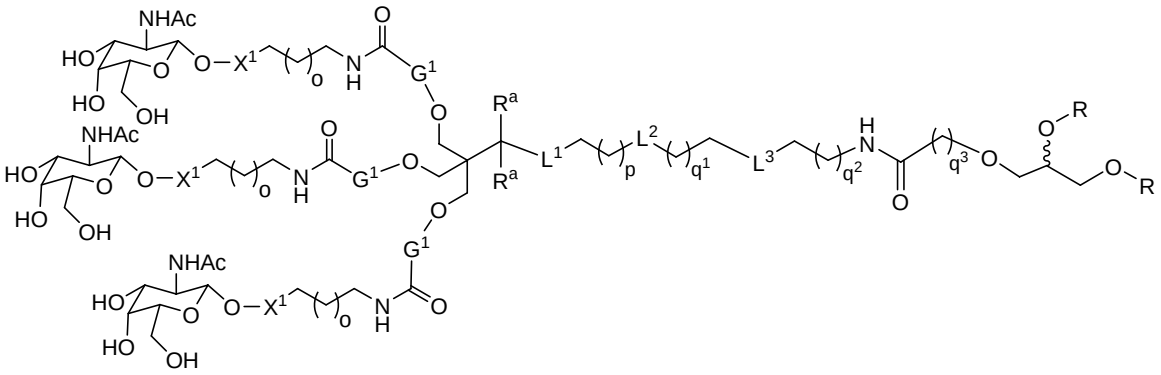
SUMMARY

[0007] The present disclosure provides lipid nanoparticle (LNP) compositions. In some examples, the LNP compositions comprise a lipid that comprises a compound described herein. In some examples, the compound described herein is a GalNAc-based lipid.

[0008] An aspect of the present disclosure provides compounds of Formula I:



Formula I

wherein,

each X^1 is independently $–(CH_2)_r–$, $–(CH_2CH_2O)_s–$, $–(OCH_2CH_2)_s–$, $–((CH_2)_m–C(O)NH)–$, or $–(C(O)NH–(CH_2)_m)–$,

each subscript "m" is independently 1-5;

each subscript "o" is independently 1-5;

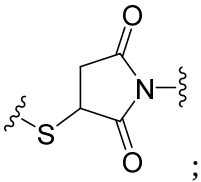
each subscript "r" is independently 1-10;

each subscript "s" is independently 1-5;

each G^1 is independently a C_1-C_6 substituted or unsubstituted alkylene;

each R^a is independently H or a C_1-C_6 substituted or unsubstituted alkyl;

L^1 is –NHC(O)–, –C(O)NH–, –NHC(O)O–, –OC(O)NH–, –NHC(O)NH–, –S-S–, or



;

subscript "p" is independently 1-5;

L^2 is $–O-(CH_2CH_2O)_n–$, $–(CH_2CH_2O)_n-O–$, or $–(OCH_2CH_2O)_n–$,

each subscript "n" is independently 1-200;

subscript "q^1" is independently 0-5;

subscript "q^2" is independently 0-5;

L^3 is absent, –NHC(O)–, or –C(O)NH–;

subscript "q^3" is independently 0-5;

each R is independently a C_{12}-C_{20} substituted or unsubstituted alkyl; and

each Y^1 is independently –NH–, –NHC(O)O–, –OC(O)NH–, –NHC(O)–, or –C(O)NH–;

each Y^2 is independently absent, $–(CH_2)_r–$, $–(CH_2CH_2O)_t–$, or $–(OCH_2CH_2)_t–$;

each subscript "t" is independently 1-5;

each Y^3 is independently absent, –NHC(O)–, or –C(O)NH–;

each Y^4 is independently absent or $–(CH_2)_r–$;

each subscript "r" is independently 1-10;

each subscript "d" is independently 0-5;

each subscript "c" is independently 0-5;

subscript "n" is independently 1-200;

subscript "a" is 1-5;

subscript "b^1" is independently 0-5;

M^2 is absent, –NHC(O)–, or –C(O)NH–;

subscript "b^2" is independently 0-5;

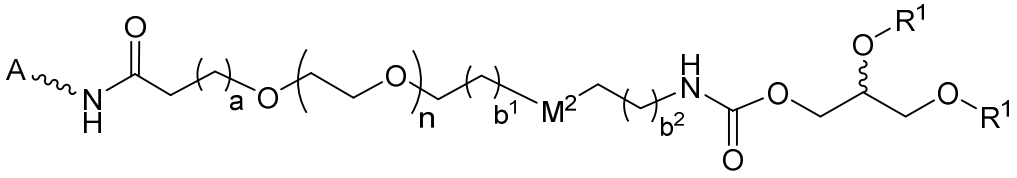
subscript "q^4" is independently 0-6;

each R^1 is independently a C_{12}-C_{20} substituted or unsubstituted alkyl; and

each of the "〰" bonds independently indicate an *R* configuration or an *S* configuration;

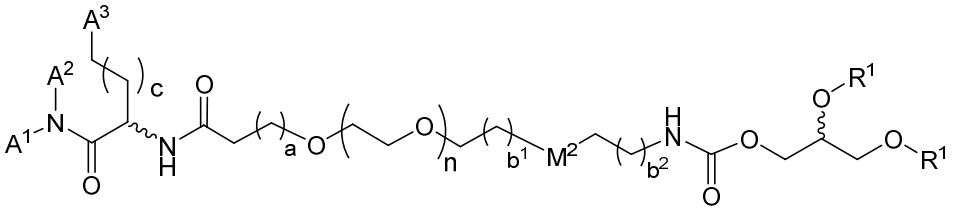
with the proviso that (1) A^1 and A^2 are the same and (2) at least one of Y^2, Y^3 and Y^4 is present.

[0011] In some examples, a compound of Formula II is a compound of Formula II-a:

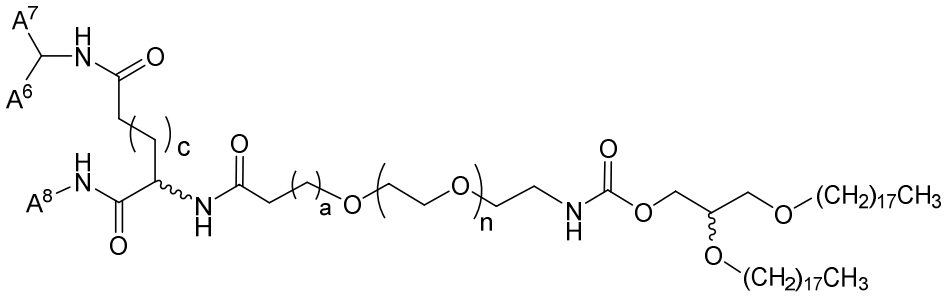


Formula II-a.

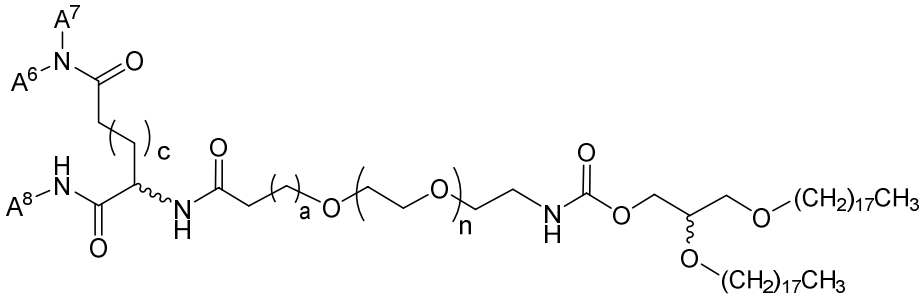
[0012] In some examples, a compound of Formula II-a is a compound of Formula II-a-1, Formula II-a-2, Formula II-a-3, Formula II-a-4, Formula II-a-5, or Formula II-a-6:



Formula II-a-1,

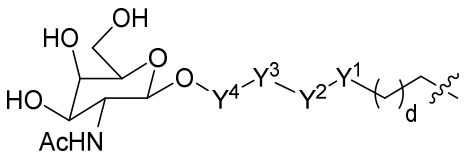


Formula III, or



Formula IV

wherein,

each A^6, A^7, and A^8 is independently  ;

each Y^1 is independently absent, –NHC(O)O–, or –OC(O)NH–;

each Y^2 and Y^4 is independently $–(CH_2)_r–$;

each subscript "r" is independently 1-10;

each Y^3 is independently absent, –NHC(O)–, or –C(O)NH–;

each subscript "d" is independently 1-5;

each subscript "c" is independently 1-5;

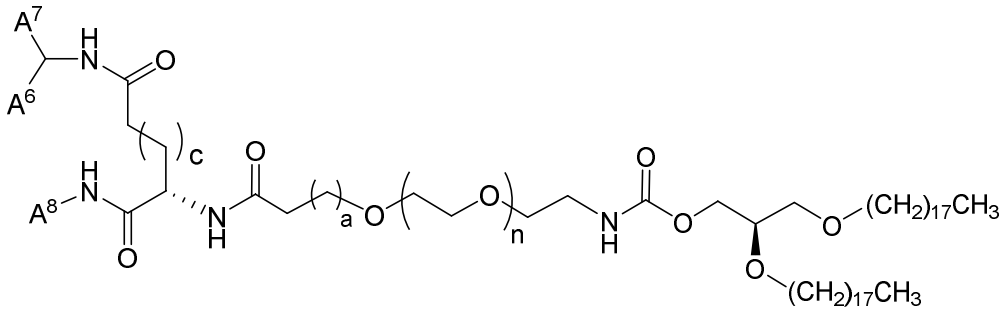
subscript "a" is 1-5;

subscript "n" is independently 10-100; and

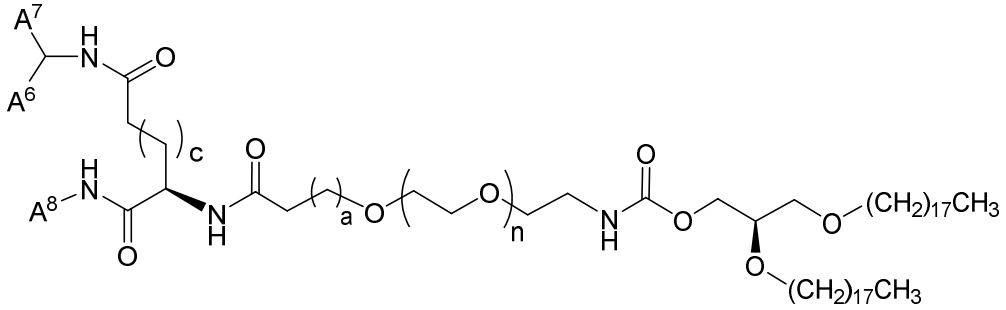
each of the "〰" bonds independently indicate an *R* configuration or an *S* configuration;

with the proviso that at least one of Y^1 or Y^3 is present.

[0014] In some examples a compound of Formula III is a compound Formula III-a or Formula III-b:

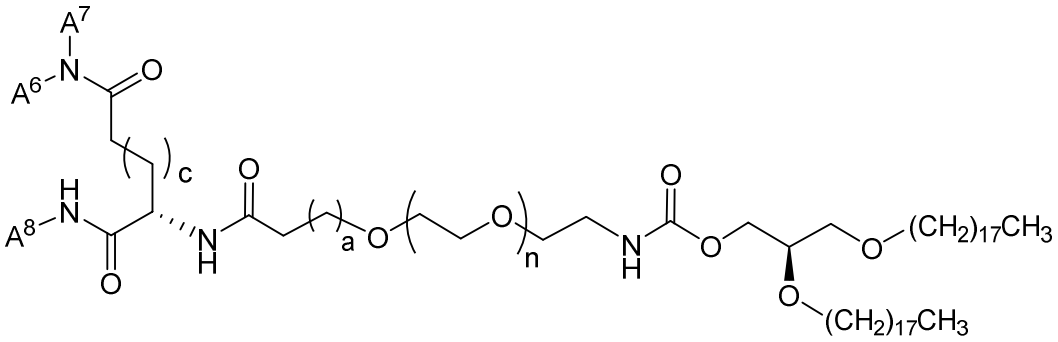


Formula III-a, or

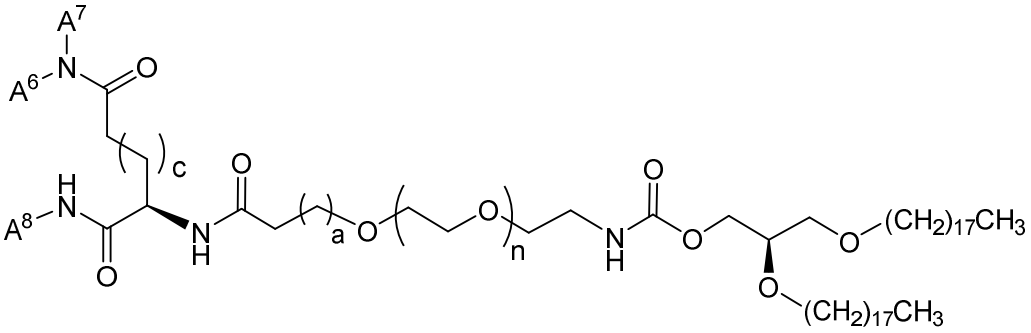


Formula III-b.

[0015] In some examples, a compound of Formula IV is a compound of Formula IV-a or Formula IV-b:

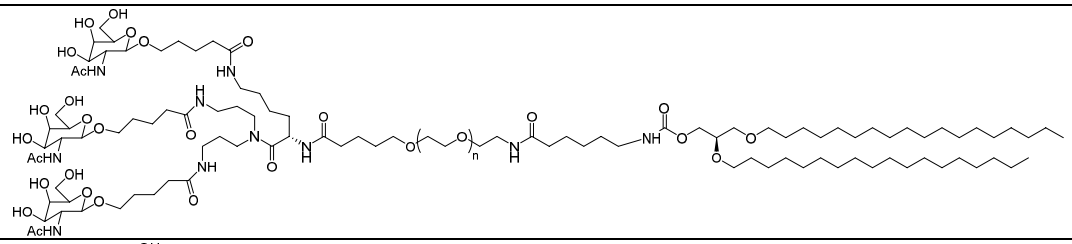
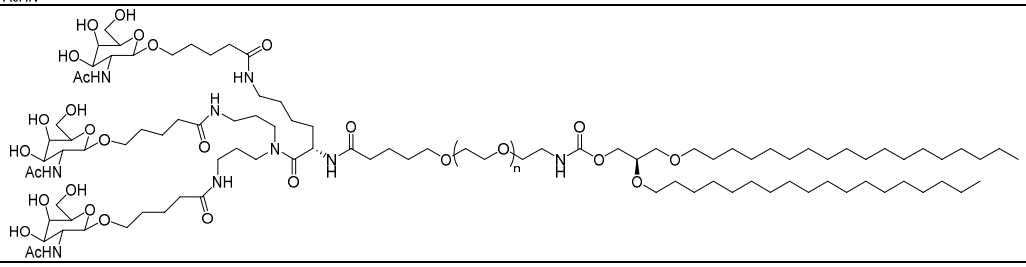
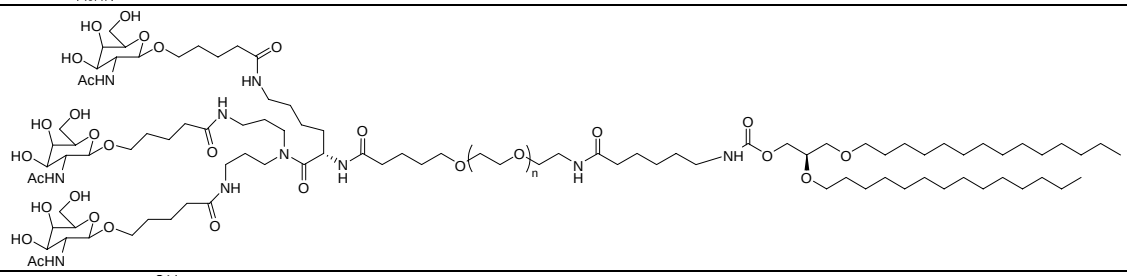
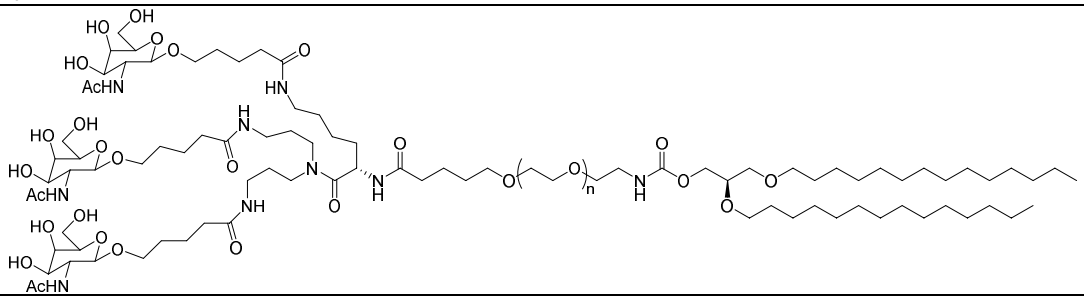
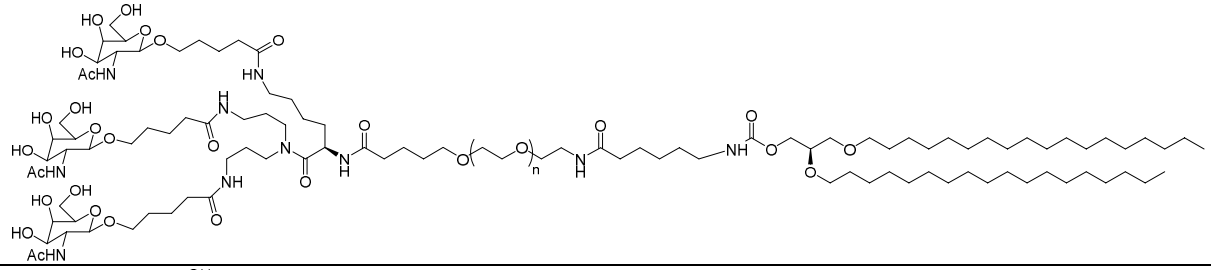
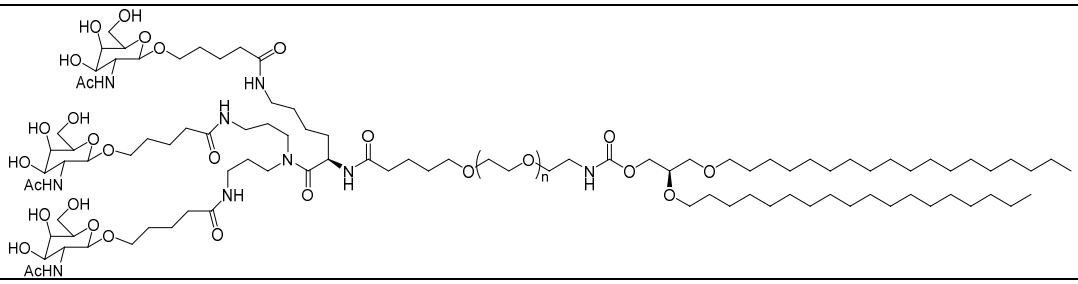


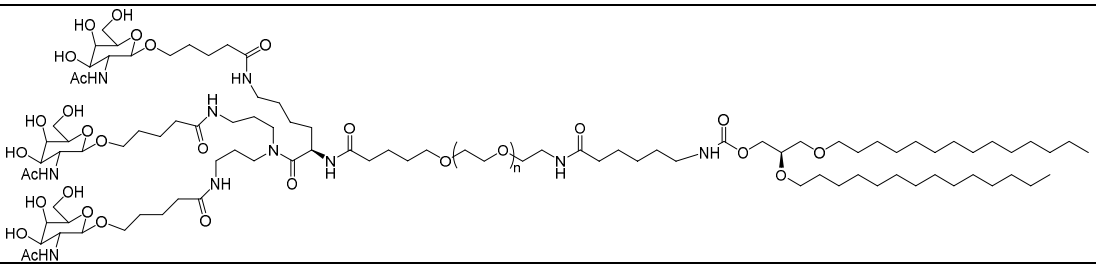
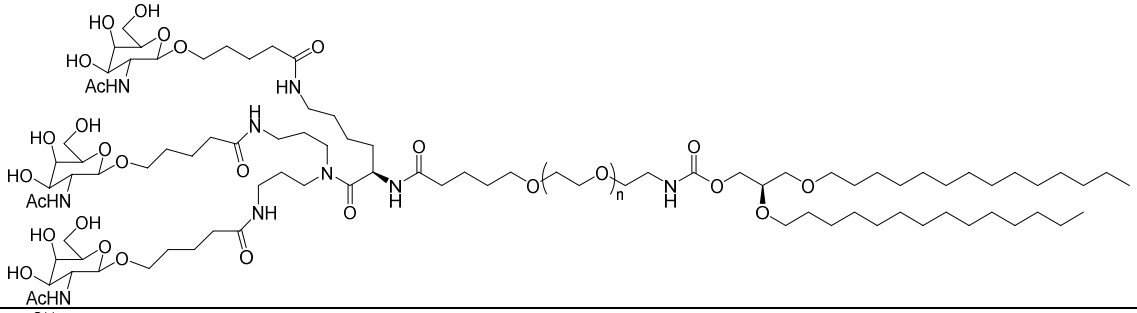
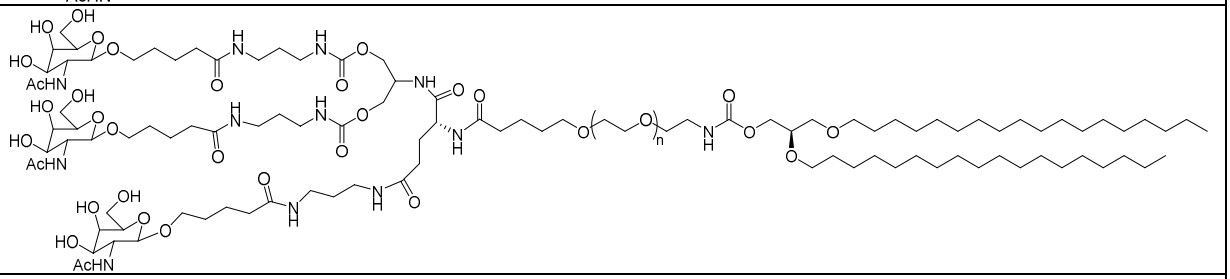
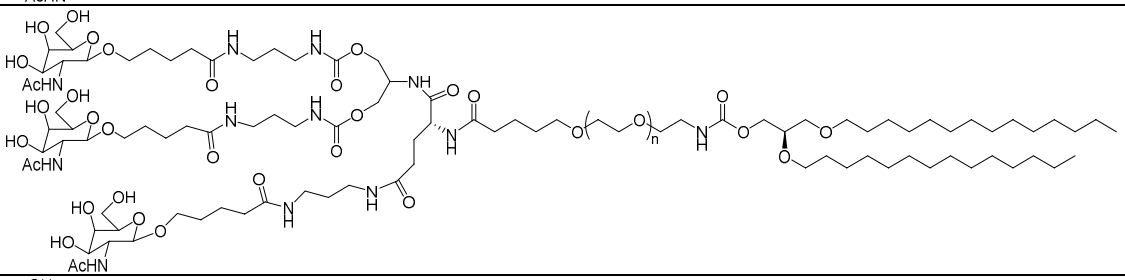
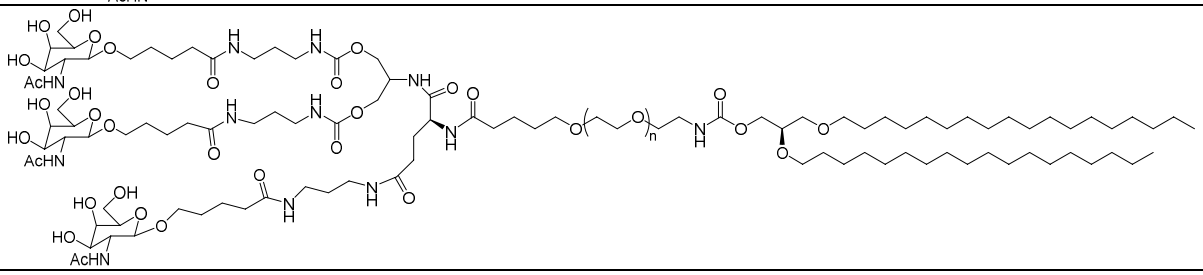
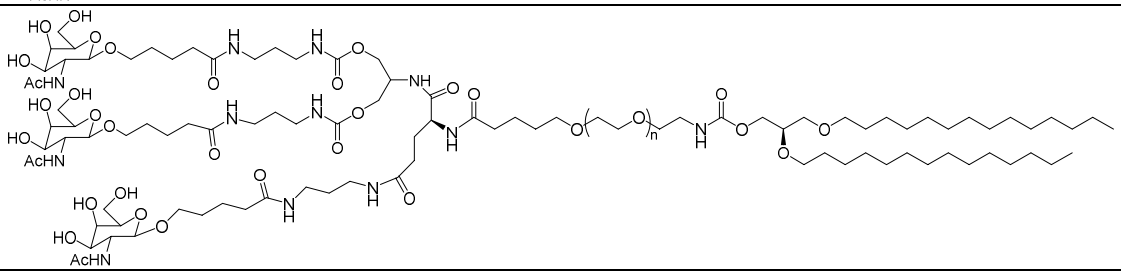
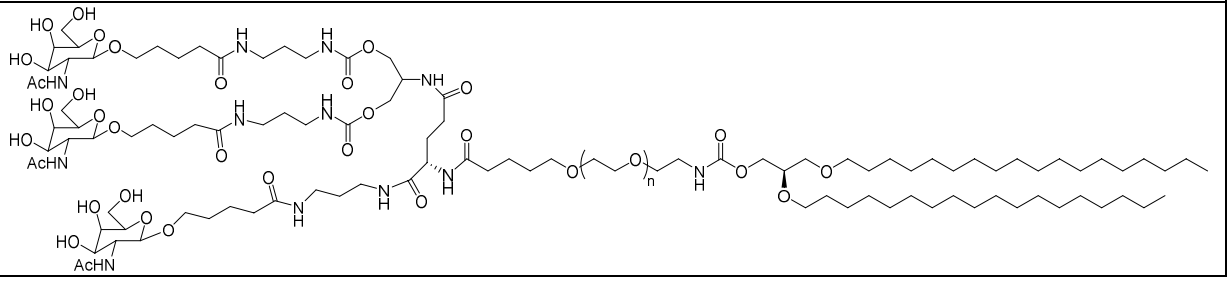
Formula IV-a, or

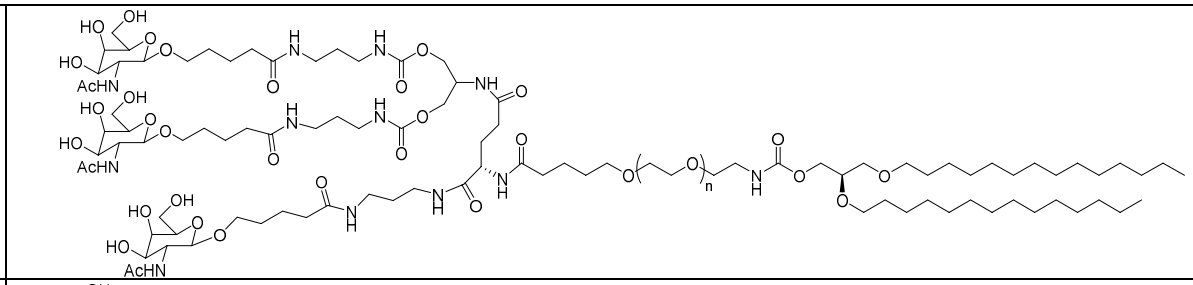
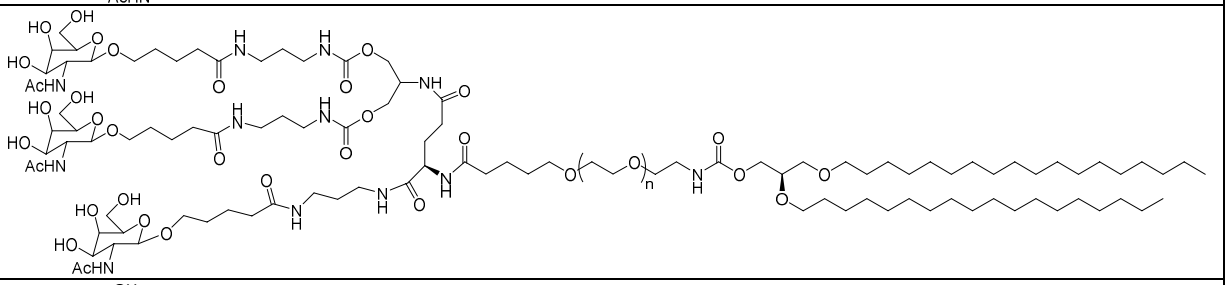
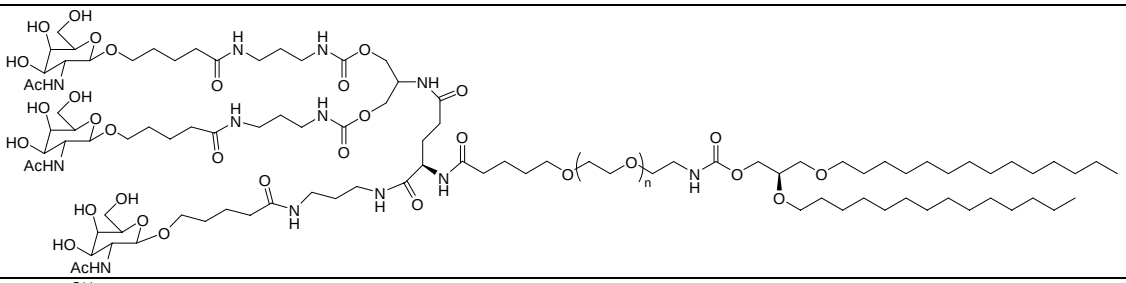
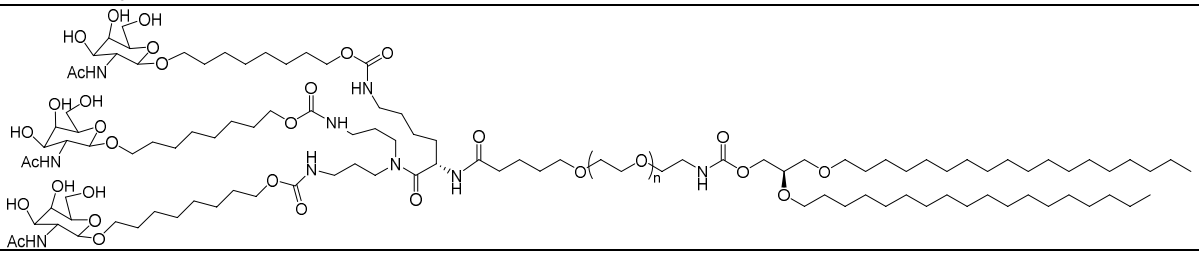
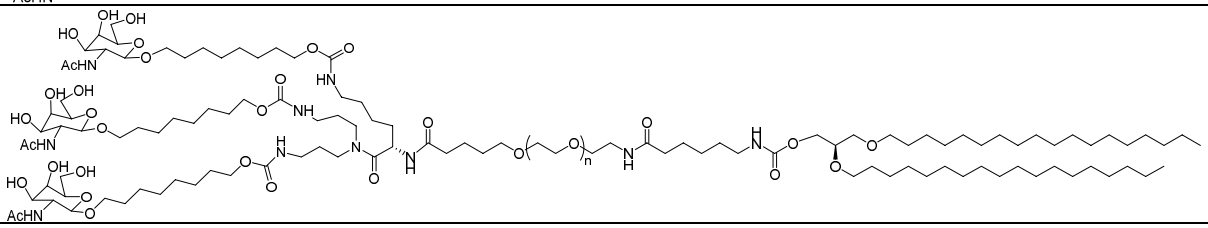
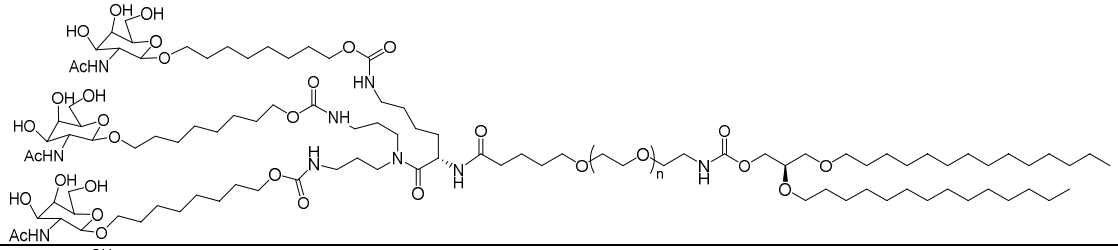
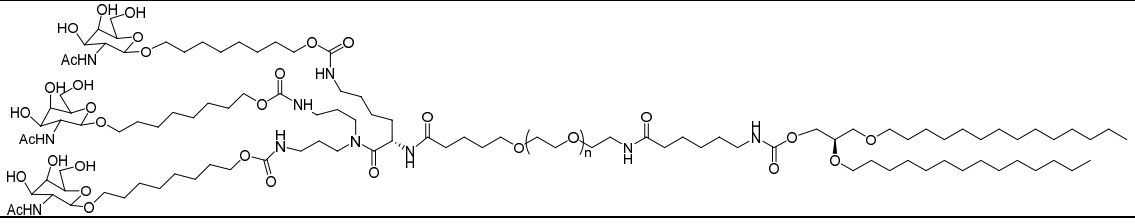


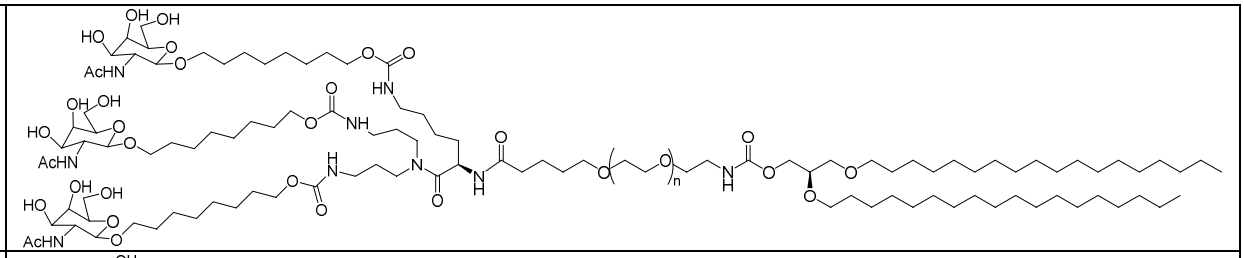
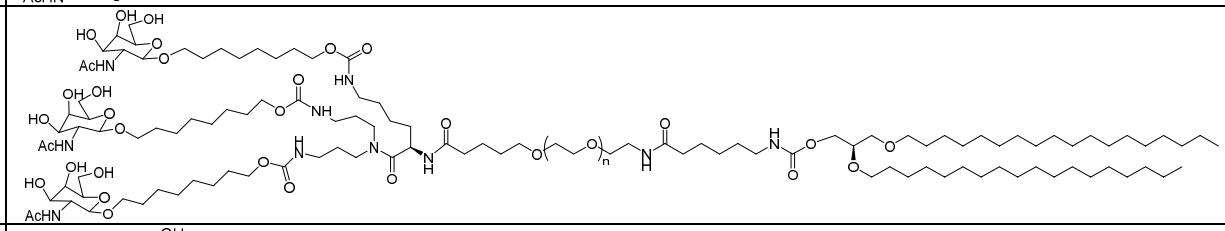
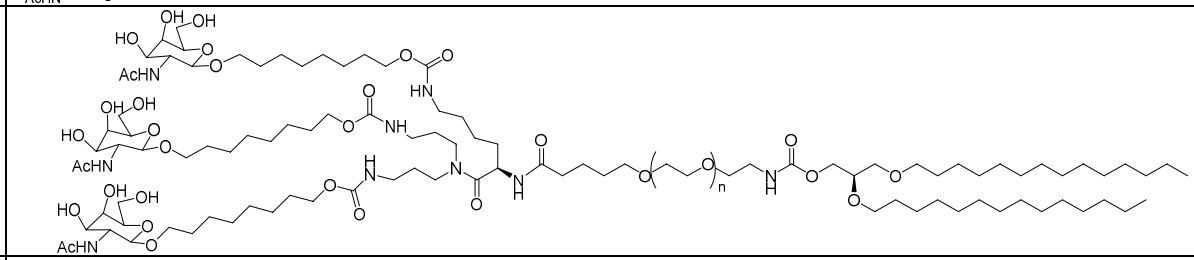
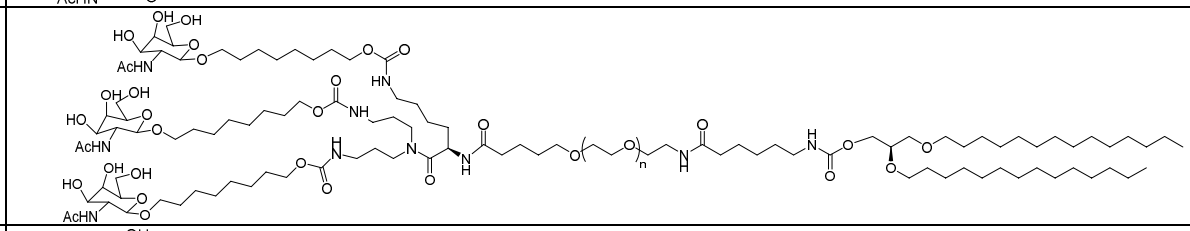
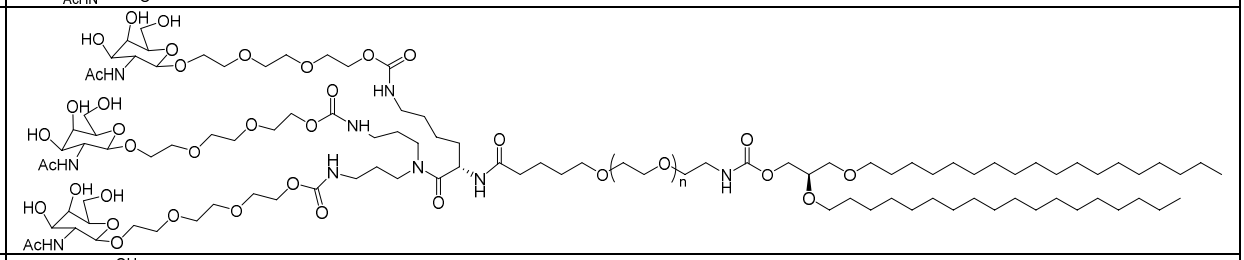
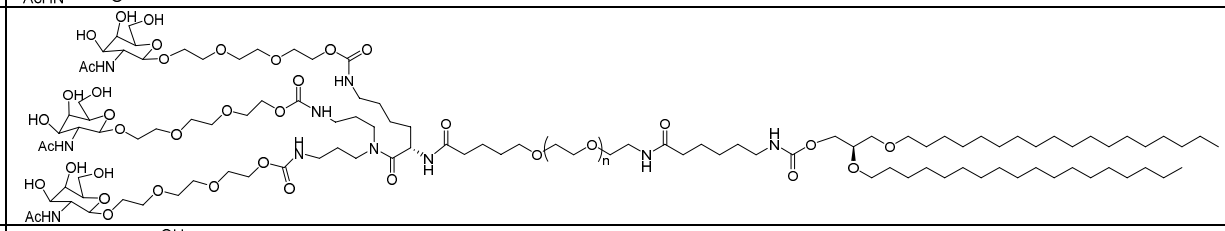
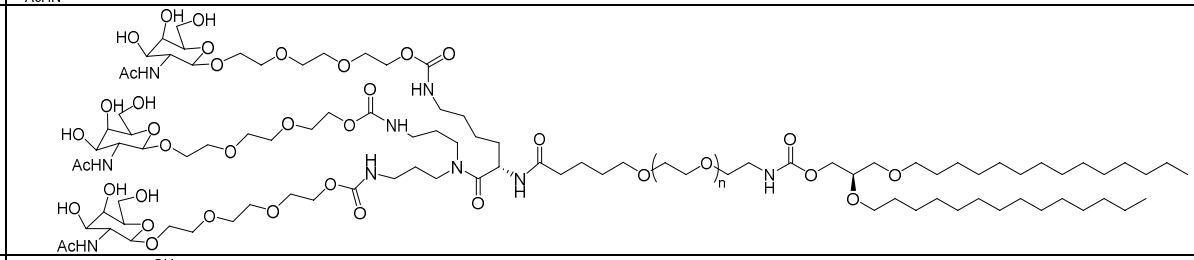
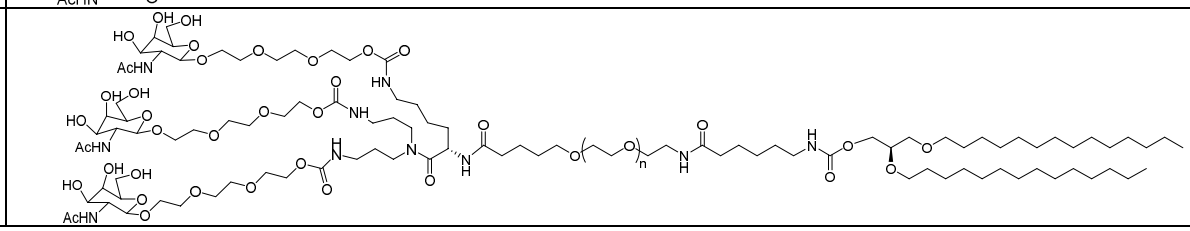
Formula IV-b.

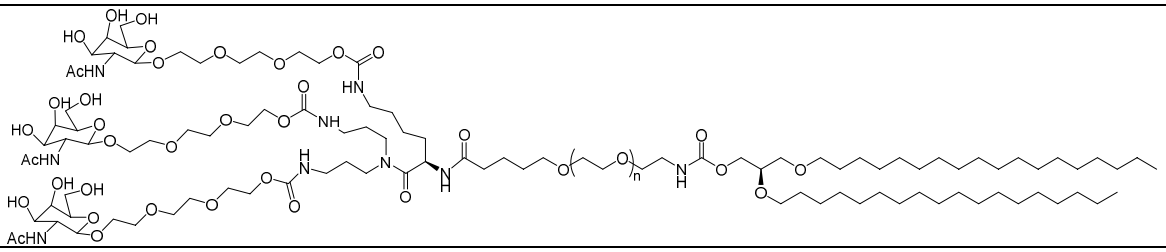
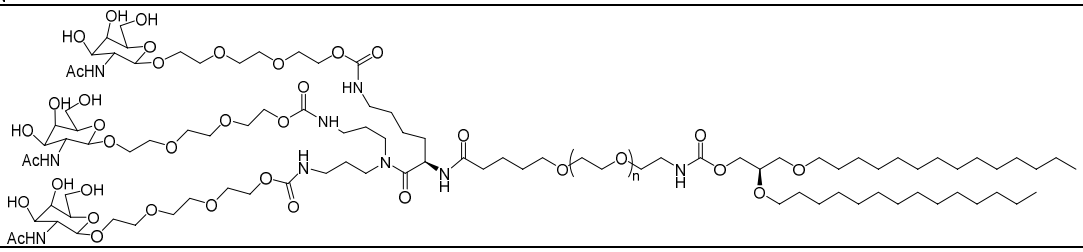
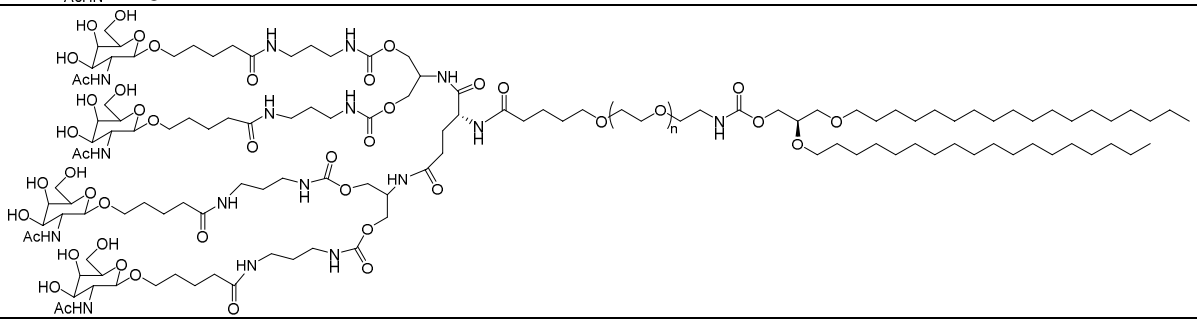
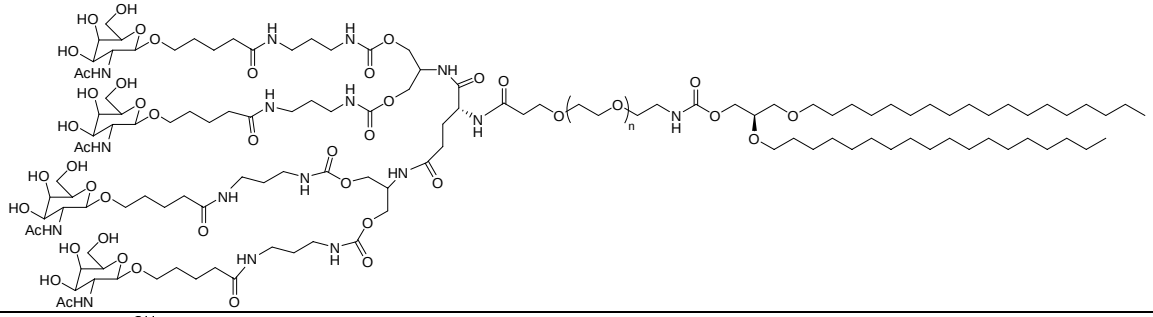
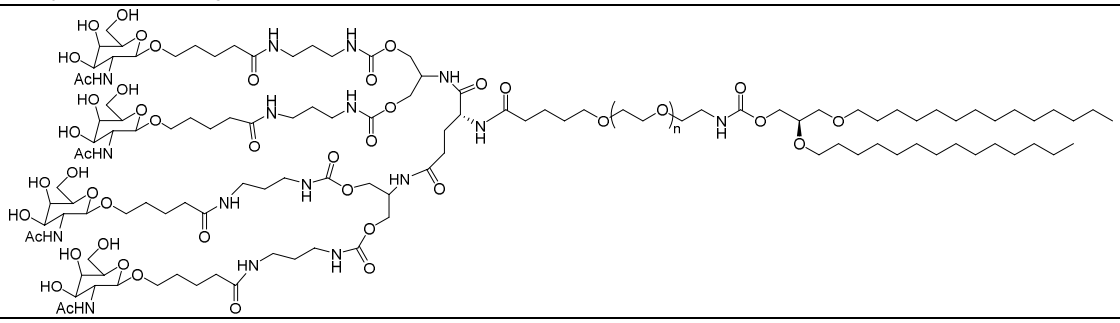
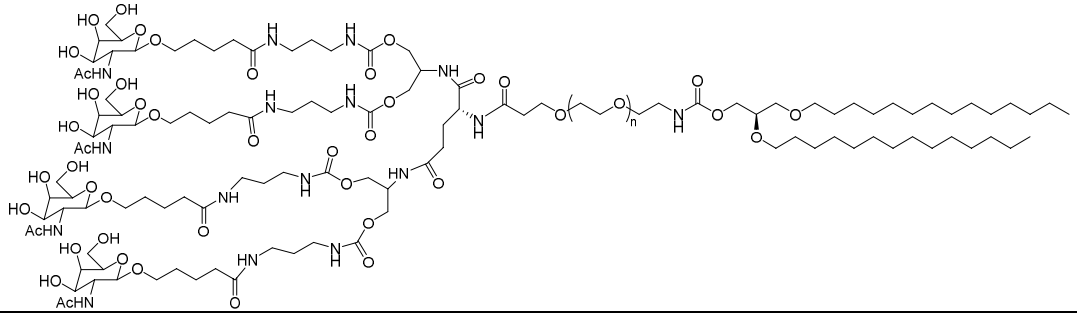
[0015a] In yet another aspect, the present disclosure provides a compound selected from the group consisting of:

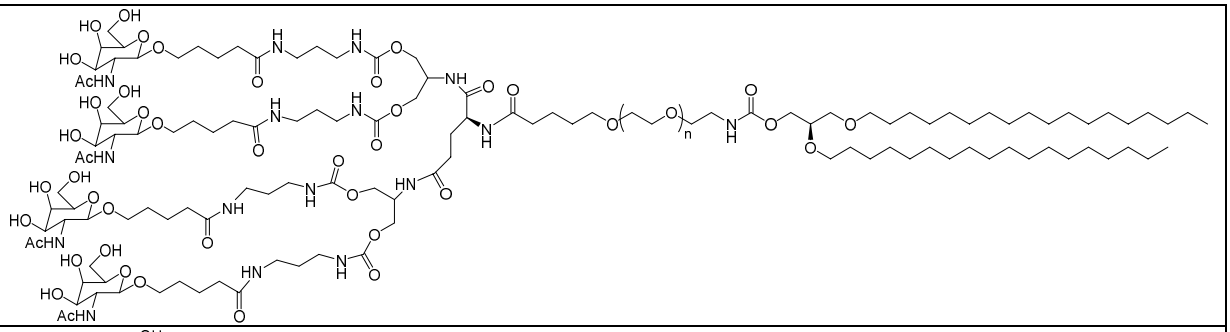
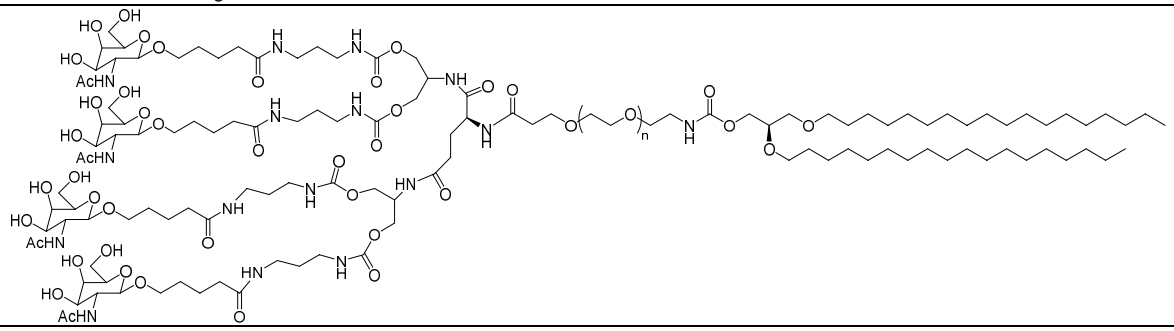
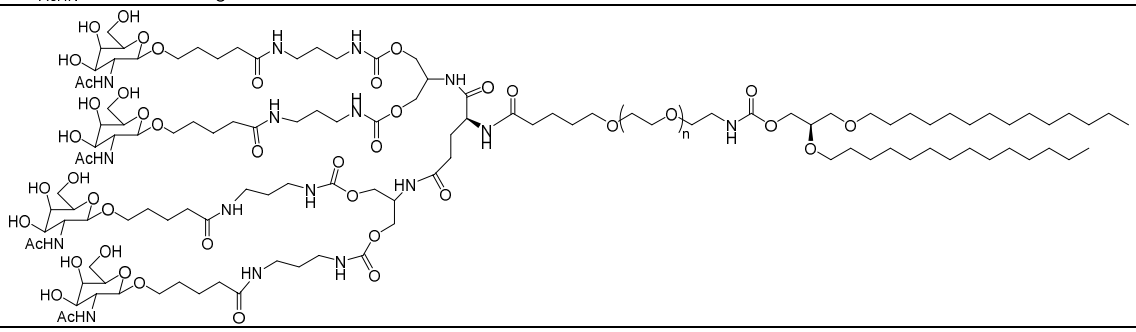
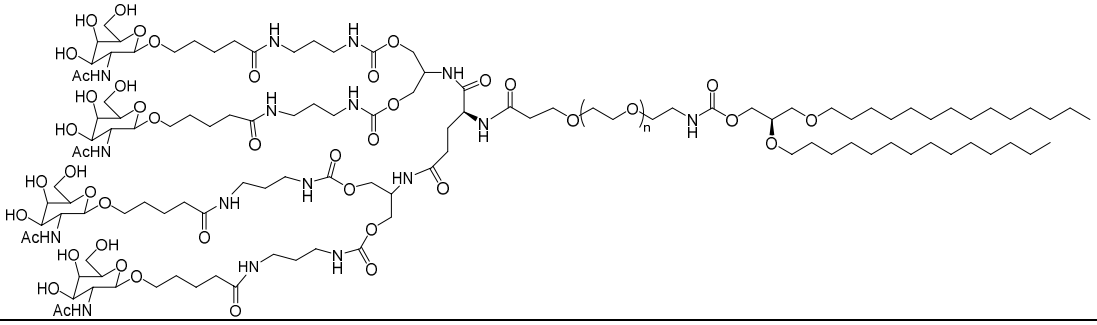
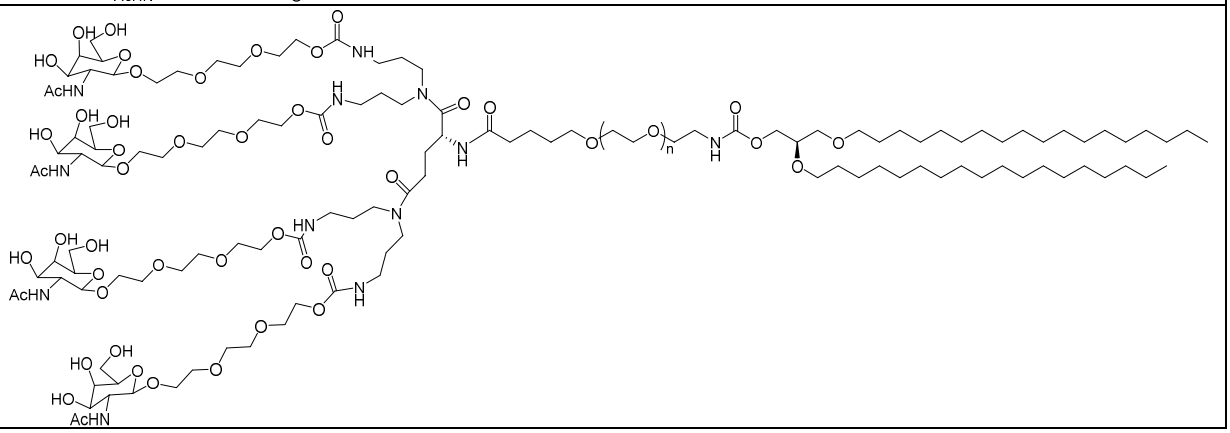
Compound No.	Structure
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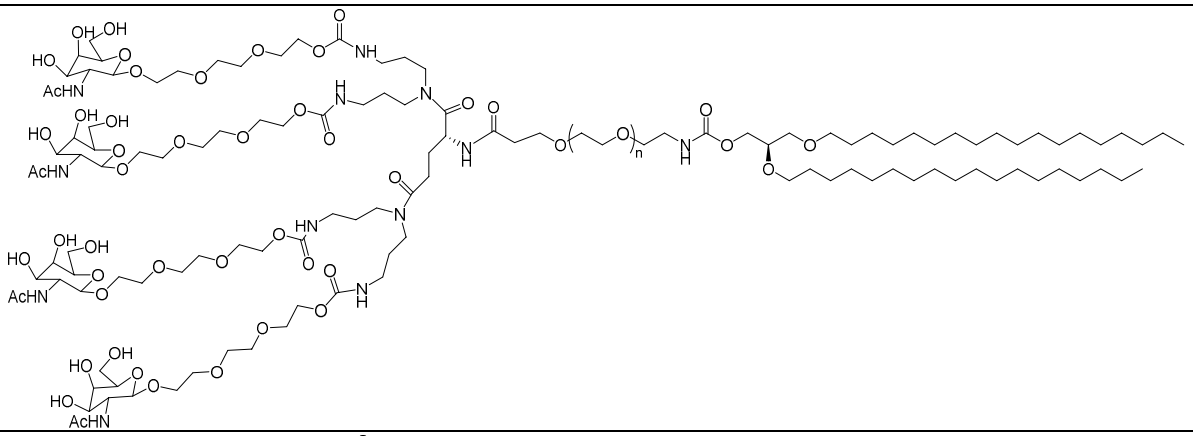
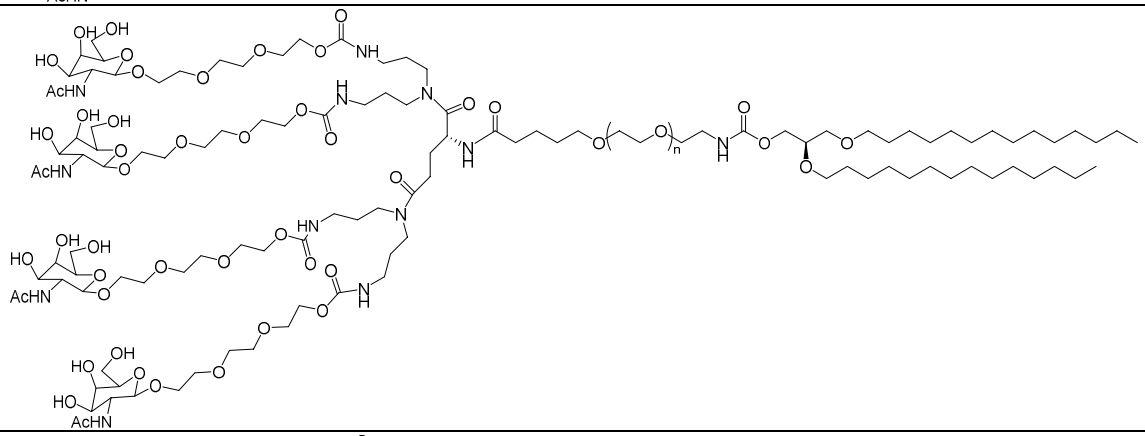
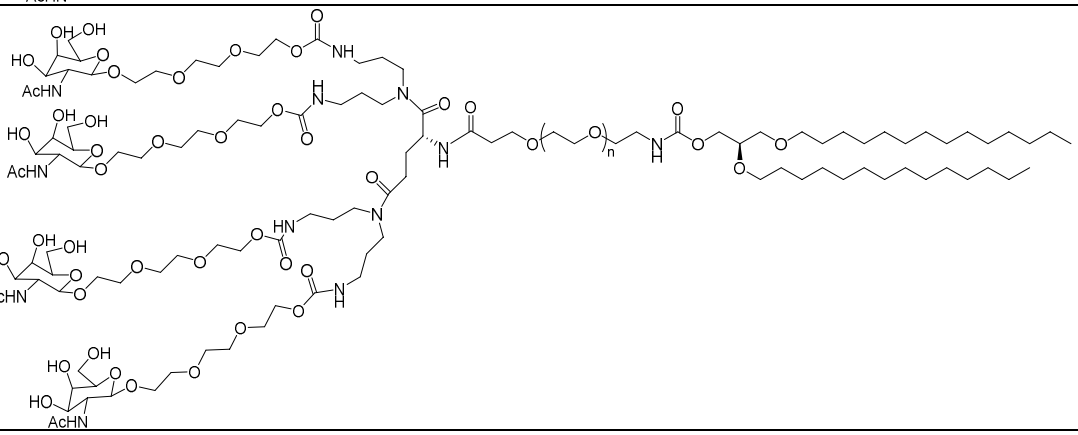
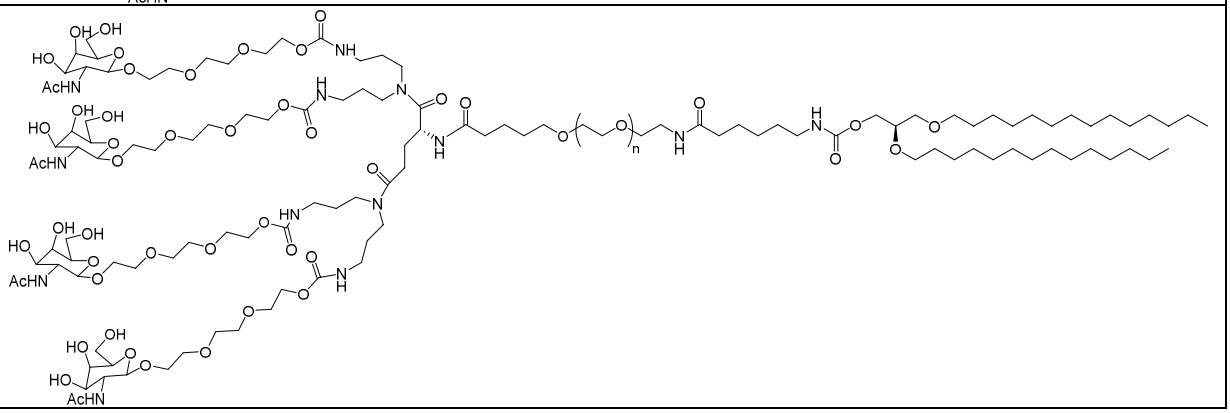
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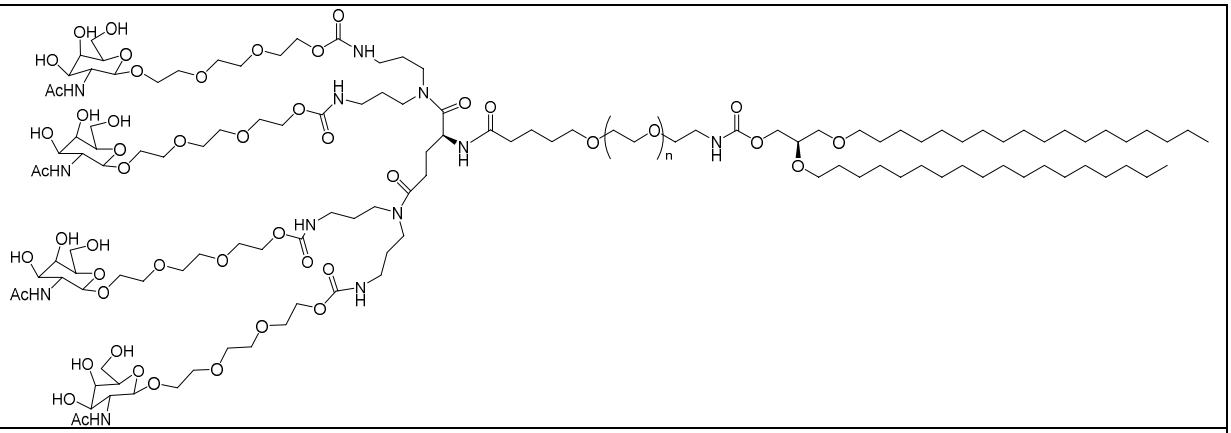
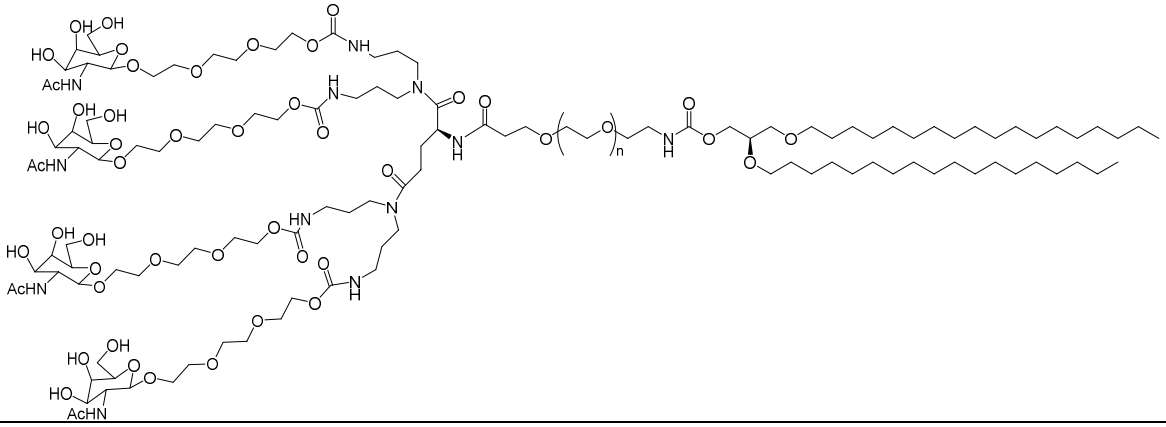
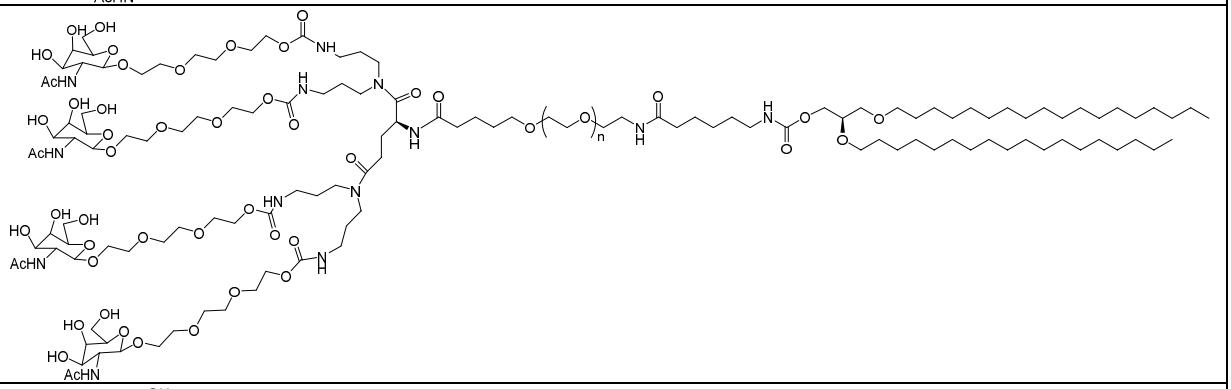
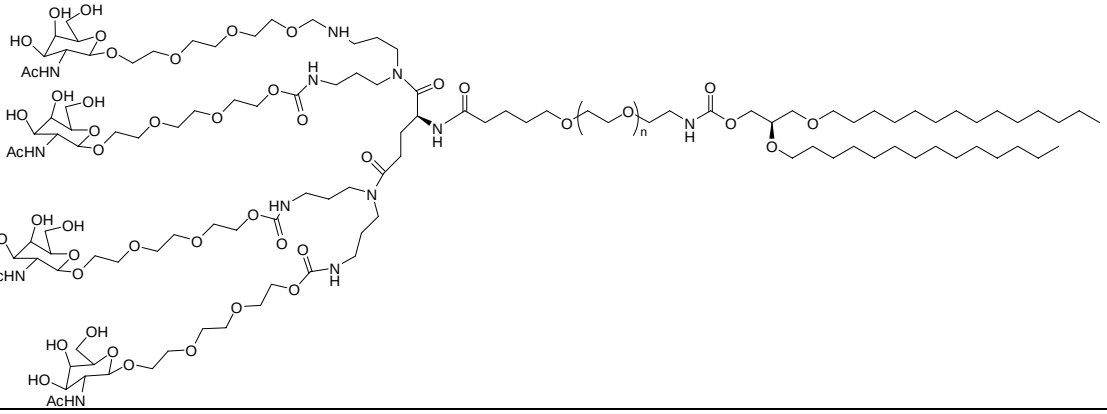
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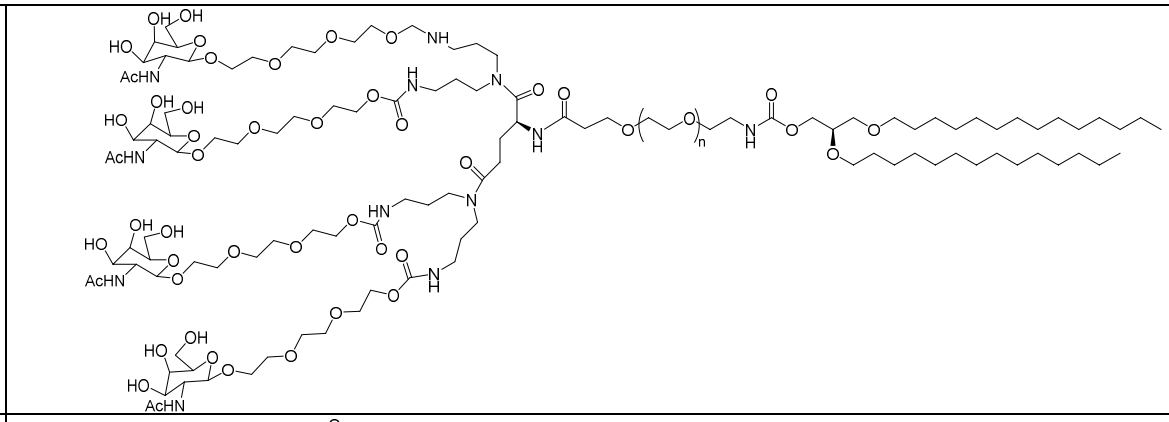
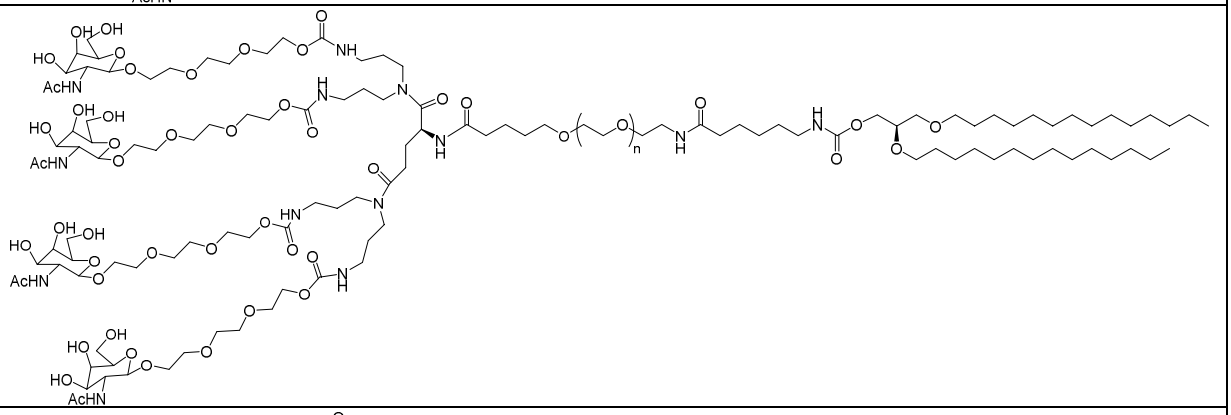
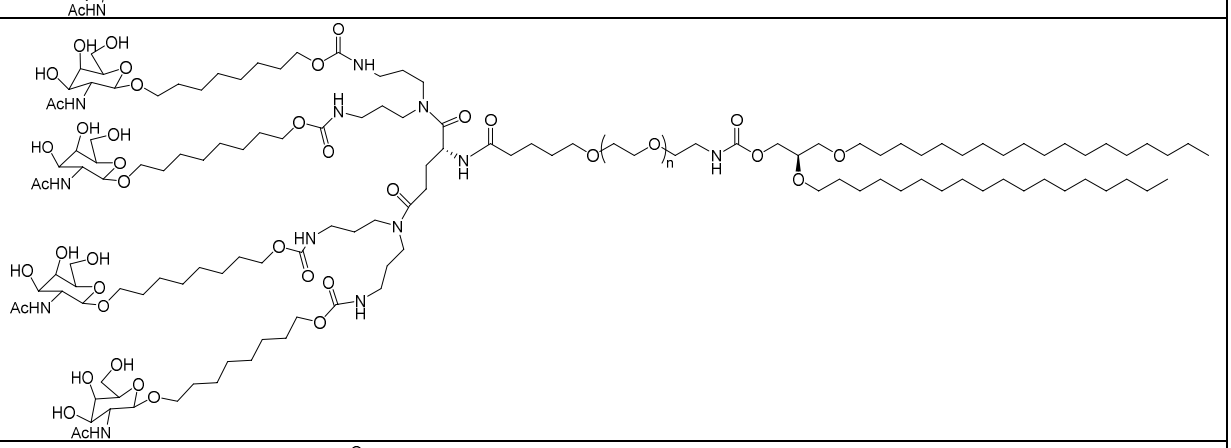
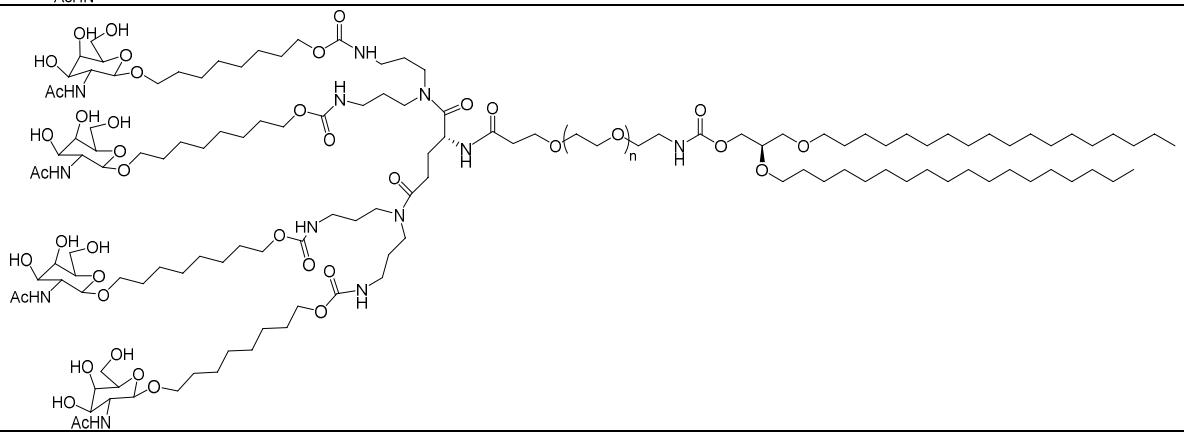
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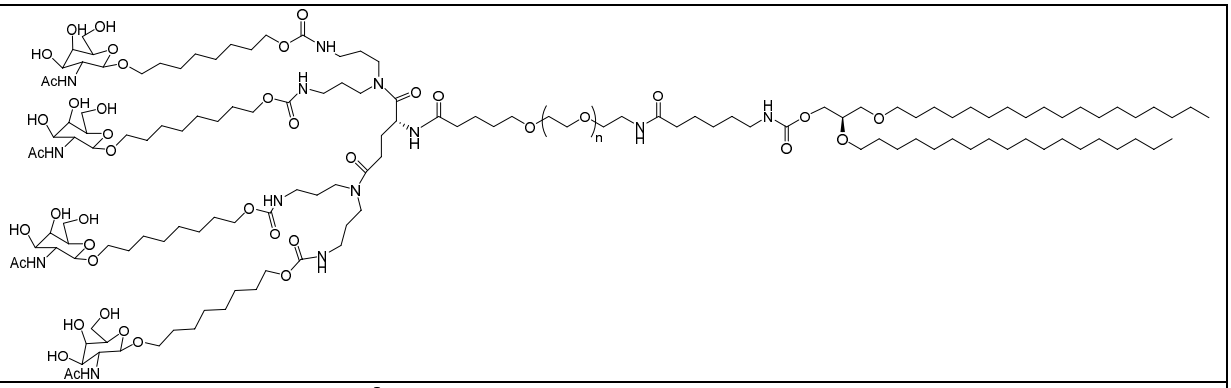
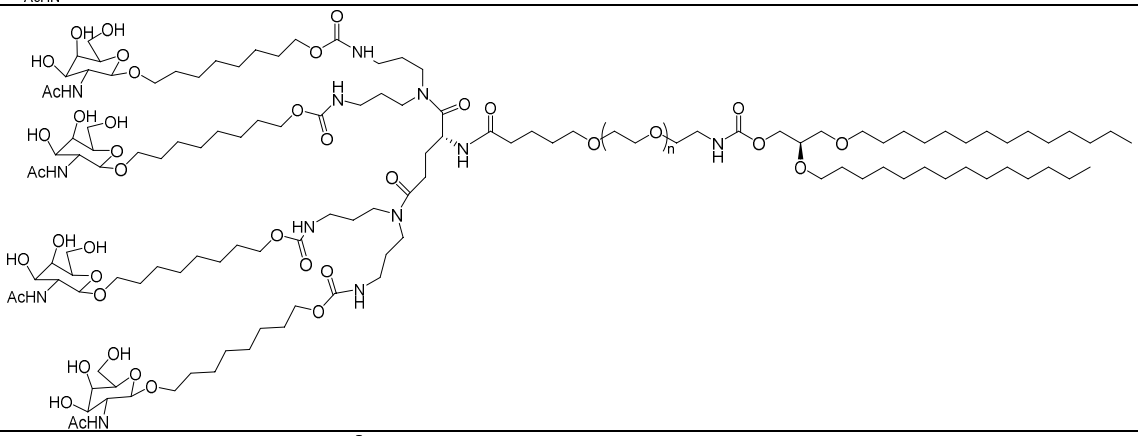
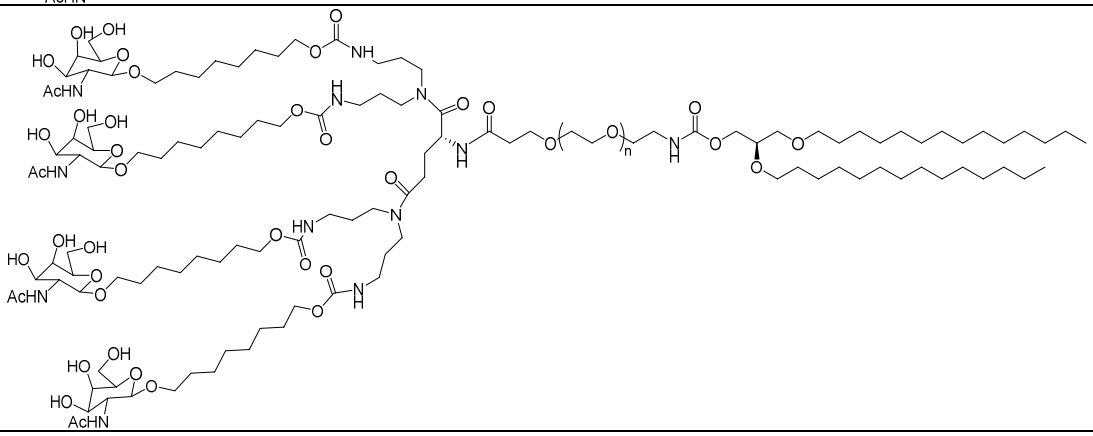
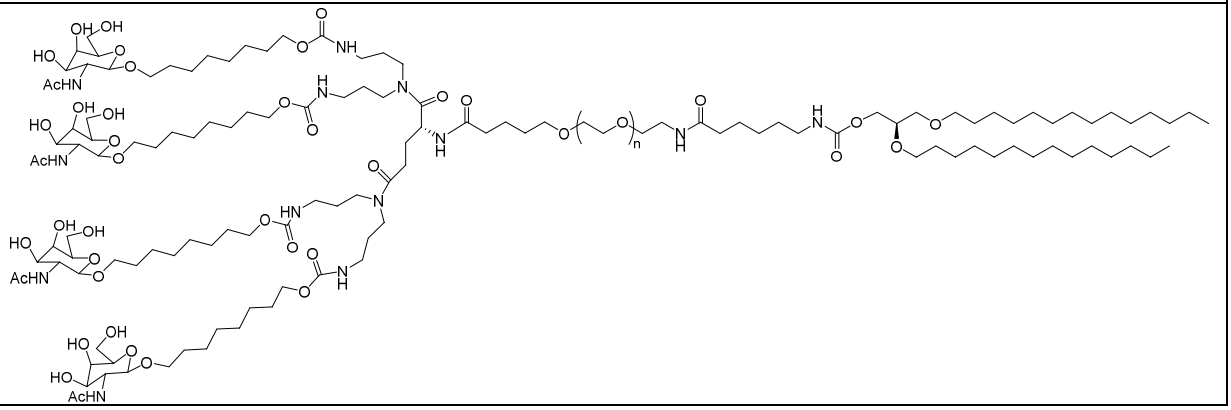
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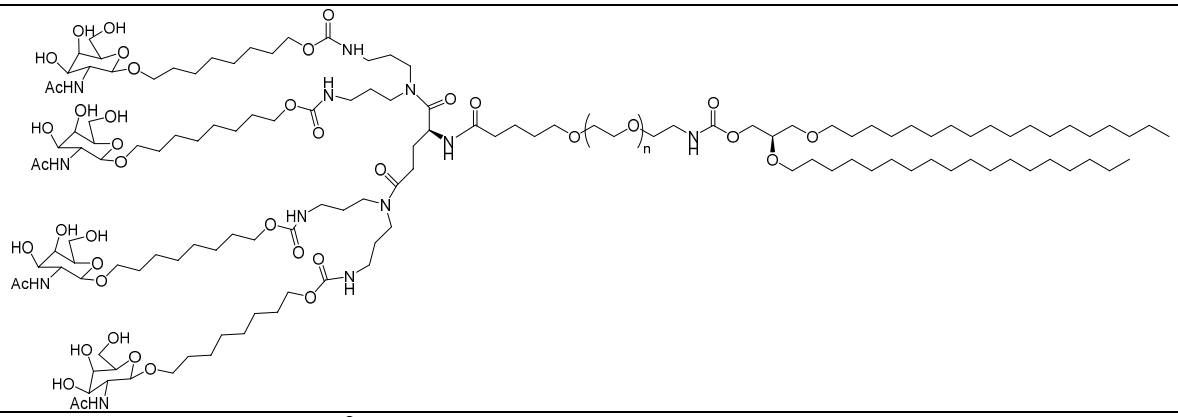
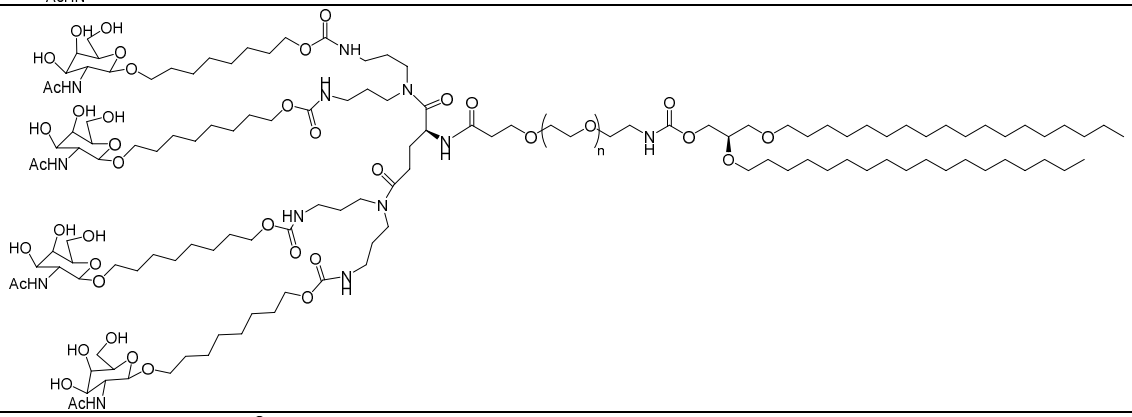
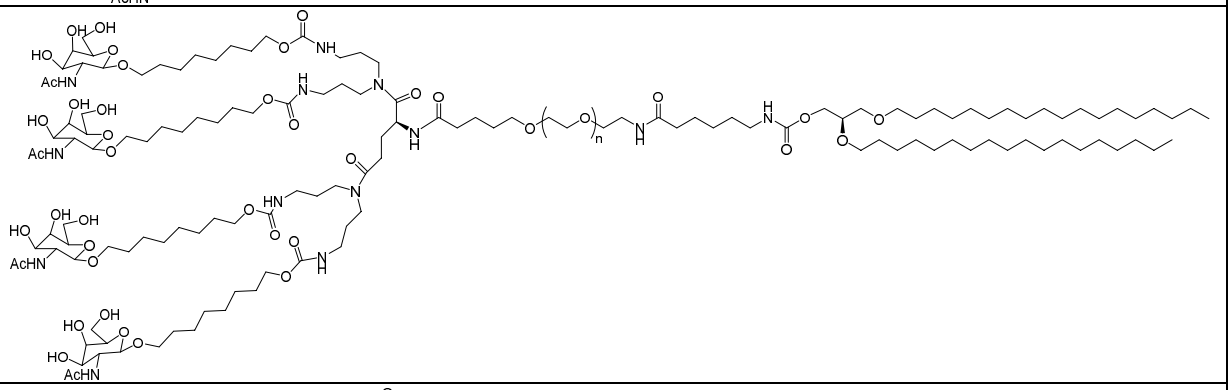
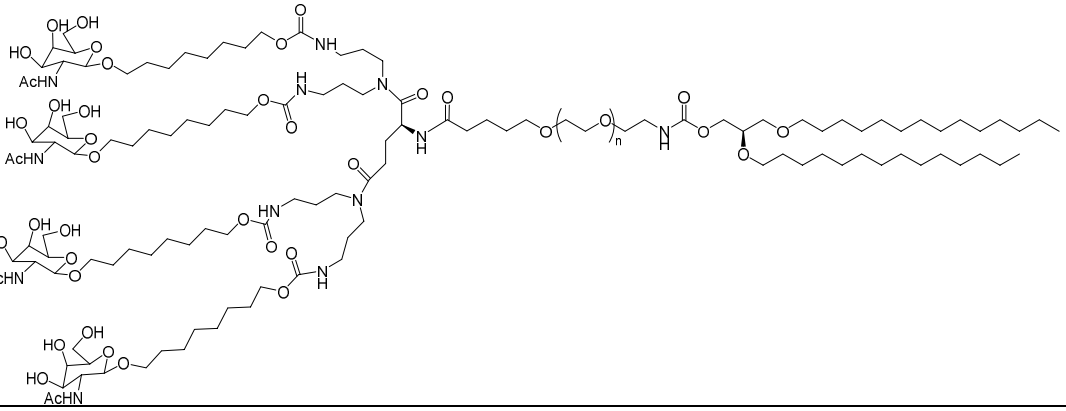
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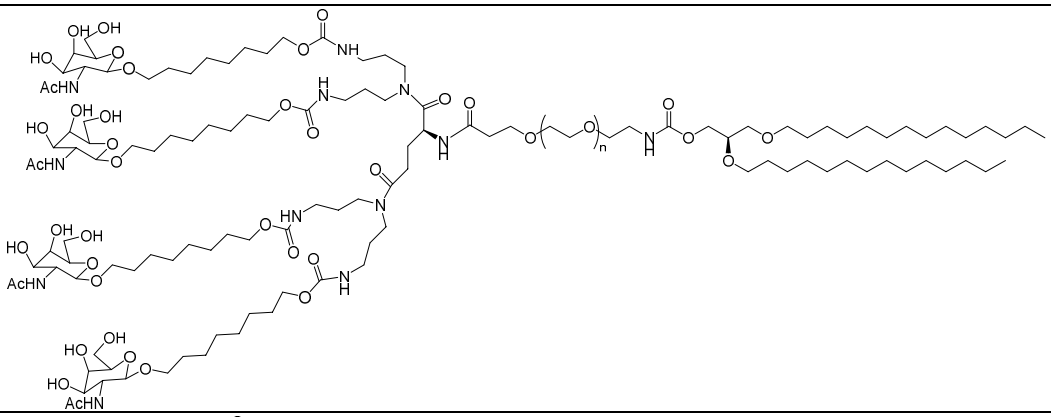
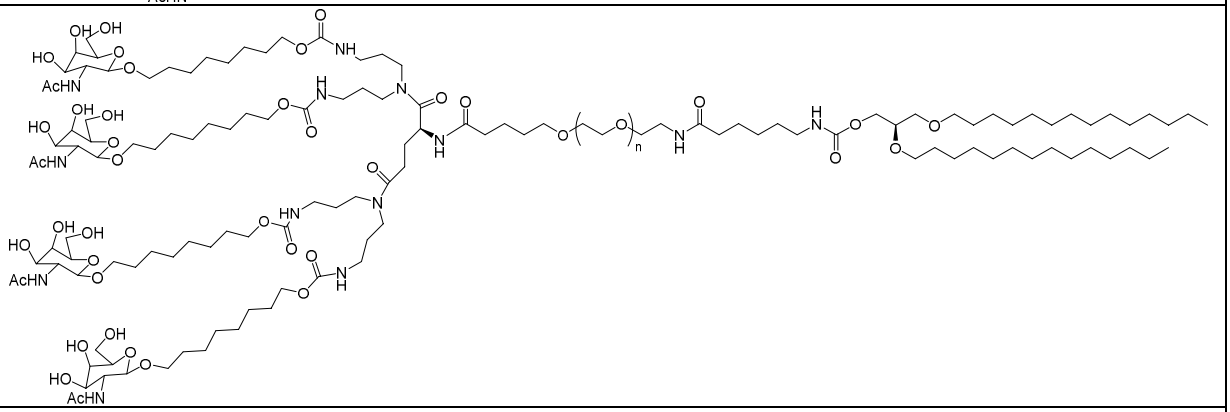
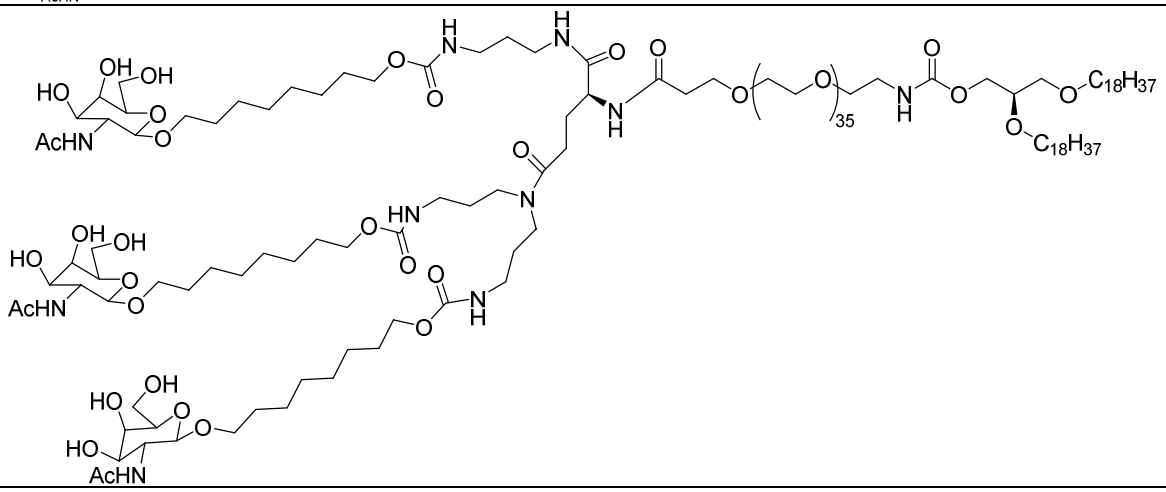
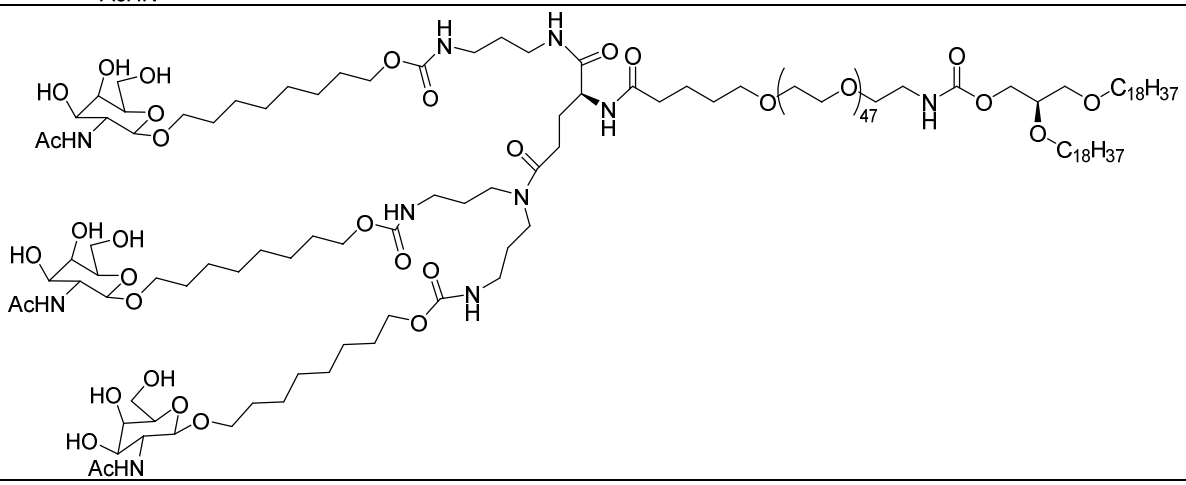
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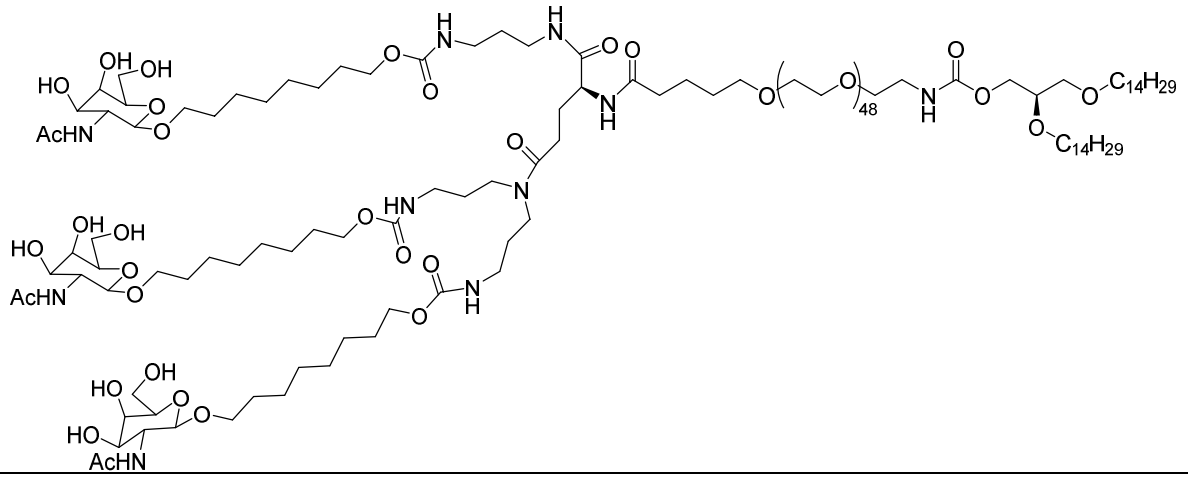
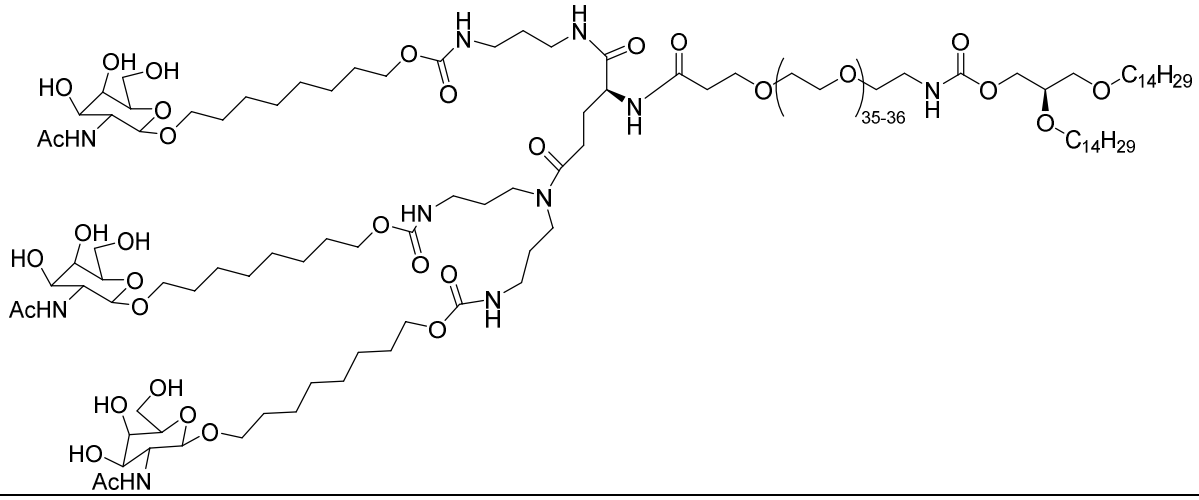
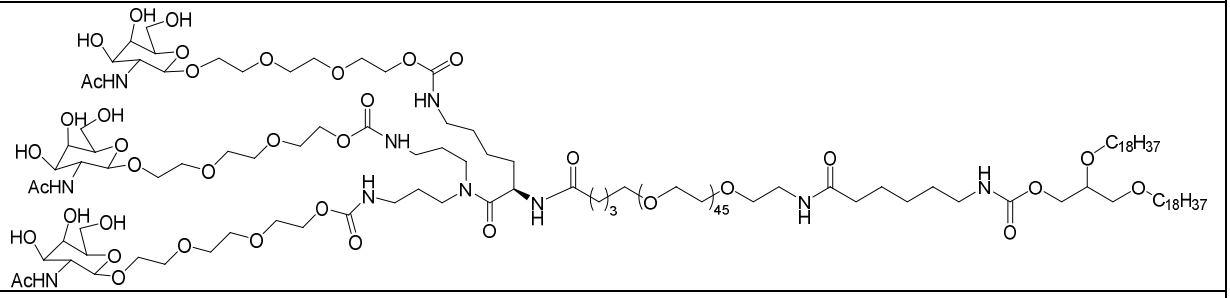
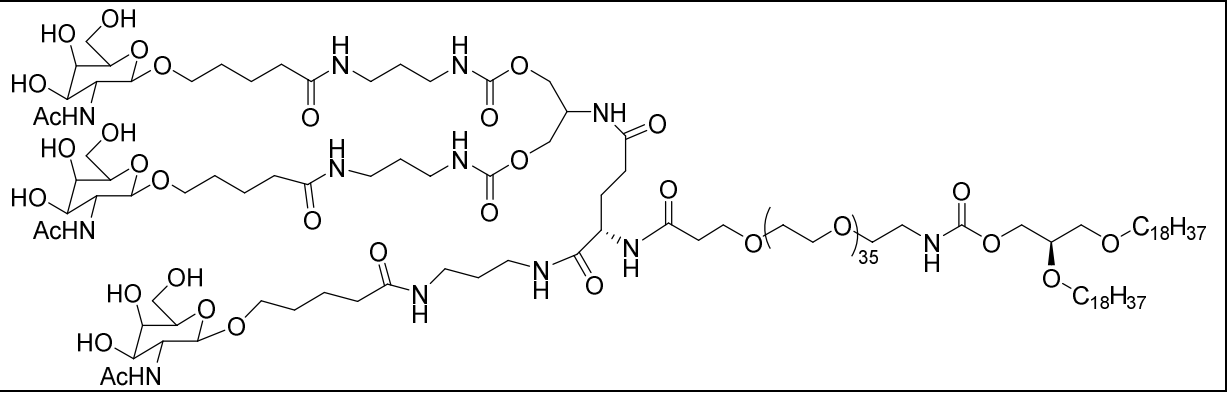
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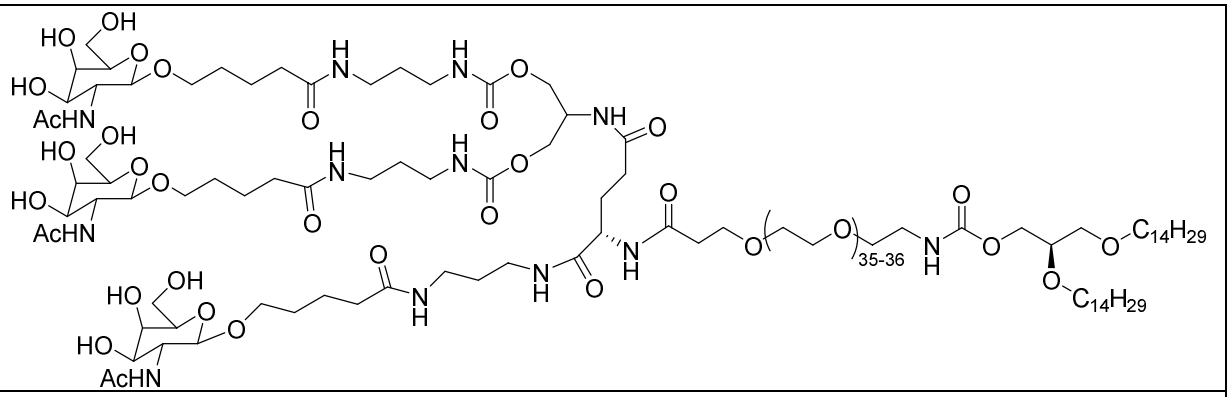
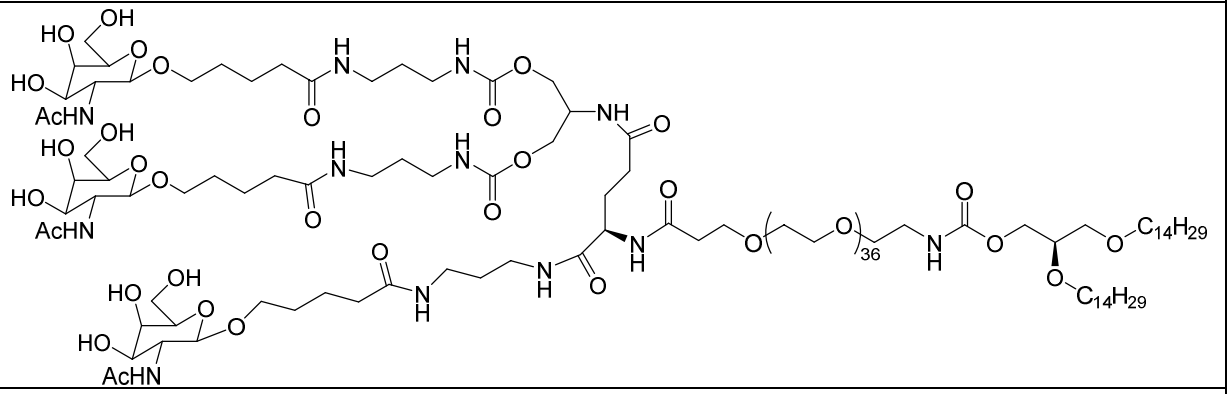
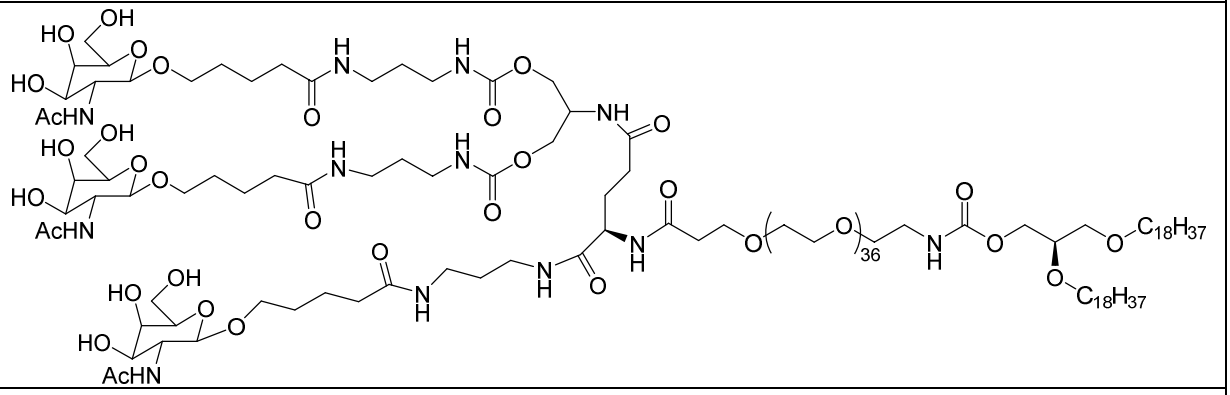
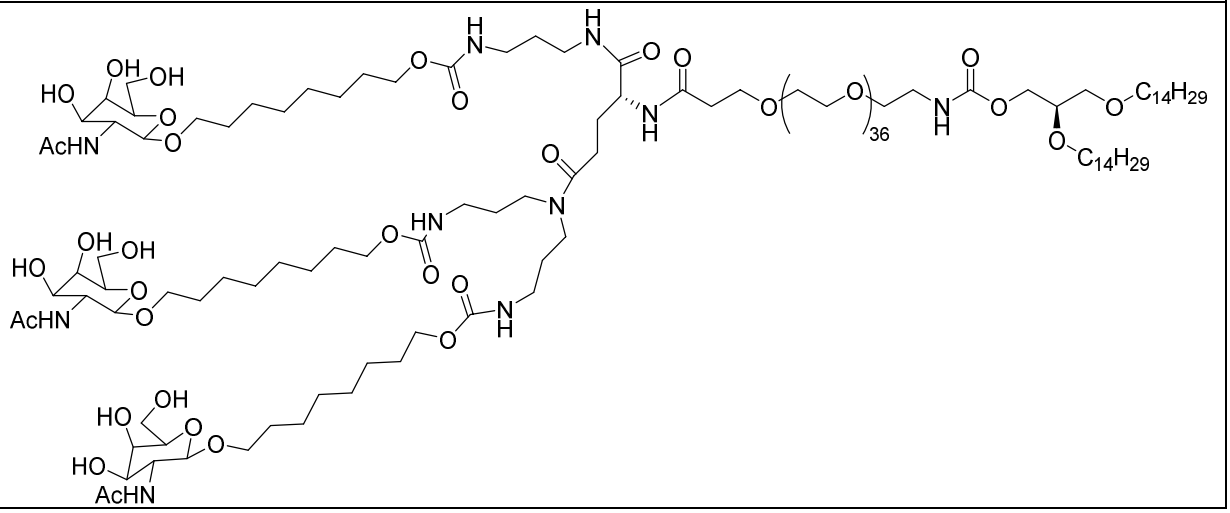
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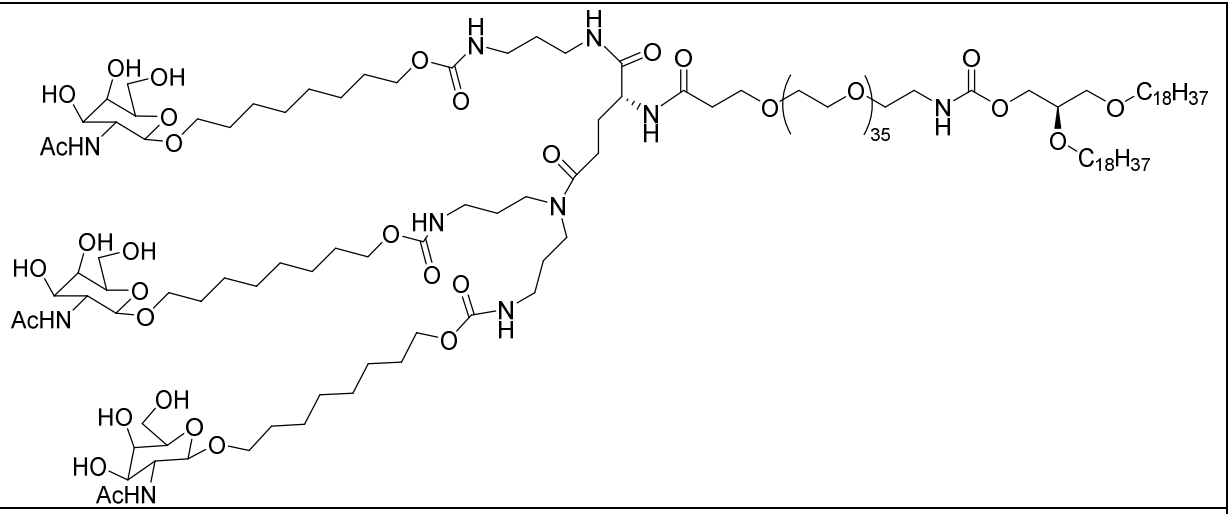
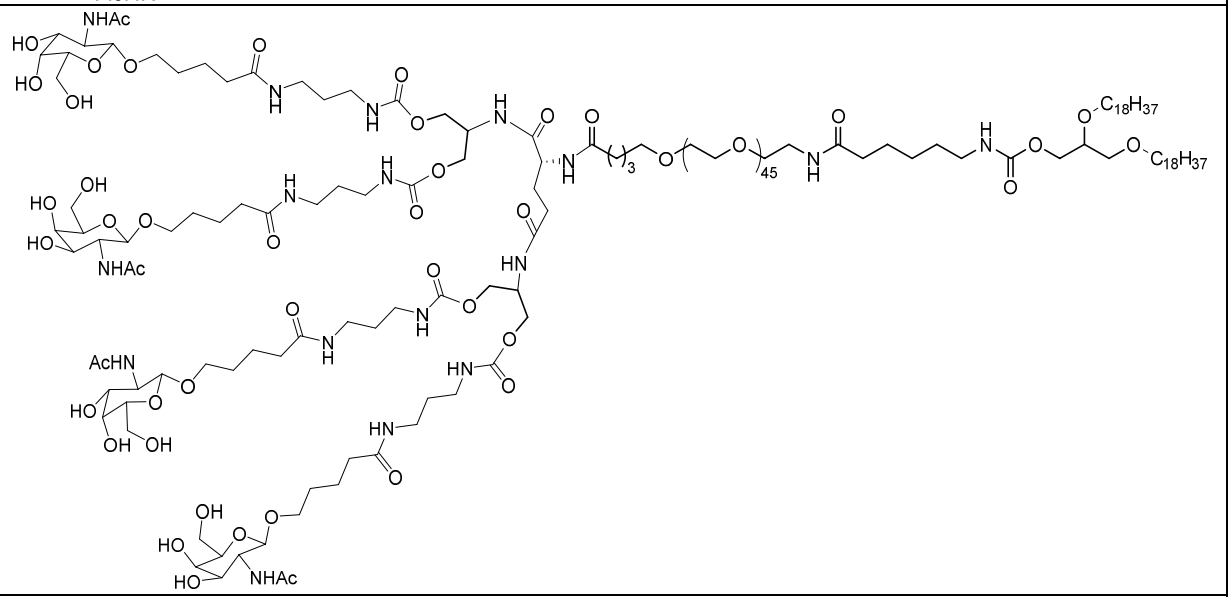
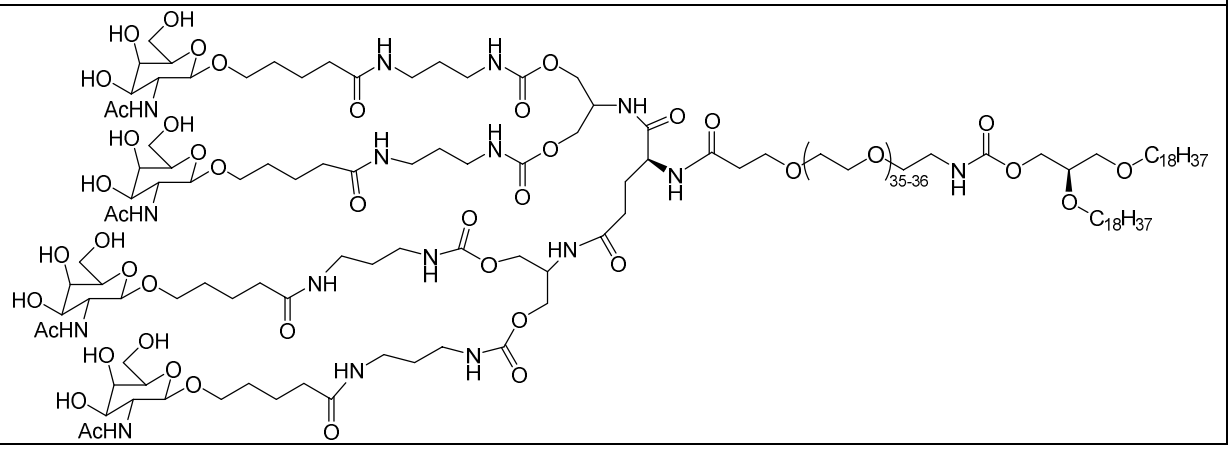
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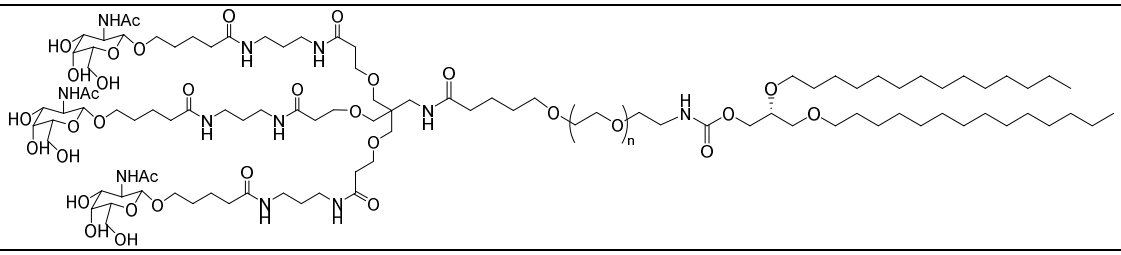
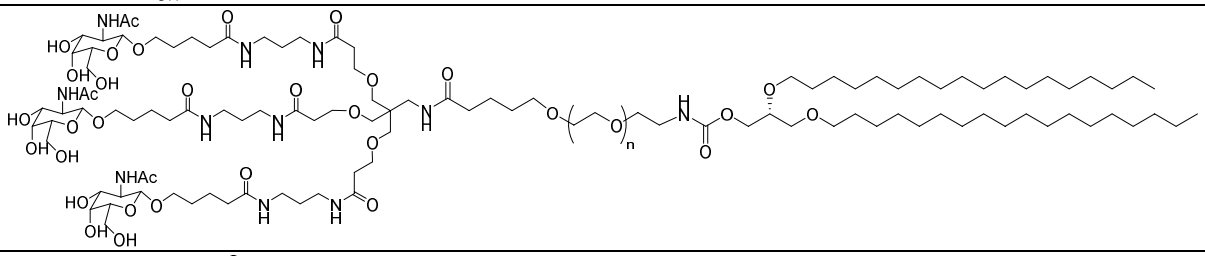
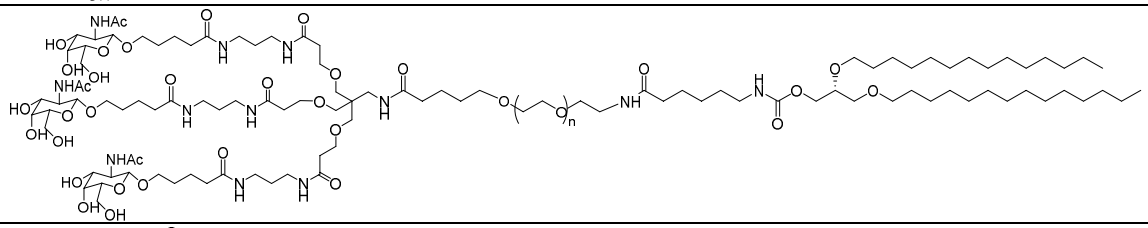
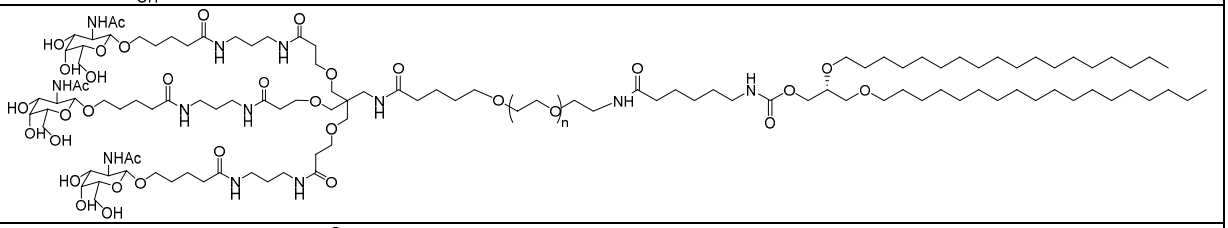
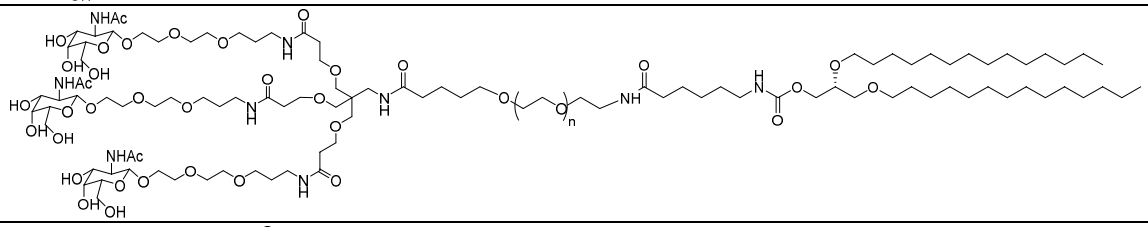
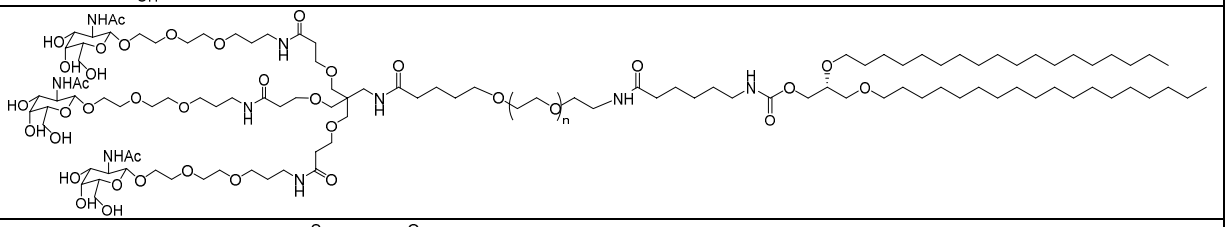
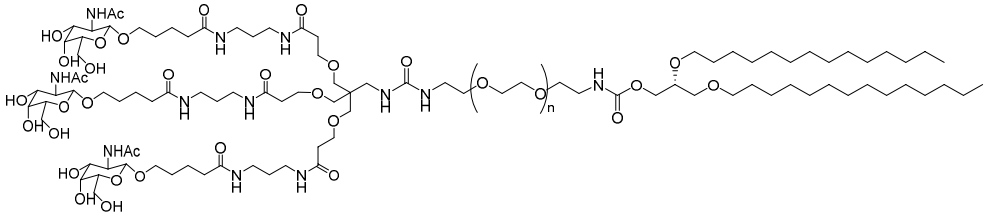
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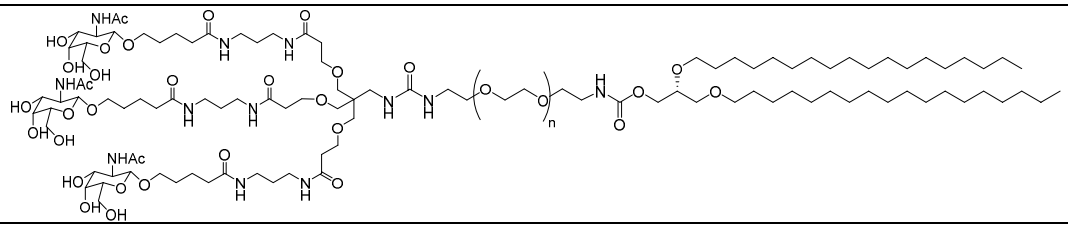
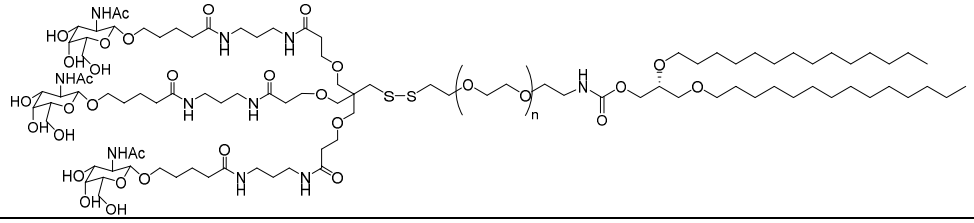
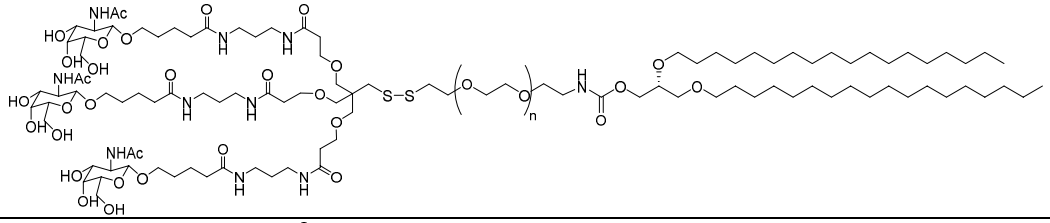
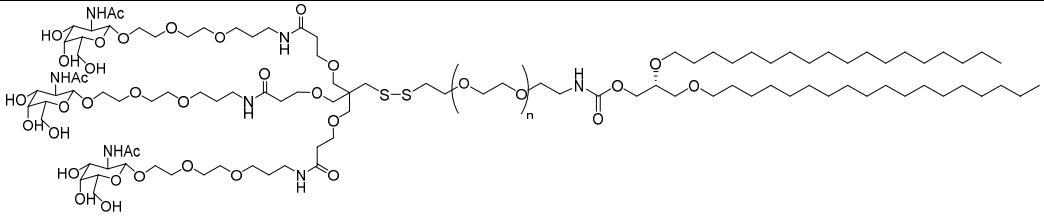
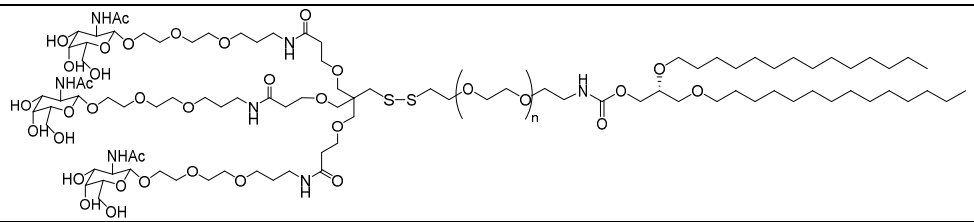
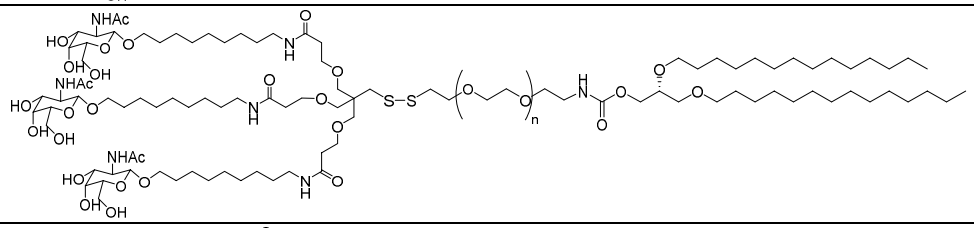
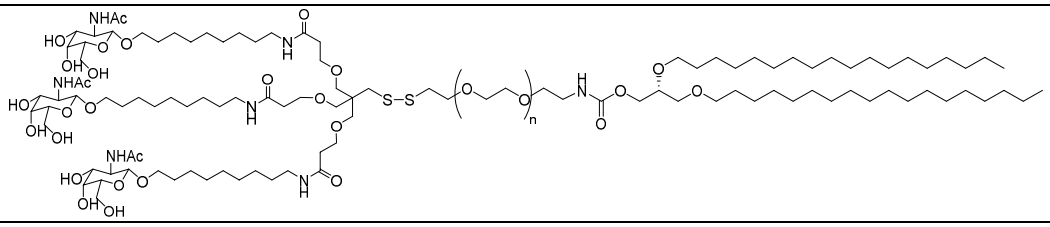
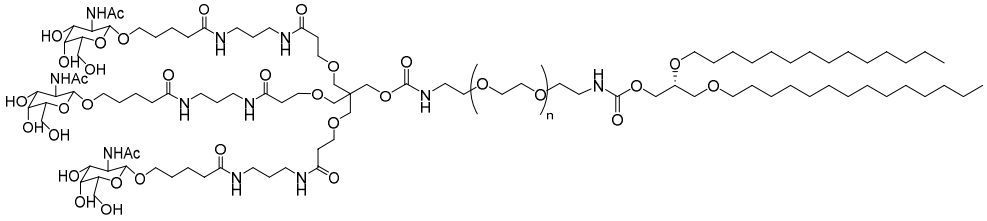
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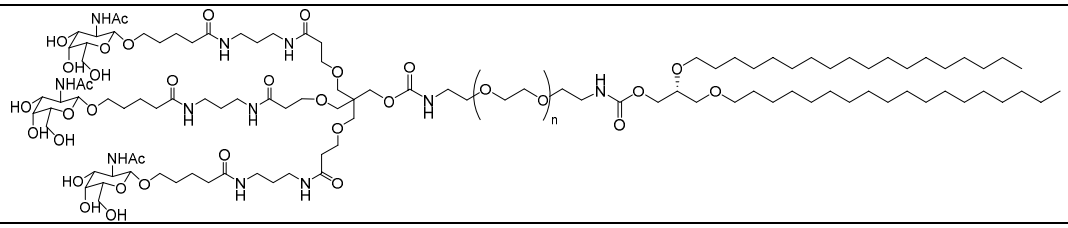
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wherein each subscript “n” is between 10-200.

[0015b] In a further aspect, the present disclosure provides a compound selected from the group consisting of:

Compound No.	Structure
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wherein each subscript “n” is between 10-200.

[0015c] In another aspect, the present disclosure provides a pharmaceutically acceptable salt of a compound as disclosed herein.

[0016] In another example, the present disclosure provides a lipid nanoparticle (LNP) composition comprising:

a lipid that comprises a compound as described herein;

a cationic lipid;

a phospholipid;

a PEG-containing lipid; and

a sterol.

[0016a] In yet another aspect, the present disclosure provides a lipid nanoparticle (LNP) composition comprising:

(A) a lipid that comprises a compound as disclosed herein or

(B) a lipid that comprises a compound as disclosed herein;

a cationic lipid;

a phospholipid;

a PEG-containing lipid; and

a sterol;

optionally, wherein the LNP composition further comprises:

(B.1) a prime editor comprising a DNA binding domain and a DNA polymerase domain, or one or more polynucleotides encoding the prime editor;

(B.2) a prime editing guide RNA (PEgRNA) or a polynucleotide encoding the PEgRNA;

(B.3) a nick guide RNA (ngRNA) or a polynucleotide encoding the ngRNA; and/or

(B.4) a second PEgRNA or a polynucleotide encoding the second PEgRNA;

optionally, wherein the LNP composition is formulated to deliver the at least one polynucleotide or one or more components of the prime editing system to target cells;

optionally, wherein the target cells are or comprise human cells, mammalian cells, liver cells, bone marrow cells, lung cells, eye cells, muscle cells, or cells in the central nervous system.

[0017] Another aspect of the present disclosure provides a pharmaceutical composition comprising the LNP composition described herein.

[0018] Another example of the present disclosure provides a method for delivering polynucleotides into a target cell comprising:

introducing into the target cell at least one lipid nanoparticle comprising a GalNAc-based lipid that comprises any one of the compounds described herein and one or more polynucleotides.

[0019] Another example of the present disclosure provides a method for delivering a prime editing system into a target cell comprising:

introducing into the target cell at least one lipid nanoparticle comprising a GalNAc-based lipid that comprises any one of the compounds described herein and one or more components of a prime editing system.

[0019a] In a further aspect, the present disclosure provides a pharmaceutical composition comprising the LNP composition as disclosed herein for use in delivering polynucleotides into a target cell comprising:

introducing into the target cell the LNP composition as disclosed herein and (i) one or more polynucleotides or (ii) one or more components of a prime editing system;

optionally, wherein the target cells are or comprise human cells, mammalian cells, liver cells, bone marrow cells, lung cells, eye cells, muscle cells, or cells in the central nervous system.

[0020] Other examples, examples, and features will be apparent from the following description and the claims.

INCORPORATION BY REFERENCE

[0021] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

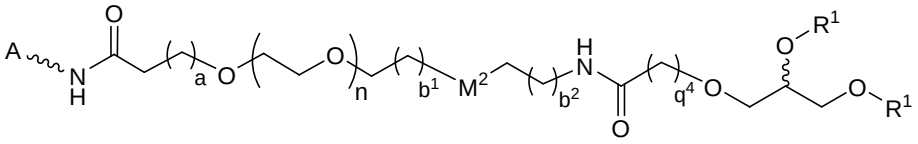
BRIEF DESCRIPTION OF THE DRAWINGS

[0022] The novel features of the methods and compositions provided herein are set forth with particularity in the appended claims. A better understanding of the features and advantages of the methods and compositions provided herein will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the methods and compositions provided herein are utilized, and the accompanying drawings of which:

[0023] **FIG. 1** shows Indel% activity for compounds disclosed herein.

WHAT IS CLAIMED IS

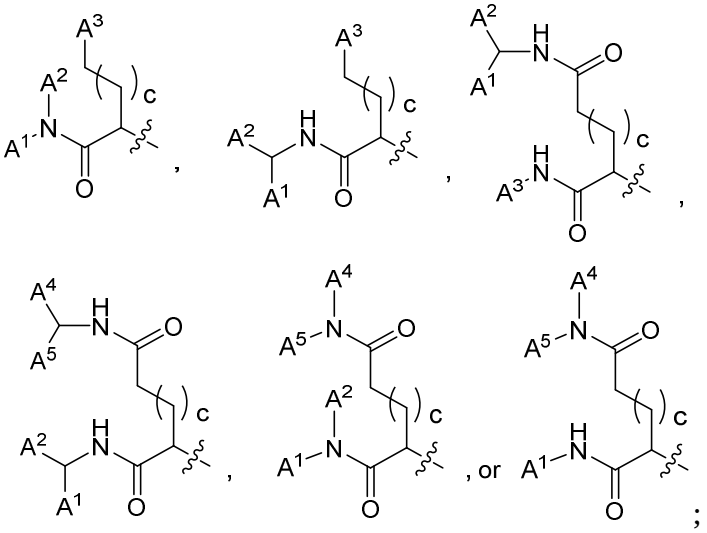
1. A compound of Formula II:

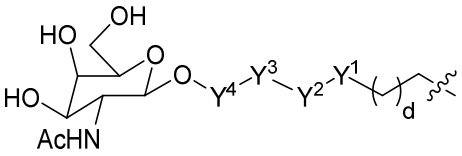


Formula II

wherein:

A is:



each A^1, A^2, A^3, A^4, and A^5 is independently ;

each Y^1 is independently –NH–, –NHC(O)O–, –OC(O)NH–, –NHC(O)–, or –C(O)NH–;

each Y^2 is independently absent, $–(CH_2)_r–$, $–(CH_2CH_2O)_t–$, or $–(OCH_2CH_2)_t–$;

each subscript "t" is independently 1-5;

each Y^3 is independently absent, –NHC(O)–, or –C(O)NH–;

each Y^4 is independently absent or $–(CH_2)_r–$;

each subscript "r" is independently 1-10;

each subscript "d" is independently 0-5;

each subscript "c" is independently 0-5;

subscript "n" is independently 1-200;

subscript "a" is 1-5;

subscript "b^1" is independently 0-5;

M^2 is absent, –NHC(O)–, or –C(O)NH–;

subscript "b^2" is independently 0-5;

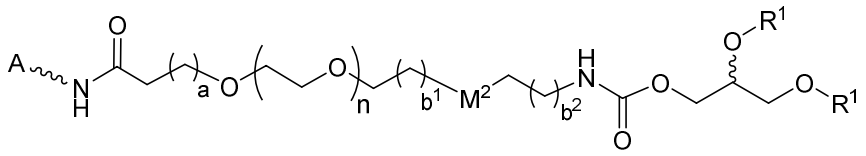
subscript "q^4" is independently 0-6;

each R^1 is independently a C_{12}-C_{20} substituted or unsubstituted alkyl; and

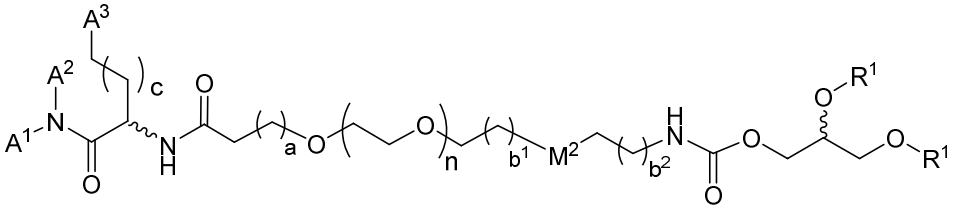
each of the "〰" bonds independently indicate an *R* configuration or an *S* configuration;

with the proviso that at least one of Y^2, Y^3 and Y^4 is present.

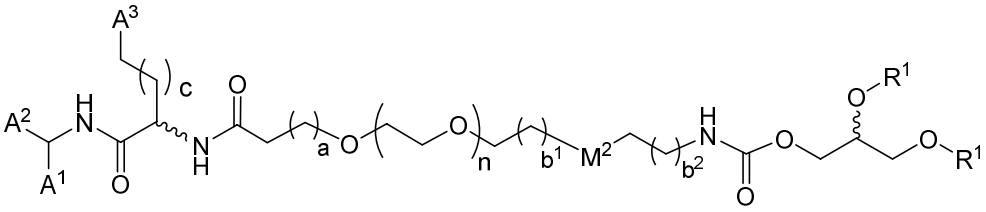
2. The compound of claim 1, wherein the compound of Formula II is a compound of Formula II-a, Formula II-a-1, Formula II-a-2, Formula II-a-3, Formula II-a-4, Formula II-a-5, or Formula II-a-6:



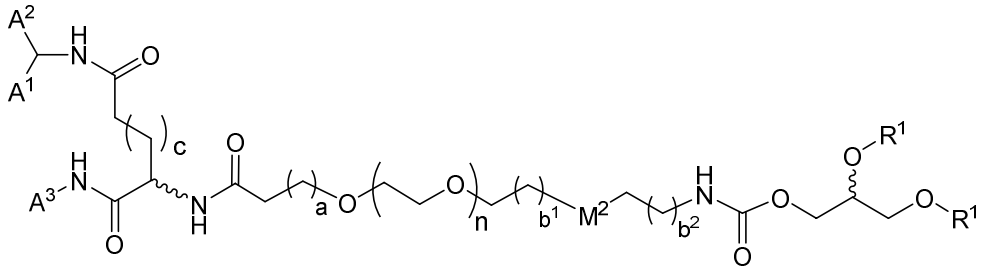
Formula II-a,



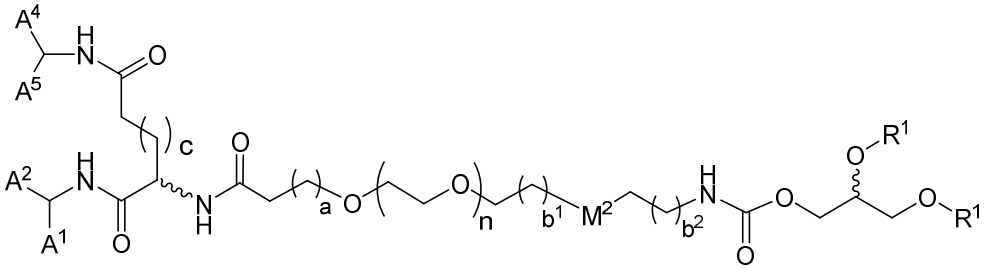
Formula II-a-1,



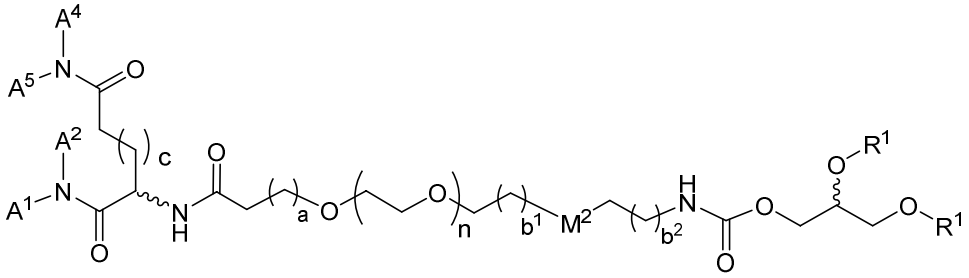
Formula II-a-2,



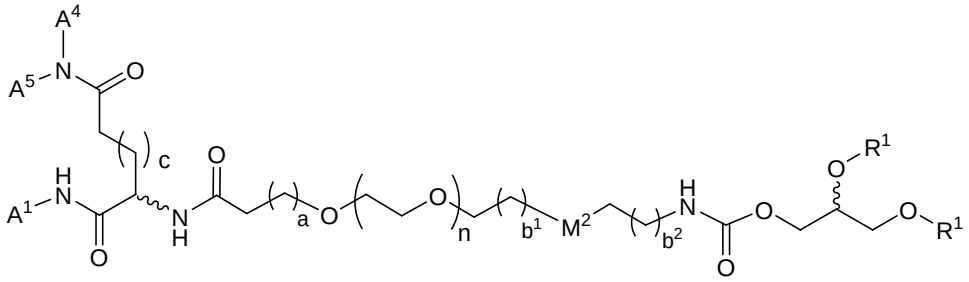
Formula II-a-3,



Formula II-a-4,



Formula II-a-5, or



Formula II-a-6.

3. The compound of claim 1 or claim 2, wherein:

(A.1) A^1, A^2, and A^3 are the same;

(A.2) A^1 and A^2 are different from A^3;

(A.3) A^1, A^2, A^4, and A^5 are the same; or

(A.4) A^1, A^2, and A^5 are the same; and/or

(B.1) each of Y^1 and Y^4 are present and each of Y^2 and Y^3 are absent; optionally, wherein:

(i.B.1) each Y^1 is –C(O)NH– and each Y^4 is $–(CH_2)_r–$; or

(ii.B.1) each Y^1 is –OC(O)NH– and each Y^4 is $–(CH_2)_r–$;

(B.2) each of Y^1, Y^2, Y^3, and Y^4 are present; optionally, wherein each Y^1 is independently –NHC(O)O–; each Y^2 is independently $–(CH_2)_r–$; each Y^3 is independently –C(O)NH–; and each Y^4 is independently $–(CH_2)_r–$; or

(B.3) each of Y^1 and Y^2 are present and each of Y^3 and Y^4 are absent; optionally,

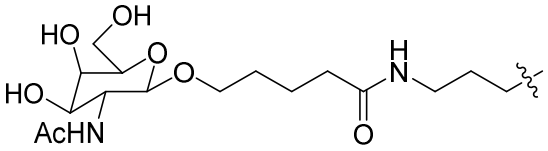
wherein each Y^1 is independently –OC(O)NH– and each Y^2 is independently $–(CH_2CH_2O)_t–$; and/or

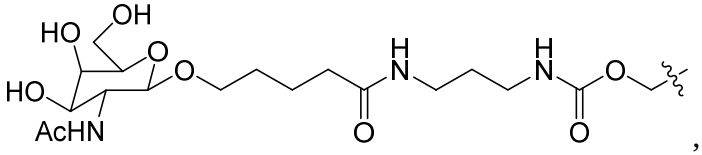
(C.1) M^2 is absent; or

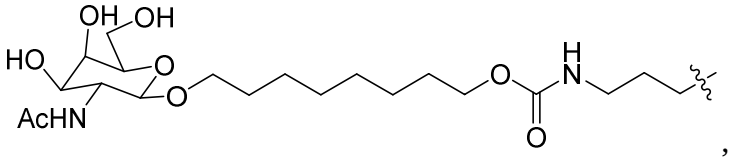
(C.2) M^2 is –NHC(O)–; and/or

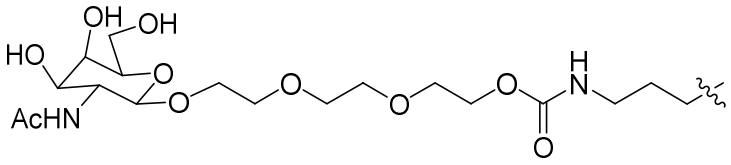
(D) each R^1 is independently a C_{14}-C_{18} unsubstituted alkyl.

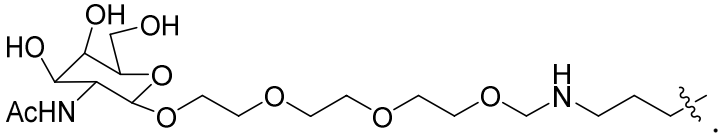
4. The compound of any one of claims 1-3, wherein each of A^1, A^2, A^3, A^4, and A^5 is selected from the group consisting of:


,

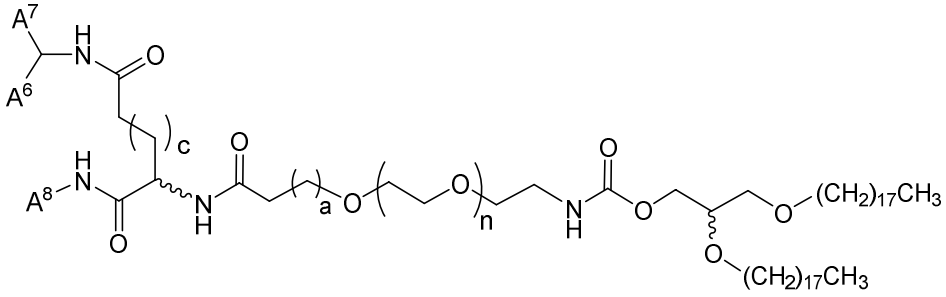

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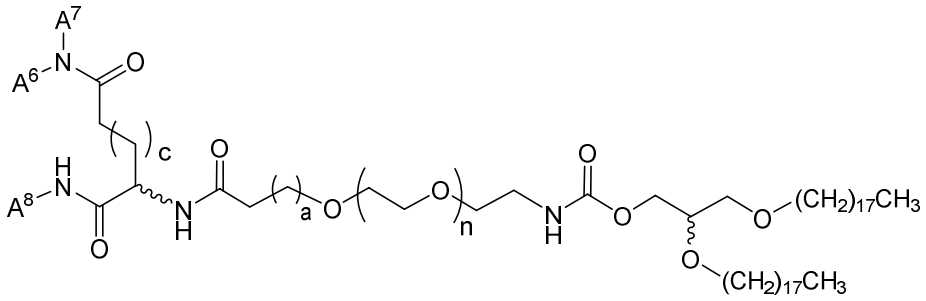

, and


.

5. A compound of Formula III or Formula IV:

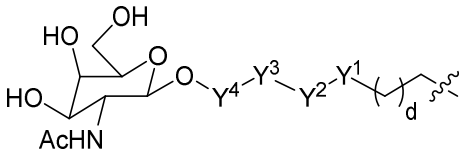


Formula III, or



Formula IV

wherein,

each A^6, A^7, and A^8 is independently  ;

each Y^1 is independently absent, –NHC(O)O–, or –OC(O)NH–;

each Y^2 and Y^4 is independently $–(CH_2)_r–$;

each subscript "r" is independently 1-10;

each Y^3 is independently absent, –NHC(O)–, or –C(O)NH–;

each subscript "d" is independently 1-5;

each subscript "c" is independently 1-5;

subscript "a" is 1-5;

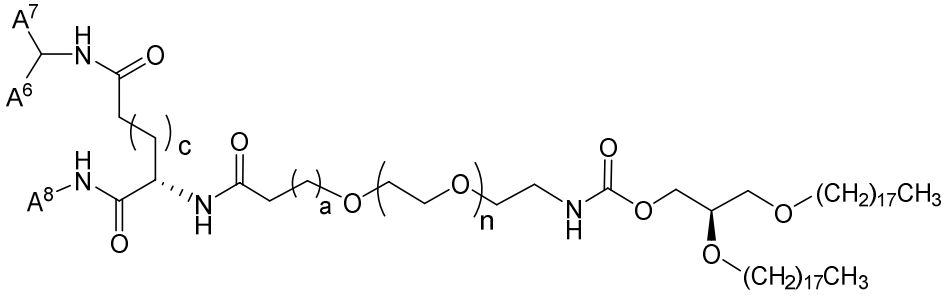
subscript "n" is independently 10-100; and

each of the "〰" bonds independently indicate an *R* configuration or an *S* configuration;

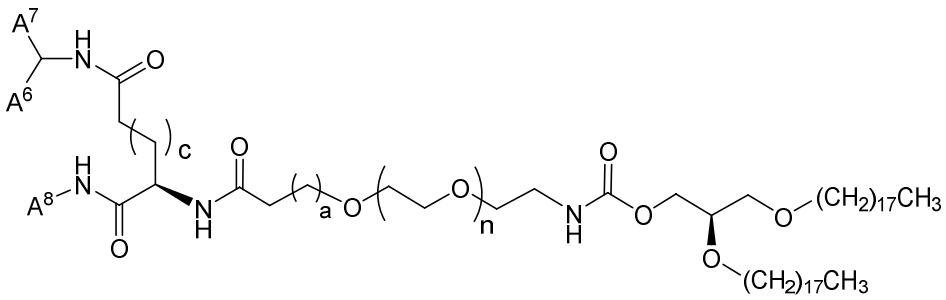
with the proviso that at least one of Y^1 or Y^3 is present.

6. The compound of claim 5, wherein the compound of:

(A) Formula III is a compound of Formula III-a or Formula III-b:

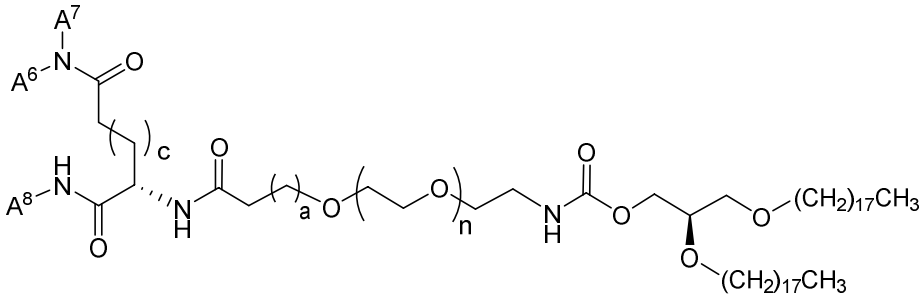


Formula III-a, or

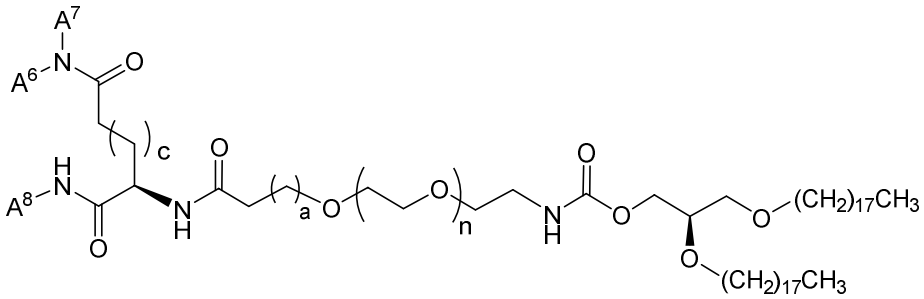


Formula III-b; or

(B) the compound of Formula IV is a compound of Formula IV-a or Formula IV-b:



Formula IV-a, or



Formula IV-b.

7. The compound of claim 6 or claim 7, wherein:

(A.1) subscript “a” is 1 or

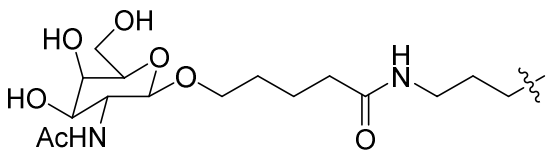
(A.2) subscript “a” is 3; and/or

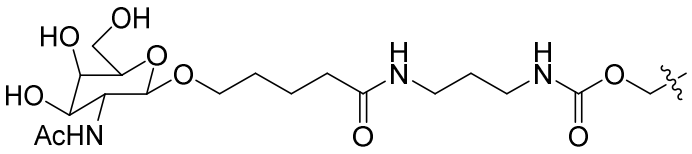
(B.1) subscript “n” is independently 34-46; or

(B.2) subscript “n” is independently between 34-36, in a range of 34-36, between 44-46 or in a range of 44-46; and/or

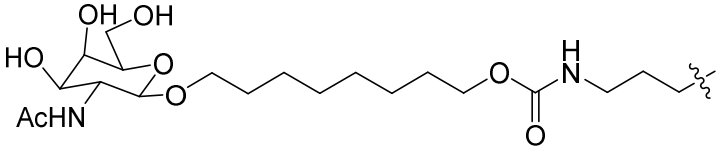
(C.1) subscript “c” is 1; and/or

(D.1) each of A^6, A^7, and A^8 is independently selected from the group consisting of:


,

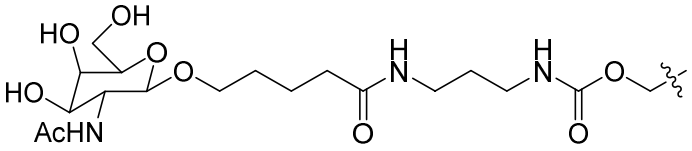


, and

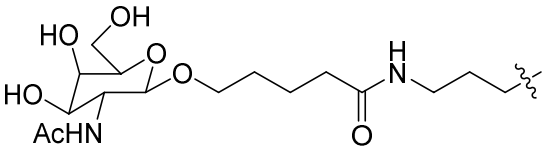


;

(D.2) A^6 and A^7 are each independently

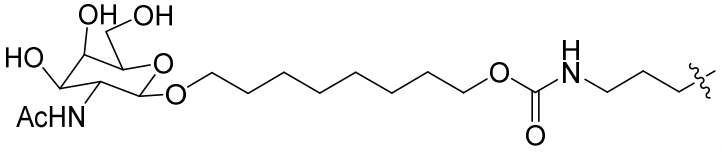


,

and A^8 is 

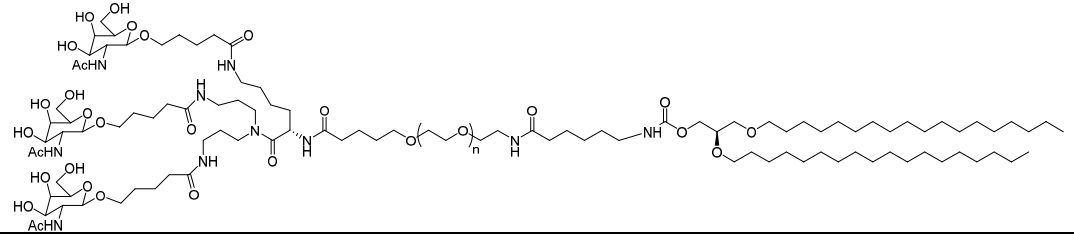
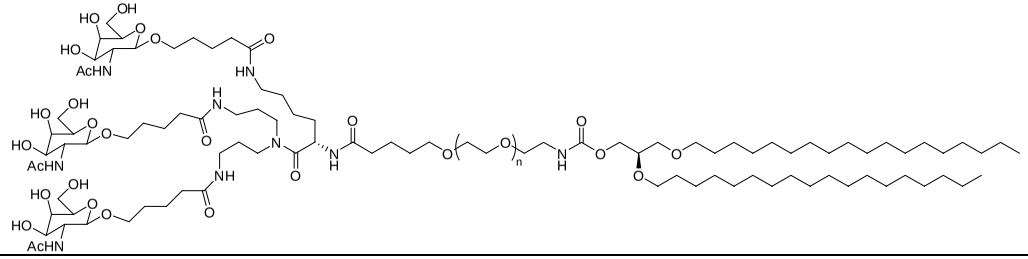
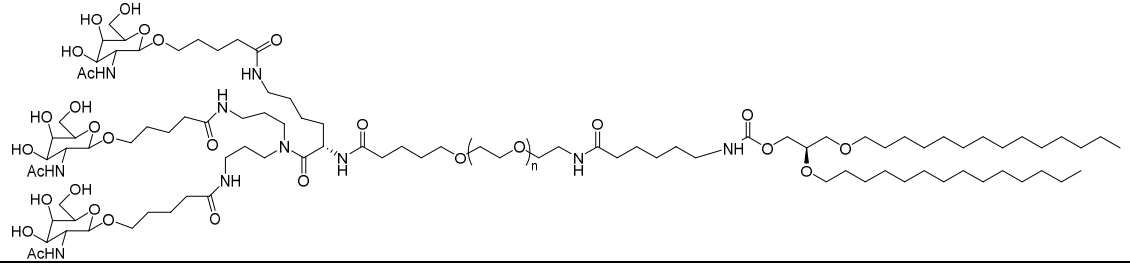
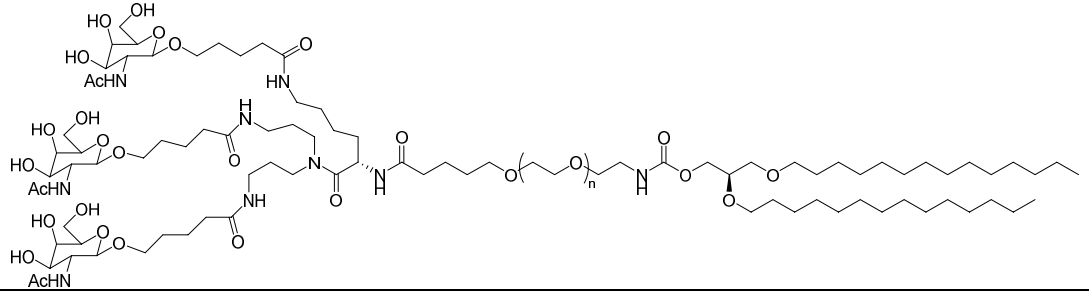
; or

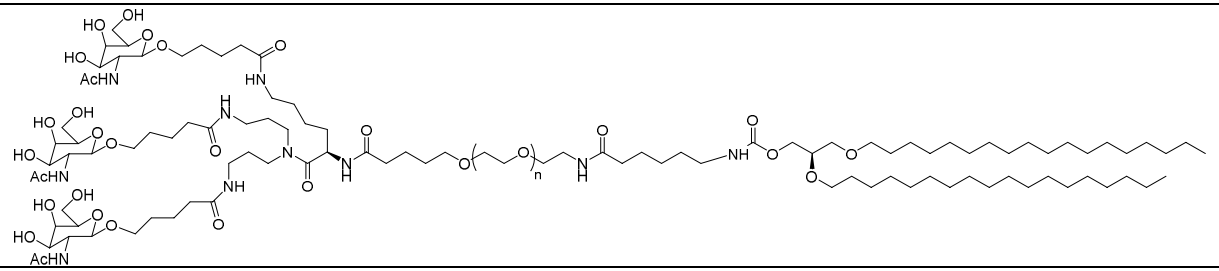
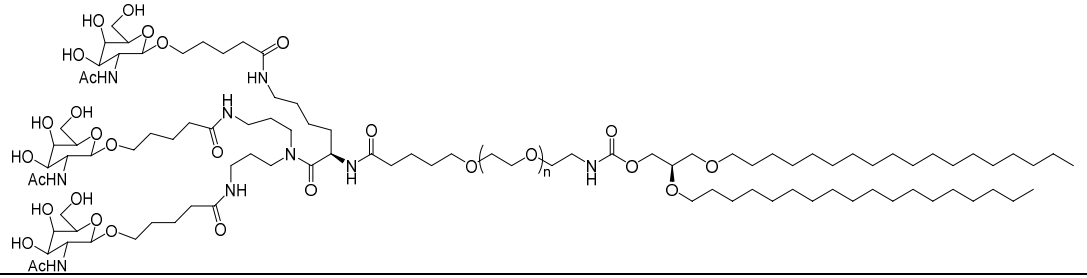
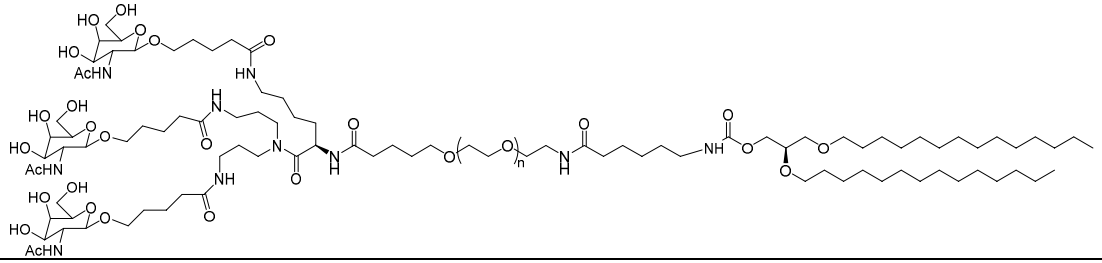
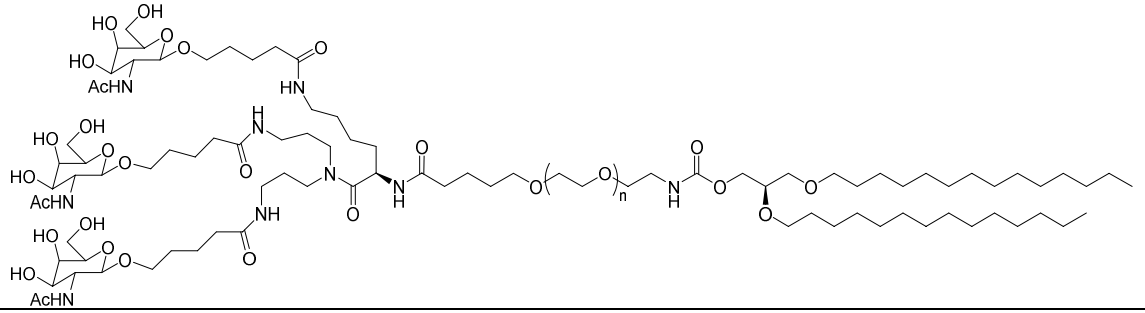
(D.3) A^6, A^7, and A^8 are each independently

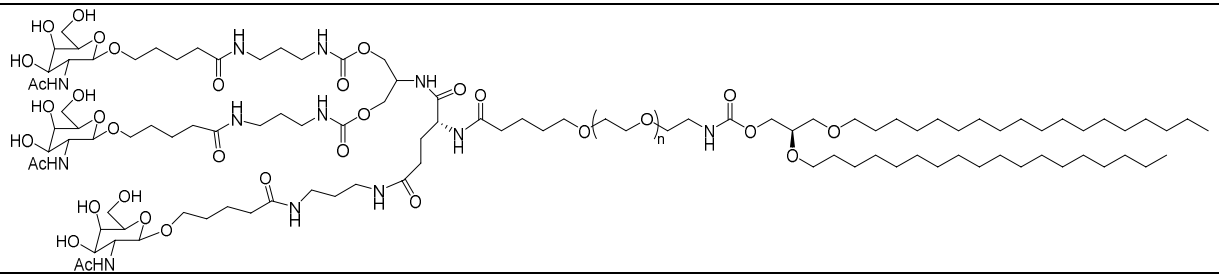
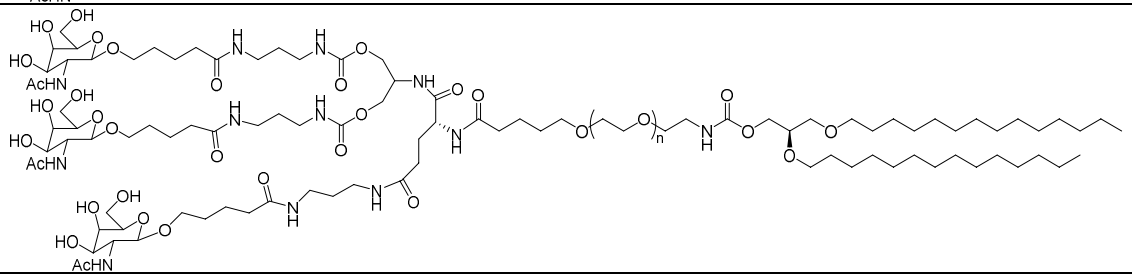
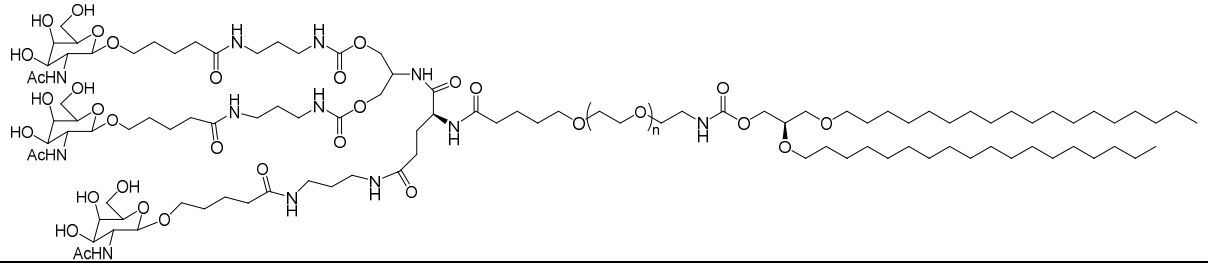
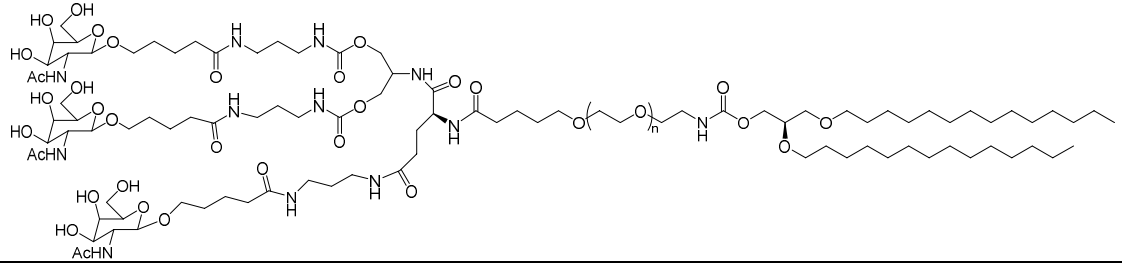


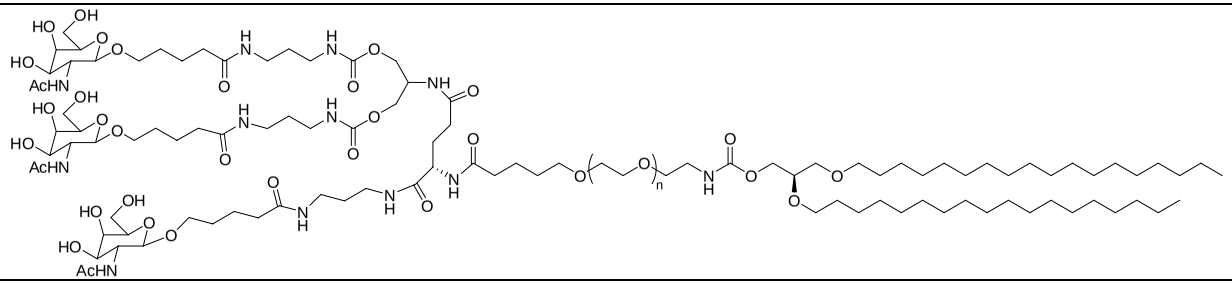
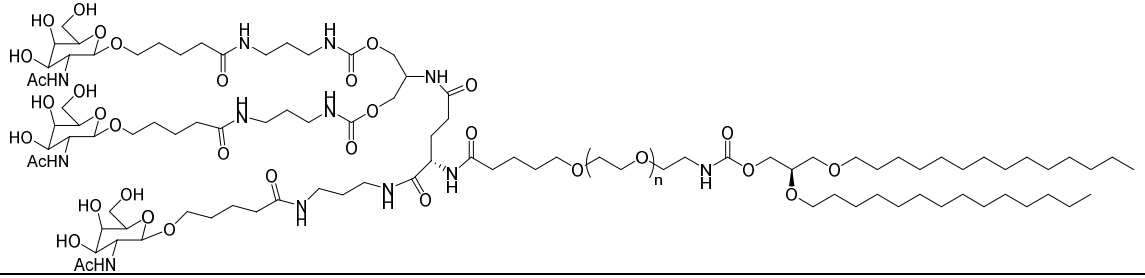
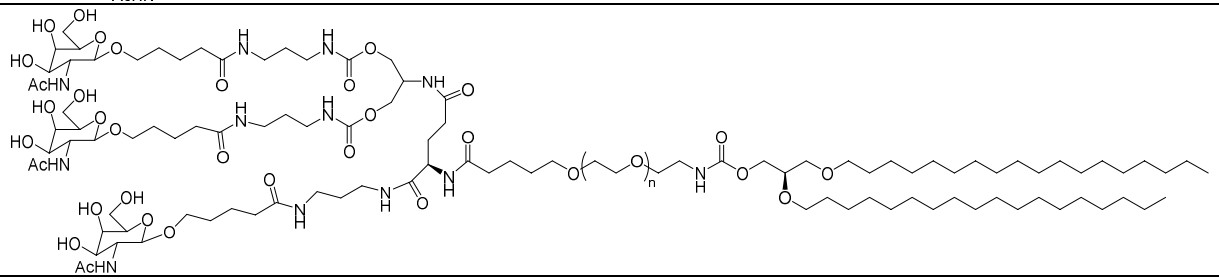
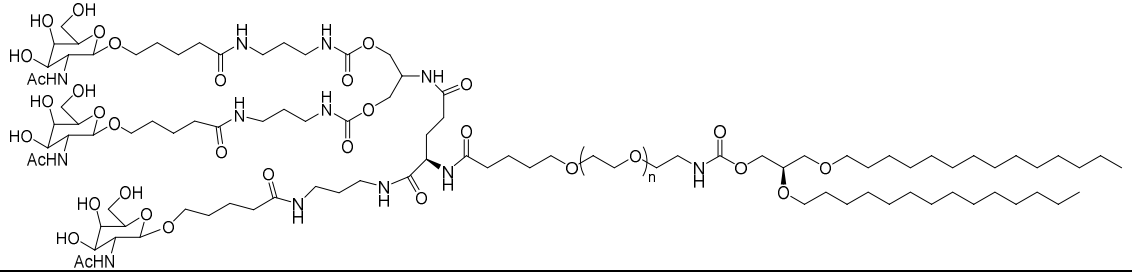
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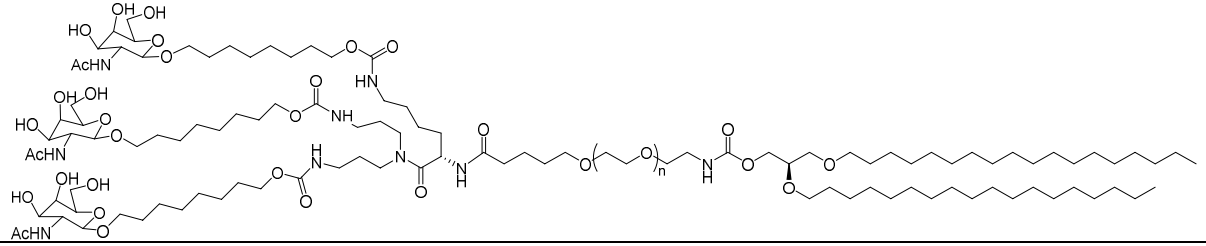
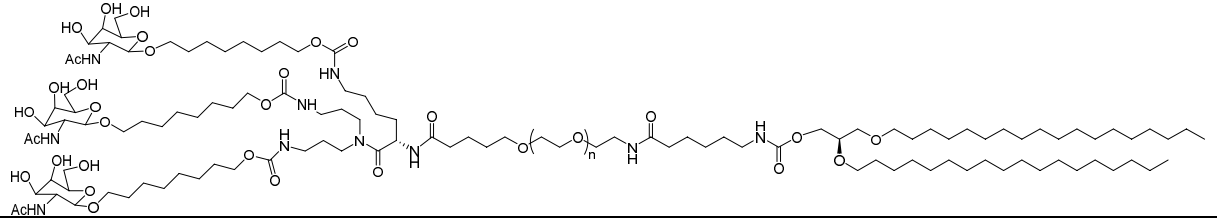
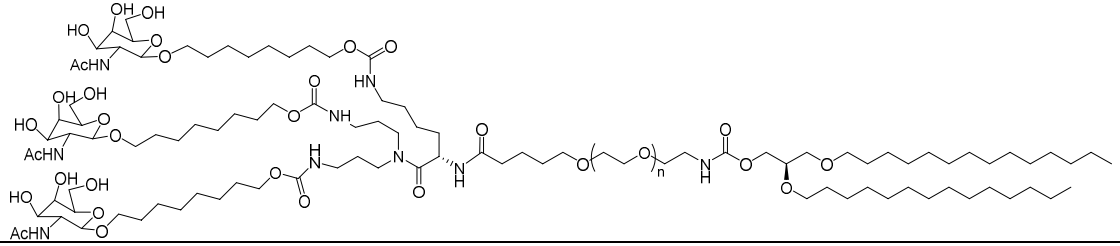
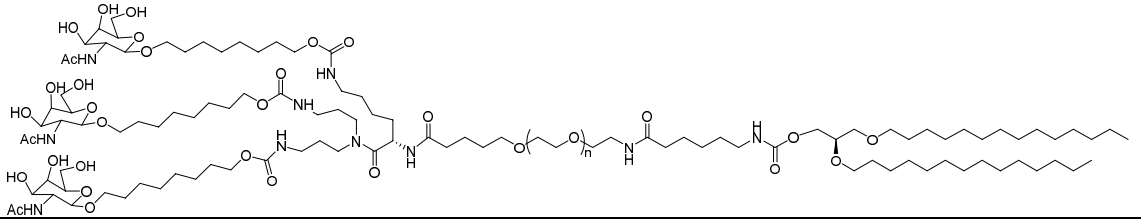
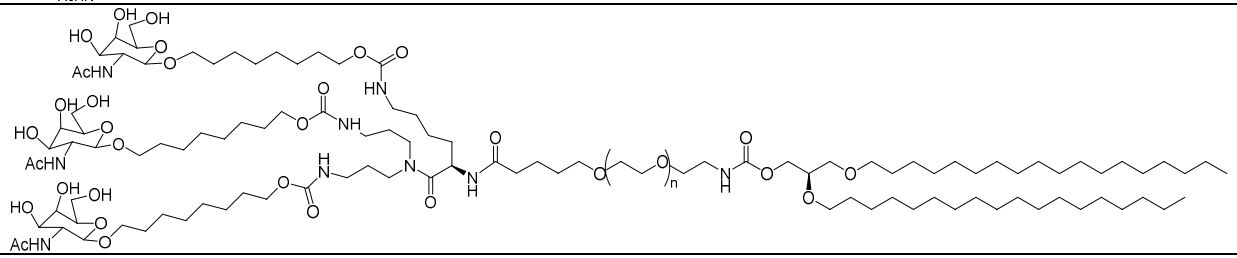
8. A compound selected from the group consisting of:

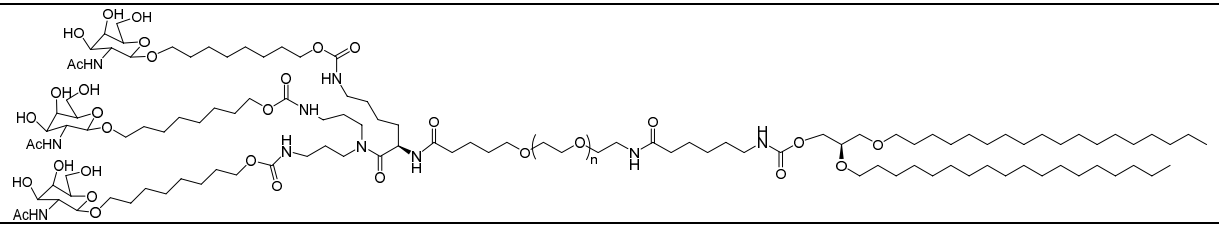
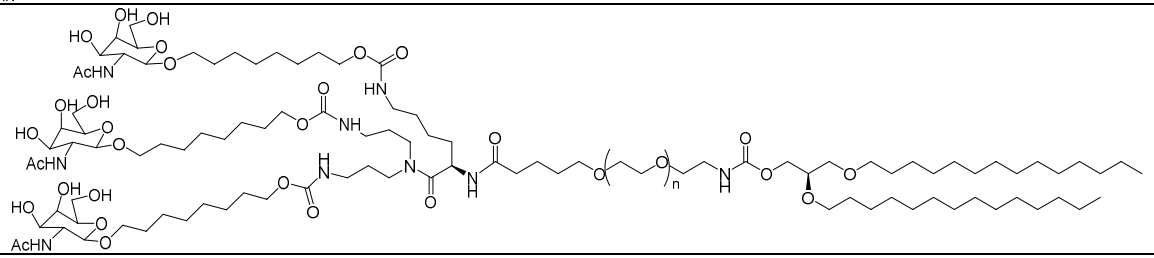
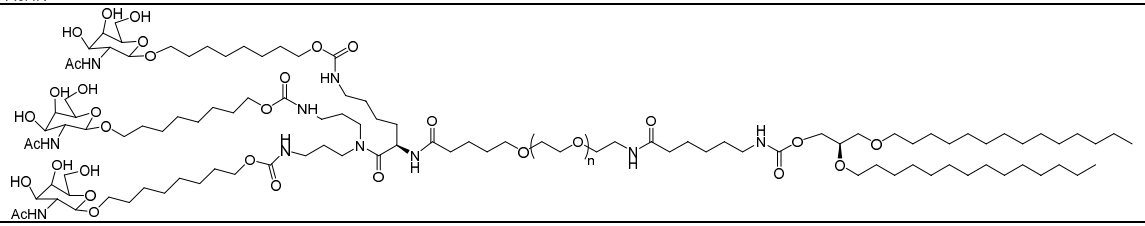
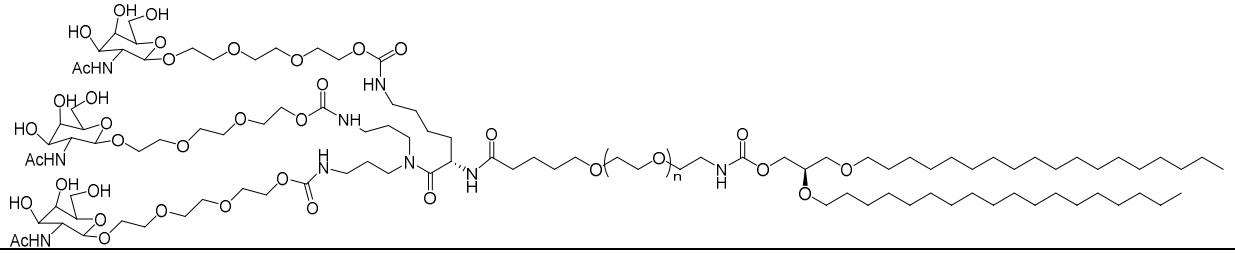
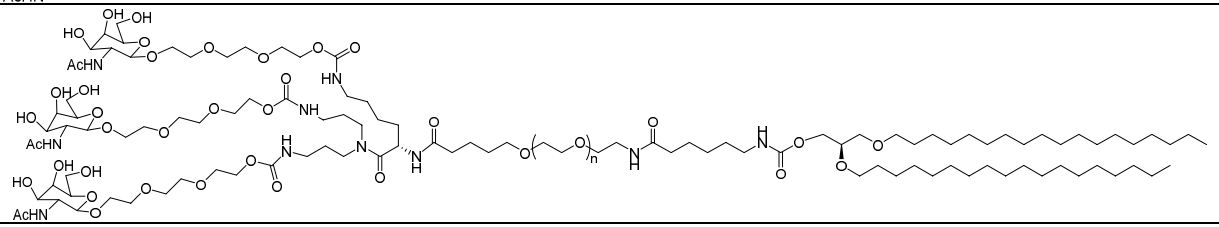
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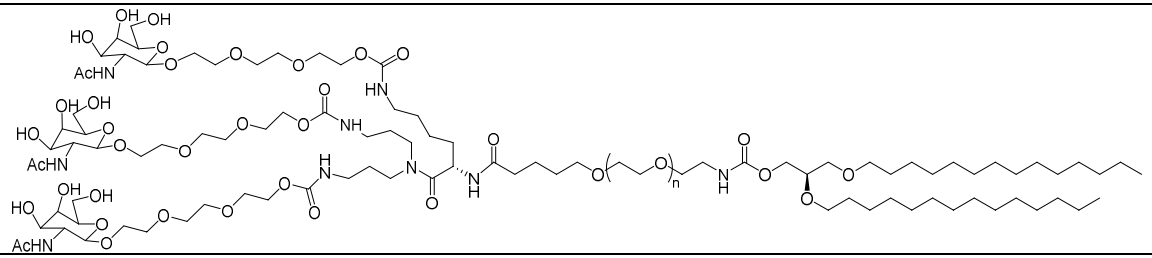
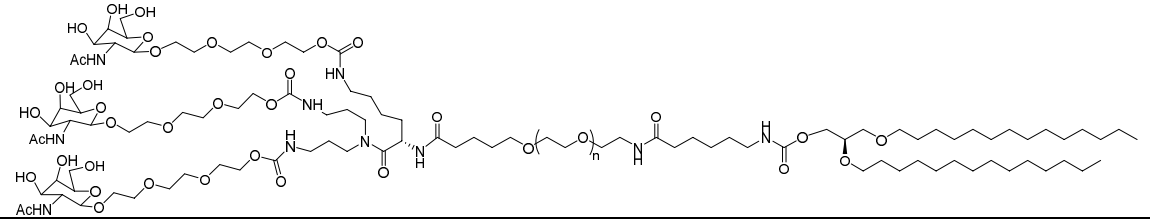
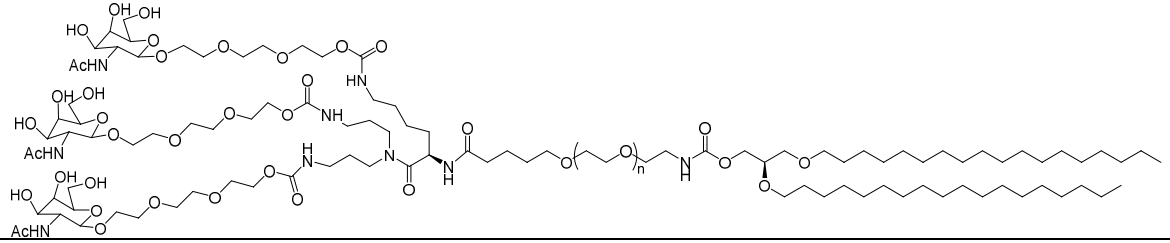
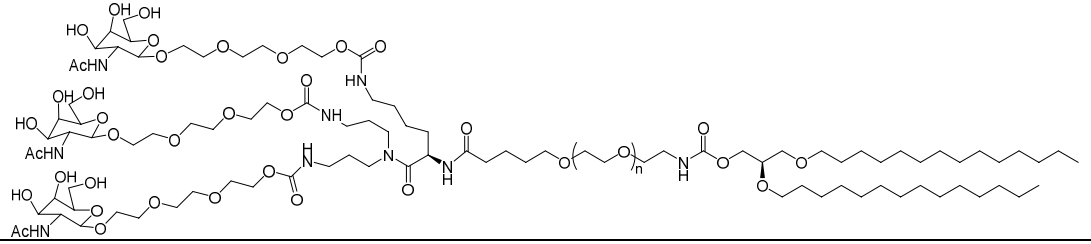
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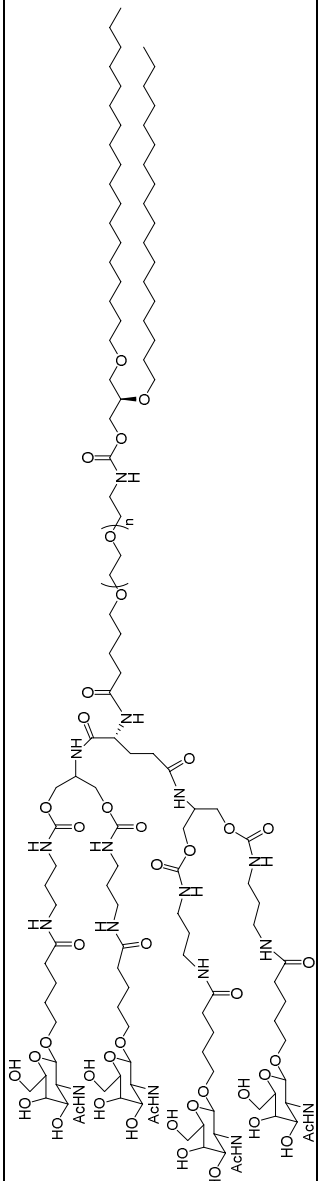
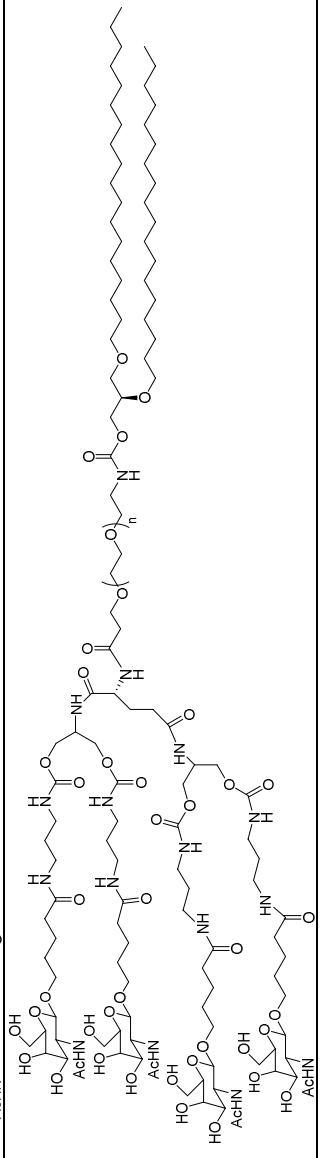
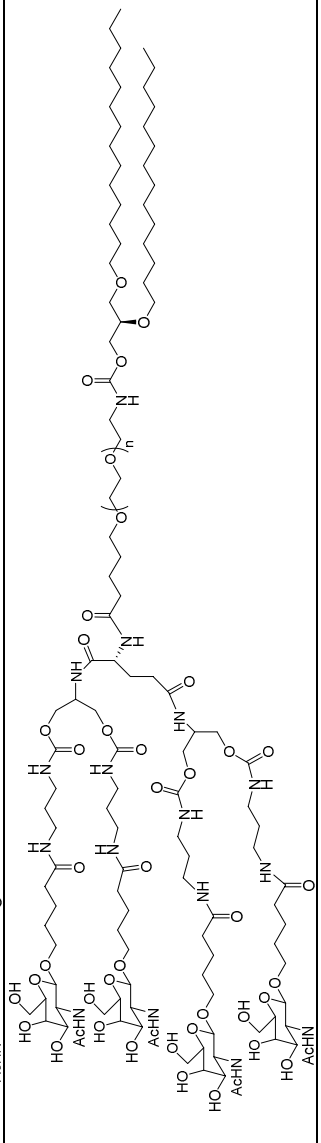
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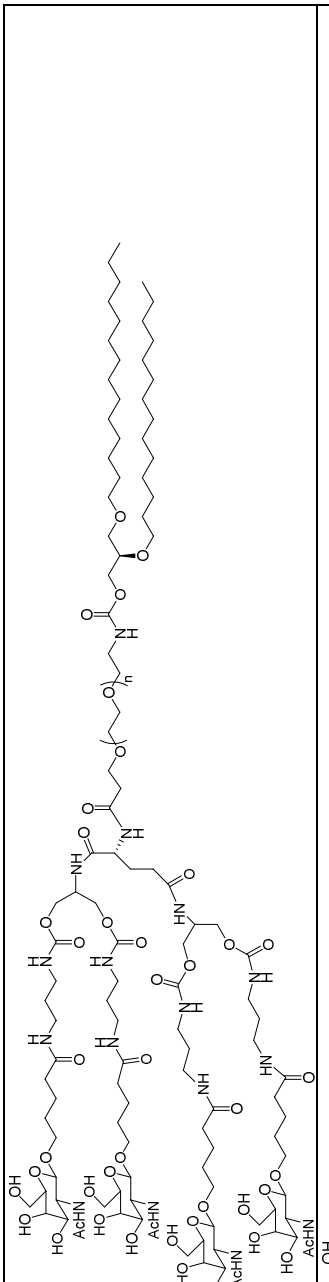
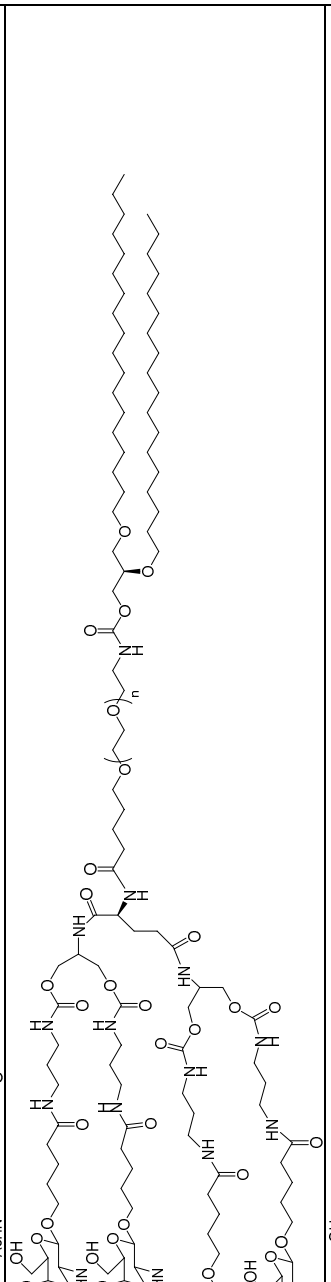
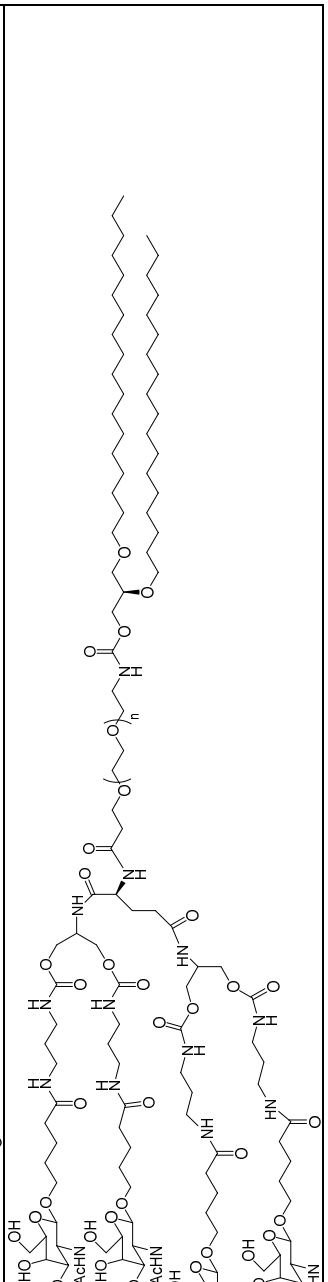
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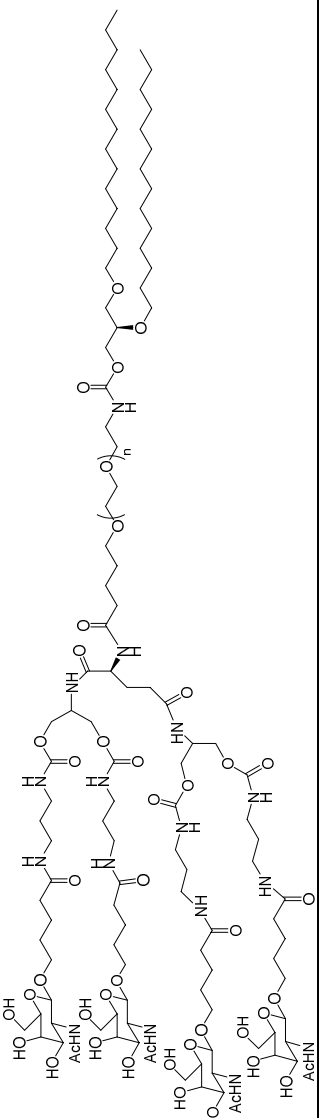
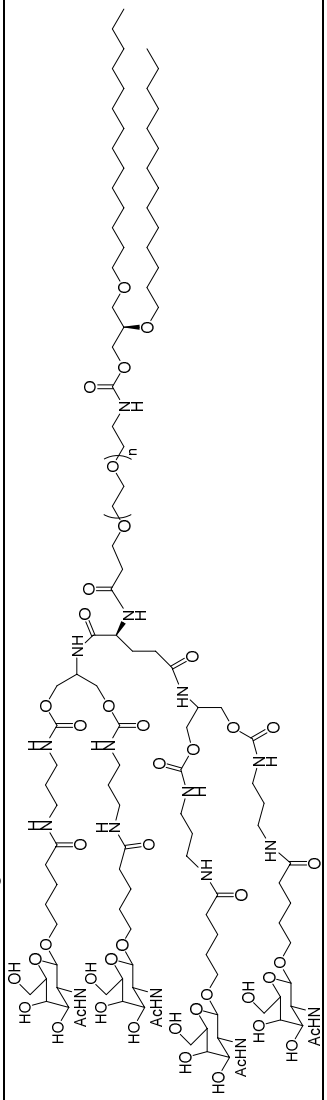
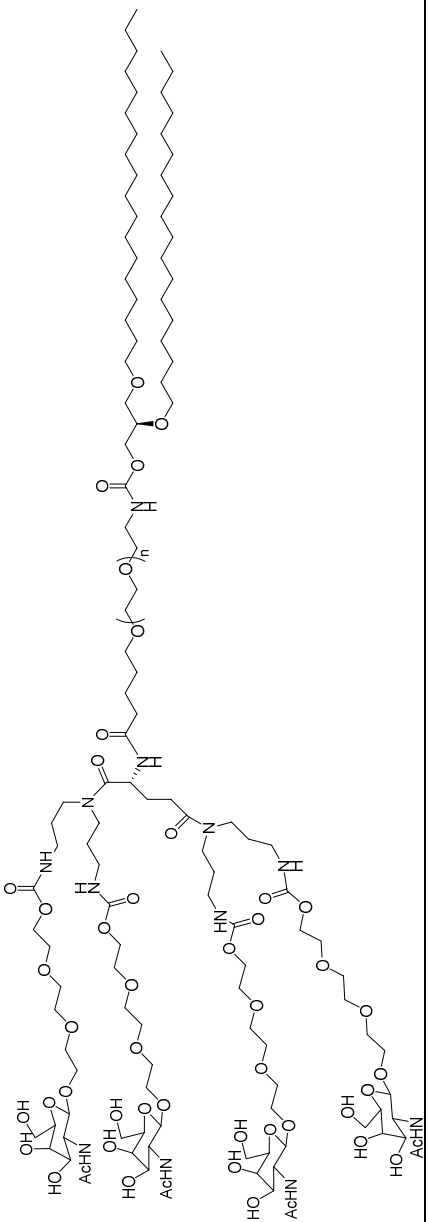
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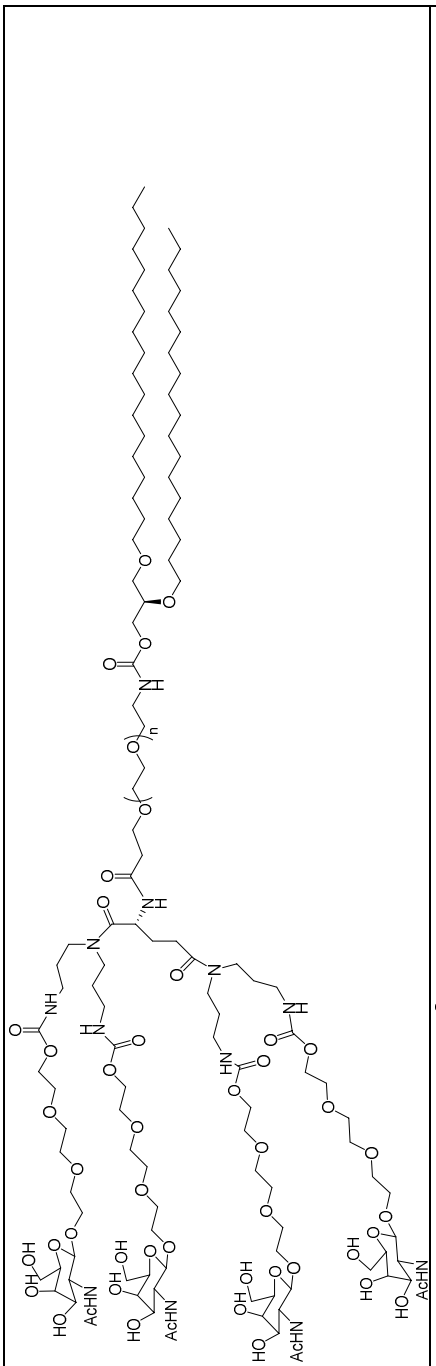
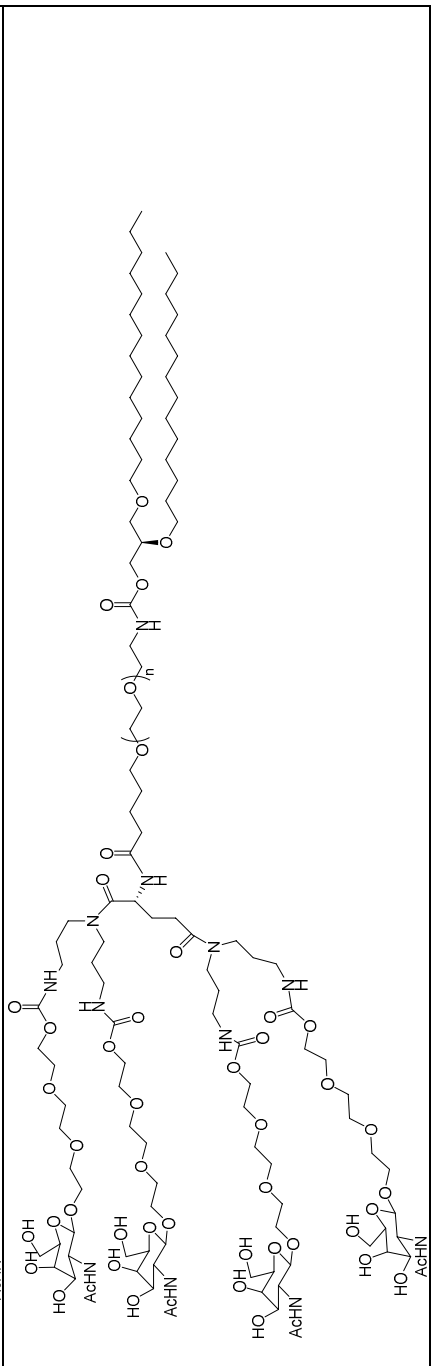
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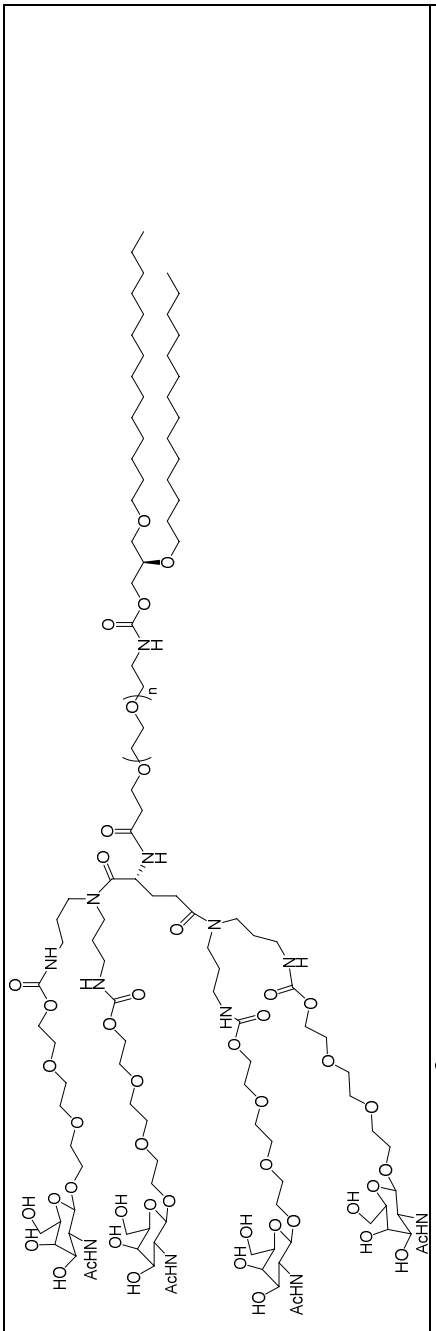
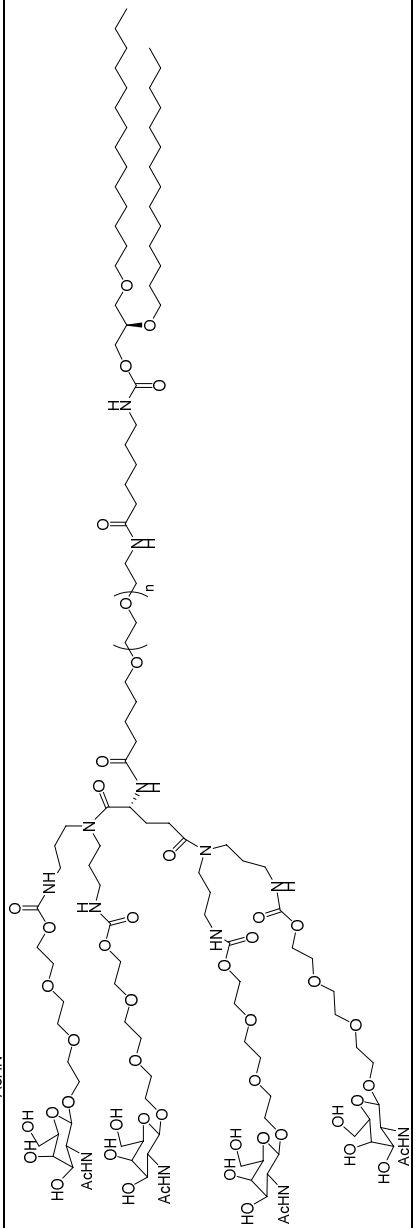
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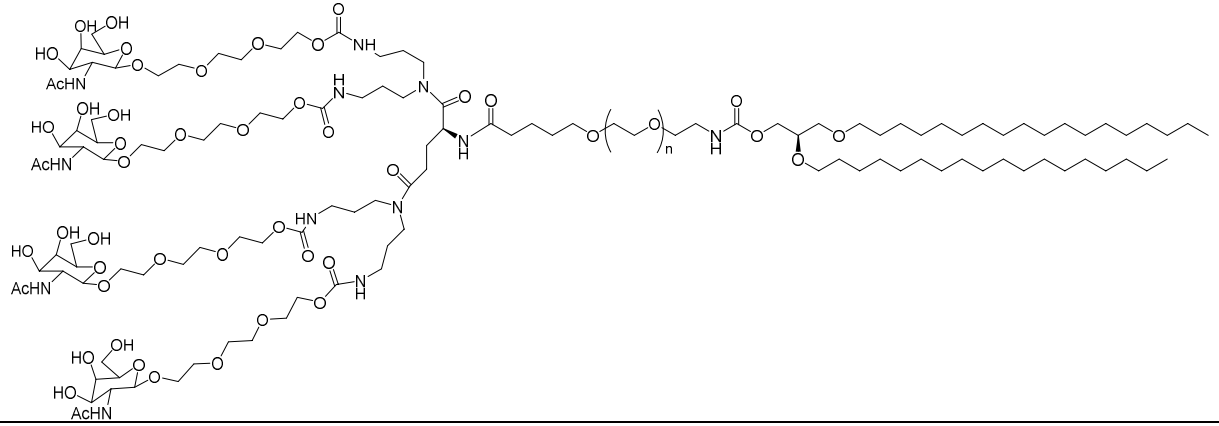
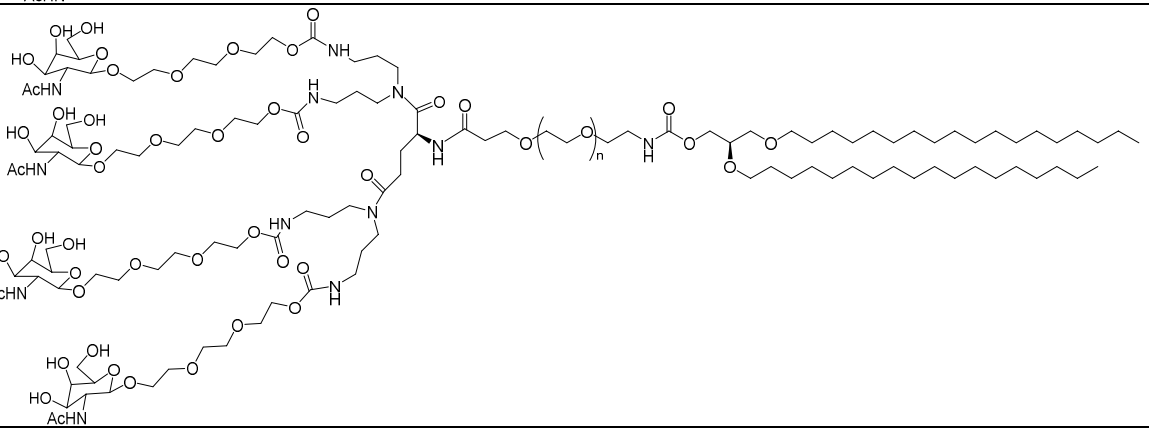
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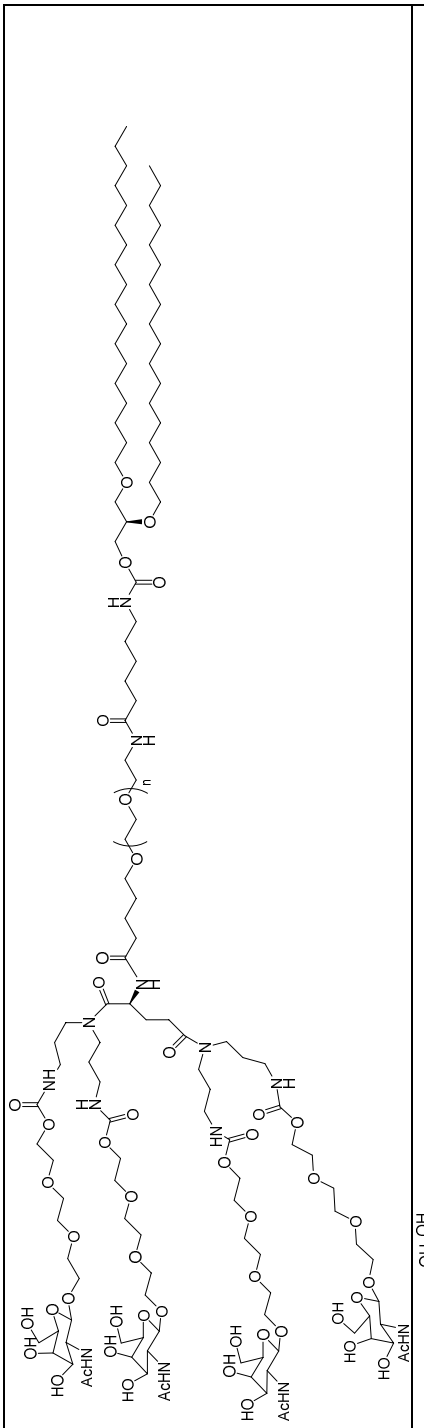
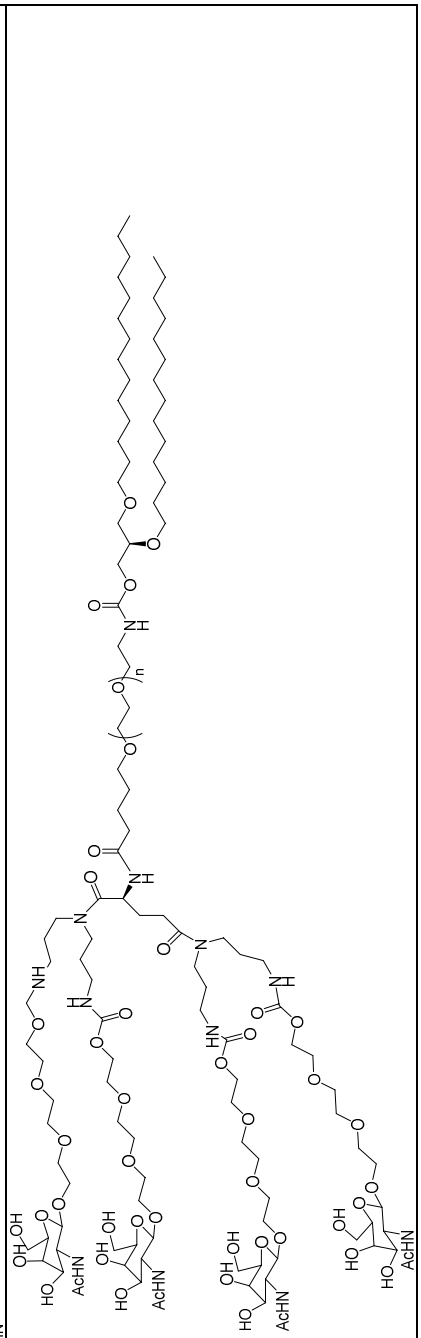
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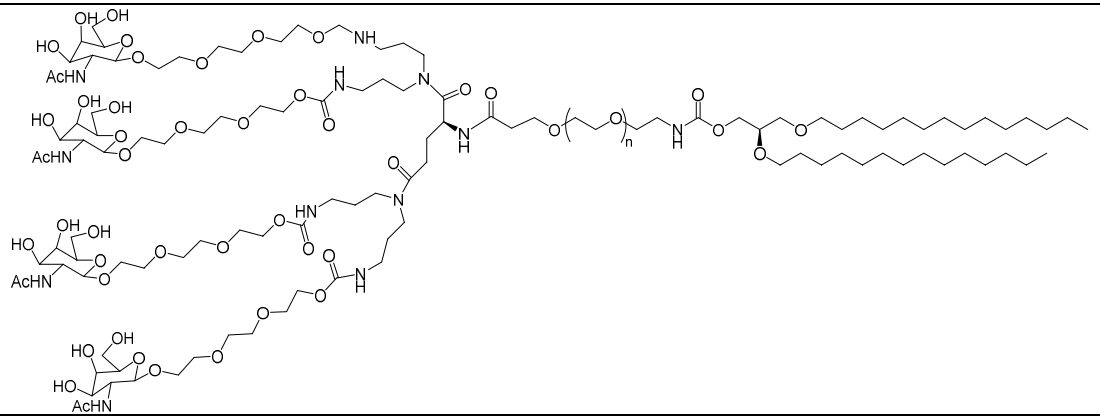
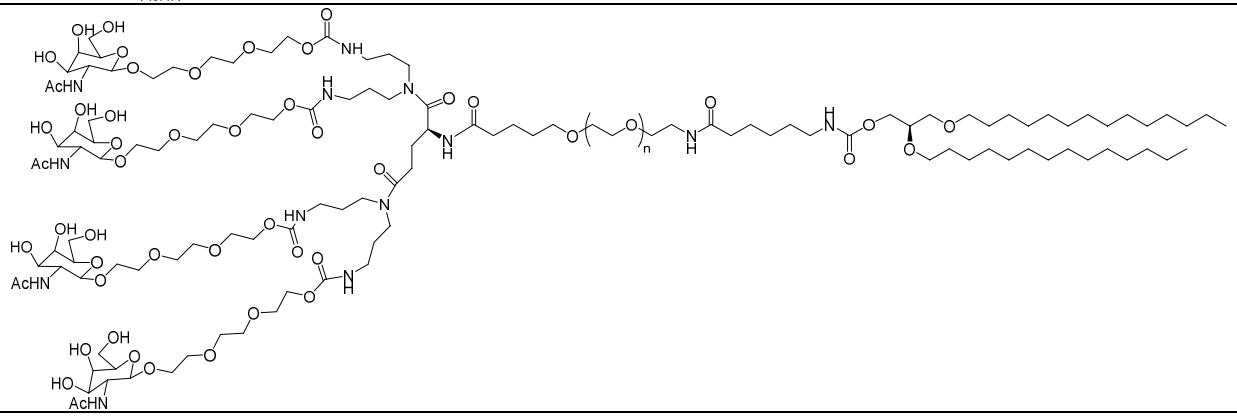
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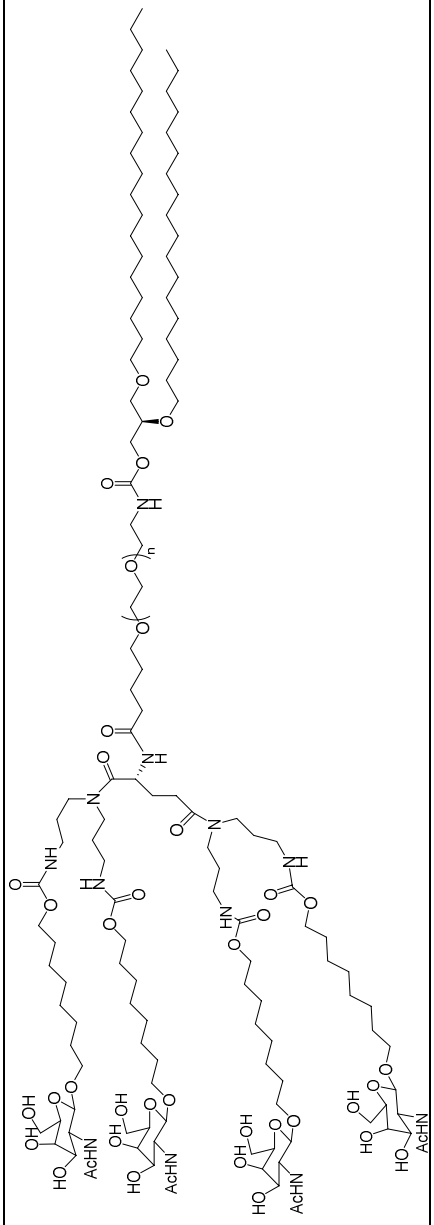
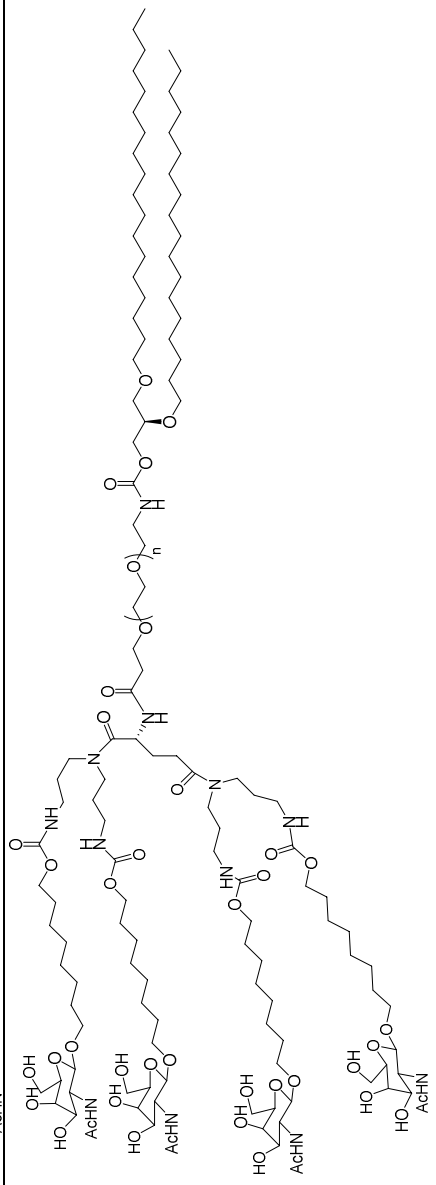
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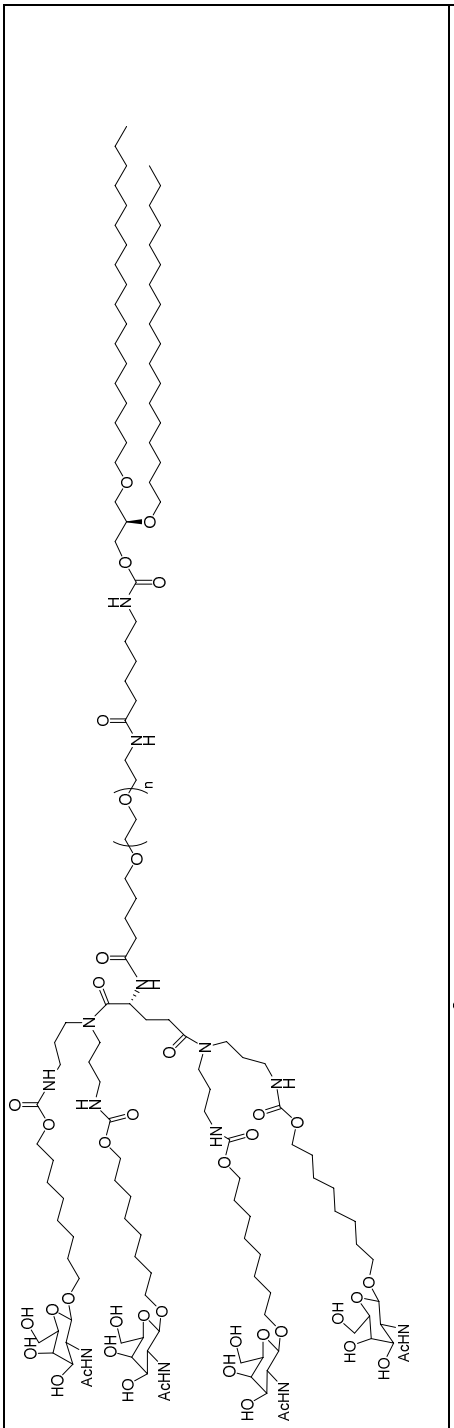
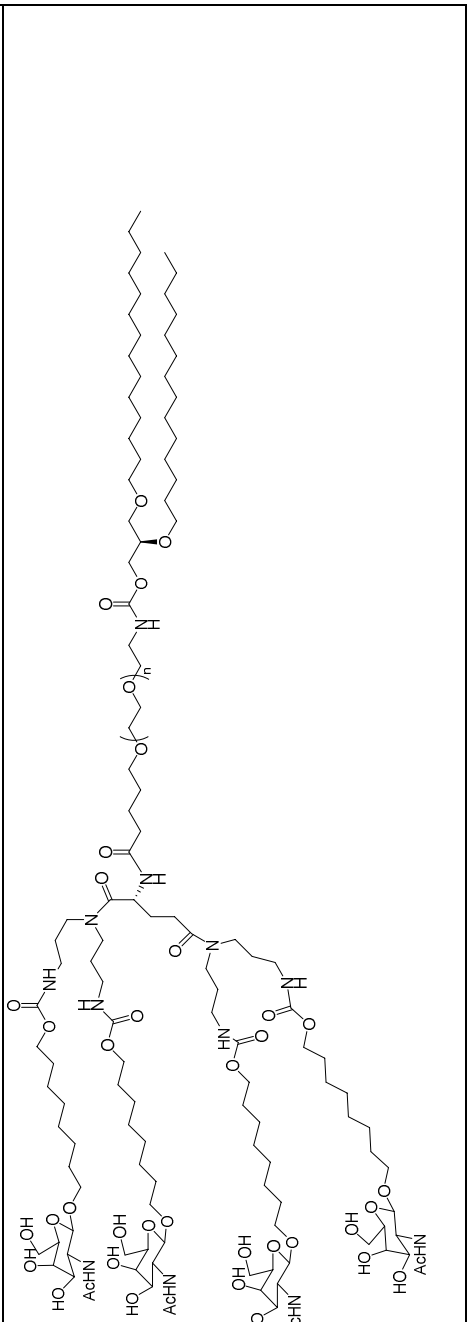
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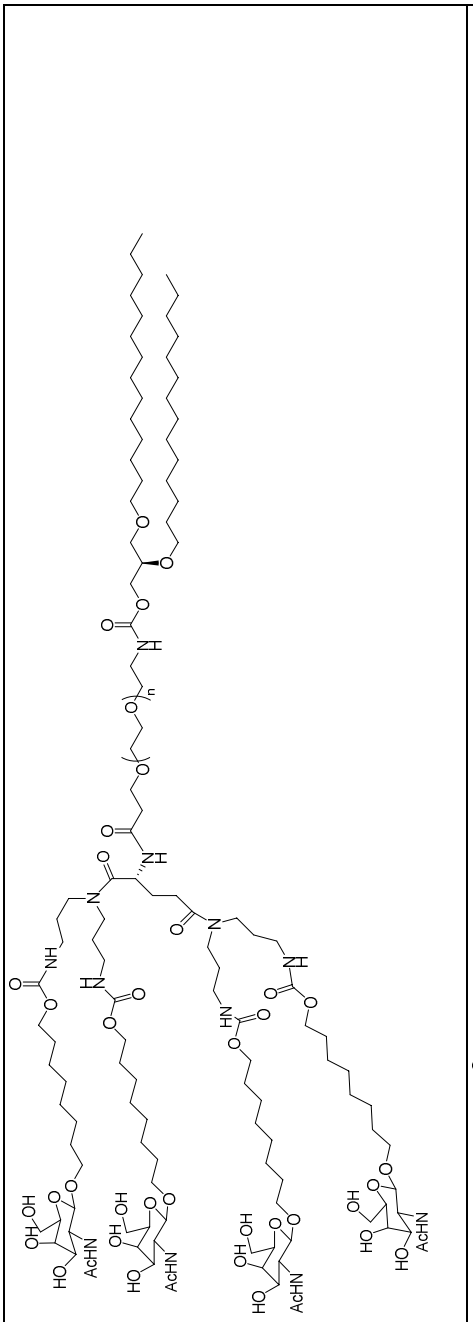
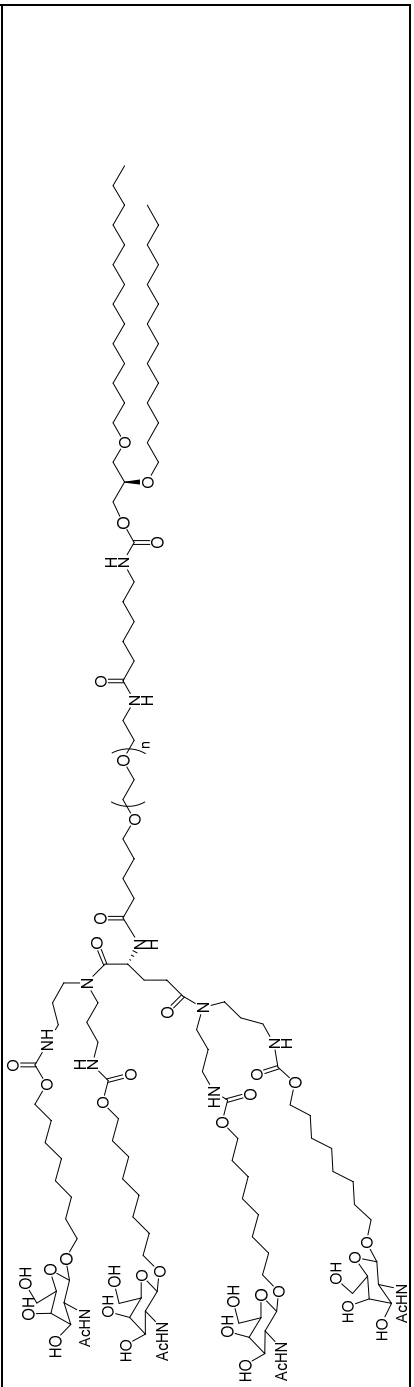
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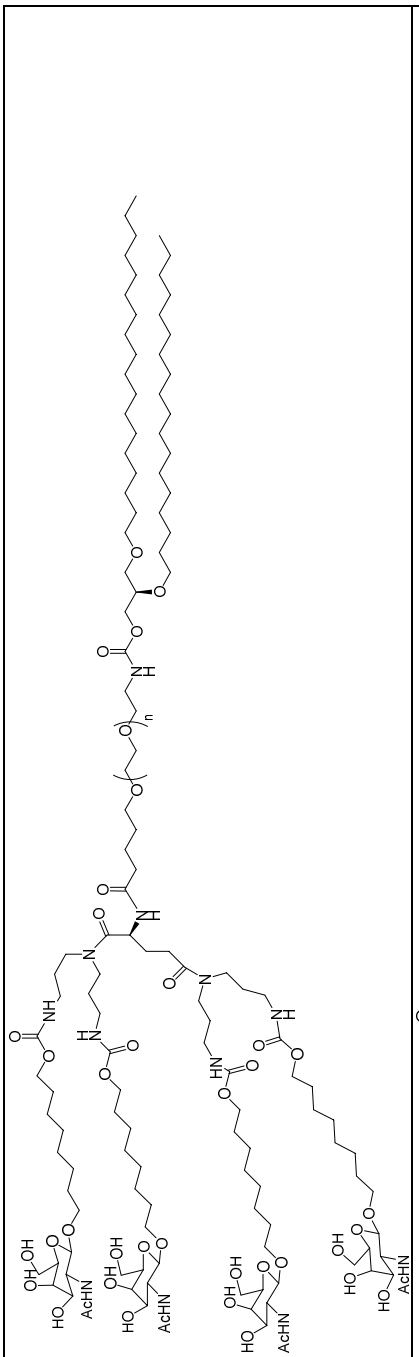
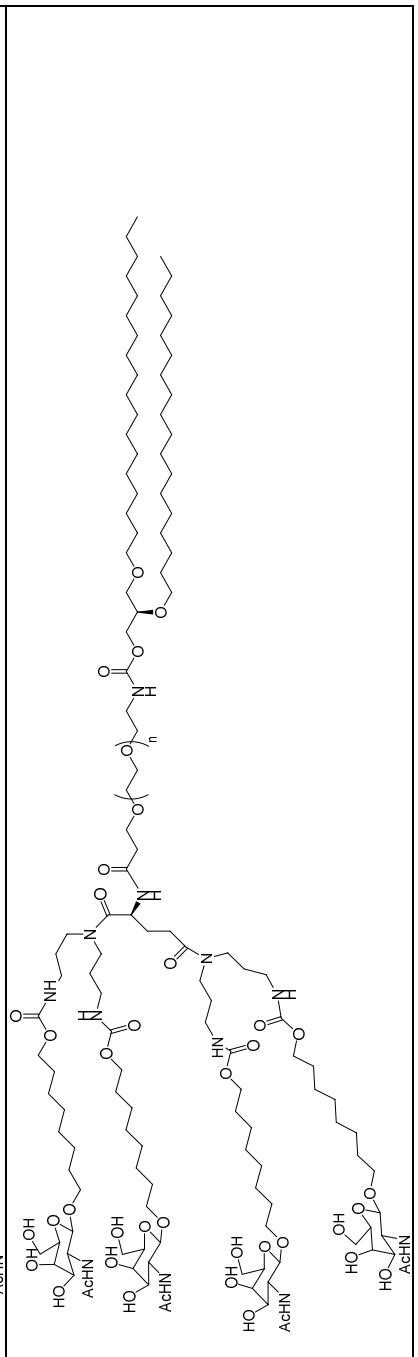
	
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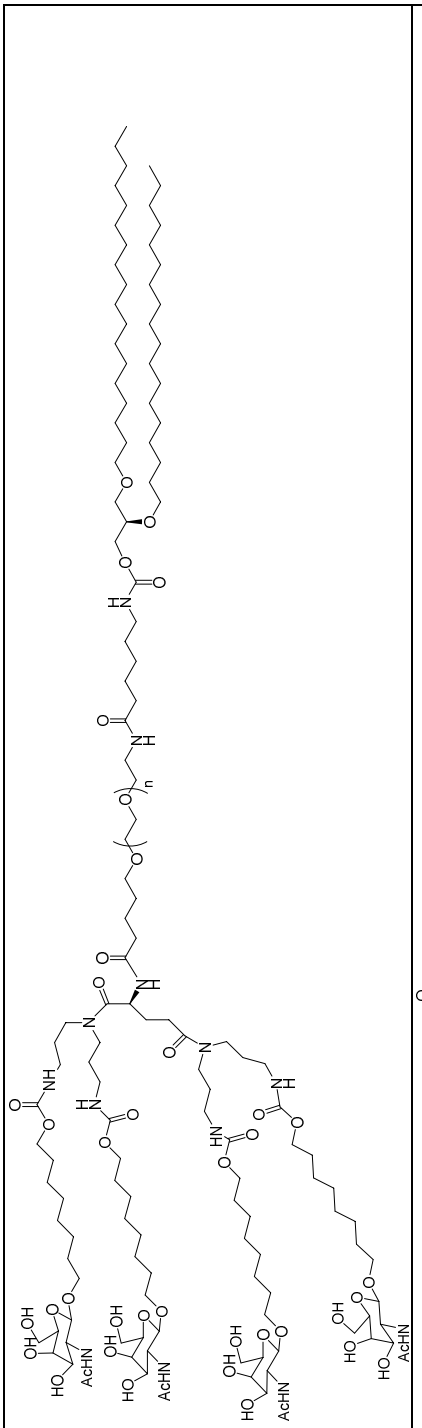
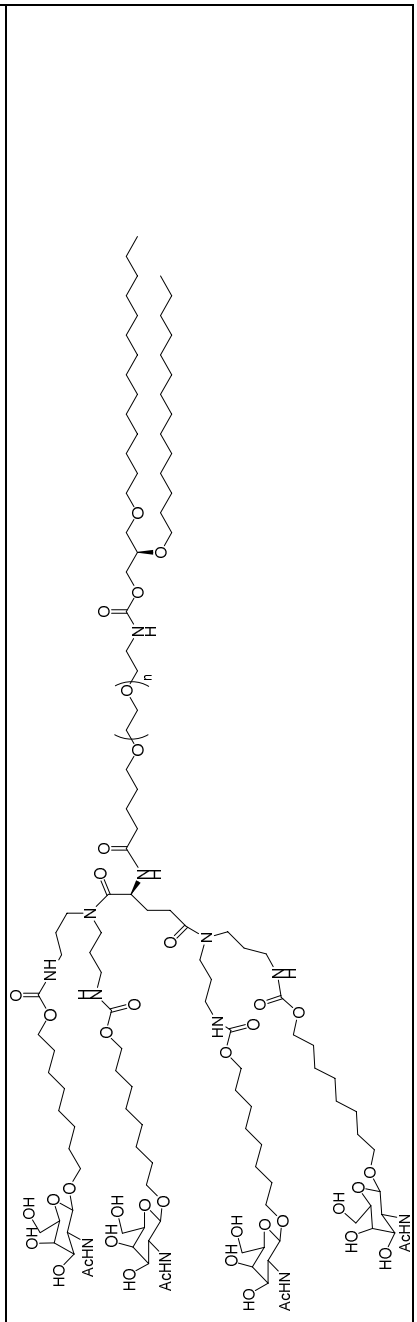
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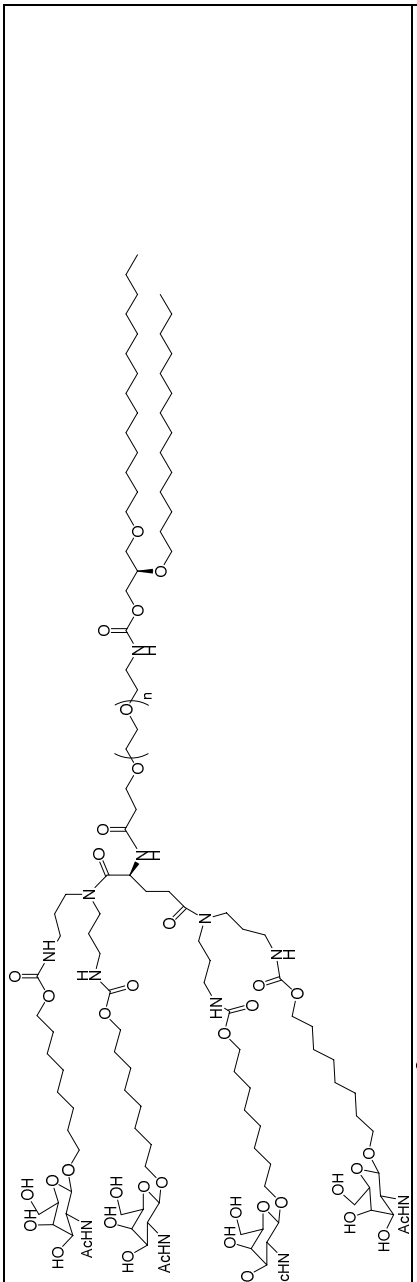
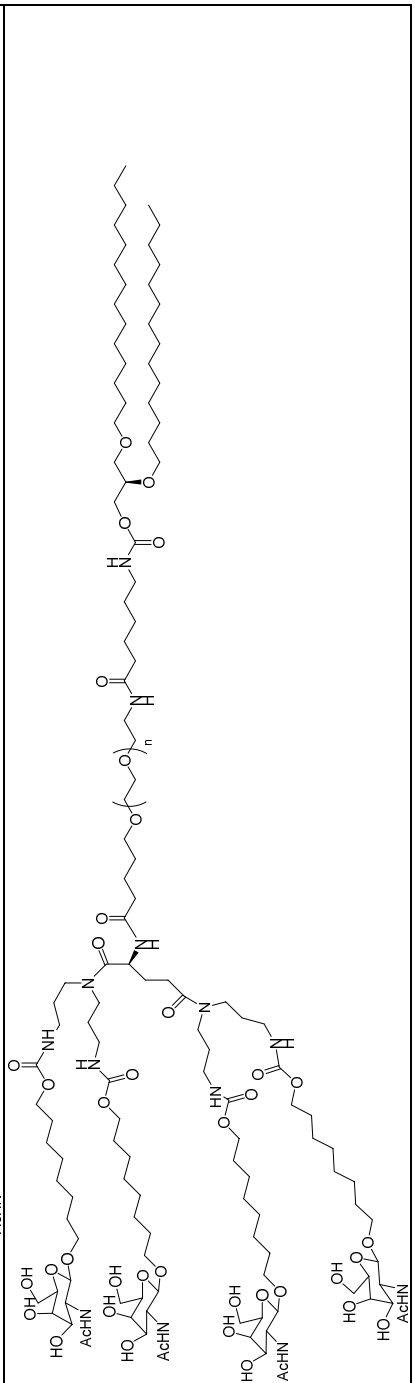
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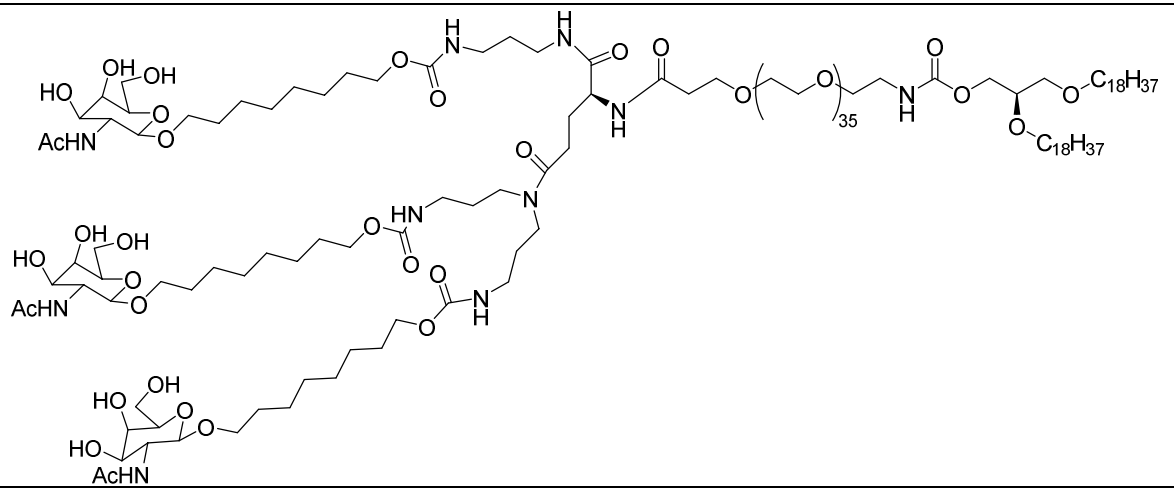
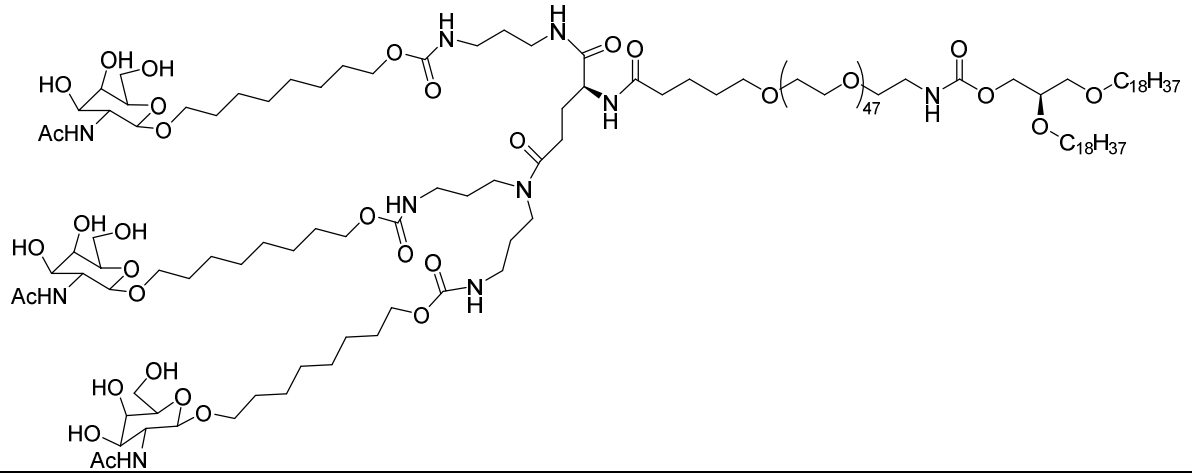
	
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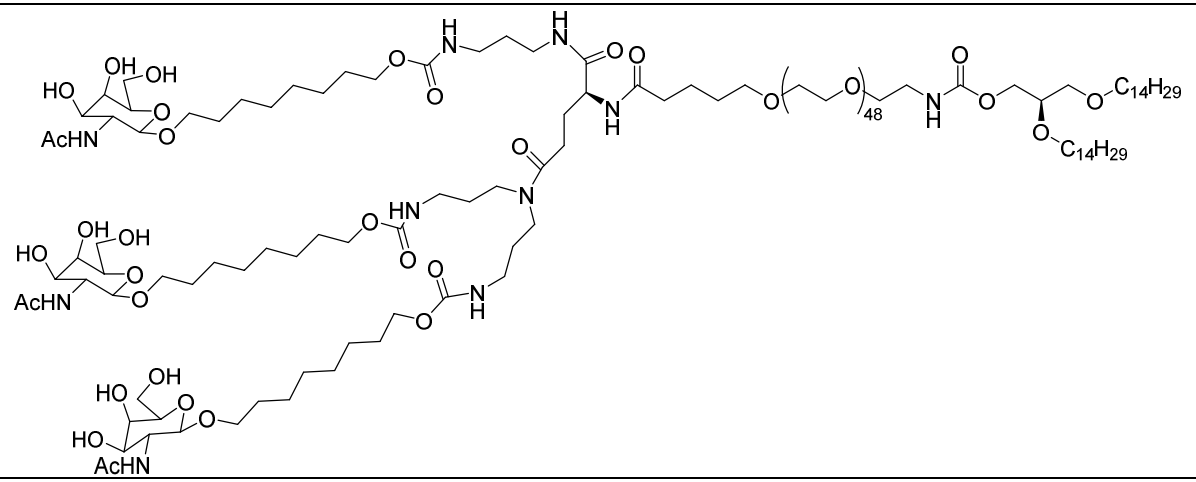
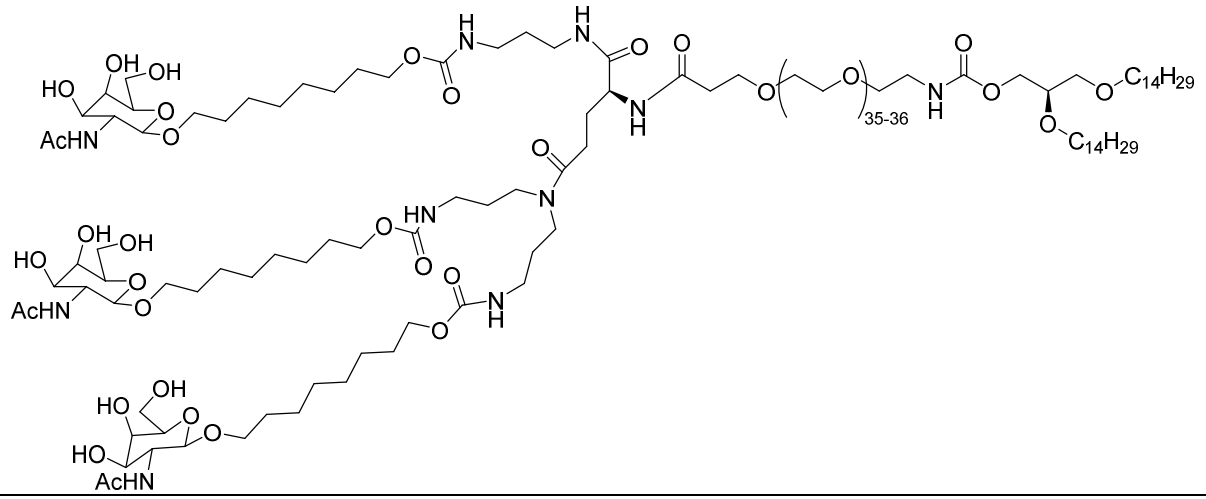
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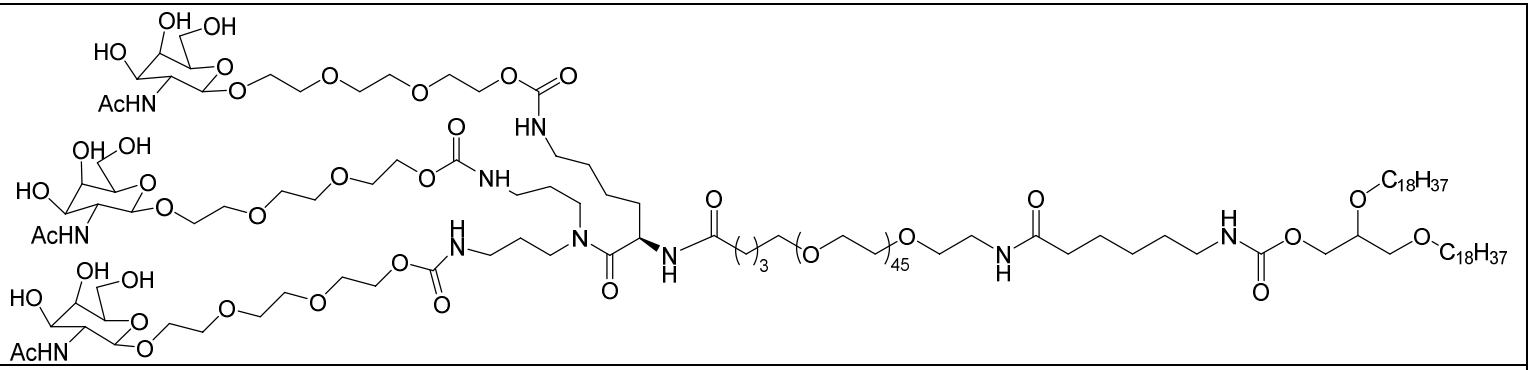
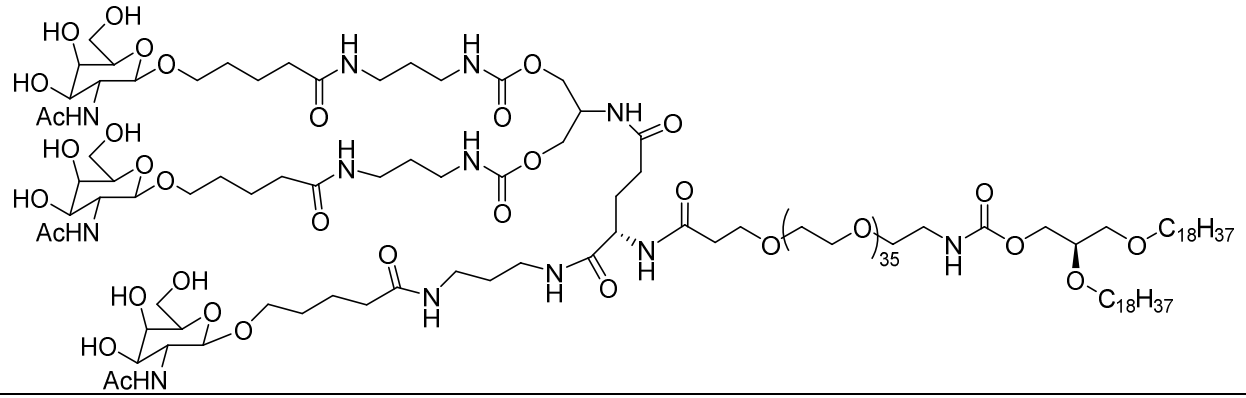
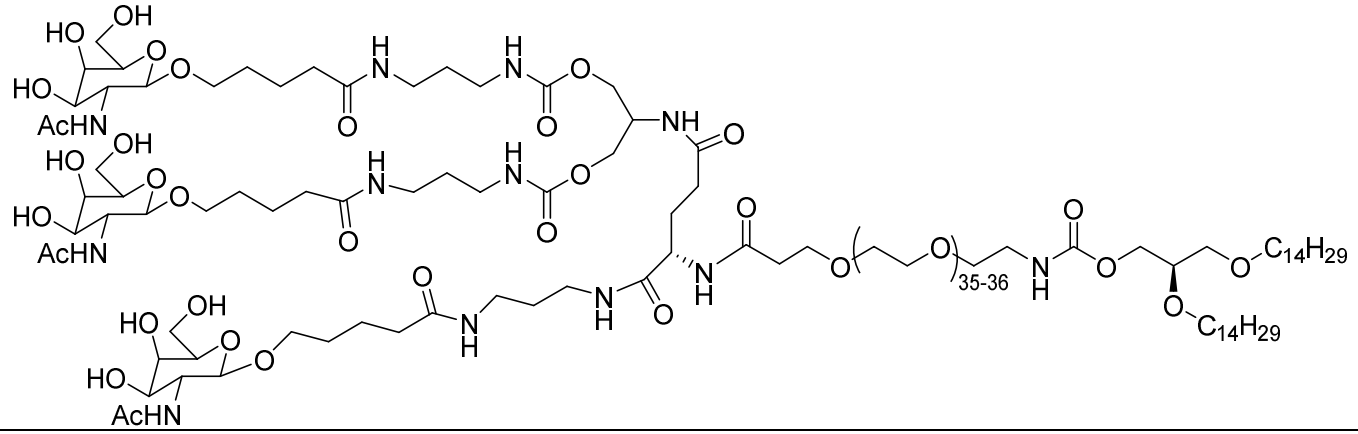
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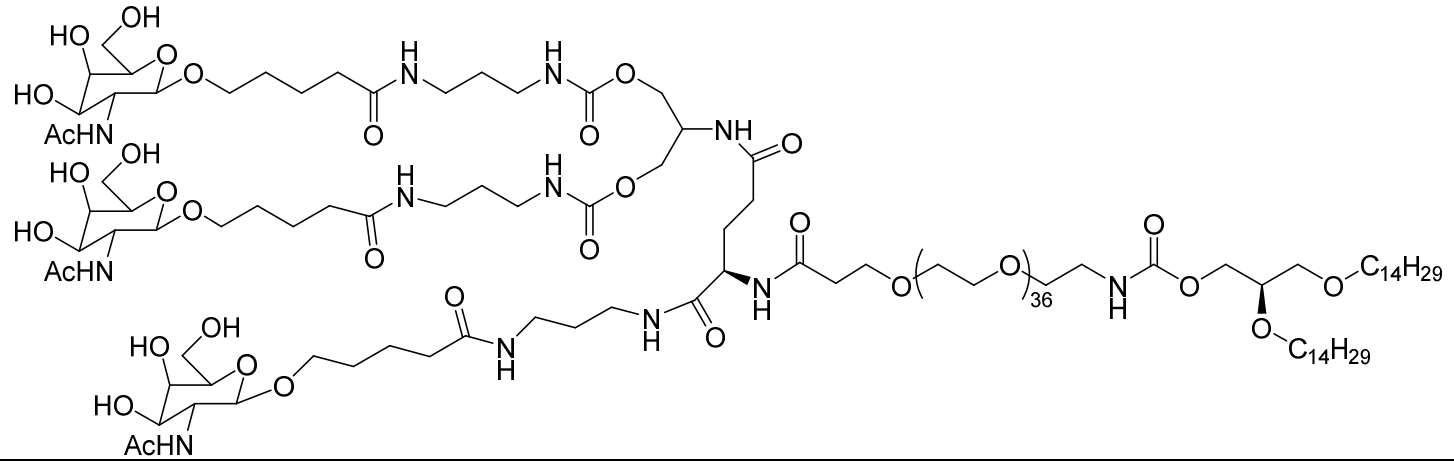
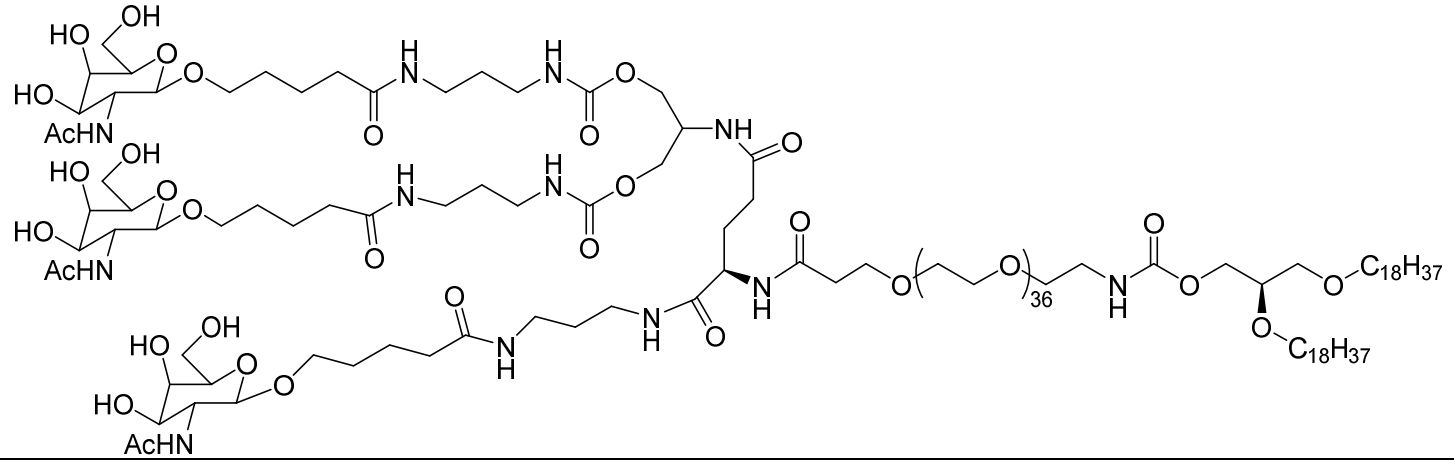
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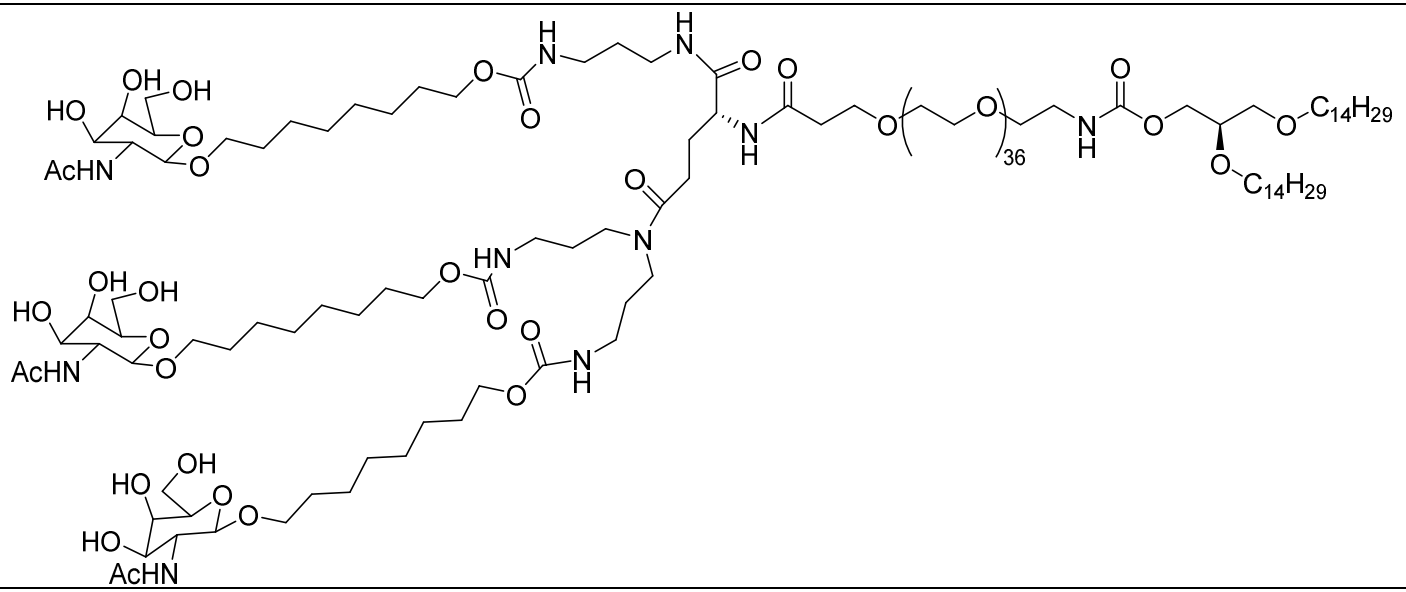
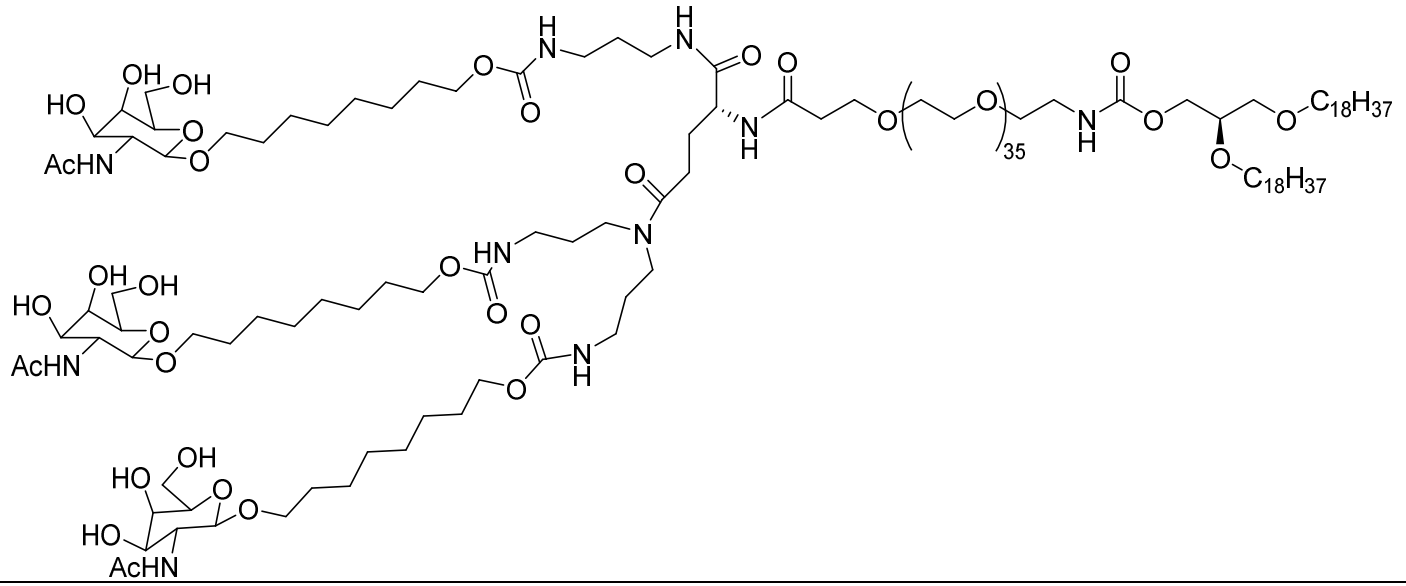
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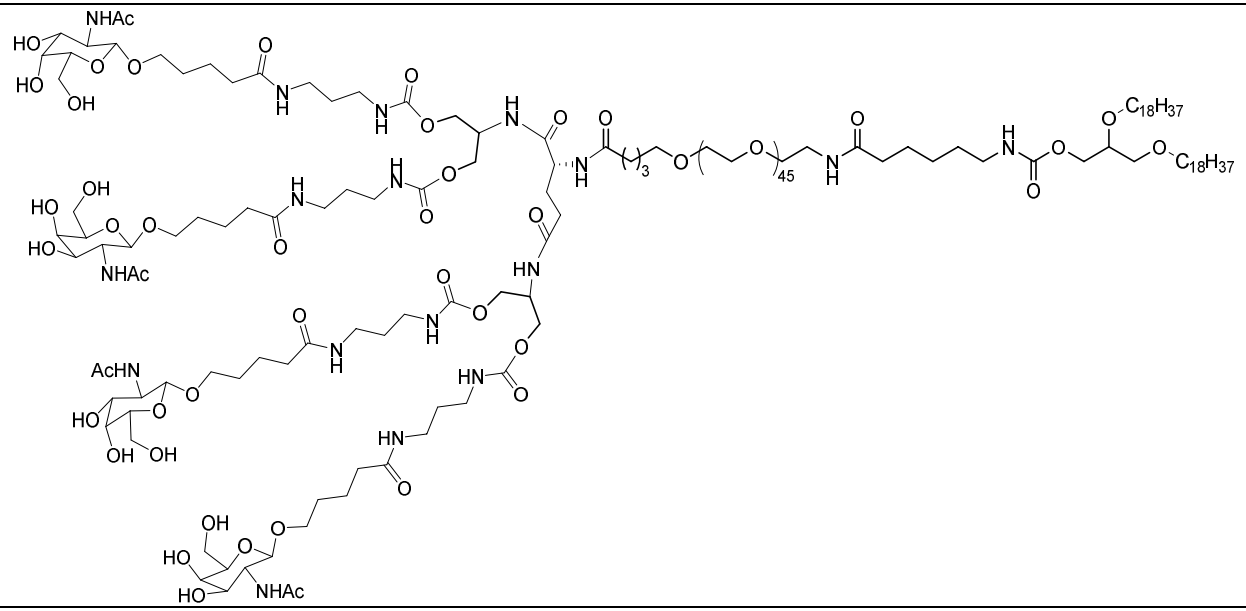
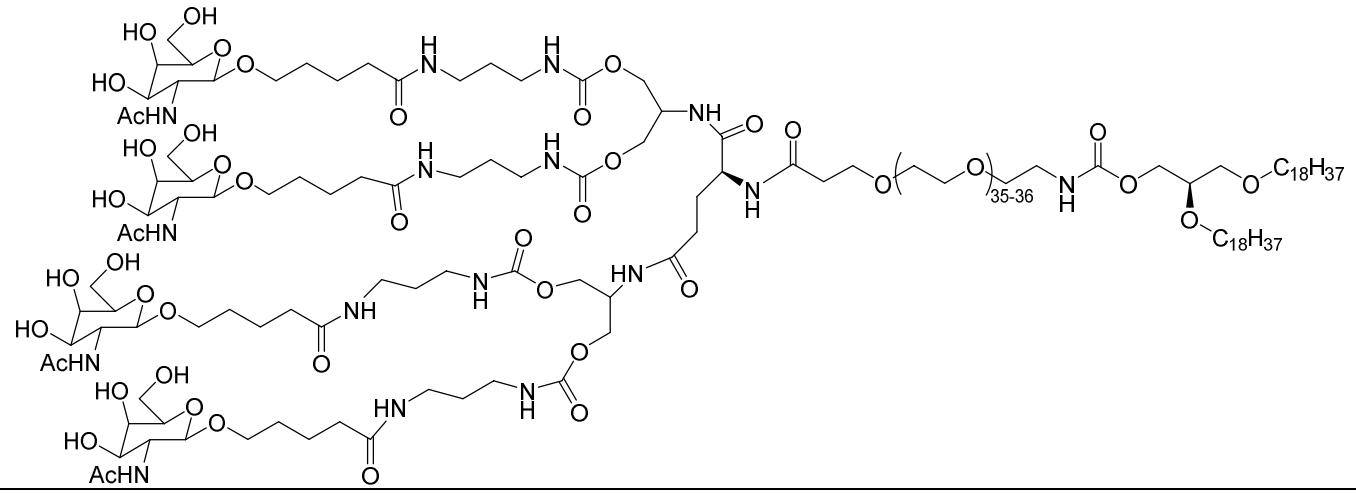
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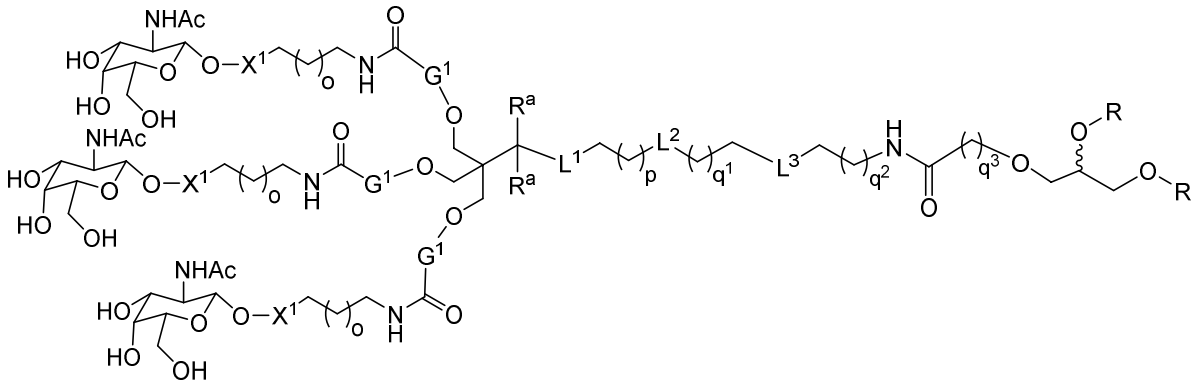
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wherein each subscript “n” is between 10-200.

9. A compound of Formula I:



Formula I

wherein,

each X^1 is independently $–(CH_2)_r–$, $–(CH_2CH_2O)_s–$, $–(OCH_2CH_2)_s–$, $–((CH_2)_m–C(O)NH)–$, or $–(C(O)NH–(CH_2)_m)–$,

each subscript "m" is independently 1-5;

each subscript "o" is independently 1-5;

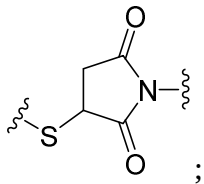
each subscript "r" is independently 1-10;

each subscript "s" is independently 1-5;

each G^1 is independently a C_1-C_6 substituted or unsubstituted alkylene;

each R^a is independently H or a C_1-C_6 substituted or unsubstituted alkyl;

L^1 is –NHC(O)–, –C(O)NH–, –NHC(O)O–, –OC(O)NH–, –NHC(O)NH–, –S-S–, or



;

subscript "p" is independently 1-5;

L^2 is $–O-(CH_2CH_2O)_n–$, $–(CH_2CH_2O)_n-O–$, or $–(OCH_2CH_2O)_n–$,

each subscript "n" is independently 1-200;

subscript "q^1" is independently 0-5;

subscript "q^2" is independently 0-5;

L^3 is absent, –NHC(O)–, or –C(O)NH–;

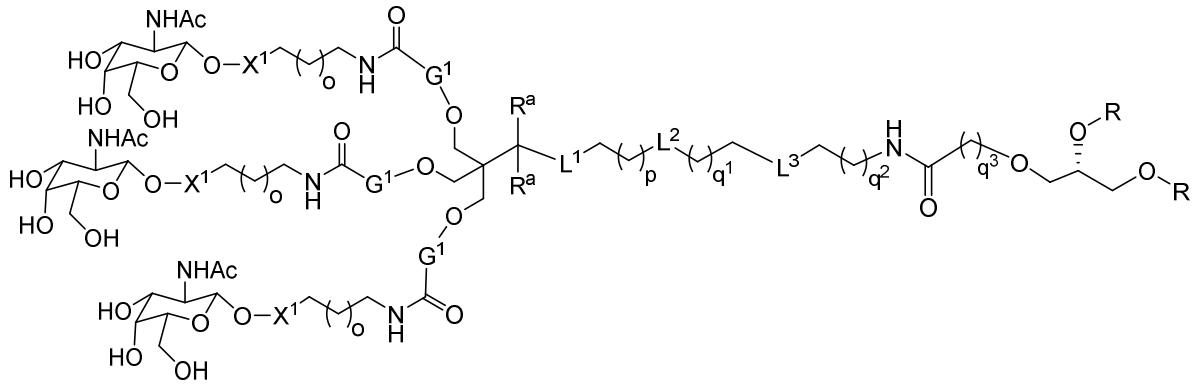
subscript "q^3" is independently 0-5;

each R is independently a C_{12}-C_{20} substituted or unsubstituted alkyl; and

the "〰" indicates an *R* configuration or an *S* configuration.

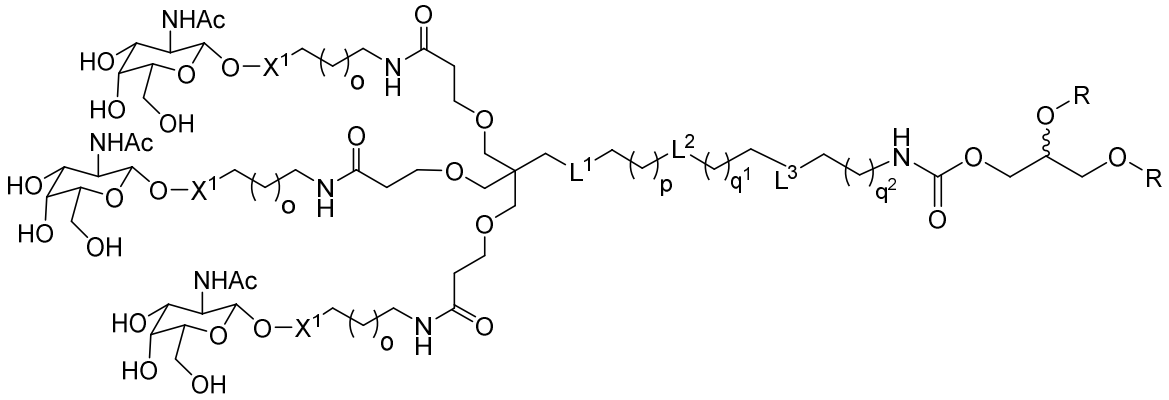
10. The compound of claim 9, wherein the compound of Formula I is a compound of

(A) Formula I-a:



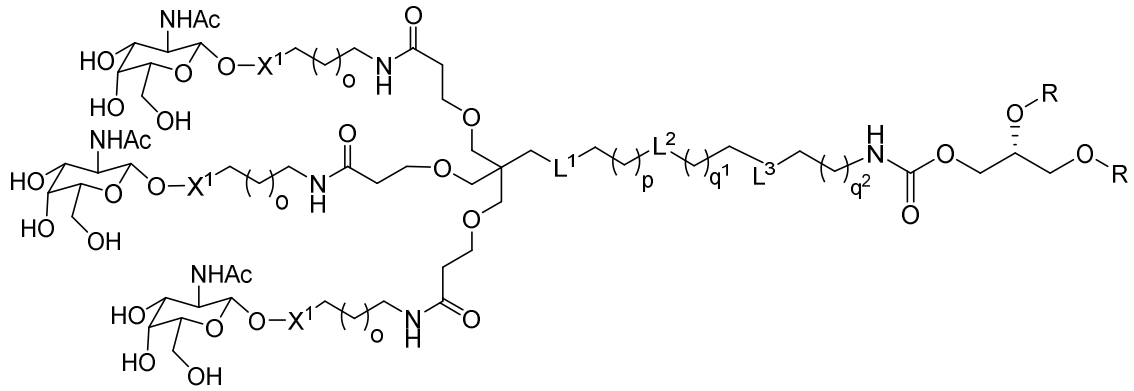
Formula I-a;

(B) Formula I-b:



Formula I-b; or

(C) Formula I-c:



Formula I-c.

11. The compound of claim 9 or claim 10, wherein:

(A.1) L^1 is –NHC(O);

(A.2) L^1 is –NHC(O)NH–;

(A.3) L^1 is –S-S–; or

(A.4) L^1 is –OC(O)NH–; and/or

(B.1) each X^1 is –$((CH_2)_m$–C(O)NH);

(B.2) each X^1 is –$(CH_2CH_2O)_s$; or

(B.3) each X^1 is –$(CH_2)_r$– and each subscript "r" is 5; and/or

(C.1) each subscript "o" is 1; and/or

(D.1) L^2 is –O-$(CH_2CH_2O)_n$–; or

(D.2) L^2 is –$(OCH_2CH_2O)_n$–; optionally,

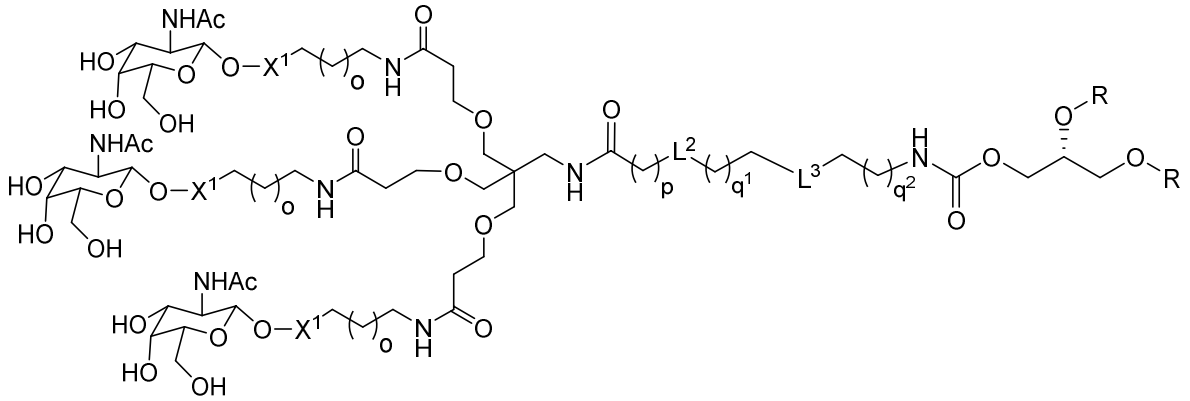
wherein each subscript "n" is 100 to 200; and/or

(E.1) L^3 is absent; or

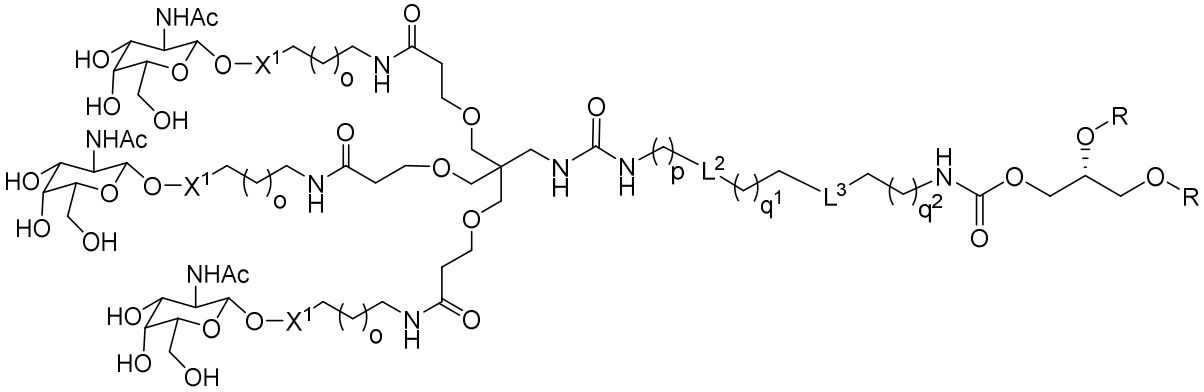
(E.2) L^3 is present and is –NHC(O)–; and/or

(F.1) each R is independently a C_{14}-C_{18} unsubstituted alkyl.

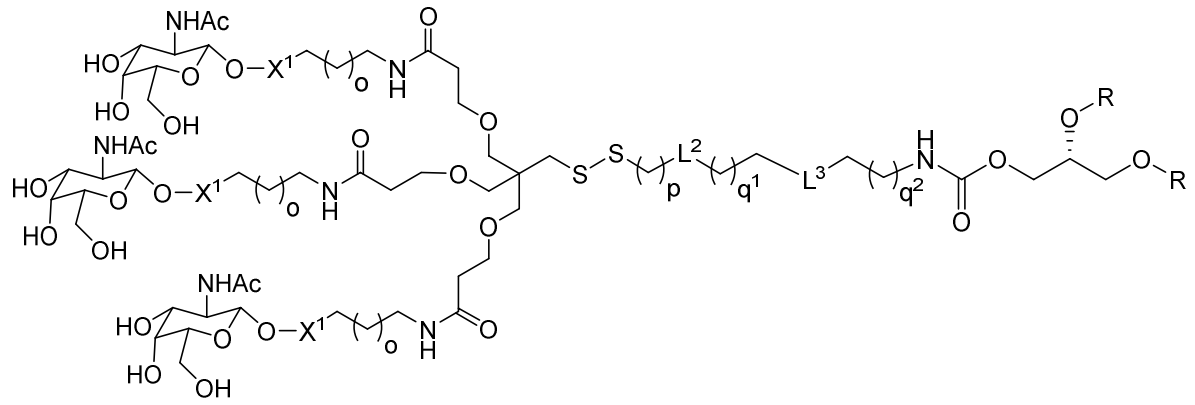
12. The compound of any one of claims 9-11, wherein the compound of Formula I is any one of a compound of Formula I-c-1 to I-c-4:



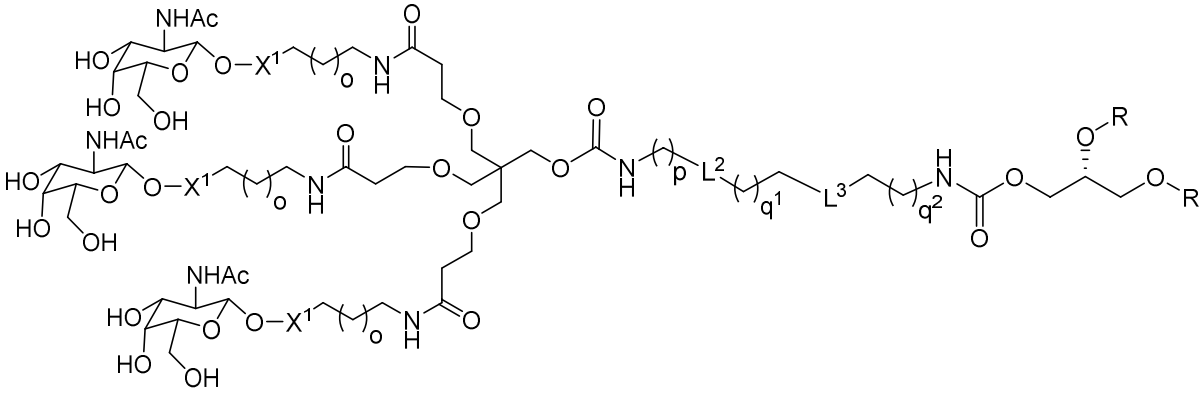
Formula I-c-1,



Formula I-c-2,

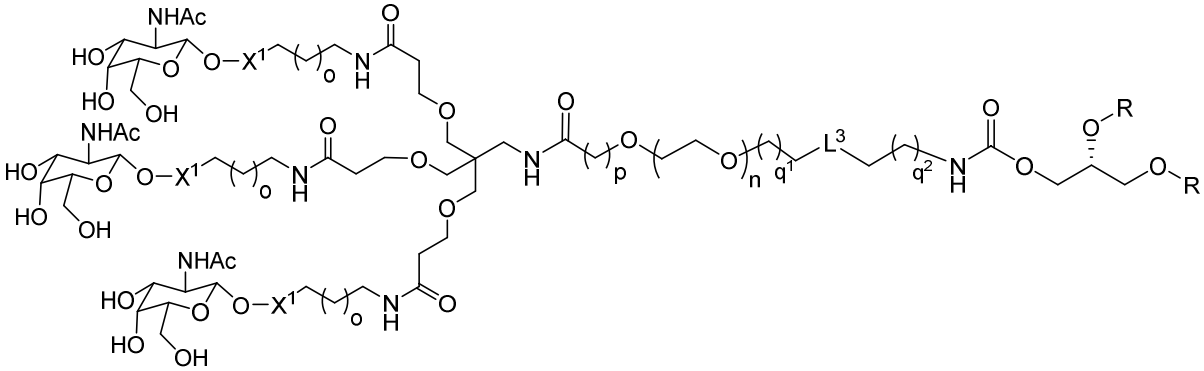


Formula I-c-3, or

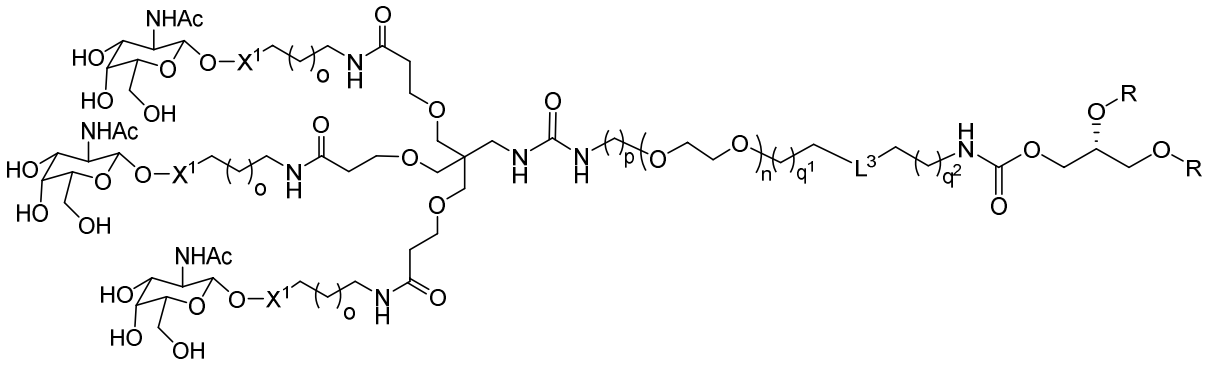


Formula I-c-4.

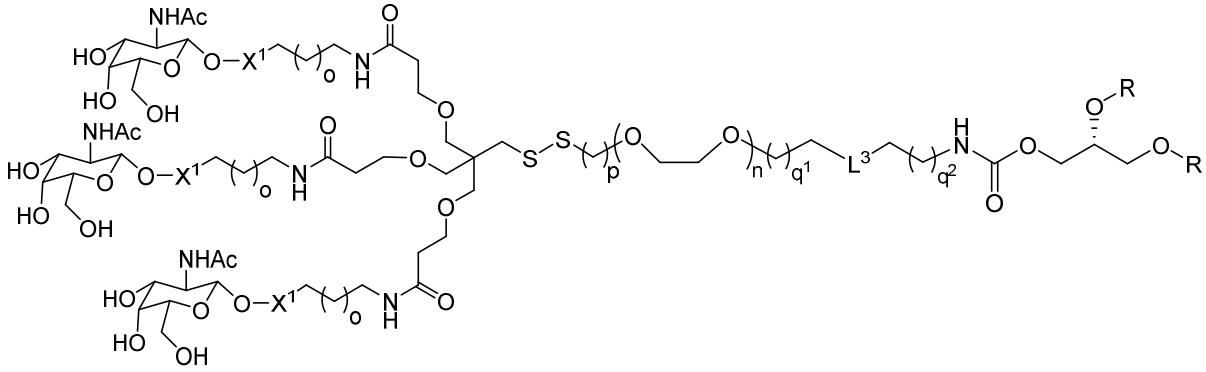
13. A compound selected from the group consisting of Formula I-c-5, I-c-6, I-c-7, and I-c-8:



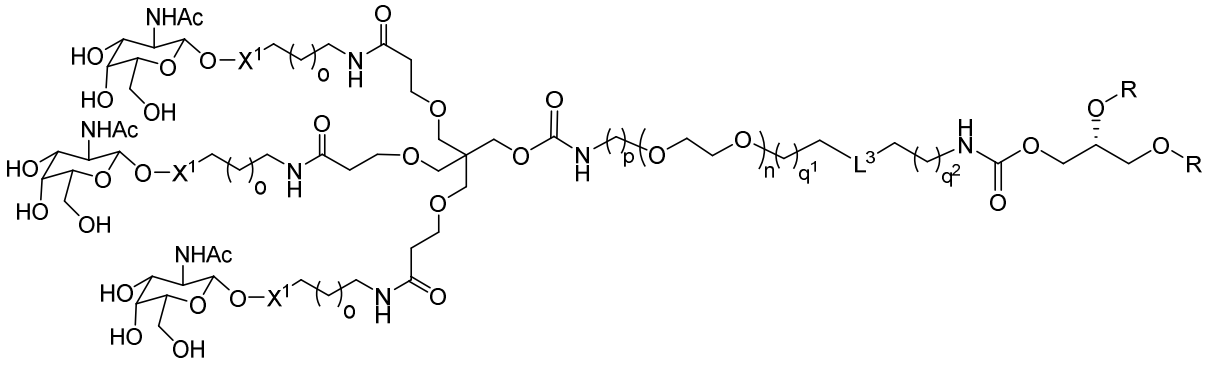
Formula I-c-5,



Formula I-c-6,



Formula I-c-7, or



Formula I-c-8

wherein,

each X^1 is independently $–(CH_2)_r–$, $–(CH_2CH_2O)_s–$, $–(OCH_2CH_2)_s–$, $–((CH_2)_m–C(O)NH)–$, or $–(C(O)NH–(CH_2)_m)–$;

each subscript “m” is independently 1-5;

each subscript “s” is independently 1-5;

each subscript “o” is independently 1-5;

each subscript “r” is independently 1-10;

each subscript “p” is independently 1-5;

each subscript “n” is independently 1-200;

each subscript “q^1” is independently 0-5;

each subscript "q^2" is independently 0-5;

each L^3 is independently absent, –NHC(O)–, or –C(O)NH–; and

each R is independently a C_{12}-C_{20} substituted or unsubstituted alkyl.

14. The compound of claim 13, wherein:

(A) each X^1 is $–((CH_2)_m–C(O)NH)–$, each subscript "m" is independently 2, and each subscript "o" is independently 1;

(B) each X^1 is $–(CH_2CH_2O)_s–$, each subscript "s" is independently 2, and each subscript "o" is independently 1;

(C) the compound is a compound of Formula I-c-7 and, optionally, each X^1 is $–(CH_2)_r–$, each subscript "r" is independently 5, and each subscript "o" is 1;

(D) the compound is a compound of Formula I-c-5, L^2 is $–O-(CH_2CH_2O)_n–$, and subscript "n" is 100 to 200; or

(E) the compound is a compound of Formula I-c-6, I-c-7, or I-c-8, each L^2 is $–(OCH_2CH_2O)_n–$ and each subscript "n" is 100 to 200.

15. The compound of claim 13 or claim 14, wherein

(i) L^3 is absent; optionally,

(i.A) wherein in Formula I-c-4, subscript "p" is 4, subscript "q^1" is 0., and subscript "q^2" is 0; or

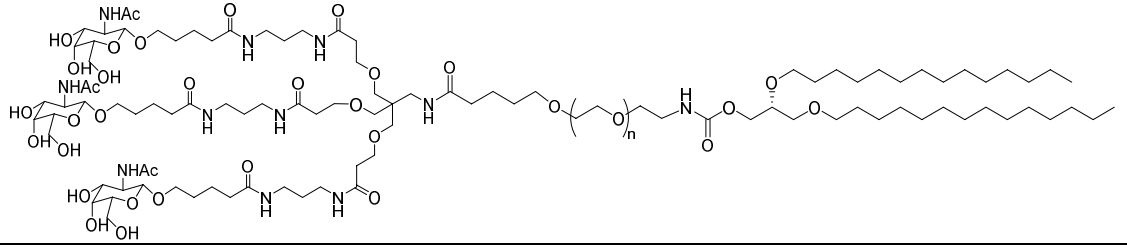
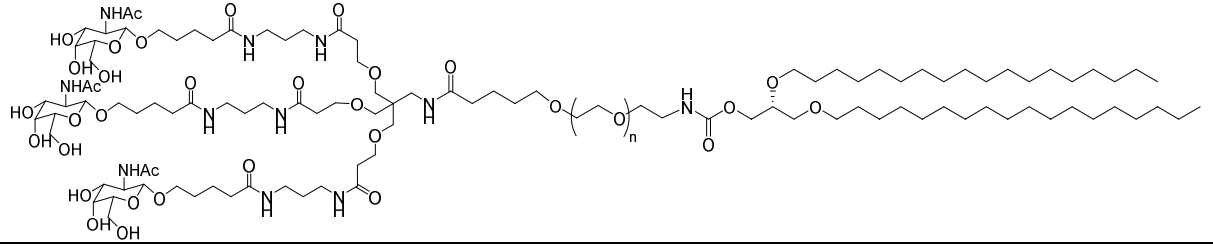
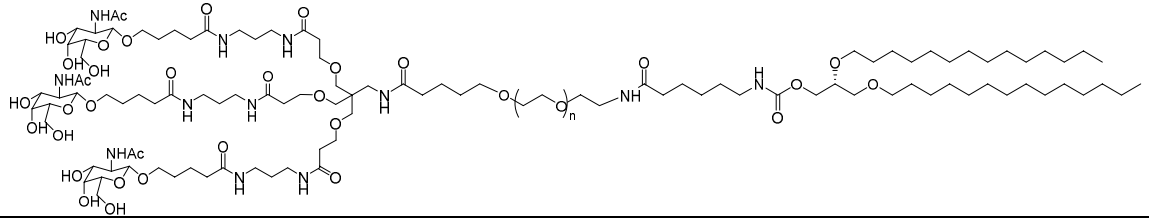
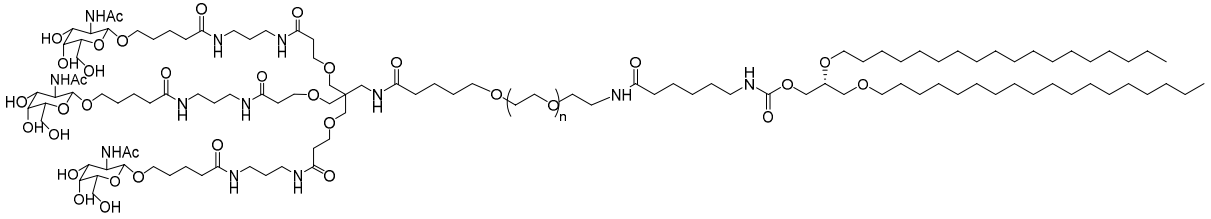
(i.B) wherein in Formulas I-c-6, I-c-7, and I-c-8, each subscript "p" is 2, subscript "q^1" is 0, and subscript "q^2" is 0; or

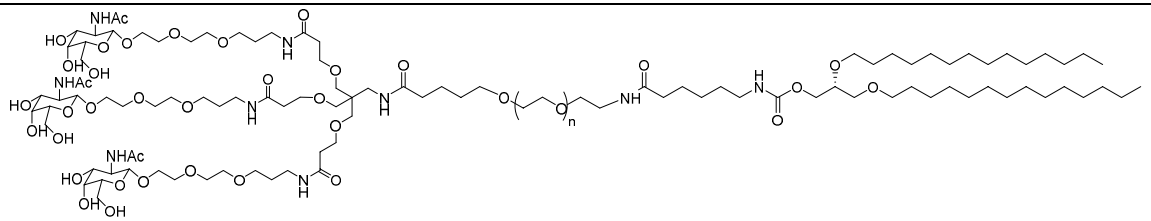
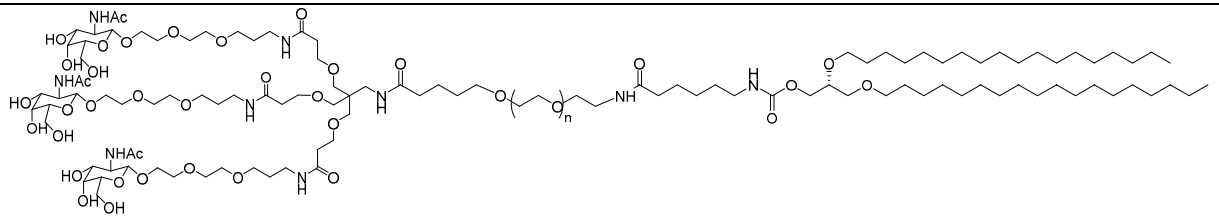
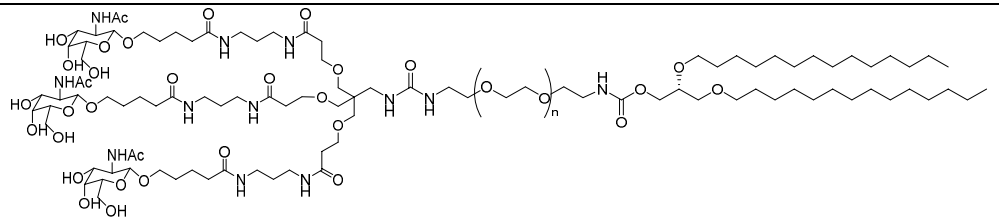
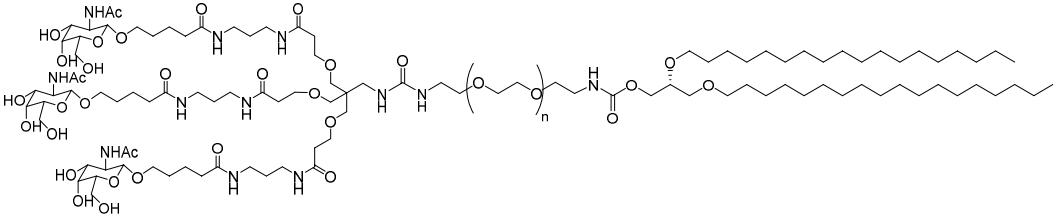
(ii) L^3 is present and is –NHC(O)–; optionally,

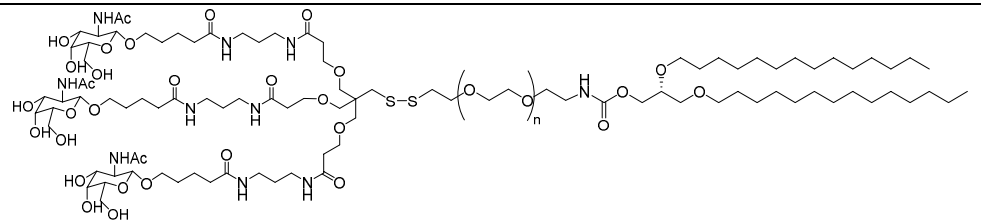
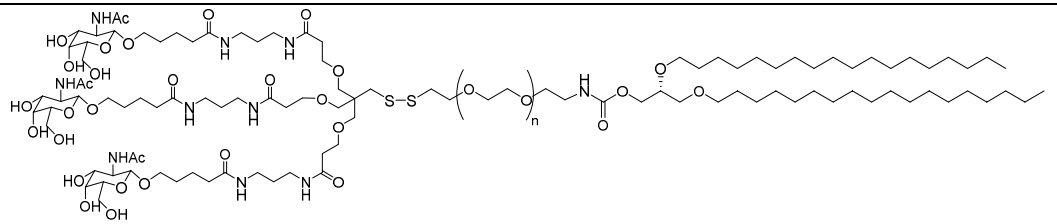
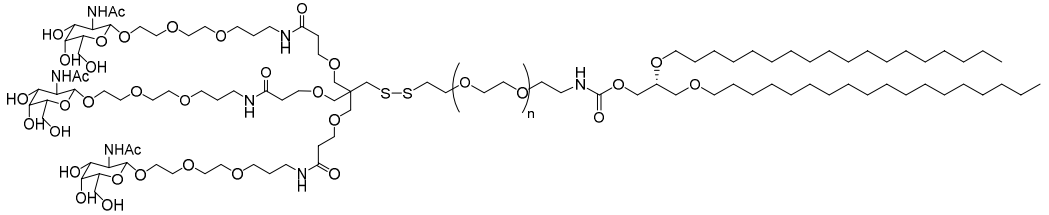
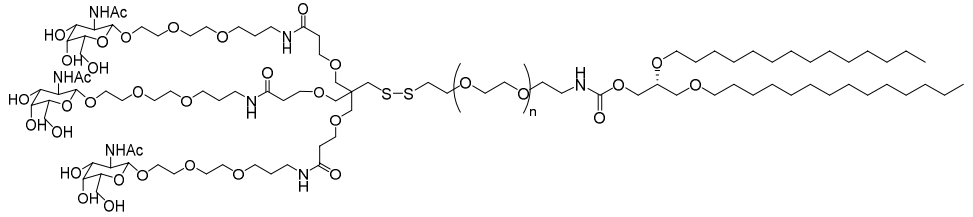
(ii.A) wherein in Formula I-a-4, subscript "p" is 4, subscript "q^1" is 1 and subscript "q^2" is 4; and/or

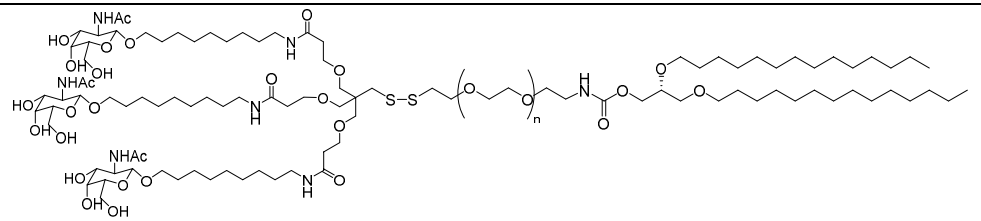
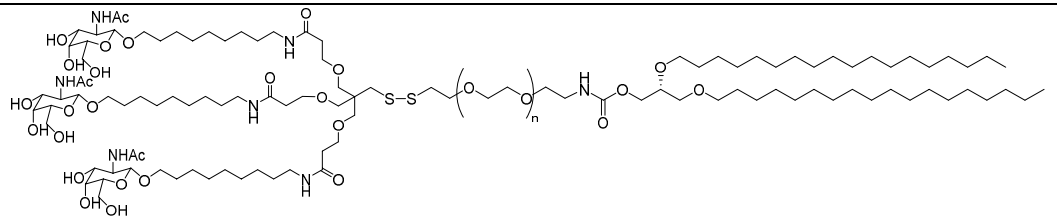
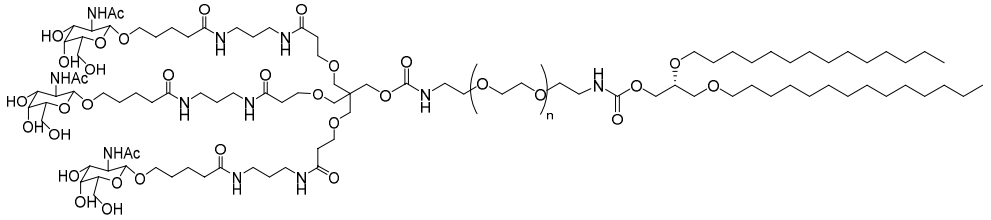
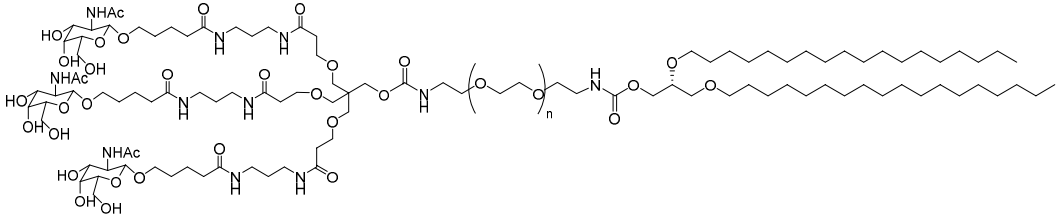
(iii) each R is independently a C_{14}-C_{18} unsubstituted alkyl.

16. A compound selected from the group consisting of:

Compound No.	Structure
1	
2	
3	
4	

5	
6	
7	
8	

9	
10	
11	
12	

13	
14	
15	
16	

wherein each subscript “n” is between 10-200.

17. A pharmaceutically acceptable salt of a compound of any one of claims 1-16.

18. A lipid nanoparticle (LNP) composition comprising:

(A) a lipid that comprises a compound of any one of claims 1-16 or

(B) a lipid that comprises a compound of any one of claims 1-16;

a cationic lipid;

a phospholipid;

a PEG-containing lipid; and

a sterol;

optionally, wherein the LNP composition further comprises:

(B.1) a prime editor comprising a DNA binding domain and a DNA polymerase domain, or one or more polynucleotides encoding the prime editor;

(B.2) a prime editing guide RNA (PEgRNA) or a polynucleotide encoding the PEgRNA;

(B.3) a nick guide RNA (ngRNA) or a polynucleotide encoding the ngRNA; and/or

(B.4) a second PEgRNA or a polynucleotide encoding the second PEgRNA;

optionally, wherein the LNP composition is formulated to deliver the at least one polynucleotide or one or more components of the prime editing system to target cells;

optionally, wherein the target cells are or comprise human cells, mammalian cells, liver cells, bone marrow cells, lung cells, eye cells, muscle cells, or cells in the central nervous system.

19. A pharmaceutical composition comprising the LNP composition of claim 18.

20. A pharmaceutical composition comprising the LNP composition of claim 18 for use in delivering polynucleotides into a target cell comprising:

introducing into the target cell the LNP composition of claim 18 and (i) one or more polynucleotides or (ii) one or more components of a prime editing system;

optionally, wherein the target cells are or comprise human cells, mammalian cells, liver cells, bone marrow cells, lung cells, eye cells, muscle cells, or cells in the central nervous system.