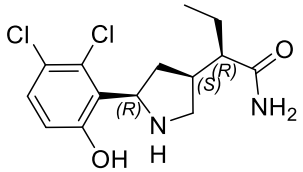
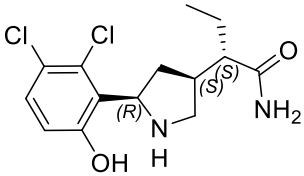
5. The compound of any one of claims 1-4, or a pharmaceutically-acceptable salt thereof, wherein R_1 and R_2 are H and H, H and Me, Me and Me, H and Et, Me and Et, Et and Et, H and CH_2OH, H and CH_2CH_2OH, H and CH_2OCH_3, H and $CH_2CH_2OCH_3$, or H and .

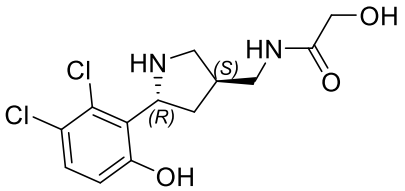
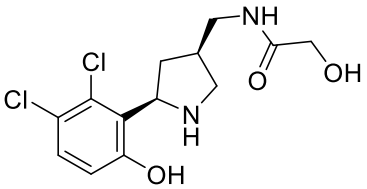
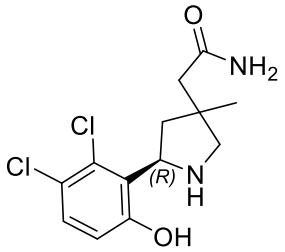
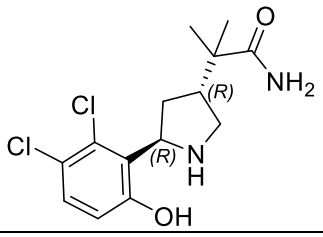
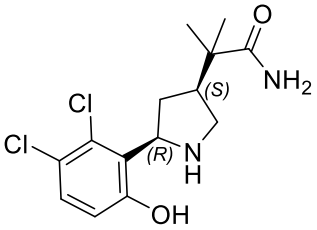
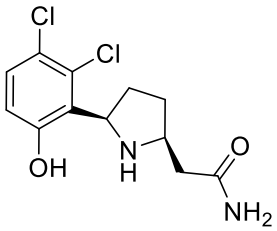
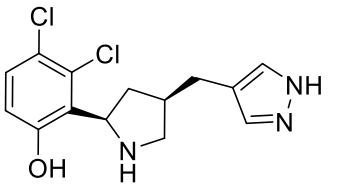
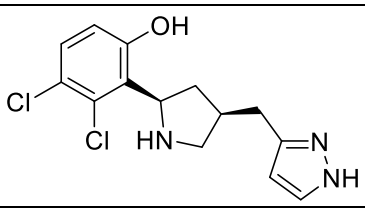
6. The compound of any one of claims 1-5, or a pharmaceutically-acceptable salt thereof, wherein each occurrence of R_6 and R_7 is independently H, -CH_3, -CH_2OH, -CH_2CH_2OH or -$CH_2CH_2CH_2OH$.

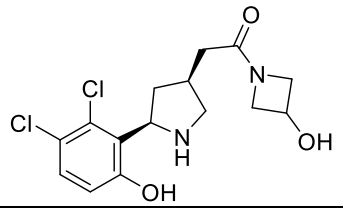
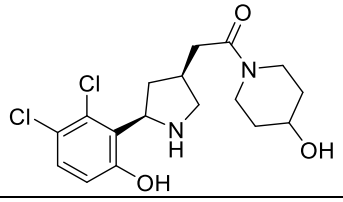
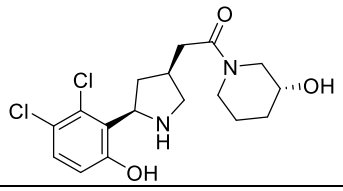
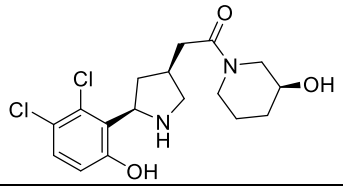
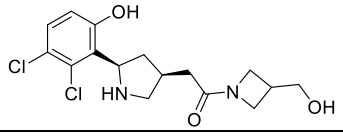
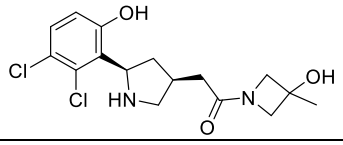
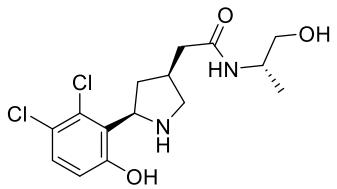
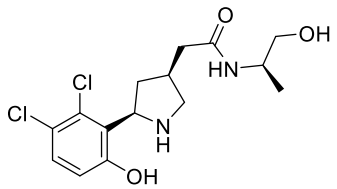
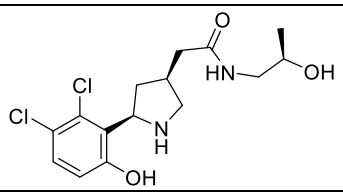
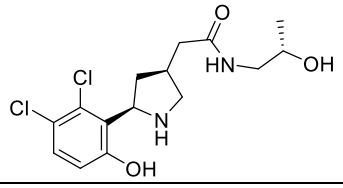
7. The compound of any one of claims 1-6, or a pharmaceutically-acceptable salt thereof, wherein each occurrence of the structural moiety  independently has the structure of  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , ,  ,  ,  ,  , or  .

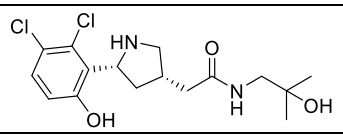
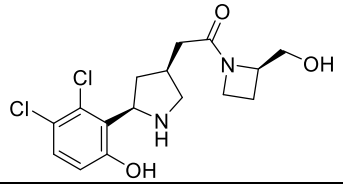
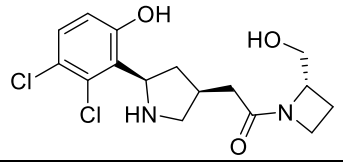
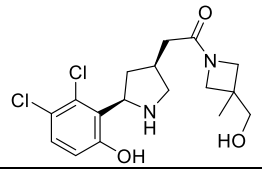
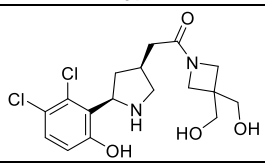
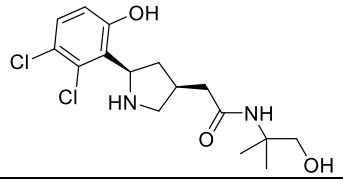
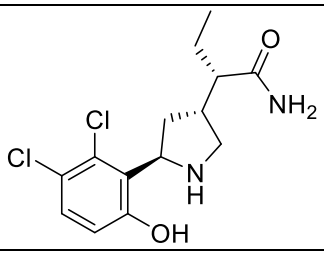
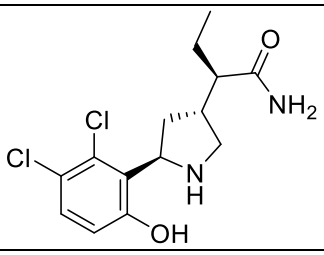
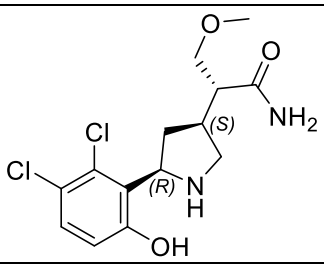
8. The compound of claim 1 selected from the group consisting of:

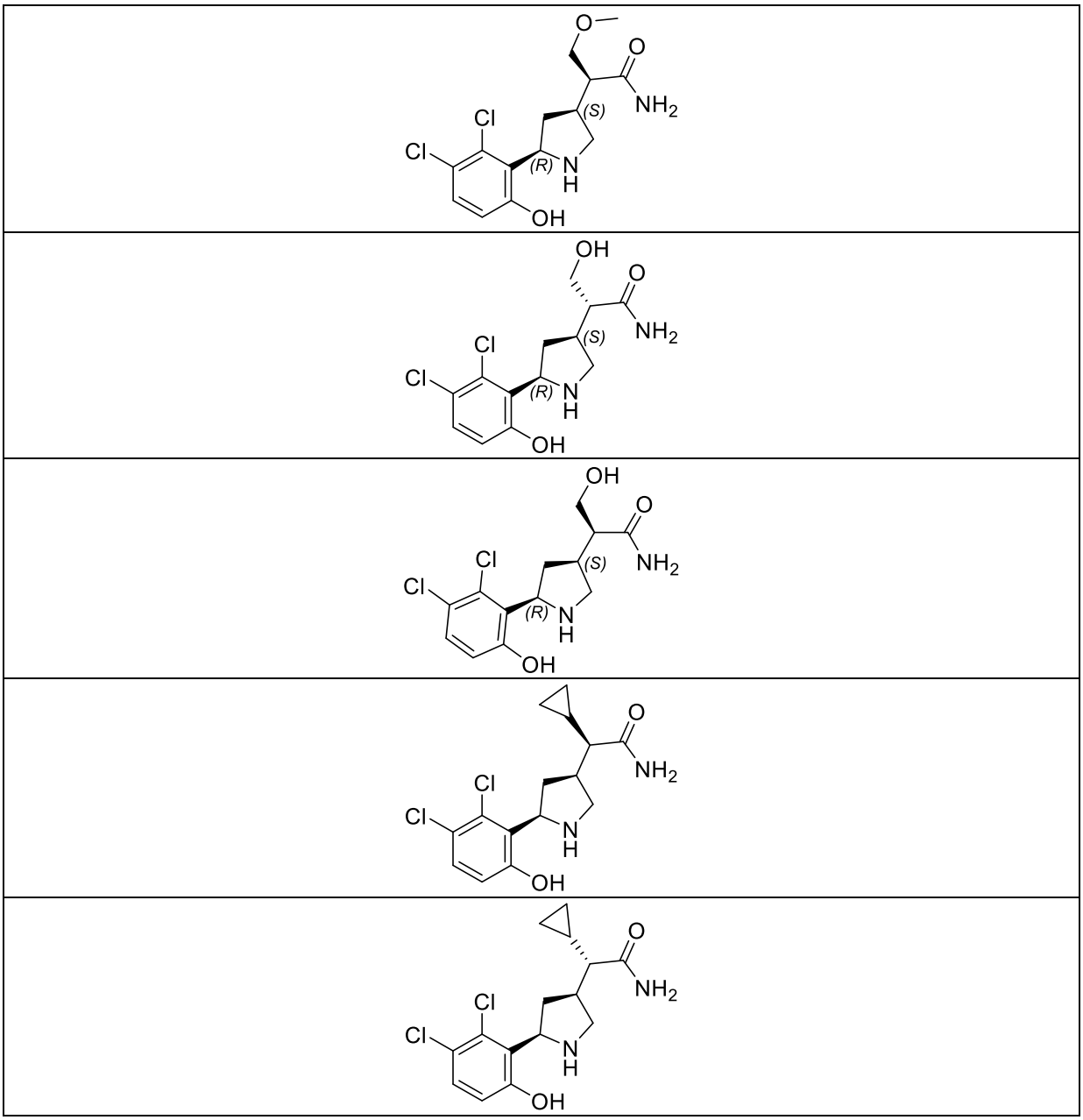









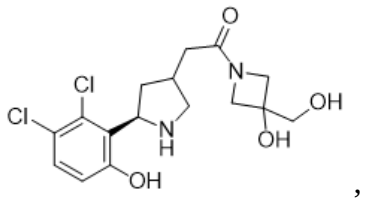













, or a pharmaceutically acceptable salt thereof.

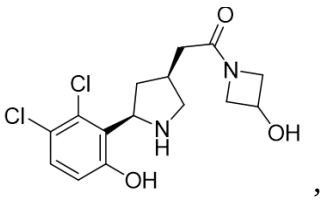
9. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

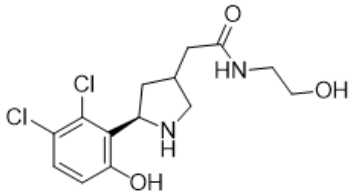
10. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

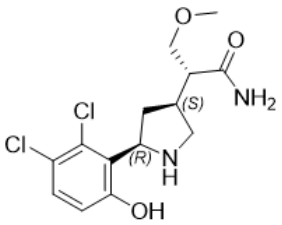
11. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

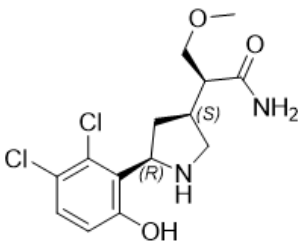
12. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

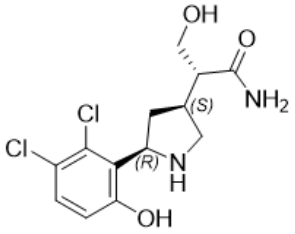
13. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

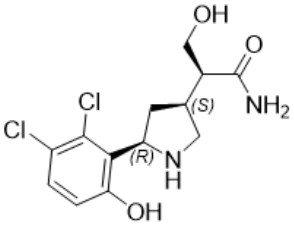
14. The compound of claim 1, wherein the compound is



,

or a pharmaceutically-acceptable salt thereof.

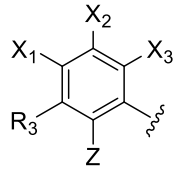
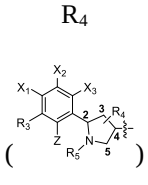
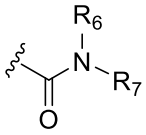
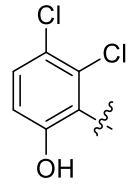
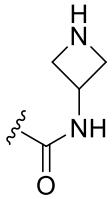
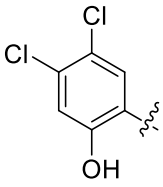
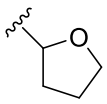
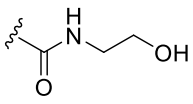
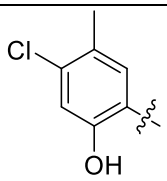
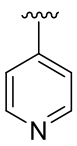
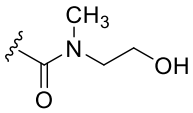
15. The compound of claim 1, wherein the compound is

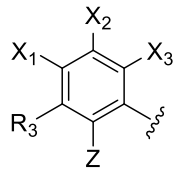
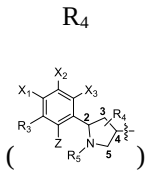
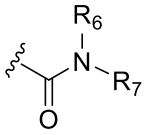
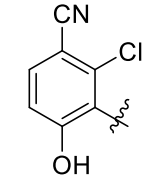
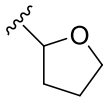
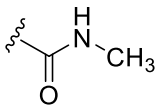
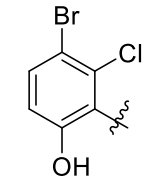
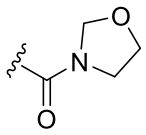
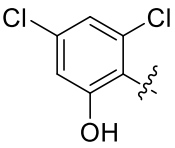
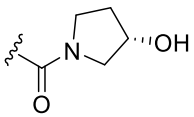
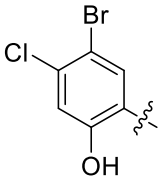
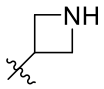
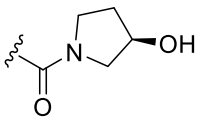
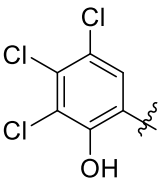
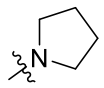
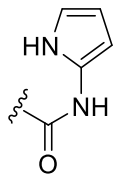
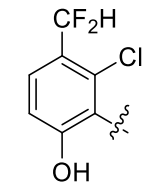
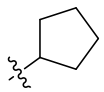
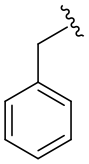
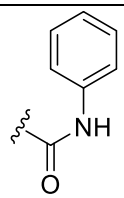
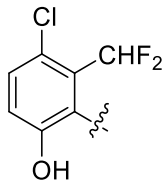
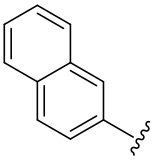
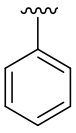
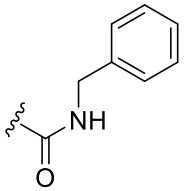


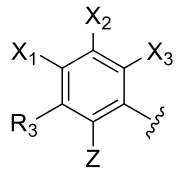
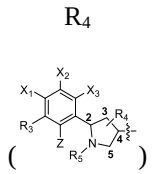
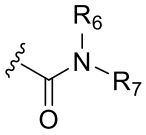
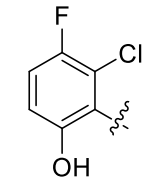
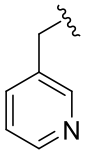
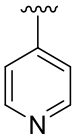
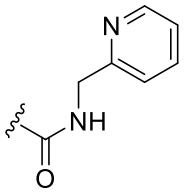
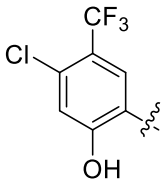
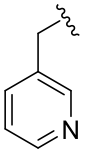
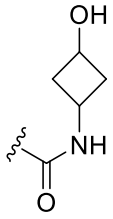
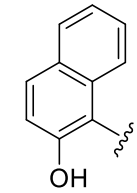
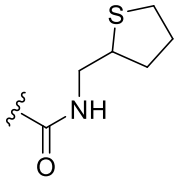
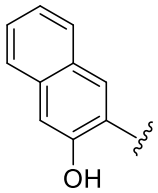
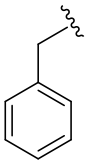
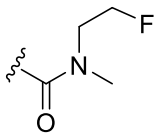
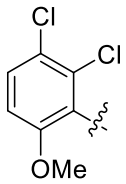
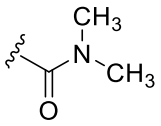
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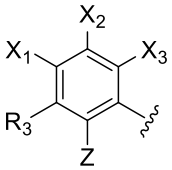
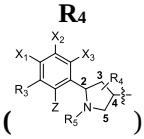
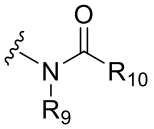
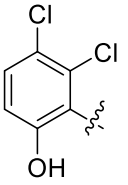
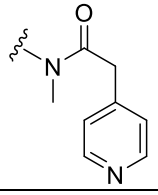
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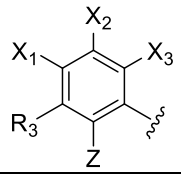
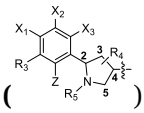
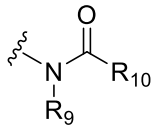
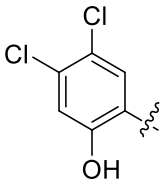
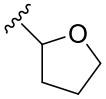
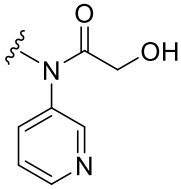
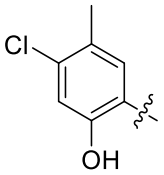
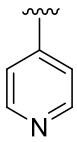
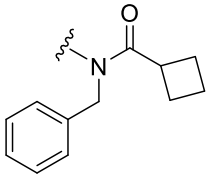
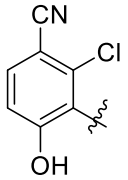
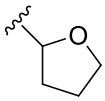
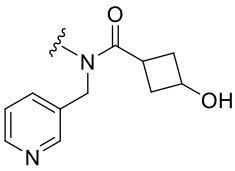
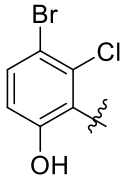
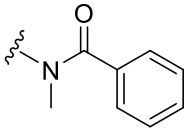
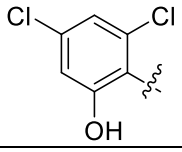
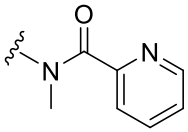
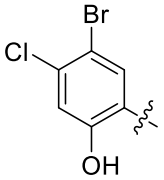
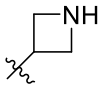
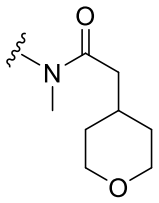
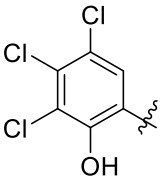
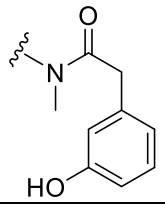
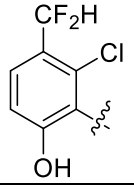
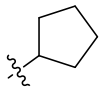
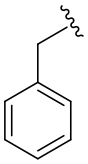
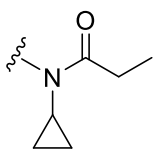
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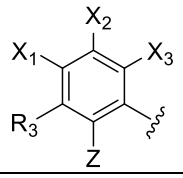
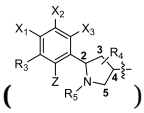
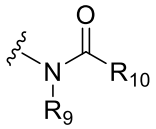
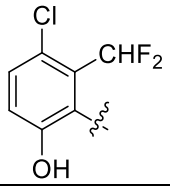
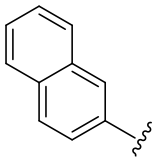
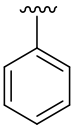
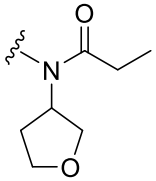
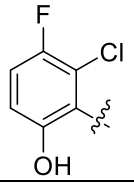
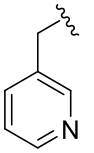
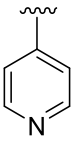
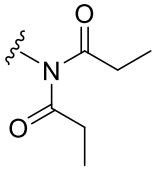
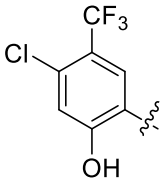
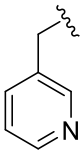
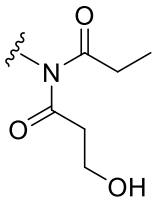
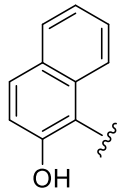
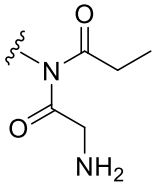
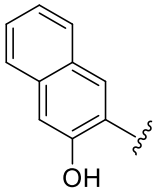
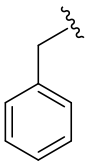
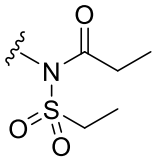
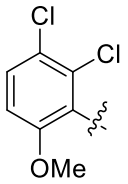
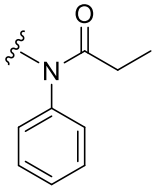
		**R_5**	**R_1**	**R_2**	**m**	
	Me (4-position)	Me	OCH_2CH_3	Et	1	
	 (4-position)		Et	Me	2	
	 (4-position)		OCF_3	Me	3	

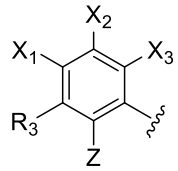
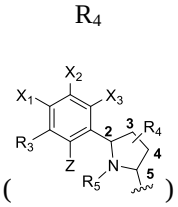
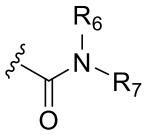
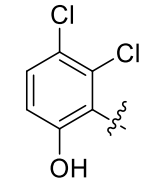
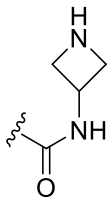
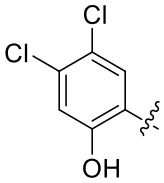
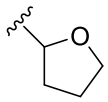
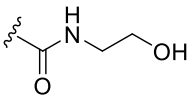
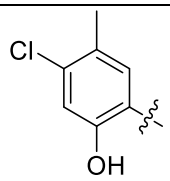
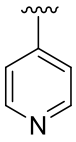
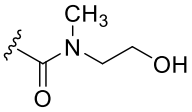
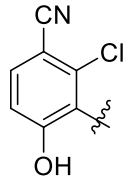
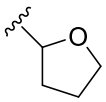
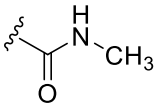
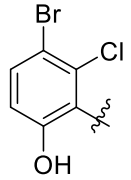
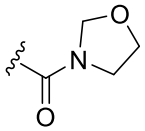
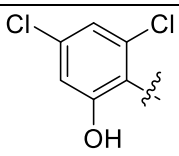
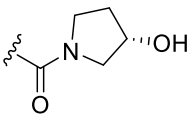
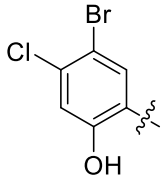
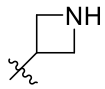
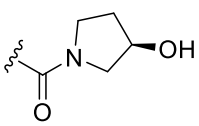
		**R_5**	**R_1**	**R_2**	**m**	
	OH (4-position)		CN	H	1	
	CH_2CH_2OH (4-position)		SCH_2CH_3	CF_3	2	
	$CH_2CH_2OCH_3$ (4-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (4-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	
	 (4-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (4-postion)			H	3	
	CH_2OCH_3 (4-position)			H	1	

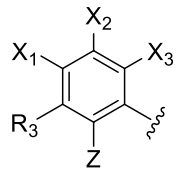
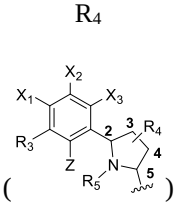
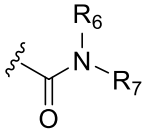
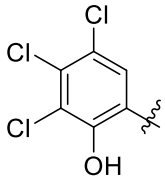
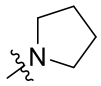
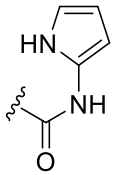
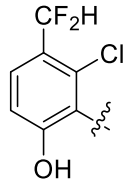
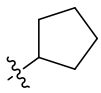
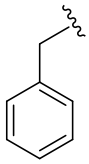
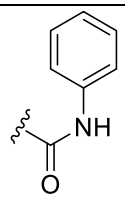
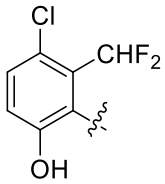
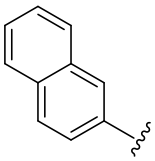
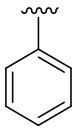
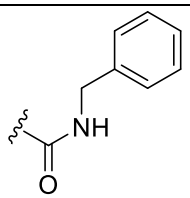
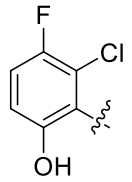
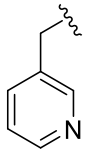
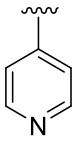
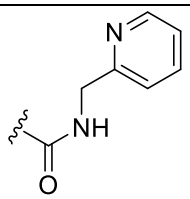
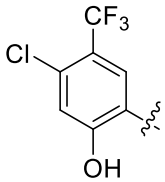
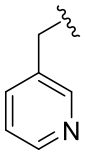
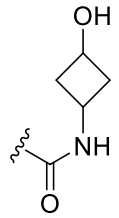
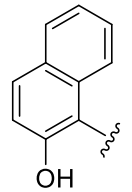
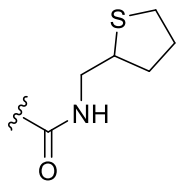
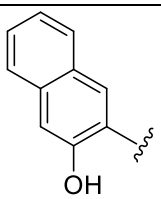
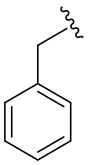
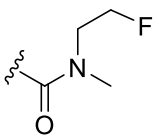
		**R5**	**R1**	**R2**	**m**	
	CH_2NHCH_3 (4-position)			H	2	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	
	Me (5-position)	(C=O)Et		H	2	
	Et (5-position)	Et	CH_2OH	H	3	

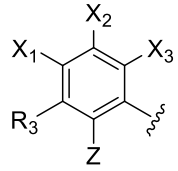
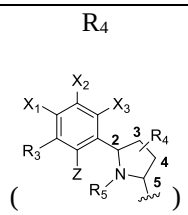
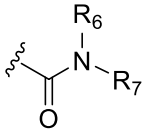
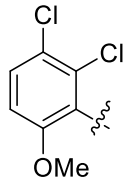
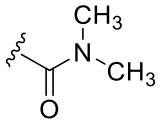
		**R5**	**R1**	**R2**	**m**	
	Me (4-position)	Me	OCH_2CH_3	Et	1	

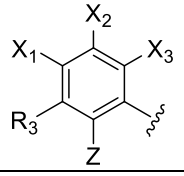
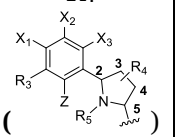
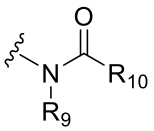
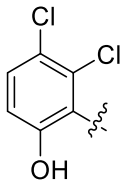
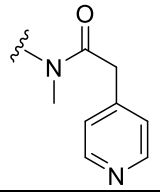
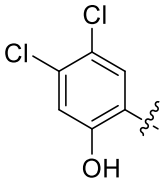
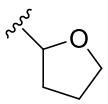
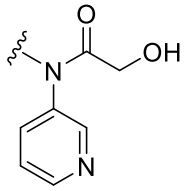
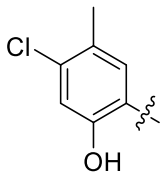
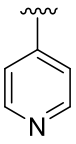
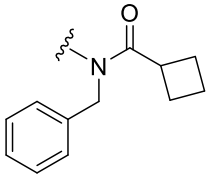
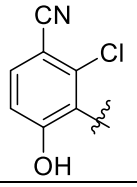
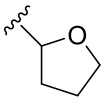
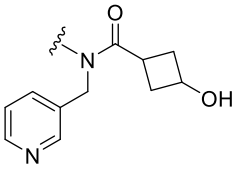
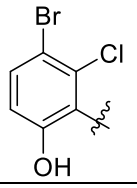
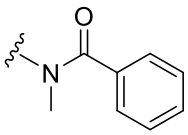
	**R_4**  ( )	**R_5**	**R_1**	**R_2**	**m**	
	 (4-position)		Et	Me	2	
	 (4-position)		OCF_3	Me	3	
	OH (4-position)		CN	H	1	
	CH_2CH_2OH (4-position)		SCH_2CH_3	CF_3	2	
	$CH_2CH_2OCH_3$ (4-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (4-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	
	 (4-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (4-postion)			H	3	

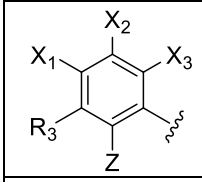
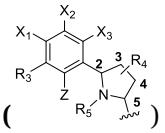
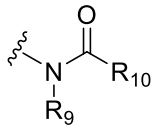
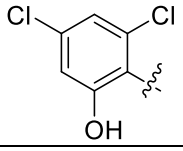
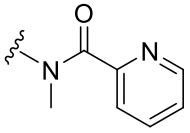
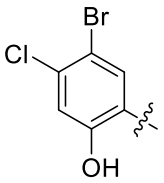
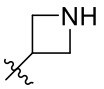
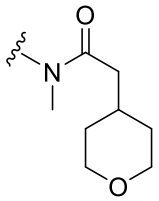
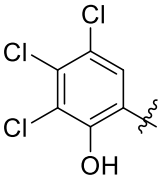
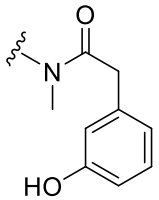
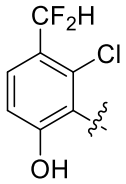
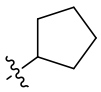
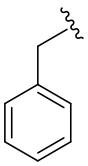
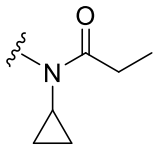
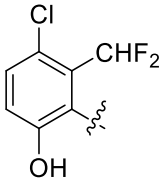
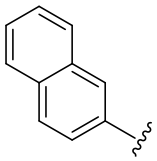
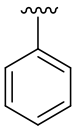
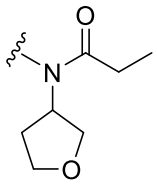
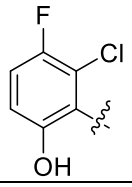
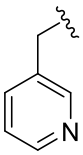
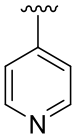
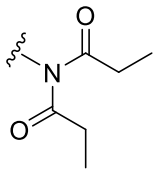
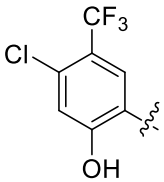
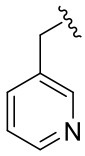
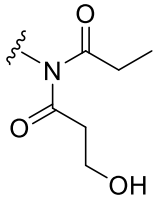
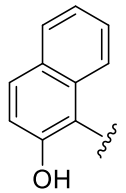
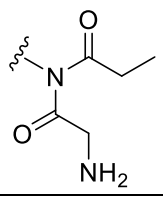
	**R4** 	**R5**	**R1**	**R2**	**m**	
	CH_2OCH_3 (4-position)			H	1	
	CH_2NHCH_3 (4-position)			H	2	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	
	Me (5-position)	(C=O)Et		H	2	
	Et (5-position)	Et	CH_2OH	H	3	

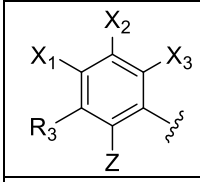
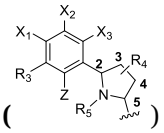
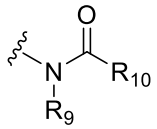
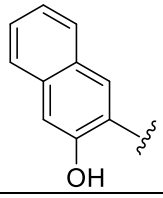
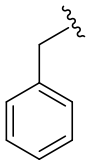
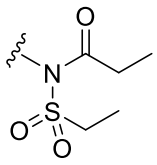
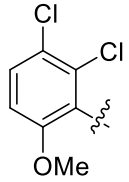
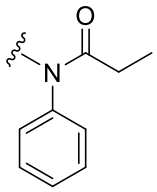
		**R_5**	**R_1**	**R_2**	**m**	
	Me (5-position)	Me	OCH_2CH_3	Et	1	
	 (5-position)		Et	Me	2	
	 (5-position)		OCF_3	Me	3	
	OH (5-position)		CN	H	1	
	CH_2CH_2OH (5-position)		SCH_2CH_3	CF_3	2	
	$CH_2CH_2OCH_3$ (5-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (5-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	

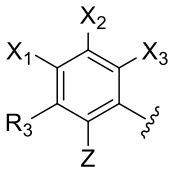
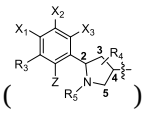
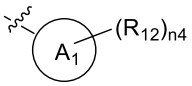
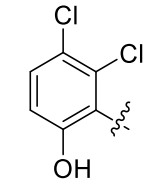
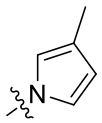
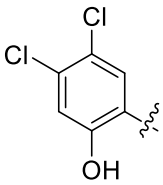
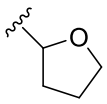
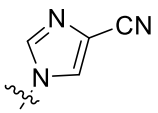
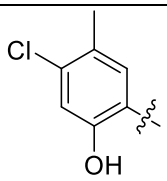
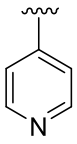
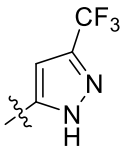
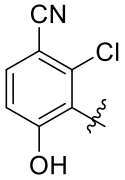
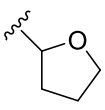
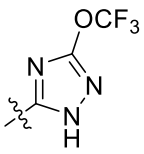
		**R_5**	**R_1**	**R_2**	**m**	
	 (5-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (5-postion)			H	3	
	CH_2OCH_3 (5-position)			H	1	
	CH_2NHCH_3 (5-position)			H	2	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	
	Me (4-position)	(C=O)Et		H	2	

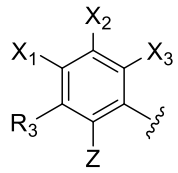
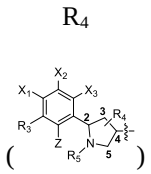
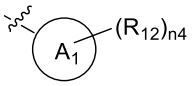
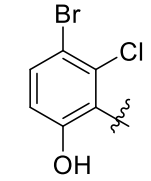
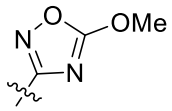
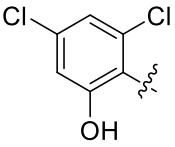
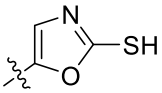
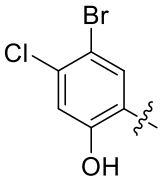
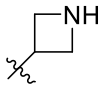
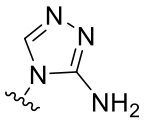
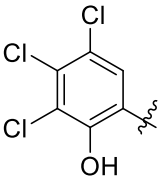
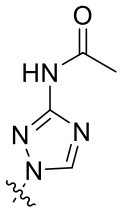
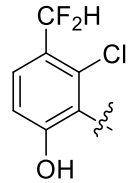
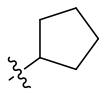
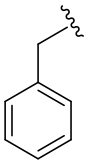
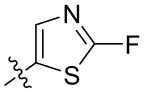
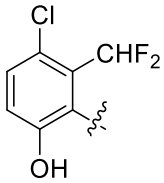
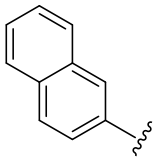
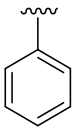
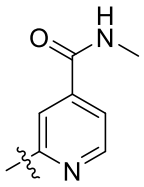
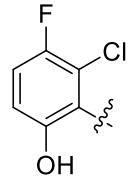
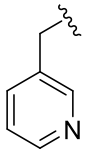
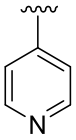
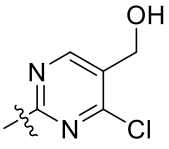
		**R_5**	**R_1**	**R_2**	**m**	
	Et (4-position)	Et	CH_2OH	H	3	

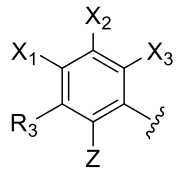
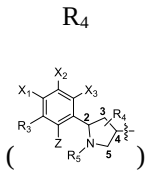
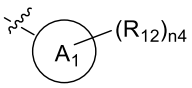
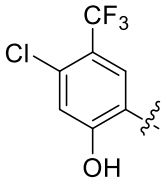
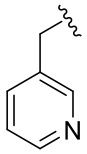
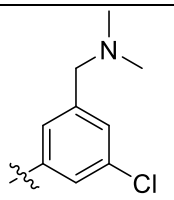
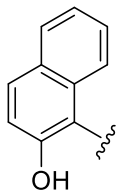
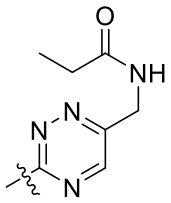
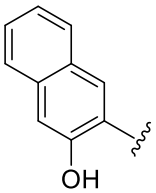
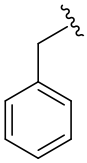
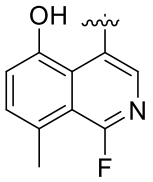
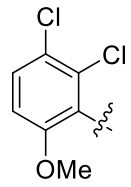
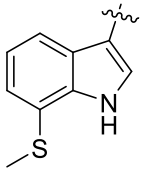
	**R_4** 	**R_5**	**R_1**	**R_2**	**m**	
	Me (5-position)	Me	OCH_2CH_3	Et	1	
	 (5-position)		Et	Me	2	
	 (5-position)		OCF_3	Me	3	
	OH (5-position)		CN	H	1	
	CH_2CH_2OH (5-position)		SCH_2CH_3	CF_3	2	

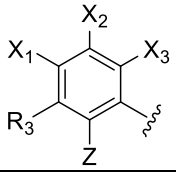
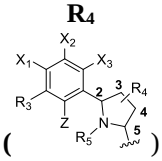
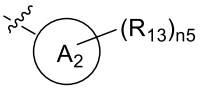
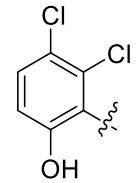
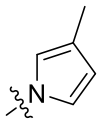
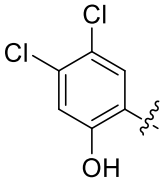
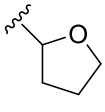
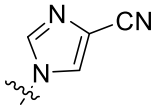
	**R4** 	**R5**	**R1**	**R2**	**m**	
	$CH_2CH_2OCH_3$ (5-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (5-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	
	 (5-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (5-postion)			H	3	
	CH_2OCH_3 (5-position)			H	1	
	CH_2NHCH_3 (5-position)			H	2	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	

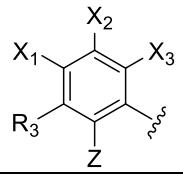
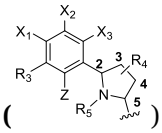
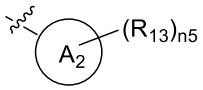
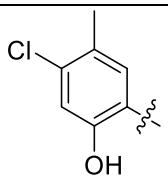
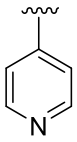
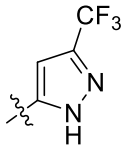
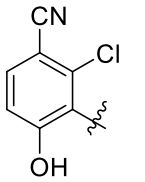
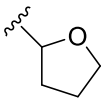
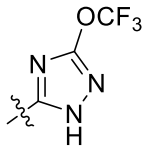
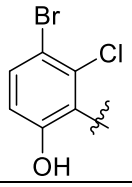
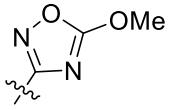
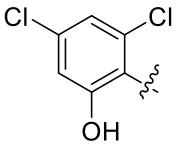
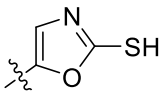
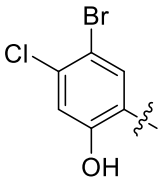
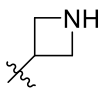
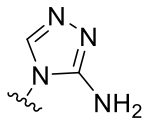
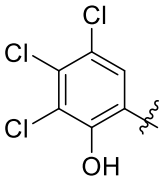
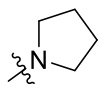
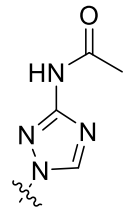
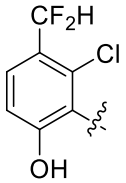
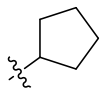
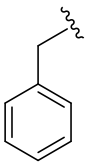
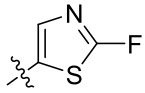
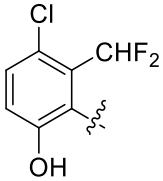
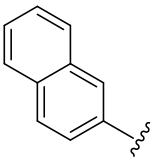
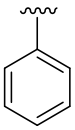
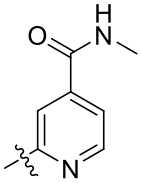
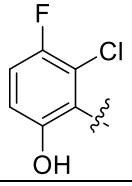
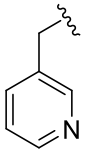
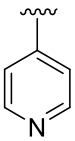
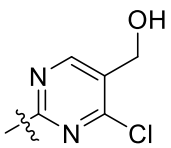
	**R4** 	**R5**	**R1**	**R2**	**m**	
	Me (4-position)	(C=O)Et		H	2	
	Et (4-position)	Et	CH_2OH	H	3	

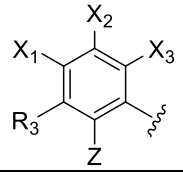
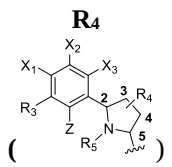
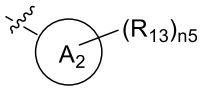
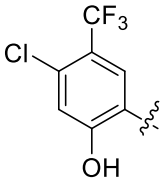
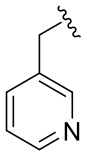
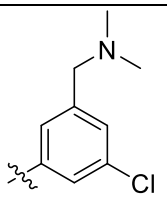
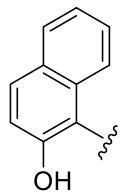
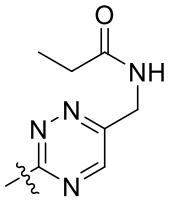
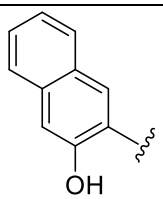
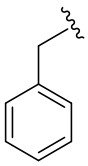
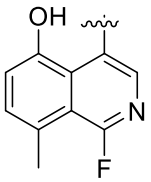
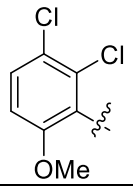
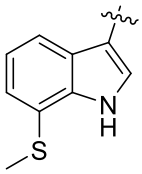
	R4 	**R5**	**R1**	**R2**	**m**	
	Me (4-position)	Me	OCH_2CH_3	Et	1	
	 (4-position)		Et	Me	2	
	 (4-position)		OCF_3	Me	3	
	OH (4-position)		CN	H	1	

		**R_5**	**R_1**	**R_2**	**m**	
	CH_2CH_2OH (4-position)		SCH_2CH_3	CF_3	2	
	$CH_2CH_2OCH_3$ (4-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (4-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	
	 (4-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (4-postion)			H	3	
	CH_2OCH_3 (4-position)			H	1	
	CH_2NHCH_3 (4-position)			H	2	

		**R_5**	**R_1**	**R_2**	**m**	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	
	Me (5-position)	(C=O)Et		H	2	
	Et (5-position)	Et	CH_2OH	H	3	

		**R_5**	**R_1**	**R_2**	**m**	
	Me (5-position)	Me	OCH_2CH_3	Et	1	
	 (5-position)		Et	Me	2	

	**R4** 	**R5**	**R1**	**R2**	**m**	
	 (5-position)		OCF_3	Me	3	
	OH (5-position)		CN	H	1	
	CH_2CH_2OH (5-position)		SCH_2CH_3	CF_3	2	
	$CH_2CH_2OCH_3$ (5-position)	$(C=O)CH_2OCH_3$	Cl	H	3	
	 (5-position)	$(C=O)CH_2NHCH_3$	NH_2	Me	1	
	 (5-position)	SO_2CH_3	$NH(C=O)CH_3$	H	2	
	 (5-postion)			H	3	
	CH_2OCH_3 (5-position)			H	1	
	CH_2NHCH_3 (5-position)			H	2	

		**R_5**	**R_1**	**R_2**	**m**	
	Et (2-position)	CF_3		H	3	
	*i*-Pr (3-position)	CH_2CH_2OH	F	F	1	
	Me (4-position)	(C=O)Et		H	2	
	Et (4-position)	Et	CH_2OH	H	3	

, or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising at least one compound according to any one of claims 1-16, or a pharmaceutically-acceptable salt thereof, and a pharmaceutically-acceptable carrier or diluent.

18. A compound according to any one of claims 1-16, or a pharmaceutically-acceptable salt thereof, for use as a medicament.

19. Use of a compound according to any one of claims 1-16, or a pharmaceutically-acceptable salt thereof, in the manufacture of a medicament for treating a condition in a human in need thereof, wherein the condition is selected from the group consisting of cancer, an immunological disorder, a central nervous system disorder, an inflammatory disorder, a gastroenterological disorder, a metabolic disorder, a cardiovascular disorder, and a kidney disease.

20. The use of claim 19, wherein the autoimmune disease is rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, or type I diabetes mellitus.

21. The use of claim 19, wherein the inflammatory disorder is an inflammatory skin condition, arthritis, psoriasis, spondylitis, parodontitits, or an inflammatory neuropathy.

22. The use of claim 19, wherein the condition is selected from the group consisting of cancer, transplant rejection, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, type I diabetes mellitus, Alzheimer's disease, inflammatory skin condition, inflammatory neuropathy, psoriasis, spondylitis, parodontitis, Crohn's disease, ulcerative colitis, obesity, type II diabetes mellitus, ischemic stroke, chronic kidney disease, nephritis, chronic renal failure, and a combination thereof.