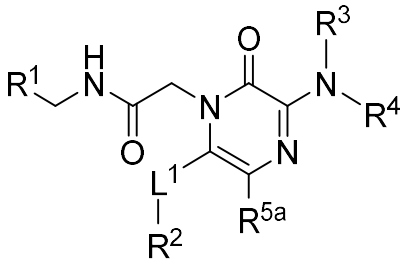
Mannan-binding lectin-associated serine protease-2 (MASP-2) has been shown to be required for the function of the lectin pathway, one of the principal complement activation pathways (Vorup-Jensen et al., J. Immunol 165:2093-2100, 2000; Ambrus et al., J Immunol. 170: 1374-1382, 2003; Schwaeble et al., PNAS 108:7523-7528, 2011). Importantly, inhibition of MASP-2 does not appear to interfere with the antibody-dependent classical complement activation pathway, which is a critical component of the acquired immune response to infection. As described in U.S. Patent No. 9,011,860 (assigned to Omeros Corporation), which is hereby incorporated by reference, discloses a fully human monoclonal antibody targeting human MASP-2 has been generated which binds to human MASP-2 with high affinity and blocks the lectin pathway complement activity and is therefore useful to treat various lectin complement pathway-associated diseases and disorders.

MASP-2-dependent complement activation has been implicated as contributing to the pathogenesis of numerous acute and chronic disease states. Therefore, a need exists for compounds that are suitable for administration/treatment of subject suffering from MASP-2 complement pathway-associated diseases and disorders, including diseases that are not suitably or efficiently treated with large molecule biologic inhibitors.

~~BRIEF~~ SUMMARY

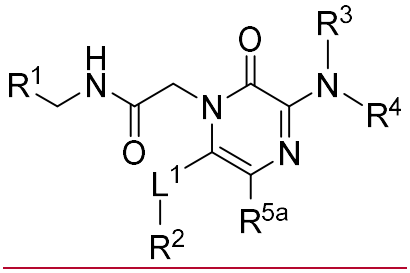
One ~~embodiment~~example provides a compound having the following Structure (I):



(I)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^1, R^2, R^3, R^4, R^{5a}, and L^1 are as defined below.

In one aspect, the present disclosure refers to a compound having the following Structure (I):



(I)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^1 is a substituted or unsubstituted heteroaryl;

R^2 is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^3 is hydrogen or alkyl;

R^4 is alkyl, a substituted or unsubstituted arylalkyl, a heterocyclyl substituted with substituents selected from the group consisting of a substituted or unsubstituted phenyl or a substituted or unsubstituted pyridinyl, or R^3 and R^4, together with the nitrogen to which they are attached form an optionally substituted 4-10 membered heterocyclyl;

R^{5a} is hydrogen or halo;

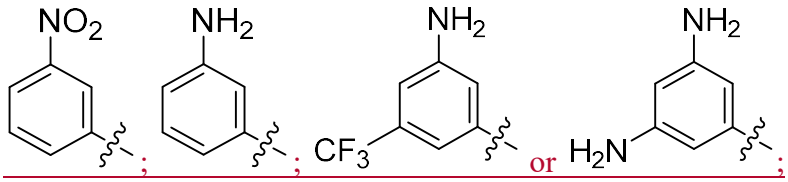
R^{5b} is hydrogen, alkyl, haloalkyl, (C=O)alkyl, (C=O)Oalkyl, (C=O)cycloalkyl, (C=O)Ocycloalkyl, (C=O)aryl, (C=O)Oaryl, (C=O)heteroaryl, (C=O)Oheteroaryl, (C=O)heterocyclyl, (C=O)Oheterocyclyl, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted heterocyclyl, a substituted or unsubstituted arylalkyl, a substituted or unsubstituted heteroarylalkyl, a substituted or unsubstituted cycloalkylalkyl, or a substituted or unsubstituted heterocyclylalkyl;

L^1 is a direct bond, $-CH_2-$, $-S(O)_t-$, NR^{5b}, -O-, -C=C-, or -C≡C-; and

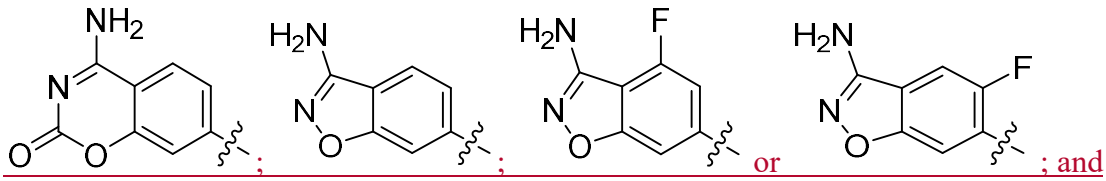
t is 0, 1, or 2,

provided that:

A) R^2 does not have one of the following structures:

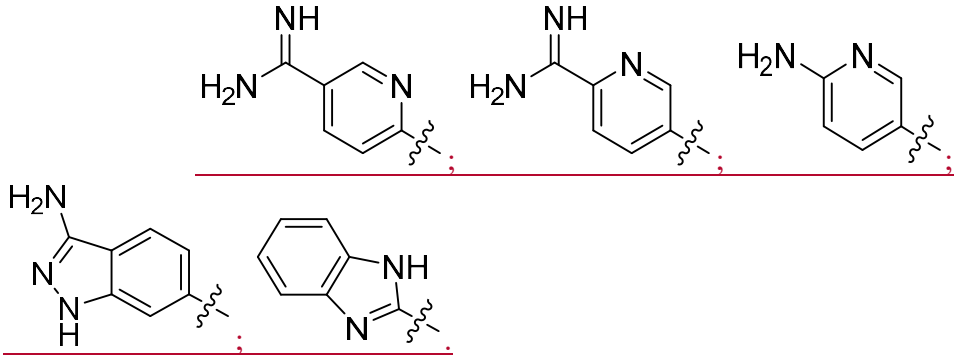


B) R^1 does not have one of the following structures:

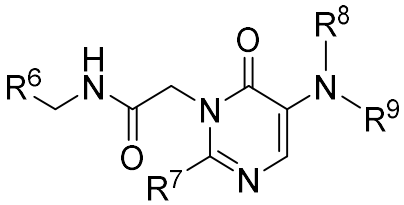


; and

C) when R^2 is unsubstituted phenyl, R^1 does not have one of the following structures:



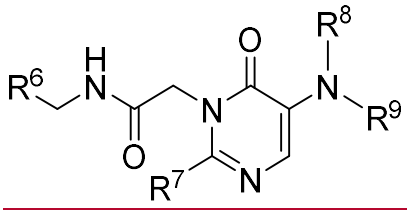
Another ~~embodiment~~example provides a compound having the following Structure (II):



(II)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^6, R^7, R^8, and R^9 are as defined below.

In one aspect, the present disclosure refers to a compound having the following Structure (II):



(II)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^6 is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^7 is alkyl, $-NR^{10a}R^{10b}$, $-SR^{10c}$, a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl;

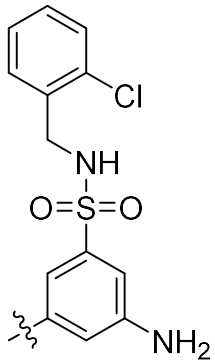
R^8 is hydrogen, alkyl, haloalkyl, cycloalkyl, or a substituted or unsubstituted arylalkyl;

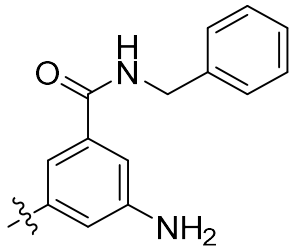
R^9 is alkyl, a substituted or unsubstituted $-S(O)_2$-arylalkyl, a substituted or unsubstituted arylalkyl, a substituted or unsubstituted heteroarylalkyl, or R^8 and R^9, together with the nitrogen to which they are attached, form an optionally substituted 4-10 membered heterocyclyl;

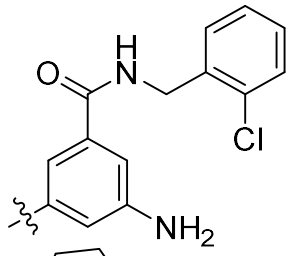
R^{10a}, R^{10b}, and R^{10c} are each independently hydrogen, alkyl, haloalkyl, or cycloalkyl;

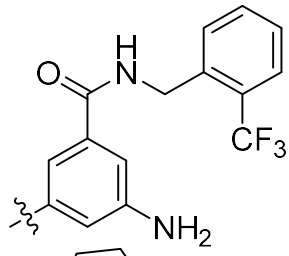
provided that:

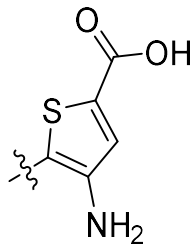
A) when R^7 is unsubstituted phenyl, 3-((methylsulfonyl)amino)phenyl, 2-methylphenyl, 3-(dimethylamino)phenyl, 3-(methylamino)phenyl, 3-methylphenyl, 3-aminomethylphenyl, 3-aminophenyl, unsubstituted pyridinyl, 3-(methylamino)-2-thienyl, 3,4-diamino-2-thienyl, 3-((methylsulfonyl)amino)-2-thienyl, 3-amino-2-thienyl, 3-amino-5-5(aminocarbonyl)phenyl, or has one of the following structures:

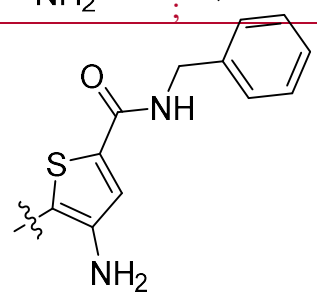


;


;


;


;


;


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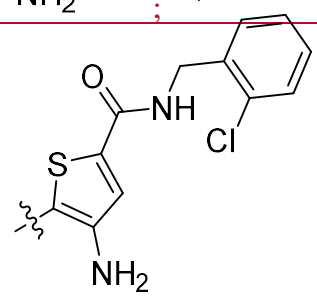
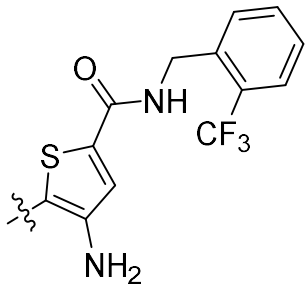
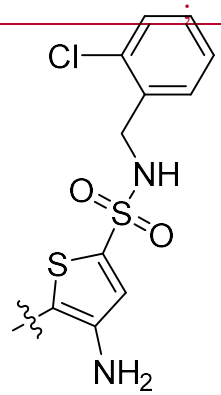
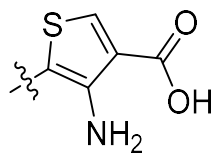


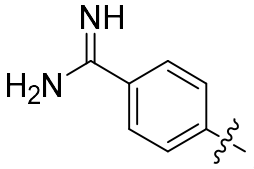
;


;


or


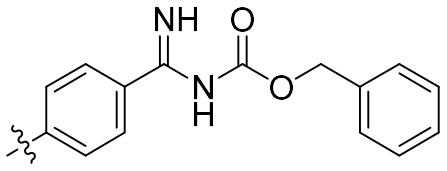
,

R^6 does not have the following structure:



; and

B) when R^7 is unsubstituted phenyl, R^6 does not have the following structure:



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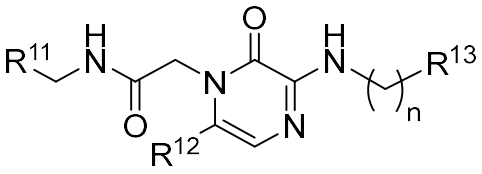
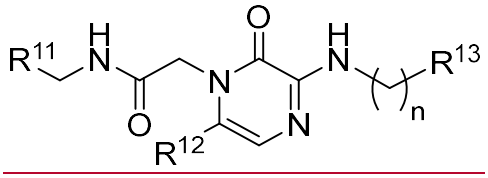
Another ~~embodiment~~example provides a compound having the following Structure (III):



(III)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^{11}, R^{12}, R^{13}, and n are as defined below.

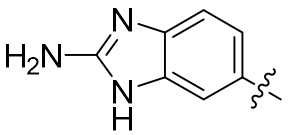
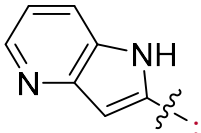
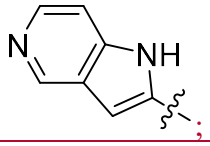
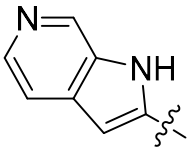
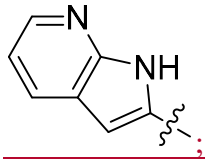
In one aspect, the present disclosure refers to a compound having the following Structure (III):



(III)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^{11} has one of the following structures:

 ;  ;  ;  or  ;

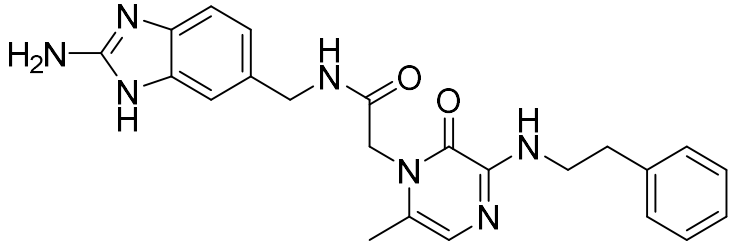
R^{12} is methyl, alkoxy, or halo;

R^{13} is a substituted or unsubstituted aryl; and

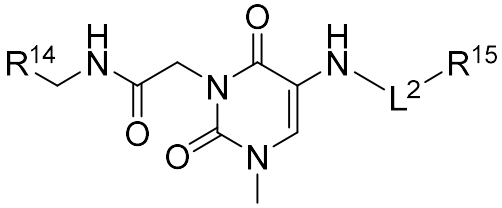
n is 1 or 2

provided that:

the compound of Structure (III) does not have the following structure:

 .

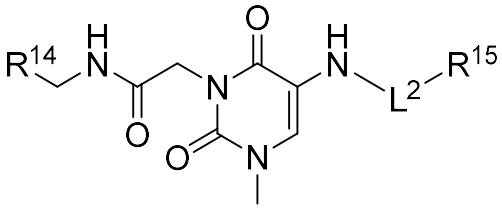
Another ~~embodiment~~example provides a compound having the following Structure (IV):



(IV)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein R^{14}, R^{15}, and L^2 are as defined below.

In one aspect, the present disclosure refers to a compound having the following Structure (IV):



(IV)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^{14} is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^{15} is a substituted or unsubstituted arylalkyl, or a substituted or unsubstituted heteroarylalkyl;

L^2 is a direct bond, -C(=O), or -$S(=O)_t$-; and

t is 0, 1, or 2.

In one aspect, the present disclosure refers to a compound having a structure found in Table 1 or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof.

Additional ~~embodiment~~examples of the present disclosure provide a pharmaceutical composition comprising a compound of Structure (I), (II), (III), or (IV),

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient.

In one aspect, the present disclosure refers to a pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof disclosed herein and a pharmaceutically acceptable carrier or excipient.

The compounds of Structures (I), (II), (III), and (IV) are useful in the treatment of MASP-2-associated diseases and disorders, and in the manufacture of medicaments for treating MASP-2-associated diseases and disorders. Accordingly, other ~~embodiment~~examples of the disclosure provide methods of treating a MASP-2-associated disease and disorder comprising administering to a patient a therapeutically effective amount of a compound of Structure (I), (II), (III), or (IV), or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure refers to use of a compound disclosed herein, in the manufacture of a medicament for treating a MASP-2-associated disease or disorder in a subject in need thereof.

These and other aspects, objects and ~~embodiment~~examples will become more apparent when read with the detailed description and figures which follow.

DETAILED DESCRIPTION

I. Definitions

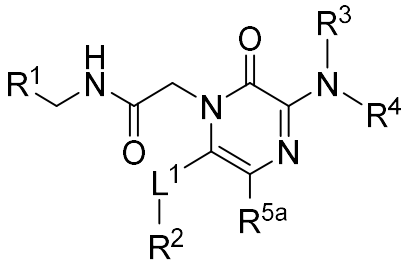
Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the subject matter of the present disclosure, suitable methods and materials are described below. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

In certain embodiments herein, reference is made to features and aspects of the disclosure, including method steps. All possible combinations of such features and aspects within the embodiments of the disclosure are included, at least to the extent that such combinations are non-contradictory. For example, if an embodiment presents aspects A, B, and C, it is understood that this also discloses embodiments including both aspects A and B, both aspects B and C, and both aspects A and C, as well as an embodiment with aspects A, B, and C.

The terms "a," "an," or "the" not only include aspects with one member, but also include aspects with more than one member. For instance, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise.

CLAIMS

1. A compound having the following Structure (I):



(I)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^1 is a substituted or unsubstituted heteroaryl;

R^2 is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^3 is hydrogen or alkyl;

R^4 is alkyl, a substituted or unsubstituted arylalkyl, a heterocyclyl substituted with substituents selected from the group consisting of a substituted or unsubstituted phenyl or a substituted or unsubstituted pyridinyl, or R^3 and R^4, together with the nitrogen to which they are attached form an optionally substituted 4-10 membered heterocyclyl;

R^{5a} is hydrogen or halo;

~~L^1 is a direct bond, $-CH_2-$, $-S(O)_t-$, NR^{5b}, $-O-$, $-C=C-$, or $-C\equiv C-$;~~

~~t is 0, 1, or 2; and~~

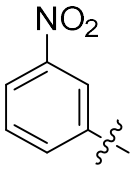
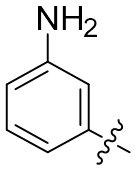
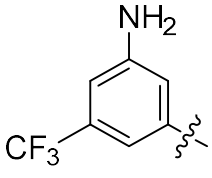
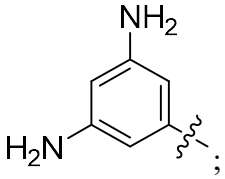
R^{5b} is hydrogen, alkyl, haloalkyl, (C=O)alkyl, (C=O)Oalkyl, (C=O)cycloalkyl, (C=O)Ocycloalkyl, (C=O)aryl, (C=O)Oaryl, (C=O)heteroaryl, (C=O)Oheteroaryl, (C=O)heterocyclyl, (C=O)Oheterocyclyl, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted heterocyclyl, a substituted or unsubstituted arylalkyl, a substituted or unsubstituted heteroarylalkyl, a substituted or unsubstituted cycloalkylalkyl, or a substituted or unsubstituted heterocyclylalkyl;~~,~~

L^1 is a direct bond, $-CH_2-$, $-S(O)_t-$, NR^{5b}, $-O-$, $-C=C-$, or $-C\equiv C-$; and

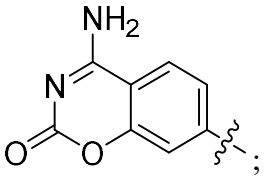
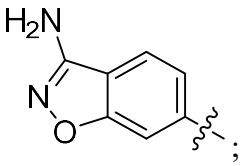
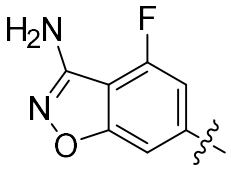
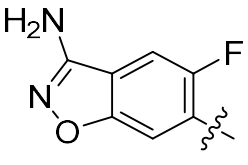
t is 0, 1, or 2,

provided that:

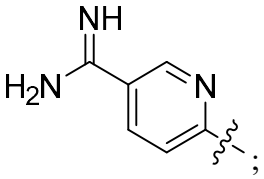
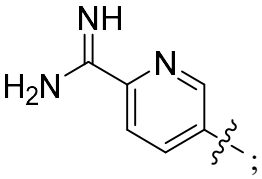
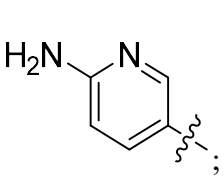
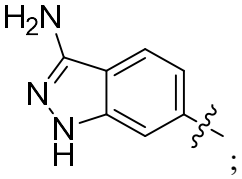
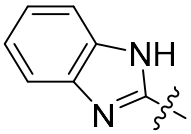
A) R^2 does not have one of the following structures:

 ;  ;  or  ;

B) R^1 does not have one of the following structures:

 ;  ;  or  ; and

C) when R^2 is unsubstituted phenyl, R^1 does not have one of the following structures:

 ;  ;  ;  ; 

.

~~2. The compound of claim 1, wherein R^1 is a substituted or unsubstituted 5-10 membered heteroaryl.~~

~~3. The compound of claim 1 or 2, wherein R^1 is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolopyridinyl, or a substituted or unsubstituted benzoimidazolyl.~~

2. The compound of ~~any one of~~ claims ~~1-3~~, wherein R^1 is substituted with one or more of R^{1a}, R^{1b}, R^{1c}, R^{1d}, and R^{1e} wherein R^{1a}, R^{1b}, R^{1c}, R^{1d}, and R^{1e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$,

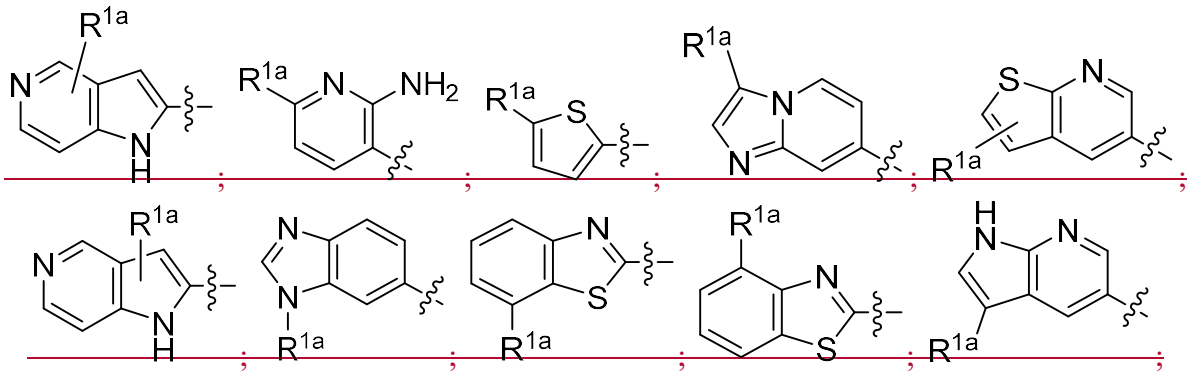
$S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

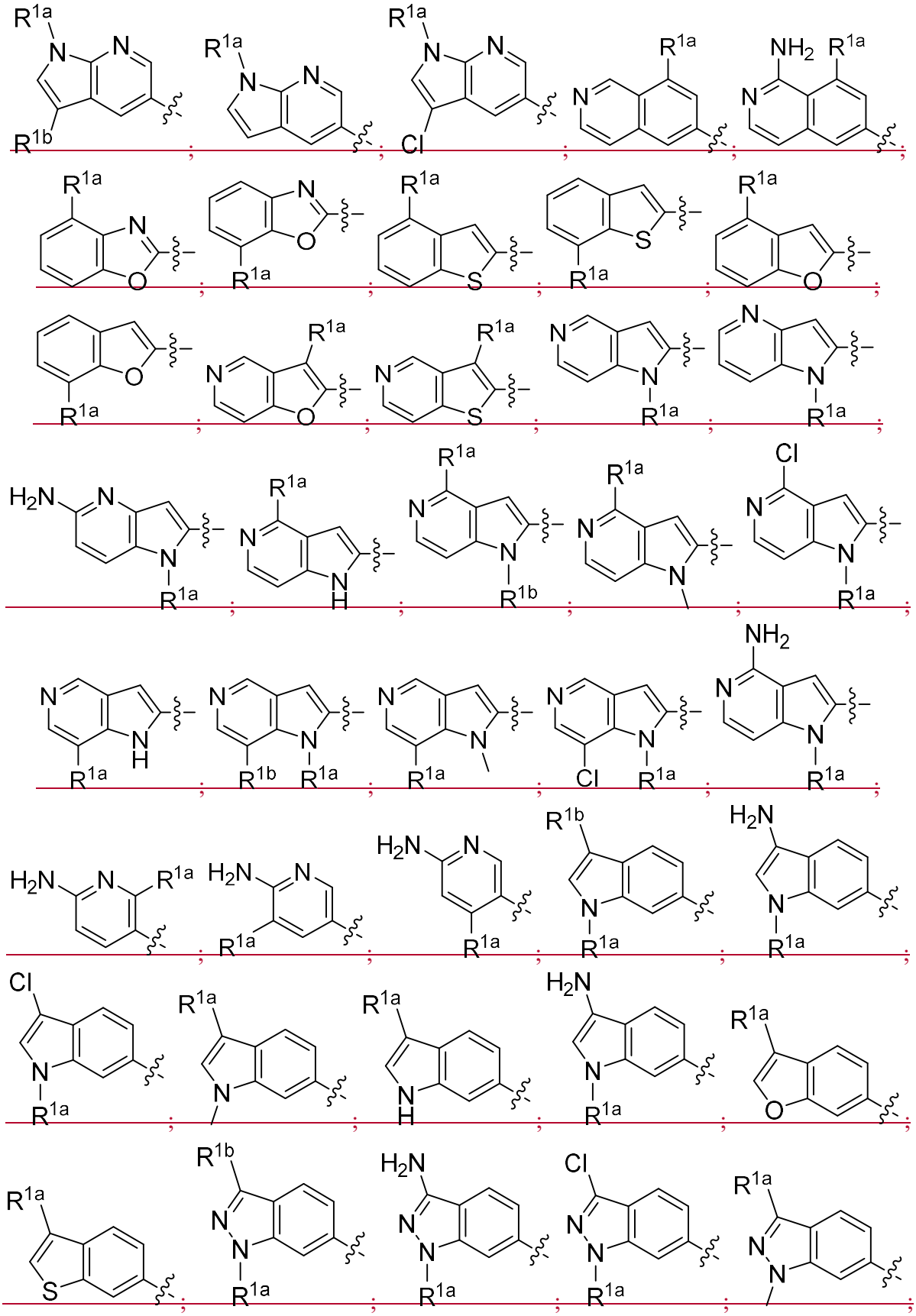
wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

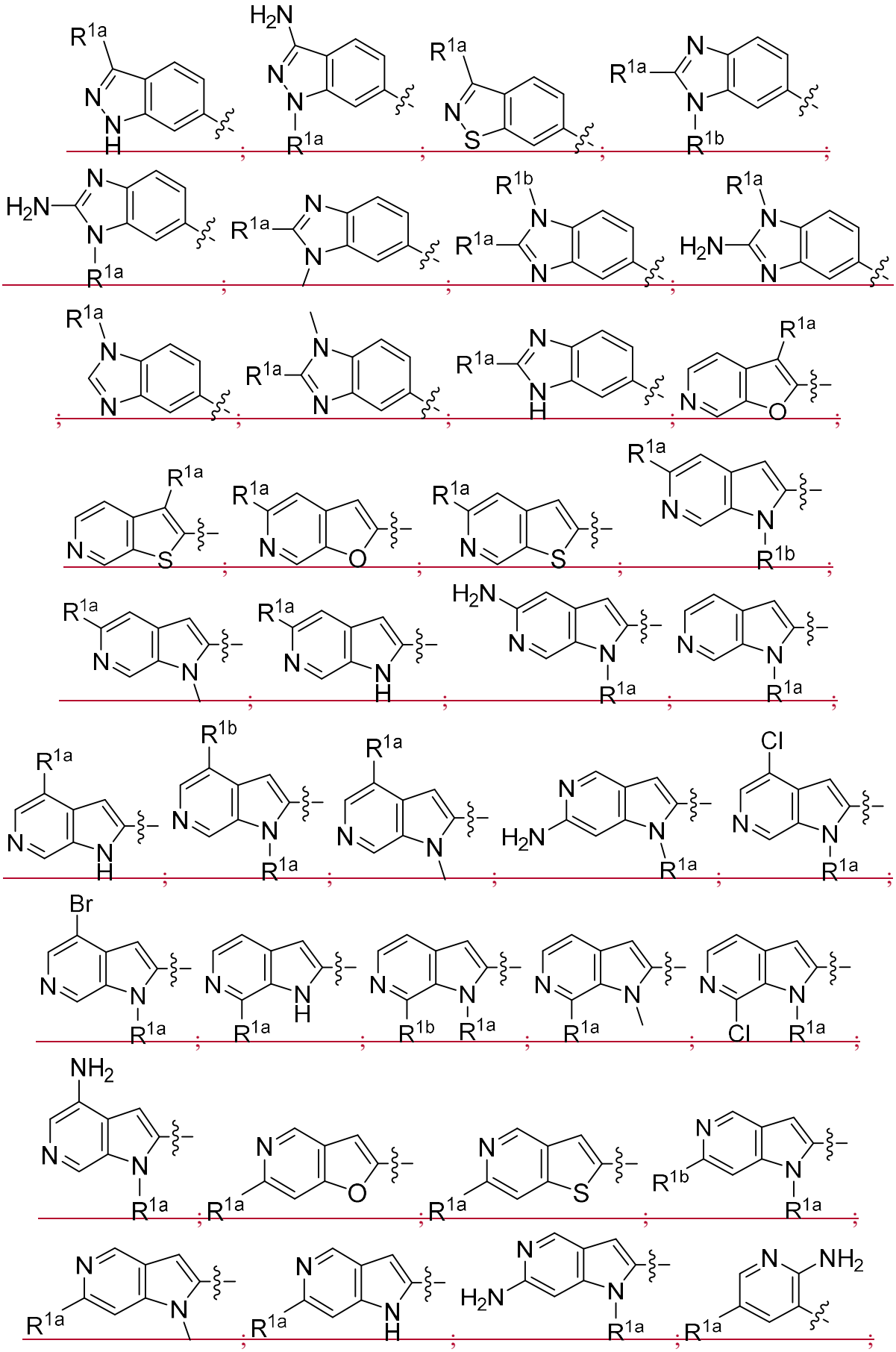
~~5. The compound of claim 4, wherein R^{1a}, R^{1b}, R^{1c}, R^{1d}, or R^{1e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{1a}, R^{1b}, R^{1c}, R^{1d}, or R^{1e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,~~

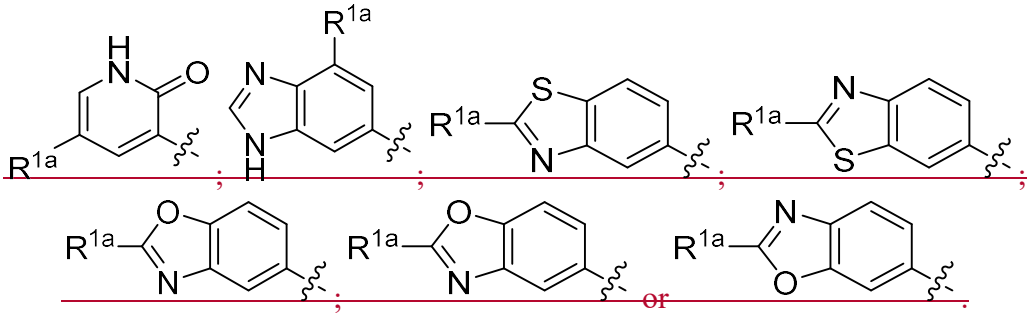
~~wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.~~

~~6. The compound of any one of claims 1-5, wherein R^1 has one of the following structures:~~









7. The compound of claim 6, wherein R^{1a} or R^{1b} is independently C_{1-6} alkyl, amino, or halo.

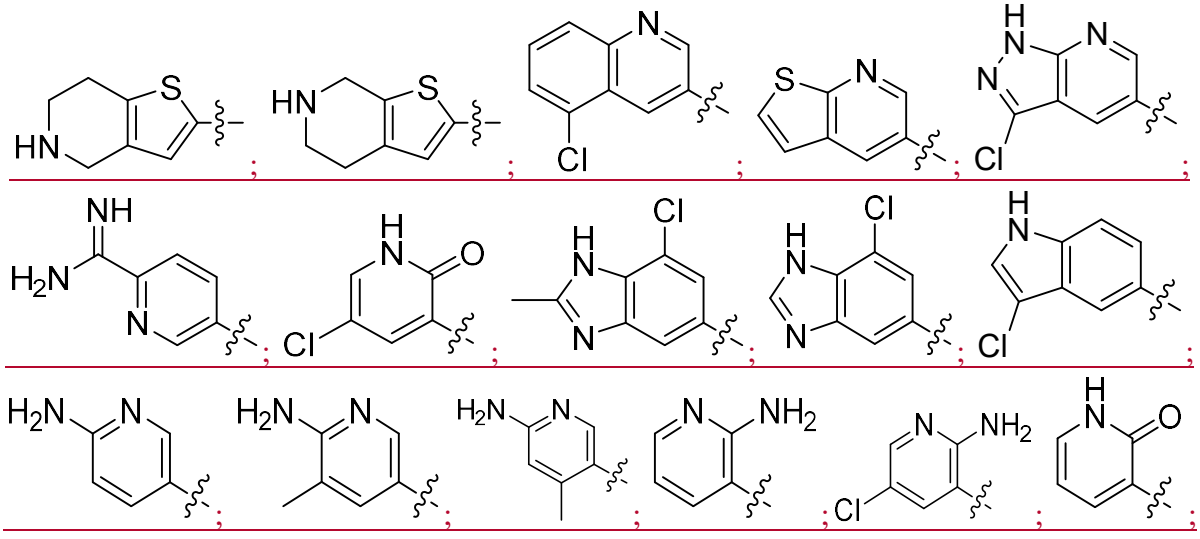
8. The compound of claim 7, wherein R^{1a} or R^{1b} is methyl.

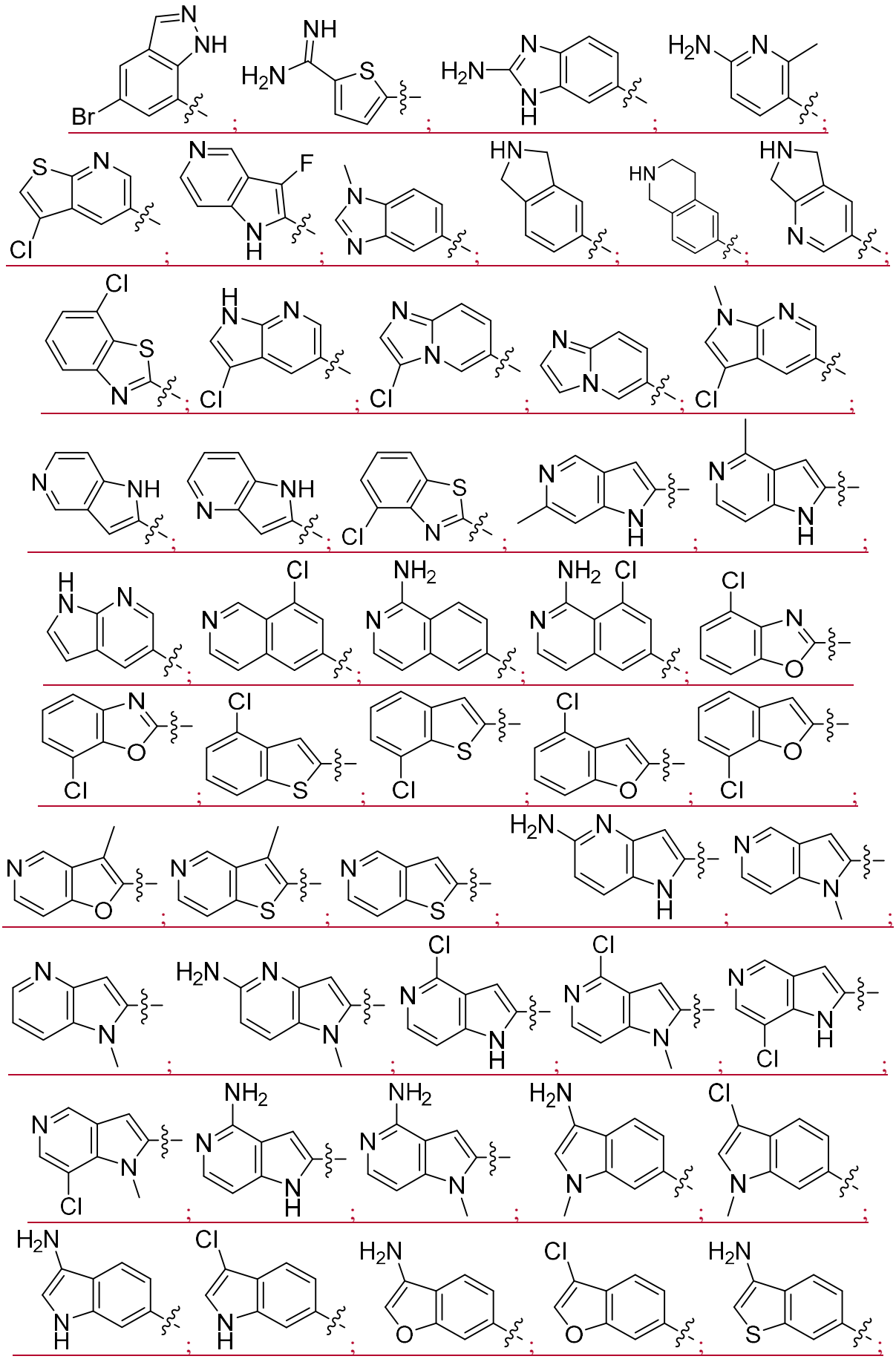
9. The compound of claim 7, wherein R^{1a} or R^{1b} is F, Cl, or Br.

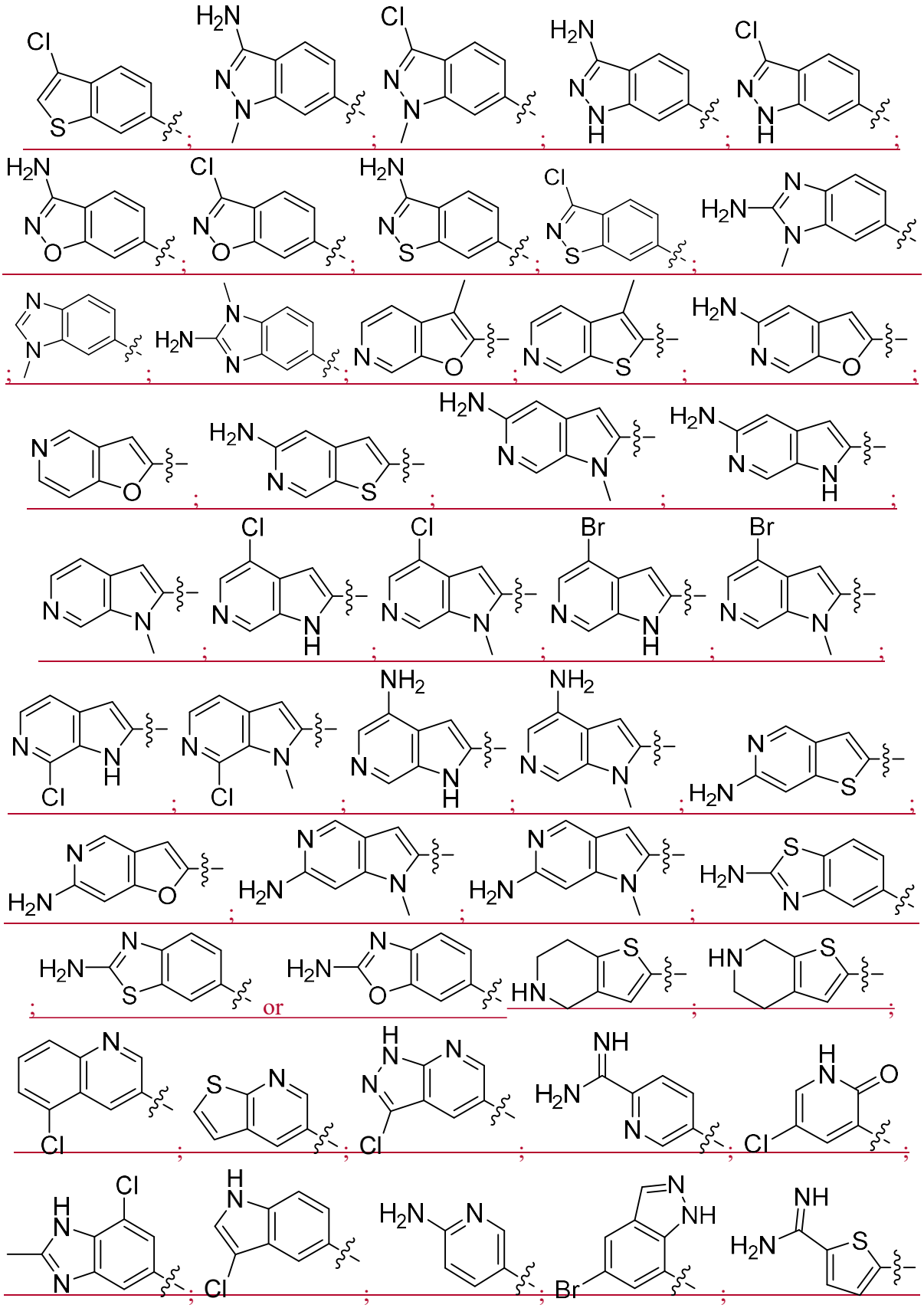
10. The compound of claim 8, wherein each R^{1a} or R^{1b} attached to nitrogen is C_{1-6} alkyl.

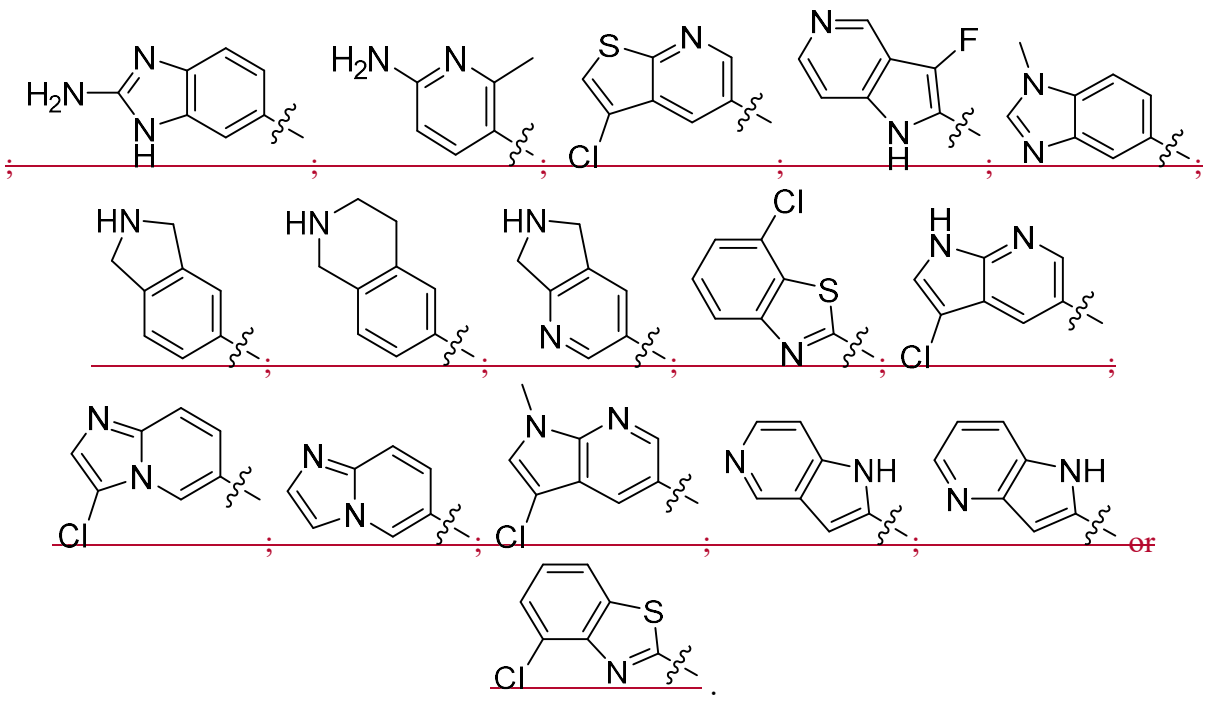
11. The compound of claim 10, wherein R^{1a} or R^{1b} is methyl or ethyl.

312. The compound of ~~any one of~~ claims 1~~-11~~, wherein R^1 has one of the following structures:

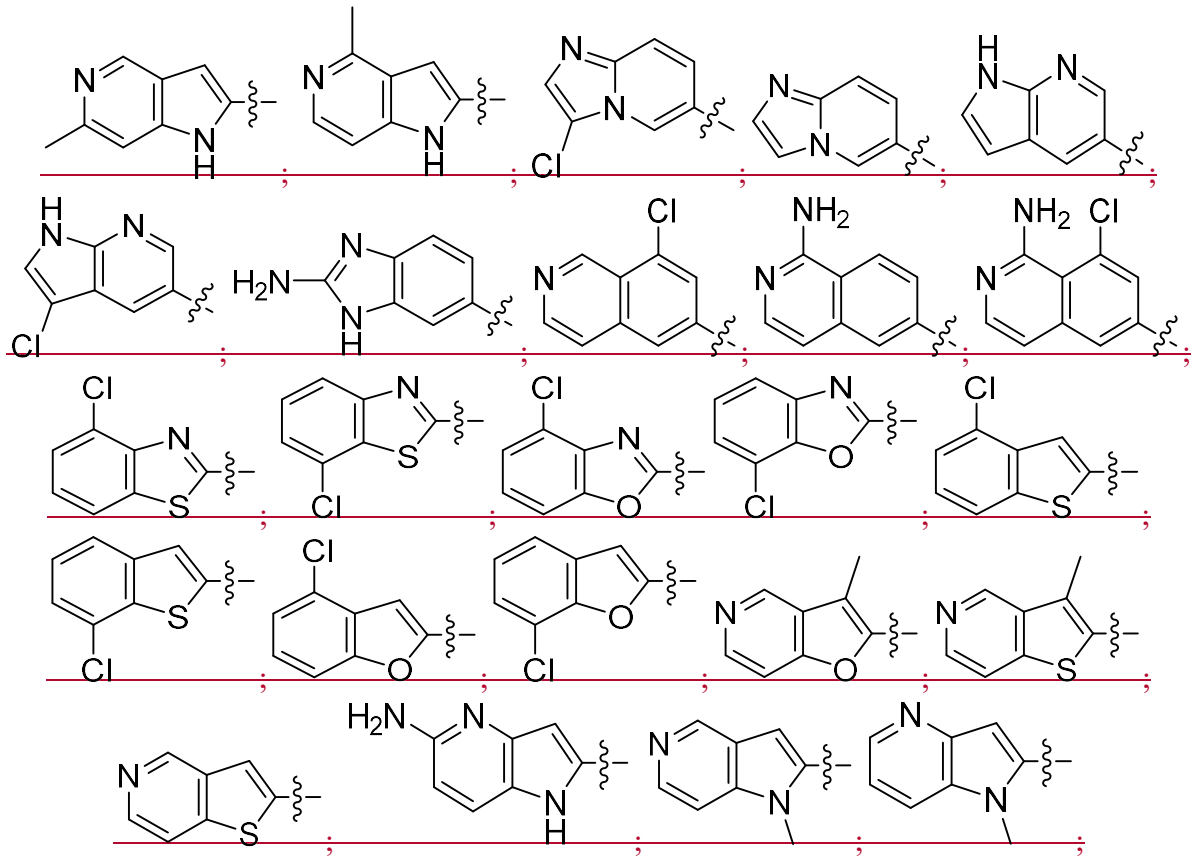


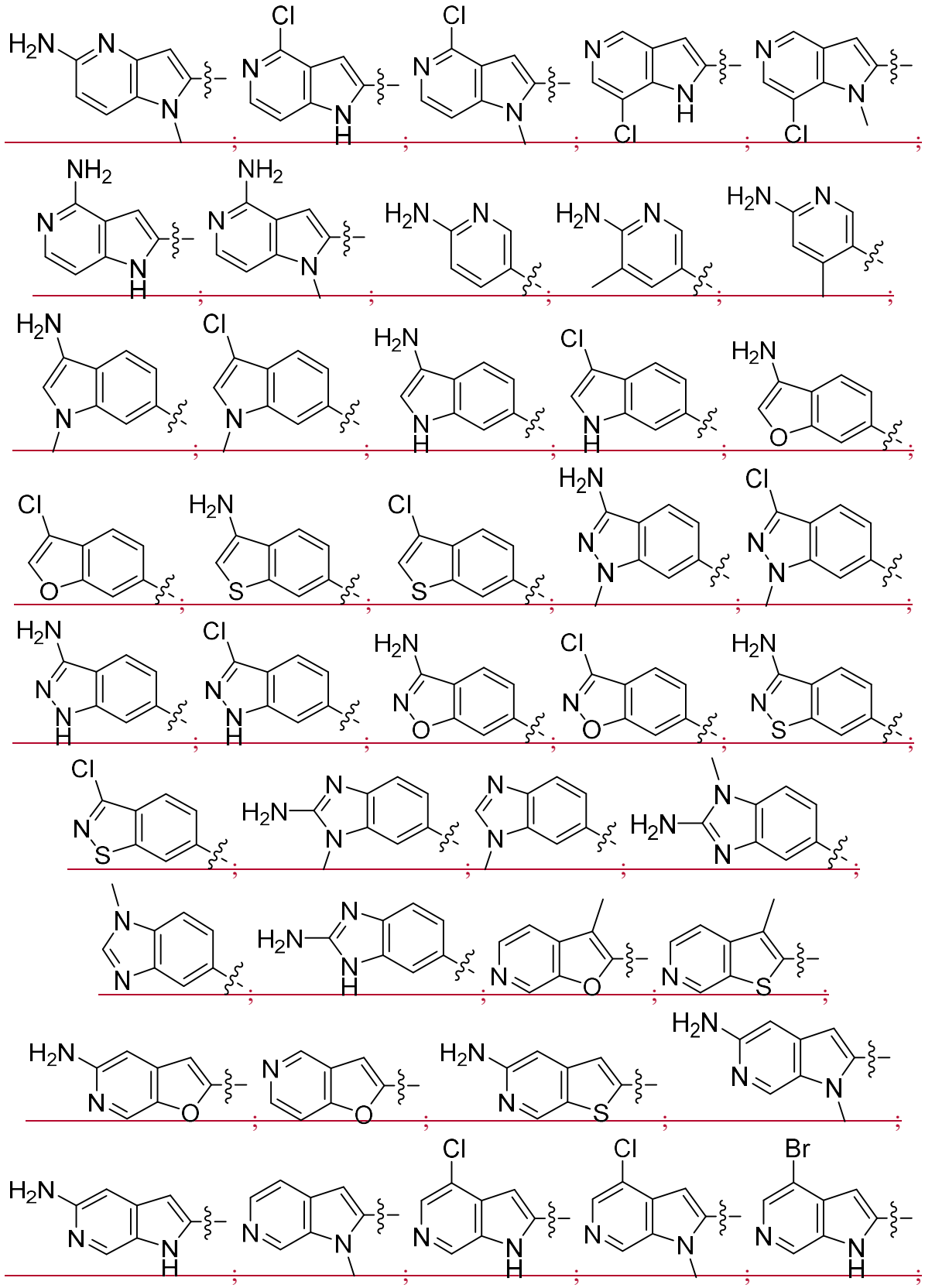


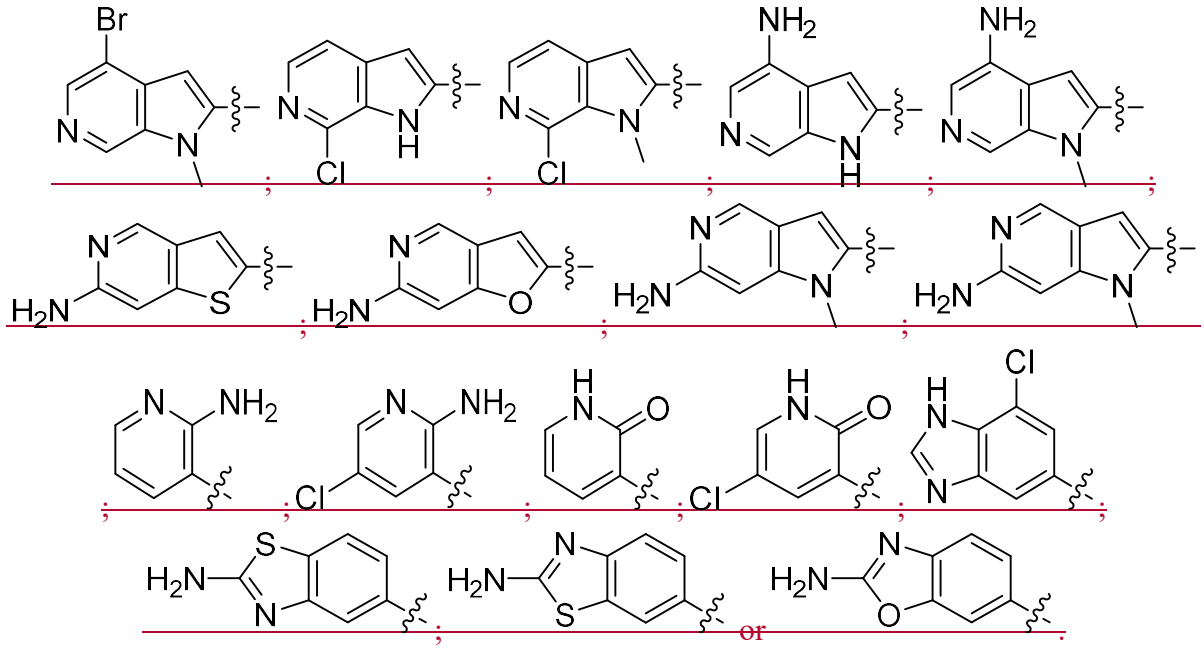




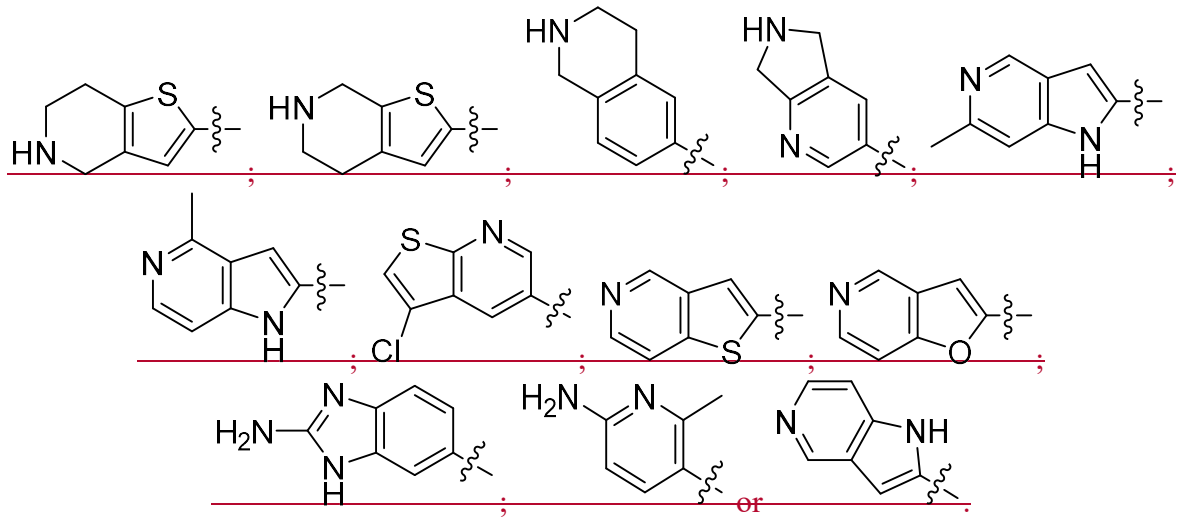
13. The compound of any one of claims 1-11, wherein R^1 has one of the following structures:







~~14. The compound of any one of claims 1-11, wherein R^1 has one of the following structures:~~



~~15. The compound of any one of claims 1-14, wherein R^2 is a substituted or unsubstituted 6-10 membered aryl.~~

~~4~~16. The compound of ~~any one of~~ claim~~s~~ 1~~-15~~, wherein R^2 is a substituted or unsubstituted phenyl.

17. The compound of any one of claims 1-16, wherein R^1 is an unsubstituted phenyl.

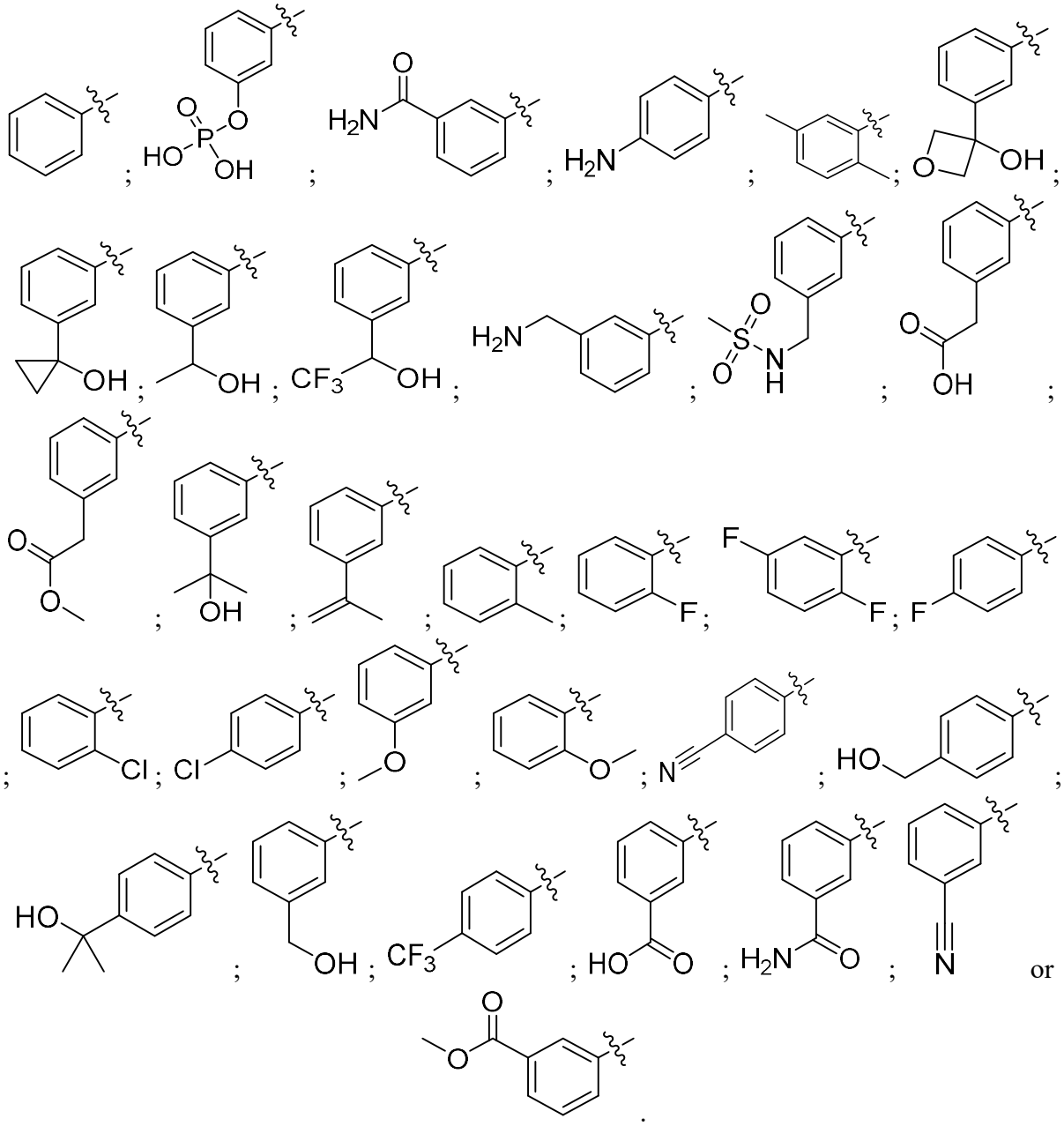
18. The compound of any one of claims 1-16, wherein R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^e$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^e$, $C(=NOR^a)NR^bR^e$, $C(=NOC(O)R^a)NR^bR^e$, $C(=NR^a)N(R^b)C(O)OR^e$, $N(R^a)C(=NR^b)NR^eR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

wherein R^a, R^b, R^e, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

19. The compound of claim 18, wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{2a}, R^{2b}, R^{2e}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

520. The compound of ~~any one of~~ claim~~s~~ 1~~-19~~, wherein R^2 has one of the following structures:



621. The compound of ~~any one of~~ claim~~s~~ 1~~-14~~, wherein R^2 is a substituted or unsubstituted 5-10 membered heteroaryl.

722. The compound of ~~any one of~~ claim~~s~~ 1~~-14 or 21~~, wherein R^2 is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolyl, a substituted or unsubstituted pyrimidinyl, a substituted or unsubstituted isoquinolinyl, a substituted or

unsubstituted pyrazolyl, a substituted or unsubstituted pyrrolopyridinyl, or a substituted or unsubstituted benzoimidazolyl.

~~23. The compound of any one of claims 1-14 or 21-22, wherein R^2 is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolyl, a substituted or unsubstituted pyrimidinyl, a substituted or unsubstituted isoquinolinyl, or a substituted or unsubstituted pyrazolyl.~~

~~24. The compound of any one of claims 1-14 or 21-23, wherein R^1 is an unsubstituted pyridinyl, an unsubstituted pyrrolyl, an unsubstituted pyrimidinyl, or an unsubstituted isoquinolinyl.~~

~~25. The compound of any one of claims 1-14 or 21-23, wherein R^2 is substituted with one or more of R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^e$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^e$, $C(=NOR^a)NR^bR^e$, $C(=NOC(O)R^a)NR^bR^e$, $C(=NR^a)N(R^b)C(O)OR^e$, $N(R^a)C(=NR^b)NR^eR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,~~

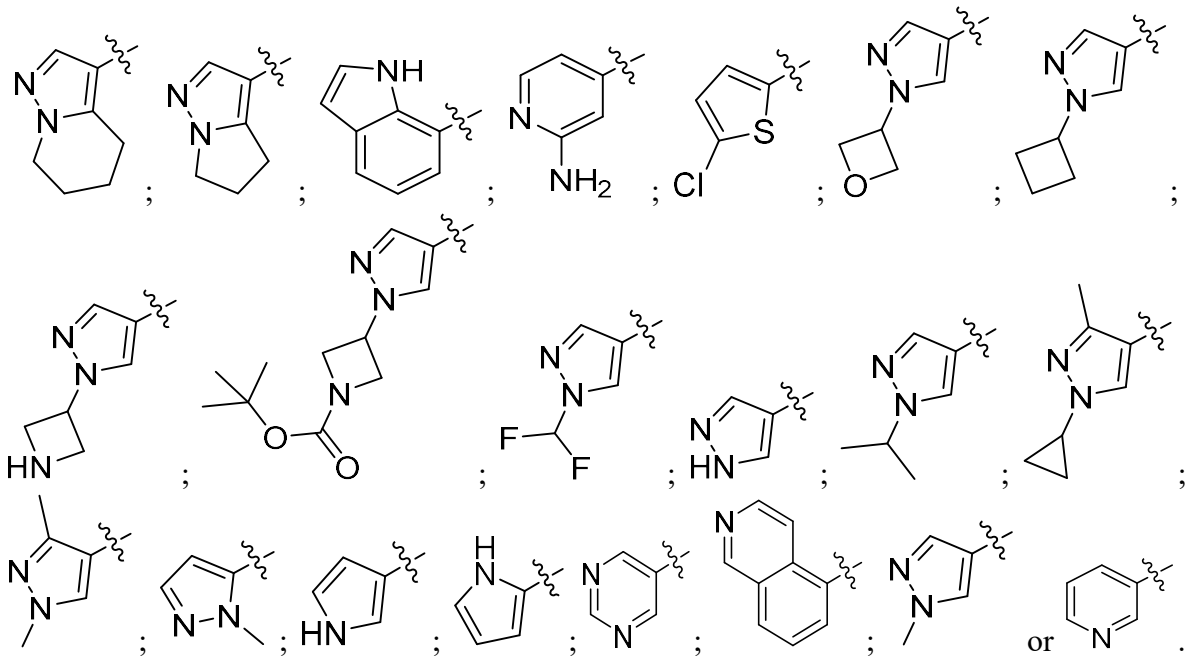
~~wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.~~

~~26. The compound of claim 25, wherein R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$,~~

~~$NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{2a}, R^{2b}, R^{2c}, R^{2d}, or R^{2e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,~~

~~wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.~~

8~~27~~. The compound of ~~any one of~~ claim~~s~~ 1~~-14~~, wherein R^2 has one of the following structures:



9~~28~~. The compound of ~~any one of~~ claim~~s~~ 1~~-27~~, wherein R^3 is hydrogen or methyl.

~~29. The compound of any one of claims 1-27, wherein R^3 is methyl.~~

130. The compound of ~~any one of~~ claim~~s~~ 1~~-27~~, wherein R^3 and R^4, together with the nitrogen to which they are attached form an optionally substituted 4-10 membered heterocyclyl.

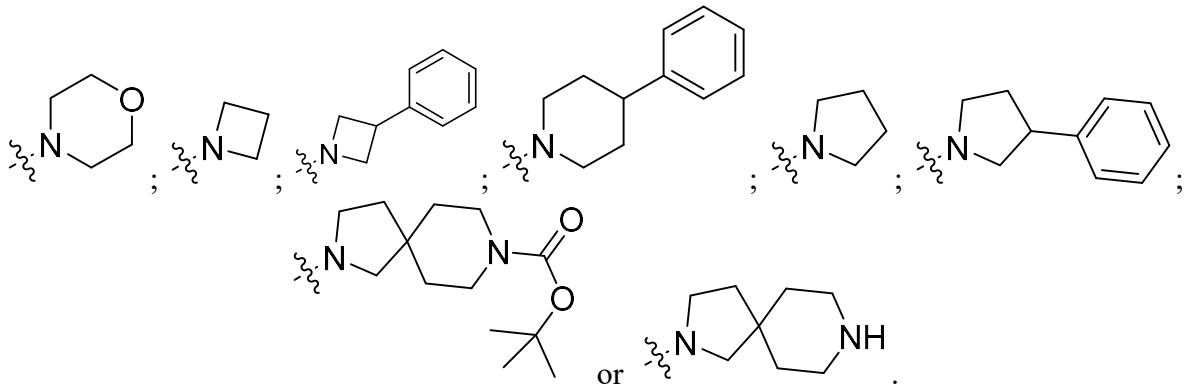
~~31. The compound of claim 30, wherein R^3 and R^4, together with the nitrogen to which they are attached form an unsubstituted 4-6 membered heterocyclyl.~~

~~32. The compound of claim 30 or 31, wherein R^3 and R^4, together with the nitrogen to which they are attached form an unsubstituted 5-membered ring.~~

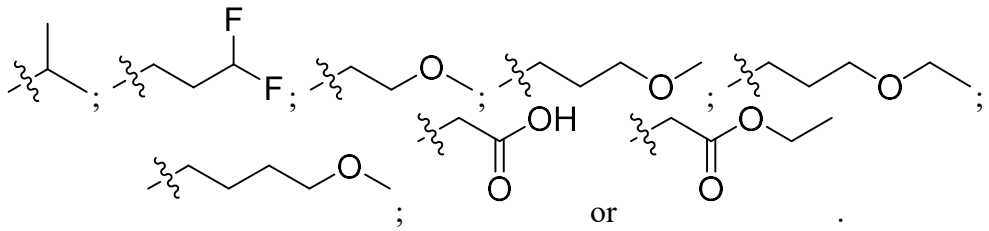
~~33. The compound of any one of claims 30-32, wherein R^3 and R^4, together with the nitrogen to which they are attached form an unsubstituted pyrrolidinyl ring.~~

~~34. The compound of claim 30 or 31, wherein R^3 and R^4, together with the nitrogen to which they are attached form an unsubstituted 6-membered ring.~~

1135. The compound of ~~any one of~~ claim~~s~~ 1~~-13~~, wherein R^3 and R^4, together with the nitrogen to which they are attached form one of the following structures:



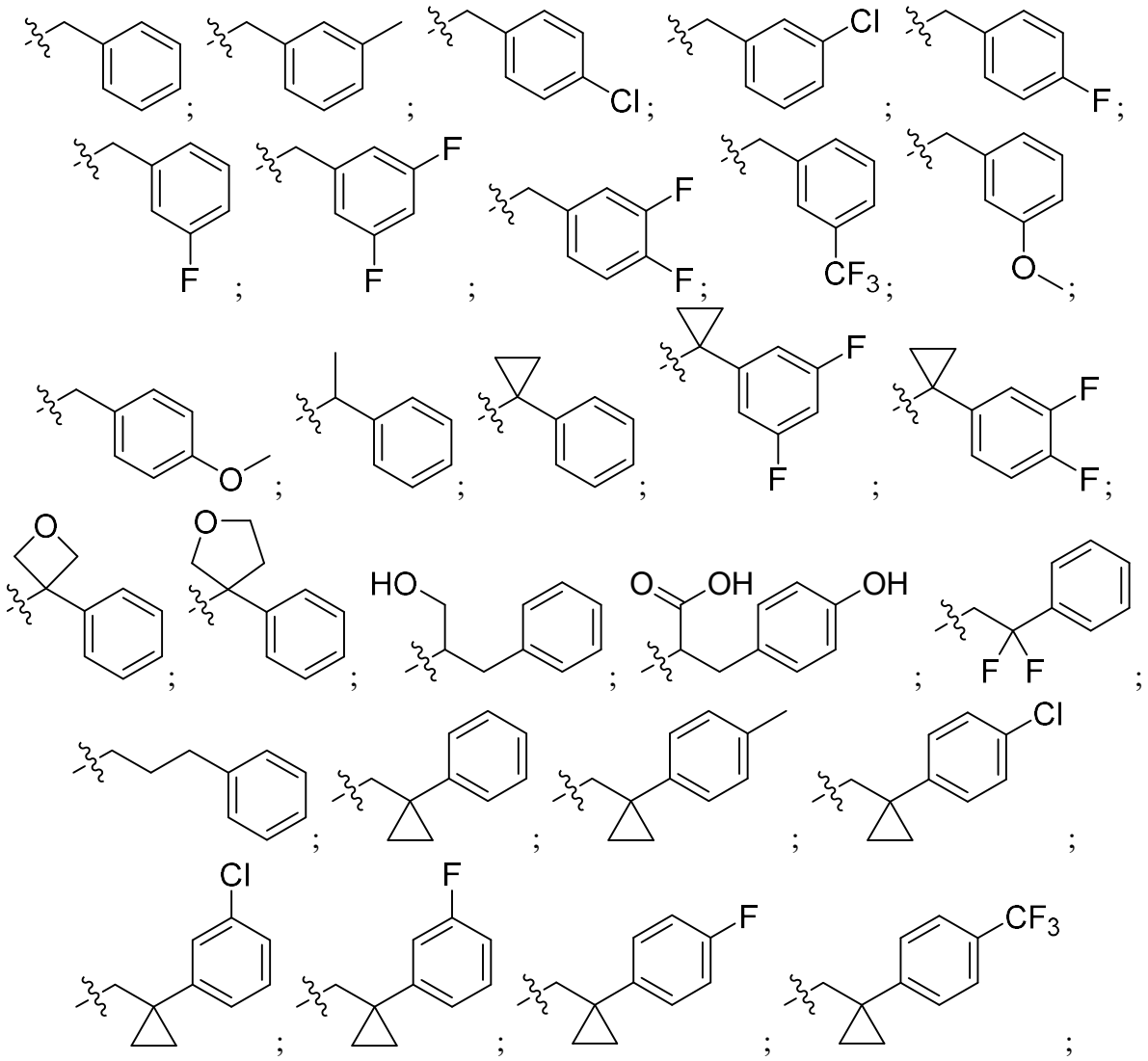
1236. The compound of ~~any one of~~ claim~~s~~ 1~~-29~~, wherein R^4 is methyl or has one of the following structures:

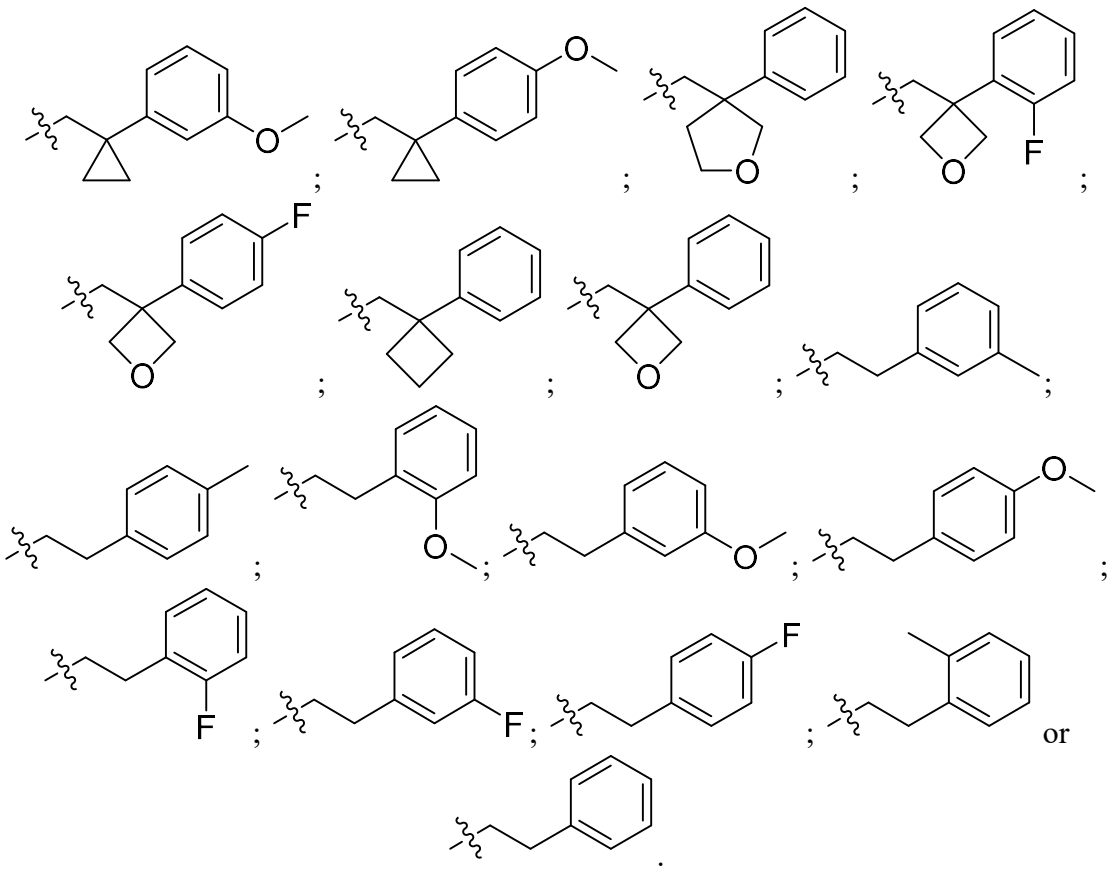


or .

1337. The compound of ~~any one of~~ claim~~s~~ 1~~-29~~, wherein R^4 is a substituted or unsubstituted arylalkyl.

1438. The compound of ~~any one of~~ claim~~s~~ 1~~-29~~, wherein R^4 has the following structure:



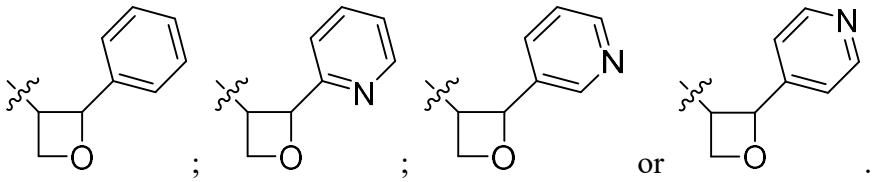


1539. The compound of ~~any one of~~ claim~~s~~ 1~~-29~~, wherein R^4 is a heterocyclyl substituted with substituents selected from the group consisting of a substituted or unsubstituted phenyl or a substituted or unsubstituted pyridinyl.

~~40. The compound of claim 39, wherein R^4 is a 4-6 membered heterocyclyl ring.~~

~~41. The compound of any one of claims 39-40, wherein R^4 comprises oxygen.~~

1642. The compound of ~~any one of~~ claim~~s~~ ~~40-4~~1, wherein R^4 has one of the following structures:



1743. The compound of ~~any one of~~ claim~~s~~ 1~~-42~~, wherein L^1 is a direct bond, -CH_2-, or -C≡C-.

~~44. The compound of any one of claims 1-43, wherein L^1 is a direct bond.~~

~~45. The compound of any one of claims 1-43, wherein L^1 is -CH_2-.~~

~~46. The compound of any one of claims 1-43, wherein L^1 is -C≡C-.~~

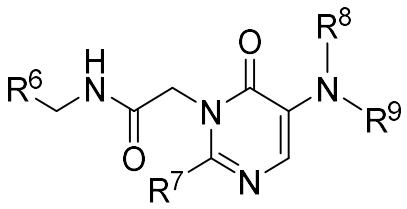
1847. The compound of ~~any one of~~ claim~~s~~ 1~~-46~~, wherein R^{5a} is hydrogen, F, Br, or Cl.

~~48. The compound of any one of claims 1-46, wherein R^{5a} is halo.~~

~~49. The compound of any one of claims 1-46, wherein R^{5a} is F, Br, or Cl.~~

~~50. The compound of any one of claims 1-46, wherein R^{5a} is Cl.~~

1951. A compound having the following Structure (II):



(II)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^6 is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^7 is alkyl, -$NR^{10a}R^{10b}$, -SR^{10c}, a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl;

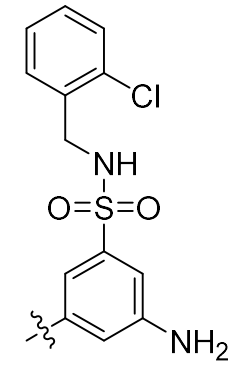
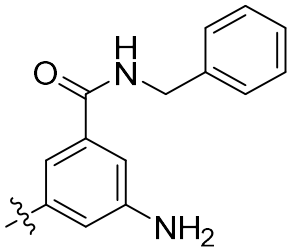
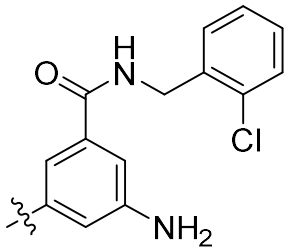
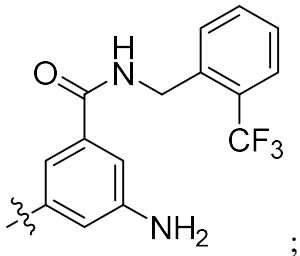
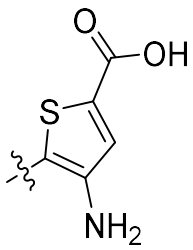
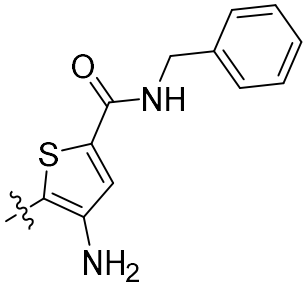
R^8 is hydrogen, alkyl, haloalkyl, cycloalkyl, or a substituted or unsubstituted arylalkyl;

R^9 is alkyl, a substituted or unsubstituted $–S(O)_2$-arylalkyl, a substituted or unsubstituted arylalkyl, a substituted or unsubstituted heteroarylalkyl, or R^8 and R^9, together with the nitrogen to which they are attached, form an optionally substituted 4-10 membered heterocyclyl;

R^{10a}, R^{10b}, and R^{10c} are each independently hydrogen, alkyl, haloalkyl, or cycloalkyl;

provided that:

A) when R^7 is unsubstituted phenyl, 3-((methylsulfonyl)amino)phenyl, 2-methylphenyl, 3-(dimethylamino)phenyl, 3-(methylamino)phenyl, 3-methylphenyl, 3-aminomethylphenyl, 3-aminophenyl, unsubstituted pyridinyl, 3-(methylamino)-2-thienyl, 3,4-diamino-2-thienyl, 3-((methylsulfonyl)amino)-2-thienyl, 3-amino-2-thienyl, 3-amino-5-5(aminocarbonyl)phenyl, or has one of the following structures:


;

;

;

;

;

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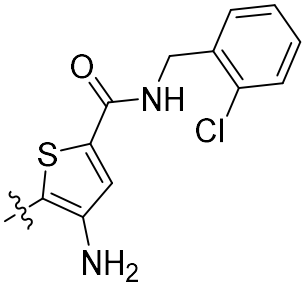
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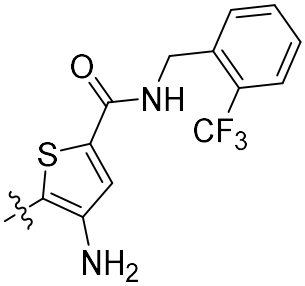
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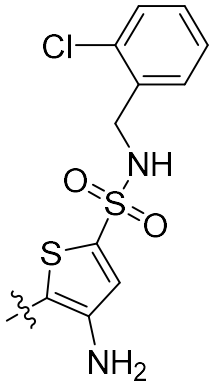
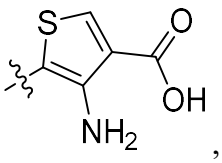
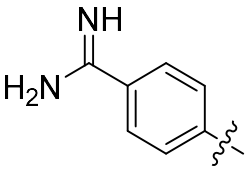
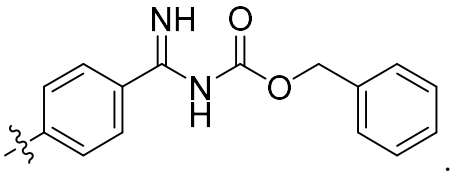

or

,

R^6 does not have the following structure:



; and

B) when R^7 is unsubstituted phenyl, R^6 does not have the following structure:



.

~~52. The compound of claim 51, wherein R^6 is a substituted or unsubstituted aryl.~~

~~53. The compound of claim 51 or 52, wherein R^6 is a substituted or unsubstituted C_6-C_{10} aryl.~~

~~54. The compound of any one of claims 51-53, wherein R^6 is a substituted or unsubstituted phenyl.~~

~~55. The compound of any one of claims 51-54, wherein R^6 is a substituted phenyl.~~

~~56. The compound of any one of claims 51-55, wherein R^6 is phenyl substituted with one or more of R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} wherein R^{6a}, R^{6b}, R^{6c}, R^{6d}, and R^{6e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^e$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^e$, $C(=NOR^a)NR^bR^e$, $C(=NOC(O)R^a)NR^bR^e$, $C(=NR^a)N(R^b)C(O)OR^e$, $N(R^a)C(=NR^b)NR^eR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10}

arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

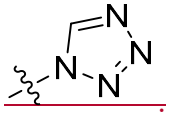
wherein R^a, R^b, R^e, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

57. The compound of claim 56, wherein R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

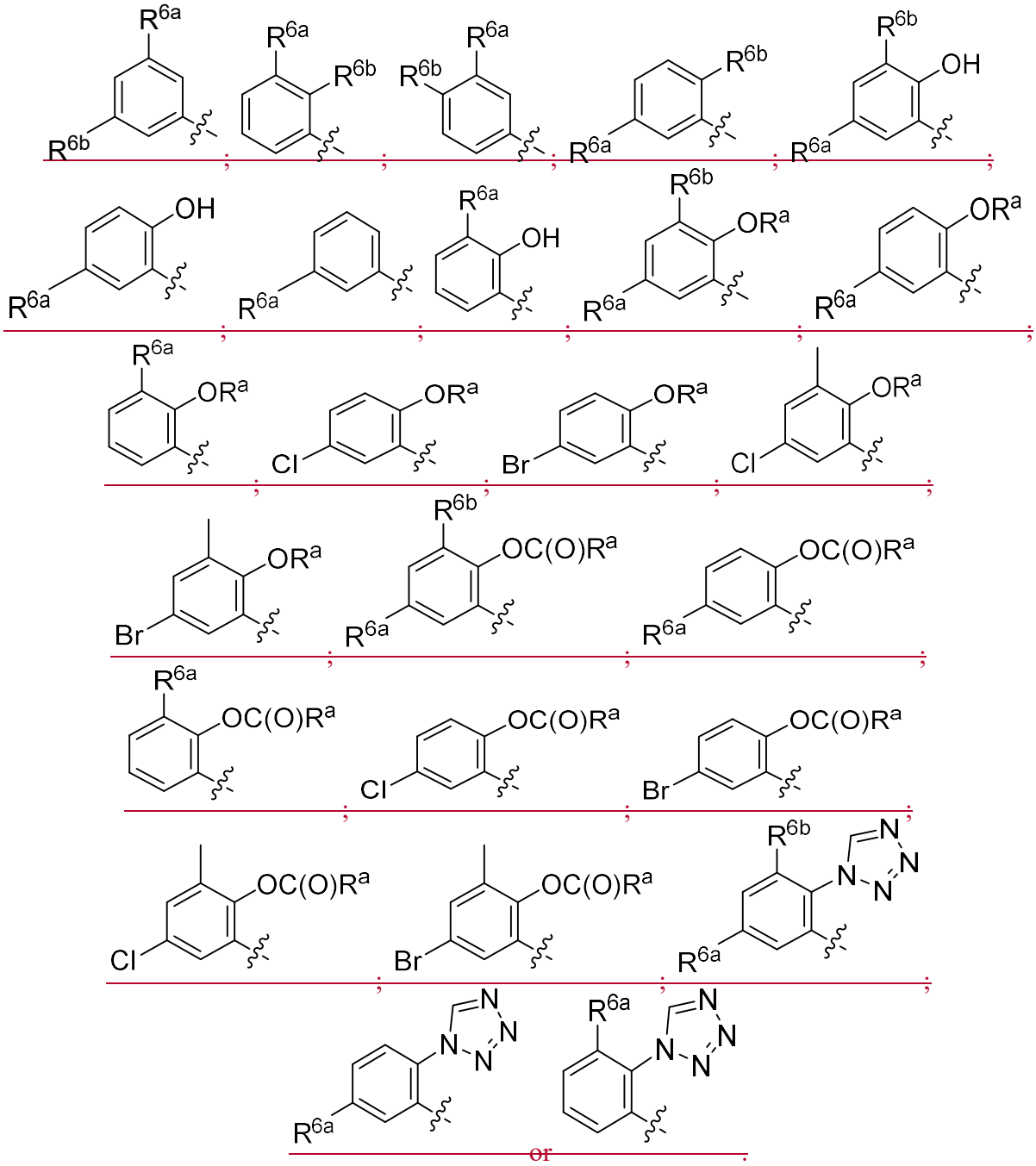
wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

58. The compound of any one of claims 51-57, wherein R^6 is phenyl substituted with at least one substituent selected from the group consisting of halo, haloalkyl, $C(=NR^a)NR^bR^e$, alkyl, and 5-10 membered heteroaryl.

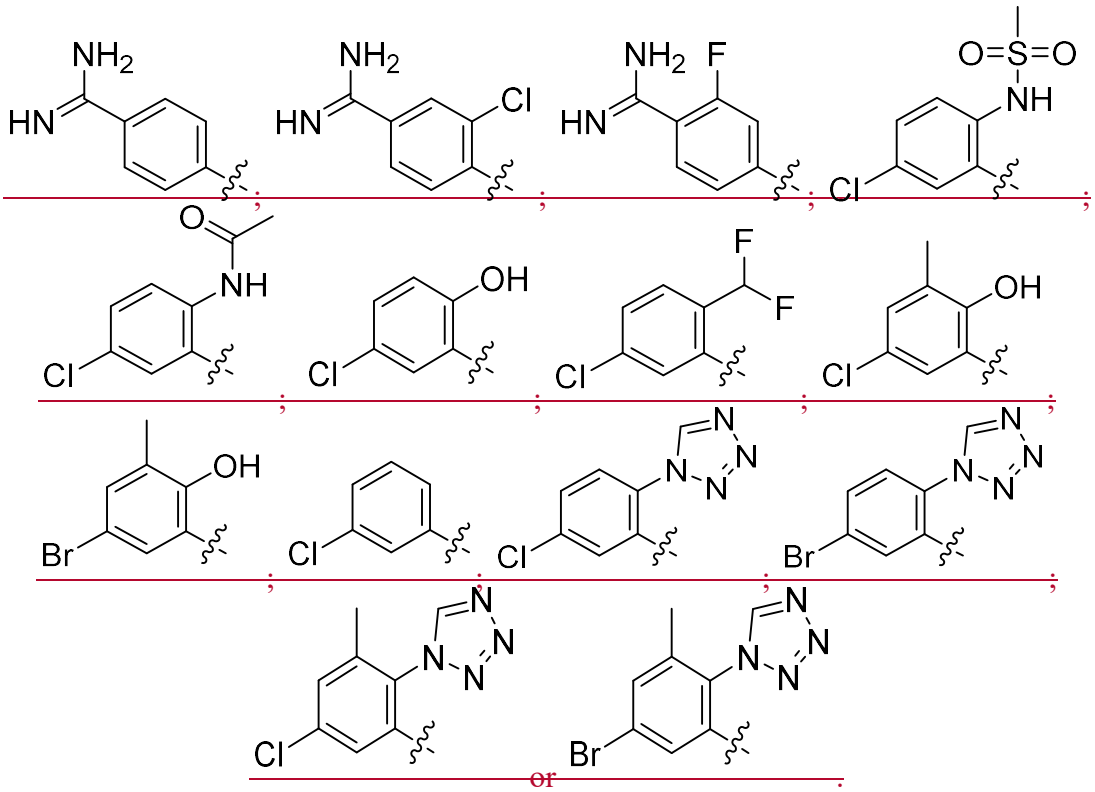
59. The compound of claim 58, wherein R^6 is substituted with at least one substituent selected from the group consisting of $-C(=NH)NH_2$, chloro, fluoro, methyl, and



60. The compound of any one of claims 57-59, wherein R^6 has one of the following structures:



61. The compound of any one of claims 51-60, wherein R^6 has one of the following structures:



62. The compound of any one of claims 51-53, wherein R^6 is an unsubstituted phenyl.

63. The compound of claim 51, wherein R^6 is a substituted or unsubstituted heteroaryl.

64. The compound of claim 51 or 63, wherein R^6 is a substituted or unsubstituted 5-10 membered heteroaryl.

65. The compound of claim 51 or 63-64, wherein R^6 is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolopyridinyl, a substituted or unsubstituted imidazopyridinyl, a substituted or unsubstituted thienopyridinyl, a substituted or unsubstituted benzoimidazolyl, a substituted or unsubstituted isoindolinyl, or a substituted or unsubstituted benzothiazolyl.

66. The compound of any one of claims 51 or 63-65, wherein R^6 is a heteroaryl substituted with one or more of R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} wherein R^{6a}, R^{6b}, R^{6c}, R^{6d},

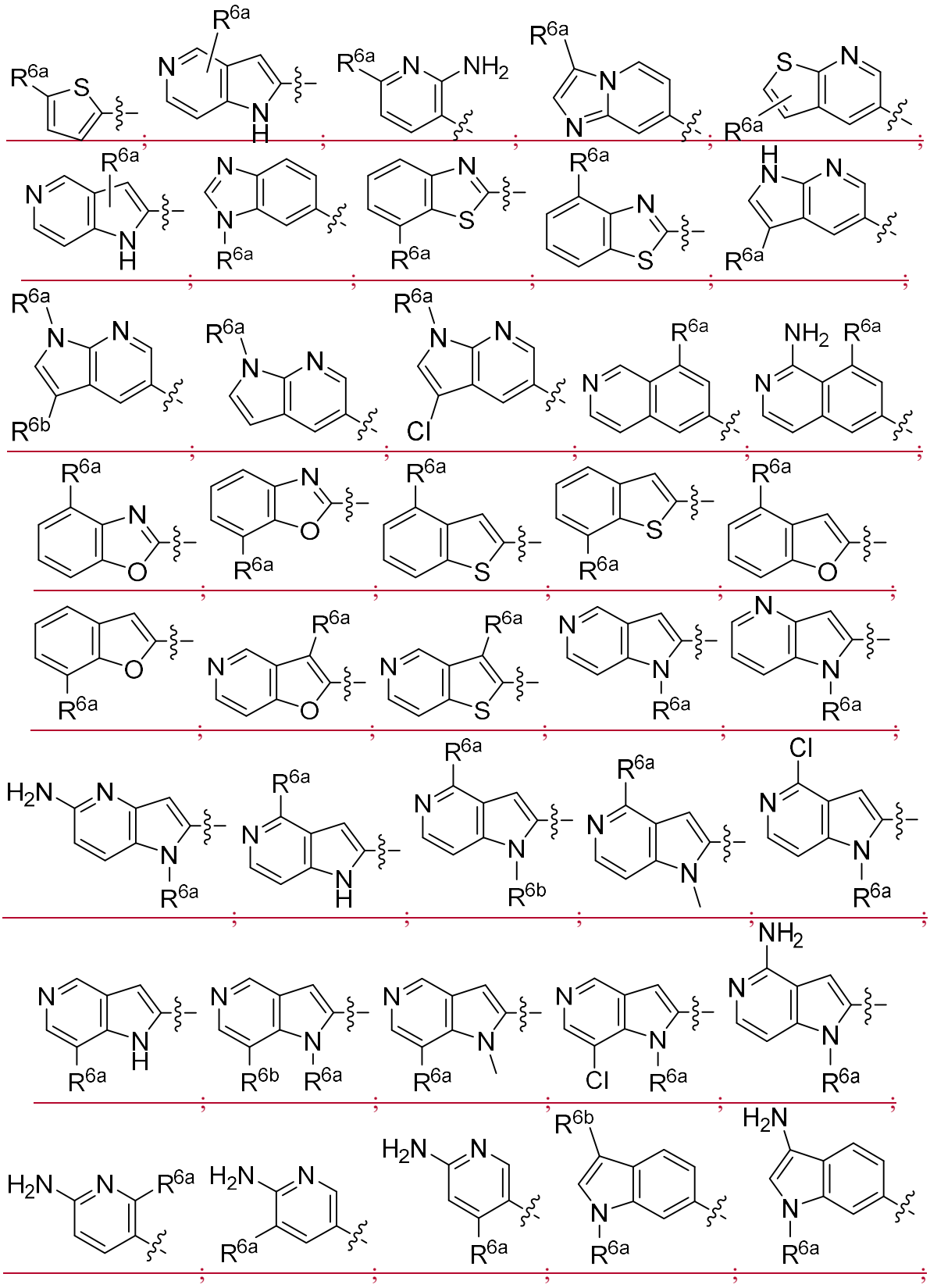
and R^{6e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^e$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^e$, $C(=NOR^a)NR^bR^e$, $C(=NOC(O)R^a)NR^bR^e$, $C(=NR^a)N(R^b)C(O)OR^e$, $N(R^a)C(=NR^b)NR^eR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

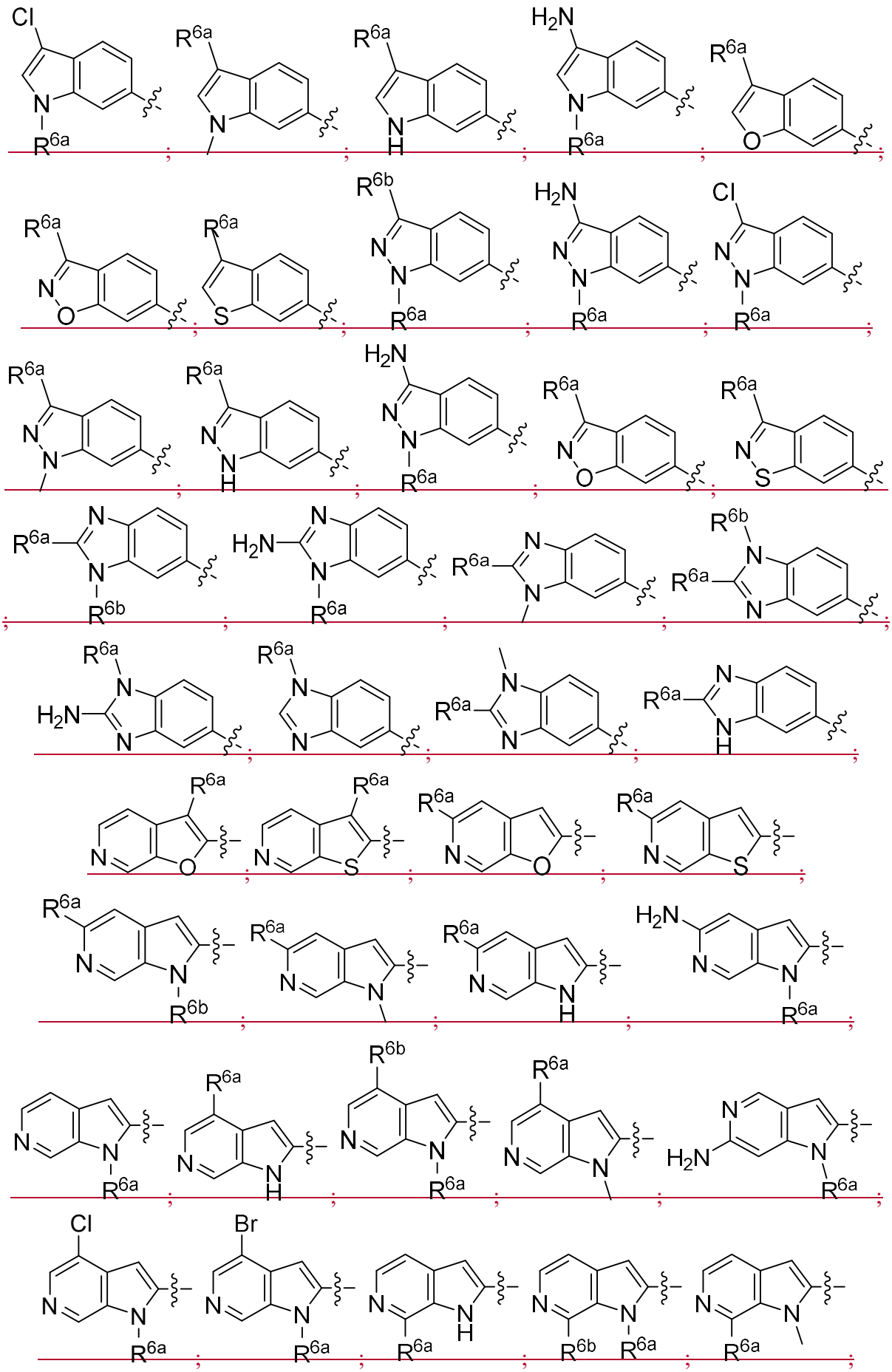
wherein R^a, R^b, R^e, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

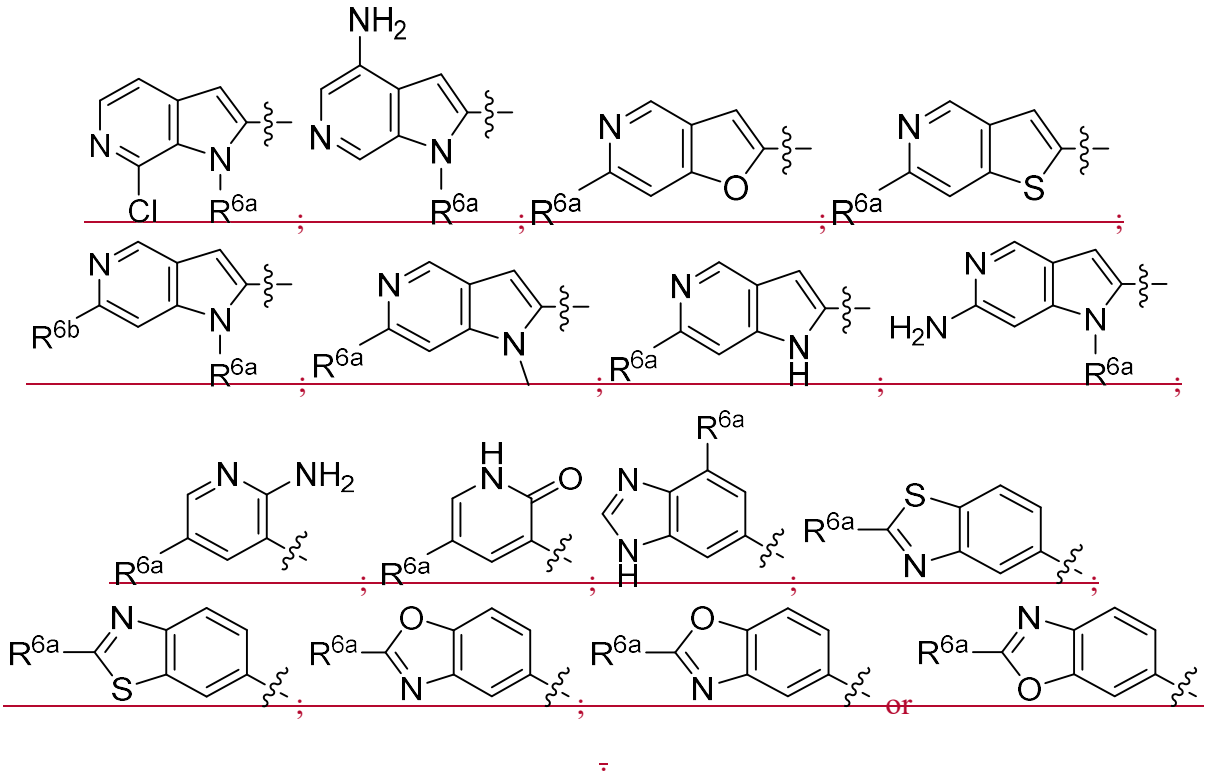
67. The compound of claim 66, wherein R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{6a}, R^{6b}, R^{6c}, R^{6d}, or R^{6e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

68. The compound of any one of claims 51 or 63-66, wherein R^6 has one of the following structures:







69. The compound of claim 68, wherein R^{6a} or R^{6b} is independently C_{1-6} alkyl, C_{1-6} deuterated alkyl, amino, or halo.

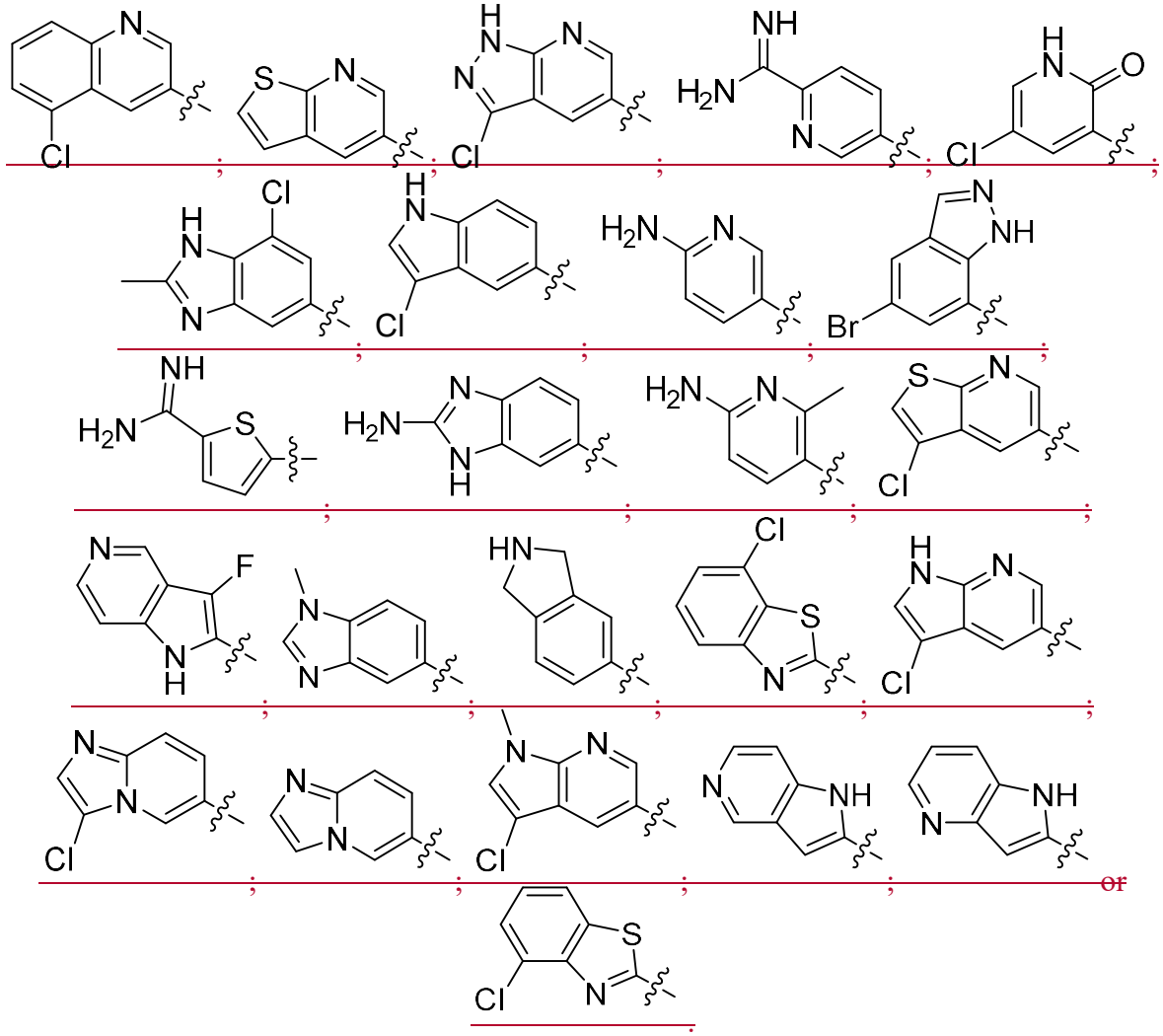
70. The compound of claim 69, wherein R^{6a} or R^{6b} is methyl.

71. The compound of claim 69, wherein R^{6a} or R^{6b} is F, Cl, or Br.

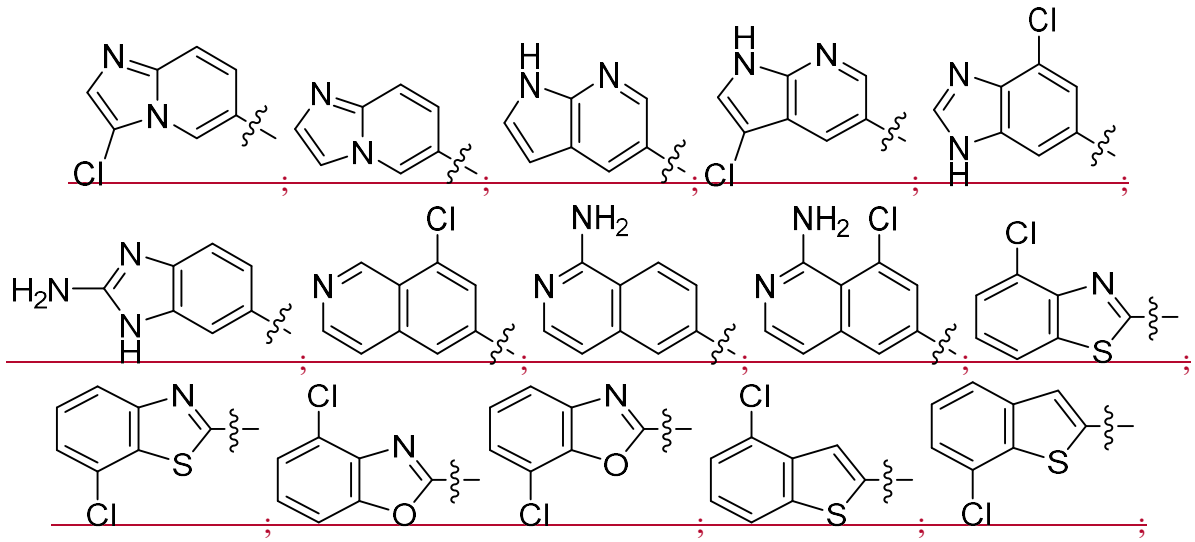
72. The compound of claim 70, wherein each R^{6a} or R^{6b} attached to nitrogen is C_{1-6} alkyl.

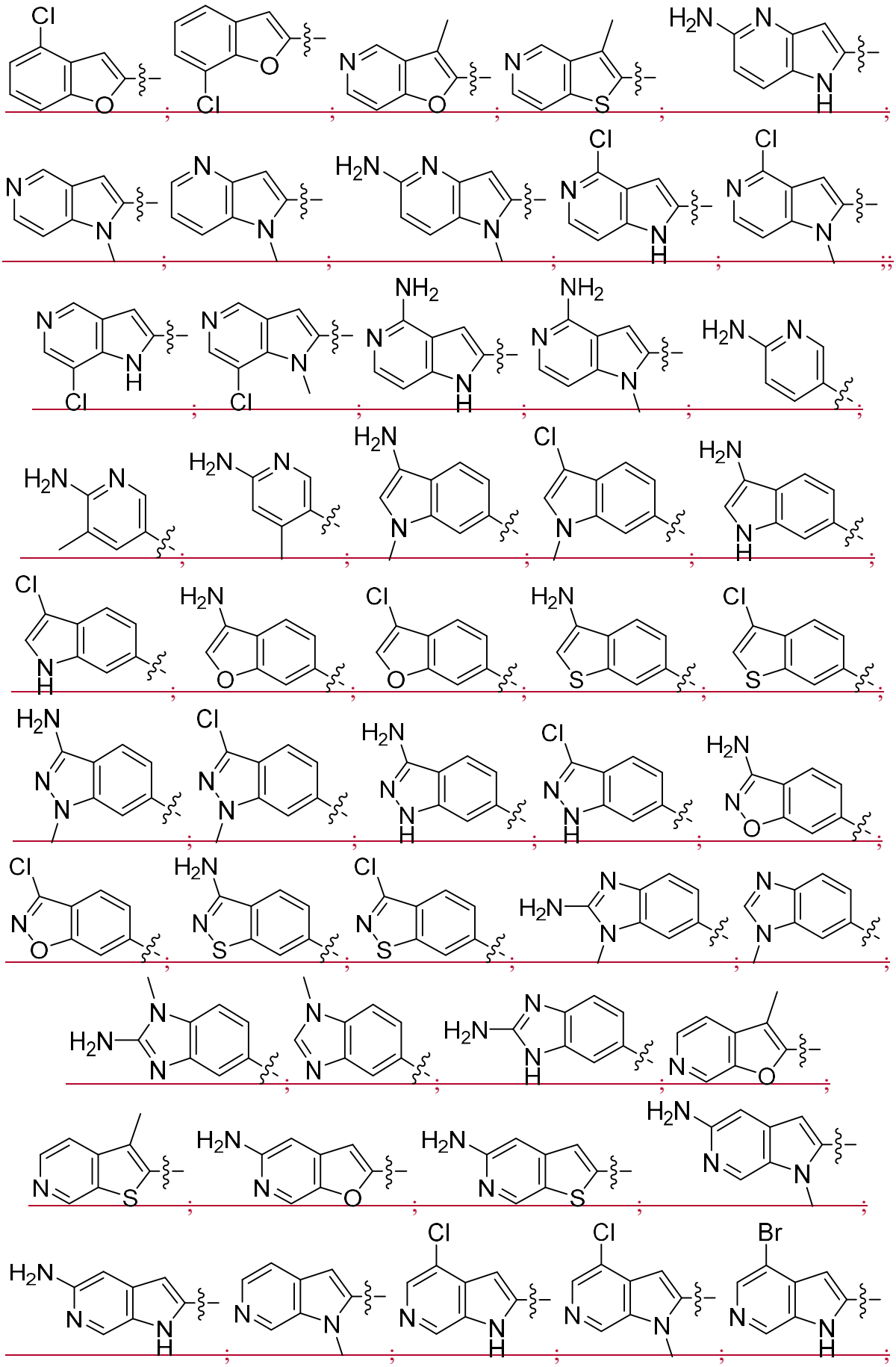
73. The compound of claim 72, wherein R^{6a} or R^{6b} is methyl or ethyl.

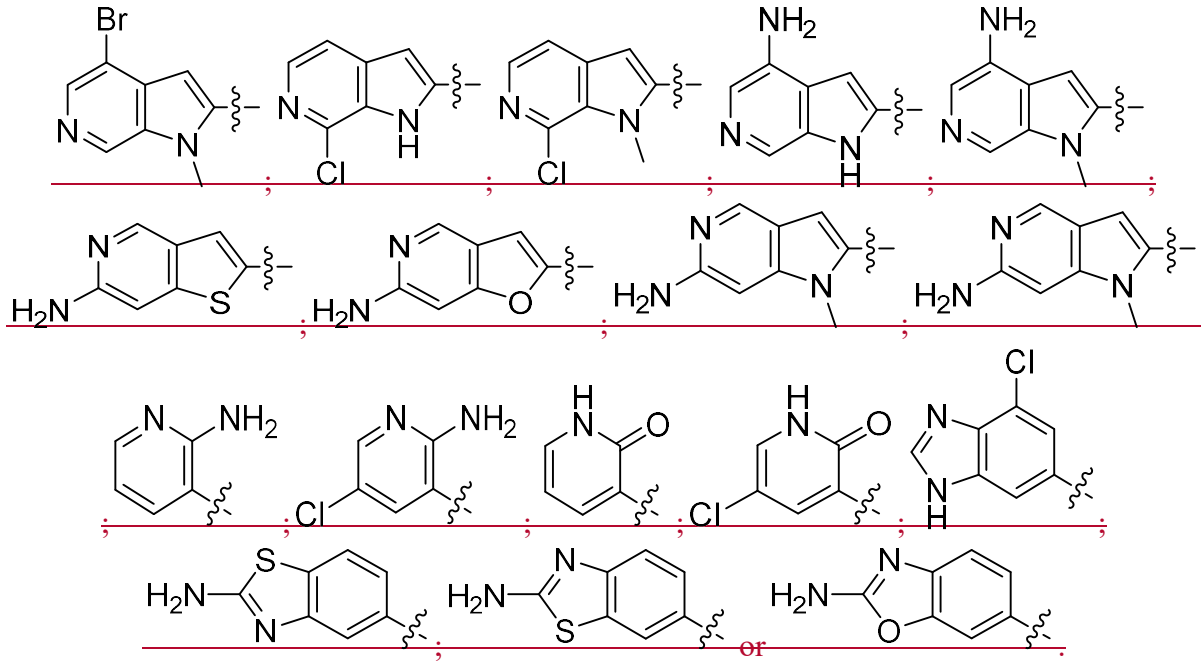
74. The compound of any one of claims 51 or 53-67, wherein R^6 has one of the following structures:



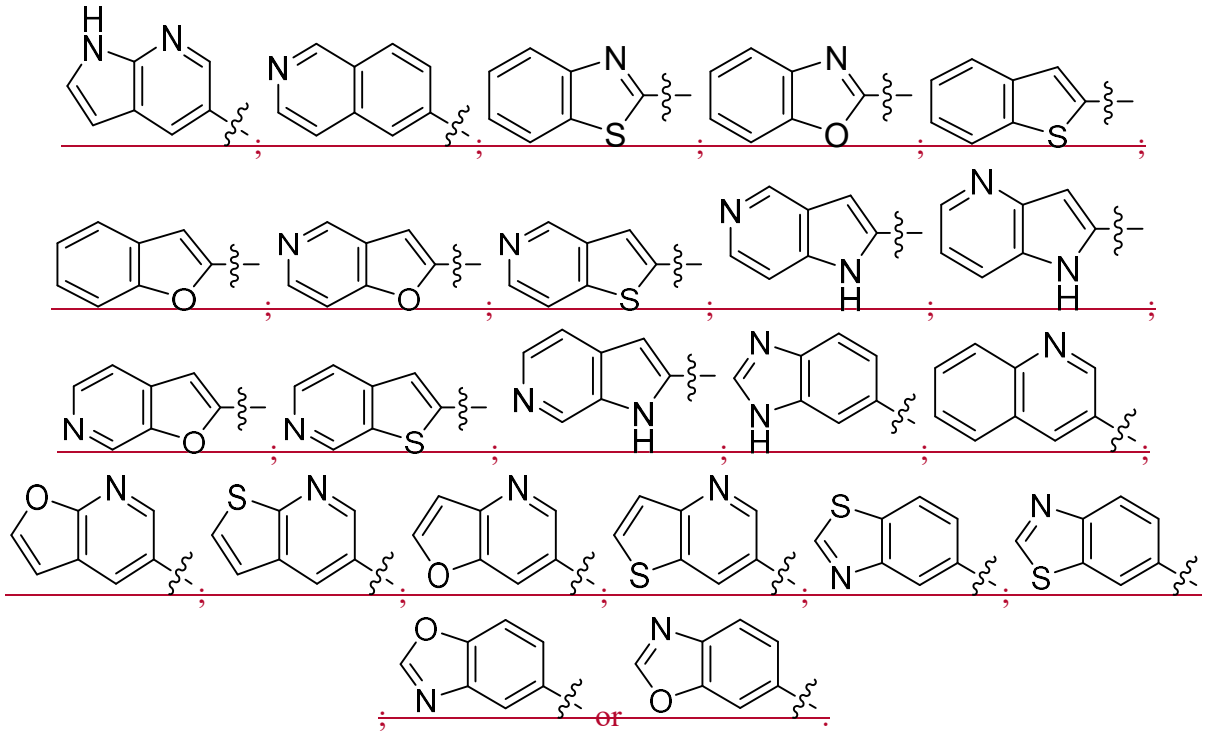
~~75. The compound of any one of claims 51 or 63-65, wherein R^6 has one of the following structures:~~







~~76. The compound of any one of claims 51 or 63-65, wherein R^6 has one of the following structures:~~

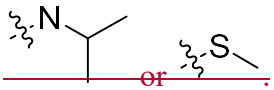


~~77. The compound of any one of claims 51-76, wherein R^7 is C_1-C_6 alkyl.~~

~~78. The compound of claim 77, wherein R^7 is methyl.~~

79. The compound of any one of claims 51-76, wherein R^7 is $-NR^{10a}R^{10b}$ or $-SR^{10c}$.

80. The compound of claim 79, wherein R^7 has one of the following structures:



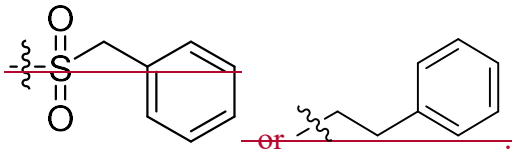
or .

81. The compound of any one of claims 51-76, wherein R^7 is a substituted or unsubstituted aryl.

82. The compound of claim 81, wherein R^7 is an unsubstituted phenyl.

83. The compound of any one of claims 51-82, wherein R^8 is hydrogen, C_1-C_6 alkyl, unsubstituted $-S(O)_2$-arylalkyl, or an unsubstituted arylalkyl.

84. The compound of claim 83, wherein R^8 is hydrogen, $-CH_3$, or has one of the following structures:

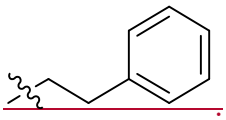


or .

85. The compound of any one of claims 51-84, wherein R^9 is a substituted or unsubstituted arylalkyl.

86. The compound of claim 85, wherein R^9 is an unsubstituted arylalkyl.

87. The compound of claim 85 or 86, wherein R^9 has the following structure:

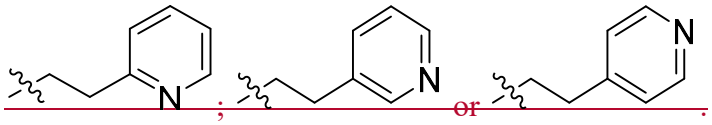


.

~~88. The compound of any one of claims 51-87, wherein R^9 is a substituted or unsubstituted heteroarylalkyl.~~

~~89. The compound of claim 88, wherein R^9 is an unsubstituted heteroarylalkyl.~~

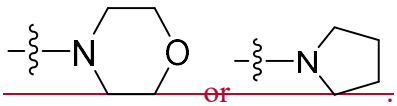
~~90. The compound of claim 88 or 89, wherein R^9 has one of the following structures:~~



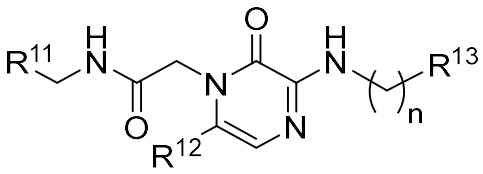
~~91. The compound of any one of claims 51-82, wherein R^8 and R^9, together with the nitrogen to which they are attached form an optionally substituted 4-7 membered heterocyclyl.~~

~~92. The compound of claim 91, wherein R^8 and R^9, together with the nitrogen to which they are attached, form an optionally substituted 4, 5, or 6 membered heterocyclyl.~~

~~93. The compound of claim 90 or 91, wherein R^8 and R^9, together with the nitrogen to which they are attached, forms one of the following structures:~~



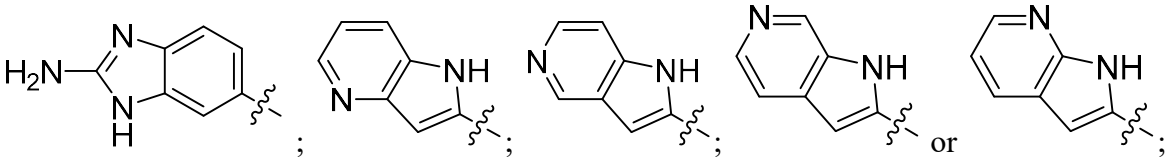
2094. A compound having the following Structure (III):



(III)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^{11} has one of the following structures:



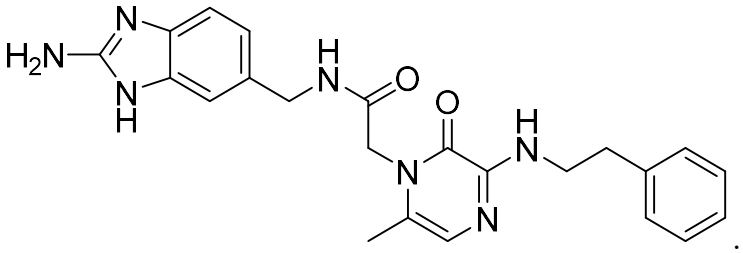
R^{12} is methyl, alkoxy, or halo;

R^{13} is a substituted or unsubstituted aryl; and

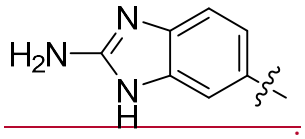
n is 1 or 2

provided that:

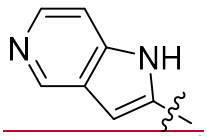
the compound of Structure (III) does not have the following structure:



~~95. The compound of claim 94, wherein R^{11} has the following structure:~~



~~96. The compound of claim 94, wherein R^{11} has the following structure:~~



~~97. The compound of any one of claims 94-96, wherein R^{12} is methyl.~~

~~98. The compound of any one of claims 94-96, wherein R^{12} is halo or butoxy.~~

~~99. The compound of claim 98, wherein R^{12} is Br.~~

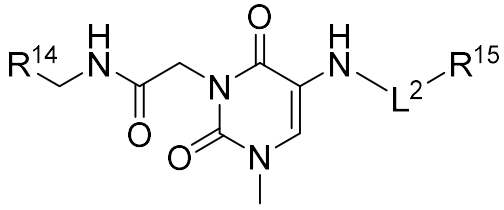
~~100. The compound of any one of claims 94-99, wherein n is 1.~~

~~101. The compound of any one of claims 94-99, wherein n is 2.~~

~~102. The compound of any one of claims 94-99, wherein R^{13} is a substituted or unsubstituted phenyl.~~

~~103. The compound of claim 102, wherein R^{13} is an unsubstituted phenyl.~~

21~~04~~. A compound having the following Structure (IV):



(IV)

or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof, wherein:

R^{14} is a substituted or unsubstituted aryl or a substituted or unsubstituted heteroaryl;

R^{15} is a substituted or unsubstituted arylalkyl, or a substituted or unsubstituted heteroarylalkyl;

L^2 is a direct bond, -C(=O), or -$S(=O)_t$-; and

t is 0, 1, or 2.

~~105. The compound of claim 104, wherein R^{14} is a substituted or unsubstituted aryl.~~

~~106. The compound of claim 104 or 105, wherein R^{14} is a substituted or unsubstituted C_6-C_{10} aryl.~~

~~107. The compound of any one of claims 104-106, wherein R^{14} is a substituted or unsubstituted phenyl.~~

108. The compound of any one of claims 104-107, wherein R^{14} is a substituted phenyl.

109. The compound of any one of claims 104-108, wherein R^{14} is phenyl substituted with one or more of R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} wherein R^{14a}, R^{14b}, R^{14c}, R^{14d}, and R^{14e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^e$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^e$, $C(=NOR^a)NR^bR^e$, $C(=NOC(O)R^a)NR^bR^e$, $C(=NR^a)N(R^b)C(O)OR^e$, $N(R^a)C(=NR^b)NR^eR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,

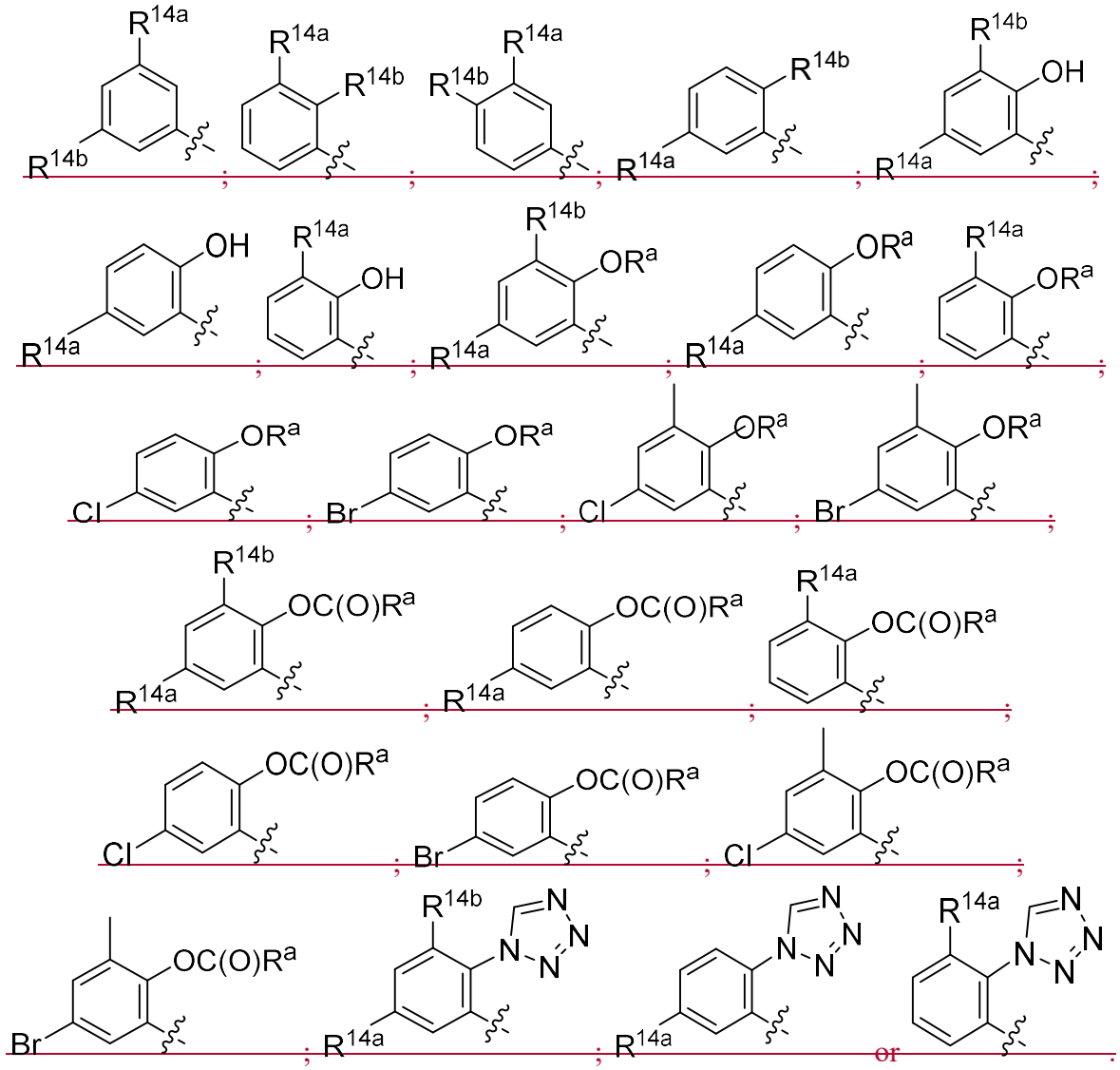
wherein R^a, R^b, R^e, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

110. The compound of claim 109, wherein R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,

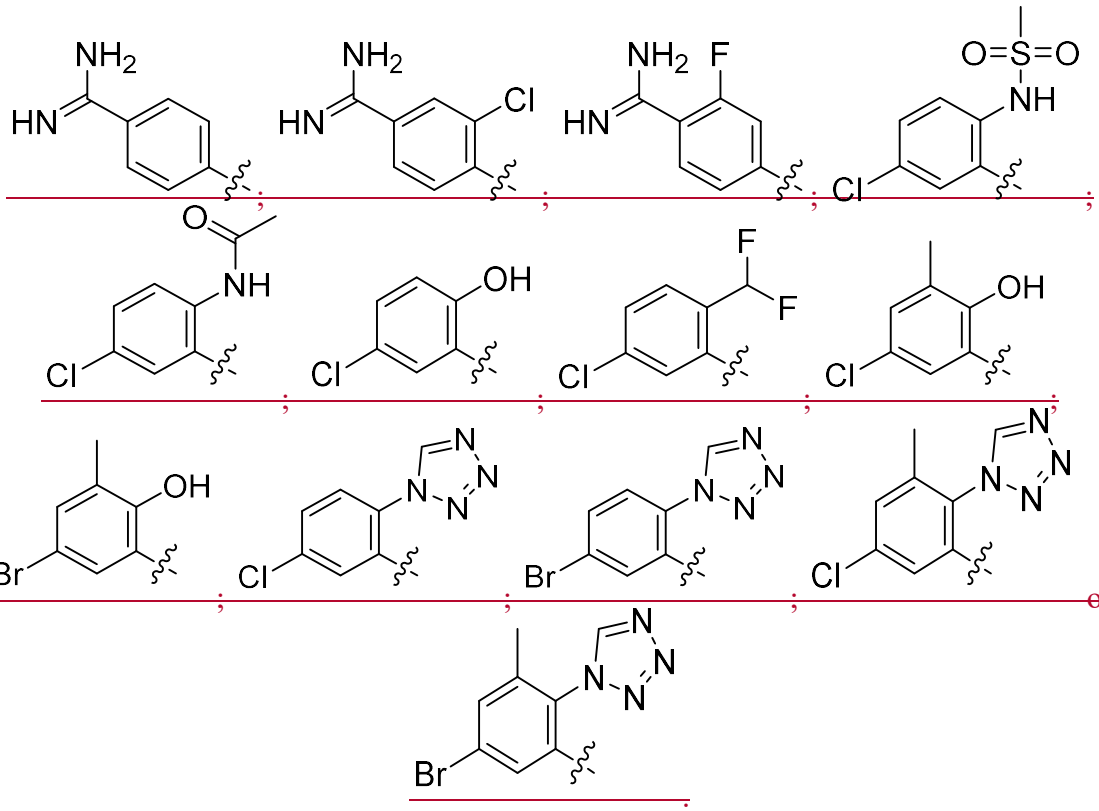
wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.

~~111. The compound of any one of claims 104-110, wherein R^{14} is phenyl substituted with at least one substituent selected from the group consisting of halo, alkyl, hydroxy, amino, and $C(=NR^a)NR^bR^e$.~~

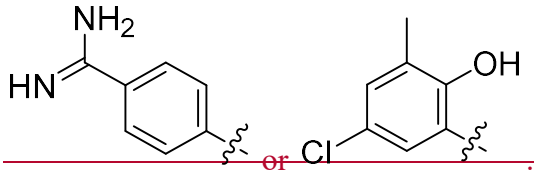
~~112. The compound of any one of claims 109-111, wherein R^{14} has one of the following structures:~~



~~113. The compound of any one of claims 104-111, wherein R^{14} has one of the following structures:~~



114. The compound of claim 109, wherein R^{14} has one of the following structures:



115. The compound of any one of claims 104-109, wherein R^{14} is an unsubstituted phenyl.

116. The compound of claim 104, wherein R^{14} is a substituted or unsubstituted heteroaryl.

117. The compound of claim 104 or 116, wherein R^{14} is a substituted or unsubstituted 5-10 membered heteroaryl.

~~118. The compound of claim 104 or 116-117, wherein R^{14} is a substituted or unsubstituted pyridinyl, a substituted or unsubstituted pyrrolopyridinyl, a substituted or unsubstituted imidazopyridinyl, a substituted or unsubstituted thienopyridinyl, a substituted or unsubstituted benzoimidazolyl, a substituted or unsubstituted isoindolinyl, or a substituted or unsubstituted benzothiazolyl.~~

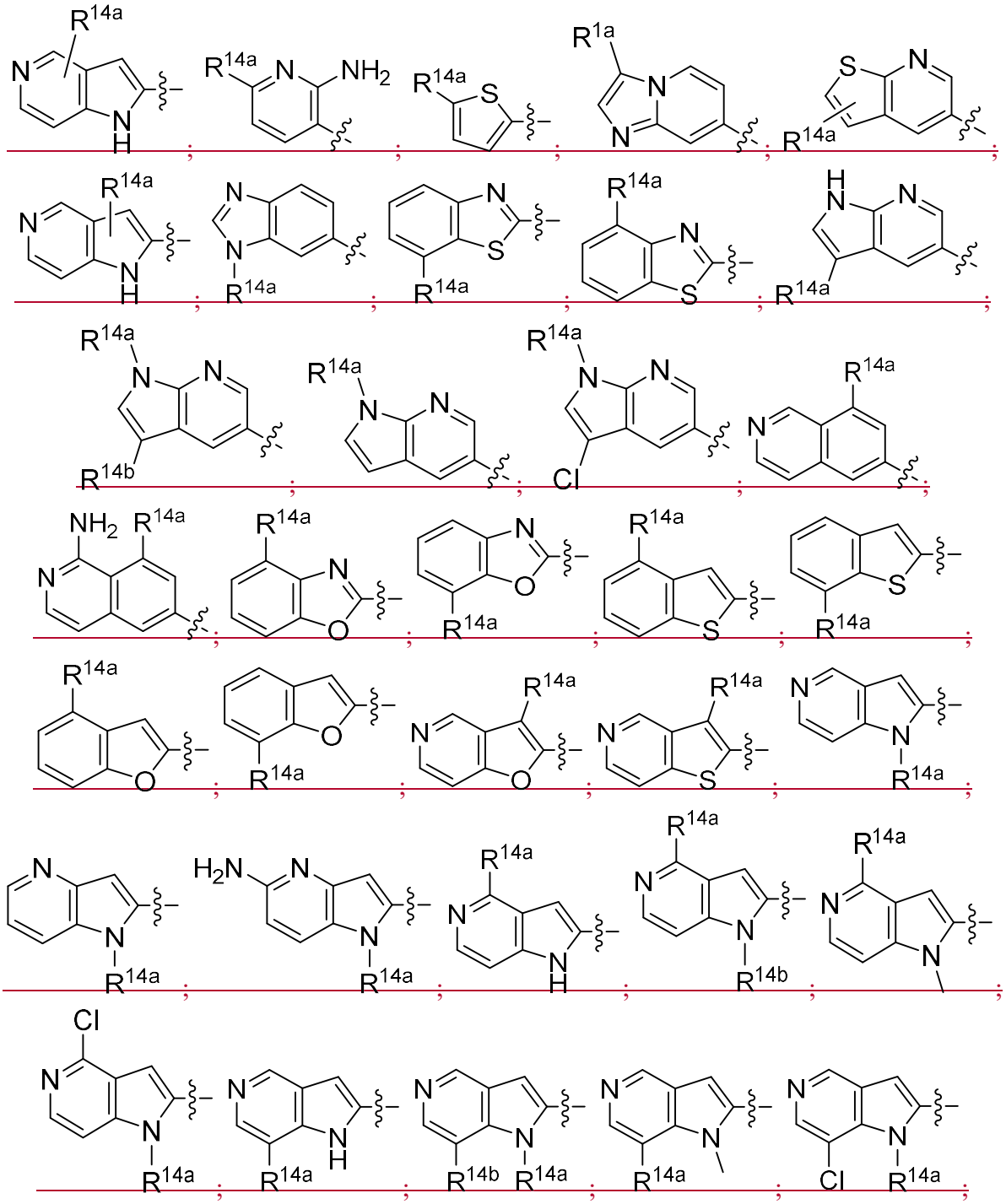
~~119. The compound of any one of claims 104 or 116-118, wherein R^{14} is a heteroaryl substituted with one or more of R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} wherein R^{14a}, R^{14b}, R^{14c}, R^{14d}, and R^{14e} are each independently selected from the group consisting of C_{1-6} alkyl, C_{1-6} deuterated alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halo, C_{1-6} haloalkyl, aminylalkyl, hydroxyalkyl, cyano, nitro, OR^a, SR^a, $C(O)R^a$, $C(O)NR^aR^b$, $C(O)OR^a$, $OC(O)R^a$, $OC(O)OR^a$, $OC(O)NR^aR^b$, NR^aR^b, $N(R^a)C(O)R^b$, $N(R^a)C(O)NR^bR^c$, $N(R^a)C(O)OR^b$, $C(=NR^a)NR^bR^c$, $C(=NOR^a)NR^bR^c$, $C(=NOC(O)R^a)NR^bR^c$, $C(=NR^a)N(R^b)C(O)OR^c$, $N(R^a)C(=NR^b)NR^cR^d$, $S(O)R^a$, $S(O)NR^aR^b$, $S(O)_2R^a$, $N(R^a)S(O)_2R^b$, $S(O)_2NR^aR^b$, oxo, substituted or unsubstituted C_{6-10} aryl, substituted or unsubstituted C_{6-10} arylalkyl, substituted or unsubstituted C_{6-10} aryloxy, substituted or unsubstituted C_{6-10} arylalkoxy, substituted or unsubstituted 5-10 membered heteroaryl, substituted or unsubstituted C_{3-10} cycloalkyl, and substituted or unsubstituted 4-10 membered heterocyclyl,~~

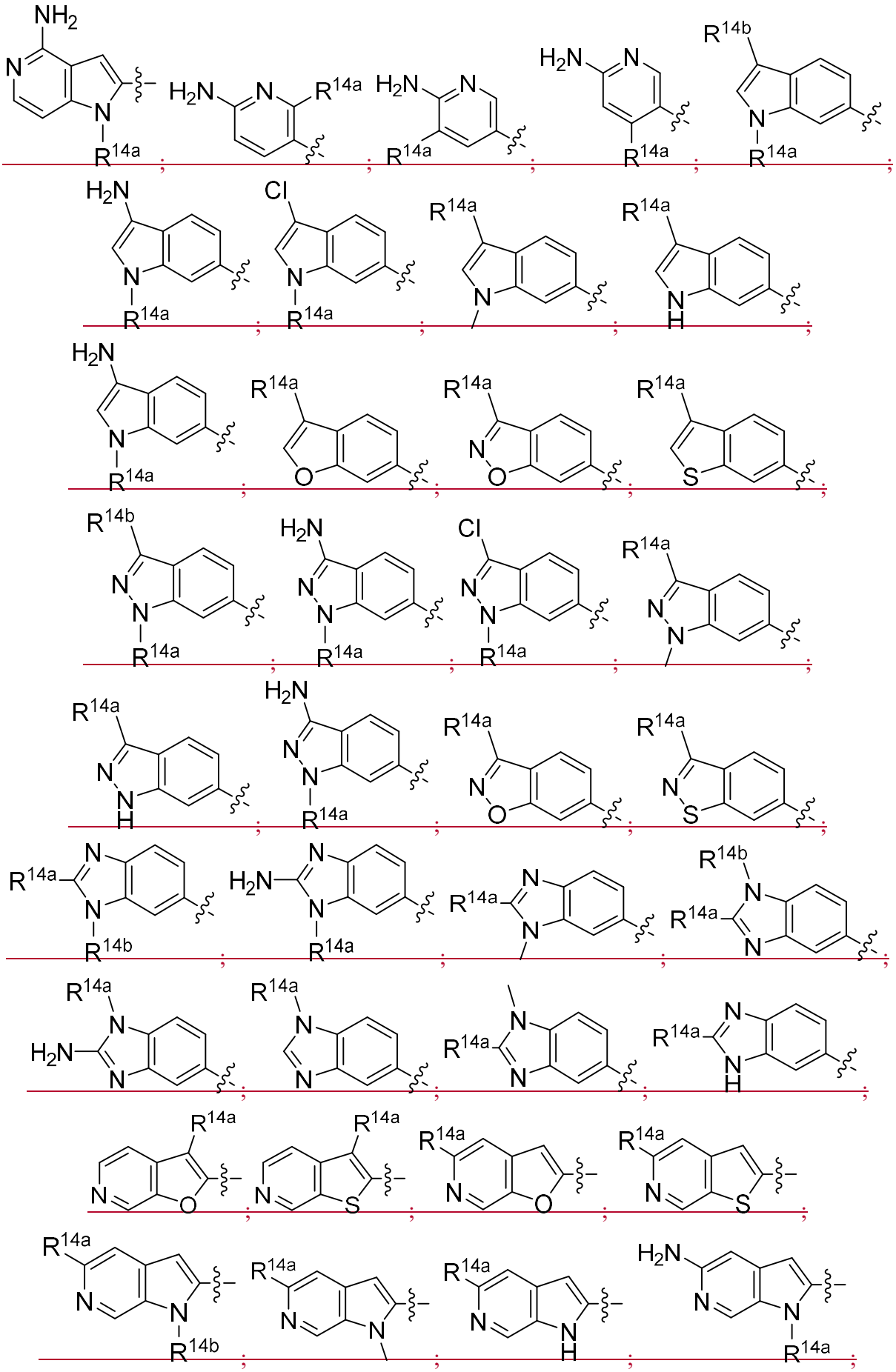
~~wherein R^a, R^b, R^c, and R^d, are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.~~

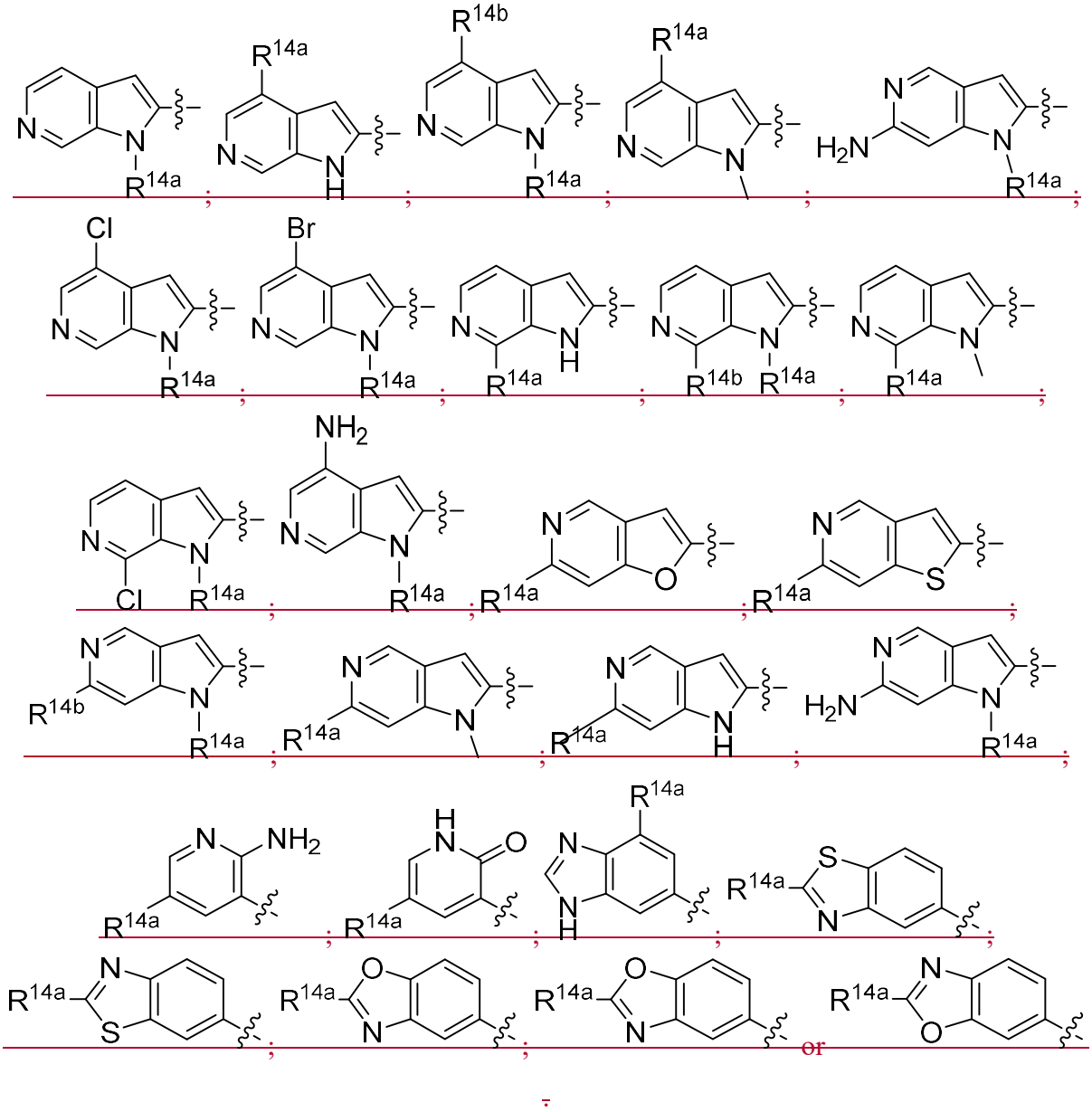
~~120. The compound of claim 119, wherein R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} is optionally substituted with one or more substituents selected from the group consisting of halo, CN, OR^e, SR^e, $C(O)R^e$, $C(O)NR^eR^f$, $C(O)OR^e$, $OC(O)R^e$, $OC(O)NR^eR^f$, NR^eR^f, $NR^eC(O)R^f$, $NR^eC(O)NR^fR^g$, $NR^eC(O)OR^f$, $C(=NR^e)NR^fR^g$, $NR^eC(=NR^f)NR^gR^h$, $S(O)R^e$, $S(O)NR^eR^f$, $S(O)_2R^e$, $NR^eS(O)_2R^f$, $S(O)_2NR^eR^f$ and oxo when R^{14a}, R^{14b}, R^{14c}, R^{14d}, or R^{14e} is a substituted C_{6-10} aryl, a substituted C_{6-10} arylalkyl, a substituted C_{6-10} aryloxy, a substituted C_{6-10} arylalkoxy, a substituted 5-10 membered heteroaryl, a substituted C_{3-10} cycloalkyl, and a substituted 4-10 membered heterocyclyl,~~

~~wherein R^e, R^f, R^g, and R^h are, at each occurrence, independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, hydroxyl, C_{1-6} alkoxy, aryl, arylalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} hydroxyalkyl, cycloalkyl, heterocyclyl, and heteroaryl.~~

~~121. The compound of any one of claims 104 or 116-120, wherein R^{14} has one of the following structures:~~







122. The compound of claim 121, wherein R^{14a} or R^{14b} is independently C_{1-6} alkyl, amino, or halo.

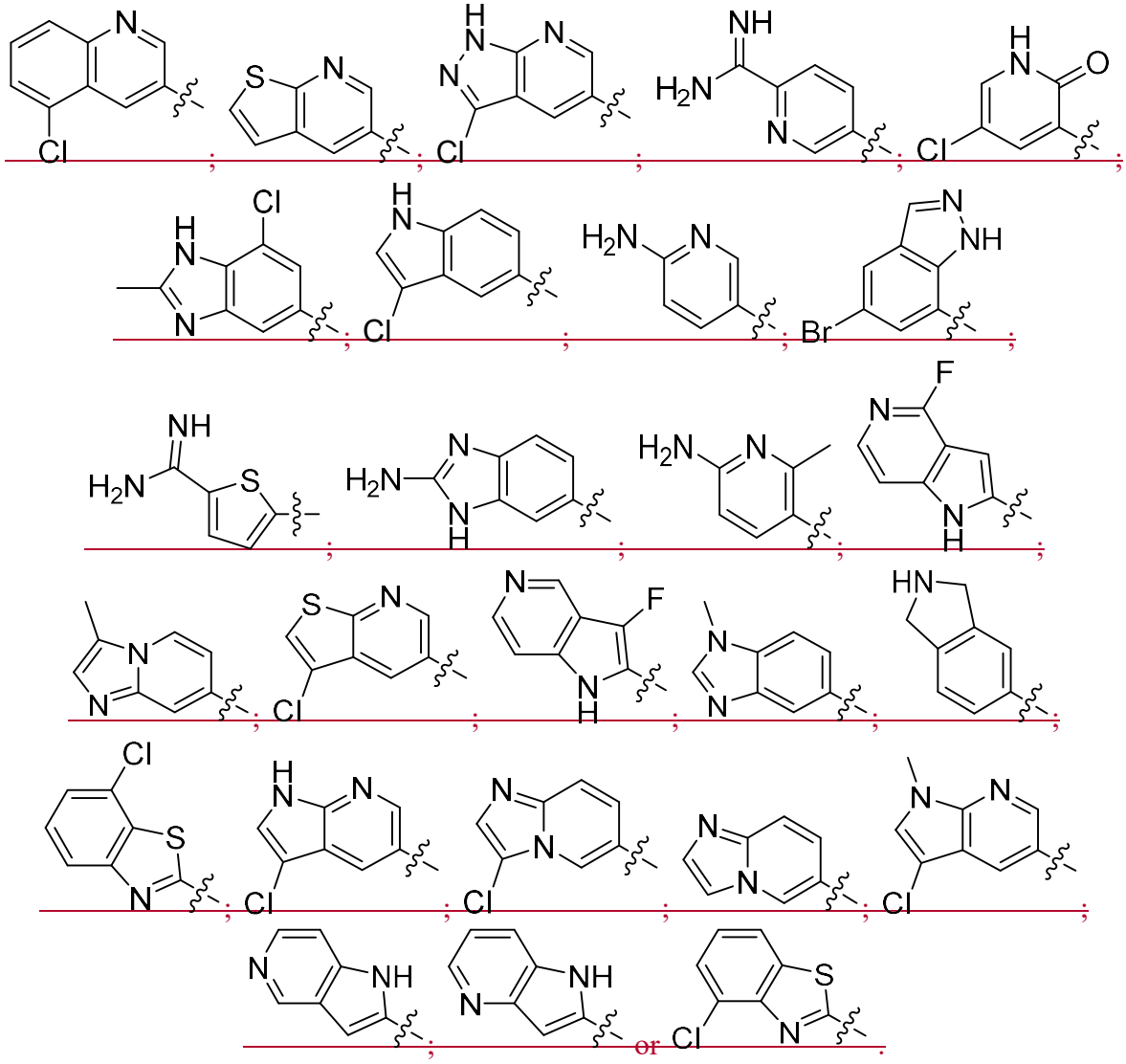
123. The compound of claim 122, wherein R^{14a} or R^{14b} is methyl.

124. The compound of claim 122, wherein R^{14a} or R^{14b} is F, Cl, or Br.

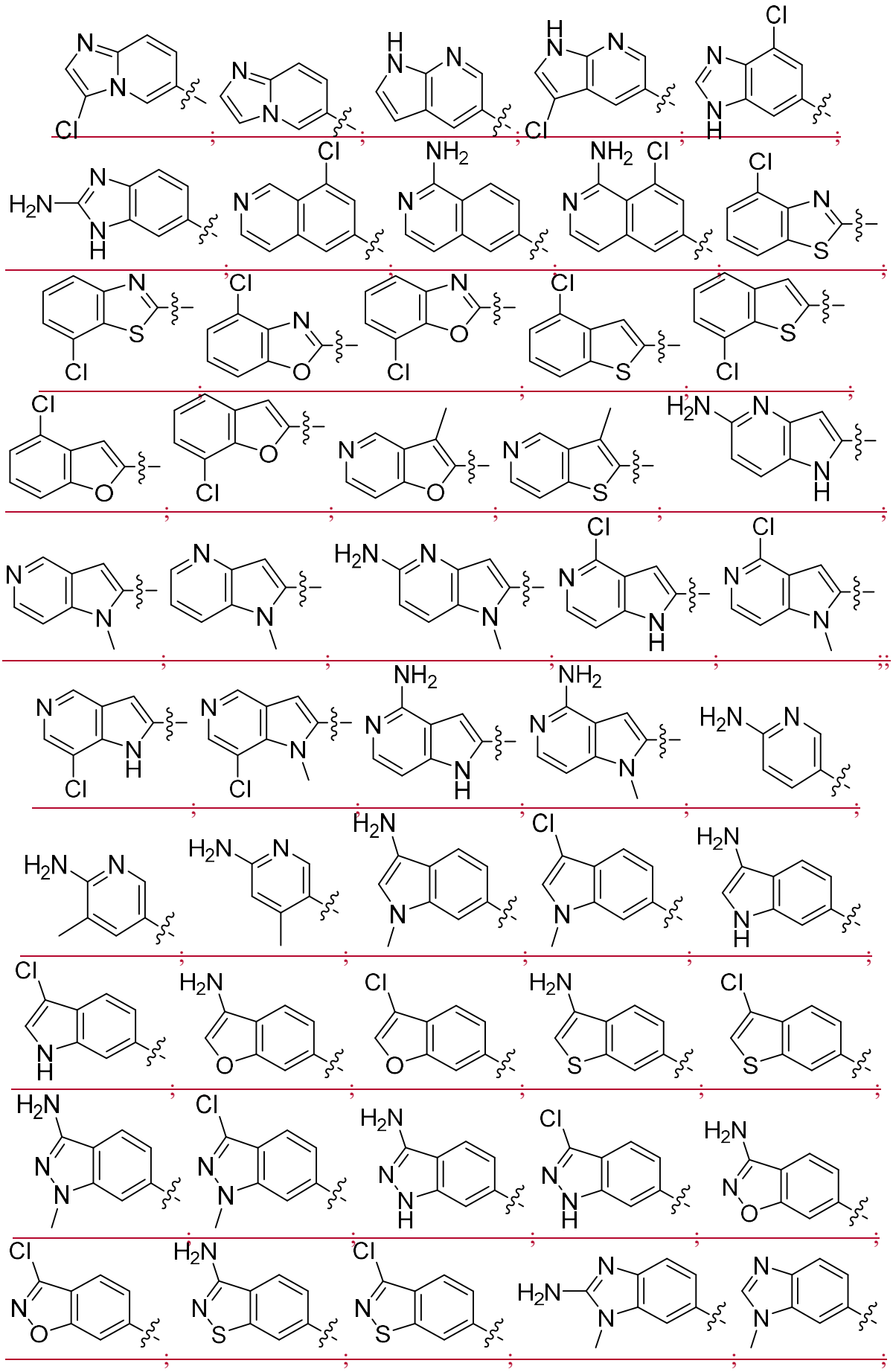
125. The compound of claim 122, wherein each R^{14a} or R^{14b} attached to nitrogen is C_{1-6} alkyl.

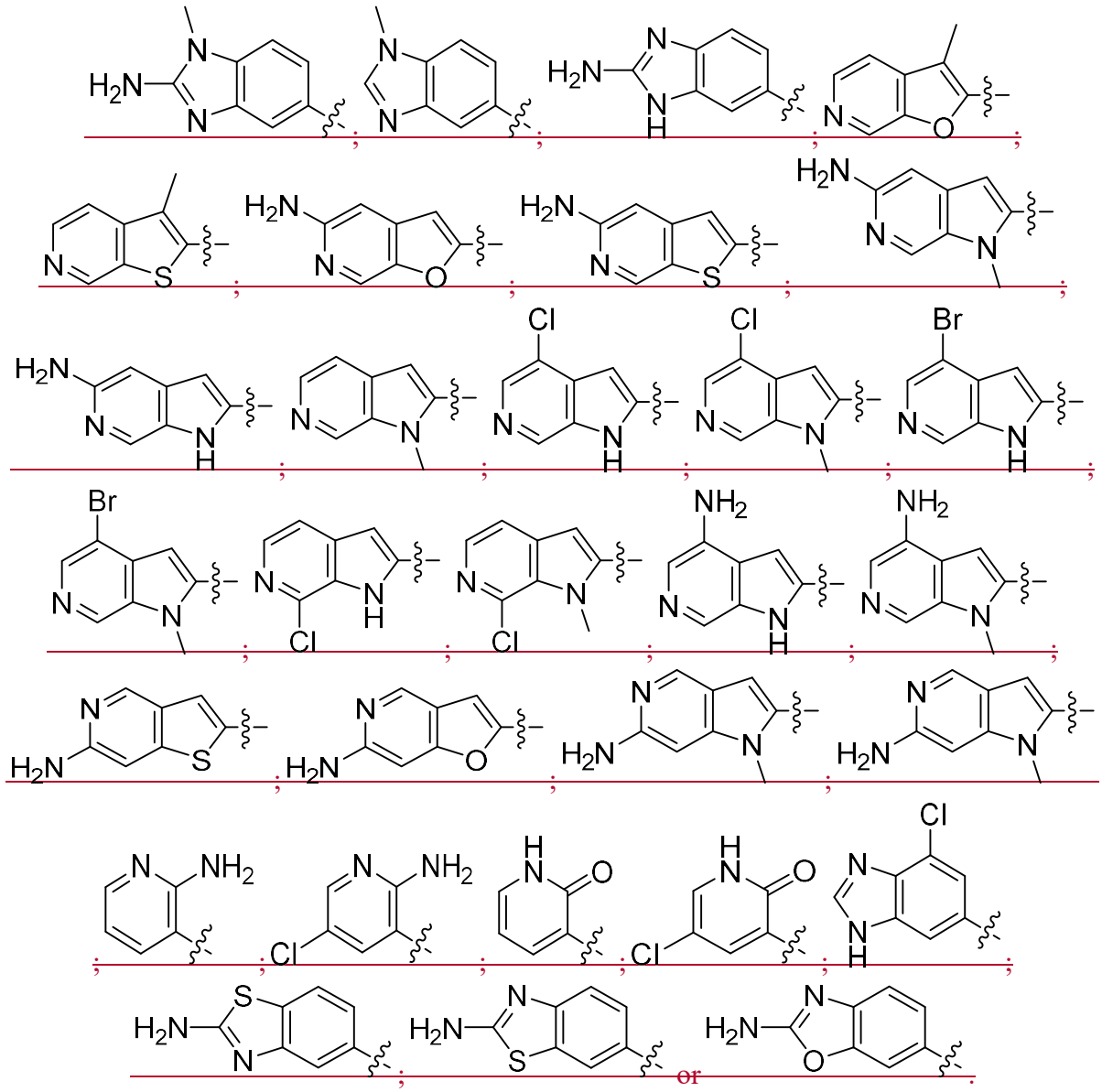
~~126. The compound of claim 125, wherein R^{14a} or R^{14b} is methyl or ethyl.~~

~~127. The compound of any one of claims 104 or 116-118, wherein R^{14} has one of the following structures:~~

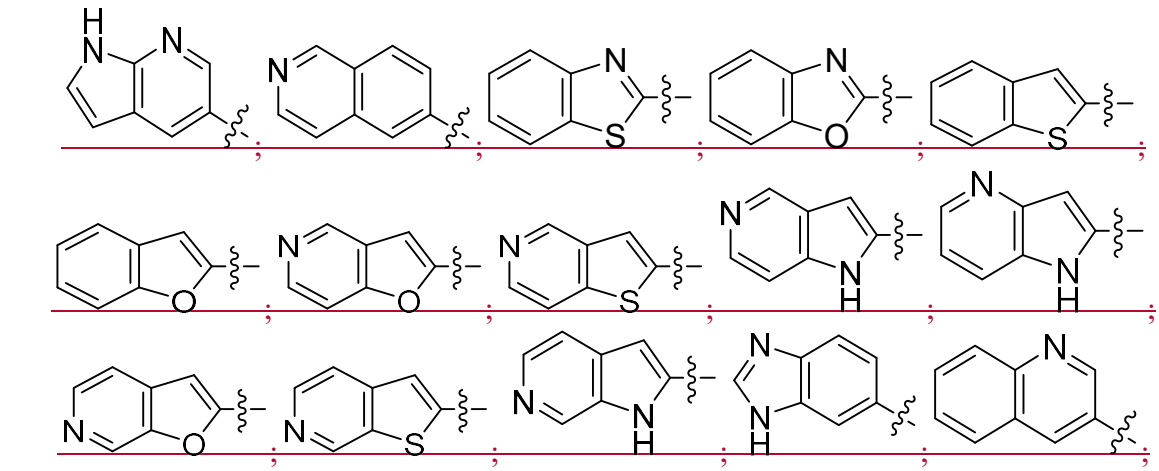


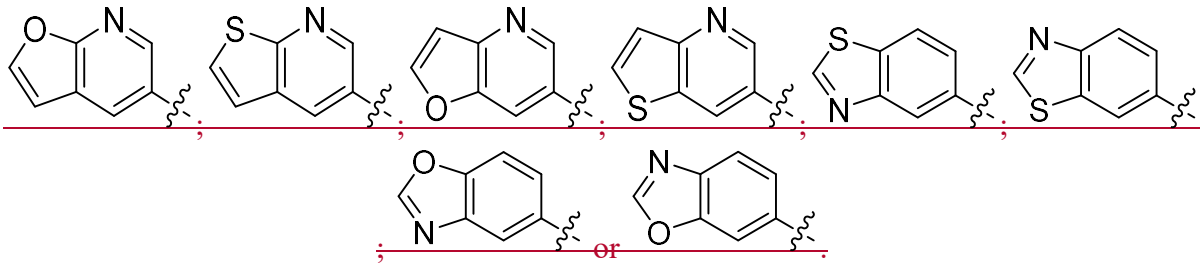
~~128. The compound of any one of claims 104 or 116-118, wherein R^{14} has one of the following structures:~~





~~129. The compound of any one of claims 104 or 116-118, wherein R^{14} has one of the following structures:~~

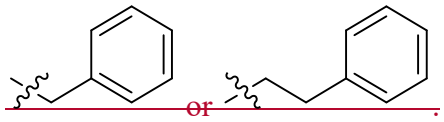




130. The compound of any one of claims 104-129, wherein R^{15} is a substituted or unsubstituted arylalkyl.

131. The compound of any one of claims 104-130, wherein R^{15} is an unsubstituted arylalkyl.

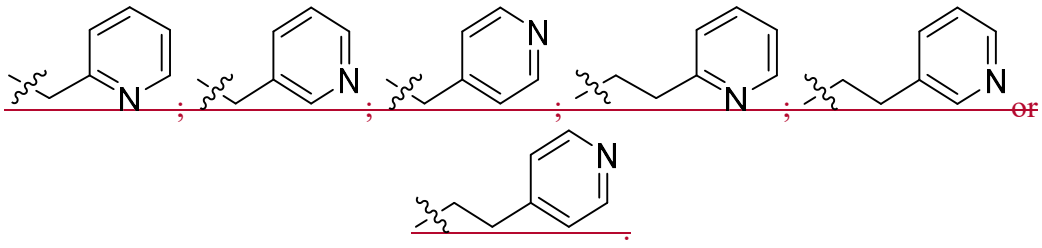
132. The compound of any one of claims 104-131, wherein R^{15} has one of the following structures:



133. The compound of any one of claims 104-129, wherein R^{15} is a substituted or unsubstituted heteroarylalkyl.

134. The compound of any one of claims 104-129 or 133, wherein R^{15} is an unsubstituted heteroarylalkyl.

135. The compound of any one of claims 104-129 or 133-134, wherein R^{15} has one of the following structures:



~~136. The compound of any one of claims 104-135, wherein L^2 is a direct bond.~~

~~137. The compound of any one of claims 104-135, wherein L^2 is -C(=O)-.~~

~~138. The compound of any one of claims 104-135, wherein L^2 is $-S(=O)_2-$.~~

~~139. The compound of any one of claims 104-135, wherein L^2 is -S-.~~

~~140. The compound of any one of claims 104-135, wherein L^2 is -S(O)-.~~

22~~141~~. A compound having a structure found in Table 1 or a stereoisomer, tautomer, or pharmaceutically acceptable salt thereof.

23~~142~~. A pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof of ~~any one of~~ claim~~s~~ 1 ~~to 141~~ and a pharmaceutically acceptable carrier or excipient.

24~~143~~. ~~A method for treating a MASP-2-associated disease or disorder in a subject in need thereof, the method comprising administering to the subject an effective amount~~ Use of a compound of ~~any one of~~ claim~~s~~ 1~~,-141 or a pharmaceutical composition according to claim 142~~ in the manufacture of a medicament for treating a MASP-2-associated disease or disorder in a subject in need thereof.

~~144. The method of claim 143, wherein the compound is administered in an amount sufficient to inhibit MASP-2 dependent complement activation in the subject.~~

~~145. The method of claim 143, wherein the subject has been diagnosed as being in need of treatment for a lectin complement-associated disease or disorder.~~

~~146. The method of claim 143, wherein disease or disorder is a thrombotic microangiopathy (TMA), a renal condition, an inflammatory reaction resulting from tissue or organ transplantation, an ischemia reperfusion injury, a complication associated with diabetes, a cardiovascular disease or disorder, an inflammatory gastrointestinal disorder, a pulmonary disorder, an ophthalmic disease or disorder, disseminated intravascular coagulation, graft-versus-host disease, veno-occlusive disease, diffuse alveolar hemorrhage, idiopathic pneumonia syndrome, capillary leak syndrome, engraftment syndrome, fluid overlaod, or combinations thereof.~~

~~147. The method of claim 143, wherein the disease or disorder is a thrombotic microangiopathy (TMA) thrombotic thrombocytopenic purpura (TTP), refractory TTP, Upshaw-Schulman Syndrome (USS), hemolytic uremic syndrome (HUS), atypical hemolytic syndrome (aHUS), non-Factor H-dependent atypical hemolytic syndrome, aHUS secondary to an infection, plasma therapy-resistant aHUS, a TMA secondary to cancer, a TMA secondary to chemotherapy, a TMA secondary to transplantation, a TMA associated with hematopoietic stem cell transplant, or combinations thereof.~~

~~148. The method of claim 143, wherein the disease or disorder is graft-versus-host disease.~~

~~149. The method of claim 143, wherein the disease or disorder is diffuse alveolar hemorrhage (DAH).~~

~~150. The method of claim 143, wherein the disease or disorder is veno-occlusive disease (VOD).~~

~~151. The method of claim 143, wherein the disease or disorder is a renal condition.~~

~~152. The method of claim 143, wherein the renal condition is mesangioproliferative glomerulonephritis, membranous glomerulonephritis,~~

~~membranoproliferative glomerulonephritis (mesangiocapillary glomerulonephritis), acute post infectious glomerulonephritis (poststreptococcal glomerulonephritis), C3 glomerulopathy, cryoglobulinemic glomerulonephritis, pauci-immune necrotizing crescentic glomerulonephritis, lupus nephritis, Henoch-Schonlein purpura nephritis, IgA nephropathy, or combinations thereof.~~

~~153. The method of claim 143, wherein the disease or disorder is renal fibrosis, proteinuria, or combinations thereof.~~

~~154. The method of claim 143, wherein the disease or disorder is an inflammatory reaction resulting from tissue or solid organ transplantation.~~

~~155. The method of claim 143, wherein the disease or disorder is an ischemia reperfusion injury (I/R).~~

~~156. The method of claim 143, wherein the disease or disorder is a complication associated with non-obese diabetes, complications associated with Type-1 diabetes, Type-2 (adult onset) diabetes, or combinations thereof.~~

~~157. The method of claim 143, wherein the disease or disorder is a cardiovascular disease or disorder.~~

~~158. The method of claim 143, wherein the disease or disorder is an inflammatory gastrointestinal disorder.~~

~~159. The method of claim 143, wherein the disease or disorder is a pulmonary disorder.~~

~~160. The method of claim 143, wherein the disease or disorder is an extracorporeal exposure-triggered inflammatory reaction.~~

~~161. The method of claim 160, wherein the method further comprises treating a subject undergoing an extracorporeal circulation procedure.~~

~~162. The method of claim 143, wherein the disease or disorder is an inflammatory arthritis, non-inflammatory arthritis, a musculoskeletal disorder, or combinations thereof.~~

~~163. The method of claim 143, wherein the disease or disorder is a skin disorder.~~

~~164. The method of claim 143, wherein the disease or disorder is peripheral nervous system (PNS) disorder or injury, a central nervous system (CNS) disorder or injury, or combinations thereof.~~

~~165. The method of claim 143, wherein the disease or disorder is sepsis or a condition resulting from sepsis.~~

~~166. The method of claim 143, wherein the disease or disorder is a urogenital disorder.~~

~~167. The method of claim 143, wherein the disease or disorder is an inflammatory reaction in a subject being treated with chemotherapeutics, radiation therapy, or combinations thereof.~~

~~168. The method of claim 143, wherein the disease or disorder is an angiogenesis-dependent cancer.~~

~~169. The method of claim 143, wherein the disease or disorder is an angiogenesis-dependent benign tumor.~~

~~170. The method of claim 143, wherein the disease or disorder is an endocrine disorder.~~

~~171. The method of claim 143, wherein the disease or disorder is an ophthalmic disease or disorder.~~

~~172. The method of claim 143, wherein the disease or disorder is an ocular angiogenic disease or condition.~~

~~173. The method of claim 143, wherein the disease or disorder is disseminated intravascular coagulation (DIC), a complement mediated coagulation disorder, or combinations thereof.~~

~~174. The method of claim 143, wherein the disease or disorder is acute radiation syndrome, dense deposit disease, Degos Disease, Catastrophic Antiphospholipid Syndrome (CAPS), Behcet's disease, cryoglobulinemia; paroxysmal nocturnal hemoglobinuria ("PNH"), cold agglutinin disease, or combinations thereof.~~

~~175. The method of claim 143, wherein the disease or disorder is atypical hemolytic uremic syndrome (aHUS).~~

~~176. The method of claim 143, wherein the disease or disorder is hematopoietic stem cell transplant-associated TMA.~~

~~177. The method of claim 143, wherein the disease or disorder is immunoglobulin A nephropathy (IgAN).~~

~~178. The method of claim 143, wherein the disease or disorder is lupus nephritis (LN).~~