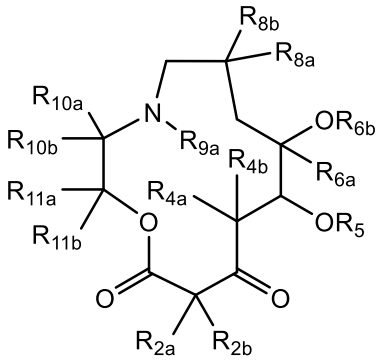
and the ribosome. See, *e.g.*, Ma *et al.*, *Curr. Med. Chem.* (2011) 18:1993-2015; Ma *et al.*, *Mini-Rev. Med. Chem.* (2010) 10:272-286. Despite greatly improved ribosomal binding, ketolides such as telithromycin and solithromycin have not addressed several of the newest forms of macrolide resistance 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:



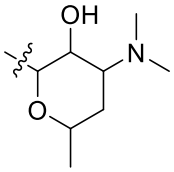
I

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, substituted 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, C_{1-10} alkyl, C_{1-10} hydroxyalkyl, allyl, haloalkyl, aryl, heteroalkenyl, heterocycloalkyl, or heteroaryl, any of which can be optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

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, optionally substituted C_{1-10} alkyl, hydroxyalkyl, optionally substituted C_{1-10} alkylene-$NR_TR_{T'}$, optionally substituted C_{1-10} alkylene-cycloalkyl-$NR_TR_{T'}$, and optionally substituted alkoxyalkyl; wherein R_T and $R_{T'}$ are each independently selected from the group consisting of H, optionally substituted alkyl, and optionally substituted C_{1-10} alkylene-heterocycloalkyl;

one of R_{10a} and R_{10b} is selected from the group consisting of H, optionally substituted C_{1-10} alkyl, optionally substituted C_{1-10} alkoxy, and the other of R_{10a} and R_{10b} is selected from the group consisting of -CO_2H, –CO_2-optionally substituted alkyl, –$CON(R_{z'})(R_{z''})$, optionally substituted C_{1-10} alkylene-R_{101}, optionally substituted C_{2-10} alkenylene-R_{101}, and optionally substituted C_{2-10} alkynylene-R_{101}; wherein:

R_{101} is selected from the group consisting of H, (C_{1-6} alkyl)-S-, (C_{1-6} alkyl)-SO-, (C_{1-6} alkyl)-SO_2-, -OH, optionally substituted -O-(C_{1-6} alkyl), -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein:

$R_{z'}$ and $R_{z''}$ are each independently H or optionally substituted alkyl;

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

R_x and $R_{x'}$ together with the atom to which they are attached form an optionally substituted 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; 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 another aspect of the present disclosure, there is provided a compound disclosed herein as depicted in Table A, or a pharmaceutically acceptable salt thereof.

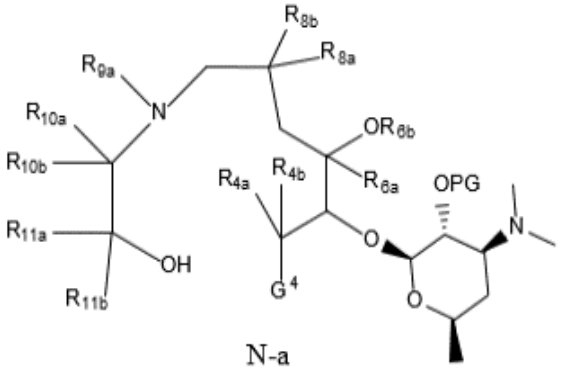
[0005c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

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

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

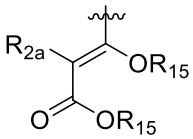
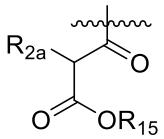
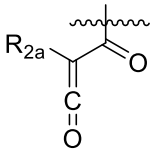
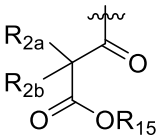
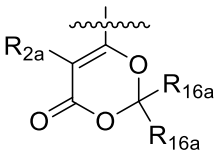
[0005f] In another aspect of the present disclosure, there is provided a compound disclosed herein or pharmaceutically acceptable salt thereof, or a pharmaceutical composition also disclosed herein, for use in the treatment of an infectious disease in a subject in need thereof.

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



N-a

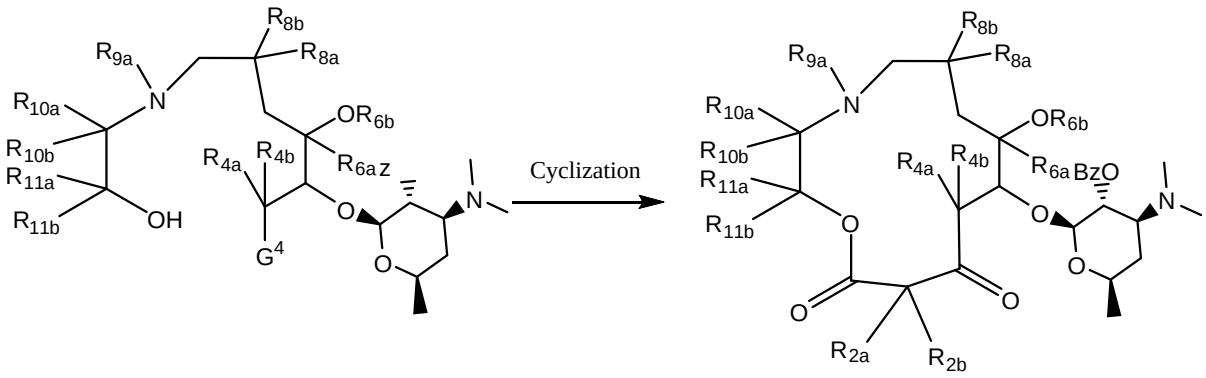
or a salt thereof, wherein R_{4a}, R_{4b}, R_5, R_{6a}, R_{6b}, R_{8a}, R_{8b}, R_{10a}, R_{10b}, R_{11a}, and R_{11b} are as disclosed herein;

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

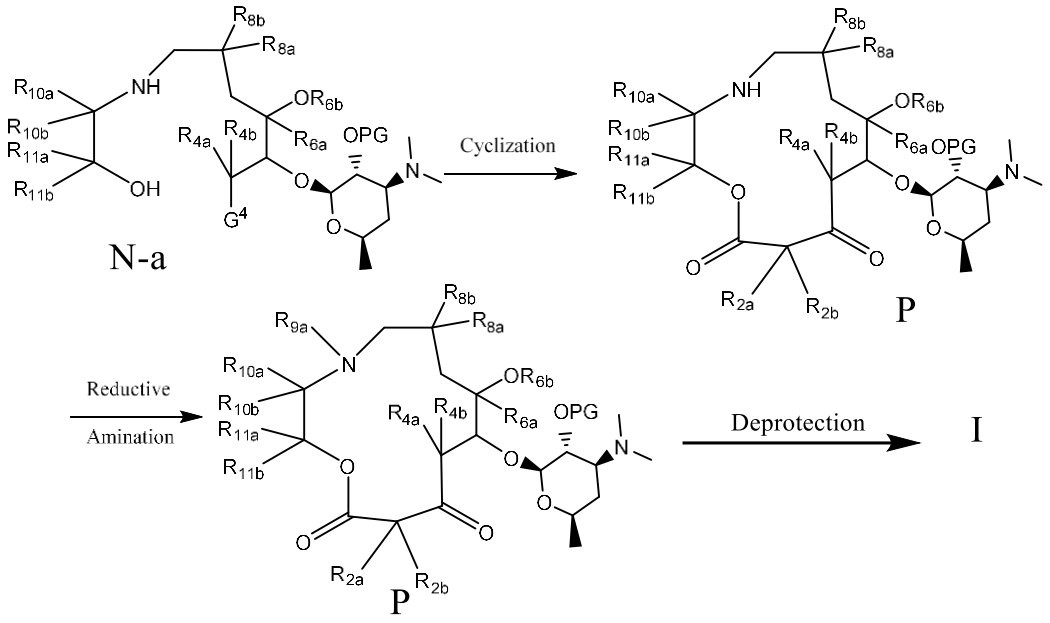
each instance of R^{16a} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and PG is a protecting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

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

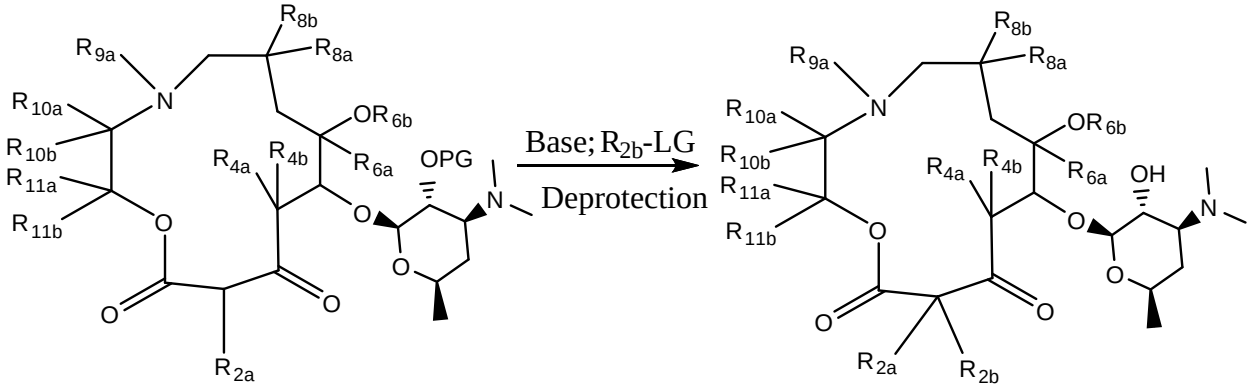


N-a I.

[0005i] In a further aspect of the present disclosure, there is provided a process of preparing a compound of formula I as disclosed herein; 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



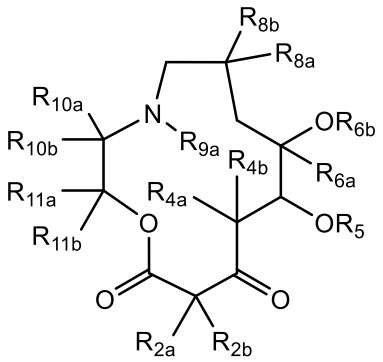
[0005j] In another aspect of the present disclosure, there is provided a process of preparing a compound of formula I as disclosed herein, comprising alkylating a compound of formula A with R_{2b}-LG in the presence of base, wherein LG is a leaving group, to provide after deprotection a compound of formula I



A I.

[0006] Disclosed herein are compounds that are novel, synthetically accessible 13-membered macrolides. The 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 $C_{1\text{-}10}$ alkyl, optionally substituted $C_{1\text{-}10}$ alkoxy, and optionally substituted $C_{1\text{-}10}$ alkenyl, wherein $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, and $C_{1\text{-}10}$ 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 $C_{1\text{-}10}$ alkyl, optionally substituted $C_{1\text{-}10}$ alkoxy, and optionally substituted $C_{1\text{-}10}$ alkenyl, wherein $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, and $C_{1\text{-}10}$ alkenyl are optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, substituted amino, alkyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

aryl, optionally substituted alkylene-heteroaryl, -C(=O)-alkyl, and -C(=O)-alkylene-$N(R_{y'})(R_{y''})$, wherein $R_{y'}$ and $R_{y''}$ are each independently H or optionally substituted alkyl; or

R_x and $R_{x'}$ together with the atom to which they are attached form an optionally substituted 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; 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.

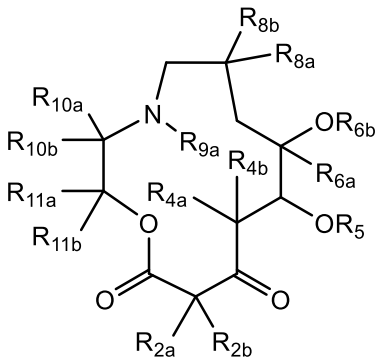
[0010] The details of certain examples of the present disclosure are set forth in the Detailed Description of Certain Embodiments, as described below. Other features, objects, and advantages of the present disclosure will be apparent from the Definitions, Drawings, Examples, and Claims.

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).

CLAIMS

1. A compound of Formula I:



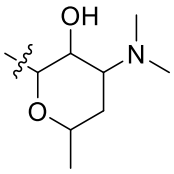
I

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, substituted 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, C_{1-10} alkyl, C_{1-10} hydroxyalkyl, allyl, haloalkyl, aryl, heteroalkenyl, heterocycloalkyl, or heteroaryl, any of which can be optionally substituted with one or more groups selected from the group consisting of halo, aryl, amino, heteroalkyl, heteroalkenyl, heterocycloalkyl, and heteroaryl;

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

R_{9a} is selected from the group consisting of H, optionally substituted $C_{1\text{-}10}$ alkyl, hydroxyalkyl, optionally substituted $C_{1\text{-}10}$ alkylene-$NR_TR_{T'}$, optionally substituted $C_{1\text{-}10}$ alkylene-cycloalkyl-$NR_TR_{T'}$, and optionally substituted alkoxyalkyl; wherein R_T and $R_{T'}$ are each independently selected from the group consisting of H, optionally substituted alkyl, and optionally substituted $C_{1\text{-}10}$ alkylene-heterocycloalkyl;

one of R_{10a} and R_{10b} is selected from the group consisting of H, optionally substituted $C_{1\text{-}10}$ alkyl, optionally substituted $C_{1\text{-}10}$ alkoxy, and the other of R_{10a} and R_{10b} is selected from the group consisting of -CO_2H, –CO_2-optionally substituted alkyl, –$CON(R_{z'})(R_{z''})$, optionally substituted $C_{1\text{-}10}$ alkylene-R_{101}, optionally substituted $C_{2\text{-}10}$ alkenylene-R_{101}, and optionally substituted $C_{2\text{-}10}$ alkynylene-R_{101}; wherein:

R_{101} is selected from the group consisting of H, ($C_{1\text{-}6}$ alkyl)-S-, ($C_{1\text{-}6}$ alkyl)-SO-, ($C_{1\text{-}6}$ alkyl)-SO_2-, -OH, optionally substituted -O-($C_{1\text{-}6}$ alkyl), -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein:

$R_{z'}$ and $R_{z''}$ are each independently H or optionally substituted alkyl;

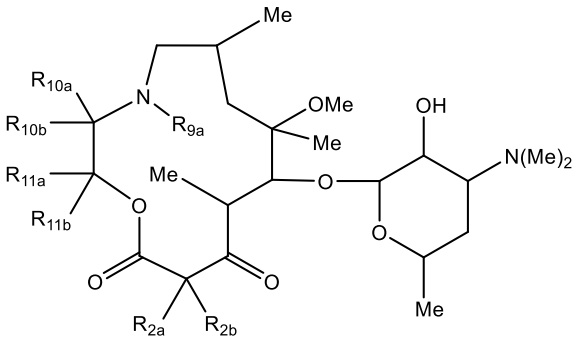
R_x and $R_{x'}$ are each independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkylene-cycloalkyl, optionally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

R_x and $R_{x'}$ together with the atom to which they are attached form an optionally substituted 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; and

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

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



IG.

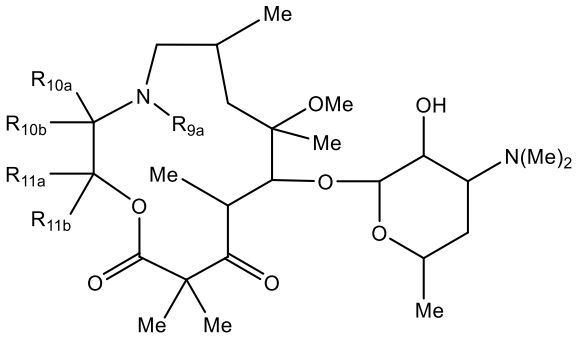
3. The compound of claim 2, or a pharmaceutically acceptable salt thereof, wherein R_{9a} is -H or C_{1-4} alkyl.

4. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein R_{11a} and R_{11b} are each methyl.

5. The compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein one of R_{2a} and R_{2b} is optionally substituted C_{1-10} alkyl.

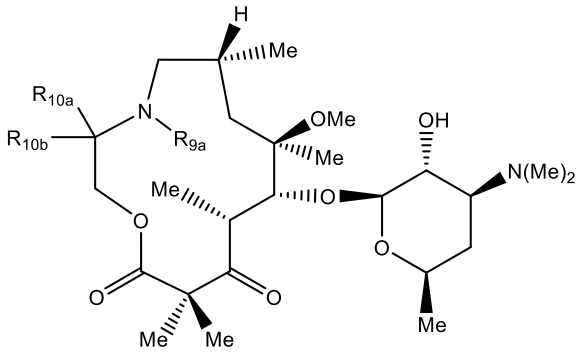
6. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein one of R_{2a} and R_{2b} is methyl and the other is halo.

7. The compound of claim 3, or a pharmaceutically acceptable salt thereof, which is a compound of formula IH:

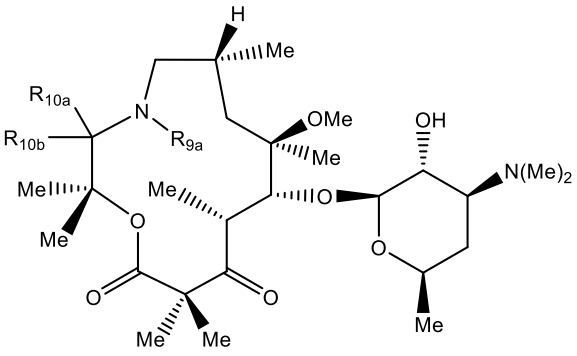


IH.

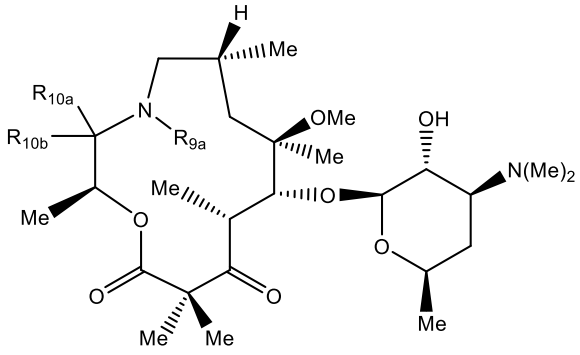
8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, which is a compound of formula IIA, IIB, IIC, or IID:



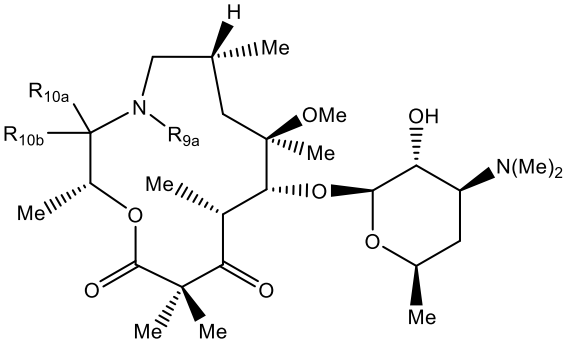
IIA;



IIB;



IIC;



IID;

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

the other of R_{10a} and R_{10b} is selected from the group consisting of -CO_2H, –CO_2-optionally substituted alkyl, –$CON(R_{z'})(R_{z''})$, optionally substituted C_{1}-$_{10}$ alkylene-R_{101}, C_{2}-$_{10}$ alkenylene-R_{101}, and C_{2}-$_{10}$ alkynylene-R_{101}; wherein

R_{101} is selected from the group consisting of H, ($C_{1\text{-}6}$ alkyl)-S-, ($C_{1\text{-}6}$ alkyl)-SO-, ($C_{1\text{-}6}$ alkyl)-SO_2-, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkylene-cycloalkyl, optionally substituted alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -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 an optionally substituted 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.

9. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein R_{9a} is –H, methyl, ethyl, propyl, isopropyl, butyl, or isobutyl.

10. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein R_{10a} is selected from the group consisting of optionally substituted C_{1-10} alkylene-R_{101}, C_{2-10} alkenylene-R_{101}, and C_{2-10} alkynylene-R_{101}; wherein:

R_{101} is selected from the group consisting of H, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein R_{101} is selected from the group consisting H, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkylene-cycloalkyl, optionally substituted alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -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 an optionally substituted 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; and

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

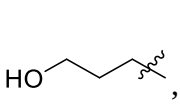
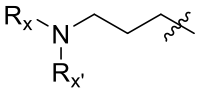
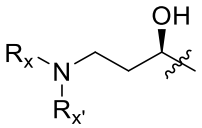
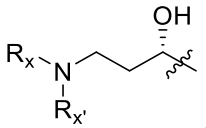
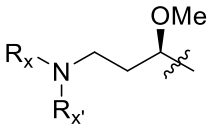
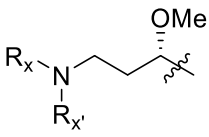
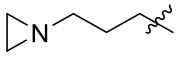
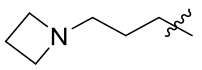
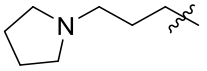
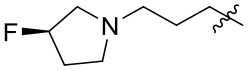
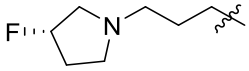
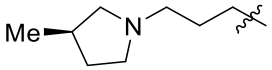
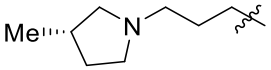
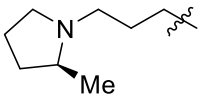
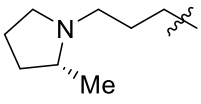
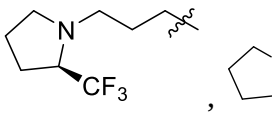
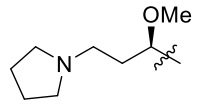
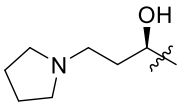
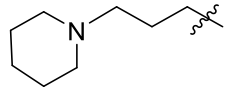
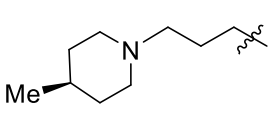
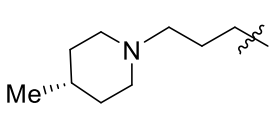
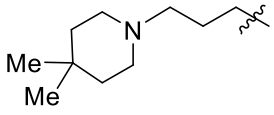
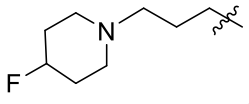
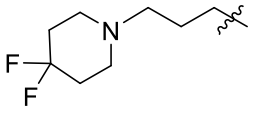
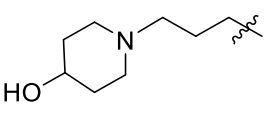
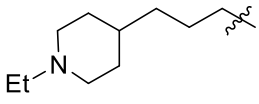
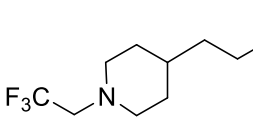
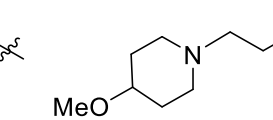
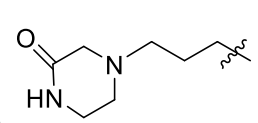
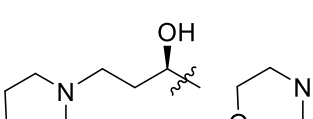
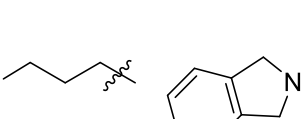
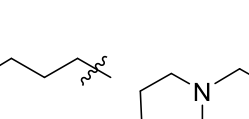
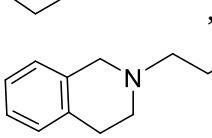
11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R_{10a} is -C_1-C_{10} alkylene-R_{101a};

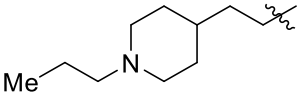
R_{101a} is selected from the group consisting of H, (C_{1-6} alkyl)-S-, (C_{1-6} alkyl)-SO-, (C_{1-6} alkyl)-SO_2-, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein R_x and $R_{x'}$ are each independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted hydroxyalkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted

heteroaryl, optionally substituted alkylene-cycloalkyl, optionally substituted alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -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 an optionally substituted 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 whereineach R_y is independently selected from the group consisting of -H and optionally substituted $C_{1\text{-}10}$ alkyl.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof,

wherein R_{10a} is selected from the group consisting of:  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , and ; wherein

$NR_xR_{x'}$ is selected from the group consisting of -N(Me)(Et), -$N(Me)_2$, -N(Me)(t-Bu), -N(Me)(iPr), -NH(Me), -NH(iPr), -$N(Et)_2$, -N(Me)(cyclopropyl), -NH(cyclopropyl), -N(Me)(cyclobutyl), -NH(cyclobutyl), -N(Me)(cyclopentyl), -NH(cyclopentyl), -N(Me)(cyclohexyl), and -NH(cyclohexyl);

$MeSCH_2CH_2$-, $MeSOCH_2CH_2$-, $MeSO_2CH_2CH_2$-, 

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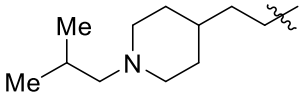
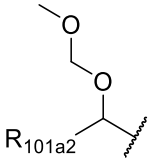


, and wherein "〰" indicates a point of attachment.

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

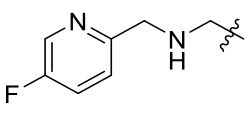
R_{10a} is an optionally substituted R_{101a2}-CH_2-, R_{101a2}-CH(OH)-, R_{101a2}-CH(OMe)-,



, or R_{101a2}-C(=O)-, wherein "〰" indicates a point of attachment; and

R_{101a2} is selected from the group consisting of -H, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein R_x and $R_{x'}$ are each independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkylene-cycloalkyl, optionally substituted alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -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 an optionally substituted 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 whereineach R_y is independently selected from the group consisting of H and optionally substituted $C_{1\text{-}10}$ alkyl.

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

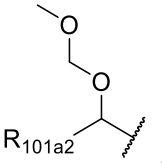
R_{101a2}-CH_2- is -CH_2NHMe, -$CH_2N(Me)_2$, -$CH_2N(Me)$(cyclopropyl), -CH_2NH(oxetanyl), -CH_2NHCH_2(cyclopropyl), and 

, wherein "〰" indicates a point of attachment.

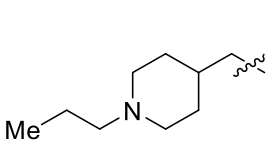
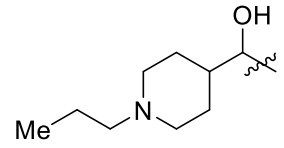
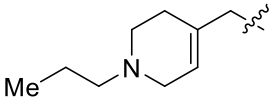
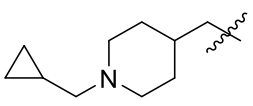
15. The compound of claim 13 or a pharmaceutically acceptable salt thereof, wherein:

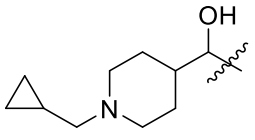
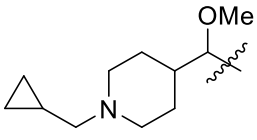
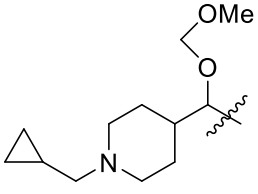
R_{10a} is R_{101a2}-CH_2-; and

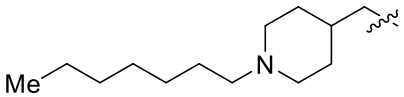
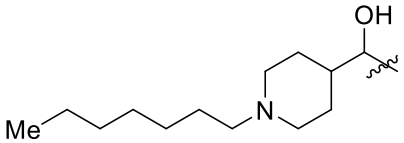
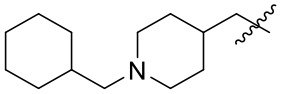
R_{101a2} is selected from the group consisting of optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl.

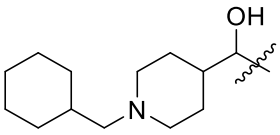
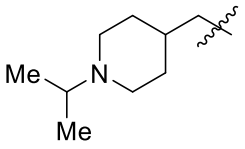
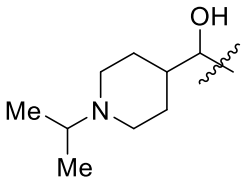
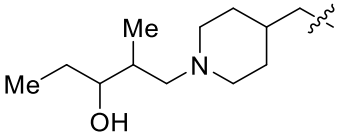
16. The compound of claim 13 or a pharmaceutically acceptable salt thereof, wherein R_{10a} is an optionally substituted R_{101a2}-CH_2-, R_{101a2}-CH(OH)-, R_{101a2}-CH(OMe)-,  , or R_{101a2}-C(=O)-, wherein "〰" indicates a point of attachment; and

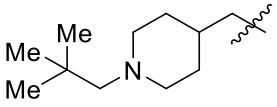
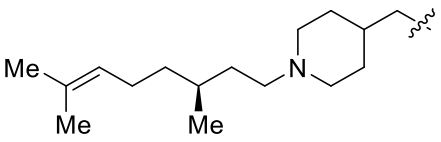
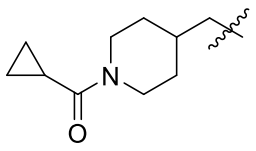
R_{101a2} is an optionally substituted piperidinyl selected from the group consisting of

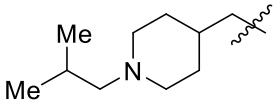
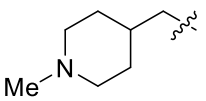
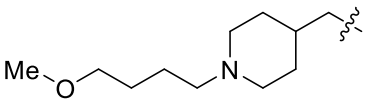
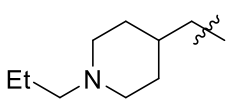
 ,  ,  ,  ,

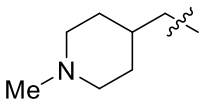
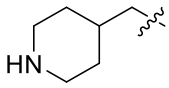
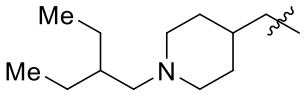
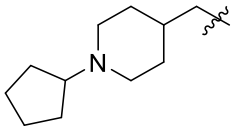
 ,  ,  ,

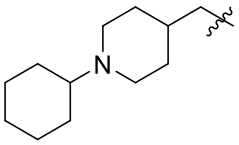
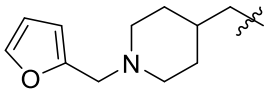
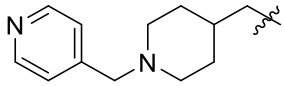
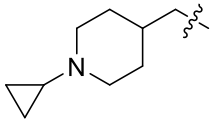
 ,  ,  ,

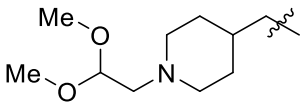
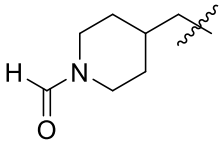
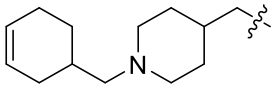
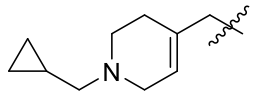
 ,  ,  ,  ,

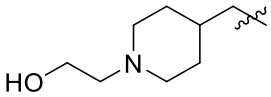
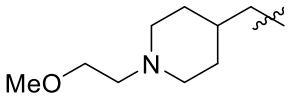
 ,  ,  ,

 ,  ,  ,  ,

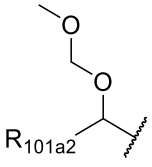
 ,  ,  ,  ,

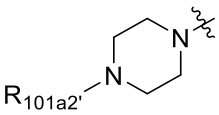
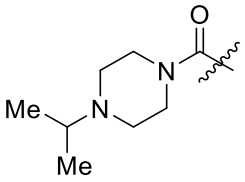
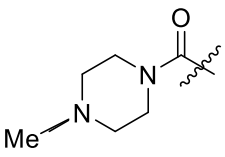
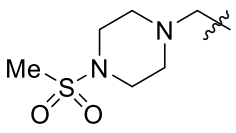
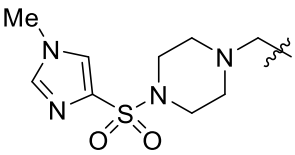
 ,  ,  ,  ,

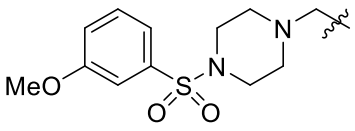
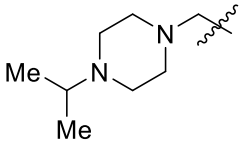
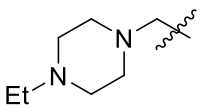
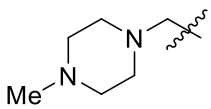
 ,  ,  ,  ,

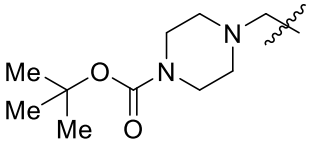
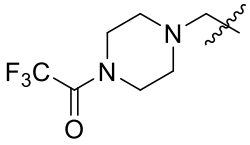
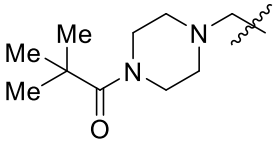
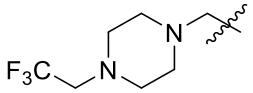
 , and  , wherein "〰" indicates a point of attachment.

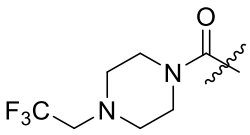
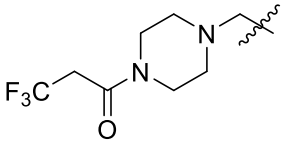
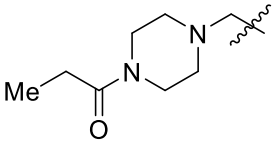
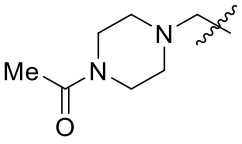
17. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein: R_{10a} is an optionally substituted R_{101a2}-CH_2-, R_{101a2}-CH(OH)-, R_{101a2}-CH(OMe)-,

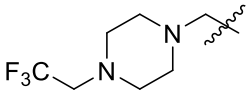
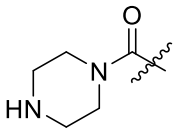
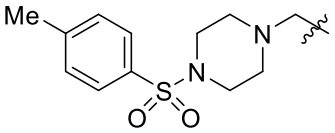
 , or R_{101a2}-C(=O)-, wherein "〰" indicates a point of attachment; and

R_{101a2} is an optionally substituted  selected from the group consisting of  ,  ,  ,  ,

 ,  ,  ,  ,

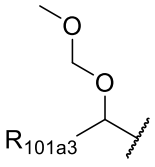
 ,  ,  ,  ,

 ,  ,  ,  ,

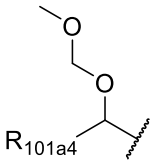
 ,  ,  , and  ,

wherein "〰" indicates a point of attachment.

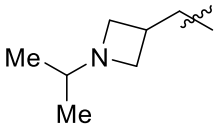
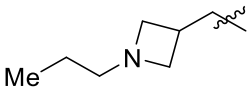
18. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein: R_{10a} is an optionally substituted R_{101a3}-CH_2-, R_{101a3}-CH(OH)-, R_{101a3}-CH(OMe)-,

 , or R_{101a3}-C(=O)-, wherein "〰" indicates a point of attachment; and R_{101a3} is an optionally substituted heteroaryl.

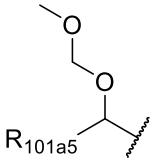
19. The compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein: R_{10a} is an optionally substituted R_{101a4}-CH_2-, R_{101a4}-CH(OH)-, R_{101a4}-CH(OMe)-,

 , or R_{101a4}-C(=O)-, wherein "〰" indicates a point of attachment; and R_{101a4} is an optionally substituted azetidinyl.

20. The compound of claim 19, or a pharmaceutically acceptable salt thereof, wherein: R_{10a} is an optionally substituted azetidinyl-CH_2- selected from the group consisting of

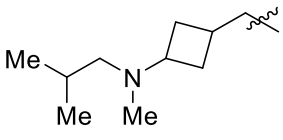
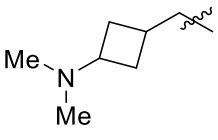
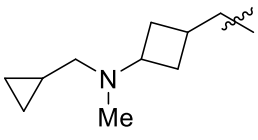
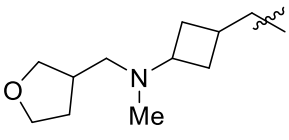
 and  , wherein "〰" indicates a point of attachment.

21. The compound of claim 14, or a pharmaceutically acceptable salt thereof, wherein: R_{10a} is an optionally substituted R_{101a5}-CH_2-, R_{101a5}-CH(OH)-, R_{101a5}-CH(OMe)-,

 , or R_{101a5}-C(=O)-, wherein "〰" indicates a point of attachment; and R_{101a5} is an optionally substituted cyclobutyl.

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

R_{101}-CH_{2}- is an optionally substituted cyclobutyl selected from the group consisting of


, 
, 
, and 
,

wherein "〰" indicates a point of attachment.

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

R_{10a} is an optionally substituted C_{2-10} alkenylene-R_{101};

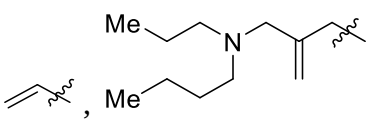
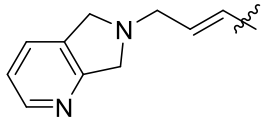
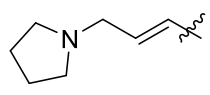
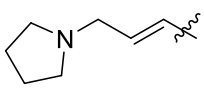
R_{101} is selected from the group consisting of -H, -OH, -O-alkyl, -$NR_xR_{x'}$, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl; wherein

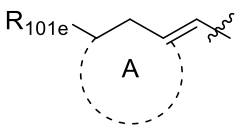
R_x and $R_{x'}$ are each independently selected from the group consisting of -H, optionally substituted alkyl, optionally substituted carbocyclyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkylene-cycloalkyl, optionally substituted alkylene-heterocycloalkyl, optionally substituted alkylene-aryl, optionally substituted alkylene-heteroaryl, -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 an optionally substituted 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.

24. The compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein R_{10a} is an optionally substituted C_{2-5} alkenylene-R_{101} selected from the group consisting of


, 
, 
, and 
.

25. The compound of claim 23 or a pharmaceutically acceptable salt thereof, wherein R_{10a} is an optionally substituted alkenylene-R_{101} which is 
, wherein A is an optionally substituted cycloalkyl or heterocycloalkyl and R_{101e} is selected from the group consisting of -H, alkyl, and -$NR_xR_{x'}$, wherein R_x and $R_{x'}$ are each independently selected from

the group consisting of -H and optionally substituted alkyl, and wherein "〰" indicates a point of attachment.

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

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

28. A kit comprising a compound of claim 1, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 27, and instructions for administering to a subject in need thereof.

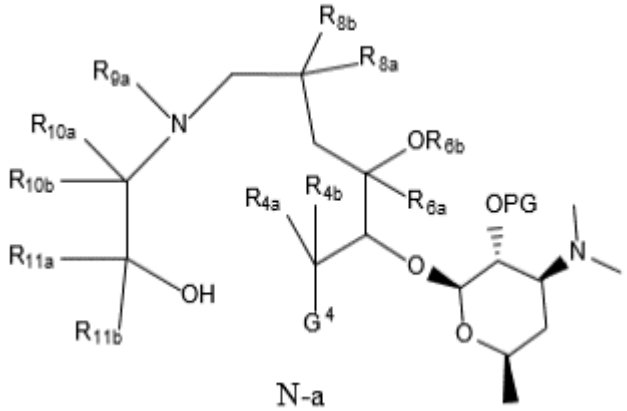
29. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 27, in the manufacture of a medicament for treating an infectious disease in a subject in need thereof.

30. The use of claim 29, wherein the infectious disease is a gram-negative or gram-positive bacterial infection or a parasitic infection.

31. A compound of claim 1 or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 27, for use in the treatment of an infectious disease in a subject in need thereof.

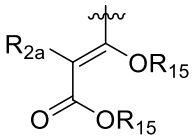
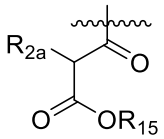
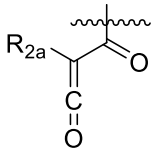
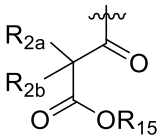
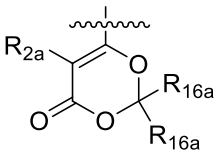
32. The compound or pharmaceutical composition for use of claim 31, wherein the infectious disease is a gram-positive or gram-negative bacterial infection or a parasitic infection.

33. A compound of formula N-a:



N-a

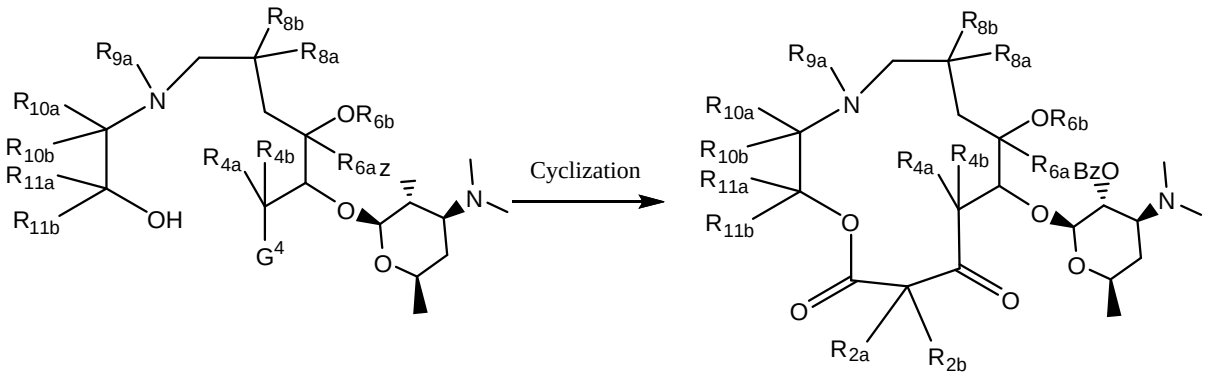
or a salt thereof, wherein R_{4a}, R_{4b}, R_5, R_{6a}, R_{6b}, R_{8a}, R_{8b}, R_{10a}, R_{10b}, R_{11a}, and R_{11b} are as defined in claim 1;

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

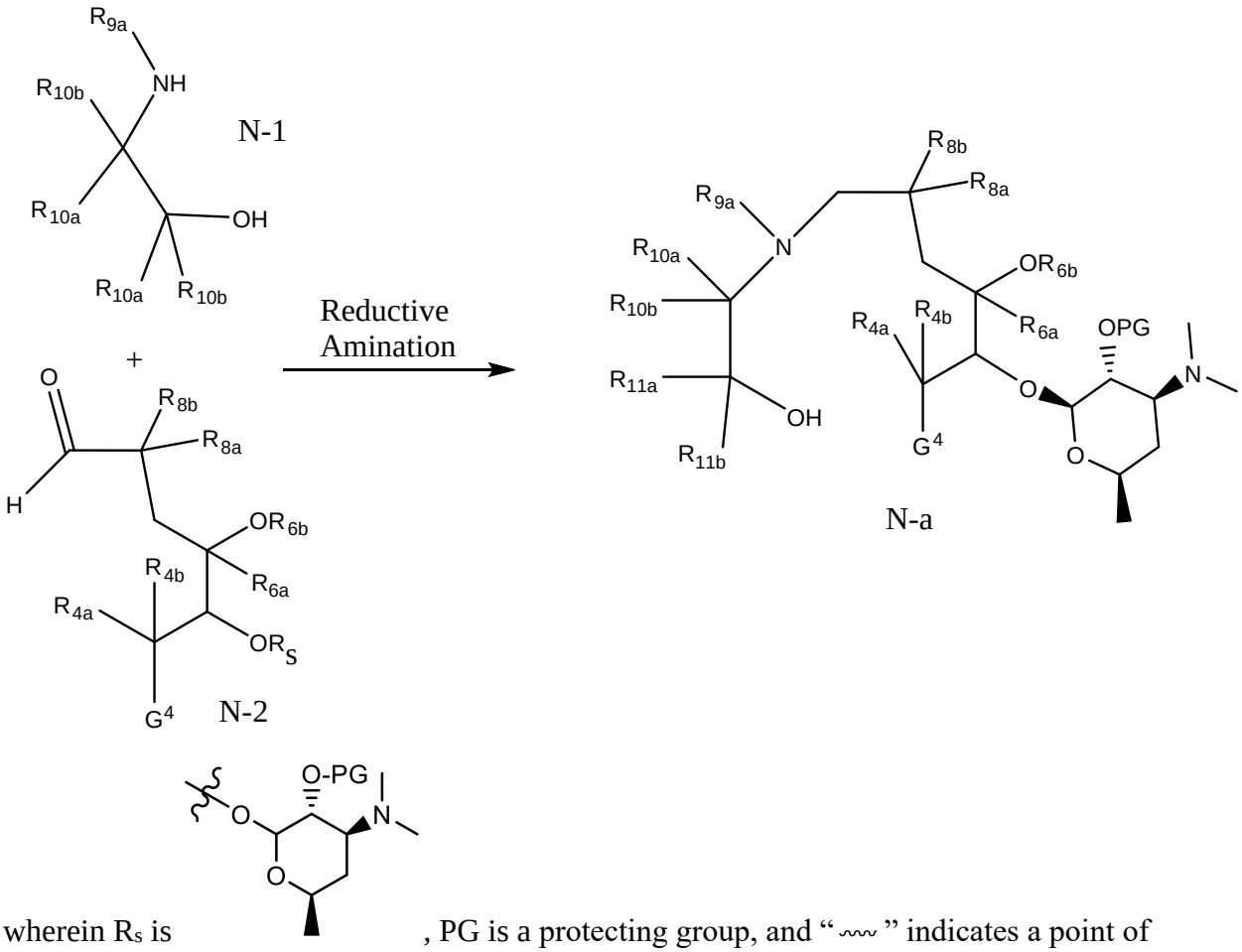
each instance of R^{16a} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl; and PG is a protecting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

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



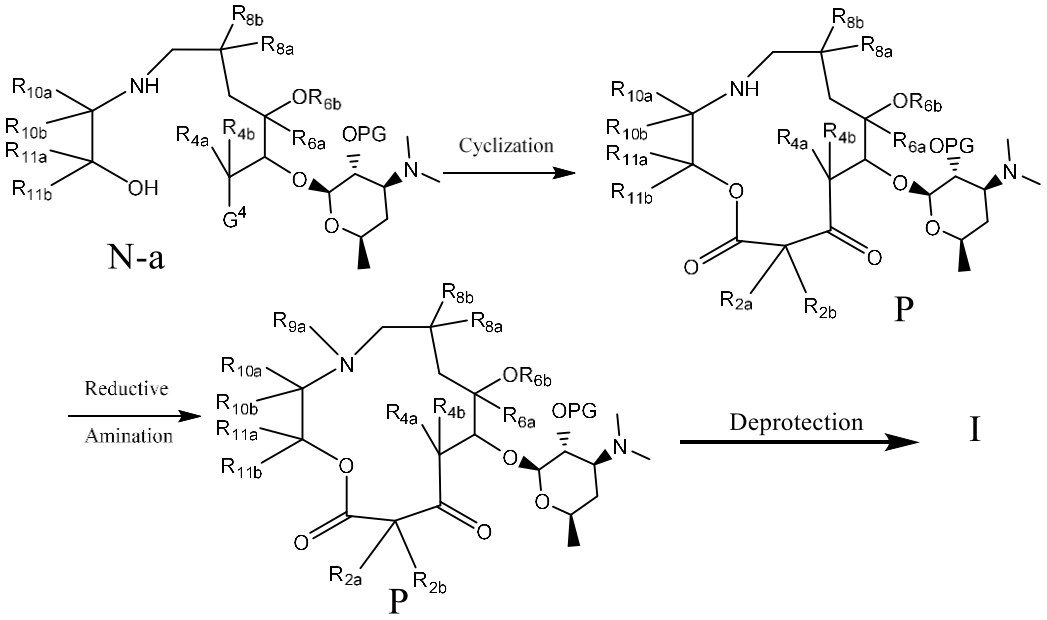
N-a I.

35. The process of claim 34, further comprising the step of preparing a compound of formula N-a, by combining N-1 with N-2 under reductive amination conditions:

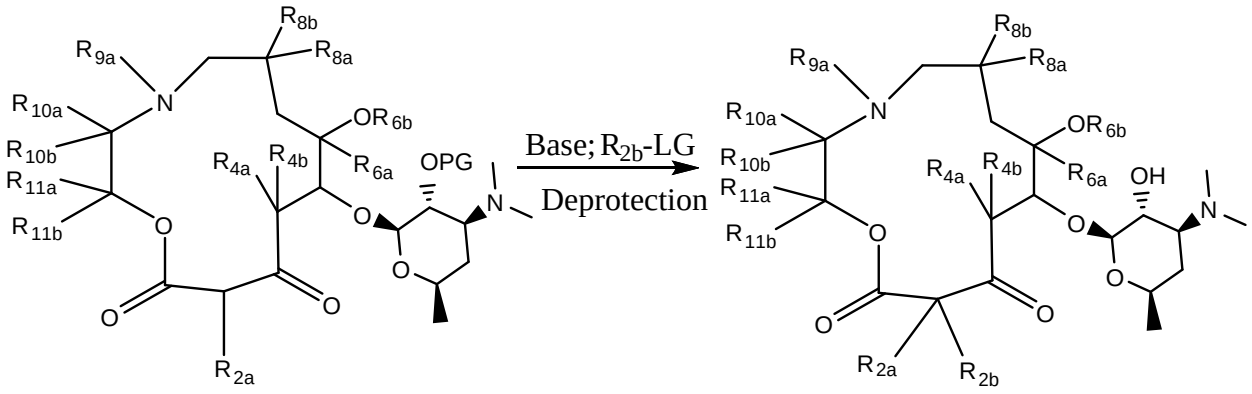


wherein R_s is , PG is a protecting group, and " 〰 " indicates a point of attachment.

36. A process of preparing a compound of formula I as defined in claim 1; 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 $C_{1\text{-}10}$ alkyl, hydroxyalkyl, or alkoxyalkyl



37. 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.