Claims

1. A method of screening for a candidate of a chemosensory receptor ligand modifier comprising

determining whether a test entity is suitable to interact with a chemosensory receptor *via* a first interacting site within the Venus flytrap domain of the chemosensory receptor.

2. A method of screening for a candidate of a chemosensory receptor ligand modifier comprising

determining whether a test entity is suitable to interact with a chemosensory receptor *via* a first interacting site within the Venus flytrap domain of the chemosensory receptor,

wherein the first interacting site is identified in light of a second interacting site identified based on the interaction between a chemosensory receptor ligand and the chemosensory receptor.

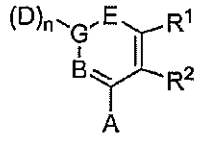
3. A method of screening for a candidate of a chemosensory receptor modifier comprising

determining whether a test entity is suitable to interact with a chemosensory receptor *via* an interacting site within the Venus flytrap domain of the chemosensory receptor,

wherein the interacting site includes an interacting residue selected from the group consisting of N143, S144, I167, S40, S144, S165, Y103, D142, P277, K65, R383, D307, E302, D278, P185, T184, T326, E302, V384, A305, I325, I306, D307, E382, I279, I67, V66, V309, S303, T242, F103, Q328, and S168 of a human T1R2 and a combination thereof,

wherein a test entity suitable to interact with the interacting site of the chemosensory receptor is indicative of a candidate of a chemosensory receptor modifier.

4. A chemosensory receptor ligand enhancer identified by the method of claim 1 and having structural Formula (I):



(I)

or a tautomer, salt, solvate, and/or ester thereof, wherein:

G forms a single bond with either D or E and a double bond with the other of D or E;

R^1 is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^3$, $-S(O)_aR^3$, $-NR^3R^4$, $-CONR^3R^4$, $-CO_2R^3$, $-NR^3CO_2R^4$, $-NR^3CONR^4R^5$, $-NR^3CSNR^4R^5$, $-NR^3C(=NH)NR^4R^5$, $-SO_2NR^3R^4$, $-NR^4SO_2R^3$, $-NR^3SO_2NR^4R^5$, $-B(OR^3)(OR^4)$, $-P(O)(OR^3)(OR^4)$ or $-P(O)(R^3)(OR^4)$;

R^2 is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^6$, $-S(O)_bR^6$, $-NR^6R^7$, $-CONR^6R^7$, $-CO_2R^6$, $-NR^6CO_2R^7$, $-NR^6CONR^7R^8$, $-NR^6CSNR^7R^8$, $-NR^6C(=NH)NR^7R^8$, $-SO_2NR^5R^6$, $-NR^5SO_2R^6$, $-NR^5SO_2NR^6R^7$, $-B(OR^5)(OR^6)$, $-P(O)(OR^5)(OR^6)$, or $-P(O)(R^5)(OR^6)$; or alternatively, R^1 and R^2, together with the atoms to which they are bonded, form an aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring wherein the ring is optionally fused to another aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring;

with the proviso that R^1 and R^2 are not both hydrogen;

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, halo, -CN, $-NO_2$, $-OR^9$, $-S(O)_cR^9$, $-NR^9COR^{10}$, $-NHOR^9$, $-NR^9R^{10}$, $-NOR^9$, $-CONR^9R^{10}$, $-CO_2R^9$, $-NR^9CO_2R^{10}$, $-NR^9CONR^{10}R^{11}$, $-NR^9CSNR^{10}R^{11}$, $-NR^9C(=NH)NR^{10}R^{11}$, $-B(OR^{10})(OR^{11})$, $-P(O)(OR^{10})(OR^{11})$ or $-P(O)(R^{10})(OR^{11})$;

B is -N- or $-C(R^{12})-$;

R^{12} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, $-NR^{13}R^{14}$,

-CN, -OR^{13}, -$S(O)_dR^{13}$, -CO_2R^{13} or -$CONR^{13}R^{14}$;

G is -C- or -$S(O)_2$-;

provided that when G is -$S(O)_2$-, then G forms a single bond with E;

when the bond between D and G is a single bond, then D is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -OR^{15}, -NH-OR^{15}, -$S(O)_eR^{15}$, -$NR^{15}R^{16}$, -NH-NHR^{15}, -CO_2R^{15}, or -$CONR^{15}R^{16}$;

when G forms a double bond with D, then D is =O, =S , =N-OR^{15}, or =N-NHR^{15};

n is 0 when G is -$S(O)_2$-, and n is 1 when G is -C-;

E is -NR^{17}-, -N- or -$C(R^{18})$-;

provided that E is -NR^{17}- only when G forms a single bond with E;

R^{17} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl or -CO_2R^{19};

R^{18} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -$NR^{20}R^{21}$, -CN, -OR^{20}, -$S(O)_fR^{20}$, -CO_2R^{20} or -$CONR^{20}R^{21}$;

a, b, c, d, e and f are independently 0, 1 or 2; and

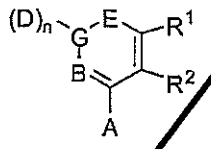
R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{18}, R^{20}, and R^{21} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively, R^3 and R^4, R^4 and R^5, R^6 and R^7, R^7 and R^8, R^9 and R^{10}, R^{10} and R^{11}, R^{13} and R^{14}, R^{15} and R^{16}, or R^{20} and R^{21}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.

5. A method of modulating the activity of a chemosensory receptor ligand comprising contacting a chemosensory receptor ligand modifier with a cell containing T1R2 Venus flytrap

domain in the presence of a chemosensory receptor ligand, wherein the chemosensory receptor ligand modifier interacts with an interacting site of the chemosensory receptor.

6. A chemosensory receptor ligand modifier, wherein in the presence of a chemosensory receptor ligand it interacts with T1R2 Venus flytrap domain *via* at least three interacting residues selected from the group consisting of N143, S144, I167, S40, S144, S165, Y103, D142, P277, K65, R383, D307, E302, D278, P185, T184, T326, E302, V384, A305, I325, I306, E382, I279, I67, V66, V309, S303, T242, F103, Q328, and S168 of a human T1R2.

7. A compound having structural Formula (I):



(I)

or a tautomer, salt, solvate, and/or ester thereof, wherein:

G forms a single bond with either D or E and a double bond with the other of D or E;

R^1 and R^2, together with the atoms to which they are bonded, form an aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring, wherein the ring is optionally fused to another aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring;

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, halo, -CN, $-NO_2$, $-OR^9$, $-S(O)_cR^9$, $-NR^9COR^{10}$, $-NHOR^9$, $-NR^9R^{10}$, $-NOR^9$, $-CONR^9R^{10}$, $-CO_2R^9$, $-NR^9CO_2R^{10}$, $-NR^9CONR^{10}R^{11}$, $-NR^9CSNR^{10}R^{11}$, $-NR^9C(=NH)NR^{10}R^{11}$, $-B(OR^{10})(OR^{11})$, $-P(O)(OR^{10})(OR^{11})$ or $-P(O)(R^{10})(OR^{11})$;

B is -N- or $-C(R^{12})-$;

R^{12} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, $-NR^{13}R^{14}$, -CN, $-OR^{13}$, $-S(O)_dR^{13}$,

$-CO_2R^{13}$ or $-CONR^{13}R^{14}$;

G is -C- or $-S(O)_2-$;

provided that when G is $-S(O)_2-$, then G forms a single bond with E;

when the bond between D and G is a single bond, then D is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, $-OR^{15}$, $-NH-OR^{15}$, $-S(O)_eR^{15}$, $-NR^{15}R^{16}$, $-NH-NHR^{15}$, $-CO_2R^{15}$, or $-CONR^{15}R^{16}$;

when G forms a double bond with D, then D is =O, =S , $=N-OR^{15}$, or $=N-NHR^{15}$;

n is 0 when G is $-S(O)_2-$, and n is 1 when G is -C-;

E is $-NR^{17}-$, -N- or $-C(R^{18})-$;

provided that E is $-NR^{17}-$ only when G forms a single bond with E;

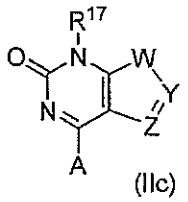
R^{17} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl or $-CO_2R^{19}$;

R^{18} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, $-NR^{20}R^{21}$, -CN, $-OR^{20}$, $-S(O)_fR^{20}$, $-CO_2R^{20}$ or $-CONR^{20}R^{21}$;

c, d, e, and f are independently 0, 1 or 2; and

R^9, R^{10}, R^{11}, R^{13}, R^{14}, R^{15}, R^{16}, R^{18}, R^{20}, and R^{21} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively, R^9 and R^{10}, R^{10} and R^{11}, R^{13} and R^{14}, R^{15} and R^{16}, or R^{20} and R^{21}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.

8. The compound of claim 7, having structural Formula (IIc):



(IIc)

wherein,

W is -S-, -N(R^{25})-, or -O-;

Y is -C(R^{26})- or -N-; and

Z is -C(R^{27})- or -N-;

R^{26} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, halo, -CN, -NO_2, -OR^{31}, -$S(O)_hR^{31}$, -$OCOR^{31}$, -$NR^{31}R^{32}$, -$CONR^{31}R^{32}$, -CO_2R^{31}, -$SO_2NR^{31}R^{32}$, -$NR^{31}SO_2R^{32}$, -$B(OR^{31})(OR^{32})$, -$P(O)(OR^{31})(OR^{32})$ or -$P(O)(R^{31})(OR^{32})$;

R^{27} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, halo, -CN, -NO_2, -OR^{33}, -$S(O)_iR^{33}$, -$OCOR^{33}$, -$NR^{33}R^{34}$, -$CONR^{33}R^{34}$, -COR^{33}, -CO_2R^{33}, -$SO_2NR^{33}R^{34}$, -$NR^{33}SO_2R^{34}$, -$B(OR^{33})(OR^{34})$, -$P(O)(OR^{33})(OR^{34})$ or -$P(O)(R^{33})(OR^{34})$; or alternatively R^{24} and R^{26}, or R^{26} and R^{27}, together with the atoms to which they are bonded form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring;

h and i are independently 0 or 1;

R^{25} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; and

R^{31}, R^{32}, R^{33}, and R^{34} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively R^{31} and R^{32},or R^{33} and R^{34}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.

9. The compound of claim 8, wherein

Y is -C(R^{26})-, and

Z is -C(R^{27})-.

10. The compound of claim 8, wherein

R^{27} is hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, -CN, -NO_2, -OR^{33}, -$S(O)_iR^{33}$, -$OCOR^{33}$, -$NR^{33}R^{34}$, -$CONR^{33}R^{34}$ or -CO_2R^{33}; and

R^{26} is hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, -CN, -NO_2, -OR^{31}, -$S(O)_hR^{31}$, -$OCOR^{31}$, -$NR^{31}R^{32}$, -$CONR^{31}R^{32}$ or -CO_2R^{31}.

11. The compound of any of claims 8, wherein

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, -NR^9COR^{10}, -$NHOR^9$, -NOR^9, -OR^9, -$NR^9CONR^{10}R^{11}$, -$NR^9CSNR^{10}R^{11}$ or -$NR^9C(=NH)NR^{10}R^{11}$, -CN, -NO_2, -$S(O)_cR^9$, -NR^9R^{10}, -$C(O)NR^9R^{10}$, -CO_2R^9 or -$NR^9CO_2R^{10}$; and

R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl.

12. The compound of any of claims 8, wherein

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, -NR^9COR^{10}, -$NHOR^9$, -NOR^9, -OR^9, -$NR^9CONR^{10}R^{11}$, -$NR^9CSNR^{10}R^{11}$ or -$NR^9C(=NH)NR^{10}R^{11}$, -CN, -NO_2, -$S(O)_cR^9$, -NR^9R^{10}, -$NR^9C(O)R^{10}$, -$C(O)NR^9R^{10}$, -CO_2R^9 or -$NR^9CO_2R^{10}$;

R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl;

R^{27} is hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, -CN, -NO_2, -OR^{33}, -$S(O)_iR^{33}$, -$OCOR^{33}$, -$NR^{33}R^{34}$, -$C(O)NR^{33}R^{34}$ or -CO_2R^{33}; and

R^{26} is hydrogen, alkyl, substituted alkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, -CN, -NO_2, -OR^{31}, -$S(O)_hR^{31}$, -$OC(O)R^{31}$, -$NR^{31}R^{32}$, -$C(O)NR^{31}R^{32}$or -CO_2R^{31}, or alternatively R^{26} and R^{27} together with the atom(s) to which they are bonded form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring.

13. The compound of claim 12, wherein

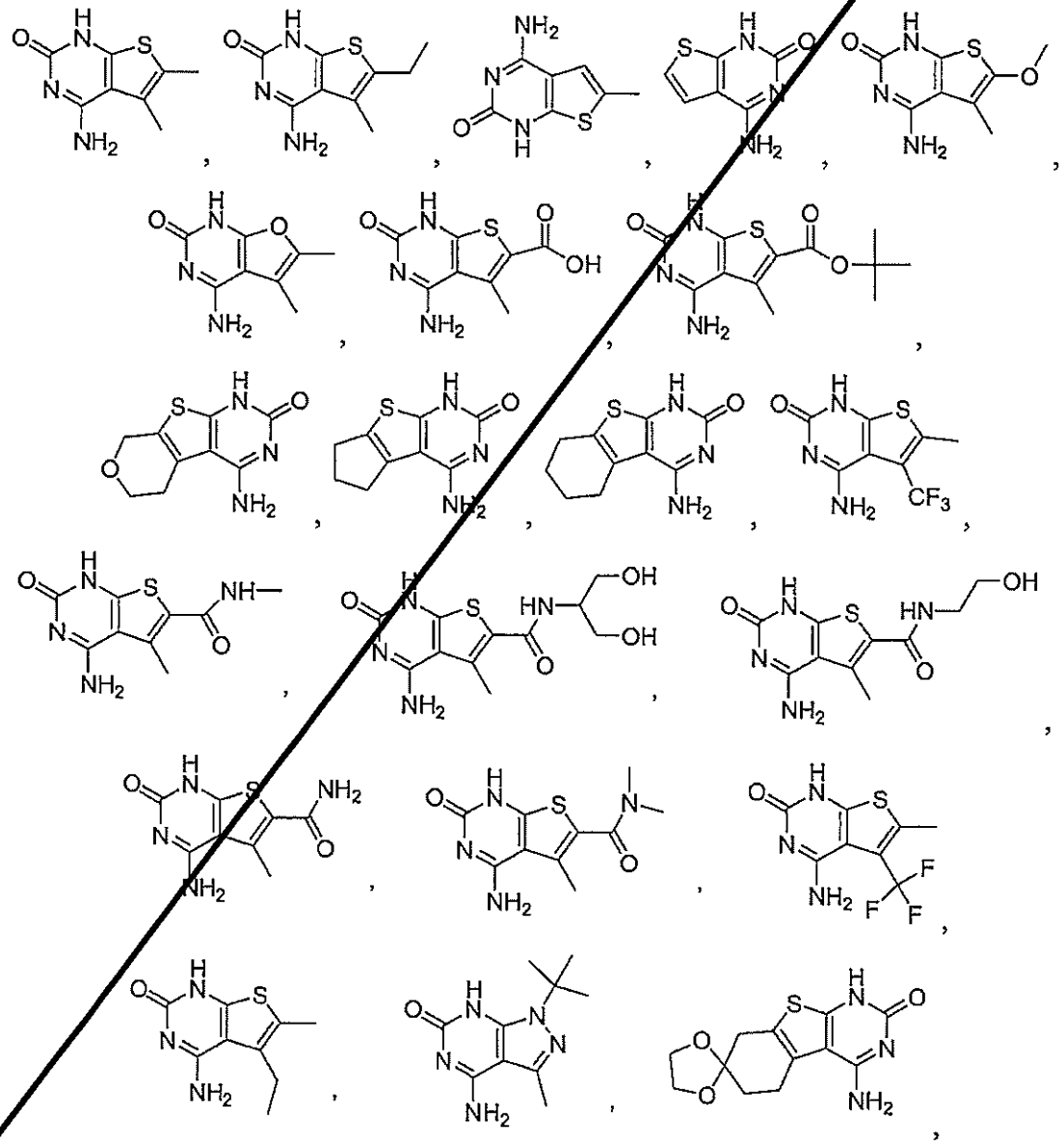
A is -NH_2;

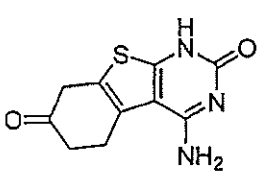
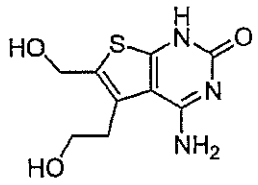
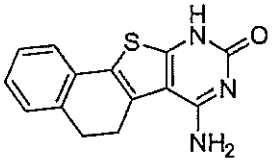
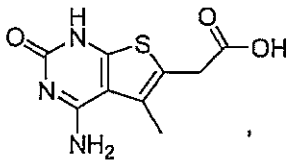
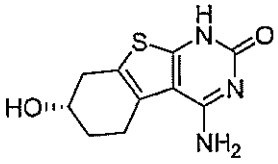
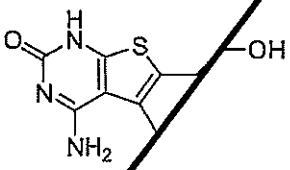
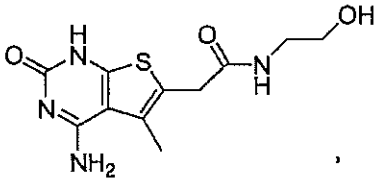
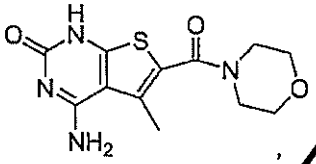
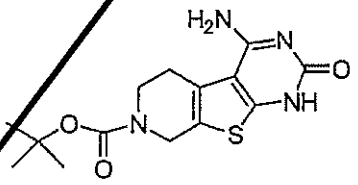
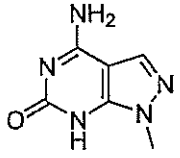
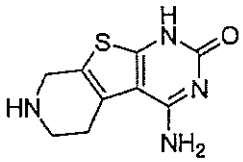
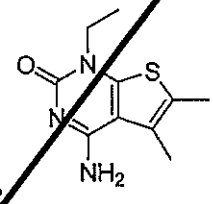
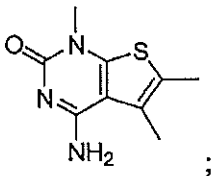
R^{17} is hydrogen, methyl, ethyl, propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *t*-butyl, phenyl or benzyl;

R^{26} and R^{27} are independently hydrogen, alkanyl, substituted alkanyl, alkoxy, carboxylic acid, carboxylic acid amide, or carboxylic acid ester;

or alternatively, R^{26} and R^{27} together with the atom(s) to which they are bonded form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring.

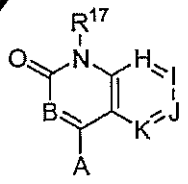
14. The compound of claim 8, having structural formula selected from the group consisting of:




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or a tautomer, salt, solvate, and/or ester thereof.

15. The compound of claim 7, having structural Formula (IIIa):


(IIIa),

wherein:

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$, $-NR^9CO_2R^{10}$, $-NR^9CONR^{10}R^{11}$, $-NR^9CSNR^{10}R^{11}$, or $-NR^9C(=NH)NR^{10}R^{11}$;

H is $-C(R^{35})-$ or -N-;

I is $-C(R^{36})$ or -N-;

J is -C(R^{37})- or -N-;

K is -C(R^{38})- or -N-;

R^{35} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, -NO_2, -OR^{39}, -$S(O)_jR^{39}$, -$OCOR^{39}$, -$NR^{39}R^{40}$, -$CONR^{39}R^{40}$, -CO_2R^{39}, -$SO_2NR^{39}R^{40}$, -$NR^{39}SO_2R^{40}$, -$B(OR^{39})(OR^{40})$, -$P(O)(OR^{39})(OR^{40})$ or -$P(O)(R^{39})(OR^{40})$;

R^{36} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, -NO_2, -OR^{41}, -$S(O)_kR^{41}$, -$OCOR^{41}$, -$NR^{41}R^{42}$, -$CONR^{41}R^{42}$, -CO_2R^{41}, -$SO_2NR^{41}R^{42}$, -$NR^{41}SO_2R^{42}$, -$B(OR^{41})(OR^{42})$, -$P(O)(OR^{41})(OR^{42})$ or -$P(O)(R^{41})(OR^{42})$;

R^{37} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl ,-CN, -NO_2, -OR^{43}, -$S(O)_lR^{43}$, -$OCOR^{43}$, -$NR^{43}R^{44}$, -$CONR^{43}R^{44}$, -CO_2R^{43}, -$SO_2NR^{43}R^{44}$, -$NR^{43}SO_2R^{44}$, -$B(OR^{43})(OR^{44})$, -$P(O)(OR^{43})(OR^{44})$ or -$P(O)(R^{43})(OR^{44})$;

R^{38} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, -NO_2, -OR^{45}, -$S(O)_mR^{45}$, -$OCOR^{45}$, -$NR^{45}R^{46}$, -$CONR^{45}R^{46}$, -COR^{45}, -CO_2R^{45}, -$SO_2NR^{45}R^{46}$, -$NR^{45}SO_2R^{46}$, -$B(OR^{45})(OR^{46})$, -$P(O)(OR^{45})(OR^{46})$ or -$P(O)(R^{45})(OR^{46})$; or alternatively R^{36} and R^{37}, or R^{37} and R^{38}, taken together with the atom to which they are bonded, form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, or substituted cycloheteroalkyl ring;

j, k, l and m are independently 0, 1 or 2; and

R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, and R^{46} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively R^{39} and R^{40}, R^{41} and R^{42}, R^{43} and R^{44}, or R^{45} and R^{46}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl

ring;

with the proviso that at most, two of H, I, J and K are -N-.

16. The compound of claim 15, wherein R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl.

17. The compound of claim 15, wherein

H is $-C(R^{35})-$;

I is $-C(R^{36})$;

J is $-C(R^{37})-$; and

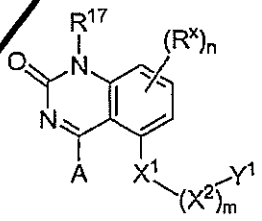
K is $-C(R^{38})-$.

18. The compound of any of claims 15, wherein

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, -CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$ or $-NR^9CO_2R^{10}$; and

R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl.

19. The compound of claim 15, having structural Formula (IIIa1):



(IIIa1)

wherein,

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NOR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$ or $-NR^9CO_2R^{10}$;

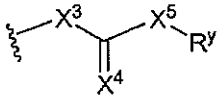
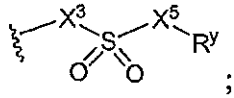
R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl;

X^1 is $-CH_2-$, $-O-$, $-NR^9-$, $-S-$, $-S(O)-$, or $-S(O)_2-$;

X^2 is alkylene, substituted alkylene, heteroalkylene, or substituted heteroalkylene;

m is 0 or 1;

Y^1 is cycloheteroalkyl, substituted cycloheteroalkyl, or


, or

;

X^3 and X^5 are independently a covalent bond, –O– or –NR^9–;

X^4 is O, NR^9, N-OR^9, or S;

R^x is halo, -NO_2, -CN, -OH, -NH_2, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

n is 0, 1, 2, or 3;

R^y is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl, -NR^9R^{10};

c is 0, 1, or 2; and

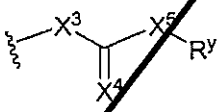
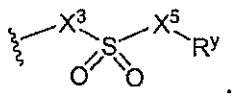
each R^9 and R^{10} is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

with the proviso that when X^1 is –O– or –S–, and m is zero; then X^3 is not –O–.

20. The compound of claim 19, wherein

X^1 is –CH_2-; and

Y^1 is


, or

.

21. The compound of claim 19, wherein

X^1 is –O–, –NR^9–, or –S–;

m is 0 or 1, and

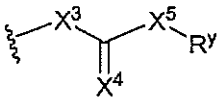
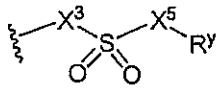
Y^1 is cycloheteroalkyl or substituted cycloheteroalkyl.

22. The compound of claim 19, wherein

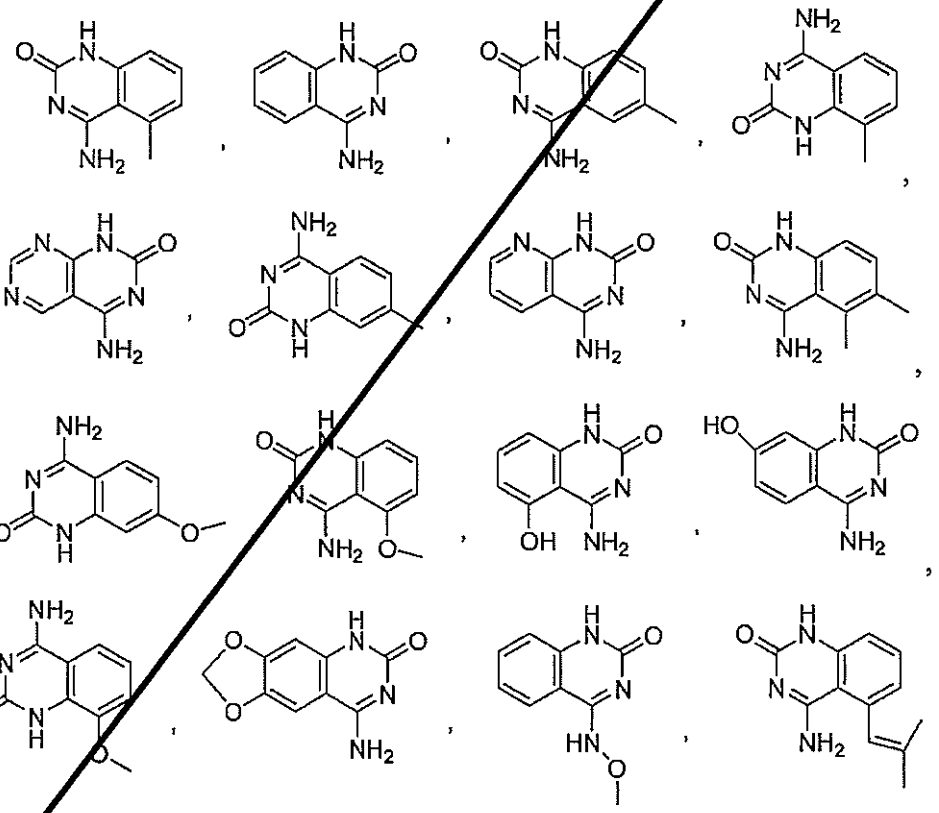
X^1 is –O–, –NR^9–, or –S–;

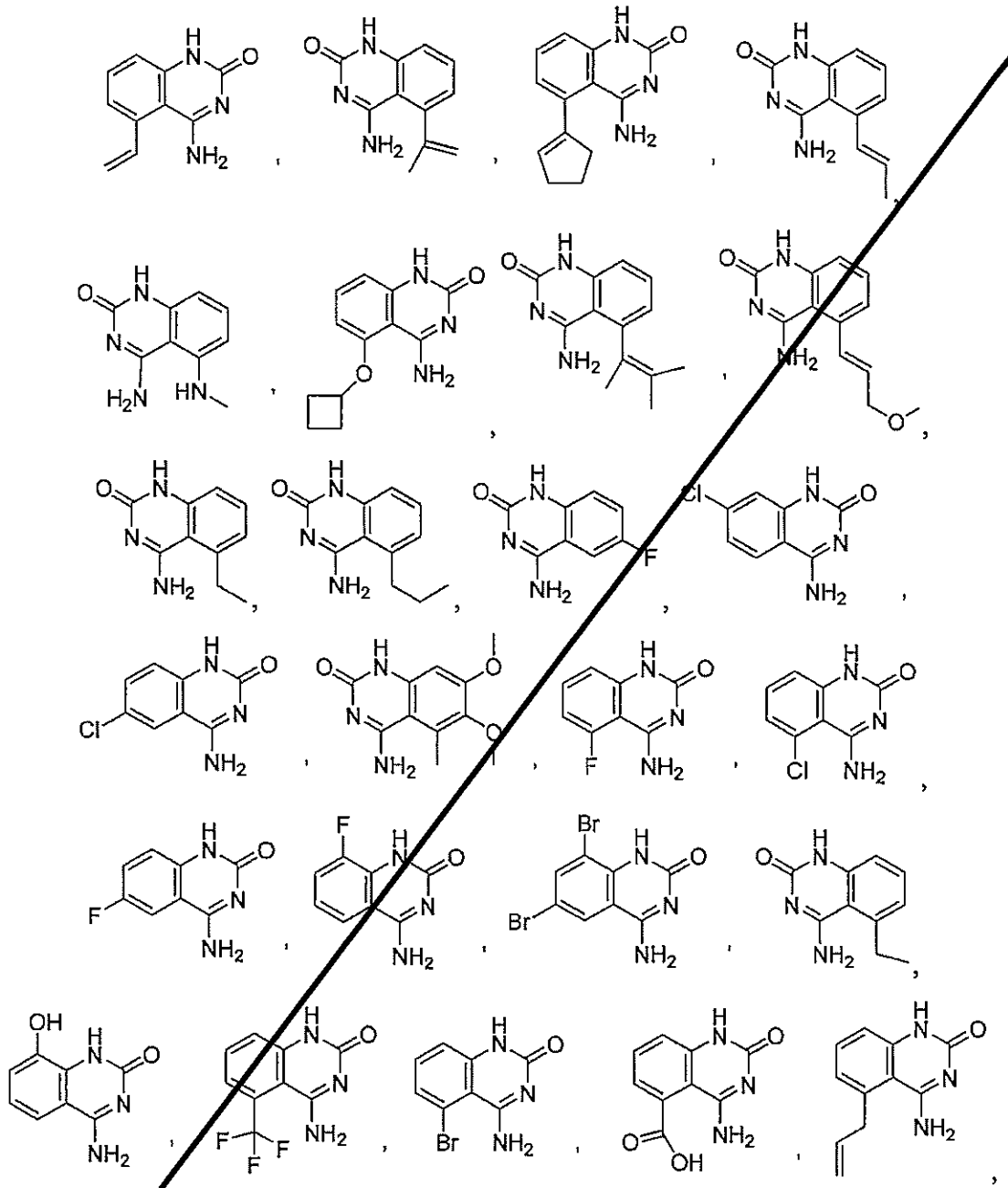
m is 1, and

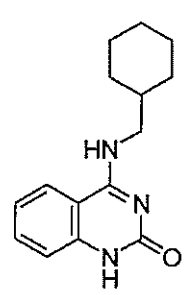
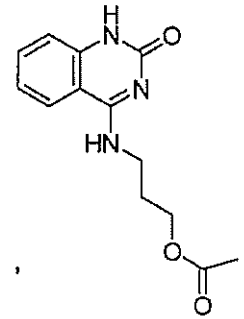
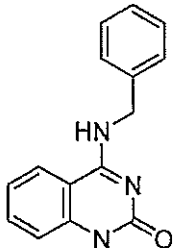
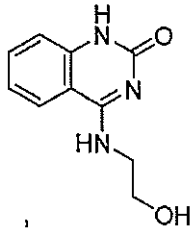
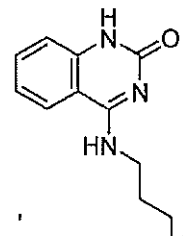
Y^1 is

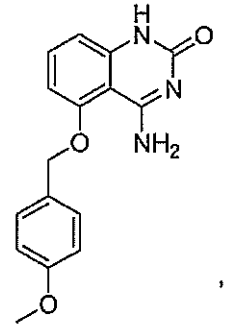
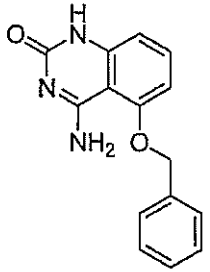
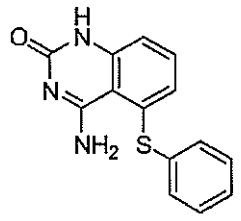
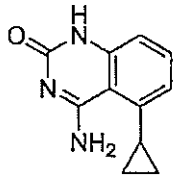

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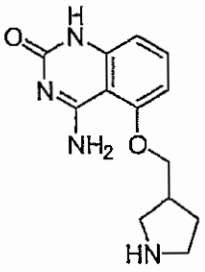
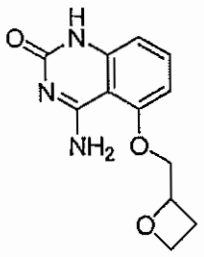
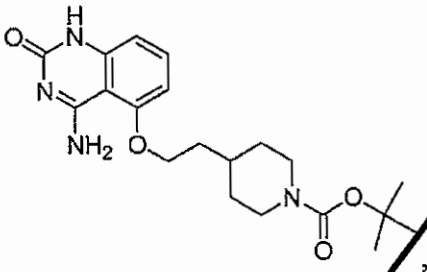
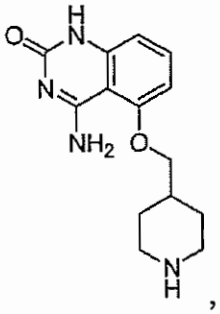
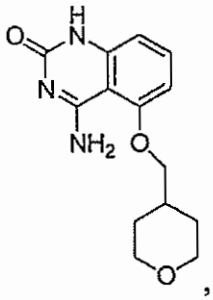
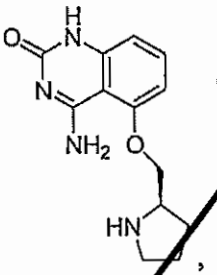
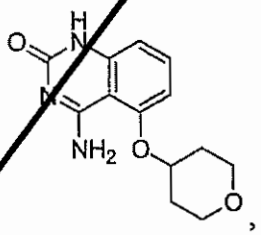
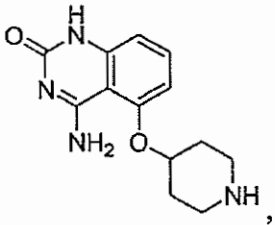
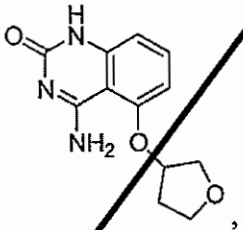
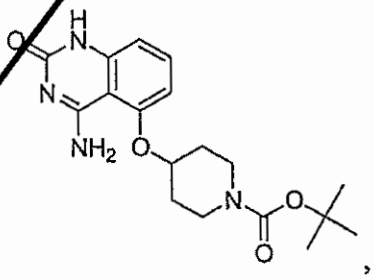
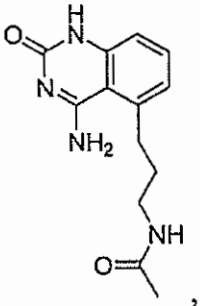
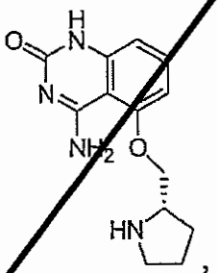
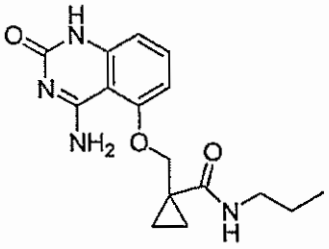
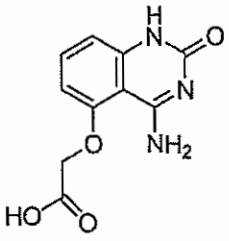
23. The compound of claim 17, having structural formula selected from the group consisting of





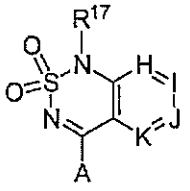







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or a tautomer, salt, solvate, and/or ester thereof.

24. The compound of claim 7, having structural Formula (IIIb):



(IIIb).

wherein

H is -C(R^{35})- or -N-;

I is -C(R^{36}) or -N-;

J is -C(R^{37})- or -N-;

K is -C(R^{38})- or -N-;

R^{35} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^{39}$, $-S(O)_jR^{39}$, $-OCOR^{39}$, $-NR^{39}R^{40}$, $-CONR^{39}R^{40}$, $-CO_2R^{39}$, $-SO_2NR^{39}R^{40}$, or $-NR^{39}SO_2R^{40}$;

R^{36} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^{41}$, $-S(O)_kR^{41}$, $-OCOR^{41}$, $-NR^{41}R^{42}$, $-CONR^{41}R^{42}$, $-CO_2R^{41}$, $-SO_2NR^{41}R^{42}$, or $-NR^{41}SO_2R^{42}$;

R^{37} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl ,-CN, $-NO_2$, $-OR^{43}$, $-S(O)_lR^{43}$, $-OCOR^{43}$, $-NR^{43}R^{44}$, $-CONR^{43}R^{44}$, $-CO_2R^{43}$, $-SO_2NR^{43}R^{44}$, or $-NR^{43}SO_2R^{44}$;

R^{38} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^{45}$, $-S(O)_mR^{45}$, $-OCOR^{45}$, $-NR^{45}R^{46}$, $-CONR^{45}R^{46}$, $-COR^{45}$, $-CO_2R^{45}$, $-SO_2NR^{45}R^{46}$, or $-NR^{45}SO_2R^{46}$; or alternatively R^{36} and R^{37}, or R^{37} and R^{38}, taken together with the atom to which they are bonded, form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, or substituted cycloheteroalkyl ring;

j, k, l and m are independently 0, 1 or 2; and

R^{39}, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, and R^{46} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, or substituted

heteroarylalkyl; or alternatively R^{39} and R^{40}, R^{41} and R^{42}, R^{43} and R^{44}, or R^{45} and R^{46}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring;

with the proviso that at most, two of H, I, J and K are -N-.

25. The compound of claim 24, wherein A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, -CN, $-NO_2$, $-OR^9$, $-S(O)_cR^9$, $-NR^9COR^{10}$, $-NHOR^9$, $-NR^9R^{10}$, $-NOR^9$, $-CONR^9R^{10}$, $-CO_2R^9$, $-NR^9CO_2R^{10}$, $-NR^9CONR^{10}R^{11}$, $-NR^9CSNR^{10}R^{11}$, or $-NR^9C(=NH)NR^{10}R^{11}$.

26. The compound of claim 24, wherein R^{17} is hydrogen, alkyl, or substituted alkyl.

27. The compound of any of claims 24, wherein

H is $-C(R^{35})-$;

I is $-C(R^{36})-$;

J is $-C(R^{37})-$; and

K is $-C(R^{38})-$.

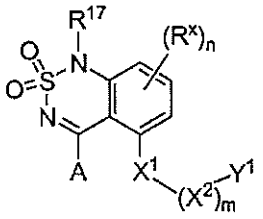
28. The compound of any of claims 24, wherein

A is $-NH_2$,

R^{17} is hydrogen, methyl, ethyl or benzyl; and

R^{35}, R^{36}, R^{37} and R^{38} are independently hydrogen, fluoro, chloro, bromo, -CN, alkanyl, substituted alkanyl, alkenyl, substitued alkenyl, alkynyl, substituted alkynyl, cycloalkanyl, substituted cycloalkanyl, cycloalkenyl, substitued cycloalkenyl, heteroalkanyl, substituted heteroalkanyl, cycloheteroalkyl, substituted cycloheteroalkyl, -O-alkanyl, -O-(substituted alkanyl), -O-alkenyl, -O-(substituted alkenyl), -NH-alkanyl, -NH-(substituted alkanyl), -NH-alkenyl, -NH-(substituted alkenyl), -S-alkanyl, -S-(substituted alkanyl), -S-alkenyl, or -S-(substituted alkenyl).

29. The compound of claim 24, having structural Formula (IIIb1):



(IIIb1)

wherein,

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NOR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$ or $-NR^9CO_2R^{10}$;

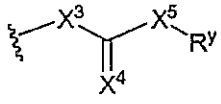
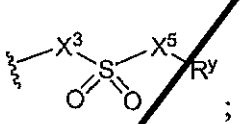
R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl;

X^1 is $-CH_2-$, $-O-$, $-NR^9-$, $-S-$, $-S(O)-$, or $-S(O)_2-$;

X^2 is alkylene, substituted alkylene, heteroalkylene, or substituted heteroalkylene;

m is 0 or 1;

Y^1 is heteroaryl, substituted heteroaryl, cycloheteroalkyl, substituted cycloheteroalkyl, or

 , or  ;

X^3 and X^5 are independently a covalent bond, $-O-$ or $-NR^9-$;

X^4 is O, NR^9, N-OR^9, or S;

R^x is halo, $-NO_2$, -CN, -OH, $-NH_2$, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

n is 0, 1, 2, or 3;

R^y is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl, $-NR^9R^{10}$; and

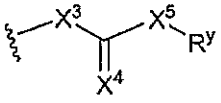
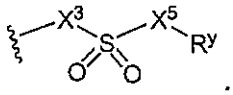
each R^9 and R^{10} is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

with the proviso that when X^1 is $-O-$ or $-S-$, and m is zero; then X^3 is not $-O-$.

30. The compound of claim 29, wherein

X^1 is $-CH_2-$; and

Y^1 is


, or 
.

31. The compound of claim 29, wherein

X^1 is –O–, $-NR^9-$, or –S–;

m is 0 or 1, and

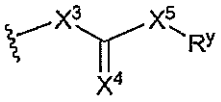
Y^1 is cycloheteroalkyl or substituted cycloheteroalkyl.

32. The compound of claim 29, wherein

X^1 is –O–, $-NR^9-$, or –S–;

m is 1, and

Y^1 is


, or 
.

33. The compound of any of claims 29, wherein

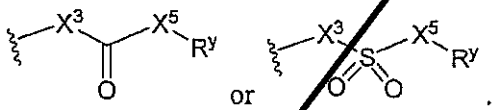
X^2 is methylene, ethylene, propylene, *iso*-propylene, butylene, *iso*-butylene, *sec*-butylene, pentylene, hexylene, heptylene, dimethylethylene, methylcyclopropylene, cyclopropylmethylene, ethenylene, propenylene, or butenylene.

34. The compound of any of claims 29, wherein Y^1 is piperidinyl, substituted piperidinyl, tetrahydrofuranyl, subsitituted tetrahydrofuranyl, tetrahydropyranyl, subsitituted tetrahydropyranyl, dihydrofuranyl, substituted dihydrofuranyl, pyrrolidinyl, substituted pyrrolidinyl, oxetanyl, substituted oxetanyl, saccharide ring or its derivative, substituted saccharide ring or its derivative.

35. The compound of any of claims 29, wherein Y^1 is pyridinyl, substituted pyridinyl, pyrrolyl, substituted pyrrolyl, furanyl, substituted furanyl, pyrazolyl, substituted pyrazolyl, isoxazolyl, substituted isoxazolyl, oxazolyl, and substituted oxazolyl.

36. The compound of any of claims 29, wherein the substituted cycloheteroalkyl comprises one or more substituents selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NOR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$, and $-NR^9CO_2R^{10}$.

37. The compound of any of claims 29, wherein Y^1 is



38. The compound of any of claims 29, wherein $-X^3-C(X^4)-X^5-$ is –C(O)-, -C(O)-NH-, -NH-C(O)-, -NH-C(O)-NH-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -NH-C(O)-O-, -O-C(O)-NH-, –C(NH)-, -C(NH)-NH-, -NH-C(NH)-, -NH-C(NH)-NH-, -C(NH)-O-, -O-C(NH)-, -O-C(NH)-O-, -NH-C(NH)-O-, -O-C(NH)-NH-, -C(NOH)-, or -C(S)-.

39. The compound of any of claims 29, wherein

A is hydrogen, alkyl, substituted alkyl, or $-NR^9R^{10}$;

R^{17} is hydrogen; and

Y^1 is piperidinyl, substituted piperidinyl, tetrahydrofuranyl, subsitituted tetrahydrofuranyl, tetrahydropyranyl, subsitituted tetrahydropyranyl, dihydrofuranyl, substituted dihydrofuranyl, pyrrolidinyl, substituted pyrrolidinyl, oxetanyl, substituted oxetanyl, monosaccharide ring, substituted monosaccharide ring, pyridinyl, substituted pyridinyl, pyrrolyl, substituted pyrrolyl, furanyl, substituted furanyl, pyrazolyl, substituted pyrazolyl, isoxazolyl, substituted isoxazolyl, oxazolyl, or substituted oxazolyl.

40. The compound of any of claims 29, wherein

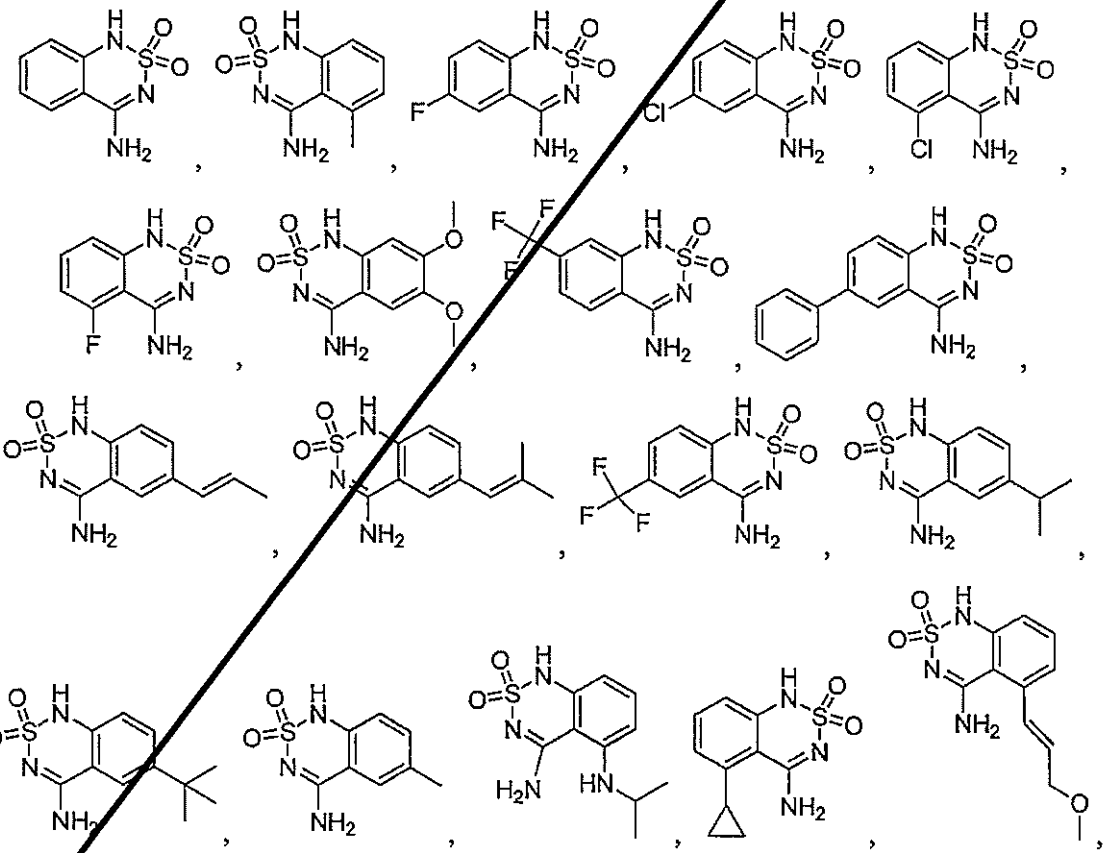
A is hydrogen, alkyl, substituted alkyl, or $-NR^9R^{10}$;

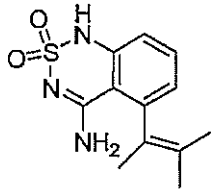
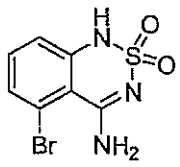
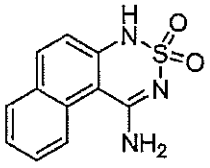
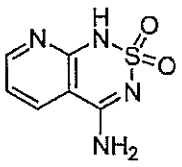
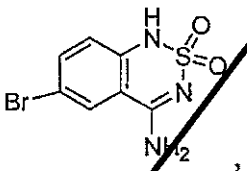
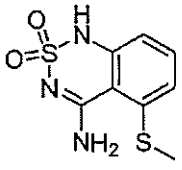
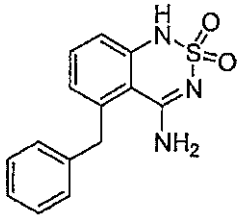
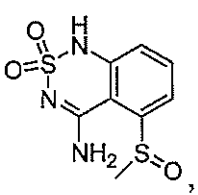
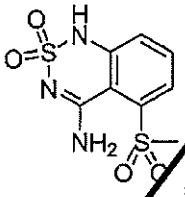
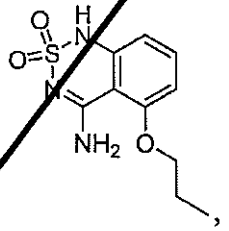
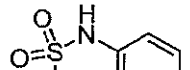
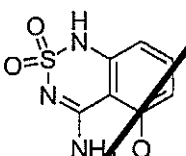
R^{17} is hydrogen;

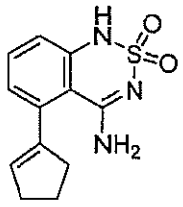
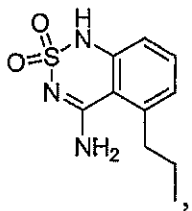
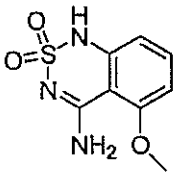
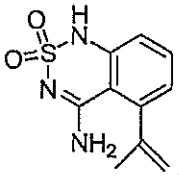
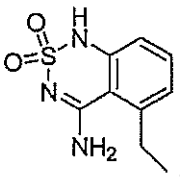
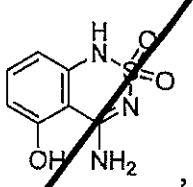
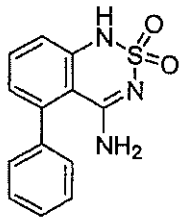
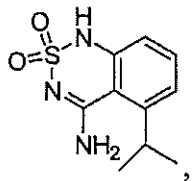
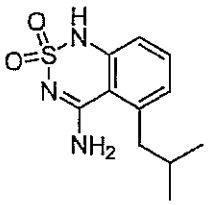
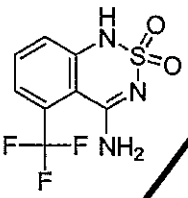
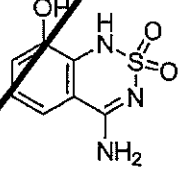
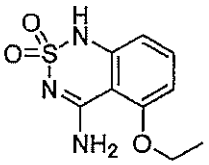
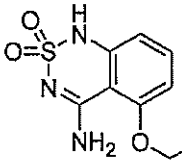
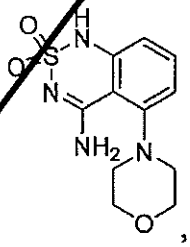
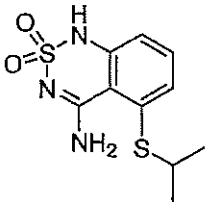
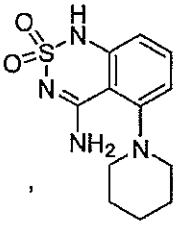
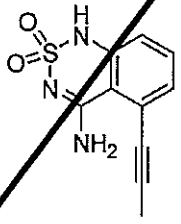
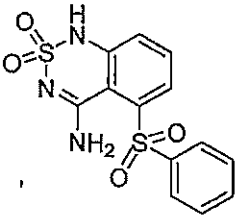
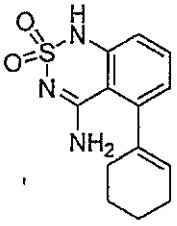
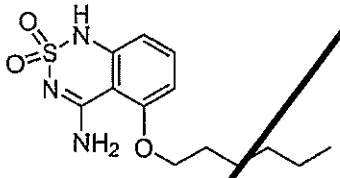
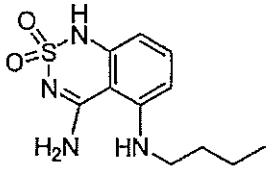
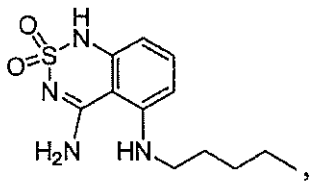
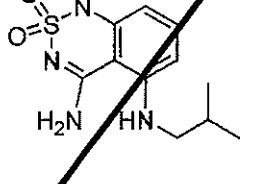
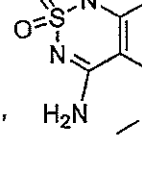
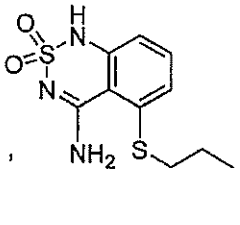
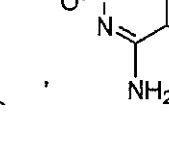
Y^1 is $-X^3-C(X^4)-X^5-$; and

$-X^3-C(X^4)-X^5-$ is –C(O)-, -C(O)-NH-, -NH-C(O)-, -NH-C(O)-NH-, -C(O)-O-, -O-C(O)-, -O-C(O)-O-, -NH-C(O)-O-, -O-C(O)-NH-, –C(NH)-, -C(NH)-NH-, -NH-C(NH)-, -NH-C(NH)-NH-, -C(NH)-O-, -O-C(NH)-, -O-C(NH)-O-, -NH-C(NH)-O-, -O-C(NH)-NH-, $-S(O)_2-$, $-NH-S(O)_2-$, $-S(O)_2-NH-$, $-O-S(O)_2-$, $-S(O)_2-O-$, -C(N-OH)-, or -C(S)-.

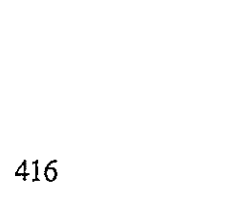
41. The compound of claim 24, having structural formula selected from the group consisting of



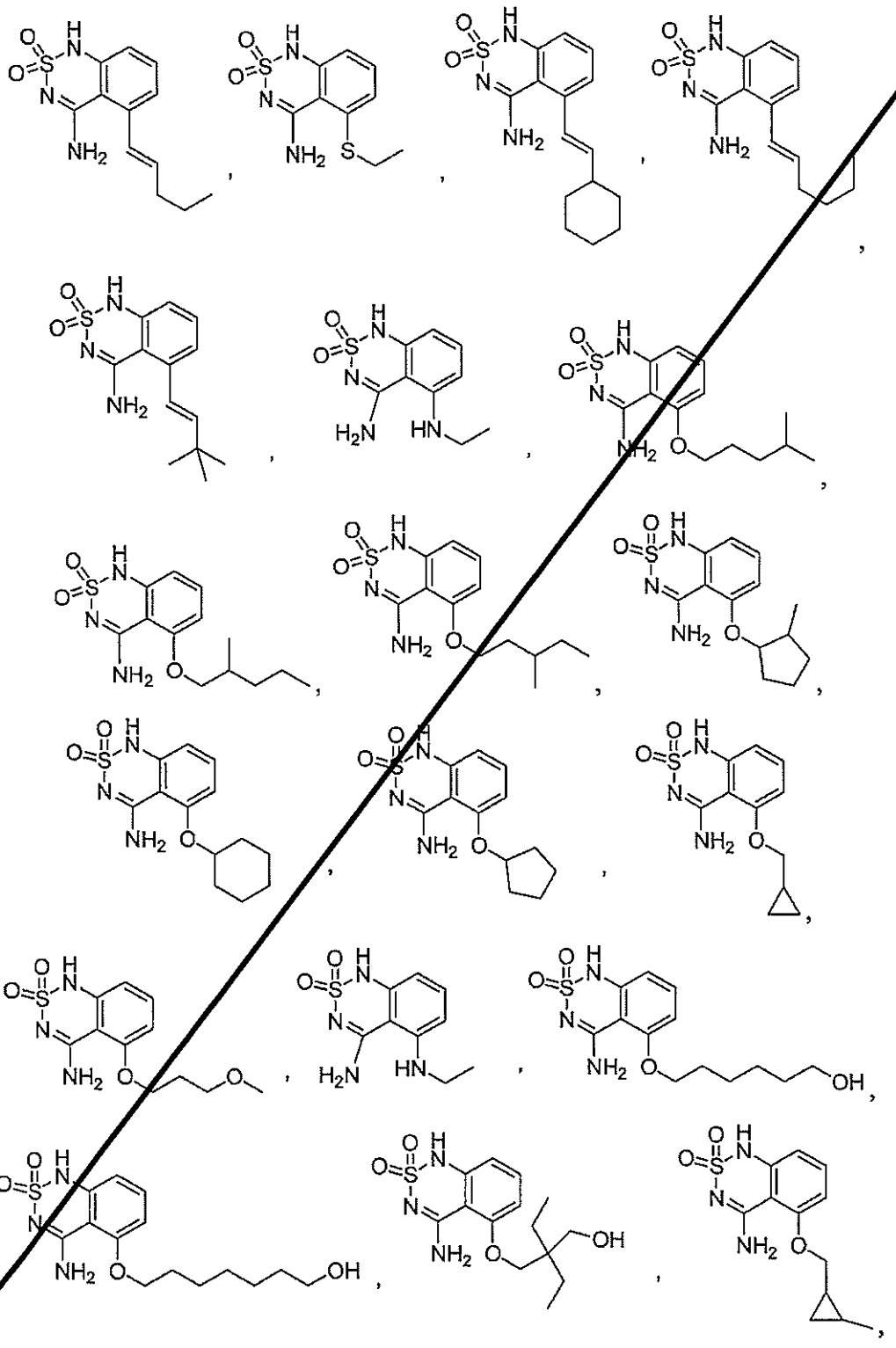

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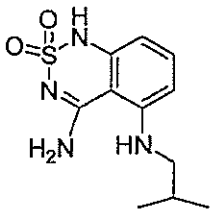
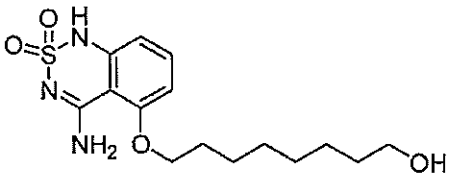
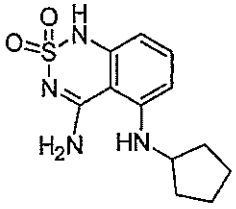
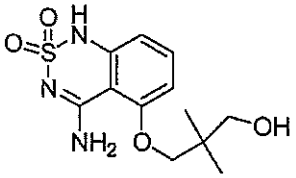
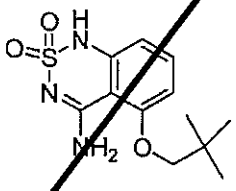
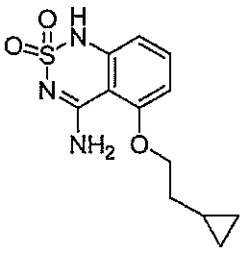
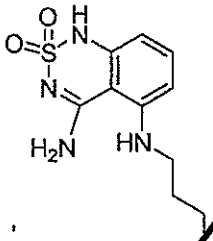
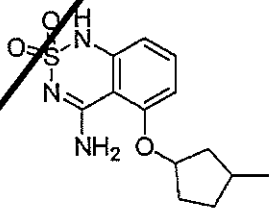
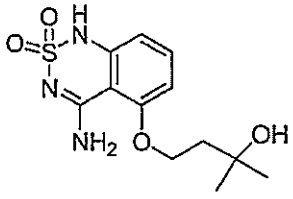
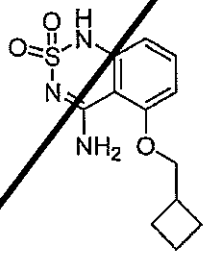
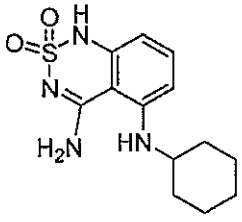
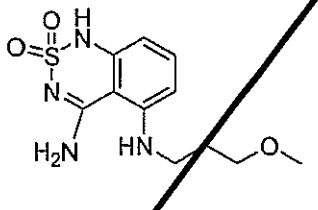
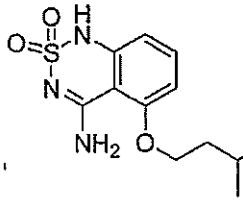
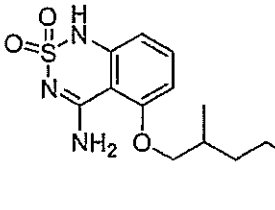

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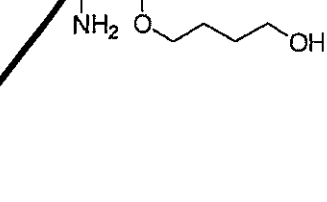
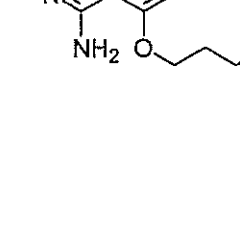
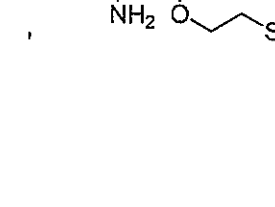
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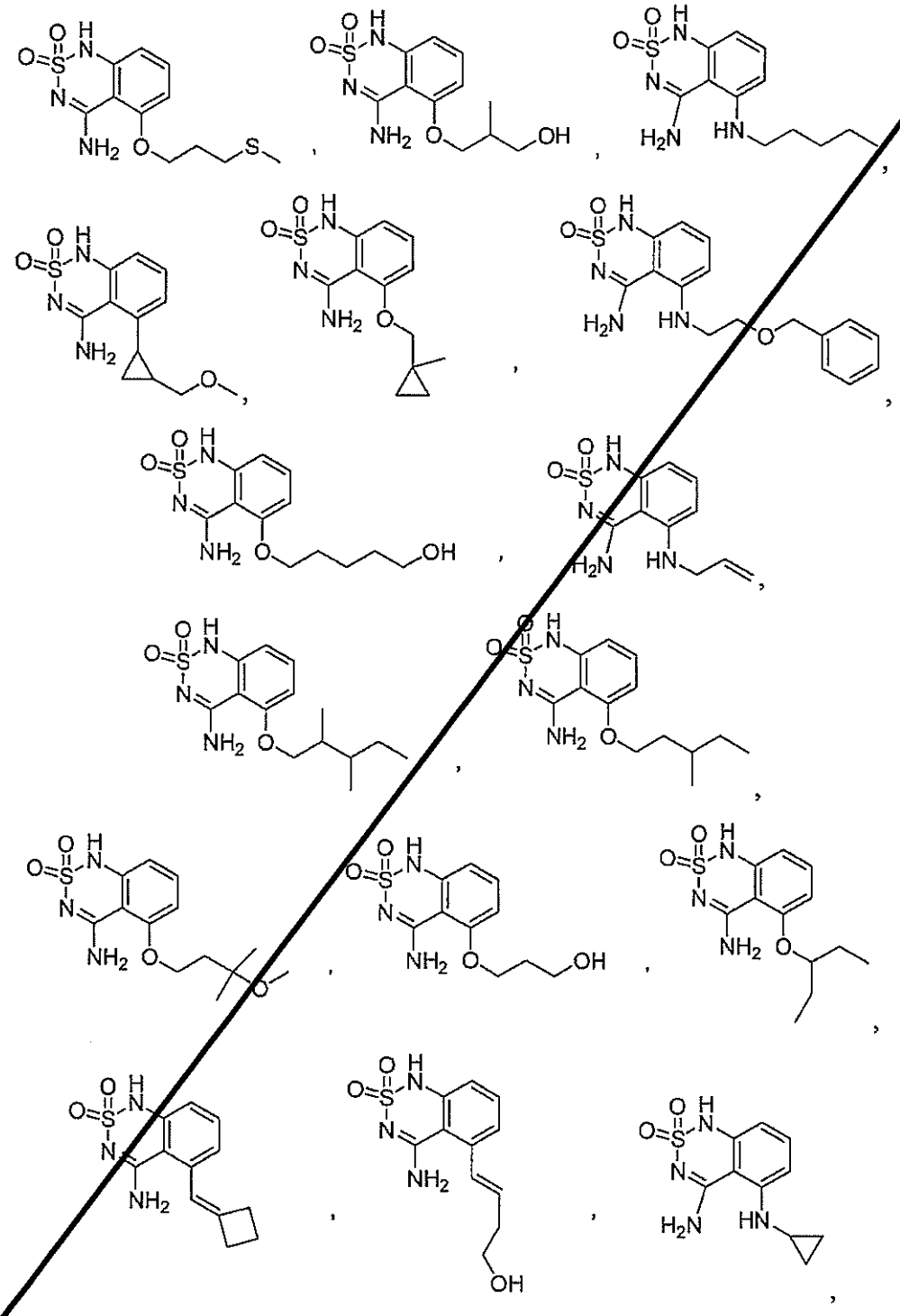


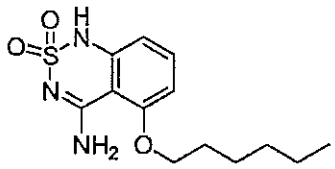
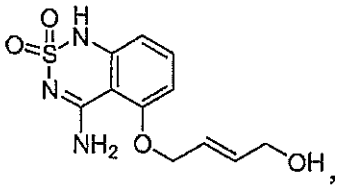
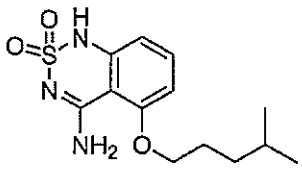
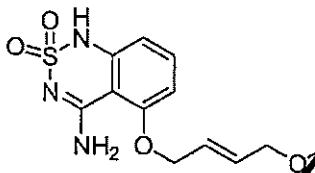
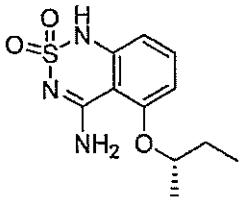
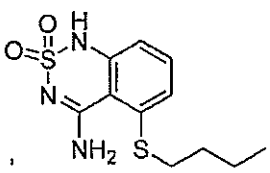
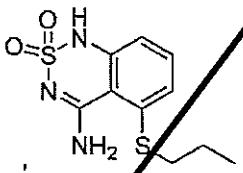
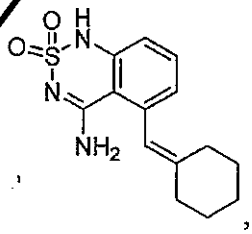
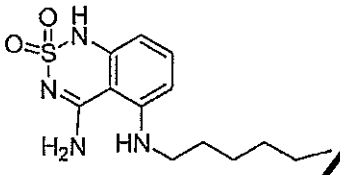
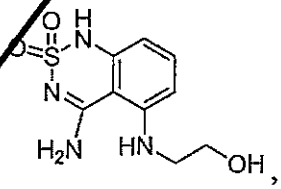
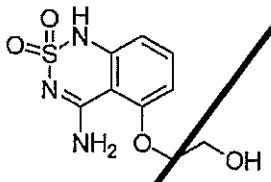
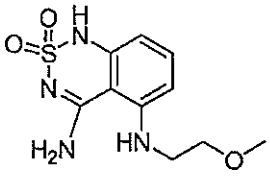
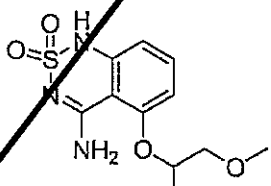
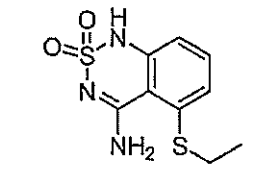

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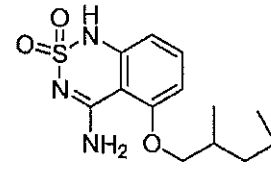
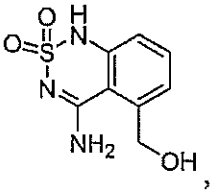
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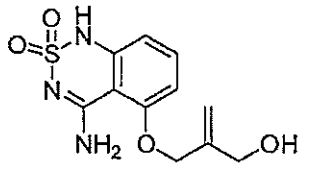
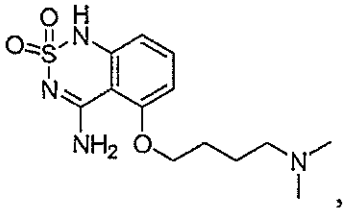
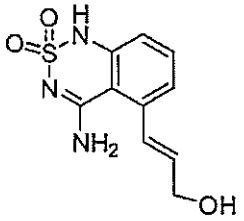
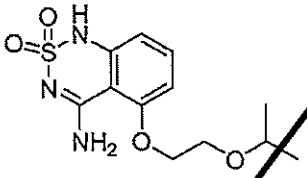
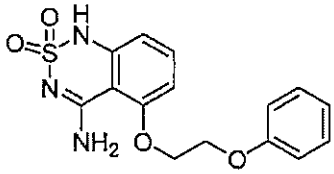
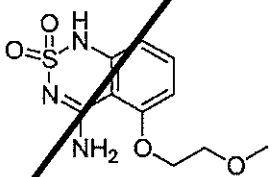
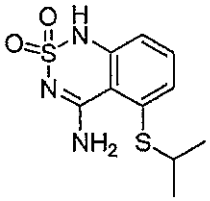
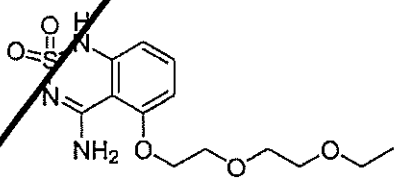
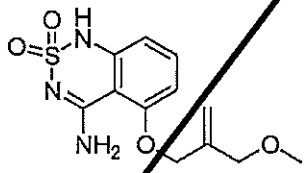
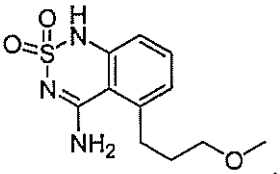
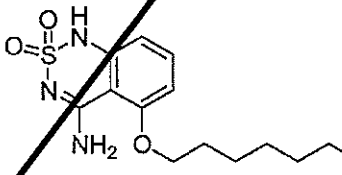
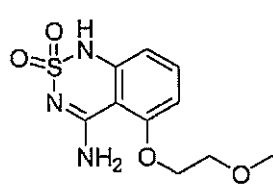
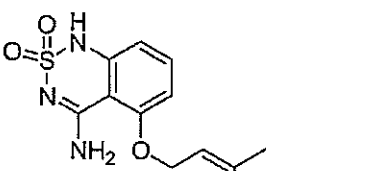
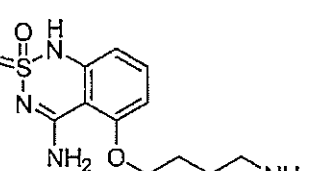



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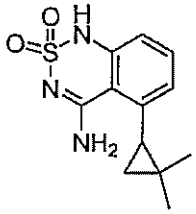
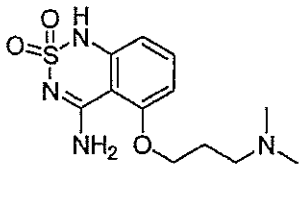
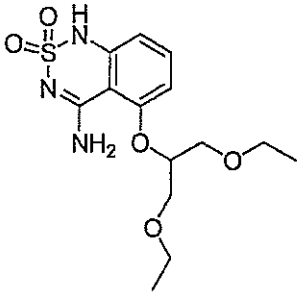
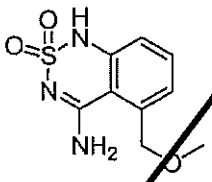
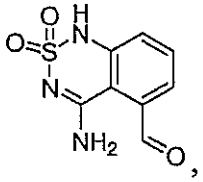
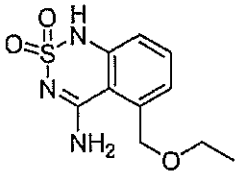
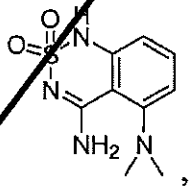
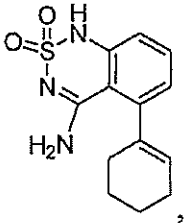
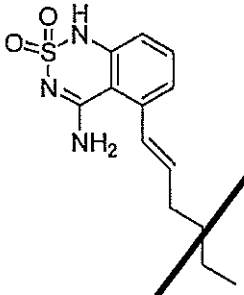
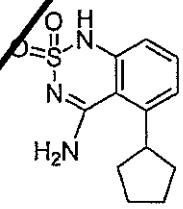
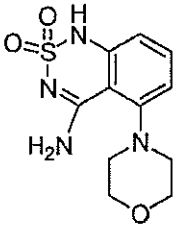
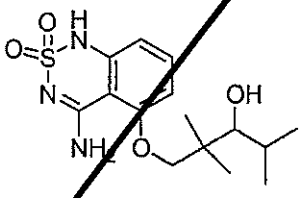
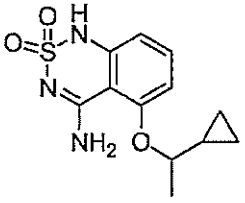
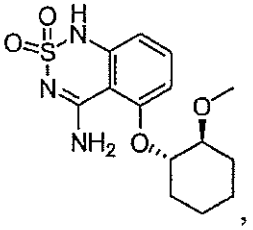
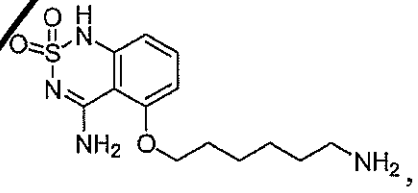
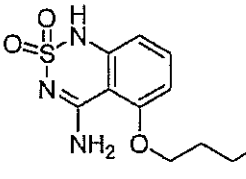
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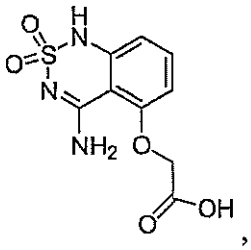
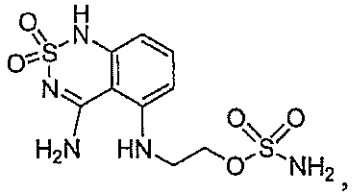
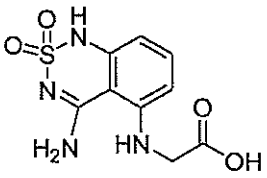
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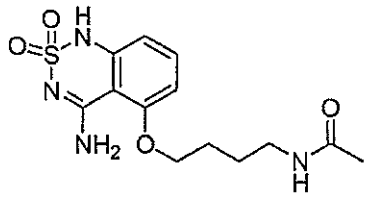
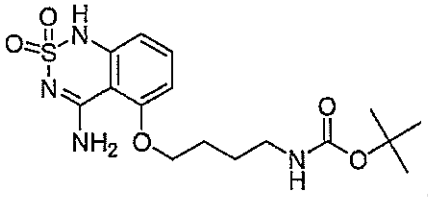
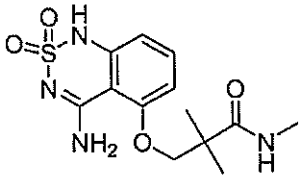
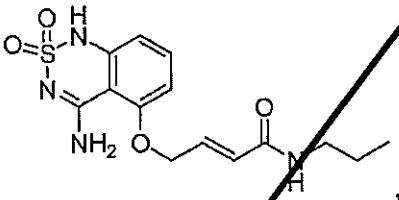
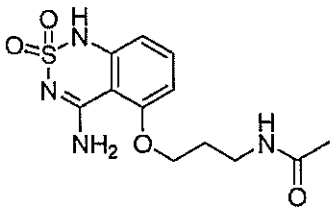
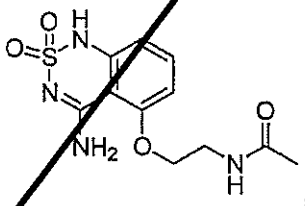
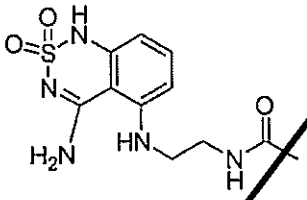
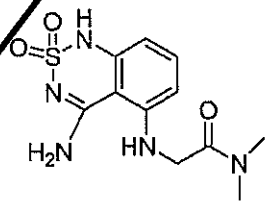
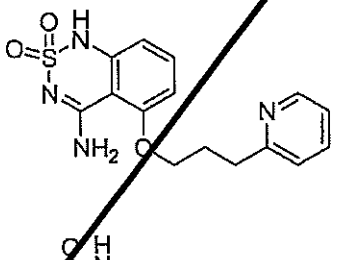
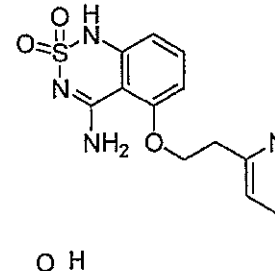
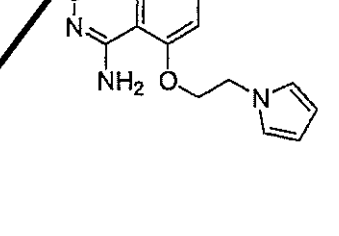
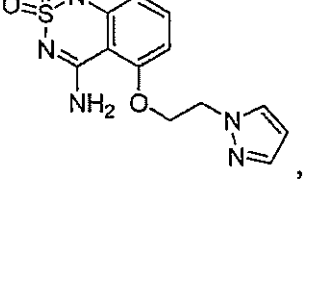
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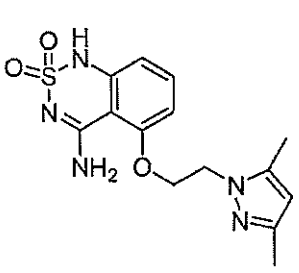
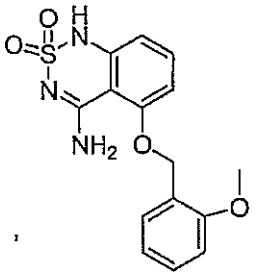
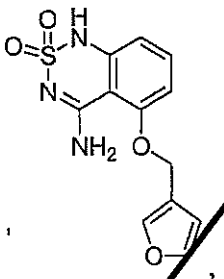
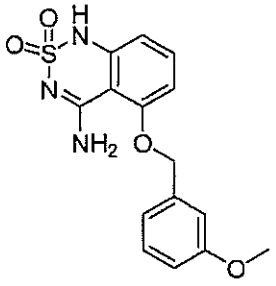
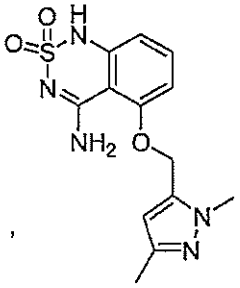
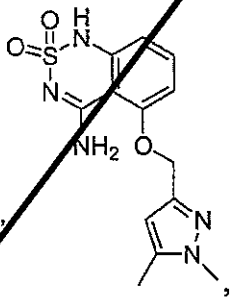
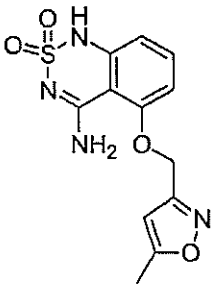
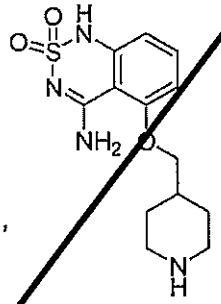
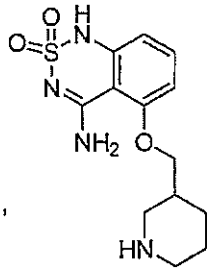
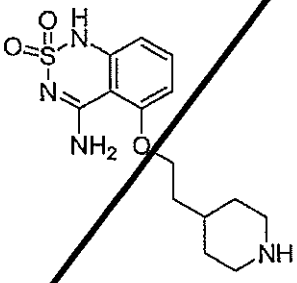
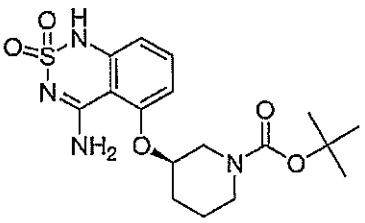
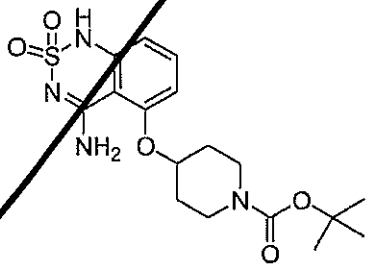
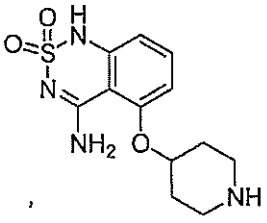
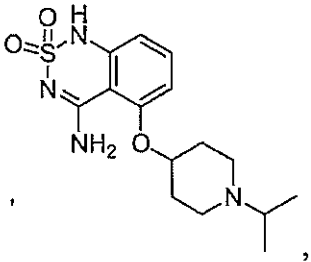
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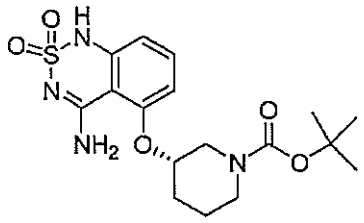
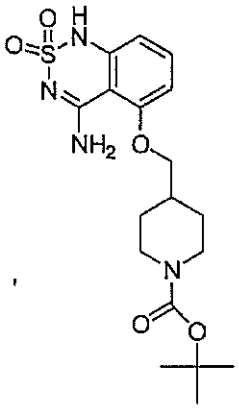
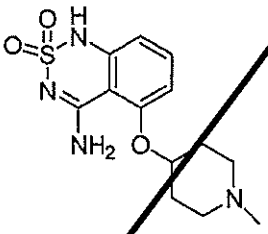
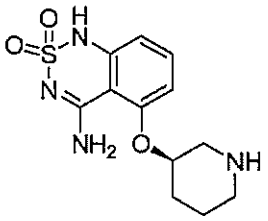
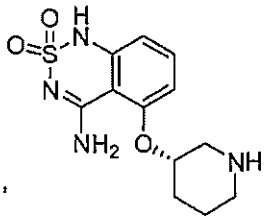
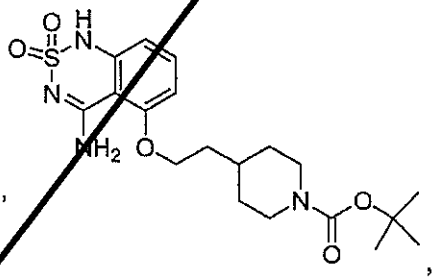
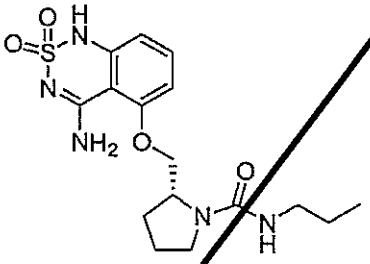
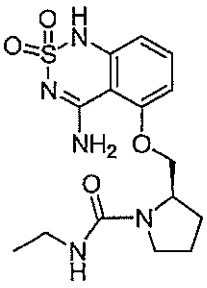
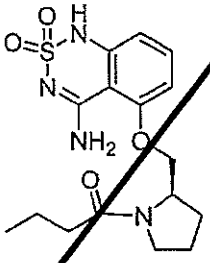
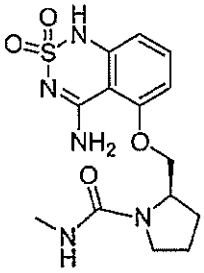
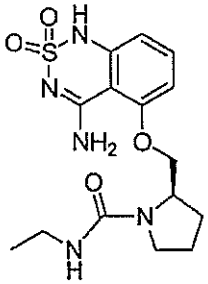

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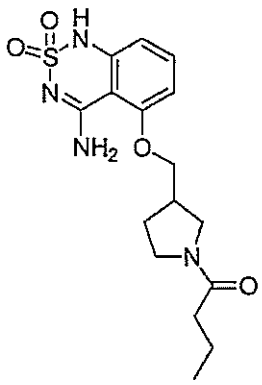
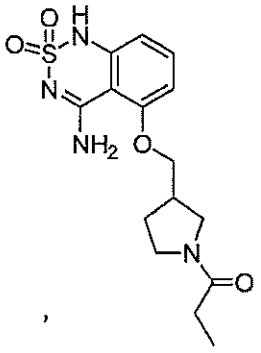
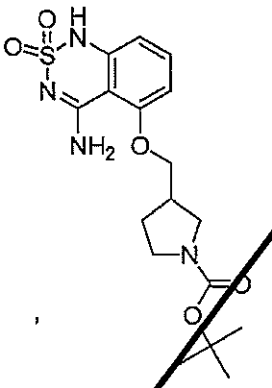
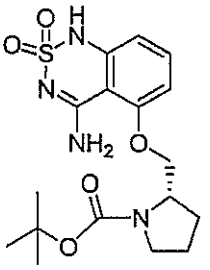
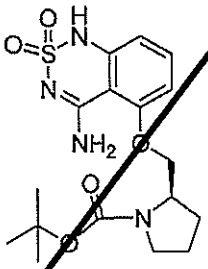
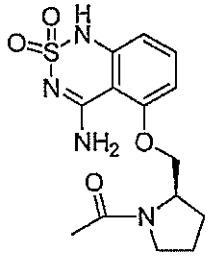
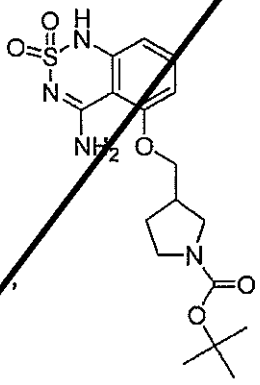
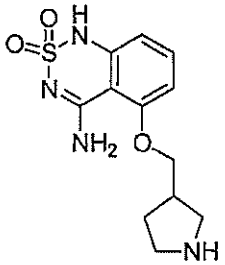
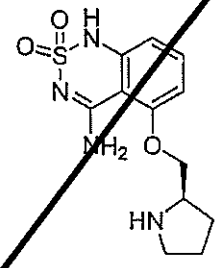
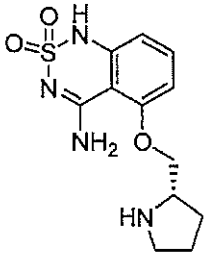
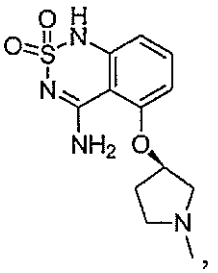

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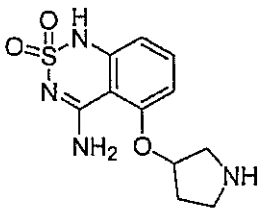
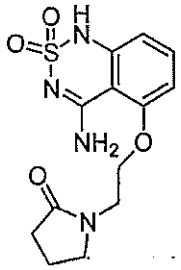
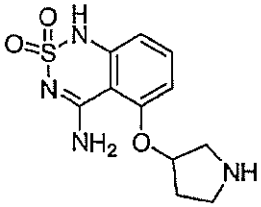
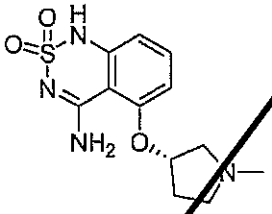
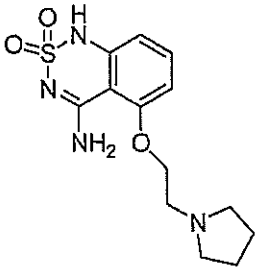
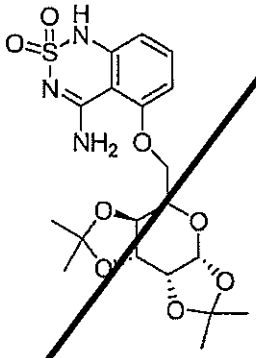
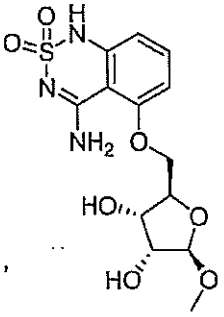
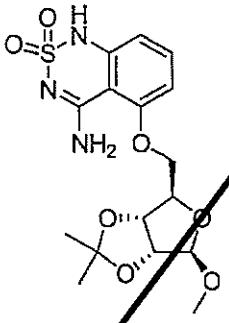
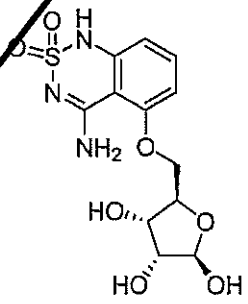
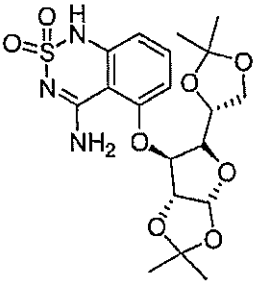
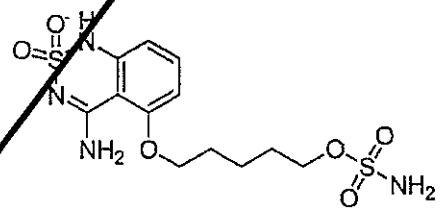
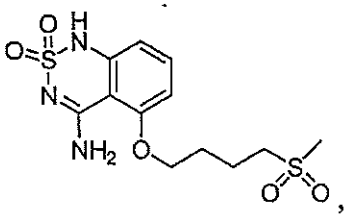
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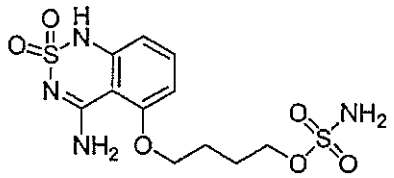
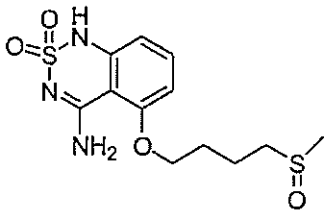
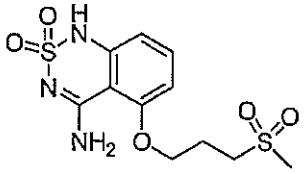
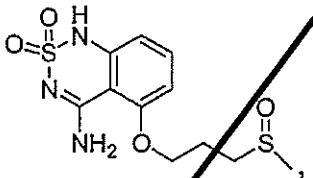
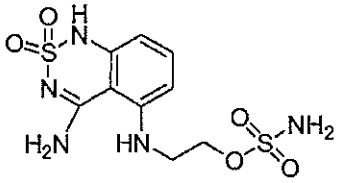
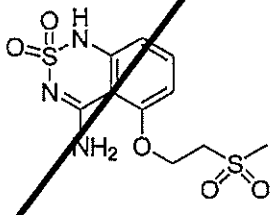
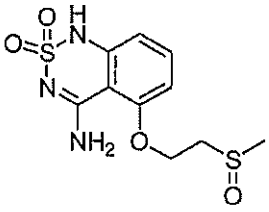
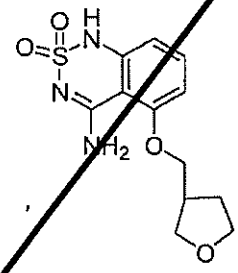
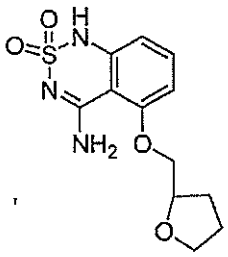
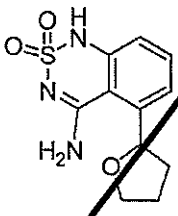
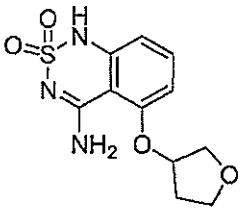
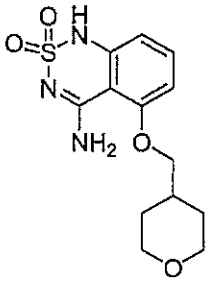
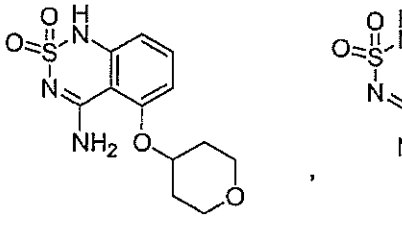
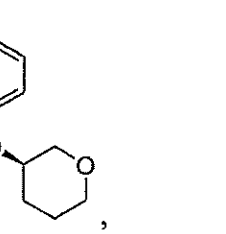
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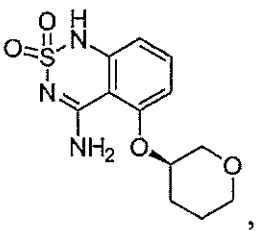
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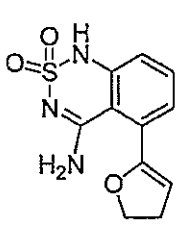
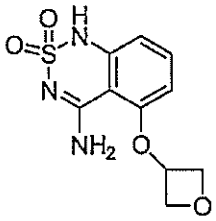
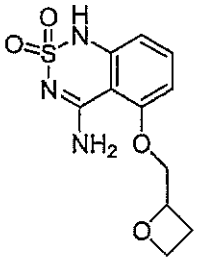
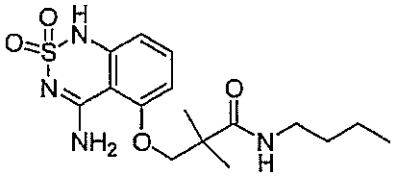
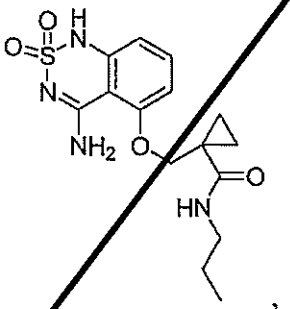
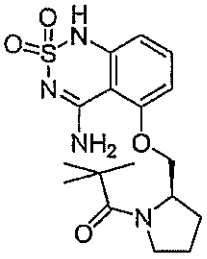
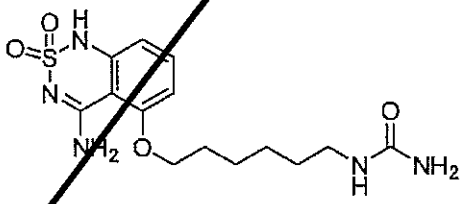
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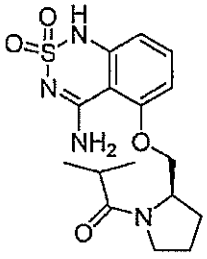
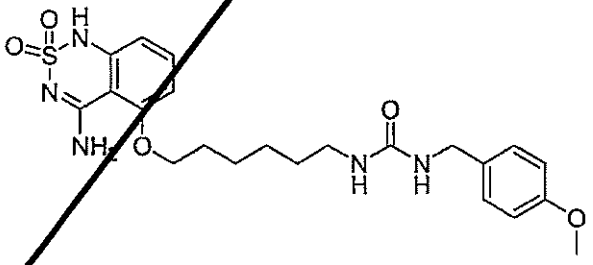
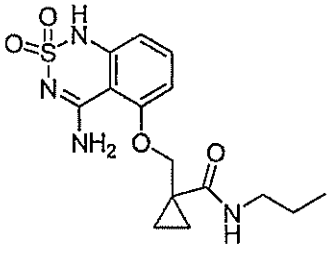
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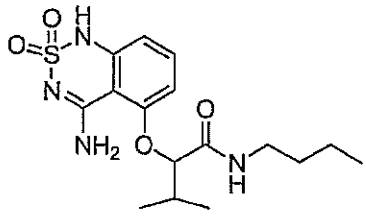
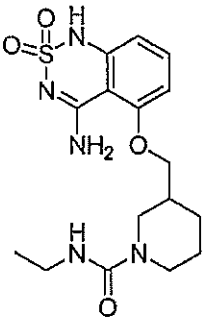
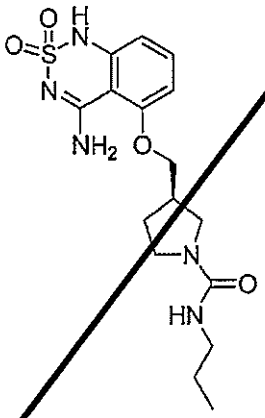
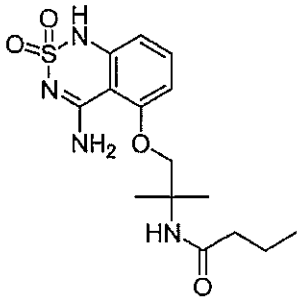
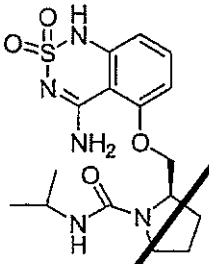
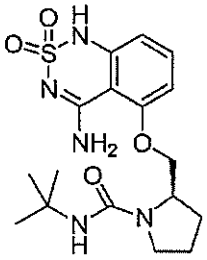
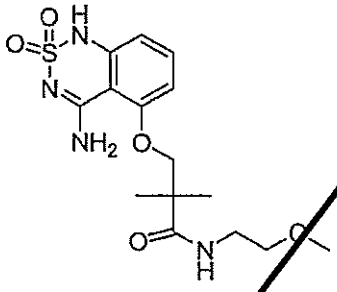
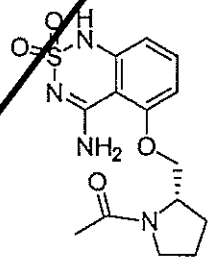
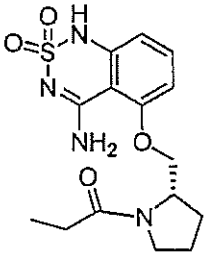
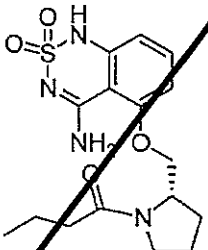
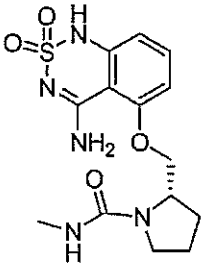
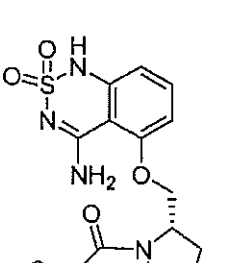
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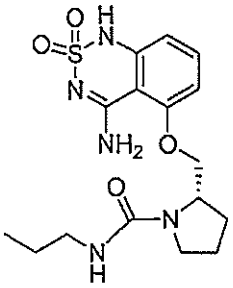
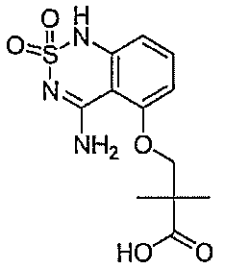
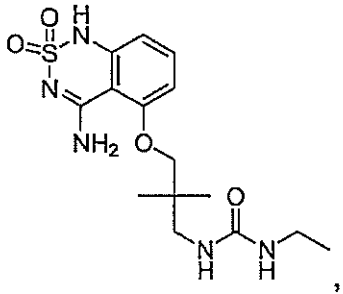
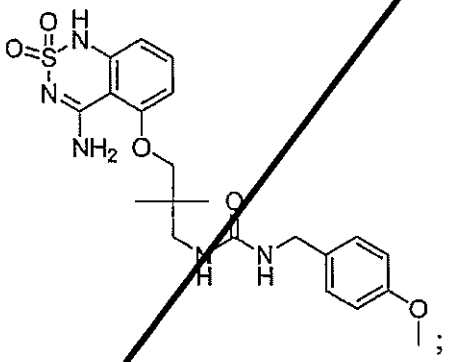
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or a tautomer, salt, solvate, and/or ester thereof.

42. An ingestible composition comprising a compound having structural Formula (I) as described in claim 7, or a tautomer, salt, solvate, and/or ester thereof.

43. The ingestible composition of claim 42, selected from the group consisting of food or beverage product, non-edible product, a pharmaceutical composition, and combinations thereof.

44. The ingestible composition of claim 43, wherein the food or beverage product is selected from the group consisting of the Soup category; the Dried Processed Food category; the Beverage category; the Ready Meal category; the Canned or Preserved Food category; the Frozen Processed Food category; the Chilled Processed Food category; the Snack Food category; the Baked Goods category; the Confectionary category; the Dairy Product category; the Ice Cream category; the Meal Replacement category; the Pasta and Noodle category; the Sauces, Dressings, Condiments category; the Baby Food category; the Spreads category; sweet coatings, frostings, or glazes; and combinations thereof.

45. The ingestible composition of claim 43, wherein the non-edible product is selected from the group consisting of nutritional products and dietary supplements, over the counter medications, oral care products, and cosmetics.

46. The ingestible composition of claim 42, wherein the compound having structural Formula (I) as described in claim 1, or a tautomer, salt, solvate, and/or ester thereof, is in a sweet flavor enhacing amount.

47. The ingestible composition of claim 46, wherein the sweet flavor enhacing amount is not a therapeutically effective amount.

48. The ingestible composition of claim 42, comprising from about 0.0001 ppm to about 10 ppm of the compound having structural Formula (I) as described in claim 1, or a tautomer, salt, solvate, and/or ester thereof.

49. The ingestible composition of claim 42, comprising from about 0.01 ppm to about 100 ppm of the compound having structural Formula (I) as described in claim 1, or a tautomer, salt, solvate, and/or ester thereof.

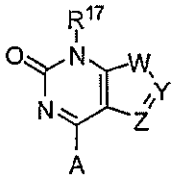
50. The ingestible composition of claim 42, comprising from about 10 ppm to about 100,000 ppm of the compound having structural Formula (I) as described in claim 1, or a tautomer, salt, solvate, and/or ester thereof.

51. The ingestible composition of claim 42, further comprising at least one sweet flavor entity, wherein the ingestible composition is not the following:

a comestible composition comprising

at least a sweet flavor entity selected from the group consisting of sucrose, sucralose, and combinations thereof; and

a compound of structural Formula (IIc):



(IIc)

or a pharmaceutically acceptable salt thereof, wherein:

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, -CN, -OR^9, -NR^9COR^{10}, -$NHOR^9$, -NR^9R^{10}, -$NR^9CO_2R^{10}$, -$NR^9CONR^{10}R^{11}$, -$NR^9CSNR^{10}R^{11}$, or -$NR^9C(=NH)NR^{10}R^{11}$;

R^{17} is hydrogen, alkyl, substituted alkyl;

W is -S-;

Y is -$C(R^{26})$-;

Z is -$C(R^{27})$-;

R^{26} is hydrogen, alkyl, substituted alkyl, -OR^{31}, -$CONR^{31}R^{32}$, or -CO_2R^{31};

R^{27} is hydrogen, alkyl, substituted alkyl, -OR^{33}, -$CONR^{33}R^{34}$, or -CO_2R^{33}; and

R^9, R^{10}, R^{11}, R^{31}, R^{32}, R^{33}, and R^{34} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; alternatively R^{10} and R^{11}, R^{31} and R^{32}, or R^{33} and R^{34} together with the atoms to which they are bonded form a heterocycloalkyl or substituted heterocycloalkyl ring;

wherein the substituted alkyl, substituted aryl, substituted arylalkyl, substituted heteroalkyl, substituted heteroaryl, substituted heteroarylalkyl, and substituted heterocycloalkyl each independently comprises one or more substituent groups selected from the group consisting of -R^a, halo, =O, -OR^b, -SR^b, =S, -NR^cR^c, =NR^b, =N-OR^b, trihalomethyl, -CN, -NO_2, -$S(O)_2R^b$, -$S(O)_2NR^b$, -$S(O)_2OR^b$, -$OS(O)_2R^b$, -$OS(O)_2OR^b$, -$P(O)(OR^b)(OR^b)$, -$C(O)R^b$, -$C(NR^b)R^b$, -$C(O)OR^b$, -$C(O)NR^cR^c$, -$C(NR^b)NR^cR^c$, -$OC(O)R^b$, -$OC(O)OR^b$, -$NR^bC(O)R^b$, -$NR^bC(O)OR^b$, -$NR^bC(O)NR^cR^c$, -$NR^bC(NR^b)R^b$ and -$NR^bC(NR^b)NR^cR^c$, where R^a is selected from the group consisting of alkyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl; each R^b is independently hydrogen or R^a; and each R^c is independently R^b or alternatively, the two R^cs are taken together with the nitrogen atom to which they are bonded form a 4-, 5-, 6- or 7-membered heterocycloalkyl.

52. The ingestible composition of claim 51, wherein the sweetener is selected from the group consisting of sucrose, fructose, glucose, galactose, mannose, lactose, tagatose, maltose, corn syrup (including high fructose corn syrup), D-tryptophan, glycine, erythritol, isomalt, lactitol, mannitol, sorbitol, xylitol, maltodextrin, maltitol, isomalt, hydrogenated glucose syrup (HGS), hydrogenated starch hydrolyzate (HSH), stevioside, rebaudioside A, other sweet Stevia-based glycosides, carrelame, other guanidine-based sweeteners, saccharin, acesulfame-K, cyclamate, sucralose, alitame, mogroside, neotame, aspartame, other aspartame derivatives, and combinations thereof.

53. The ingestible composition of claim 51, wherein the at least one sweet entity comprises
at least one natural sweetener; and
at least one artificial or synthesized sweetener.

54. The ingestible composition of claim 53, wherein the natural sweetener is a saccharide sweetener, a natural sugar, or a semi-synthetic "sugar alcohol" sweetener.

55. The ingestible composition of claim 53, wherein the artificial or synthesized sweetener is a non-caloric sweet flavor compound, a reduced caloric sweet flavor compound, or a non-target caloric sweet flavor compound.

56. The ingestible composition of claim 54, wherein the natural sweetener is selected from a group consisting of sucrose, fructose, glucose, tagatose, maltose, galactose, mannose, lactose, glycine, corn syrup or other syrups or sweetener concentrates derived from natural fruit and vegetable sources, erythritol, isomalt, lactitol, mannitol, sorbitol, xylitol, maltodextrin, and mogroside.

57. The ingestible composition of claim 55, wherein the artificial or synthesized sweetener is selected from a group consisting of aspartame, saccharin, acesulfame-K, cyclamate, sucralose, alitame, aspartame, neotame, aspartame derivatives, D-tryptophan, hydroganeted glucose syrup

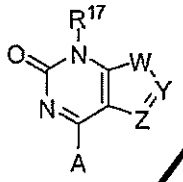
(HGS), hydrogenated starch hydrolyzate (HSH), stevioside, rebaudioside A, sweet Ste*via*-based glycosides, carrelame, and guanidine-based sweeteners.

58. A sweetening composition comprising a compound having structural Formula (I) as described in claim 7, or a tautomer, salt, solvate, and/or ester thereof, wherein the sweetening composition is not the following:

a comestible composition comprising

at least a sweet flavor entity selected from the group consisting of sucrose, sucralose, and combinations thereof; and

a compound of structural Formula (IIc):



(IIc)

or a pharmaceutically acceptable salt thereof, wherein:

A is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, -CN, -OR^9, -NR^9COR^{10}, -$NHOR^9$, -NR^9R^{10}, -$NR^9CO_2R^{10}$, -$NR^9CONR^{10}R^{11}$, -$NR^9CSNR^{10}R^{11}$, or -$NR^9C(=NH)NR^{10}R^{11}$;

R^{17} is hydrogen, alkyl, substituted alkyl;

W is -S-;

Y is -$C(R^{26})$-;

Z is -$C(R^{27})$-;

R^{26} is hydrogen, alkyl, substituted alkyl, -OR^{31}, -$CONR^{31}R^{32}$, or -CO_2R^{31};

R^{27} is hydrogen, alkyl, substituted alkyl, -OR^{33}, -$CONR^{33}R^{34}$, or -CO_2R^{33}; and

R^9, R^{10}, R^{11}, R^{31}, R^{32}, R^{33}, and R^{34} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; alternatively R^{10} and R^{11}, R^{31} and R^{32}, or R^{33} and R^{34} together with the atoms to which they are bonded form a heterocycloalkyl or substituted heterocycloalkyl ring;

wherein the substituted alkyl, substituted aryl, substituted arylalkyl, substituted heteroalkyl, substituted heteroaryl, substituted heteroarylalkyl, and substituted heterocycloalkyl each independently comprises one or more substituent groups selected from the group consisting of $-R^a$, halo, =O, $-OR^b$, $-SR^b$, =S, $-NR^cR^c$, $=NR^b$, $=N-OR^b$, trihalomethyl, -CN, $-NO_2$, $-S(O)_2R^b$, $-S(O)_2NR^b$, $-S(O)_2OR^b$, $-OS(O)_2R^b$, $-OS(O)_2OR^b$, $-P(O)(OR^b)(OR^b)$, $-C(O)R^b$, $-C(NR^b)R^b$, $-C(O)OR^b$, $-C(O)NR^cR^c$, $-C(NR^b)NR^cR^c$, $-OC(O)R^b$, $-OC(O)OR^b$, $-NR^bC(O)R^b$, $-NR^bC(O)OR^b$, $-NR^bC(O)NR^cR^c$, $-NR^bC(NR^b)R^b$ and $-NR^bC(NR^b)NR^cR^c$, where R^a is selected from the group consisting of alkyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl and heteroarylalkyl; each R^b is independently hydrogen or R^a; and each R^c is independently R^b or alternatively, the two R^cs are taken together with the nitrogen atom to which they are bonded form a 4-, 5-, 6- or 7-membered heterocycloalkyl.

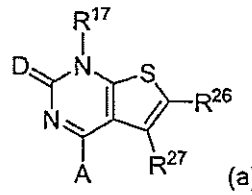
59. A method of enhancing the sweet taste of an ingestible composition comprising contacting the ingestible composition or precursors thereof with the compound having structural Formula (I) as described in claim 7, or a tautomer, salt, solvate, and/or ester thereof.

60. A method of enhancing the sweet taste of an ingestible composition comprising contacting the ingestible composition or precursors thereof with the sweetening composition of claim 53.

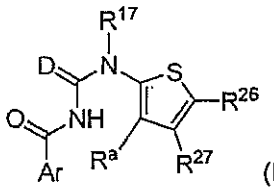
61. A method of treating a condition associated with a chemosensory receptor comprising administering to a subject in need of such treatment an effective amount of the compound having structural Formula (I) as described in claim 7, or a tautomer, salt, solvate, and/or ester thereof.

62. The method of claim 61, wherein the condition associated with a chemosensory receptor is taste, a condition associated with gastrointestinal system or metabolic disorders, or a condition associated with a functional gastrointestinal disorder.

63. A process of preparing a compound having structural Formula (a):


(a),

comprising reacting a compound having structural Formula (b)


(b)

with a base,

wherein:

D is oxygen or sulfur;

A is $-NH_2$ or $-OR^b$;

R^{17} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R^{26} and R^{27} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^{31}$, $-S(O)_hR^{31}$, $-NR^{31}R^{32}$, $-CONR^{31}R^{32}$, $-CO_2R^{31}$, $-SO_2NR^{31}R^{32}$, or $-NR^{31}SO_2R^{32}$; or alternatively R^{26} and R^{27}, together with the atoms to which they are bonded, form a cycloalkyl, substituted cycloalkyl, heterocycloalkyl, or substituted heterocycloalkyl ring;

Ar is aryl or substituted aryl; and

R^a is -CN, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^b)_2$;

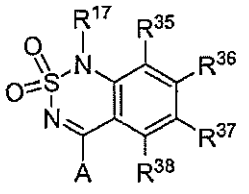
each R^b is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, or substituted heteroarylalkyl;

h is 0, 1 or 2; and

R^{31} and R^{32} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively

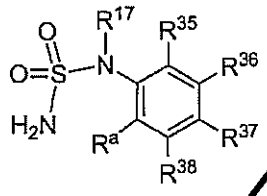
R^{31} and R^{32}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.

64. A process of preparing a compound having structural Formula (e):



(e),

comprising reacting a compound having structural Formula (f)



(f),

with a base,

wherein:

A is $-NH_2$ or $-OR^b$;

R^{17} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R^{35}, R^{36}, R^{37}, and R^{38} are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl, -CN, $-NO_2$, $-OR^{41}$, $-S(O)_kR^{41}$, $-NR^{41}R^{42}$, $-CONR^{41}R^{42}$, $-CO_2R^{41}$, $-SO_2NR^{41}R^{42}$, and $-NR^{41}SO_2R^{42}$; or alternatively, R^{35} and R^{36}, R^{36} and R^{37}, or R^{37} and R^{38}, together with the atoms to which they are bonded, form a cycloalkyl, substituted cycloalkyl, heterocycloalkyl, or substituted heterocycloalkyl ring;

R^a is is -CN, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^b)_2$;

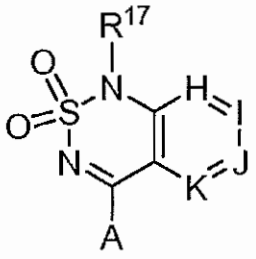
each R^b is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, or substituted heteroarylalkyl; and

R^{41} and R^{42} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl,

heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively R^{41} and R^{42}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.

CLAIMS

1. A compound having structural Formula (IIIb):



(IIIb), or a salt or solvate thereof;

wherein

A is $-NH_2$;

H is $-C(R^{35})-$ or $-N-$;

I is $-C(R^{36})$ or $-N-$;

J is $-C(R^{37})-$ or $-N-$;

K is $-C(R^{38})-$;

R^{17} is hydrogen;

R^{35} is hydrogen;

R^{36} is hydrogen;

R^{37} is hydrogen, fluoro, chloro, or bromo; and

R^{38} is alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, cycloalkanyl, substituted cycloalkanyl, cycloalkenyl, substituted cycloalkenyl, heteroalkanyl, substituted heteroalkanyl, cycloheteroalkyl, substituted cycloheteroalkyl, –O–alkanyl, –O-(substituted alkanyl), –O-heteroalkanyl, –O-(substituted heteroalkanyl), –O-alkenyl, –O-(substituted alkenyl), –NH-alkanyl, –NH-(substituted alkanyl), –NH-alkenyl, –NH-(substituted alkenyl), –S-alkanyl, –S-(substituted alkanyl), –S-alkenyl, or –S-(substituted alkenyl).

2. The compound of claim 1, wherein

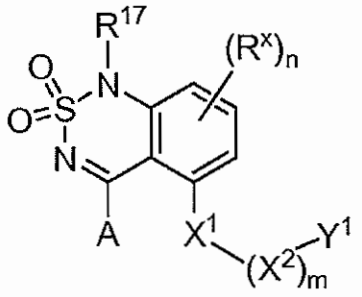
H is $-C(R^{35})-$;

I is $-C(R^{36})-$;

J is $-C(R^{37})-$; and

K is $-C(R^{38})-$.

3. A compound having structural Formula (IIIb1):



(IIIb1) , or a salt or solvate thereof;

wherein,

A is hydrogen, –CN, $–OR^9$, $–NO_2$, $–S(O)_cR^9$, $–NOR^9$, $–NHOR^9$, $–NR^9COR^{10}$, $–NR^9R^{10}$, $–CONR^9R^{10}$, $–CO_2R^9$ or $–NR^9CO_2R^{10}$;

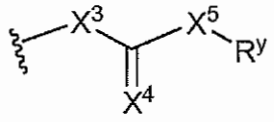
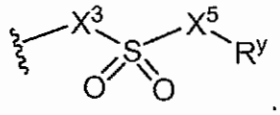
R^{17} is hydrogen, alkyl, substituted alkyl, arylalkyl, or substituted arylalkyl;

X^1 is $–CH_2–$, –O–, $–NR^9–$, –S–, –S(O)–, or $–S(O)_2–$;

X^2 is alkylene, substituted alkylene, heteroalkylene, or substituted heteroalkylene;

m is 0 or 1;

Y^1 is heteroaryl, substituted heteroaryl, cycloheteroalkyl, substituted cycloheteroalkyl, or

 , or  ;

X^3 and X^5 are independently a covalent bond, –O– or $–NR^9–$;

X^4 is O, NR^9, $N–OR^9$, or S;

R^x is halo, $–NO_2$, –CN, –OH, $–NH_2$, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

n is 0, 1, 2, or 3;

R^y is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl, $–NR^9R^{10}$; and

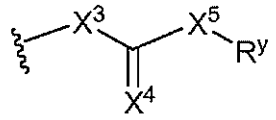
each R^9 and R^{10} is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl;

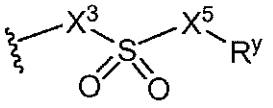
with the proviso that when X^1 is –O– or –S–, and m is zero; then X^3 is not –O–.

4. The compound of claim 3, wherein

X^1 is $-CH_2-$; and

Y^1 is



, or


.

5. The compound of claim 3, wherein

X^1 is –O–, $-NR^9-$, or –S–;

m is 0 or 1, and

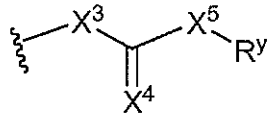
Y^1 is cycloheteroalkyl or substituted cycloheteroalkyl.

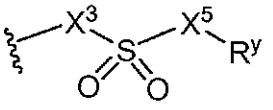
6. The compound of claim 3, wherein

X^1 is –O–, $-NR^9-$, or –S–;

m is 1, and

Y^1 is



, or


.

7. The compound of claim 3, wherein

X^2 is methylene, ethylene, propylene, iso-propylene, butylene, iso-butylene, sec-butylene, pentylene, hexylene, heptylene, dimethylethylene, methylcyclopropylene, cyclopropylmethylene, ethenylene, propenylene, or butenylene.

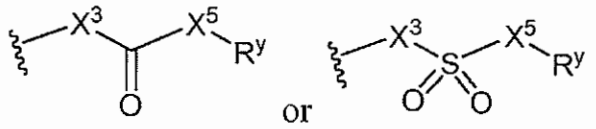
8. The compound of claim 3, wherein Y^1 is piperidinyl, substituted piperidinyl, tetrahydrofuranyl, substituted tetrahydrofuranyl, tetrahydropyranyl, substituted tetrahydropyranyl, dihydrofuranyl, substituted dihydrofuranyl, pyrrolidinyl, substituted

pyrrolidinyl, oxetanyl, substituted oxetanyl, saccharide ring or its derivative, substituted saccharide ring or its derivative.

9. The compound of claim 3, wherein Y^1 is pyridinyl, substituted pyridinyl, pyrrolyl, substituted pyrrolyl, furanyl, substituted furanyl, pyrazolyl, substituted pyrazolyl, isoxazolyl, substituted isoxazolyl, oxazolyl, and substituted oxazolyl.

10. The compound of claim 3, wherein the substituted cycloheteroalkyl comprises one or more substituents selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, –CN, $-OR^9$, $-NO_2$, $-S(O)_cR^9$, $-NOR^9$, $-NHOR^9$, $-NR^9COR^{10}$, $-NR^9R^{10}$, $-CONR^9R^{10}$, $-CO_2R^9$, and $-NR^9CO_2R^{10}$.

11. The compound of claim 3, wherein Y^1 is



12. The compound of claim 3, wherein $-X^3-C(X^4)-X^5-$ is –C(O)–, –C(O)–NH–, –NH–C(O)–, –NH–C(O)–NH–, –C(O)–O–, –O–C(O)–, –O–C(O)–O–, –NH–C(O)–O–, –O–C(O)–NH–, –C(NH)–, –C(NH)–NH–, –NH–C(NH)–, –NH–C(NH)–NH–, –C(NH)–O–, –O–C(NH)–, –O–C(NH)–O–, –NH–C(NH)–O–, –O–C(NH)–NH–, –C(N–OH)–, or –C(S)–.

13. The compound of claim 3, wherein

A is hydrogen, or $-NR^9R^{10}$;

R^{17} is hydrogen; and

Y^1 is piperidinyl, substituted piperidinyl, tetrahydrofuranyl, substituted tetrahydrofuranyl, tetrahydropyranyl, substituted tetrahydropyranyl, dihydrofuranyl, substituted dihydrofuranyl, pyrrolidinyl, substituted pyrrolidinyl, oxetanyl, substituted oxetanyl, monosaccharide ring, substituted monosaccharide ring, pyridinyl, substituted pyridinyl, pyrrolyl, substituted pyrrolyl, furanyl, substituted furanyl, pyrazolyl, substituted pyrazolyl, isoxazolyl, substituted isoxazolyl, oxazolyl, or substituted oxazolyl.

14. The compound of claim 3, wherein

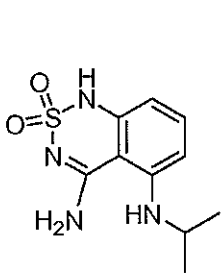
A is hydrogen, or $-NR^9R^{10}$;

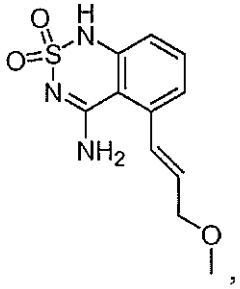
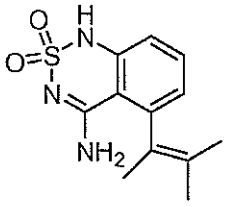
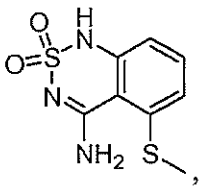
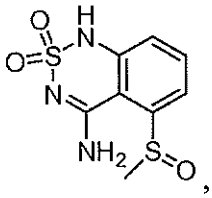
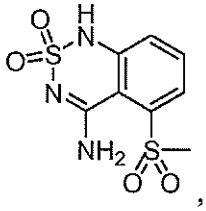
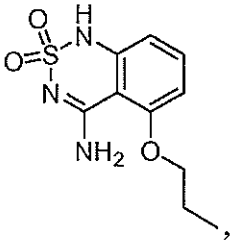
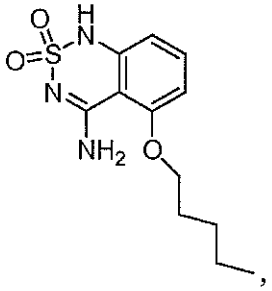
R^{17} is hydrogen;

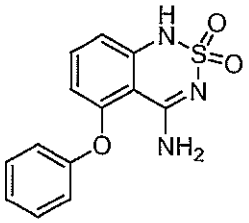
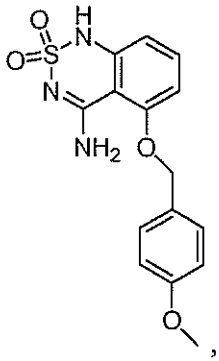
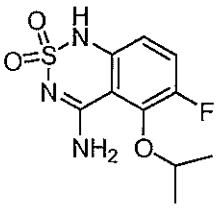
Y^1 is $-X^3-C(X^4)-X^5-$; and

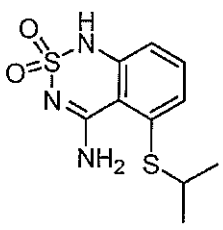
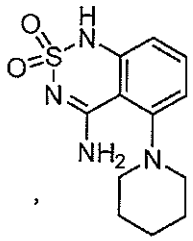
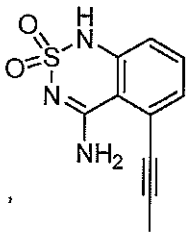
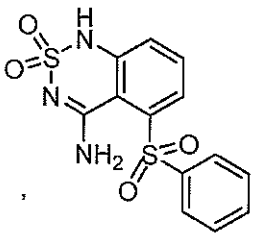
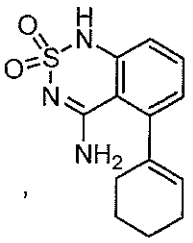
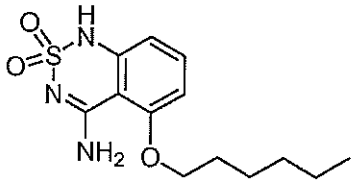
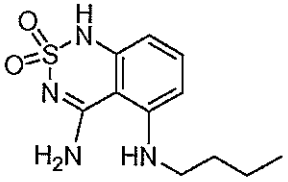
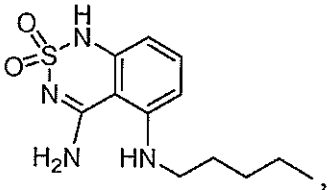
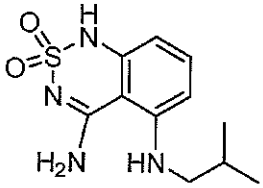
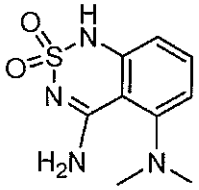
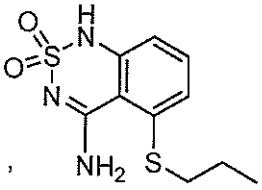
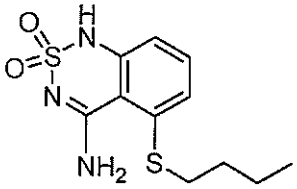
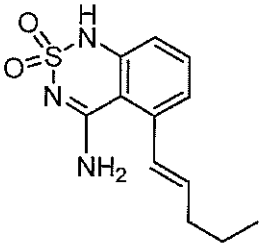
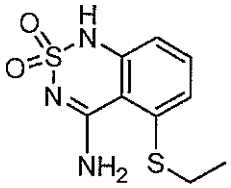
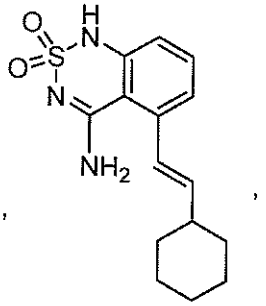
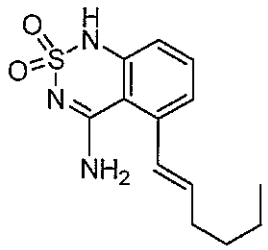
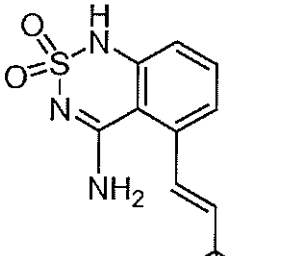
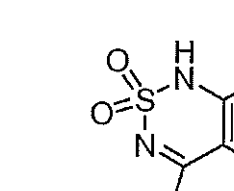
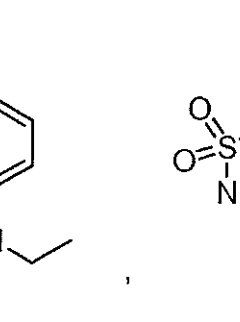
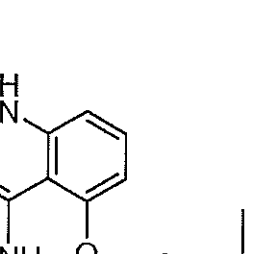
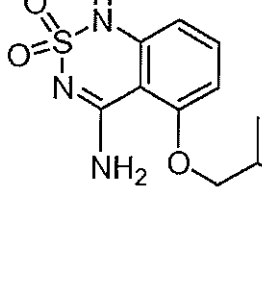
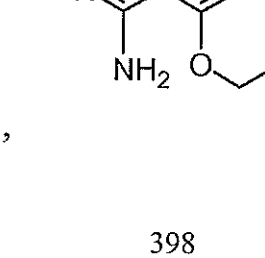
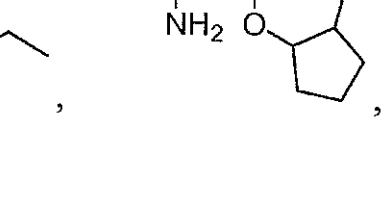
$-X^3-C(X^4)-X^5-$ is $-C(O)-$, $-C(O)-NH-$, $-NH-C(O)-$, $-NH-C(O)-NH-$, $-C(O)-O-$, $-O-C(O)-$, $-O-C(O)-O-$, $-NH-C(O)-O-$, $-O-C(O)-NH-$, $-C(NH)-$, $-C(NH)-NH-$, $-NH-C(NH)-$, $-NH-C(NH)-NH-$, $-C(NH)-O-$, $-O-C(NH)-$, $-O-C(NH)-O-$, $-NH-C(NH)-O-$, $-O-C(NH)-NH-$, $-S(O)_2-$, $-NH-S(O)_2-$, $-S(O)_2-NH-$, $-O-S(O)_2-$, $-S(O)_2-O-$, $-C(N-OH)-$, or $-C(S)-$.

15. The compound of claim 1 or 3, having structural formula selected from the group consisting of


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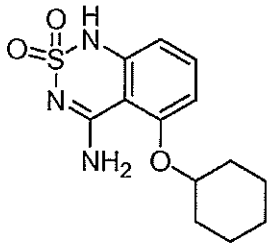
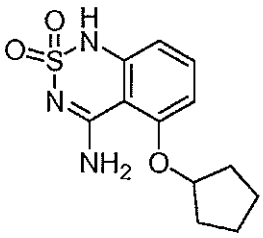
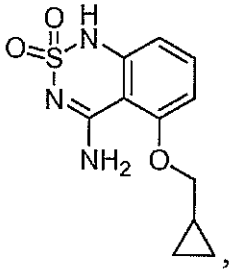
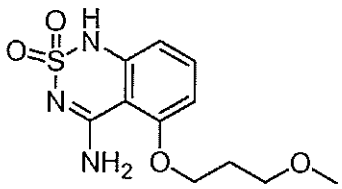
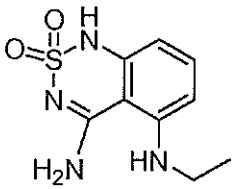
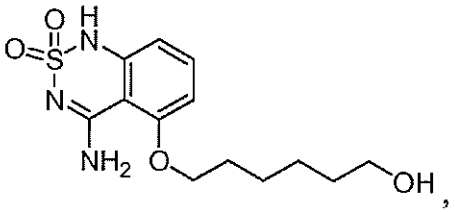
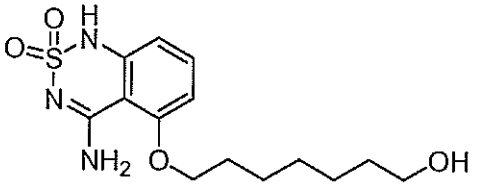
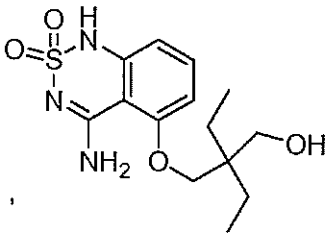
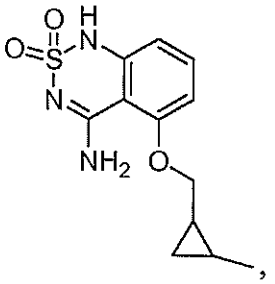
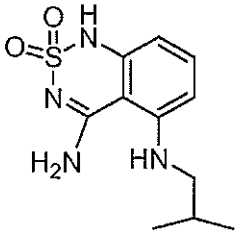
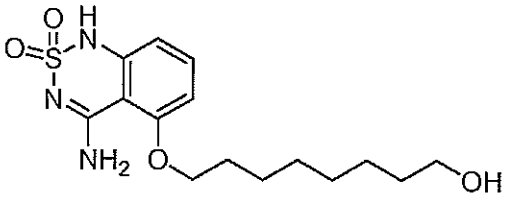
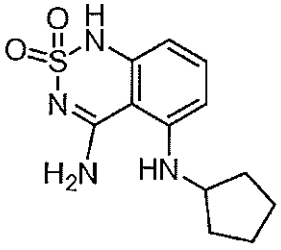
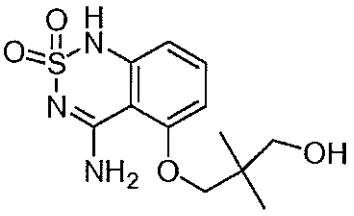
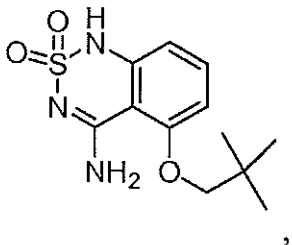
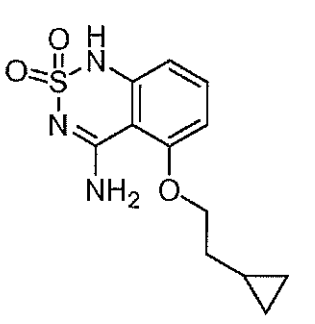
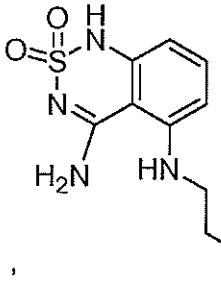
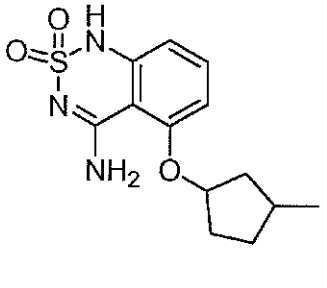

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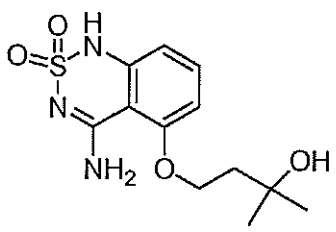
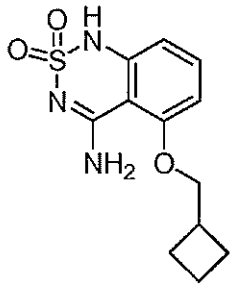
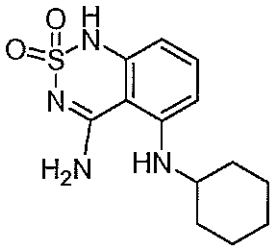
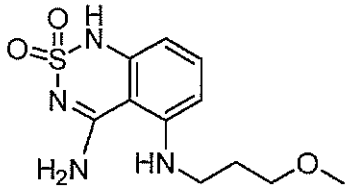
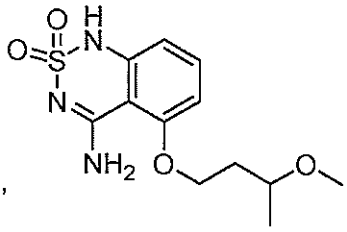
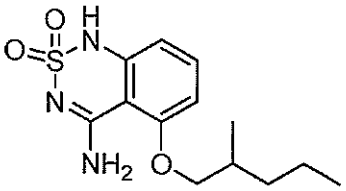
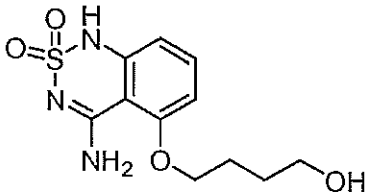
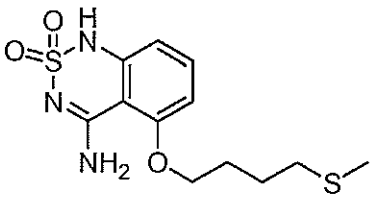
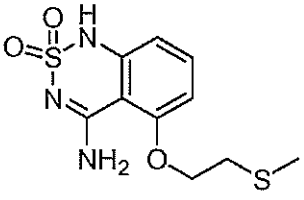
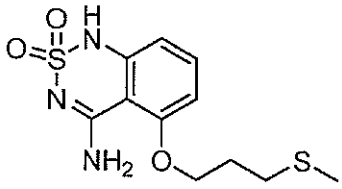
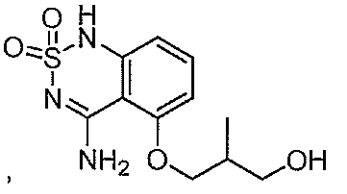
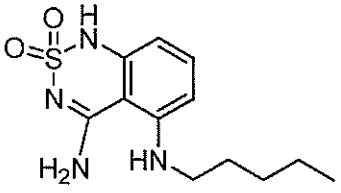
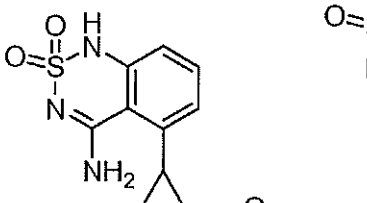
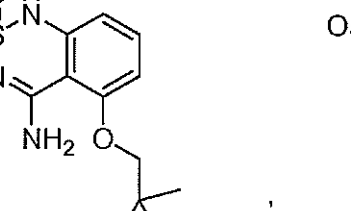
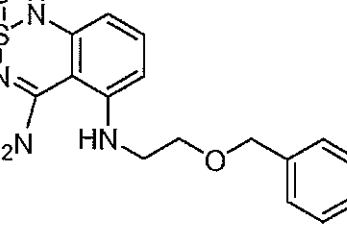
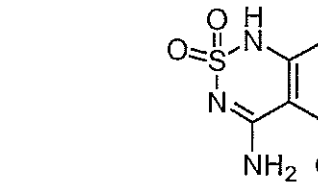
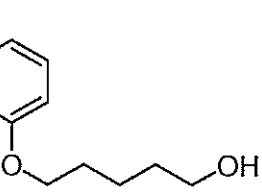
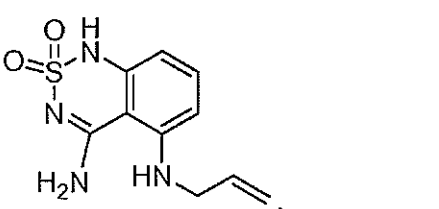
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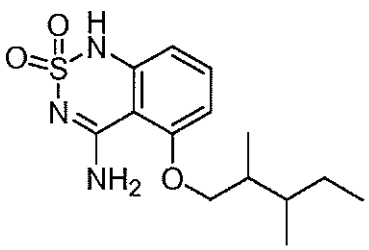
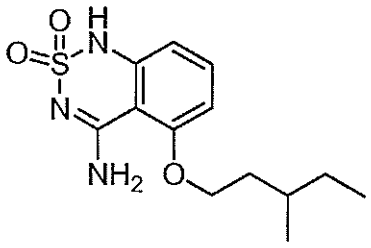
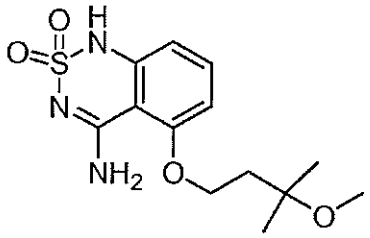
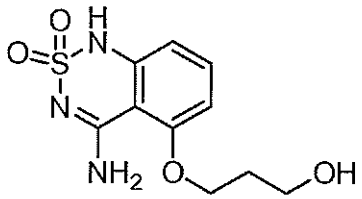
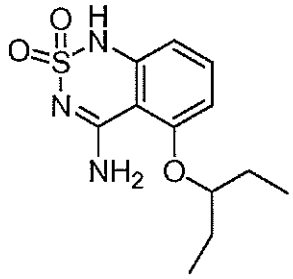
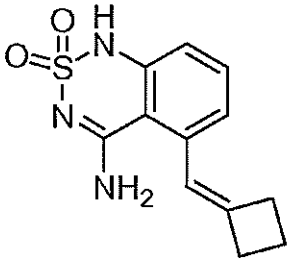
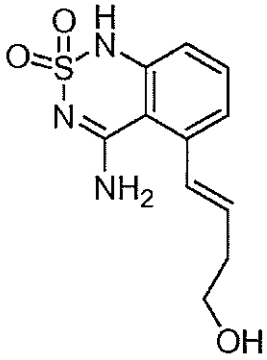
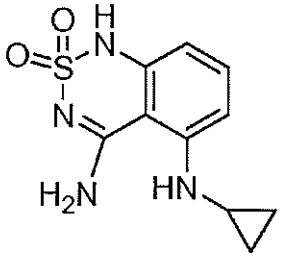
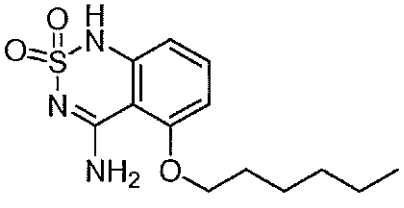
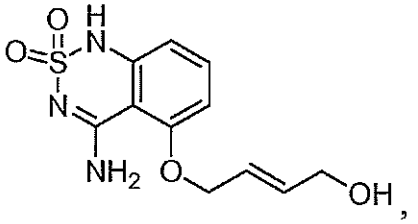
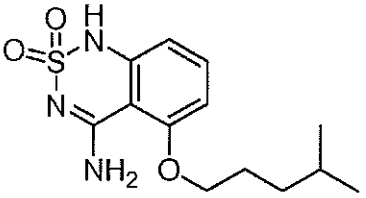
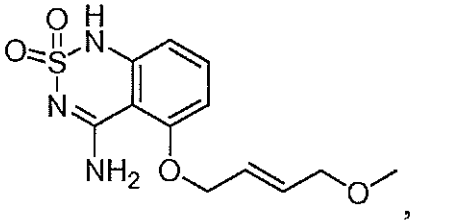
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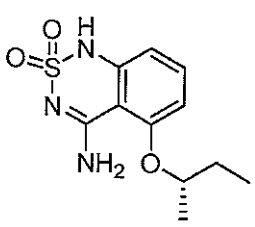
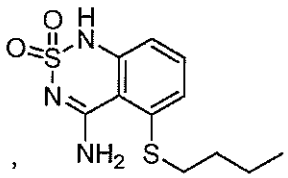
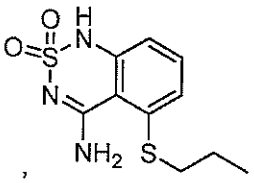
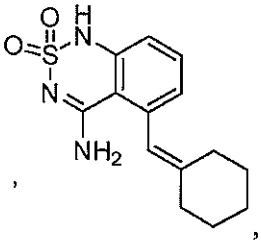
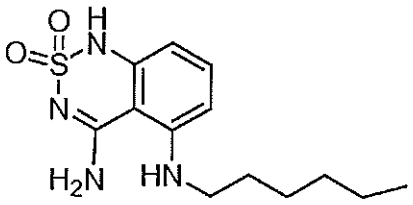
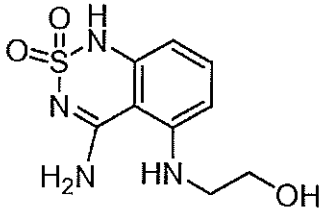
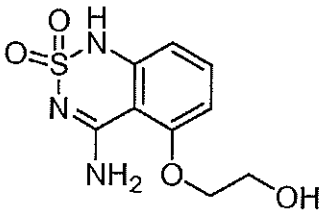
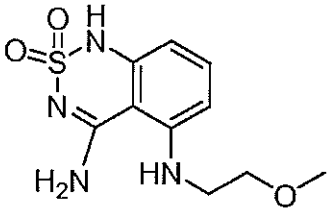
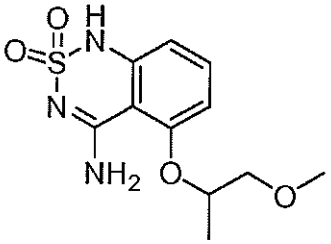
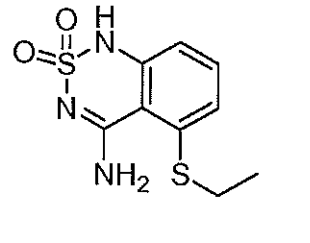
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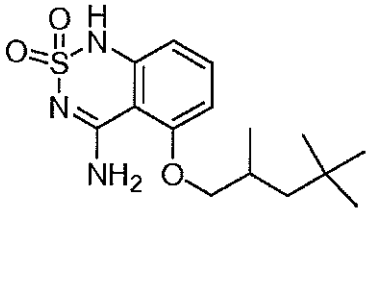
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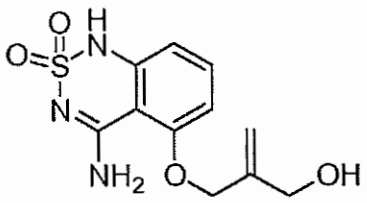
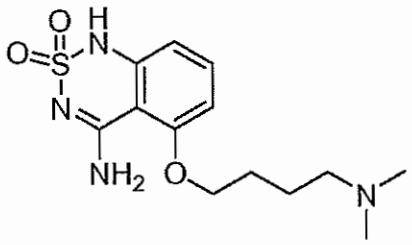
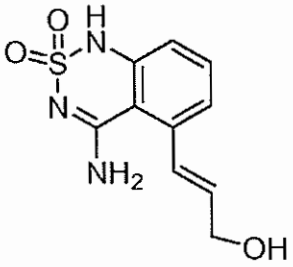
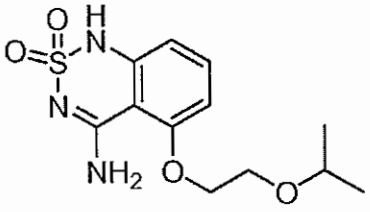
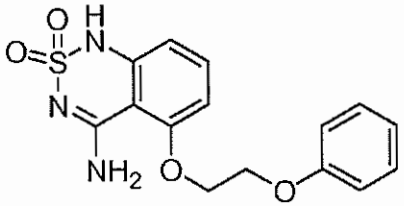
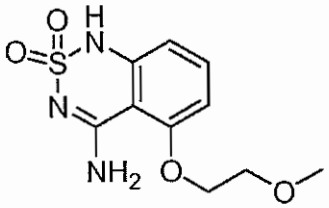
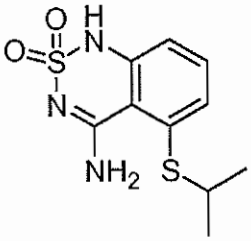
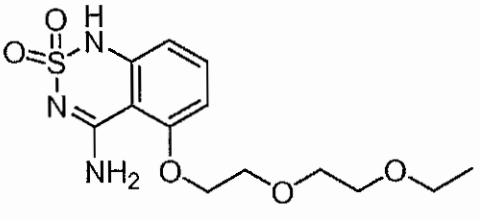

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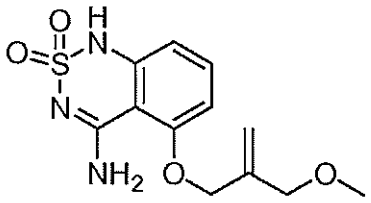
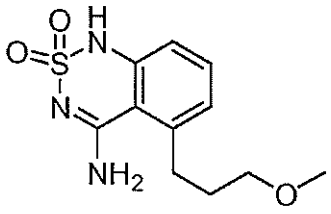
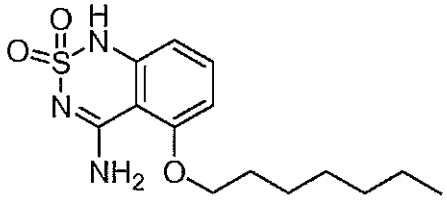
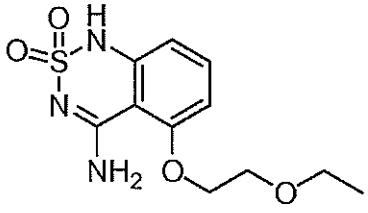
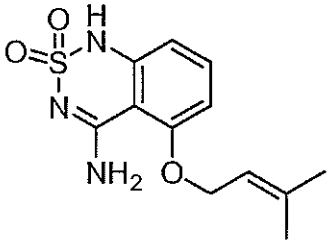
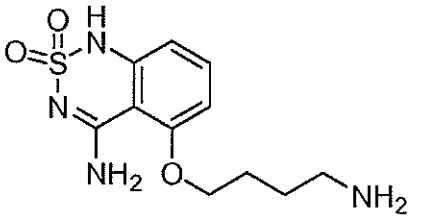
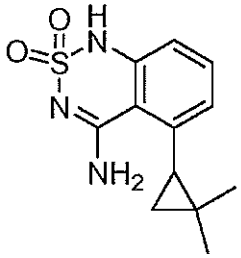
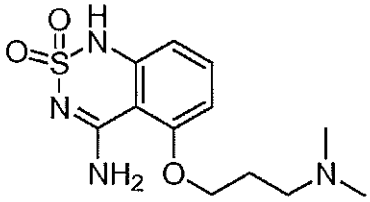
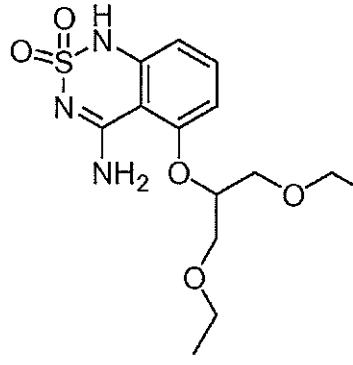
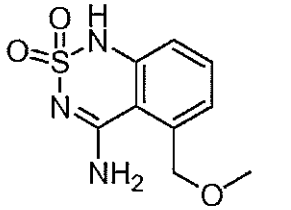
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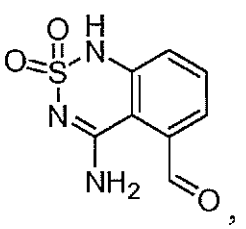
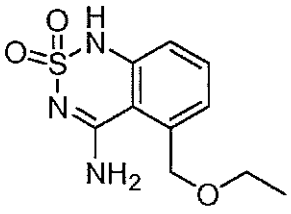
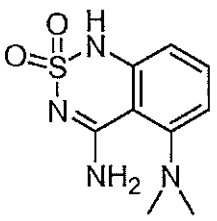
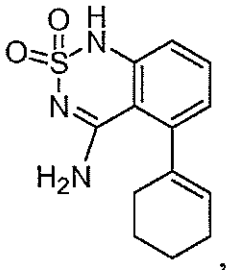
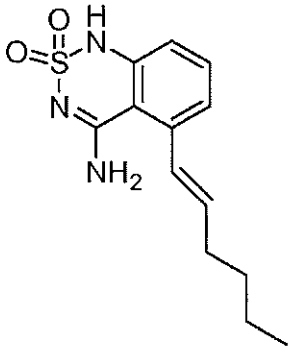
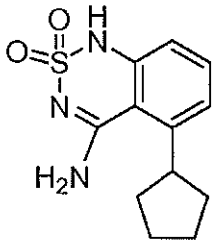
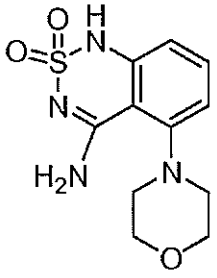
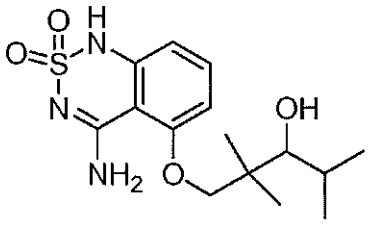
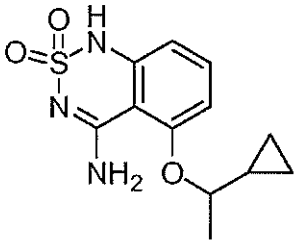
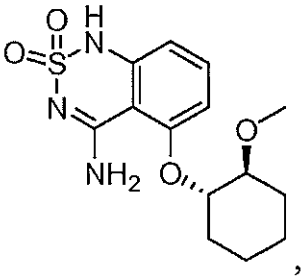
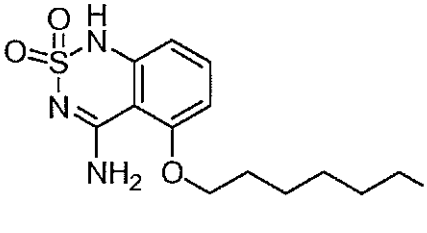
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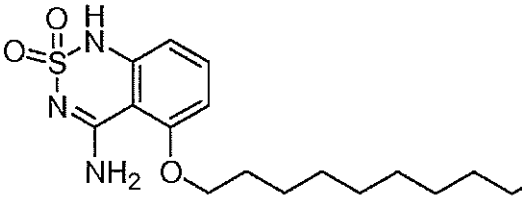
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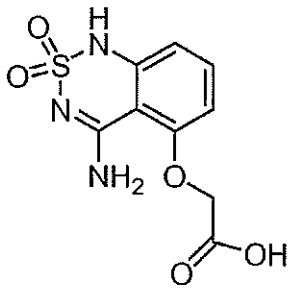
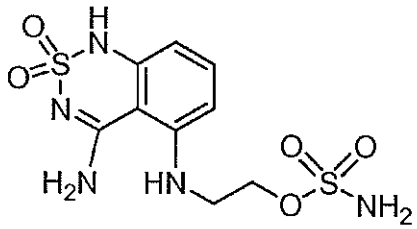
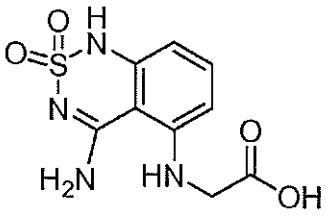
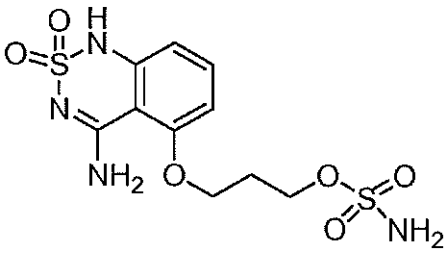
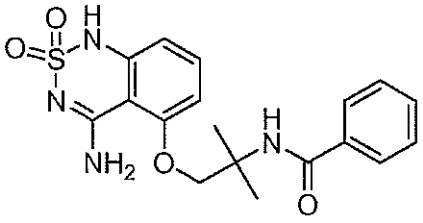
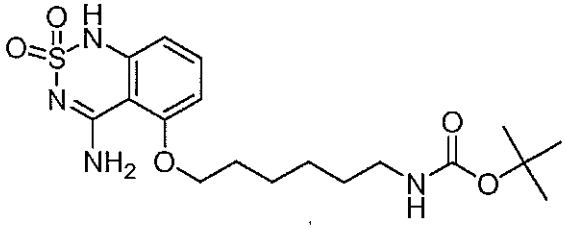
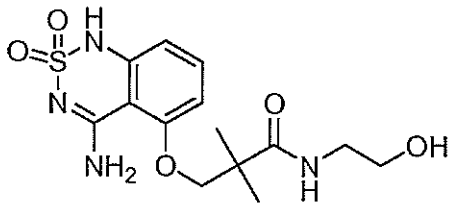
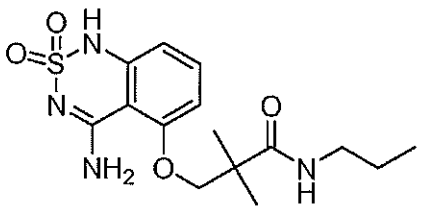

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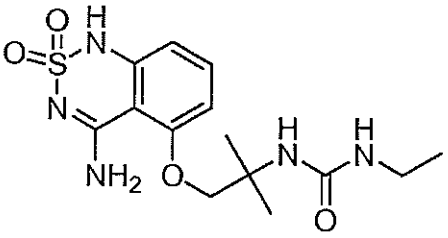
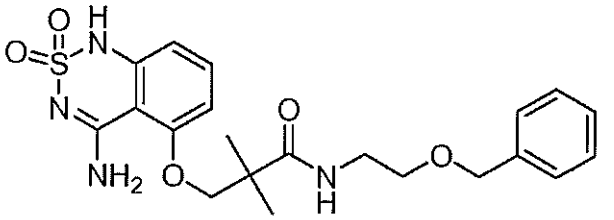
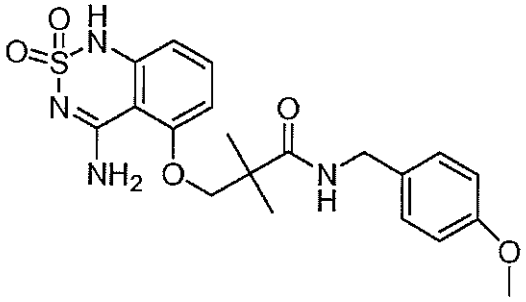
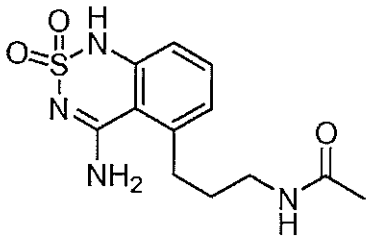
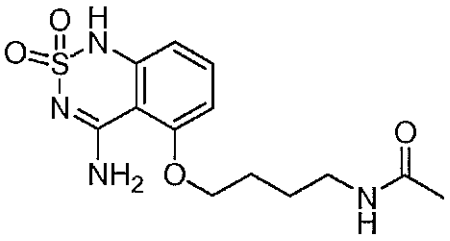
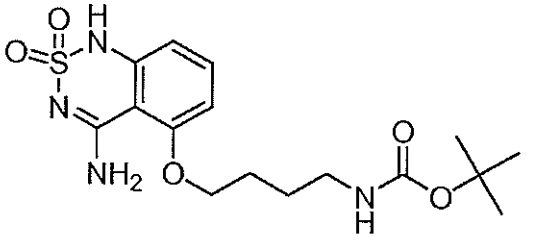
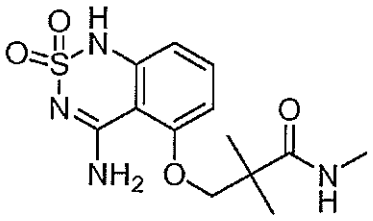
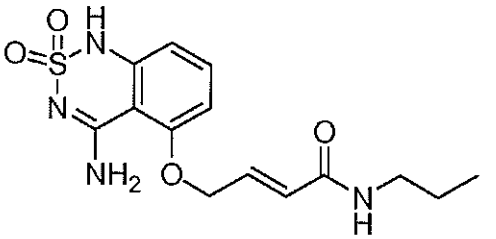
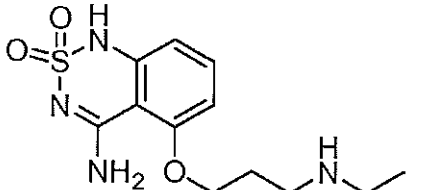

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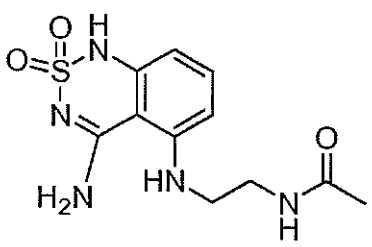
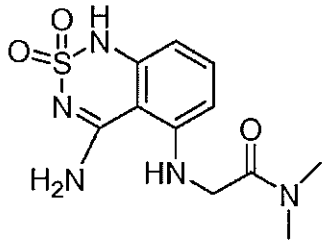
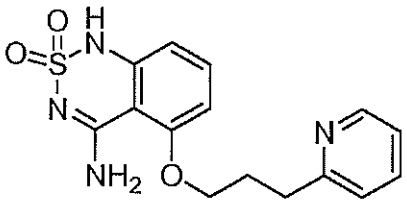
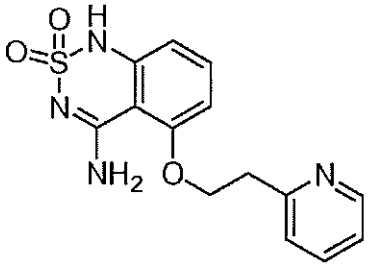
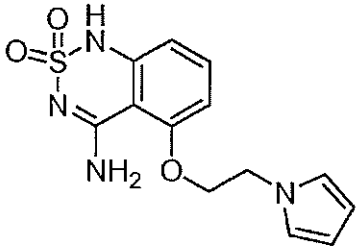
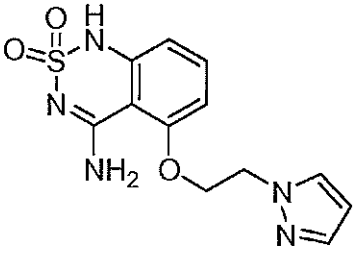
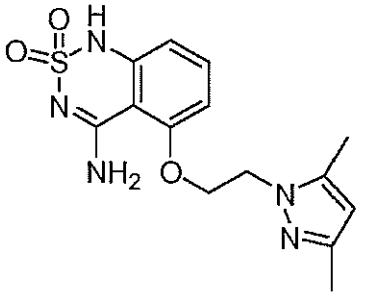
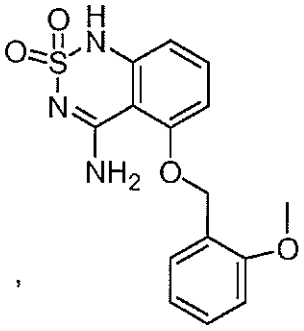
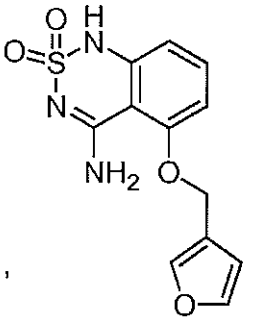
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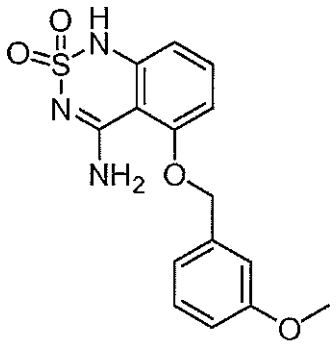
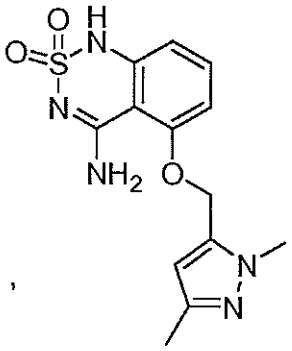
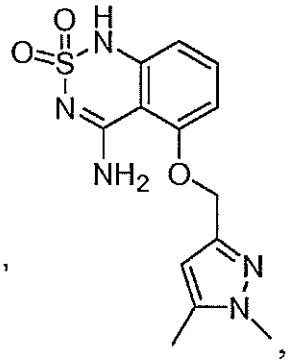
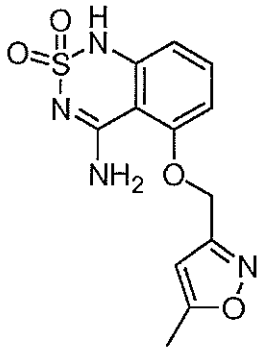
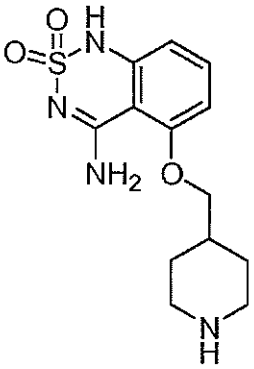
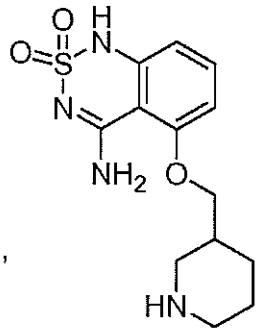
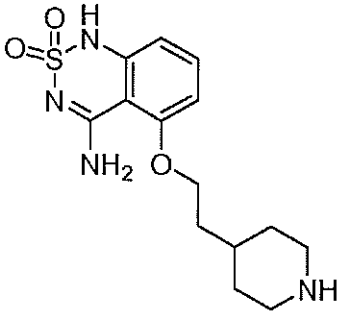
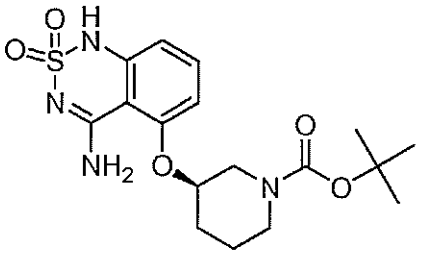
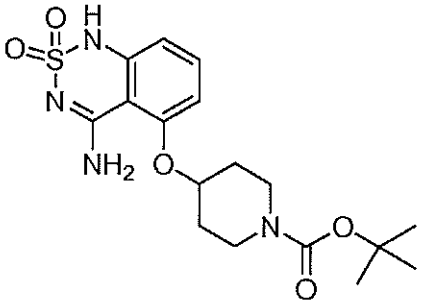
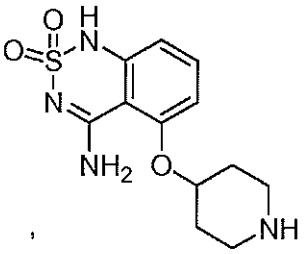
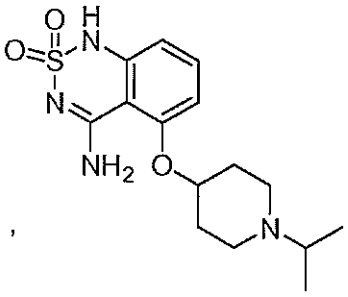

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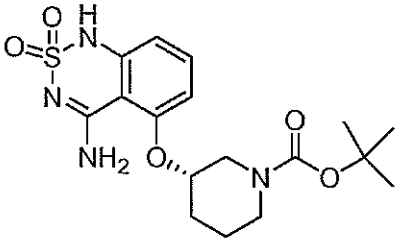
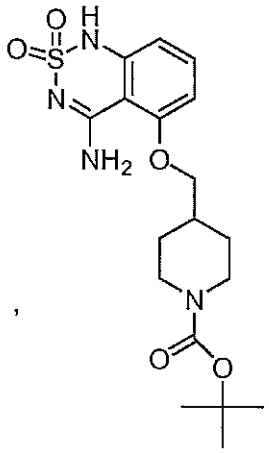
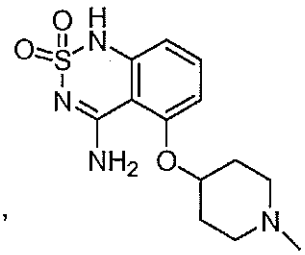
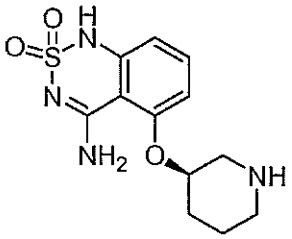
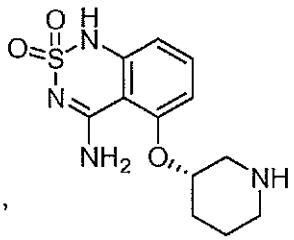
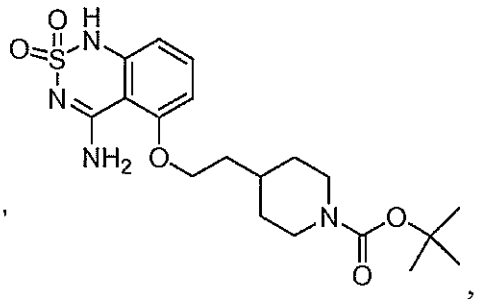
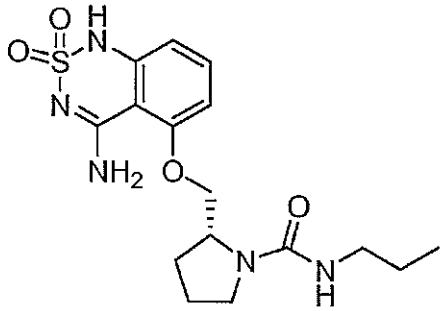
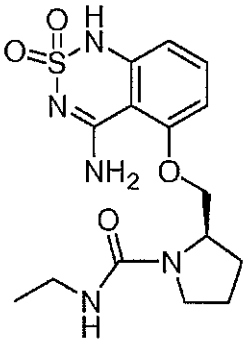
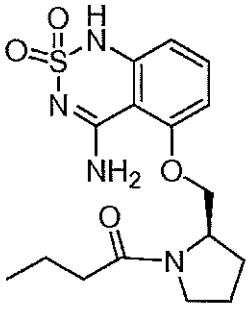
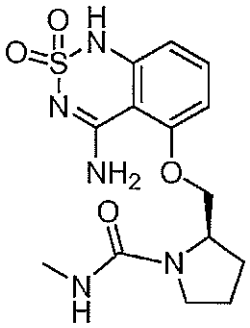
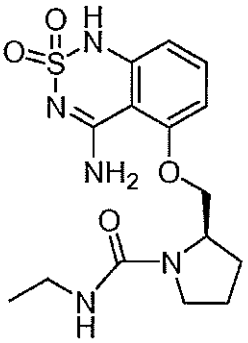

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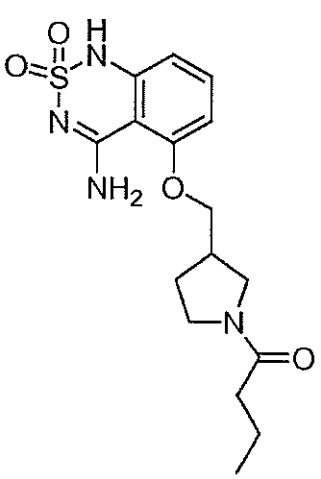
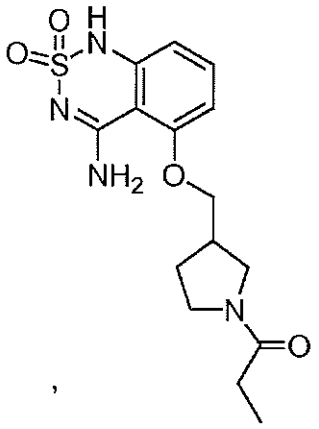
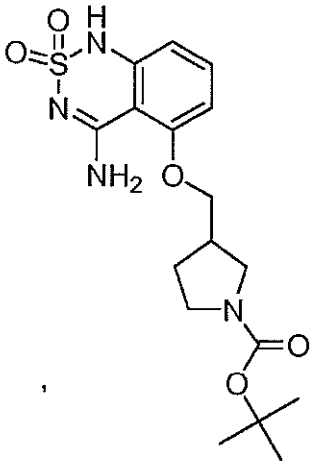
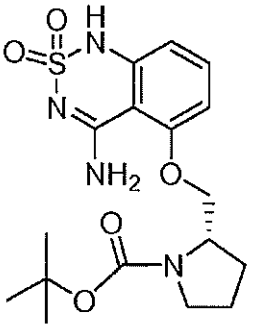
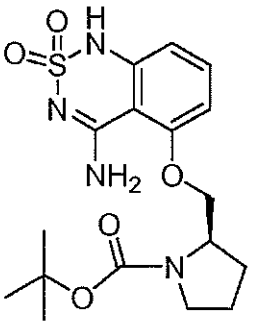
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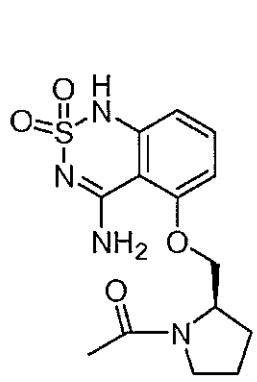
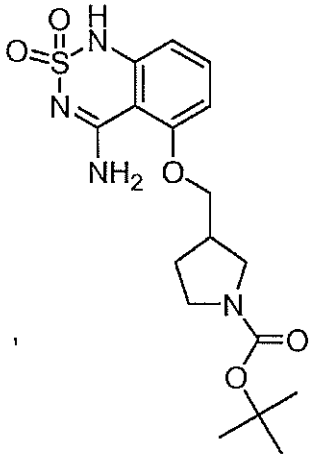
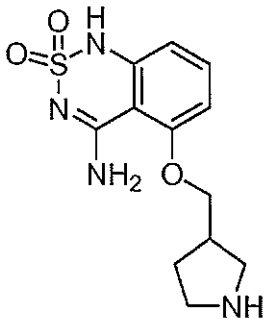
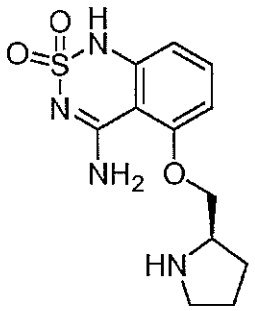
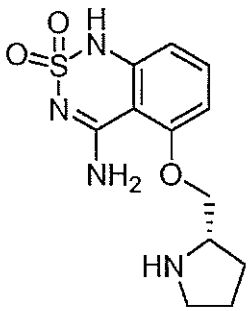
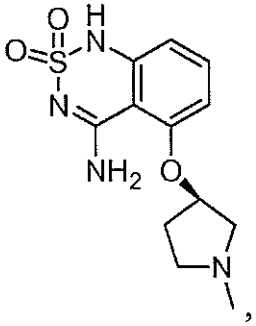
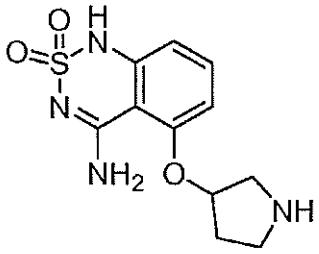
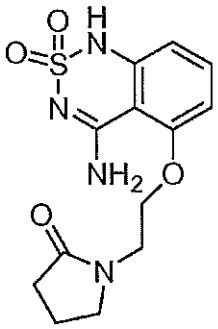
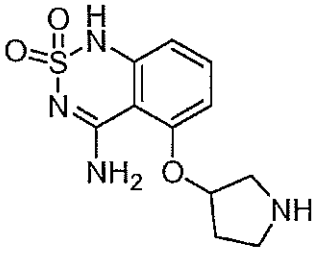
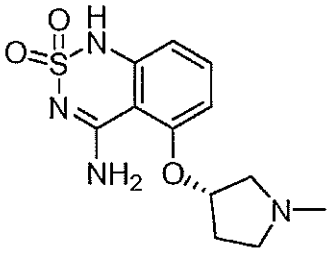
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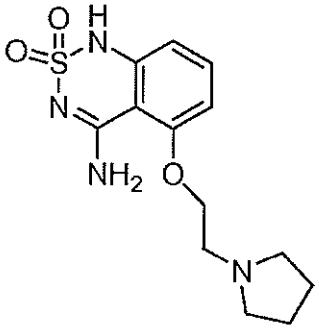
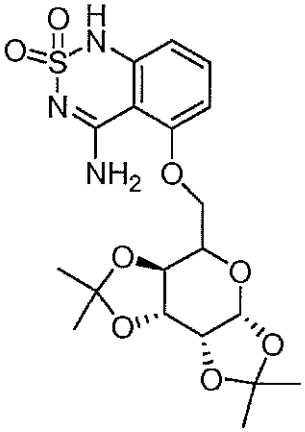
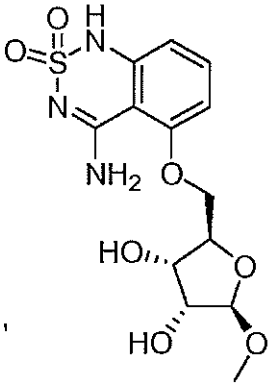
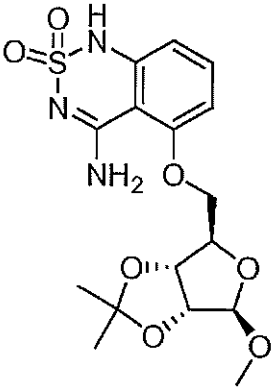
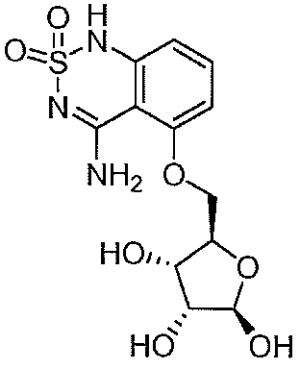
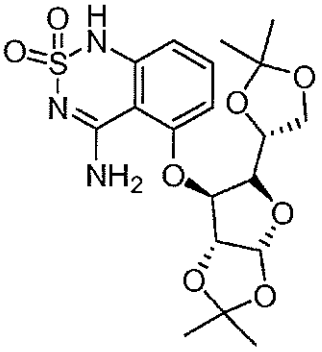
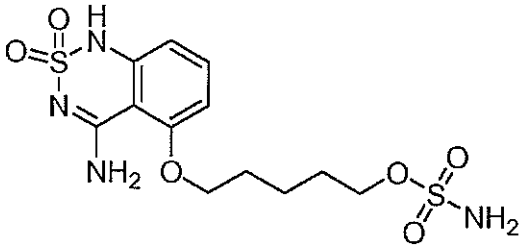
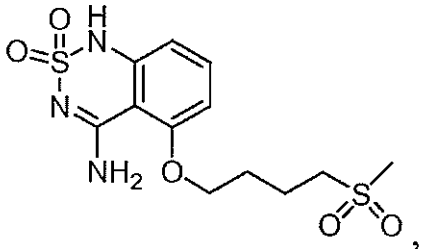
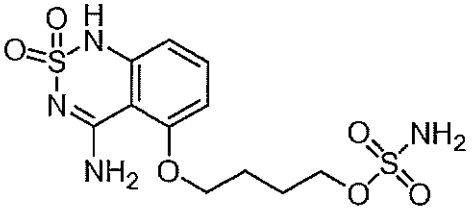
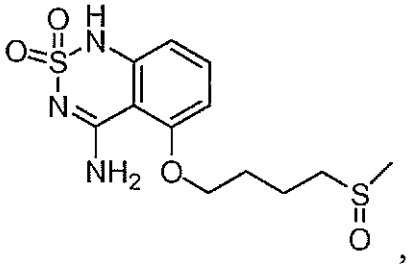

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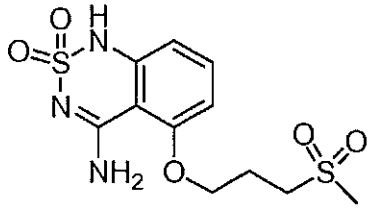
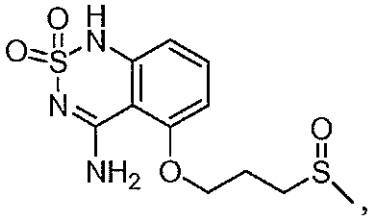
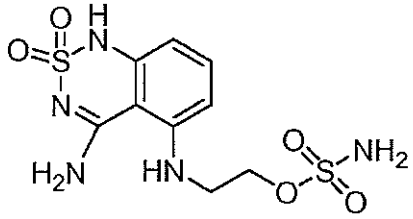
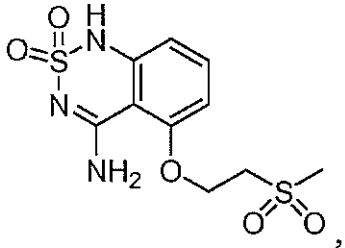
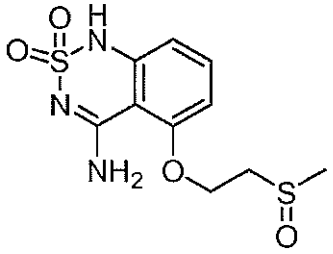
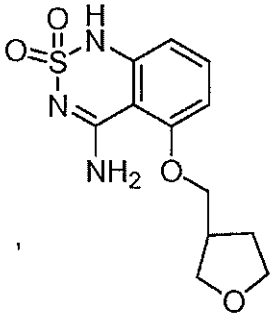
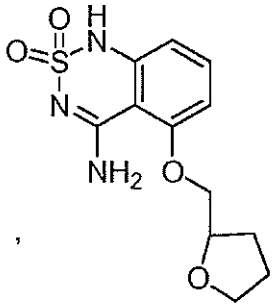
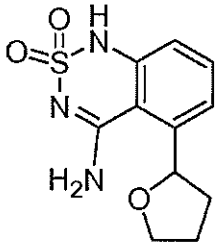
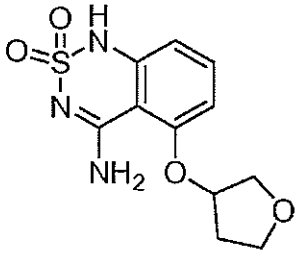
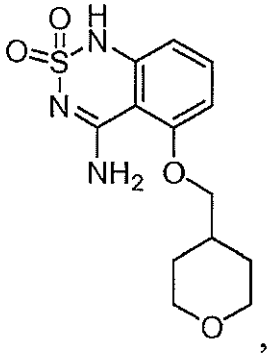

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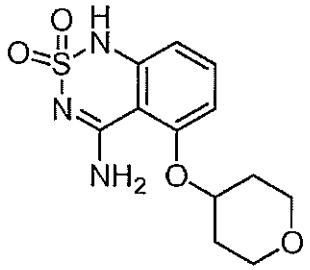
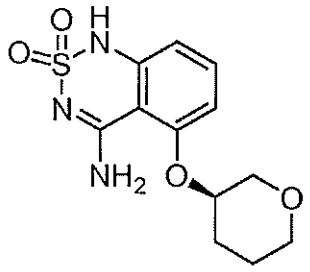
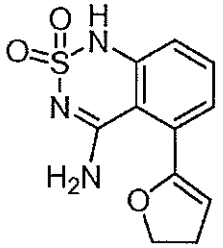
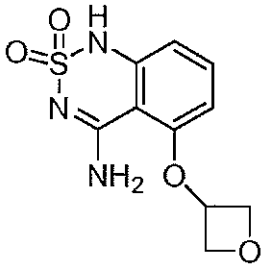
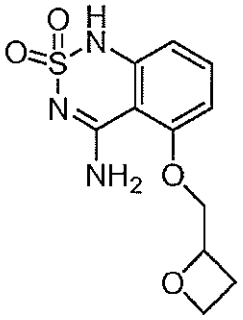
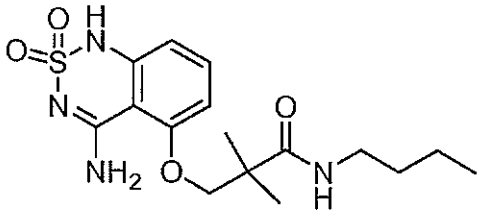
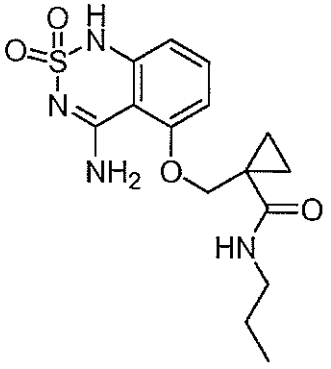
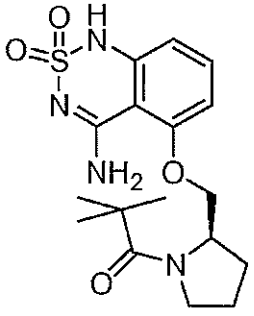
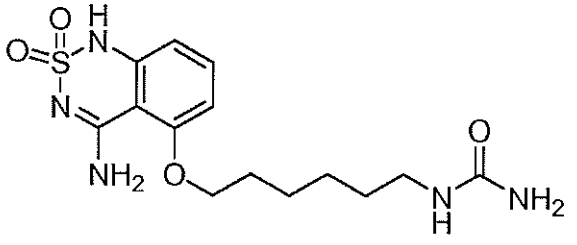

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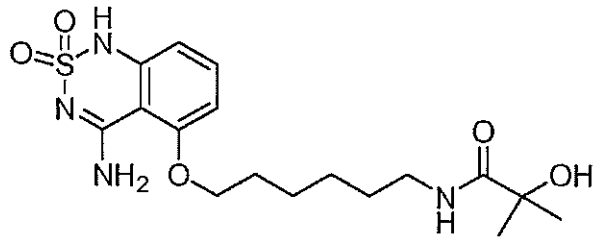
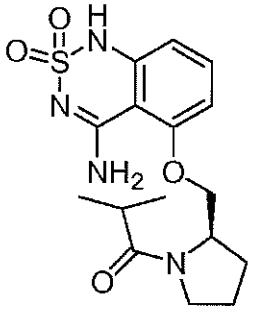
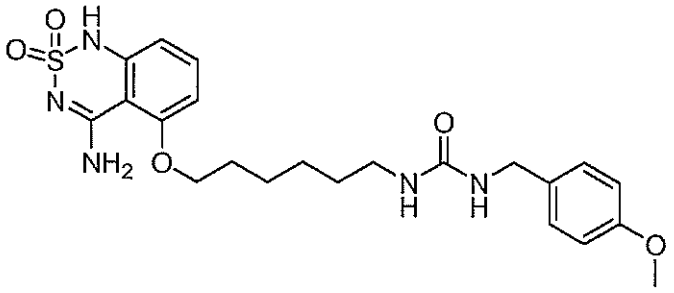
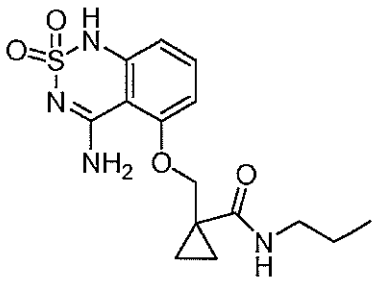
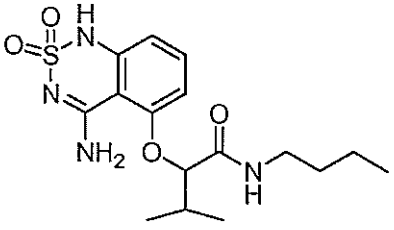
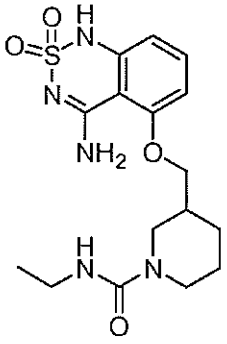
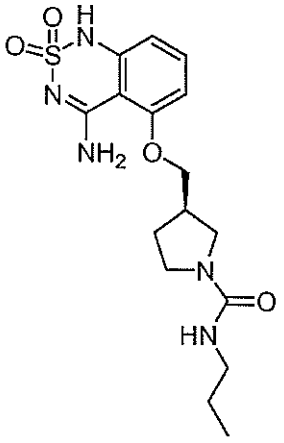
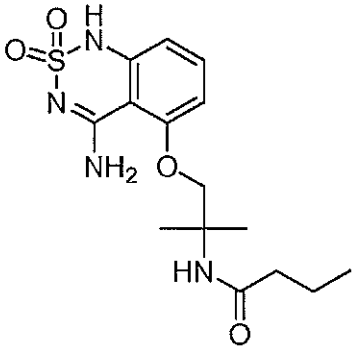
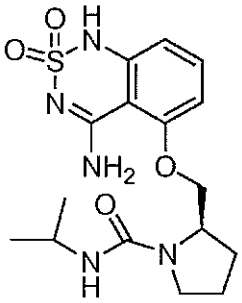
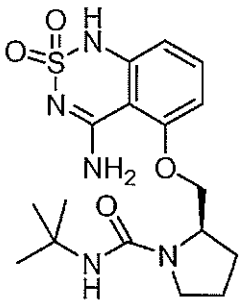

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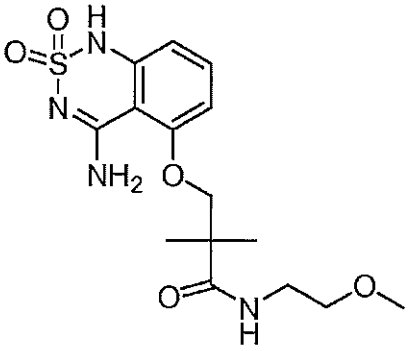
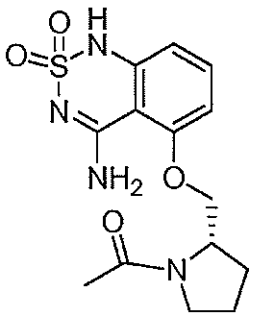
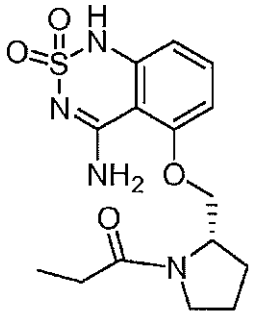
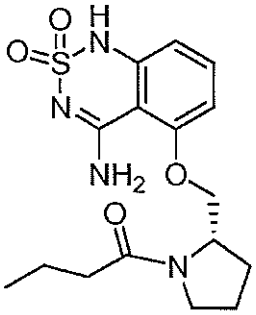
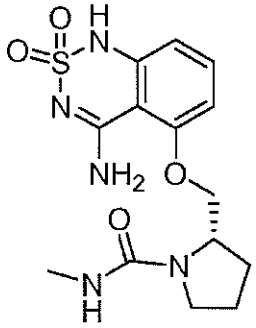
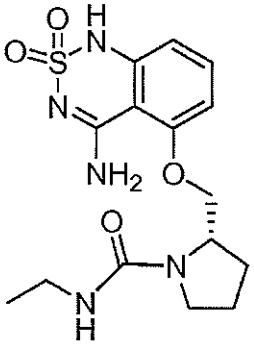
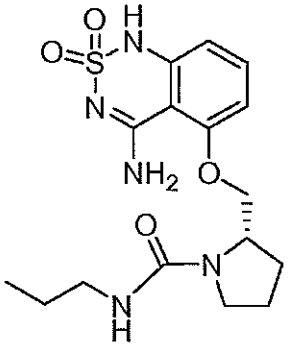
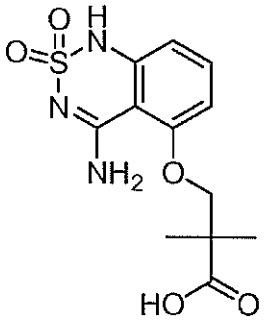
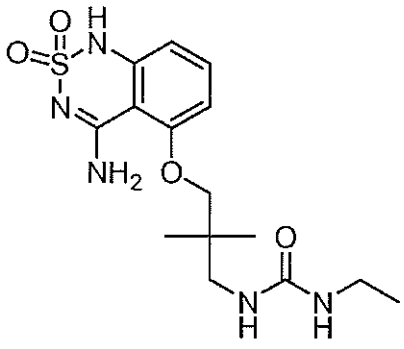
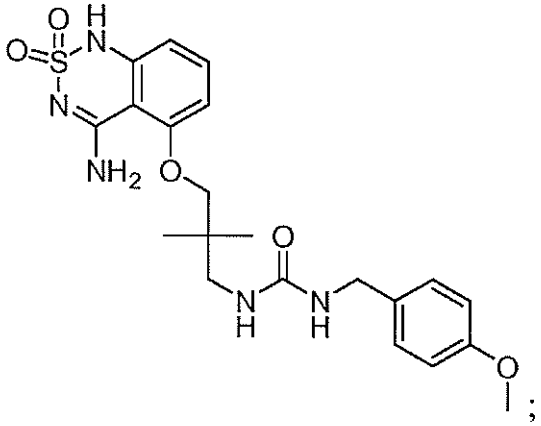

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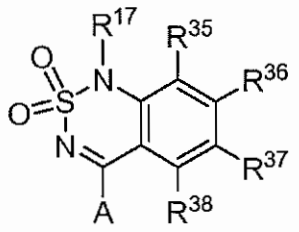

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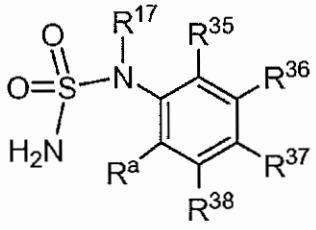
or a salt or solvate thereof.

16. A process of preparing a compound having structural Formula (e):



(e),

comprising reacting a compound having structural Formula (f)



(f),

with a base,

wherein:

A is $-NH_2$ or $-OR^b$;

R^{17} is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, or substituted arylalkyl;

R^{35}, R^{36}, R^{37}, and R^{38} are each independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, halo, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl, $-CN$, $-NO_2$, $-OR^{41}$, $-S(O)_kR^{41}$, $-NR^{41}R^{42}$, $-CONR^{41}R^{42}$, $-CO_2R^{41}$, $-SO_2NR^{41}R^{42}$, and $-NR^{41}SO_2R^{42}$; or alternatively, R^{35} and R^{36}, R^{36} and R^{37}, or R^{37} and R^{38}, together with the atoms to which they are bonded, form a cycloalkyl, substituted cycloalkyl, heterocycloalkyl, or substituted heterocycloalkyl ring;

R^a is $-CN$, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^b)_2$;

each R^b is independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, or substituted heteroarylalkyl; and

R^{41} and R^{42} are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, acyl, substituted acyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted heteroarylalkyl; or alternatively R^{41} and R^{42}, together with the atoms to which they are bonded, form a cycloheteroalkyl or substituted cycloheteroalkyl ring.