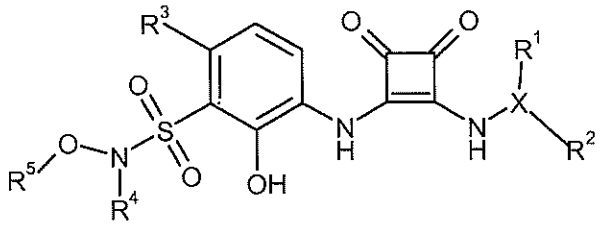
Claims:

1. A compound of formula I



(I)

or solvates, hydrates or pharmaceutically acceptable salts thereof, wherein

R^1 is H, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen atoms or OH groups, or an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, wherein the ether group is optionally substituted by one or more substituents each independently selected from OH, halogen, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups and a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^2 is a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen atoms or OH groups, or an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, wherein the ether group is optionally substituted by one or more substituents each independently selected from OH, halogen, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups and a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups; or

R^1 and R^2 together with the carbon atom to which they are attached form 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, or a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^3 is hydrogen, halogen or cyano;

R^4 is H, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl or (C_1-C_4 alkyl)-R^6, wherein the alkyl groups are each optionally substituted by one or more halogen atoms;

R^5 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, (C_1-C_4 alkyl)-C_3-C_8 cycloalkyl or (C_1-C_4 alkyl)-C_5-C_8 cycloalkenyl, wherein the alkyl groups are each optionally substituted by one or more halogen atoms; or

R^4 and R^5, together with the nitrogen and oxygen atoms to which they are attached, form a 5 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^6 is selected from a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, NR^7R^9, $NR^7(SO_2)R^9$, $(SO_2)NR^7R^8$, $(SO_2)R^9$, $NR^7C(O)R^9$, $C(O)NR^7R^9$, $NR^7C(O)NR^8R^9$, $NR^7C(O)OR^9$, $C(O)OR^7$, $OC(O)R^9$, $OC(O)NR^7$, $C(O)R^9$, SR^7 , CN and NO_2;

R^7 and R^8 are each independently selected from H, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl and -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl;

R^9 is selected from H, C_1-C_6 alkyl, -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl, a 3 to 10 membered carbocyclic group and a 3 to 10 membered heterocyclic group, wherein each of the alkyl groups and ring systems is optionally substituted by OH, halo, C_1-C_3 alkyl and C_1-C_3 alkoxy;

X is CR^{14} or N;

Z is independently selected from OH; a 3 to 10 membered carbocyclic group; a 3 to 10 membered heterocyclic group; benzyl; C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups; C_1-C_6 alkoxy optionally substituted by one or more halogen atoms, CN or OH groups; -Oaryl; -Obenzyl; $-O(CH_2)_aC(O)E$; $NR^{10}(SO_2)R^{12}$;

$(SO_2)NR^{10}R^{11}$; $(SO_2)R^{12}$; $NR^{10}C(O)R^{12}$; $C(O)NR^{10}R^{12}$; $NR^{10}C(O)NR^{11}R^{12}$; $NR^{10}C(O)OR^{12}$; $NR^{10}R^{12}$; $C(O)OR^{10}$; $OC(O)R^{12}$; $OC(O)NR^{10}$; $C(O)R^{12}$; SR^{12} ; CN; NO_2; and halogen; or

where there are two or more Z substitutents, two Z substituents together with the atoms to which they are attached optionally form a 5- to 7-membered carbocyclic or a 4- to 7-membered heterocyclic substituent fused to the ring system;

a is 0, 1, 2, 3 or 4, wherein the alkylene group is optionally substituted by OH or NH_2 when a is 1, 2, 3 or 4;

E is $NR^{10}R^{12}$ or OR^{12};

each R^{10} and R^{11} are independently selected from H, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl and -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl;

each R^{12} is selected from H, C_1-C_6 alkyl, -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl, a 3 to 10 membered carbocyclic group and a 3 to 10 membered heterocyclic group, wherein each of the ring systems is optionally substituted by OH, halo, C_1-C_3 alkyl and C_1-C_3 alkoxy; and

R^{14} is H or C_1-C_6 alkyl.

2. A compound according to Claim 1, wherein R^1 is H or C_1-C_4 alkyl.

3. A compound according to Claim 1 or Claim 2, wherein
R^1 is H or C_1-C_4 alkyl;
R^2 is C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, a 4 to 6 membered carbocyclic group optionally substituted by one or more Z groups, or a 4 to 6 membered heterocyclic group optionally substituted by one or more Z groups; or
R^1 and R^2, together with the carbon atom to which they are attached form a 4 to 6 membered carbocyclic group optionally substituted by one or more Z groups or a 4 to 6 membered heterocyclic group optionally substituted by one or more Z groups.

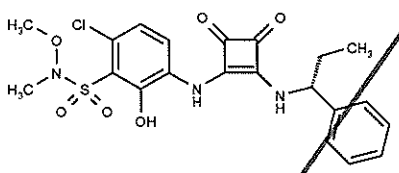
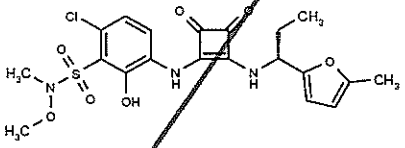
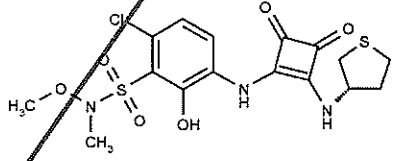
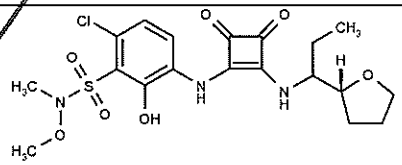
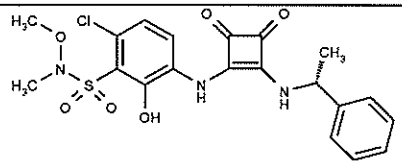
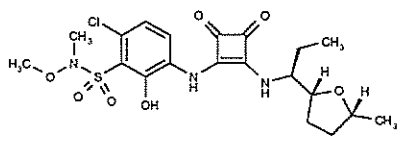
4. A compound according to any preceding claim, wherein R^3 is halogen.

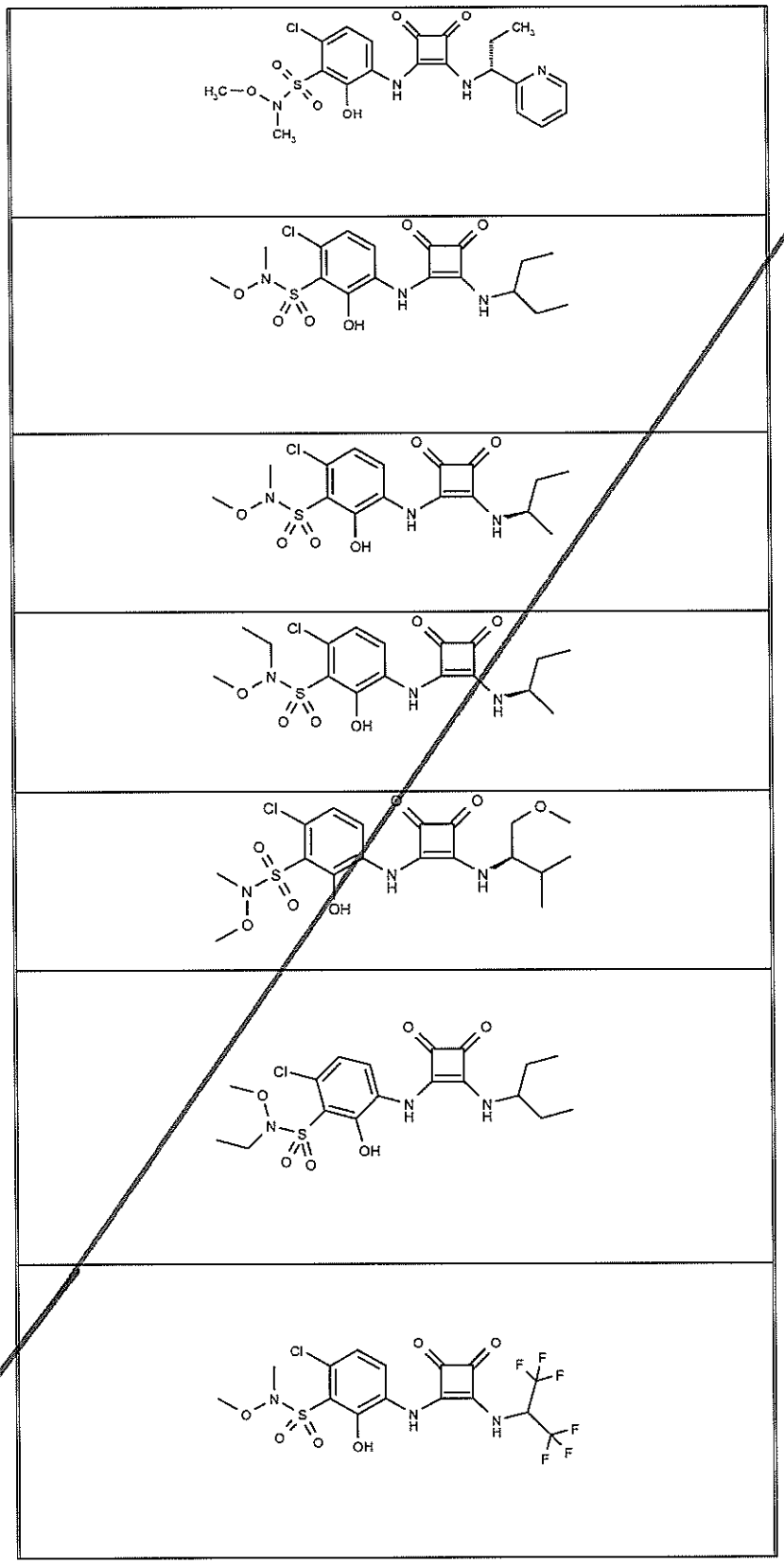
5. A compound according to any preceding claim, wherein R^4 is H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl or (C_1-C_3 alkyl)-C_3-C_6 cycloalkyl.

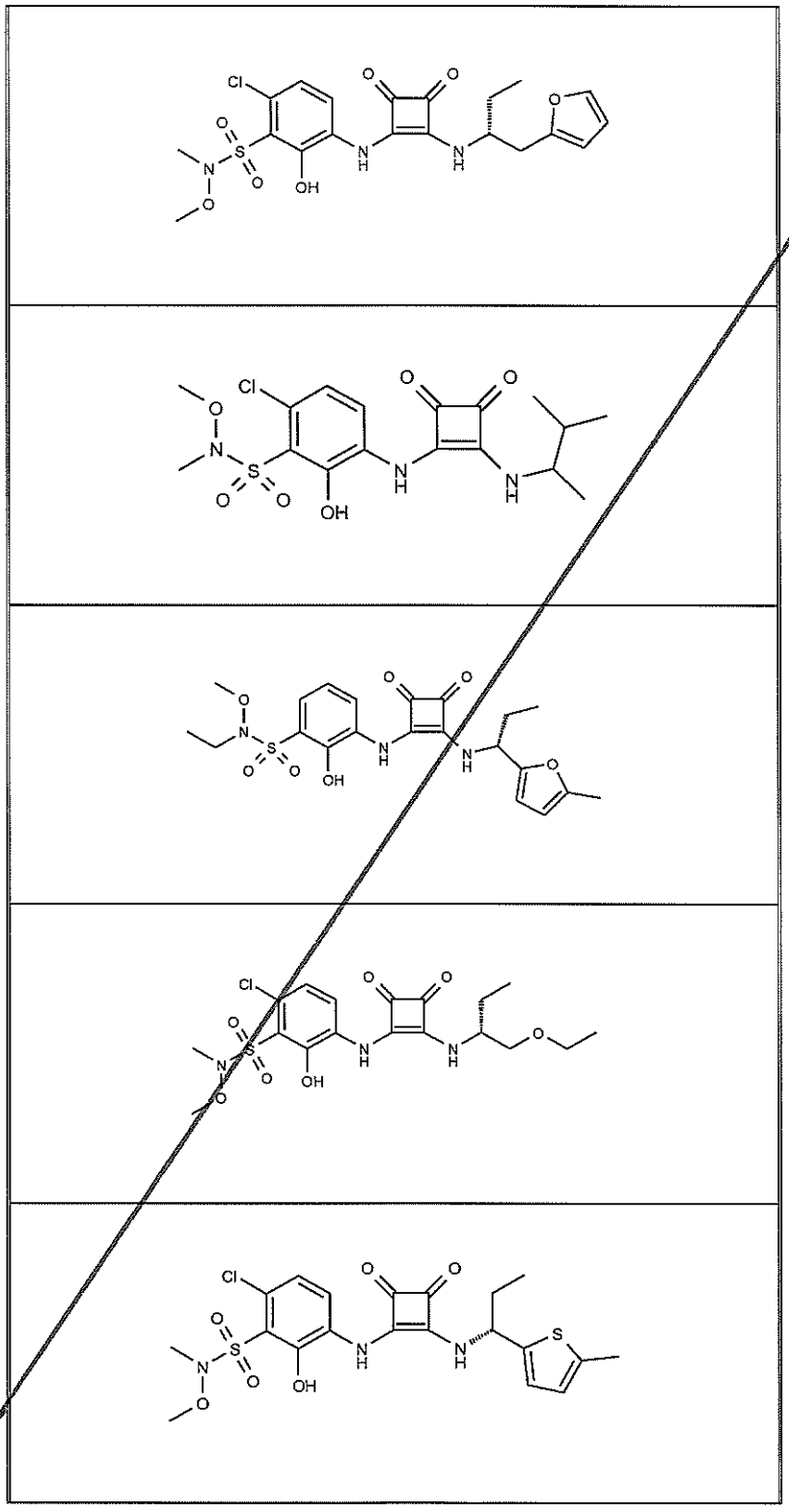
6. A compound according to any preceding claim, wherein R^5 is C_1-C_6 alkyl.

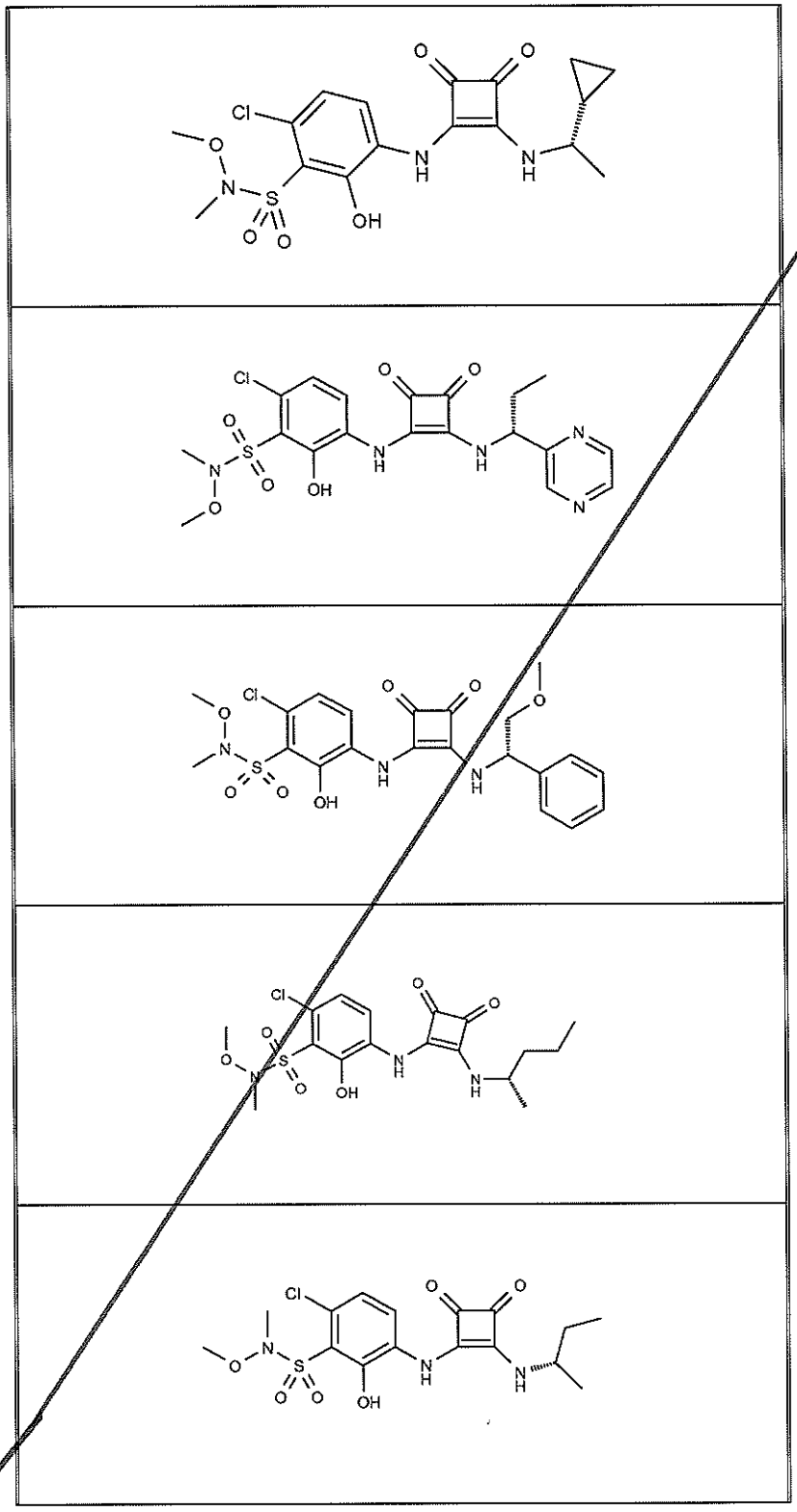
7. A compound according to any preceding claim, wherein X is CH.

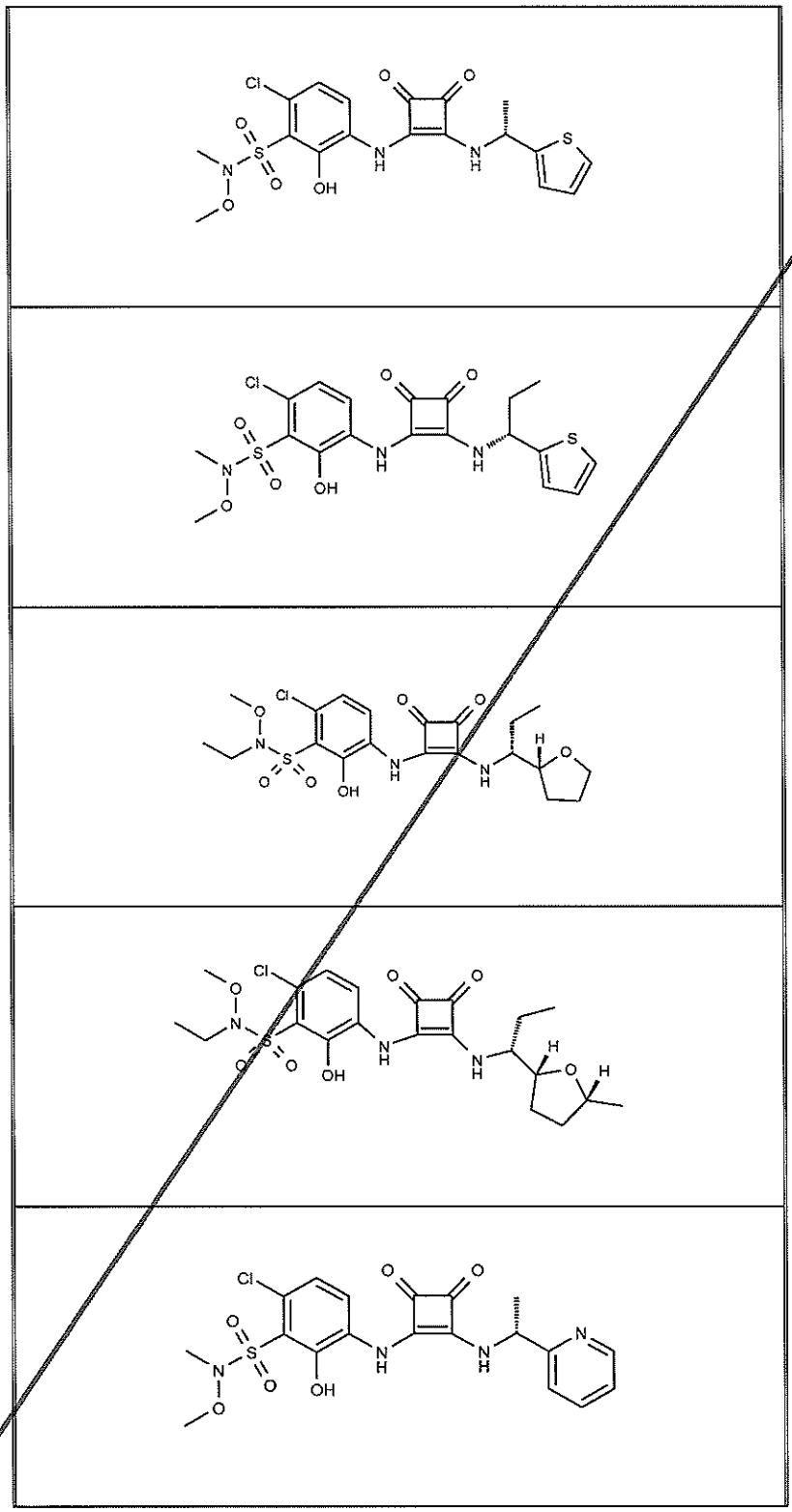
8. A compound according to Claim 1 which is selected from:

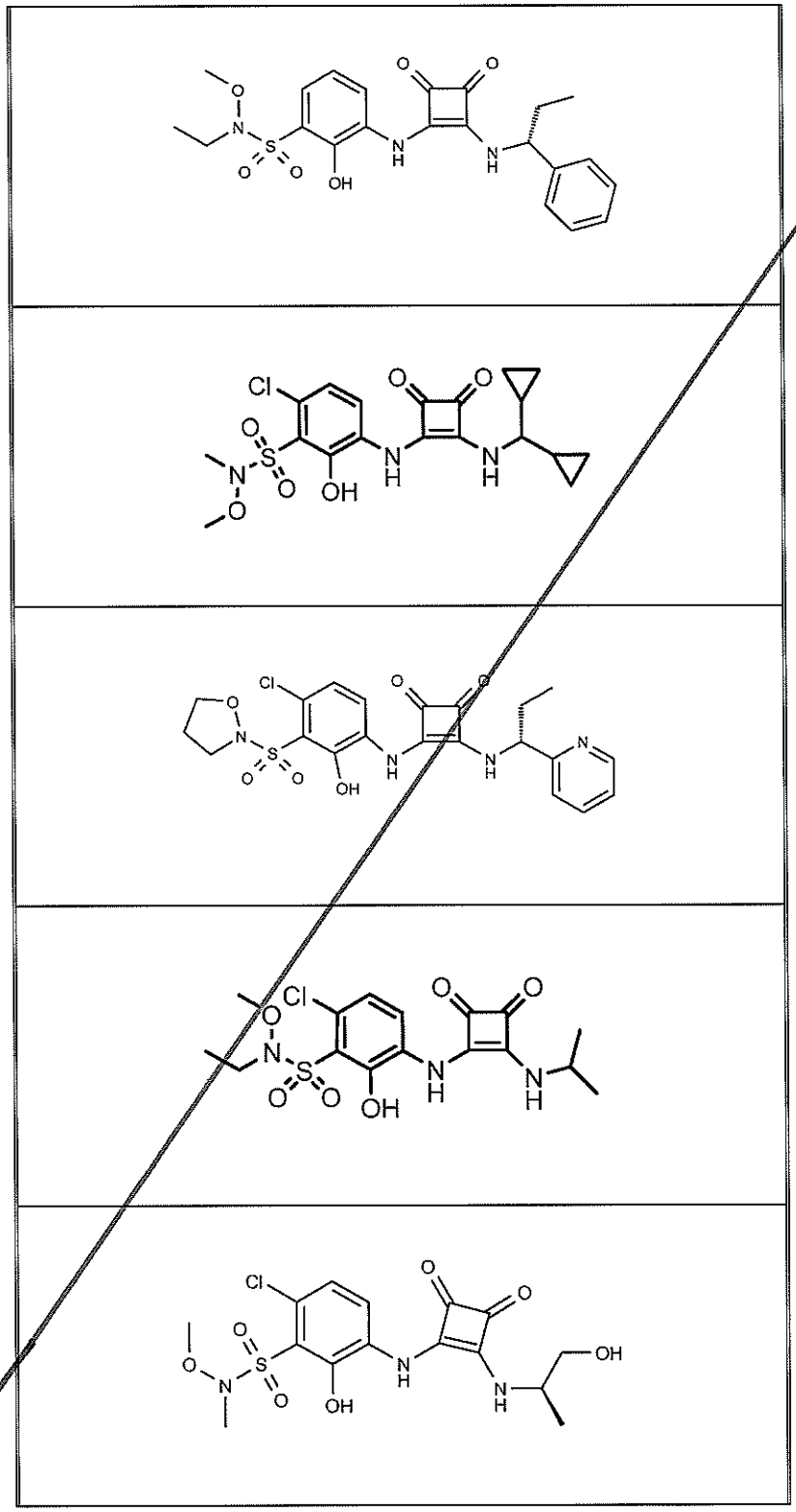
Structure







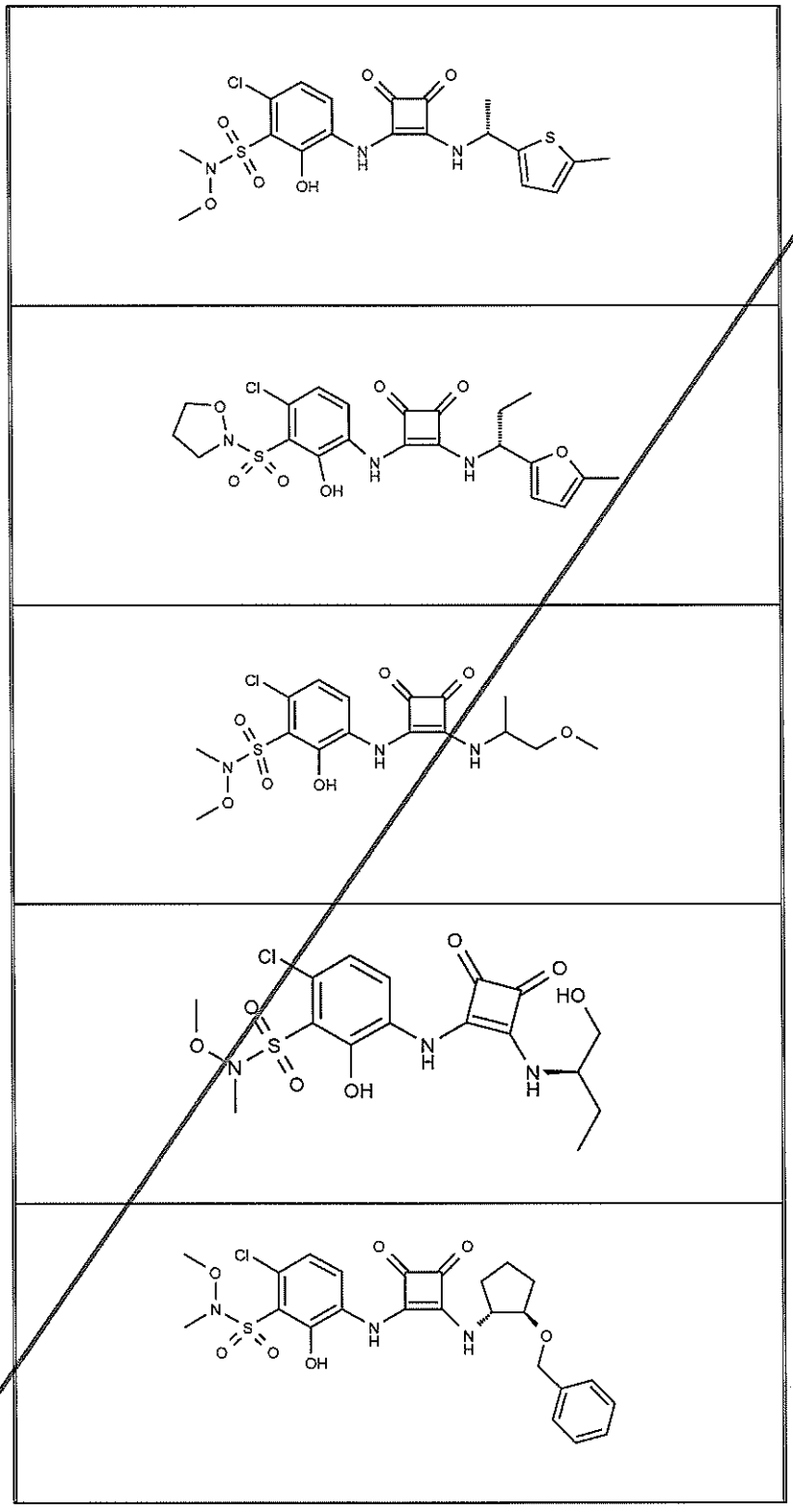


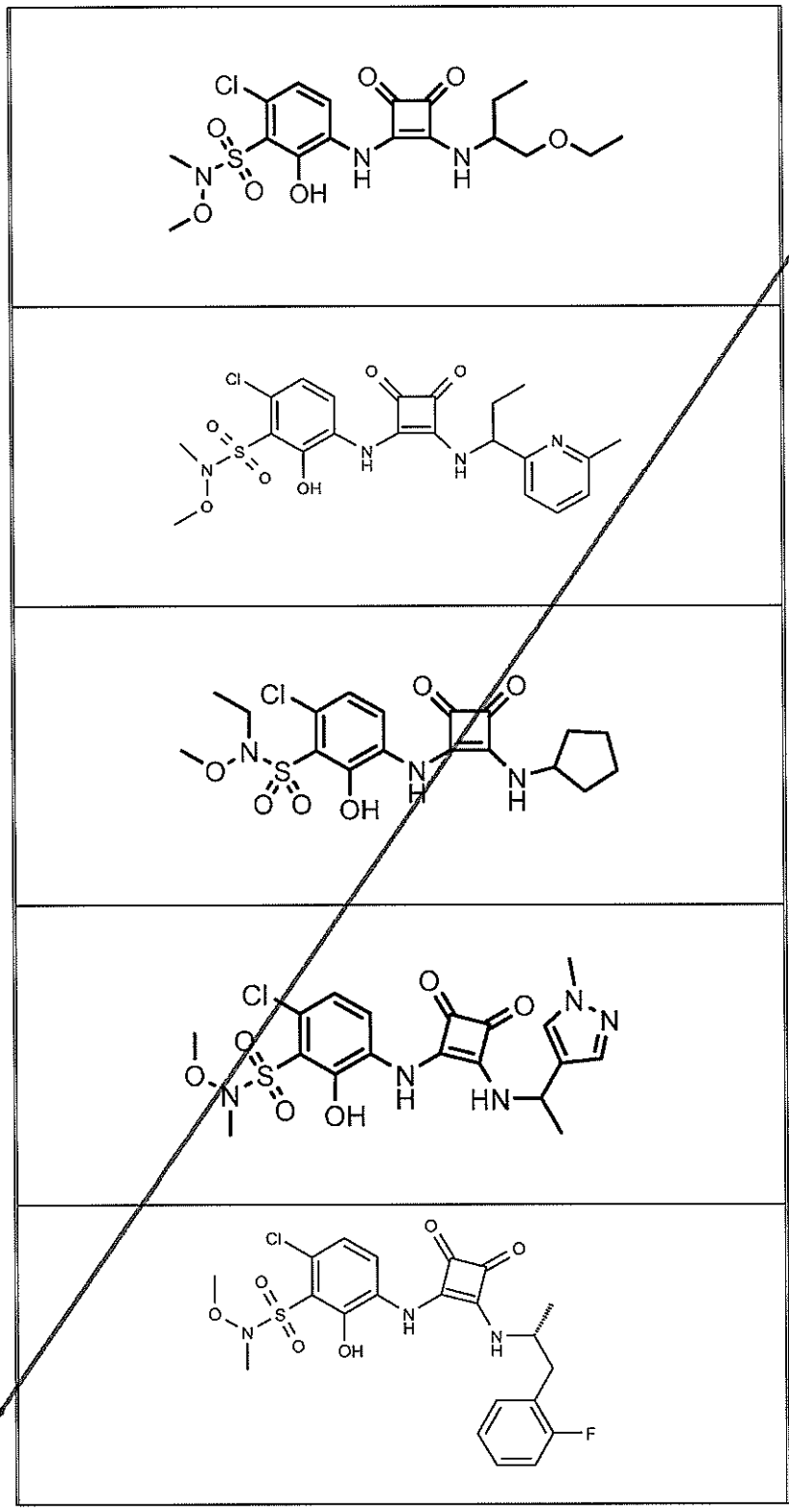


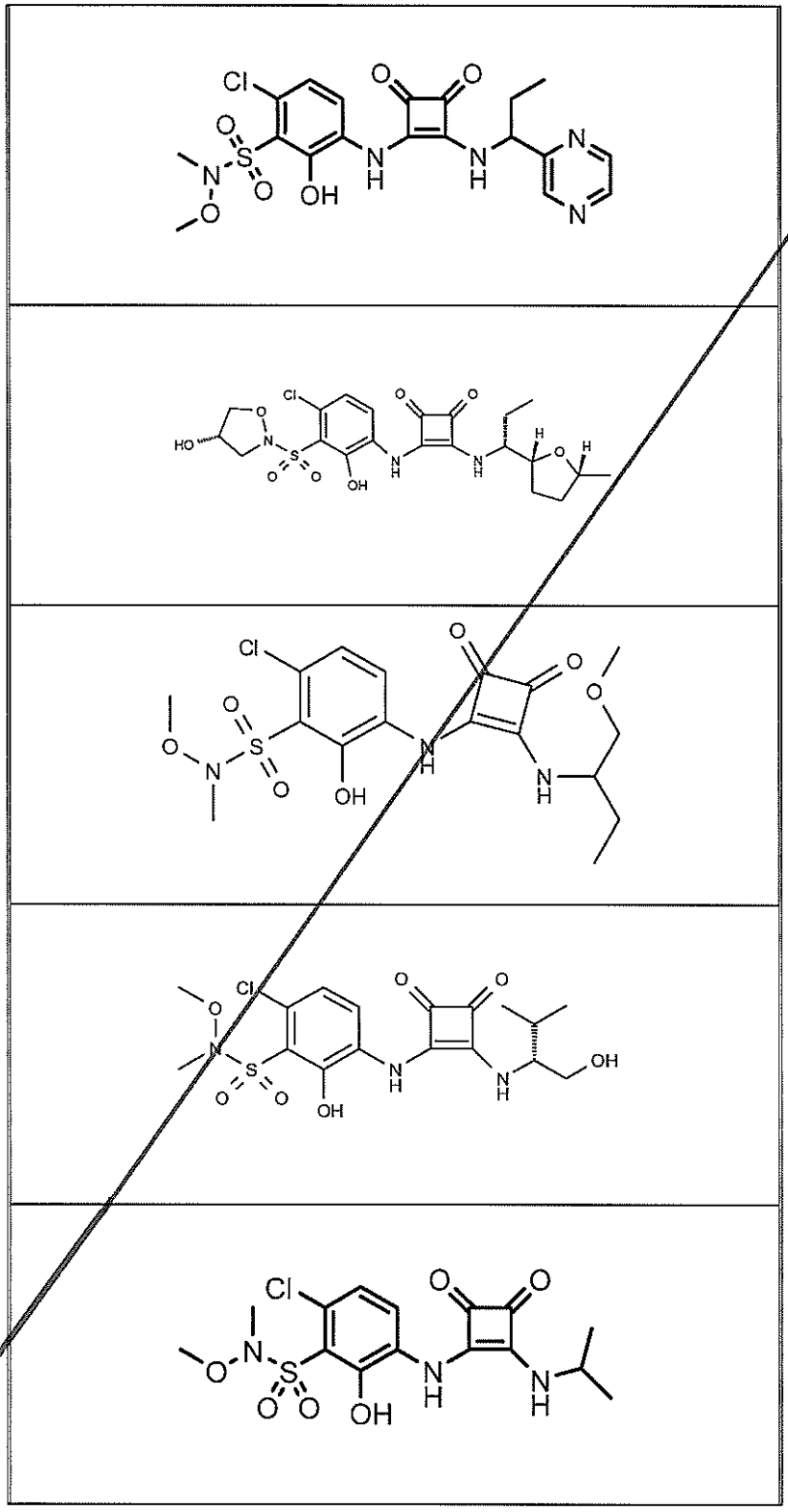


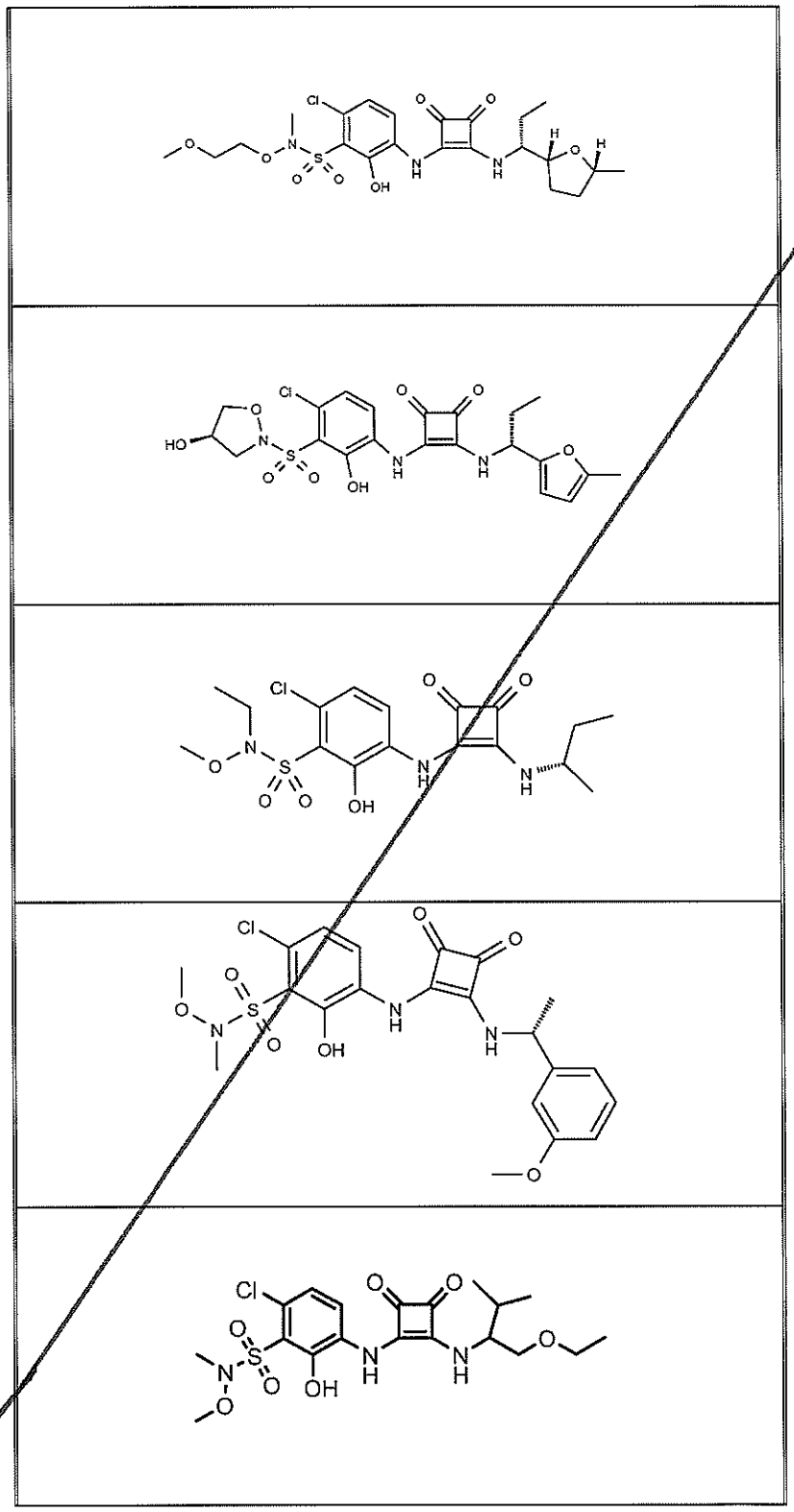


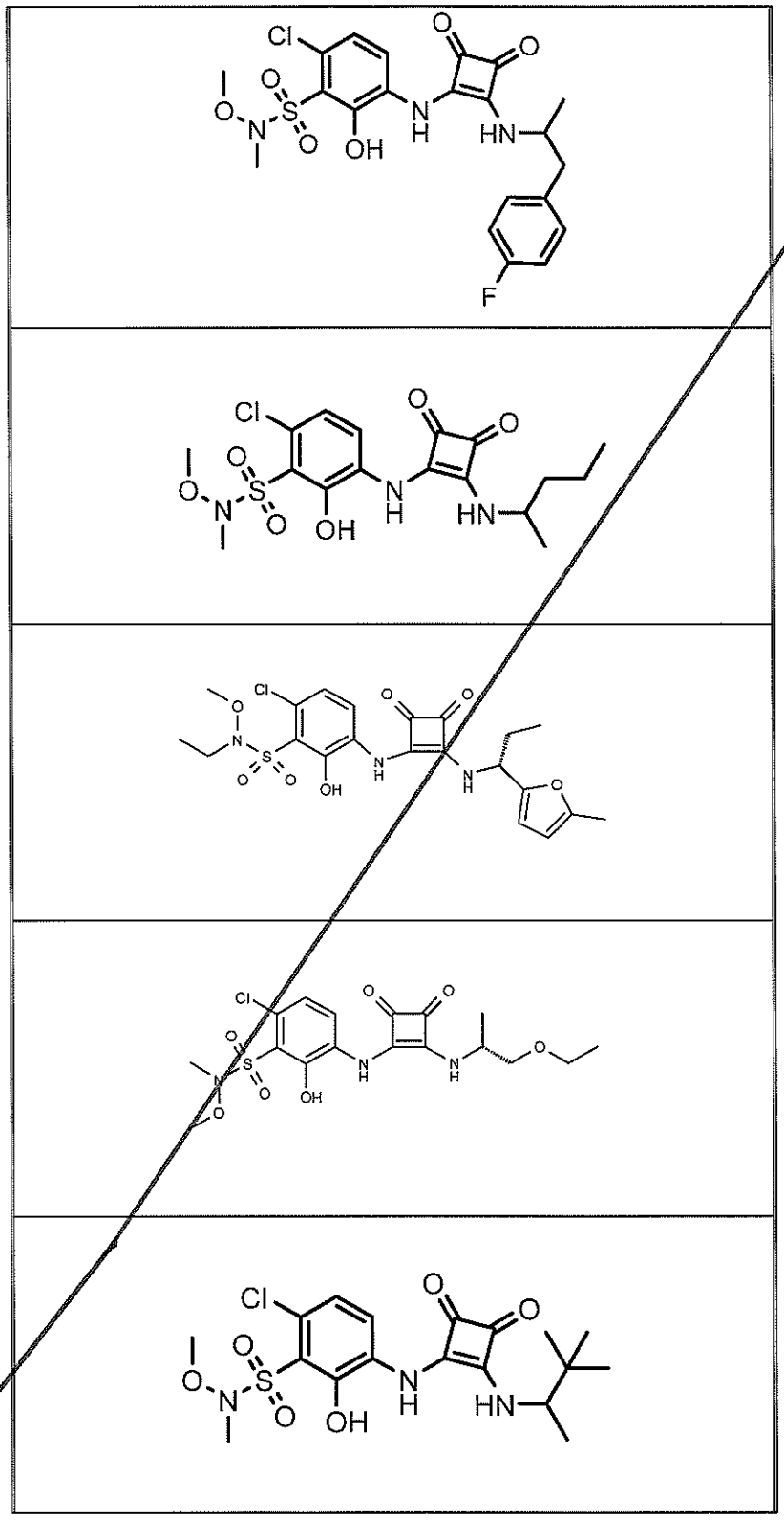


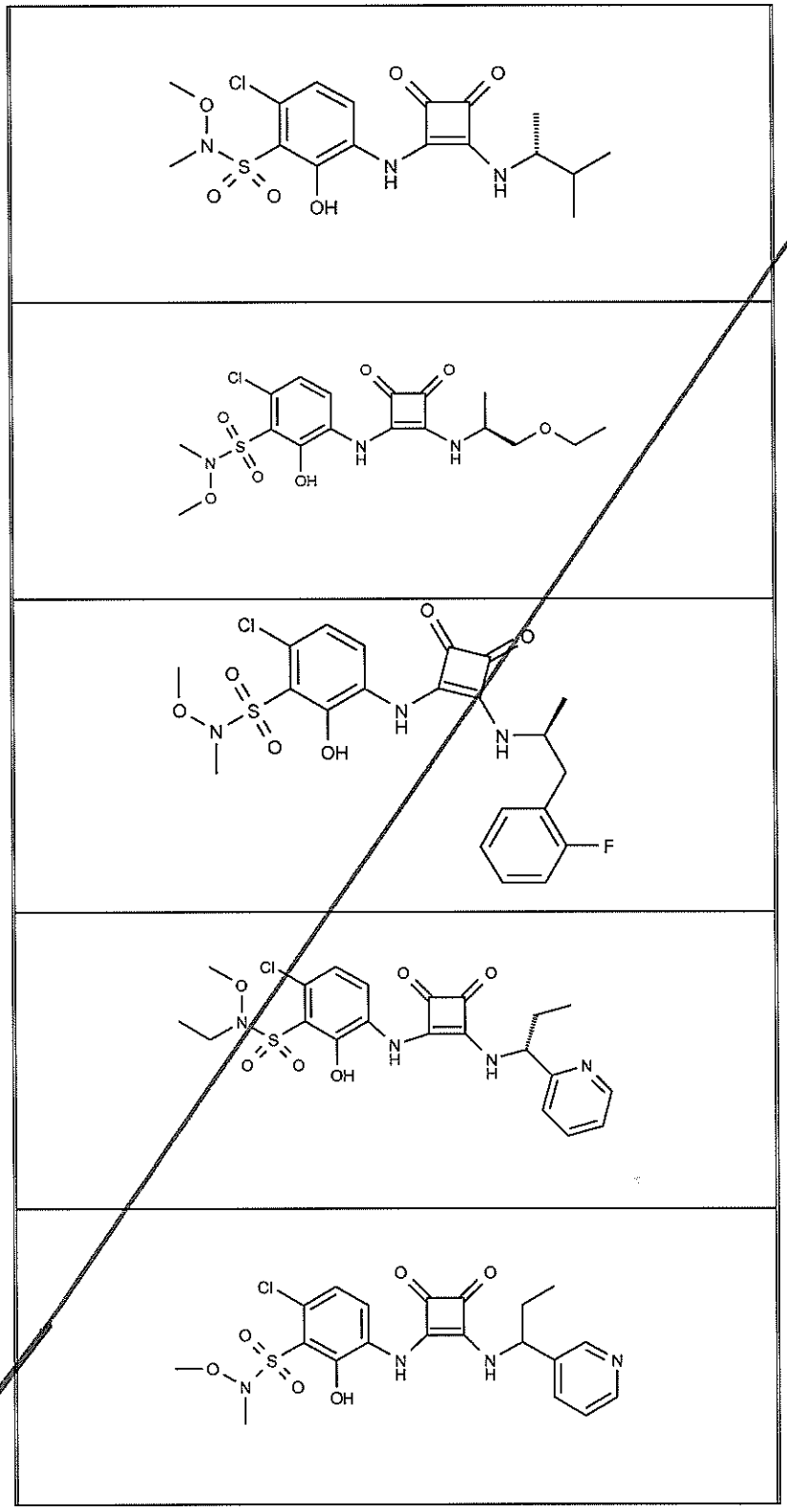


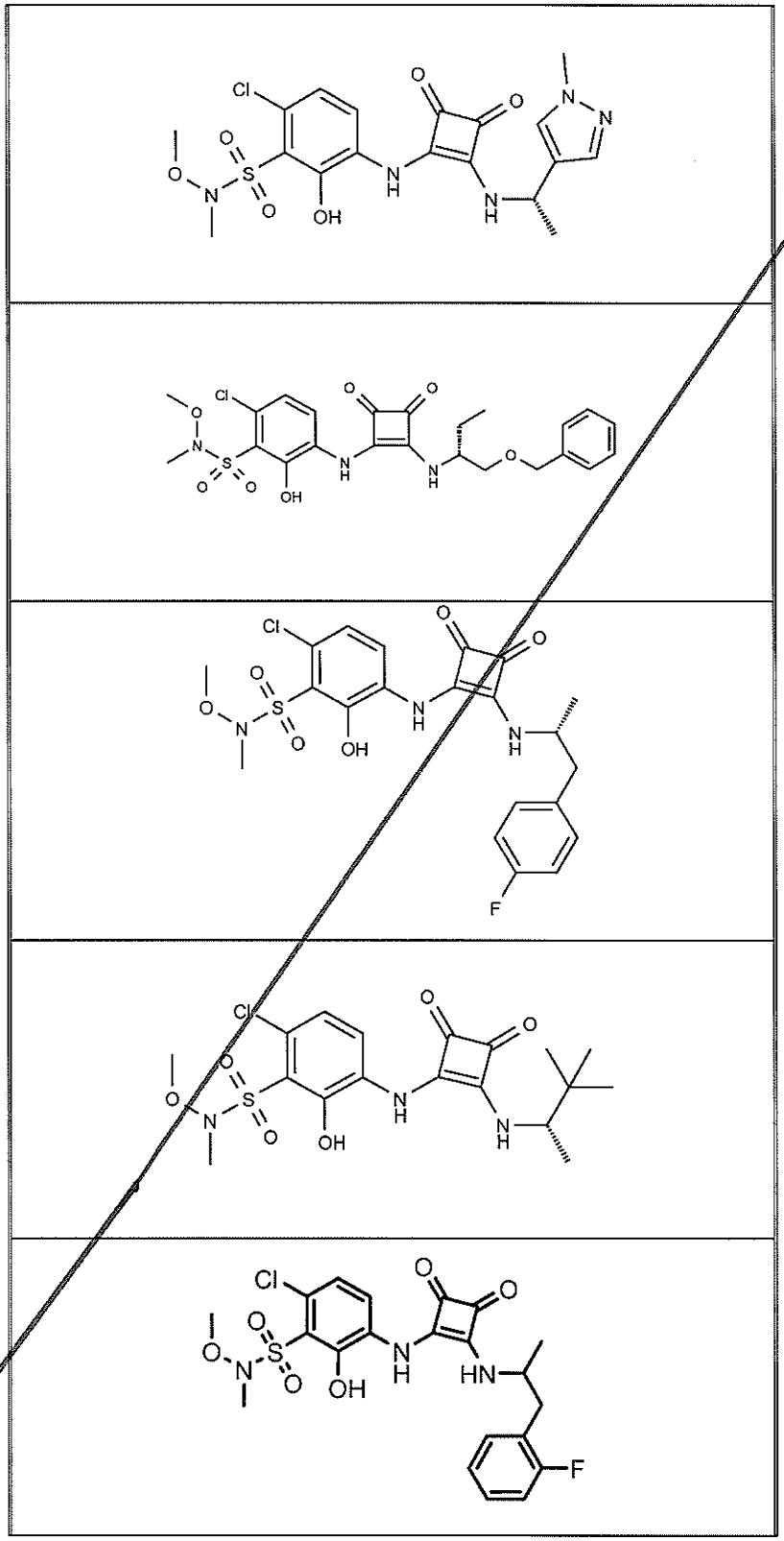


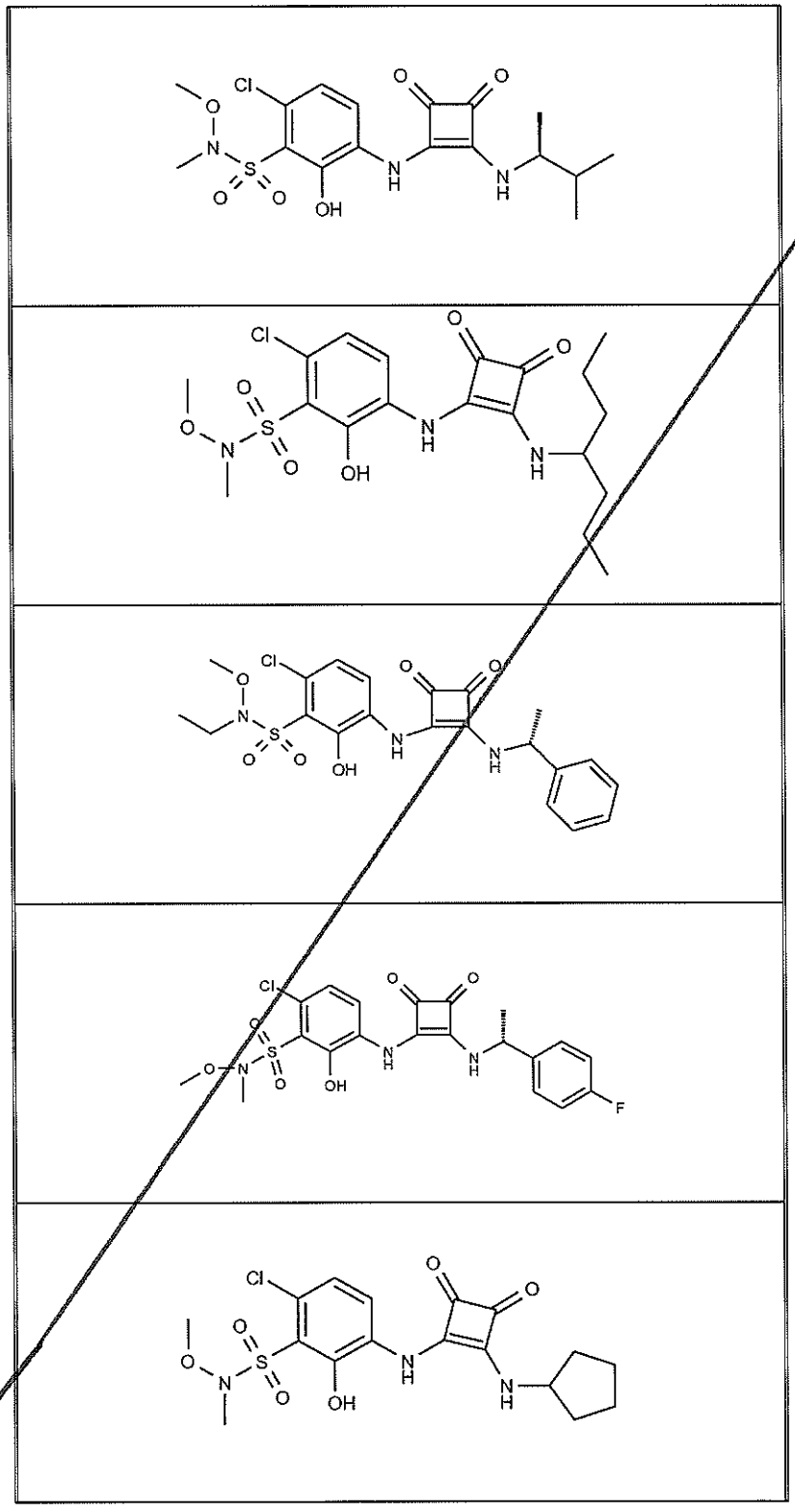


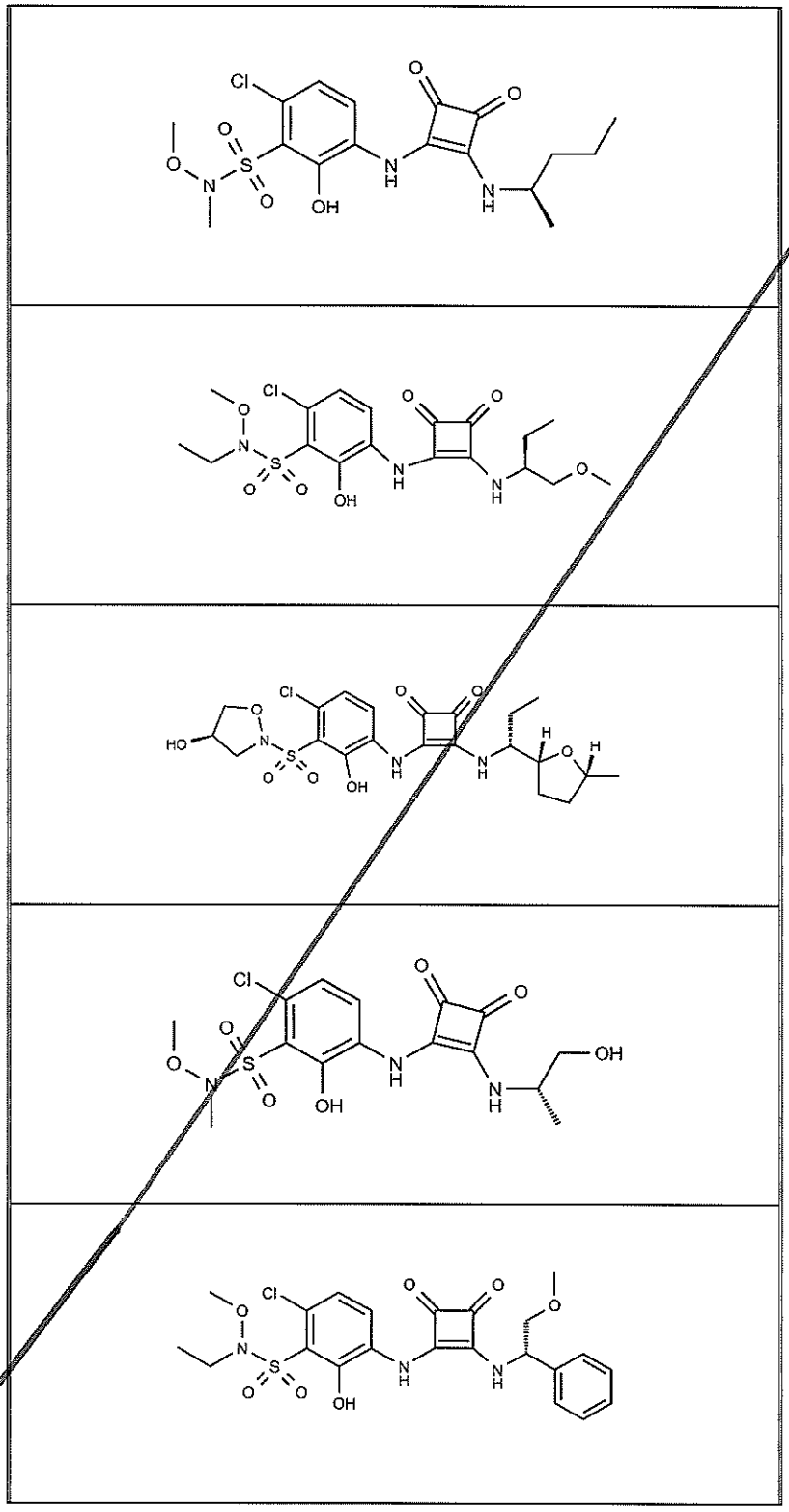


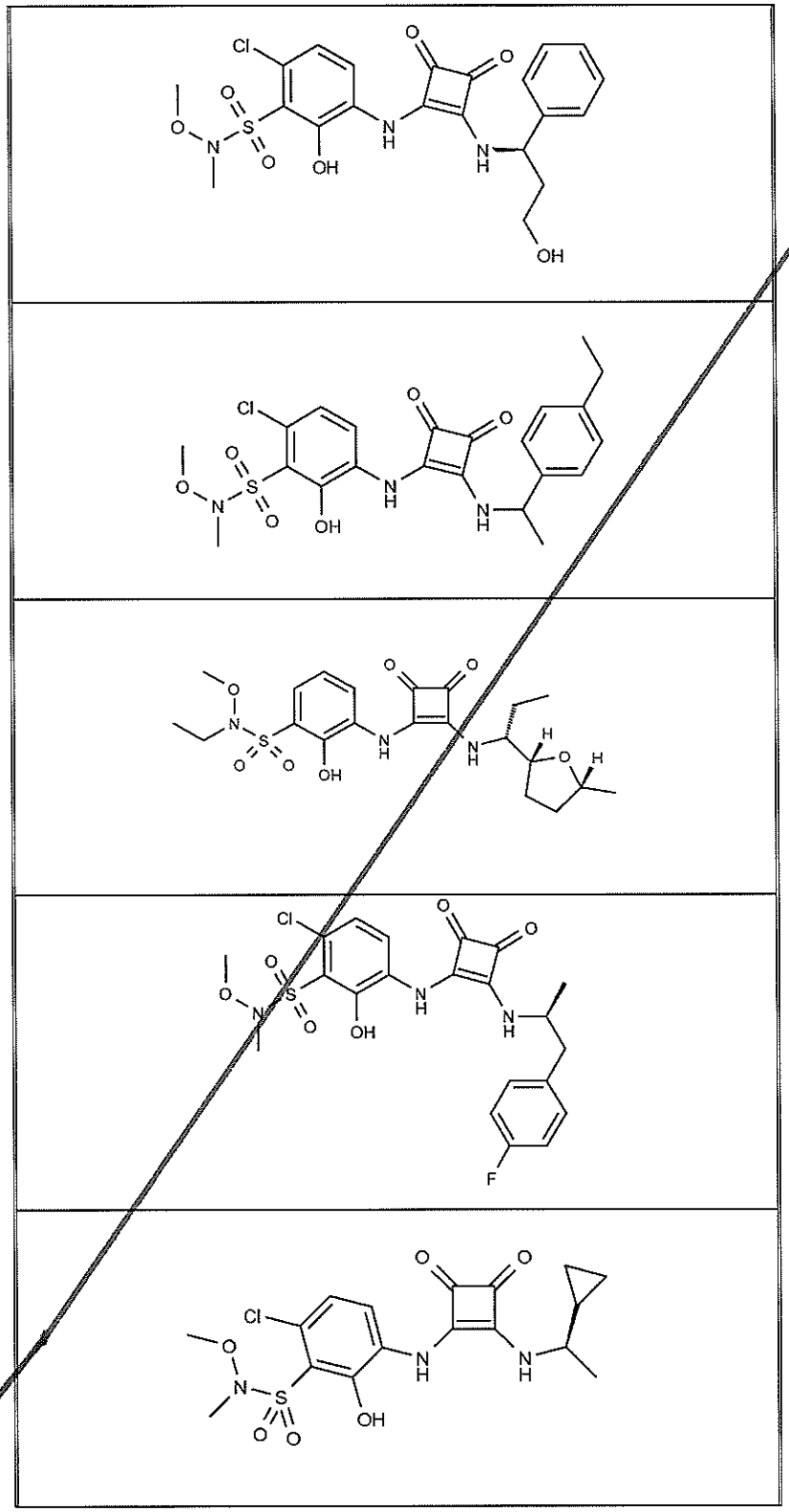


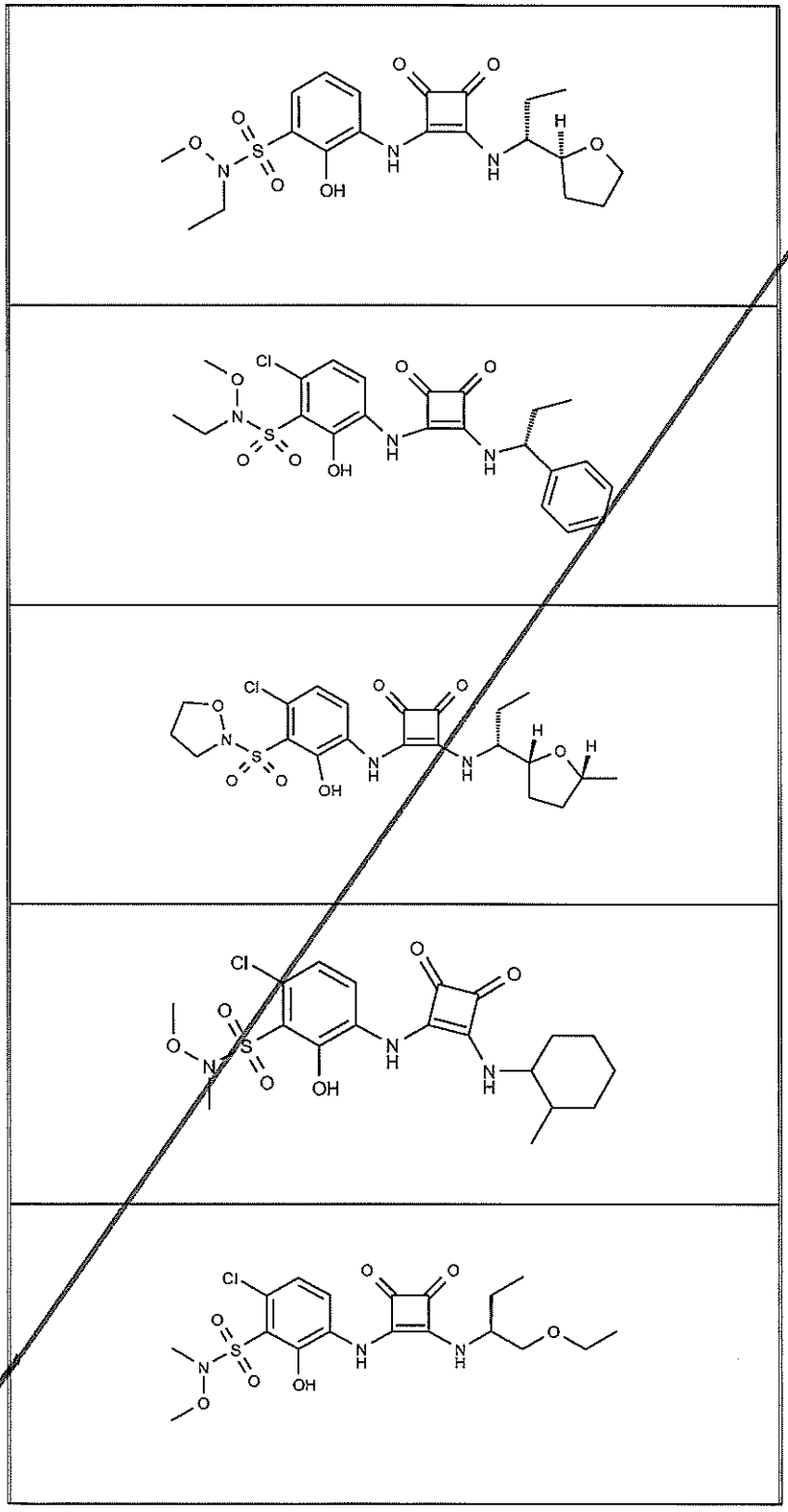


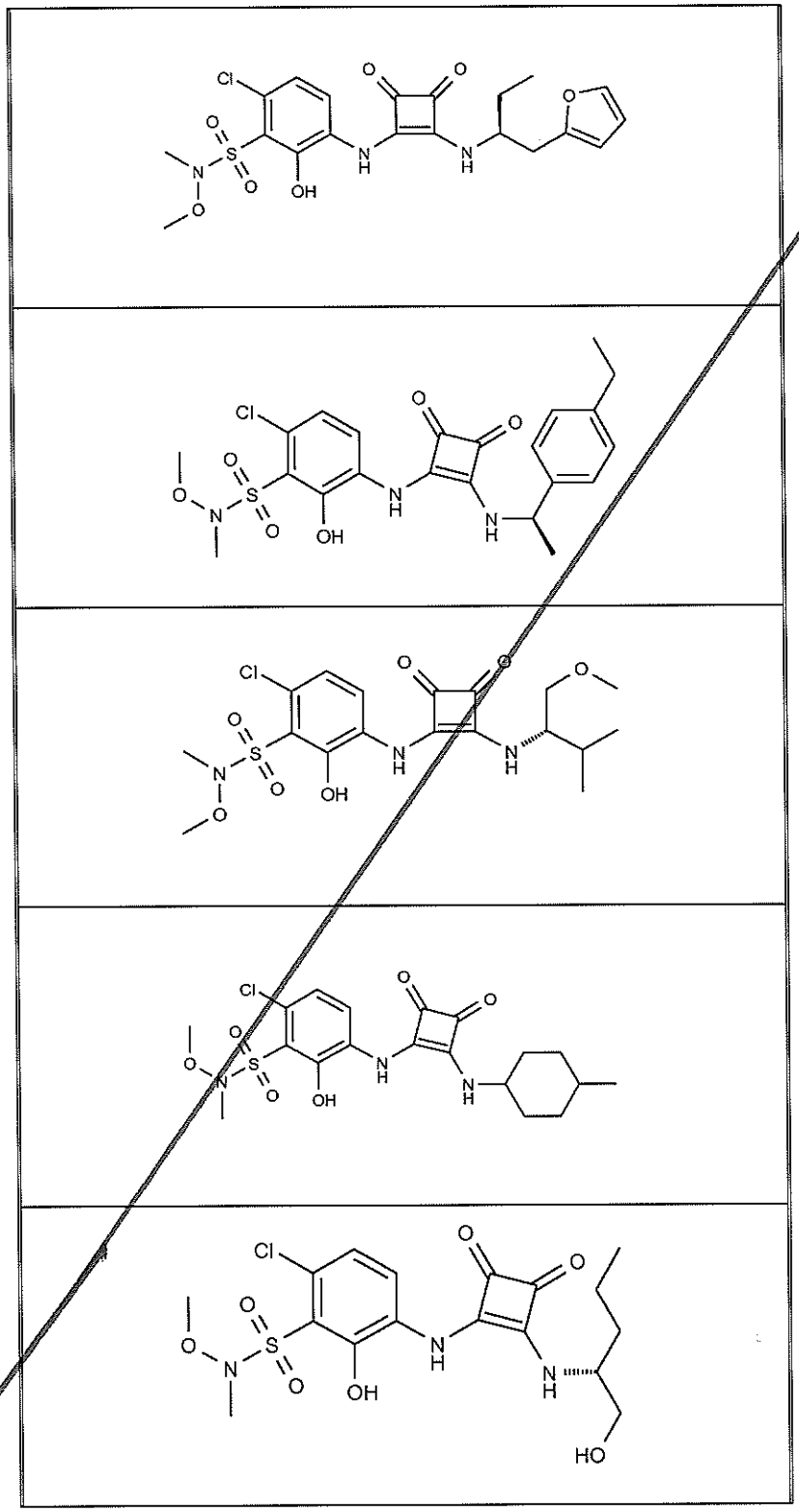


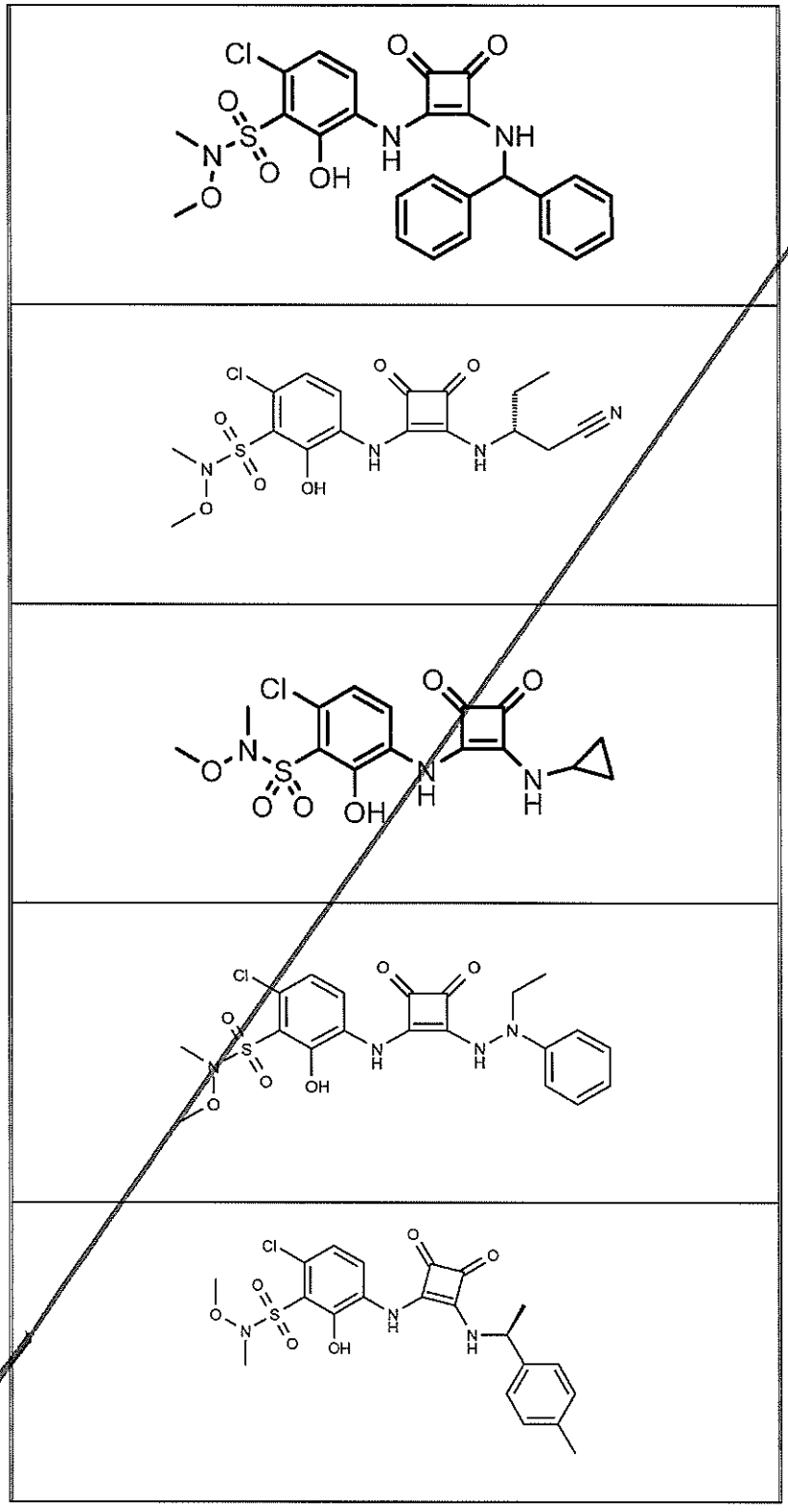


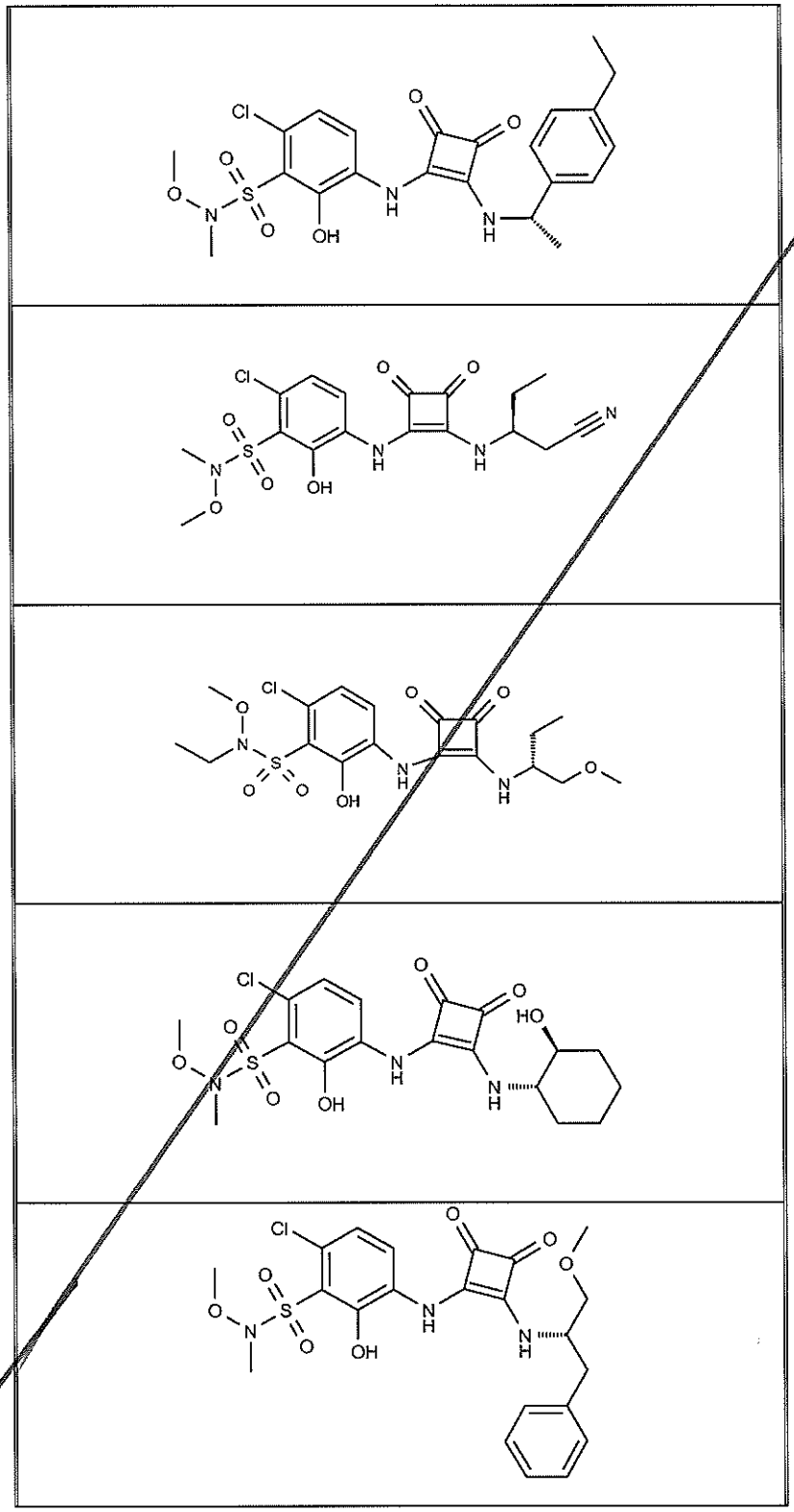


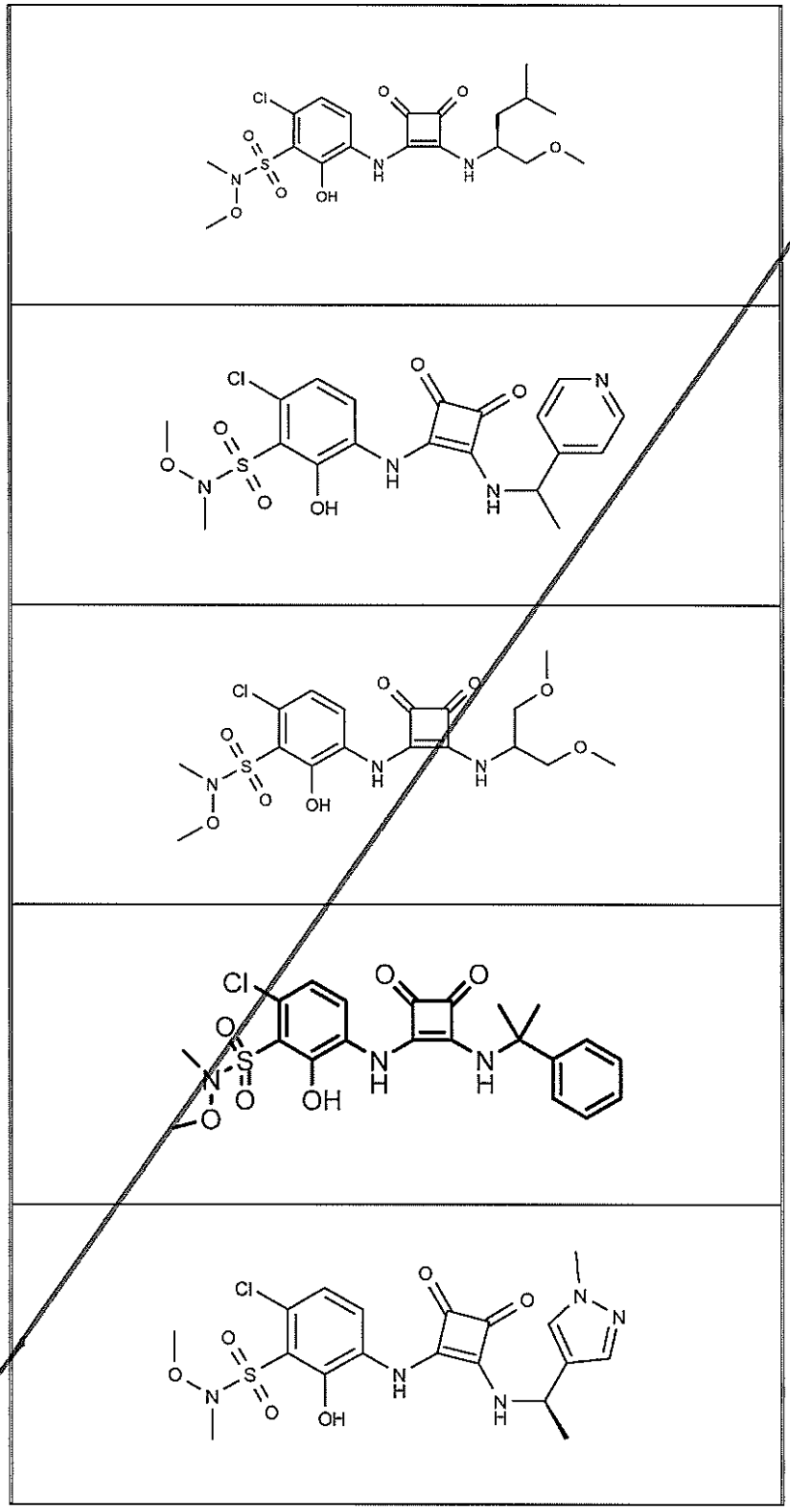


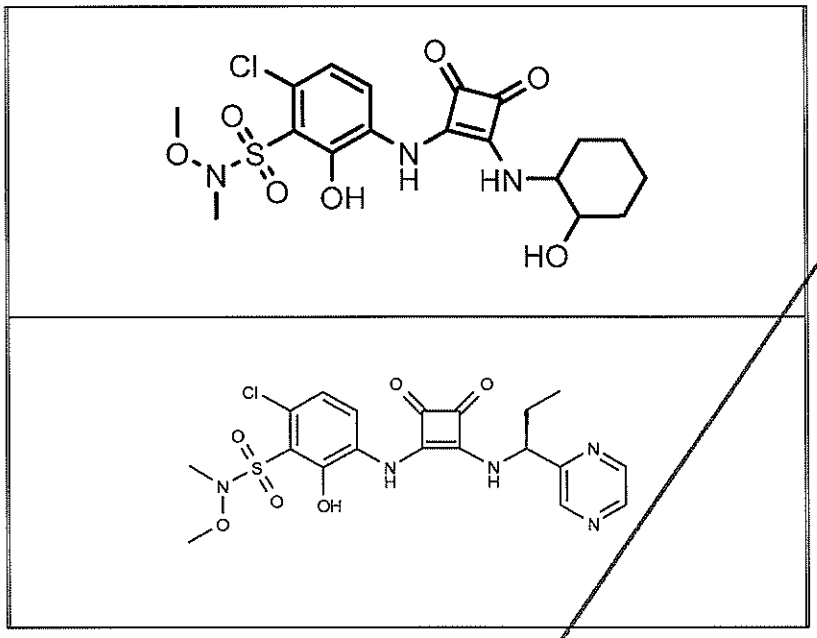












9. A compound according to any one of claims 1 to 8 for use as a pharmaceutical.

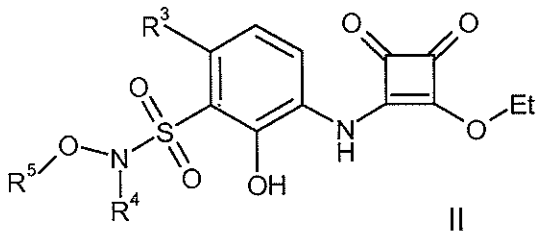
10. Use of a compound according to any of Claims 1 to 8 in the manufacture of a medicament for the treatment of inflammatory or allergic conditions or diseases.

11. Use according to Claim 10, wherein the condition is COPD.

12. A pharmaceutical composition comprising a compound according to any of Claims 1 to 8 together with a pharmaceutically acceptable carrier or excipient.

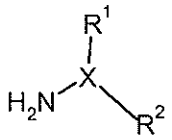
13. A method for the prevention or treatment of a CXCR2 receptor mediated condition or disease comprising administering an effective amount of at least one compound according to any of claims 1 to 8 to a subject in need of such treatment.

14. A process for the preparation of a compound according to any of Claims 1 to 8, the process comprising reacting a compound of formula II



II

wherein R^3, R^4 and R^5 are as defined in Claim 1, with a compound of formula III

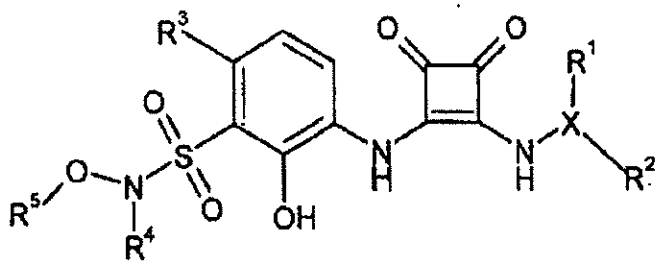


III

Wherein X, R^1 and R^2 are as defined in Claim 1; and isolating the product.

Claims

1. A compound of formula I



(I)

or solvates, hydrates or pharmaceutically acceptable salts thereof, wherein

R^1 is H, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen atoms or OH groups, or an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, wherein the ether group is optionally substituted by one or more substituents each independently selected from OH, halogen, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups and a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^2 is a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, (C_1-C_4 alkyl)- 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen atoms or OH groups, or an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, wherein the ether group is optionally substituted by one or more substituents each independently selected from OH, halogen, a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups and a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups; or

R^1 and R^2 together with the carbon atom to which they are attached form 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, or a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^3 is hydrogen, halogen or cyano;

R^4 is H, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl or (C_1-C_4 alkyl)-R^6, wherein the alkyl groups are each optionally substituted by one or more halogen atoms;

R^5 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_5-C_8 cycloalkenyl, (C_1-C_4 alkyl)-C_3-C_6 cycloalkyl or (C_1-C_4 alkyl)-C_5-C_8 cycloalkenyl, wherein the alkyl groups are each optionally substituted by one or more halogen atoms; or

R^1 and R^6, together with the nitrogen and oxygen atoms to which they are attached, form a 5 to 10 membered heterocyclic group optionally substituted by one or more Z groups;

R^6 is selected from a 3 to 10 membered carbocyclic group optionally substituted by one or more Z groups, a 3 to 10 membered heterocyclic group optionally substituted by one or more Z groups, NR^7R^9, $NR^7(SO_2)R^9$, $(SO_2)NR^7R^8$, $(SO_2)R^9$, $NR^7C(O)R^9$, $C(O)NR^7R^9$, $NR^7C(O)NR^8R^9$, $NR^7C(O)OR^9$, $C(O)OR^7$, $OC(O)R^9$, $OC(O)NR^7$, $C(O)R^9$, SR^7, CN and NO_2;

R^7 and R^8 are each independently selected from H, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl and -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl;

R^9 is selected from H, C_1-C_6 alkyl, -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl, a 3 to 10 membered carbocyclic group and a 3 to 10 membered heterocyclic group, wherein each of the alkyl groups and ring systems is optionally substituted by OH, halo, C_1-C_3 alkyl and C_1-C_3 alkoxy;
X is CR^{14} or N;
Z is independently selected from OH; a 3 to 10 membered carbocyclic group; a 3 to 10 membered heterocyclic group; benzyl; C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups; C_1-C_6 alkoxy optionally substituted by one or more halogen atoms, CN or OH groups; -Oaryl; -Obenzyl; -$O(CH_2)_aC(O)E$; $NR^{10}(SO_2)R^{12}$; $(SO_2)NR^{10}R^{11}$; $(SO_2)R^{12}$; $NR^{10}C(O)R^{12}$; $C(O)NR^{10}R^{12}$; $NR^{10}C(O)NR^{11}R^{12}$; $NR^{10}C(O)OR^{12}$; $NR^{10}R^{12}$; $C(O)OR^{10}$; $OC(O)R^{12}$; $OC(O)NR^{10}$; $C(O)R^{12}$; SR^{13}; CN; NO_2; and halogen; or where there are two or more Z substitutents, two Z substituents together with the atoms to which they are attached optionally form a 5- to 7-membered carbocyclic or a 4- to 7-membered heterocyclic substituent fused to the ring system;
a is 0, 1, 2, 3 or 4, wherein the alkylene group is optionally substituted by OH or NH_2 when a is 1, 2, 3 or 4;
E is $NR^{10}R^{12}$ or OR^{12};
each R^{10} and R^{11} are independently selected from H, C_1-C_6 alkyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl and -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl;
each R^{12} is selected from H, C_1-C_6 alkyl, -(C_1-C_3 alkylene)-C_3-C_{10} cycloalkyl, a 3 to 10 membered carbocyclic group and a 3 to 10 membered heterocyclic group, wherein each of the ring systems is optionally substituted by OH, halo, C_1-C_3 alkyl and C_1-C_3 alkoxy; and
R^{14} is H or C_1-C_6 alkyl.

2. A compound according to Claim 1, wherein R^1 is H or C_1-C_4 alkyl.

3. A compound according to Claim 1 or Claim 2, wherein
R^1 is H or C_1-C_4 alkyl;
R^2 is C_1-C_6 alkyl optionally substituted by one or more halogen atoms, CN or OH groups, an ether group containing 2 to 10 carbon atoms and 1 to 3 oxygen atoms, a 4 to 6 membered carbocyclic group optionally substituted by one or more Z groups, or a 4 to 6 membered heterocyclic group optionally substituted by one or more Z groups; or
R^1 and R^2, together with the carbon atom to which they are attached form a 4 to 6 membered carbocyclic group optionally substituted by one or more Z groups or a 4 to 6 membered heterocyclic group optionally substituted by one or more Z groups.

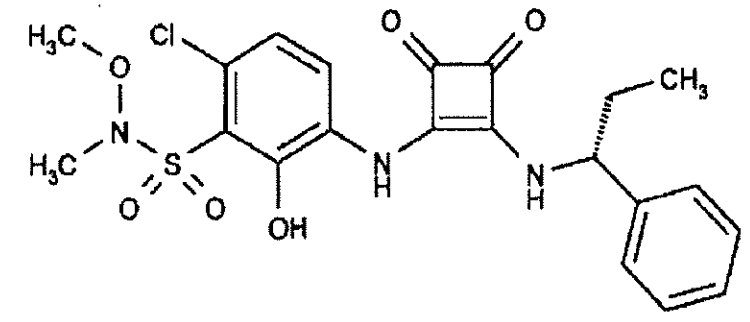
4. A compound according to any preceding claim, wherein R^3 is halogen.

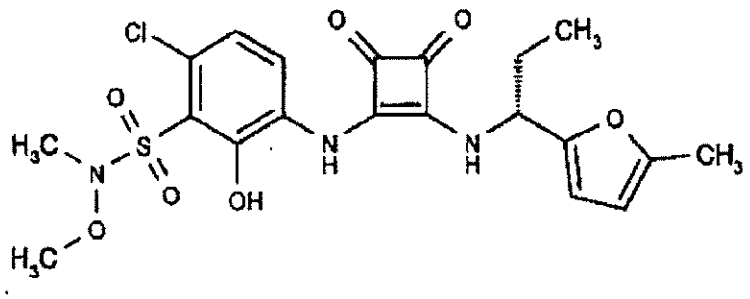
5. A compound according to any preceding claim, wherein R^4 is H, C_1-C_4 alkyl, C_3-C_6 cycloalkyl or (C_1-C_3 alkyl)-C_3-C_6 cycloalkyl.

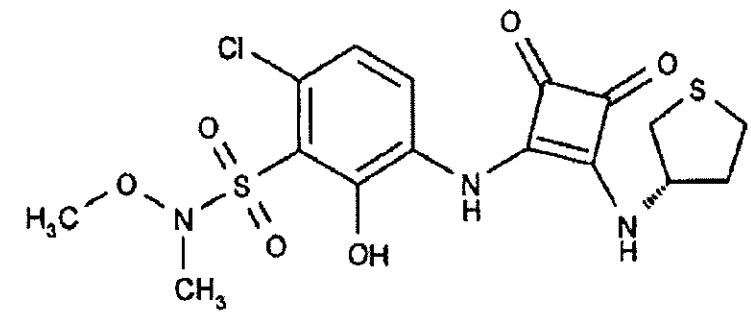
6. A compound according to any preceding claim, wherein R^5 is C_1-C_6 alkyl.

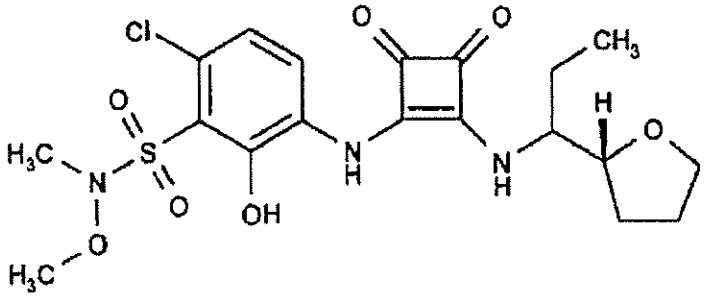
7. A compound according to any preceding claim, wherein X is CH.

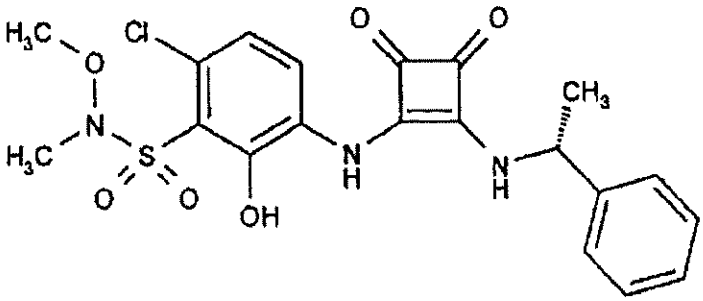
8. A compound according to Claim 1 which is selected from:

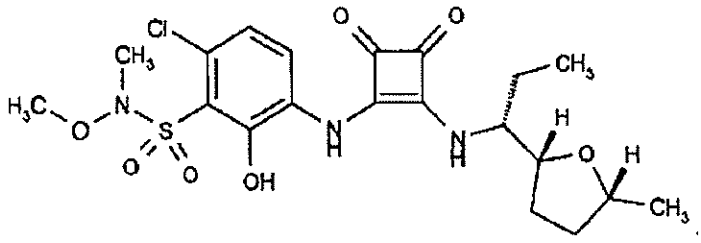


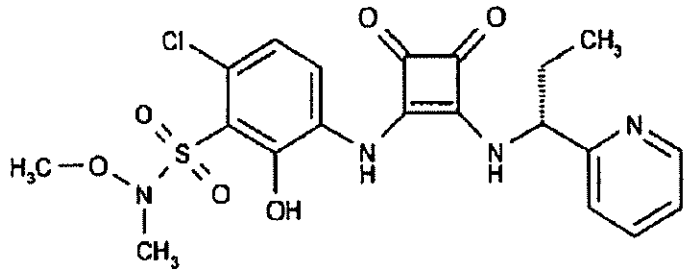


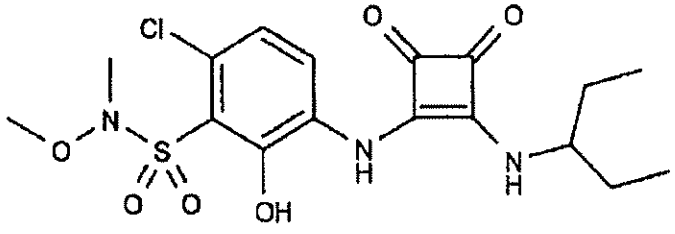


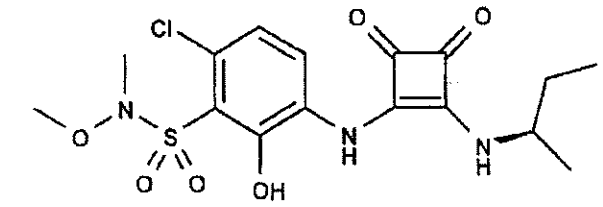


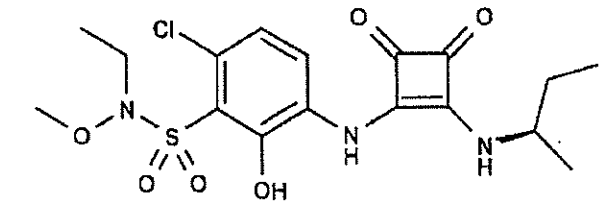


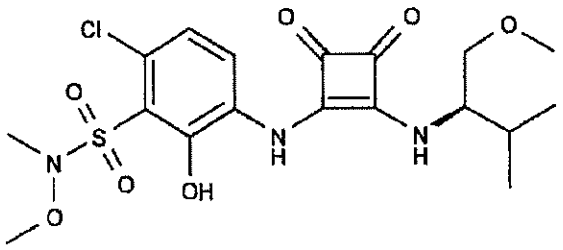


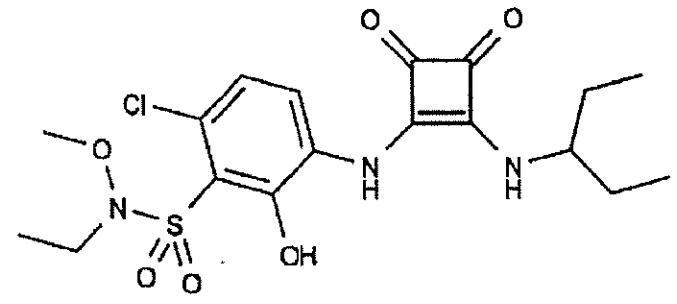


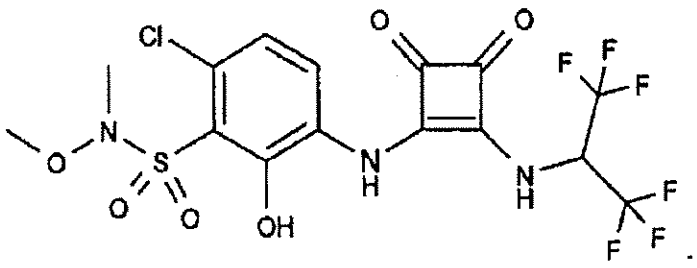


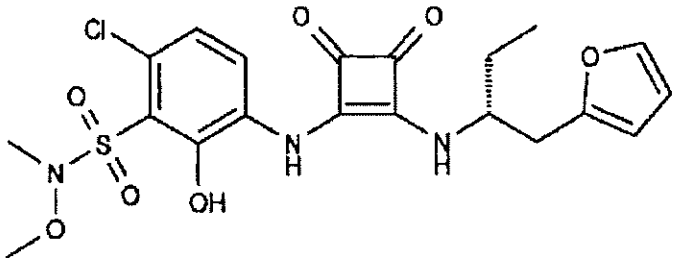


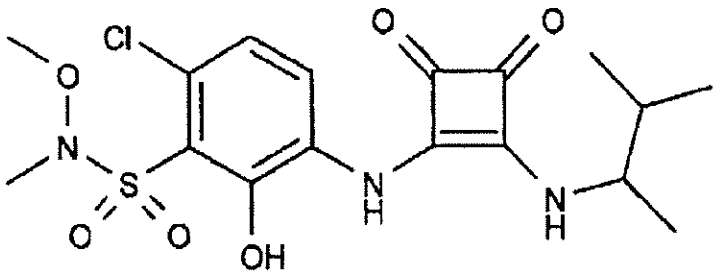


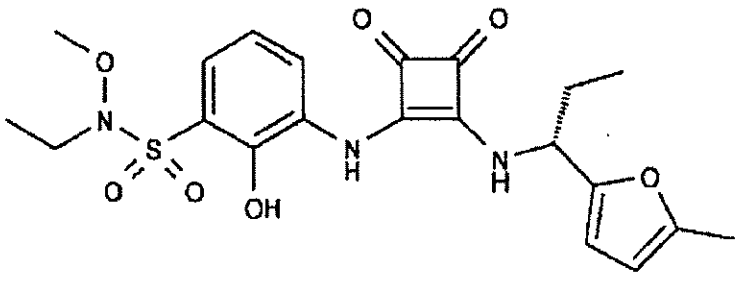


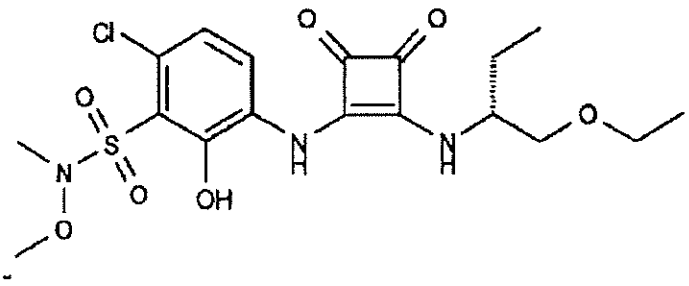


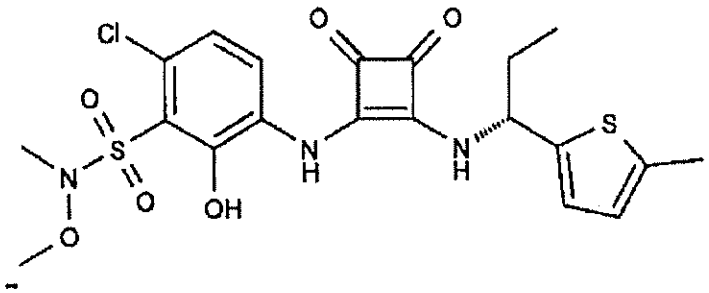


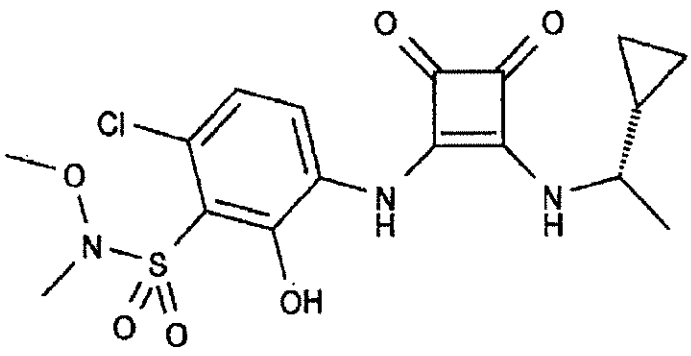


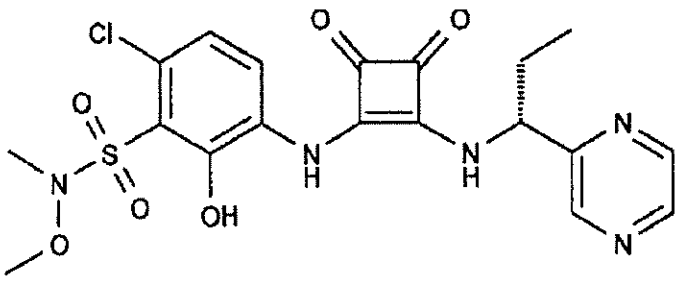


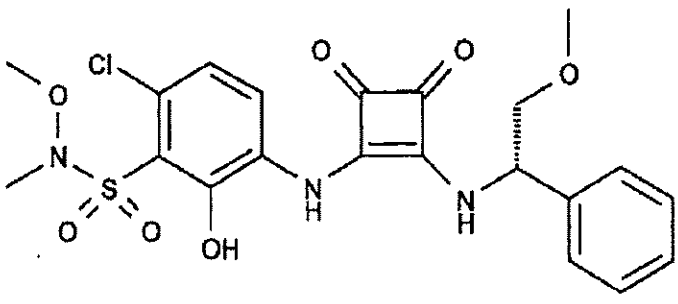


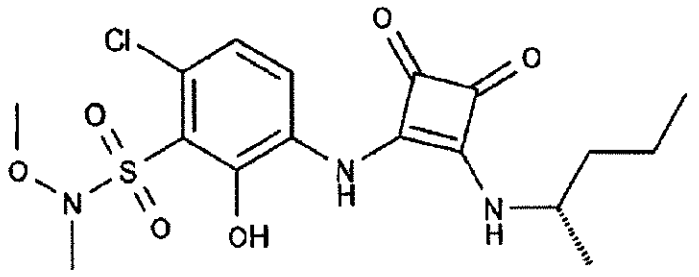


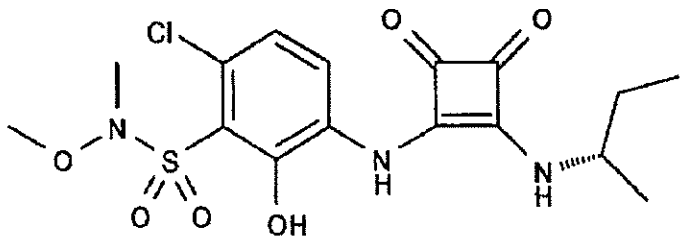


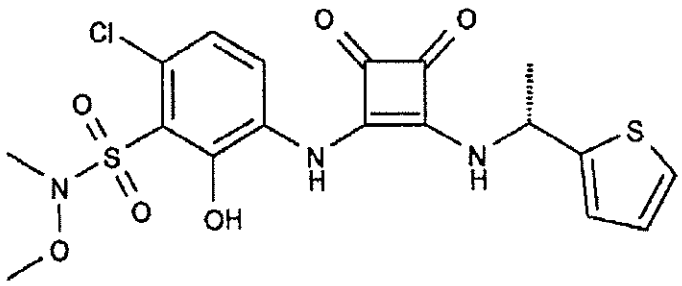


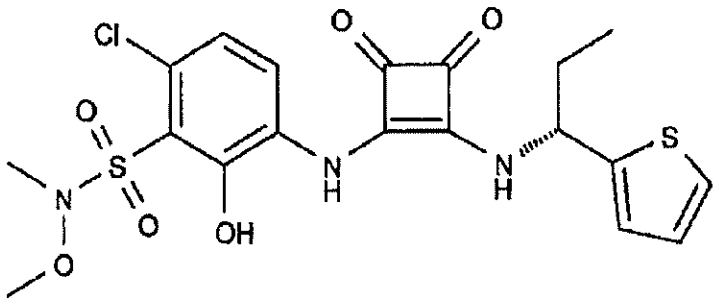


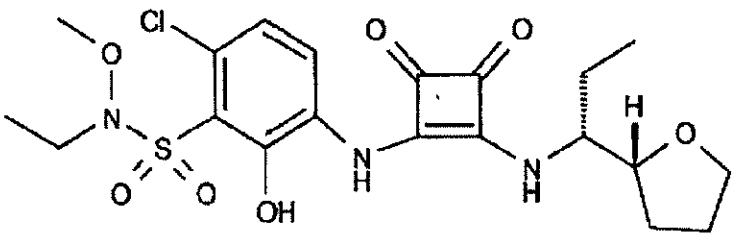


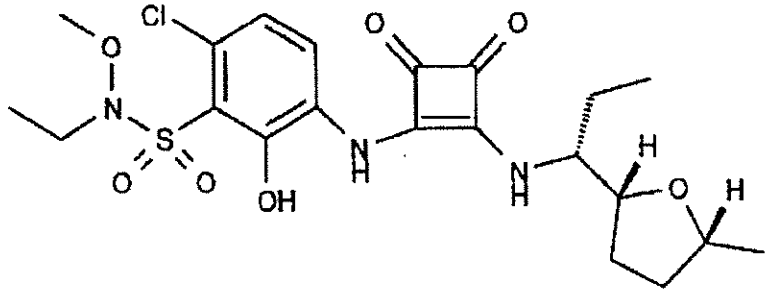


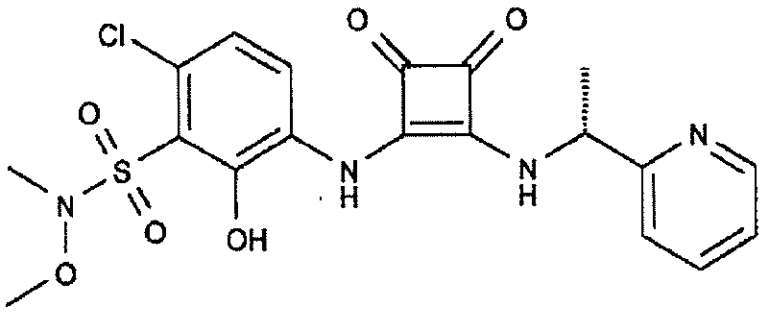


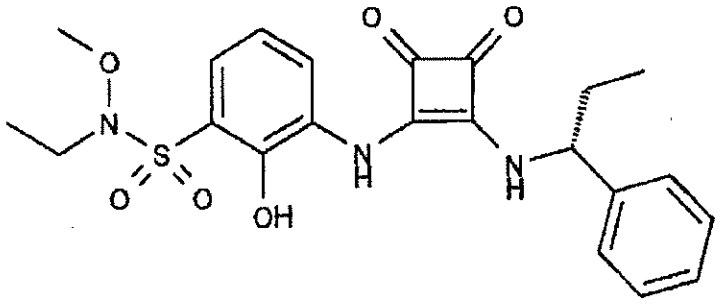


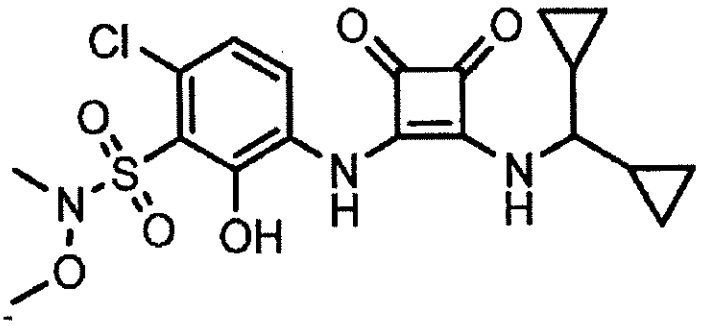


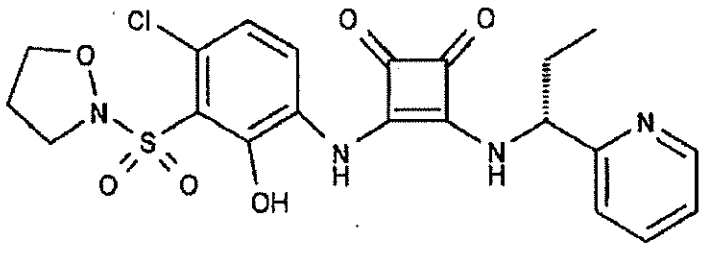


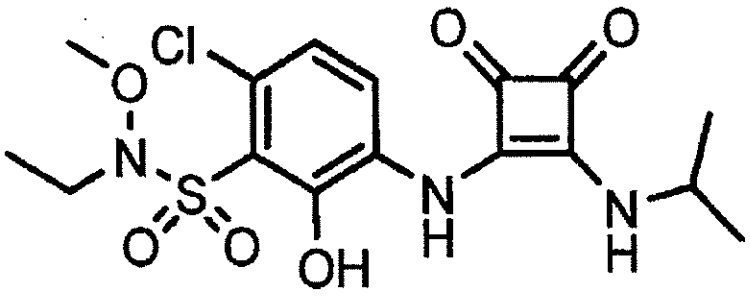


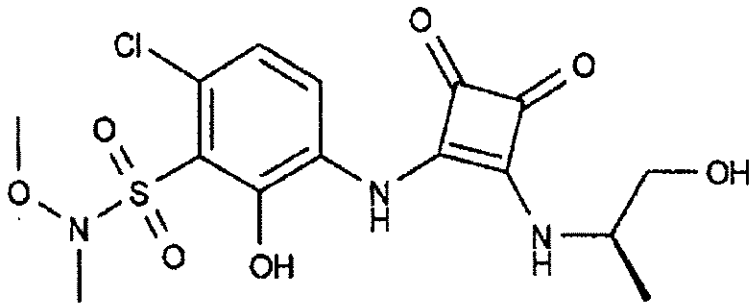


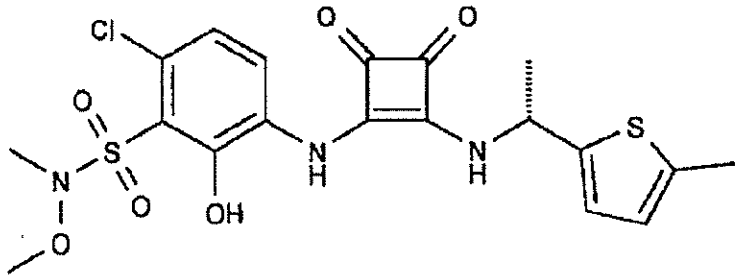


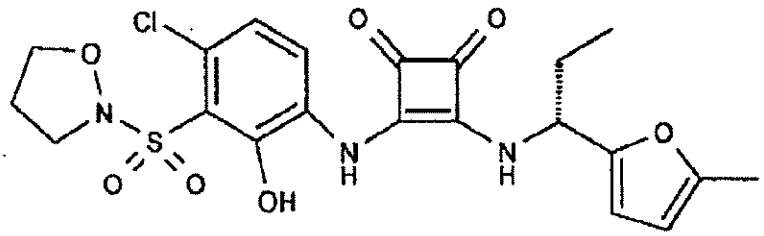


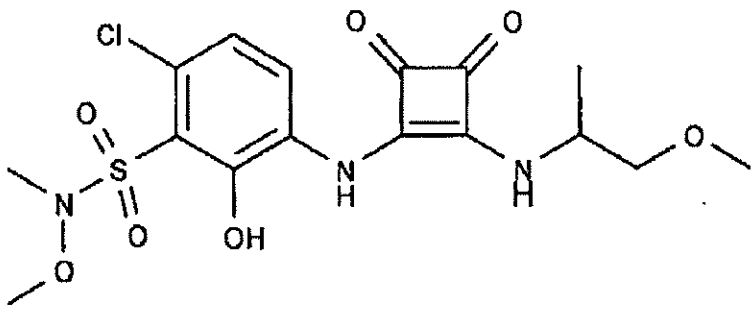


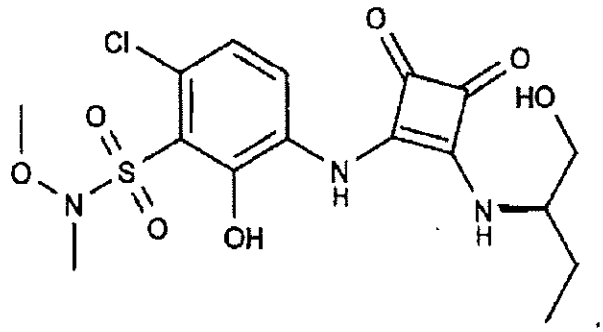


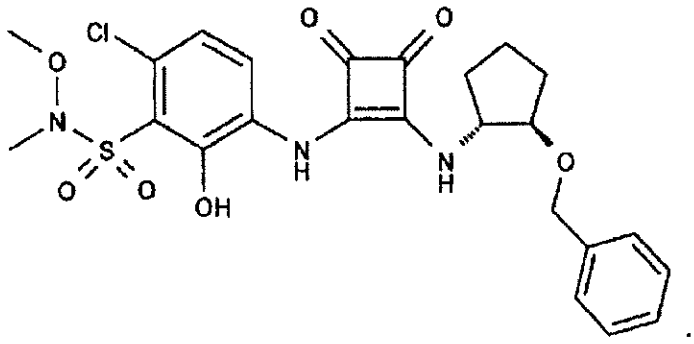


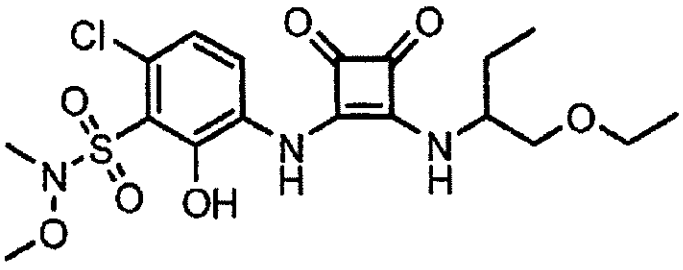


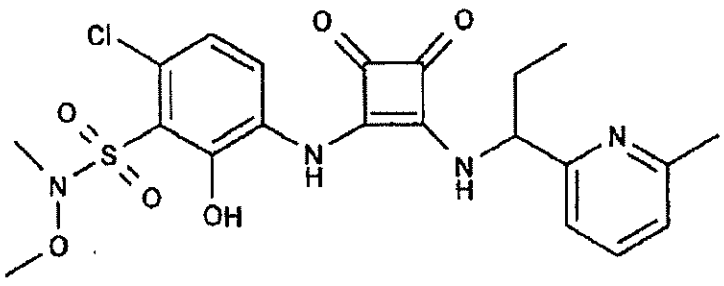


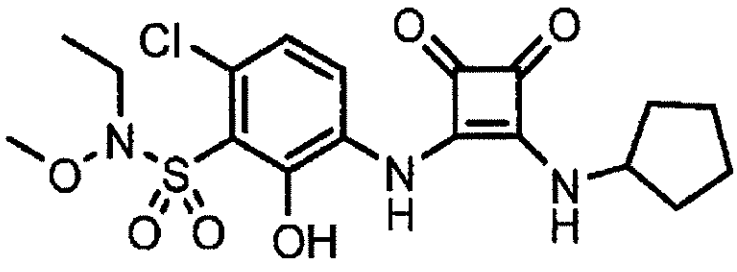


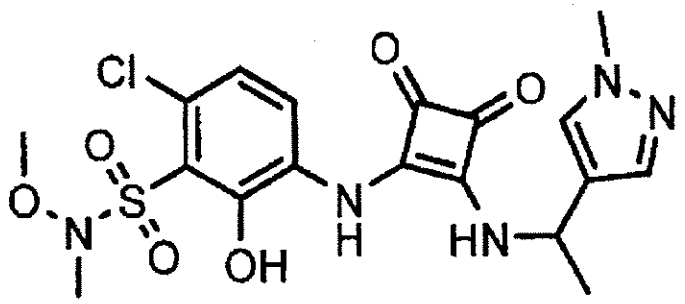


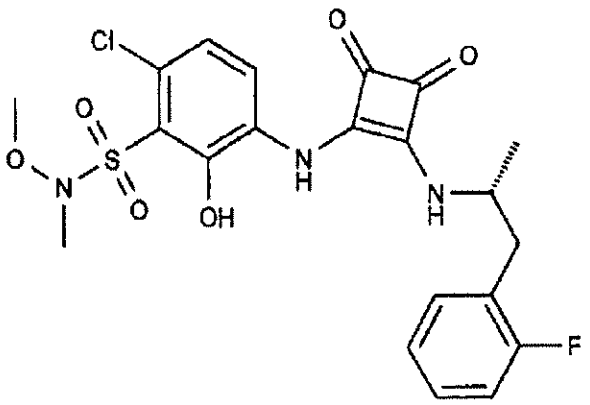


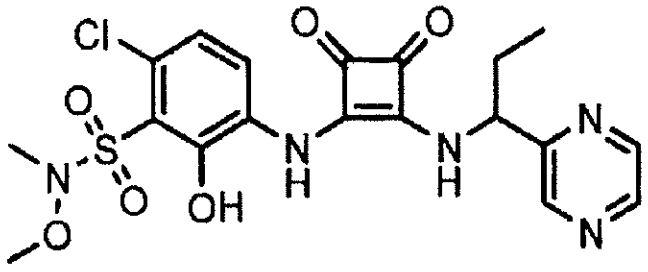


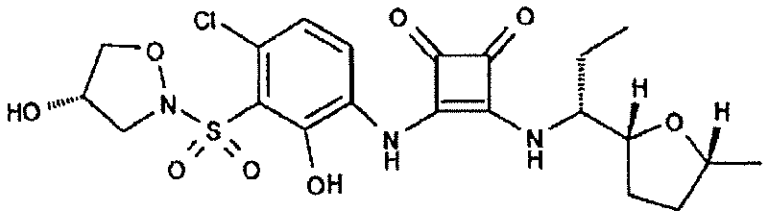


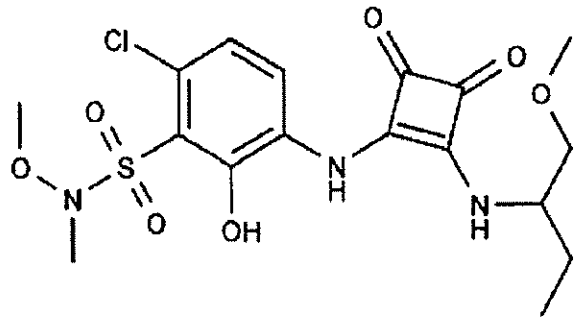


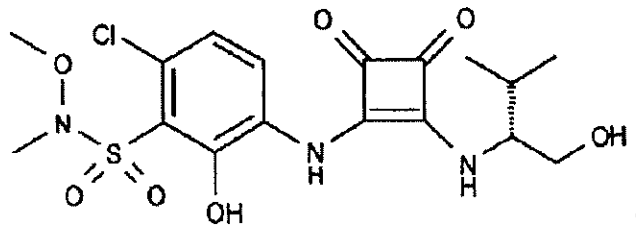


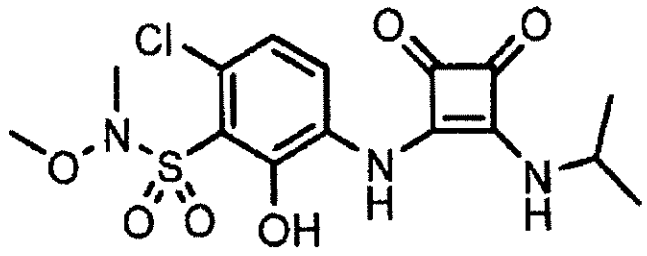


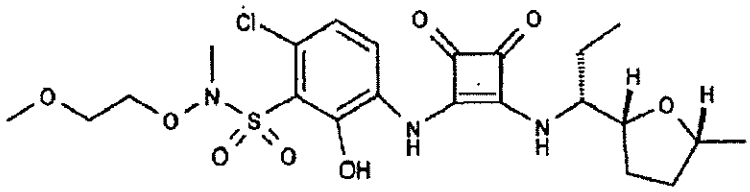


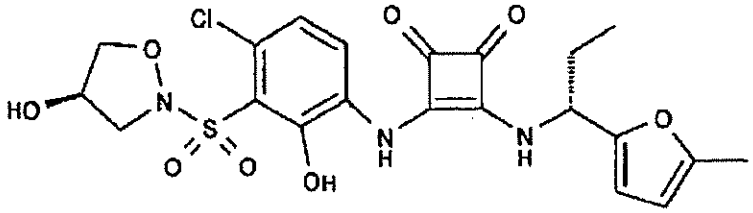


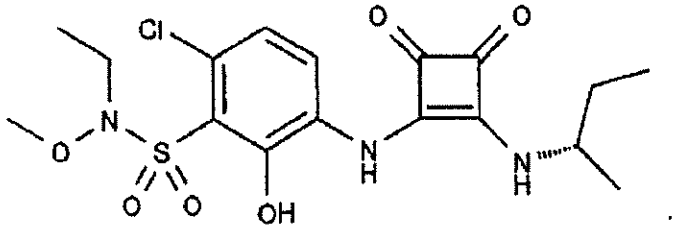


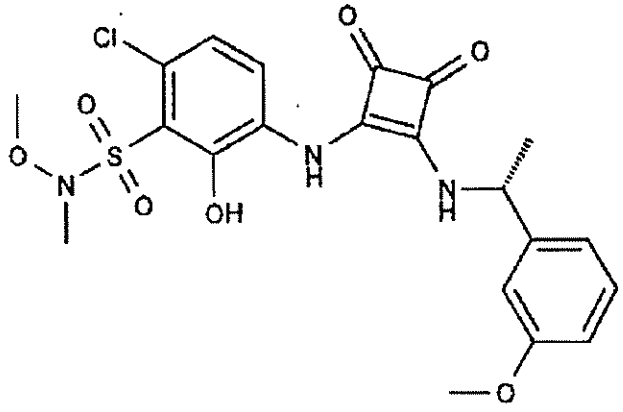


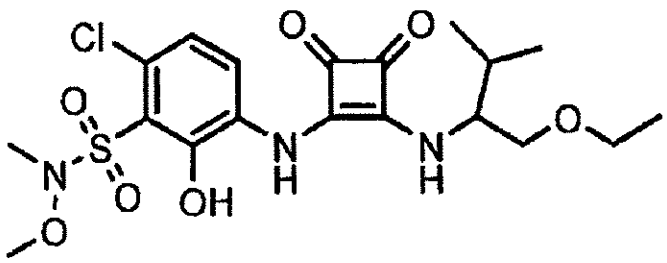


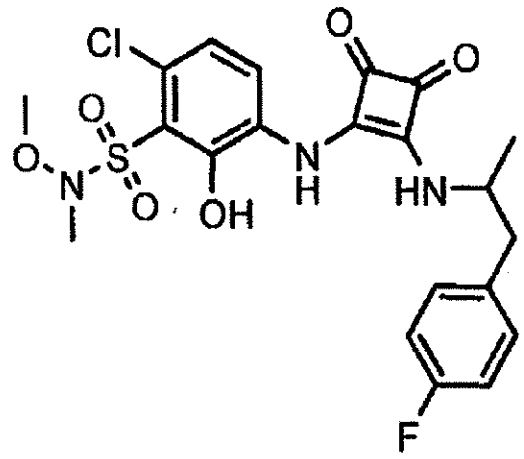


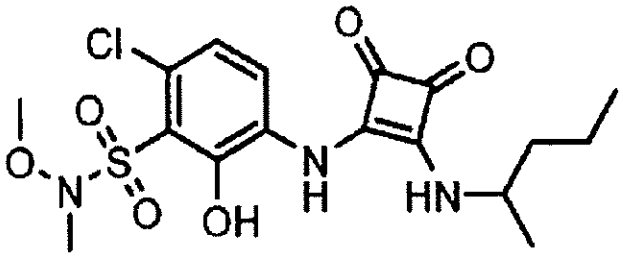


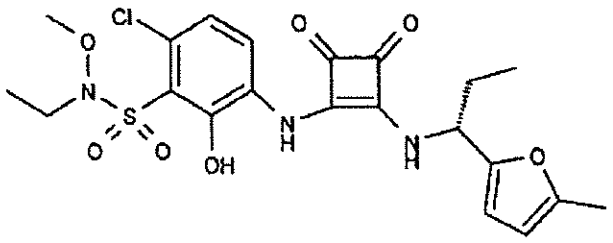


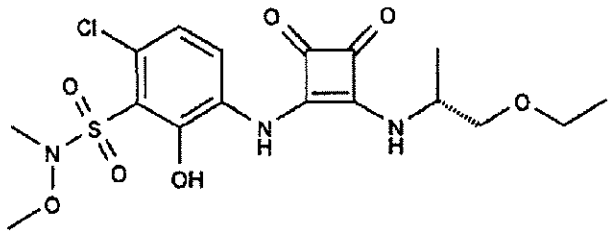


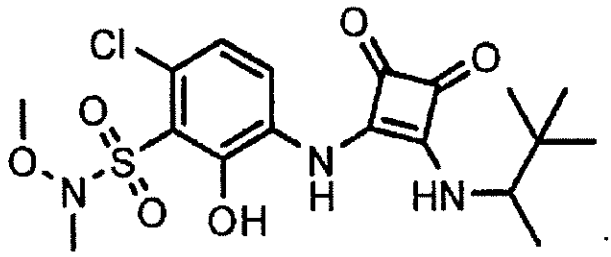


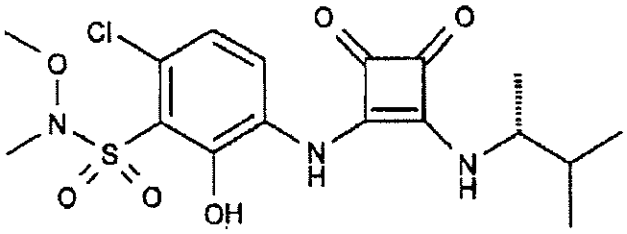


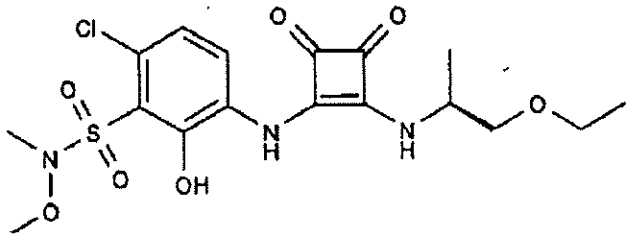


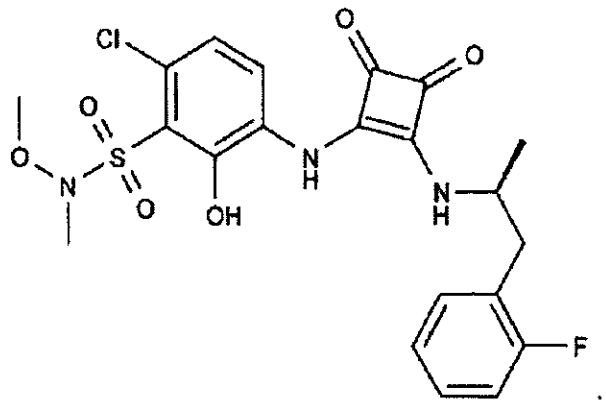


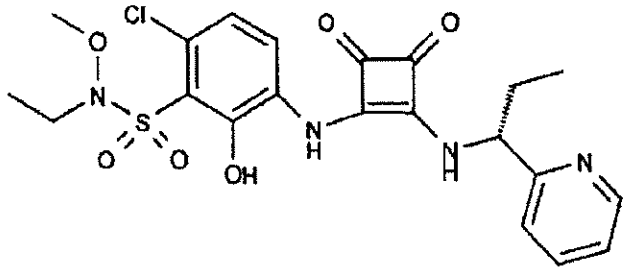


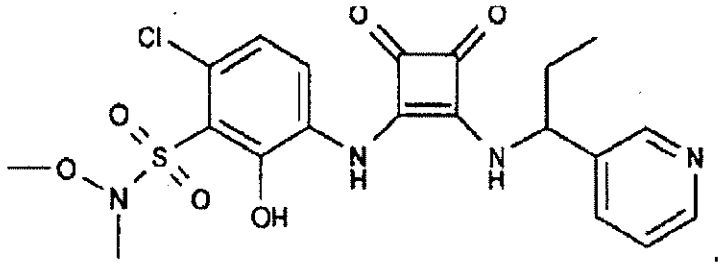


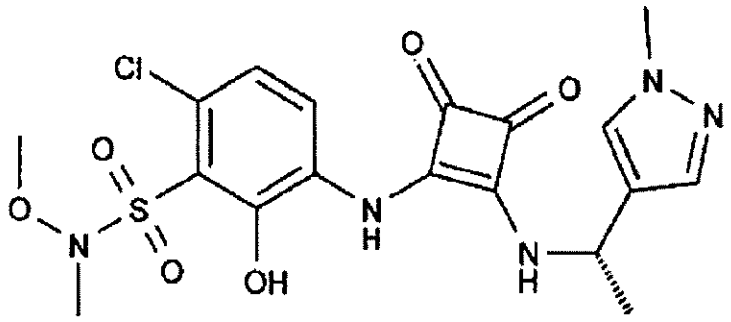


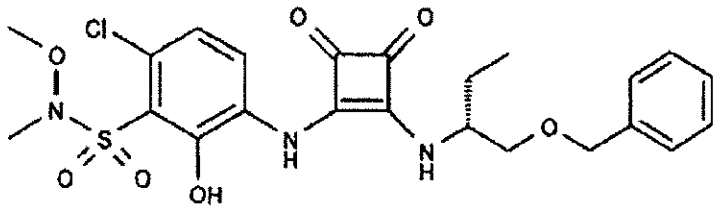


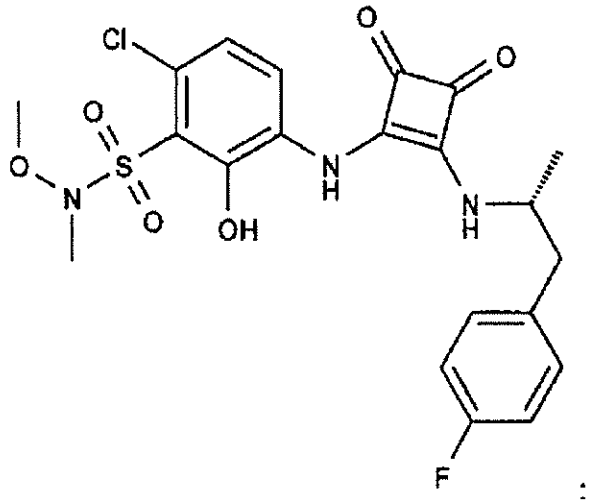


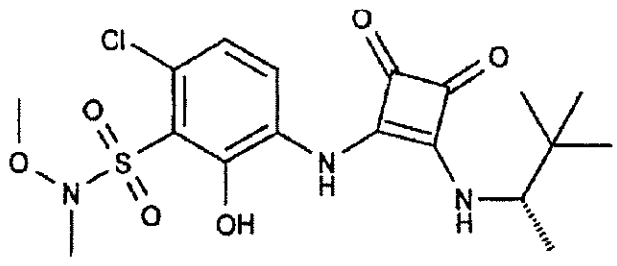


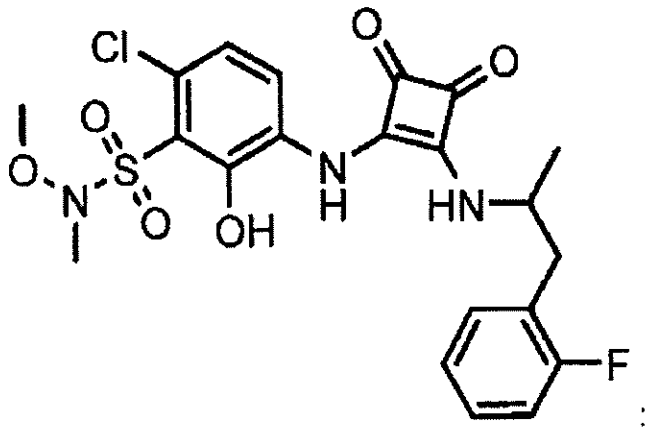


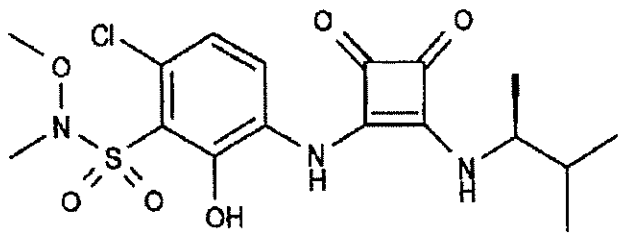


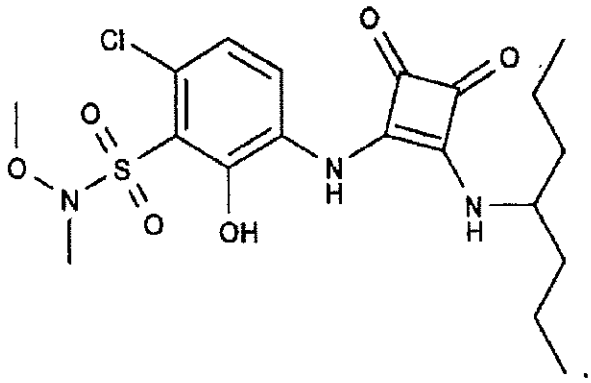


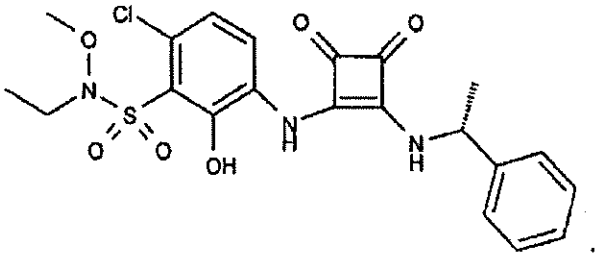


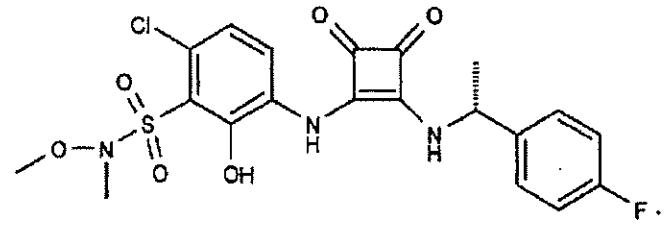


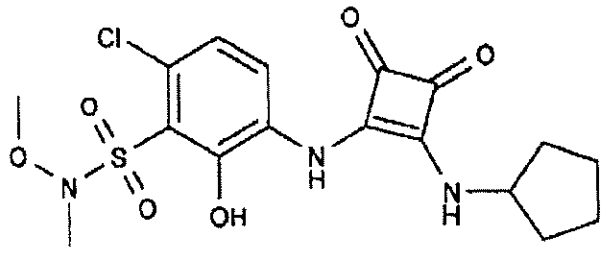


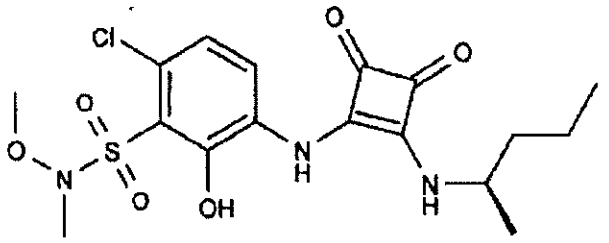


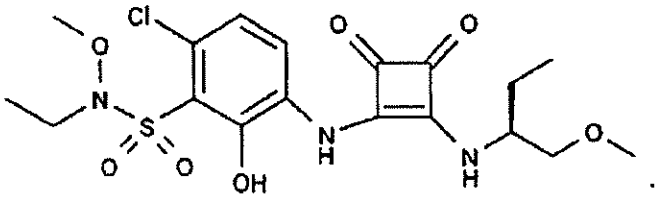


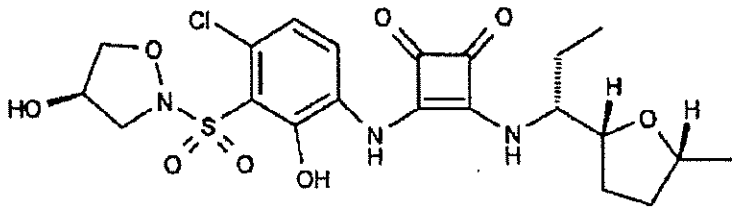


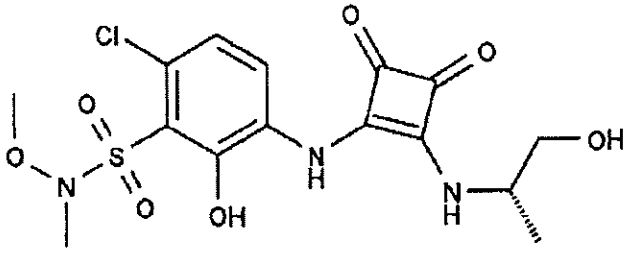


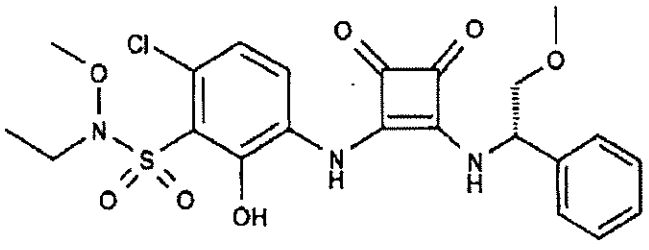


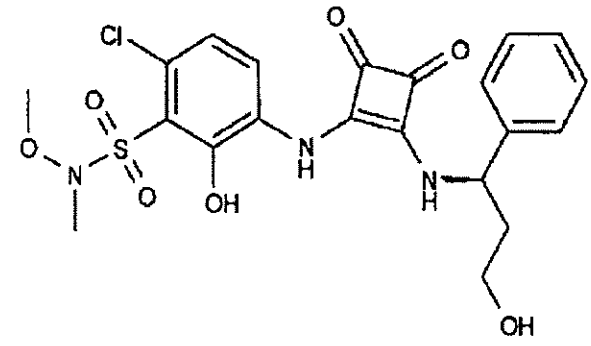


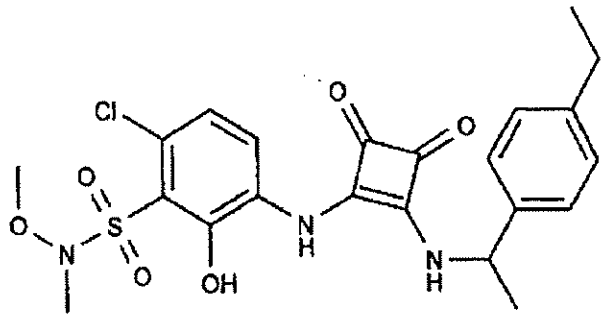


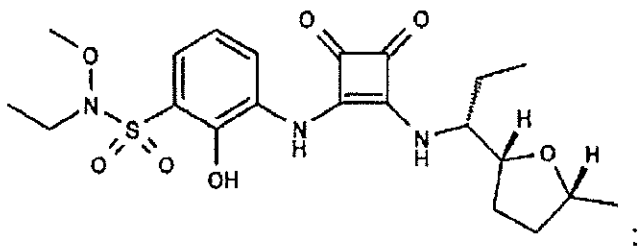


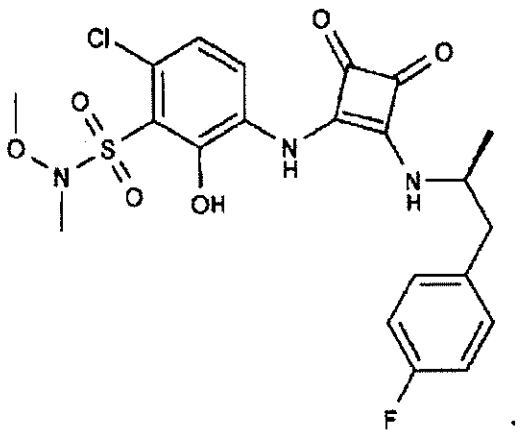


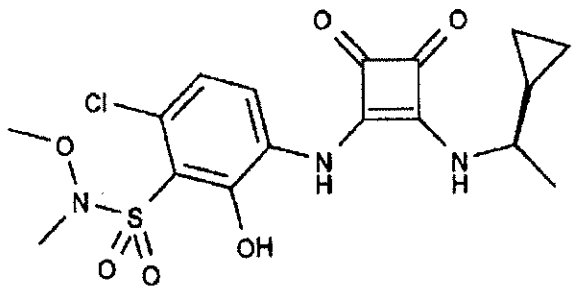


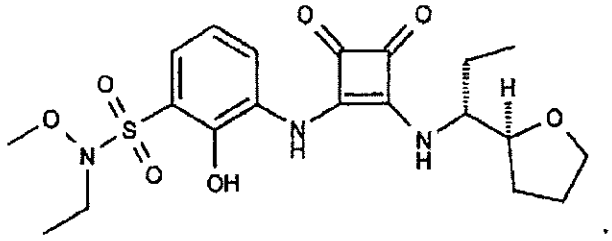


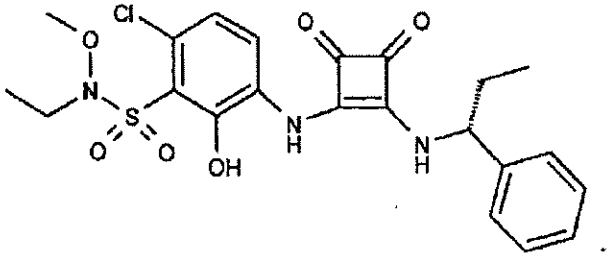


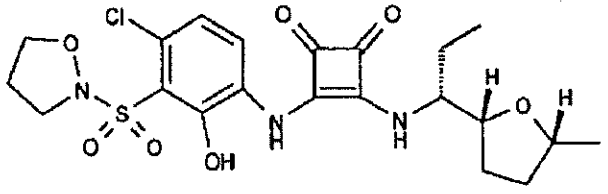


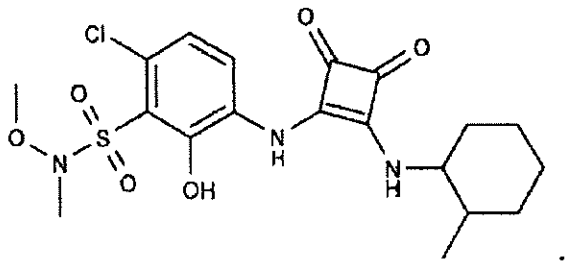


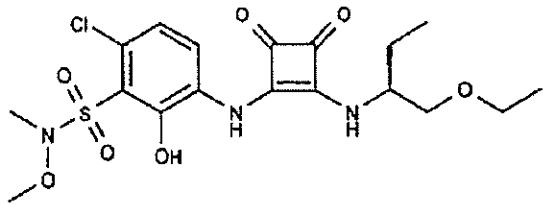


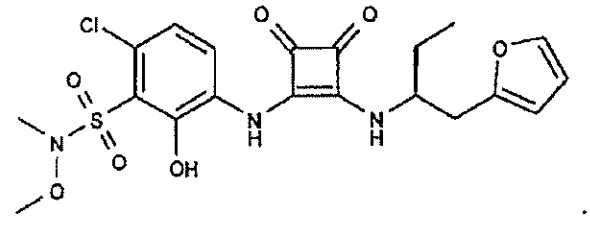


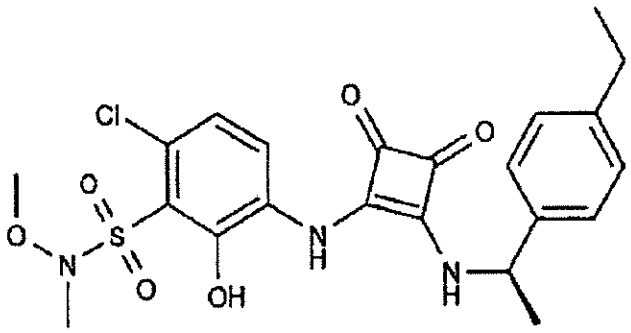


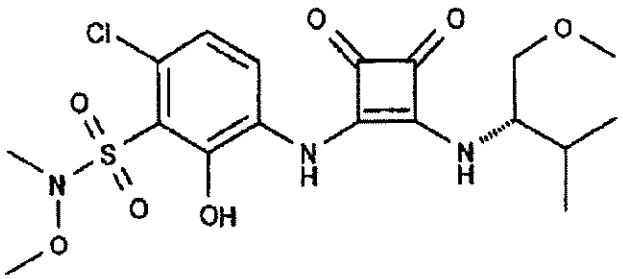


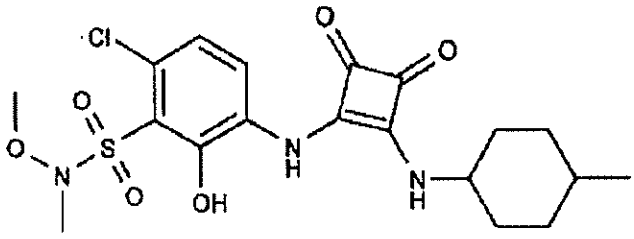


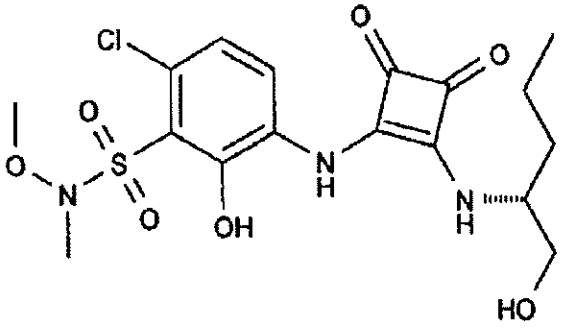


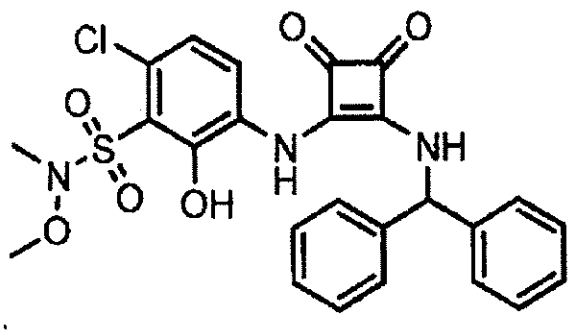


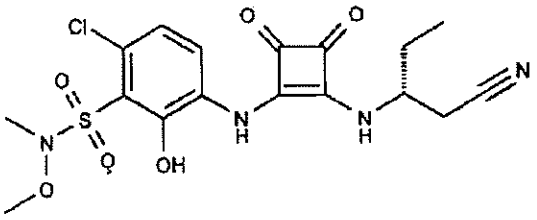


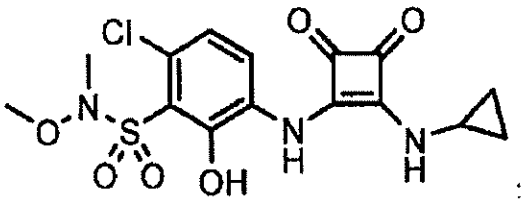


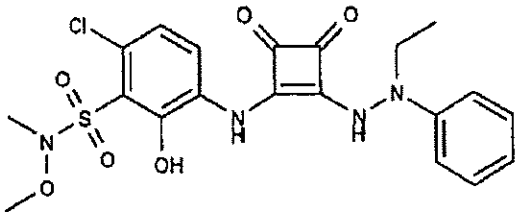


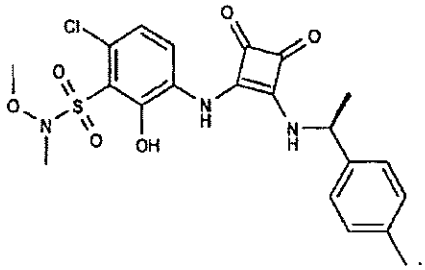


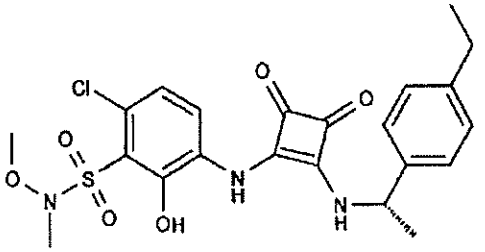


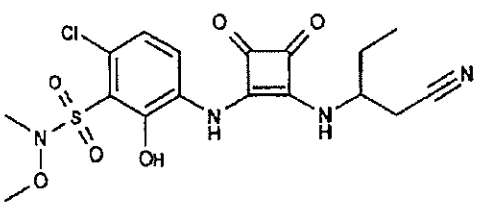


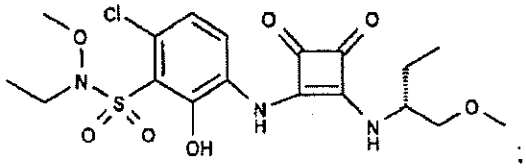


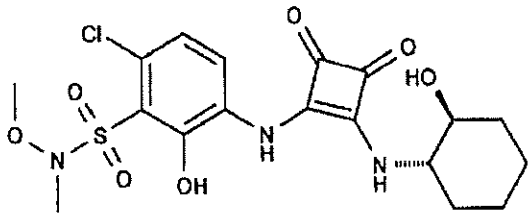


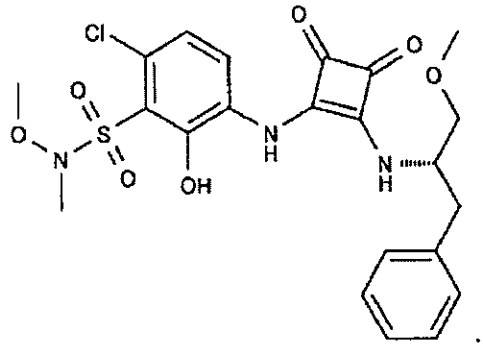


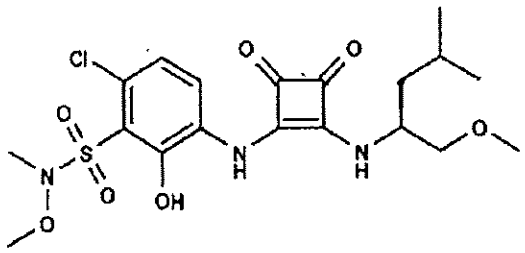


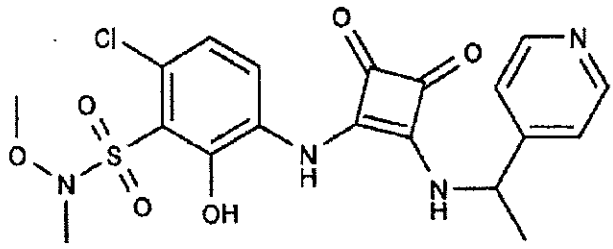


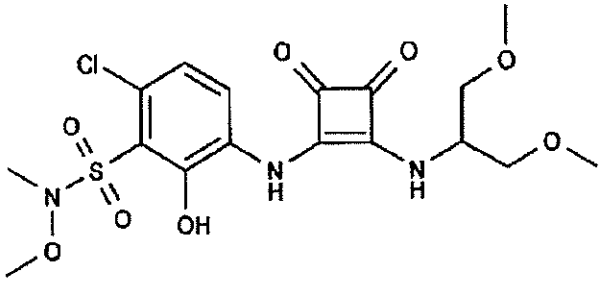


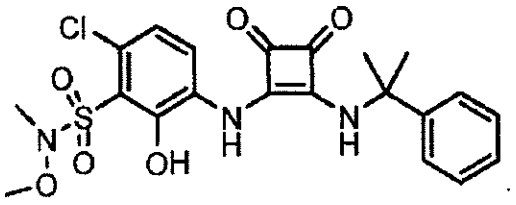


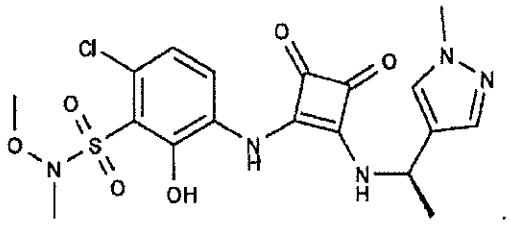


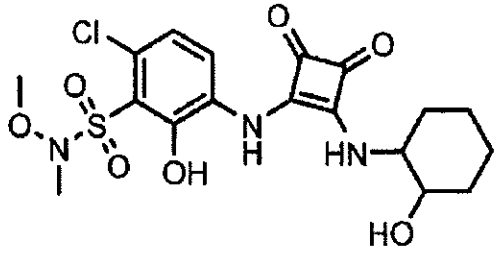




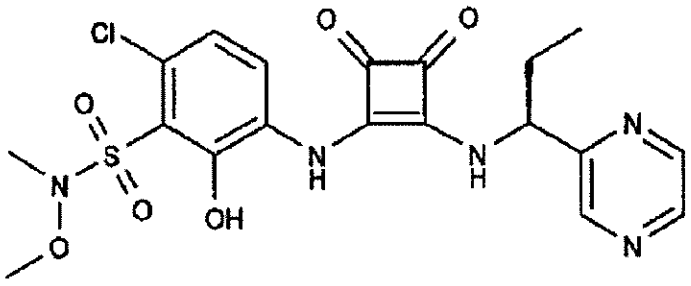




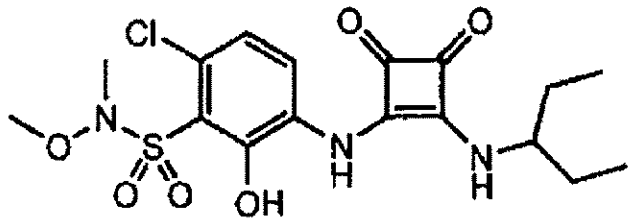




and



9. The compound of Claim 1, wherein the compound is 6-chloro-3-[2-(1-ethyl-propylamino)-3,4-dioxo-cyclobut-1-enylamino]-2-hydroxy-N-methoxy-N-methyl-benzenesulfonamide with the structure



,or a pharmaceutically acceptable salt thereof.

10. A compound according to any one of claims 1 to 9, in free or pharmaceutically acceptable salt form, for use

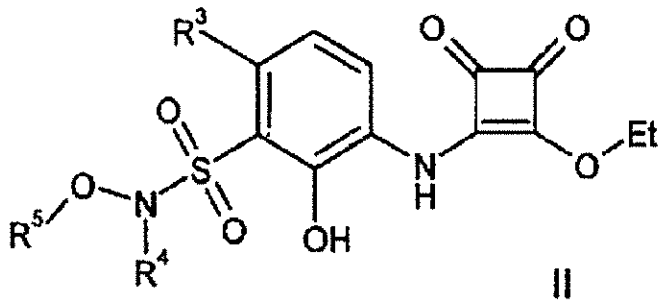
as a pharmaceutical.

11. Use of a compound according to any of Claims 1 to 9, in free or pharmaceutically acceptable salt form, in the manufacture of a medicament for the treatment of inflammatory or allergic conditions or diseases.

12. Use according to Claim 11, wherein the condition is COPD.

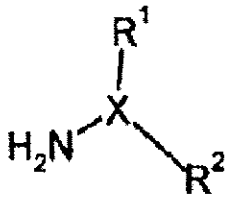
13. A pharmaceutical composition comprising a compound according to any of Claims 1 to 9, in free or pharmaceutically acceptable salt form, together with a pharmaceutically acceptable carrier or excipient.

14. A process for the preparation of a compound according to any of Claims 1 to 9, the process comprising reacting a compound of formula II



II

wherein R^3, R^4 and R^5 are as defined in Claim 1, with a compound of formula III



III

wherein X, R^1 and R^2 are as defined in Claim 1; and isolating the product.

15. A combination of a compound according to any of Claims 1 to 9, in free or pharmaceutically acceptable salt form, with another drug substance.

16. A combination according to Claim 15, wherein the other drug substance is an antiinflammatory, bronchodilatory, antihistamine or anti-tussive drug substance.