(a) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(b) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, where P_9 is H or a hydroxyl protecting group; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, where P_{10} is alkyl or a hydroxyl protecting group;

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP"; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, where P_{10} is alkyl or a hydroxyl protecting group; or

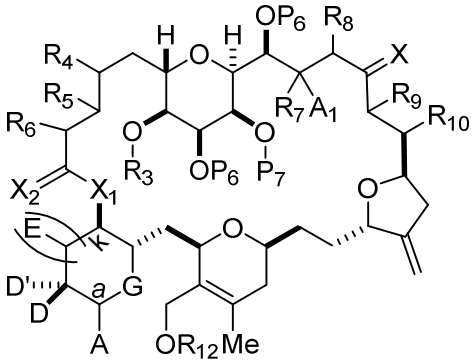
(iii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form acetal; and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, where P_9 is H or a hydroxyl protecting group;

R_9 is H, OP", or Y, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

each P", when present, is independently H or a hydroxyl protecting group; and

P_8 is H or silyl; and

where the macrocyclic intermediate in the synthesis of a halichondrin macrolide or an analog thereof is a compound of formula (IB):



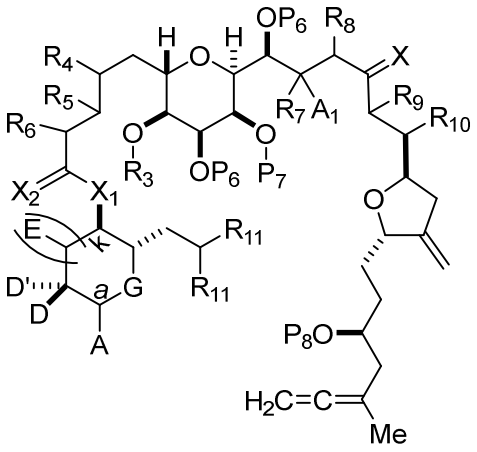
(IB)

or a salt or a tautomer thereof.

In another aspect, the disclosure provides a method of preparing a macrocyclic intermediate in the synthesis of a halichondrin macrolide or an analog thereof, the method comprising reacting a compound of formula (IA) with R_{12}OH and a Lewis acid, the reaction producing the macrocyclic intermediate by forming a bond in the structure of the halichondrin macrolide or an analog thereof,

wherein R_{12} is optionally substituted acyl;

wherein the compound of formula (IA) is:

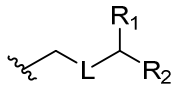


(IA),

or a salt or a tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or $–C(O)–$;

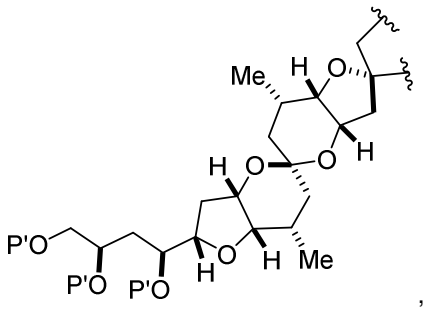
R_1 is H, or R_1 and P_1 combine to form a bond;

(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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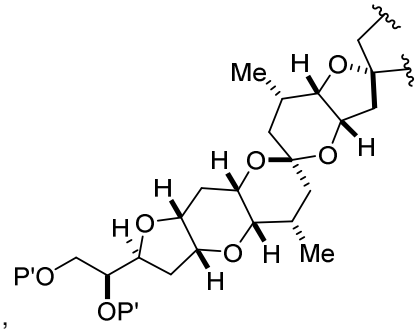

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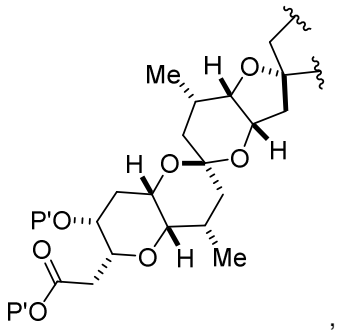


, wherein each P' is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)–, $–CH_2–$, or –O–;

X_2 is =O or X_2, together with the carbon atom to which it is attached, is $–(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $–SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene, provided that, when X_1 is –O–, X_2 is =O;

Y is SO_2R_C or $COOR_C$, where, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H;

or

A_1 is H or OP", and:

(a) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(b) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP"; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group; or

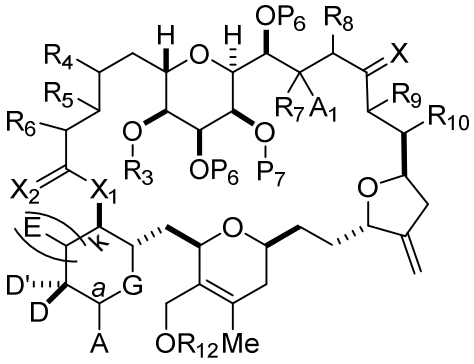
(iii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form acetal; and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group;

R_9 is H, OP", or Y, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

each P", when present, is independently H or a hydroxyl protecting group; and

P_8 is H or silyl; and

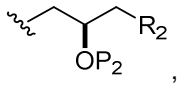
wherein the macrocyclic intermediate in the synthesis of a halichondrin macrolide or an analog thereof is a compound of formula (IB):



(IB)

or a salt or a tautomer thereof.

In some examples, the Lewis acid is an oxophilic Lewis acid (e.g., boron trifluoride or a solvate thereof).



where

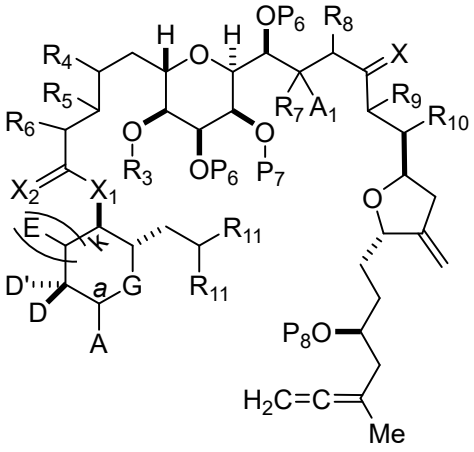
(i) R_2 is $–(CH_2)_nNP_3P_4$, where n is 0, P_3 is an N-protecting group, and P_2 and P_4 combine to form an alkylidene; or

(ii) R_2 is $–(CH_2)_nOP_5$, where n is 0, P_2 is H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo;

can be used for the synthesis of eribulin or its salt (e.g., eribulin mesylate).

In another aspect, the disclosure provides the compounds of formula (IA), (IB), (IC), (ID), (IDa), (IDb), (IDc), (IDd), (IE), (IF), (IH), (IHa), (IHb), (IJ), or (IN). In some examples, disclosure provides the compounds of formula (IDb), (IDc), (IDd), (IF), (IH), (IHa), or (IHb).

The structure of the compound of formula (IA) is as follows:

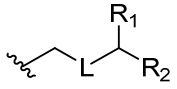


(IA),

or a salt or a tautomer thereof,

where

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, where P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:

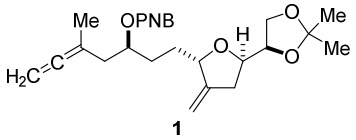


(1),

where

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or $–C(O)–$;

R_1 is H, or R_1 and P_1 combine to form a bond;



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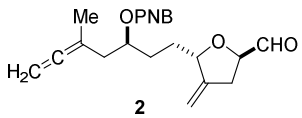

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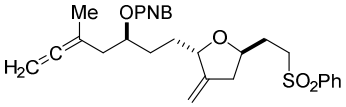

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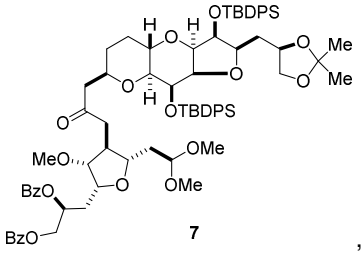

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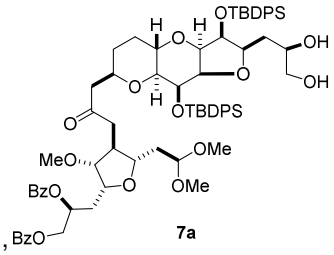

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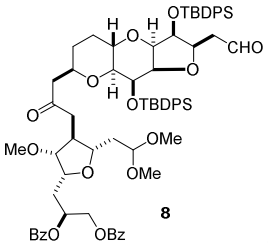

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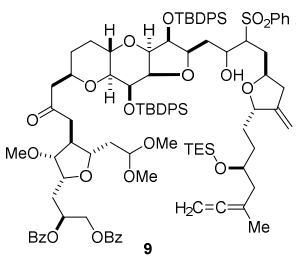

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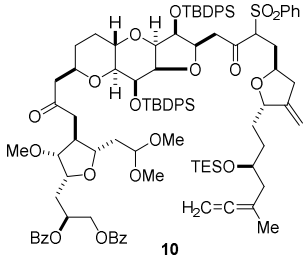

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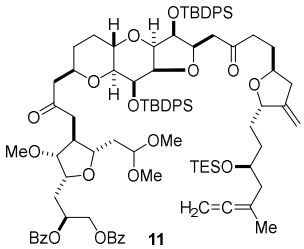

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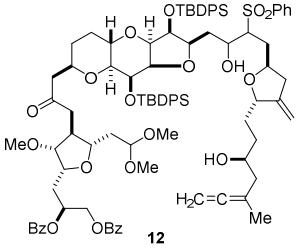

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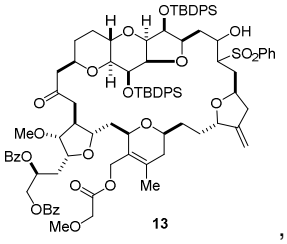

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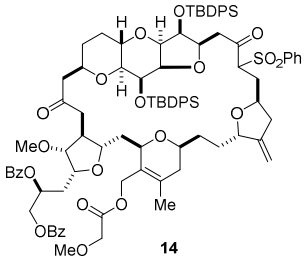

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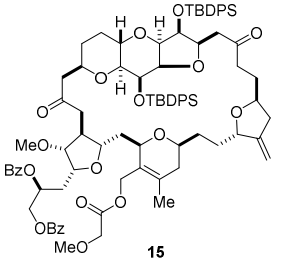

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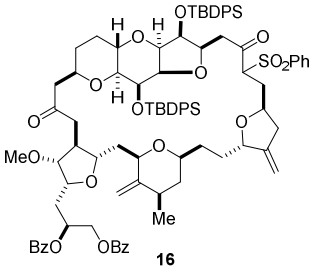

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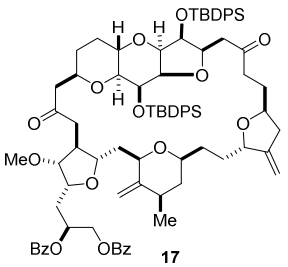

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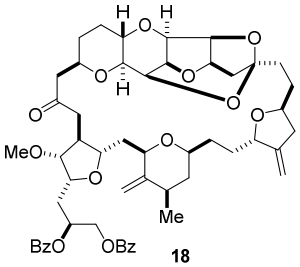

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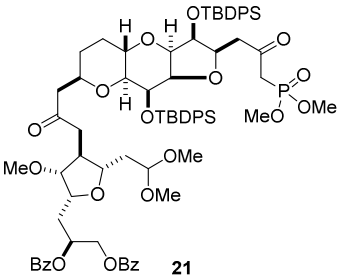

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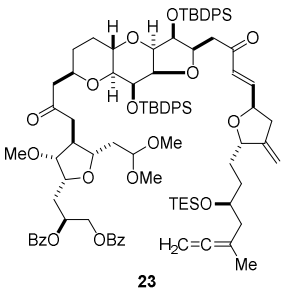

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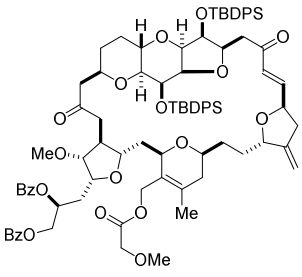

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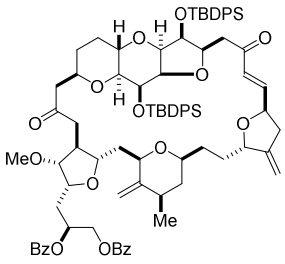

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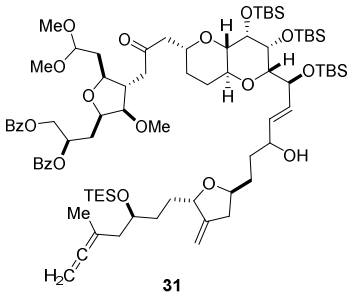

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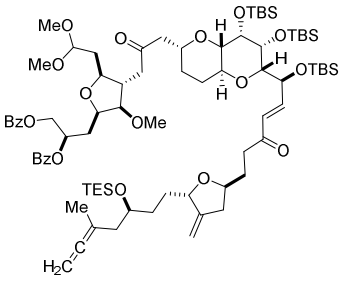

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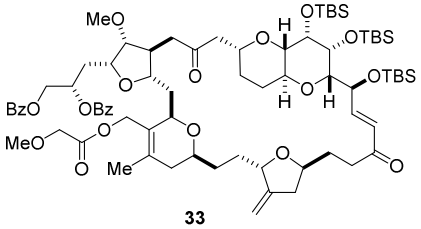

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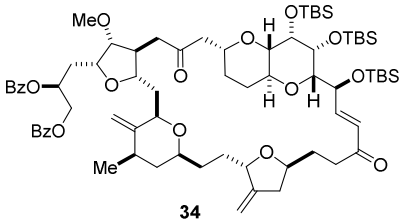

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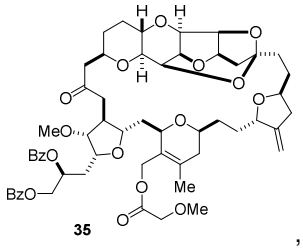

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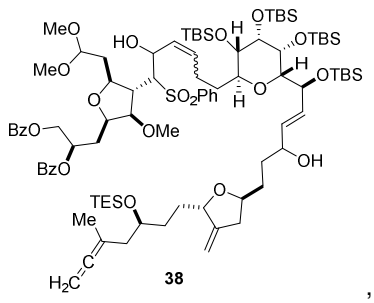

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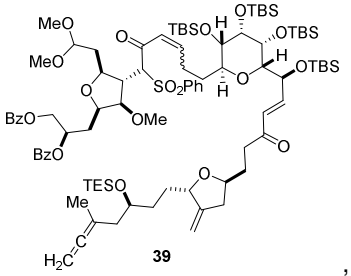

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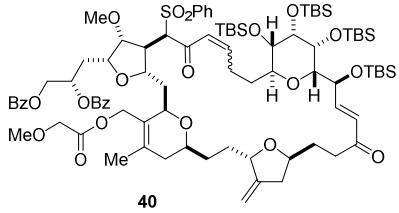

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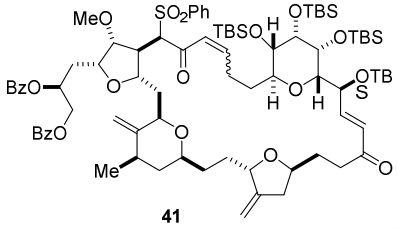

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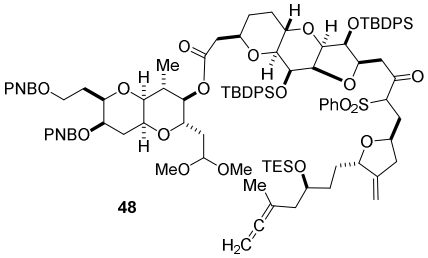

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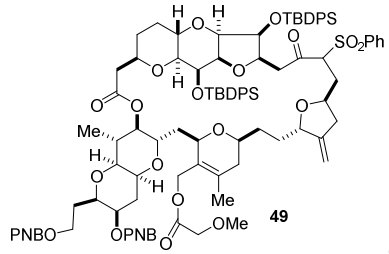

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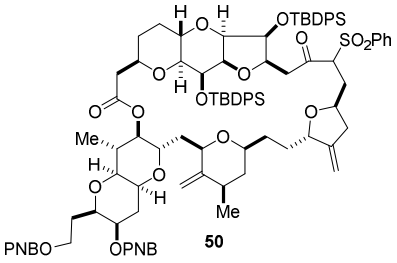

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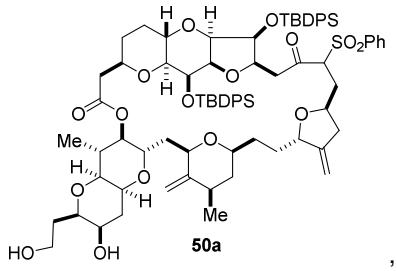

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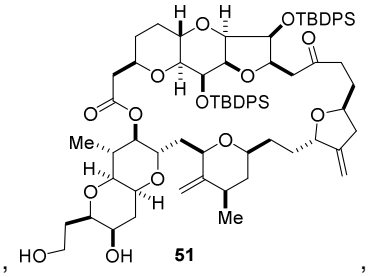

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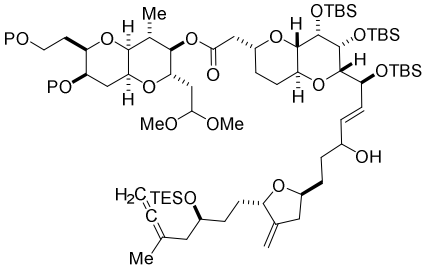

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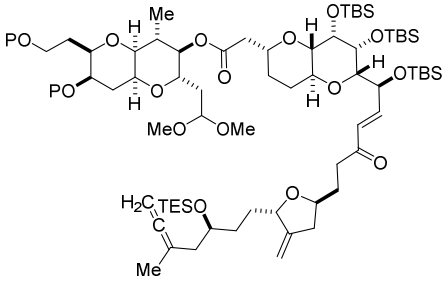

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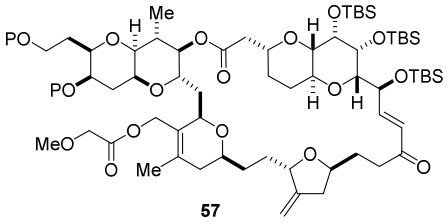

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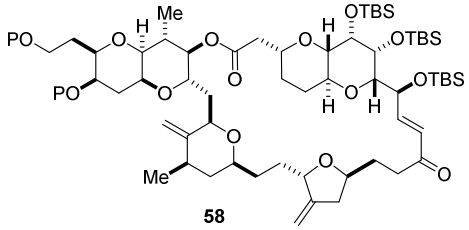

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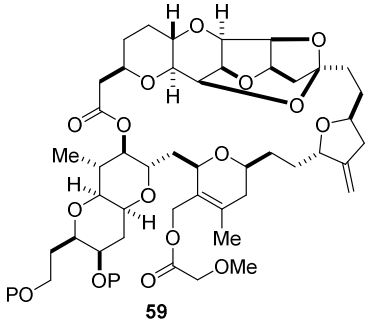

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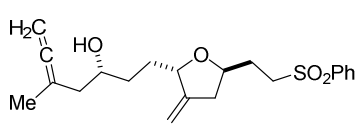

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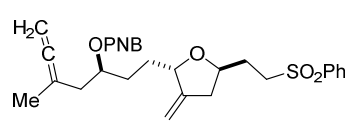

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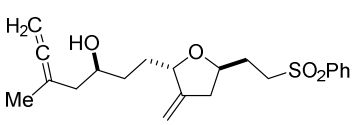

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Definitions

Compounds useful in the invention may be isotopically labeled compounds. Useful isotopes include hydrogen, carbon, nitrogen, and oxygen (e.g., ^{2}H, ^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, and ^{17}O). Isotopically-labeled compounds can be prepared by synthesizing a compound using a readily available isotopically-labeled reagent in place of a non-isotopically-labeled reagent.

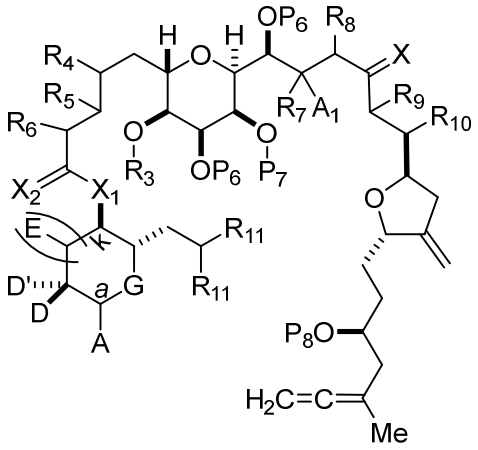
For any of the following chemical definitions, a number following an atomic symbol indicates that total number of atoms of that element that are present in a particular chemical moiety. As will be understood, other atoms, such as hydrogen atoms, or substituent groups, as described herein, may be present, as necessary, to satisfy the valences of the atoms. For example, an unsubstituted C_2 alkyl group has the formula $–CH_2CH_3$. When used with the groups defined herein, a reference to the number of carbon atoms includes the divalent carbon in acetal and ketal groups but does not include the carbonyl carbon in acyl, ester, carbonate, or carbamate groups. A reference to the number of oxygen, nitrogen, or sulfur atoms in a heteroaryl group only includes those atoms that form a part of a heterocyclic ring.

Claims

1. A method of preparing a macrocyclic intermediate in the synthesis of a halichondrin macrolide or an analog thereof, the method comprising reacting a compound of formula (IA) with $R_{12}OH$ and a Lewis acid, the reaction producing the macrocyclic intermediate by forming a bond in the structure of the halichondrin macrolide or an analog thereof,

wherein R_{12} is optionally substituted acyl;

wherein the compound of formula (IA) is:

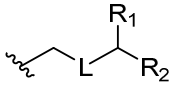


(IA),

or a salt or a tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or $–C(O)–$;

R_1 is H, or R_1 and P_1 combine to form a bond;

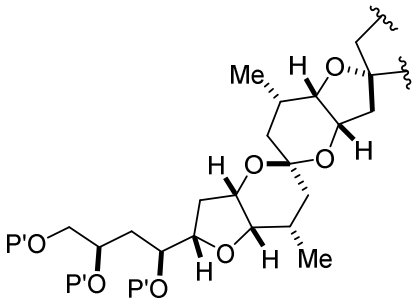
(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl

protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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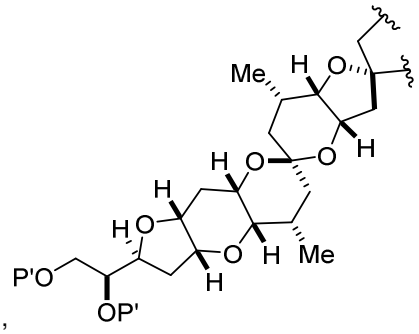

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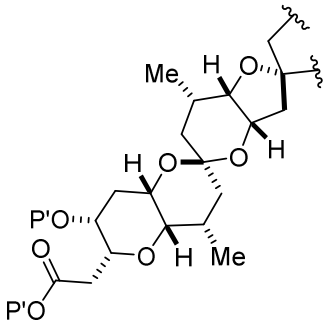


, wherein each P' is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)–, $–CH_2–$, or –O–;

X_2 is =O or X_2, together with the carbon atom to which it is attached, is $–(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $–SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene, provided that, when X_1 is –O–, X_2 is =O;

Y is SO_2R_C or $COOR_C$, where, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H;

or

A_1 is H or OP", and:

(a) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(b) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP"; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group; or

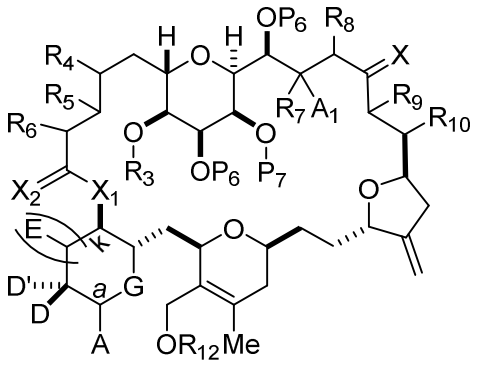
(iii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form acetal; and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group;

R_9 is H, OP", or Y, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

each P", when present, is independently H or a hydroxyl protecting group; and

P_8 is H or silyl; and

wherein the macrocyclic intermediate in the synthesis of a halichondrin macrolide or an analog thereof is a compound of formula (IB):



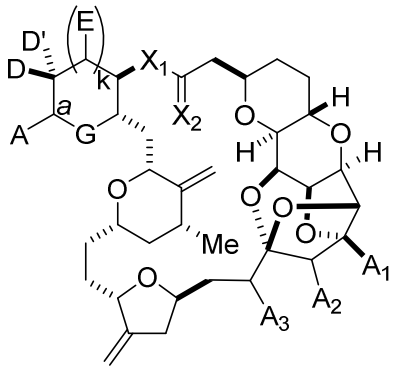
(IB)

or a salt or a tautomer thereof.

2. The method of claim 1, wherein the Lewis acid is an oxophilic Lewis acid.

3. The method of claim 2, wherein the oxophilic Lewis acid is boron trifluoride or a solvate thereof.

4. A method of preparing

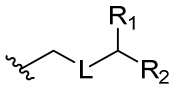


a halichondrin macrolide or an analog thereof,

or a salt thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or $–C(O)–$;

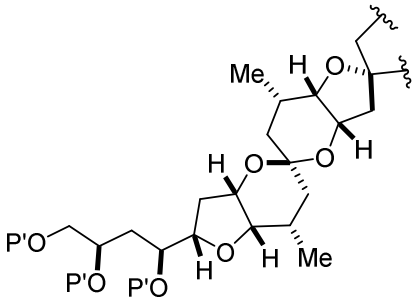
R_1 is H, or R_1 and P_1 combine to form a bond;

(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is H or an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene, or (c) each of P_2 and P_4 is H;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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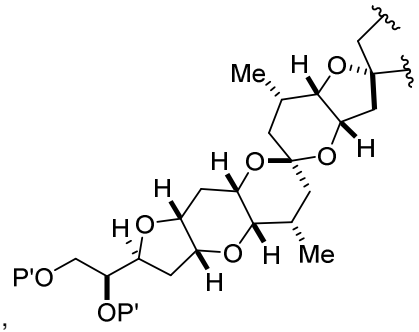

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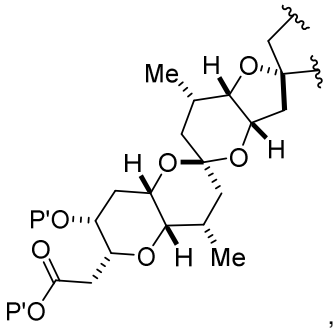


, wherein each P' is independently H or a hydroxyl protecting group;

each of A_1, A_2, and A_3 is independently H or OP", wherein each P" is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

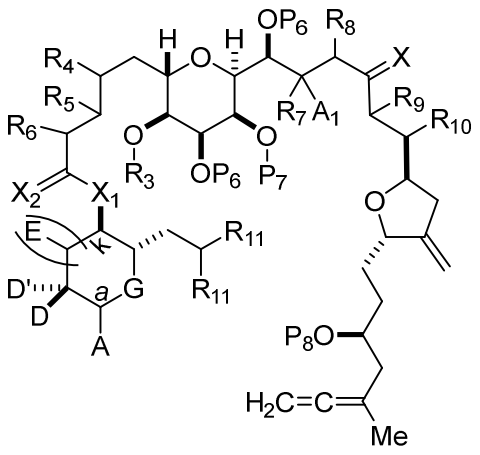
n, when present, is 0, 1, or 2;

k is 0 or 1; and

X_1 is $–CH_2–$ or –O–, and X_2 is =O;

the method comprising:

(A) producing a compound of formula (IB) from a compound of formula (IA) and $R_{12}OH$, wherein R_{12} is optionally substituted acyl, and the compound of formula (IA) is of the following structure:

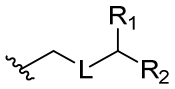


(IA)

or a salt or a tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or $–C(O)–$;

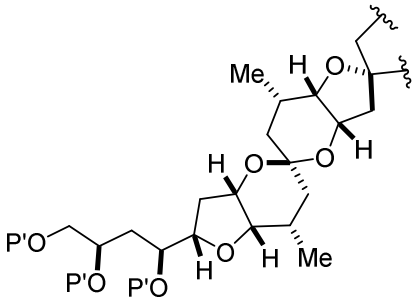
R_1 is H, or R_1 and P_1 combine to form a bond;

(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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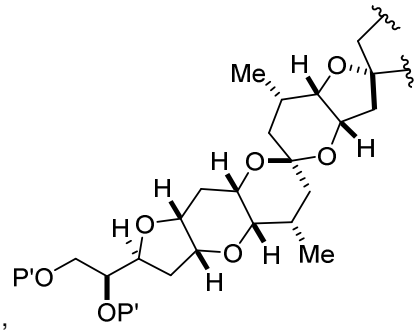

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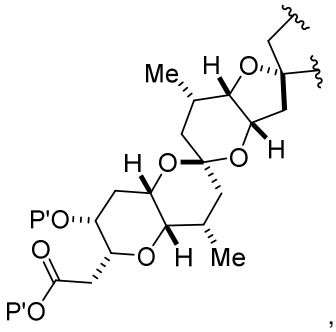


, wherein each P' is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)–, $–CH_2–$, or –O–, and X_2 is =O or X_2, together with the carbon atom to which it is attached, is $–(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $–SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene, provided that, when X_1 is –O–, X_2 is =O; and wherein Y is SO_2R_C or $COOR_C$, where, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H; or

A_1 is H or OP", and:

(i) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(ii) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP"; and each R_{11} is –OP$_{10}$, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group; or

(iii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form acetal; and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group;

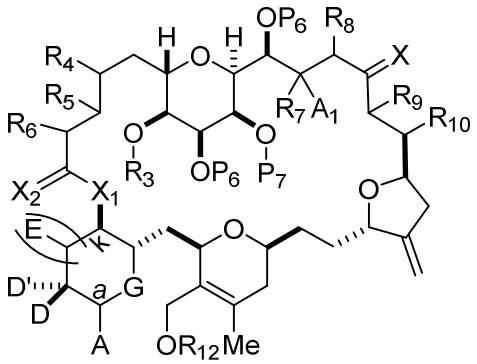
R_9 is H, OP", SO_2R_C, or $COOR_C$, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

each P", when present, is independently H or a hydroxyl protecting group; and

P_8 is H or silyl;

and

the compound of formula (IB) is of the following structure:



(IB)

or a salt or a tautomer thereof;

wherein

R_{12} is optionally substituted acyl;

(B) producing the halichondrin macrolide or the analog thereof from compound (IB).

5. The method of claim 4, wherein the producing the compound of formula (IB) comprises reacting the compound of formula (IA) with R_{12}OH and a Lewis acid.

6. The method of claim 5, wherein the Lewis acid is an oxophilic Lewis acid.

7. The method of any one of claims 4 to 6, wherein the producing the halichondrin macrolide or the analog thereof comprises reacting the compound of formula (IB) with an allylic reducing agent.

8. The method of any one of claims 1 to 7, wherein R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H.

9. The method of any one of claims 1 to 7, wherein R_5 and R_6, together with the atom to which each is attached, combine to form a double bond, R_4 is H, and R_3 is a hydroxyl protecting group.

10. The method of any one of claims 1 to 9, wherein P_6 is a hydroxyl protecting group, and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP_9))–.

11. The method of any one of claims 1 to 10, wherein R_7 and P_7 combine to form a bond, and R_8 is H.

12. The method of any one of claims 1 to 10, wherein P_7 is a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond.

13. The method of any one of claims 1 to 12, wherein R_9 is H or SO_2R_C, and R_{10} is H.

14. The method of any one of claims 1 to 13, wherein P_8 is silyl.

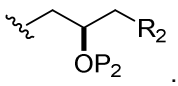
15. The method of any one of claims 1 to 14, wherein each R_{11} is $–OP_{10}$, wherein P_{10} is alkyl.

16. The method of any one of claims 1 to 15, wherein G is O.

17. The method of any one of claims 1 to 16, wherein D is H.

18. The method of any one of claims 1 to 17, wherein D' is OP_1, wherein P_1 is alkyl.

19. The method of any one of claims 1 to 18, wherein the stereogenic center designated by *a* is (*R*), and A is of the following structure:

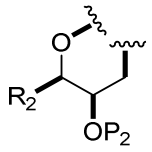


.

20. The method of any one of claims 1 to 19, wherein k is 0 and X_1 is $–CH_2–$.

21. The method of any one of claims 1 to 20, wherein R_2 is $–(CH_2)_nNP_3P_4$ or $–(CH_2)_nOP_5$, wherein n is 0.

22. The method of any one of claims 1 to 17, wherein A and D combine to form the following structure:



,

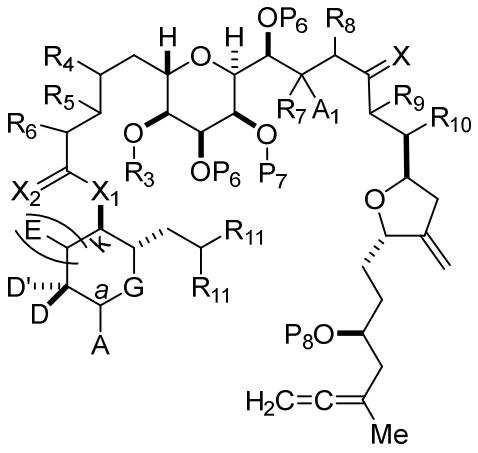
wherein, the bond to oxygen atom originates at the carbon atom, to which D is attached in formula (IA), and

wherein R_2 is $–(CH_2)_nNP_3P_4$ or $–(CH_2)_nOP_5$, wherein n is 2.

23. The method of claim 22, wherein k is 1, and E is optionally substituted alkyl.

24. The method of claim 22 or 23, wherein X_1 is –O–.

25. A compound of formula (IA):

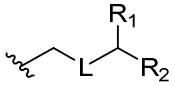


(IA),

or a salt or a tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is –(CH(OP$_2$))–, –(C(OH)(OP$_2$))–, or –C(O)–;

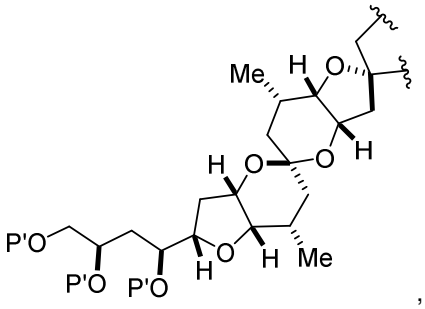
R$_1$ is H, or R$_1$ and P$_1$ combine to form a bond;

(i) R$_2$ is H, wherein P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

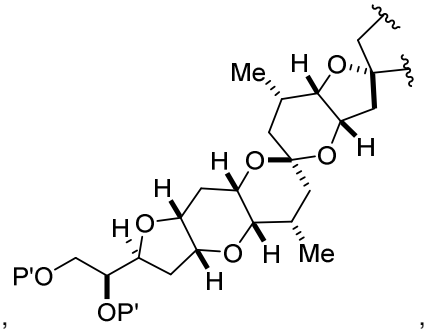
(ii) R$_2$ is –(CH$_2$)$_n$NP$_3$P$_4$, wherein P$_3$ is an N-protecting group, and (a) P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P$_4$ is an N-protecting group, or (b) P$_2$ and P$_4$ combine to form an alkylidene;

(iii) R$_2$ is –(CH$_2$)$_n$OP$_5$, wherein P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P$_5$ is H, optionally substituted alkyl, or a hydroxyl protecting group; or P$_2$ and P$_5$, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

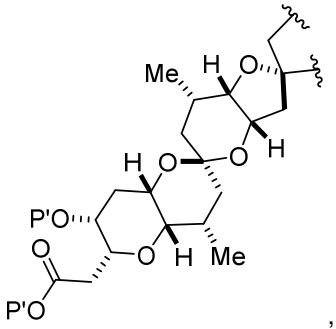
(iv) R$_2$ and P$_2$ combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



,



, and



, wherein each P' is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH$_2$, or NR$_N$, wherein R$_N$ is H, an N-protecting group, or optionally substituted alkyl;

each Q$_1$ is independently OR$_A$, SR$_A$, SO$_2$R$_A$, OSO$_2$R$_A$, NR$_B$R$_A$, NR$_B$(CO)R$_A$, NR$_B$(CO)(CO)R$_A$, NR$_B$(CO)NR$_B$R$_A$, NR$_B$(CO)OR$_A$, (CO)OR$_A$, O(CO)R$_A$, (CO)NR$_B$R$_A$, or O(CO)NR$_B$R$_A$, wherein each of R$_A$ and R$_B$ is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)–, –CH_2–, or –O–;

X_2 is =O or X_2, together with the carbon atom to which it is attached, is –($C(R_X)_2$)–; wherein each R_X is independently H, –OR_{X1}, or –SR_{X1}, provided that at least one R_X, when present, is –OR_{X1} or –SR_{X1}; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene, provided that, when X_1 is –O–, X_2 is =O;

Y is SO_2R_C or $COOR_C$, where, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H;

or

A_1 is H or OP", and:

(i) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(ii) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –($CH(OP_9)$)–, wherein P_9 is H or a hydroxyl protecting group; and each R_{11} is –OP_{10}, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP"; and each R_{11} is –OP_{10}, or both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group; or

(iii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form acetal; and X is =O or X combines with the carbon atom, to which it is attached, to form –($CH(OP_9)$)–, wherein P_9 is H or a hydroxyl protecting group;

R_9 is H, OP", or Y, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

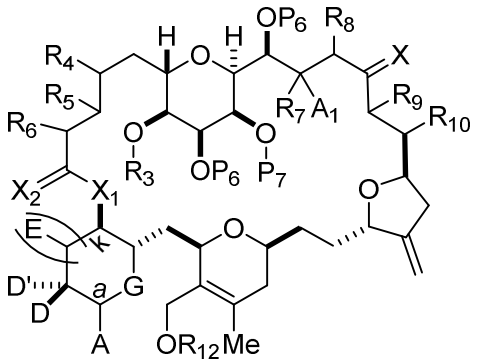
each P", when present, is independently H or a hydroxyl protecting group; and

P_8 is H or silyl.

26. The compound of claim 25, wherein P_8 is silyl.

27. The compound of claim 25 or 26, wherein each R_{11} is –OP_{10}, wherein P_{10} is alkyl.

28. A compound of formula (IB):

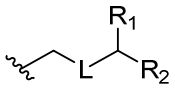


(IB)

or a salt or a tautomer thereof.

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, oxo, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$, $–(C(OH)(OP_2))–$, or –C(O)–;

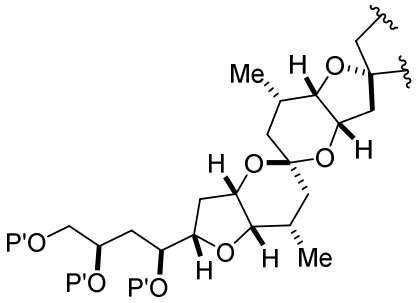
R_1 is H, or R_1 and P_1 combine to form a bond;

(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is H, optionally substituted alkyl, or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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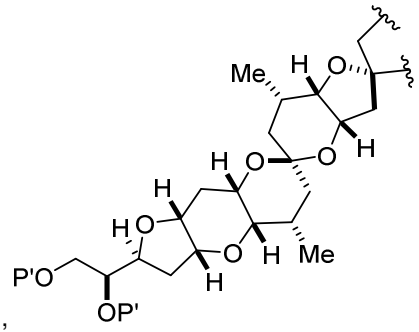
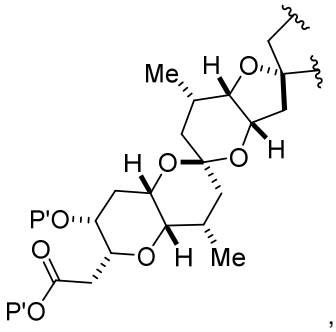


, and


, wherein each P' is independently H or a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently H, alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)–, $–CH_2–$, or –O–;

X_2 is =O or X_2, together with the carbon atom to which it is attached, is $–(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $–SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene, provided that, when X_1 is –O–, X_2 is =O;

Y is SO_2R_C or $COOR_C$, where, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H;

or

A_1 is H or OP", and:

(a) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

(b) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

(i) each P_6 is independently H or a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal; X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–, wherein P_9 is H or a hydroxyl protecting group; or

(ii) both P_6 and X, together with the atoms to which each is attached, combine to form ketal, P_7 and R_7 combine to form a bond, and R_8 is H or OP";

R_9 is H, OP", or Y, and R_{10} is H; or R_9 and R_{10}, together with the atoms to which each is attached, combine to form a double bond;

each P", when present, is independently H or a hydroxyl protecting group; and

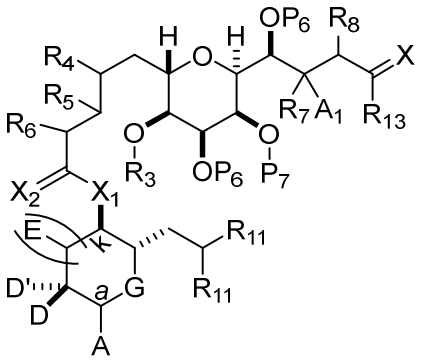
R_{12} is optionally substituted acyl.

29. The compound of any one of claims 25 to 28, wherein R_9 is H or SO_2R_C, and R_{10} is H.

30. The compound of any one of claims 25 to 29, wherein P_6 is a hydroxyl protecting group, and X is =O or X combines with the carbon atom, to which it is attached, to form –(CH(OP$_9$))–.

31. The compound of any one of claims 25 to 30, wherein A_1 is H.

32. A compound of formula (IC)

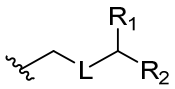


(IC),

or a salt or tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is –(CH(OP$_2$))– or –C(O)–;

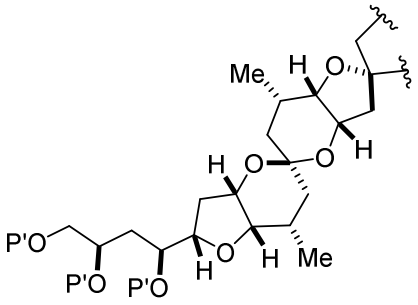
R$_1$ is H, or R$_1$ and P$_1$ combine to form a bond;

(i) R$_2$ is H, wherein P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R$_2$ is –(CH$_2$)$_n$NP$_3$P$_4$, wherein P$_3$ is an N-protecting group, and (a) P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P$_4$ is an N-protecting group, or (b) P$_2$ and P$_4$ combine to form an alkylidene;

(iii) R$_2$ is –(CH$_2$)$_n$OP$_5$, wherein P$_2$ is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P$_5$ is optionally substituted alkyl or a hydroxyl protecting group; or P$_2$ and P$_5$, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R$_2$ and P$_2$ combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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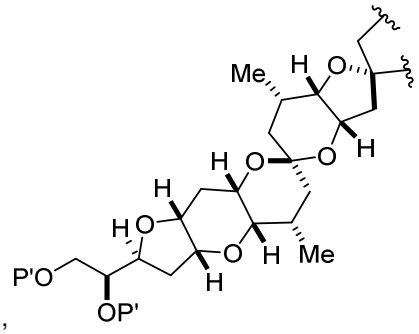

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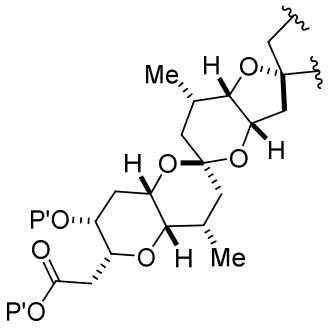


, wherein each P' is independently a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH$_2$, or NR$_N$, wherein R$_N$ is H, an N-protecting group, or optionally substituted alkyl;

each Q$_1$ is independently OR$_A$, SR$_A$, SO$_2$R$_A$, OSO$_2$R$_A$, NR$_B$R$_A$, NR$_B$(CO)R$_A$, NR$_B$(CO)(CO)R$_A$, NR$_B$(CO)NR$_B$R$_A$, NR$_B$(CO)OR$_A$, (CO)OR$_A$, O(CO)R$_A$, (CO)NR$_B$R$_A$, or O(CO)NR$_B$R$_A$, wherein each of R$_A$ and R$_B$ is independently alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl,

alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)– or $–CH_2–$;

X_2 is =O or X_2, together with the carbon atom to which it is attached, is $-(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $-SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene;

Y is SO_2R_C or $COOR_C$, wherein, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

(i) each P_6 is independently a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal;

each R_{11} is independently $–OP_{10}$, or

both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

or

(ii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form an acetal;

R_{13} is H or $–CH_2P(O)(OR_E)_2$, wherein each R_E, when present, is independently optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

X is =O or X combines with the carbon atom, to which it is attached, to form $–(CH(OP_9))–$, wherein P_9 is H or a hydroxyl protecting group;

A_1 and R_7 combine to form oxo, P_7 is H or a hydroxyl protecting group, and R_8 is H;

or

A_1 is H or OP", and:

(i) P_7 is H or a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

or

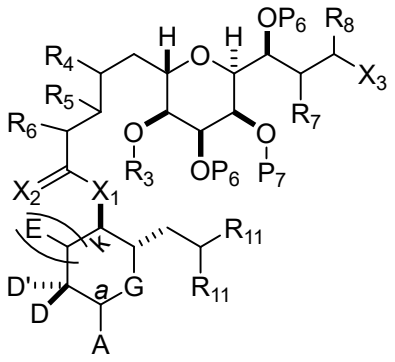
(ii) P_7 and R_7 combine to form a bond, and R_8 is H or OP";

and

each P", when present, is independently H or a hydroxyl protecting group.

33. The compound of any one of claims 25 to 32, wherein A_1 is H.

34. A compound of formula (IE):

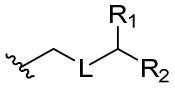


(IE),

or a salt or tautomer thereof,

wherein

each of D and D' is independently H, optionally substituted alkyl, or OP_1, provided that only one of D and D' is OP_1, wherein P_1 is H, alkyl, or a hydroxyl protecting group; and A is a group of formula (1) or a C_{1-6} saturated or C_{2-6} unsaturated hydrocarbon skeleton, the skeleton being unsubstituted or having from 1 to 10 substituents independently selected from the group consisting of cyano, halo, azido, and Q_1, the group of formula (1) having the structure:



(1),

wherein

L is $–(CH(OP_2))–$ or $–C(O)–$;

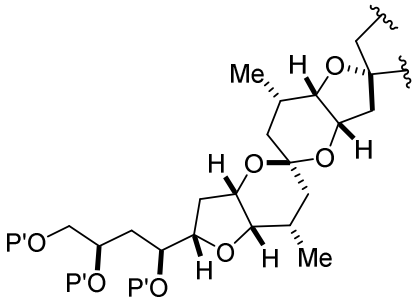
R_1 is H, or R_1 and P_1 combine to form a bond;

(i) R_2 is H, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group;

(ii) R_2 is $–(CH_2)_nNP_3P_4$, wherein P_3 is an N-protecting group, and (a) P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_4 is an N-protecting group, or (b) P_2 and P_4 combine to form an alkylidene;

(iii) R_2 is $–(CH_2)_nOP_5$, wherein P_2 is absent, H, optionally substituted alkyl, or a hydroxyl protecting group, and P_5 is optionally substituted alkyl or a hydroxyl protecting group; or P_2 and P_5, together with the atoms to which each is attached, combine to form a ketal, a cyclic carbonate, a dicarbonyl-dioxo, or silylene-dioxo; or

(iv) R_2 and P_2 combine to form an optionally substituted ethylene or a structure selected from the group consisting of:



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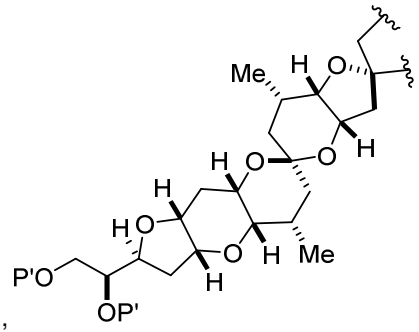

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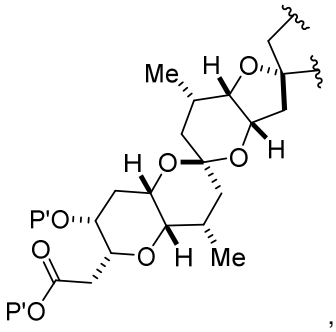


, wherein each P' is independently a hydroxyl protecting group;

E is H, optionally substituted alkyl, or optionally substituted alkoxy;

G is O, S, CH_2, or NR_N, wherein R_N is H, an N-protecting group, or optionally substituted alkyl;

each Q_1 is independently OR_A, SR_A, SO_2R_A, OSO_2R_A, NR_BR_A, $NR_B(CO)R_A$, $NR_B(CO)(CO)R_A$, $NR_B(CO)NR_BR_A$, $NR_B(CO)OR_A$, $(CO)OR_A$, $O(CO)R_A$, $(CO)NR_BR_A$, or $O(CO)NR_BR_A$, wherein each of R_A and R_B is independently alkyl, haloalkyl, hydroxyalkyl, aminoalkyl, aryl, haloaryl, hydroxyaryl, alkoxyaryl, arylalkyl, alkylaryl, haloarylalkyl, alkylhaloaryl, (alkoxyaryl)alkyl, heterocyclic radical, or heterocyclic radical-alkyl;

n, when present, is 0, 1, or 2;

k is 0 or 1;

X_1 is –CH(Y)– or $–CH_2–$,

X_2 is =O or X_2, together with the carbon atom to which it is attached, is $–(C(R_X)_2)–$; wherein each R_X is independently H, $–OR_{X1}$, or $–SR_{X1}$, provided that at least one R_X, when present, is $–OR_{X1}$ or $–SR_{X1}$; wherein each R_{X1} is independently optionally substituted alkyl, or both R_{X1} combine to form optionally substituted alkylene;

Y is SO_2R_C or $COOR_C$, wherein, when Y is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when Y is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl;

R_3 and R_5 combine to form a bond, and each of R_4 and R_6 is H; or R_3 is H or a hydroxyl protecting group, R_5 and one of R_4 and R_6, together with the atoms to which each is attached, combine to form a double bond, and the remaining R_4 or R_6 is H;

R_7 and P_7 combine to form a bond, and R_8 is H; or P_7 is a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond;

(i) each P_6 is independently a hydroxyl protecting group, or both P_6, together with the atoms to which each is attached, combine to form a ketal or acetal;

each R_{11} is independently $–OP_{10}$, or

both R_{11} combine to form oxo, wherein P_{10} is alkyl or a hydroxyl protecting group;

or

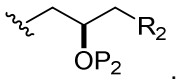
(ii) both P_6 and both R_{11}, together with the atoms to which they are attached, combine to form an acetal;

X_3 is $–CH_2OP_A$, $–CH=CH_2$, or $–CH(OP_A)CH_2OP_A$, wherein each R_E is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl, and wherein each P_A is independently H or a hydroxyl protecting group, or both P_A combine to form a cyclic protected diol.

35. The compound of claim 34, wherein each P_A is H, or both P_A combine to form a cyclic protected diol.

36. The compound of any one of claims 32 to 35, wherein each R_{11} is $–OP_{10}$, wherein P_{10} is alkyl.

37. The compound of any one of claims 25 to 36, wherein the stereogenic center designated by *a* is (*R*), and A is of the following structure:



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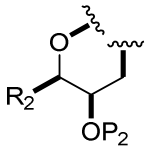
38. The compound of any one of claims 25 to 37, wherein k is 0 and X_1 is $–CH_2–$.

39. The compound of any one of claims 25 to 38, wherein R_2 is $–(CH_2)_nNP_3P_4$ or $–(CH_2)_nOP_5$, wherein n is 0.

40. The compound of any one of claims 25 to 36, wherein A and D combine to form the following structure:



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wherein, the bond to oxygen atom originates at the carbon atom, to which D is attached in formula (IA), and

wherein R_2 is $–(CH_2)_nNP_3P_4$ or $–(CH_2)_nOP_5$, wherein n is 2.

41. The compound of claim 40, wherein k is 1, and E is optionally substituted alkyl.

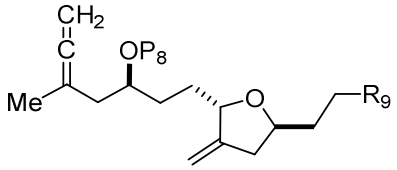
42. The compound of claim 40 or 41, wherein X_1 is –O–.

43. The compound of any one of claims 25 to 42, wherein R_5 and R_6, together with the atom to which each is attached, combine to form a double bond, R_4 is H, and R_3 is a hydroxyl protecting group.

44. The compound of any one of claims 25 to 43, wherein R_7 and P_7 combine to form a bond, and R_8 is H.

45. The compound of any one of claims 25 to 43, wherein P_7 is a hydroxyl protecting group, and R_7 and R_8, together with the atoms to which each is attached, combine to form a double bond.

46. A compound of formula (ID):



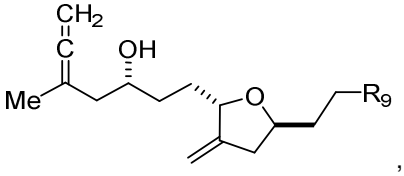
(ID),

wherein

P_8 is H or a hydroxyl protecting group; and

R_9 is SO_2R_C or $COOR_C$, when R_9 is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when R_9 is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl.

47. A compound of formula (IDa):



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(IDa)

wherein

R_9 is SO_2R_C or $COOR_C$, when R_9 is SO_2R_C, R_C is optionally substituted aryl or optionally substituted non-enolizable alkyl, and when R_9 is $COOR_C$, R_C is optionally substituted alkyl, optionally substituted aryl, or optionally substituted arylalkyl.

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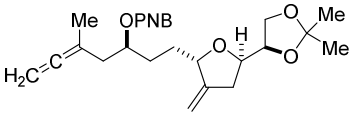
48. The compound of claim 46 or 47, wherein R_9 is SO_2R_C.

49. A compound selected from the group consisting of:



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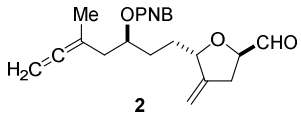

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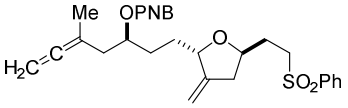

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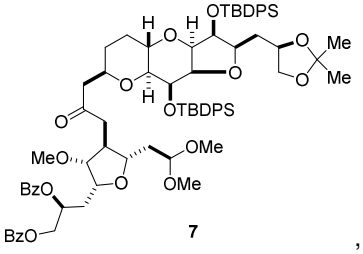

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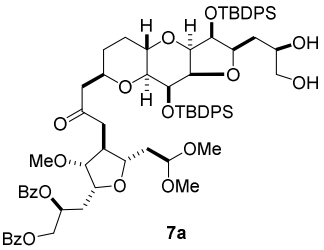

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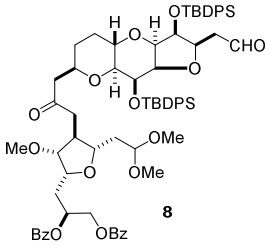

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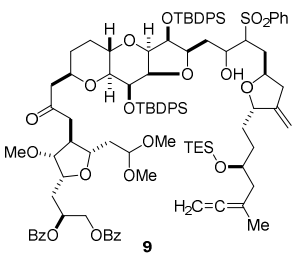

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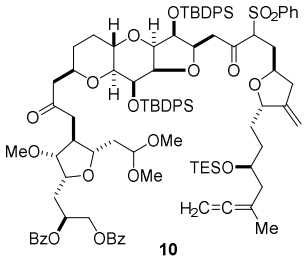

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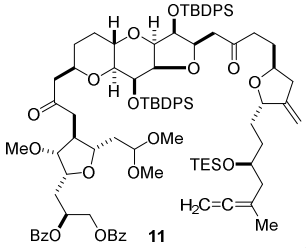

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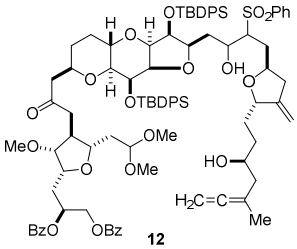

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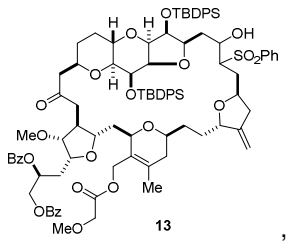

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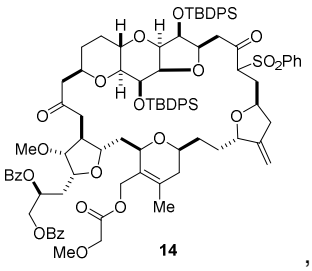

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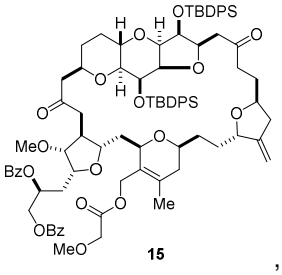

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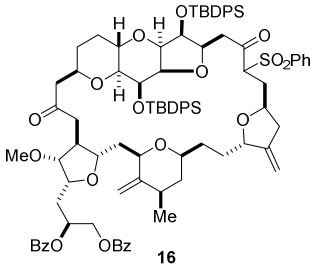

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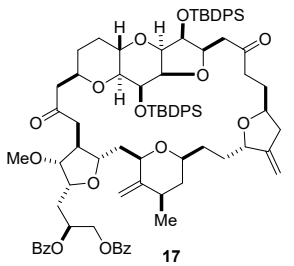

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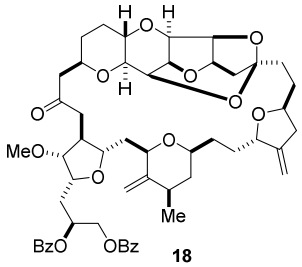

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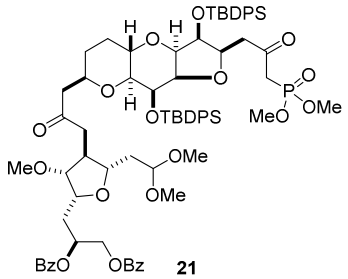

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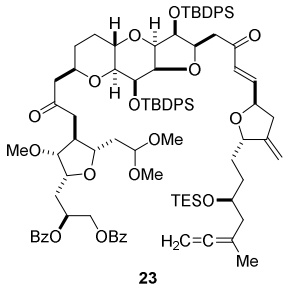

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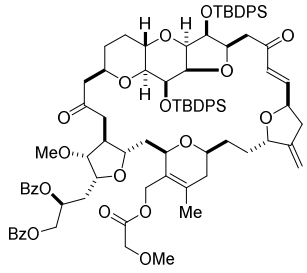

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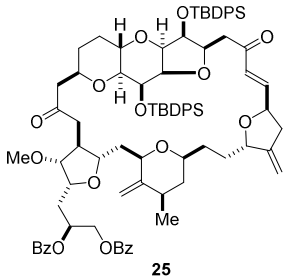

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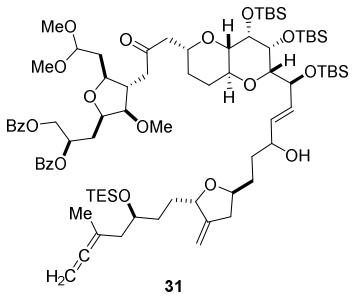

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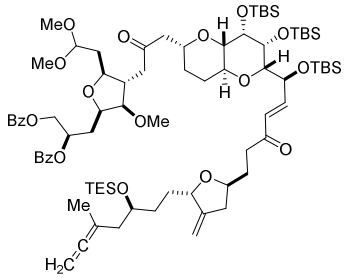

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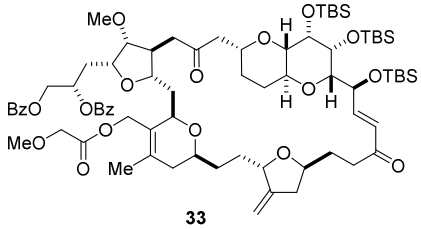

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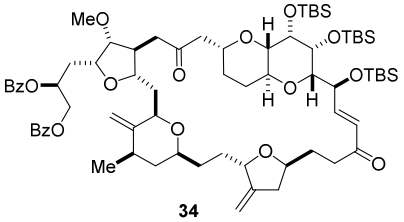

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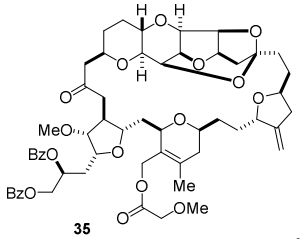

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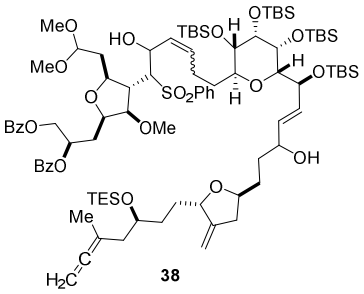

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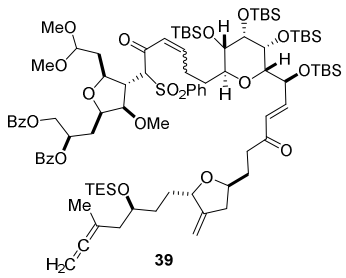

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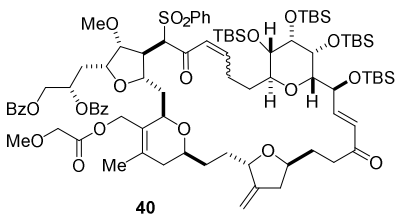

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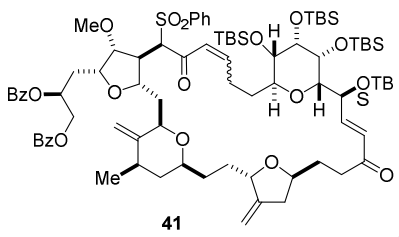

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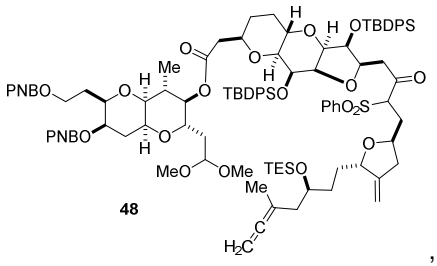

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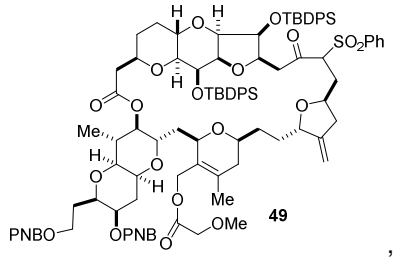

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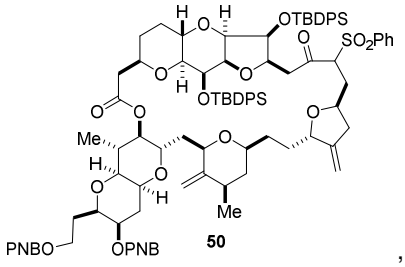

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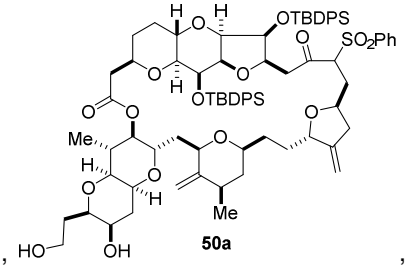

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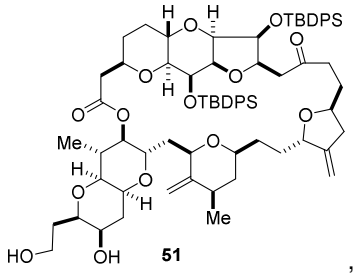

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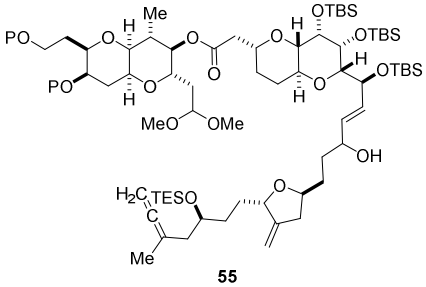

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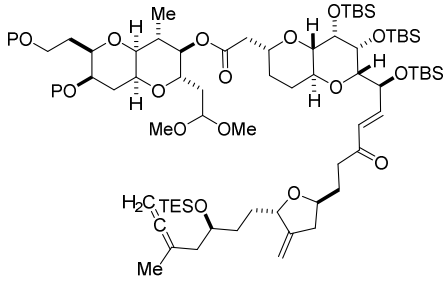

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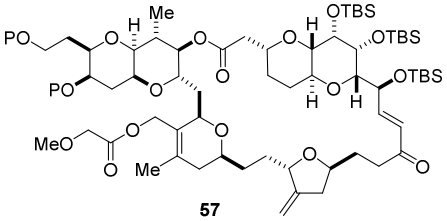

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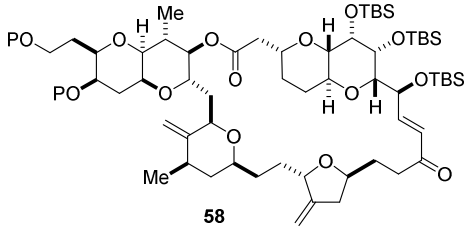

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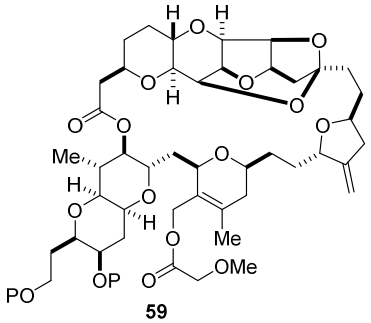

59

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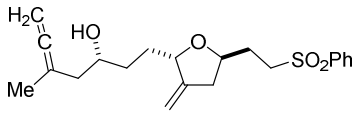

85

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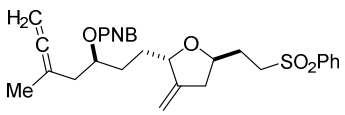

86

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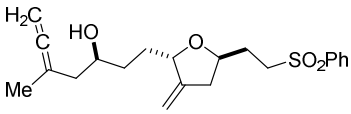

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wherein P is TBDPS, Ac, or PNB.