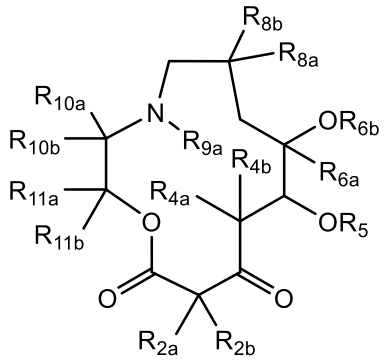
992-998. Ketolides such as telithromycin and solithromycin defeat the efflux mechanism of resistance by replacement of the C3 cladinose sugar with a carbonyl group (hence the name "ketolides") and are thought to exhibit greatly increased binding by virtue of favorable interactions between the novel aryl-alkyl sidechain and the ribosome. See, *e.g.*, Ma *et al.*, *Curr. Med. Chem.* (2011) 18:1993-2015; Ma *et al.*, *Mini-Rev. Med. Chem.* (2010) 10:272-286. Despite greatly improved ribosomal binding, ketolides such as telithromycin and solithromycin have not addressed several of the newest forms of macrolide resistance that have evolved in nosocomial settings, especially ribosome methylation and RNA point mutations.

[0005] Accordingly, the discovery and development of new antibiotics effective against drug-resistant bacteria, especially Gram-negative bacteria, represents a currently unmet medical need.

SUMMARY

[0005a] In an aspect of the present disclosure, there is provided a compound of Formula I:



I

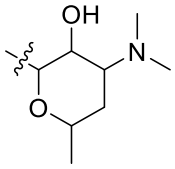
or a pharmaceutically acceptable salt thereof, wherein:

one of R_{2a} and R_{2b} is selected from the group consisting of H, halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

and the other of R_{2a} and R_{2b} is selected from the group consisting of halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

each of R_{4a} and R_{4b} is independently selected from the group consisting of -H, and optionally substituted C_{1-10} alkyl;

R_5 is selected from the group consisting of -H, an oxygen protecting group, and



, wherein " ~~~ " indicates a point of attachment

R_{6a} is optionally substituted C_{1-10} alkyl;

R_{6b} is -H, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} hydroxyalkyl, and optionally substituted allyl;

R_{8a} and R_{8b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl;

R_{9a} is selected from the group consisting of -H, -CO_2-alkylene-aryl, -C(=O)-alkyl, and optionally substituted C_{1-10} alkyl;

one of R_{10a} and R_{10b} is selected from the group consisting of –H, optionally substituted C_{1-10} alkyl, -CO_2H, and –CO_2-alkyl; and

the other of R_{10a} and R_{10b} is selected from the group consisting of optionally substituted saturated or partially unsaturated cycloalkyl containing at least one double bond, optionally substituted saturated or partially unsaturated heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R_{11a} and R_{11b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl.

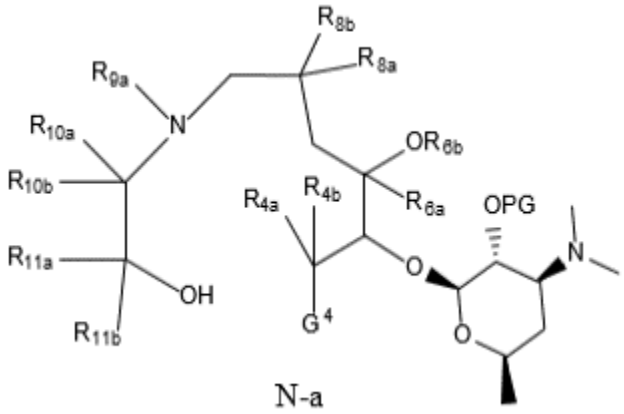
[0005b] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising the compound disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0005c] In another aspect of the present disclosure, there is provided a kit comprising the compound disclosed herein, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition disclosed herein, and instructions for administering to a subject in need thereof.

[0005d] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating an infectious disease in a subject in need thereof.

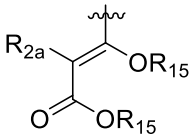
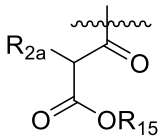
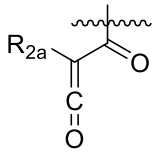
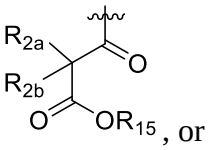
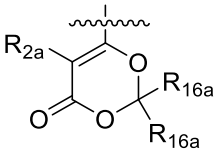
[0005e] In another aspect of the present disclosure, there is provided a compound disclosed herein, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition disclosed herein, for use in the treatment of an infectious disease in a subject in need thereof.

[0005f] In a further aspect of the present disclosure, there is provided a compound of formula N-a:



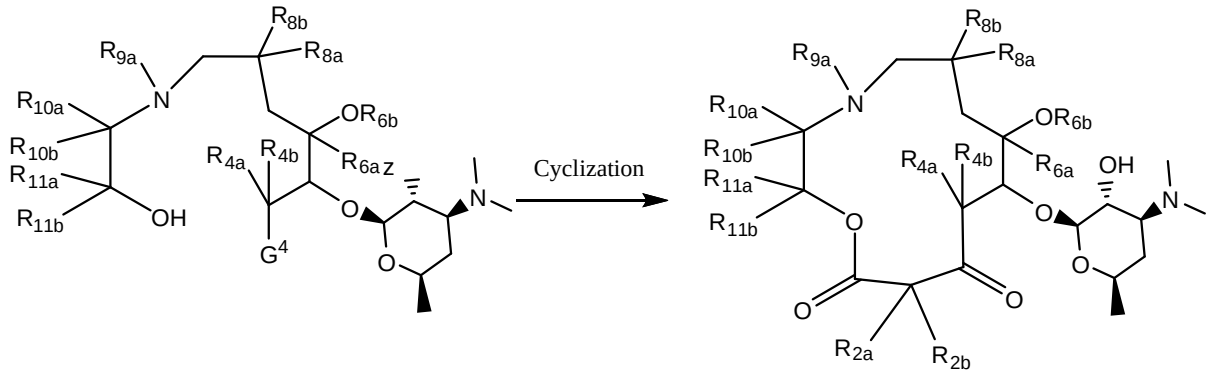
N-a

or a salt thereof, wherein R_{4a}, R_{4b}, R_5, R_{6a}, R_{6b}, R_{8a}, R_{8b}, R_{10a}, R_{10b}, R_{11a}, and R_{11b} are as disclosed herein;

G^4 is , , , , or ;

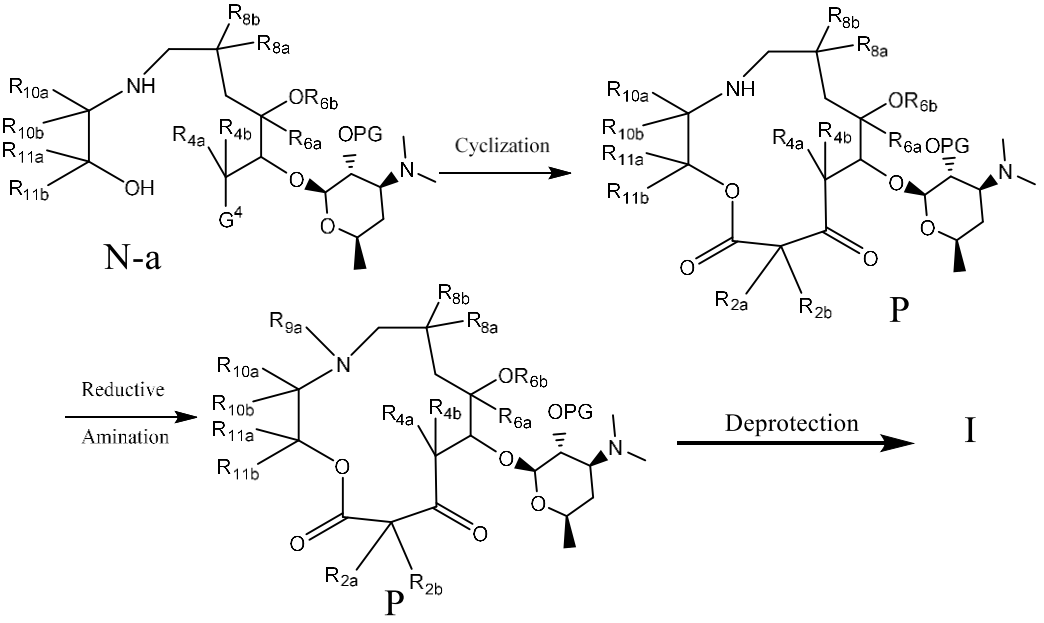
each instance of R^{15} is independently silyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{15} groups are joined to form an optionally substituted heterocyclyl or heteroaryl ring; and each instance of R^{16a} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and PG is a protecting group.

[0005g] In another aspect of the present disclosure, there is provided a process of preparing a compound of formula I disclosed herein, comprising cyclization of a compound of formula N-a:



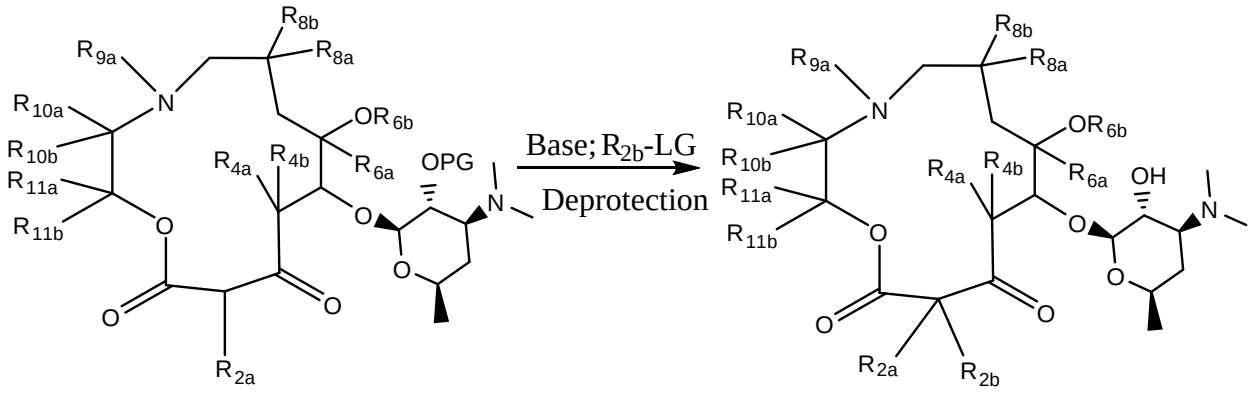
N-a I.

[0005h] In a further aspect of the present disclosure, there is provided a process of preparing a compound of formula I as disclosed herein wherein R_{9a} is C_{1-10} alkyl, hydroxyalkyl, or alkoxyalkyl; comprising cyclizing a compound of formula N-a wherein R_{9a} is H to provide a compound of formula P wherein R_{9a} is H; followed by reductive amination and deprotection to provide a compound of formula I wherein R_{9a} is C_{1-10} alkyl, hydroxyalkyl, or alkoxyalkyl



[0005i] In another aspect of the present disclosure, there is provided a process of preparing a compound of formula I as disclosed herein, comprising alkylating a compound of formula A

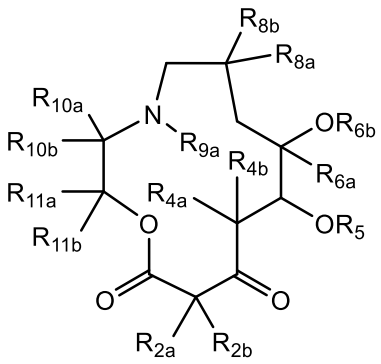
with R_{2b}-LG in the presence of base, wherein LG is a leaving group, to provide after deprotection a compound of formula I



A I.

[0006] Disclosed herein are compounds that are novel, synthetically accessible 13-membered macrolides. The disclosed compounds are novel antibiotics with unexpectedly potent antimicrobial activity.

[0007] In one example, the present disclosure provides compounds of Formula (**I**):



I

or a pharmaceutically acceptable salt thereof, wherein:

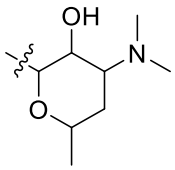
one of R_{2a} and R_{2b} is selected from the group consisting of H, halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl; and

the other of R_{2a} and R_{2b} is selected from the group consisting of halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10}

alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

each of R_{4a} and R_{4b} is independently selected from the group consisting of -H, and optionally substituted C_{1-10} alkyl;

R_5 is selected from the group consisting of -H, an oxygen protecting group, and



, wherein " 〰 " indicates appoint of attachment;

R_{6a} is optionally substituted C_{1-10} alkyl;

R_{6b} is -H, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} hydroxyalkyl, and optionally substituted allyl;

R_{8a} and R_{8b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl;

R_{9a} is selected from the group consisting of -H, -CO_2-alkylene-aryl, -C(=O)-alkyl, and optionally substituted C_{1-10} alkyl;

one of R_{10a} and R_{10b} is selected from the group consisting of –H, optionally substituted C_{1-10} alkyl, -CO_2H, and –CO_2-alkyl; and

the other of R_{10a} and R_{10b} is selected from the group consisting of optionally substituted saturated or partially unsaturated cycloalkyl containing at least one double bond, optionally substituted saturated or partially unsaturated heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R_{11a} and R_{11b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl.

[0008] The disclosed compounds have anti-microbial activity and may be used to treat and/or prevent infectious diseases. Pharmaceutical compositions of the compounds and methods of treatment and prevention using the compounds or compositions thereof are provided herein. Infectious diseases which may be treated with compounds of the present disclosure include, but are not limited to, bacterial infections caused by *Staphylococcus*, *Acinetobacter*, *Klebsiella*, *Escherichia*, and *Pseudomonas* species.

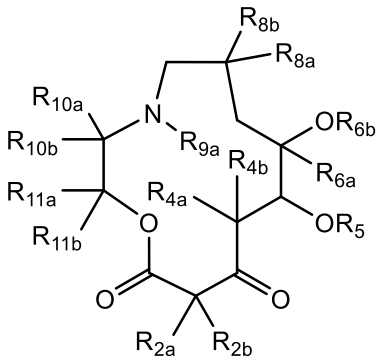
[0009] Methods of preparing the compounds are also provided herein. The present disclosure also provides intermediates in the preparation of the compounds described herein.

[0010] The details of certain examples of the present disclosure are set forth in the Detailed Description of Certain Embodiments, as described below. Other features, objects, and advantages of the present disclosure will be apparent from the Definitions, Drawings, Examples, and Claims.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

[0011] The compounds disclosed herein include 13-membered azaketolides. The disclosed compounds may have reduced structural complexity over known macrolides, providing compounds that may be accessed by less demanding synthetic routes over routes required for other macrolides. Despite their reduced structural complexity, the disclosed 13-membered azaketolides provide unexpected and potent activity against various microorganisms, including Gram negative bacteria. Also disclosed are methods for the preparation of the compounds, pharmaceutical compositions comprising the compounds, and methods of using the compounds (*e.g.*, treatment of an infectious disease).

[0012] In certain embodiments, provided are compounds of formula I:



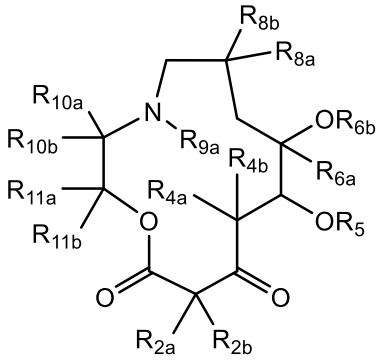
I

or a pharmaceutically acceptable salt thereof, wherein:

one of R_{2a} and R_{2b} is selected from the group consisting of H, halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl; and

CLAIMS

1. A compound of Formula I:



I

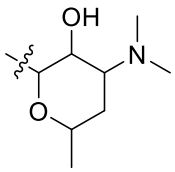
or a pharmaceutically acceptable salt thereof, wherein:

one of R_{2a} and R_{2b} is selected from the group consisting of H, halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

and the other of R_{2a} and R_{2b} is selected from the group consisting of halo, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and optionally substituted C_{1-10} alkenyl, wherein C_{1-10} alkyl, C_{1-10} alkoxy, and C_{1-10} alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

each of R_{4a} and R_{4b} is independently selected from the group consisting of -H, and optionally substituted C_{1-10} alkyl;

R_5 is selected from the group consisting of -H, an oxygen protecting group, and



, wherein "〰" indicates a point of attachment

R_{6a} is optionally substituted C_{1-10} alkyl;

R_{6b} is -H, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} hydroxyalkyl, and optionally substituted allyl;

R_{8a} and R_{8b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl;

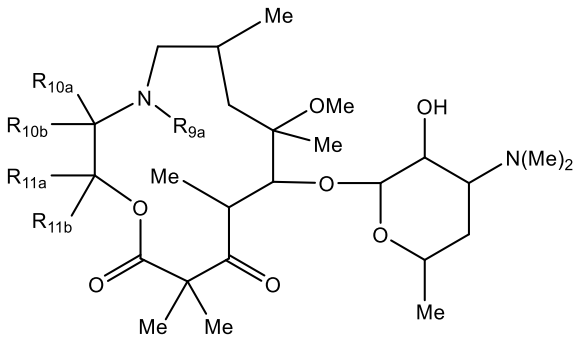
R_{9a} is selected from the group consisting of -H, -CO_2-alkylene-aryl, -C(=O)-alkyl, and optionally substituted C_{1-10} alkyl;

one of R_{10a} and R_{10b} is selected from the group consisting of –H, optionally substituted C_{1-10} alkyl, -CO_2H, and –CO_2-alkyl; and

the other of R_{10a} and R_{10b} is selected from the group consisting of optionally substituted saturated or partially unsaturated cycloalkyl containing at least one double bond, optionally substituted saturated or partially unsaturated heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; and

R_{11a} and R_{11b} are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl.

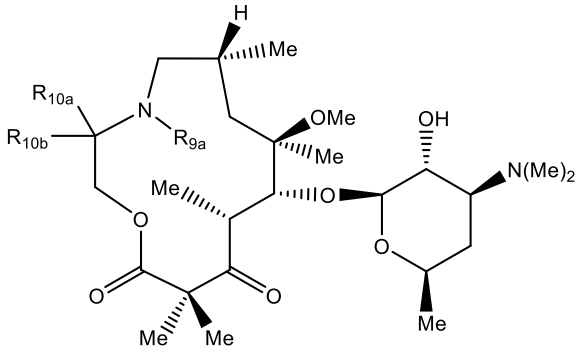
2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, which is a compound of formula IH:



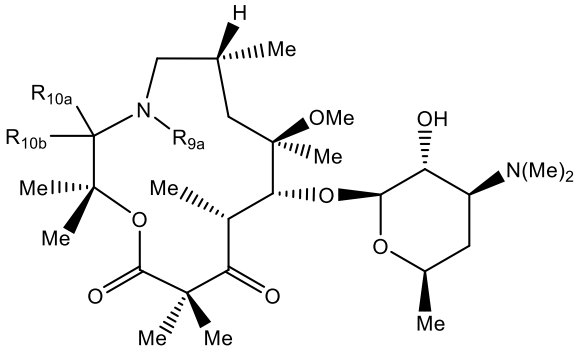
IH.

3. The compound of claim 2, or a pharmaceutically acceptable salt thereof, wherein one of R_{10a} and R_{10b} is methyl.

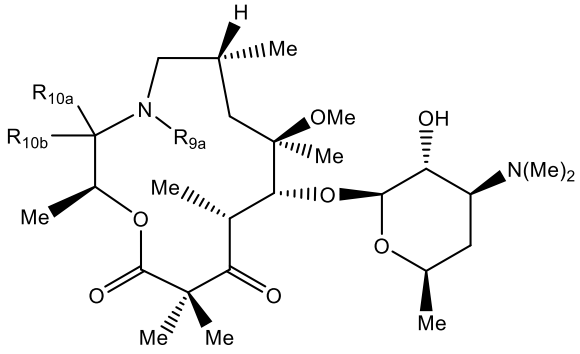
4. The compound of claim 2, or a pharmaceutically acceptable salt thereof, which is a compound of formula IIA, IIB, IIC, or IID:



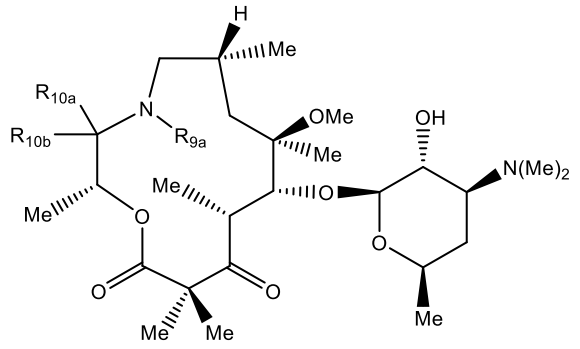
IIA;



IIB;



IIC;



IID.

5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein:

one of R_{10a} and R_{10b} is selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl, $-CO_2H$, and $–CO_2$-alkyl;

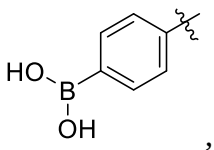
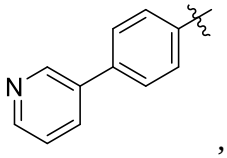
and the other of R_{10a} and R_{10b} is selected from the group consisting of optionally substituted saturated or partially unsaturated cycloalkyl, optionally substituted saturated or partially unsaturated heterocycloalkyl, optionally substituted aryl, and an optionally substituted heteroaryl.

6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted -arylene-R_{101};

R_{101} is selected from the group consisting of -H, halo, optionally substituted aryl, and optionally substituted heteroaryl.

7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is phenyl, bromophenyl, aminophenyl, , or , wherein "〰" indicates a point of attachment.

8. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted -heteroarylene-R_{101b};

R_{101b} is selected from the group consisting of -H, halo, optionally substituted aryl, and optionally substituted heteroaryl.

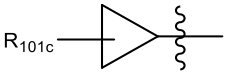
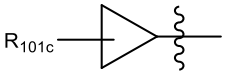
9. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted pyridyl.

10. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted saturated or partially unsaturated cycloalkyl selected from the group consisting of optionally substituted cyclopropyl, optionally substituted cyclobutyl, optionally substituted saturated or partially unsaturated cyclopentyl, optionally substituted saturated or partially unsaturated cyclohexyl, and optionally substituted saturated or partially unsaturated cycloheptyl.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted cyclopropyl  or , wherein "〰" indicates a point of attachment;

R_{101c} is selected from the group consisting of -H, halo, -OH, alkoxy, -$NR_xR_{x'}$, and alkylene-$R_{101c'}$, wherein $R_{101c'}$ is selected from the group consisting of -H, halo, -OH, alkoxy, and $NR_xR_{x'}$, wherein:

at each occurrence R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-N($R_{y'}$)($R_{y''}$); or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl; and wherein

$R_{y'}$ and $R_{y''}$ are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl; or

$R_{y'}$ and $R_{y''}$, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein R_{101c} is alkylene-$R_{101c'}$, wherein $R_{101c'}$ is selected from the group consisting of -H, halo, -OH, alkoxy, and -$NR_xR_{x'}$, wherein:

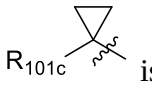
at each occurrence R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-N($R_{y'}$)($R_{y''}$); or

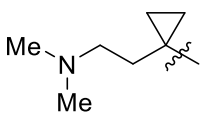
R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl; and wherein:

$R_{y'}$ and $R_{y''}$ are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl; or

$R_{y'}$ and $R_{y''}$, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein



is selected from the group consisting of


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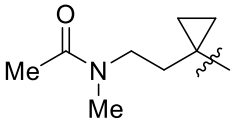
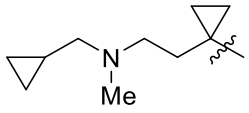
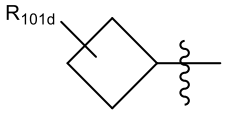


, and


, wherein "〰" indicates a point of attachment.

14. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted cyclobutyl , wherein "〰" indicates a point of attachment;

R_{101d} is selected from the group consisting of -H, halo, -OH, alkoxy, $-NR_xR_{x'}$, and -alkylene-$R_{101d'}$, wherein $R_{101d'}$ is selected the group consisting of -H, halo, -OH, alkoxy, and $-NR_xR_{x'}$, wherein:

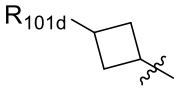
at each occurrence R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_{y'})(R_{y''})$; or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl; and wherein

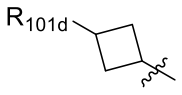
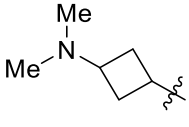
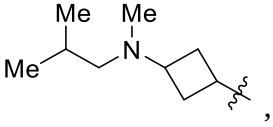
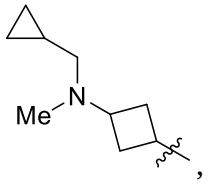
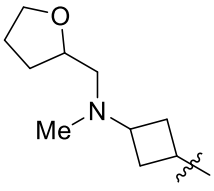
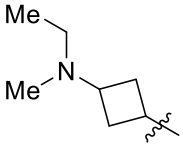
$R_{y'}$ and $R_{y''}$ are each independently selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl; or

$R_{y'}$ and $R_{y''}$, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

15. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is , wherein "〰" indicates a point of attachment.

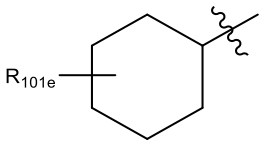
16. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein

 is selected from the group consisting of , , , , and , wherein "〰" indicates a point of attachment.

17. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted saturated or partially unsaturated cyclopentyl, optionally substituted saturated or partially unsaturated cyclohexyl, or optionally substituted saturated or partially unsaturated cycloheptyl.

18. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is 

wherein "〰" indicates a point of attachment;

R_{101e} is selected from the group consisting of -H, halo, -OH, alkoxy, $-NR_xR_{x'}$, halo, -OH, alkoxy, $-NR_{x'}R_{x'}$, -alkylene-$R_{101e'}$, wherein $R_{101e'}$ is selected from the group consisting of -H, halo, -OH, alkoxy, and $-NR_{x'}R_{x'}$ wherein:

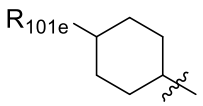
at each occurrence R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_{y'})(R_{y''})$; or

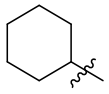
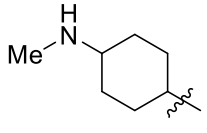
R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl; and wherein

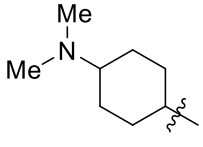
$R_{y'}$ and $R_{y''}$ are each independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl; or

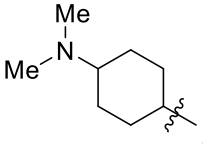
$R_{y'}$ and $R_{y''}$, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

19. The compound of claim 18, or a pharmaceutically acceptable salt thereof, wherein



is selected from the group consisting of , 

, 

, and 

, wherein "〰" indicates a point of attachment.

20. The compound of claim 18, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted heterocycloalkyl selected from the group consisting of optionally substituted aziridinyl, optionally substituted saturated or partially unsaturated pyrrolidinyl, and optionally substituted saturated or partially unsaturated piperidinyl.

21. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is azetidinyl optionally substituted with R_{101f}, wherein the point of attachment is on the azetidinyl;

R_{101f} is selected from the group consisting of -H, halo, optionally substituted alkyl, -OH, -CO_2H, -CO_2-alkyl, alkoxy, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, $NR_xR_{x'}$, -C(=O)-alkyl, -C(=O)- optionally substituted heterocycloalkyl, alkenyl, -C(=O)-optionally substituted alkylene-$R_{101f'}$, -alkylene-C(=O)-$R_{101f'}$ and -alkylene-$R_{101f'}$, wherein $R_{101f'}$ is selected from the group consisting of -H, halo, -OH, alkoxy, -CO_2H, CO_2- optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted hetercycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl, and -$NR_xR_{x'}$, wherein:

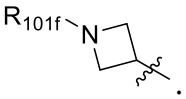
R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_y)_2$; or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, 7-, optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NR_y, and N-C_1-C_{10} alkyl; and wherein

each R_y is independently selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl; or

each R_y, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, 7, 8-, 9-, or 10-membered monocyclic or bicyclic ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

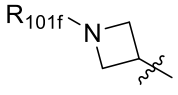
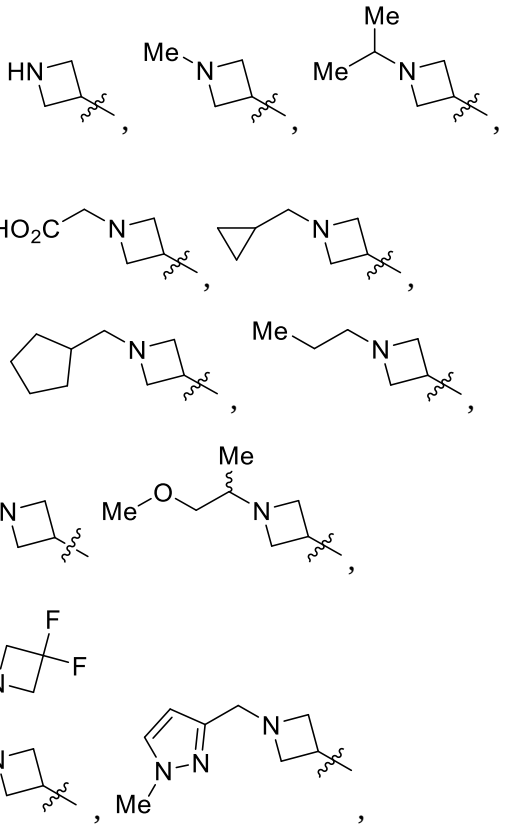
22. The compound of claim 21, or a pharmaceutically acceptable salt thereof, wherein:

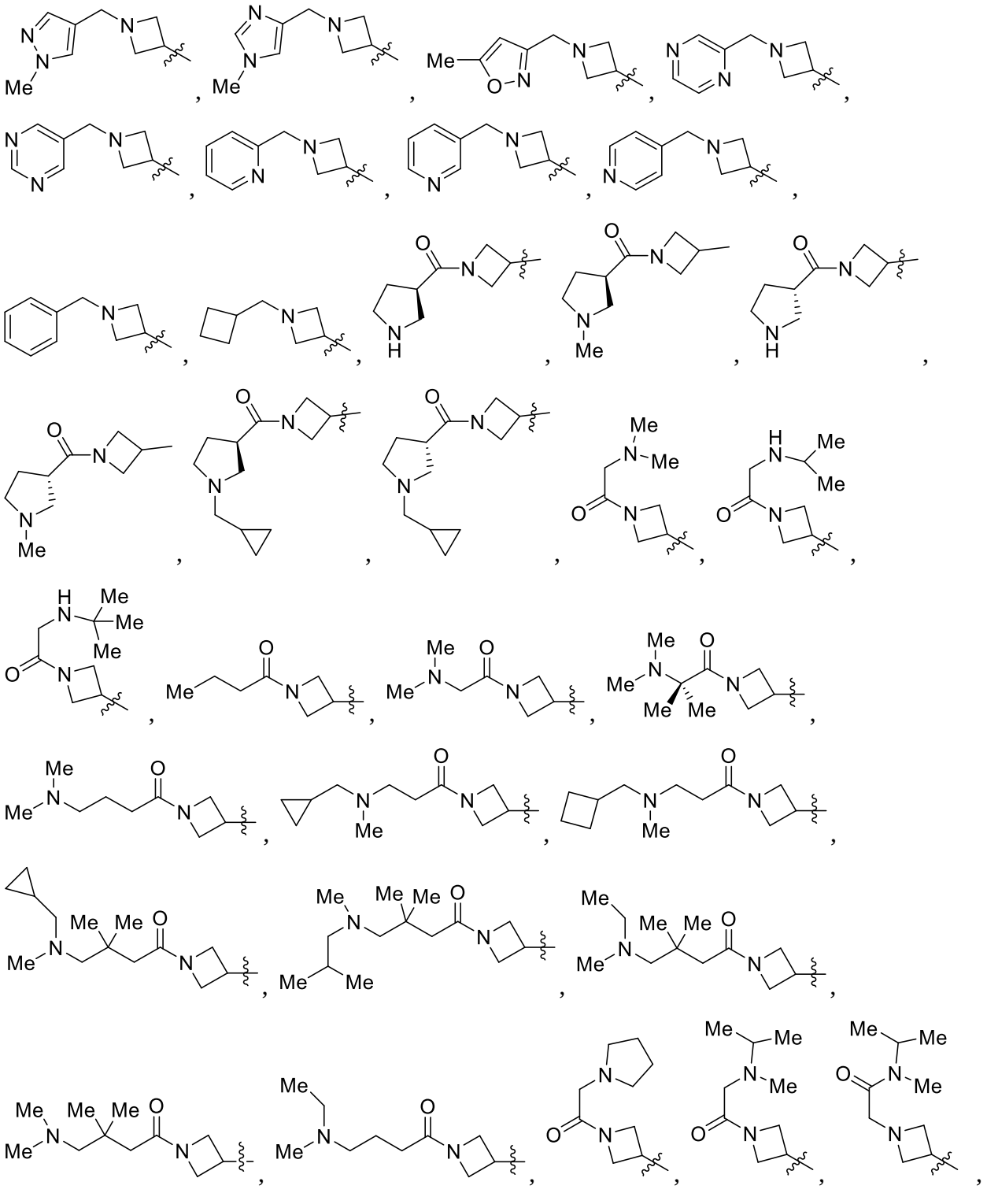
R_{10a} is .

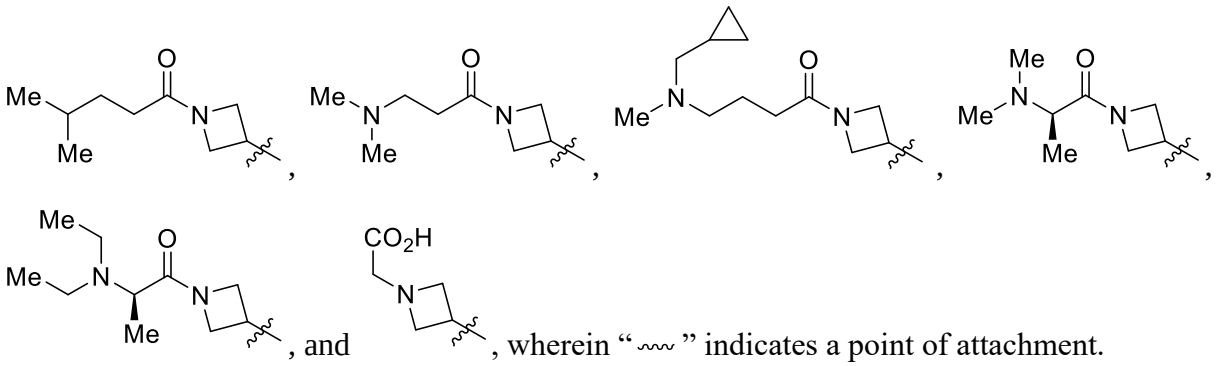
23. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein R_{101f} is selected from the group consisting of -CH_2-oxiranyl, -CH_2-oxetanyl, -CH_2-tetrahydrofuryl, aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, -CH_2-phenyl, -CH_2-pyridyl, -CH_2-pyrazinyl, -CH_2-pyrazolyl, -CH_2-imidazolyl, and -CH_2-oxazolyl.

24. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein R_{101f} is -C(=O)-$R_{101f'}$, wherein $R_{101f'}$ is selected from the group consisting of -CH_2-heterocycloalkyl, -CH_2-$NR_xR_{x'}$, -$C(Me)_2$-$NR_xR_{x'}$, -CH_2CH_3, -$CH_2CH_2CH_3$, -CH_2CH_2-$NR_xR_{x'}$, -$CH_2CH_2CH_2$-$NR_xR_{x'}$, -CH_2-heterocycloalkyl, -CHMe-$NR_xR_{x'}$, -CH_2-$NR_xR_{x'}$, and -CH_2-$C(Me)_2$-CH_2-$NR_xR_{x'}$.

25. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein R_{101f} is –CH_2-C(=O)-$R_{101f'}$, wherein $R_{101f'}$ is selected from the group consisting of -$NR_xR_{x'}$ and heterocycloalkyl.

26. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein  is selected from the group consisting of 





, and , wherein "〰" indicates a point of attachment.

27. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is saturated or partially unsaturated pyrrolidinyl optionally substituted with R_{101g}, wherein the point of attachment is the pyrrolidinyl;

R_{101g} is selected from the group consisting of -H, alkyl and -C(=O)-alkylene-$NR_xR_{x'}$; wherein:

R_{101g} is selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$NR_xR_{x'}$, wherein:

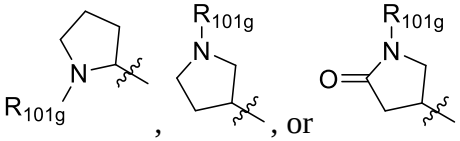
R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_y)_2$; or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NR_y, and N-C_1-C_{10} alkyl; and wherein

each R_y is independently selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl; or

each R_y, together with the atom to which they are attached, form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

28. The compound of claim 27, or a pharmaceutically acceptable salt thereof, wherein:

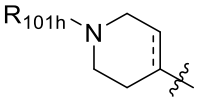
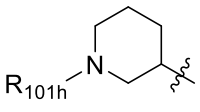
R_{10a} is 

, , or , wherein "〰" indicates a point of attachment.

29. The compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is optionally substituted saturated or partially unsaturated piperidinyl.

30. The compound of claim 29, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is , or , wherein "〰" indicates a point of attachment

R_{101h} is selected from the group consisting of -H, optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted alkoxy, optionally substituted hydroxyalkyl, optionally substituted alkenyl, optionally substituted -alkylene-cycloalkyl, optionally substituted -alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -SO_2-optionally substituted alkyl, -C(=O)-optionally substituted alkyl, -C(=O)-optionally substituted alkylene-cycloalkyl, -C(=O)-optionally substituted alkylene-heterocycloalkyl, and -C(=O)- optionally substituted alkylene-$NR_xR_{x'}$; wherein

R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_y)_2$; or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NR_y, and N-C_1-C_{10} alkyl; and wherein

each R_y is independently selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl; or

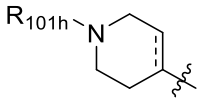
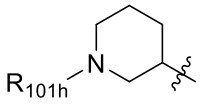
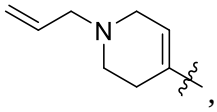
each R_y, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

31. The compound of claim 30, or a pharmaceutically acceptable salt thereof, wherein R_{101h} is selected from the group consisting of -H, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, neopentyl, trifluoromethyl, CF_3-CH_2-, CHF_2-CH_2-, -CH_2-cyclopropyl, -CH_2-cyclobutyl, -CH_2-cyclopentyl, -CH_2-cyclohexyl, –CHMe-CH_2-OMe, -CH_2-CH=$C(Me)_2$, -CH_2-CH=$C(Me)_2$, -CH_2-oxiranyl, -CH_2-oxetanyl, -CH_2-tetrahydrofuryl, aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, -CH_2-phenyl, -CH_2-pyridyl, -CH_2-pyrazinyl, -CH_2-pyrazolyl, -CH_2-imidazolyl, and -CH_2-oxazolyl.

32. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein R_{101h} is -C(=O)-$R_{101h'}$, wherein $R_{101h'}$ is selected from the group consisting of -CH_2-heterocycloalkyl, -CH_2-$NR_xR_{x'}$, and -$C(Me)_2$-$NR_xR_{x'}$.

33. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein R_{101h} is -C(=O)-$R_{101h'}$, wherein $R_{101h'}$ is selected from the group consisting of -CH_2CH_3, -$CH_2CH_2CH_3$, -CH_2CH_2-$NR_xR_{x'}$, -$CH_2CH_2CH_2$-$NR_xR_{x'}$, -CH_2-heterocycloalkyl, -CHMe-$NR_xR_{x'}$, -CH_2-$NR_xR_{x'}$, -CH_2-$C(Me)_2$-CH_2-$NR_xR_{x'}$, -$NR_xR_{x'}$ heterocycloalkyl, -SO_2-Me, -CH_2-CHOH-CH_2OH, -CH_2-$CHNH_2$-CH_2OH, and -CHMe-CH_2-OMe.

34. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein:


and

are selected from the group consisting of

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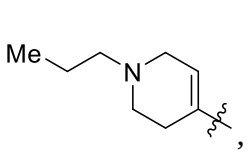
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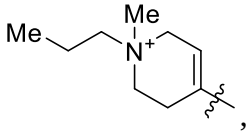
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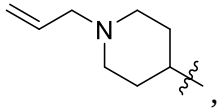
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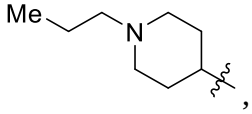
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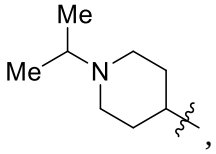
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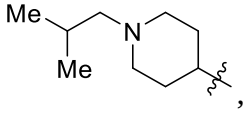
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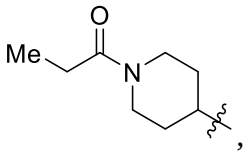
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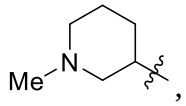
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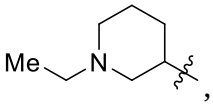
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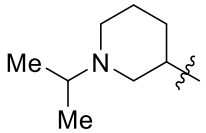
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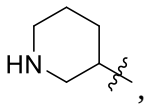
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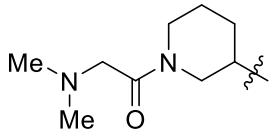
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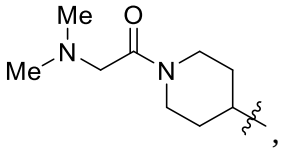
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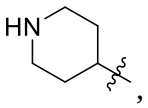
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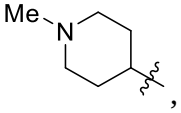
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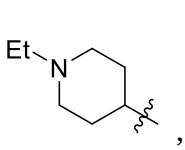
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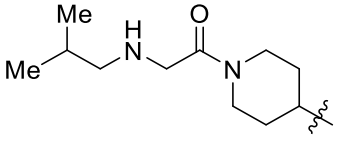
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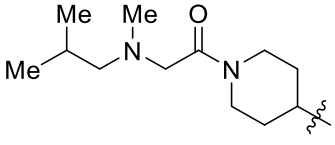
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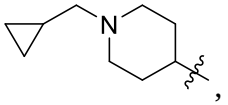
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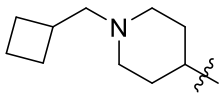
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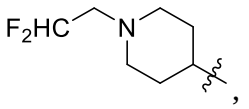
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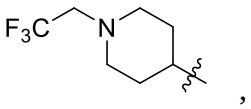
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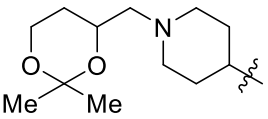
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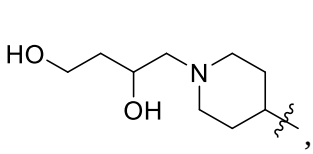
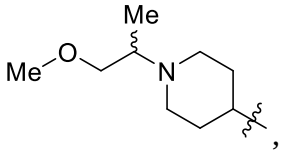
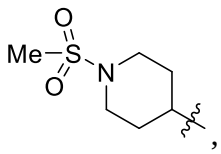
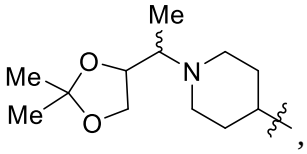
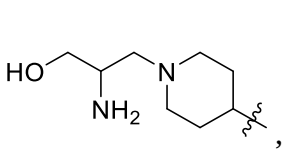
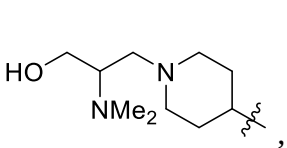
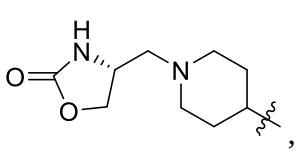
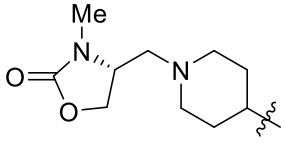
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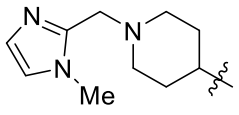
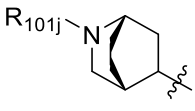

, wherein "〰" indicates a point of attachment.

35. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is , wherein "〰" indicates a point of attachment;

R_{101j} is selected from the group consisting of -H, optionally substituted alkyl, haloalkyl, alkoxy, hydroxyalkyl, optionally substituted alkenyl, -alkylene-optionally substituted cycloalkyl, -alkylene- optionally substituted heterocycloalkyl, alkylene- optionally substituted aryl, alkylene-optionally substituted heteroaryl, -SO_2-alkyl, -C(=O)-alkyl, -C(=O)-alkylene- optionally substituted cycloalkyl, -C(=O)-alkylene-heterocycloalkyl, and -C(=O)-alkylene-$NR_xR_{x'}$; wherein

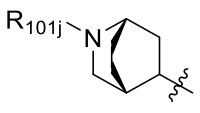
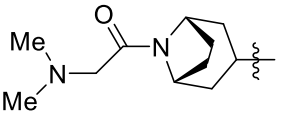
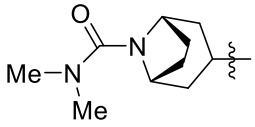
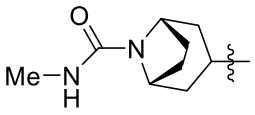
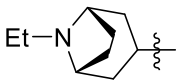
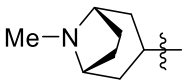
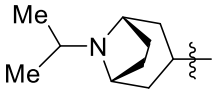
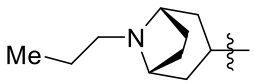
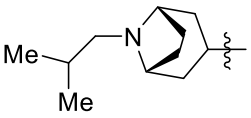
R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, -C(=O)-alkyl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_y)_2$; or

R_x and $R_{x'}$ together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NR_y, and N-C_1-C_{10} alkyl; and wherein

each R_y is independently selected from the group consisting of -H and optionally substituted C_{1-10} alkyl; or

each R_y, together with the atom to which they are attached form a 3-, 4-, 5-, 6-, or 7-membered ring optionally containing an additional heteroatom selected from the group consisting of O, S, SO, SO_2, NH, and N-C_1-C_{10} alkyl.

36. The compound of claim 35, or a pharmaceutically acceptable salt thereof, wherein:

, is selected from the group consisting of , , , , , , and , , wherein "〰" indicates a point of attachment.

37. A compound of claim 1 as depicted in Table A, or a pharmaceutically acceptable salt thereof.

38. A pharmaceutical composition comprising the compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

39. A kit comprising the compound of claim 1, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 38, and instructions for administering to a subject in need thereof.

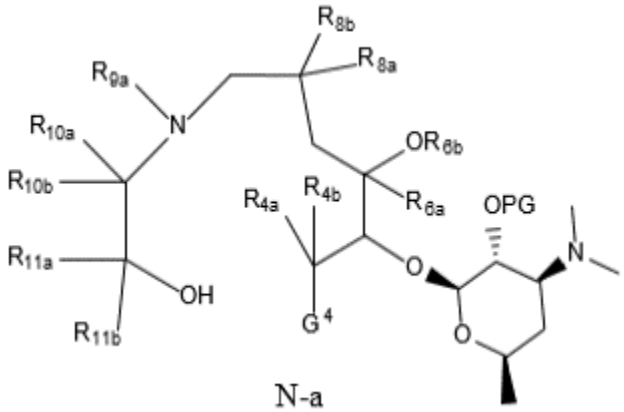
40. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 38, in the manufacture of a medicament for treating an infectious disease in a subject in need thereof.

41. The use of claim 40, wherein the infectious disease is a gram-positive or gram negative bacterial infection or a parasitic infection.

42. A compound of claim 1, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 38, for use in the treatment of an infectious disease in a subject in need thereof.

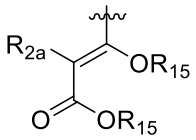
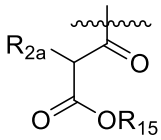
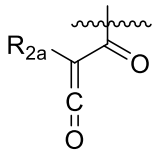
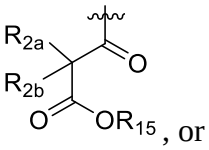
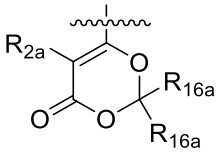
43. The compound or pharmaceutical composition for use of claim 42, wherein the infectious disease is a gram-positive or gram-negative bacterial infection or a parasitic infection.

44. A compound of formula N-a:



N-a

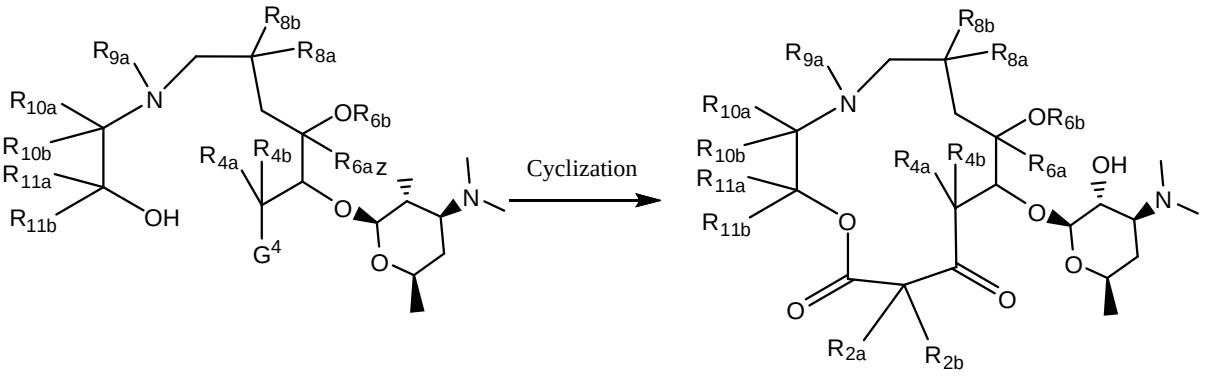
or a salt thereof, wherein R_{4a}, R_{4b}, R_5, R_{6a}, R_{6b}, R_{8a}, R_{8b}, R_{10a}, R_{10b}, R_{11a}, and R_{11b} are as defined in claim 1;

G^4 is , , , , or ;

each instance of R^{15} is independently silyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, or two R^{15} groups are joined to form an optionally substituted heterocyclyl or heteroaryl ring; and

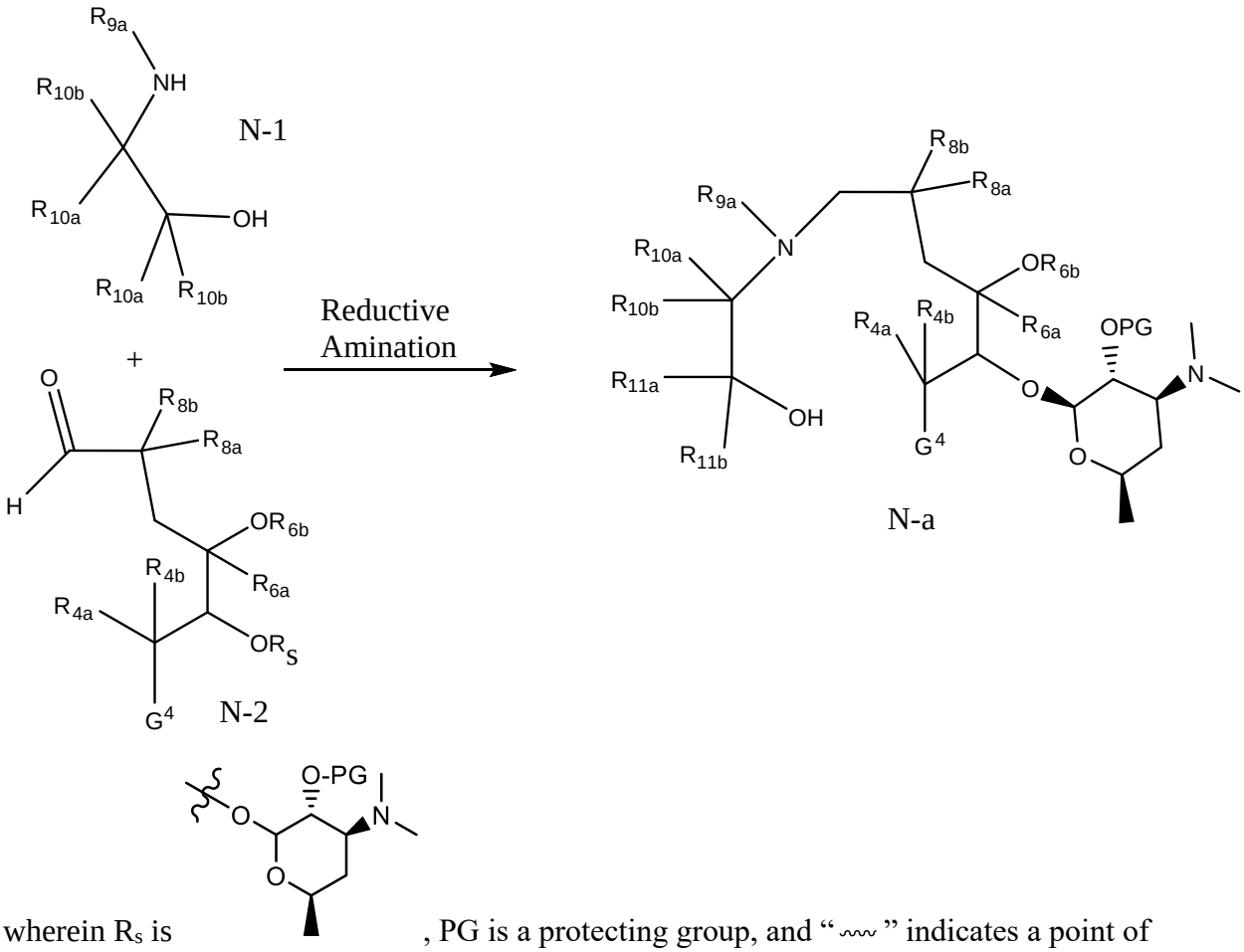
each instance of R^{16a} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and PG is a protecting group.

45. A process of preparing a compound of formula I of claim 1, comprising cyclization of a compound of formula N-a:



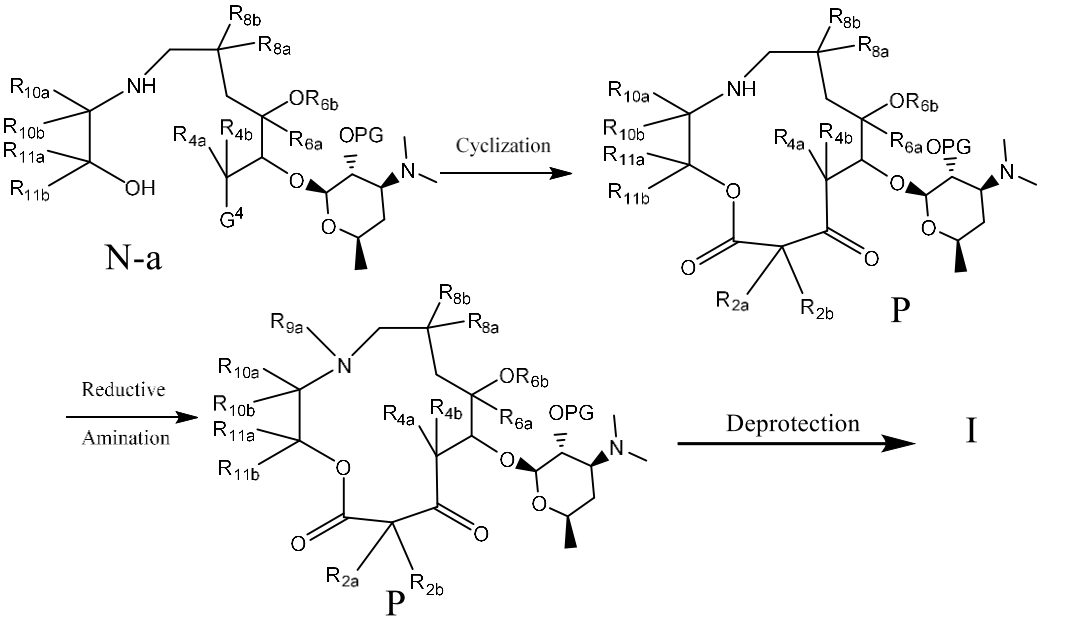
N-a I.

46. The process of claim 45, further comprising the step of preparing a compound of formula N-a, by combining N-1 with N-2 under reductive amination conditions:

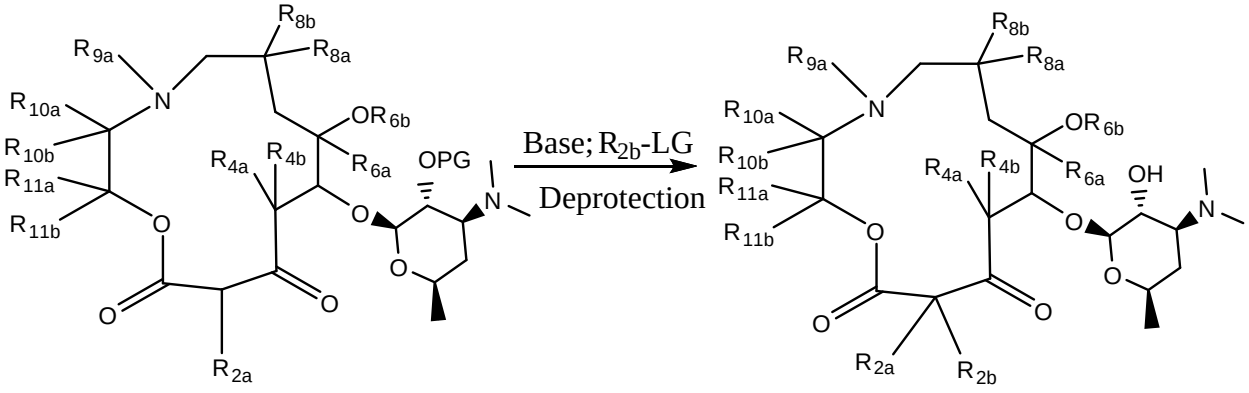


wherein R_s is , PG is a protecting group, and "〰" indicates a point of attachment.

47. A process of preparing a compound of formula I as defined in claim 1 wherein R_{9a} is C_{1-10} alkyl, hydroxyalkyl, or alkoxyalkyl; comprising cyclizing a compound of formula N-a wherein R_{9a} is H to provide a compound of formula P wherein R_{9a} is H; followed by reductive amination and deprotection to provide a compound of formula I wherein R_{9a} is C_{1-10} alkyl, hydroxyalkyl, or alkoxyalkyl



48. A process of preparing a compound of formula I as defined in claim 1, comprising alkylating a compound of formula A with R_{2b}-LG in the presence of base, wherein LG is a leaving group, to provide after deprotection a compound of formula I



A I.