

1. A compound of structural Formula **HVII**:

(H)

(H)

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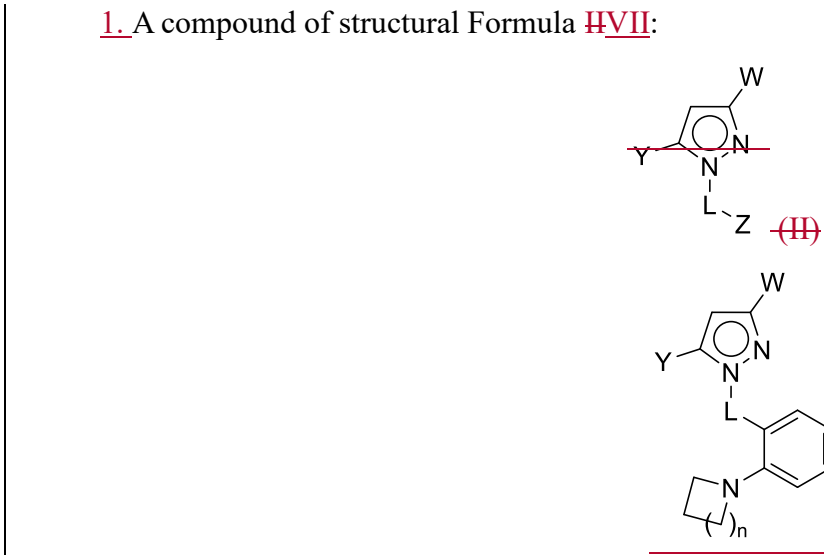
(H)

(H)

1. A compound of structural Formula **HVII**:

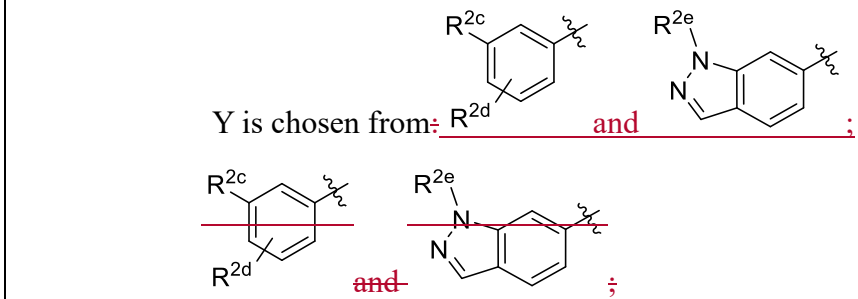
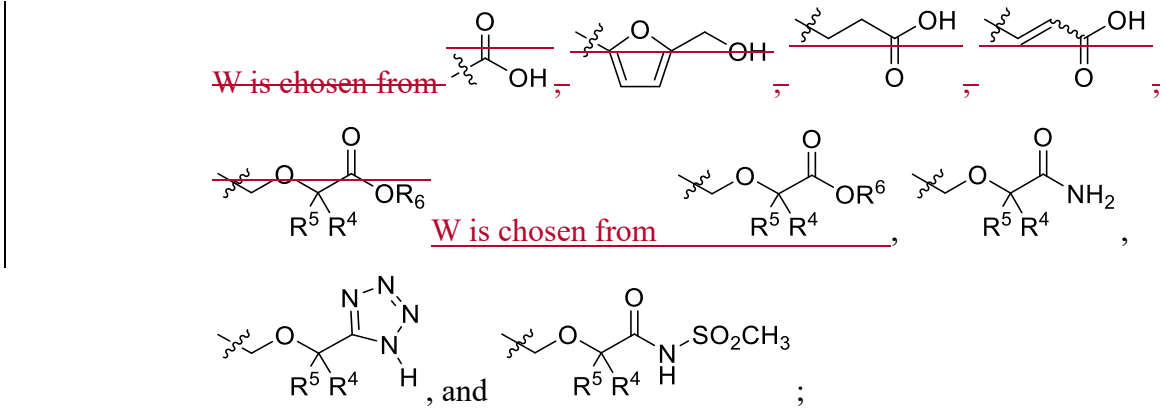
(H)

(H)



or a salt thereof, wherein:

L is chosen from a bond and methylene;

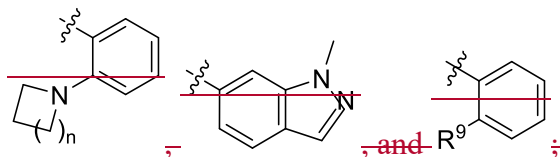


R^{2c} is chosen from H, C₁-C₄alkoxy and C₃-C₄cycloalkoxy;

R^{2d} is chosen from null and C₁-C₄alkoxy;

R^{2e} is C₁-C₄alkyl;

~~Z is chosen from:~~



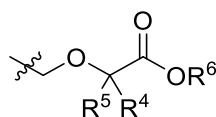
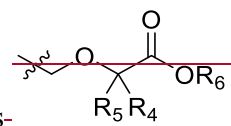
n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);

R⁴ and R⁵ are independently chosen from C₁-C₃alkyl; and

R⁶ is chosen from H and C₁-C₄alkyl; ~~and.~~

~~R⁹ is chosen from halo and C₁-C₄alkoxy.~~

2. The compound as recited in claim 1, or a salt thereof, wherein W is-

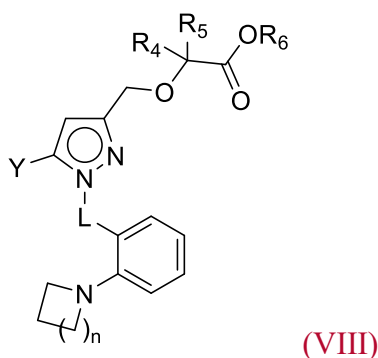


; R⁴ and R⁵, together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or heterocycloalkyl ring; and R⁶ is chosen from H and C₁-C₄alkyl.

3. The compound as recited in claim 2, or a salt thereof, wherein ~~R⁹n~~ ~~is chosen from chloro and ethoxyl,~~ forming azetidin-1-yl.

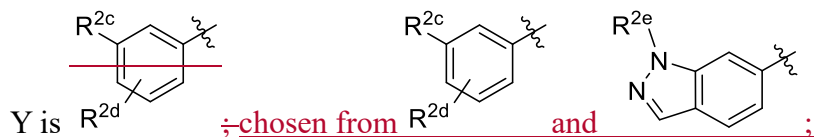
4. The compound as recited in claim 3, or a salt thereof, wherein L is a bond.

5. The compound as recited in claim ~~4~~1, wherein: compound has structural Formula VIII:



or a salt thereof, wherein

L is chosen from a bond and methylene;



R^{2c} is chosen from H, C₁-C₄alkoxy and C₃-C₄cycloalkoxy; ~~and~~

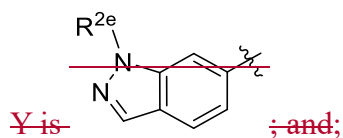
R^{2d} is chosen from null and C₁-C₄alkoxy;

~~1. The compound as recited in claim 5, wherein:~~

~~R^{2e} is chosen from methoxy, methylpropoxy, cyclopropoxy, and cyclobutoxy; and~~

~~R^{2d} is chosen from null and methoxy.~~

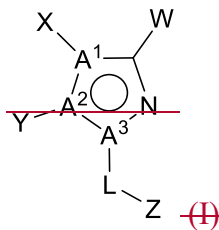
~~2. The compound as recited in claim 6, wherein:~~



R^{2e} is C₁-C₄alkyl;

~~3. The compound as recited in claim 7, wherein R^{2e} is chosen from ethyl and propyl.~~

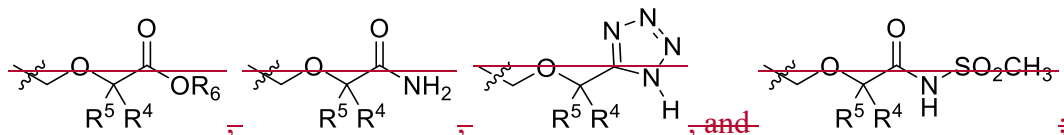
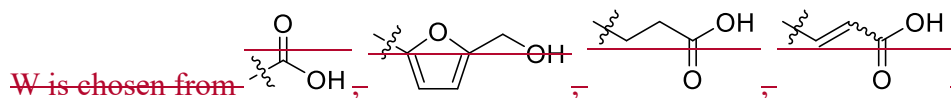
~~4. A compound of structural Formula I~~



~~or a salt thereof, wherein:~~

~~A^1 , A^2 , and A^3 are independently chosen from N and C, wherein at least one of A^1 , A^2 , and A^3 is N;~~

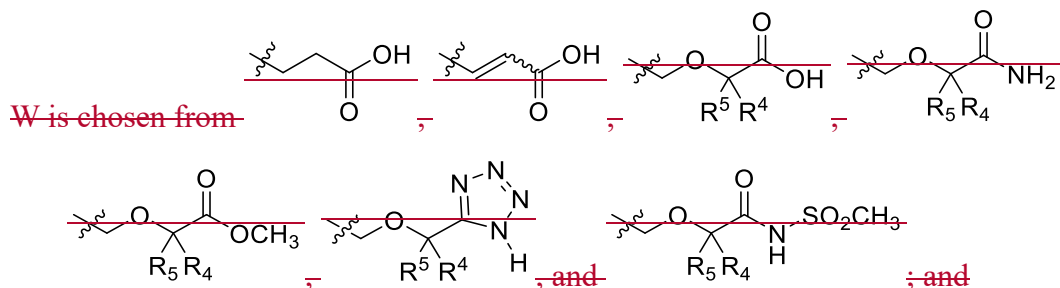
~~L is chosen from a bond, methylene, and ethylene;~~



~~X is H or null, or is chosen from alkenylamino, alkyl, aminoalkenyl, and aminoalkyl, any of which is optionally substituted with one to three R^1 groups;~~

~~Y is chosen from alkenyl, alkenylamino, alkyl, aminoalkenyl, aminoalkyl, aryl, arylmethyl, arylamino, aryloxy, cycloalkyl, heterocycloalkyl, and heteroaryl, any of which is optionally substituted with one to three R²-groups, or~~
~~X and Y together with the atoms to which they are attached may form an aryl, cycloalkyl, heteroaryl, or heterocycloalkyl ring, any of which is optionally substituted with one to three R⁷-groups; and~~
~~Z is chosen from alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, any of which is optionally substituted with one to three R³-groups;~~
~~each R¹ is independently chosen from alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, amino, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, aryl, heteroaryl;~~
~~each R² is independently chosen from alkyl, alkenyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, or~~
~~two R², together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;~~
~~each R³ is independently chosen from alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, cycloalkoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, and is optionally substituted with one to three R⁸-groups, or~~
~~two R³, together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;~~
~~R⁴ and R⁵ are independently chosen from H and C₁-C₆alkyl, wherein R⁴ and R⁵ together comprise no more than 6 carbons, or~~
~~R⁴ and R⁵, together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or heterocycloalkyl ring;~~
~~R⁶ is chosen from H and C₁-C₄alkyl;~~
~~each R⁷ is independently chosen from alkyl, alkenyl, alkoxy, haloalkyl, haloalkoxy, amino, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, aryl, and heteroaryl; and~~
~~each R⁸ is independently chosen from cyano, halo, hydroxy, and oxo.~~

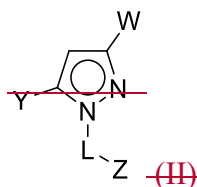
5. ~~The compound as recited in claim 9, or a salt thereof, wherein exactly one of A¹, A², and A³ is N.~~
6. ~~The compound as recited in claim 10, or a salt thereof, wherein A¹ and A² are C; and A³ is N.~~
7. ~~The compound as recited in claim 11, or a salt thereof, wherein X is hydrogen.~~
8. ~~The compound as recited in claim 12, or a salt thereof, wherein~~



~~R⁴ and R⁵ are independently chosen from H and C₁-C₆alkyl, with R⁴ and R⁵ together having no more than 6 carbons, or~~

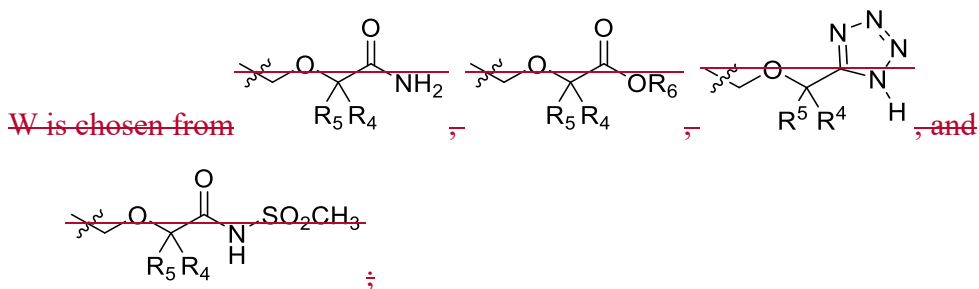
~~R⁴ and R⁵, together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or heterocycloalkyl ring.~~

9. ~~The compound as recited in claim 12, or a salt thereof, wherein:~~
- ~~Y is chosen from aryl and heteroaryl, any of which is optionally substituted with one to three R² groups; and~~
- ~~each R² is independently chosen from alkyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, carboxamido, sulfonamido, halo, aryl, and heteroaryl.~~
10. ~~The compound as recited in claim 9, having structural Formula II:~~



~~or a salt thereof, wherein:~~

~~L is chosen from a bond, methylene, and ethylene;~~



Y is chosen from aryl, arylmethyl, arylamino, aryloxy, cycloalkyl, heterocycloalkyl, and heteroaryl, any of which is optionally substituted with one to three R^2 groups;

Z is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R^3 groups;

each R^2 is independently chosen from alkyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, or

two R^2 , together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;

each R^3 is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, cycloalkoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, and is optionally substituted with one to three R^8 groups, or

two R^3 , together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;

R^4 and R^5 are independently chosen from H and C_1 - C_6 alkyl, wherein R^4 and R^5 together comprise no more than 6 carbons and wherein at least one of R^4 and R^5 is C_1 - C_6 alkyl, or

R^4 and R^5 , together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or heterocycloalkyl ring;

R^6 is chosen from H and C_1 - C_4 alkyl; and

each R^8 is independently chosen from cyano, halo, hydroxy, and oxo.

11. The compound as recited in claim 15, or a salt thereof, wherein:

each R^2 is independently chosen from alkyl, alkoxy, alkoxyalkyl, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, and halo, or two R^2 , together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring.

12. The compound as recited in claim 16, or a salt thereof, wherein Z is chosen from phenyl, pyridinyl, pyridazinyl, pyrimidinyl, and pyrazinyl, any of which is optionally substituted with one or two R^3 groups.

13. The compound as recited in claim 17, or a salt thereof, wherein each R^3 is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, amino, aminoalkyl, and halo, and is optionally substituted with one or two R^8 groups.

14. The compound as recited in claim 18, or a salt thereof, wherein Y is heteroaryl, and is substituted with one or two R^2 groups.

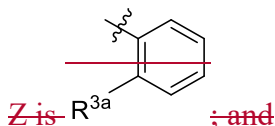
15. The compound as recited in claim 19, or a salt thereof, wherein Y is chosen from pyridinyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, pyrazolyl, imidazolyl, triazolyl, benzothiophenyl, benzofuranyl, quinolinyl, isoquinolinyl, cinnolinyl, indazolyl, and indolyl, any of which is optionally substituted with one or two R^2 groups.

16. The compound as recited in claim 20, wherein Y is chosen from thienyl, furyl, benzothiophenyl, benzofuranyl, indazolyl, and indolyl and is optionally substituted with one or two R^2 groups.

17. The compound as recited in claim 21, wherein each R^3 is independently chosen from alkyl, haloalkyl, alkoxy, and haloalkoxy.

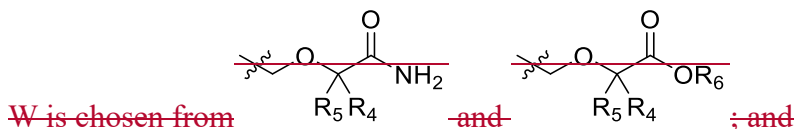
18. The compound as recited in claim 22, wherein each R^2 is independently chosen from alkyl, alkoxy, cycloalkoxy, cycloalkylmethoxy, and halo.

19. The compound as recited in claim 23 wherein



R^{3a} is chosen from H, alkyl, alkoxy, haloalkyl, haloalkoxy, amino, aminoalkyl, halo, cyano, and hydroxy.

20. The compound as recited in claim 24, wherein



~~R⁴ and R⁵ are independently chosen from H, methyl, and ethyl, and wherein at most one of R⁴ and R⁵ is H.~~

~~21. The compound as recited in claim 15, wherein R⁴ and R⁵ are independently chosen from C₁-C₆alkyl, wherein R⁴ and R⁵ together comprise no more than 6 carbons.~~

~~22. The compound as recited in claim 26, wherein exactly one of R⁴ and R⁵ is methyl.~~

~~23. The compound as recited in claim 27, wherein~~

~~Y is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R² groups; and~~

~~each R² is independently chosen from alkyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, cycloalkyl, and heterocycloalkyl.~~

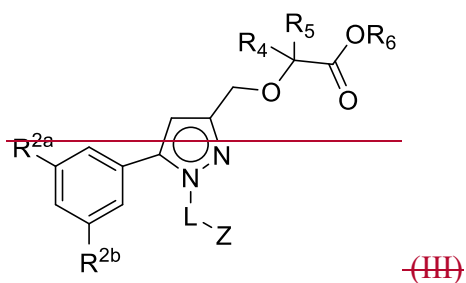
~~24. The compound as recited in claim 28, wherein each R³ is independently chosen from alkyl, alkoxy, cycloalkoxy, amino, cycloalkyl, and heterocycloalkyl.~~

~~25. The compound as recited in claim 29, wherein Y is phenyl, and is optionally substituted with one or two R² groups.~~

~~26. The compound as recited in claim 30, wherein each R² is independently chosen from alkoxy, cycloalkoxy, and cycloalkylmethoxy.~~

~~27. The compound as recited in claim 29, wherein Z is phenyl, and is optionally substituted with one or two R³ groups.~~

~~28. The compound as recited in claim 15, having structural Formula III:~~



~~or a salt thereof, wherein:~~

~~L is chosen from a bond, methylene, and ethylene;~~

~~Z is chosen from aryl and heteroaryl, either of which is optionally substituted with one or two R³ groups;~~

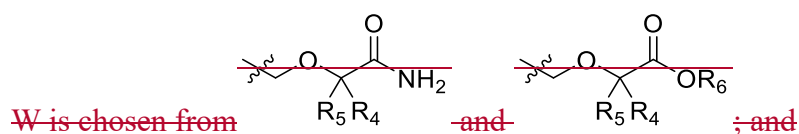
R^{2a} and R^{2b} are independently chosen from H, alkyl, alkoxy, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, halo, cycloalkyl, and heterocycloalkyl;
each R^3 is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, amino, aminoalkyl, carboxamido, halo, cyano, hydroxy, and cycloalkyl, and is optionally substituted with one or two R^8 groups;
 R^4 and R^5 are independently chosen from H and C_1 - C_6 alkyl, wherein R^4 and R^5 together comprise no more than 6 carbons and wherein at least one of R^4 and R^5 is C_1 - C_6 alkyl, or
 R^4 and R^5 , together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or heterocycloalkyl ring;
 R^6 is chosen from H and methyl; and
each R^8 is independently chosen from cyano, halo, hydroxy, and oxo.

29. The compound as recited in claim 33, wherein Z is chosen from phenyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, quinolinyl, isoquinolinyl, cinnolinyl, indazolyl, and indolyl, any of which is optionally substituted with one or two R^3 groups.

30. The compound as recited in claim 34 wherein R^{2a} is selected from alkyl, alkoxy, haloalkyl, haloalkoxy, and halo.

31. The compound as recited in claim 35, wherein each R^3 is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, amino, aminoalkyl, halo, cyano, and hydroxy.

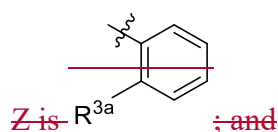
32. The compound as recited in claim 36, wherein



R^4 and R^5 are independently chosen from H, methyl, and ethyl, and wherein at most one of R^4 and R^5 is H.

33. The compound as recited in claim 37, wherein Z is phenyl, and is optionally substituted with one or two R^3 groups.

34. The compound as recited in claim 38, wherein



~~R^{3a} is chosen from H, alkyl, alkoxy, haloalkyl, haloalkoxy, amino, aminoalkyl, halo, cyano, and hydroxy.~~

~~35. The compound as recited in claim 37, wherein Z is chosen from pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, quinolinyl, isoquinolinyl, cinnolinyl, indazolyl, and indolyl, any of which is optionally substituted with one or two R³ groups.~~

~~36. The compound as recited in claim 40, wherein Z is chosen from quinolinyl, isoquinolinyl, cinnolinyl, indazolyl, and indolyl, any of which is optionally substituted with one or two R³ groups.~~

~~37. The compound as recited in claim 41, wherein Z is chosen from indazolyl and indolyl, any of which is optionally substituted with one or two R³ groups.~~

~~38. The compound as recited in claim 35, wherein R^{2b} is chosen from H and alkoxy.~~

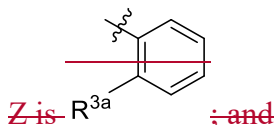
~~39. The compound as recited in claim 43, wherein R^{2a} is alkoxy.~~

~~40. The compound as recited in claim 44, wherein each R³ is independently chosen from alkyl, alkoxy, amino, aminoalkyl, haloalkyl, haloalkoxy, halo, cyano, and hydroxy.~~

~~41. The compound as recited in claim 45, wherein R⁴ and R⁵ are independently chosen from H, methyl, and ethyl, and wherein at most one of R⁴ and R⁵ is H.~~

~~42. The compound as recited in claim 46, wherein Z is phenyl, and is optionally substituted with one or two R³ groups.~~

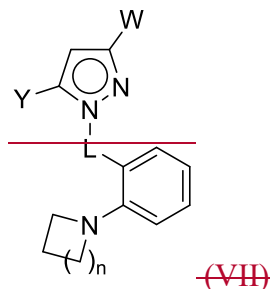
~~43. The compound as recited in claim 47, wherein~~



~~R^{3a} is chosen from H, alkyl, alkoxy, amino, aminoalkyl, haloalkyl, haloalkoxy, halo, cyano, and hydroxy.~~

~~44. The compound as recited in claim 48, wherein Z is chosen from indazolyl and indolyl, any of which is optionally substituted with one or two R³ groups.~~

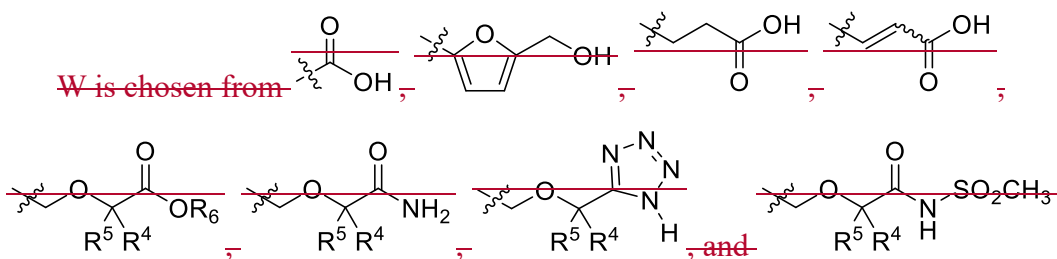
~~45. The compound as recited in claim 9, wherein the compound has structural Formula VII:~~



or a salt thereof, wherein:

~~L is chosen from a bond and methylene;~~

~~W is chosen from~~



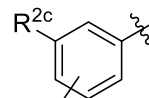
~~Y is chosen from alkenyl, alkenylamino, alkyl, aminoalkenyl, aminoalkyl, aryl, arylmethyl, arylamino, aryloxy, cycloalkyl, heterocycloalkyl, and heteroaryl, any of which is optionally substituted with one to three R² groups;~~

~~each R² is independently chosen from alkyl, alkenyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl;~~

~~n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);~~

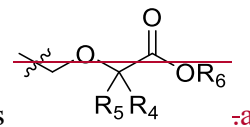
~~R⁴ and R⁵ are independently chosen from C₁-C₃alkyl; and~~

~~R⁶ is chosen from H and C₁-C₄alkyl.~~



6. The compound as recited in claim 505, or a salt thereof, wherein Y is R^{2d}; R^{2c} is chosen from arylH, C₁-C₄ alkoxy and heteroaryl, either of which is optionally substituted with one to three R² groups. C₃-C₄ cycloalkoxy; and R^{2d} is chosen from null and C₁-C₄ alkoxy.

7. The compound as recited in claim 51, wherein each R² is independently chosen from alkoxy, cycloalkoxy, haloalkoxy, alkyl, halo, and haloalkyl.5, or a salt thereof, wherein n is 1, forming azetidin-1-yl.

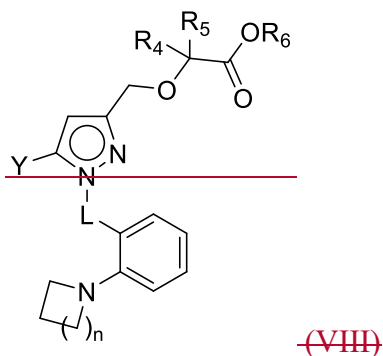


8. The compound as recited in claim ~~527~~, or a salt thereof, wherein ~~WL~~ is bond.

~~46-9.~~ The compound as recited in claim ~~53~~, wherein ~~n is 1, forming azetidin-1-yl.~~

~~47.~~ The compound as recited in claim ~~54~~, wherein ~~L is a bond.~~

~~48.~~ The compound as recited in claim ~~9~~, wherein compound has structural Formula VIII:



8. or a salt thereof, wherein ÷

~~L is chosen from a bond and methylene;~~

Y is chosen from phenyl, indazolyl, thienyl, indazolyl, and indolyl, any of which is optionally substituted with one or two R^2 -groups;

~~n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);~~

~~each R^2 is independently chosen from alkyl, alkoxy, alkylthio, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, and halo;~~

~~R^4 and R^5 are independently chosen from C_1 - C_3 alkyl; and~~

~~R^6 is chosen from H and C_1 - C_4 alkyl.~~

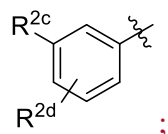
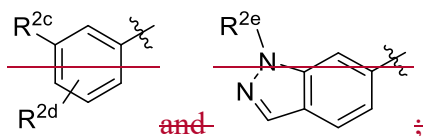
~~49.~~ The compound as recited in claim ~~56~~, wherein Y is chosen from phenyl and indazolyl, either of which is optionally substituted with one or two R^2 -groups.

~~50.~~ The compound as recited in claim ~~57~~, wherein each R^2 is independently chosen from alkoxy, cycloalkoxy, haloalkoxy, alkyl, halo, and haloalkyl.

~~51.~~ The compound as recited in claim ~~58~~, wherein ~~n is 1, forming azetidin-1-yl.~~

~~52.~~ The compound as recited in claim ~~59~~, wherein ~~L is a bond.~~

53. ~~The compound as recited in claim 60, wherein Y is phenyl substituted with one or two R² groups independently chosen from alkoxy, cycloalkoxy, haloalkoxy, alkyl, halo, and haloalkyl.~~
54. ~~The compound as recited in claim 61, wherein each R² is independently chosen from C₁-C₄alkoxy, cyclopropoxy, cyclobutoxy, and C₁-C₃alkyl.~~
55. ~~The compound as recited in claim 60, wherein Y is indazolyl substituted with an R² groups chosen from methyl, ethyl, and propyl.~~
56. ~~The compound as recited in claim 60, wherein Y is chosen from:~~

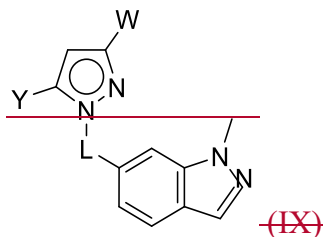


~~R^{2c} is chosen from H, C₁-C₄alkoxy and C₁-C₄cycloalkoxy; and~~

~~R^{2d} is chosen from null and C₁-C₄alkoxy; and~~

~~R^{2e} is C₁-C₄alkyl.~~

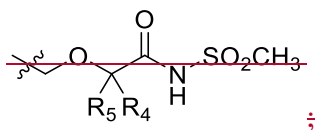
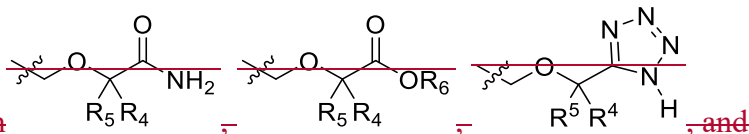
57. 10. The compound as recited in claim 9, ~~wherein the compound has structural Formula IX:~~



~~or a salt thereof, wherein:~~

~~L is chosen from a bond and methylene;~~

~~W is chosen from~~



~~Y is chosen from aryl, arylmethyl, arylamino, aryloxy, cycloalkyl, heterocycloalkyl, and heteroaryl, any of which is optionally substituted with one to three R²-groups;~~

~~Z is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R³-groups;~~

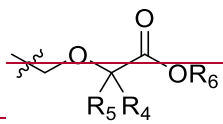
~~each R² is independently chosen from alkyl, alkoxy, alkoxyalkyl, alkylthio, haloalkyl, haloalkoxy, cycloalkoxy, cycloalkylmethoxy, heterocycloalkylmethoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl;~~

~~R⁴ and R⁵ are independently chosen from C₁-C₃alkyl; and~~

~~R⁶ is chosen from H and C₁-C₄alkyl.~~

~~58. The compound as recited in claim 65, wherein Y is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R²-groups.~~

~~59. The compound as recited in claim 66, wherein each R² is independently chosen from alkoxy, cycloalkoxy, haloalkoxy, alkyl, halo, and haloalkyl.~~



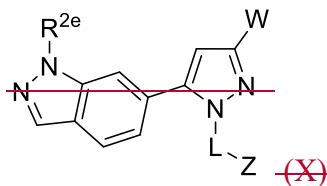
~~60. The compound as recited in claim 67, wherein W is~~

~~61. The compound as recited in claim 68, wherein L is a bond.~~

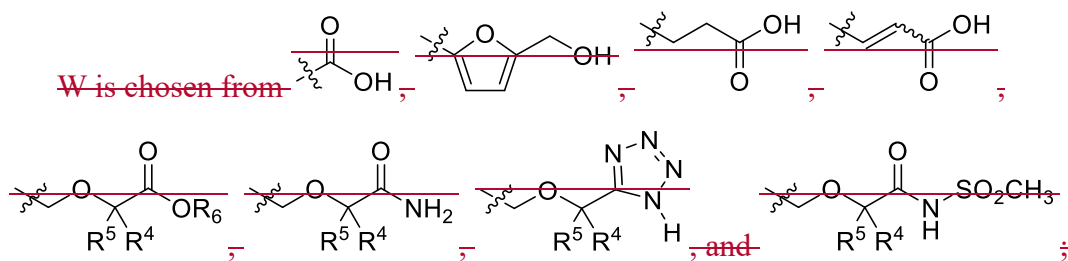
~~62. The compound as recited in claim 69, wherein Y is phenyl substituted with one or two R² groups independently chosen from alkoxy, cycloalkoxy, haloalkoxy, alkyl, halo, and haloalkyl.~~

~~63. The compound as recited in claim 70, wherein each R² is independently chosen from C₁-C₄alkoxy, cyclopropoxy, cyclobutoxy, and C₁-C₃alkyl.~~

~~64. The compound as recited in claim 9, wherein the compound has structural Formula X:~~



~~or a salt thereof, wherein:~~



~~R^{2e} is C₁-C₄alkyl;~~

~~L is chosen from a bond and methylene;~~

~~Z is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R³ groups;~~

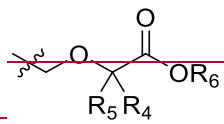
~~each R³ is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, cycloalkoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, and is optionally substituted with one to three R⁸ groups; or~~

~~two R³, together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;~~

~~R⁴ and R⁵ are independently chosen from C₁-C₃alkyl;~~

~~R⁶ is chosen from H and C₁-C₄alkyl; and~~

~~each R⁸ is independently chosen from cyano, halo, hydroxy, and oxo.~~

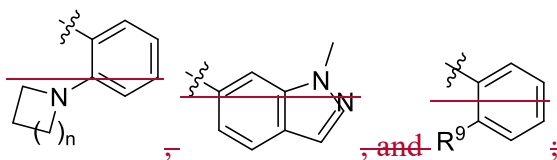


~~65. The compound as recited in claim 72, wherein W is~~

~~66. The compound as recited in claim 73, wherein L is a bond.~~

~~67. The compound as recited in claim 74, wherein Z is chosen from phenyl and indazolyl, either of which is optionally substituted with one to three R³ groups.~~

~~68. The compound as recited in claim 75, wherein Z is chosen from:~~



~~n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);~~

~~R⁴ and R⁵ are independently chosen from C₁-C₃alkyl;~~

~~R⁶ is chosen from H and C₁-C₄alkyl; and~~

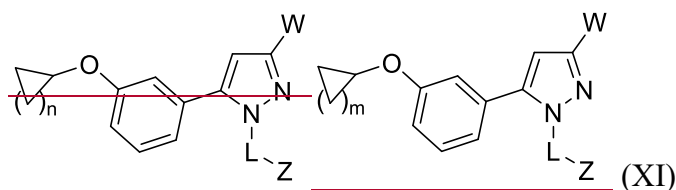
~~R^9 is chosen from halo, amino, and C_1 - C_4 alkoxy.~~

69. The compound as recited in claim 76, wherein R⁹ is chosen from chloro, dimethylamino, and ethoxy.

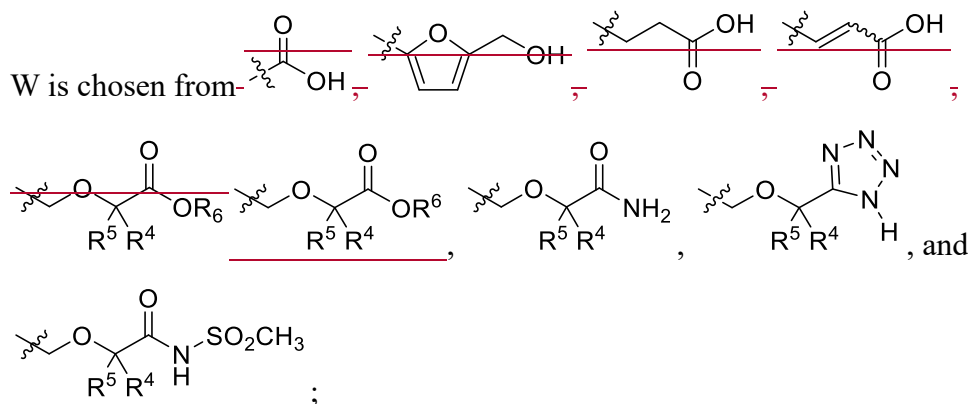
~~70. The compound as recited in claim 77, wherein R⁹ is chosen from chloro and ethoxy.~~

~~71. The compound as recited in claim 76, wherein n is 1, forming azetidin-1-yl.~~

~~The compound as recited in claim 91~~, wherein the compound has structural Formula XI:



or a salt thereof, wherein:



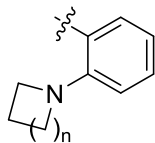
am is 1, 2, or 3 (forming a cyclopropyl, cyclobutyl, or cyclopentyl);

L is chosen from a bond and methylene;

~~Z is chosen from aryl and heteroaryl, either of which is optionally substituted with one to three R³-groups;~~

each R³ is independently chosen from alkyl, alkoxy, haloalkyl, haloalkoxy, cycloalkoxy, amino, aminoalkyl, carboxamido, sulfonamido, halo, cyano, hydroxy, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, and is optionally substituted with one to three R⁸ groups, or

two R³, together with the intervening atoms, form a 5-7 membered cycloalkyl or heterocycloalkyl ring;



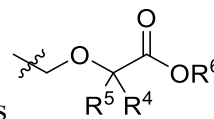
Z is  ;

n is 1 or 2;

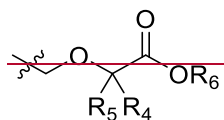
R⁴ and R⁵ are independently chosen from C₁-C₃alkyl;

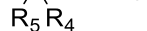
R⁶ is chosen from H and C₁-C₄alkyl; ~~and~~

~~each R⁸ is independently chosen from cyano, halo, hydroxy, and oxo.~~



11. The compound as recited in claim ~~80~~10, or a salt thereof, wherein W is  ; R⁴
and R⁵, together with the atoms to which they are attached, form a 3-7 membered cycloalkyl or

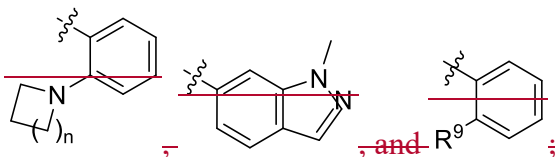


heterocycloalkyl ring; and R⁶ is  chosen from H and C₁-C₄alkyl.

12. The compound as recited in claim ~~84~~11, or a salt thereof, wherein L is a bond.

~~The~~13. A compound of structural Formula VII as recited in claim 82, wherein Z is 1 chosen from
phenyl and indazolyl, either of which is optionally substituted with one to three R³ groups.

~~72. The compound as recited in claim 83, wherein Z is chosen from:~~



n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);

R⁴ and R⁵ are independently chosen from C₁-C₃alkyl;

R⁶ is chosen from H and C₁-C₄alkyl; and

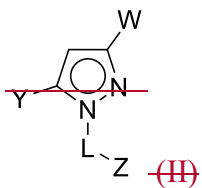
R⁹ is chosen from halo, amino, and C₁-C₄alkoxy.

~~73. The compound as recited in claim 84, wherein R⁹ is chosen from chloro, dimethylamino, and ethoxy.~~

~~74. The compound as recited in claim 85, wherein R⁹ is chosen from chloro and ethoxy.~~

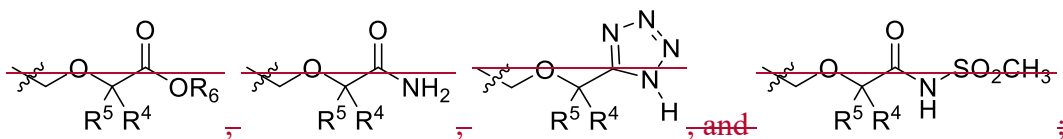
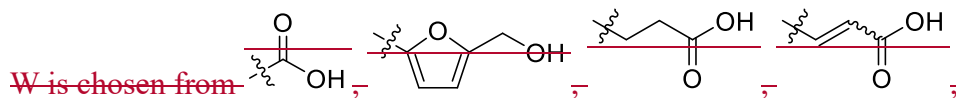
~~75. The compound as recited in claim 84, wherein n is 1, forming azetidin-1-yl.~~

~~76. The compound as recited in claim 9, wherein the compound has structural Formula II:~~

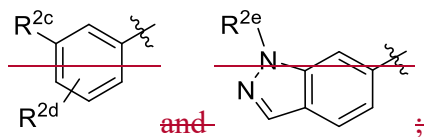


or a salt thereof, wherein:

L is chosen from a bond and methylene;

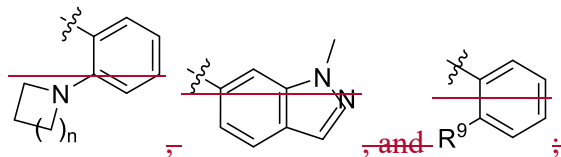


Y is chosen from:



R^{2e} is C₁-C₄alkyl;

Z is chosen from:

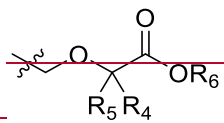


n is 1 or 2 (forming an azetidin-1-yl or pyrrolidin-1-yl);

R⁴ and R⁵ are independently chosen from C₁-C₃alkyl;

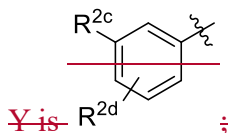
R⁶ is chosen from H and C₁-C₄alkyl; and

R⁹ is chosen from halo and C₁-C₄alkoxy;



77. The compound as recited in claim 88, wherein W is

78. The compound as recited in claim 89, wherein:



~~R^{2e} is chosen from C₁-C₄alkoxy and C₁-C₄cycloalkoxy; and~~

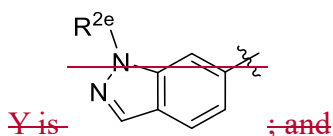
~~R^{2d} is chosen from null and C₁-C₄alkoxy.~~

~~79. The compound as recited in claim 90, wherein:~~

~~R^{2e} is chosen from methoxy, methylpropoxy, cyclopropoxy, and cyclobutoxy; and~~

~~R^{2d} is chosen from null and methoxy.~~

~~80. The compound as recited in claim 89 wherein:~~



~~R^{2e} is C₁-C₄alkyl.~~

~~81. The compound as recited in claim 92, wherein R^{2e} is chosen from ethyl and propyl.~~

~~82. The compound as recited in claim 89, wherein L is a bond.~~

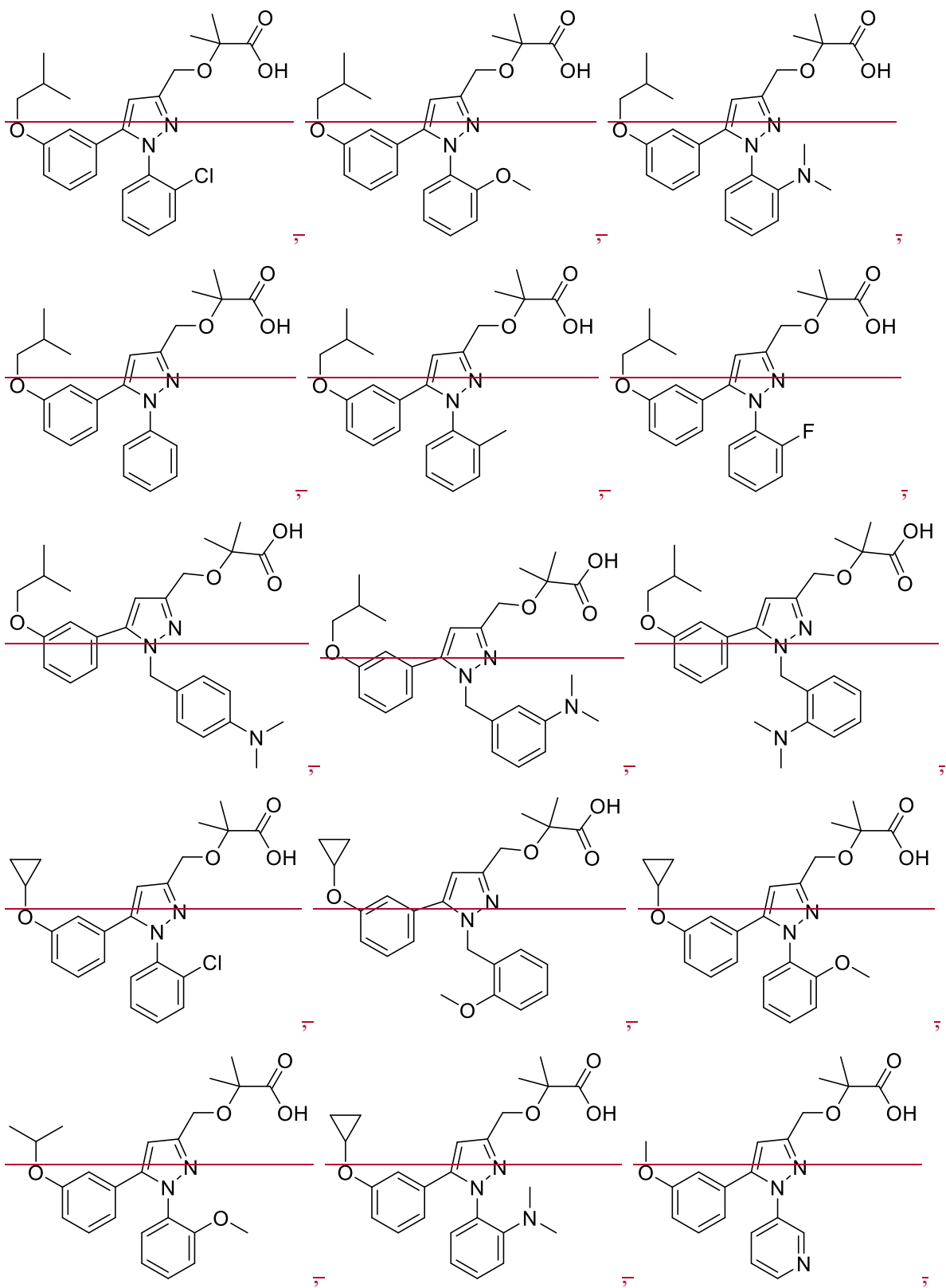


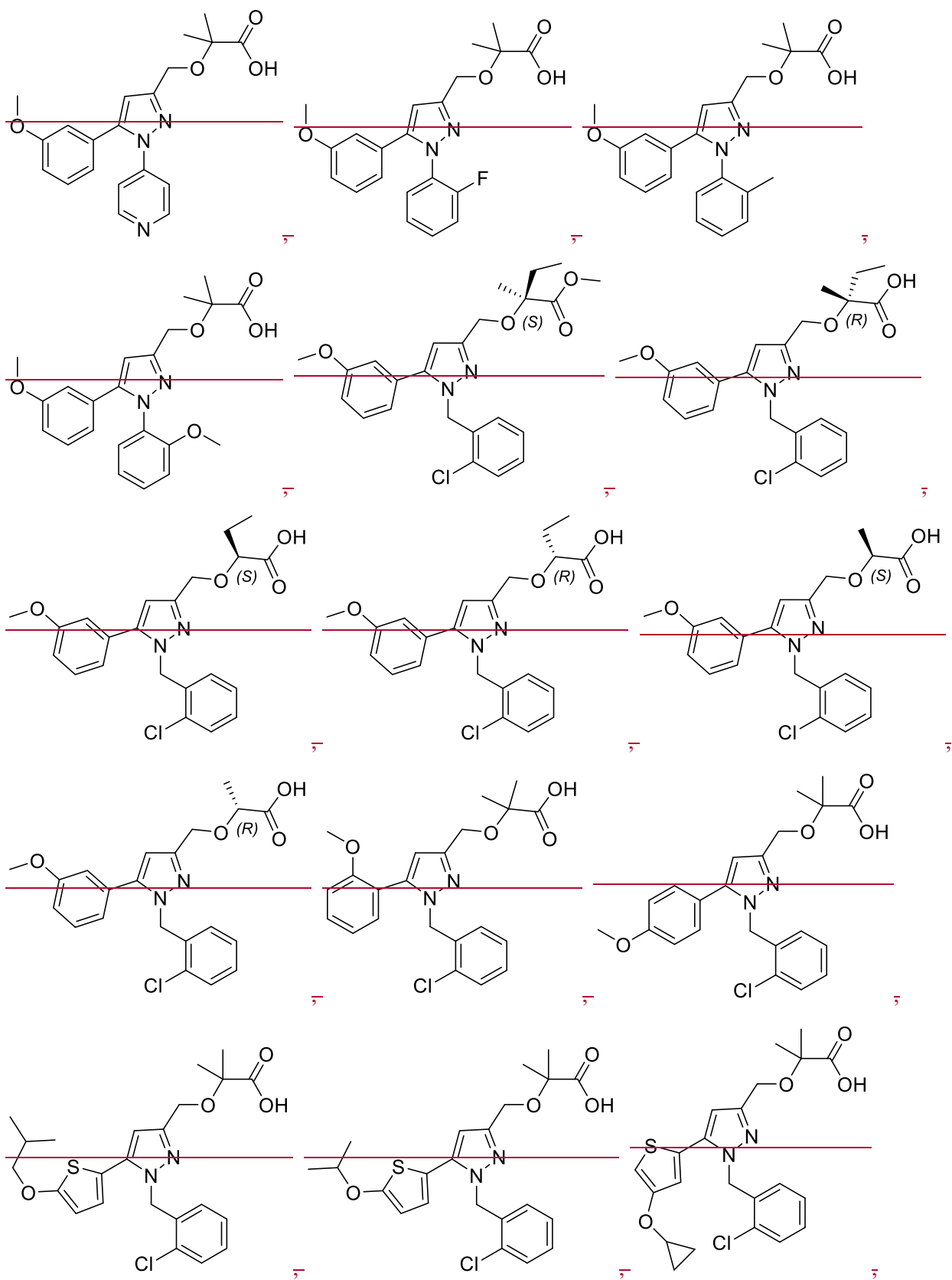
~~84. The compound as recited in claim 95, wherein n is 1, forming azetidin-1-yl.~~

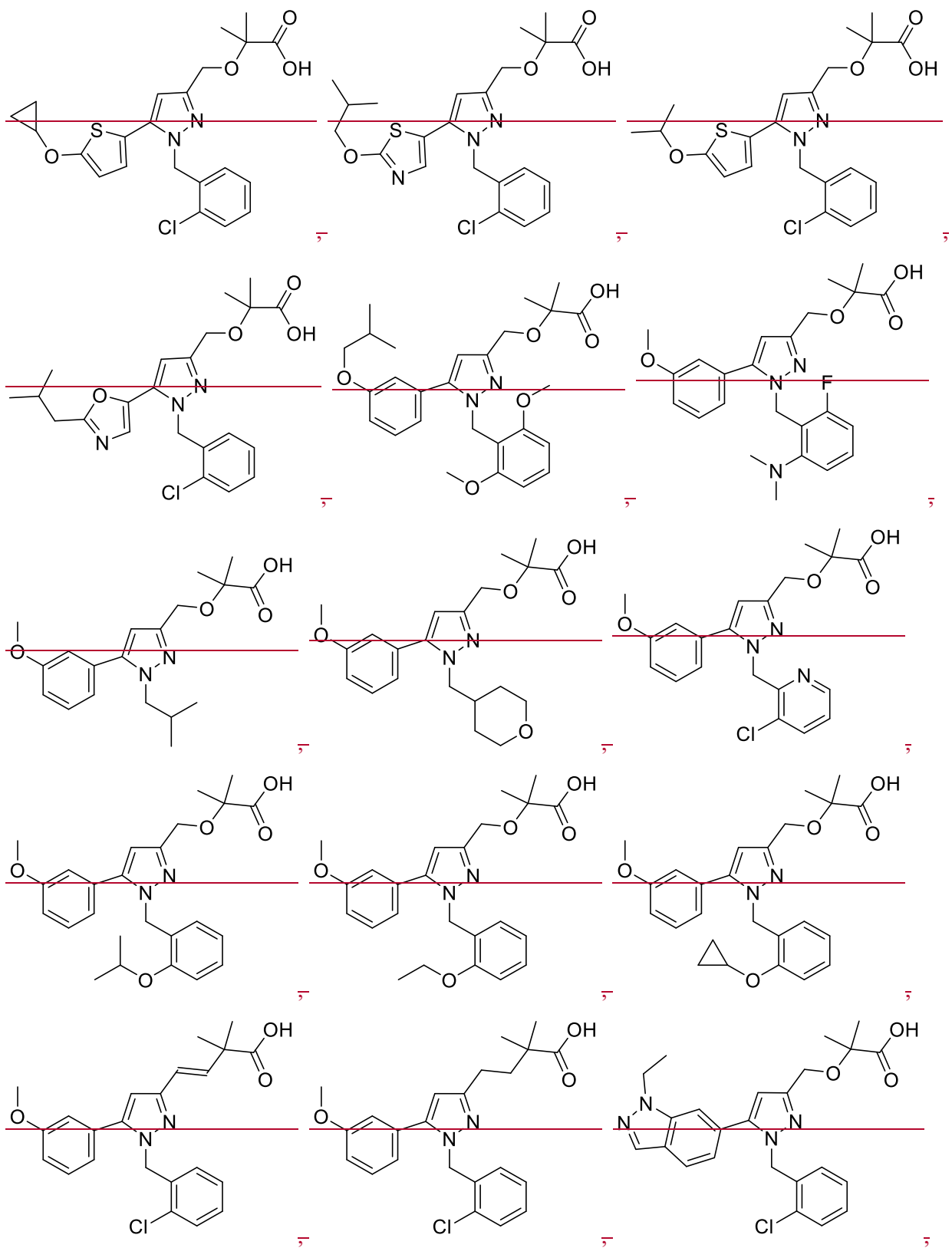


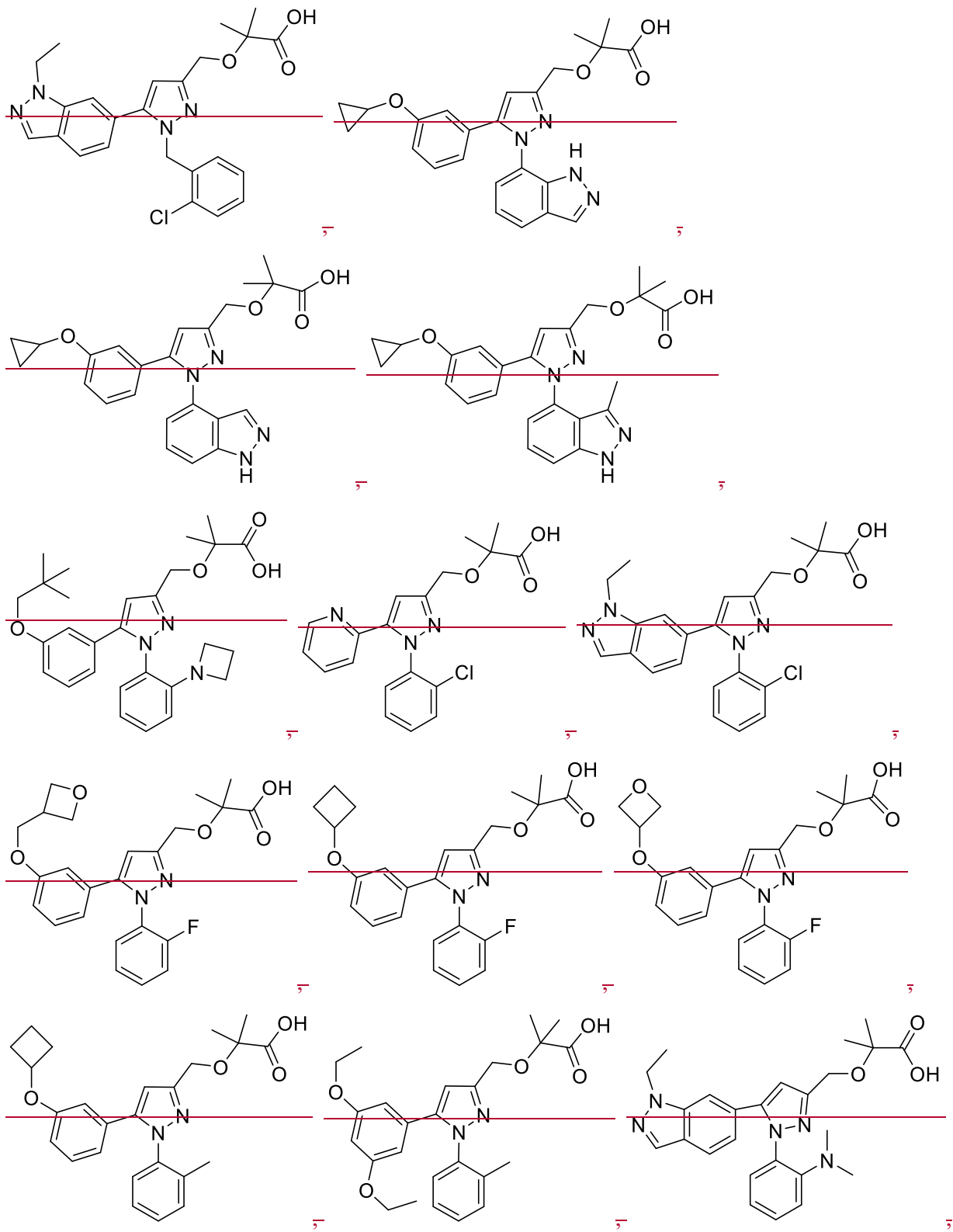
~~87. The compound as recited in claim 98, wherein R⁹ is chosen from chloro and ethoxy.~~

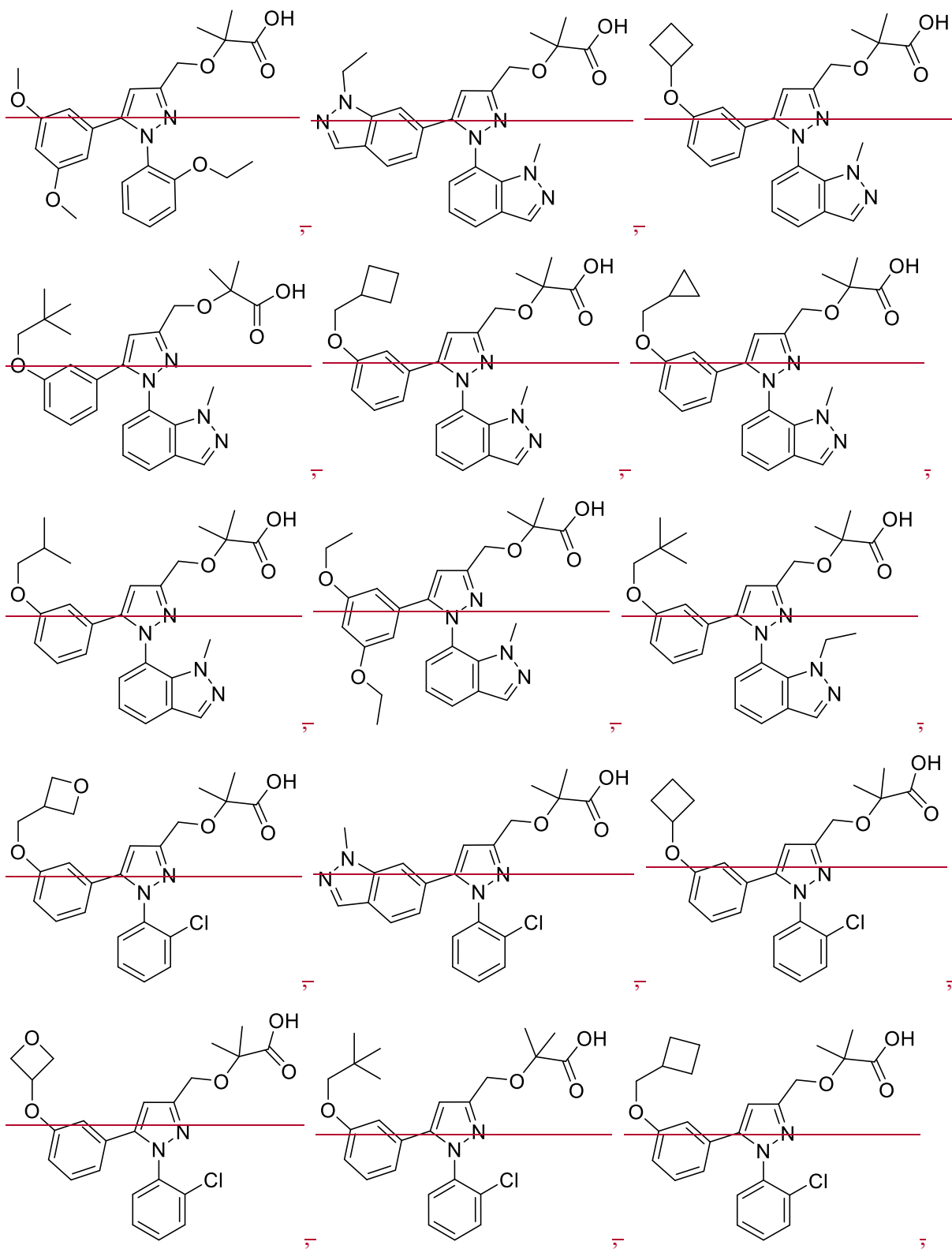
~~88. A compound chosen from:~~

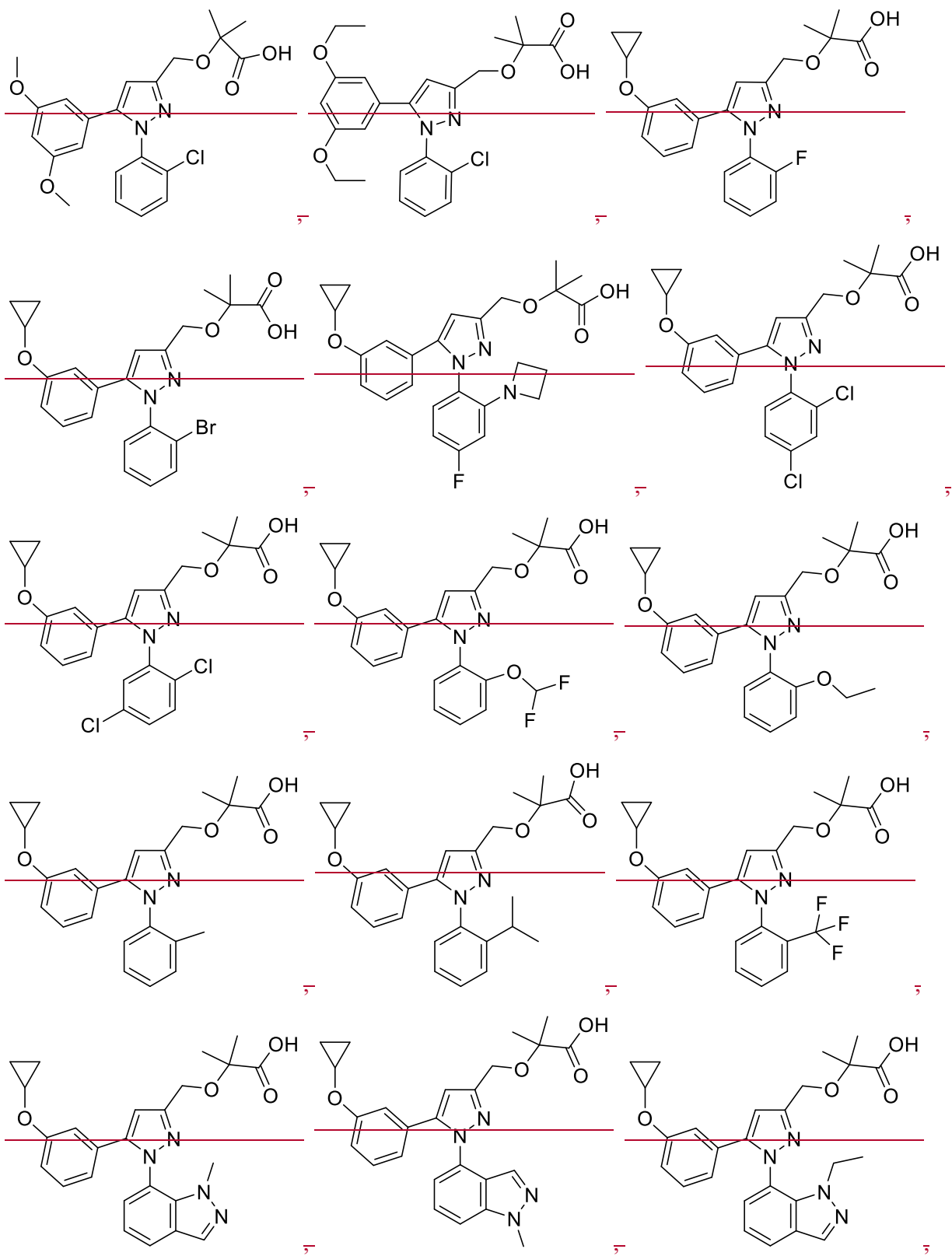


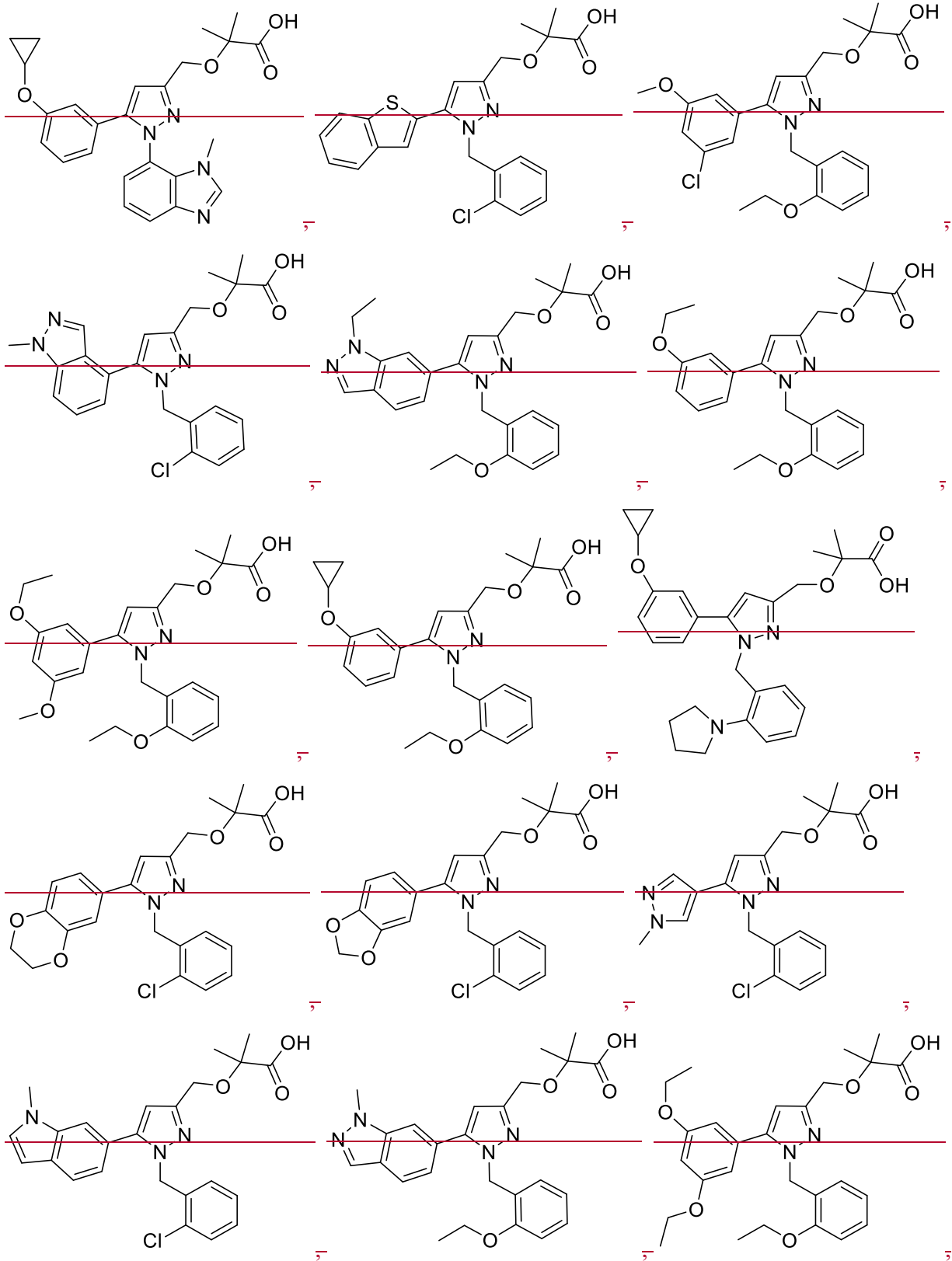


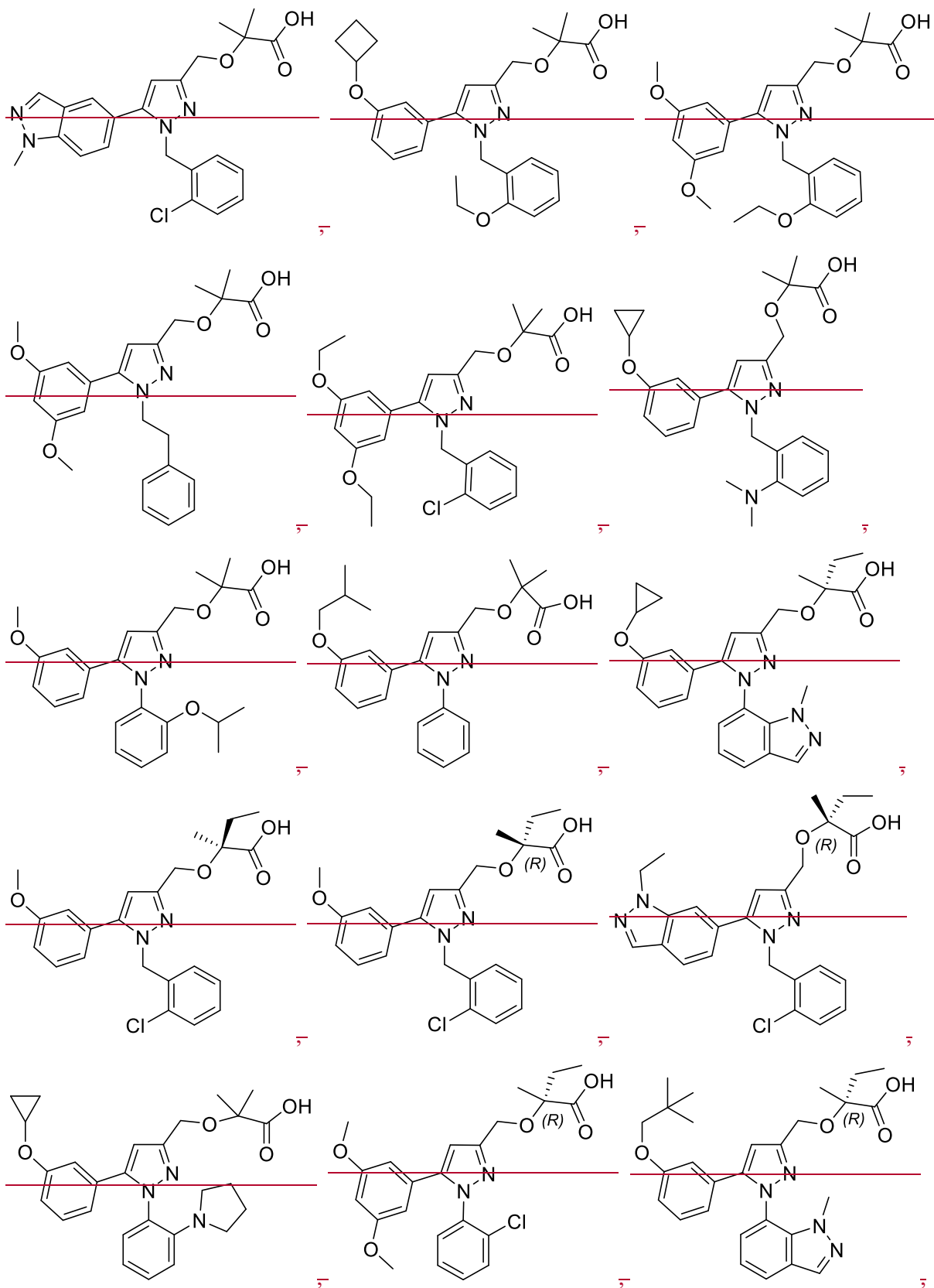


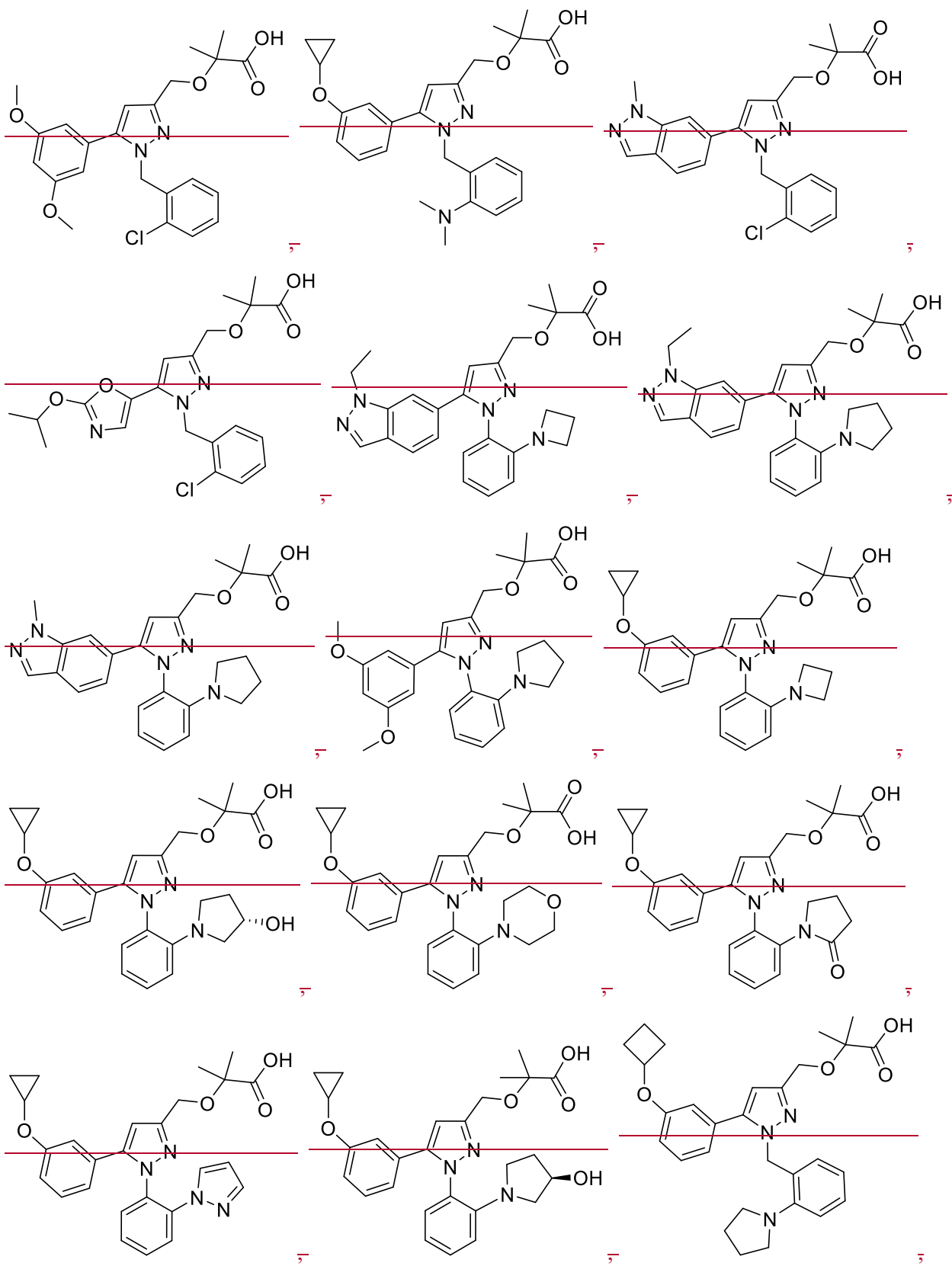


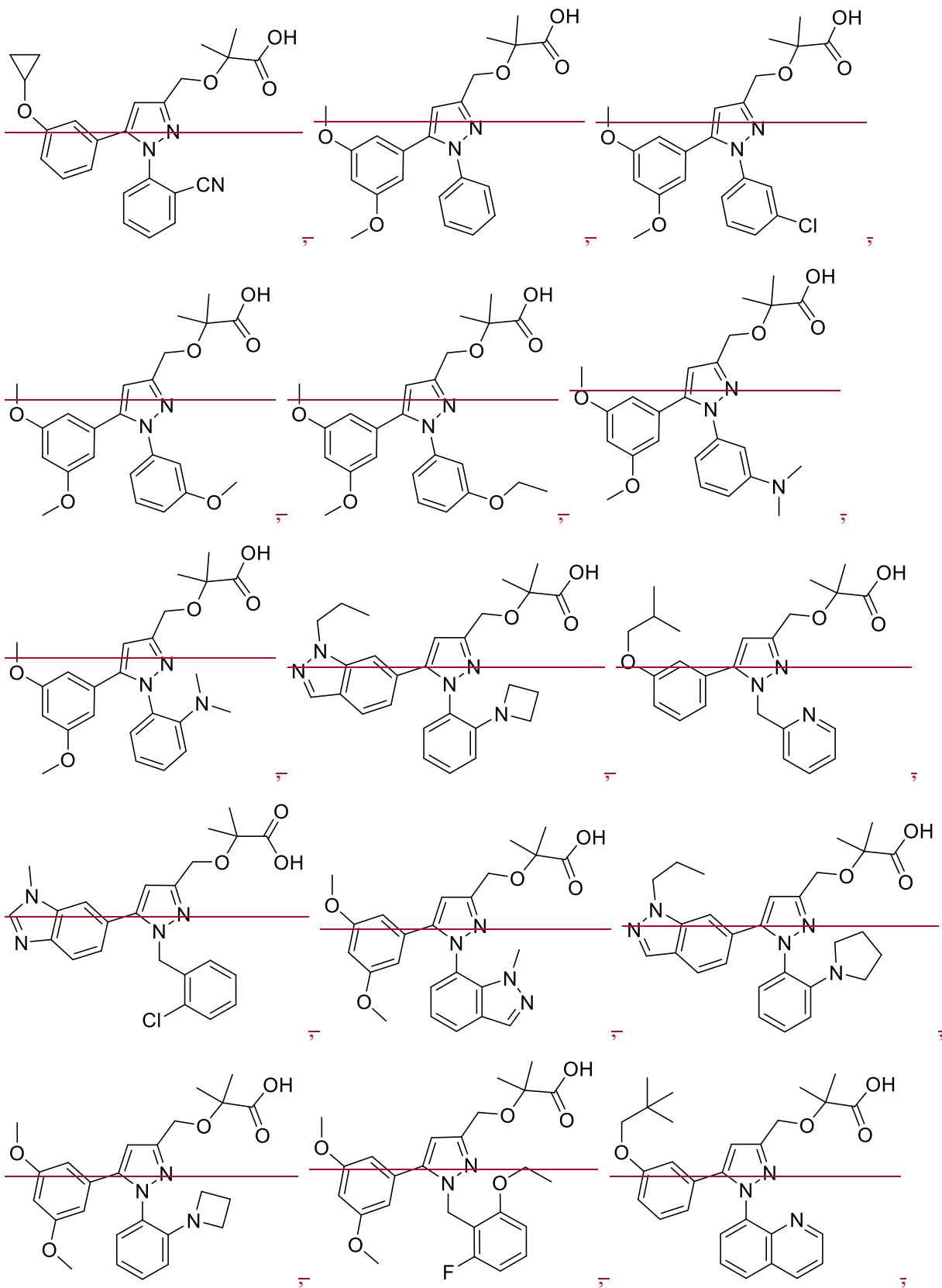


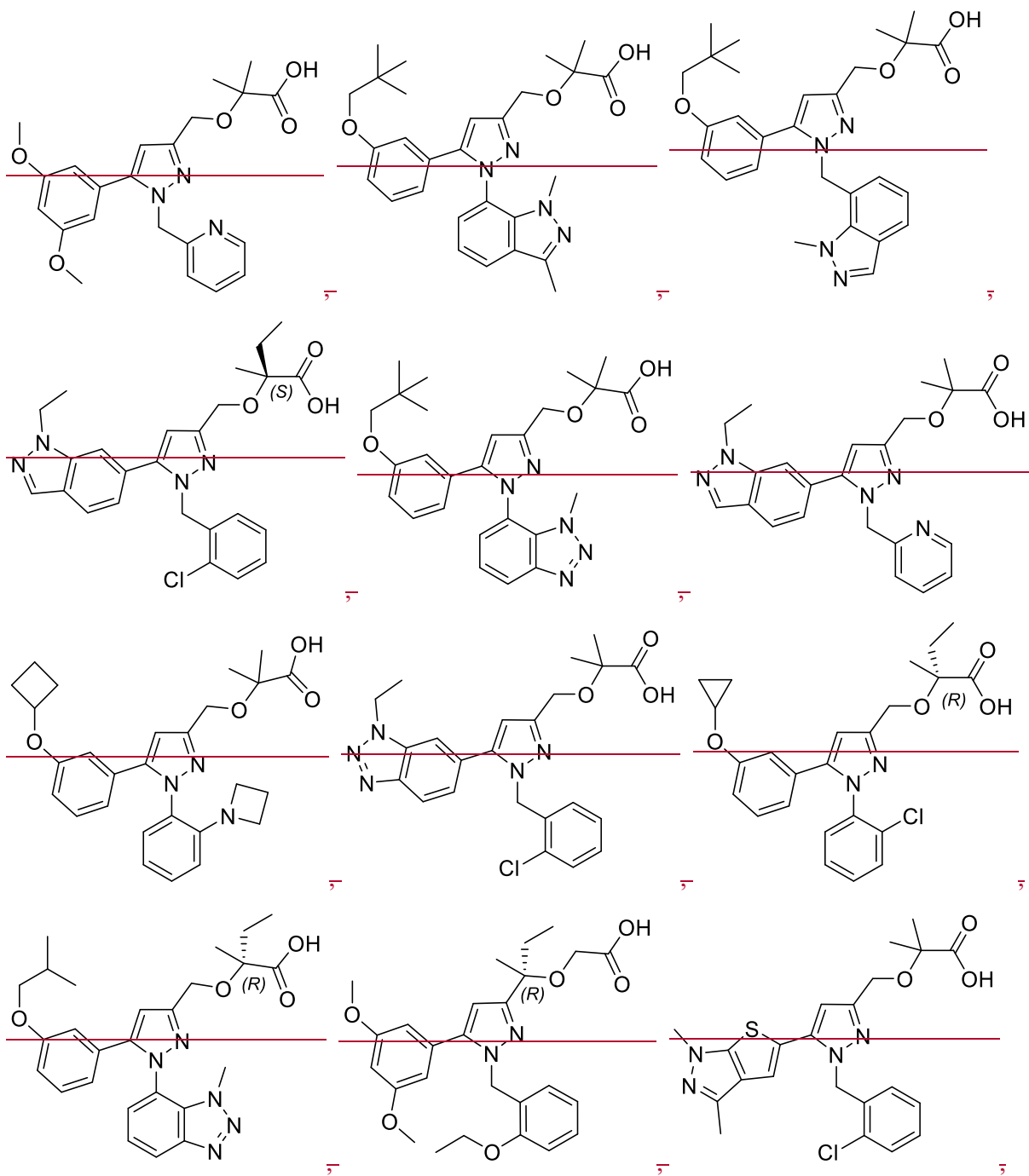


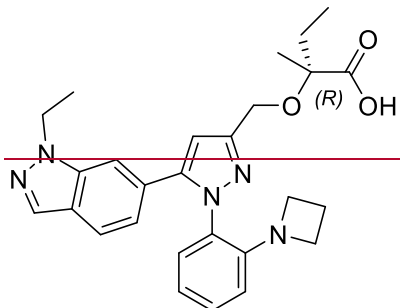
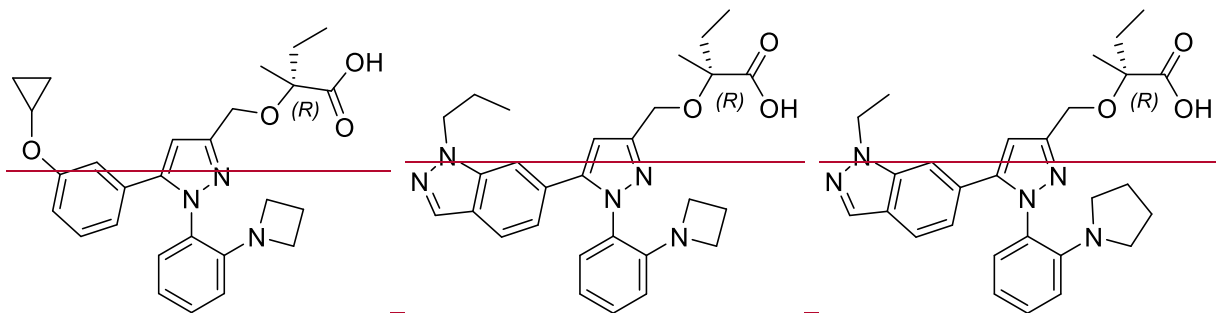






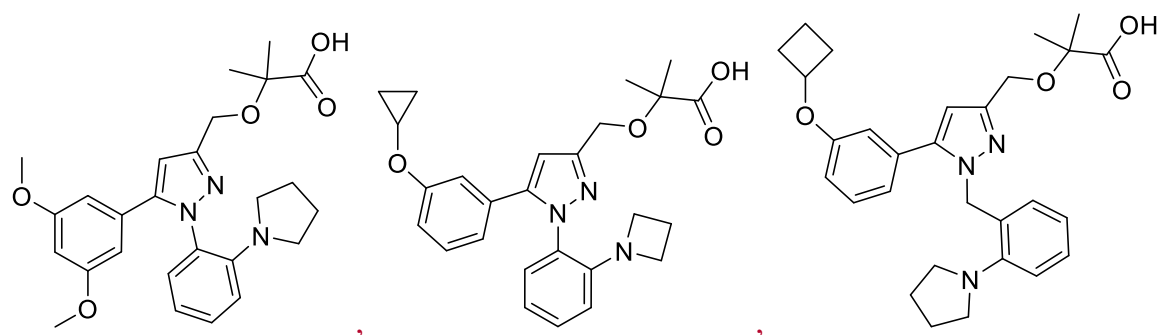
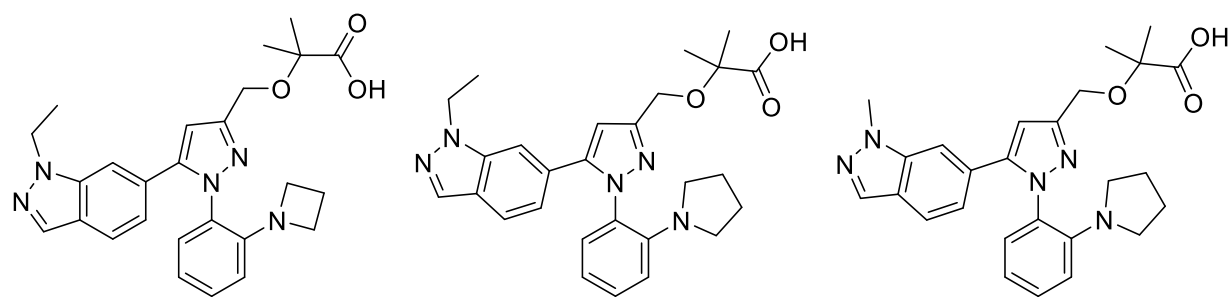
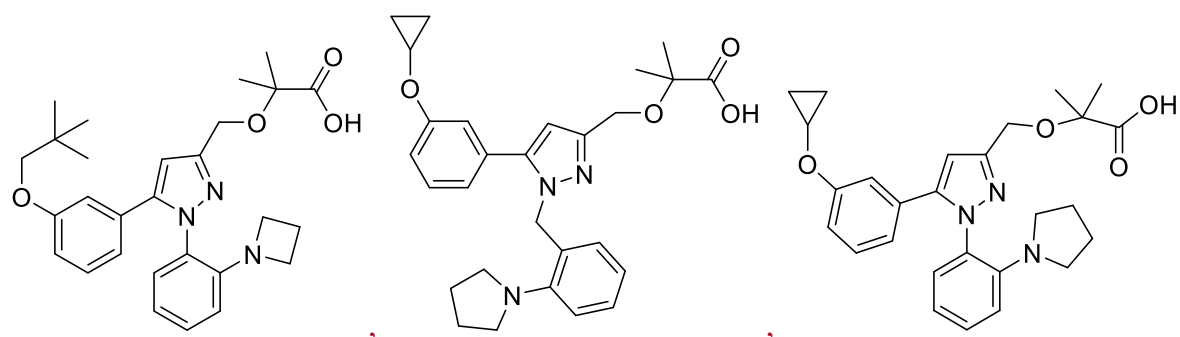


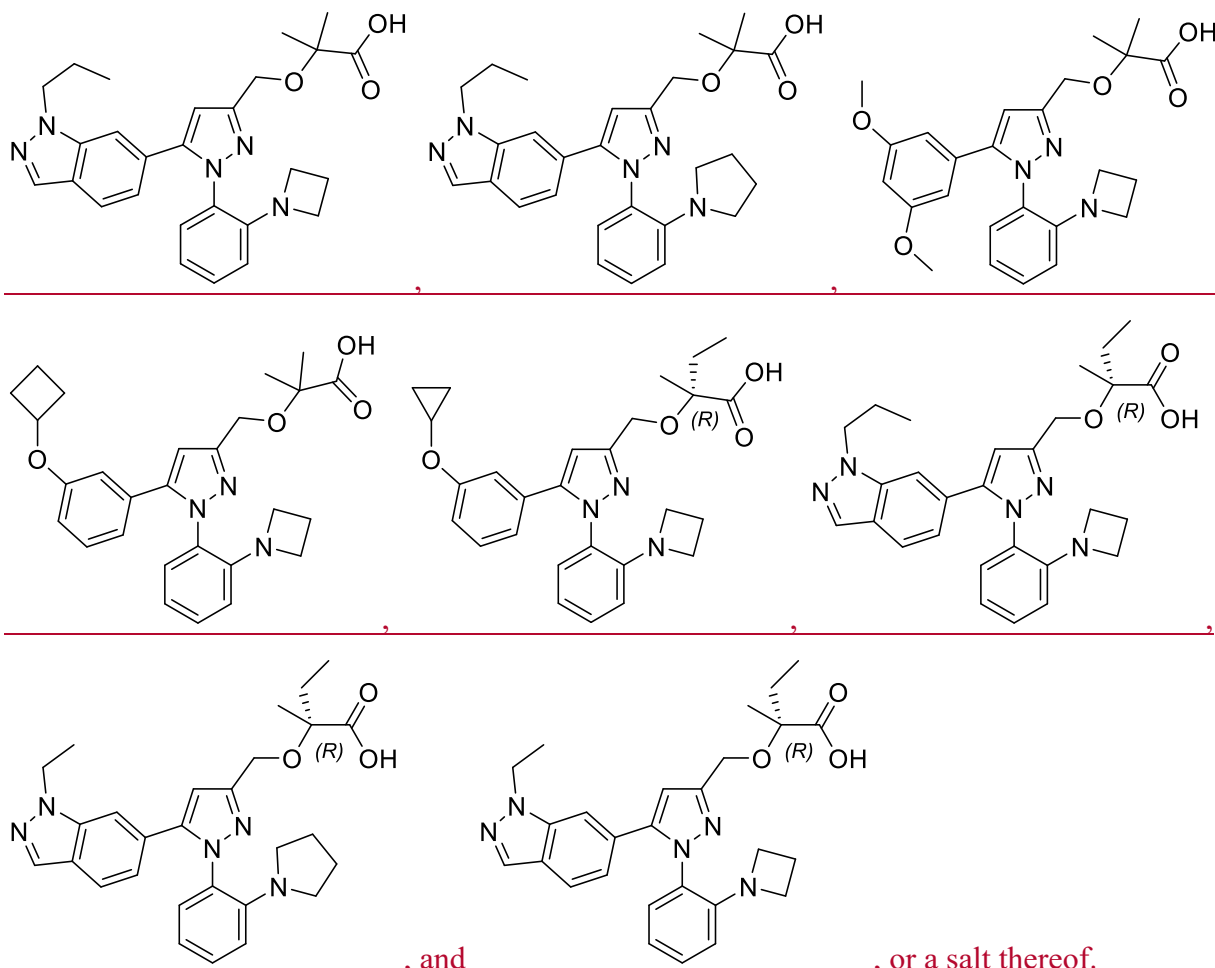




and

, or a salt thereof.





14. An isolated enantiomer of a compound as recited in claim ~~100~~13 or a salt thereof.

15. A pharmaceutical composition comprising a compound as recited in any of claims 1–14, or a salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

~~89-16. A pharmaceutical composition comprising a compound as recited in any of claims 1–101, 14 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.~~

~~A method~~salt thereof for use in inhibiting activity of the monocarboxylate transporter MCT4, or a mutant thereof, in a biological sample comprising the step of contacting said biological sample with a compound as recited in any of claims 1–~~101~~14, or a salt thereof.

~~90-17. A method for pharmaceutical composition comprising a compound as recited in any of claims 1–14 or a salt thereof for use in~~ inhibiting activity of the monocarboxylate transporter MCT4, or a mutant thereof, in a patient ~~comprising the step of administering to the patient a compound as recited in any of claims 1–101, or a salt thereof.~~

91. A method for selectively inhibiting activity of the monocarboxylate transporter MCT4, or a mutant thereof, over the monocarboxylate transporter MCT1, or a mutant thereof, in a patient comprising the step of administering to the patient a compound as recited in any of claims 1-101, or a salt thereof.
92. The method as recited in claim 105 wherein the inhibition is at least 100-fold selective for MCT4 over MCT1.
93. A method for treating a monocarboxylate transporter MCT4-mediated disorder in a subject in need thereof, comprising the step of administering to said patient a compound as recited in any of claims 1-101, or a pharmaceutically acceptable salt thereof.
94. The method as recited in claim 107, wherein the subject is a human.
95. The method as recited in claim 107, wherein the monocarboxylate transporter MCT4-mediated disorder is chosen from an inflammatory disorder and a proliferative disorder.
96. The method as recited in claim 107, wherein the monocarboxylate transporter MCT4-mediated disorder is a proliferative disorder.
97. The method as recited in claim 110, wherein the proliferative disorder is cancer.
98. The method as recited in claim 111, wherein the cancer is chosen from adenocarcinoma, adult T-cell leukemia/lymphoma, bladder cancer, blastoma, bone cancer, breast cancer, brain cancer, carcinoma, myeloid sarcoma, cervical cancer, colorectal cancer, esophageal cancer, gastrointestinal cancer, glioblastoma multiforme, glioma, gallbladder cancer, gastric cancer, head and neck cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, intestinal cancer, kidney cancer, laryngeal cancer, leukemia, lung cancer, lymphoma, liver cancer, small cell lung cancer, non-small cell lung cancer, mesothelioma, multiple myeloma, ocular cancer, optic nerve tumor, oral cancer, ovarian cancer, pituitary tumor, primary central nervous system lymphoma, prostate cancer, pancreatic cancer, pharyngeal cancer, renal cell carcinoma, rectal cancer, sarcoma, skin cancer, spinal tumor, small intestine cancer, stomach cancer, T-cell lymphoma, testicular cancer, thyroid cancer, throat cancer, urogenital cancer, urothelial carcinoma, uterine cancer, vaginal cancer, and Wilms' tumor.
99. The method as recited in claim 107, wherein the monocarboxylate transporter MCT4-mediated disorder is an inflammatory disorder.

- 100.—The method as recited in claim 113, wherein the inflammatory disorder is chosen from Crohn's disease, ulcerative colitis, idiopathic pulmonary fibrosis, muscular dystrophy, rheumatoid arthritis, and systemic sclerosis (scleroderma).
- 101.—A method of treating a monocarboxylate transporter MCT4-mediated disorder in a subject in need thereof, comprising the sequential or co-administration of a compound as recited in any of claims 1-101 or a pharmaceutically acceptable salt thereof, and another therapeutic agent.
- 102.—The method as recited in claim 115, wherein the therapeutic agent is a protein kinase inhibitor.
- 103.—The method as recited in claim 116, wherein the protein kinase inhibitor is chosen from Aurora B, EGFR, PLK-1, CDKs inhibitors.
- 104.—The method as recited in claim 115, wherein the therapeutic agent is chosen from an antimetabolite, bcr-abl inhibitor, DNA damaging agent, EGFR inhibitor, microtubule stabilizing inhibitor, mitotic arrest inhibitor, S-phase inhibitor, and a taxane.
- 105.—The method as recited in claim 118, wherein the therapeutic agent is a DNA damaging agent chosen from an alkylating agent, anthracycline, antimetabolite agent, crosslinking agent, DNA replication inhibitor, intercalator, microtubule disruptor, PARP inhibitor, radiomimetic agent, radiosensitizer, strand break agent, and topoisomerase II inhibitor.
- 106.—The method as recited in claim 115, wherein the therapeutic agent is chosen from aminoglutethimide, amsacrine, anastrozole, asparaginase, barasertib, beg, bicalutamide, bleomycin, buserelin, busulfan, camptothecin, capecitabine, carboplatin, carmustine, chlorambucil, chloroquine, cisplatin, cladribine, clodronate, colchicine, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daunorubicin, demethoxyviridin, dichloroacetate, dienestrol, diethylstilbestrol, docetaxel, doxorubicin, epirubicin, estradiol, estramustine, etoposide, everolimus, exemestane, filgrastim, fludarabine, fludrocortisone, fluorouracil, fluoxymesterone, flutamide, gemcitabine, genistein, goserelin, hydroxyurea, idarubicin, ifosfamide, imatinib, interferon, irinotecan, irinotecan, letrozole, leucovorin, leuprolide, levamisole, lomustine, lonidamine, mechlorethamine, medroxyprogesterone, megestrol, melphalan, mercaptopurine, mesna, metformin, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, nocodazole, olaparib, octreotide, oxaliplatin, paclitaxel, pamidronate, pentostatin, perifosine, plicamycin, porfimer, procarbazine, raltitrexed,

~~rituximab, sorafenib, streptozocin, sunitinib, suramin, tamoxifen, temozolomide, temsirolimus, teniposide, testosterone, thioguanine, thiotepa, titanocene dichloride, topotecan, trastuzumab, tretinoin, vinblastine, vincristine, vindesine, and vinorelbine.~~

~~107.—The method as recited in claim 107 wherein the method further comprises administering non-chemical methods of cancer treatment.~~

~~108.—The method as recited in claim 121, wherein the method further comprises administering radiation therapy.~~

~~109.—The method as recited in claim 121, wherein the method further comprises administering surgery, thermoablation, focused ultrasound therapy, cryotherapy, or any combination thereof.~~

~~110.—A compound as recited in any of claims 1–101, or a pharmaceutically acceptable salt thereof, for use in human therapy.~~

~~111.—A compound as recited in any of claims 1–101, or a pharmaceutically acceptable salt thereof, for use in treating a monocarboxylate transporter MCT4-mediated disorder.~~

~~112.—Use of a compound as recited in any of claims 1–101, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament to treat a monocarboxylate transporter MCT4-mediated disorder.~~

~~113.—The method as recited in claim 107, wherein the monocarboxylate transporter MCT4-mediated disorder is a metabolic disease.~~

~~114.—The method as recited in Claim 127 wherein said disease is a metabolic disease.~~

~~115.—The method as recited in claim 128 wherein said metabolic disease is chosen from metabolic syndrome, diabetes, dyslipidemia, fatty liver disease, non-alcoholic steatohepatitis, obesity, and insulin resistance.~~

~~116.—The method of claim 129 wherein said diabetes is Type II diabetes.~~

~~117.—The method of claim 130 wherein said dyslipidemia is hyperlipidemia.~~

~~118.—A method for achieving an effect in a patient comprising the administration of a therapeutically effective amount of a compound as recited in any of claims 1–101 to a patient, wherein the effect is selected from the group consisting of reduction of triglycerides, reduction of cholesterol, and reduction of hemoglobin A1c.~~

~~119.—The method of claim 132 wherein said cholesterol is chosen from LDL and VLDL cholesterol.~~

120. — ~~The method of claim 133 wherein said triglycerides are chosen from plasma triglycerides and liver triglycerides.~~

⋮