2-(2-carboxyphenyl)-1,3-dioxane, 2-(4-carboxyphenyl)-1,3-dioxane, or 2-C_{1-6}-alkylOC(=O)-1,3-dioxane; each of which is optionally substituted with one to four R^3;

R^3 at each occurrence is independently selected from the group consisting of halo, hydroxy, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, aryl, and heteroaryl; or

two R^3 groups when attached to adjacent carbons are taken together with the carbons to which they are attached to form a fused C_3-C_6 cycloalkyl; or

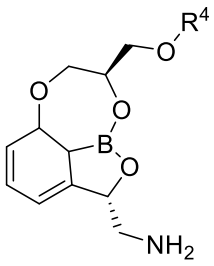
two R^3 groups when attached to the same carbon are taken together with the carbon to which they are attached to form a spiro C_3-C_6 cycloalkyl;

wherein each R^3 is optionally independently substituted with one to three fluoro, hydroxy, or C_1-C_3 alkyl.

In one preferred example of Formula I, R^1 and R^2 are both alkyl.

In yet another preferred example of Formula I, R^1 and R^2 are both C_1-C_6 alkyl-C(=O)-.

In another example, provided herein is a compound of Formula II:



II

or a pharmaceutically acceptable salt thereof;

wherein:

R^4 is selected from C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl.

In another example, provided herein is a pharmaceutical composition comprising a therapeutically effective amount of a compound of Formula I or Formula II, or a pharmaceutically acceptable salt, complex, or tautomer thereof, and a pharmaceutically acceptable carrier.

In another example, provided herein is a pharmaceutical composition comprising a compound of Formula I or Formula II, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

In another aspect, provided herein is a pharmaceutical composition comprising a therapeutically effective amount of a compound disclosed herein, or a pharmaceutically acceptable salt, complex, or tautomer thereof, and a pharmaceutically acceptable carrier.

In another aspect, provided herein is a compound disclosed herein, or a pharmaceutically acceptable salt, complex, or tautomer thereof, for use in therapy.

In another aspect, provided herein is compound disclosed herein, or a pharmaceutically acceptable salt, complex, or tautomer thereof, for use in treating a microbial infection

In another aspect, provided herein is a use of a compound disclosed herein disclosed herein, or a pharmaceutically acceptable salt, complex, or tautomer thereof, in the manufacture of a medicament for treating a microbial infection.

In an additional example, provided herein is a method for the treatment of a microbial infection in a mammal comprising administering to the mammal in need thereof a therapeutically effective amount of a compound of Formula I or Formula II, or a pharmaceutically acceptable salt, complex, or tautomer thereof. The compound of Formula I or Formula II or a pharmaceutically acceptable salt, complex, or tautomer thereof may be administered orally, parenterally, transdermally, topically, rectally, or intranasally in a pharmaceutical composition, including a solution or a powder composition for inhalation.

In an additional example, the compound or a pharmaceutically acceptable salt, complex, or tautomer thereof is administered to the mammal orally in a pharmaceutical composition.

In an additional example, provided herein is a method for treating mycobacteria microbial infections in humans or other warm-blooded animals by administering to the subject in need thereof a therapeutically effective amount of a compound of Formula I or Formula II or a pharmaceutically acceptable salt thereof. The compound of Formula I or Formula II may be administered orally, parenterally, transdermally, topically, rectally, or intranasally in a pharmaceutical composition.

In another example, provided herein are compositions and methods for the treatment of microbial infections caused by microorganisms selected from Gram-negative bacteria, including, but not limited to, *Pseudomonas aeruginosa, Acinetobacter baumannii, Escherichia coli,* and *Klebsiela pneumoniae.*

In one example, the method is for the treatment of a skin, soft tissue, respiratory, blood, intra-abdominal, urinary, or eye infection.

In yet another example, provided herein are novel intermediates and processes for preparing compounds of Formula I.

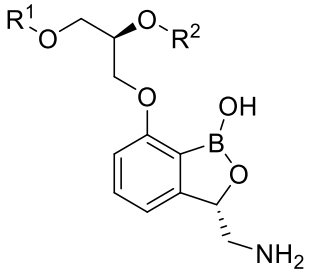
DETAILED DESCRIPTION

Unless otherwise stated, the following terms used in the specification and Claims have the meanings given below:

The carbon atom content of various hydrocarbon-containing moieties is indicated by a prefix designating the minimum and maximum number of carbon atoms in the moiety, i.e., the prefix C_{i-j} indicates a moiety of the integer "i" to the integer "j" carbon atoms, inclusive. Thus, for example, C_{1-7} alkyl refers to alkyl of one to seven carbon atoms, inclusive.

WHAT IS CLAIMED IS:

1. A compound of Formula I:



I,

or a pharmaceutically acceptable salt, complex, or tautomer thereof;

wherein:

R^1 is selected from H, C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; and

R^2 is selected from C_{1-24}alkyl-C(=O)-, C_{1-24}alkoxy-C(=O)-, C_{3-7}cycloalkyl-C(=O)-, heteroalkyl-C(=O)-, aryl-C(=O)-, heteroaryl-C(=O)-, and (5-methyl-1,3-dioxol-2-one-4-yl)methyl; or

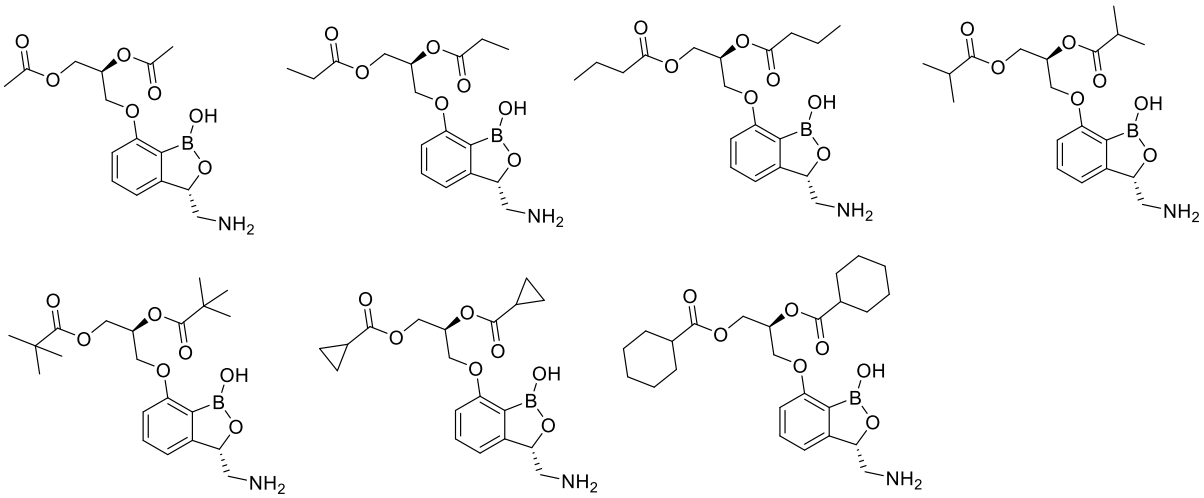
R^1 and R^2 taken together form a heterocyclic group selected from 1,3-dioxane, 2-C_{1-6}-alkyl-1,3-dioxane, 2,2-di(C_{1-6}-alkyl)-1,3-dioxane, 2-methyl-1,3-dioxane, 2-aryl-1,3-dioxane, 2-(2-carboxyphenyl)-1,3-dioxane, 2-(4-carboxyphenyl)-1,3-dioxane, or 2-C_{1-6}-alkylOC(=O)-1,3-dioxane; each of which is optionally substituted with one to four R^3;

R^3 at each occurrence is independently selected from the group consisting of halo, hydroxy, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, aryl, and heteroaryl; or

two R^3 groups when attached to adjacent carbons and taken together with the carbons to which they are attached are a fused C_3-C_6 cycloalkyl; or

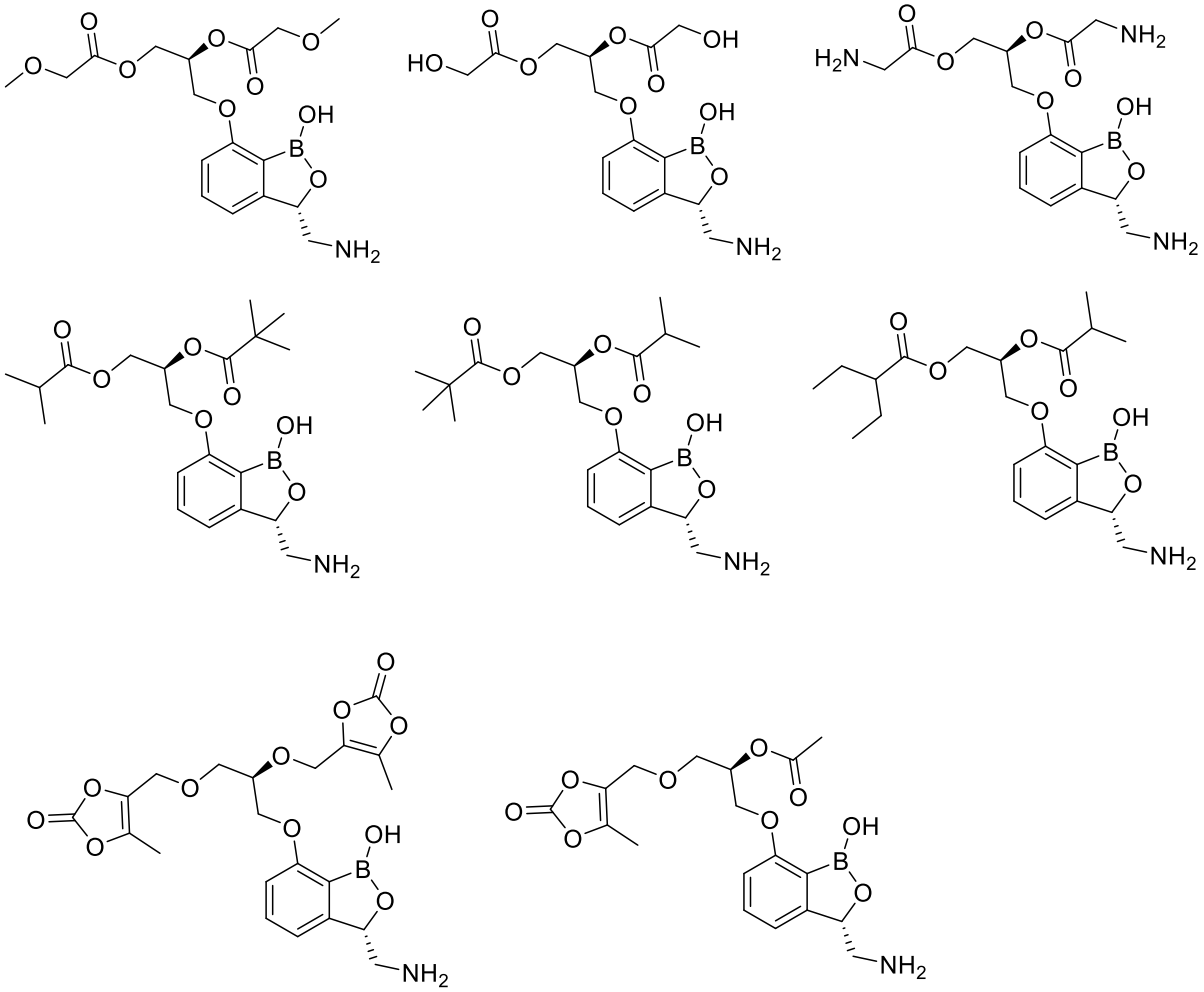
two R^3 groups when attached to the same carbon and taken together with the carbon to which they are attached are a spiro C_3-C_6 cycloalkyl; wherein each R^3 is optionally independently substituted with one to three fluoro or hydroxy, and C_1-C_3 alkyl.

2. The compound of claim 1 selected from:



or a pharmaceutically acceptable salt, complex, or tautomer thereof.

3. The compound of claim 1 selected from:



or a pharmaceutically acceptable salt, complex, or tautomer thereof.

4. The compound according to any one of claims 1-3, or a pharmaceutically acceptable salt, complex, or tautomer thereof, wherein the pharmaceutically acceptable salt is a hydrochloride salt.

5. The compound of any of claims 1-3, or a pharmaceutically acceptable salt, complex, or tautomer thereof, for use in treating a microbial infection.

6. The compound for use according to claim 5, or a pharmaceutically acceptable salt, complex, or tautomer thereof, wherein the compound or a pharmaceutically acceptable salt, complex, or tautomer thereof is to be administered to the mammal orally, parenterally, transdermally, topically, rectally, or intranasally in a pharmaceutical composition.

7. The compound for use according to claim 6, or a pharmaceutically acceptable salt, complex, or tautomer thereof, wherein the compound or a pharmaceutically acceptable salt, complex, or tautomer thereof is to be administered to the mammal orally in a pharmaceutical composition.

8. The compound for use according to claim 5, or a pharmaceutically acceptable salt, complex, or tautomer thereof, wherein the microbial infection is caused by a Gram-negative bacteria selected from *Pseudomonas aeruginosa, Acinetobacter baumannii, Escherichia coli, and Klebsiela pneumoniae.*

9. The compound for use according to claim 5, or a pharmaceutically acceptable salt, complex, or tautomer thereof, wherein the infection is a skin, soft tissue, respiratory, blood, intraabdominal, urinary or eye infection.

10. Use of a compound of any of claims 1-4, or a pharmaceutically acceptable salt, complex, or tautomer thereof, in the manufacture of a medicament for treating a microbial infection.

11. The use according to claim 10, wherein the compound or a pharmaceutically acceptable salt, complex, or tautomer thereof is to be administered to the mammal orally, parenterally, transdermally, topically, rectally, or intranasally in a pharmaceutical composition.

12. The use according to claim 11, wherein the compound or a pharmaceutically acceptable salt, complex, or tautomer thereof is to be administered to the mammal orally in a pharmaceutical composition.

13. The use according to claim 10 wherein the microbial infection is caused by a Gram-negative bacteria selected from *Pseudomonas aeruginosa, Acinetobacter baumannii, Escherichia coli,* and *Klebsiela pneumoniae.*

14. The use according to claim 10, wherein the infection is a skin, soft tissue, respiratory, blood, intraabdominal, urinary or eye infection.

15. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any of claims 1-4, or a pharmaceutically acceptable salt, complex, or tautomer thereof, and a pharmaceutically acceptable carrier.

16. A compound of any of claims 1-4, or a pharmaceutically acceptable salt, complex, or tautomer thereof, for use in therapy.