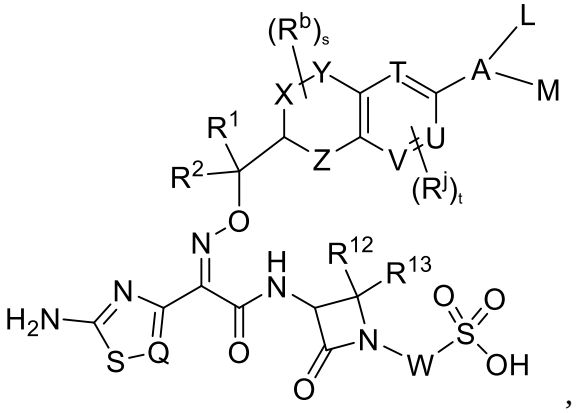
strains. Because monobactams are inherently resistant to hydrolysis by MBLs, several companies have begun developing novel monobactam compounds for the treatment of infections caused by Gram-negative bacteria. Monobactam compounds comprising a siderophore moiety are disclosed in WO 2007/065288, WO2012/073138, *J. Medicinal Chemistry* 56: 5541-5552 (2013), and *Bioorganic and Medicinal Chemstry Letters* 22:5989 (2012).

WO2017/106064 discloses biaryl monobactam compounds and their use to treat bacterial infections. U.S. Patent Application Publication No US 2015/0045340 and No. US 2014/0275007 disclose oxamazin monobactams and their use as antibacterial agents. U.S. Patent Application Publication No. US 2015/0266867 discloses novel monobactam compounds for the use as antibacterial agents. WO 2013/110643 discloses novel amidine substituted monobactam derivatives and their use as antimicrobial reagents. WO 2015/103583 discloses monobactam derivatives useful for treating infectious disease which is bacterial infection.

The need for new antibiotics to overcome multidrug resistance continues. Compounds disclosed in this invention are designed to fill this medical need, through administration either on their own or in combination with a suitable β-lactamase inhibitor.

SUMMARY

The disclosure relates to the design and synthesis of monobactam analogs, a novel class of highly potent antibiotics effective against a broad range of Gram-negative bacteria. These compounds and their pharmaceutically acceptable salts may be useful as therapeutic agents for clinical treatment of various infections caused by Gram-negative bacteria, including strains that are multidrug resistant. The compounds can be used alone or in combination with a suitable β-lactamase inhibitor. The present disclosure, in one aspect, includes compounds of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

wherein C_1-C_3 alkyl unsubstituted or substituted with one to three R^b;

each n is independently 0, 1, 2, 3, 4, 5 or 6;
each m is independently 0, 1 or 2;
each p is independently 1 or 2;
each q is independently 0, 1, 2, 3, 4, 5 or 6;
each s is independently 0, 1, 2 or 3;
each t is independently 0, 1, 2 or 3;
each u is independently 0, 1, 2, 3, 4, 5 or 6; and
each v is independently 0, 1, or 2.

The present disclosure also relates to a pharmaceutical composition for treating a bacterial infection in a subject, including infection with multidrug resistant Gram-negative bacterial strains, comprising a monobactam compound of the disclosure and a pharmaceutically acceptable carrier, diluent or excipient.

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

The Compounds of Formula (I), also referred to herein as the "monobactam compounds", and pharmaceutically acceptable salts thereof can be useful, for example, for inhibiting the growth of Gram-negative bacterial strains, including but not limited to, *Pseudomonas*, *Klebsiella* and *Acinetobacter* strains, including *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter baumannii*, and/or for treating or preventing the clinical maifestations thereof in a patient.

The present disclosure is also directed to methods of treating Gram-negative bacterial infections in a subject in need of treatment thereof, comprising administering to the subject an effective amount of a monobactam compound of the disclosure. In specific examples of the disclosure, the method includes administration of a beta lactamase inhibitor compound.

In another aspect, there is provided a compound as defined herein, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition as defined herein for use in treating a bacterial infection.

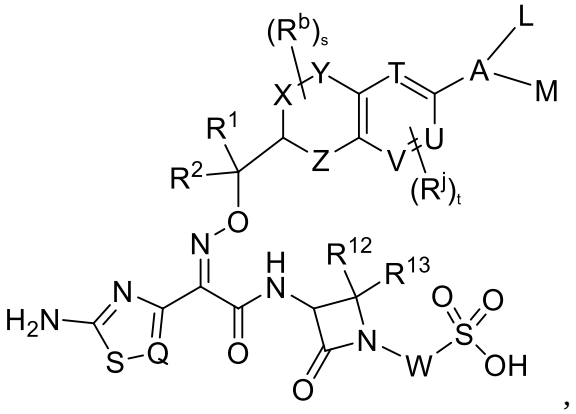
In another aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition as defined herein in the manufacture of a medicament for treating a bacterial infection.

In another aspect, there is provided use of a compound as defined herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a bacterial infection, in combination with a beta-lactamase inhibitor compound for treating a bacterial infection, or in combination with a beta-lactamase inhibitor compound in the manufacture of a medicament for treating a bacterial infection.

Embodiments, sub-embodiments, examples and features of the present disclosure are either further described in or will be apparent from the ensuing description, examples and appended claims.

WHAT IS CLAIMED

1. A compound of Formula I



(I)

or a pharmaceutically acceptable salt thereof, wherein:

T is CH or N, provided that no more than two of T, U and V is N;
U is CH or N;
V is CH or N;

W is
1) a bond, or
2) O;

Q is
1) N, or
2) CR^3;

X is
1) O, or
2) CH_2;

Y is
1) O,
2) NR^8,
3) S, or

4) CH_2,

provided that when Y is O, NR^8 or S then X is not O;

Z is

1) O,
2) S,
3) CH_2, or
4) NH,

provided that when Z is O, S or NH, then X is not O;

A is

1) –C(=NH)-NH,
2) $-(CH_2)_qN(R^7)$-AryC,
3) $-(CH_2)_qO$-AryC,
4) AryC,
5) $-(CH_2)_qN(R^7)$-HetC,
6) $-(CH_2)_qO$-HetC,
7) HetC, or
8) C_3-C_7 cycloalkyl,

wherein CH_2 and C_3-C_7 cycloalkyl are unsubstituted or substituted with one to four R^i;

AryC is a 5- to 6-membered monocyclic aromatic ring with 0, 1, 2, or 3 ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^i, wherein AryC is optionally fused to a 4- to 7- membered heterocycloalkyl ring containing one to two heteroatoms selected from O, S and $–NR^g$;

HetC is a 4- to 7-membered saturated or monounsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^i;

L is

1) absent,
2) R^4,
3) $-NHR^4$,
4) $-N(R^4)_2$,
5) $-OR^4$,
6) $-(CH_2)_nR^4$,

7) -C(O)R^4 ,
8) -C(NH)R^4, or
9) -S(O)$_m$$R^4$,

wherein L is unsubstituted or substituted with 1-4 substituents selected from R^e ;

M is

1) R^5,
2) -NHR^5,
3) -N(R^5)$_2$,
4) -OR^5,
5) -(CH$_2$)$_u$$R^5$,
6) -C(O)R^5,
7) -C(NH)R^5, or
8) -S(O)$_v$$R^5$,

wherein M is unsubstituted or substituted with 1 - 4 substituents selected from R^6;

R^1 is

1) hydrogen,
2) -C_1-C_8 alkyl,
3) -C_3-C_7 cycloalkyl,
4) -C(O)OR^e,
5) -C(O)N$R^c$$R^d$,
6) tetrazolyl,
7) oxadiazolonyl,
8) HetA,
9) AryA,
10) -S(O)$_m$$R^e$,
11) -S(O)$_m$N$R^c$$R^d$, or
12) -P(O)(R^e)$_p$,

wherein -C_1-C_8 alkyl and -C_3-C_7 cycloalkyl are unsubstituted or substituted with one to three R^a;

R^2 is

1) hydrogen,
2) -C_1-C_8 alkyl,
3) -C_3-C_7 cycloalkyl,
4) -C(O)OR^e,

5) -C(O)NR^{c}R^d,
6) tetrazolyl,
7) oxadiazolonyl,
8) HetA,
9) AryA,
10) -S(O)$_m$R^e,
11) -S(O)$_m$NR^{c}R^d, or
12) -P(O)(R^e)$_p$,

wherein -C$_1$-C$_8$ alkyl and -C$_3$-C$_7$ cycloalkyl are unsubstituted or substituted with one to three R^a,

provided that when R^1 is -C(O)OR^e, -C(O)NR^{c}R^d, -S(O)$_m$R^e, -S(O)$_m$NR^{c}R^d, or -P(O)(R^e)$_p$, then R^2 is not -C(O)OR^e, -C(O)NR^{c}R^d, -S(O)$_m$R^e, -S(O)$_m$NR^{c}R^d, or -P(O)(R^e)$_p$;

HetA is a 4- to 7- membered saturated or monounsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^c;

AryA is a 5- to 6-membered monocyclic aromatic ring with 0, 1, 2, or 3 ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to four R^c;

R^3 is

1) hydrogen,
2) C$_1$-C$_4$ alkyl,
3) halogen, or
4) C$_3$-C$_7$cycloalkyl,

wherein C$_1$-C$_4$ alkyl and C$_3$-C$_7$cycloalkyl are unsubstituted or substituted with one to three R^a;

each occurrence of R^4 is independently:

1) hydrogen,
2) -C$_1$-C$_{10}$ alkyl,
3) -C$_2$-C$_8$ alkenyl,
4) -(CH$_2$)$_n$OR^e,
5) -S(O)$_m$R^e,
6) -S(O)$_m$NR^{c}R^d,
7) -(CH$_2$)$_n$NR^{c}R^d,

8) -OC(O)R^e,
9) -C(O)OR^e,
10) -CN,
11) -C(O)N$R^c$$R^d$,
12) -NR^cC(O)R^e,
13) -NR^cC(O)OR^e,
14) -NR^cC(O)N$R^c$$R^d$,
15) -NR^cS(O)$_m$$R^e$,
16) =NR^{11},
17) -C_3-C_7 cycloalkyl,
18) -O-C_3-C_6cycloalkyl,
19) -C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
20) -O-C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
21) HetB,
22) -O-HetB,
23) -C_1-C_{10}alkylene-HetB,
24) -O-C_1-C_{10}alkylene-HetB,
25) AryB,
26) -O-AryB,
27) -C_1-C_{10}alkylene-AryB, or
28) -O-C_1-C_{10}alkylene-AryB,

wherein R^4 is unsubstituted or substituted with one to four R^6;

AryB is a 5- to 6-membered monocyclic aromatic ring with 0, 1, 2, or 3 ring atoms independently selected from N, O and S, unsubstituted or substituted with one to four R^c;

HetB is a 4- to 7-membered saturated or monounsaturated monocyclic ring with 1, 2, or 3 heteroatom ring atoms independently selected from N, N as a quaternary salt, O and S, unsubstituted or substituted with one to three R^a;

R^5 is

1) hydrogen,
2) C_1-C_{10} alkyl,
3) -C_2-C_8 alkenyl,
4) -$(CH_2)_u$OR^e,
5) -S(O)$_v$$R^e$,
6) -S(O)$_v$N$R^c$$R^d$,

7) -$(CH_2)_u NR^c R^d$,
8) -$OC(O)R^e$,
9) -$C(O)OR^e$,
10) -CN,
11) -$C(O)NR^c R^d$,
12) -$NR^c C(O)R^e$,
13) -$NR^c C(O)OR^e$,
14) -$NR^c C(O)NR^c R^d$,
15) -$NR^c S(O)_v R^e$,
16) =NR^{11},
17) -C_3-C_7 cycloalkyl,
18) -O-C_3-C_6cycloalkyl,
19) -C_1-C_{10}alkylene-C_3-C_6cycloalkyl,
20) -O-C_1-C_{10} alkylene-C_3-C_6cycloalkyl,
21) HetB,
22) -O-HetB,
23) -C_1-C_{10}alkylene-HetB,
24) -O-C_1-C_{10} alkylene-HetB,
25) AryB,
26) -O-AryB,
27) -C_1-C_{10}alkylene-AryB, or
28) -O-C_1-C_{10}alkylene-AryB,

wherein R^5 is unsubstituted or substituted with one to four R^6;

each occurrence of R^6 is independently:

1) halogen,
2) -C_1-C_6alkyl,
3) -OR^e,
4) -$S(O)_v R^e$,
5) -$S(O)_v NR^c R^d$,
6) -$C(O)R^e$,
7) -$OC(O)R^e$,
8) -$C(O)OR^e$,
9) -CN,
10) -$C(O)NR^c R^d$,
11) -$C(NH)NR^c R^d$,
12) -$(CH_2)_u NR^c R^d$,

13) -$(CH_2)_u NR^c R^d$,
14) -$N(R^c)(C(O)R^e)$,
15) -$N(R^c)(C(O)OR^e)$,
16) -$N(R^c)(C(O)NR^c R^d)$,
17) -$N(R^c)(S(O)_v R^e)$, or
18) HetB;

R^7 is
1) hydrogen,
2) C_1-C_3 alkyl, or
3) C_3-C_7 cycloalkyl,
wherein C_1-C_3 alkyl and C_3-C_7 cycloalkyl are unsubstituted or substituted with one to three R^a;

R^8 is
1) hydrogen,
2) C_1-C_4 alkyl, or
3) C_3-C_7 cycloalkyl;

R^9 is
1) hydrogen,
2) C_1-C_4 alkyl, or
3) C_3-C_7 cycloalkyl;

R^{10} is
1) hydrogen,
2) C_1-C_4 alkyl, or
3) C_3-C_7 cycloalkyl;

R^{11} is
1) hydrogen,
2) C_1-C_4 alkyl, or
3) C_3-C_7 cycloalkyl;

R^{12} and R^{13} are independently:
1) hydrogen,
2) -SC_1-C_3alkyl,

3) C_1-C_3 alkyl,
4) -(C_1-C_3alkylene)$_n$OC_1-C_3alkyl, or
5) -(C_1-C_3alkylene)$_n$NC_1-C_3alkyl,

wherein -SC_1-C_3alkyl, C_1-C_3 alkyl, -(C_1-C_3alkylene)$_n$OC_1-C_3alkyl and -(C_1-C_3alkylene)$_n$NC_1-C_3alkyl are unsubstituted or substituted with one to seven fluorines, or, alternatively, R^{12} and R^{13} together with the carbon to which they are attached, form a monocyclic C_4-C_7 cycloalkyl or a monocyclic C_4-C_7 heterocycloalkyl with 1, 2, or 3 heteroatom ring atoms independently selected from N, O and S, wherein C_4-C_7 cycloalkyl and C_4-C_7 heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from -F, -OH and -OC_1-C_3alkyl;

R^{14} is
1) hydrogen,
2) C_1-C_4 alkyl, or
3) C_3-C_7 cycloalkyl;

each occurrence of R^a is independently:
1) hydrogen,
2) halogen,
3) C_1-C_3alkyl,
4) -NR^cR^d, or
5) -OR^e;

each occurrence of R^b is independently:
1) hydrogen,
2) -C_1-C_6 alkyl,
3) -OC_1-C_6 alkyl,
4) OH,
5) N(R^9)$_2$, or
6) halogen,

wherein -C_1-C_3 alkyl is unsubstituted or substituted with one to three R^a;

each occurrence of R^c and R^d is independently:
1) hydrogen,
2) -C_1-C_{10} alkyl,
3) -C_2-C_{10} alkenyl,
4) -C_3-C_6 cycloalkyl,

5) -C_1-C_{10} alkylene-C_3-C_6 cycloalkyl,
6) HetA,
7) -C_1-C_{10}alkylene-HetB,
8) AryB,
9) -C_1-C_{10} alkylene-AryB, or
10) -C_1-C_{10} alkylene-HetB,

or, alternatively, R^c and R^d together with the nitrogen atom to which they are attached, form a 4- to 7-membered hetercycloalkyl optionally containing one to two additional heteroatoms independently selected from O, S and -NR^g, and wherein each R^c and R^d is unsubstituted or substituted with one to three R^f;

each occurrence of R^e is independently:

1) hydrogen,
2) -C_1-C_{10}alkyl,
3) -C_2-C_{10} alkenyl,
4) -OH,
5) -OC_1-C_4 alkyl,
6) -C_3-C_6 cycloalkyl,
7) -C_1-C_{10} alkylene-C_3-C_6 cycloalkyl,
8) HetB,
9) -C_1-C_{10} alkylene-HetB,
10) AryB,
11) -C_1-C_{10} alkylene-AryB,
12) -C_1-C_{10} alkylene–HetB, or
13) halogen,

wherein each R^e is unsubstituted or substituted with one to three R^h;

each occurrence of R^f is independently:

1) halogen,
2) -C_1-C_{10} alkyl,
3) -OH,
4) -OC_1-C_4 alkyl,
5) -$S(O)_m$$C_1$-$C_4$ alkyl,
6) -CN,
7) -CF_3,
8) -$OCHF_2$,
9) -OCF_3, or

10) NH_2,

wherein -C_1-C_{10} alkyl is unsubstituted or substituted with one to three substituents independently selected from –OH, halogen, cyano, and -$S(O)_2CH_3$;

each occurrence of R^g is independently:

1) hydrogen,
2) -$C(O)R^e$, or
3) -C_1-C_{10} alkyl,

wherein -C_1-C_{10}alkyl is unsubstituted or substituted with one to five fluorines;

each occurrence of R^h is independently:

1) halogen,
2) -C_1-C_{10}alkyl,
3) -OH,
4) -OC_1-C_4 alkyl,
5) -$S(O)_mC_1$-C_4 alkyl,
6) -CN,
7) -CF_3,
8) -$OCHF_2$, or
9) -OCF_3,

wherein -C_1-C_{10} alkyl is unsubstituted or substituted with one to three substituents independently selected from: -OH, halogen, cyano, or–$S(O)_2CH_3$;

each occurrence of R^i is independently:

1) -C_1-C_8 alkyl,
2) -C_2-C_8 alkenyl,
3) -C_2-C_8 alkynyl,
4) halogen,
5) -OR^e ,
6) -$S(O)_mR^e$,
7) -$S(O)_mNR^cR^d$,
8) -$C(O)R^e$,
9) -$OC(O)R^e$,
10) -$C(O)OR^e$,
11) -CN,
12) -$C(O)NR^cR^d$,
13) -NR^cR^d,

14) $-(CH_2)_nNR^cR^d$,
15) $-NR^cC(O)R^e$,
16) $-NR^cC(O)OR^e$,
17) $-NR^cC(O)NR^cR^d$,
18) $-NR^cS(O)_mR^e$,
19) =NH,
20) $-CF_3$,
21) $-OCF_3$, or
22) $-OCHF_2$;

each occurrence of R^j is independently:
1) hydrogen,
2) C_1-C_3 alkyl,
3) OR^{10},
4) $=NR^{10}$,
5) $N(R^{10})_2$, or
6) halogen,

wherein C_1-C_3 alkyl unsubstituted or substituted with one to three R^b;

each n is independently 0, 1, 2, 3, 4, 5 or 6;
each m is independently 0, 1 or 2;
each p is independently 1 or 2;
each q is independently 0, 1, 2, 3, 4, 5 or 6;
each s is independently 0, 1, 2 or 3;
each t is independently 0, 1, 2 or 3;
each u is independently 0, 1, 2, 3, 4, 5 or 6; and
each v is independently 0, 1, or 2.

2. A compound of Claim 1 wherein

T, U and V are each CH;

or a pharmaceutically acceptable salt thereof.

3. The compound of Claim 1 wherein

W is O;

or a pharmaceutically acceptable salt thereof.

4. The compound of Claim 1 wherein

Q is CR^3; and

R^3 is hydrogen;

or a pharmaceutically acceptable salt thereof.

5. The compound of Claim 1 wherein

X is CH_2;

or a pharmaceutically acceptable salt thereof.

6. The compound of Claim 5 wherein

Y is O or CH_2; and

Z is O or CH_2;

or a pharmaceutically acceptable salt thereof.

7. The compound of Claim 1 wherein

Y is CH_2; and

Z is O;

or a pharmaceutically acceptable salt thereof.

8. The compound of Claim 1 wherein R^1 and R^2 are independently selected from:

1) hydrogen,
2) -C_1-C_8 alkyl, and
3) -C(O)OR^e,

wherein -C_1-C_8 alkyl is unsubstituted or substituted with one to three R^a,

provided that if R^1 is –C(O)OR^e, then R^2 is not –C(O)OR^e;

or a pharmaceutically acceptable salt thereof.

9. The compound of Claim 1 wherein

R^1 and R^2 are independently selected from

1) -C_1-C_8 alkyl, and
2) -C(O)OR^e,

provided if R^1 is -C(O)OR^e, then R^2 is -C_1-C_8 alkyl, and if R^2 is -C(O)OR^e, then R^1 is -C_1-C_8 alkyl; or a pharmaceutically acceptable salt thereof.

10. The compound of Claim 1 wherein

R^{12} and R^{13} are independently C_1-C_3 alkyl, wherein C_1-C_3 alkyl is unsubstituted or substituted with one to seven fluorines,

or alternatively R^{12} and R^{13} together with the carbon to which they are attached form a monocyclic C_4-C_6 cycloalkyl unsubstituted or substituted with one to three substituents independently selected from -F, -OH and -OC_1-C_3alkyl;

or a pharmaceutically acceptable salt thereof.

11. The compound of Claim 1 wherein

A is

1) –C(=NH)-NH,
2) AryC, or
3) HetC,

wherein A is unsubstituted or substituted with one to four R^i;

or a pharmaceutically acceptable salt thereof.

12. The compound of Claim 1 wherein

A is

1) AryC, or
2) HetC,

wherein A is unsubstituted or substituted with one to four R^i;

or a pharmaceutically acceptable salt thereof.

13. The compound of Claim 1 wherein

L is

1) absent, or
2) R^4,

wherein L is unsubstituted or substituted with 1-4 substituents selected from R^e; and

each occurrence of R^4 is independently:

1) hydrogen,

2) -C_1-C_{10} alkyl,
3) -$(CH_2)_nOR^e$,
4) -$(CH_2)_nNR^cR^d$, or
5) -C_1-C_{10}alkylene-HetB,

wherein R^4 is unsubstituted or substituted with one to four R^6;
or a pharmaceutically acceptable salt thereof.

14. The compound of Claim 13 wherein
each occurrence of R^4 is independently:
1) -C_1-C_{10} alkyl,
2) -$(CH_2)_nNR^cR^d$, or
3) -C_1-C_{10}alkylene-HetB,

wherein R^4 is unsubstituted or substituted with one to four R^6;
or a pharmaceutically acceptable salt thereof.

15. The compound of Claim 1 wherein
M is
1) R^5, or
2) -NHR^5,

wherein M is unsubstituted or substituted with 1 – 4 substituents selected from R^6; and

R^5 is
1) hydrogen,
2) C_1-C_6 alkyl,
3) -C_1-C_4alkyl-$(NR^cR^d)_2$,
4) -$(CH_2)_uNR^cR^d$, or
5) -C_1-C_{10}alkylene-HetB,

wherein R^5 is unsubstituted or substituted with one to four R^6;
or a pharmaceutically acceptable salt thereof.

16. The compound of Claim 15 wherein
R^5 is
1) -C_1-C_4alkyl-$(NR^cR^d)_2$, or
2) -$(CH_2)_uNR^cR^d$,

wherein R^5 is unsubstituted or substituted with one to four R^6;
or a pharmaceutically acceptable salt thereof.

17. The compound of Claim 1 wherein

T, U and V are CH;

W is O;

Q is CR^3;

X is CH_2;

Y is O or CH_2;

Z is O or CH_2;

R^1 and R^2 are independently selected from:

1) hydrogen,
2) -C_1-C_8 alkyl, and
3) –C(O)OR^e,

wherein -C_1-C_8 alkyl is unsubstituted or substituted with one to three R^a, provided that if R^1 is –C(O)OR^e, then R^2 is independently selected from hydrogen and -C_1-C_8 alkyl;

R^3 is hydrogen;

R^{12} and R^{13} are independently C_1-C_3 alkyl, wherein C_1-C_3 alkyl is unsubstituted or substituted with one to seven fluorines,

or alternatively R^{12} and R^{13} together with the carbon to which they are attached form a monocyclic C_4-C_6 cycloalkyl unsubstituted or substituted with one to three substituents independently selected from -F, -OH and -OC_1-C_3alkyl;

A is

1) –C(=NH)-NH,
2) AryC, or
3) HetC,

wherein A is unsubstituted or substituted with one to four R^i;

L is

1) absent, or
2) R^4,

wherein L is unsubstituted or substituted with 1-4 substituents selected from R^e;

each occurrence of R^4 is independently:

1) hydrogen,
2) -C_1-C_{10} alkyl,
3) -$(CH_2)_nOR^e$,
4) -$(CH_2)_nNR^cR^d$, or
5) –C_1-C_{10}alkylene-HetB,

wherein R^4 is unsubstituted or substituted with one to four R^6;

M is

1) R^5, or
2) -NHR^5,

wherein M is unsubstituted or substituted with 1 – 4 substituents selected from R^6; and

R^5 is

1) hydrogen,
2) -C_1-C_6 alkyl,
3) -C_1-C_4alkyl-$(NR^cR^d)_2$,
4) -$(CH_2)_uNR^cR^d$, or
5) –C_1-C_{10}alkylene-HetB,

wherein R^5 is unsubstituted or substituted with one to four R^6;
or a pharmaceutically acceptable salt thereof.

18. The compound of Claim 1 wherein

T, U and V are CH;
W is O;
Q is CR^3;
R^3 is hydrogen;

X is CH_2;
Y is CH_2;
Z is O;

R^1 and R^2 are independently selected from

1) -C_1-C_6 alkyl, and
2) -$C(O)OR^e$,

wherein -C_1-C_6 alkyl is unsubstituted or substituted with one to three R^a, provided that if R^1 is –C(O)OR^e, then R^2 is -C_1-C_6 alkyl;

R^{12} and R^{13} are independently C_1-C_3 alkyl, wherein C_1-C_3 alkyl is unsubstituted or substituted with one to seven fluorines;

A is

1) AryC, or
2) HetC,

wherein A is unsubstituted or substituted with one to four R^i;

L is

1) absent, or
2) R^4,

wherein L is unsubstituted or substituted with 1-4 substituents selected from R^e;

each occurrence of R^4 is independently:

1) -C_1-C_{10} alkyl,
2) -$(CH_2)_n NR^c R^d$, or
3) -C_1-C_{10}alkylene-HetB,

wherein R^4 is unsubstituted or substituted with one to four R^6;

M is

1) R^5, or
2) -NHR^5,

wherein M is unsubstituted or substituted with 1 – 4 substituents selected from R^6;

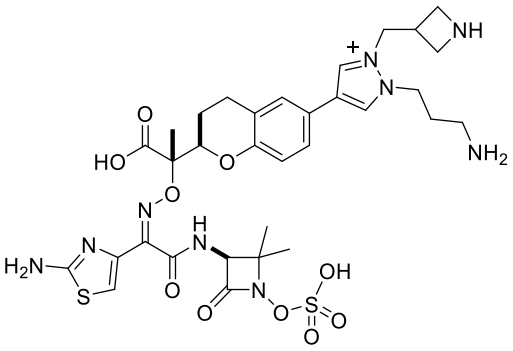
R^5 is

1) -C_1-C_4alkyl-$(NR^c R^d)_2$, or
2) -$(CH_2)_u NR^c R^d$,

wherein R^5 is unsubstituted or substituted with one to four R^6;

or a pharmaceutically acceptable salt thereof.

19. The compound of Claim 1 which is selected from: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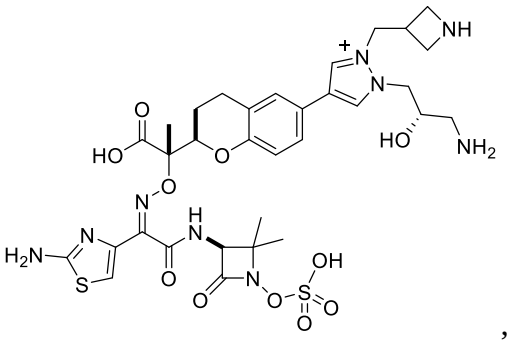
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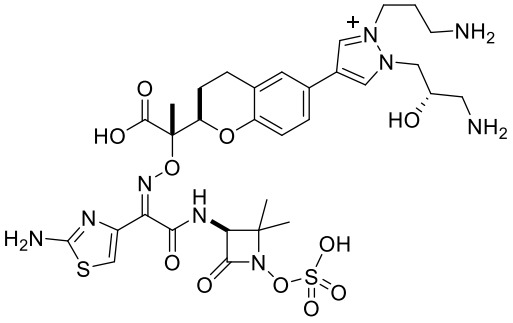
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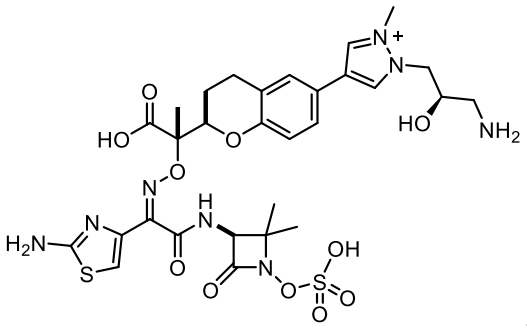
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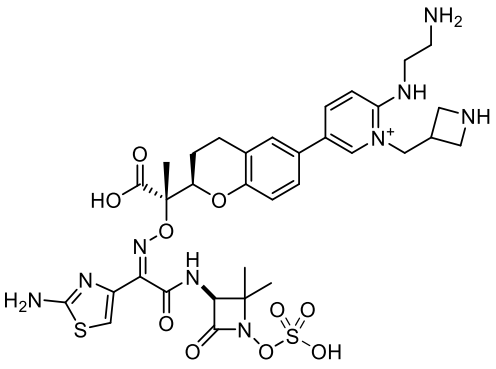
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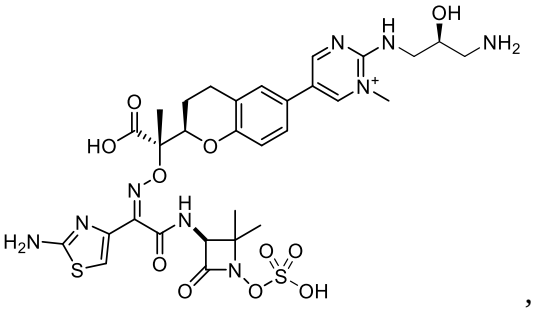
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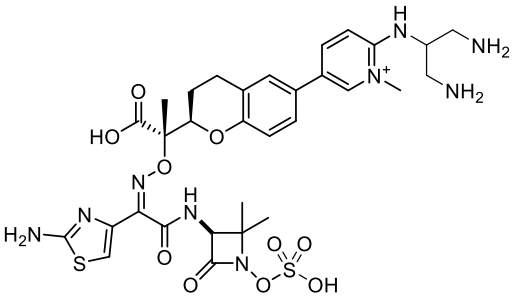
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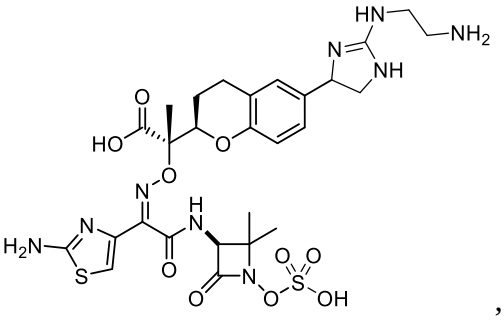
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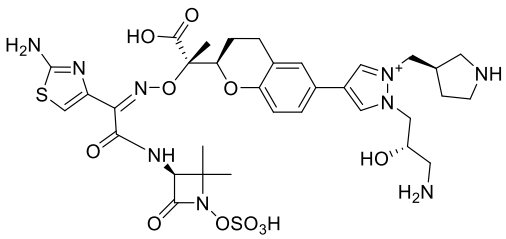
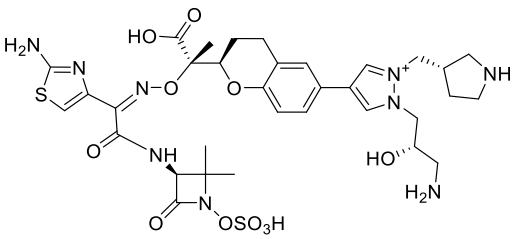
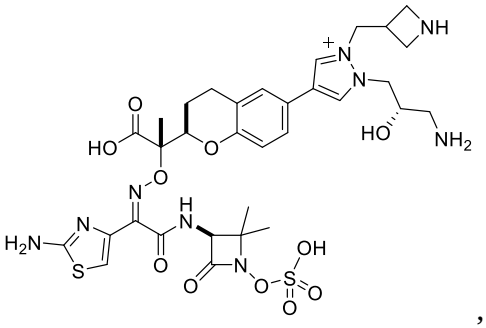


, and



or a pharmaceutically acceptable salt thereof.

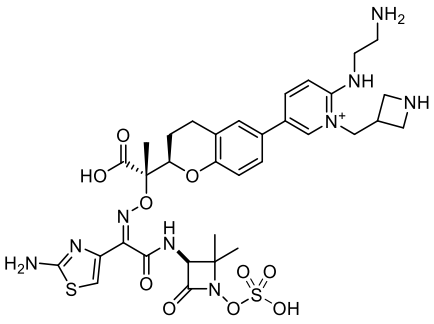
20. The compound of Claim 1 which is:



,

or a pharmaceutically acceptable salt thereof.

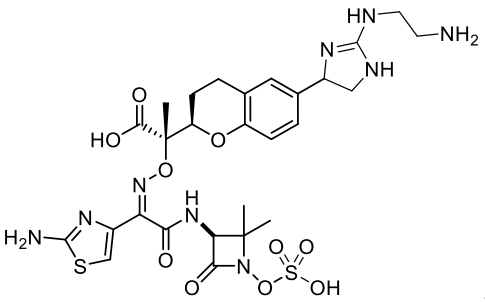
21. The compound of Claim 1 which is:



,

or a pharmaceutically acceptable salt thereof.

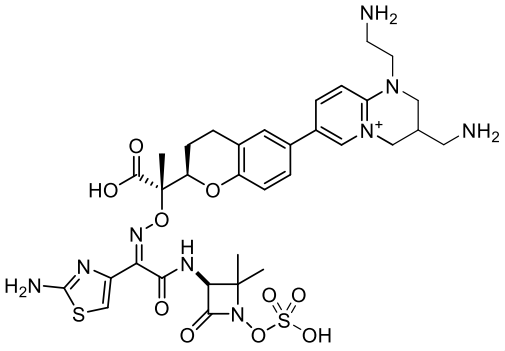
22. The compound of Claim 1 which is:



,

or a pharmaceutically acceptable salt thereof.

23. The compound of Claim 1 which is:



,

or a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising a therapeutically effective amount of a compound acccording to any one of Claims 1 to 23, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

25. A pharmaceutical composition according to Claim 24, which further comprises a therapeutically effective amount of a beta-lactamase inhibitor compound.

26. A pharmaceutical composition according to Claim 25, wherein the beta-lactamase inhibitor compound is selected from the group consisting of relebactam, tazobactam, clavulanic acid, sulbactam, and avibactam.

27. A compound according to any one of Claims 1 to 23, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition according to any one of claims 24 to 26 for use in treating a bacterial infection.

28. Use of a compound according to any one of Claims 1 to 23, or a pharmaceutically acceptable salt thereof, optionally in combination with a beta-lactamase inhibitor compound or a pharmaceutical composition according to any one of claims 24 to 26 in the manufacture of a medicament for treating a bacterial infection.

29. Use of a compound according to any one of Claims 1 to 23, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a bacterial infection, in combination with a beta-lactamase inhibitor compound for treating a bacterial infection, or in combination with a beta-lactamase inhibitor compound in the manufacture of a medicament for treating a bacterial infection.

30. The compound or the pharmaceutical composition for use of Claim 27 or the use of claim 28 or 29, wherein the beta-lactamase inhibitor compound is selected from the group consisting of relebactam, tazobactam, clavulanic acid, sulbactam, and avibactam.

31. The compound or the pharmaceutical composition for use of claim 27 or 30 or the use of claim 28 or 29, wherein the bacterial infection is due to Pseudomonas spp., Klebsiella spp., Enterobacter spp., Escherichia spp., Morganella spp., Citrobacter spp., Serratia spp. or Acintetobacter spp.