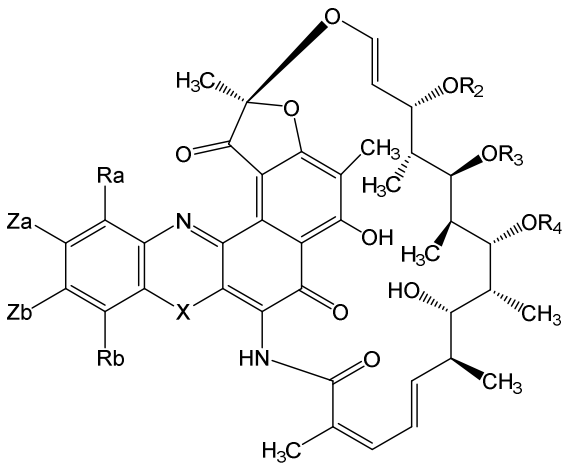
WHAT IS CLAIMED IS:

1. A compound having the structure of formula (A):



(A)

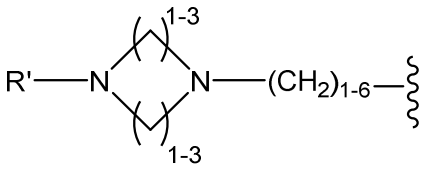
or a pharmaceutically acceptable salt thereof, wherein:

X is selected from -O- and -NR*-;

Za and Zb are independently selected from a hydrogen, -OR_1, -Cl, -Br, and -R_N, with the proviso that at least one of Za or Zb is not a hydrogen, wherein:

R_1 is selected from a hydrogen, R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon; a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, -NO_2, -NO_3, -O-NO, -N_3, -NH_2, -NHR*, -$N(R^*)_2$, -$N(R^*)_3^+$, -N(R*)-OH, -O-$N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, -CO_2H, -CO_2R^*, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*,-(C=O)-NH_2, -(C=O)-$N(R^*)_2$, -(C=O)-$NHNH_2$, -O-(C=O)-$NHNH_2$, -(C=S)-NH_2, -(C=S)-$N(R^*)_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, -SO_2R^*, -SO_2-$N(R^*)_2$, -S(=O)-OR*, -S(=O)-R*, -$Si(R^*)_3$, -CF_3, -O-CF_3 and combinations thereof, with the provisos that R_1 is not an n-butyl group, and when X is -O- and Ra is hydrogen, R_1 is not hydrogen;

R_N is selected from:



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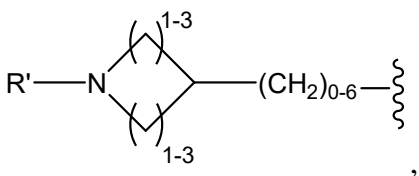

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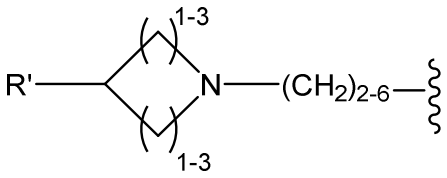

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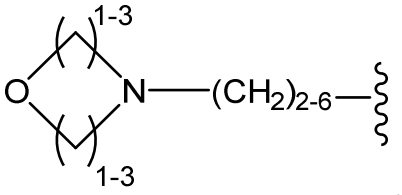

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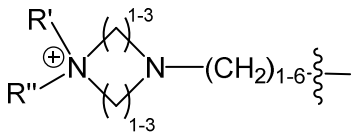

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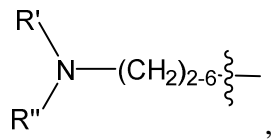

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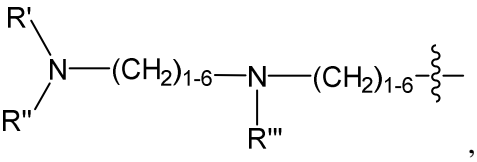

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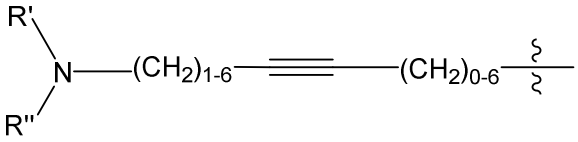

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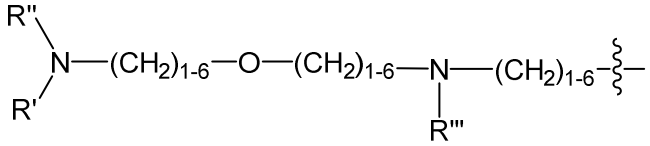


wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from Fluorenylmethyloxycarbonyl (F_{MOC}) and *tert*-Butyloxycarbonyl (B_{OC}), or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R_2, R_3, and R_4 are independently selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, and -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

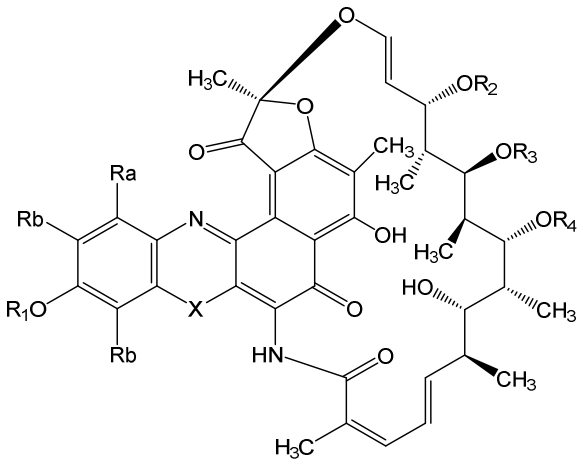
R_a is selected from hydrogen, -Cl, -OR*, -F, -Br, -I, -OH, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -SR*, $-SO_2R^*$, and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R_b is selected from hydrogen, -F, -Cl, -Br, -I, -OH, -OR*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-3 heteroatoms selected from halogen, O, and S, and wherein R_b is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations

thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

2. The compound of claim 1 having a structure according to formula (I):



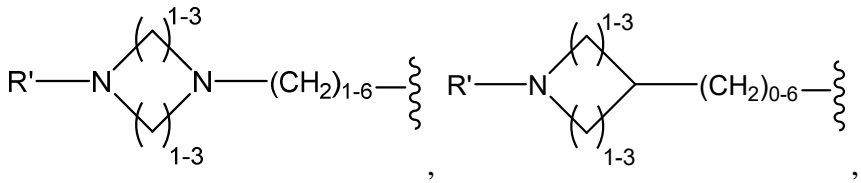
(I)

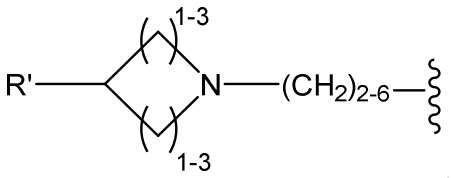
or a pharmaceutically acceptable salt thereof wherein:

X is selected from -O- and -NR*-;

R_1 is selected from R_N, a hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, -NO_2, -NO_3, -O-NO, -N_3, -NH_2, -NHR*, -$N(R^*)_2$, -$N(R^*)_3^+$, -N(R*)-OH, -O-$N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, -CO_2H, -CO_2R^*, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*, -(C=O)-NH_2, -(C=O)-$N(R^*)_2$, -(C=O)-$NHNH_2$, -O-(C=O)-$NHNH_2$, -(C=S)-NH_2, -(C=S)-$N(R^*)_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, -SO_2R^*, -SO_2-$N(R^*)_2$, -S(=O)-OR*, -S(=O)-R*, -$Si(R^*)_3$, -CF_3, -O-CF_3 and combinations thereof, with the provisos that R_1 is not an n-butyl group, and when X is -O- and Ra is hydrogen, R_1 is not hydrogen;

R_N is selected from:





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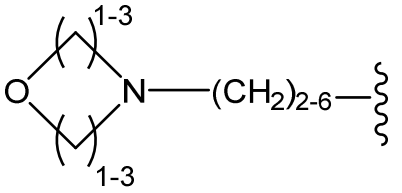

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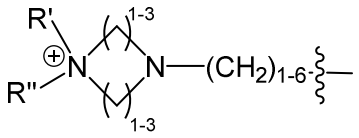

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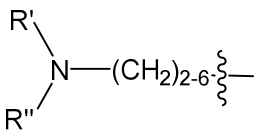

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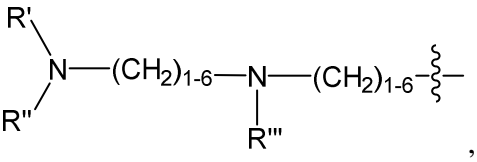

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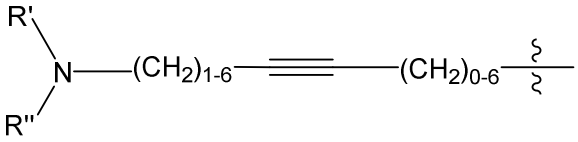

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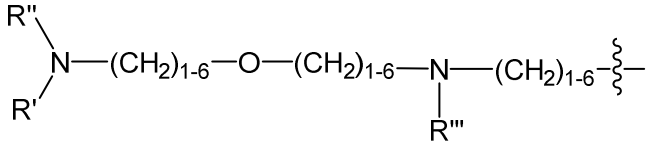


; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R_2, R_3, and R_4 are independently selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, or -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

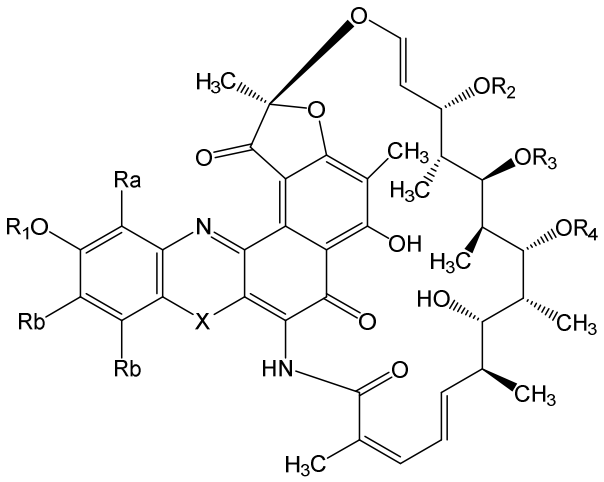
R_a is selected from hydrogen, F, -Cl, -Br, -I, -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -SR*, $-SO_2R^*$, and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R_b is selected from hydrogen, -F, -Cl, -Br, -I, -OH, -OR*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-3 heteroatoms selected from halogen, O, and S, and wherein R_b is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations

thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

3. The compound of claim 1 having a structure according to formula (I')



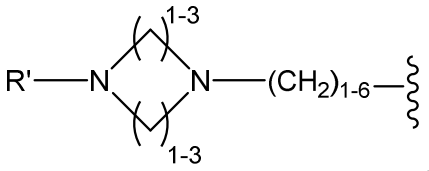
(I')

or a pharmaceutically acceptable salt thereof wherein:

X is selected from -O- and -NR*-;

R_1 is selected from R_N, a hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, $-NO_2$, $-NO_3$, -O-NO, $-N_3$, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-OH, $-O-N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*, $-(C=O)-NH_2$, $-(C=O)-N(R^*)_2$, $-(C=O)-NHNH_2$, $-O-(C=O)-NHNH_2$, $-(C=S)-NH_2$, $-(C=S)-N(R^*)_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, $-SO_2R^*$, $-SO_2-N(R^*)_2$, -S(=O)-OR*, -S(=O)-R*, $-Si(R^*)_3$, $-CF_3$, $-O-CF_3$ and combinations thereof, with the provisos that R_1 is not an n-butyl group, and when X is -O- and Ra is hydrogen, R_1 is not hydrogen;

R_N is selected from: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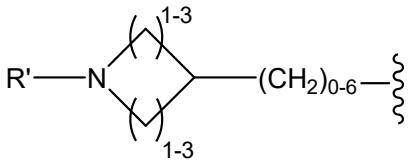
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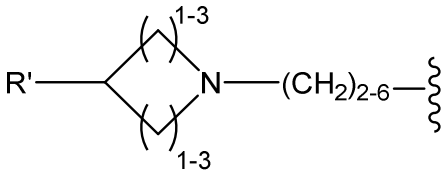
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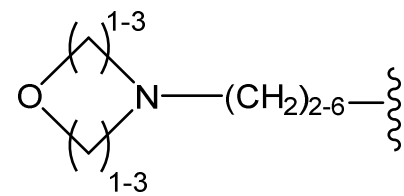
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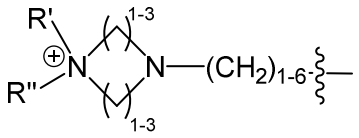
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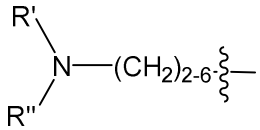
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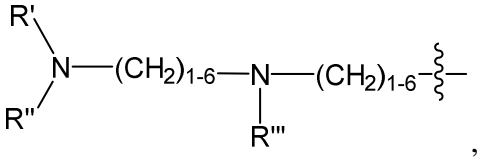
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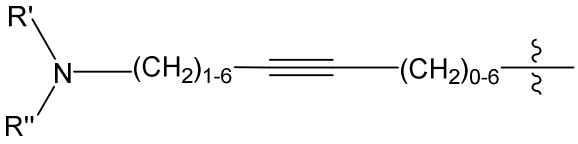
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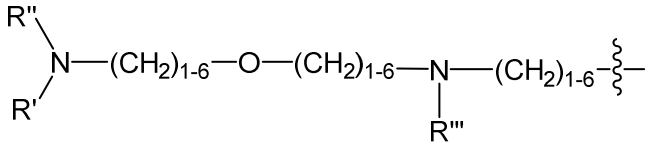

wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and B_{OC}, or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R_2, R_3, and R_4 are independently selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, or -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

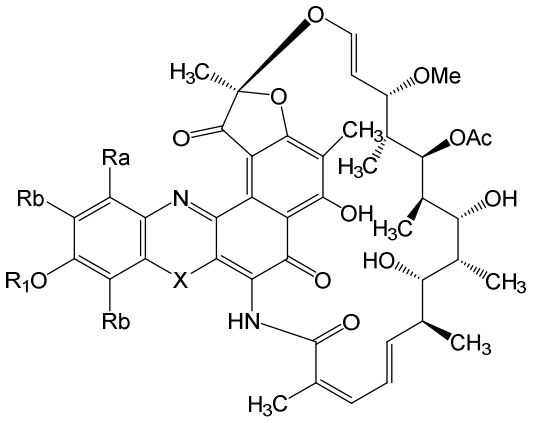
R_a is selected from hydrogen, F, -Cl, -Br, -I, -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -SR*, SO_2R^*, and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R_b is selected from hydrogen, -F, -Cl, -Br, -I, -OH, -OR*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-3 heteroatoms selected from halogen, O, and S, and wherein R_b is optionally substituted with one or more

of -F, -Cl, -Br, -I, -OH, -OR*; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

4. The compound of claim 1 or 2, having the structure of formula (II):



(II)

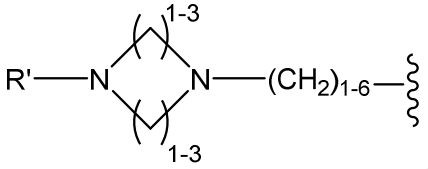
or a pharmaceutically acceptable salt thereof wherein:

X is selected from -O- and -NR*-;

R_a is selected from hydrogen, -Cl, and -OR*;

R_1 is selected from R_N, hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, $-NO_2$, $-NO_3$, -O-NO, $-N_3$, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-OH, $-O-N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*, $-(C=O)-NH_2$, $-(C=O)-N(R^*)_2$, $-(C=O)-NHNH_2$, $-O-(C=O)-NHNH_2$, $-(C=S)-NH_2$, $-(C=S)-N(R^*)_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, $-SO_2R^*$, $-SO_2-N(R^*)_2$, -S(=O)-OR*, -S(=O)-R*, $-Si(R^*)_3$, $-CF_3$, $-O-CF_3$ and combinations thereof, with a proviso that R_1 is not an n-butyl group;

R_N is selected from:



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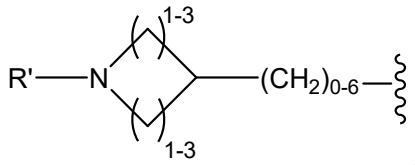

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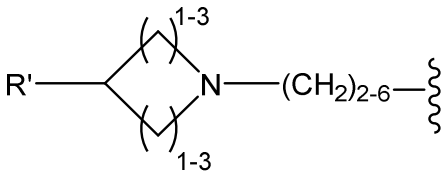

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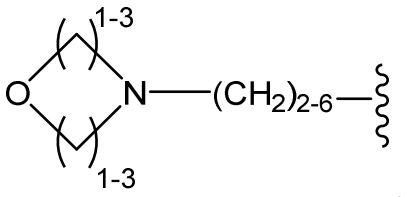

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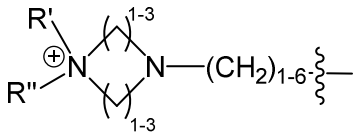

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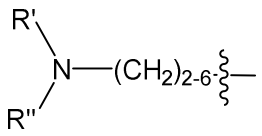

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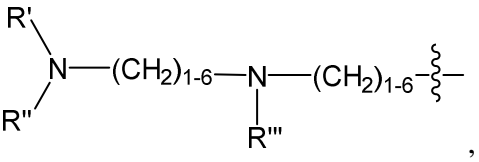

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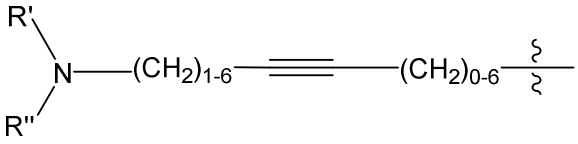

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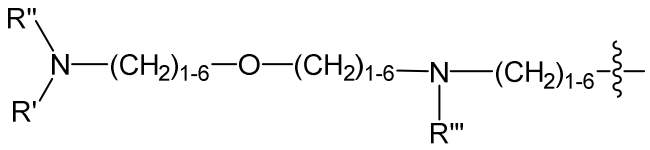
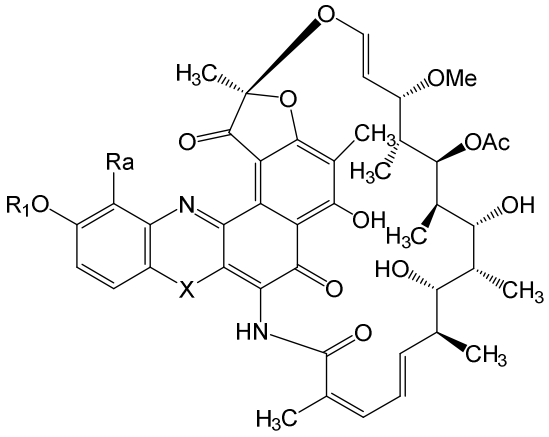


; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

5. The compound of claim 1 or 3, having a structure according to formula (II'):



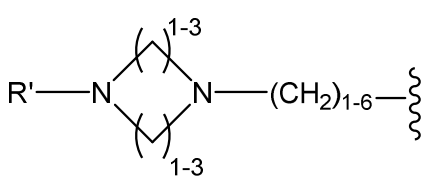
(II')

wherein:

X is selected from -O- and -NR*-;

R_a is selected from hydrogen, -Cl, and -OR*;

R_1 is selected from R_N, hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, $-NO_2$, $-NO_3$, -O-NO, $-N_3$, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-OH, $-O-N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*, $-(C=O)-NH_2$, $-(C=O)-N(R^*)_2$, $-(C=O)-NHNH_2$, $-O-(C=O)-NHNH_2$, $-(C=S)-NH_2$, $-(C=S)-N(R^*)_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, $-SO_2R^*$, $-SO_2-N(R^*)_2$, -S(=O)-OR*, -S(=O)-R*, $-Si(R^*)_3$, $-CF_3$, $-O-CF_3$ and combinations thereof, with a proviso that R_1 is not an n-butyl group; R_N is selected from:



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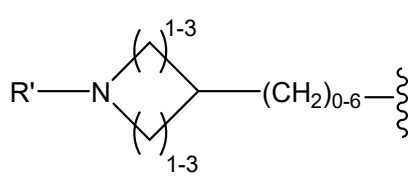

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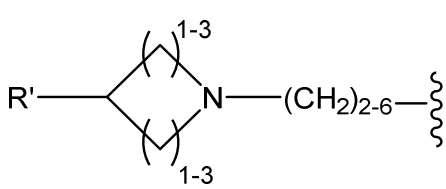

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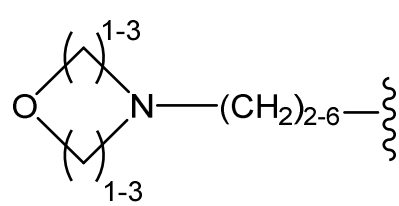

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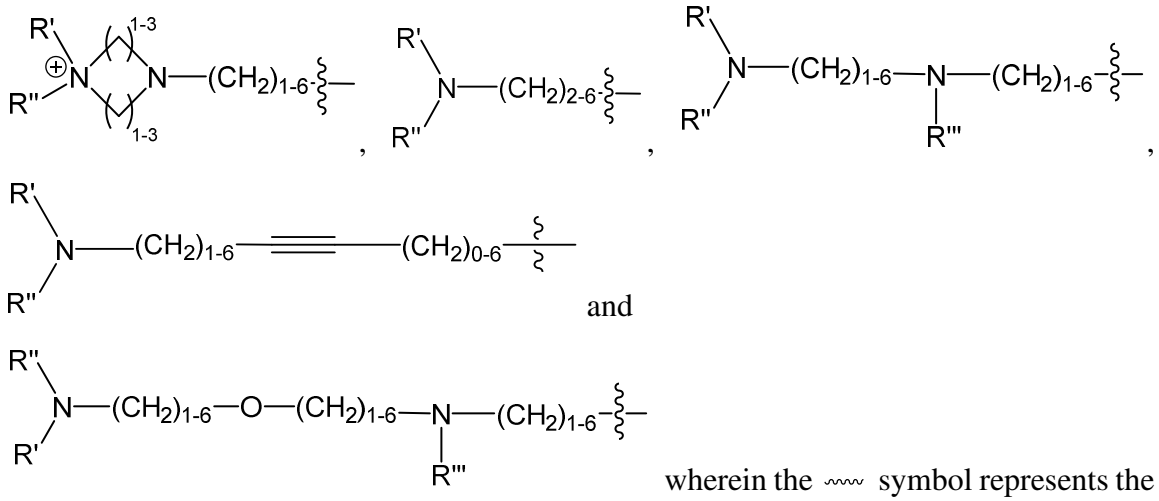
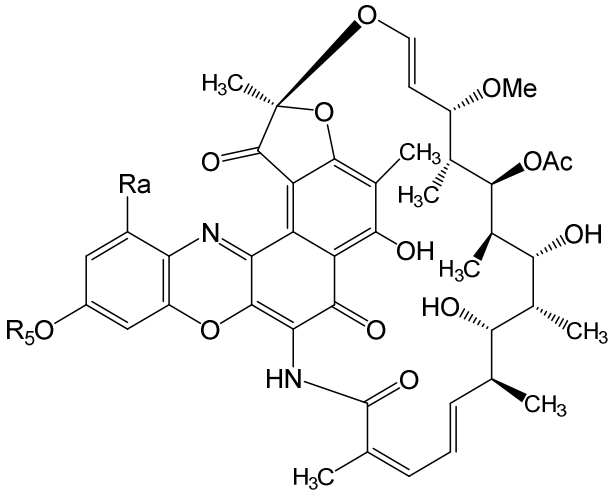


and

wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

6. The compound of claims 1, 2 or 4 having a structure according to formula (III):



(III)

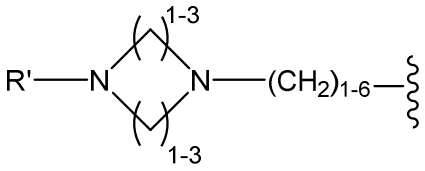
or a pharmaceutically acceptable salt thereof wherein:

R_a is selected from hydrogen and -OR*;

R_5 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_5 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NH_2, -NHR*, -$N(R^*)_2$, -$N(R^*)_3^+$, -(C=O)-R*, -CHO, -CO_2H, -CO_2R^* and combinations thereof, with a proviso that R_5 is not an n-butyl group;

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof; and

R_N is selected from: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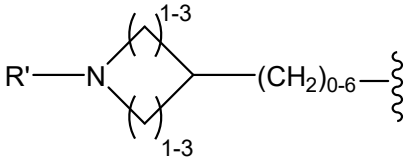
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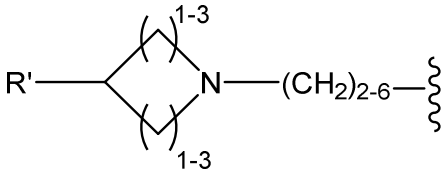
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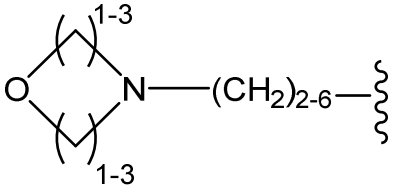
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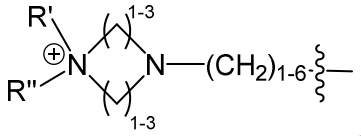
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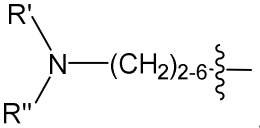
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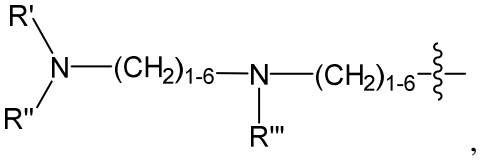
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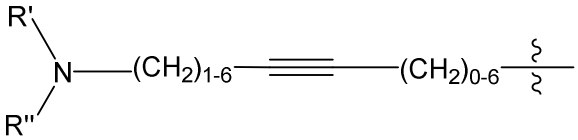
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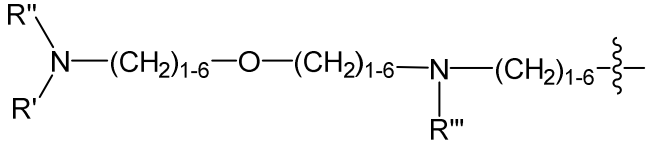
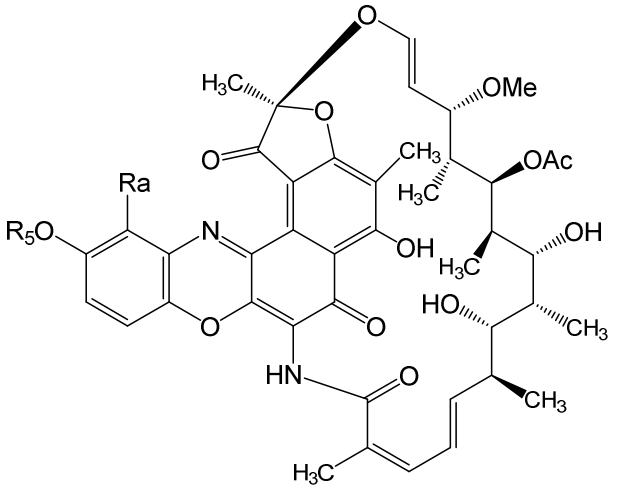

; wherein the 〰 symbol represents the

point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure.

7. The compound of claims 1, 3, or 5 having a structure according to formula (III'):



(III')

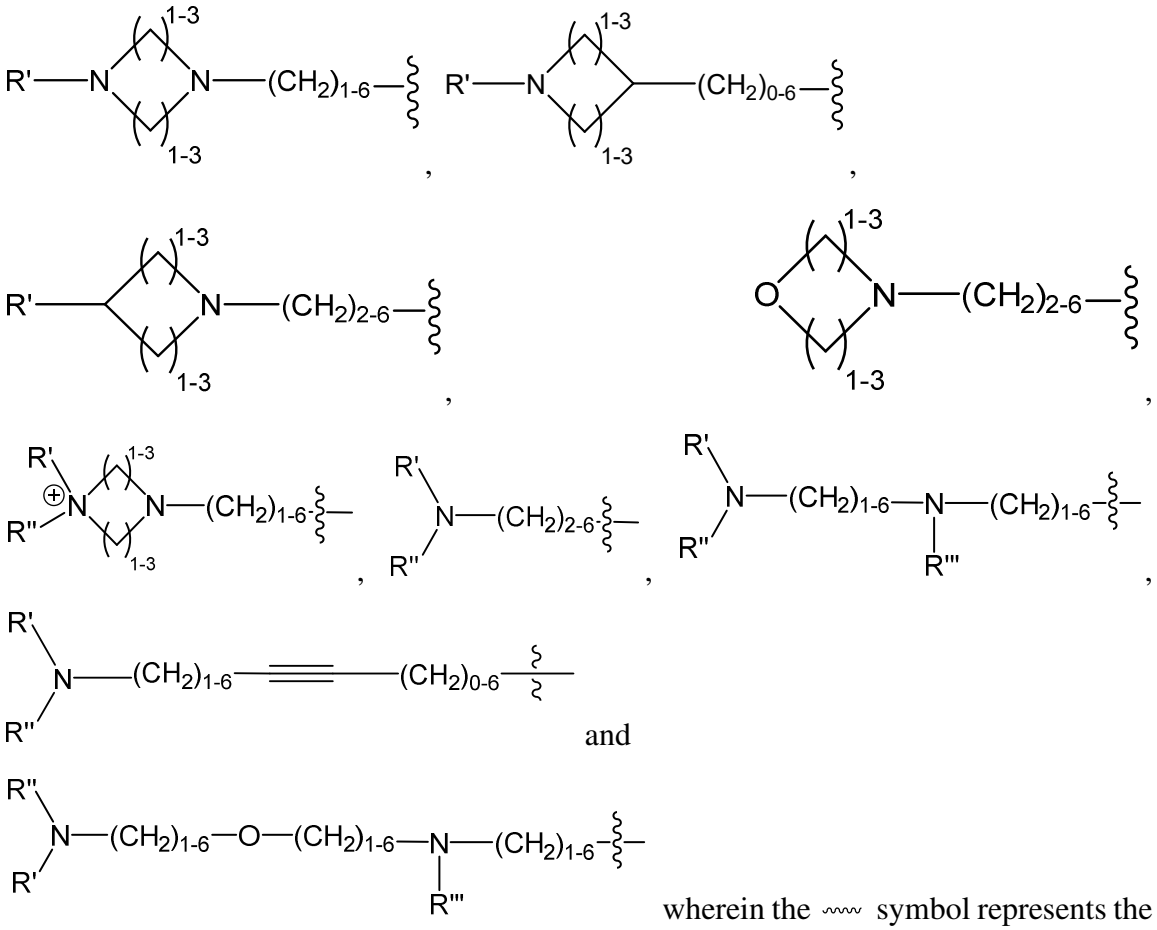
or a pharmaceutically acceptable salt thereof wherein:

R_a is selected from hydrogen and -OR*;

R_5 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_5 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and combinations thereof, with a proviso that R_5 is not an n-butyl group;

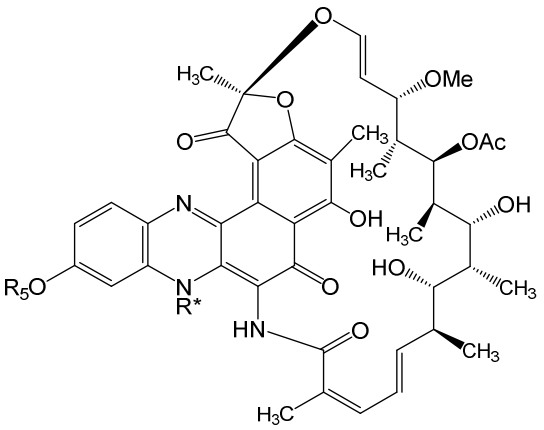
R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof; and

R_N is selected from:



wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure.

8. The compound of claims 1, 2 or 4 having a structure according to formula (IV):



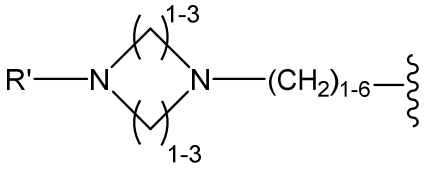
(IV)

or a pharmaceutically acceptable salt thereof wherein:

R_a is selected from hydrogen and -OR*;

R_5 is selected from R_N, hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_6-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_5 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NH_2, -NHR*, -$N(R^*)_2$, -$N(R^*)_3^+$, -(C=O)-R*, -CHO, -CO_2H, -CO_2R^* and combinations thereof;

R_N is selected from:



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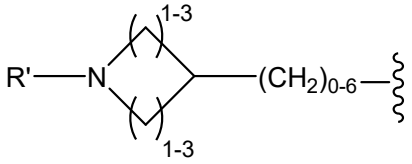

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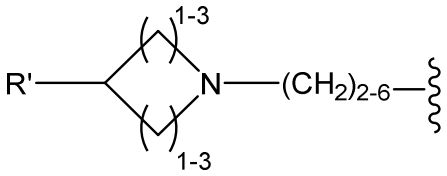

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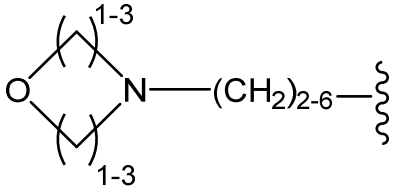

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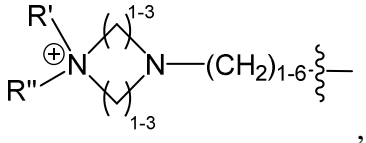

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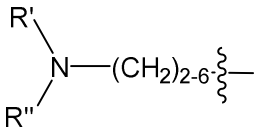

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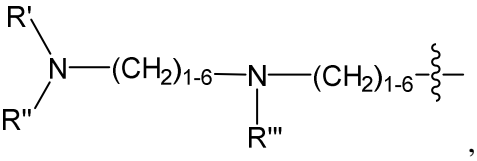

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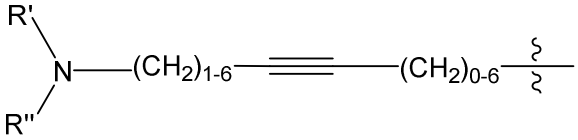

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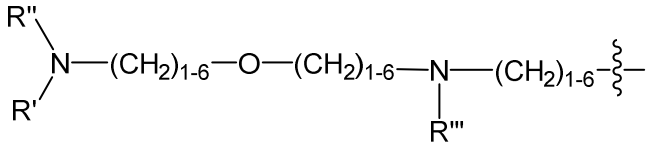
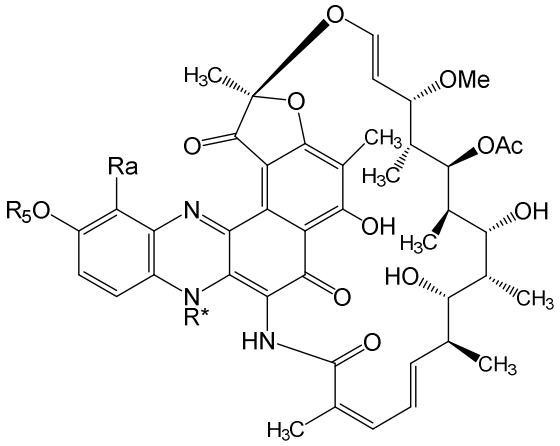


; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20}

hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

9. The compound of claims 1, 3, or 5 having a structure according to formula (IV'):



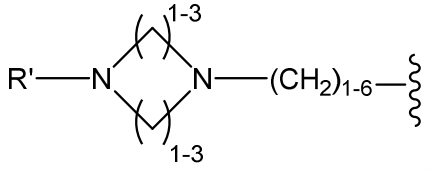
(IV')

or a pharmaceutically acceptable salt thereof wherein:

R_a is selected from hydrogen and -OR*;

R_5 is selected from R_N, hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_6-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_5 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and combinations thereof;

R_N is selected from:



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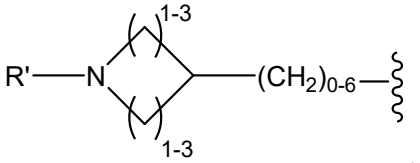

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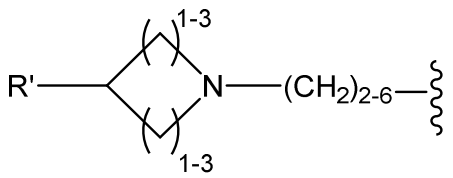

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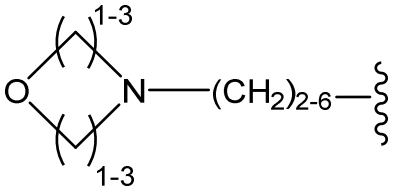

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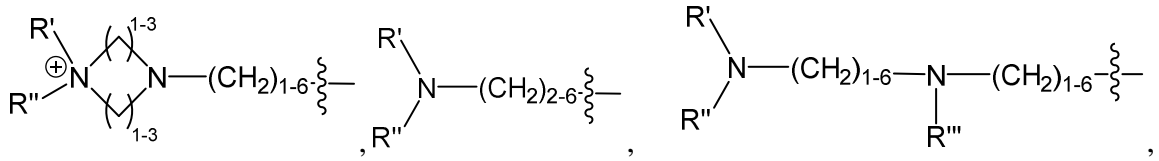

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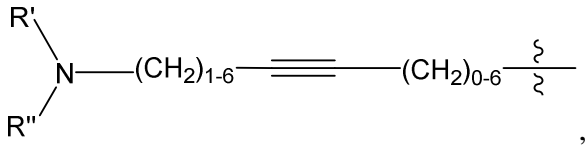

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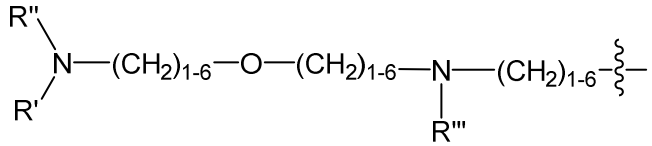
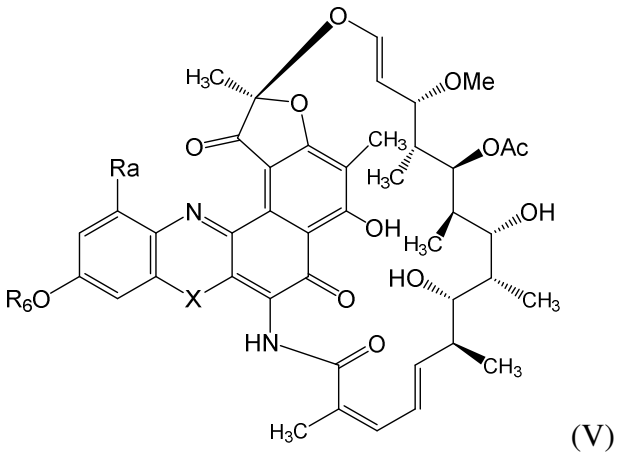


; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

10. The compound of claims 1, 2 or 4 having a structure according to formula (V):



(V)

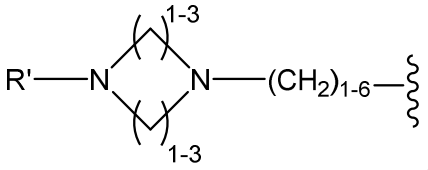
or a pharmaceutically acceptable salt thereof wherein:

X is selected from -O- and -NR*-;

R_a is selected from hydrogen and -OR*;

R_6 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_6 is optionally substituted with one or more of -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-(C=O)-R*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and combinations thereof, with a proviso that R_6 is not an n-butyl group;

R_N is selected from:



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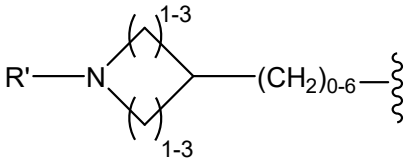

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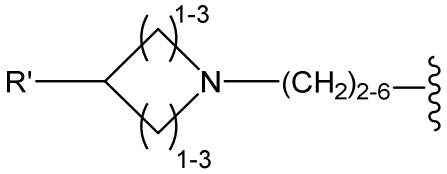

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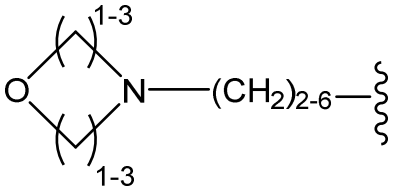

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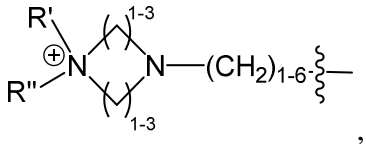

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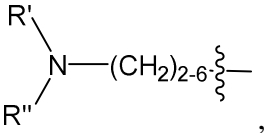

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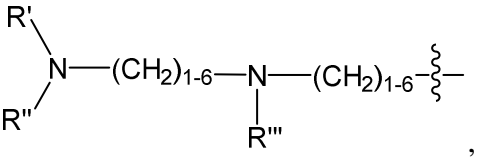

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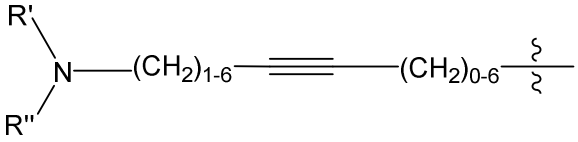

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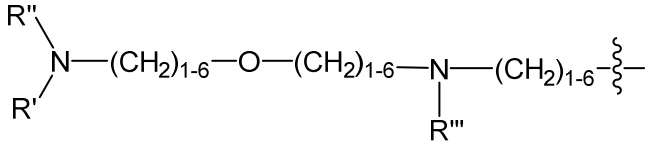
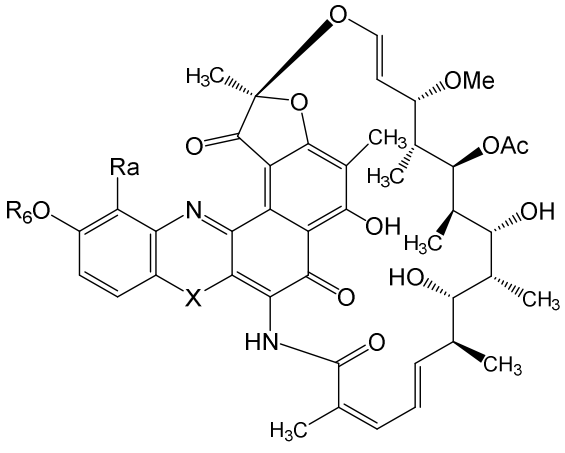


wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

11. The compound of claims 1, 3, or 5 having a structure according to formula (V'):



(V')

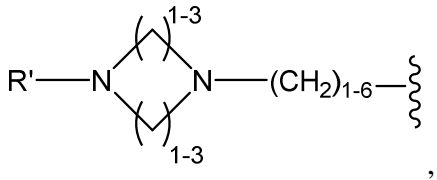
or a pharmaceutically acceptable salt thereof wherein:

X is selected from -O- and -NR*-;

R_a is selected from hydrogen and -OR*;

R_6 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_6 is optionally substituted with one or more of -OH, -OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-(C=O)-R*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and combinations thereof, with a proviso that R_6 is not an n-butyl group;

R_N is selected from:



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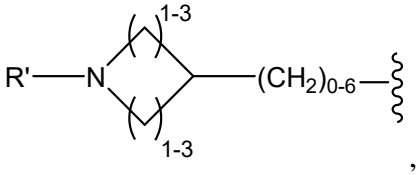

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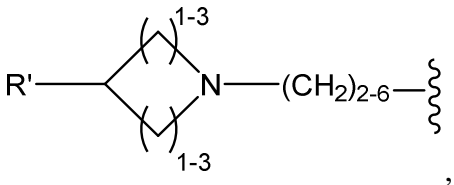

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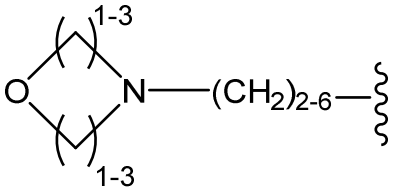

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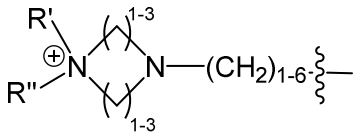

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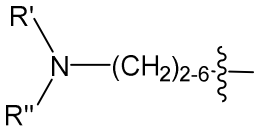

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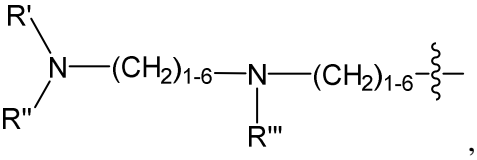

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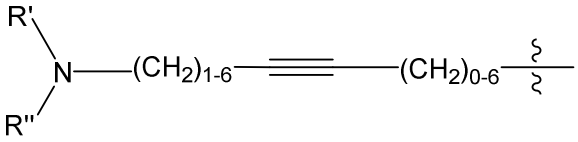

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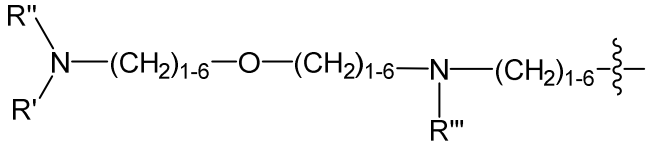
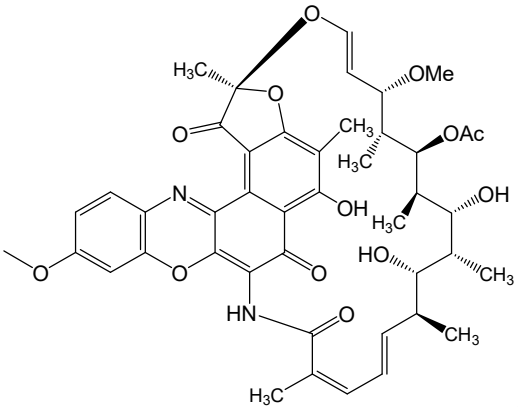


wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_5-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

12. A compound having the structure selected from the group consisting of: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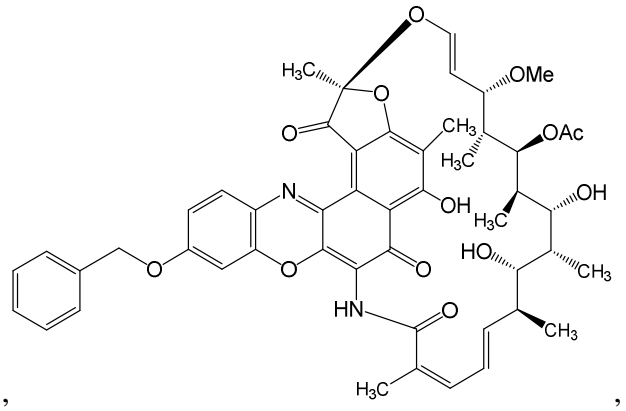
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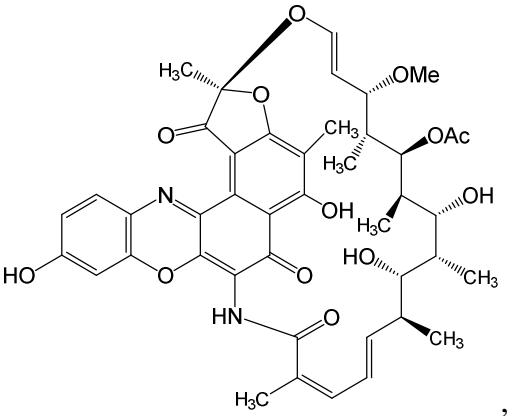
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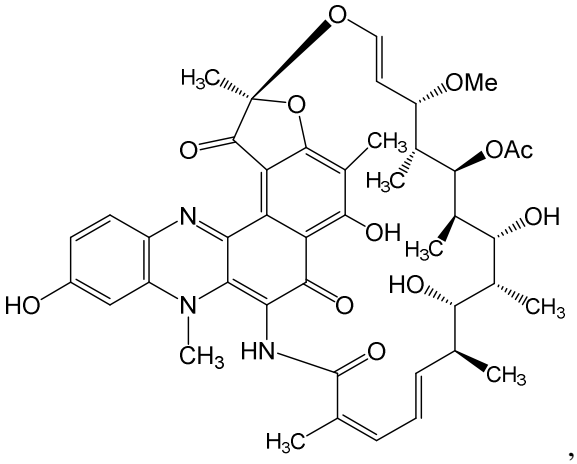
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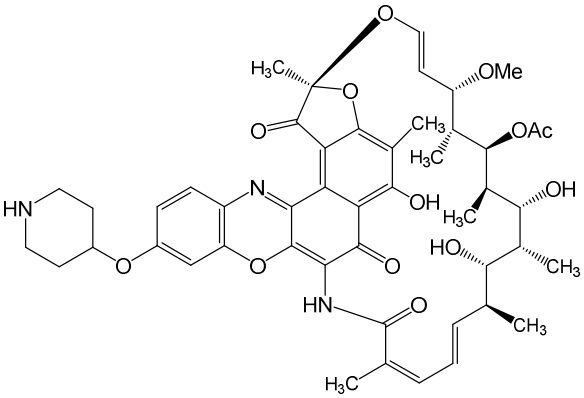
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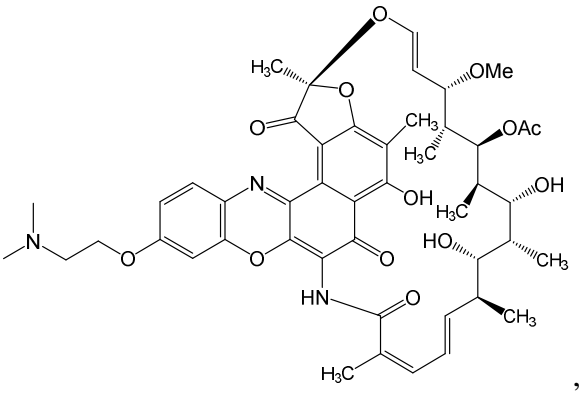
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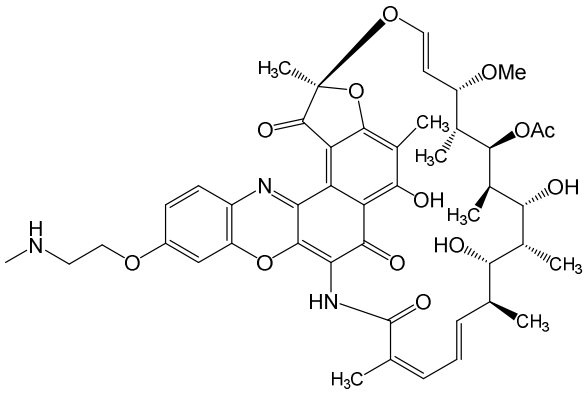

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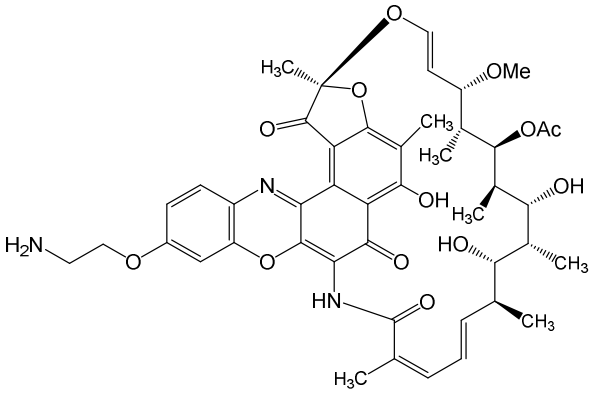

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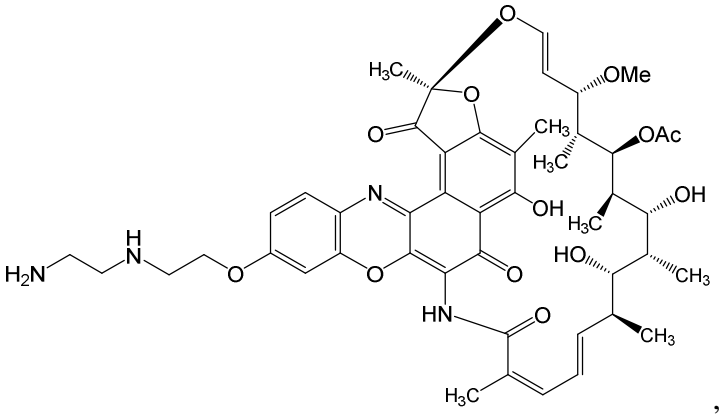

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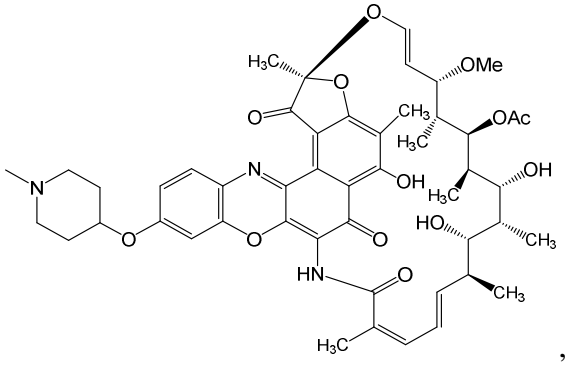

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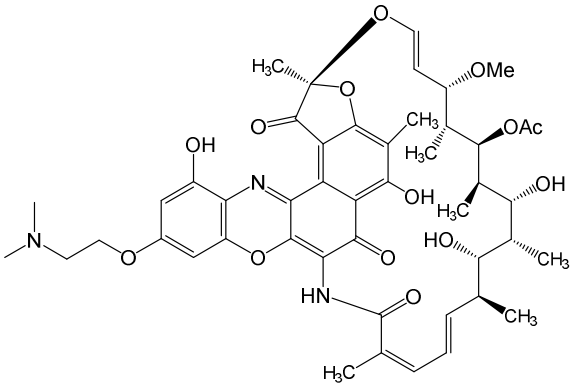

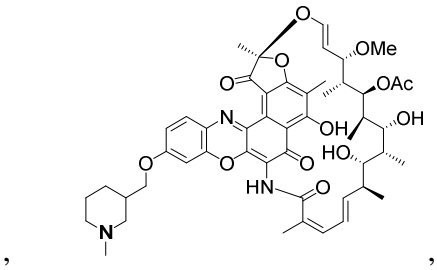
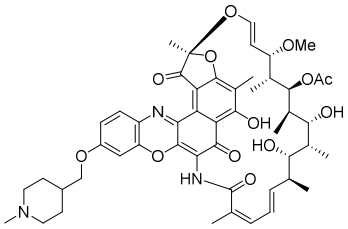
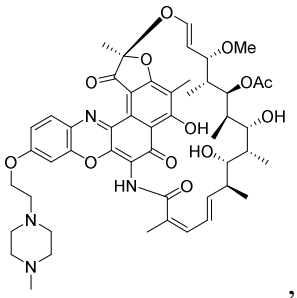
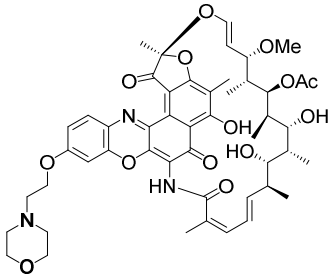
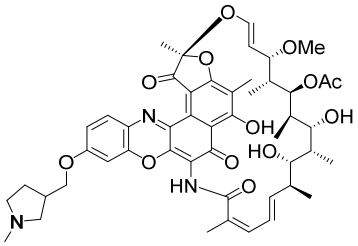
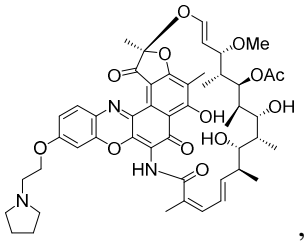
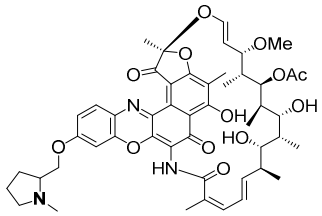
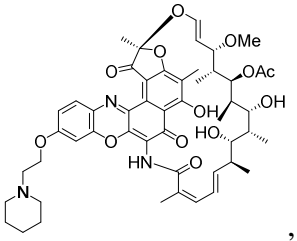
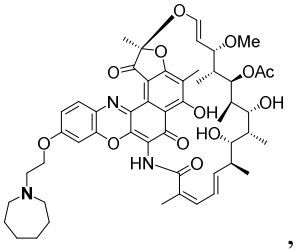
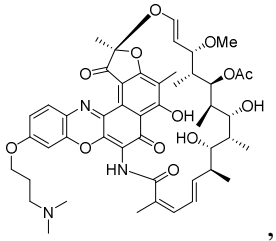
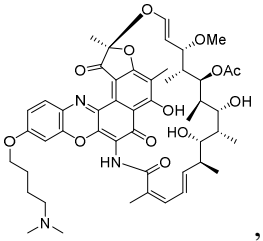
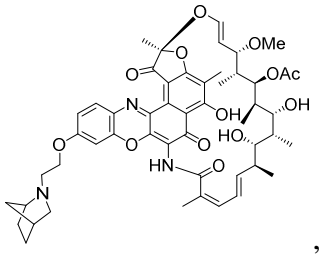
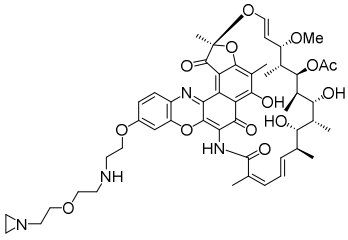
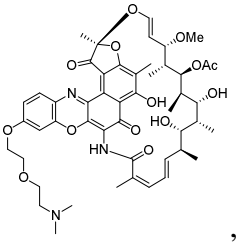
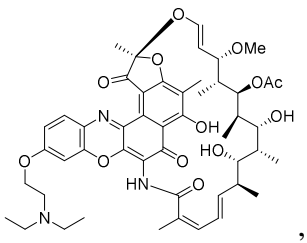
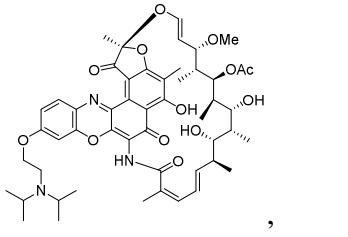
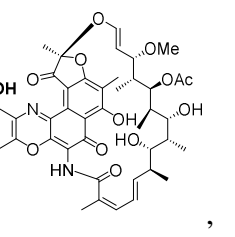
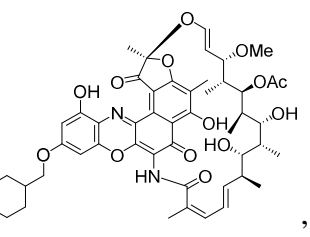



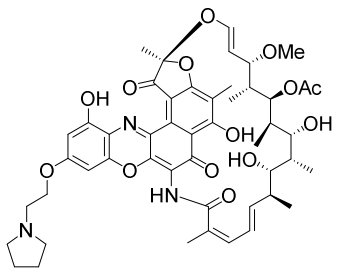
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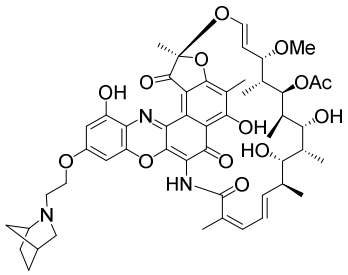
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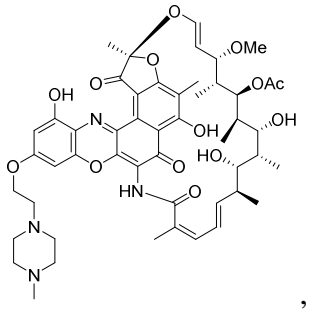
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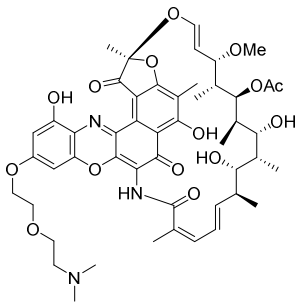
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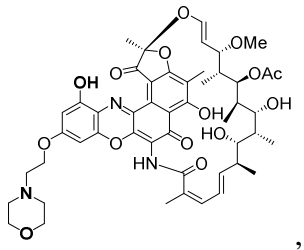
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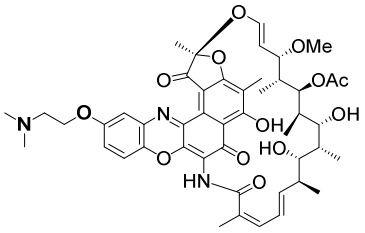
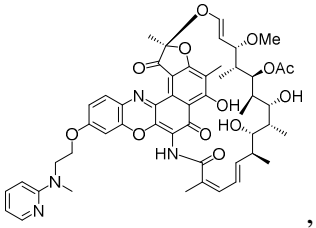
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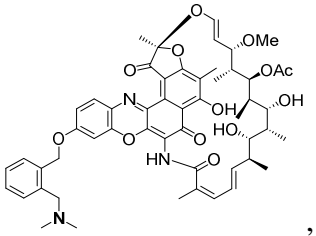
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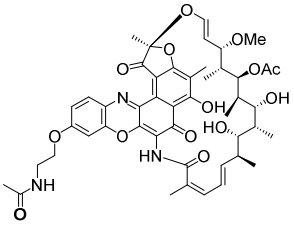
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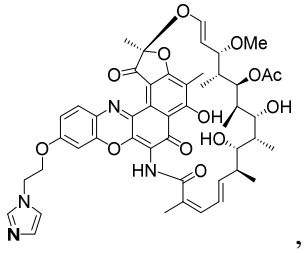
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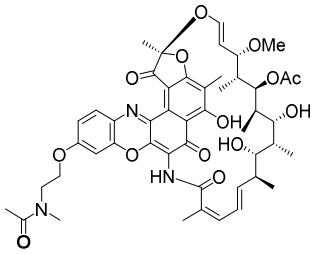
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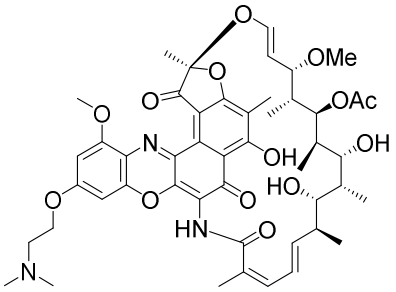
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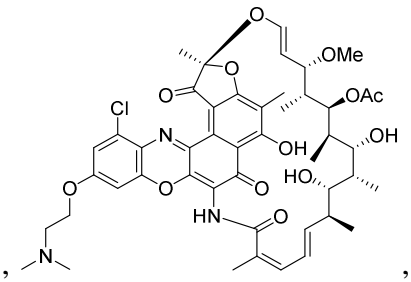
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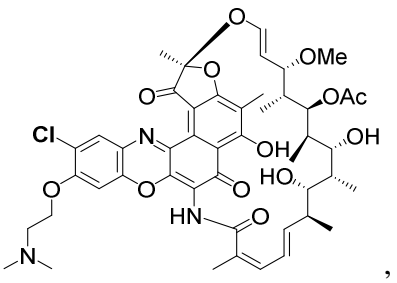
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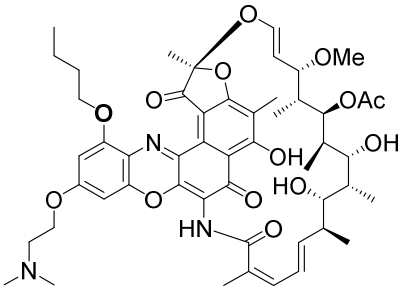
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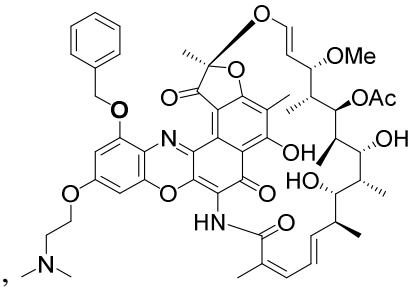
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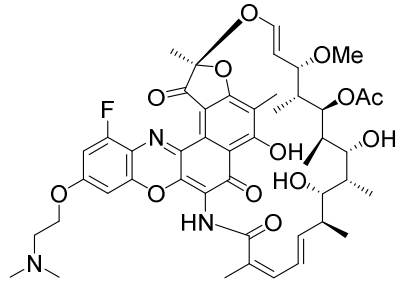
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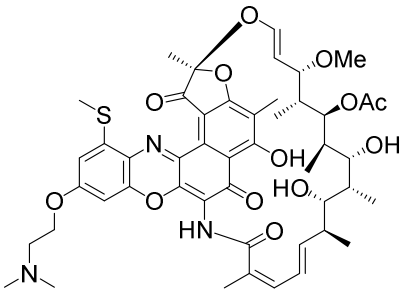
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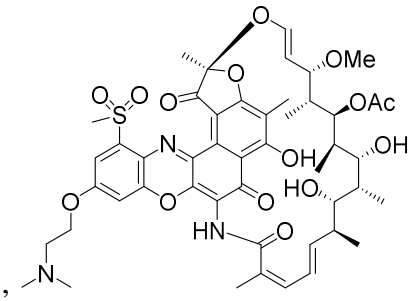
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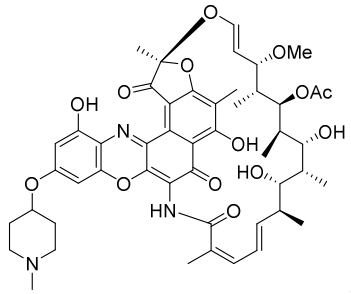
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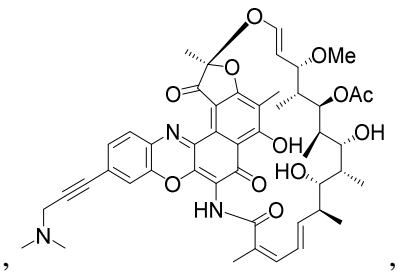
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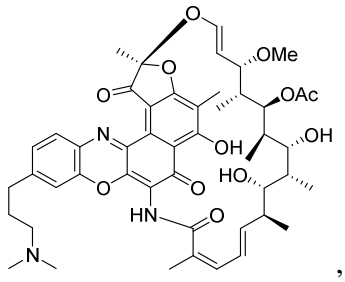
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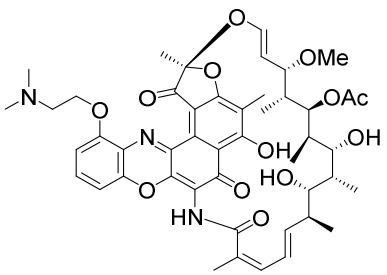
or a pharmaceutically acceptable salt thereof.

13. A compound having the structure

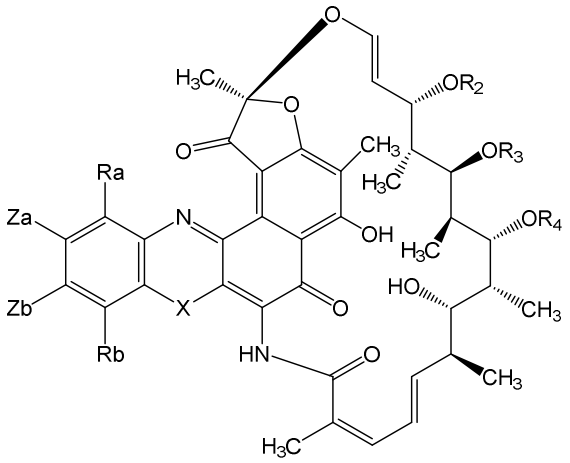


or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising the compound of any of claims 1-13 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

15. A pharmaceutical dosage form comprising the compound of any of claims 1-13 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition of claim14.

16. Use of a compound having the structure of formula (A):



(A)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preventing or inhibiting growth of a bacterium, wherein:

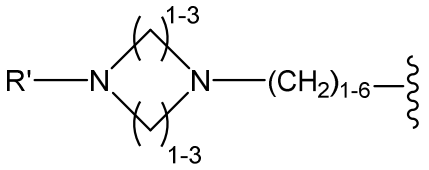
X is selected from -O-, -S- and -NR*-;

Za and Zb are independently selected from a hydrogen, $-OR_1$, -Cl, -Br and $-R_N$, with the proviso that at least one of Za or Zb is not a hydrogen, wherein:

R_1 is selected from a hydrogen, R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, $-NO_2$, $-NO_3$, -O-NO, $-N_3$, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -N(R*)-OH, $-O-N(R^*)_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*,$-(C=O)-NH_2$, $-(C=O)-N(R^*)_2$, $-(C=O)-NHNH_2$, $-O-(C=O)-NHNH_2$,

-(C=S)-NH_2, -(C=S)-$N(R^*)_2$, -$N(R^*)$-CHO, -$N(R^*)$-(C=O)-R^*, -SCN, -NCS, -NSO, -SSR*, -SO_2R^*, -SO_2-$N(R^*)_2$, -S(=O)-OR*, -S(=O)-R^*, -$Si(R^*)_3$, -CF_3, -O-CF_3 and combinations thereof, with the provisos that R_1 is not an n-butyl group, and when X is -O- and Ra is hydrogen, R_1 is not hydrogen;

R_N is selected from:



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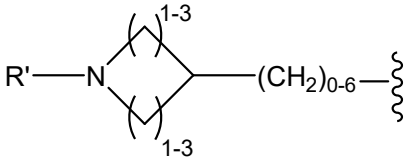

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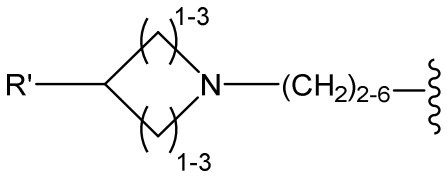

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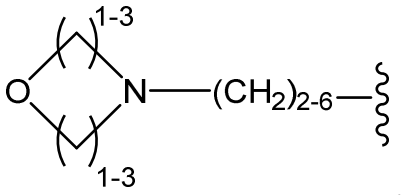

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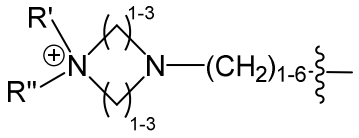

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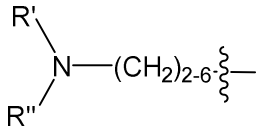

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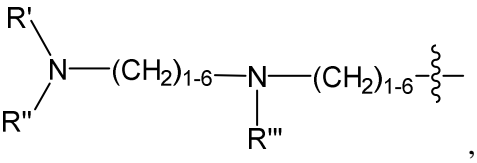

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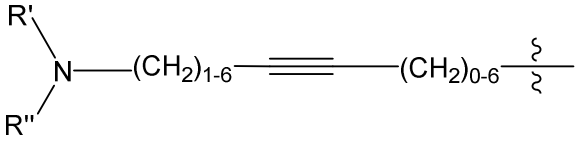

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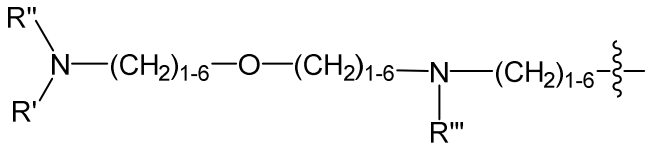


; wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from Fluorenylmethyloxycarbonyl (F_{MOC}) and *tert*-Butyloxycarbonyl (B_{OC}), or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R_2, R_3, and R_4 are independently selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, and -(C=O)-R^*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

R_a is selected from hydrogen, -Cl, -OR*, -F, -Br, -I, -OH, -NH_2, -NHR*, -$N(R^*)_2$, -$N(R^*)_3^+$, -(C=O)-R^*, -CHO, -CO_2H, -CO_2R^*, -SR*, SO_2R^*, and an aliphatic C_1-C_{20} hydrocarbon,

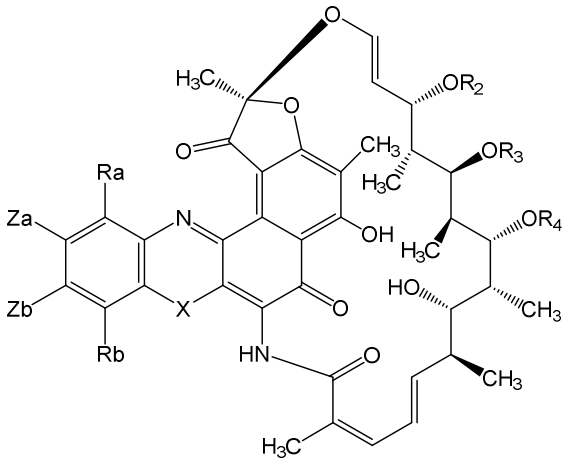
which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R_b is selected from hydrogen, -F, -Cl, -Br, -I, -OH, -OR*, -(C=O)-R*, -CHO, -CO_2H, -CO_2R* and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-3 heteroatoms selected from halogen, O, and S, and wherein R_b is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

17. Use of a compound having the structure of any of claims 1-13 in the manufacture of a medicament for preventing or inhibiting growth of a bacterium.

18. Use of a compound having the structure of formula (A):



(A)

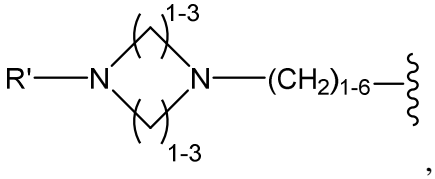
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a bacterial infection in a subject in need of such treatment, wherein:

X is selected from -O-, -S- and -NR*-;

Za and Zb are independently selected from a hydrogen, -OR_1, -Cl, -Br and -R_N, with the proviso that at least one of Za or Zb is not a hydrogen wherein:

R_1 is selected from a hydrogen, R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon; a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, -NO_2, -NO_3, -O-NO, -N_3, -NH_2, -NHR*, -N(R*)$_2$, -N(R*)$_3^+$, -N(R*)-OH, -O-N(R*)$_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, -CO_2H, -CO_2R*, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*,-(C=O)-NH_2, -(C=O)-N(R*)$_2$, -(C=O)-$NHNH_2$, -O-(C=O)-$NHNH_2$, -(C=S)-NH_2, -(C=S)-N(R*)$_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, -SO_2R*, -SO_2-N(R*)$_2$, -S(=O)-OR*, -S(=O)-R*, -Si(R*)$_3$, -CF_3, -O-CF_3 and combinations thereof, with the provisos that R_1 is not an n-butyl group, and when X is -O- and Ra is hydrogen, R_1 is not hydrogen;

R_N is selected from:



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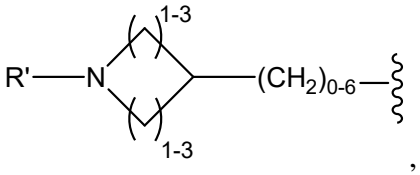

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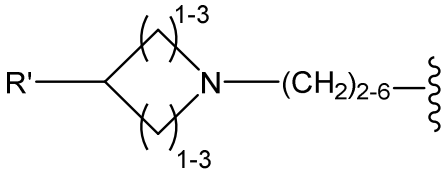

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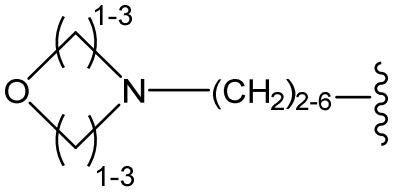

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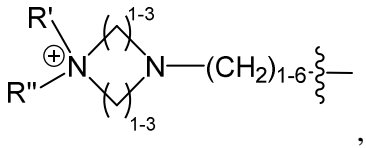

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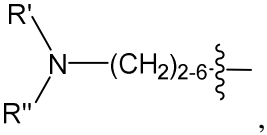

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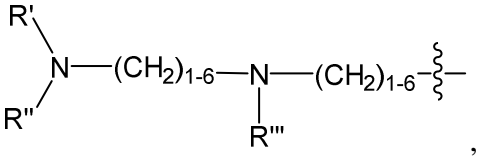

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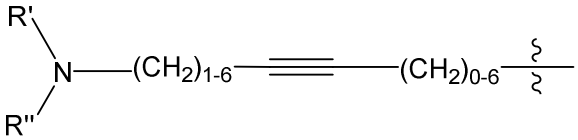

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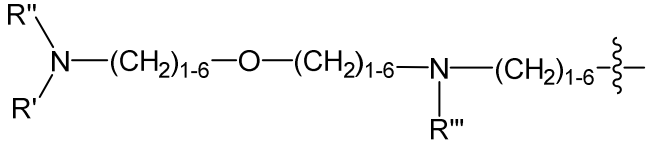


; wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic

hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R_2, R_3, and R_4 are independently selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, and -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

R_a is selected from hydrogen, -Cl, -OR*, -F, -Br, -I, -OH, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -SR*, SO_2R^*, and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R_b is selected from hydrogen, -F, -Cl, -Br, -I, -OH, -OR*, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$ and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-3 heteroatoms selected from halogen, O, and S, and wherein R_b is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof.

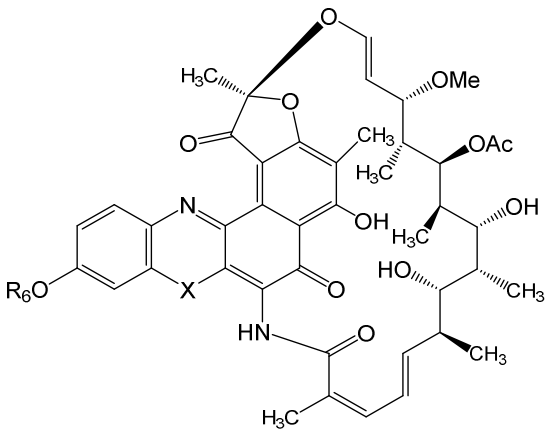
19. Use of a compound having the structure of any of claims 1-13 in the manufacture of a medicament for treating a bacterial infection in a subject in need of such treatment.

20. The use of any of claims 18-19, wherein the subject is human.

21. The use of any of claims 18-20, further comprising administering a second therapeutic agent.

22. The use of claim21, wherein the second therapeutic agent is a second antibiotic.

23. A method of manufacturing a compound having the structure of formula (V):

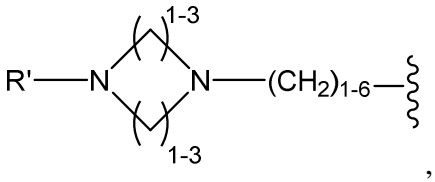


(V),

wherein X is selected from -O- and NR*-;

R_6 is selected from a hydrogen, R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof,

R_N is selected from:



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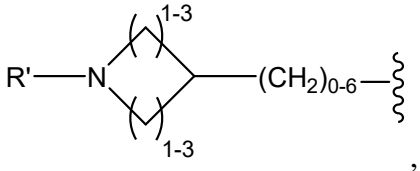

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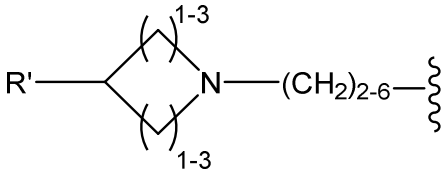

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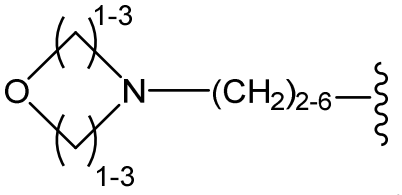

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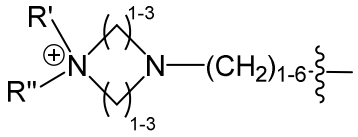

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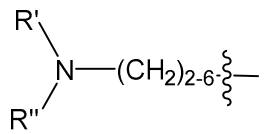

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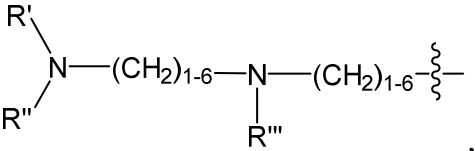

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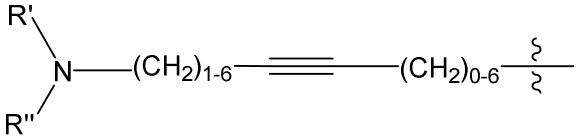

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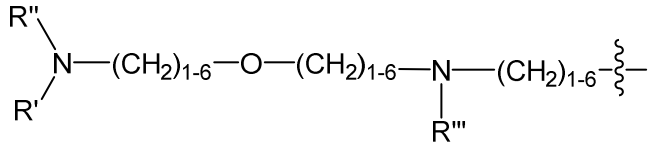
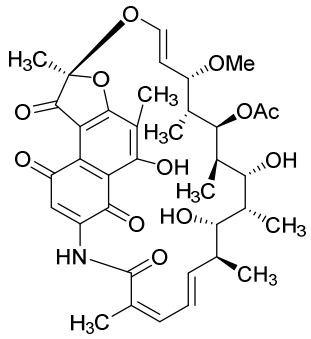


; wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

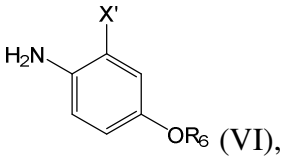
R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof,

comprising the steps of:

(a) contacting Rifamycin S having the structure:



with a compound having the structure of formula (VI):

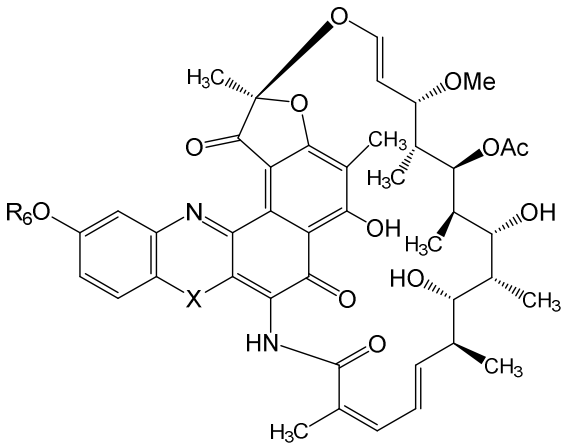


(VI),

wherein X' is selected from -OH and -NHR*, and

(b) treating the product of step (a) with an oxidizing agent.

24. A method of manufacturing a compound having the structure (V'):

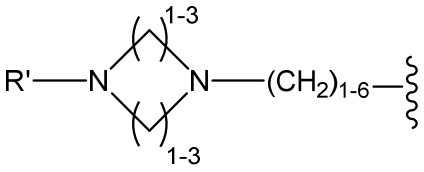


(V'),

wherein X is selected from -O- and NR*-;

R_6 is selected from a R_N, hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof,

R_N is selected from: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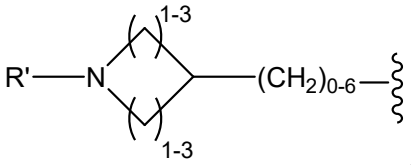
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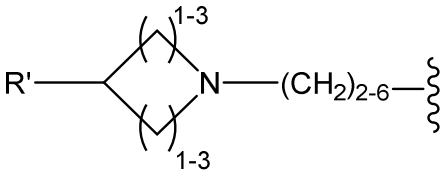
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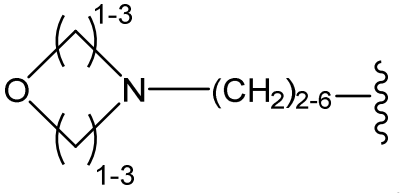
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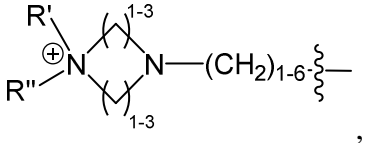
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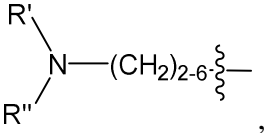
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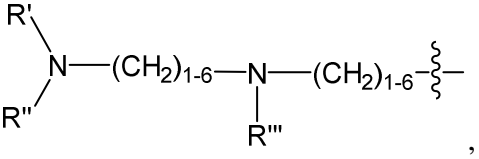
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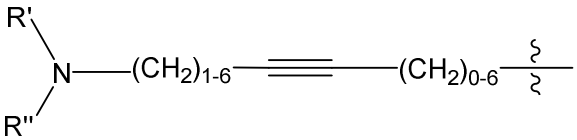
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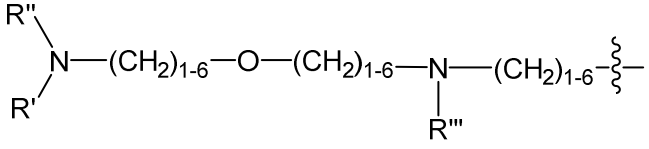
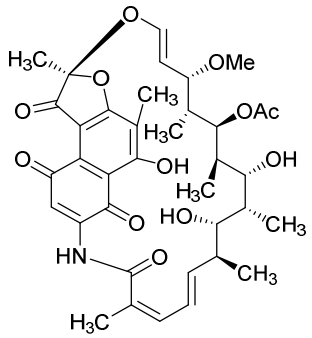

; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic

hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

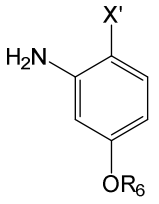
R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof,

comprising the steps of:

(a) contacting Rifamycin S having the structure:



with a compound having the structure of formula (VI'):

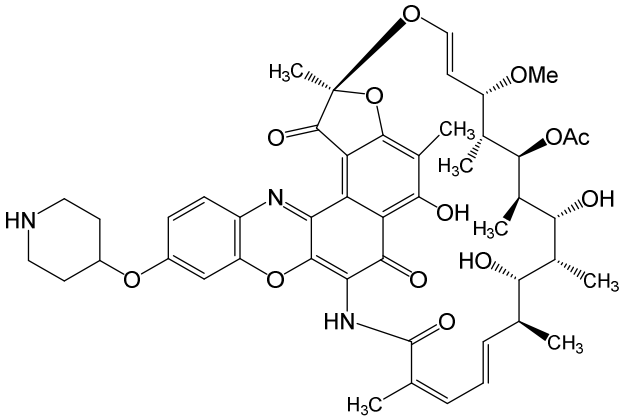


(VI'),

wherein X' is selected from -OH and -NHR*, and

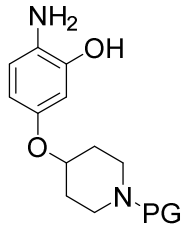
(b) treating the product of step (a) with an oxidizing agent.

25. A method of manufacturing a compound having the structure:



comprising the steps of:

(a) contacting Rifamycin S with a compound having the structure of formula (VII):



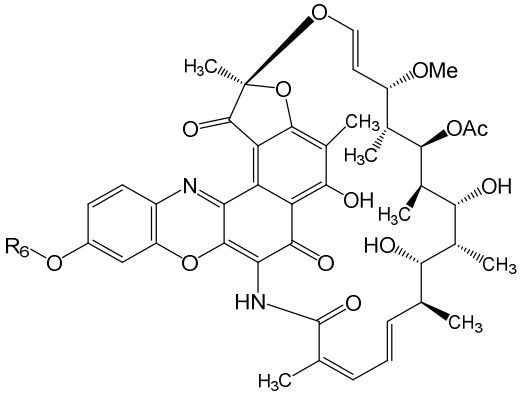
(VII),

wherein PG is a protecting group;

(b) treating the product of step (a) with an oxidizing agent, and

(c) removing the protecting group PG.

26. A method of manufacturing a compound having the structure of formula (XI):

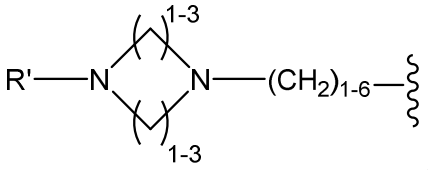


(XI)

wherein R_6 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-

8 heteroatoms selected from halogen, O, N, and S and combinations thereof and wherein R_6 is optionally substituted with one or more of -F; -Cl; -Br; -I; -OH, -OR*; -NO; $-NO_2$; $-NO_3$; -O-NO; $-N_3$; $-NH_2$; -NHR*; $-N(R^*)_2$; $-N(R^*)_3^+$; -N(R*)-OH; $-O-N(R^*)_2$; -N(R*)-O-R*; -CN; -NC; -(C=O)-R*; -CHO; $-CO_2H$; $-CO_2R^*$; -(C=O)-S-R*; -O-(C=O)-H; -O-(C=O)-R*; -S-(C=O)-R*; $-(C=O)-NH_2$; $-(C=O)-N(R^*)_2$; $-(C=O)-NHNH_2$; $-O-(C=O)-NHNH_2$; $-(C=S)-NH_2$; $-(C=S)-N(R^*)_2$; -N(R*)-CHO; -N(R*)-(C=O)-R*; -SCN; -NCS; -NSO; -SSR*; $-SO_2R^*$; $-SO_2-N(R^*)_2$; $-S(=O)-OR^*$; -S(=O)-R*; $-Si(R^*)_3$; $-CF_3$; $-O-CF_3$ and combinations thereof,

R_N is selected from:



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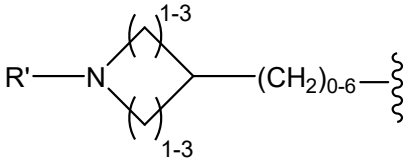

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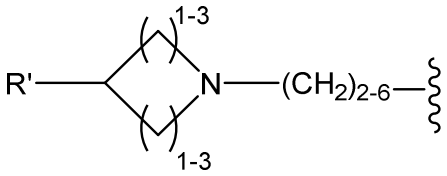

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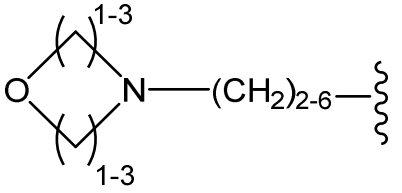

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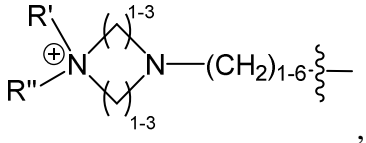

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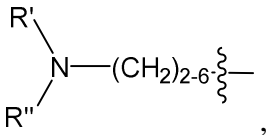

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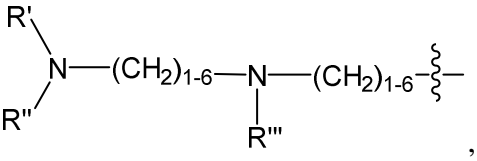

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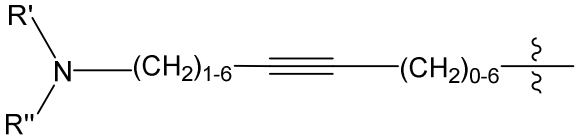

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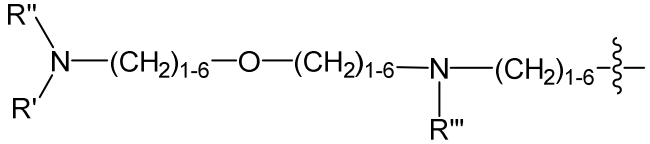
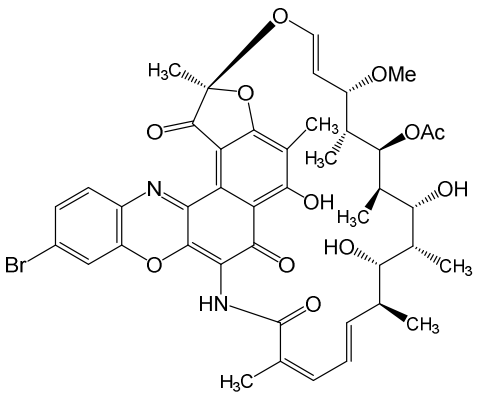


wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20}

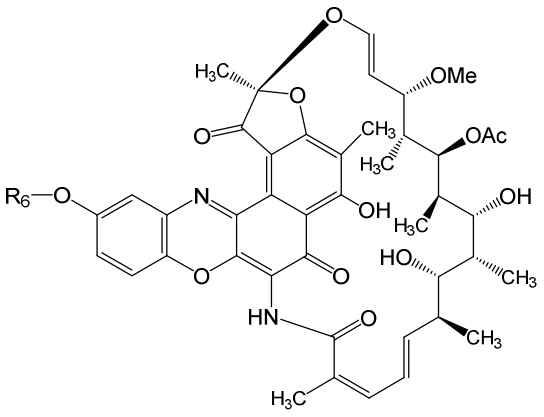
hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof, comprising contacting a compound having the structure of formula (XII):



(XII)

with an alcohol having the structure R_6-OH.

27. A method of manufacturing a compound having the structure of formula (XI'):

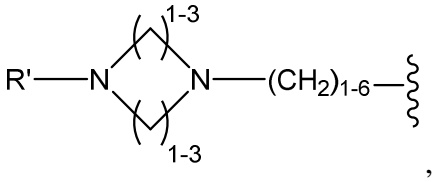


(XI')

wherein R_6 is selected from R_N, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof and wherein R_6 is optionally substituted with one or more of -F; -Cl; -Br; -I; -OH, -OR*; -NO; -NO_2; -NO_3; -O-NO; -N_3; -NH_2; -NHR*; -N(R*)$_2$; -N(R*)$_3^+$; -N(R*)-OH; -O-N(R*)$_2$; -N(R*)-O-R*; -CN; -NC; -(C=O)-R*; -CHO; -CO_2H; -CO_2R*; -(C=O)-S-R*; -O-(C=O)-H; -O-(C=O)-R*; -S-(C=O)-R*; -(C=O)-NH_2; -(C=O)-N(R*)$_2$; -(C=O)-$NHNH_2$; -O-(C=O)-

$NHNH_2$; -(C=S)-NH_2; -(C=S)-$N(R^*)_2$; -$N(R^*)$-CHO; -$N(R^*)$-(C=O)-R^*; -SCN; -NCS; -NSO; -SSR*; -SO_2R^*; -SO_2-$N(R^*)_2$; -S(=O)-OR^*; -S(=O)-R^*; -$Si(R^*)_3$; -CF_3; -O-CF_3 and combinations thereof,

R_N is selected from:



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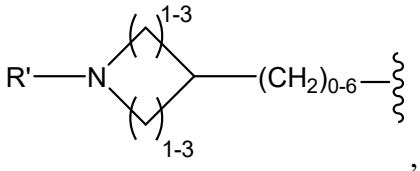

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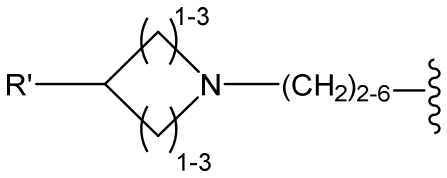

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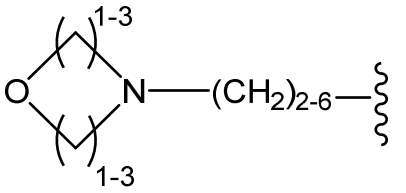

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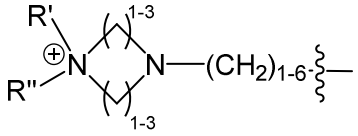

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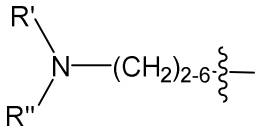

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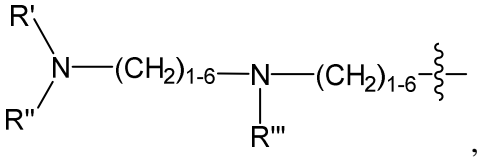

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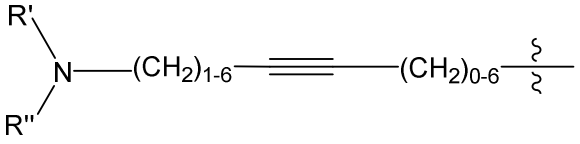
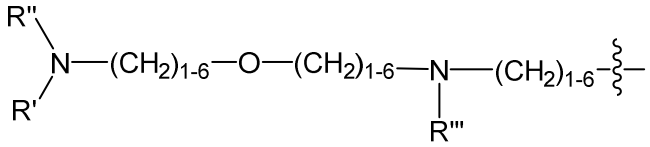


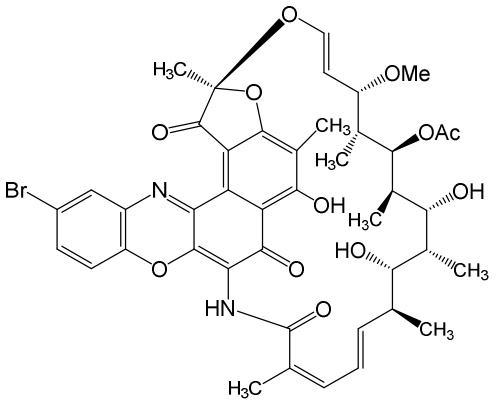
and



wherein the ~~~ symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations

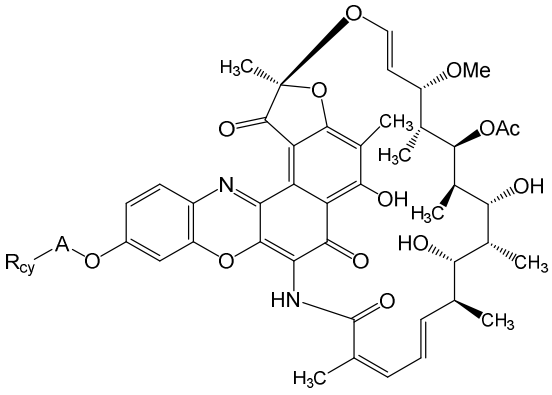
thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof, comprising contacting a compound having the structure of formula (XII'):



(XII')

with an alcohol having the structure R_6-OH.

28. A method of manufacturing a compound having the structure of formula (XIII):



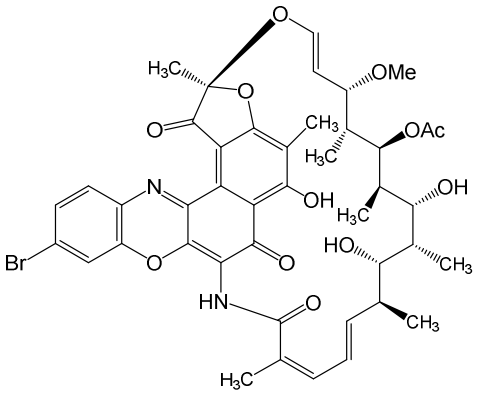
(XIII)

wherein A is selected from a bond (A is absent) or an aliphatic C_1-C_{20} hydrocarbon;

R_{cy} is a C_3-C_{14} cycloaliphatic hydrocarbon which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof and wherein R_{cy} is optionally substituted with one or more of -F; -Cl; -Br; -I; -OH, -OR*; -NO; -NO_2; -NO_3; -O-NO; -N_3; -NH_2; -NHR*; -N(R*)$_2$; -N(R*)$_3^+$; -N(R*)-OH; -O-N(R*)$_2$; -N(R*)-O-R*; -CN; -NC; -(C=O)-R*; -CHO; -CO_2H; -CO_2R*; -(C=O)-S-R*; -O-(C=O)-H; -O-(C=O)-R*; -S-(C=O)-R*; -(C=O)-NH_2; -(C=O)-N(R*)$_2$; -(C=O)-$NHNH_2$; -O-(C=O)-$NHNH_2$; -(C=S)-NH_2; -(C=S)-N(R*)$_2$; -N(R*)-CHO; -N(R*)-(C=O)-R*; -SCN; -NCS; -NSO; -SSR*; -SO_2R*; -SO_2-N(R*)$_2$; -S(=O)-OR*; -S(=O)-R*; -Si(R*)$_3$; -CF_3; -O-CF_3 and combinations thereof, and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof,

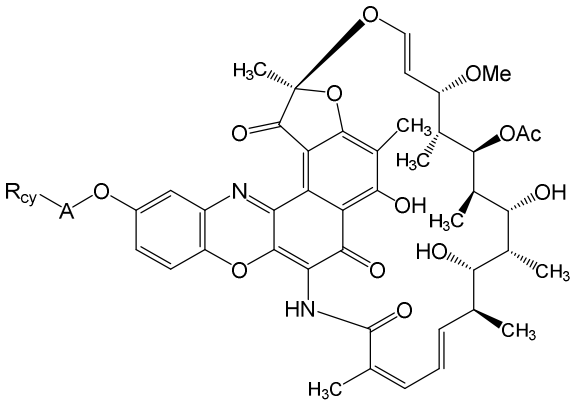
comprising contacting a compound having the structure of formula (XII):



(XII)

with an alcohol having the structure R_{cy}-A-OH.

29. A method of manufacturing a compound having the structure of formula (XIII'):



(XIII')

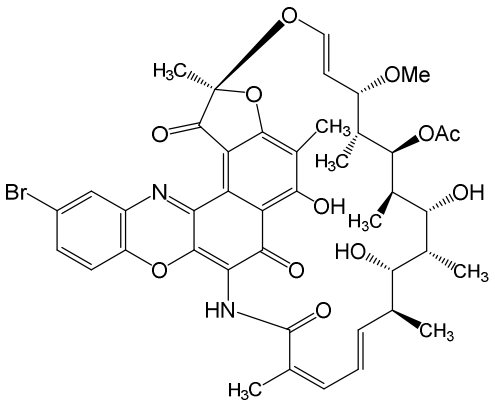
wherein A is selected from a bond (A is absent) or an aliphatic C_1-C_{20} hydrocarbon;

R_{cy} is a C_3-C_{14} cycloaliphatic hydrocarbon which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof and wherein R_{cy} is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*, -NO, -NO_2, -NO_3, -O-NO, -N_3, -NH_2, -NHR*, -N(R*)$_2$, -N(R*)$_3^+$, -N(R*)-OH, -O-N(R*)$_2$, -N(R*)-O-R*, -CN, -NC, -(C=O)-R*, -CHO, -CO_2H, -CO_2R*, -(C=O)-S-R*, -O-(C=O)-H, -O-(C=O)-R*, -S-(C=O)-R*, -(C=O)-NH_2, -(C=O)-N(R*)$_2$, -(C=O)-$NHNH_2$, -O-(C=O)-$NHNH_2$, -(C=S)-

NH_2, -(C=S)-N(R*)$_2$, -N(R*)-CHO, -N(R*)-(C=O)-R*, -SCN, -NCS, -NSO, -SSR*, -SO_2R*, -SO_2-N(R*)$_2$, -S(=O)-OR*, -S(=O)-R*, -Si(R*)$_3$, -CF_3, -O-CF_3 and combinations thereof; and

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof;

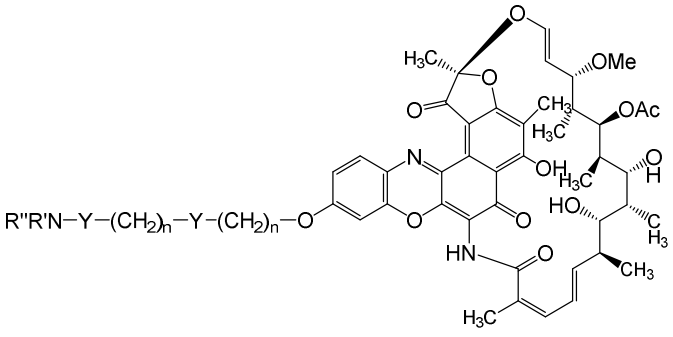
comprising contacting a compound having the structure of formula (XII'):



(XII')

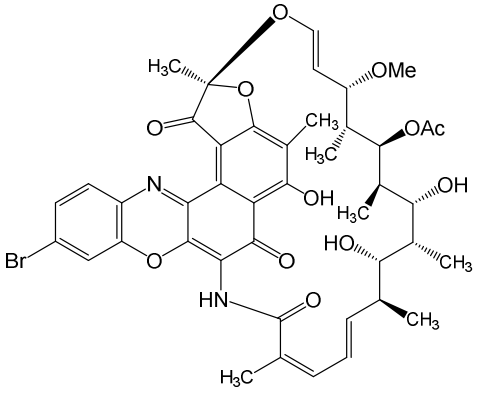
with an alcohol having the structure R_{cy}-A-OH.

30. A method of manufacturing a compound having the structure of formula (XIV):



(XIV),

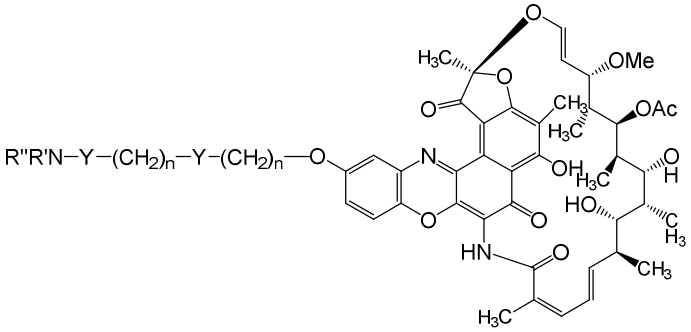
wherein Y is at each occurrence selected from -O- and -NR'R"-; n is independently at each occurrence an integer from 1-6, and R', R'', and R''' are each independently selected from a hydrogen, an aliphatic C_1-C_{20} hydrocarbon; said method comprising contacting a compound having the structure of formula (XII):



(XII)

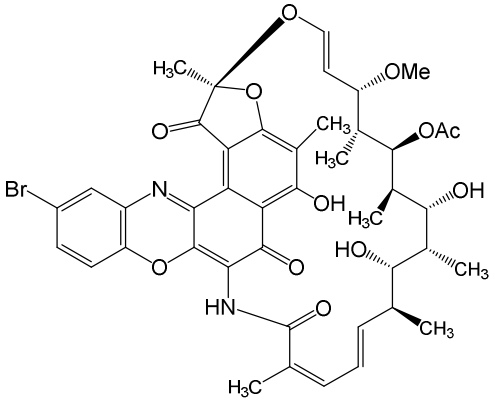
with an alcohol having the structure $R''R'N-Y-(CH_2)_n-Y-(CH_2)_n-OH$.

31. A method of manufacturing a compound having the structure of formula (XIV'):



(XIV'),

wherein Y is at each occurrence selected from -O- and -NR'R"-; n is independently at each occurrence an integer from 1 to 6, and R', R'', and R''' are each independently selected from a hydrogen and an aliphatic C_1-C_{20} hydrocarbon; said method comprising contacting a compound having the structure of formula (XII'):



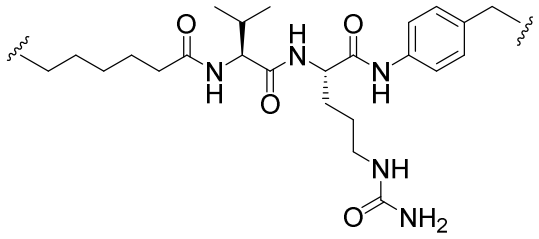
(XII')

with an alcohol having the structure $R''R'N-Y-(CH_2)_n-Y-(CH_2)_n-OH$.

32. An antibody-drug conjugate comprising an antibody, or an antigen-binding fragment thereof, conjugated to the compound of any of claims 1-13 via a linker or through a linker-spacer.

33. The antibody-drug conjugate of claim32, wherein the antibody, or the antigen-binding fragment thereof, binds an infectious disease-related target.

34. The antibody-drug conjugate of any one of claims 32-33, wherein the linker or linker spacer is selected from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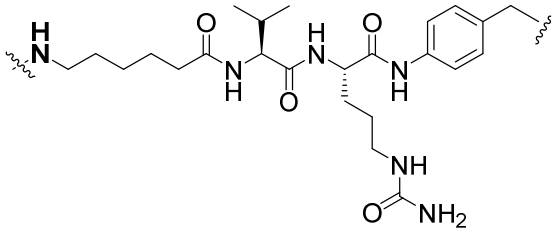
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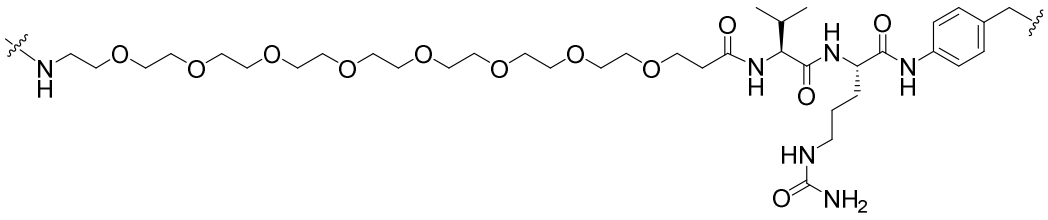
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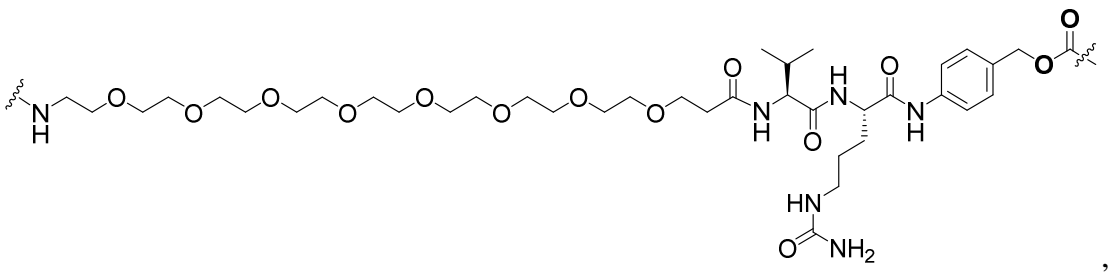
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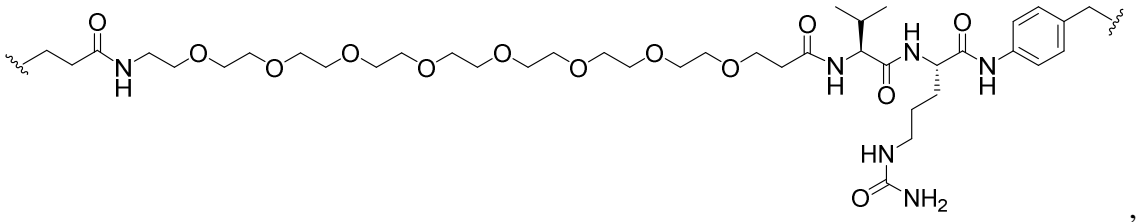

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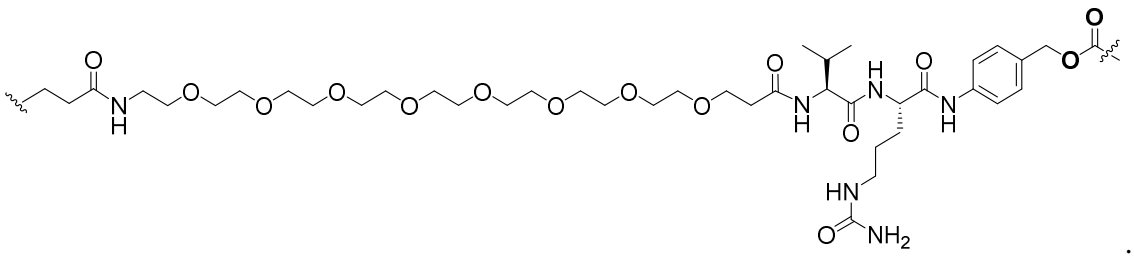
or



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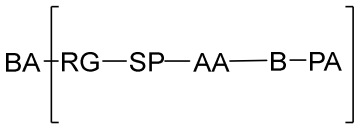
35. An antibody-drug conjugate having the structure according to Formula (XVIII):



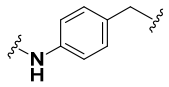
(**XVIII**), wherein

BA is an antibody, or an antigen-binding fragment thereof;

RG is selected from a maleimide, a N-hydroxysuccinimide, primary amine, or a succinimide;

SP is absent or a spacer group residue selected from the group consisting of $C_{1\text{-}6}$ alkyl, -NH-, -C(O)-, $-CH_2-CH_2-C(O)-NH-$, $-(CH)_u-C(O)-NH-$, $(-CH_2-CH_2-O)_e$, $-NH-CH_2-CH_2-(-O-CH_2-CH_2)_e-C(O)-$, $-C(O)-(CH_2)_u-C(O)-$, $-C(O)-NH-(CH_2)_v-$, $-(CH)_u-C(O)-NH-(CH_2-CH_2-O)_e-(CH)_u-C(O)-NH-$, $-(CH)_2-C(O)-NH-(CH_2-CH_2-O)_8-(CH)_2-C(O)-NH-$, and combinations thereof, wherein independently at each occurrence subscript **e** is an integer from 0 to 20, subscript **u** is an integer from 1 to 8, and subscript **v** is an integer from 1 to 8;

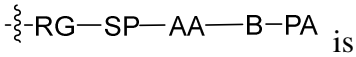
AA is a linker selected from valine-citrulline; citrulline-valine; valine-alanine; alanine-valine; valine-glycine, or glycine-valine;

B is absent or  , wherein the  indicates the atom through which the **B** is bonded to the adjacent groups in the formula;

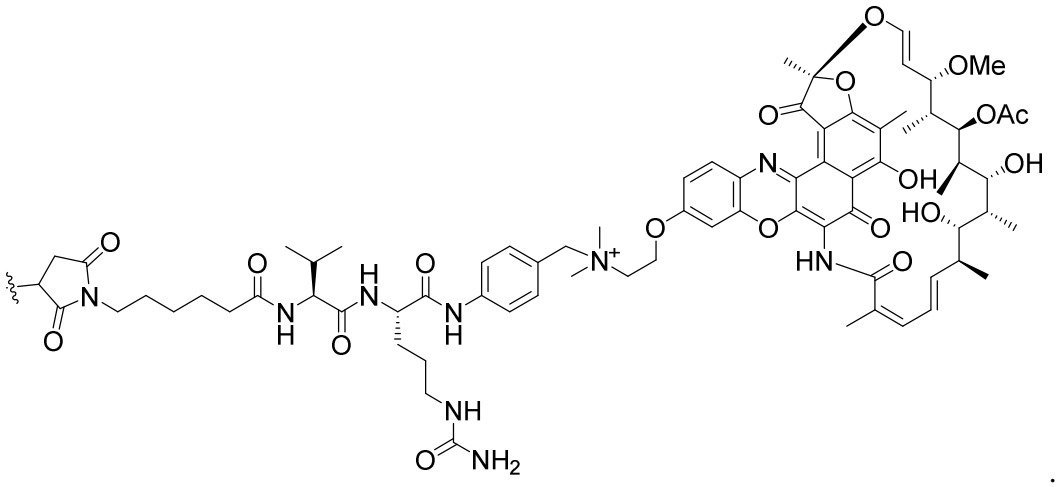
n is an integer from 1 to 30, and

PA is the compound of any of claims 1-13.

36. The antibody-drug conjugate of claim35, wherein



is



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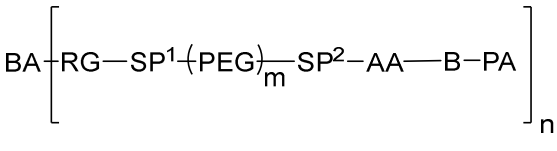
37. An antibody-drug conjugate having the structure according to Formula (XIX):



(**XIX**), wherein

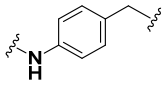
BA is an antibody, or an antigen-binding fragment thereof;

RG is selected from a maleimide, a N-hydroxysuccinimide, or a succinimide;

SP^1 and **SP^2** are independently absent or a spacer group selected from the group consisting of $C_{1\text{-}6}$ alkyl, -NH-, -C(O)-, $-CH_2-CH_2-C(O)-NH-$, $-(CH)_u-C(O)-NH-$, $(-CH_2-CH_2-O)_e$, $-NH-CH_2-CH_2-(-O-CH_2-CH_2)_e-C(O)-$, $-C(O)-(CH_2)_u-C(O)-$, $-C(O)-NH-(CH_2)_v-$, and combinations thereof, wherein subscript **e** is an integer from 0 to 4, subscript **u** is an integer from 1 to 8, and subscript **v** is an integer from 1 to 8;

AA is a linker selected from valine-citrulline; citrulline-valine; valine-alanine; alanine-valine; valine-glycine, or glycine-valine;

PEG is a polyethylene glycol chain comprising between 1 and 30 polyethylene glycol residues;

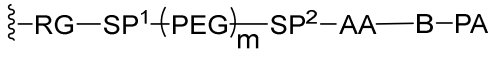
B is absent or  , wherein the  indicates the atom through which the **B** is bonded to the adjacent groups in the formula;

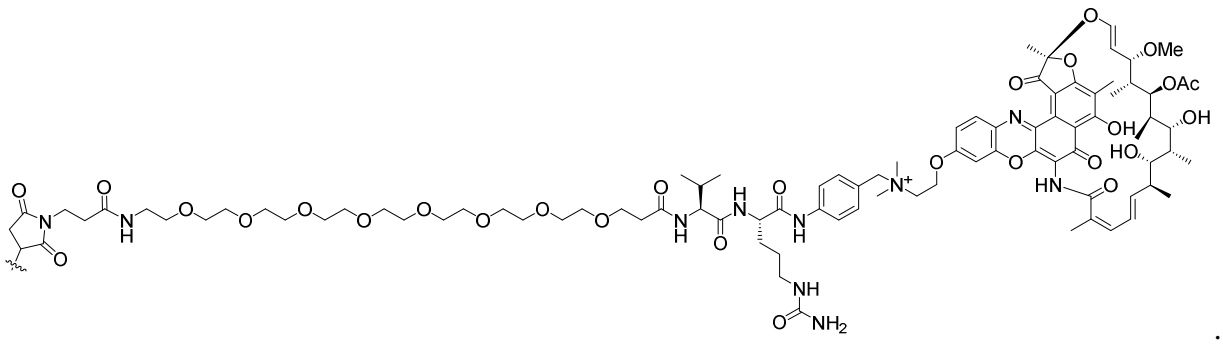
n is an integer from 1 to 30;

m is an integer from 0 to 20,

and **PA** is the compound of any of claims 1-13.

38. The antibody-drug conjugate of claim37, wherein

 is



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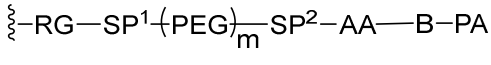
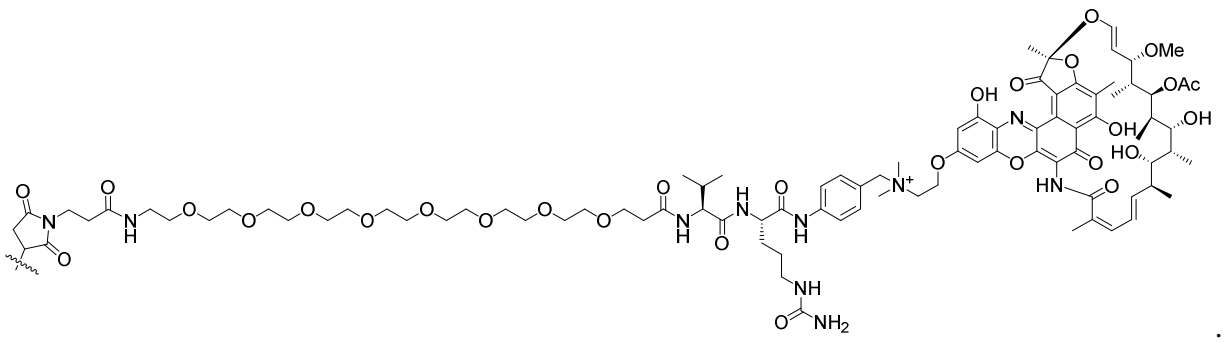
39. The antibody-drug conjugate of claim37, wherein

 is



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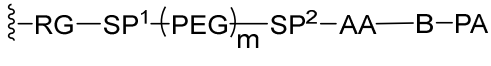
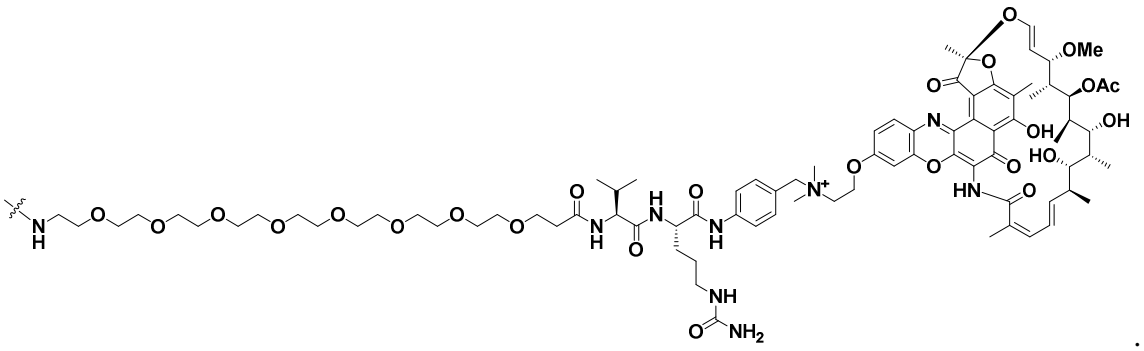
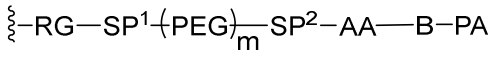
40. The antibody-drug conjugate of claim37, wherein

 is



41. The antibody-drug conjugate of claim37, wherein



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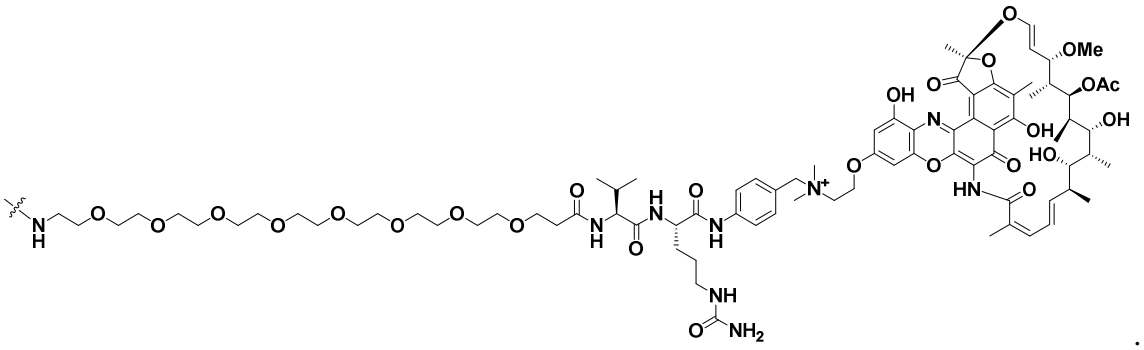
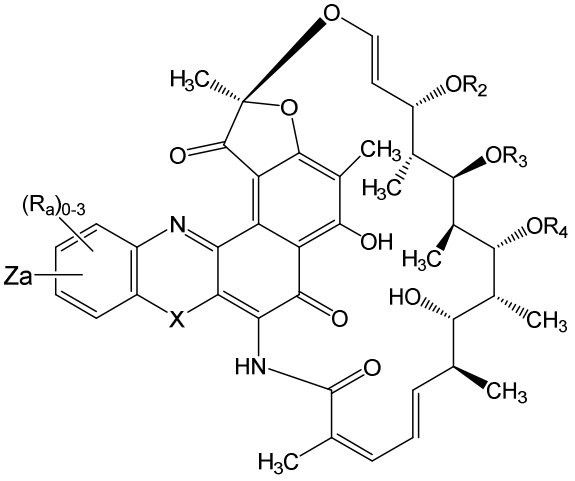


42. An antibody-drug conjugate comprising an antibody, or an antigen-binding fragment thereof, conjugated via a linker or through a linker-spacer to a rifamycin analog having the structure of Formula (XX):



(XX),

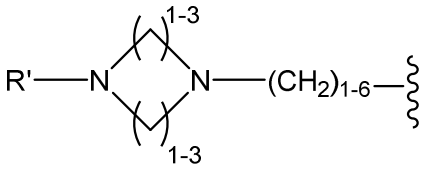
wherein:

X is selected from -O-, -S-, and -NR*-;

Za is selected from $-OR_1$ and $-R_N$;

R_1 is selected from a bond; an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_1 is optionally substituted with one or more of -F; -Cl; -Br; -I; -OH, -OR*; -NO; $-NO_2$; $-NO_3$; -O-NO; $-N_3$; $-NH_2$; -NHR*; $-N(R^*)_2$; $-N(R^*)_3^+$; -N(R*)-OH; $-O-N(R^*)_2$; -N(R*)-O-R*; -CN; -NC; -(C=O)-R*; -CHO; $-CO_2H$; $-CO_2R^*$; -(C=O)-S-R*; -O-(C=O)-H; -O-(C=O)-R*; -S-(C=O)-R*; $-(C=O)-NH_2$; $-(C=O)-N(R^*)_2$; $-(C=O)-NHNH_2$; $-O-(C=O)-NHNH_2$; $-(C=S)-NH_2$; $-(C=S)-N(R^*)_2$; -N(R*)-CHO; -N(R*)-(C=O)-R*; -SCN; -NCS; -NSO; -SSR*; $-SO_2R^*$; $-SO_2-N(R^*)_2$; -S(=O)-OR*; -S(=O)-R*; $-Si(R^*)_3$; $-CF_3$; $-O-CF_3$ and combinations thereof**;**

R_N is selected from:



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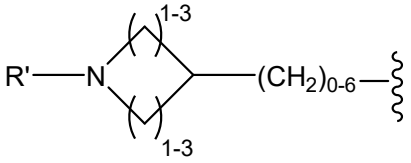

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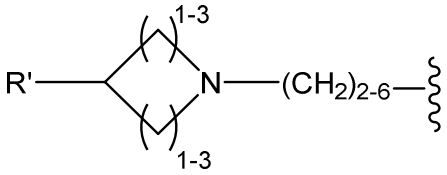

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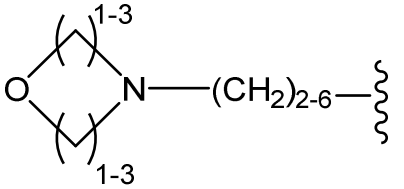

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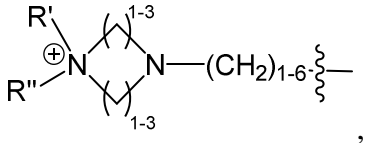

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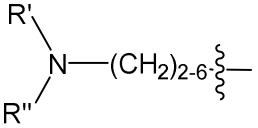

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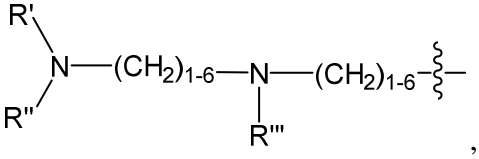

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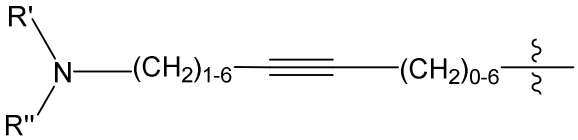

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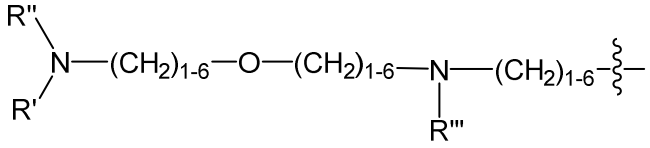


; wherein the ~~~ symbol represents the

point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from F_{MOC} and $B_{OC,}$ or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

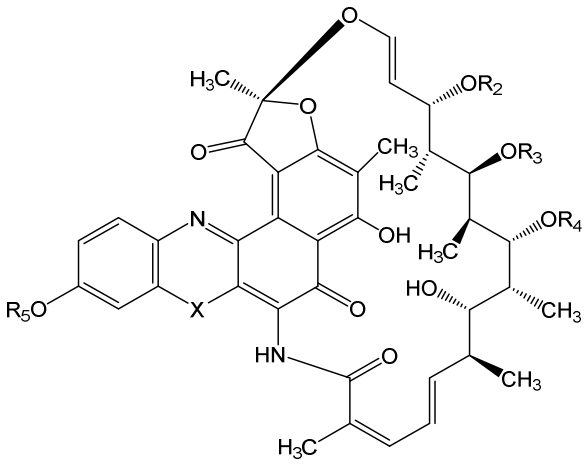
R_2, R_3, and R_4 are independently selected from hydrogen, a straight chained, branched or cyclic aliphatic C_1-C_{20} hydrocarbon, or -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;

R_a is independently at each occurrence selected from hydrogen, -F, -Cl, -Br, -I, -OH, OR*, $-NH_2$, -NHR*, $-N(R^*)_2$, $-N(R^*)_3^+$, -(C=O)-R*, -CHO, $-CO_2H$, $-CO_2R^*$, -SR*, SO_2R^*, and an aliphatic C_1-C_{20} hydrocarbon, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and wherein R_a is optionally substituted with one or more of -F, -Cl, -Br, -I, -OH, -OR*;

R* is independently at each occurrence selected from hydrogen, an aliphatic C_1-C_{20} hydrocarbon, an aromatic C_1-C_{20} hydrocarbon, a heteroaromatic C_1-C_{20} hydrocarbon, a cyclic aliphatic C_1-C_{20} hydrocarbon, a heterocyclic C_1-C_{20} hydrocarbon, and combinations thereof, which further comprises 0-8 heteroatoms selected from halogen, O, N, and S and combinations thereof, and

wherein the group Za is bonded to the linker.

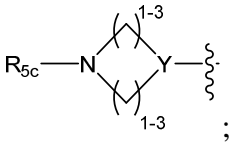
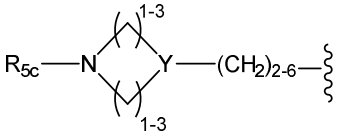
43. An antibody-drug conjugate comprising an antibody, or an antigen-binding fragment thereof, conjugated via a linker or through a linker-spacer to a rifamycin analog having the structure of Formula (XXI):



(XXI),

wherein:

X is selected from -O-, -S-, and -NR*-;

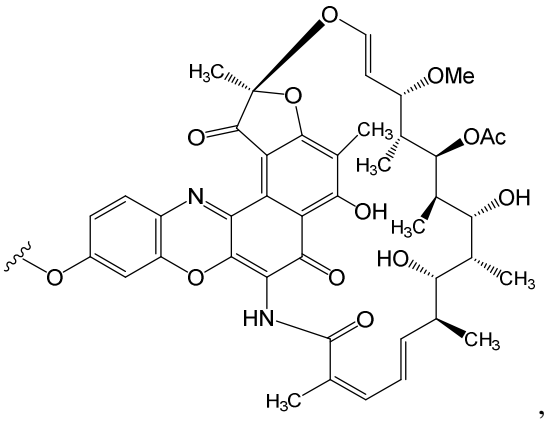
R_5 is selected from a bond; an aliphatic C_1-C_{20} hydrocarbon which further comprises 0-8 heteroatoms selected from halogen, O, N, and S;  ; or  ; wherein **Y** is C or N;

R_2, R_3, and R_4 are independently selected from a hydrogen, a straight chained, branched or cyclic aliphatic C_1-C_{20} hydrocarbon, or -(C=O)-R*, each of which further comprises 0-8 heteroatoms selected from halogen, O, N, and S, and

R_{5c} is a bond or an aliphatic C_1-C_8 hydrocarbon,

wherein the group R_5 is bonded to the linker.

44. The antibody-drug conjugate of claims 42-43, wherein the compound is selected from the group consisting of: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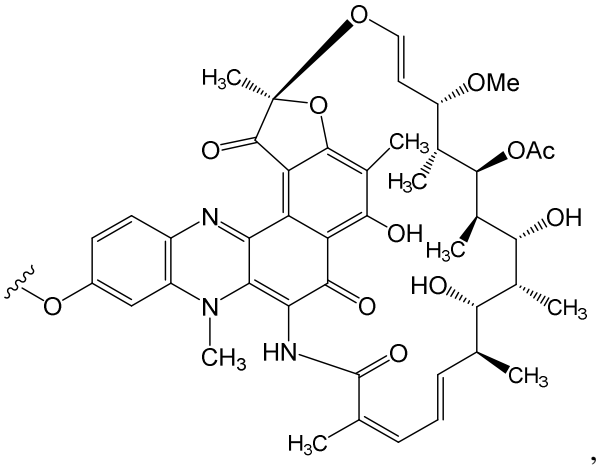
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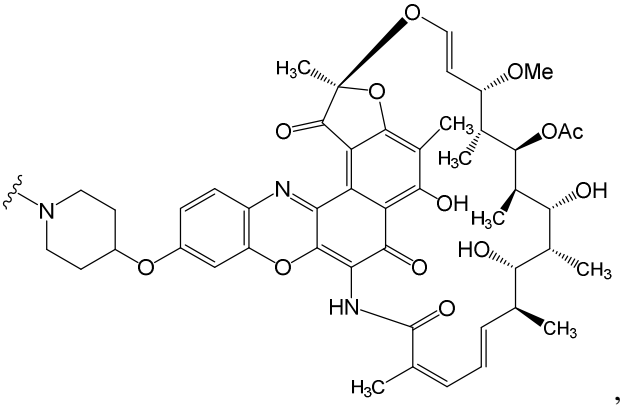
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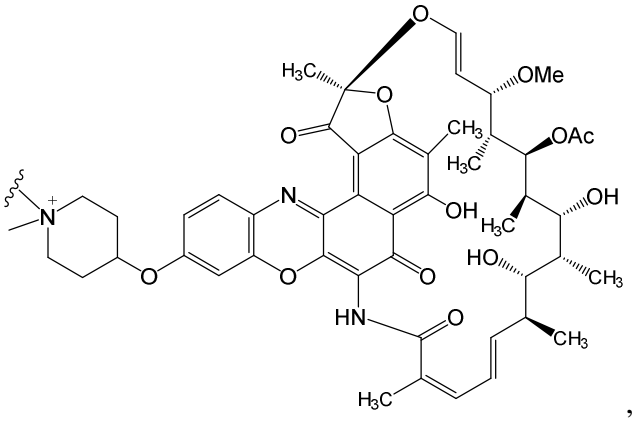
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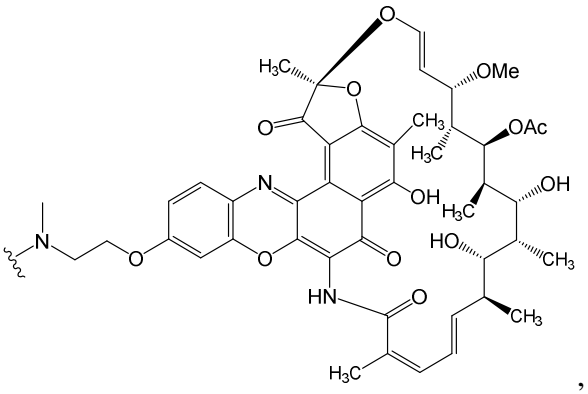
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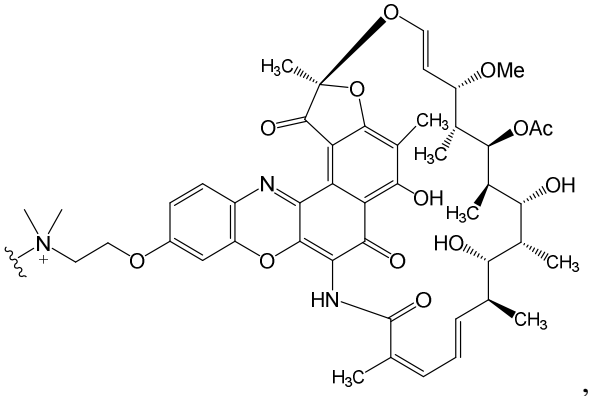
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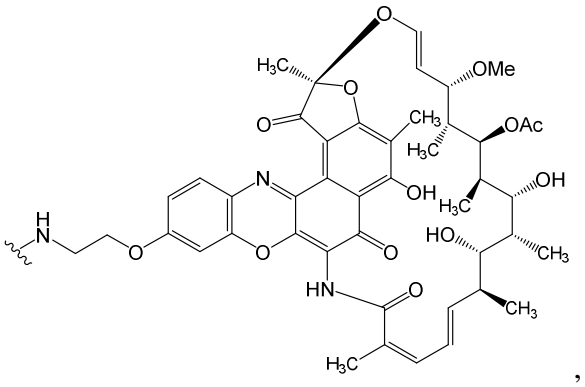
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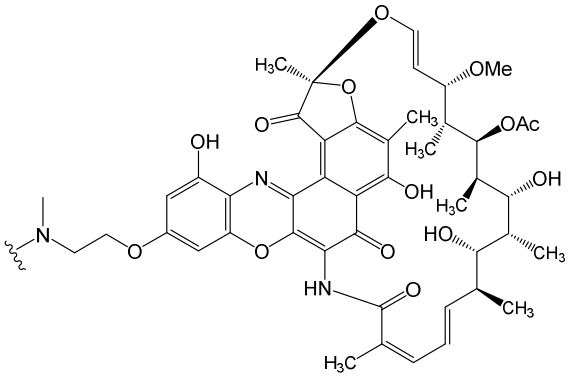
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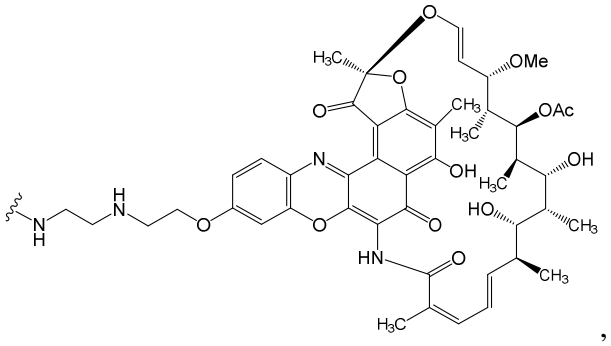
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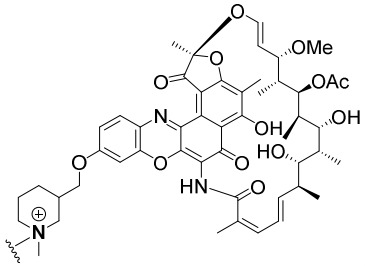
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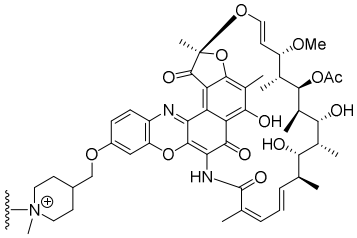
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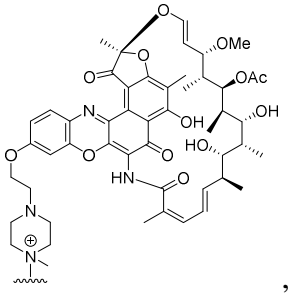
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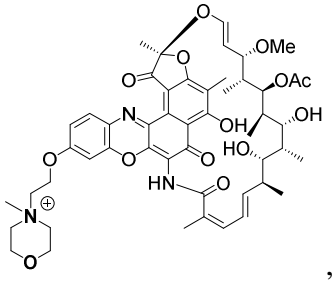
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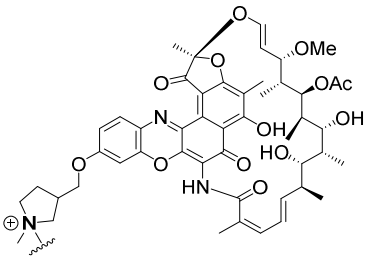
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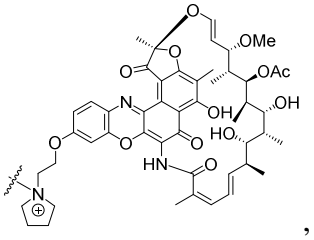
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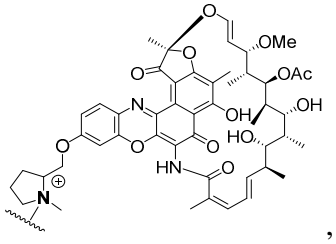
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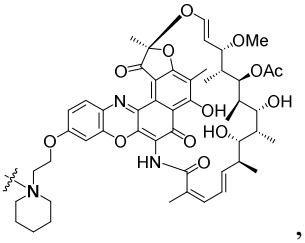
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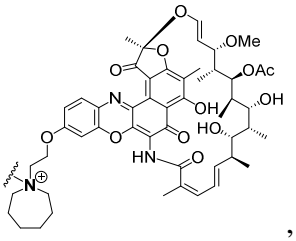
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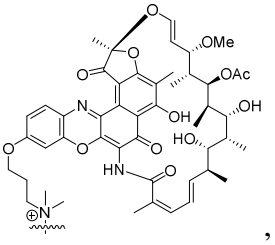
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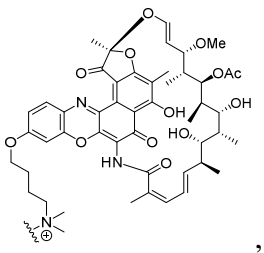
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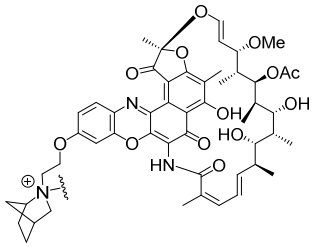
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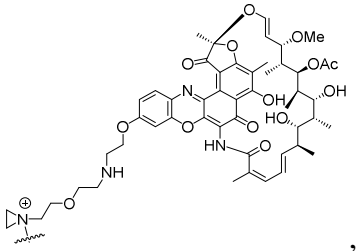
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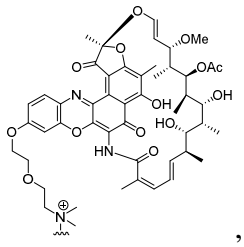
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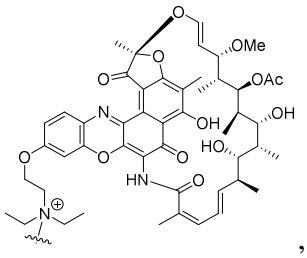
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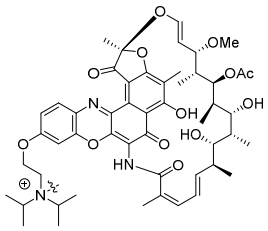
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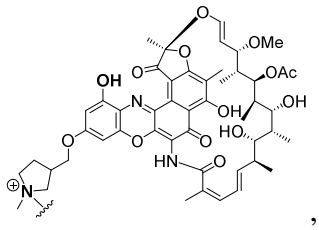
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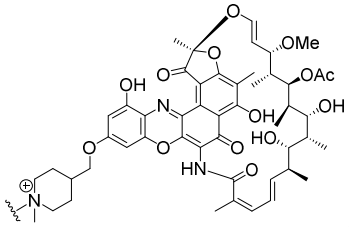
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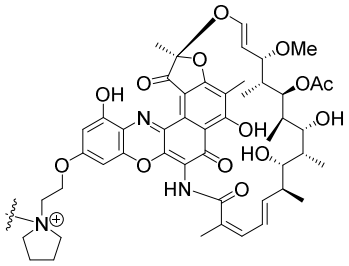
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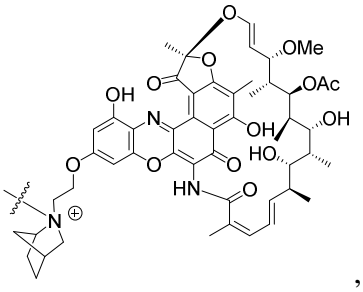
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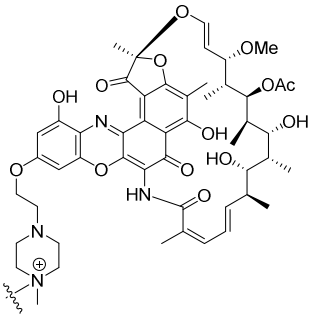
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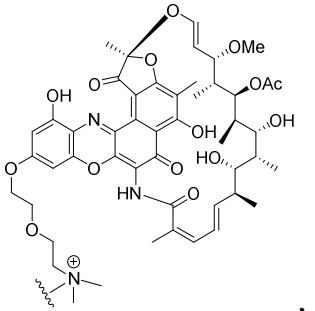
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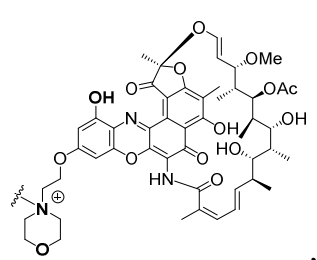
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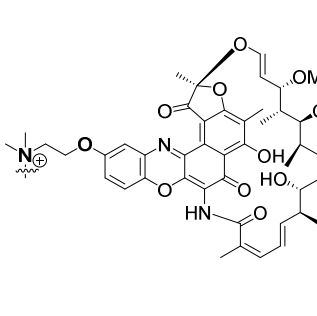
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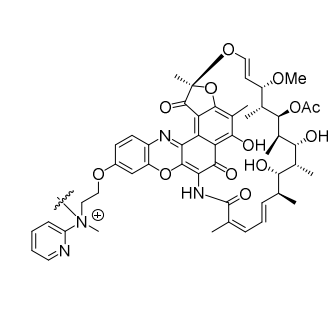
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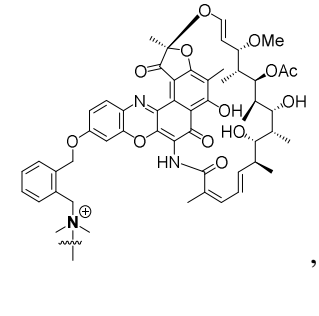
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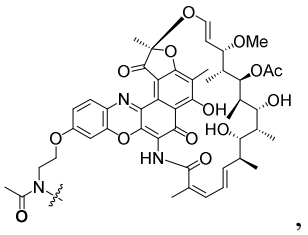
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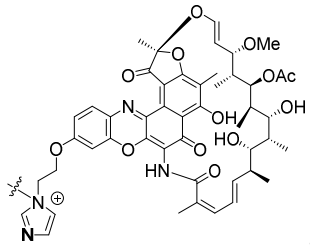
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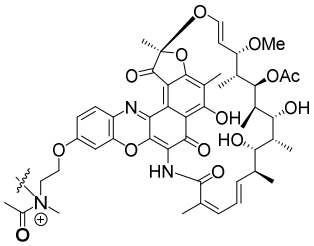
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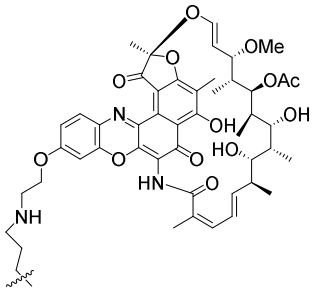
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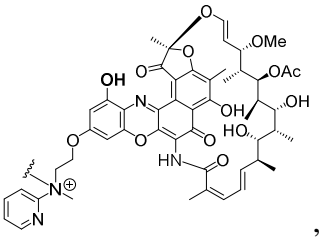
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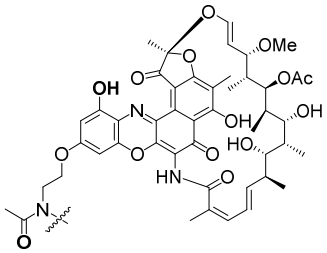
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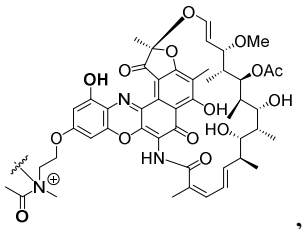
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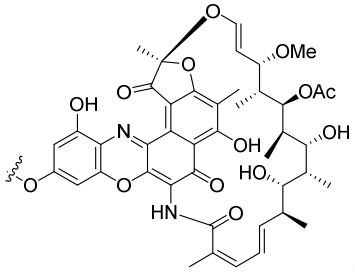
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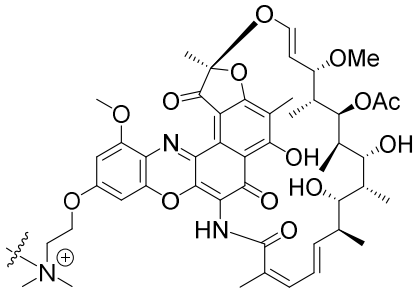
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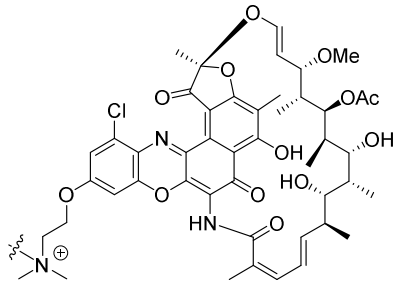
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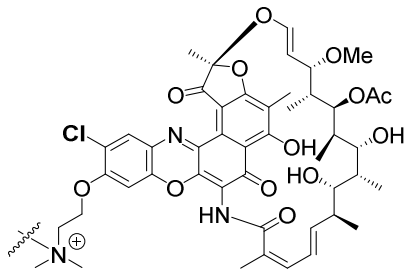
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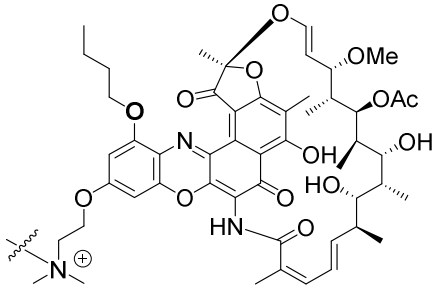
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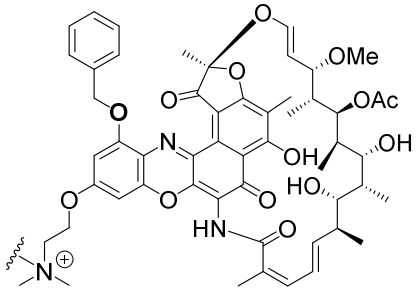
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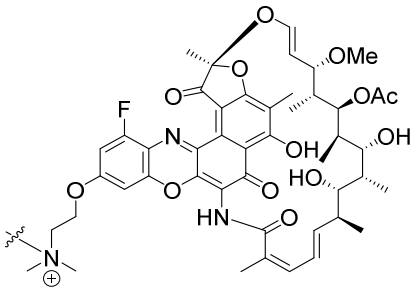
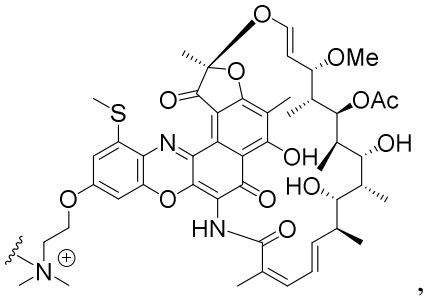
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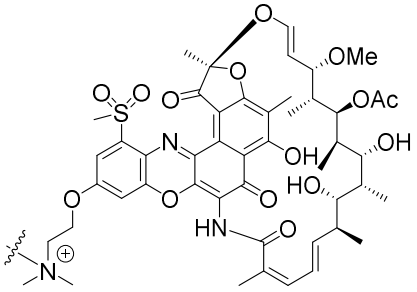
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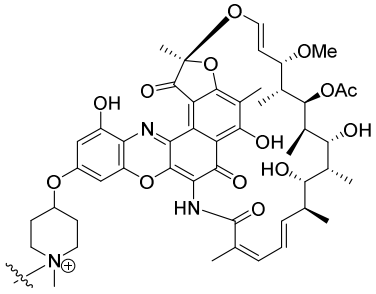
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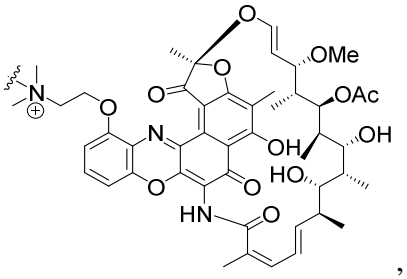
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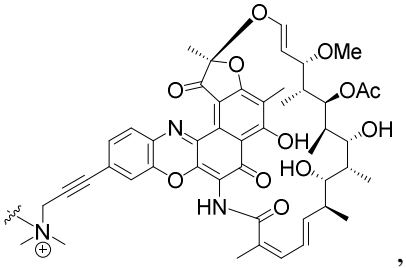
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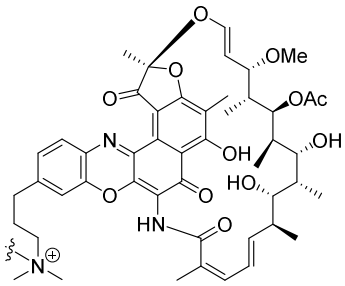
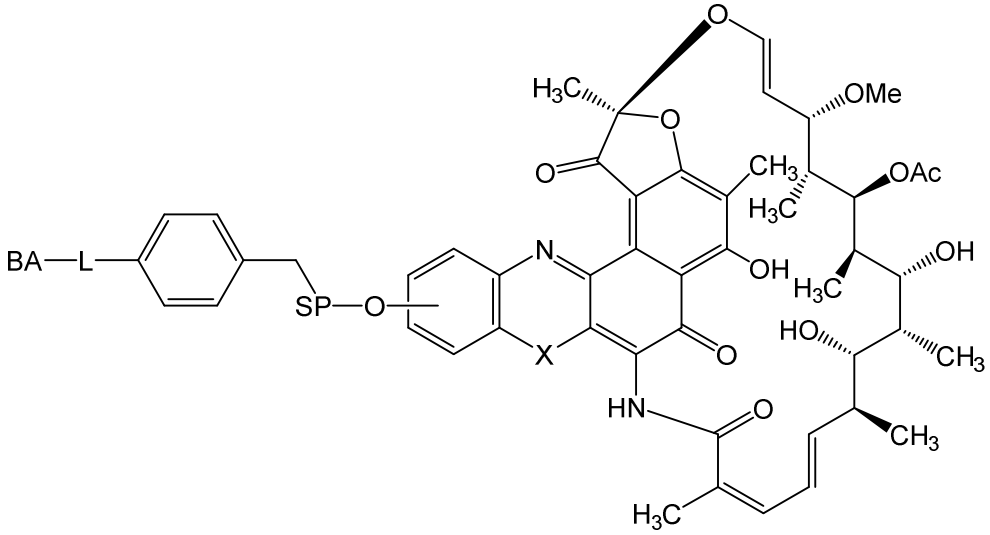

,

wherein the ⌇— is the bond to the linker.

45. An antibody-drug conjugate having the structure of Formula (XXII):

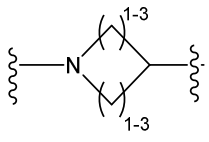
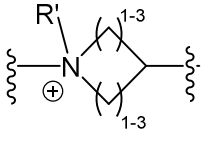
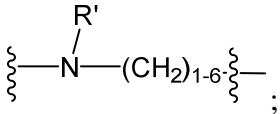
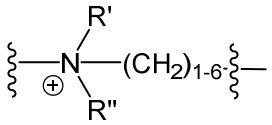
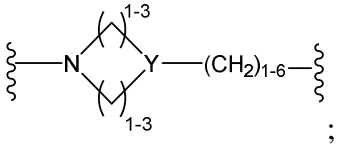
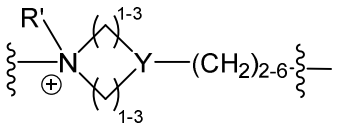
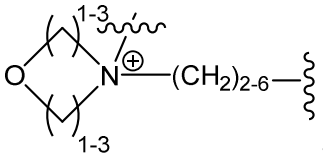
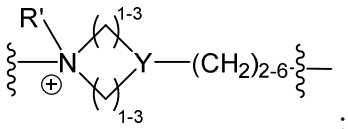
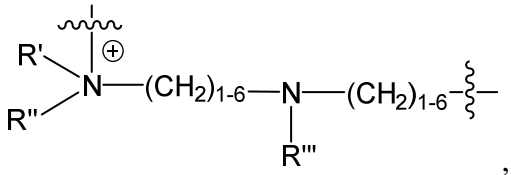
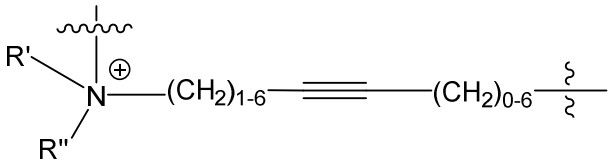
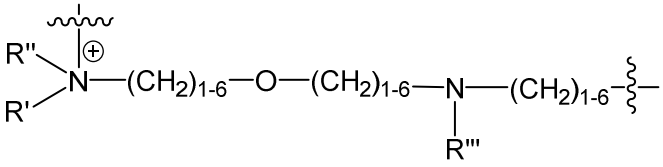


(XXII),

wherein:

BA is an antibody, or an antigen-binding fragment thereof;

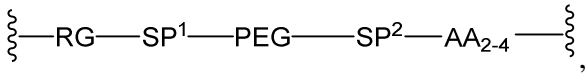
L is a linker;

SP is a spacer group selected from  ;  ;  ;  ;  ;  ;  ;  ;  ,   and ;

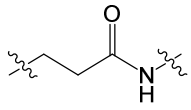
Y is C or N; wherein the 〰 symbol represents the point of attachment; and R', R" and R''' are selected from a hydrogen, a C_1-C_6 aliphatic hydrocarbon, and a protecting group selected from Fluorenylmethyloxycarbonyl (F_{MOC}) and *tert*-Butyloxycarbonyl (B_{OC}), or wherein R' and R'' together form an aliphatic monocyclic, an aliphatic bicyclic, or an aliphatic polycyclic structure;

R' and R" are independently at each occurrence selected from a hydrogen and a C_{1-6} alkyl, and

X is selected from -O-, -S-, and -NR*.

46. The antibody-drug conjugate of claim45, wherein L is a linker having the formula  , wherein

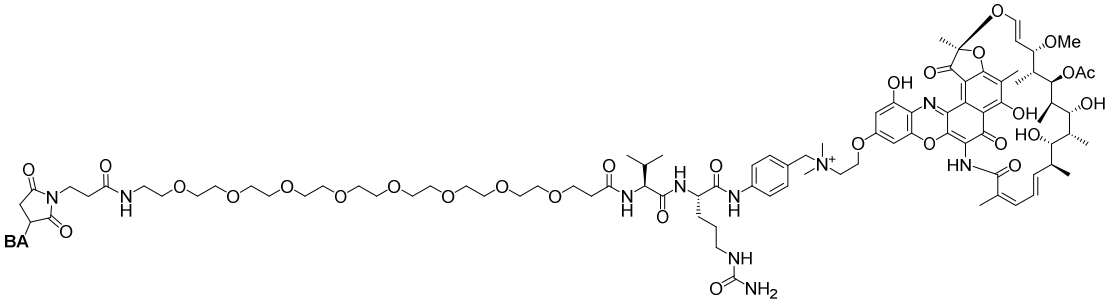
RG is selected from a maleimide, a N-hydroxysuccinimide, or a succinimide;

SP^1 and SP^2 are independently absent or a spacer group selected from the group consisting of  ; C_{1-6} alkyl, -NH-, -C(O)-, $-CH_2-CH_2-C(O)-NH-$, $-(CH)_u-C(O)-NH-$, $(-CH_2-CH_2-O)_e$, $-NH-CH_2-CH_2-(-O-CH_2-CH_2)_e-C(O)-$, $-C(O)-(CH_2)_u-C(O)-$, $-C(O)-NH-(CH_2)_v-$, and combinations thereof, wherein subscript **e** is an integer from 0 to 4, subscript **u** is an integer from 1 to 8, and subscript **v** is an integer from 1 to 8;

AA_{2-4} is a peptide unit comprising from 2 to 4 amino acids, and

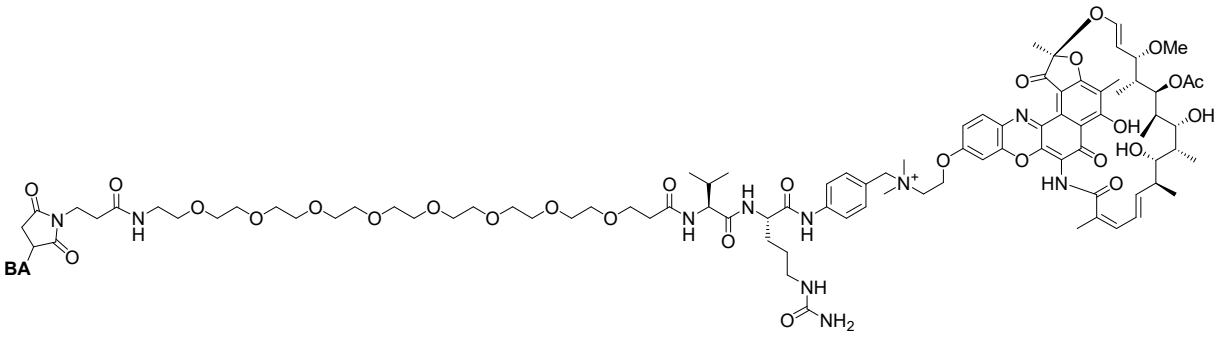
PEG is a polyethylene glycol chain comprising between 1 and 30 polyethylene glycol residues.

47. The antibody-drug conjugate of any of claims 45-46, wherein the antibody-drug conjugate has a structure:



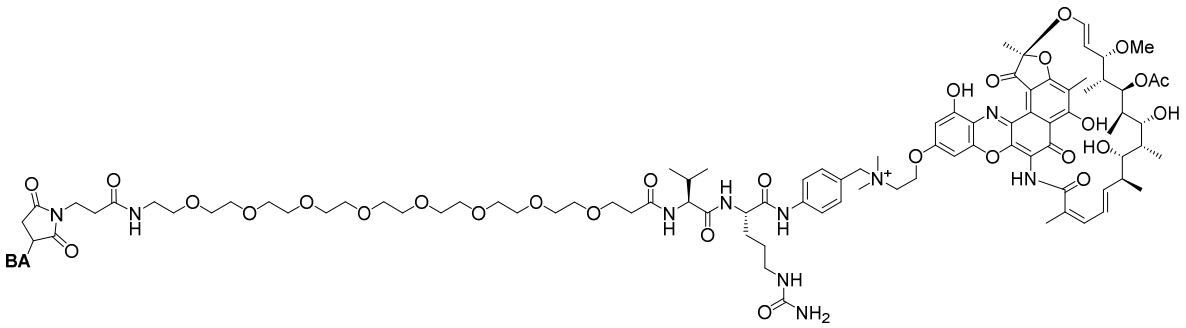
wherein BA is an antibody, or an antigen-binding fragment thereof.

48. The antibody-drug conjugate of any of claims 45-46, wherein the antibody-drug conjugate has a structure:



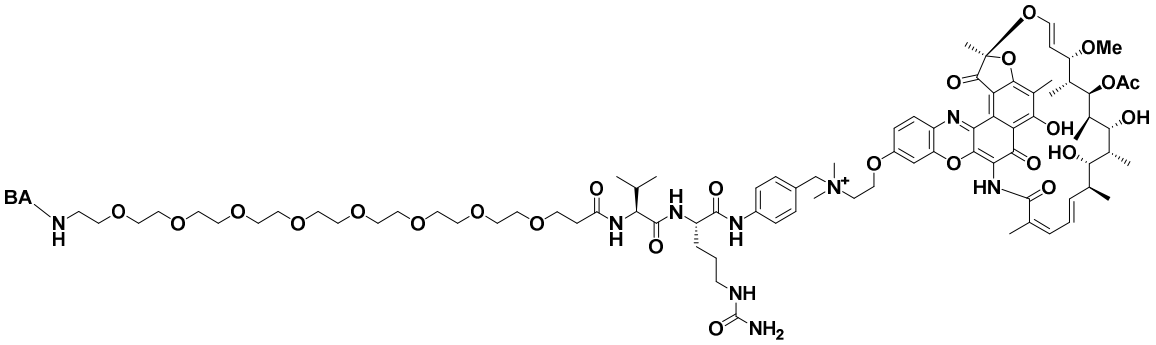
wherein BA is an antibody, or an antigen-binding fragment thereof.

49. The antibody-drug conjugate of any of claims 45-46, wherein the antibody-drug conjugate has a structure:



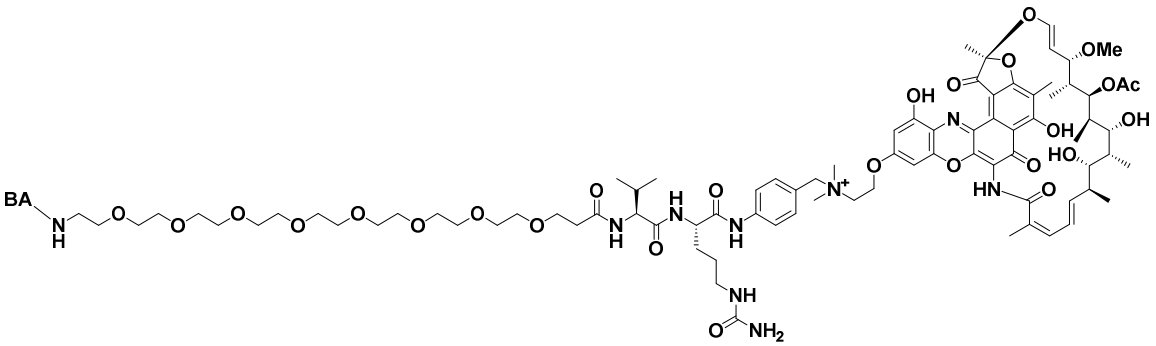
wherein BA is an antibody, or an antigen-binding fragment thereof.

50. The antibody-drug conjugate of any of claims 45-46, wherein the antibody-drug conjugate has a structure:



wherein BA is an antibody, or an antigen-binding fragment thereof.

51. The antibody-drug conjugate of any of claims 45-46, wherein the antibody-drug conjugate has a structure:



wherein BA is an antibody, or an antigen-binding fragment thereof.

52. The antibody-drug conjugate of any of claims 35-51, wherein the antibody, or an antigen-binding fragment thereof, binds an infectious disease-related target.

53. Use of an antibody-drug conjugate of any of claims 32-52 in the manufacture of a medicament for preventing or inhibiting growth of a bacterium.

54. Use of an antibody-drug conjugate of any of claims 32-52 in the manufacture of a medicament for treating a bacterial infection.

55. The use of claim54, wherein the subject is human.

56. The use of any of claims 54-55, further comprising administering a second therapeutic agent.

57. The use of claim56, wherein the second therapeutic agent is a second antibiotic.

58. The use of any of claims 53-57, wherein the antibody-drug conjugate is to be administered to the subject orally, topically, intranasally, intravenously, intramuscularly, or subcutaneously.

59. Use of the compounds of any one of claims 1-13, or the pharmaceutical composition of claim 14, or the antibody-drug conjugate of any of claims 32-52 in the manufacture of a medicament for preventing or treating cellulitis, bacteremia, dermonecrosis, eyelid infection, eye infection, neonatal conjunctivitis, osteomyelitis, impetigo, boils, scalded skin syndrome, food poisoning, pneumonia, surgical infection, urinary tract infection, burn infection, meningitis, endocarditis, septicemia, toxic shock syndrome, septic arthritis,

mastitis, infection associated with a prosthetic joint, infection associated with a catheter, or infection associated with an implant, in a subject.