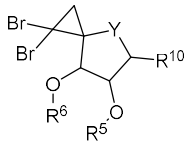
In another aspect the present disclosure concerns a compound of formula (H):



(H)

or a salt or solvate thereof, wherein:

Y is –O– or –CH_2–;

R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^5 and R^6 taken together are a diol protecting group; and

R^{10} is a nucleobase or nucleobase derivative.

The present disclosure will now be further described. In the following passages, different aspects of the disclosure are defined in more detail. Each aspect so defined may be combined with any other aspect or aspects unless clearly indicated to the contrary. In particular, any feature indicated as being preferred or advantageous may be combined with any other feature or features indicated as being preferred or advantageous.

Detailed description

When describing the compounds of the invention, the terms used are to be construed in accordance with the following definitions, unless a context dictates otherwise.

When any variable occurs more than one time in any constituent or in any formula, its definition in each occurrence is independent of its definition at every other occurrence.

Whenever the term “substituted” is used in the present invention, it is meant, unless otherwise is indicated or is clear from the context, to indicate that one or more hydrogens, in particular from 1 to 3 hydrogens, preferably 1 or 2 hydrogens, more preferably 1 hydrogen, on the atom or radical indicated in the expression using “substituted” are replaced with a selection from the indicated group, provided that the normal valency is not exceeded, and that the substitution results in a chemically stable compound, i.e. a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into a therapeutic agent.

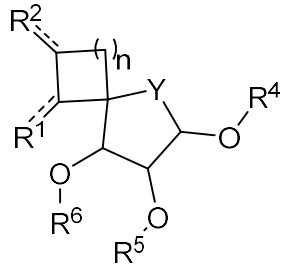
When two or more substituents are present on a moiety they may, unless otherwise is indicated or is clear from the context, replace hydrogens on the same atom or they may replace hydrogen atoms on different atoms in the moiety.

The prefix “C_{x-y}” (where x and y are integers) as used herein refers to the number of carbon atoms in a given group. Thus, a C_{1-4}alkyl group contains from 1 to 4 carbon atoms, a C_{1-3}alkyl group contains from 1 to 3 carbon atoms and so on.

The term “halo” as a group or part of a group is generic for fluoro, chloro, bromo, iodo unless otherwise is indicated or is clear from the context.

Claims

1. A compound of Formula (A)



(A)

or a salt or solvate thereof, wherein:

Y is –O– or –CH_2–;

n is 0 or 1;

when n is 1, R^1 is hydrogen and R^2 is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, =O or =CR^a_2; or

when n is 1, R^2 is hydrogen and R^1 is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, -O-aryl, =O or =CR^a_2;

when n is 0, one of R^1 and R^2 is hydrogen and the other is -$(CH_2)_mNR^a_2$,-$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$ or =CH_2;

wherein the bond towards R^1 or R^2 ⎓ is a single bond when R^1 or R^2 is hydrogen, -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group or -O-aryl, or a double bond when R^1 or R^2 is =O, =CH_2 or =CR^a_2;

each R^a is, independently, hydrogen or C_{1-6} alkyl;

each R^b is hydrogen or both R^b are taken together to form a boronic acid protecting group;

R^c is C_{1-6} alkyl or aryl;

PG is a hydroxyl protecting group;

m is 0 or 1;

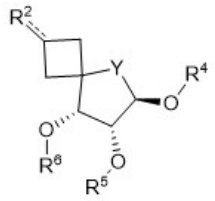
x is 0, 1 or 2;

R^4, R^5 and R^6 are each independently hydrogen or a hydroxyl protecting group; or R^5 and R^6 taken together are a diol protecting group;

or R^4 and R^5 taken together are a diol protecting group;

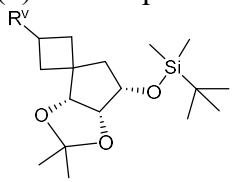
provided that:

(a) the compound is not a compound of formula:



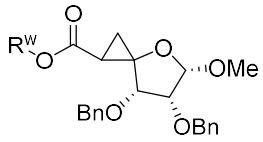
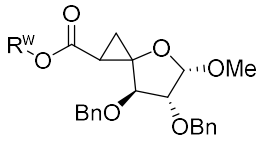
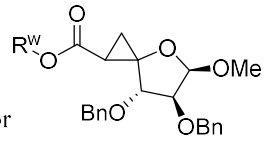
, wherein Y is –O– or –CH_2–; R^4 is hydrogen or a hydroxyl protecting group such as for example $C_{1\text{-}4}$alkyl, t-butyldimethylsilyl, $C_{1\text{-}4}$alkyl-O-$C_{1\text{-}4}$alkyl, tetrahydropyranyl, allyl, t-butyldiphenylsilyl, benzyl, -C(=O)-$C_{1\text{-}4}$alkyl, or -C(=O)-phenyl; R^2 is -OH, =O, -CH_2-OH or =CH_2; and R^5 and R^6 are each independently -C(=O)-$C_{1\text{-}4}$alkyl, benzoyl, benzyl, or -CH_2-naphthyl, wherein benzyl, -CH_2-naphthyl, and benzoyl are optionally substituted with one or two substituents each independently selected from -CH_3 and -OCH_3; or R^5 and R^6 taken together are -C($C_{1\text{-}4}$alkyl)$_2$-; or wherein Y is –O– or –CH_2, R^4 is methyl, R^2 is =O, or =CH_2, and R^5 and R^6 are each independently hydrogen or –C(=O)-$C_{1\text{-}4}$alkyl; and

(b) the compound is not a compound of formula:



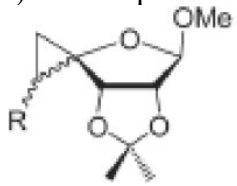
, wherein R^v is =O, -OH or =CH_2; and

(c) the compound is not a compound of formula:



or


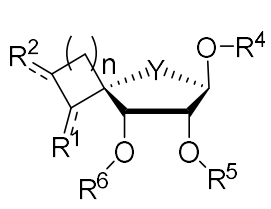
, wherein R^w is methyl or H; and

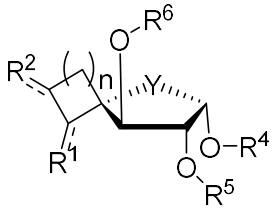
(d) the compound is not a compound of formula:

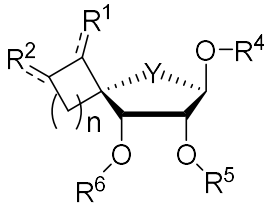


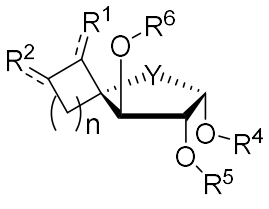
, wherein R is CO_2Et or CH_2OH or any stereoisomer thereof.

2. The compound of claim 1, wherein the compound is a compound of formula (A-1a), (A-3a), (A-1b) or (A-3b):


(A-1a)


(A-3a)


(A-1b)


(A-3b)

or a salt or solvate thereof.

3. The compound of claim 1 or 2, wherein the hydroxyl protecting group is selected from a silyl group, C_{1-4}alkyl, C_{1-4}alkyl-O-C_{1-4}alkyl, tetrahydropyranyl, allyl, benzyl, -CH_2-naphthyl, or benzoyl, -C(=O)-C_{1-4}alkyl, or -C(=O)-phenyl; wherein benzyl, -CH_2-naphthyl, and benzoyl, are optionally substituted with one or two substituents each independently selected from -CH_3 and -OCH_3; and/or the diol protecting group is $C(C_{1-4}alkyl)_2$-.

4. The compound of any one of claims 1 to 3, wherein Y is O.

5. The compound of any one of claims 1 to 3, wherein Y is CH_2.

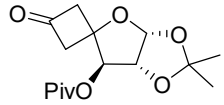
6. The compound of any one of claims 1 to 5, wherein n is 1.

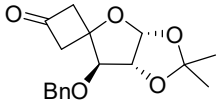
7. The compound of claim 6, wherein:
R^1 is hydrogen and R^2 -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, =O or $=CR^a_2$; or
R^2 is hydrogen and R^1 is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, -O-aryl, =O or $=CR^a_2$.

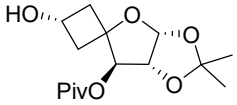
8. The compound of any one of claims 1 to 5, wherein n is 0.

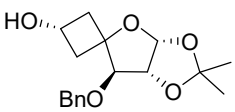
9. The compound of claim 8, wherein one of R^1 and R^2 is hydrogen and the other is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$C(O)OR^a$, -$C(O)NR^a_2$ or -$B(OR^b)_2$.

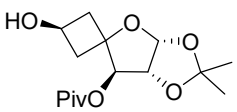
10. The compound of claim 1, wherein the compound is selected from:

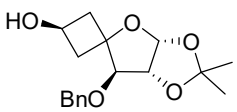


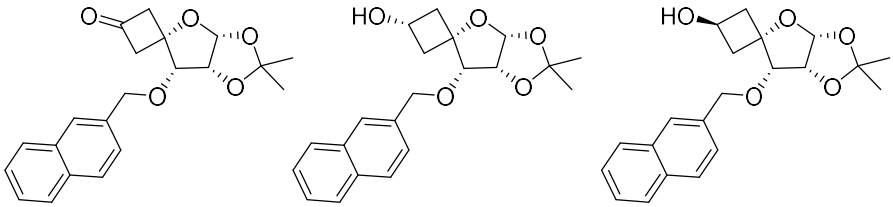


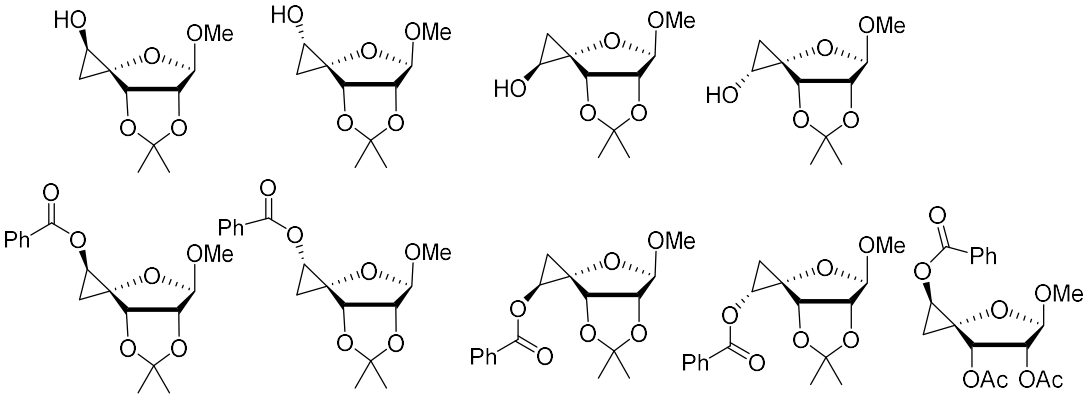


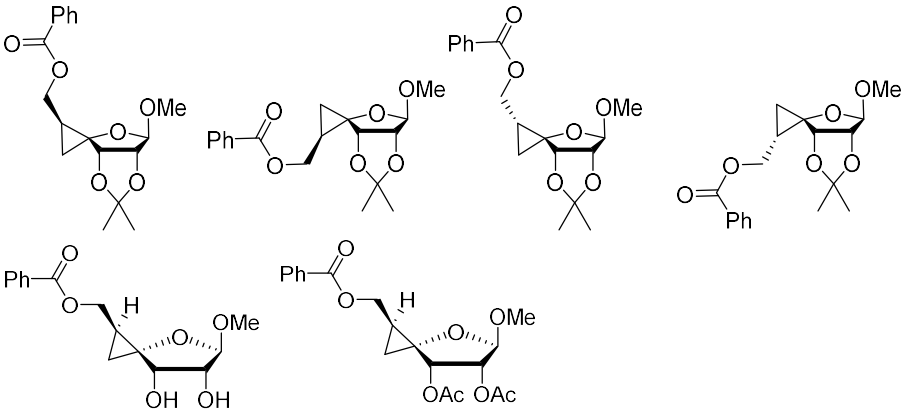


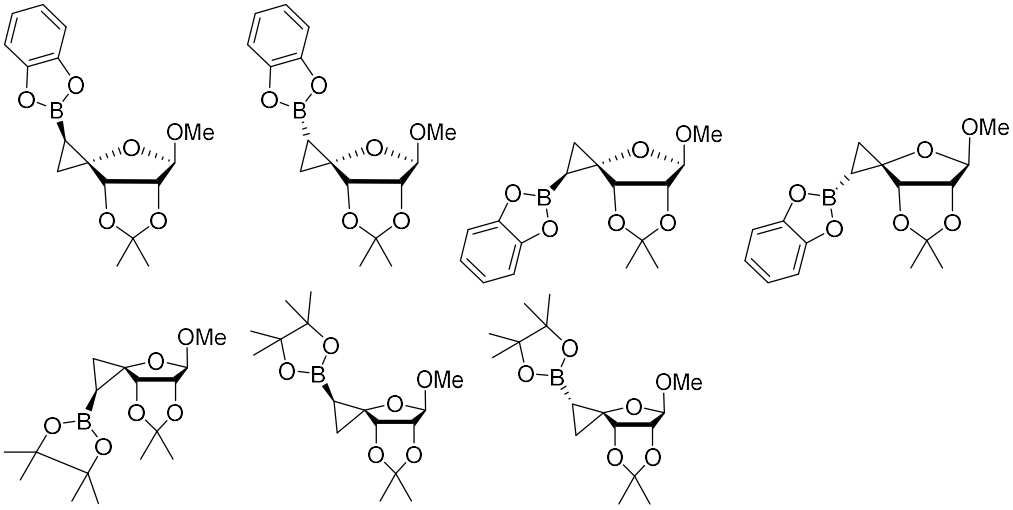


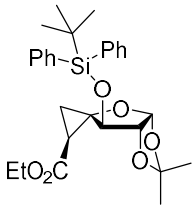
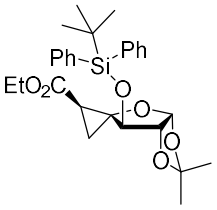
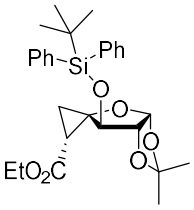
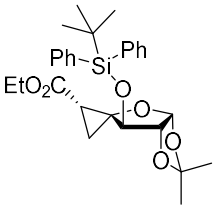
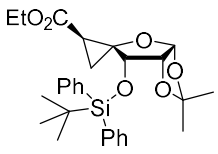
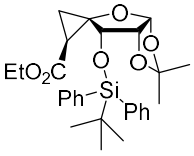
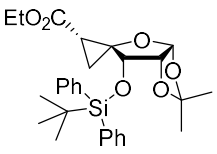
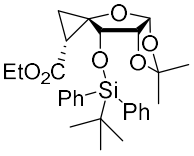
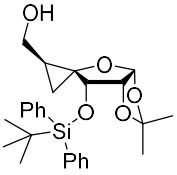
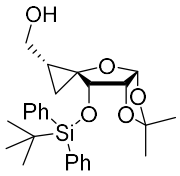
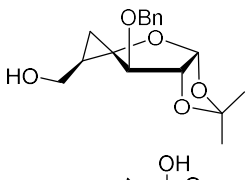
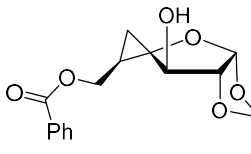
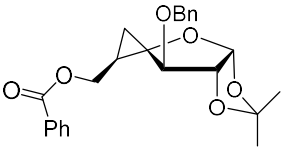
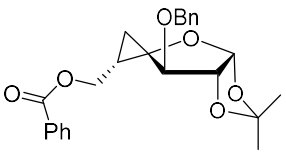


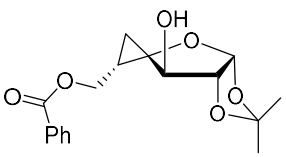
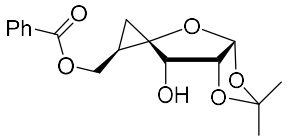
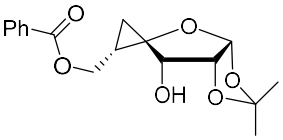
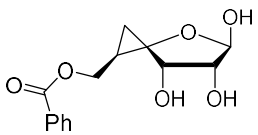
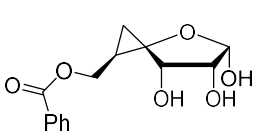
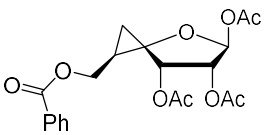
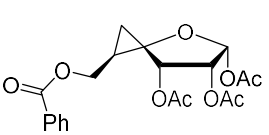
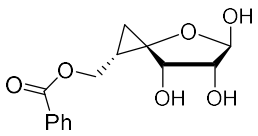
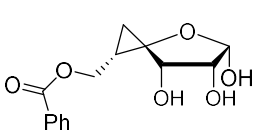
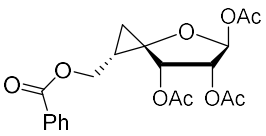
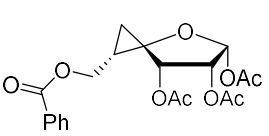
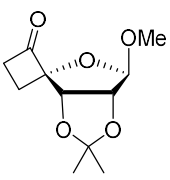
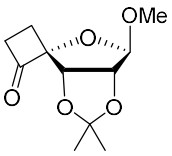


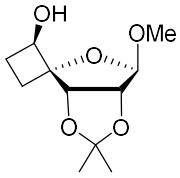
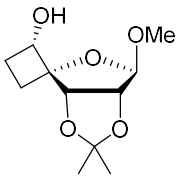
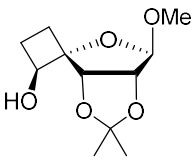
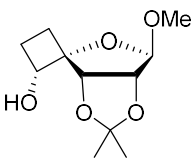
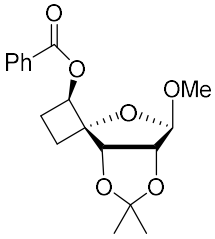
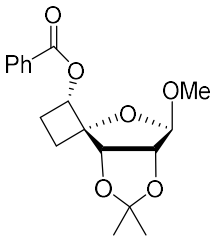
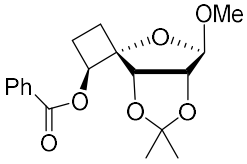
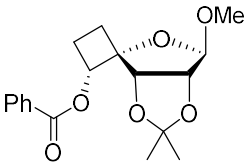
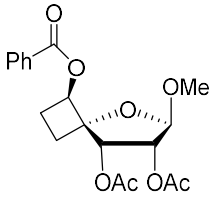
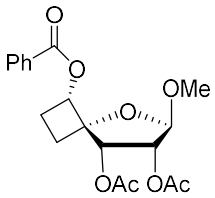
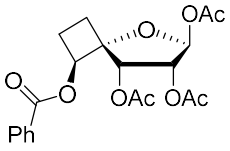
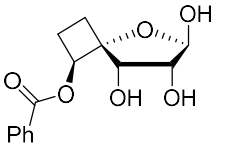
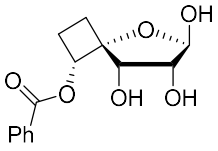
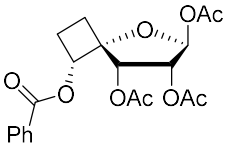
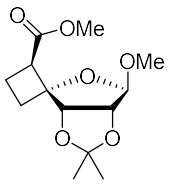
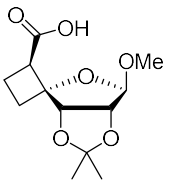
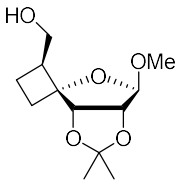
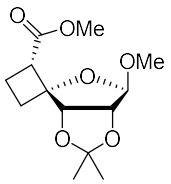
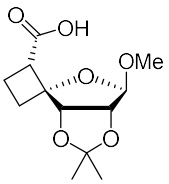
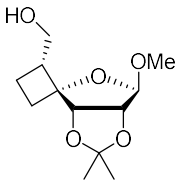
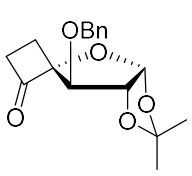
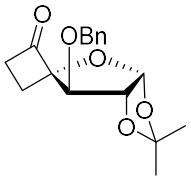
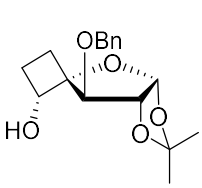
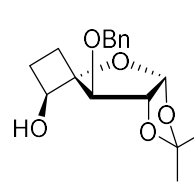
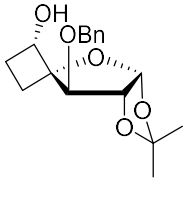
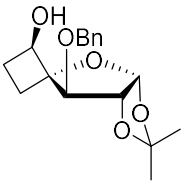


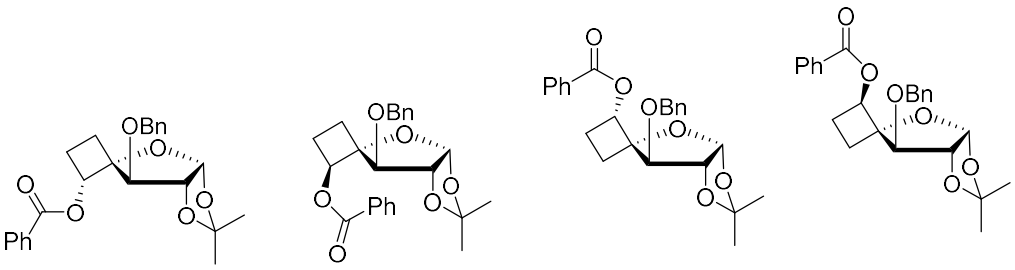




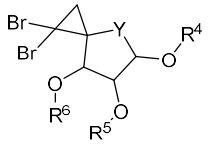
















or a salt or solvate thereof.

11. A compound of formula (B):



(B)

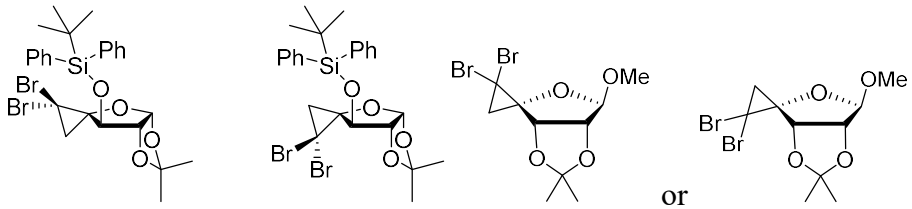
or a salt or solvate thereof, wherein:

Y is –O– or –CH_2–;

R^4, R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^5 and R^6 taken together are a diol protecting group;

or R^4 and R^5 taken together are a diol protecting group.

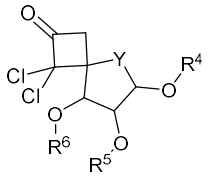
12. The compound of claim 11, wherein the compound is selected from:



or

or a salt or solvate thereof.

13. A compound of formula (C):



(C)

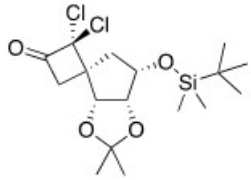
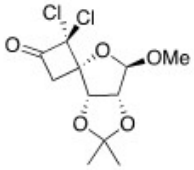
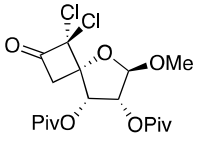
wherein:

Y is –O– or –CH_2–;

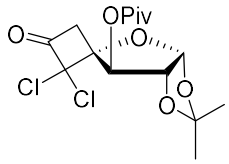
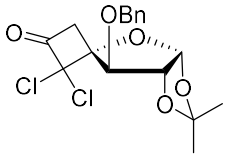
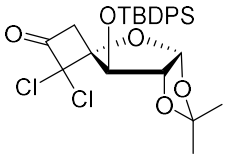
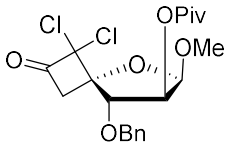
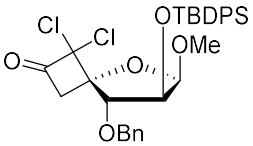
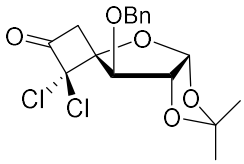
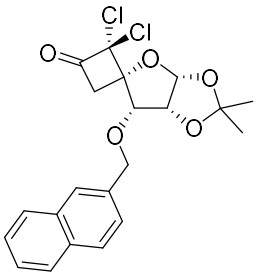
R^4, R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^4 and R^5 taken together are a diol protecting group; or

R^5 and R^6 taken together are a diol protecting group;

provided that the compound is not:

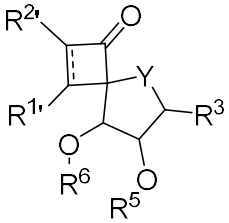


or

.

14. The compound of claim 13, wherein the compound is selected from:

or a salt or solvate thereof.

15. A compound of formula (D):



(D)

or a salt or solvate thereof, wherein:

Y is –O– or –CH_2–;

wherein ⎓ is a single bond or a double bond; and

when ⎓ is a single bond, one of $R^{1'}$ and $R^{2'}$ is hydrogen or C_{1-6} alkyl and the other is a silyl group, C_{1-6} alkyl optionally substituted with a silyl group, -O-C_{1-6} alkyl, -$B(OR^b)_2$ -S-C_{1-6} alkyl, -S-aryl, -O-aryl or $C(O)R^a$;

when ⎯⎯ is a double bond, one of $R^{1'}$ and $R^{2'}$ is hydrogen or C_{1-6} alkyl and the other is a silyl group, C_{1-6} alkyl optionally substituted with a silyl group, -O-C_{1-6} alkyl, , or C(O)R^a; and

R^a is hydrogen or C_{1-6} alkyl;

each R^b is hydrogen or both R^b are taken together to form a boronic acid protecting group;

R^3 is OR^4 or R^{10};

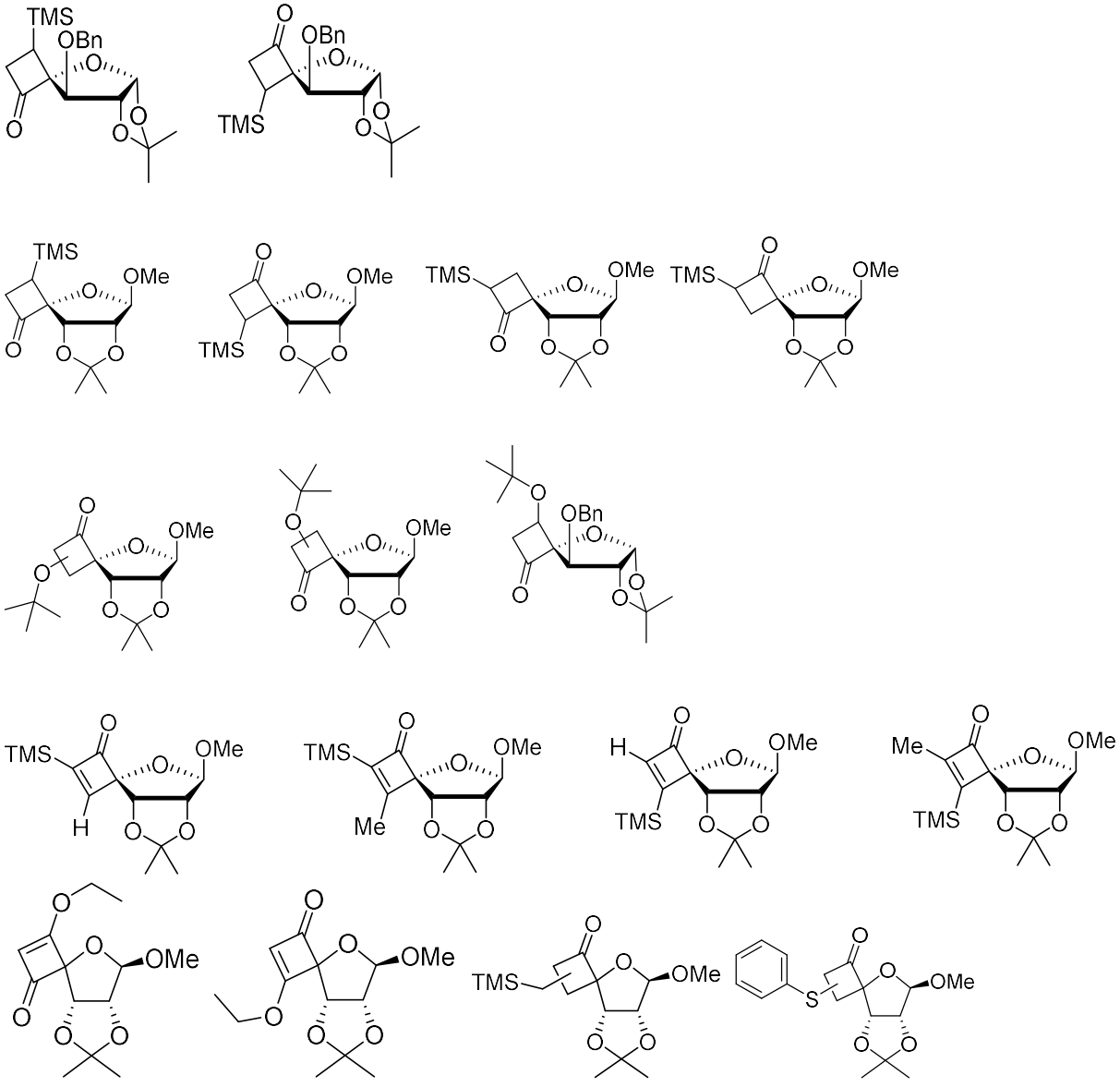
R^{10} is a nucleobase or nucleobase derivative;

R^4, R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^4 and R^5 taken together are a diol protecting group; or

R^5 and R^6 taken together are a diol protecting group.

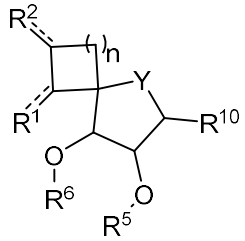
16. The compound of claim 15, wherein R^3 is OR^4.

17. The compound of claim 15, wherein the compound is selected from:



or a salt or solvate thereof.

18. A compound of formula (E):



(E)

or a salt or solvate thereof, wherein:

Y is –O- or –CH_2–;

n is 0 or 1;

when n is 1, R^1 is hydrogen and R^2 is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, =O or =CR^a_2; or

when n is 1, R^2 is hydrogen and R^1 is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group, -O-aryl, =O or =CR^a_2;

when n is 0, one of R^1 and R^2 is hydrogen and the other is -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$ or =CH_2;

wherein the bond towards R^1 or R^2 ⎓ is a single bond when R^1 or R^2 is hydrogen, -$(CH_2)_mNR^a_2$, -$(CH_2)_mOR^a$, -$(CH_2)_mOPG$, -$(CH_2)_mC(O)OR^a$, -$(CH_2)_mC(O)NR^a_2$, -$(CH_2)_mC(O)R^a$, -$(CH_2)_mB(OR^b)_2$, -$(CH_2)_mS(O)_xR^c$, a silyl group, C_{1-6} alkyl substituted with a silyl group or -O-aryl, or a double bond when R^1 or R^2 is =O, =CH_2 or =CR^a_2;

each R^a is, independently, hydrogen or C_{1-6} alkyl;

both R^b are hydrogen or both R^b are taken together to form a boronic acid protecting group;

R^c is C_{1-6} alkyl or aryl;

x is 0, 1 or 2;

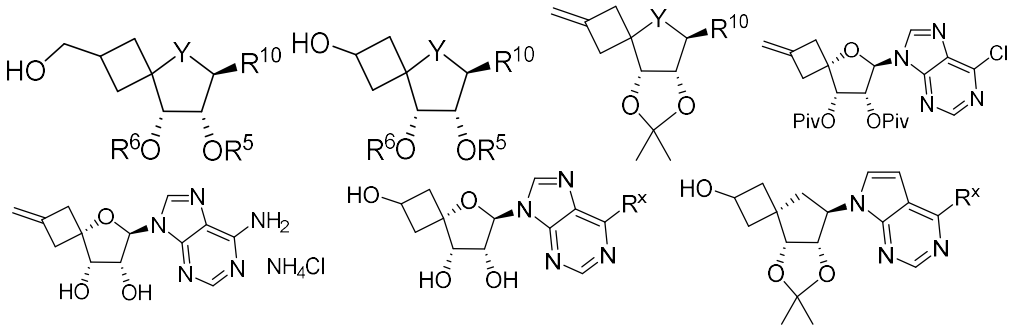
m is 0 or 1;

R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^5 and R^6 taken together are a diol protecting group;

R^{10} is a nucleobase or nucleobase derivative;

PG is a hydroxyl protecting group;

provided that the compound is not any of:



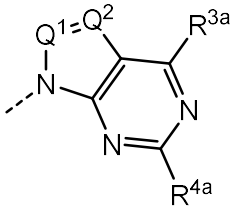
wherein

R^5 is hydrogen or –C(=O)-C_{1-4}alkyl;

R^6 is hydrogen or –C(=O)-C_{1-4}alkyl; or R^5 and R^6 taken together are -$C(CH_3)_2$-

Y is –O- or –CH_2–;

R^{10} is



Q^1 is CR^{6a};

Q^2 is N or CR^{6b};

R^{6a} and R^{6b} each independently represent hydrogen, halogen, C_{1-4}alkyl, –$NR^{9a}R^{9b}$, or C_{1-4}alkyl substituted with one, two or three halo atoms;

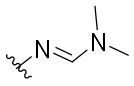
R^{9a} and R^{9b} each independently represent hydrogen or C_{1-4}alkyl;

R^{3a} is hydrogen, halo, -$NR^{7a}R^{7b}$, C_{1-4}alkyl, C_{2-4}alkenyl, C_{3-6}cycloalkyl, –OH, or –O-C_{1-4}alkyl;

R^{7a} is hydrogen;

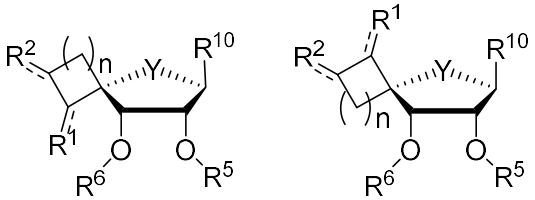
R^{7b} is hydrogen, C_{3-6}cycloalkyl, or C_{1-4}alkyl;

R^{4a} is hydrogen, halo, -$NR^{8a}R^{8b}$, or C_{1-4}alkyl; and

R^x is ;

or a salt or solvate thereof.

19. The compound of claim 18, wherein the compound is a compound of formula (G-1a) or (G-1b):



(G-1a) (G-1b)

or a salt or solvate thereof.

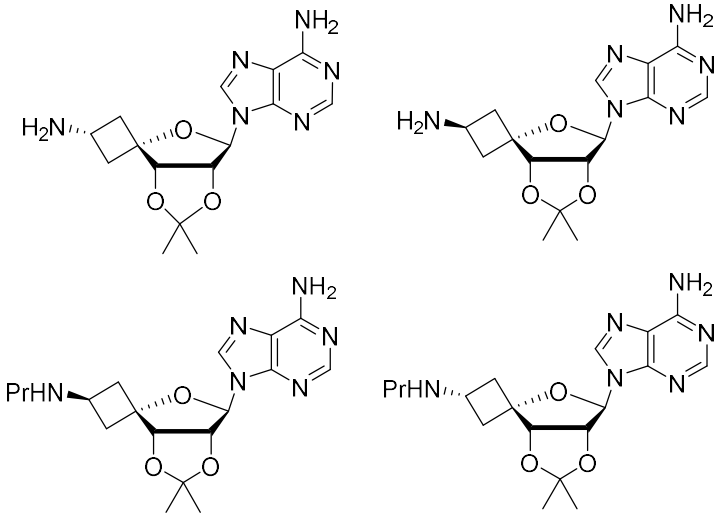
20. The compound of any one of claims 18 or 19, wherein n is 1.

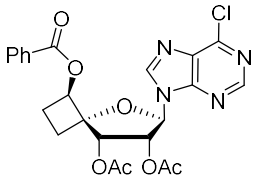
21. The compound of claim 20, wherein:
R^1 is hydrogen and R^2 is $-(CH_2)_mNR^a_2$, $-(CH_2)_mOR^a$, $-(CH_2)_mC(O)OR^a$, $-(CH_2)_mC(O)NR^a_2$, $-(CH_2)_mC(O)R^a$, $-(CH_2)_mS(O)_xR^c$, a silyl group, C_1-$_6$ alkyl substituted with a silyl group, =O or $=CR^a_2$; or
R^2 is hydrogen and R^1 is $-(CH_2)_mNR^a_2$, $-(CH_2)_mOR^a$, $-(CH_2)_mOPG$, $-(CH_2)_mC(O)OR^a$, $-(CH_2)_mC(O)NR^a_2$, $-(CH_2)_mC(O)R^a$, $-(CH_2)_mS(O)_xR^c$, a silyl group, C_1-$_6$ alkyl substituted with a silyl group, -O-aryl, =O or $=CR^a_2$.

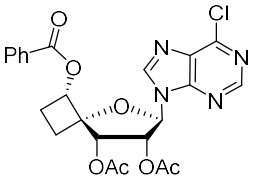
22. The compound of any one of claims 18 or 19, wherein n is 0.

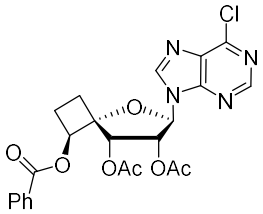
23. The compound of claim 20, wherein one of R^1 and R^2 is hydrogen and the other is $-(CH_2)_mNR^a_2$, $-(CH_2)_mOR^a$, $-(CH_2)_mOPG$, $-(CH_2)_mC(O)OR^a$, $-(CH_2)_mC(O)NR^a_2$, $-(CH_2)_mC(O)R^a$, $-(CH_2)_mB(OR^b)_2$, or $=CH_2$.

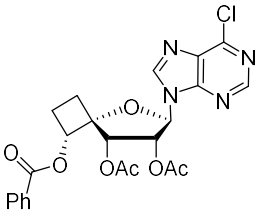
24. The compound of claim 18, wherein the compound is selected from:

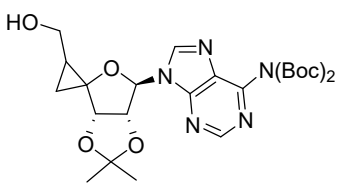


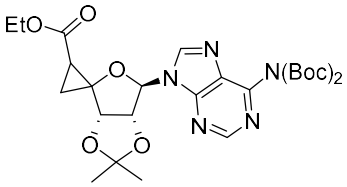


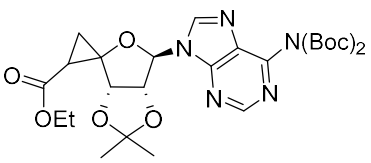


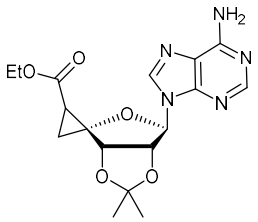


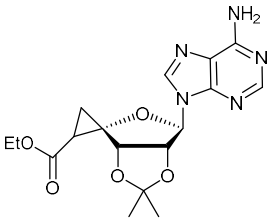


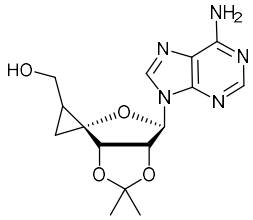


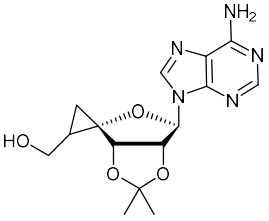


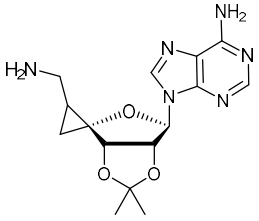


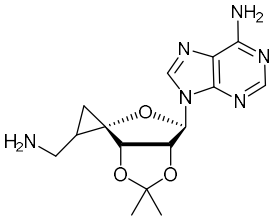


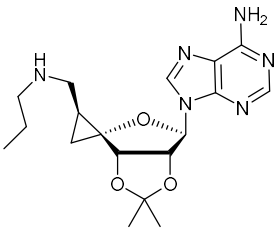


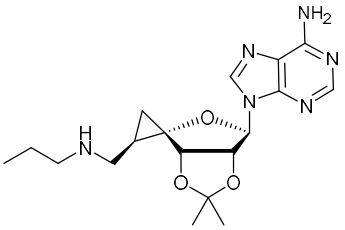


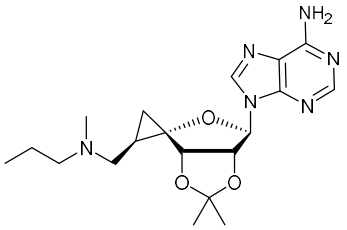


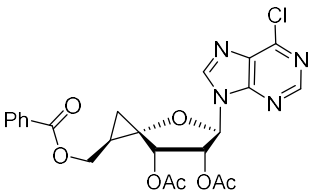


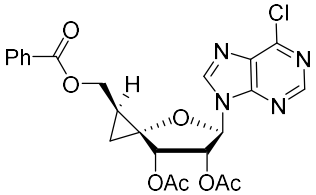


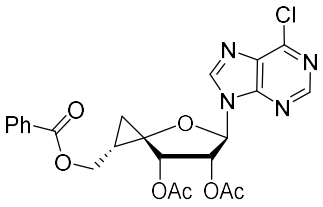


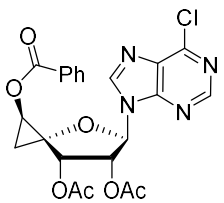






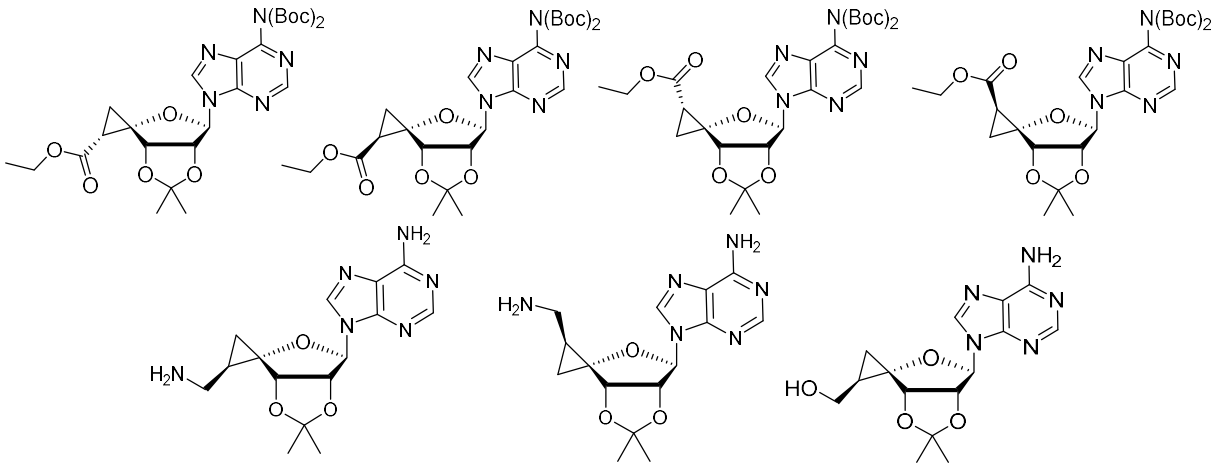






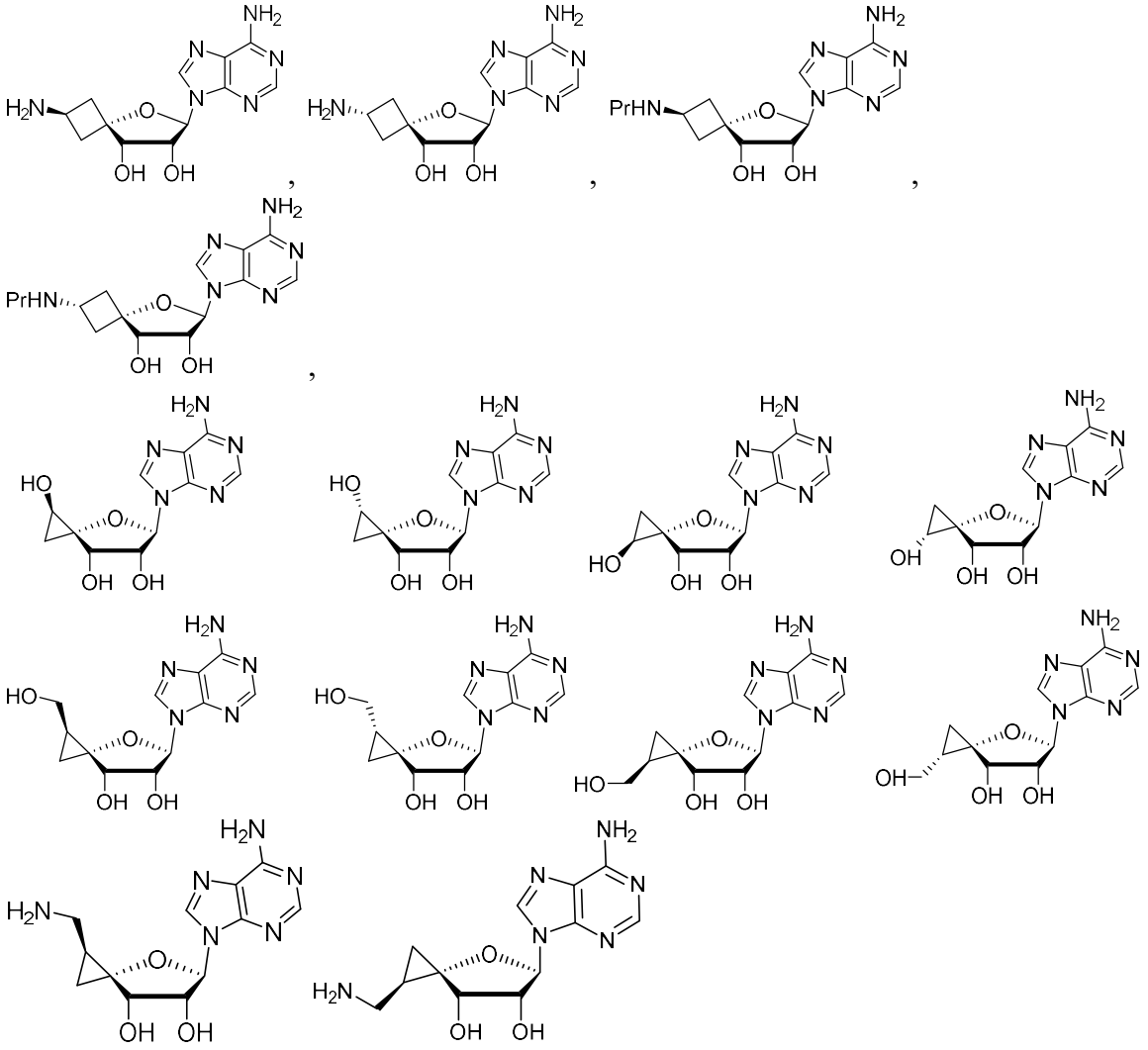
or a salt or solvate thereof.

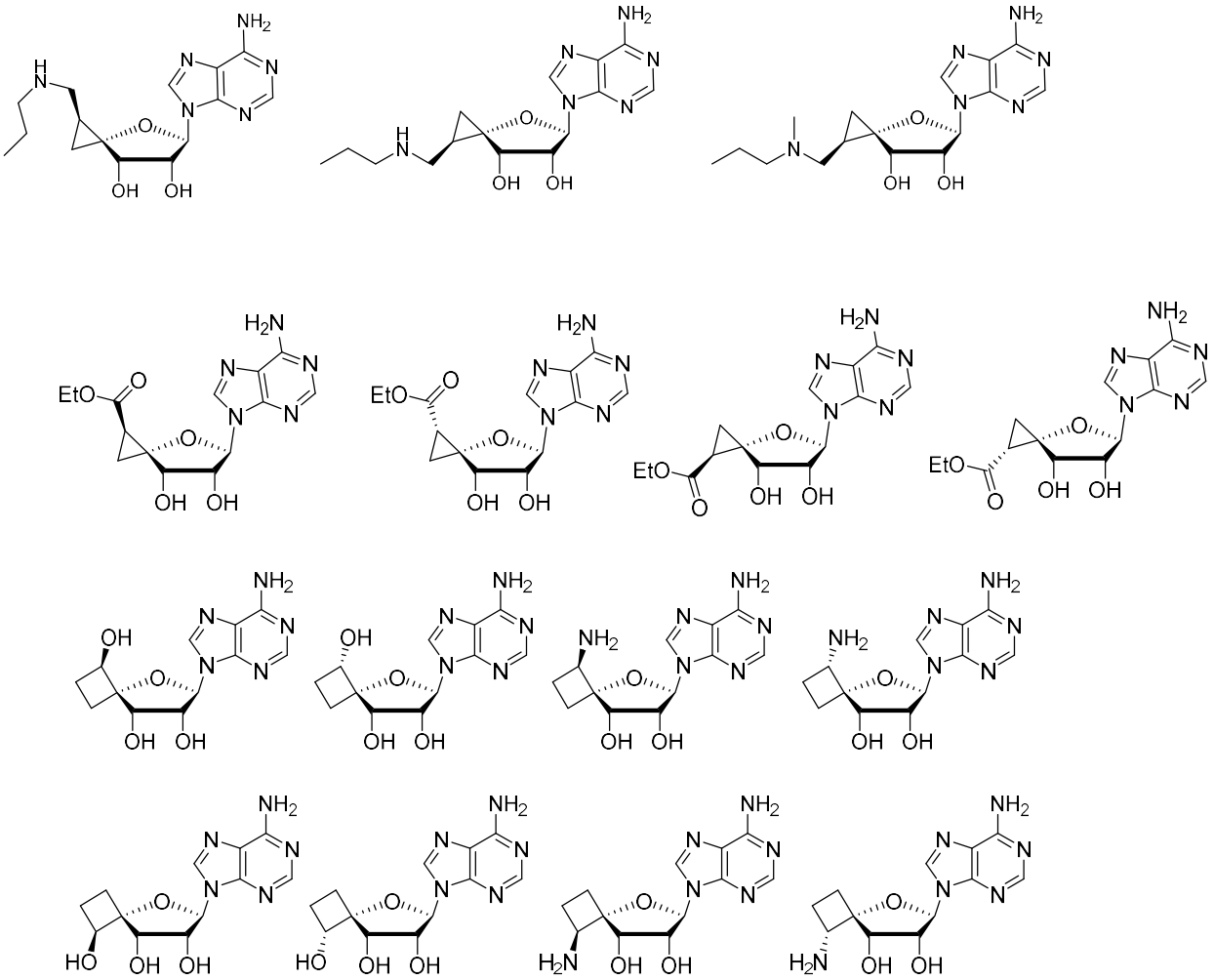
25. The compound of claim 24, wherein the compound is selected from:



or a salt or solvate thereof.

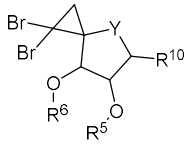
26. The compound of claim 18, wherein the compound is selected from:





or a salt or solvate thereof.

27. A compound of formula (H):



(H)

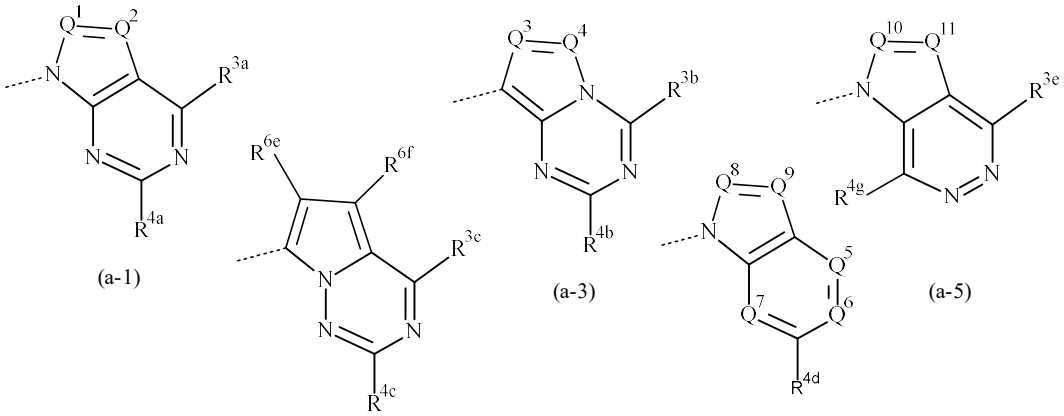
or a salt or solvate thereof, wherein:

Y is –O– or –CH_2–;

R^5 and R^6 are each, independently, hydrogen or a hydroxyl protecting group; or R^5 and R^6 taken together are a diol protecting group; and

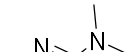
R^{10} is a nucleobase or nucleobase derivative.

28. The compound of any one of claims 15 to 27, wherein R^{10}, when present, is cytosine, thymine, uracil, or a modified or protected form thereof, or a bicyclic aromatic heterocyclic ring system selected from the group consisting of (a-1), (a-2), (a-3), (a-4) and (a-5):



(a-1) (a-2) (a-3) (a-4) (a-5)

R^{3a}, R^{3b}, R^{3c}, R^{3d} and R^{3e} each independently are hydrogen, halo, $-NR^{7a}R^{7b}$, C_{1-4}alkyl, C_{2-4}alkenyl, C_{3-6}cycloalkyl, –OH, or –O-C_{1-4}alkyl;

R^{7a} is hydrogen, -C(O)O-C_{1-4}alkyl or  ;

R^{7b} is hydrogen, C_{3-6}cycloalkyl, C_{1-4}alkyl, or -C(O)O-C_{1-4}alkyl;

R^{4a}, R^{4b}, R^{4c}, R^{4d}, R^{4e}, R^{4f} and R^{4g} each independently are hydrogen, halo, $-NR^{8a}R^{8b}$, or C_{1-4}alkyl;

R^{8a} and R^{8b} each independently are hydrogen or C_{1-4}alkyl;

Q^1 is N or CR^{6a};

Q^2 is N or CR^{6b};

Q^3 is N or CR^{6c};

Q^4 is N or CR^{6d};

provided that maximum one of Q^3 and Q^4 is N;

Q^8 is N or CR^{6g};

Q^9 is N or CR^{6h};

Q^{10} is N or CR^{6i};

Q^{11} is N or CR^{6j};

Q^5 is CR^{3d}; Q^6 is N; and Q^7 is CR^{4f}; or

Q^5 is CR^{3d}; Q^6 is CR^{4e}; and Q^7 is N; or

Q^5 is N; Q^6 is CR^{4e}; and Q^7 is CR^{4f}; or

Q^5 is N; Q^6 is CR^{4e}; and Q^7 is N; or

Q^5 is N; Q^6 is N; and Q^7 is CR^{4f}; or

Q^5 is N; Q^6 is N; and Q^7 is N;

R^{6a}, R^{6b}, R^{6c}, R^{6d}, R^{6e}, R^{6f}, R^{6g}, R^{6h}, R^{6i} and R^{6j} each independently are hydrogen, halogen, C_{1-4}alkyl, $-NR^{9a}R^{9b}$, or C_{1-4}alkyl substituted with one, two or three halo atoms;

R^{9a} and R^{9b} each independently are hydrogen or C_{1-4}alkyl.