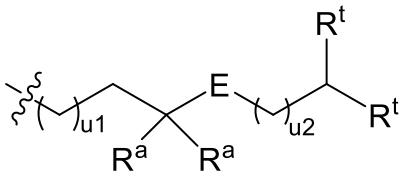
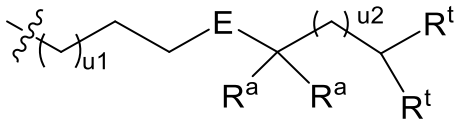
WHAT IS CLAIMED:

1. A lipid comprising at least one head group and at least one tail group of formula (TI) or (TI')



(TI) or


(TI'), a pharmaceutically acceptable salt thereof, or a stereoisomer of any of the foregoing,

wherein:

E is each independently -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -C(O)N(R^7)-, -C(O-R_{13})-O-, -C(O)O(CH_2)$_r$-, -C(O)N(R^7) (CH_2)$_r$-, -S-S-, or -C(O-R_{13})-O-(CH_2)$_r$-, wherein each R^7 is independently H, alkyl, alkenyl, cycloalkyl, hydroxyalkyl, or aminoalkyl; R_{13} is branched or unbranched C_3-C_{10} alkyl; and r is 1, 2, 3, 4, or 5;

R^a is each independently C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl;

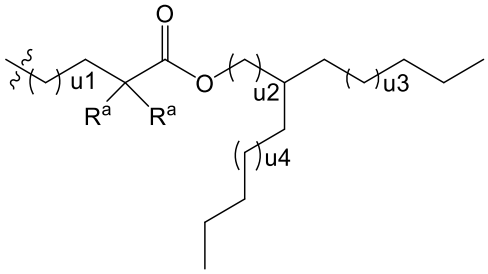
u1 and u2 are each independently 0, 1, 2, 3, 4, 5, 6, or 7;

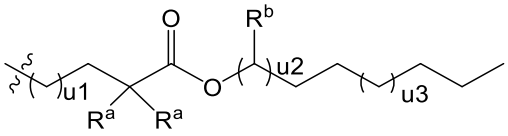
R^t is each independently H, C_1-C_{16} branched or unbranched alkyl or C_1-C_{16} branched or unbranched alkenyl, optionally interrupted with heteroatom or substituted with OH, SH, or halogen, or cycloalkyl or substituted cycloalkyl;

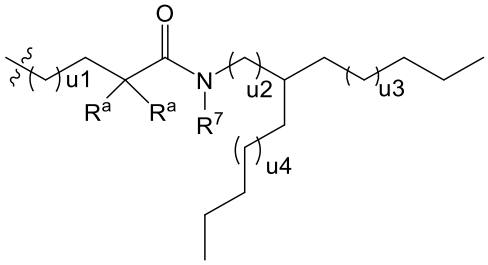
 represents the bond connecting the tail group to the head group; and

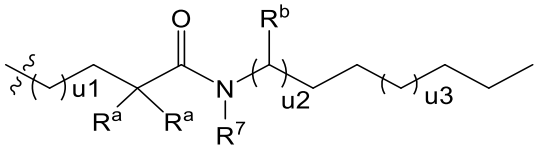
wherein the lipid has a pKa from about 4 to about 8.

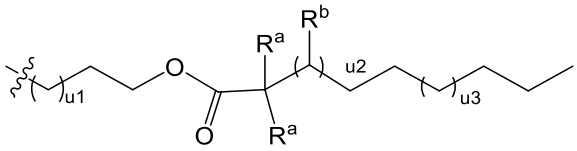
2. The lipid of claim 1, wherein the lipid comprises at least one tail group of the following formulas:



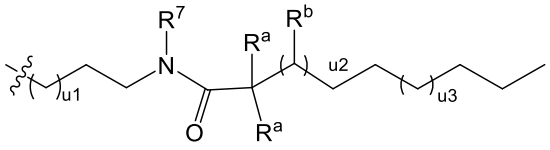
(TII),


(TIII),


(TIV),


(TV),


(TII'), and



(TIII'),

wherein

R^7 is each independently H or methyl;
R^b is in each occasion independently H or C_1-C_4 alkyl; and
u3 and u4 are each independently 0, 1, 2, 3, 4, 5, 6, or 7, and
wherein the lipid has a pKa from about 4 to about 8.

3. The lipid of claim 2, wherein the lipid comprises two, three, four, or more tail groups of formula (TII), (TIII), (TIV), (TV), (TII'), or (TIII'), and wherein each tail group may be the same or different.

4. The lipid of any one of claims 1-3, wherein:

each R^a is methyl; and/or
u1 is 3-5, u2 is 0-3, and u3 and u4 are each independently 1-7.

5. The lipid of claim 2, wherein the lipid comprises:

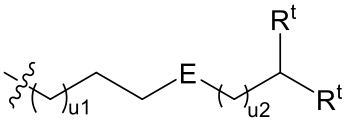
(i) at least one tail of formula (TIII), wherein each R^a is methyl, R^b is in each occasion independently H, ethyl, or butyl, u1 is 3-5, u2 is 0-3, and u3 is 1-7; optionally wherein the lipid comprises at least two, three, or four tails of formula (TIII), wherein the two, three, or four tails of formula (TIII) are the same or different;

(ii) at least one tail of formula (TII), wherein each R^a is methyl, u1 is 3-5, u2 is 0-3, u3 is 1-4, and u4 is 1-4, optionally wherein the lipid has at least two, three, or four tails of formula (TII), wherein the two, three, or four tails of formula (TII) are the same or different;(iii) at least one tail of formula (TII) and at least one tail of formula (TIII), optionally wherein the lipid has at least two tails of formula (TII) and at least two tails of formula (TIII), wherein the at least two tails of formula (TII) are the same or different and at least two tails of formula (TIII) are the same or different;

(iv)at least one tail of formula (TIV), wherein each R^a is methyl, u1 is 3-5, u2 is 0-3, u3 is 1-4, and u4 is 1-4; optionally, wherein the lipid comprises at least two, three, or four tails of formula (TIV), wherein the two, three, or four tails of formula (TIV) are the same or different; (v) at least two, three, or four tails of formula (TV), wherein the two, three, or four tails of formula (TV) are the same or different;(vi) at least two, three, or four tails of formula (TII'), wherein the two, three, or four tails of formula (TII') are the same or different; (vii) at least two, three, or four tails of formula (TIII'), wherein the two, three, or four tails of formula (TIII') are the same or different; (viii) at least one tail selected from the group consisting of formula (TII), (TIII), and (TII'), and at least one tail selected from the group consisting of (TIV), (TV), and (TIII');.(ix) at least two tails selected from the group consisting of (TII), (TIII), and (TII');(x) at least two tails selected from the group consisting of (TIV), (TV), and (TIII');.(xi) at least two tails selected from the group consisting of formula (TII), (TIII), and (TII'), and at least one tail selected from the group consisting of (TIV), (TV), and (TIII');(xii) at least one tail selected from the group consisting of formula (TII), (TIII), and (TII'), and at least two tails selected from the group consisting of (TIV), (TV), and (TIII'); (xiii) at least two tails selected from the group consisting of formula (TII),

(TIII), and (TII'), and at least two tails selected from the group consisting of (TIV), (TV), and (TIII');(xiv) at least three tails selected from the group consisting of (TII), (TIII), and (TII'); (xv) at least three tails selected from the group consisting of (TIV), (TV), and (TIII'); (xvi) at least three tails selected from the group consisting of formula (TII), (TIII), and (TII'), and at least one tail selected from the group consisting of (TIV), (TV), and (TIII'); (xvii) at least one tail selected from the group consisting of formula (TII), (TIII), and (TII'), and at least three tails selected from the group consisting of (TIV), (TV), and (TIII');(xviii) at least two tails of formula (TII) or (TIII), and at least two tails of formula (TIV) or (TV); (xix) at least two tails of formula (TII) or (TIII), and at least two tails of formula (TII') or (TIII'); or(xx) at least two tails of formula (TIV) or (TV), and at least two tails of formula (TII') or (TIII').

6. The lipid of one of claims 1-5, further comprising at least one tail of formula (TNG-I):



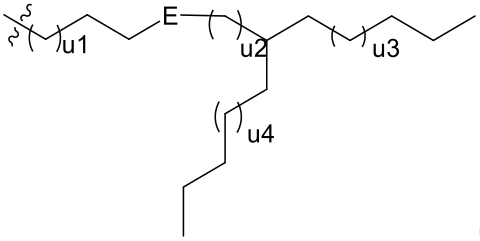
(TNG-I), wherein

E is each independently, -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -S-S-, or -C(O)N(R^7)-;

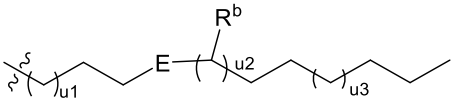
u1 and u2 are each independently 0, 1, 2, 3, 4, 5, 6, or 7; and

R^7 is independently H, alkyl, alkenyl, cycloalkyl, hydroxyalkyl, or aminoalkyl.

7. The lipid of claim 6, wherein the at least one tail of formula (TNG-I) is represented by



(TNG-II) or

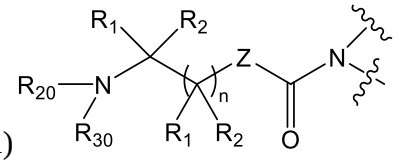


(TNG-III), wherein

u3 and u4 are each independently 0, 1, 2, 3, 4, 5, 6, or 7; and

R^b is in each occasion independently H or C_1-C_4 alkyl.

8. The lipid of one of claims 1-6, wherein the head group has a structure of one of the following formulas:



(i) (HA-I),

wherein:

R_{20} and R_{30} are each independently H, C_1-C_5 branched or unbranched alkyl, or C_2-C_5 branched or unbranched alkenyl, optionally interrupted with one or more heteroatoms or substituted with OH, SH, halogen, or cycloalkyl groups; or

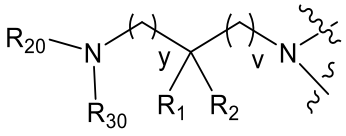
R_{20} and R_{30}, together with the adjacent N atom, form a 3 to 7 membered heterocylic or heteroaromatic ring containing one or more heteroatoms, optionally substituted with one or more OH, SH, halogen, alkyl, or cycloalkyl groups;

each of R_1 and R_2 is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, OH, halogen, SH, or $NR_{10}R_{11}$; or R_1 and R_2 together form a cyclic ring;

each of R_{10} and R_{11} is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl; or R_{10} and R_{11} together form a heterocyclic ring;

n is 0, 1, 2, 3 or 4;

Z is absent, O, S, or NR_{12}, wherein R_{12} is H or C_1-C_7 branched or unbranched alkyl; provided that when Z is not absent, the adjacent R_1 and R_2 cannot be OH, $NR_{10}R_{11}$, SH;

(ii)  (HA-V), wherein:

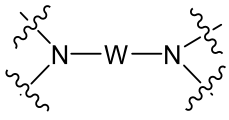
R_1 is H, C_1-C_3 alkyl, OH, halogen, SH, or $NR_{10}R_{11}$;

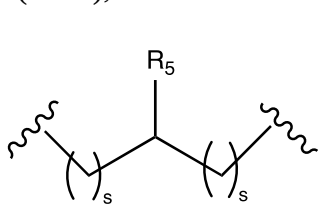
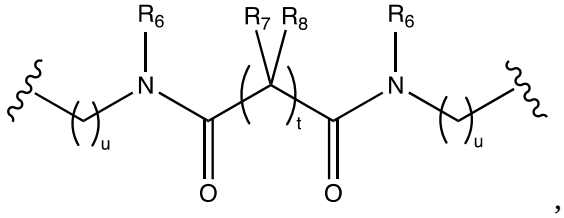
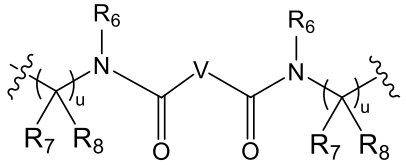
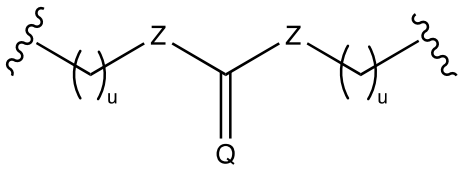
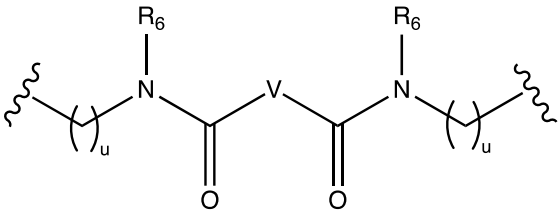
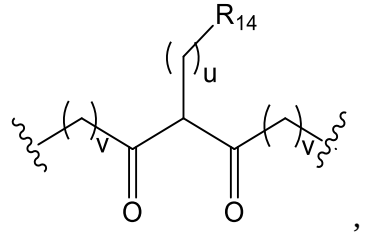
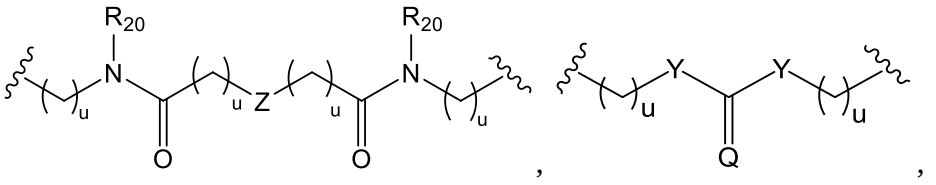
R_2 is OH, halogen, SH, or $NR_{10}R_{11}$; or R_1 and R_2 can be taken together to form a cyclic ring;

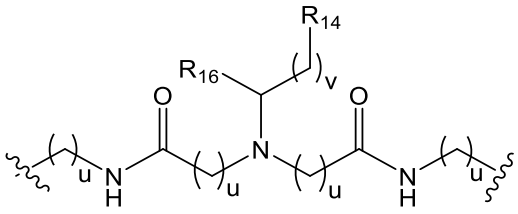
R_{10} and R_{11} are each independently H or C_1-C_3 alkyl; or R_{10} and R_{11} can be taken together to form a heterocyclic ring;

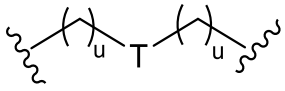
R_{20} and R_{30} are each independently H, C_1-C_5 branched or unbranched alkyl, C_2-C_5 branched or unbranched alkenyl; or R_{20} and R_{30} can be taken together to form a cyclic ring; and

each of v and y is independently 1, 2, 3, or 4;

(iii)  (HB-I),

wherein W is , , , , , , , , .



, or 

,

wherein

R_5 is OH, SH, $(CH_2)_sOH$, or $NR_{10}R_{11}$;

each R_6 is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, or cycloalkyl;

each R_7 and R_8 are independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, halogen, $(CH_2)_vOH$, $(CH_2)_vSH$, $(CH_2)_sN(CH_3)_2$, or $NR_{10}R_{11}$, wherein each R_{10} and R_{11} is independently H or C_1-C_3 alkyl, or R_{10} and R_{11} are taken together to form a heterocyclic ring; or R_7 and R_8 are taken together to form a ring;

each R_{20} is independently H, or C_1-C_3 branched or unbranched alkyl;

R_{14} is a heterocyclic, $NR_{10}R_{11}$, $C(O)NR_{10}R_{11}$, $NR_{10}C(O)NR_{10}R_{11}$, or $NR_{10}C(S)NR_{10}R_{11}$, wherein each R_{10} and R_{11} is independently H, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, optionally substituted with one or more NH and/or oxo groups, or R_{10} and R_{11} are taken together to form a heterocyclic ring;

R_{16} is H, =O, =S, or CN;

each of s, u, and t is independently 1, 2, 3, 4, or 5;

each v is independently 0, 1, 2, 3, 4, or 5;

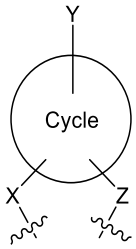
each Y is a divalent heterocyclic;

each Z is independently absent, O, S, or NR_{12}, wherein R_{12} is H, C_1-C_7 branched or unbranched alkyl, or C_2-C_7 branched or unbranched alkenyl;

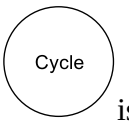
Q is O, S, CH_2, or NR_{13}, wherein each R_{13} is H, C_1-C_5 alkyl;

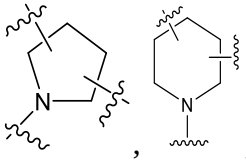
V is branched or unbrachned C_2-C_{10} alkylene, C_2-C_{10} alkenylene, C_2-C_{10} alkynylene, or C_2-C_{10} heteroalkylene, optionally substituted with one or more OH, SH, and/or halogen groups; and

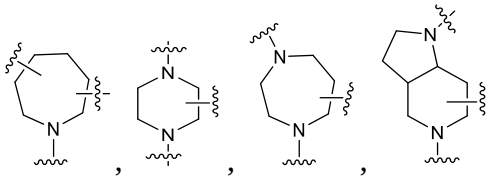
T is –NHC(O)O-, –OC(O)NH-, or a divalent heterocyclic; or

(iv) 

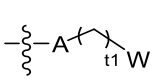
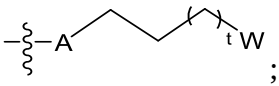
(HC-I), wherein:



is selected from the group consisting of 

, , 

, , , , and 
;

Y is alkyl, hydroxy, hydroxyalkyl, , or ;

A is absent, -O-, -N(R^7)-, -O-alkylene-, -alkylene-O-, -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -C(O)N(R^7)-, -N(R^7)C(O)N(R^7)-, -S-, or -S-S-;

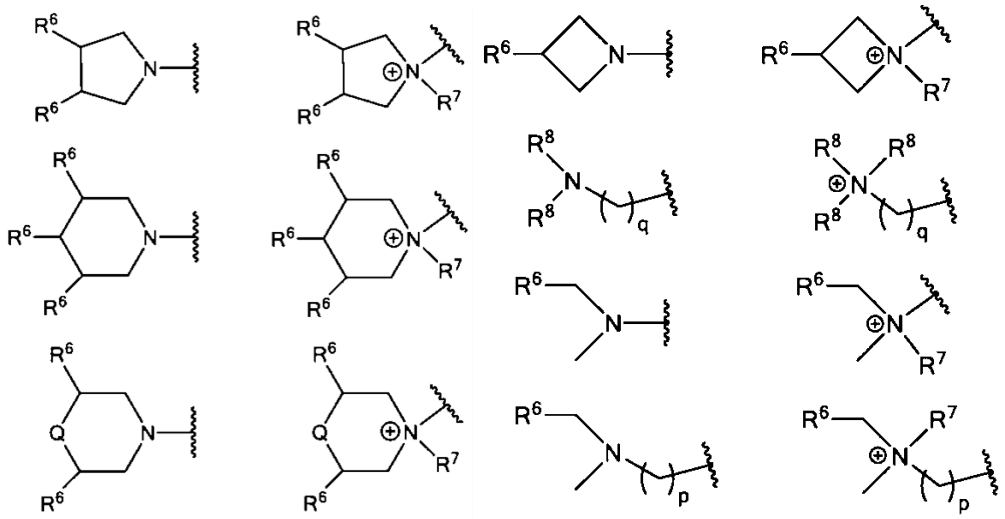
each of X and Z is independently absent, -O-, -C(O)-, -N(R^7)-, alkylene, -O-alkylene-, -alkylene-O-, -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -C(O)N(R^7)-, or -S-;

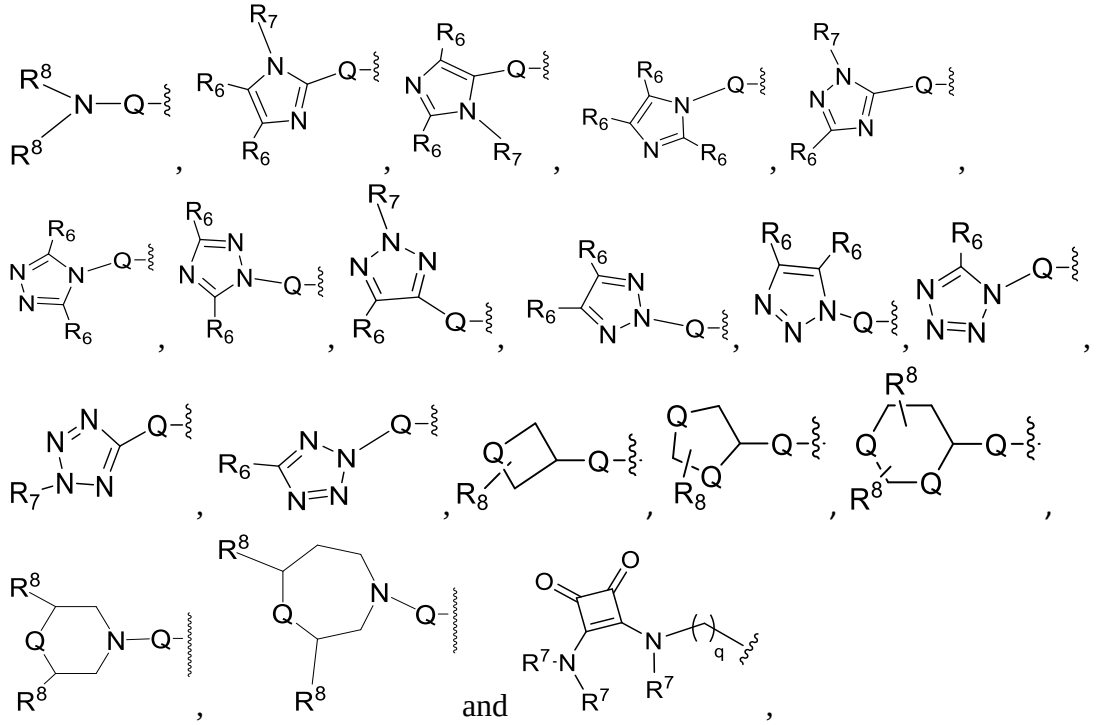
each R^7 is independently H, alkyl, alkenyl, cycloalkyl, hydroxy, alkoxy, hydroxyalkyl, alkylamino, alkylaminoalkyl, or aminoalkyl;

t is 0, 1, 2, or 3;

t1 is an integer from 0 to 10; and

W is hydroxyl, substituted or unsubstituted hydroxyalkyl, or one of the following moieties:





wherein:

each Q is independently absent, -O-, -C(O)-, -C(S)-, -C(O)O-, -$(CH_2)_q$-

$C(R^7)_2$, -C(O)N(R^7)-, -C(S)N(R^7)-, or -N(R^7);

R^6 is independently H, alkyl, hydroxyl, hydroxyalkyl, alkoxy, -O-alkylene-O-alkyl, -O-alkylene-N(R^7)$_2$, amino, alkylamino, aminoalkyl, thiol, thiolalkyl, or $N^+(R^7)_3$–alkylene-Q-;

each R^8 is independently H, alkyl, hydroxyalkyl, amino, aminoalkyl, alkylamino, thiol, thiolalkyl, heterocyclyl, heteroaryl; or two R^8 together with the nitrogen atom form a ring, optionally substituted with one or more alkyl, hydroxy, hydroxyalkyl, alkoxy, alkylaminoalkyl, alkylamino, or aminoalkyl;

q is 0, 1, 2, 3, 4, or 5; and

p is 0, 1, 2, 3, 4, or 5.

9. The lipid of claim 8, wherein the head group has a structure of (i) formula (HA-I), and wherein:

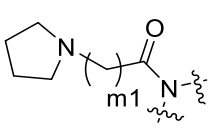
R_{20} and R_{30} together with the adjacent N atom form a 3 to 7 membered heterocylic or heteroaromatic ring containing one or more heteroatoms, optionally substituted with one or more OH, SH, halogen, alkyl, or cycloalkyl groups;

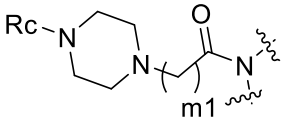
Z is absent, O, S, or NH;

each R_1 and R_2 are H; and/or

n is 0, 1, or 2.

10. The lipid of claim 9, wherein the head group has a structure of:



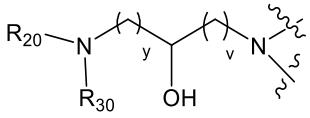
or


, wherein:

Rc is H, alkyl, or alkyl substituted with OH; and

m1 is 1, 2, or 3.

11. The lipid of claim 8, wherein the head group has a structure of (ii) formula (HA-V), having a structure of formula (HA-VI):



(HA-VI), optionally wherein each R_{20} and R_{30} are independently C_1-C_3 alkyl.

12. The lipid of claim 8, the head group has a structure of (iii) formula (HB-I), and wherein:

R_5 is OH or $(CH_2)_sOH$; and s is 1 or 2;

each R_6, R_7, and R_8 are independently H or C_1-C_3 alkyl;

each of u and t is independently 1, 2, or 3;

each v is independently 0, 1, 2, or 3;

R_{16} is H or =O;

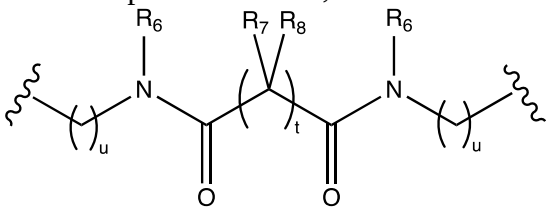
each Z is independently absent, O, or NR_{12}, wherein R_{12} is H or C_1-C_3 alkyl;

T is a divalent heterocylic;

Q is O or CH_2; and

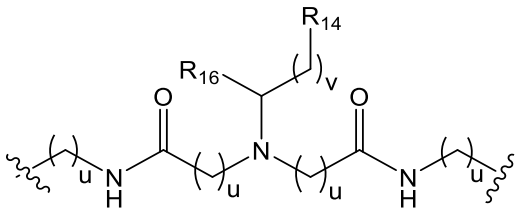
V is C_2-C_6 alkylene or C_2-C_6 alkenylene.

13. The lipid of claim 12, wherein W is

(a)  , wherein:

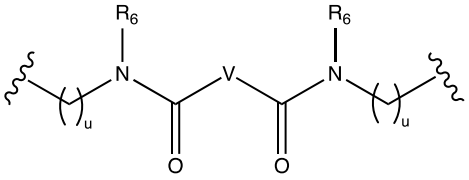
each R_6, R_7, and R_8 are independently H or methyl; and

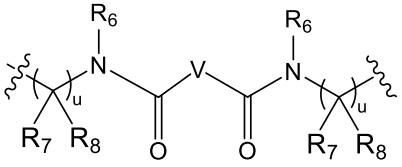
each of u and t is independently 1, 2, or 3;

(b)  , wherein:

R_{16} is H or =O;

R_{14} is a nitrogen-containing 5- or 6- membered heterocyclic $NR_{10}R_{11}$, $C(O)NR_{10}R_{11}$, $NR_{10}C(O)NR_{10}R_{11}$, or $NR_{10}C(S)NR_{10}R_{11,}$ wherein each R_{10} and R_{11} is independently H or C_1-C_3 alkyl; and

each of u and v is independently 1, 2, or 3;(c)  or

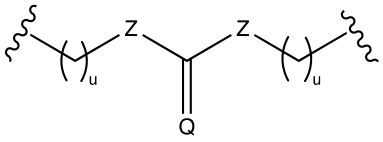
 , wherein:

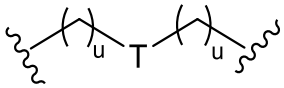
each R_6 is independently H or methyl;

each R_7 is independently H;

each R_8 is methyl;

each u is independently 1, 2, or 3; and

V is C_2-C_6 alkylene or C_2-C_6 alkenylene; or(d) is  or

 ,

wherein:

each u is independently 1, 2, or 3;

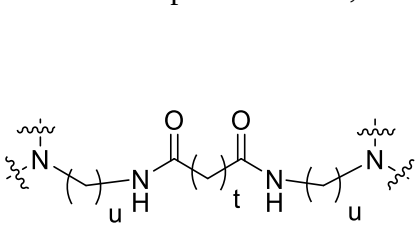
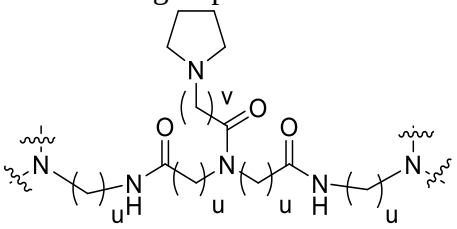
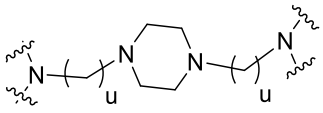
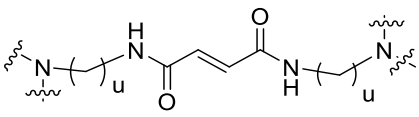
Q is O;

each Z is independently $NR_{12;}$

R_{12} is H or C_1-C_3 alkyl; and

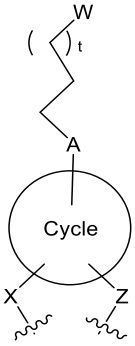
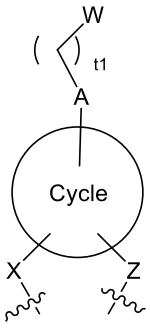
T is a divalent nitrogen-containing 5- or 6- membered heterocyclic.

14. The lipid of claim 8, wherein the head group has the structure of:

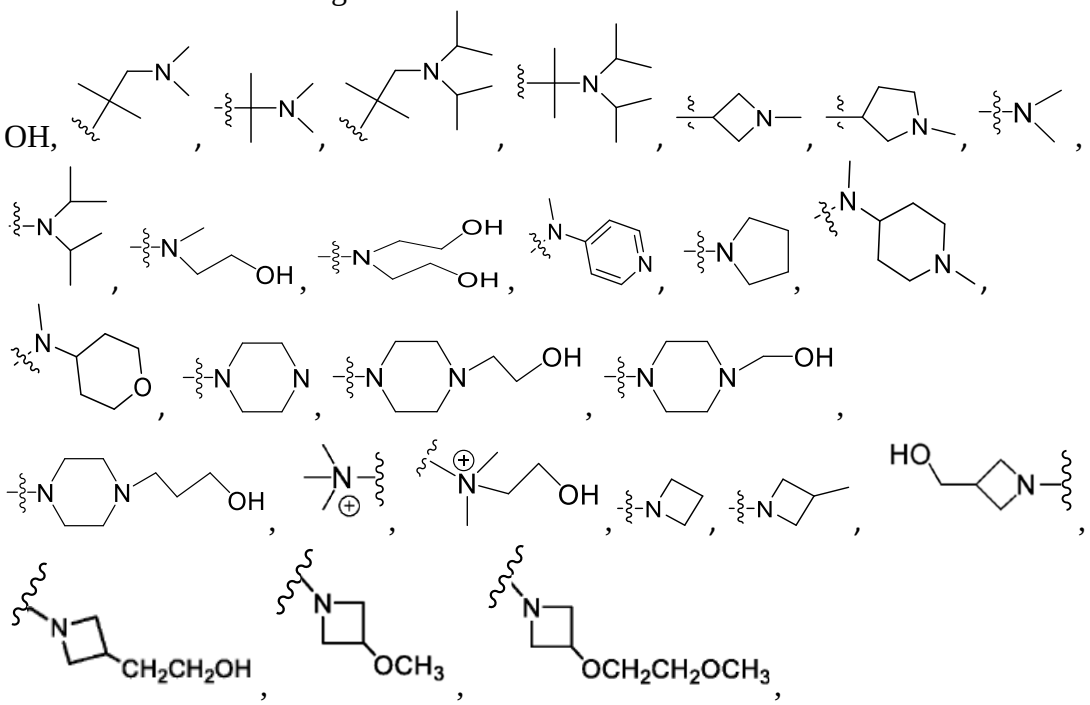





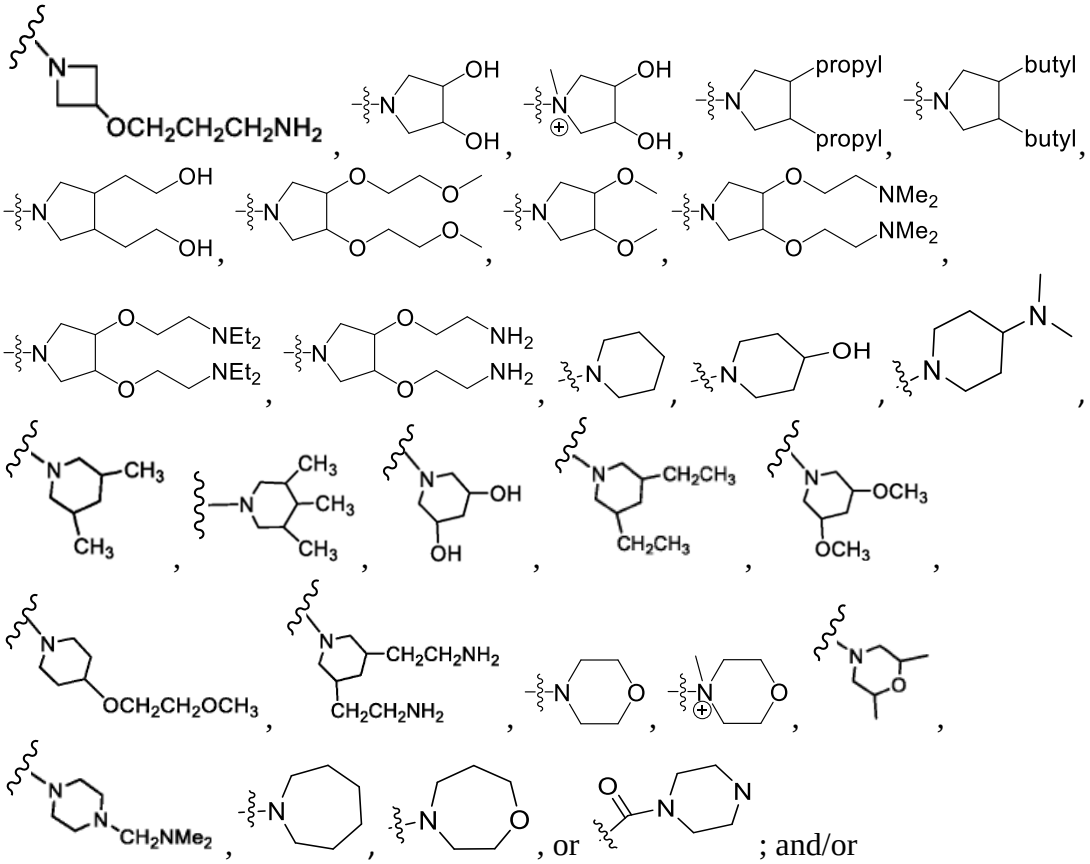
, wherein each of u and t is independently 1 or 2.

15. The lipid of claim 8, wherein the head group has a structure of (iv) formula (HC-I), having a structure of formula (HC-IA):

(HC-IA) or (HC-IB),
wherein W is one of the following:





; and/or

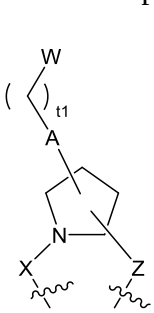
wherein:

A is absent, -O-, -N(R^7)-, -OC(O)-, or -C(O)O-;

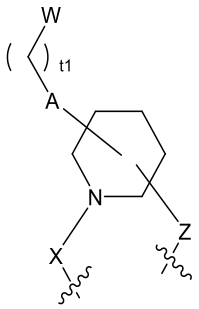
X is absent, -O-, or –C(O)-; and

Z is –O-, –C(O)O-, or –OC(O)-.

16. The lipid of claim 15, wherein the head group has a structure of formula

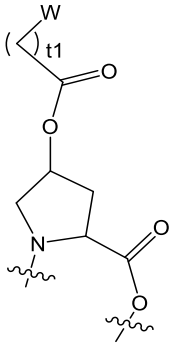


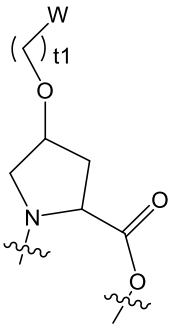
(HC-IIA) or



(HC-IIC).

17. The lipid of claim 16, wherein the head group has a structure of formula

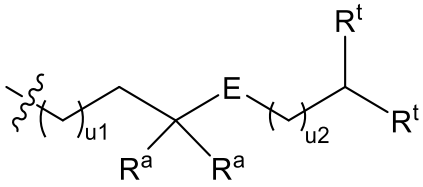


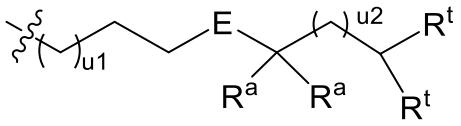
(HC-IIID) or


(HC-IIIE), wherein t1 is 0, 1, 2, or 3.

18. A lipid comprising at least one head group and at least one tail group, wherein:

at least one tail group has a structure of formula (TI) or (TI')



(TI) or


(TI'),

wherein:

E is each independently a biodegradable group;

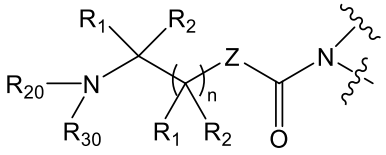
R^a is each independently C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl;

u1 and u2 are each independently 0, 1, 2, 3, 4, 5, 6, or 7;

R^t is each independently H, C_1-C_{16} branched or unbranched alkyl or C_1-C_{16} branched or unbranched alkenyl, optionally interrupted with heteroatom or substituted with OH, SH, or halogen, or cycloalkyl or substituted cycloalkyl; and

 represents the bond connecting the tail group to the head group; and

the head group has a structure of one of the following formulas:

i) 

(HA-I),

wherein:

R_{20} and R_{30} are each independently H, C_1-C_5 branched or unbranched alkyl, or C_2-C_5 branched or unbranched alkenyl, optionally interrupted with one or more heteroatoms or substituted with OH, SH, halogen, or cycloalkyl groups; or

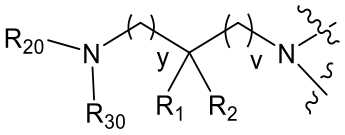
R_{20} and R_{30}, together with the adjacent N atom, form a 3 to 7 membered heterocylic or heteroaromatic ring containing one or more heteroatoms, optionally substituted with one or more OH, SH, halogen, alkyl, or cycloalkyl groups;

each of R_1 and R_2 is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, OH, halogen, SH, or $NR_{10}R_{11}$; or R_1 and R_2 together form a cyclic ring;

each of R_{10} and R_{11} is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl; or R_{10} and R_{11} together form a heterocyclic ring;

n is 0, 1, 2, 3 or 4; and

Z is absent, O, S, or NR_{12}, wherein R_{12} is H or C_1-C_7 branched or unbranched alkyl; provided that when Z is not absent, the adjacent R_1 and R_2 cannot be OH, $NR_{10}R_{11}$, SH;

ii)  (HA-V).

wherein:

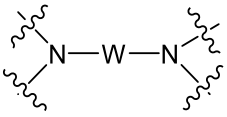
R_1 is H, C_1-C_3 alkyl, OH, halogen, SH, or $NR_{10}R_{11}$;

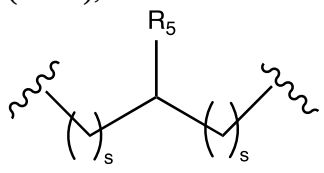
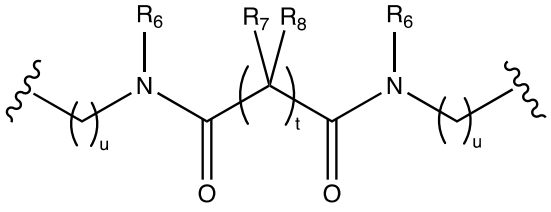
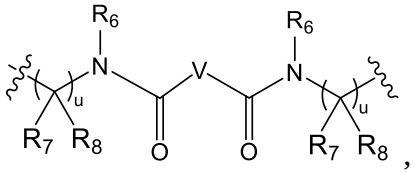
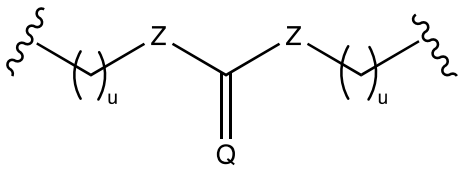
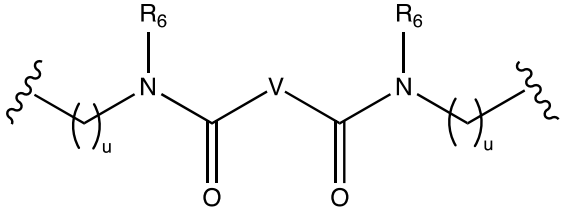
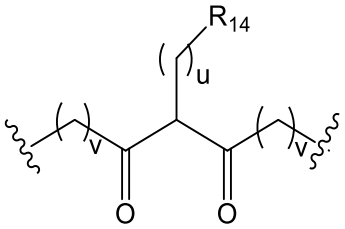
R_2 is OH, halogen, SH, or $NR_{10}R_{11}$; or R_1 and R_2 can be taken together to form a cyclic ring;

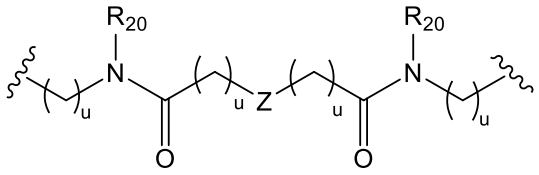
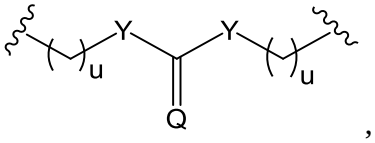
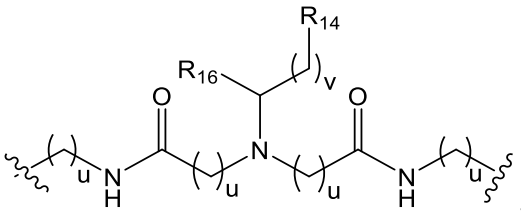
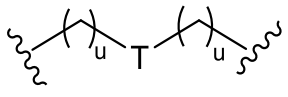
R_{10} and R_{11} are each independently H or C_1-C_3 alkyl; or R_{10} and R_{11} can be taken together to form a heterocyclic ring;

R_{20} and R_{30} are each independently H, C_1-C_5 branched or unbranched alkyl, C_2-C_5 branched or unbranched alkenyl; or R_{20} and R_{30} can be taken together to form a cyclic ring; and

each of v and y is independently 1, 2, 3, or 4;

iii)  (HB-I),

wherein W is , , , , , , .

wherein

R_5 is OH, SH, $(CH_2)_sOH$, or $NR_{10}R_{11}$;

each R_6 is independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, or cycloalkyl;

each R_7 and R_8 are independently H, C_1-C_3 branched or unbranched alkyl, C_2-C_3 branched or unbranched alkenyl, halogen, $(CH_2)_vOH$, $(CH_2)_vSH$, $(CH_2)_sN(CH_3)_2$, or $NR_{10}R_{11}$, wherein each R_{10} and R_{11} is independently H or C_1-C_3 alkyl, or R_{10} and R_{11} are taken together to form a heterocyclic ring; or R_7 and R_8 are taken together to form a ring;

each R_{20} is independently H, or C_1-C_3 branched or unbranched alkyl;

R_{14} is a heterocyclic, $NR_{10}R_{11}$, $C(O)NR_{10}R_{11}$, $NR_{10}C(O)NR_{10}R_{11}$, or $NR_{10}C(S)NR_{10}R_{11}$, wherein each R_{10} and R_{11} is independently H, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, C_3-C_7 cycloalkenyl, optionally substituted with one or more NH and/or oxo groups, or R_{10} and R_{11} are taken together to form a heterocyclic ring;

R_{16} is H, =O, =S, or CN;

each of s, u, and t is independently 1, 2, 3, 4, or 5;

each v is independently 0, 1, 2, 3, 4, or 5;

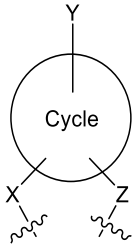
each Y is a divalent heterocyclic;

each Z is independently absent, O, S, or NR_{12}, wherein R_{12} is H, C_1-C_7 branched or unbranched alkyl, or C_2-C_7 branched or unbranched alkenyl;

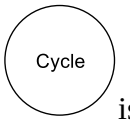
Q is O, S, CH_2, or NR_{13}, wherein each R_{13} is H, C_1-C_5 alkyl;

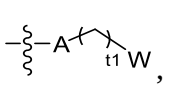
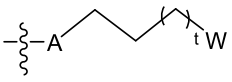
V is branched or unbrachned C_2-C_{10} alkylene, C_2-C_{10} alkenylene, C_2-C_{10} alkynylene, or C_2-C_{10} heteroalkylene, optionally substituted with one or more OH, SH, and/or halogen groups; and

T is –NHC(O)O-, –OC(O)NH-, or a divalent heterocyclic; and

iv)  (HC-I),

wherein:

 is cyclic or heterocyclic moiety;

Y is alkyl, hydroxy, hydroxyalkyl, , or ;

A is absent, -O-, -N(R^7)-, -O-alkylene-, -alkylene-O-, -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -C(O)N(R^7)-, -N(R^7)C(O)N(R^7)-, -S-, or -S-S-;

each of X and Z is independently absent, -O-, -C(O)-, -N(R^7)-, -O-alkylene-, -alkylene-O-, -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -C(O)N(R^7)-, or -S-;

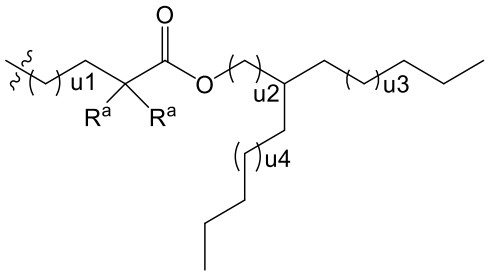
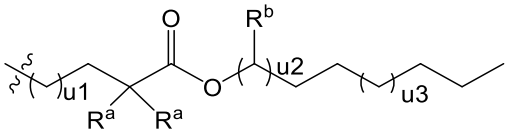
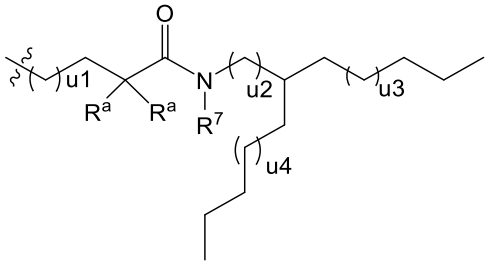
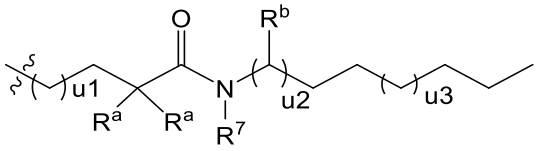
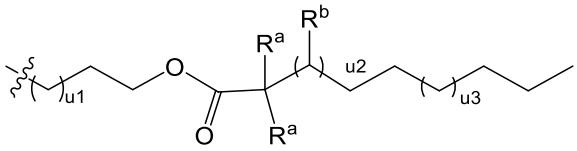
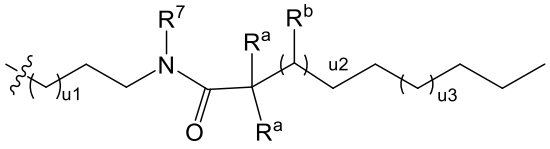
each R^7 is independently H, alkyl, alkenyl, cycloalkyl, hydroxy, alkoxy, hydroxyalkyl, alkylamino, alkylaminoalkyl, or aminoalkyl;

t1 is an integer from 0 to 10; and

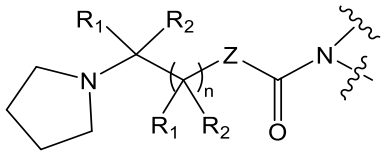
W is hydroxyl, substituted or unsubstituted hydroxyalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminocarbonyl, or substituted or unsubstituted heterocyclyl or heteroaryl; and

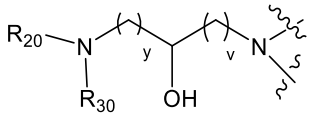
wherein the lipid has a pKa from about 4 to about 8.

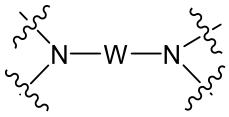
19. The lipid of claim 18, wherein at least one tail group has the structure of at least one of the following formulas:

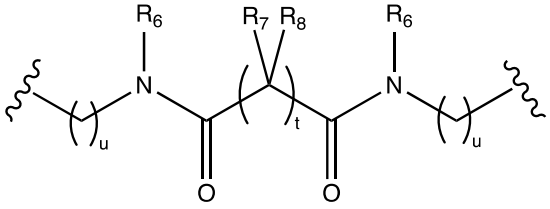

(TII),

(TIII),

(TIV),

(TV),

(TII'), and/or

(TIII'), wherein each R^a is methyl; u1 is 3-5, u2 is 0-3; and u3 and u4 are each independently 1-7; and

wherein the head group has the structure of one of the following formulas

i) 
(HA-III);

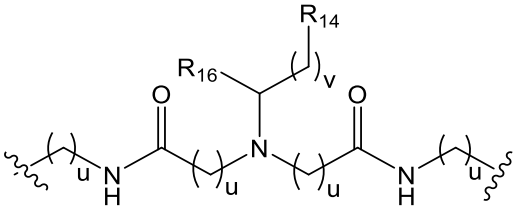
ii)  (HA-VI), wherein each R_{20} and R_{30} are independently C_1-C_3 alkyl.

iii)  (HB-I), wherein:

W is , wherein:

each R_6, R_7, and R_8 are independently H or methyl; and

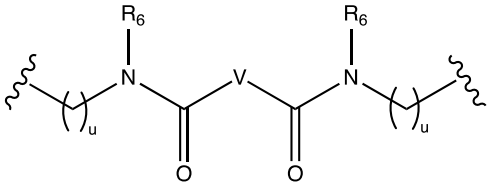
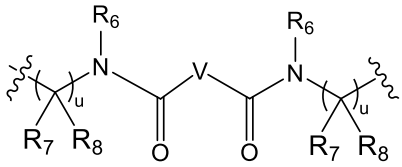
each of u and t is independently 1, 2, or 3; or

W is , wherein:

R_{16} is H or =O;

R_{14} is a nitrogen-containing 5- or 6- membered heterocyclic, $NR_{10}R_{11}$, $C(O)NR_{10}R_{11}$, $NR_{10}C(O)NR_{10}R_{11}$, or $NR_{10}C(S)NR_{10}R_{11}$, wherein each R_{10} and R_{11} is independently H or C_1-C_3 alkyl; and

each of u and v is independently 1, 2, or 3; or

W is  or , wherein:

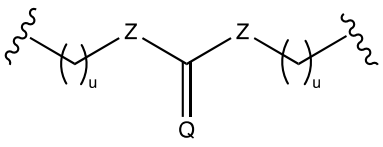
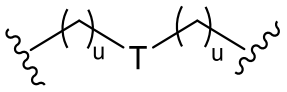
each R_6 is independently H or methyl;

each R_7 is independently H;

each R_8 is methyl;

each u is independently 1, 2, or 3; and

V is C_2-C_6 alkylene or C_2-C_6 alkenylene; or

W is  or , wherein:

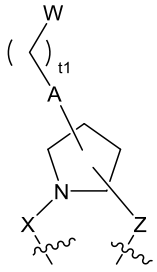
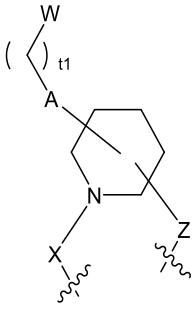
each u is independently 1, 2, or 3;

Q is O;

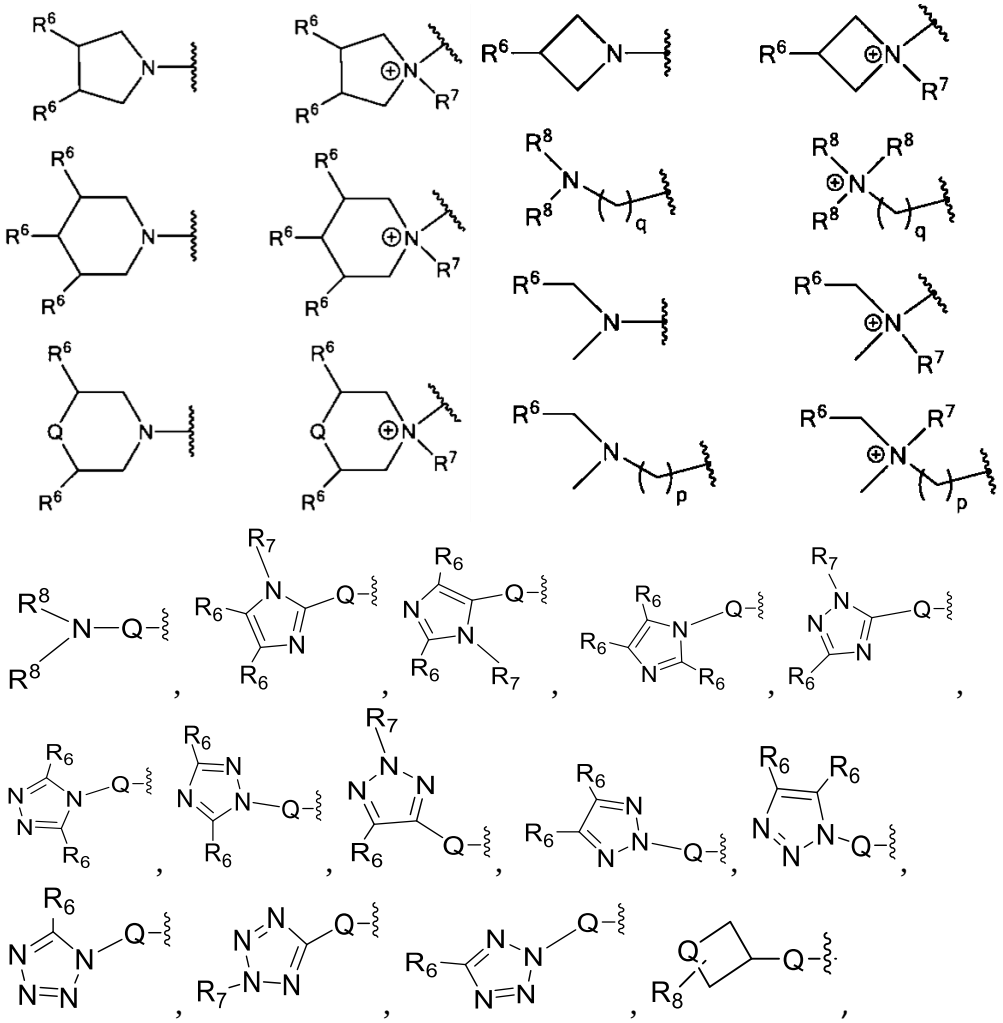
each Z is independently $NR_{12;}$ and

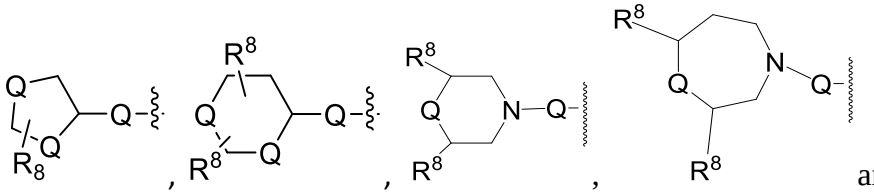
T is a divalent nitrogen-containing 5- or 6- membered heterocyclic;

and

iv)  (HC-IIA) or  (HC-IIC), wherein:

W is hydroxyl, substituted or unsubstituted hydroxyalkyl, one of the following moieties:




, wherein

each Q is independently absent, -O-, -C(O)-, -C(S)-, -C(O)O-, -$(CH_2)_q$-$C(R^7)_2$-, -C(O)N(R^7)-, -C(S)N(R^7)-, or -N(R^7);

R^6 is independently H, alkyl, hydroxyl, hydroxyalkyl, alkoxy, -O-alkylene-O-alkyl, -O-alkylene-N(R^7)$_2$, amino, alkylamino, aminoalkyl, thiol, thiolalkyl, or N^+(R^7)$_3$–alkylene-Q-;

each R^8 is independently H, alkyl, hydroxyalkyl, amino, aminoalkyl, alkylamino, thiol, thiolalkyl, heterocyclyl, heteroaryl; or two R^8 together with the nitrogen atom form a ring, optionally substituted with one or more alkyl, hydroxy, hydroxyalkyl, alkoxy, alkylaminoalkyl, alkylamino, or aminoalkyl;

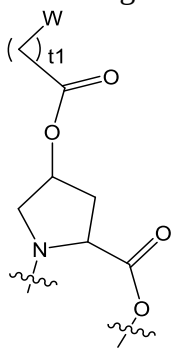
q is 0, 1, 2, 3, 4, or 5; and

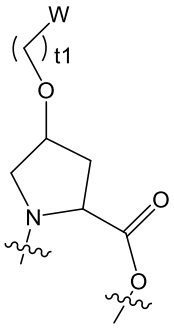
p is 0, 1, 2, 3, 4, or 5.

20. The lipid of claim 19, wherein:

at least one tail group has the structure of formula (TII), wherein each R^a is methyl, u1 is 3-5, u2 is 0-3, u3 is 1-4, and u4 is 1-4; optionally wherein the lipid has at least two, three, or four tails of formula (TII), wherein the two, three, or four tails of formula (TII) are the same or different; and

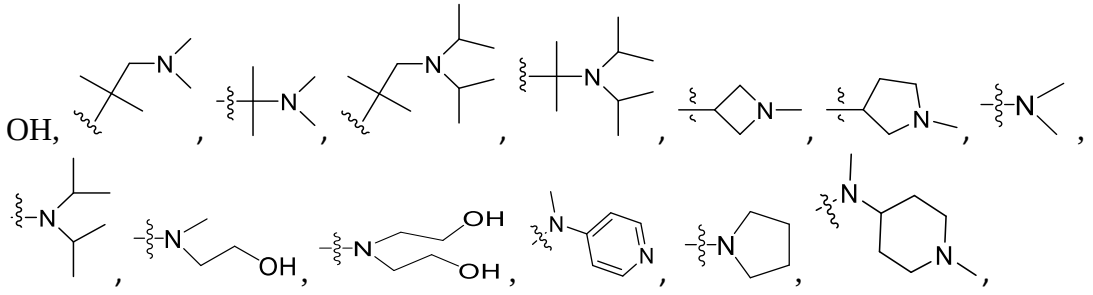
the head group has a structure of formula

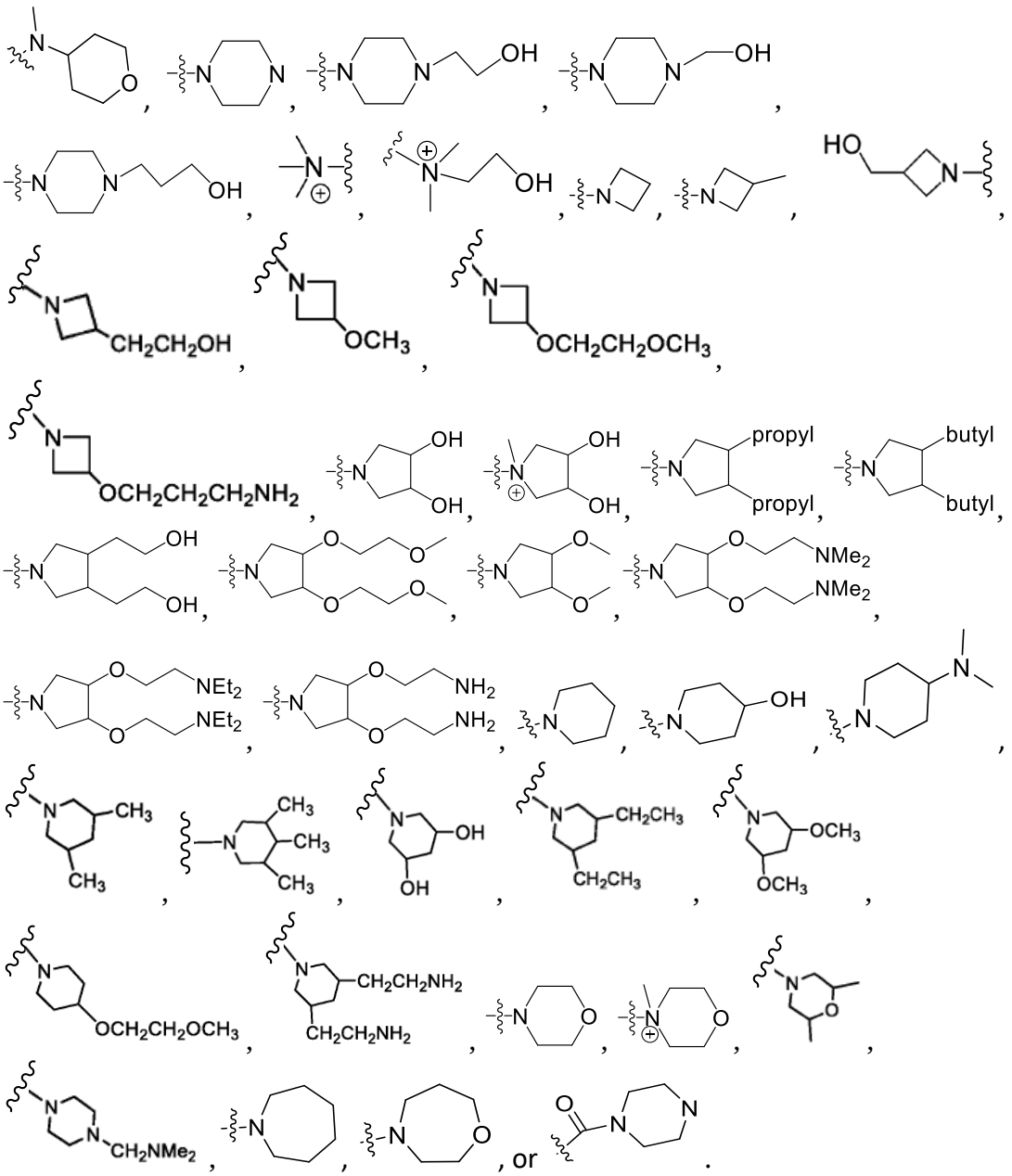

(HC-IIID) or


(HC-IIIE), wherein:

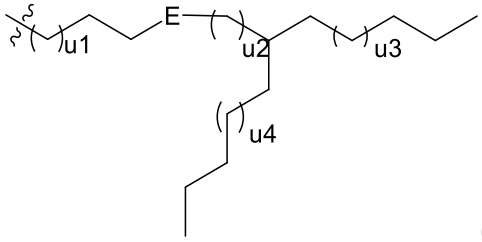
t1 is 0, 1, 2, or 3; and

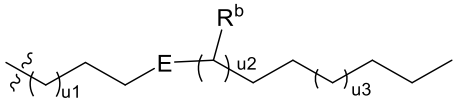
W is one of the following:





21. The lipid of claim 20, further comprising one or more tail groups of formula



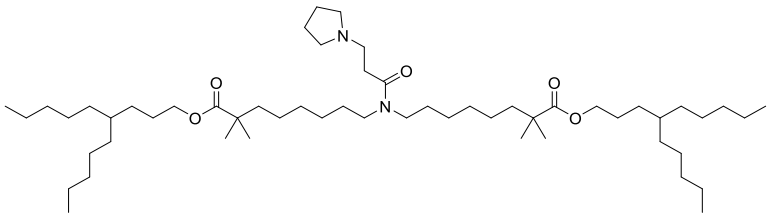
(TNG-II) or  (TNG-III), wherein

E is each independently -OC(O)-, -C(O)O-, -N(R^7)C(O)-, -S-S-, or -C(O)N(R^7)-;
u1 is each independently 0, 1, 2, 3, 4, 5, 6, or 7;
R^7 is independently H, alkyl, alkenyl, cycloalkyl, hydroxyalkyl, or aminoalkyl;
u3 and u4 are each independently 0, 1, 2, 3, 4, 5, 6, or 7; and

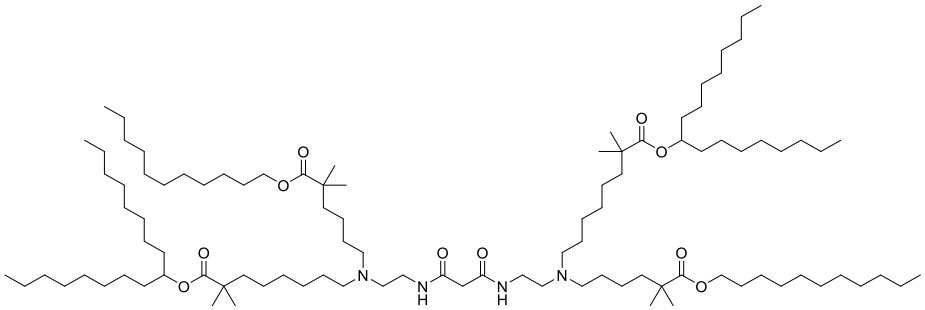
R^b is in each occasion independently H or C_1-C_4 alkyl.

22. The lipid of claim 1 or claim 18, having one of the following structures:

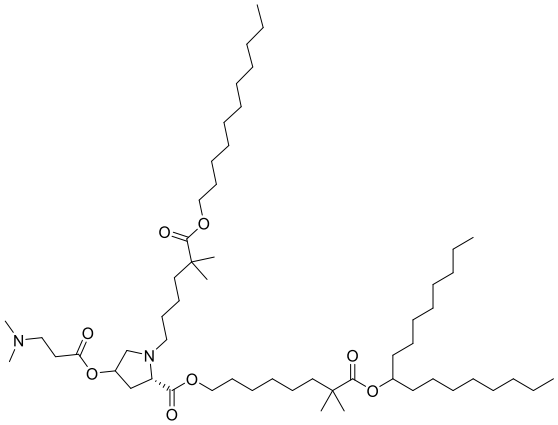
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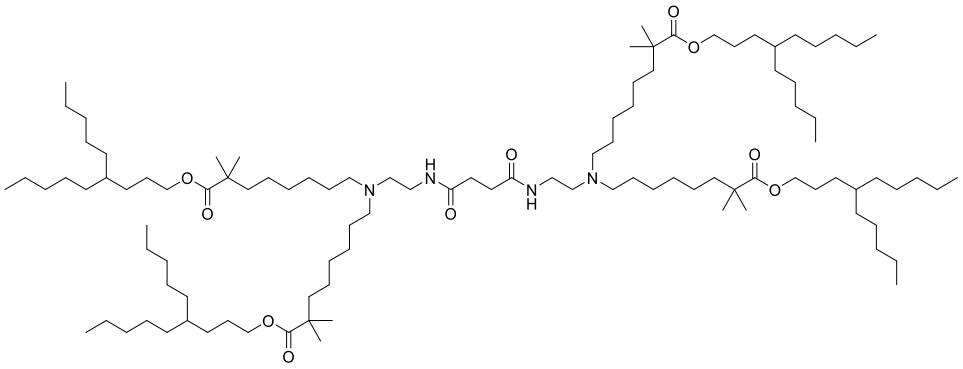
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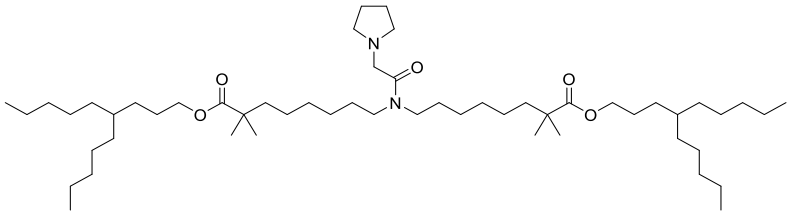
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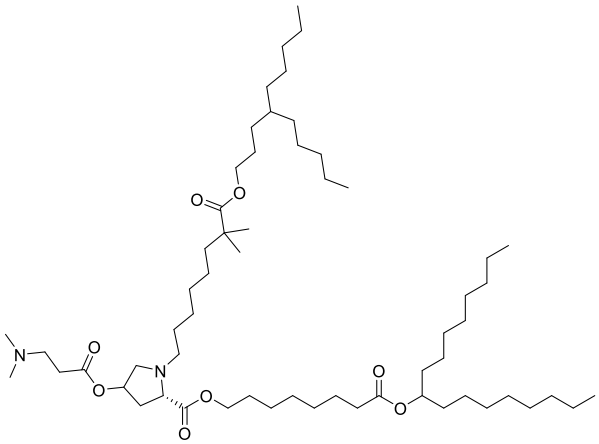
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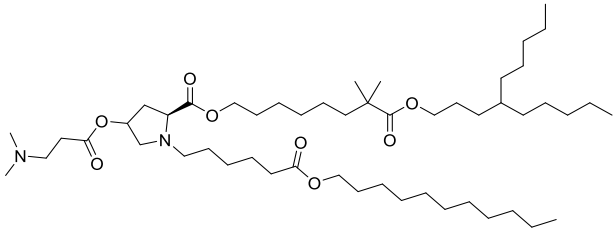
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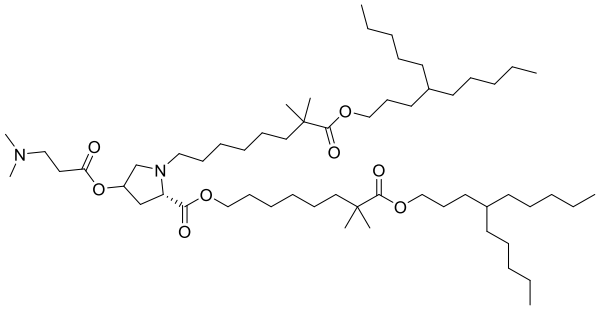
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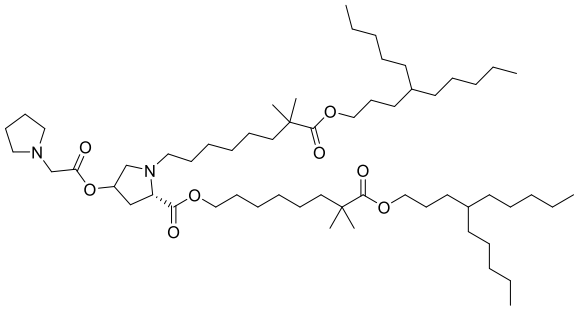
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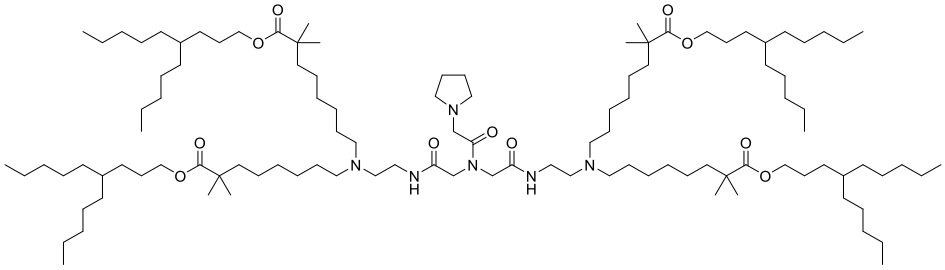
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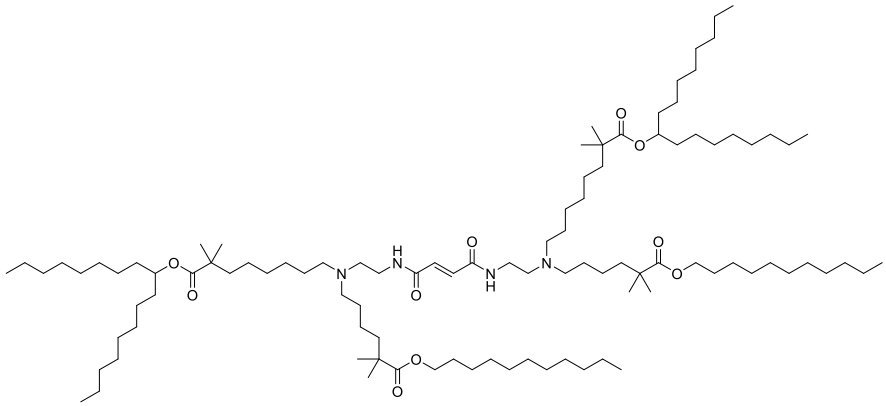
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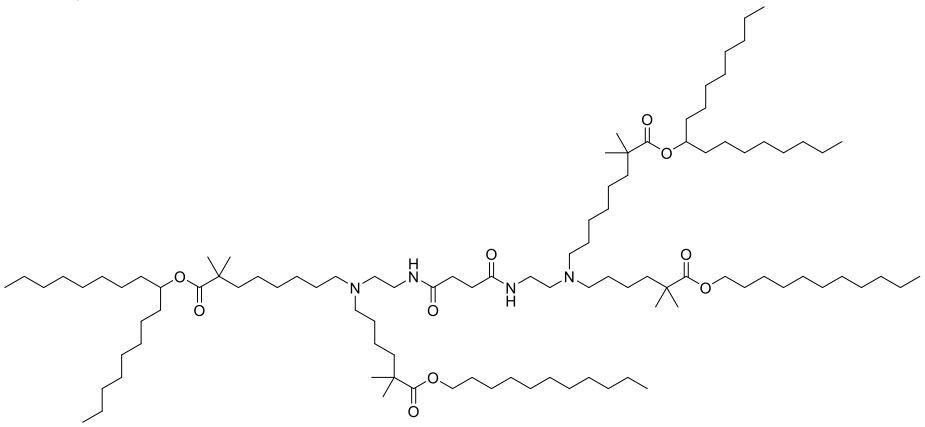
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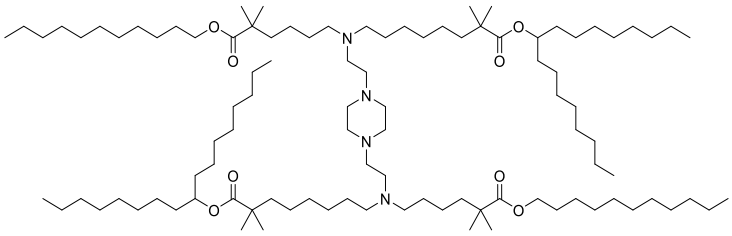
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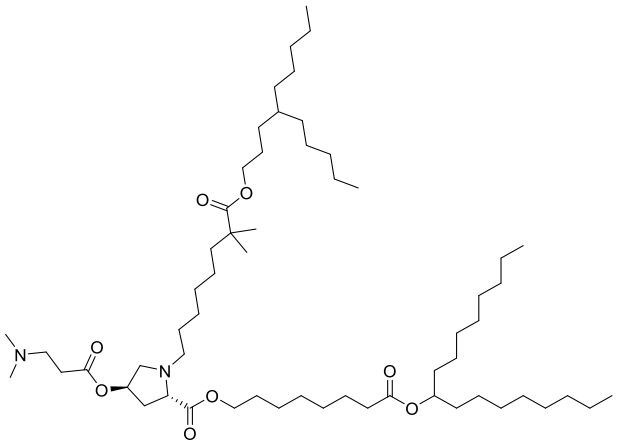
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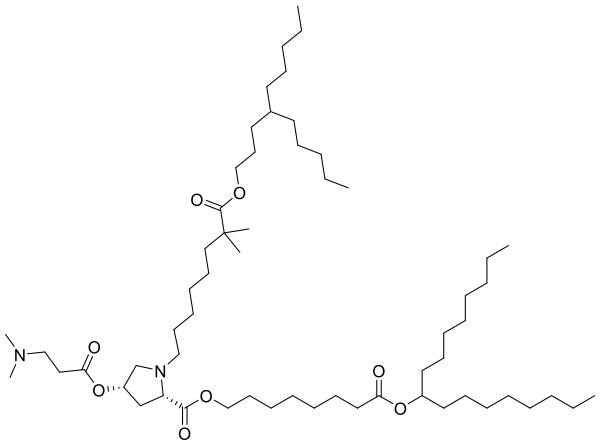
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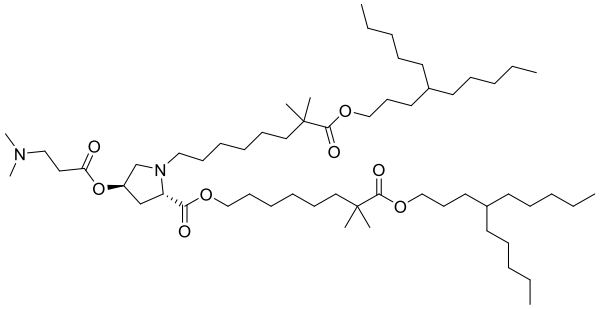
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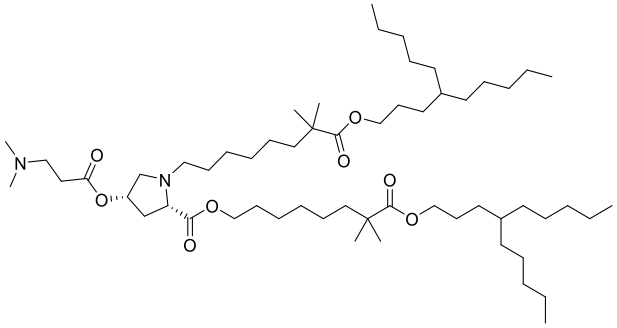
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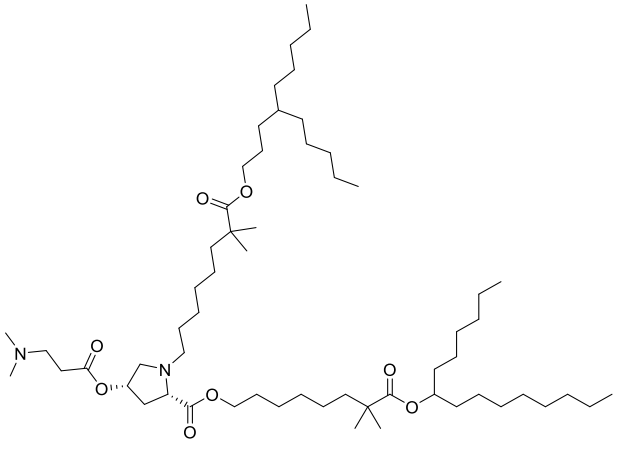
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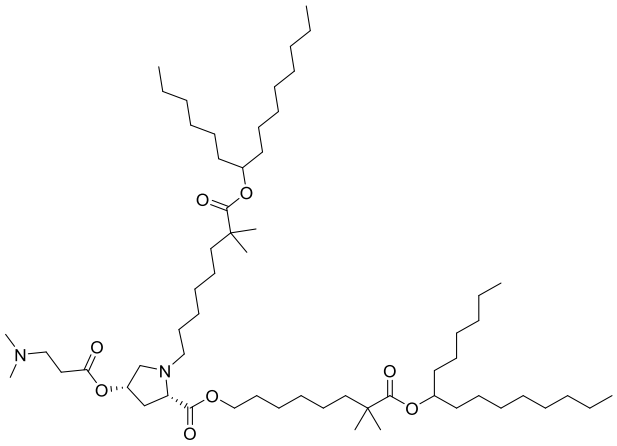
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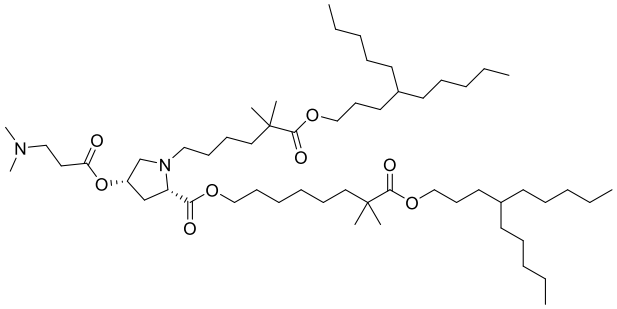
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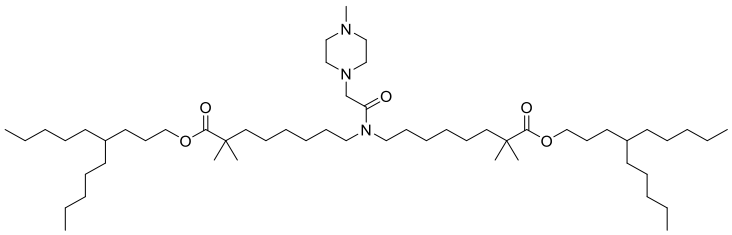
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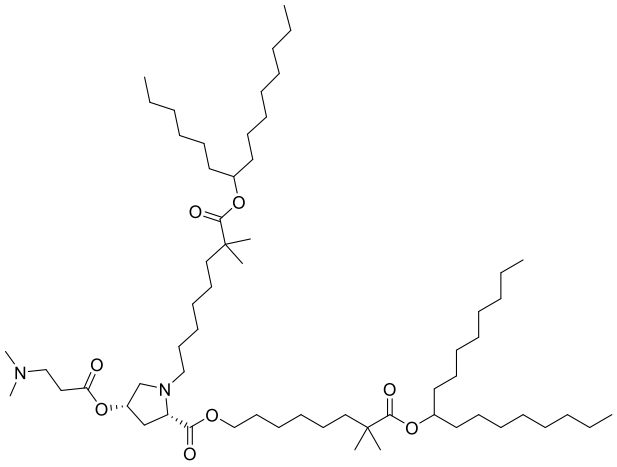
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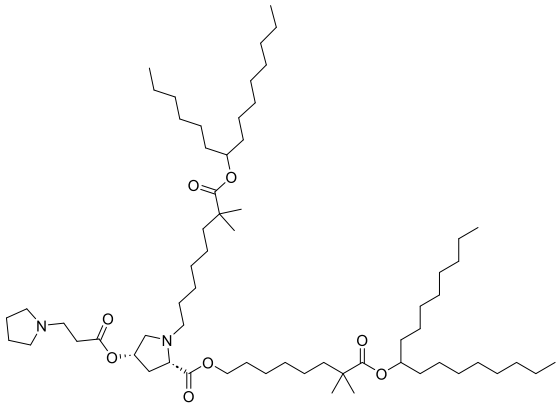
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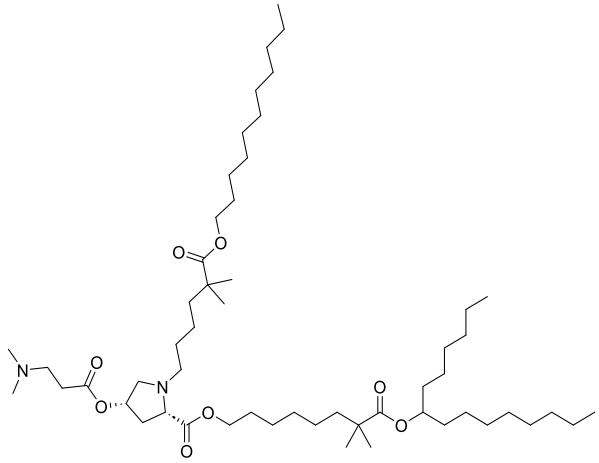
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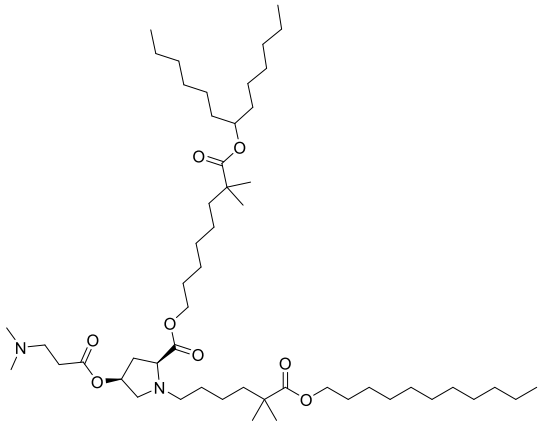
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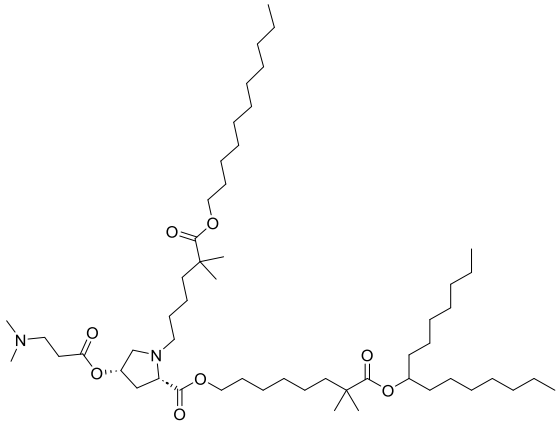
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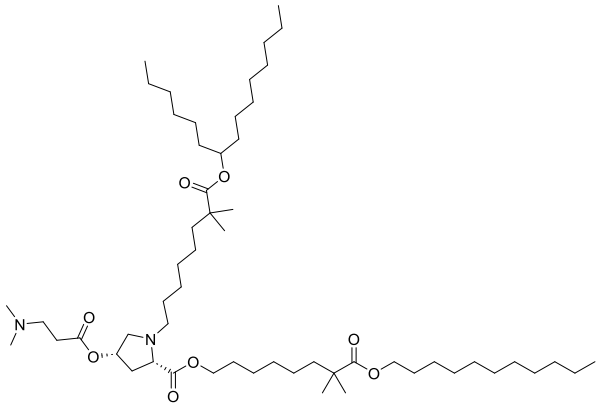
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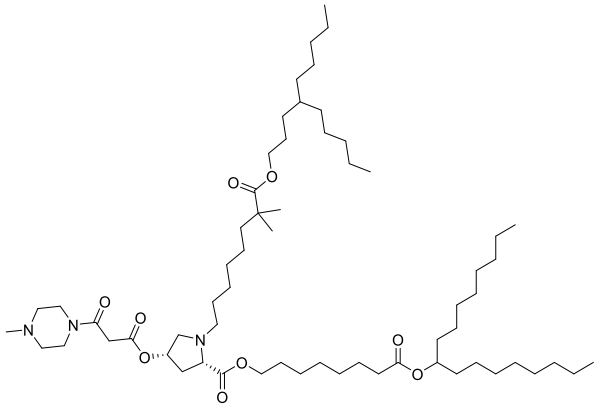
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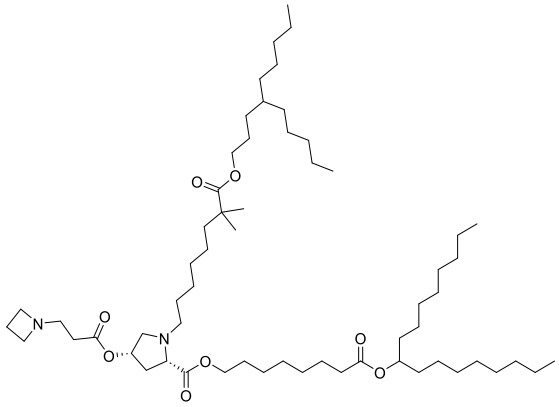
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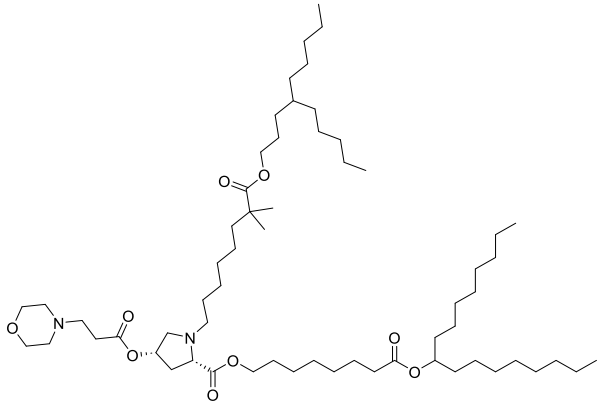
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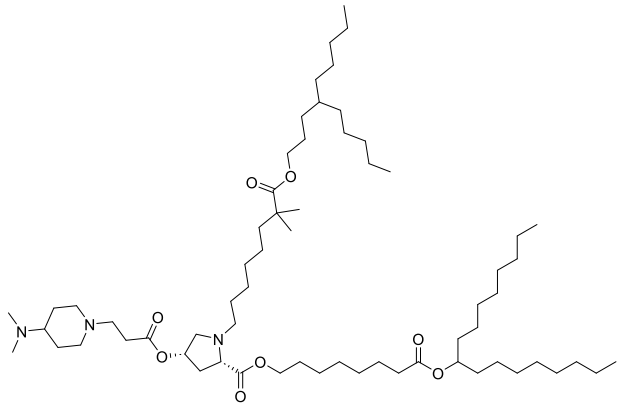
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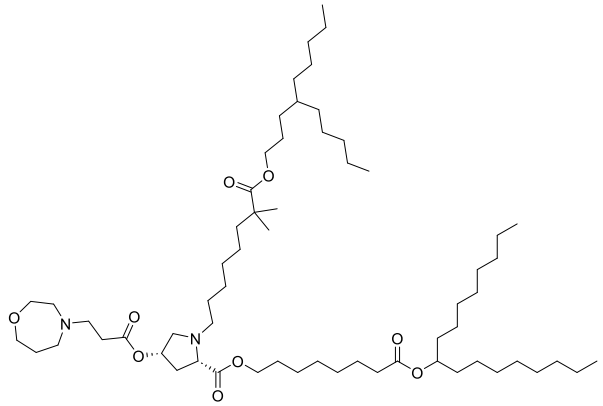
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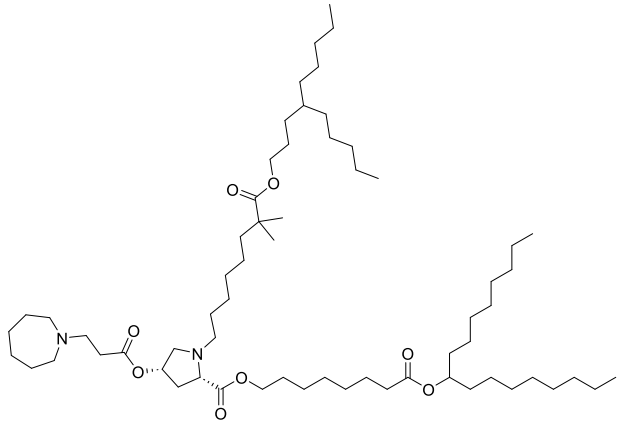
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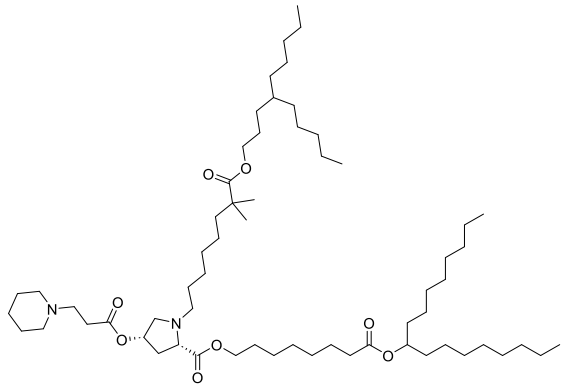
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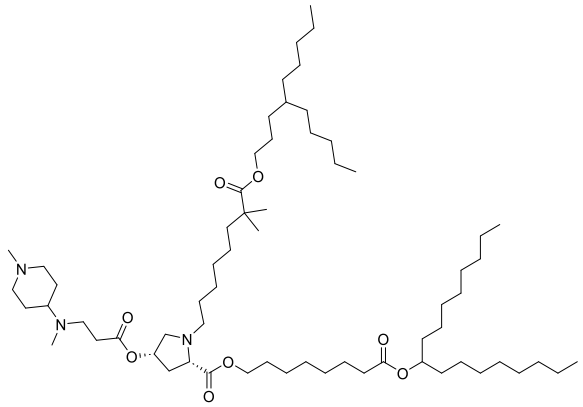
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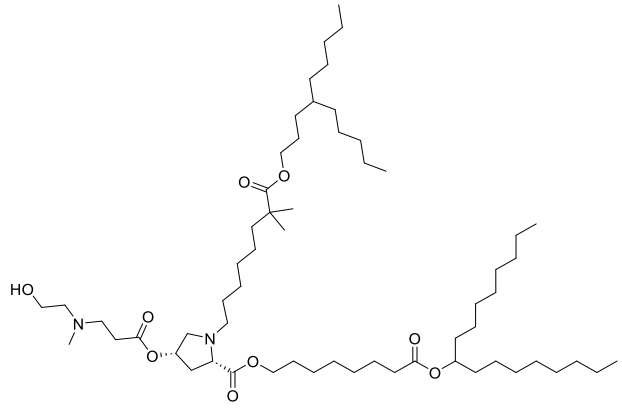
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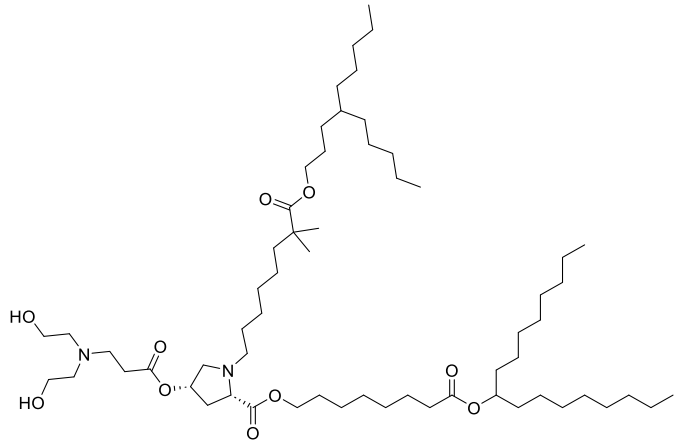
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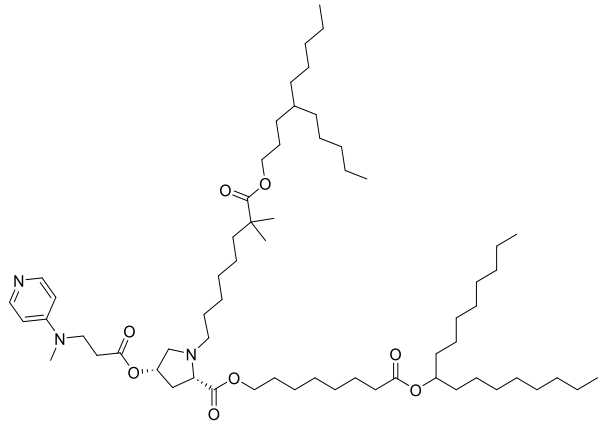
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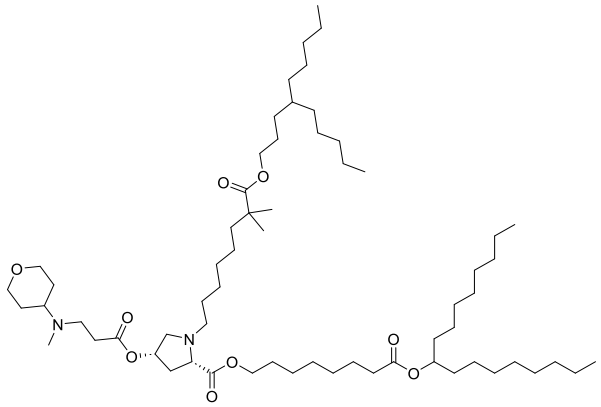
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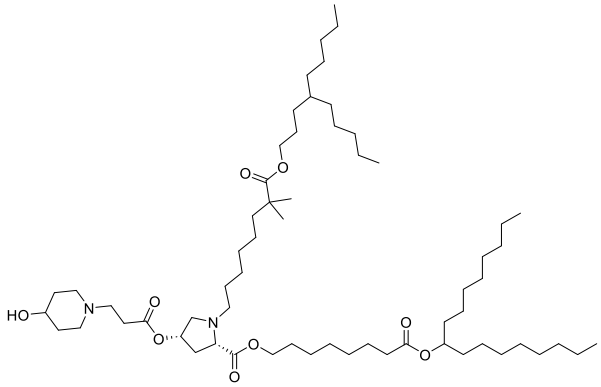
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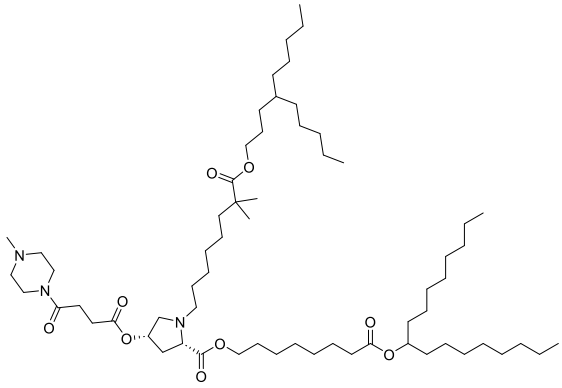
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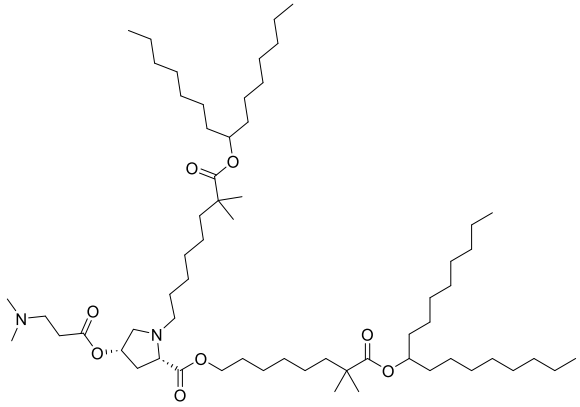
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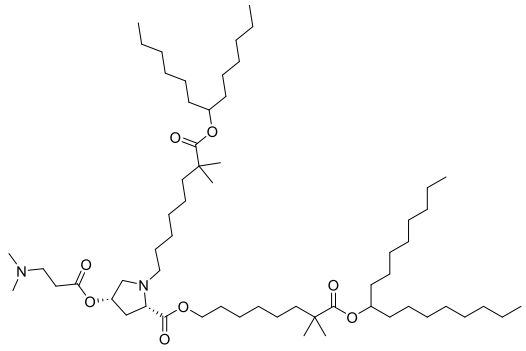
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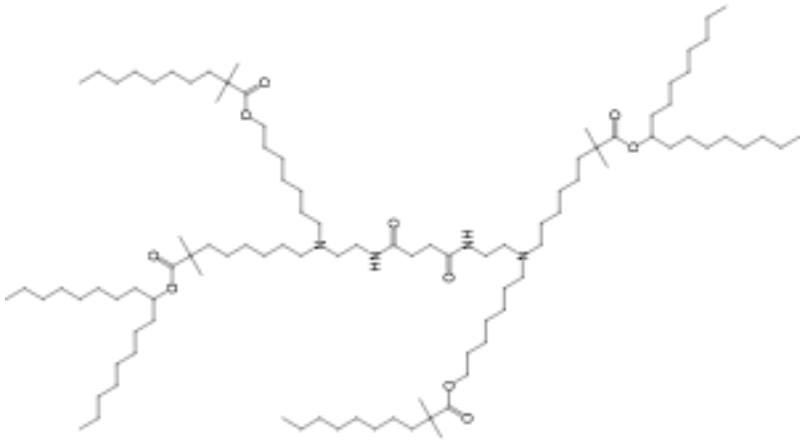
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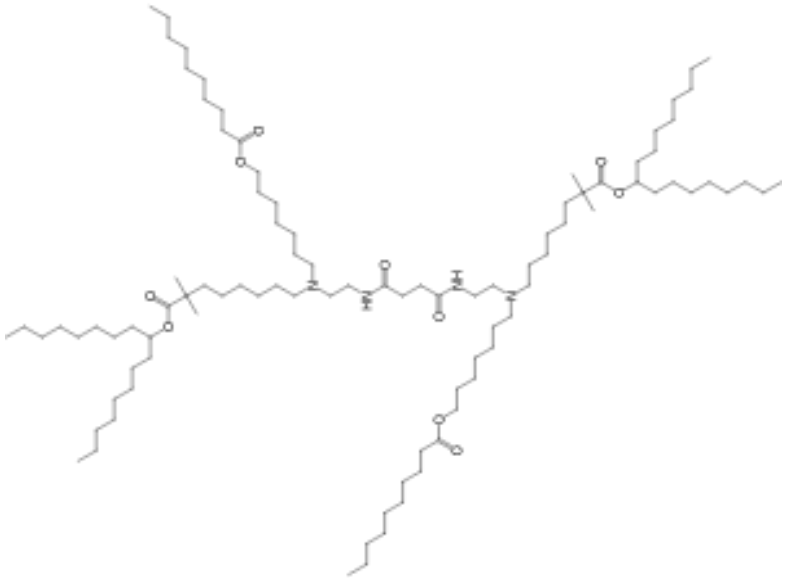
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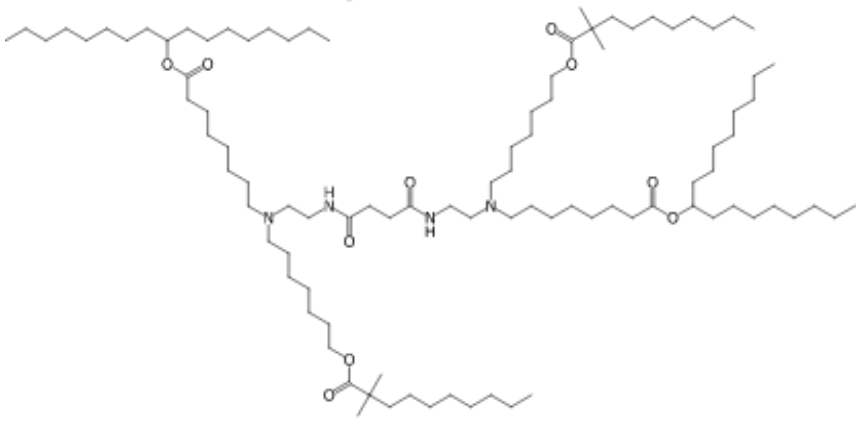
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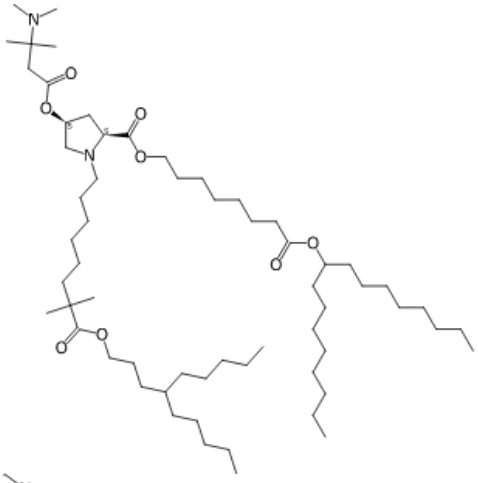


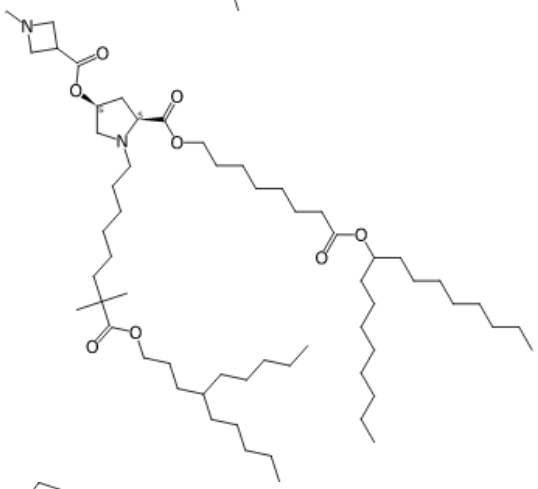
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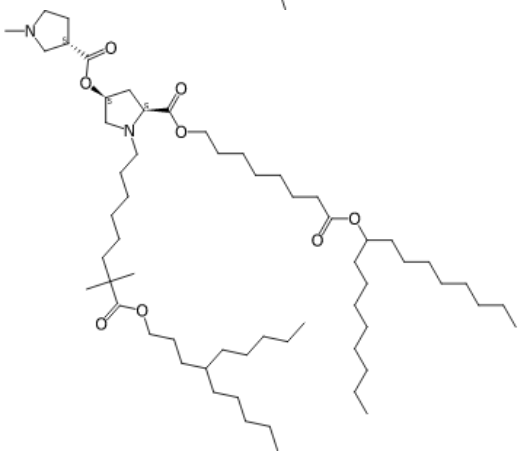


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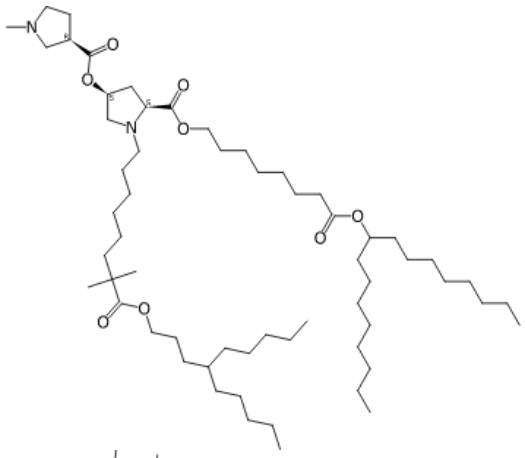


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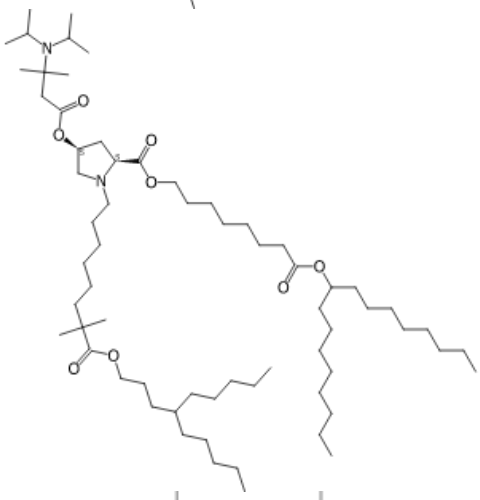
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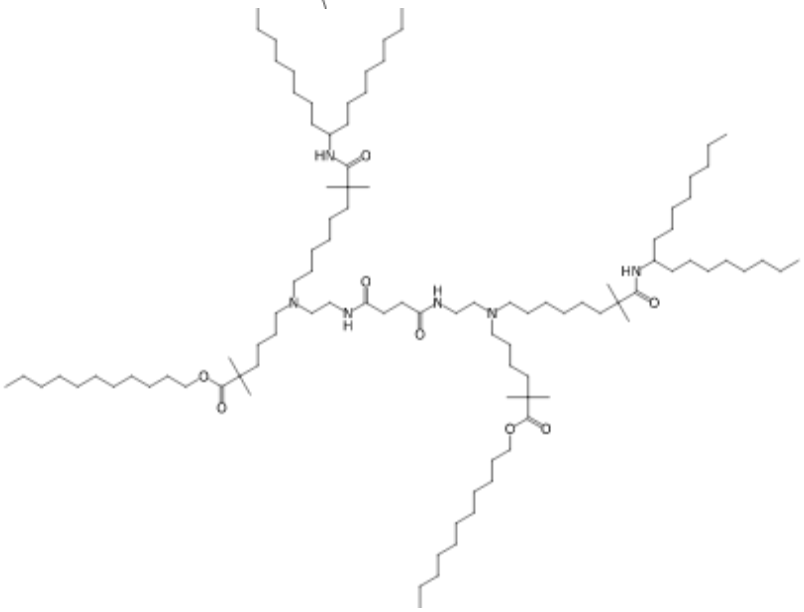
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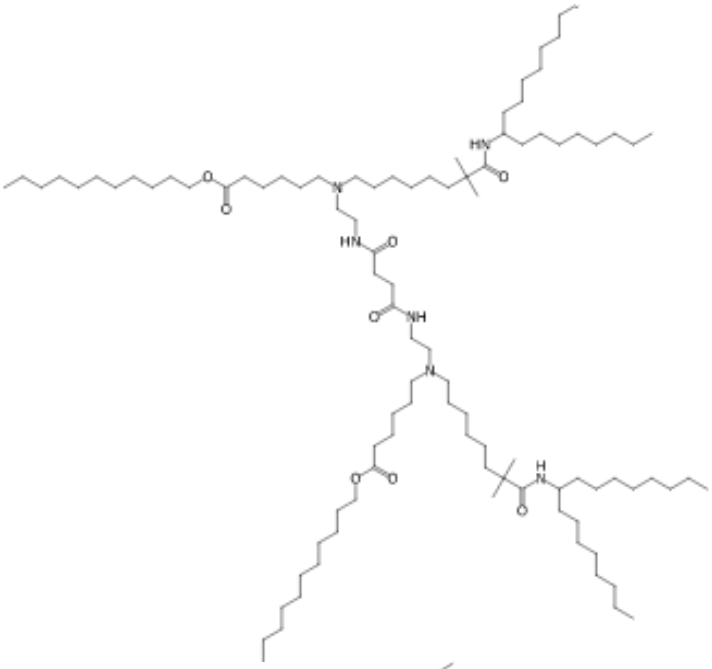
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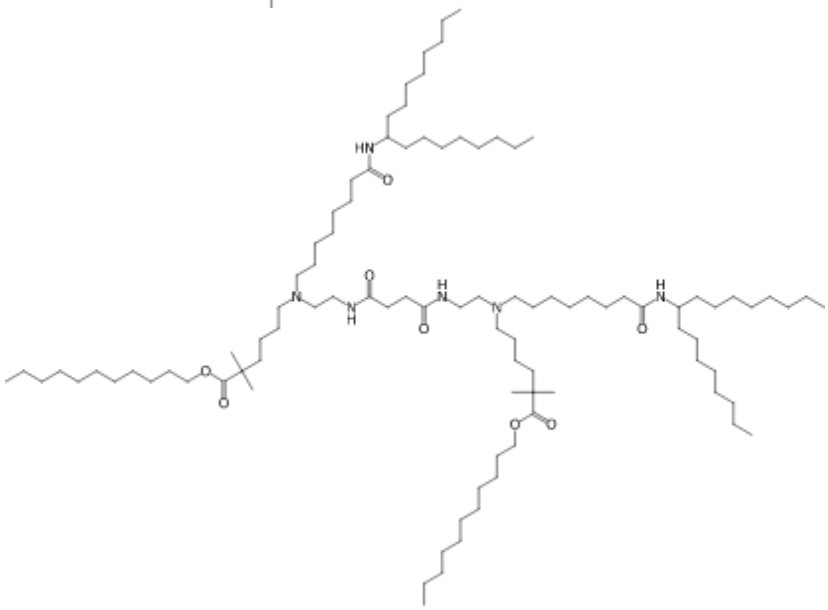
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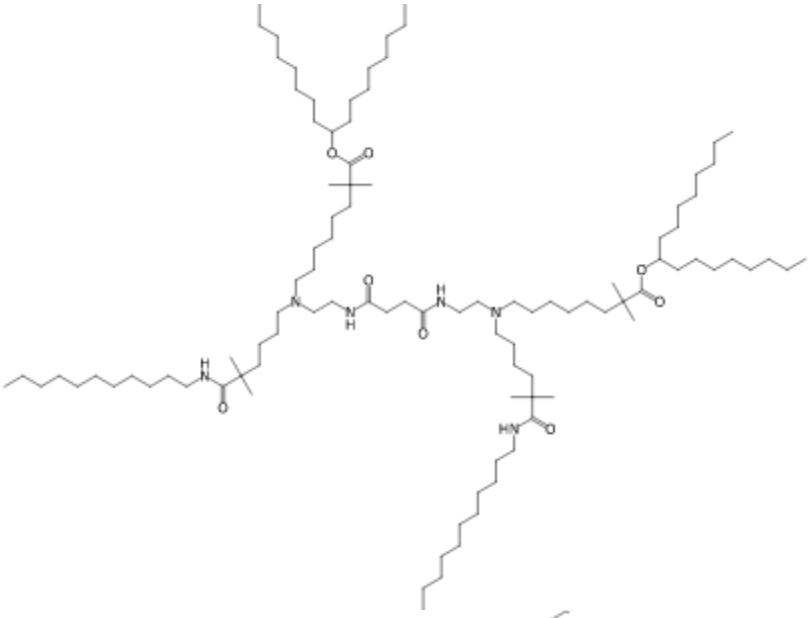
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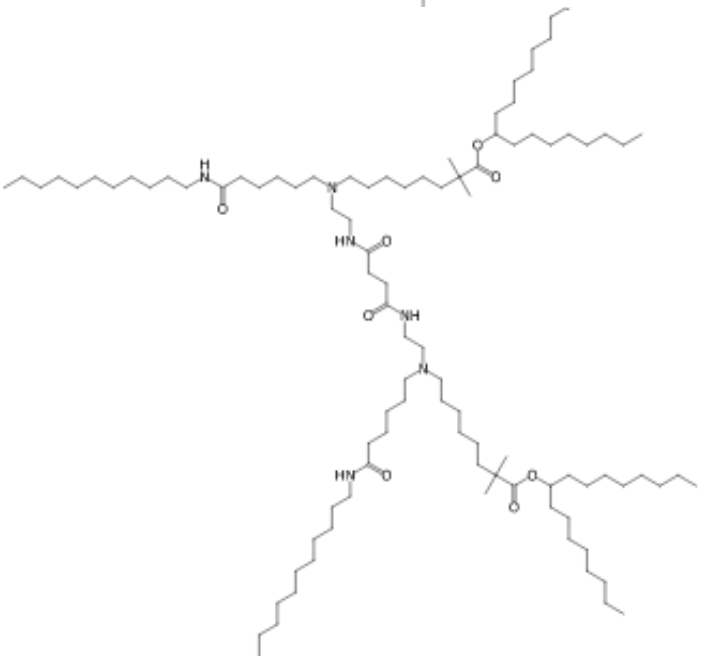
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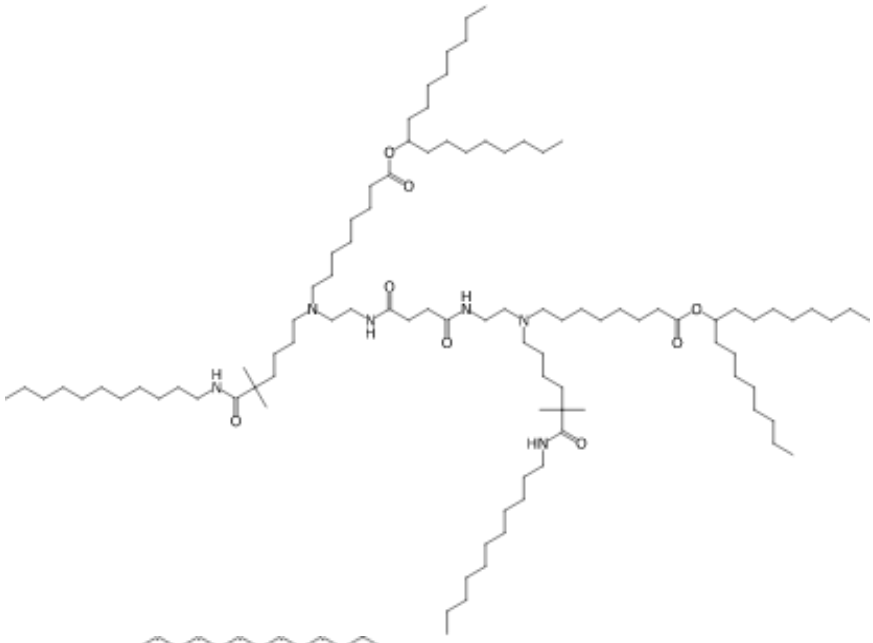
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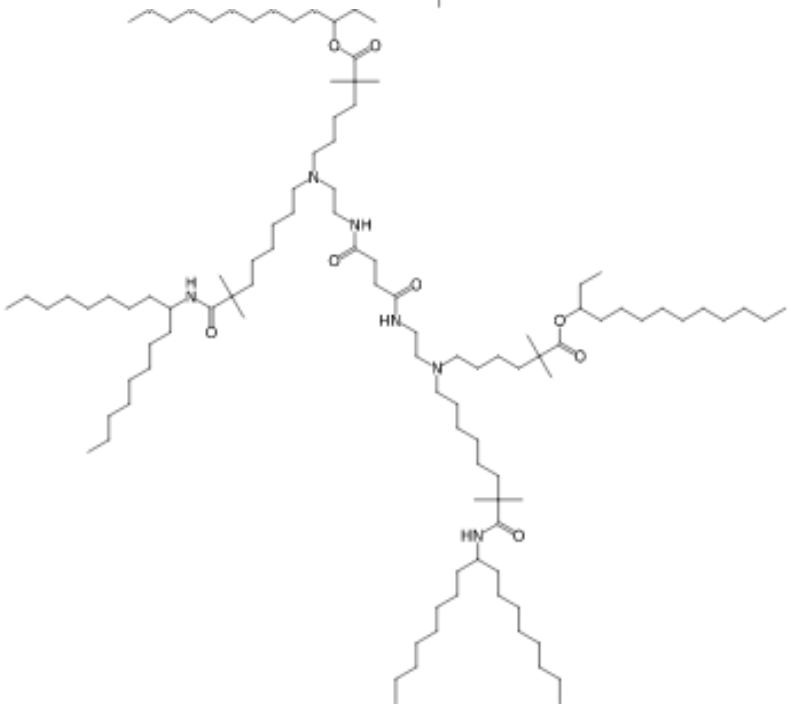
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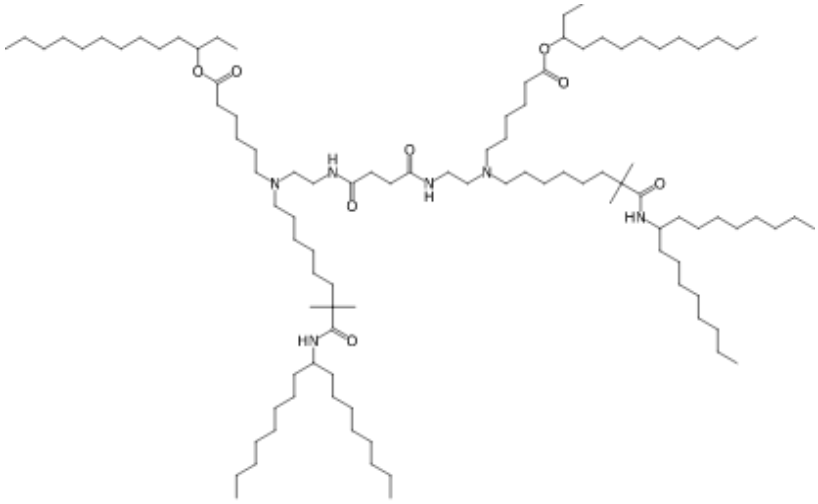
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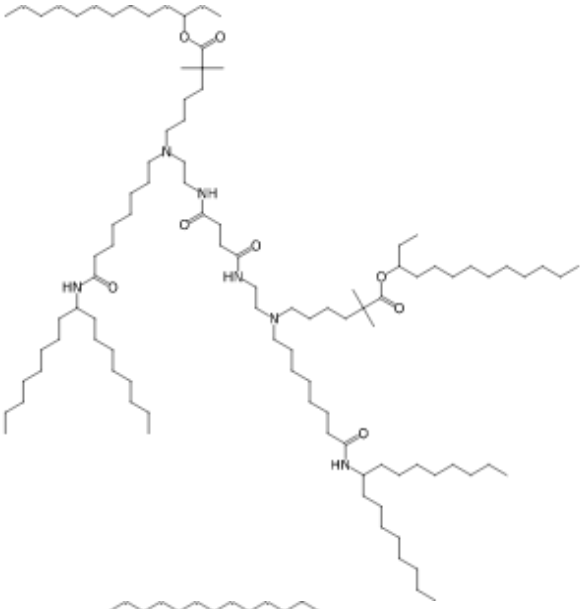
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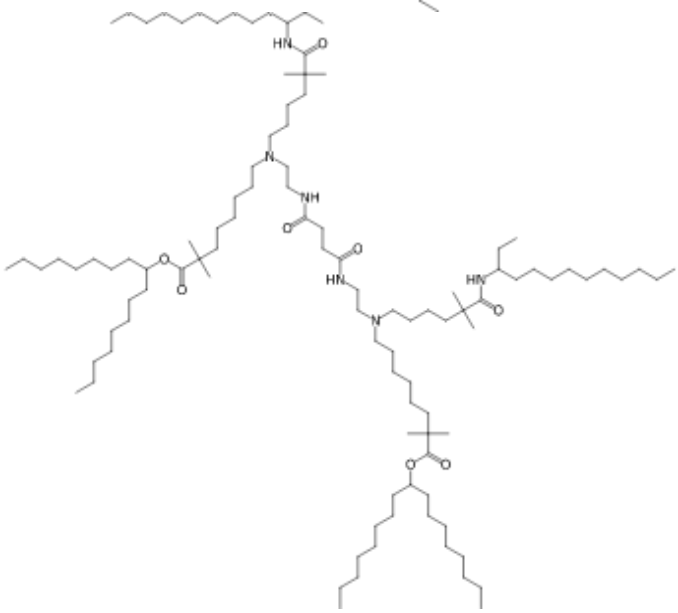
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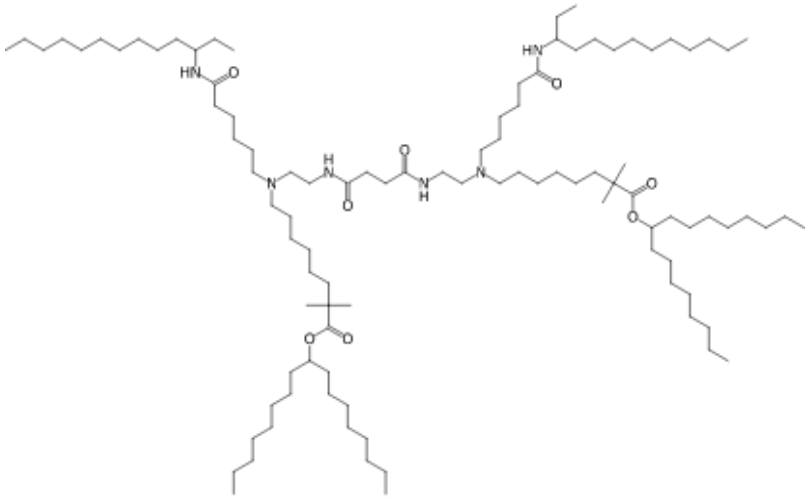
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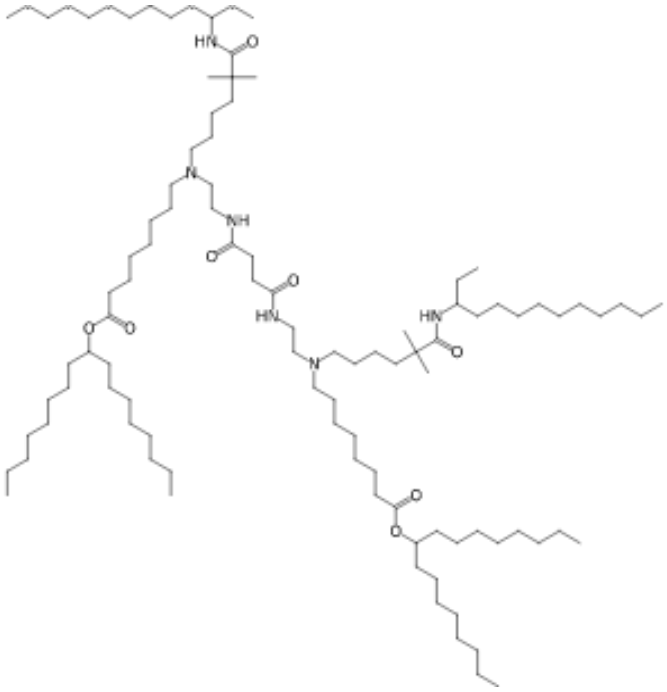
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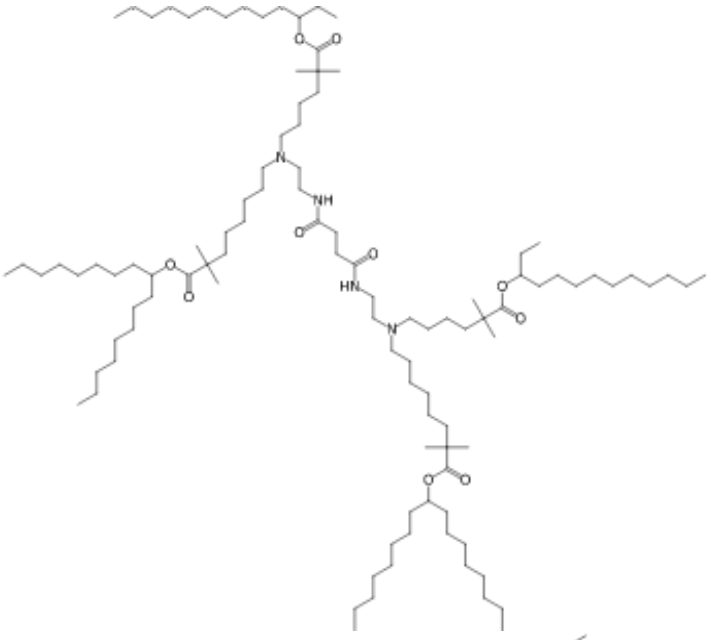
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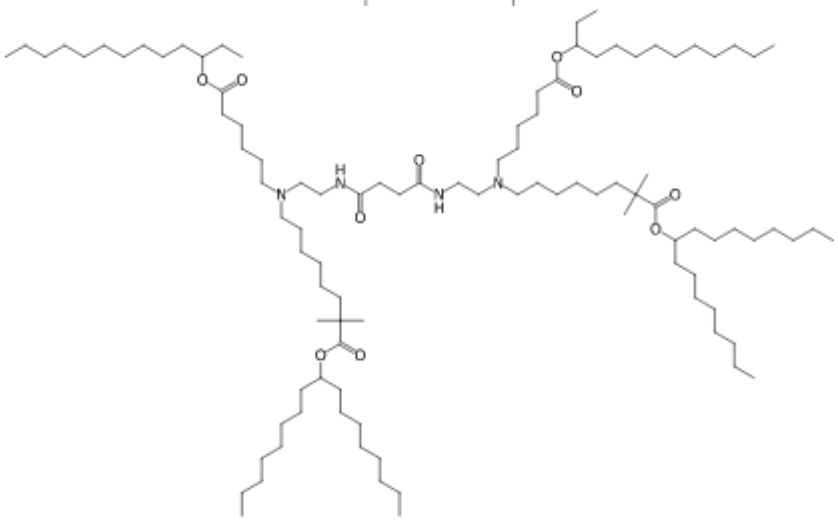
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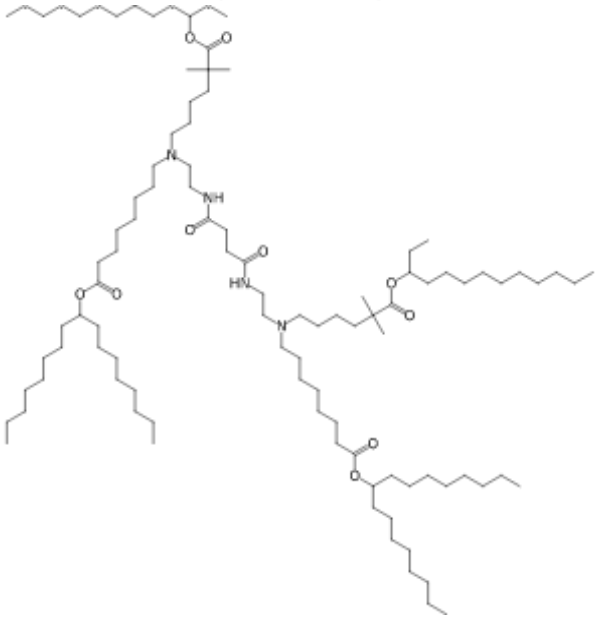
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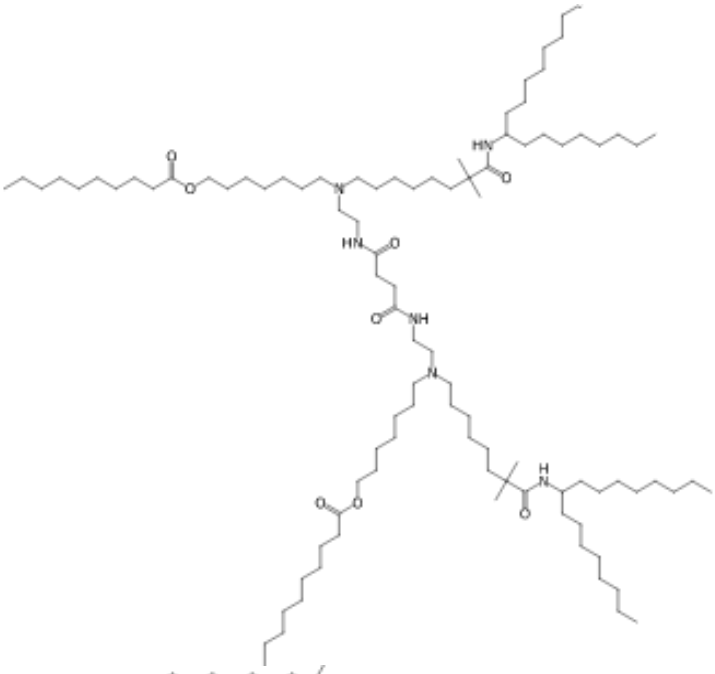
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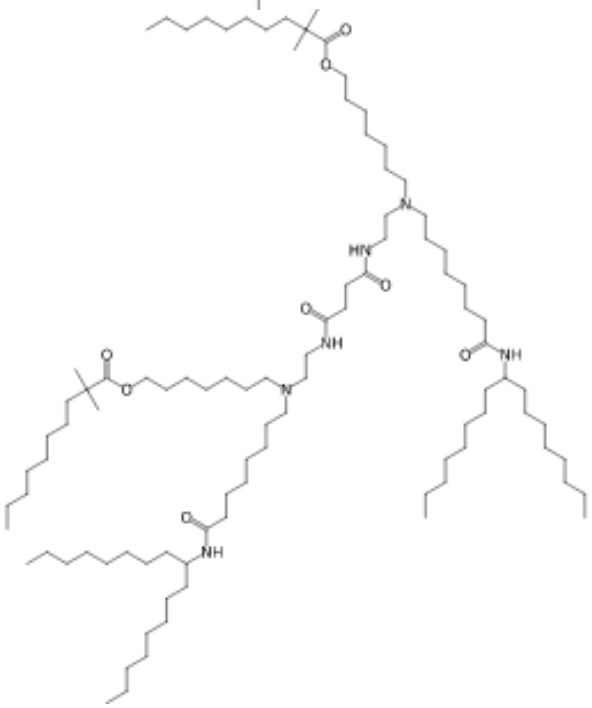
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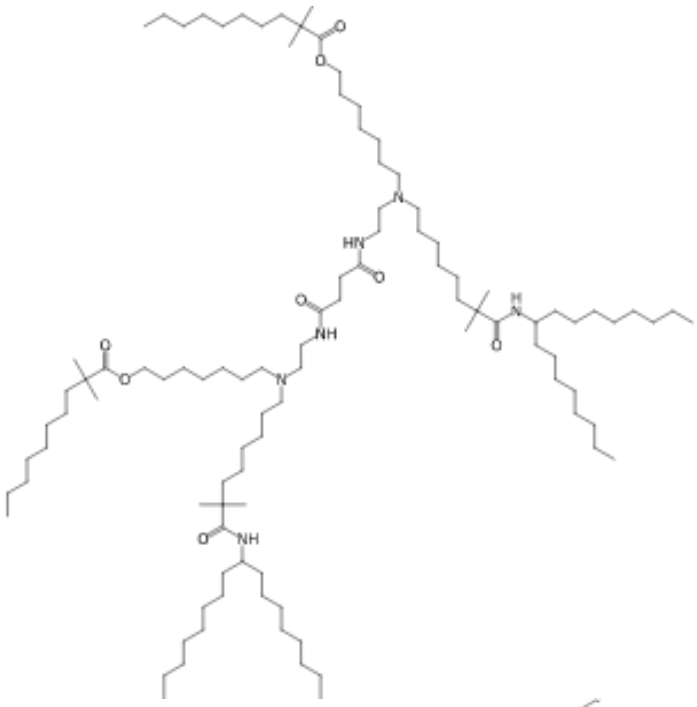
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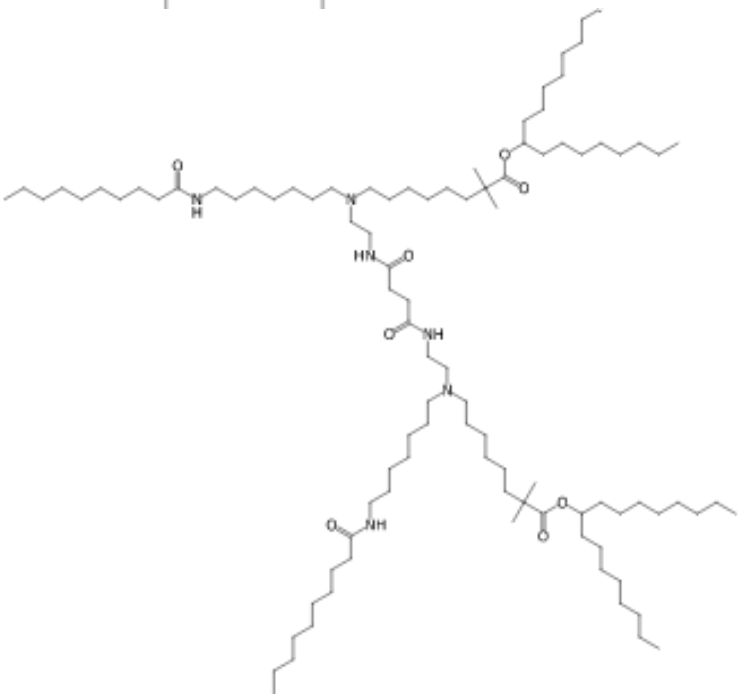
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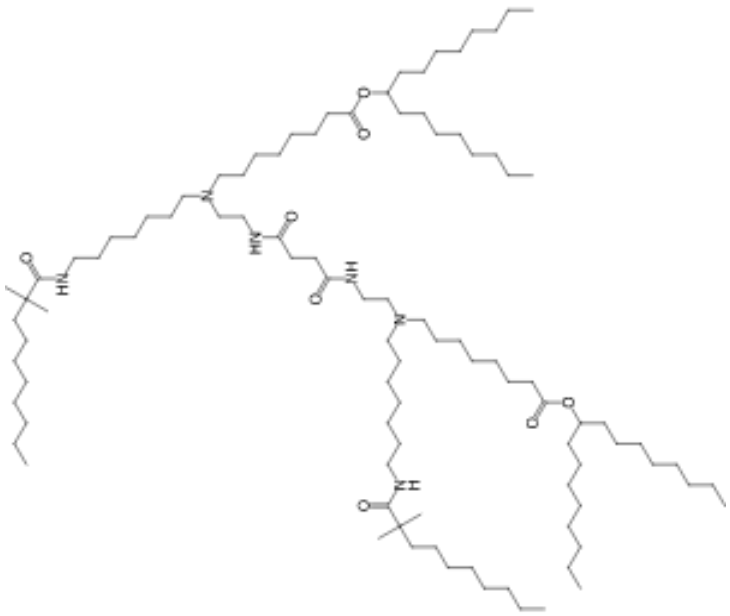
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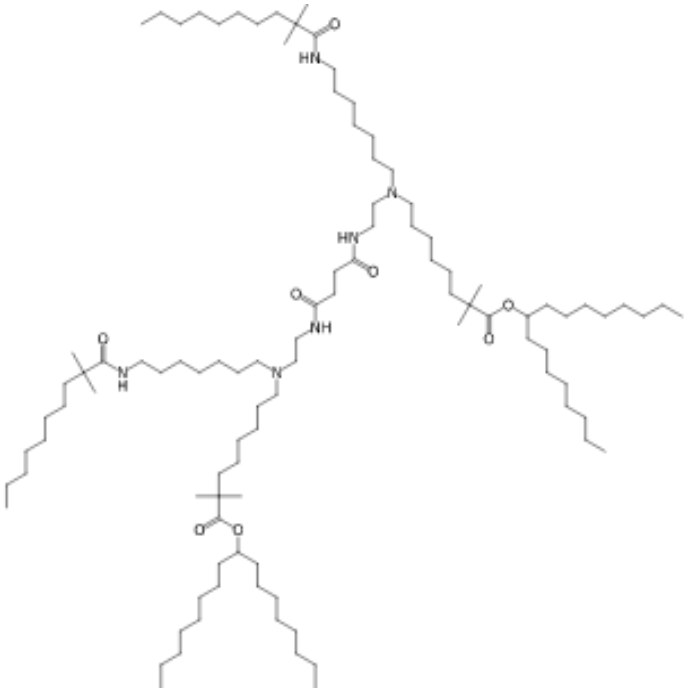
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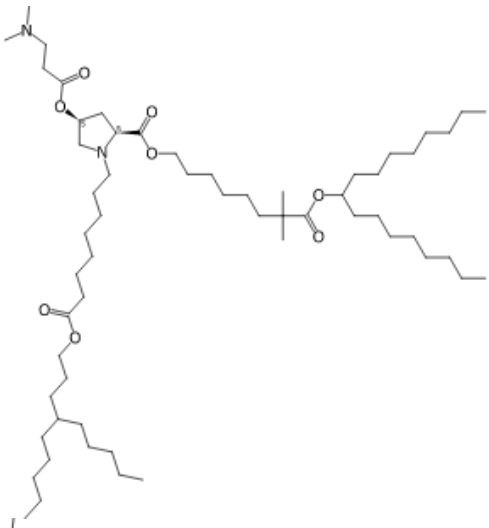
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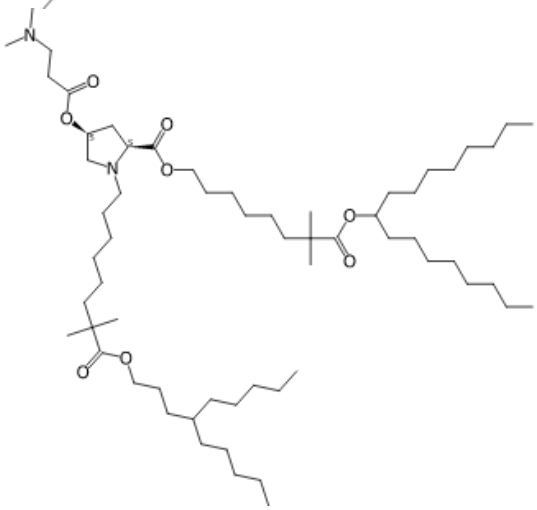
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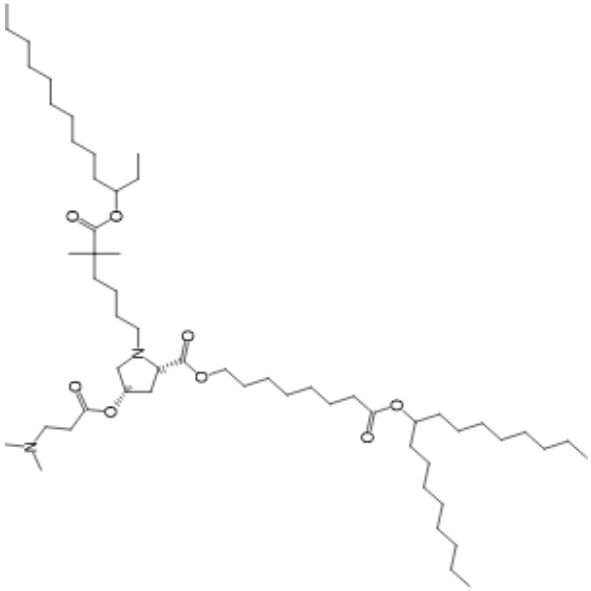
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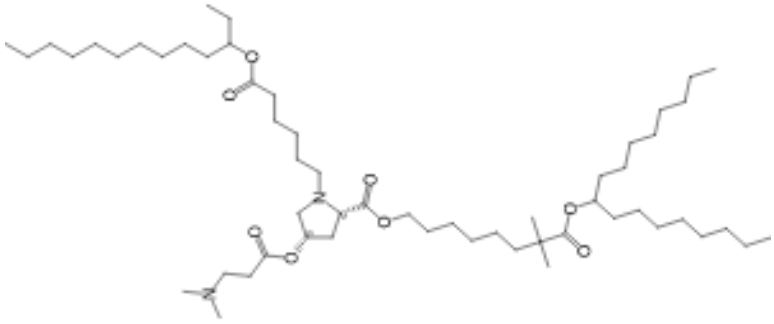
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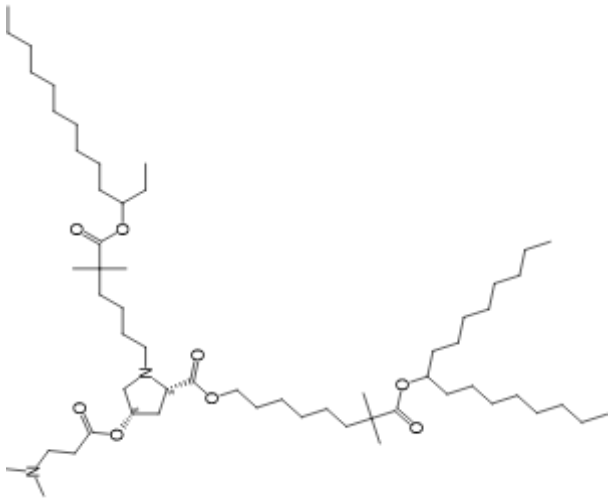
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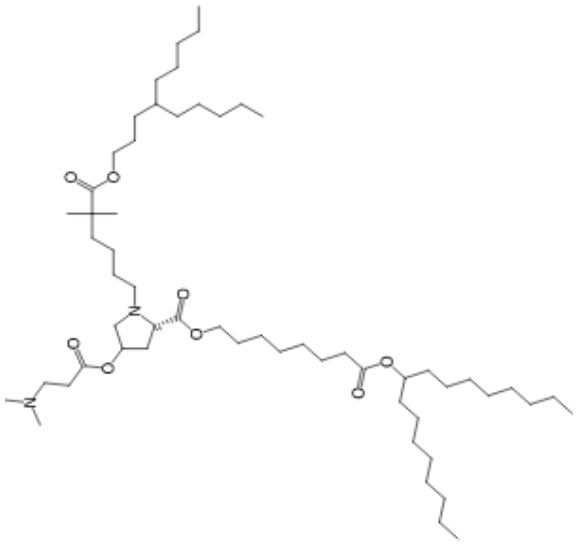
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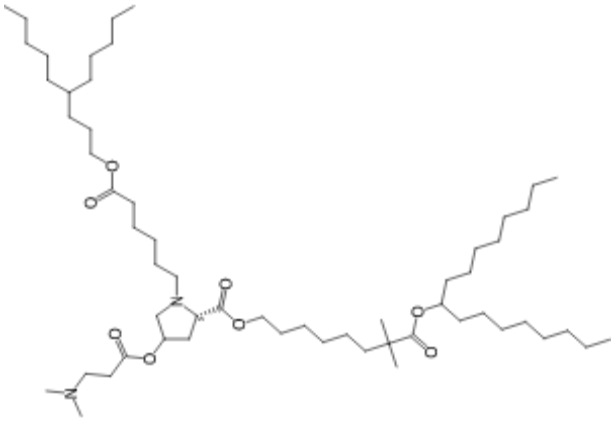
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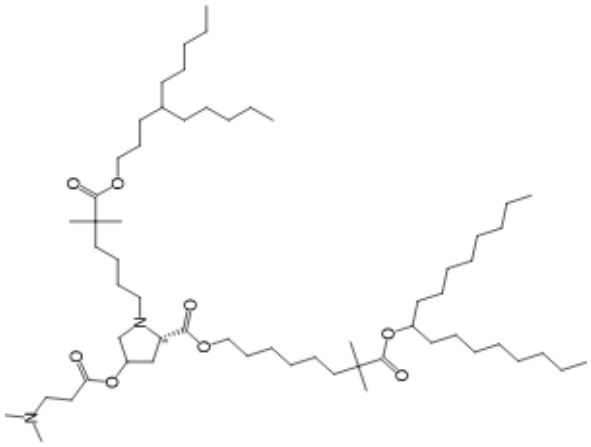
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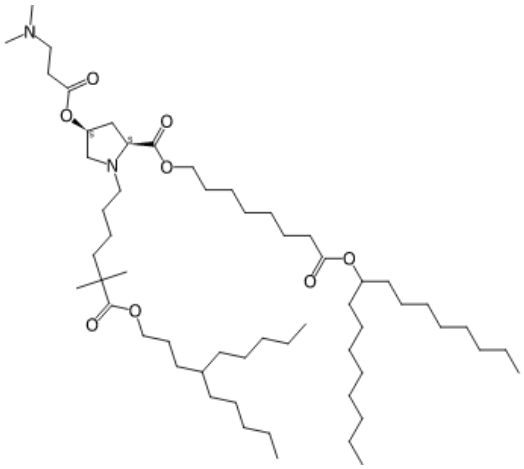
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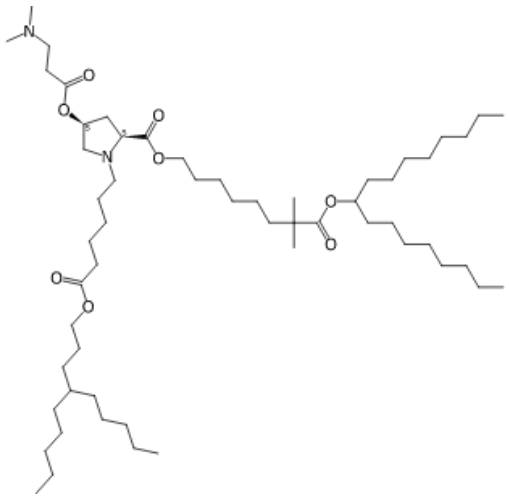
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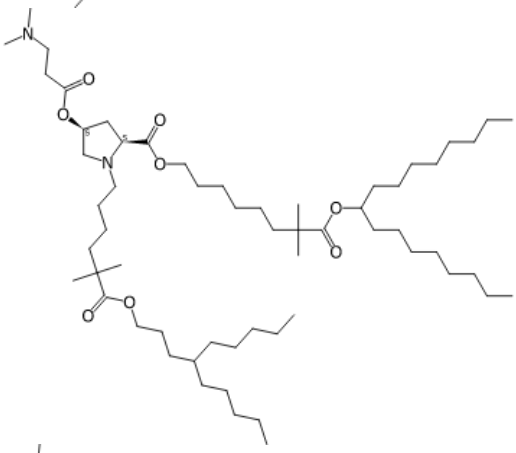
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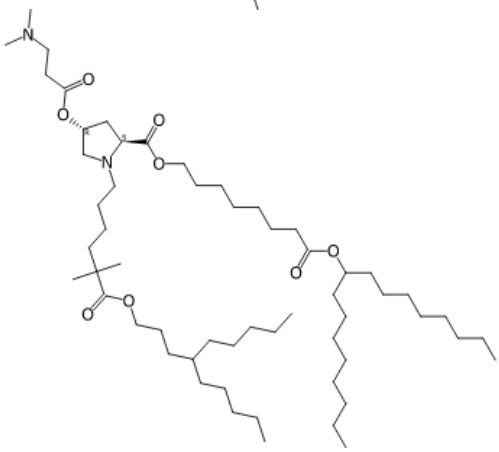
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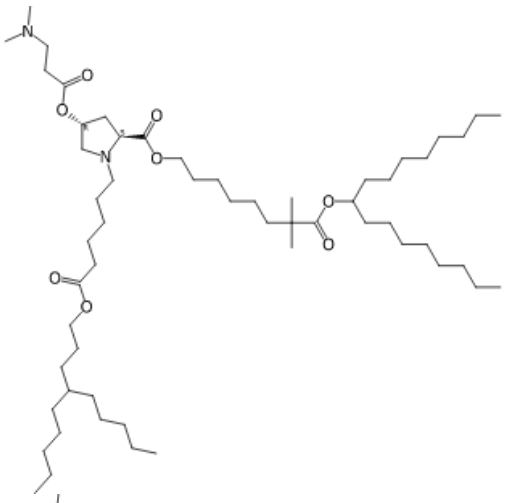
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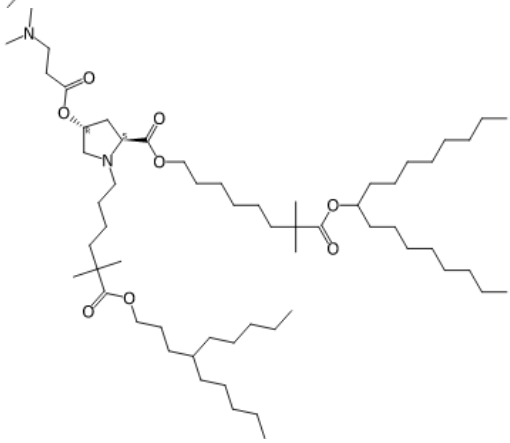
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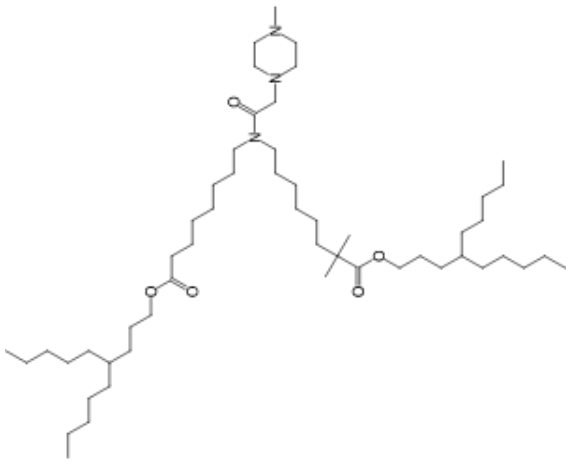
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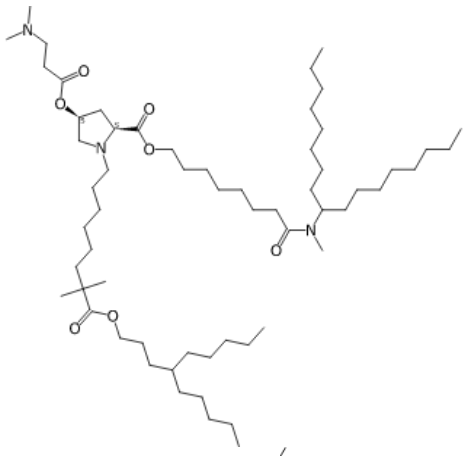
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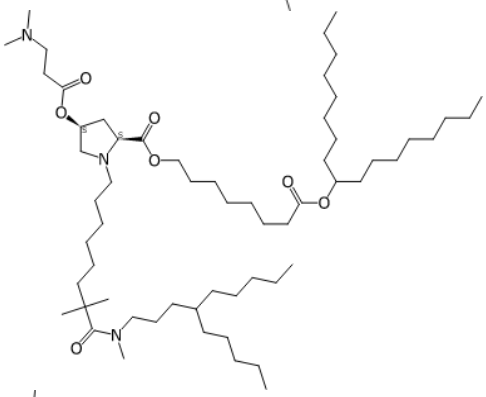
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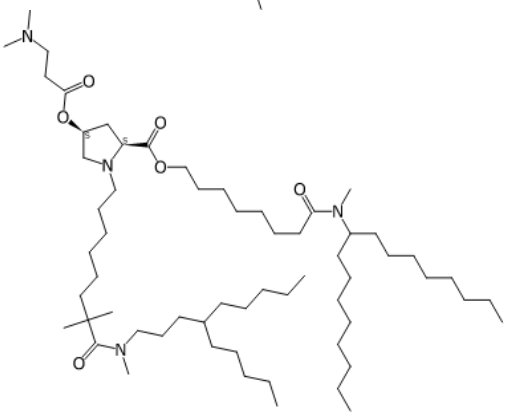
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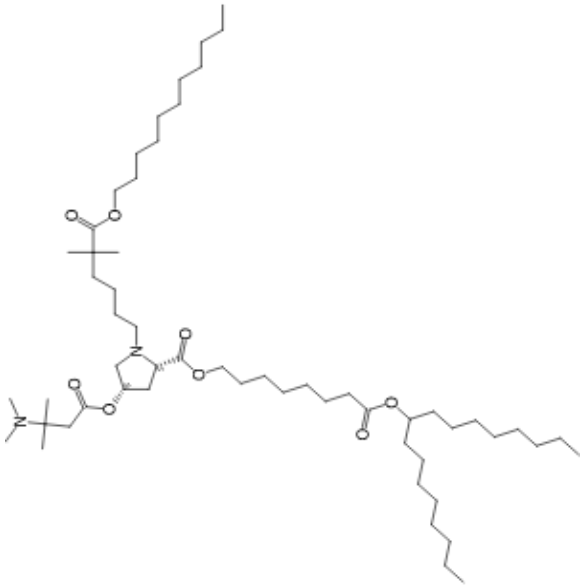
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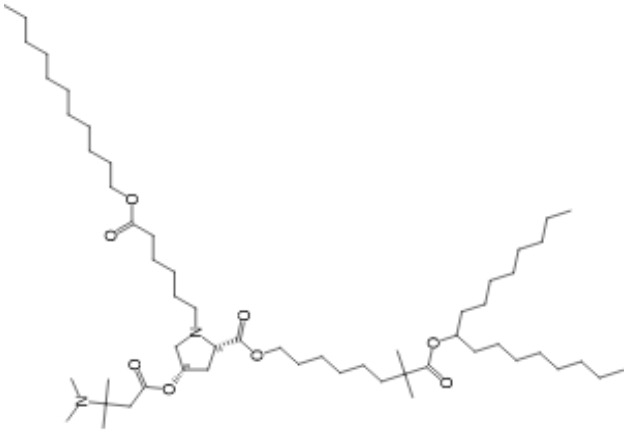
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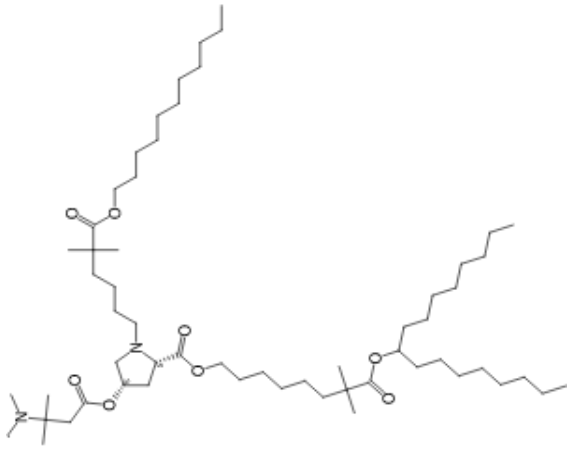
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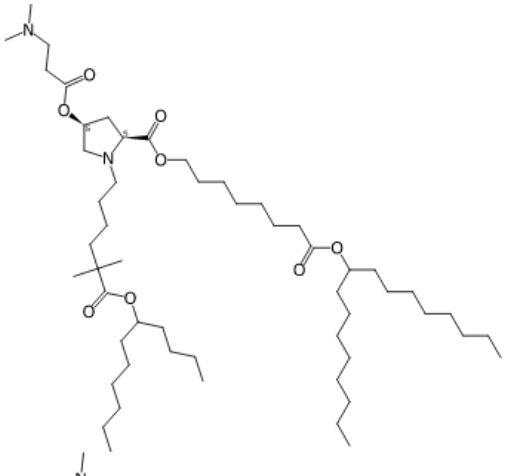
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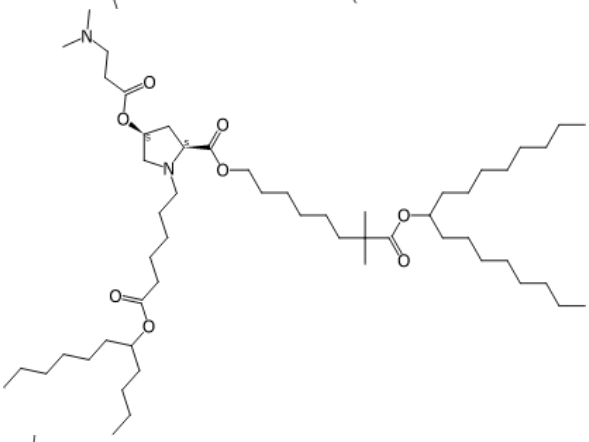
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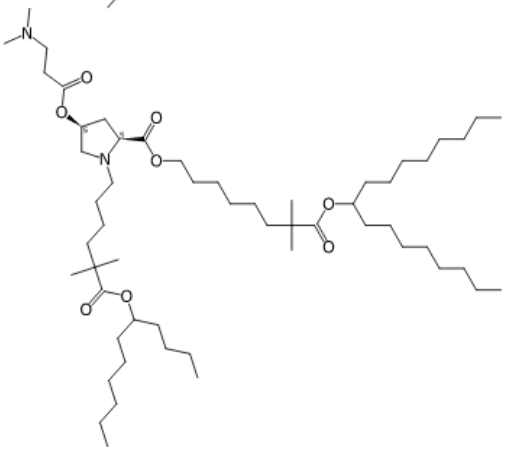
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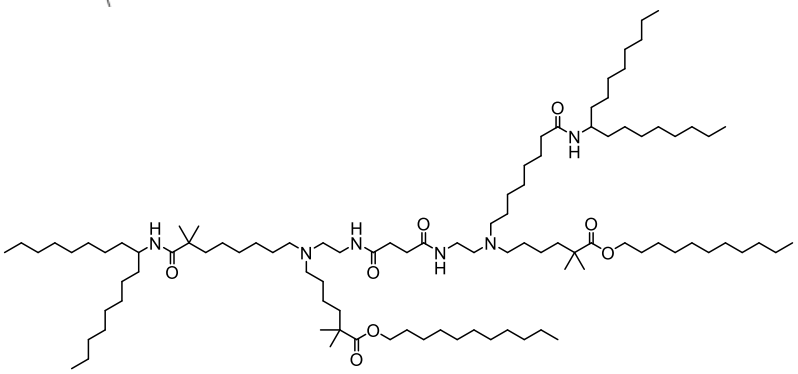
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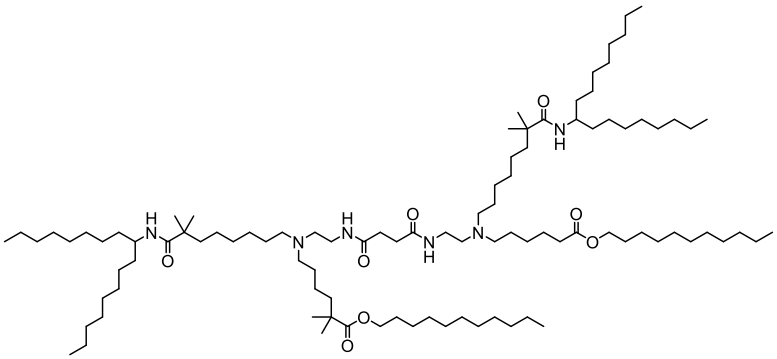
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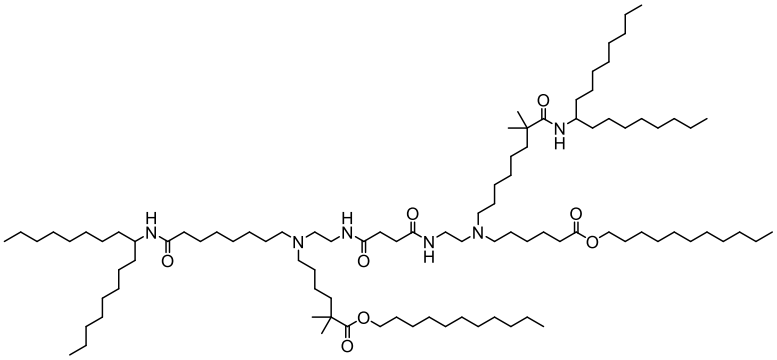
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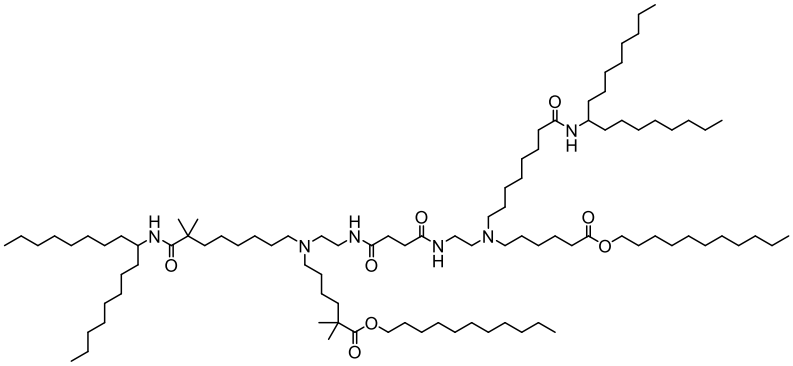
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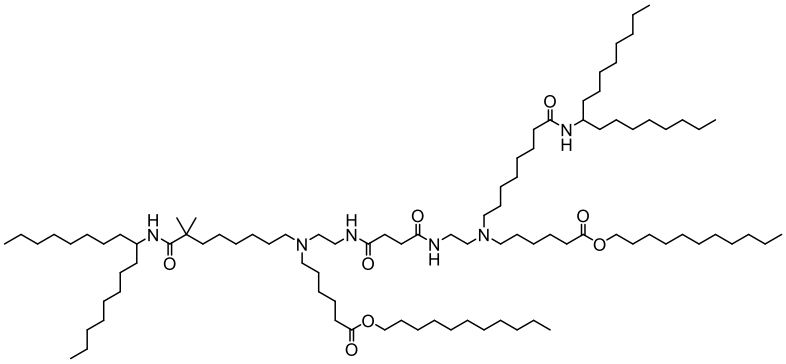
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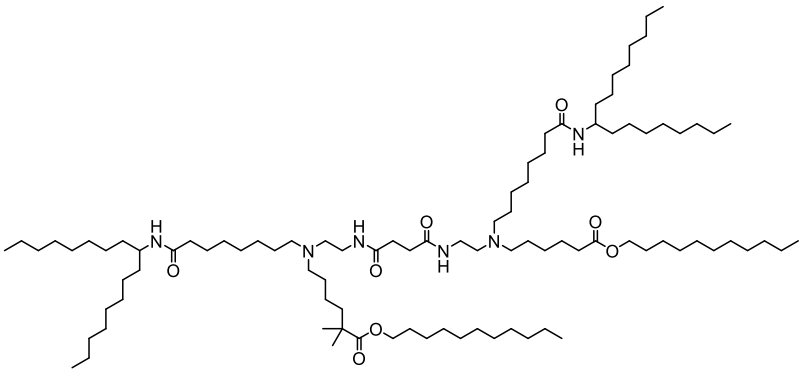
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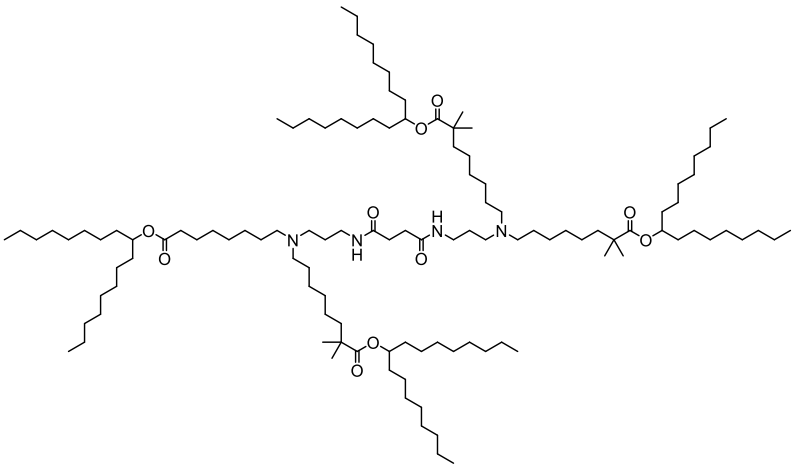
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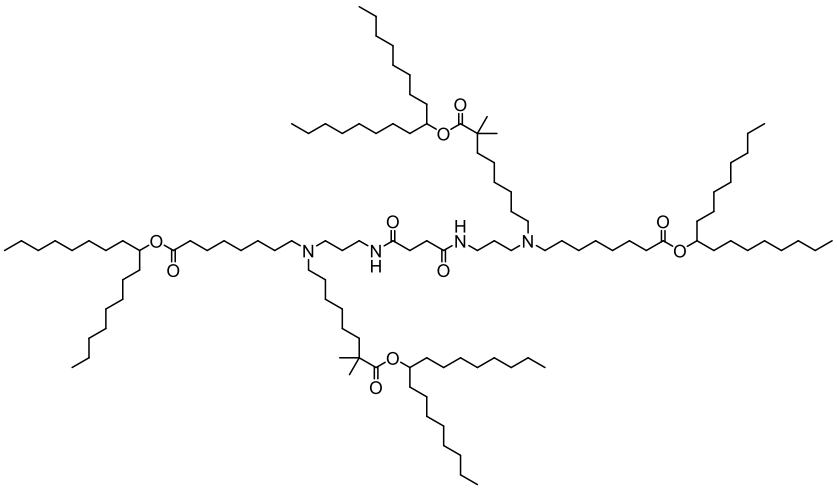
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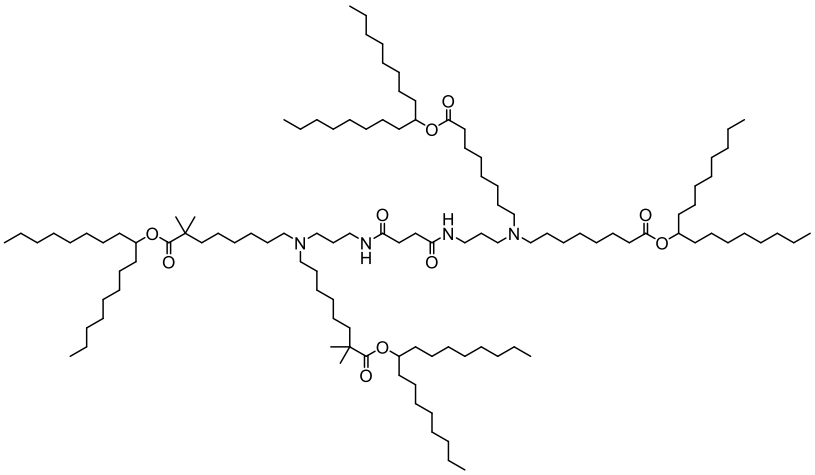
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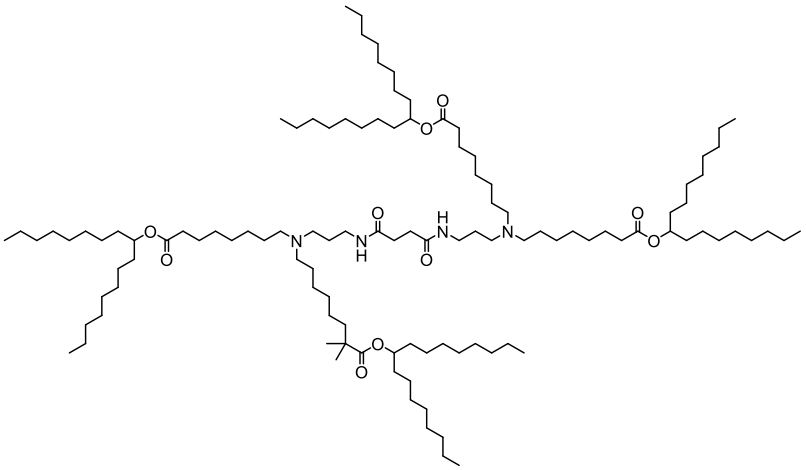
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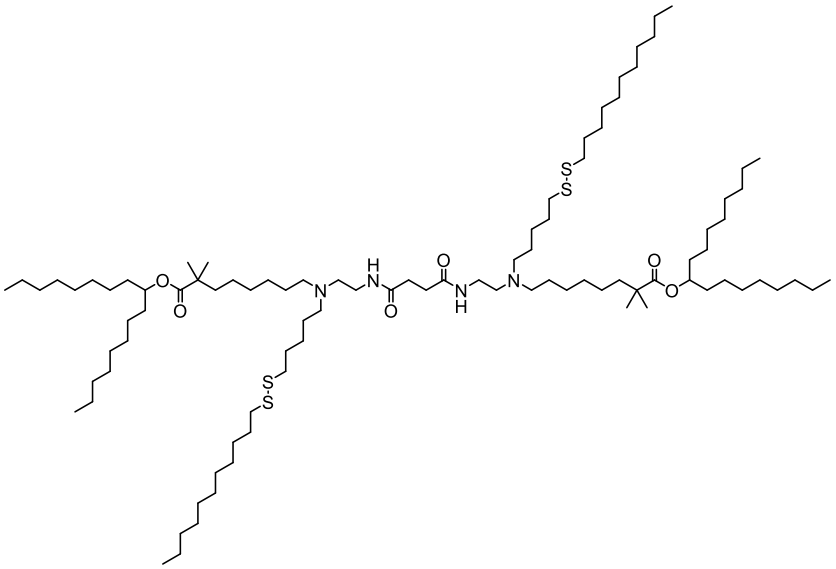
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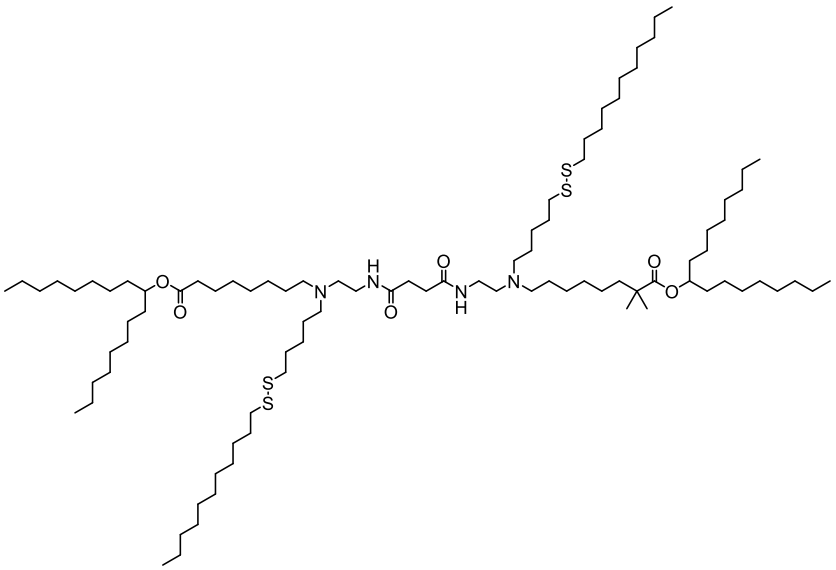
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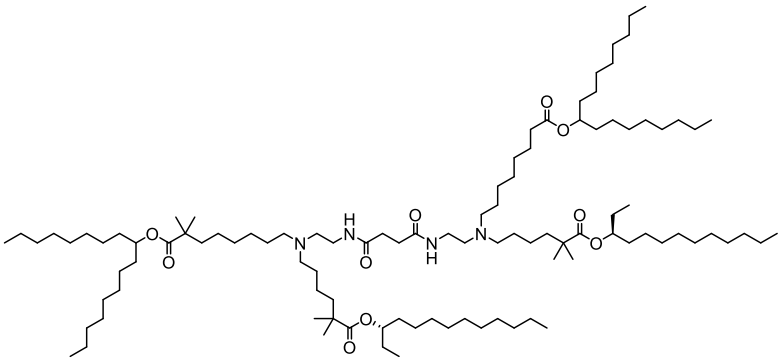
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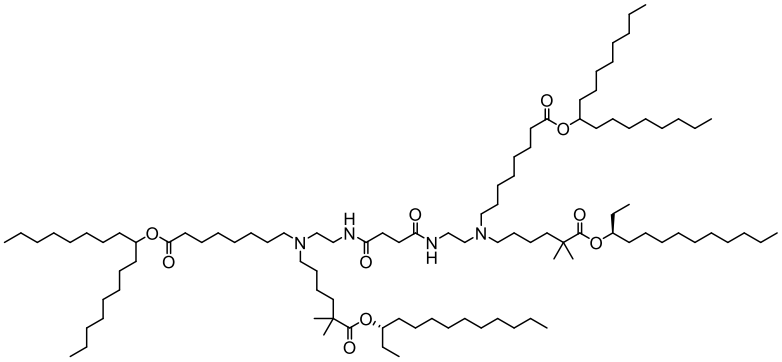
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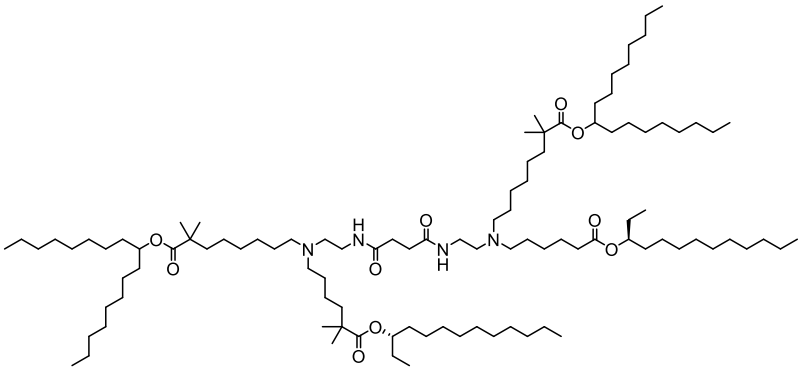
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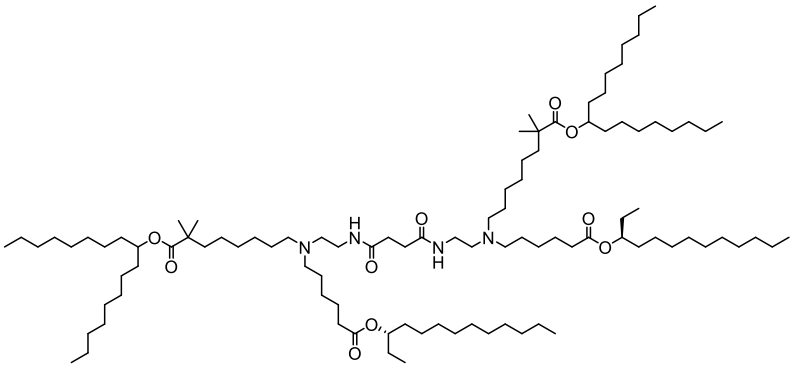
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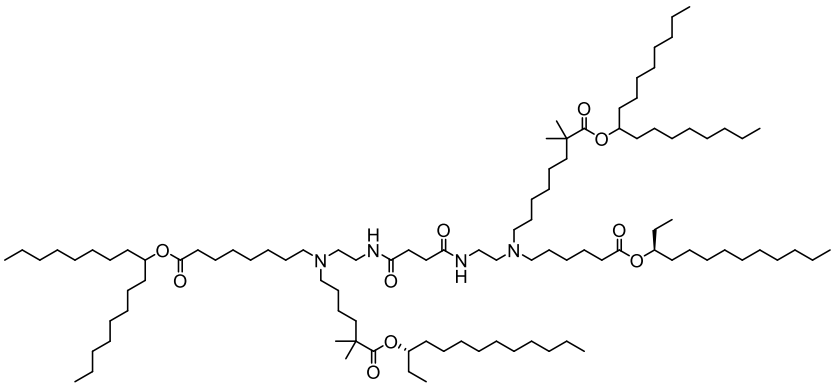
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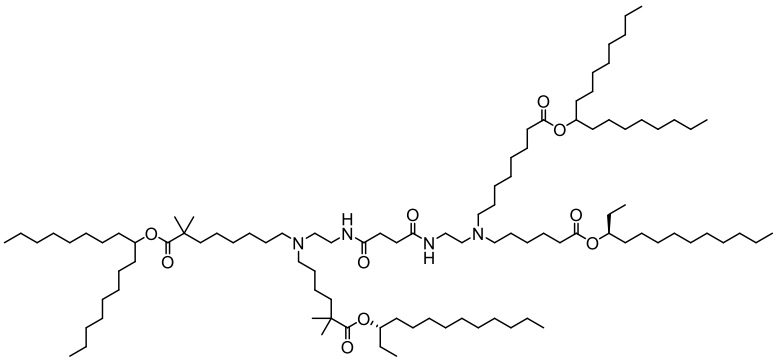
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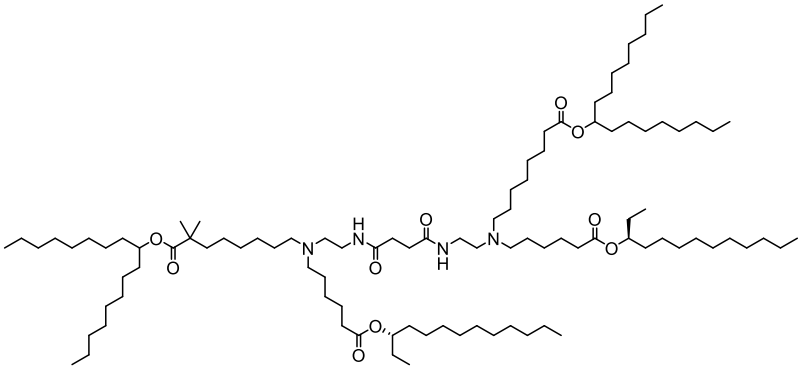
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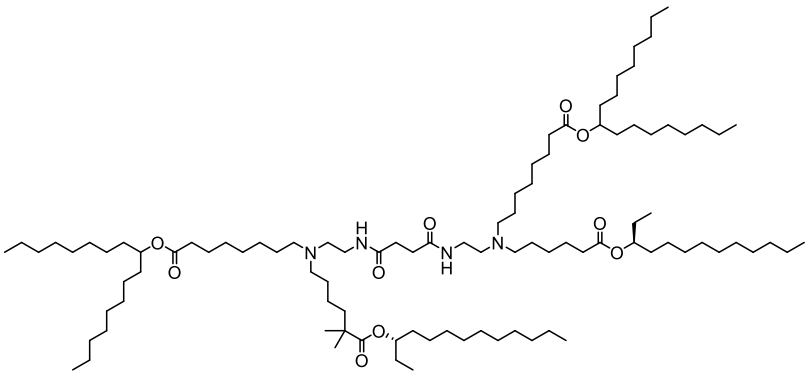
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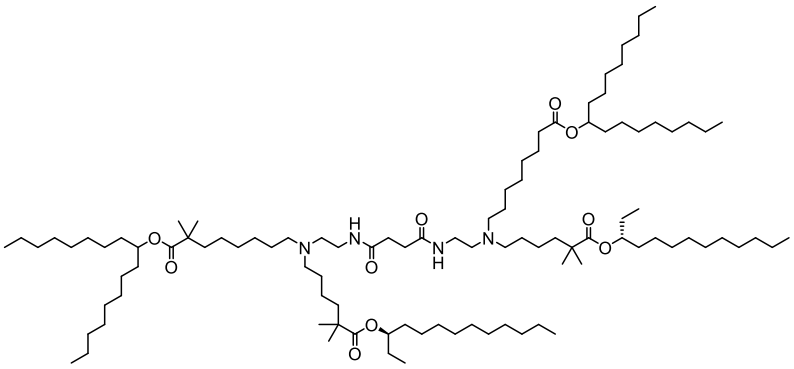
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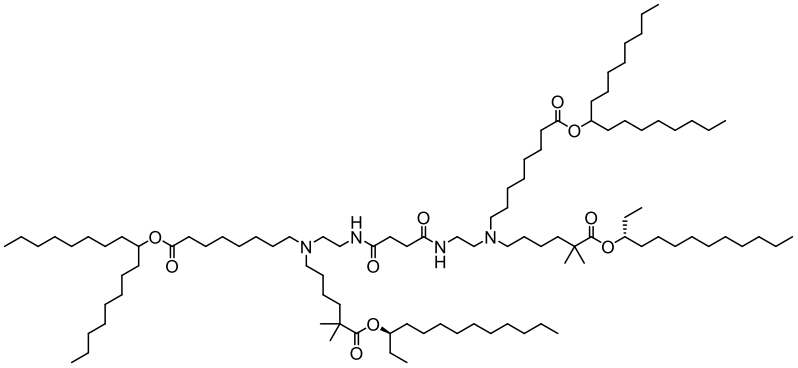
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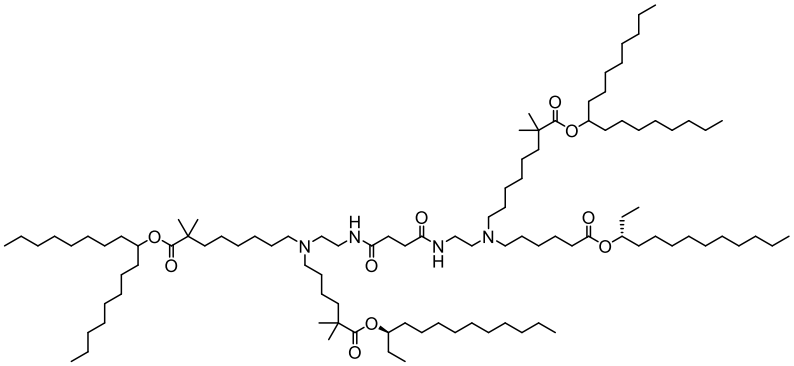
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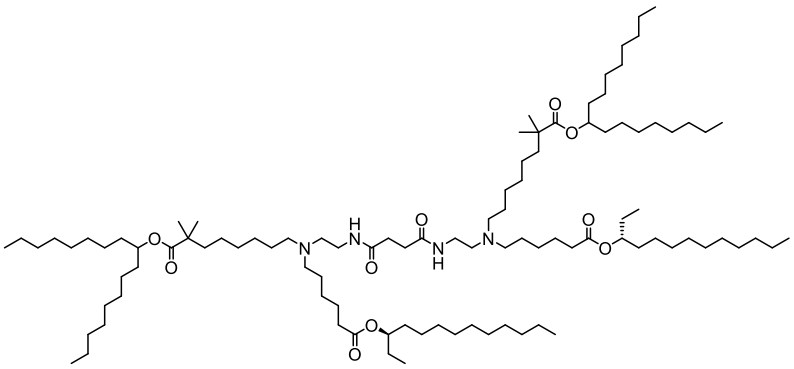
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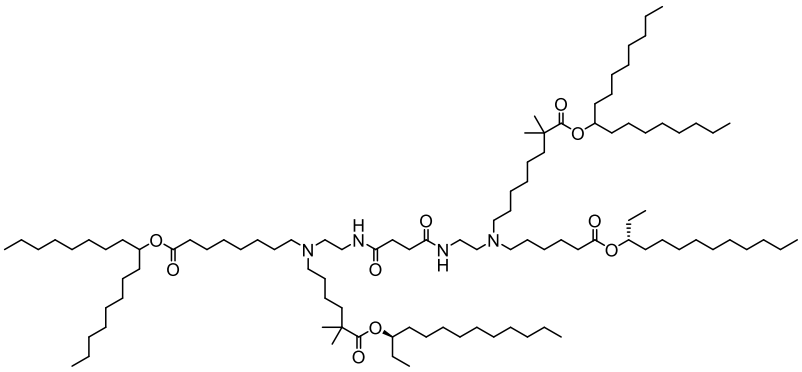
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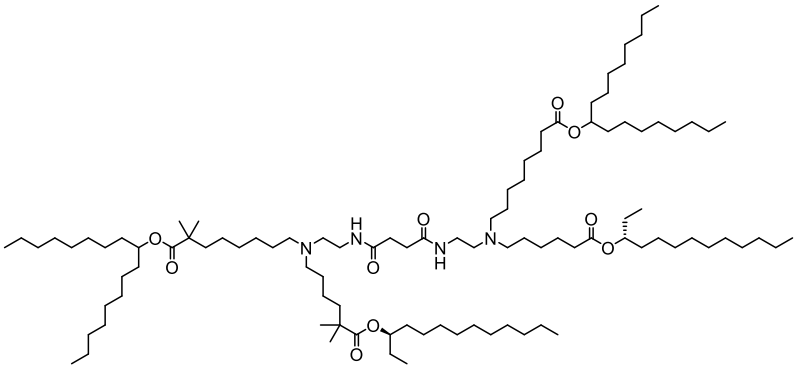
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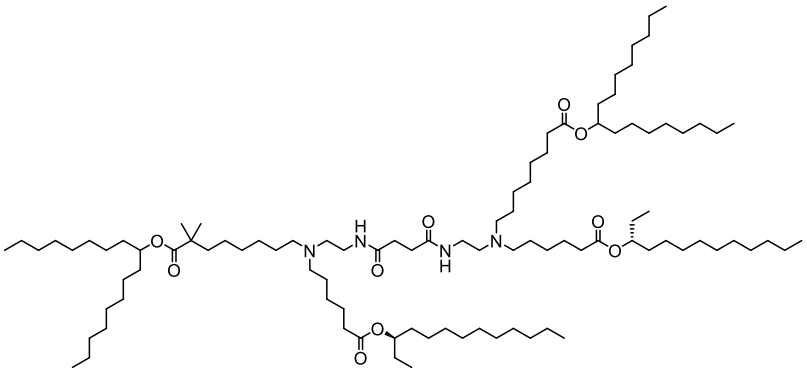
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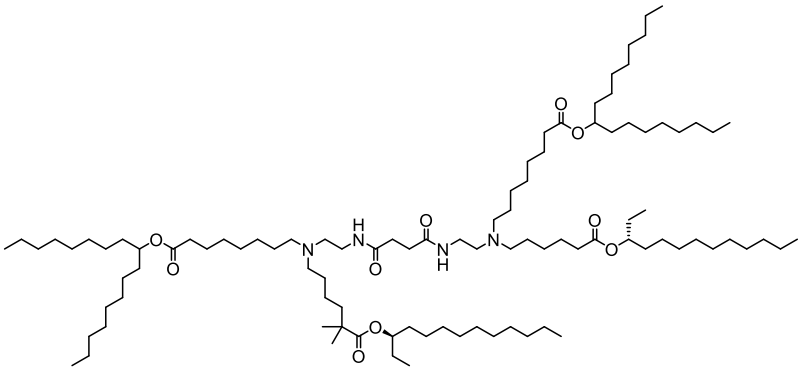
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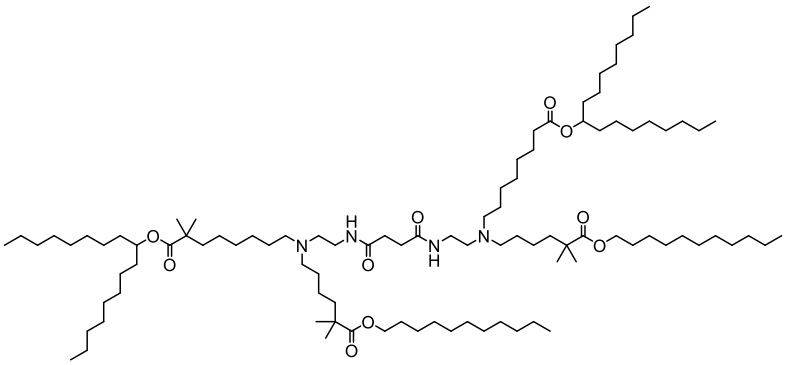
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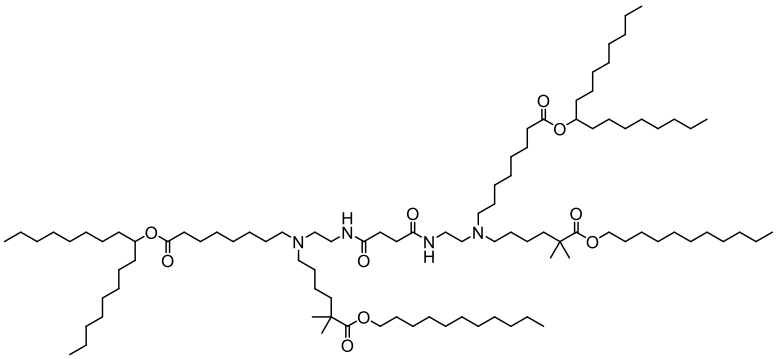
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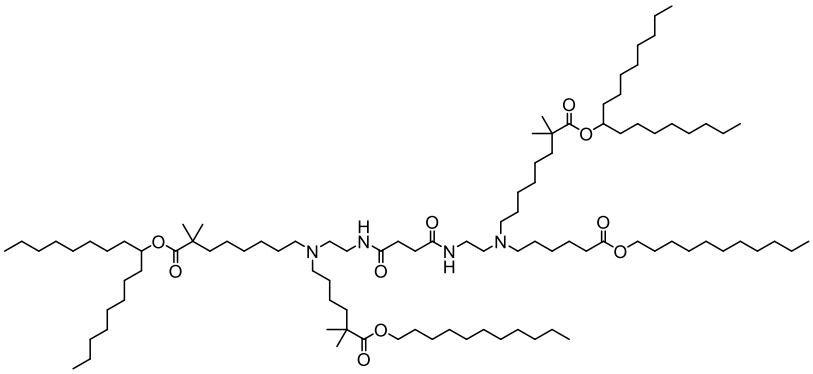
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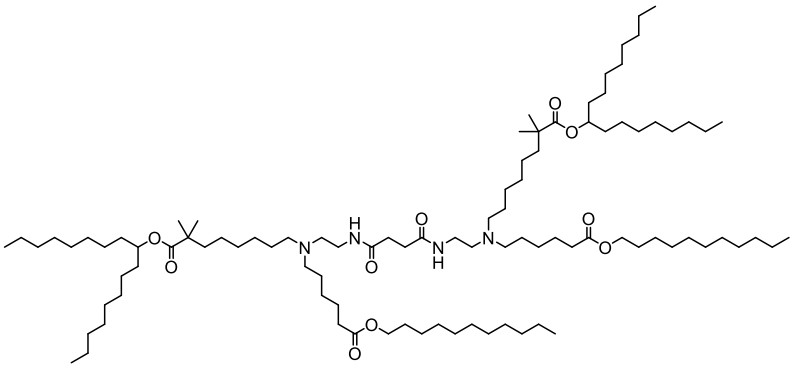
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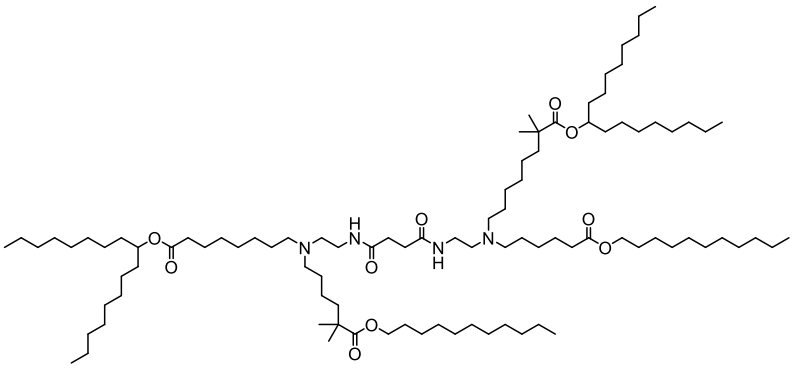
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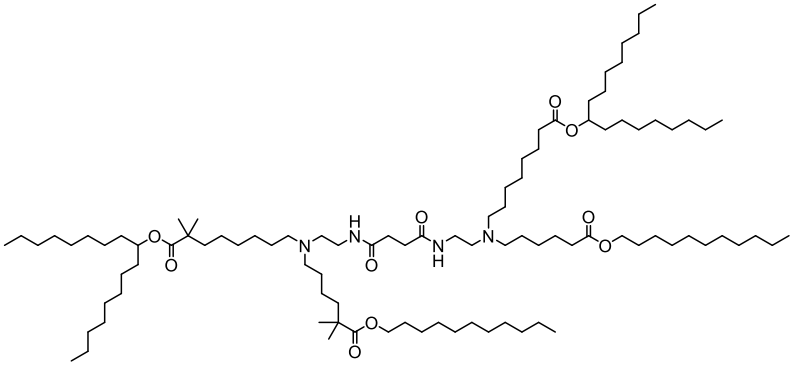
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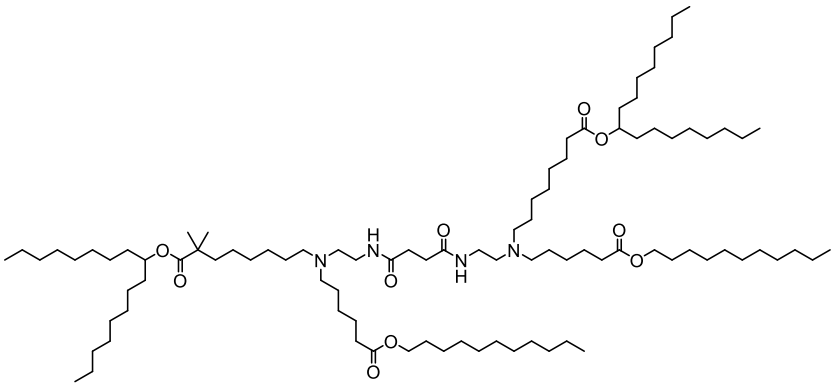
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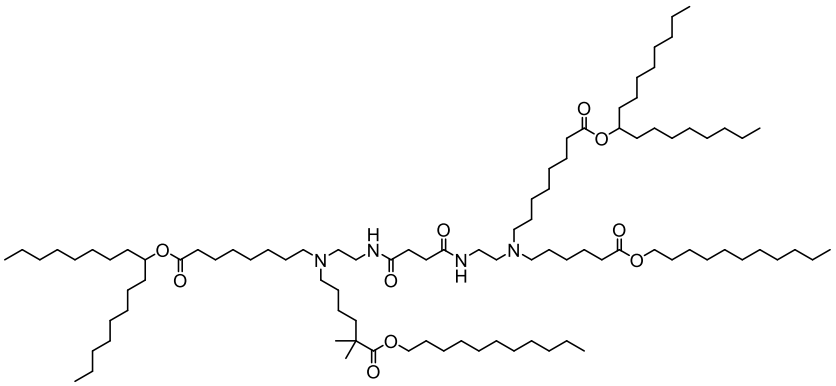
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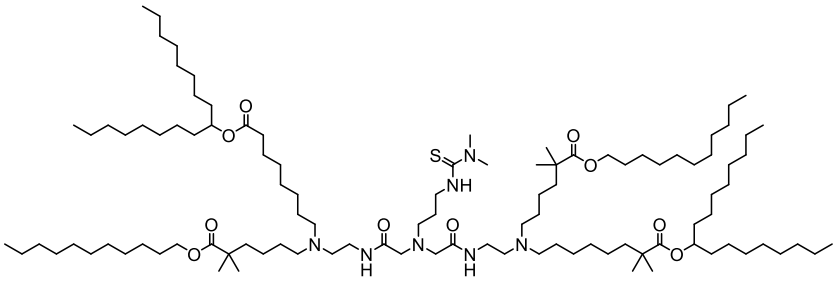
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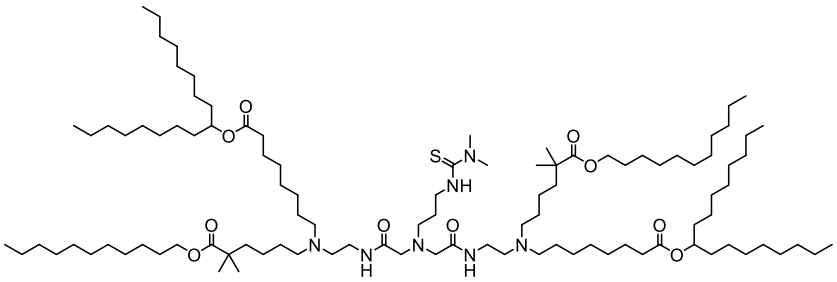
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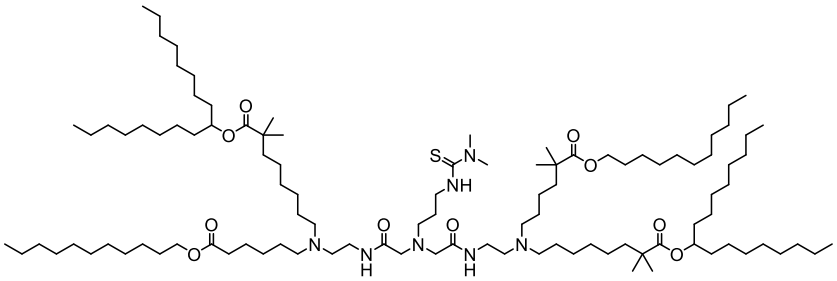
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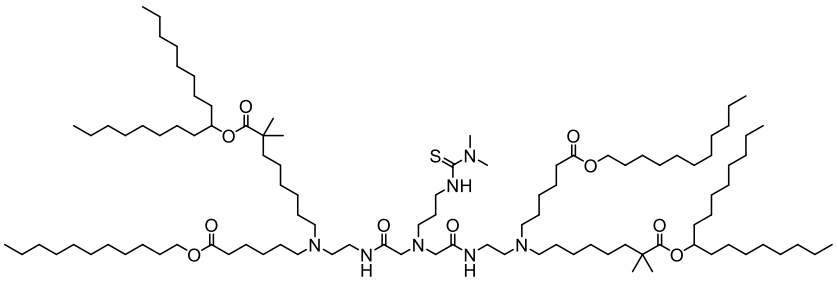
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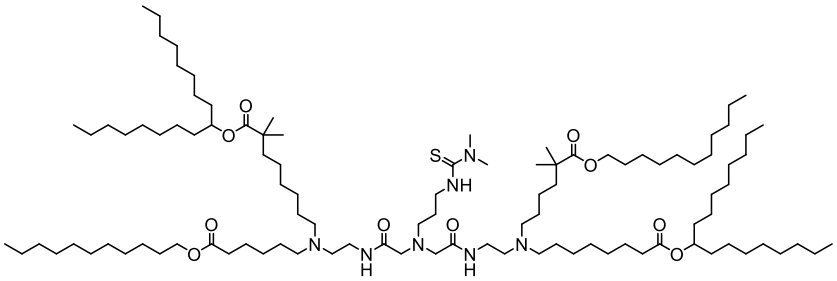
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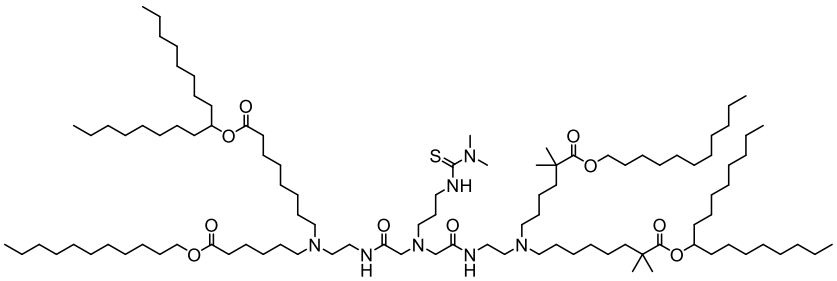
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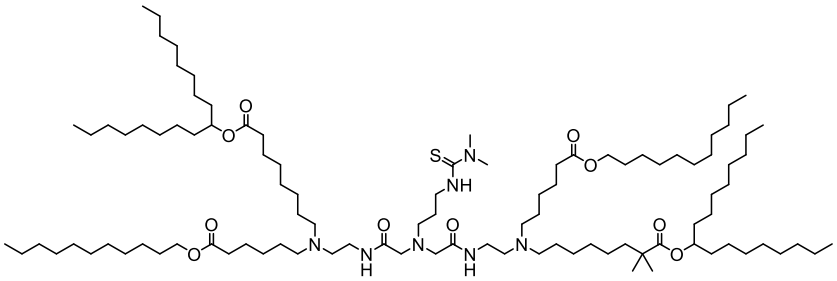
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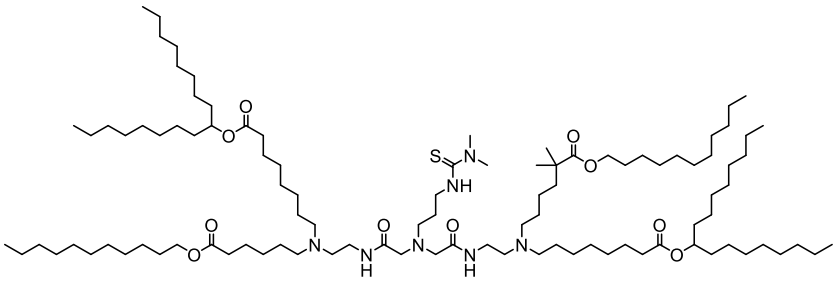
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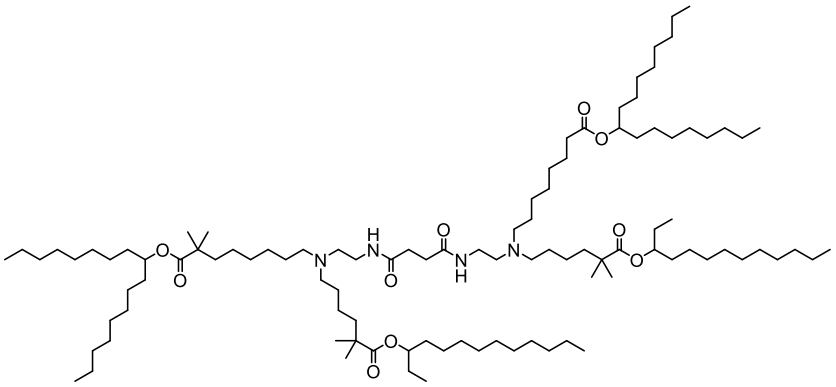
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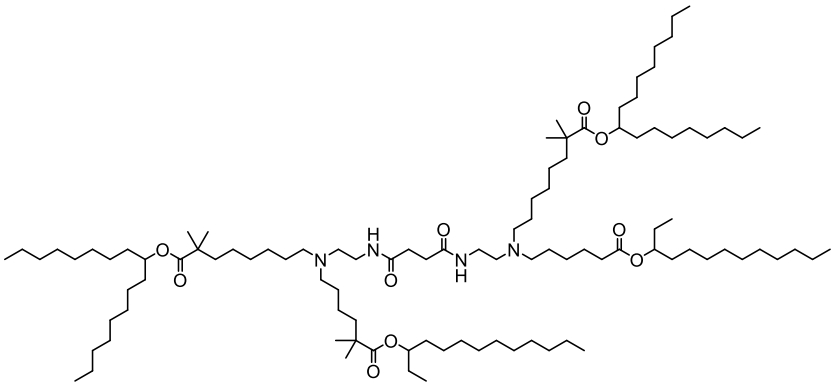
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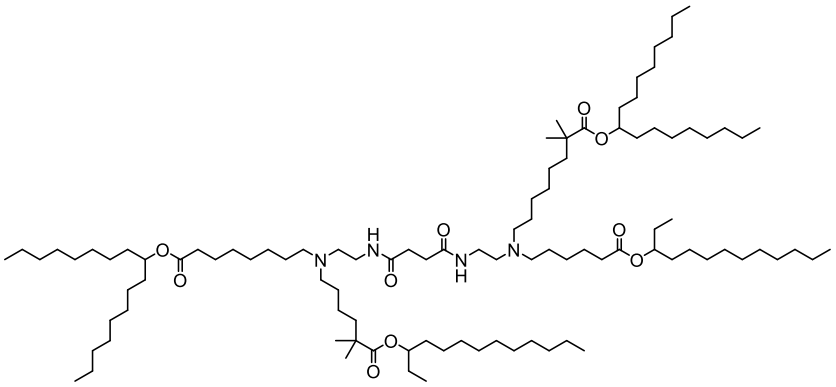
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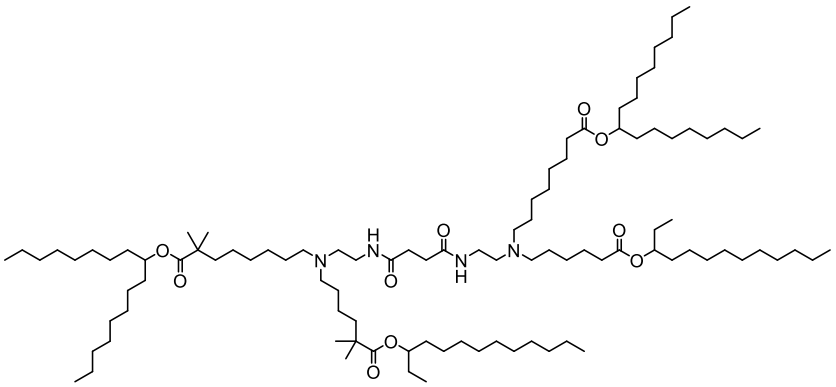
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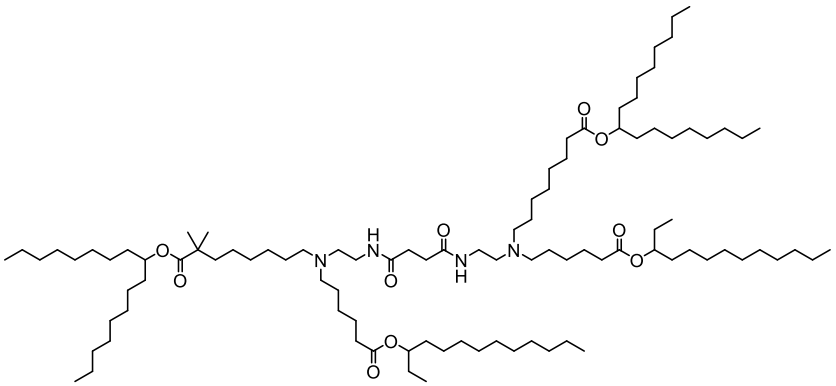
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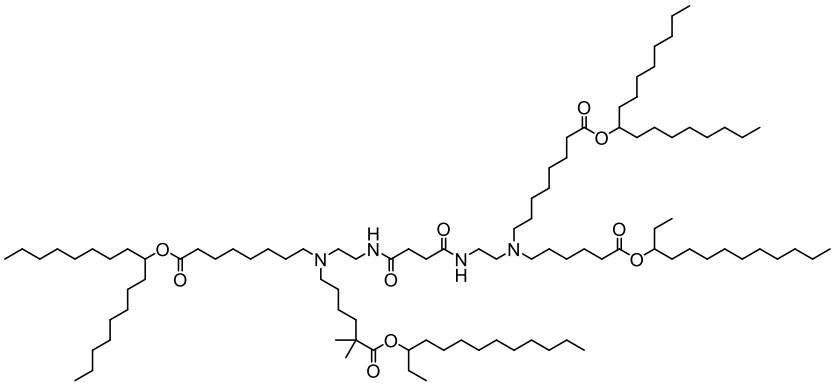
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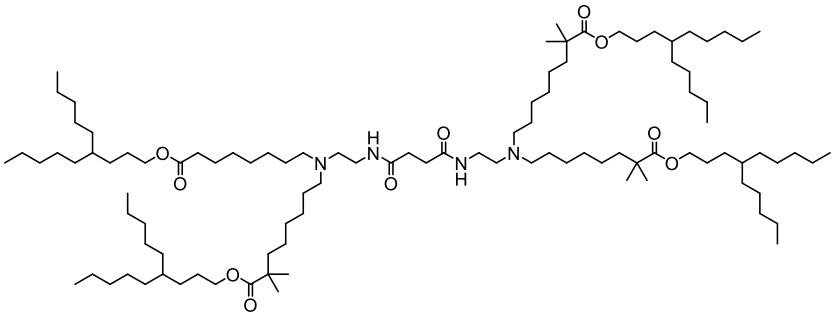
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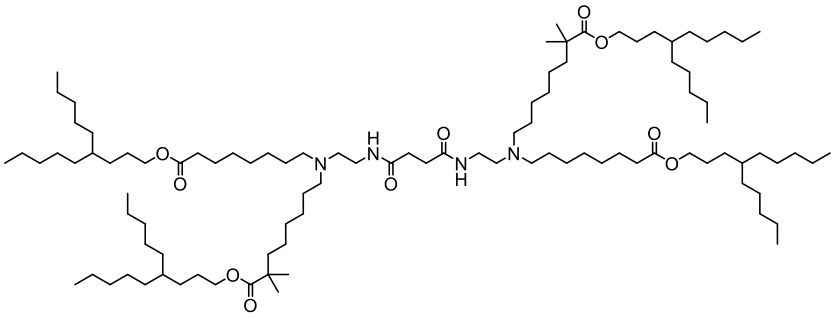
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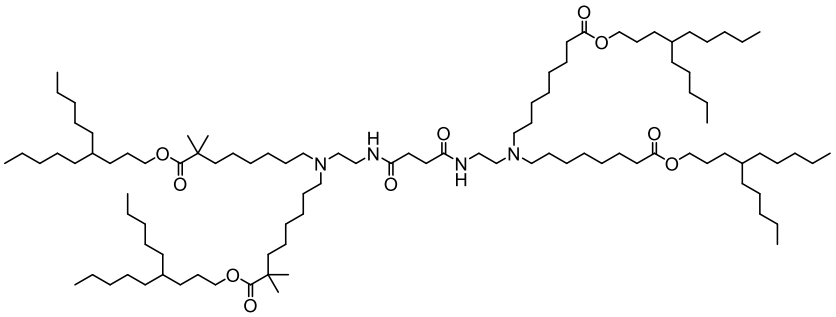
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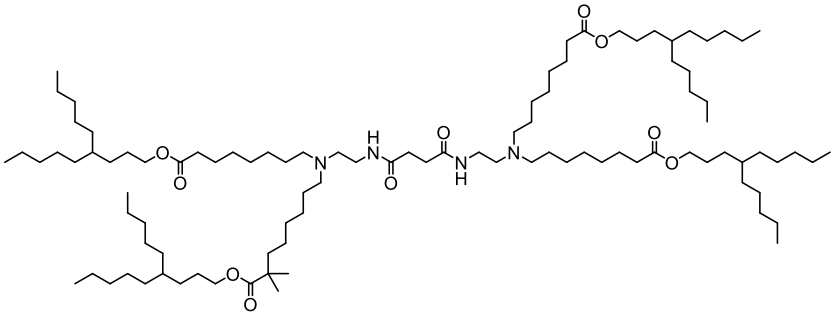
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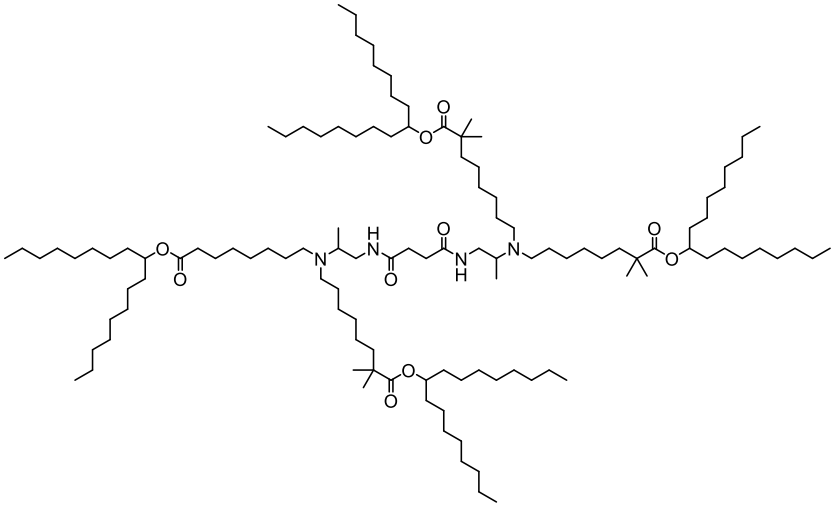
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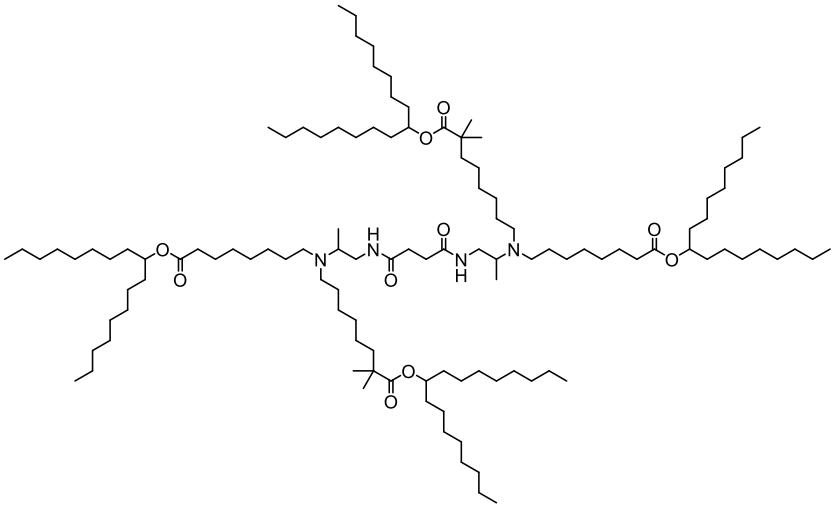
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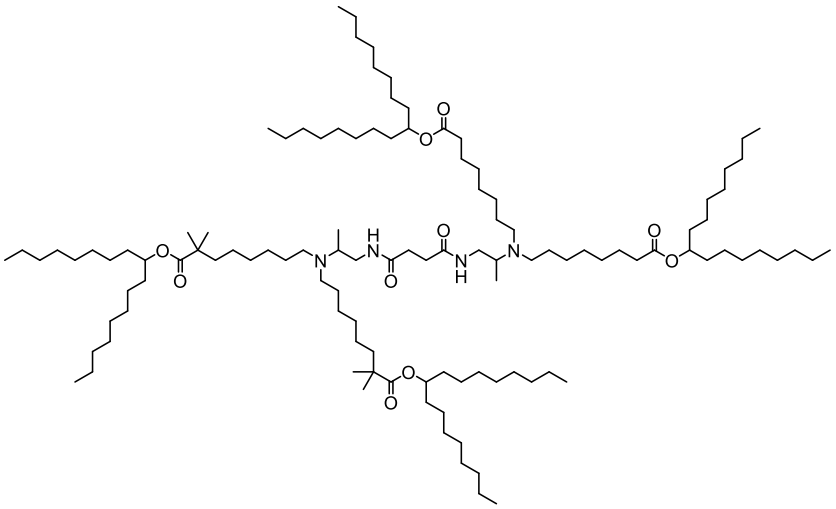
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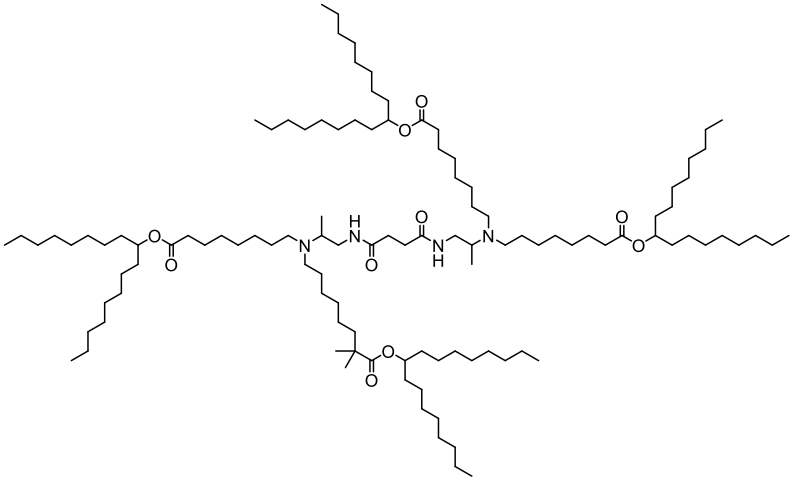
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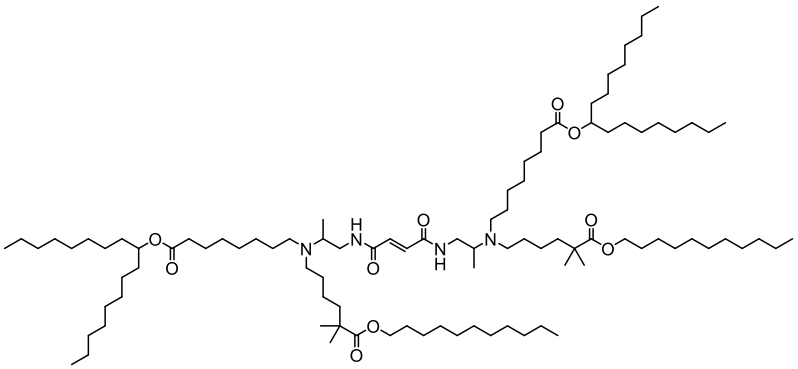
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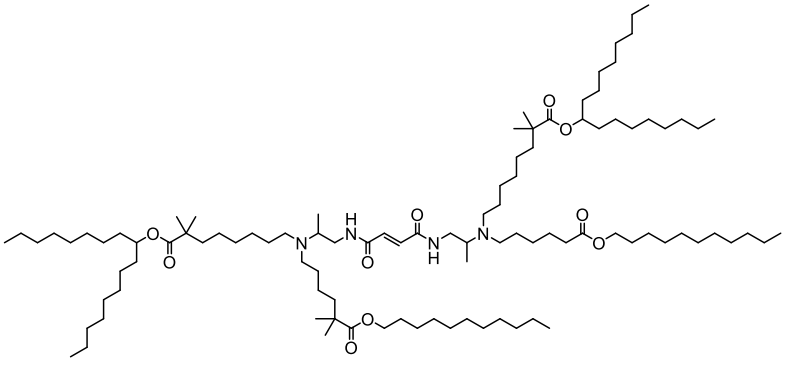
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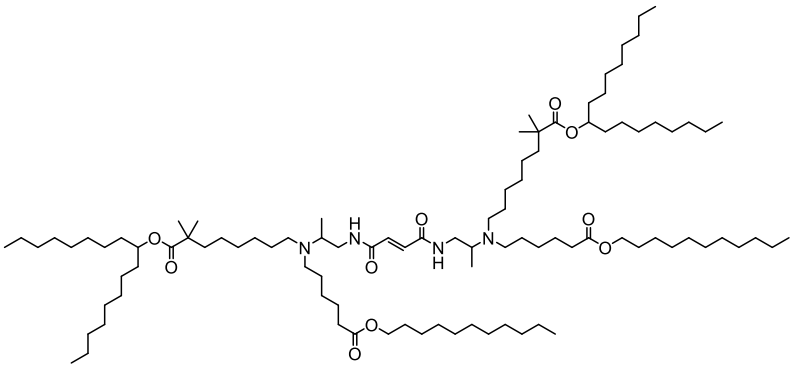
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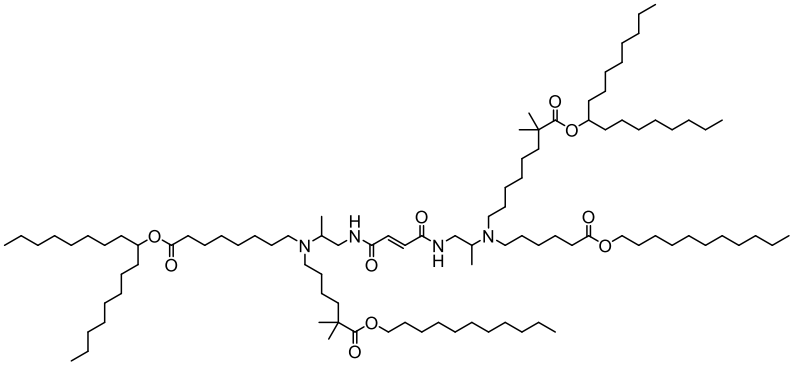
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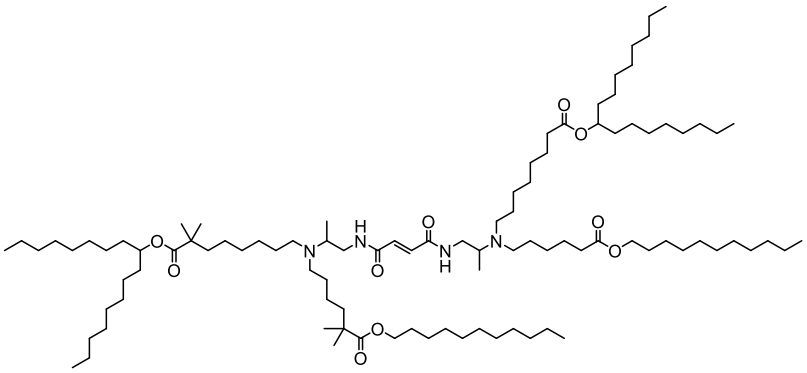
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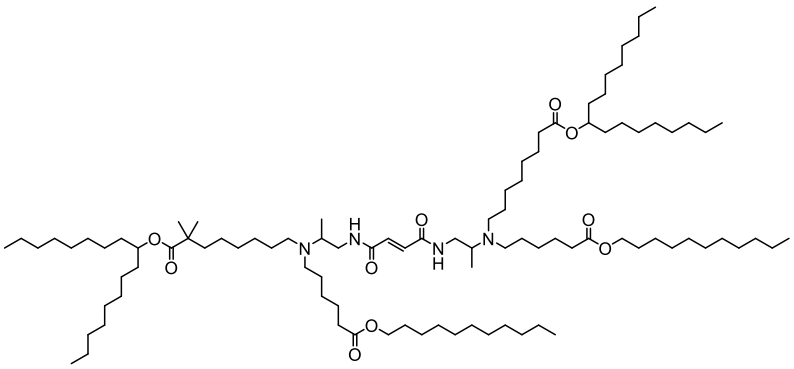
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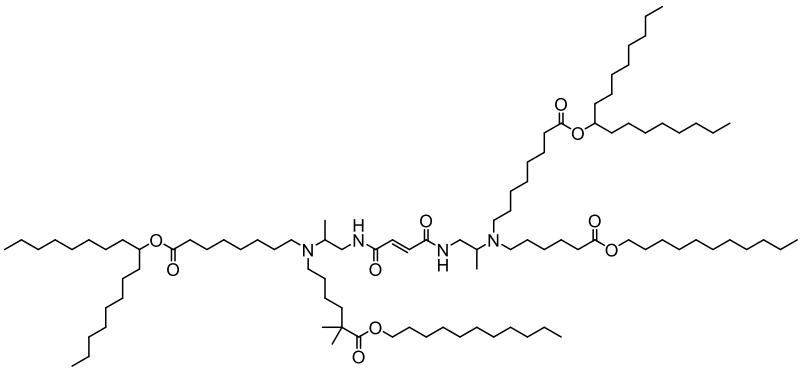
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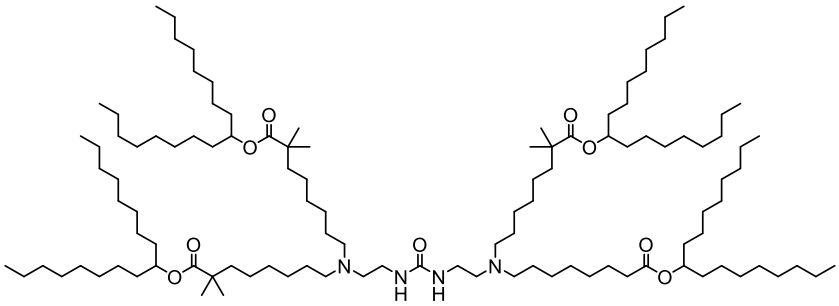
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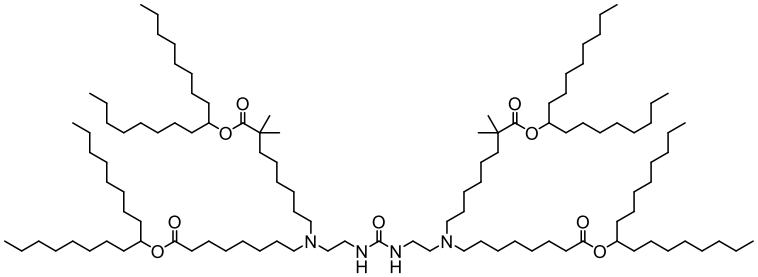
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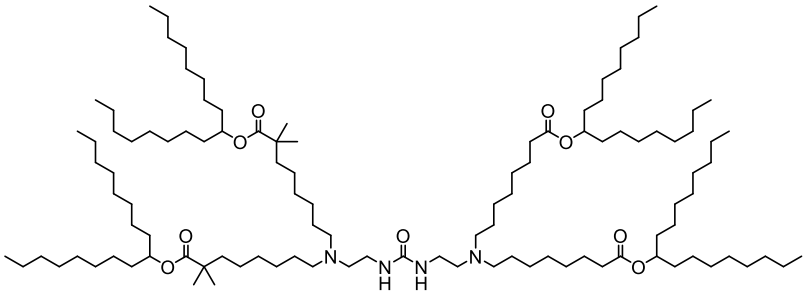
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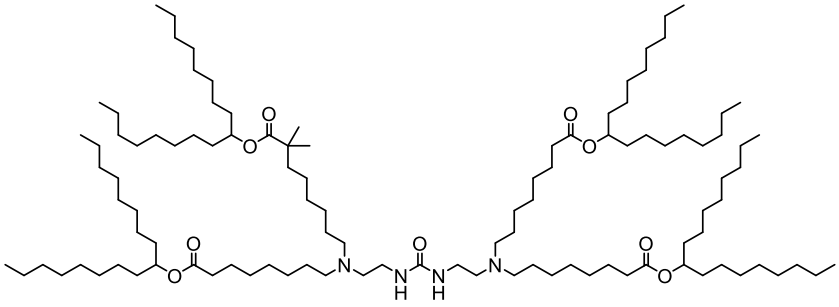
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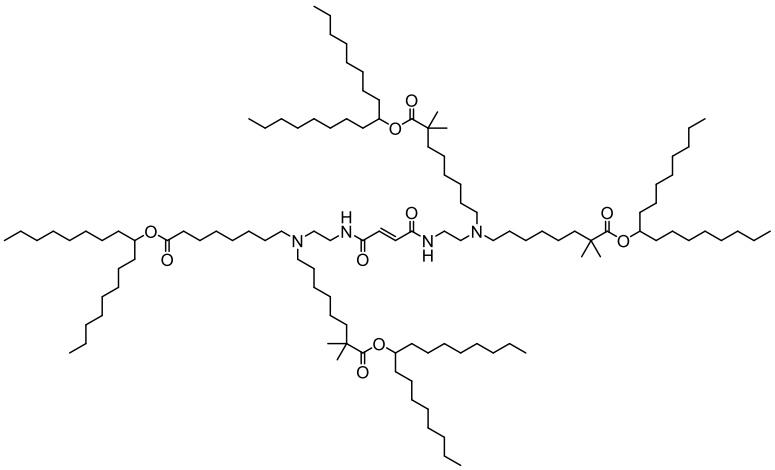
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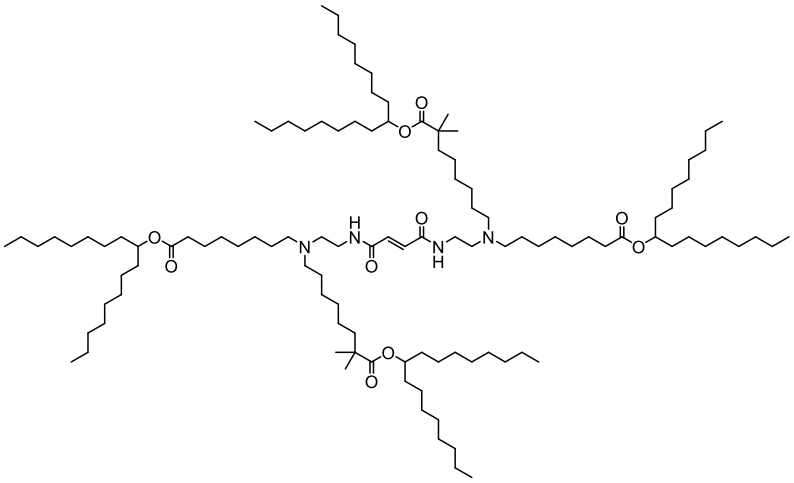
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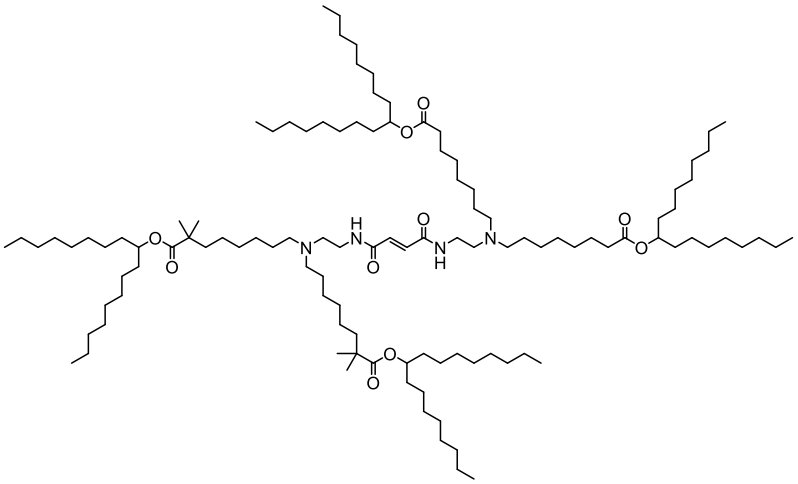
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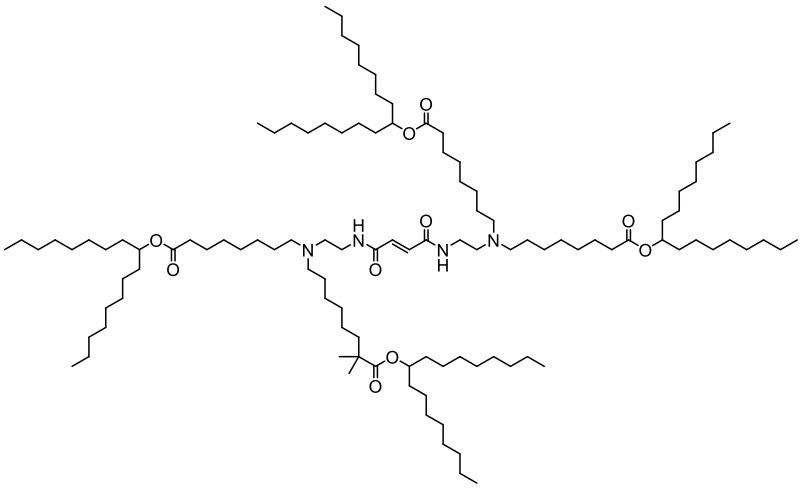
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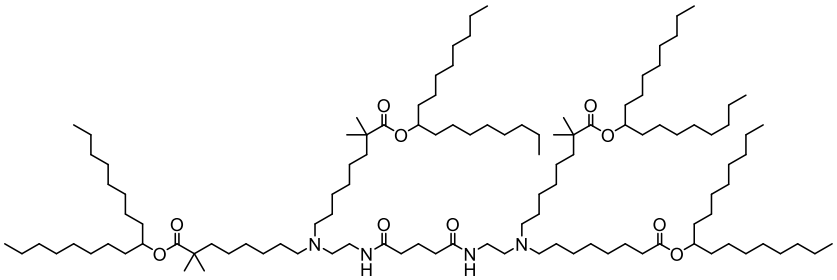
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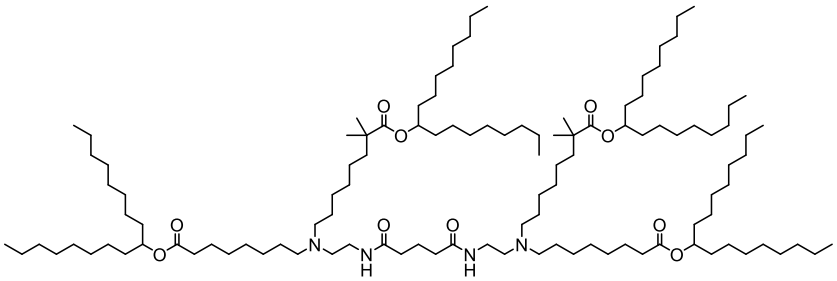
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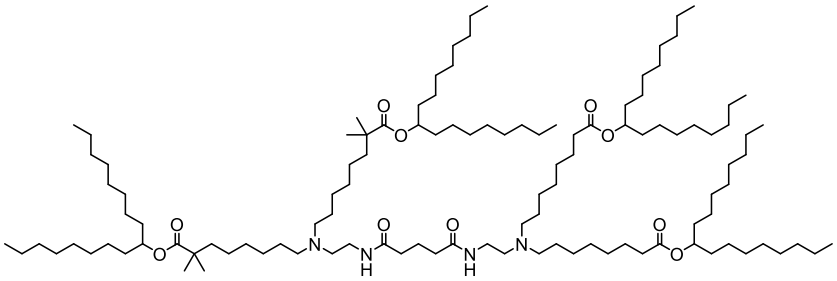
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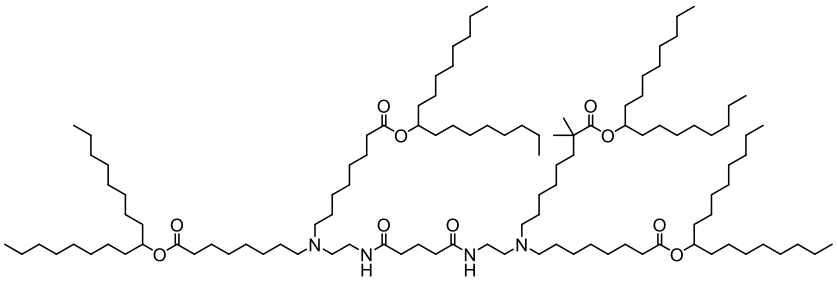
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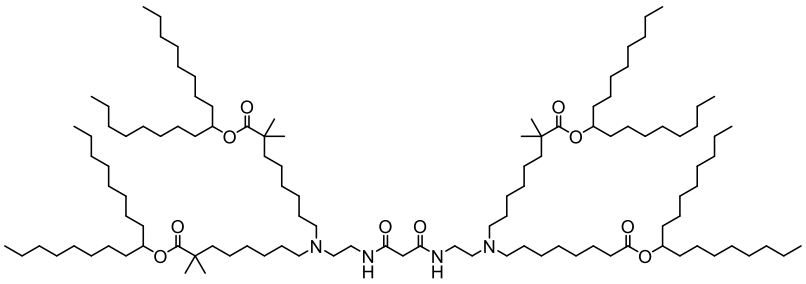
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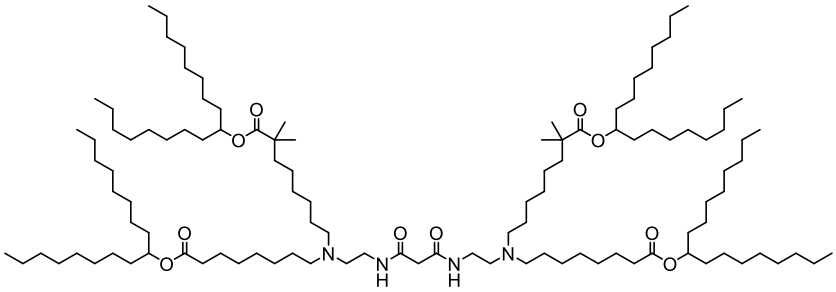
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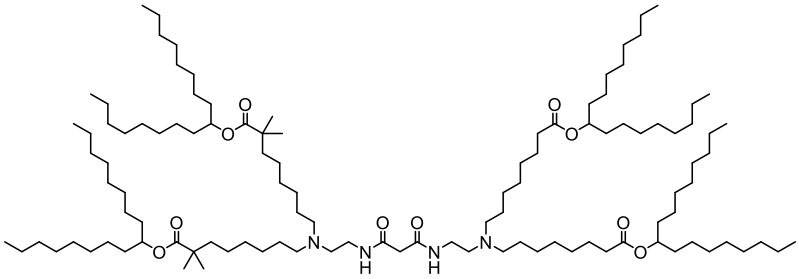
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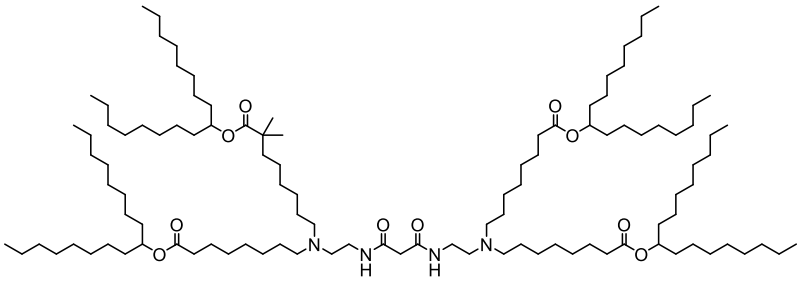
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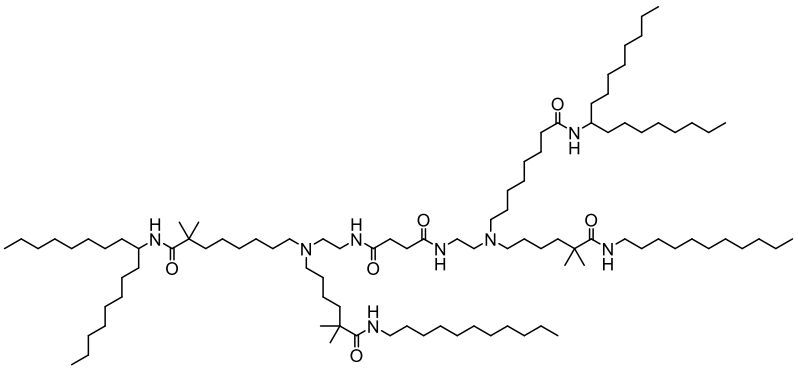
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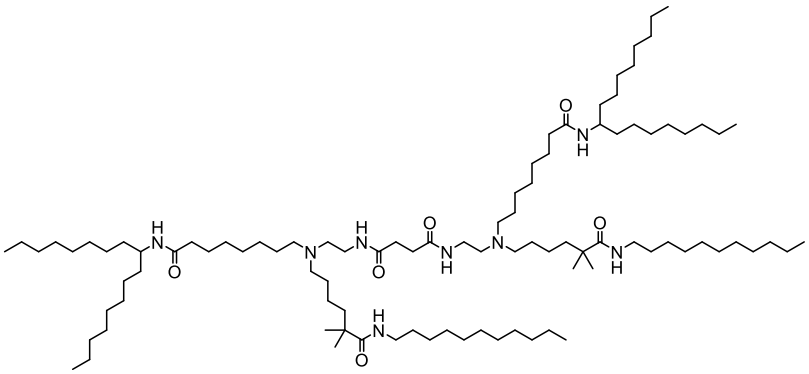
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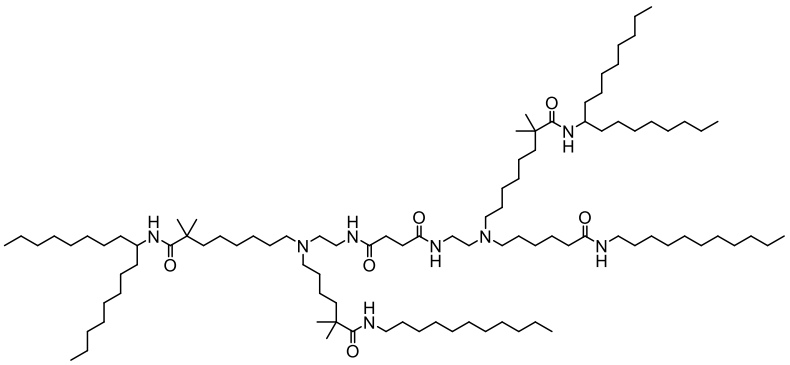
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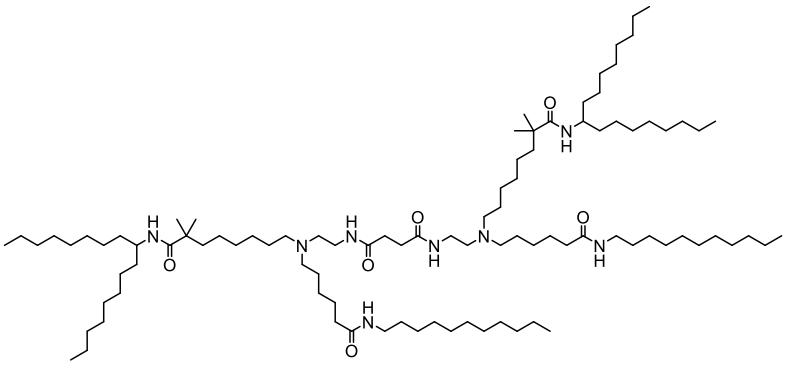
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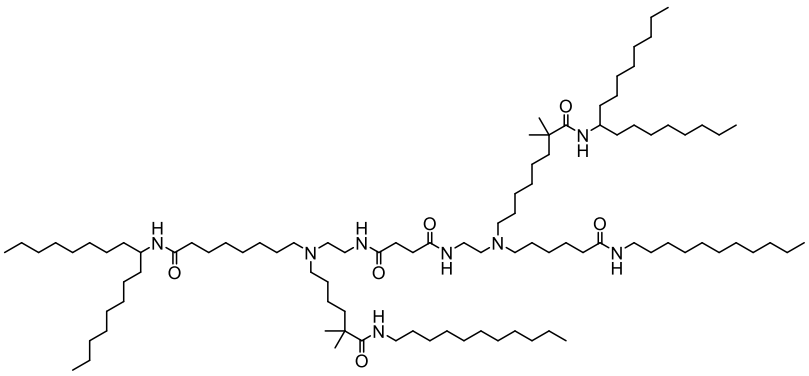
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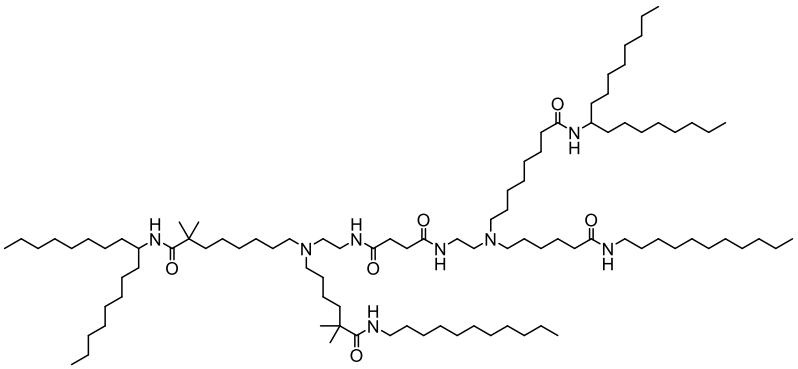
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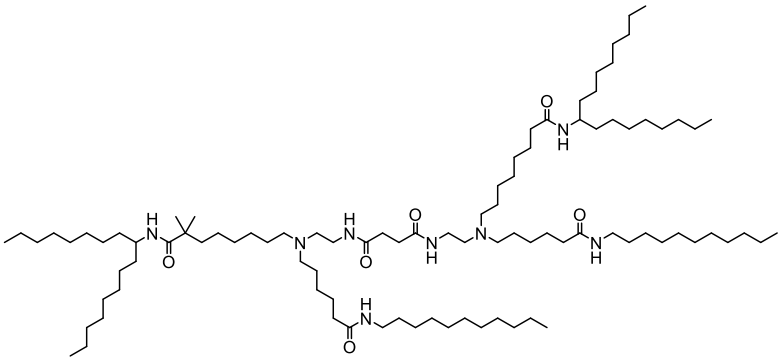
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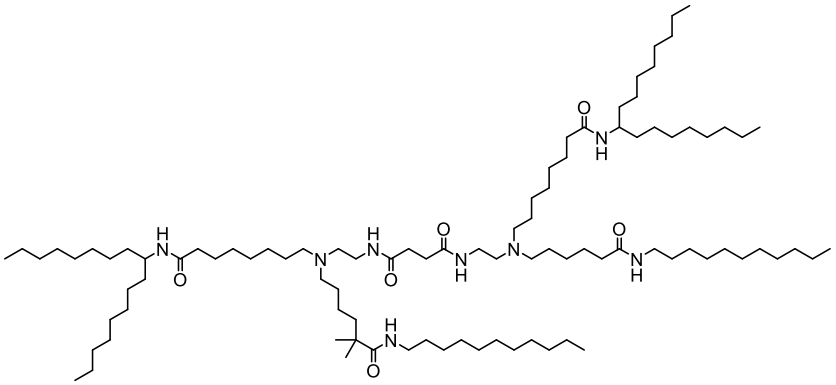
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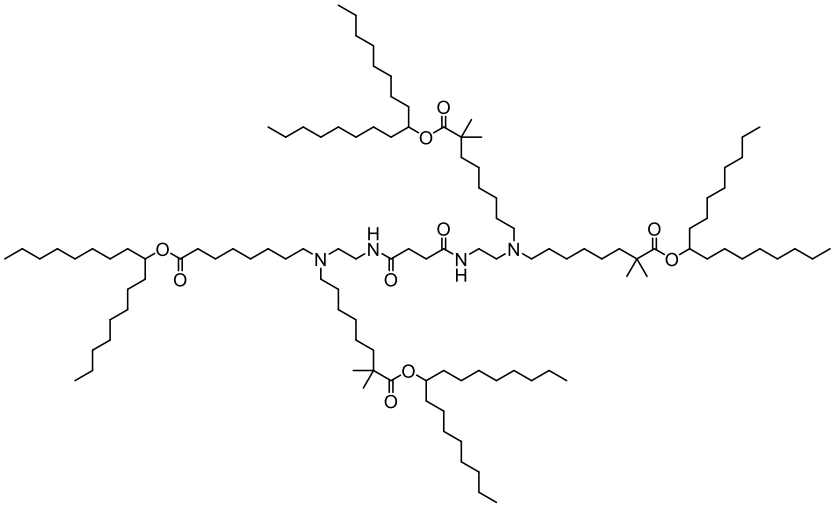
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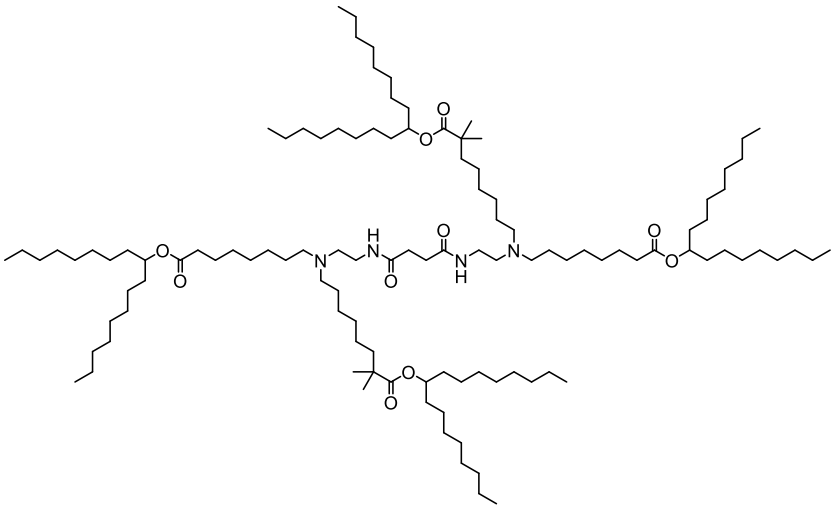
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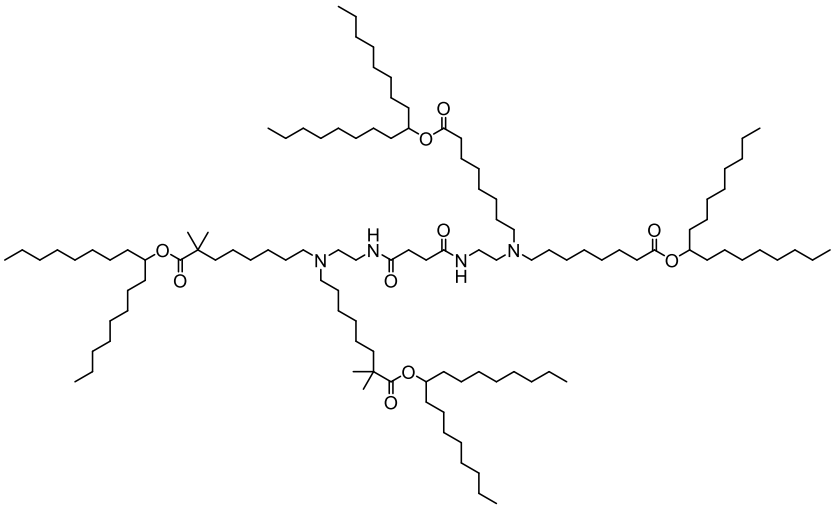
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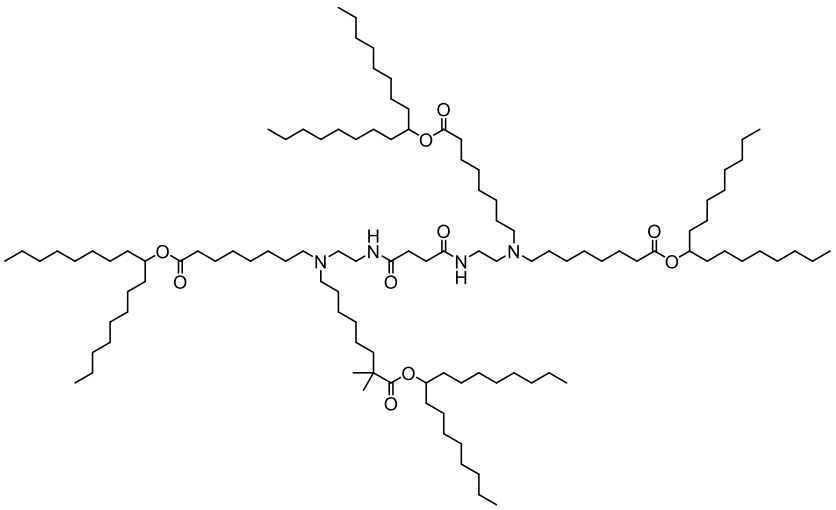
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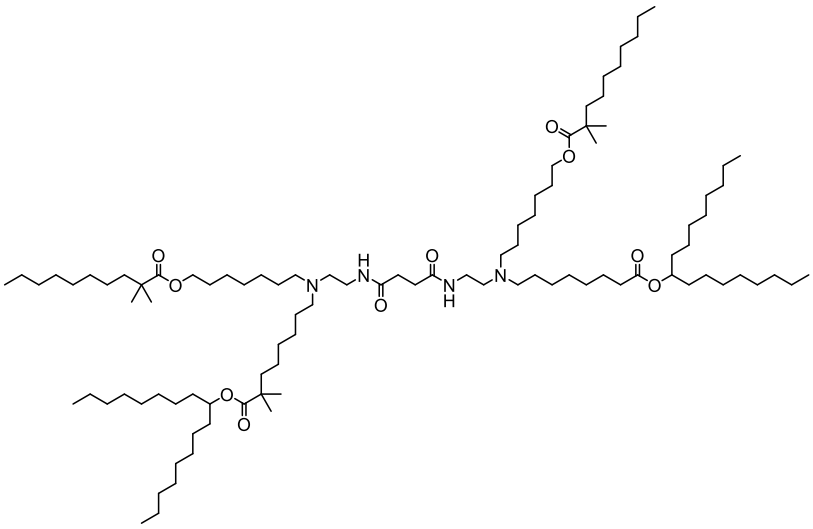
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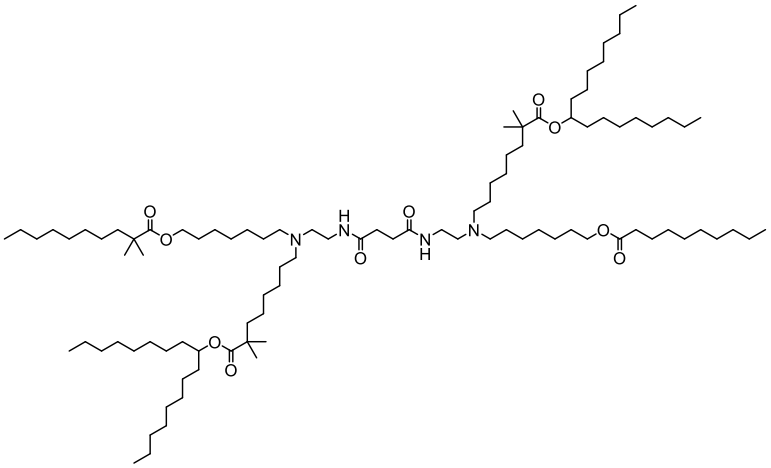
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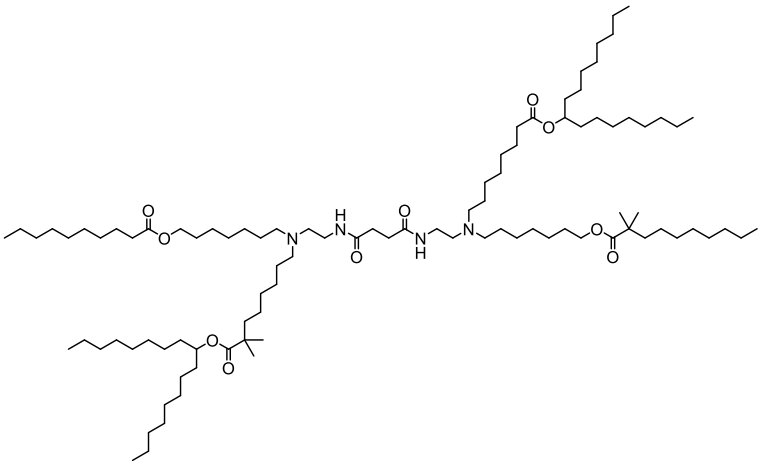
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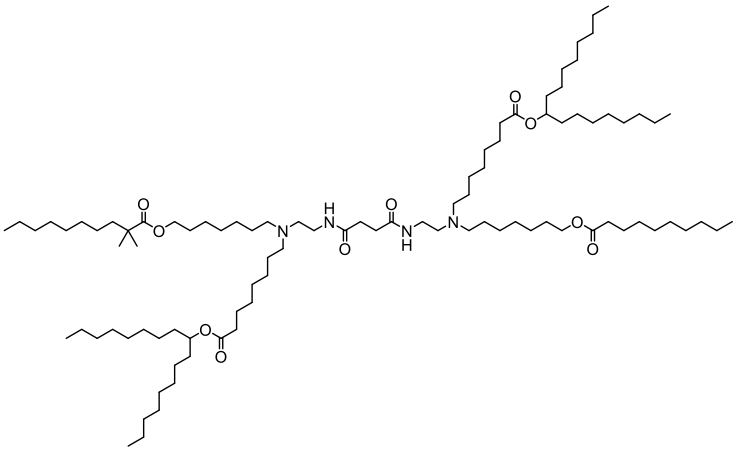
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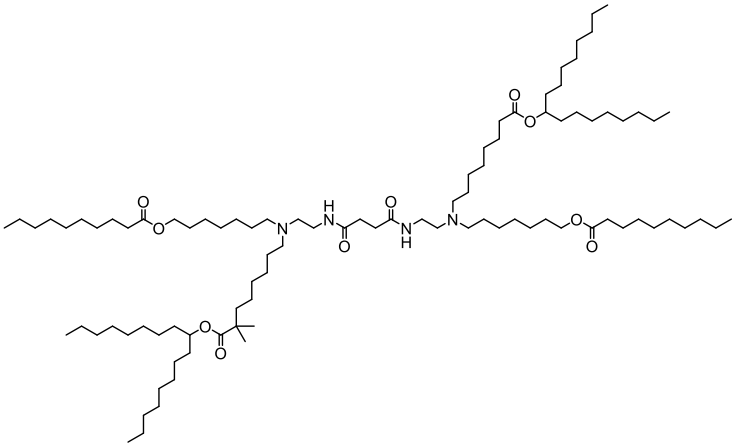
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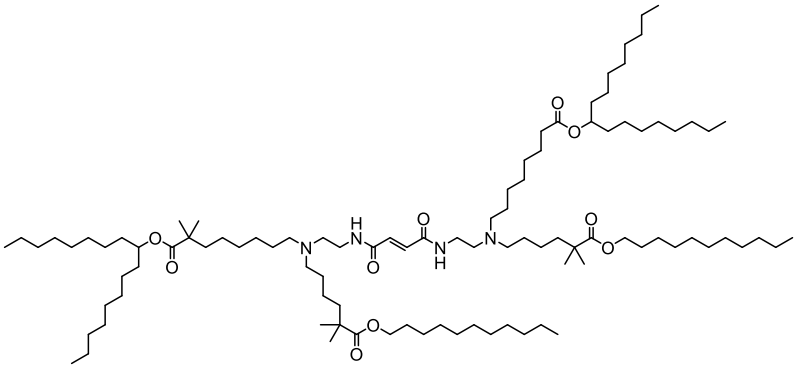
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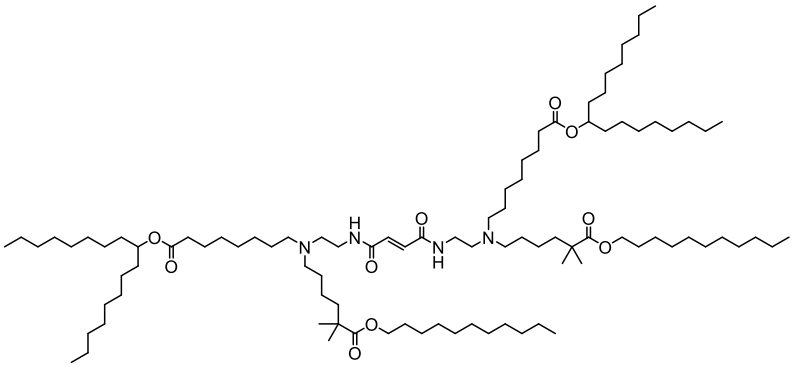
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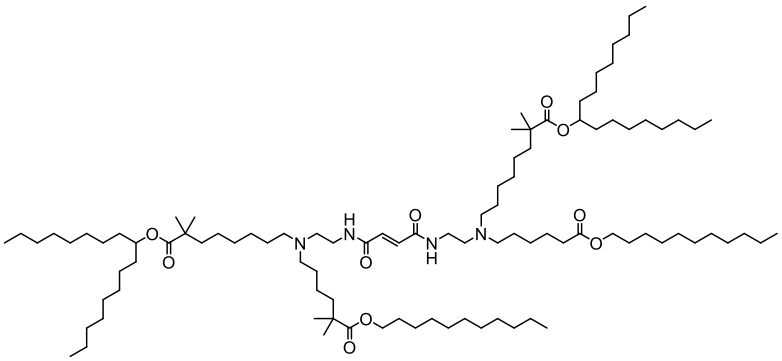
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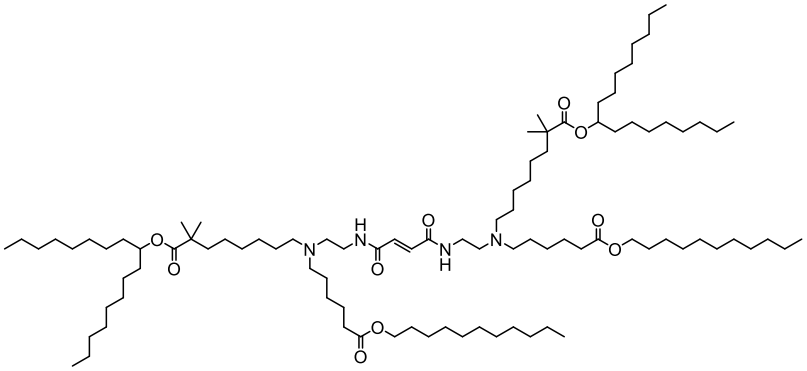
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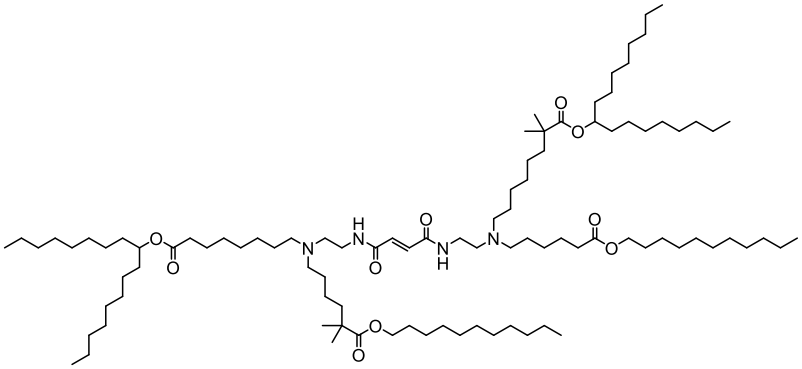
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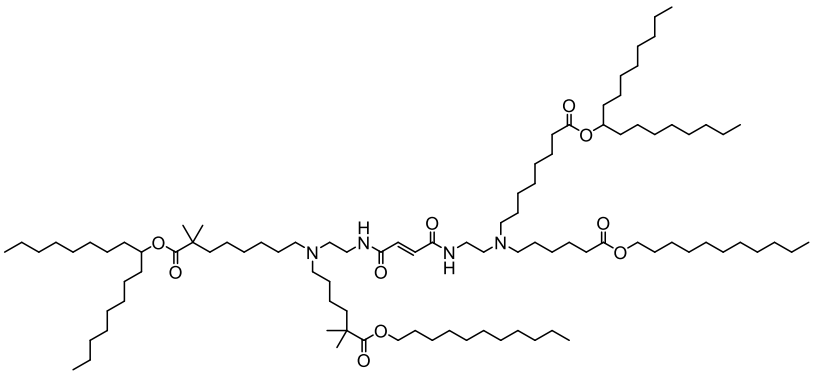
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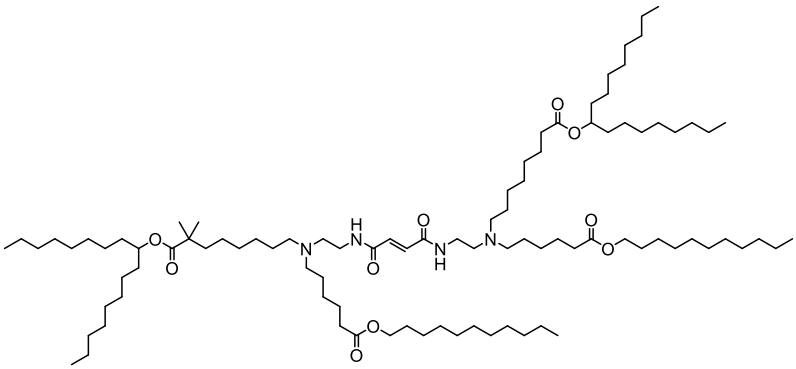
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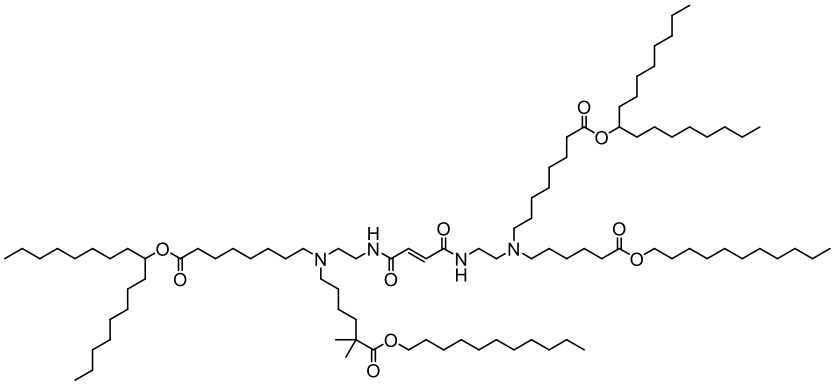
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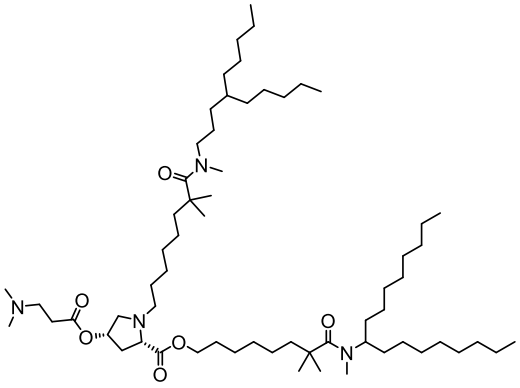
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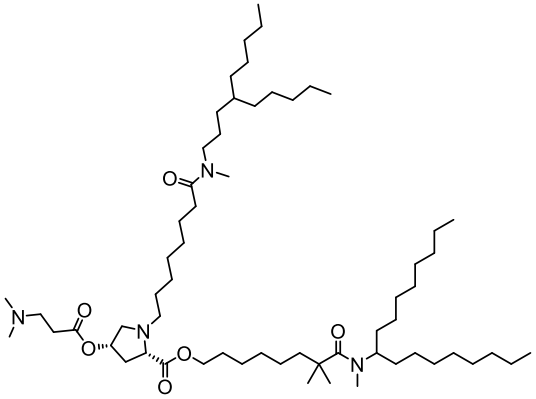
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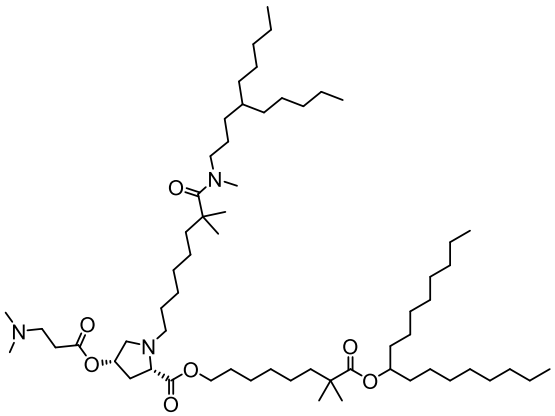
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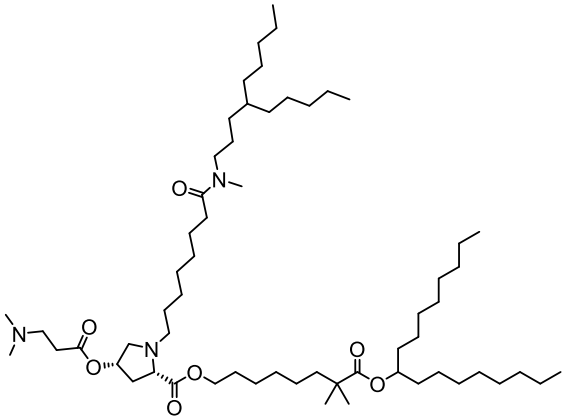
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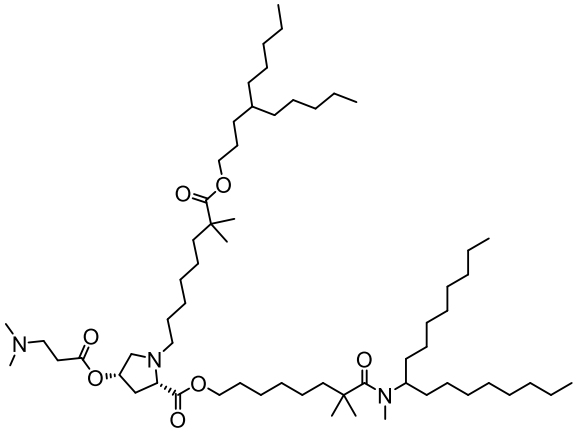
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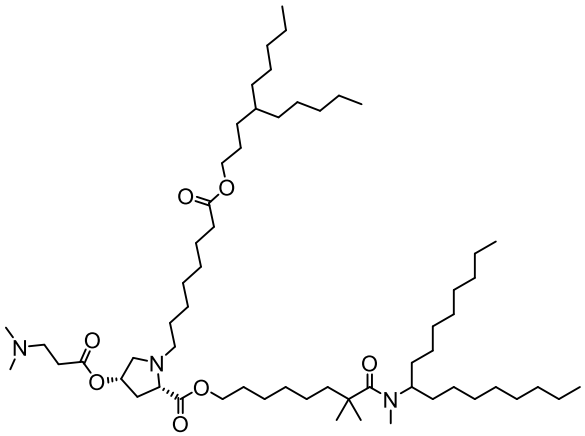
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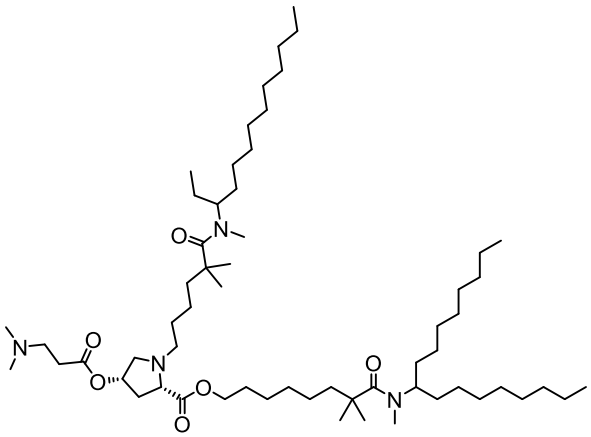
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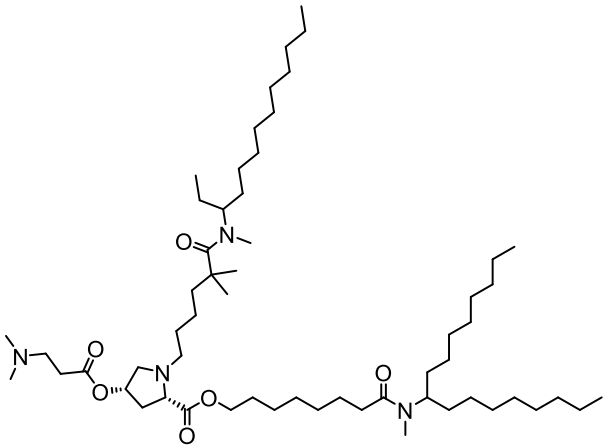
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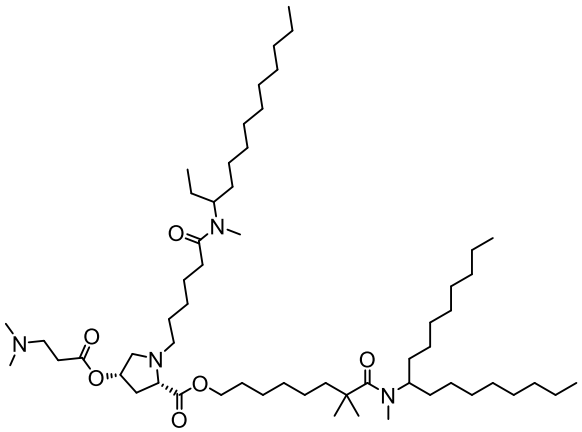
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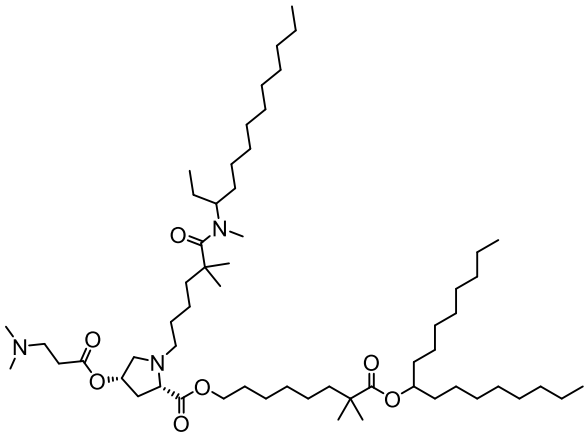
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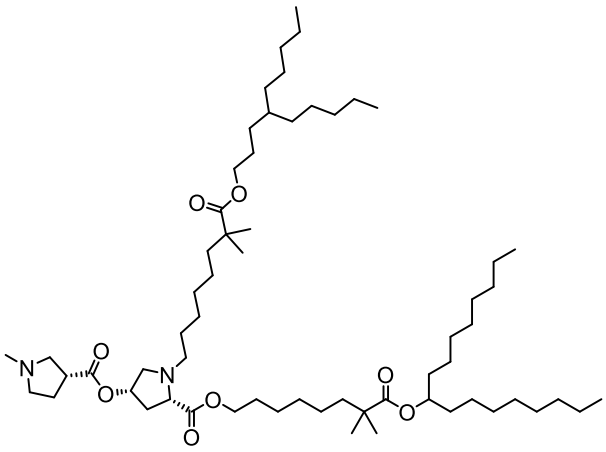
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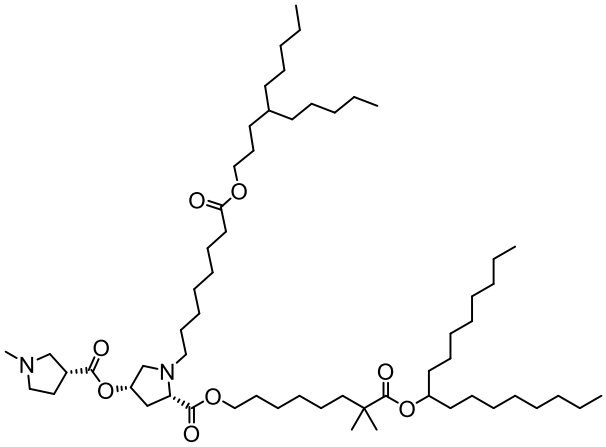
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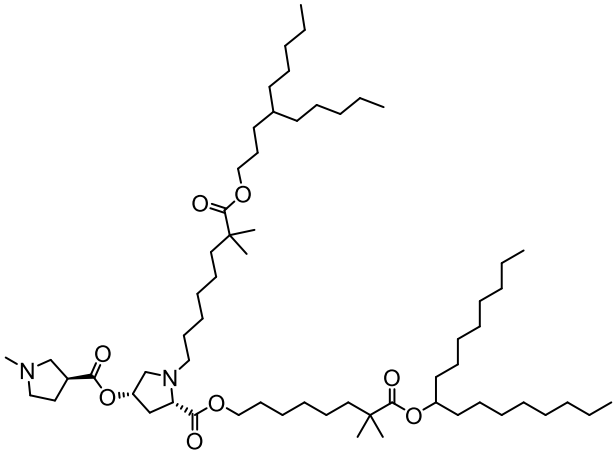
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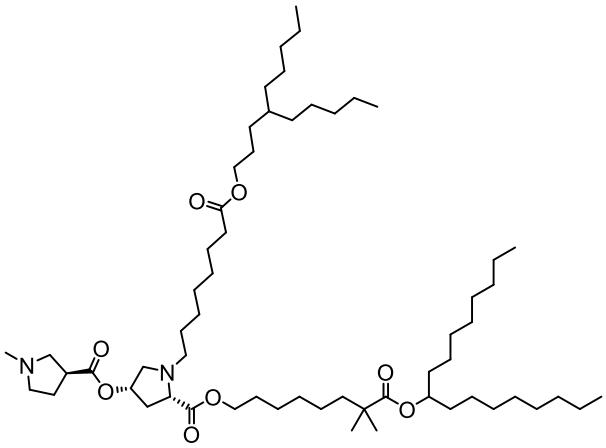
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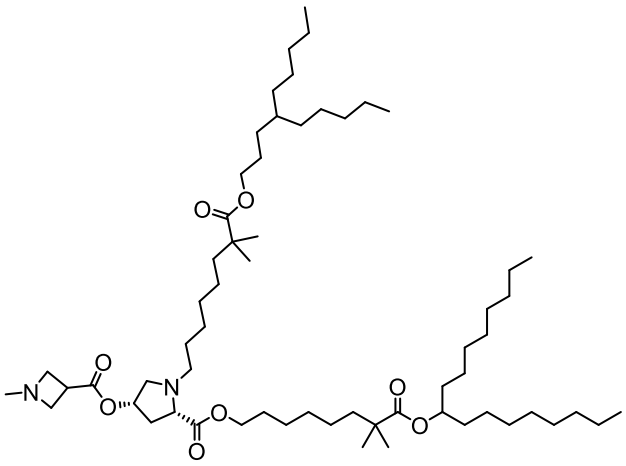
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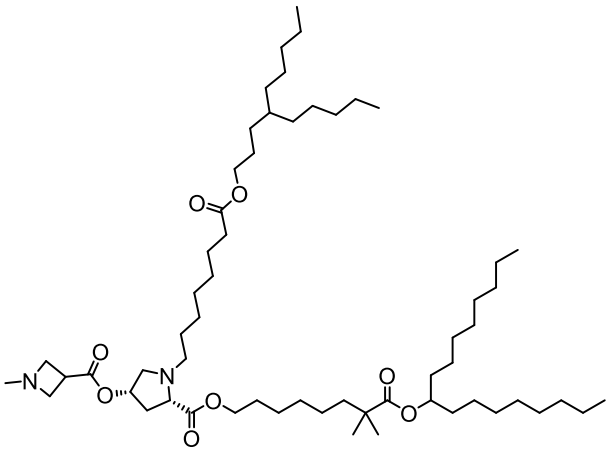
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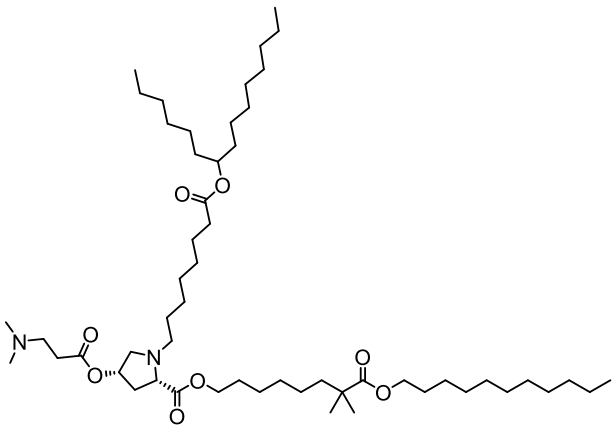
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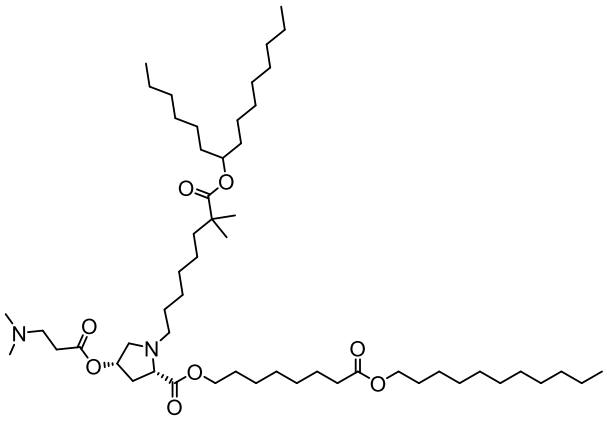
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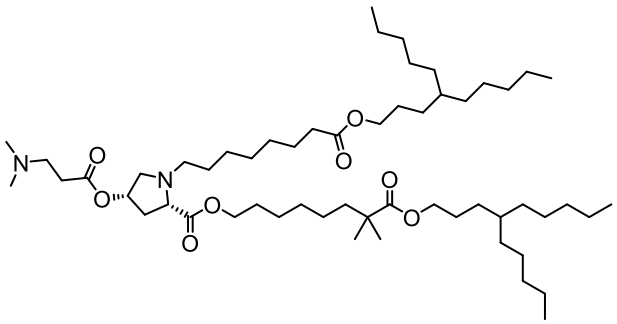
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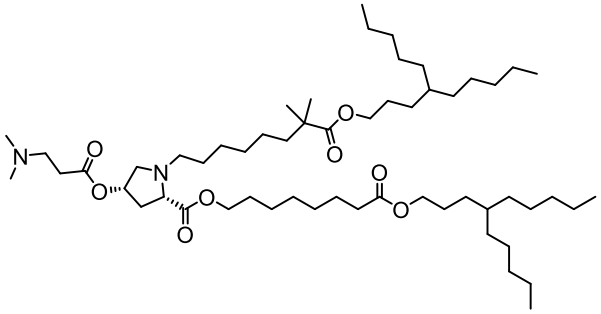
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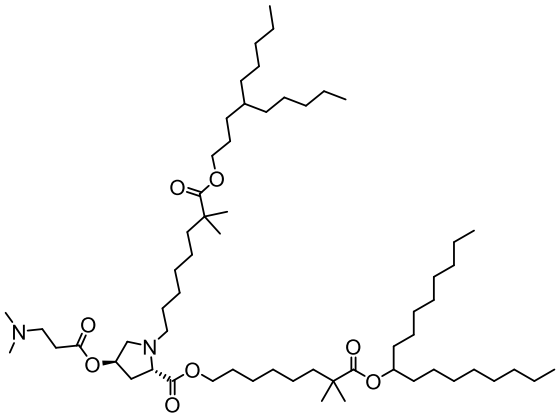
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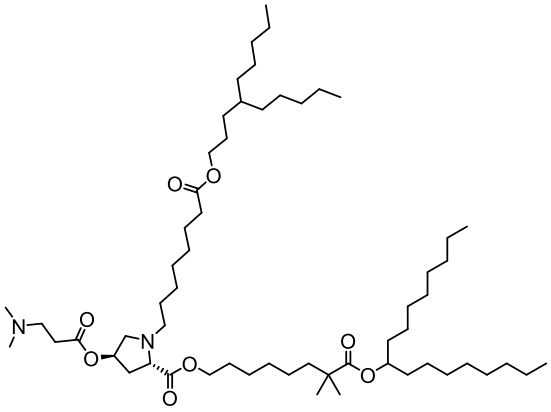
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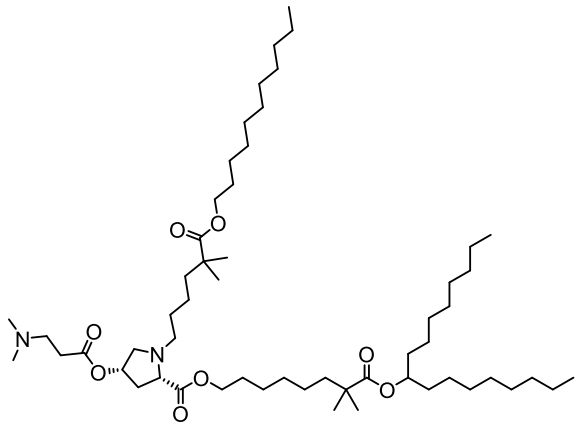
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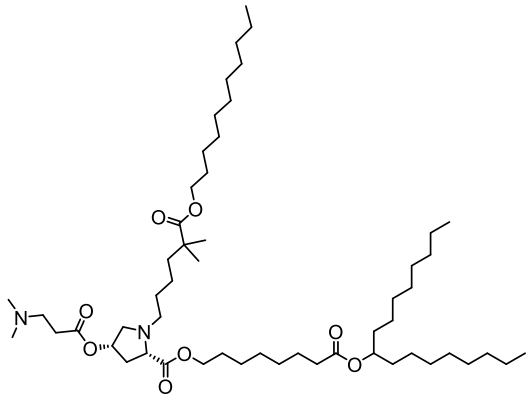
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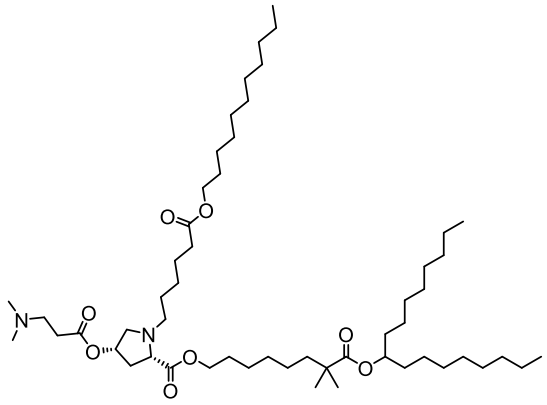
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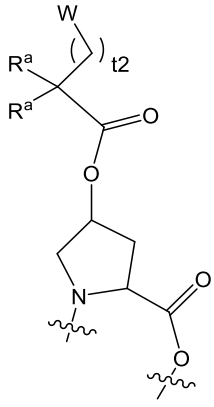
B24



B25



23. A lipid comprising at least two lipophilic tail groups and a head group of formula (G-HC-IIID):



, a pharmaceutically acceptable salt thereof, or a stereoisomer of any of the

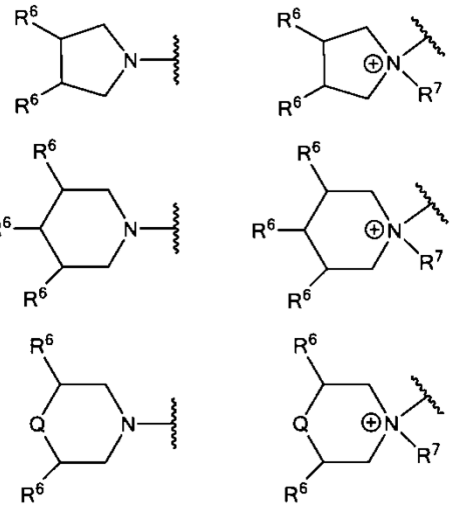
foregoing,

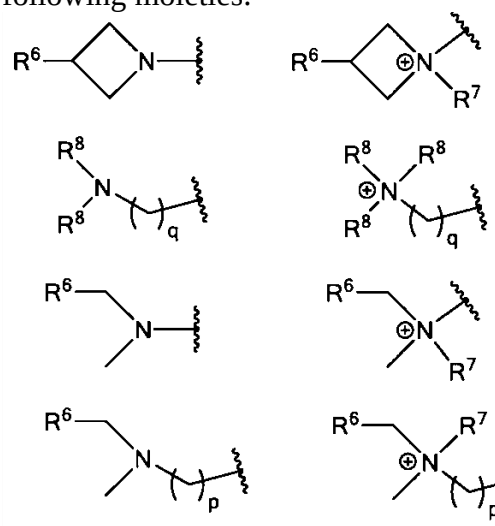
wherein:

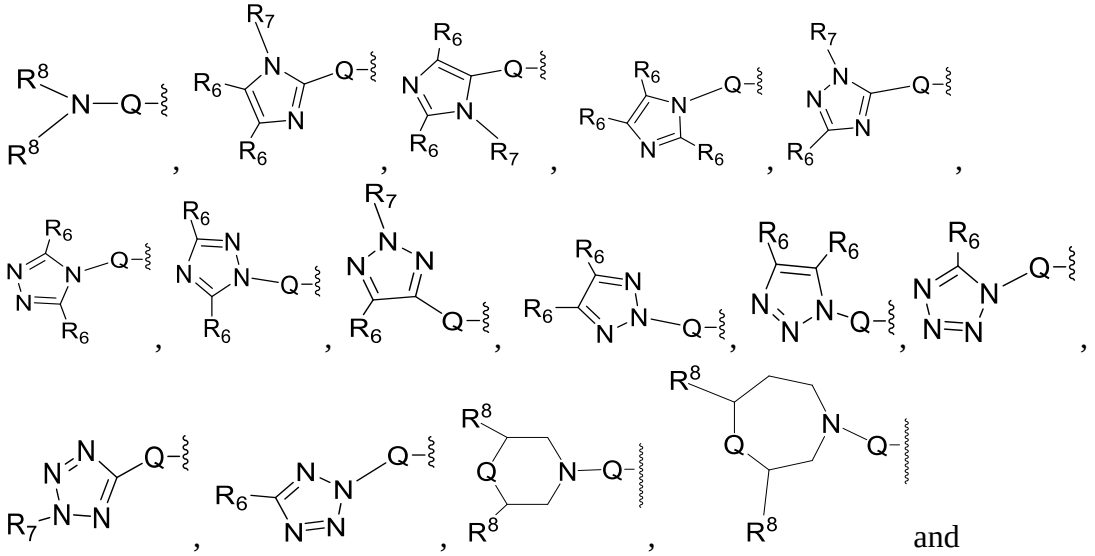
R^a is each independently C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl;

t2 is an integer from 0 to 5;

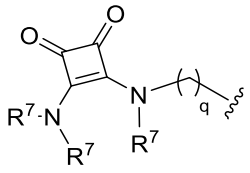
W is hydroxyl, substituted or unsubstituted hydroxyalkyl,or one of the following moieties:







and


, wherein

each Q is independently absent, -O-, -C(O)-, -C(S)-, -C(O)O-, -$C(R^7)_2$-, -C(O)N(R^7)-, -C(S)N(R^7)-, or -N(R^7);

R^6 is independently H, alkyl, hydroxyl, hydroxyalkyl, alkoxy, -O-alkylene-O-alkyl, -O-alkylene-$N(R^7)_2$, amino, alkylamino, aminoalkyl, thiol, thiolalkyl, or $N^+(R^7)_3$–alkylene-Q-;

each R^8 is independently H, alkyl, hydroxyalkyl, amino, aminoalkyl, alkylamino, thiol, thiolalkyl, heterocyclyl, heteroaryl; or two R^8 together with the nitrogen atom form a ring, optionally substituted with one or more alkyl, hydroxy, hydroxyalkyl, alkoxy, alkylaminoalkyl, alkylamino, or aminoalkyl;

q is 0, 1, 2, 3, 4, or 5; and

p is 0, 1, 2, 3, 4, or 5; and


represents the bond connecting the head group to the tail groups.

24. A composition comprising the lipid of any one of claims 1-23, and one or more lipid components different than the lipid, optionally wherein the composition is a LNP composition.

25. The composition of claim 24, wherein the lipid component comprises one or more of a sterol, a PEG lipid, a phospholipid, and a neutral lipid.

26. A pharmaceutical composition comprising a composition of any one of claims 1-25; a therapeutic agent selected from the group consisting of a nucleic acid molecule, a protein, and a small molecule drug; and a pharmaceutically acceptable excipient.

27. The pharmaceutical composition of claim 26, wherein the therapeutic agent is an RNA or DNA; optionally wherein the therapeutic agent is a RNA comprising a mRNA.