DESCRIPTION

NITROGEN-CONTAINING CHAIN COMPOUND, PREPARATION METHOD, COMPOSITION COMPRISING THE SAME, AND USE

The present application claims priority to Chinese Patent Application No. 202410407999.5 filed on April 3, 2024, and Chinese Patent Application No. 202411391626.X filed on September 30, 2024. The entire contents of the above-mentioned Chinese patent applications are incorporated herein by reference.

TECHNICAL FIELD

The present disclosure relates to a nitrogen-containing chain compound, a preparation method, a composition comprising the same, and use.

BACKGROUND ART

Nucleic acid drugs are an important direction in current basic and applied research. Nucleic acid drugs can be used for the prevention and/or treatment of viral and bacterial infectious diseases, tumors, metabolic diseases, etc., and their production cost is lower and their cycle is shorter, which is conducive to the rapid development of personalized drugs. However, nucleic acids are negatively charged macromolecules that are difficult to penetrate cell membranes, and nucleic acids have poor stability. The development of various nucleic acid packaging and delivery systems can, to a certain extent, overcome the instability of nucleic acid drugs and improve their delivery efficiency.

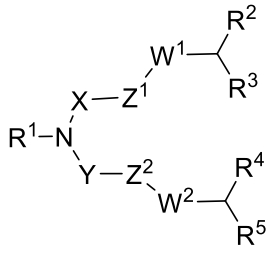
Lipid nanoparticles have been proven to be useful as carriers for delivering bioactive substances (such as small molecule drugs, proteins and nucleic acids) into cells and/or intracellular compartments. By designing and optimizing the types and amounts of the components in lipid nanoparticles, optimizing nucleic acid drug delivery systems is of greater significance for improving the efficacy of nucleic acid drug prevention and treatment, especially lipid compounds that can be used to deliver RNA prophylactic agents and/or therapeutic agents, as well as related methods and compositions.

In view of the importance of ionizable lipid compounds that can be used to deliver nucleic acid drugs, there is an urgent need to develop ionizable lipid compounds with novel structures.

SUMMARY OF DISCLOSURE

The present invention aims to provide a novel ionizable lipid compound that can be used for delivering nucleic acid drugs, thereby increasing the variety of ionizable lipid compounds and the options for delivery carriers for nucleic acid prophylactic agents and/or therapeutic agents. In order to solve the above technical problems, the present disclosure provides a nitrogen-containing chain compound, a preparation method, a composition comprising the same, and use. The LNP formulation prepared with the nitrogen-containing chain compound of the present disclosure has relatively uniform nanoparticle size, higher encapsulation efficiency, and a high expression activity *in vivo*.

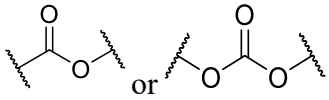
The present disclosure provides a compound I or a pharmaceutically acceptable salt thereof,



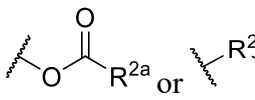
I

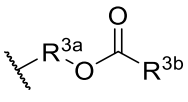
wherein R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

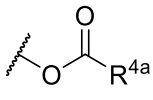
X and Y are independently C_{1-12} alkylene;

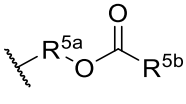
Z^1 and Z^2 are independently  ;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is  , R^{2a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-6} alkyl; R^{2b} is C_{1-6} alkylene, and R^{2c} is C_{1-15} alkyl;

R^3 is C_{1-15} alkyl or  , R^{3a} is C_{1-6} alkylene, and R^{3b} is C_{1-15} alkyl;

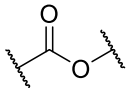
R^4 is H, C_{1-15} alkyl,  or -C_{3-10} cycloalkyl-C_{1-15} alkyl; R^{4a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa}; R^{4aa} is H or C_{1-6} alkyl;

R^5 is C_{1-15} alkyl or , R^{5a} is C_{1-6} alkylene, and R^{5b} is C_{1-15} alkyl.

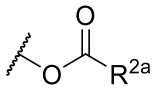
In some preferred embodiments of the present disclosure, some groups of the compound I or the pharmaceutically acceptable salt thereof are defined as follows, and groups not mentioned are as described in any embodiment of the present disclosure (referred to simply as "in an embodiment of the present disclosure").

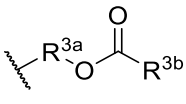
In an embodiment of the present disclosure, R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

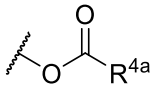
X and Y are independently C_{1-12} alkylene;

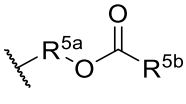
Z^1 and Z^2 are independently ;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is , R^{2a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-6} alkyl;

R^3 is C_{1-15} alkyl or , R^{3a} is C_{1-6} alkylene, and R^{3b} is C_{1-15} alkyl;

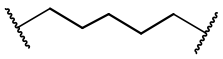
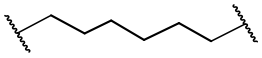
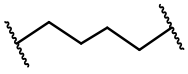
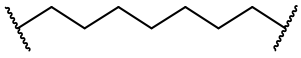
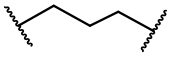
R^4 is H, C_{1-15} alkyl,  or -C_{3-10} cycloalkyl-C_{1-15} alkyl; R^{4a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa}; R^{4aa} is H or C_{1-6} alkyl;

R^5 is C_{1-15} alkyl or , R^{5a} is C_{1-6} alkylene, and R^{5b} is C_{1-15} alkyl.

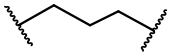
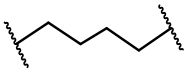
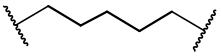
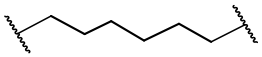
In an embodiment of the present disclosure, in R^1, R^{2aa}, and R^{4aa}, the "C_{1-6} alkyl" in the C_{1-6} alkyl substituted with one or more hydroxyl groups and the C_{1-6} alkyl is each independently C_{1-4} alkyl, such as methyl, ethyl, n-propyl, or n-butyl.

In an embodiment of the present disclosure, in R^1, R^{2aa}, and R^{4aa}, the "C_{1-6} alkyl" in the C_{1-6} alkyl substituted with one or more hydroxyl groups and the C_{1-6} alkyl is each independently a straight-chain or branched-chain C_{1-6} alkyl.

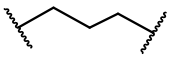
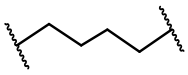
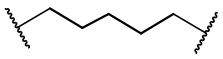
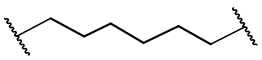
In an embodiment of the present disclosure, in X, Y, R^{2a}, and R^{4a}, the "C_{1-12} alkylene" in the C_{1-12} alkylene, the -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, and the -C_{1-12} alkylene-C_{3-6}

cycloalkyl-R^{4aa} is each independently C_{3-7} alkylene, such as , , ,  or .

In an embodiment of the present disclosure, in X, Y, R^{2a}, and R^{4a}, the "C_{1-12} alkylene" in the C_{1-12} alkylene, the -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, and the -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa} is each independently a straight-chain or branched-chain C_{1-12} alkylene.

In an embodiment of the present disclosure, in W^1, W^2, R^{3a}, and R^{5a}, the C_{1-6} alkylene is each independently methylene, -CH_2CH_2-, , ,  or .

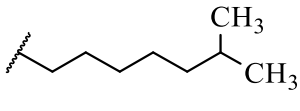
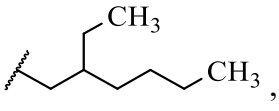
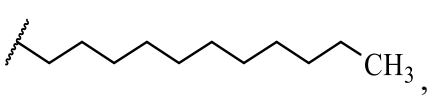
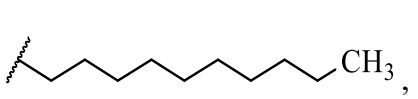
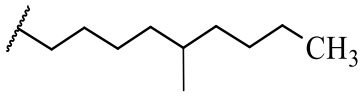
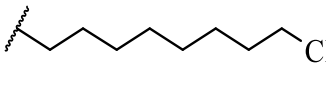
In an embodiment of the present disclosure, in R^{2b}, the C_{1-6} alkylene is C_{1-3} alkylene, such as methylene.

In an embodiment of the present disclosure, in W^1, W^2, R^{3a}, R^{5a}, and R^{2b}, the C_{1-6} alkylene is each independently methylene, -CH_2CH_2-, , ,  or .

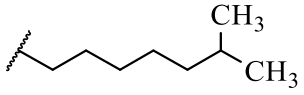
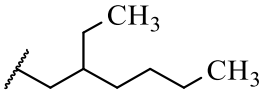
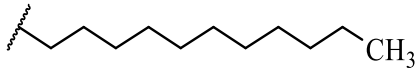
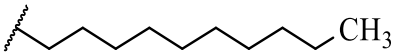
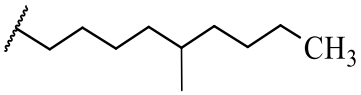
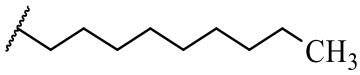
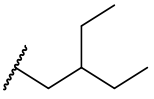
In an embodiment of the present disclosure, in W^1, W^2, R^{3a}, and R^{5a}, the C_{1-6} alkylene is each independently a straight-chain or branched-chain C_{1-6} alkylene.

In an embodiment of the present disclosure, in R^{2b}, the C_{1-6} alkylene is a straight-chain or branched-chain C_{1-6} alkylene.

In an embodiment of the present disclosure, in W^1, W^2, R^{3a}, R^{5a}, and R^{2b}, the C_{1-6} alkylene is each independently a straight-chain or branched-chain C_{1-6} alkylene.

In an embodiment of the present disclosure, in R^{2a}, R^3, R^{3b}, R^4, R^{4a}, R^5, and R^{5b}, the "C_{1-15} alkyl" in the C_{1-15} alkyl and the -C_{3-10} cycloalkyl-C_{1-15} alkyl is C_{3-12} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or .

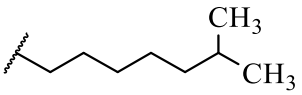
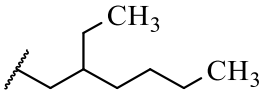
In an embodiment of the present disclosure, in R^{2c}, the C_{1-15} alkyl is C_{3-12} alkyl, such as n-pentyl or n-heptyl.

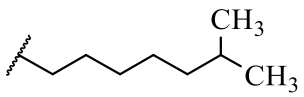
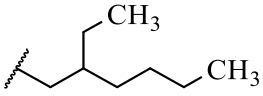
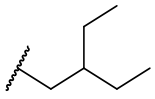
In an embodiment of the present disclosure, in R^{2a}, R^3, R^{3b}, R^4, R^{4a}, R^5, R^{5b}, and R^{2c}, the "C_{1-15} alkyl" in the C_{1-15} alkyl and the -C_{3-10} cycloalkyl-C_{1-15} alkyl is C_{3-12} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , , ,  or .

In an embodiment of the present disclosure, in R^{2a}, R^3, R^{3b}, R^4, R^{4a}, R^5, and R^{5b}, the "C_{1-15} alkyl" in the C_{1-15} alkyl and the -C_{3-10} cycloalkyl-C_{1-15} alkyl is a straight-chain or branched-chain C_{1-15} alkyl.

In an embodiment of the present disclosure, in R^{2c}, the C_{1-15} alkyl is a straight-chain or branched-chain C_{1-15} alkyl.

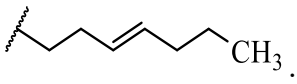
In an embodiment of the present disclosure, in R^{2a}, R^3, R^{3b}, R^4, R^{4a}, R^5, R^{5b}, and R^{2c}, the "C_{1-15} alkyl" in the C_{1-15} alkyl and the -C_{3-10} cycloalkyl-C_{1-15} alkyl is a straight-chain or branched-chain C_{1-15} alkyl.

In an embodiment of the present disclosure, in R^{2a}, the C_{1-15} alkyl is C_{3-10} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl,  or .

In an embodiment of the present disclosure, in R^{2a}, the C_{1-15} alkyl is C_{3-10} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, ,  or .

In an embodiment of the present disclosure, in R^{2a}, the C_{1-15} alkyl is a straight-chain or branched-chain C_{1-15} alkyl.

In an embodiment of the present disclosure, in R^{2a} and R^{4a}, the C_{1-15} alkenyl is C_{3-10} alkenyl,

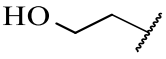
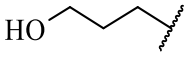
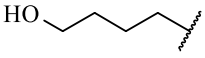
such as .

In an embodiment of the present disclosure, in R^{2a} and R^{4a}, the C_{1-15} alkenyl is a straight-chain or branched-chain C_{1-15} alkenyl.

In an embodiment of the present disclosure, in R^{2a} and R^{4a}, the "C_{3-6} cycloalkyl" in the -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa} and the -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa} is cyclopropyl or cyclobutyl.

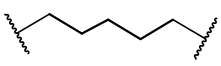
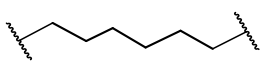
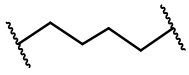
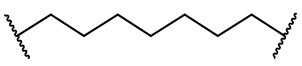
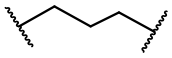
In an embodiment of the present disclosure, in R^4, the "C_{3-10} cycloalkyl" in the -C_{3-10} cycloalkyl-C_{1-15} alkyl is C_{3-6} cycloalkyl, such as a cyclohexyl.

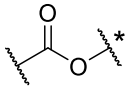
In an embodiment of the present disclosure, R^1 is C_{1-6} alkyl substituted with one hydroxyl group.

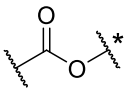
In an embodiment of the present disclosure, R^1 is ,  or .

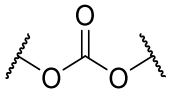
In an embodiment of the present disclosure, in R^1, only a terminal carbon at an end not attached to an N atom is substituted with a hydroxyl group.

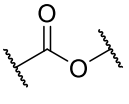
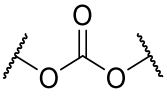
In an embodiment of the present disclosure, X and Y are independently C_{3-7} alkylene.

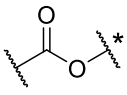
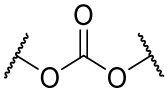
In an embodiment of the present disclosure, the X and the Y are independently , , ,  or .

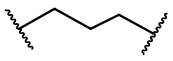
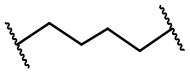
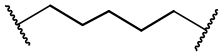
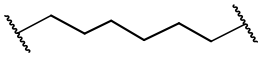
In an embodiment of the present disclosure, Z^1 is , and the asterisk (*) indicates an attachment to W^1.

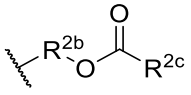
In an embodiment of the present disclosure, Z^2 is , and the asterisk (*) indicates an attachment to W^2.

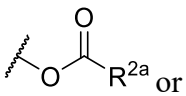
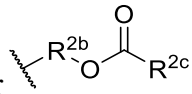
In an embodiment of the present disclosure, Z^2 is .

In an embodiment of the present disclosure, $Z^2$is  or ; preferably, Z^2 is

 or , and the asterisk (*) indicates an attachment to W^1.

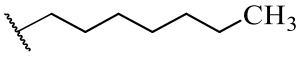
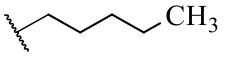
In an embodiment of the present disclosure, W^1 and W^2 are independently a chemical bond, methylene, -CH_2CH_2-, , ,  or .

In an embodiment of the present disclosure, R^2 is .

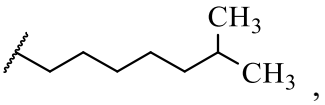
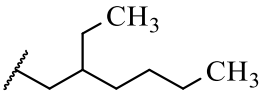
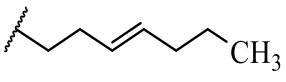
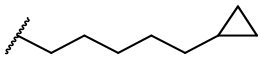
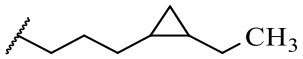
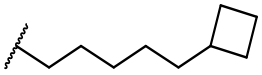
In an embodiment of the present disclosure, R^2 is  or , R^{2a} is C_{3-10} alkyl, C_{3-10} alkenyl, or -C_{3-7} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-3} alkyl; R^{2b} is C_{1-3} alkylene, and R^{2c} is C_{3-10} alkyl.

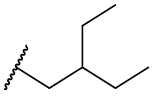
In an embodiment of the present disclosure, R^{2b} is C_{1-3} alkylene, and R^{2c} is C_{3-10} alkyl.

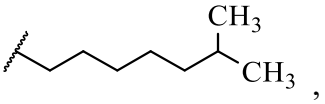
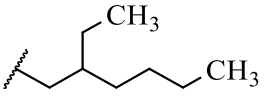
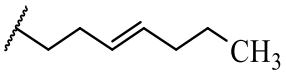
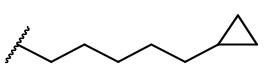
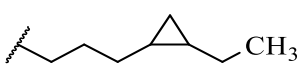
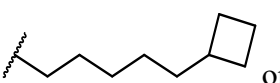
In an embodiment of the present disclosure, R^{2b} is methylene.

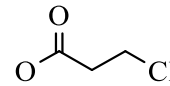
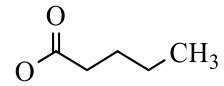
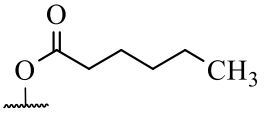
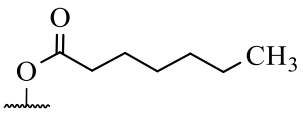
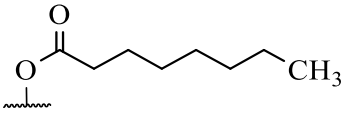
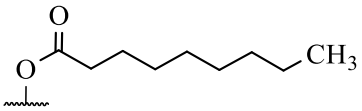
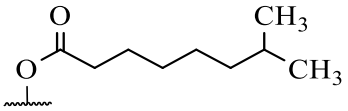
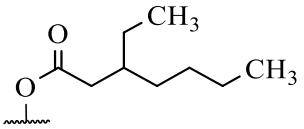
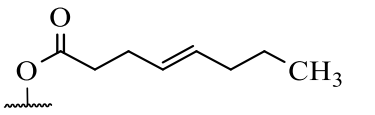
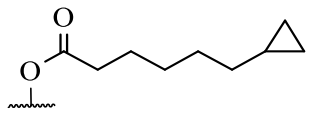
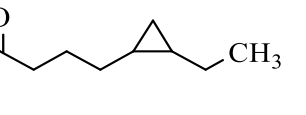
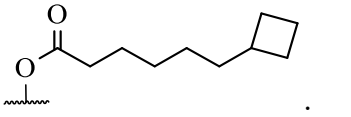
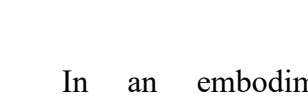
In an embodiment of the present disclosure, R^{2c} is  or .

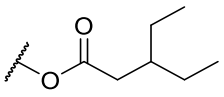
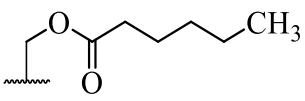
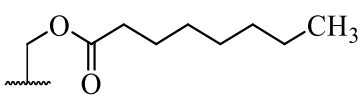
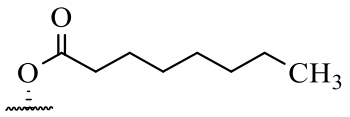
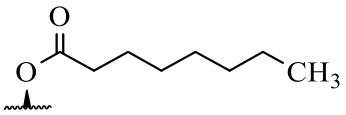
In an embodiment of the present disclosure, R^{2a} is C_{3-10} alkyl, C_{3-10} alkenyl, or -C_{3-7} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-3} alkyl.

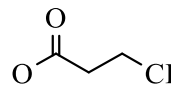
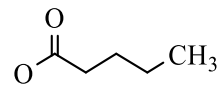
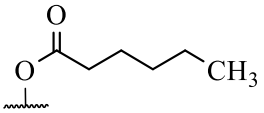
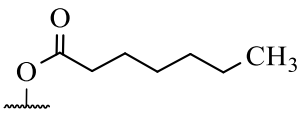
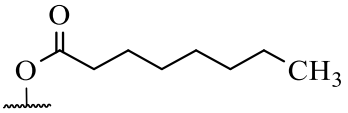
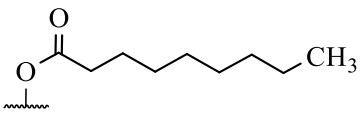
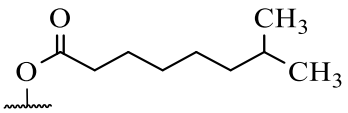
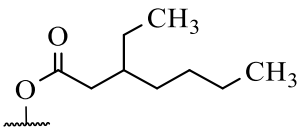
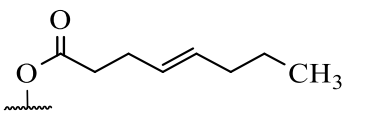
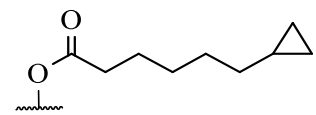
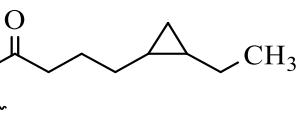
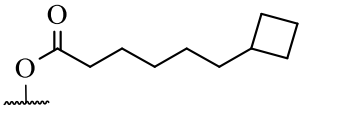
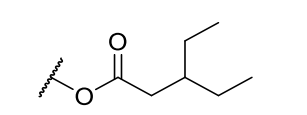
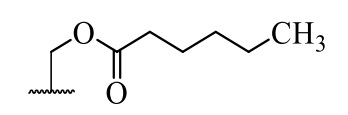
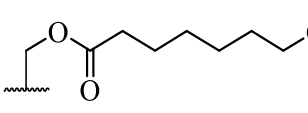
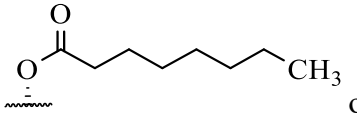
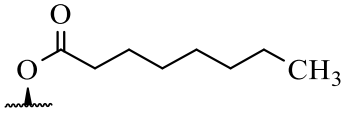
In an embodiment of the present disclosure, R^{2a} is n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or .

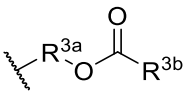
In an embodiment of the present disclosure, R^{2a} is .

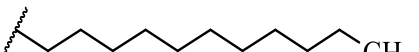
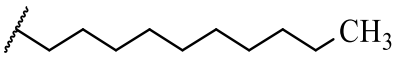
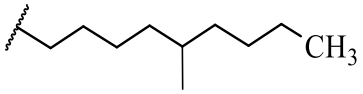
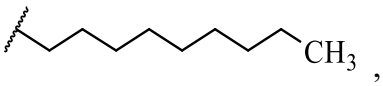
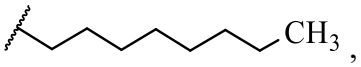
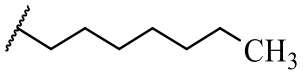
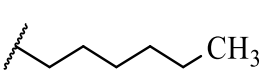
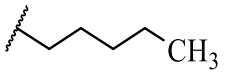
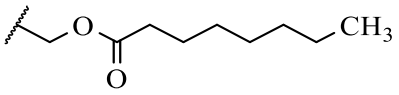
In an embodiment of the present disclosure, R^{2a} is n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or .

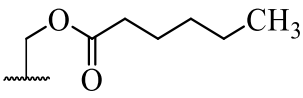
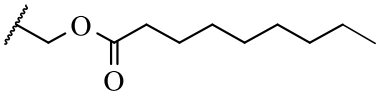
In an embodiment of the present disclosure, R^2 is , , , , , , , , , , , , , , or .

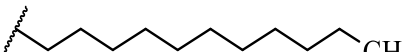
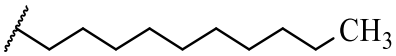
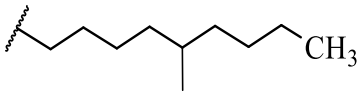
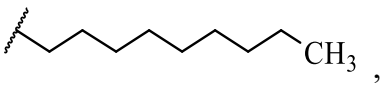
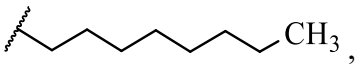
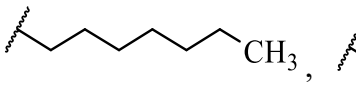
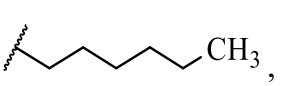
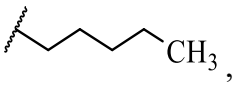
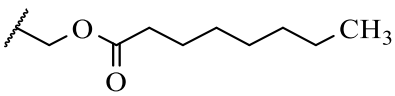
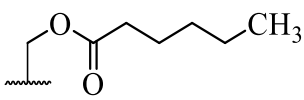
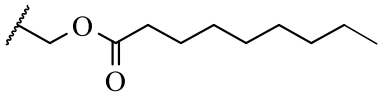
In an embodiment of the present disclosure, R^2 is , , , , or .

In an embodiment of the present disclosure, R^2 is , , , , , , , , , , , , , , , , , , , or .

In an embodiment of the present disclosure, R^3 is C_{4-12} alkyl or , R^{3a} is C_{1-3} alkylene, and R^{3b} is C_{6-12} alkyl.

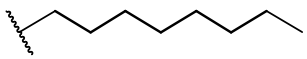
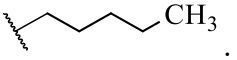
In an embodiment of the present disclosure, R^3 is , , , , , , , , or .

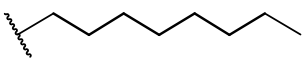
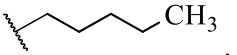
In an embodiment of the present disclosure, R^3 is  or .

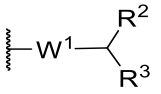
In an embodiment of the present disclosure, R^3 is , , , , , , , , , , or .

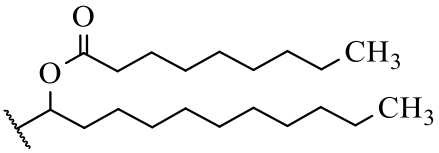
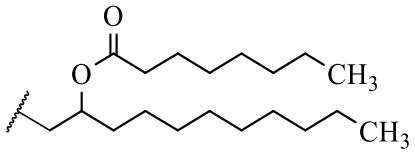
In an embodiment of the present disclosure, R^{3a} is methylene.

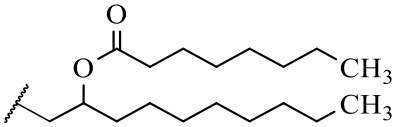
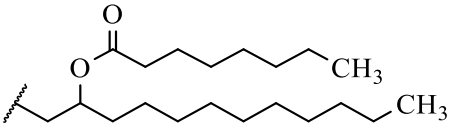
In an embodiment of the present disclosure, R^{3b} is n-heptyl.

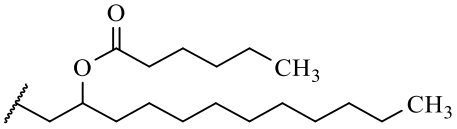
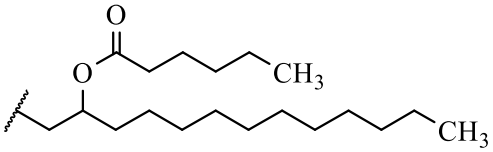
In an embodiment of the present disclosure, R^{3b} is  or .

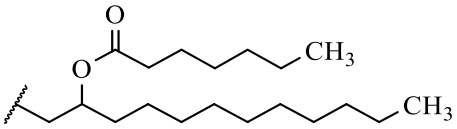
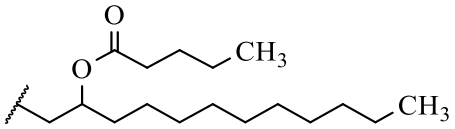
In an embodiment of the present disclosure, R^{3b} is n-heptyl, , or .

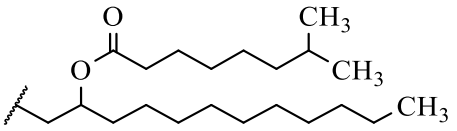
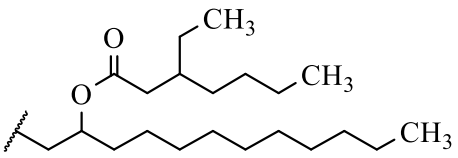
In an embodiment of the present disclosure,  is

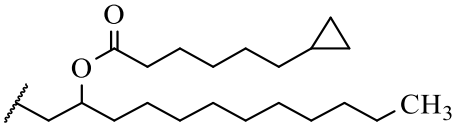
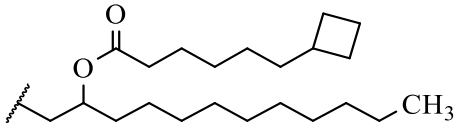
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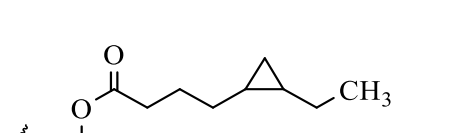
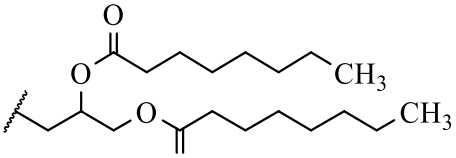
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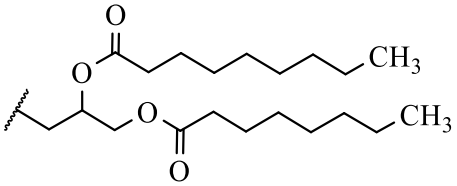
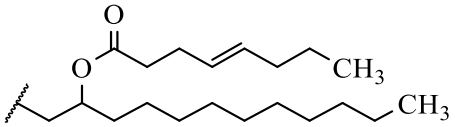
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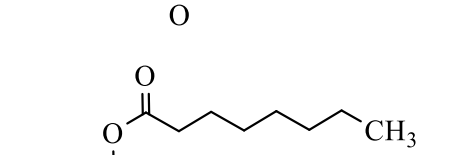
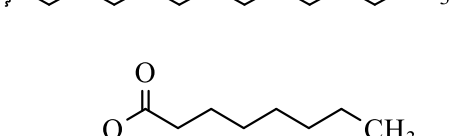
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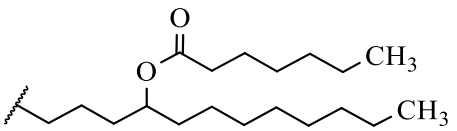
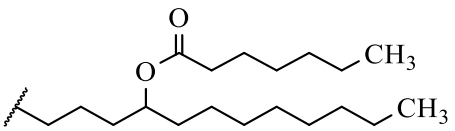
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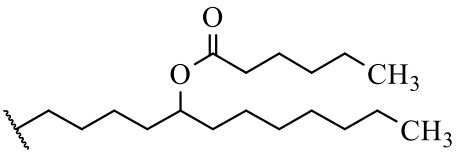
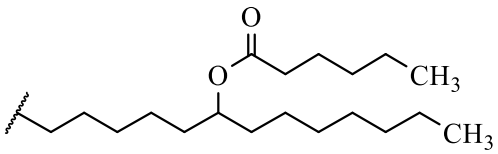
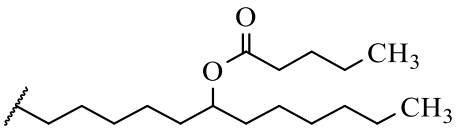
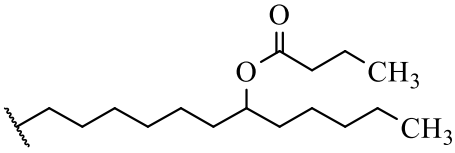
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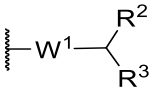
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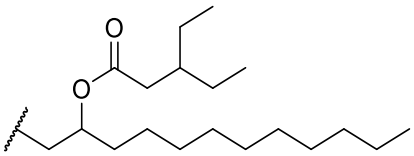
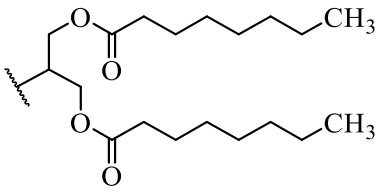
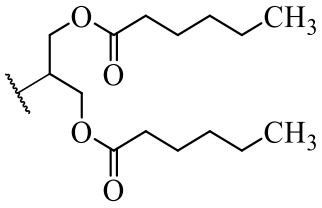
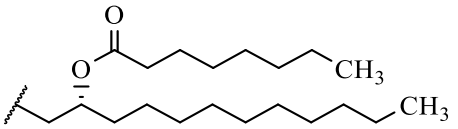
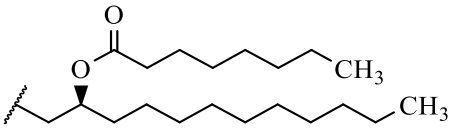
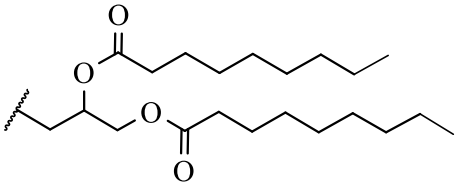
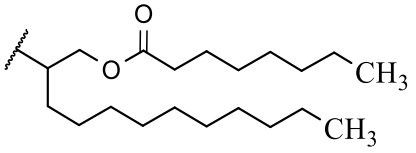
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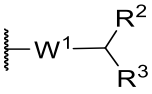
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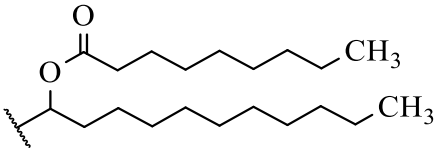
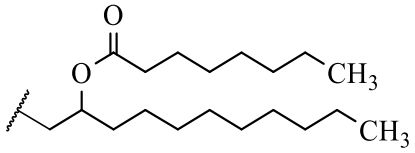
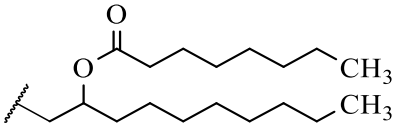
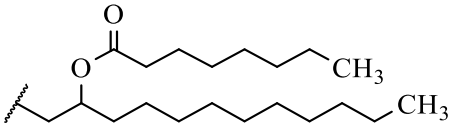
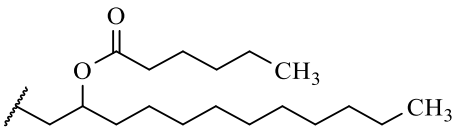
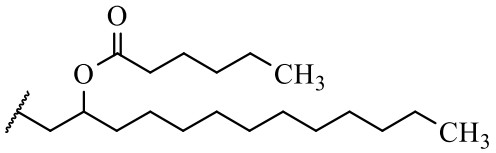
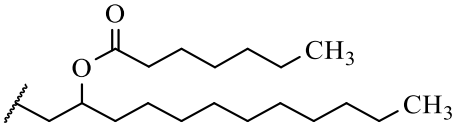
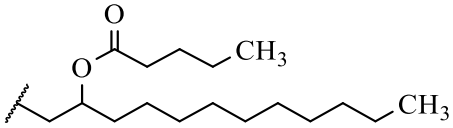
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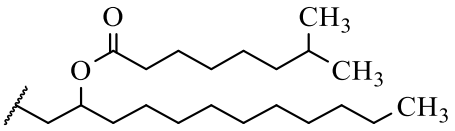
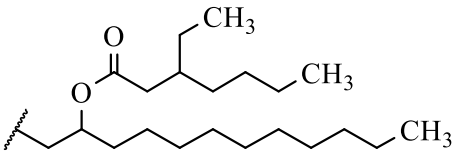
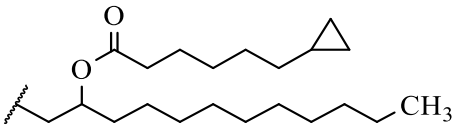
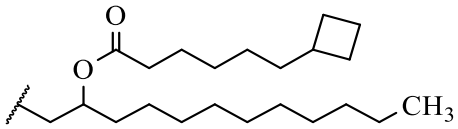
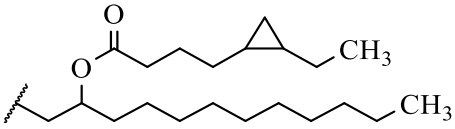
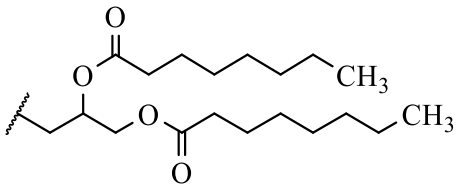
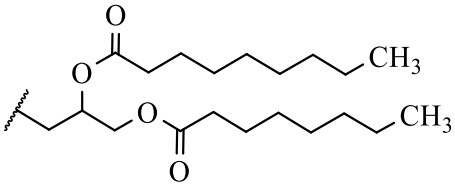
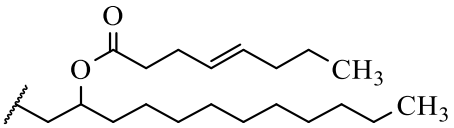
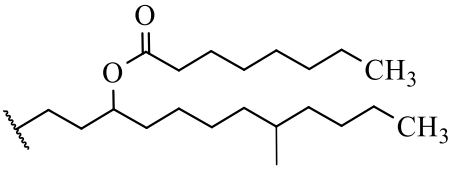
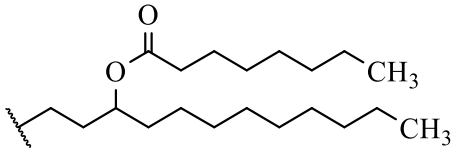

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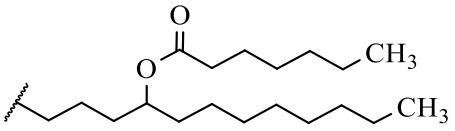
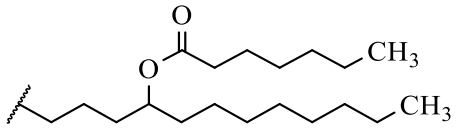

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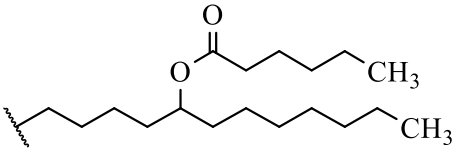
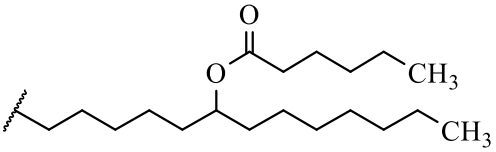
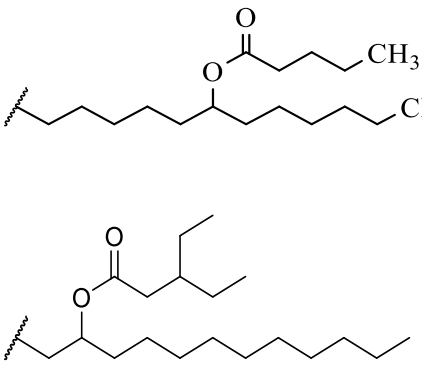
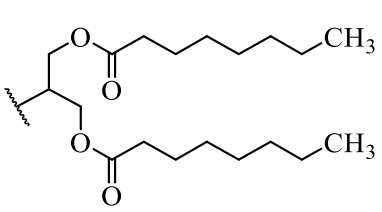
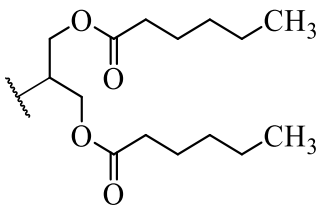
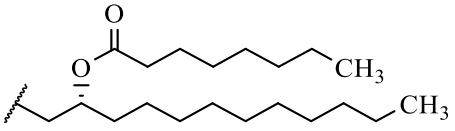
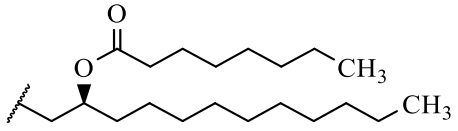

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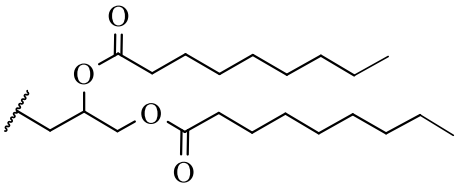
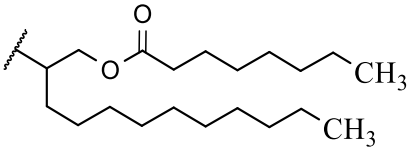

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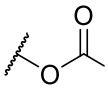
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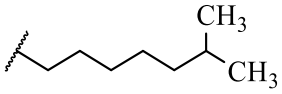
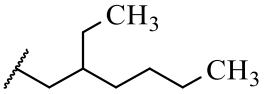
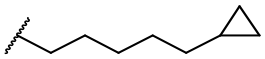
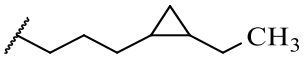
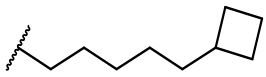
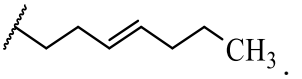
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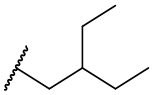
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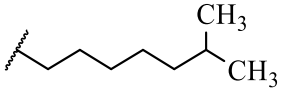
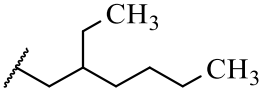
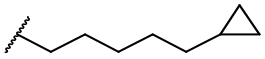
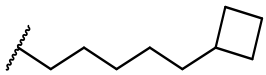
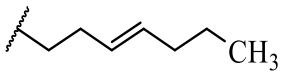
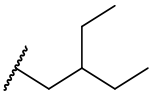
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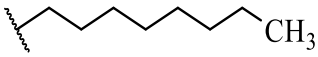
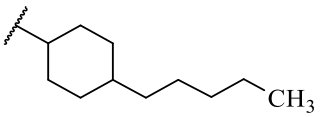
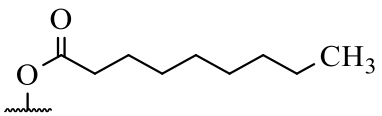
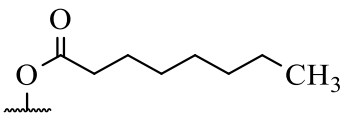
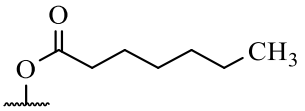
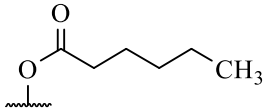
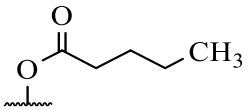
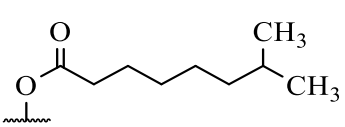
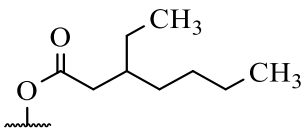
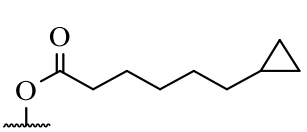
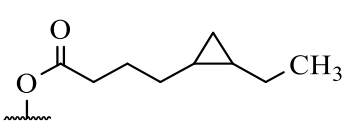
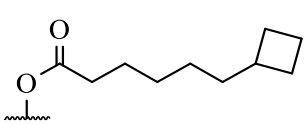
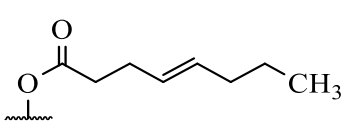
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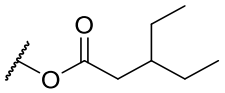
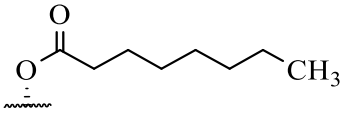
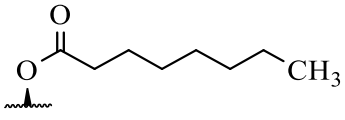
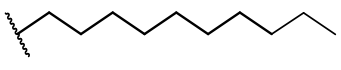
In an embodiment of the present disclosure, R^4 is H, C_{3-10} alkyl,  or -C_{3-6} cycloalkyl-C_{3-10} alkyl; R^{4a} is C_{3-10} alkyl, C_{3-10} alkenyl, or -C_{3-7} alkylene-C_{3-6} cycloalkyl-R^{4aa}; R^{4aa} is H or C_{1-3} alkyl.

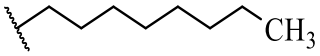
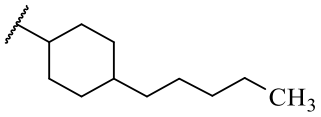
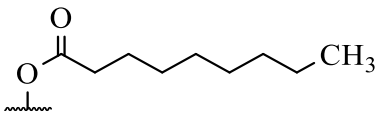
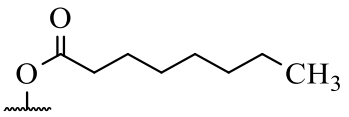
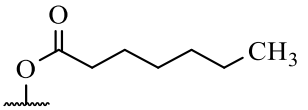
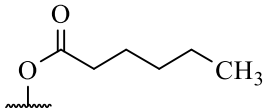
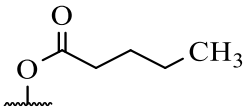
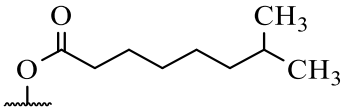
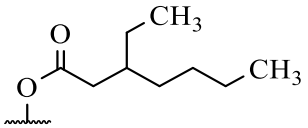
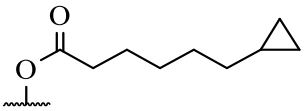
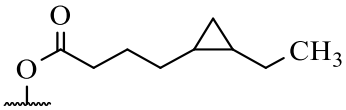
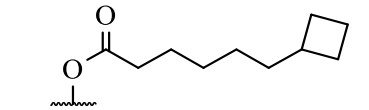
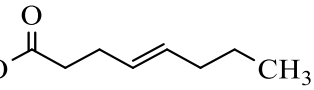
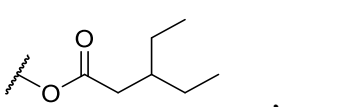
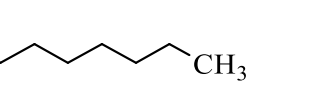
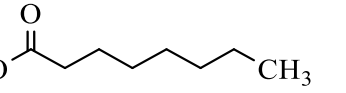
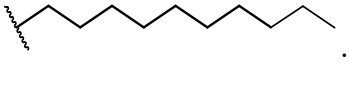
In an embodiment of the present disclosure, R^{4a} is n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or .

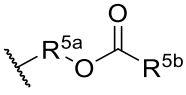
In an embodiment of the present disclosure, R^{4a} is .

In an embodiment of the present disclosure, R^{4a} is n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , , ,  or .

In an embodiment of the present disclosure, R^4 is H, , , , , , , , , , , ,  or .

In an embodiment of the present disclosure, R^4 is , ,  or .

In an embodiment of the present disclosure, R^4 is H, , , , , , , , , , , , , , , , , , , , , , or .

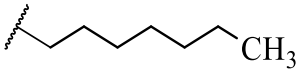
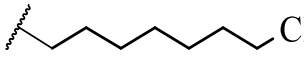
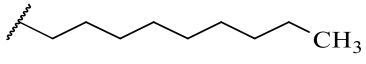
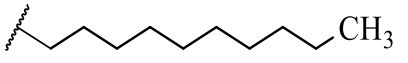
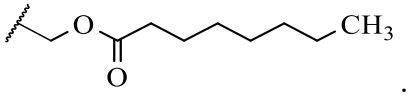
In an embodiment of the present disclosure, R^5 is C_{6-10} alkyl or , R^{5a} is C_{1-3} alkylene, and R^{5b} is C_{6-10} alkyl.

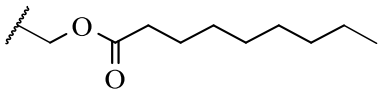
In an embodiment of the present disclosure, R^{5a} is methylene.

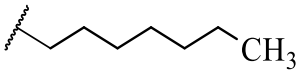
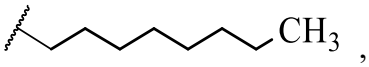
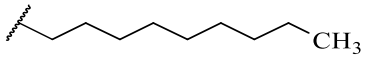
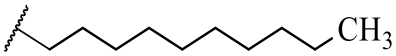
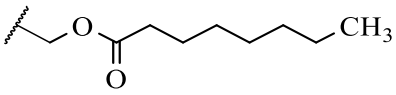
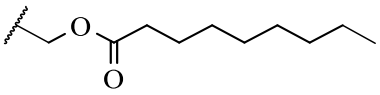
In an embodiment of the present disclosure, R^{5b} is n-heptyl.

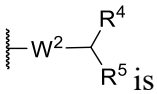
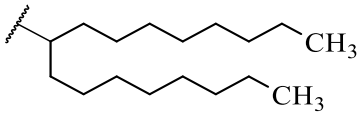
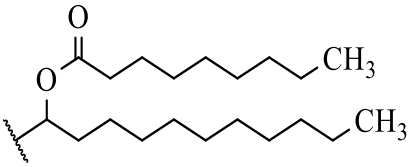
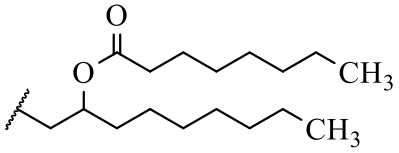
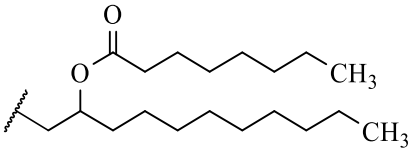
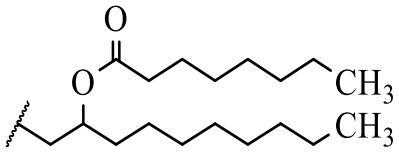
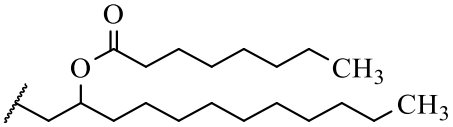
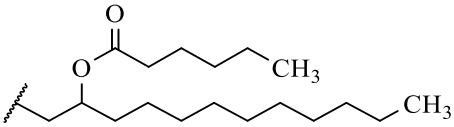
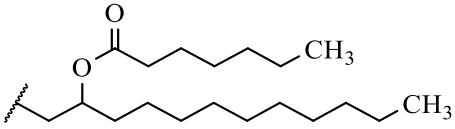
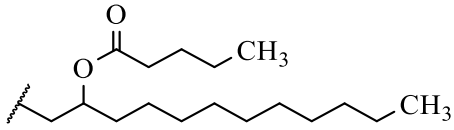
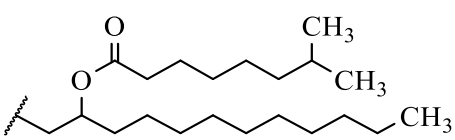
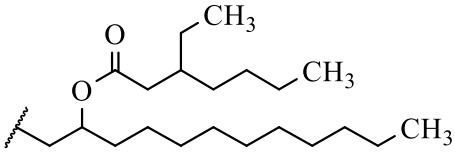
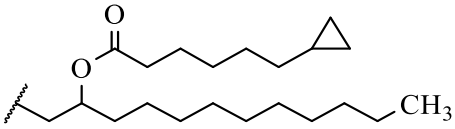
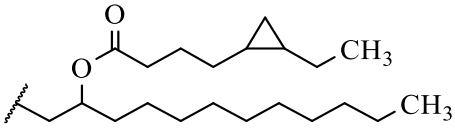
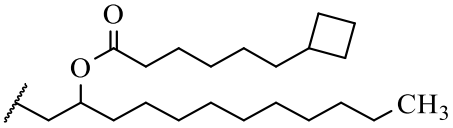
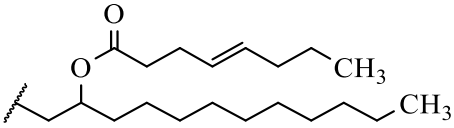
In an embodiment of the present disclosure, R^{5b} is n-octyl.

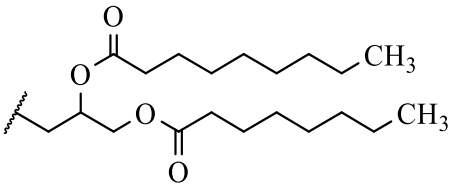
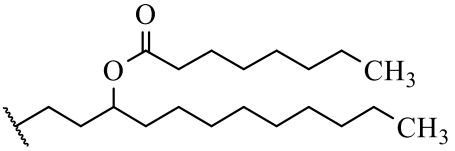
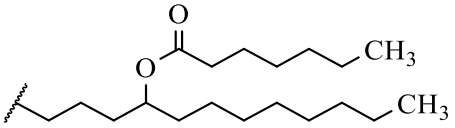
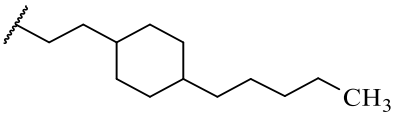
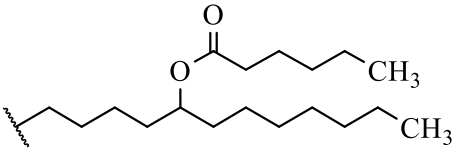
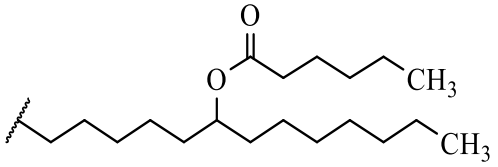
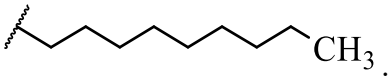
In an embodiment of the present disclosure, R^{5b} is n-heptyl or n-octyl.

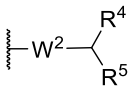
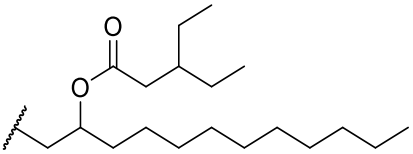
In an embodiment of the present disclosure, R^5 is , , ,  or .

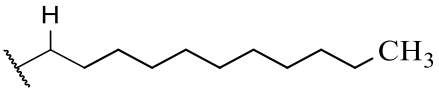
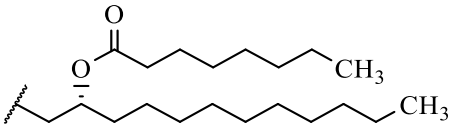
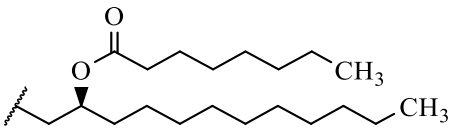
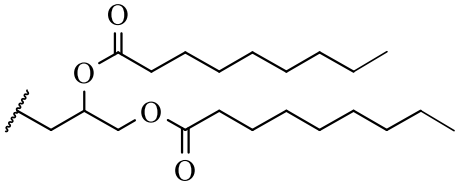
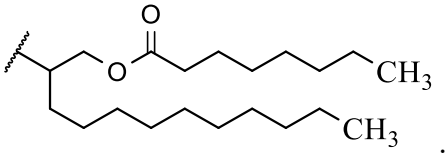
In an embodiment of the present disclosure, R^5 is .

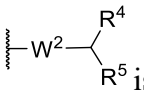
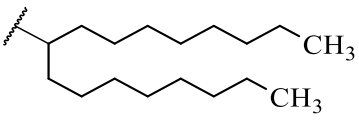
In an embodiment of the present disclosure, R^5 is , , , ,  or .

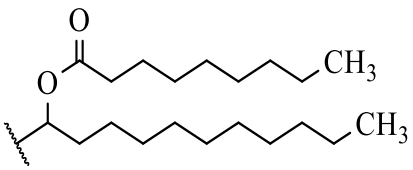
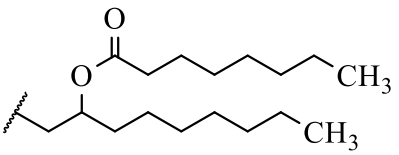
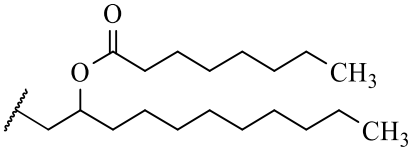
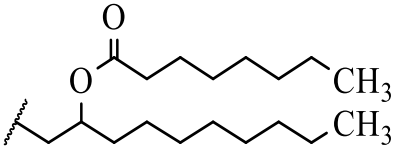
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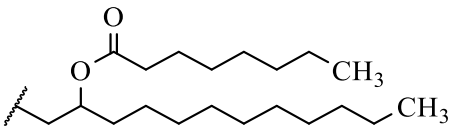
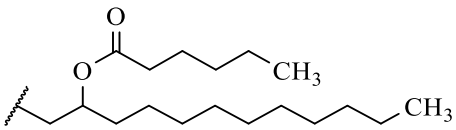
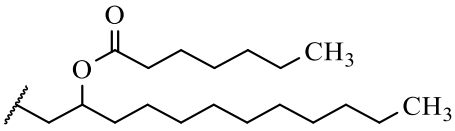
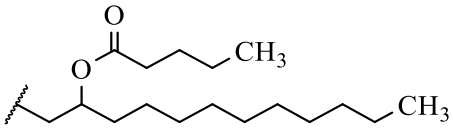
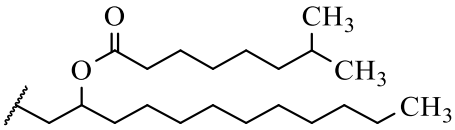
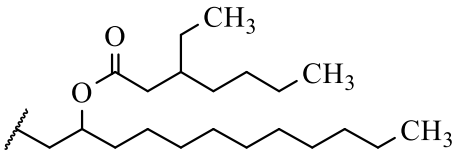
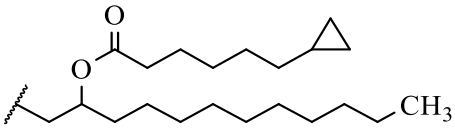
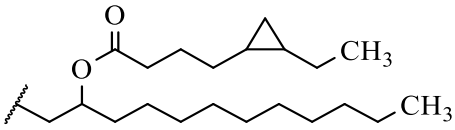
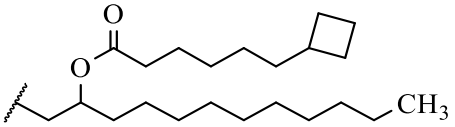
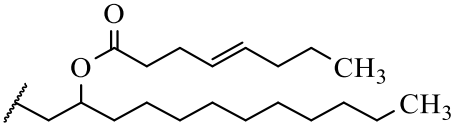
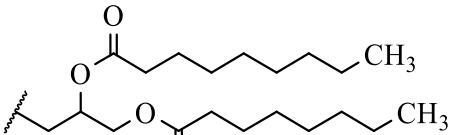
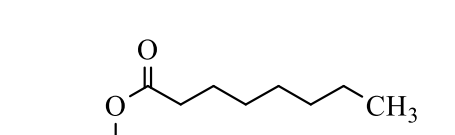

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In an embodiment of the present disclosure,  is ,

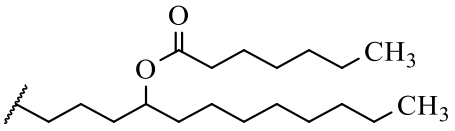
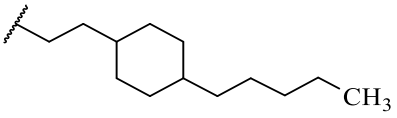
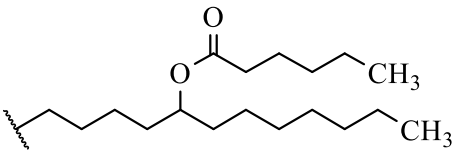
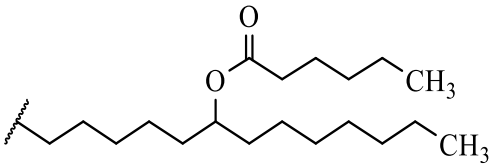
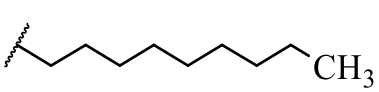
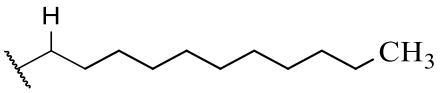
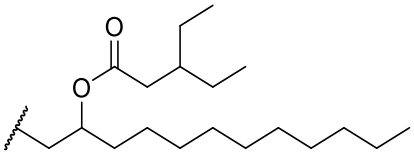
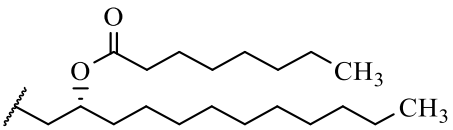
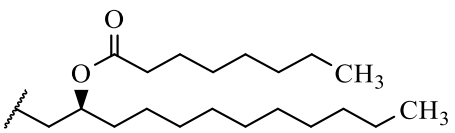
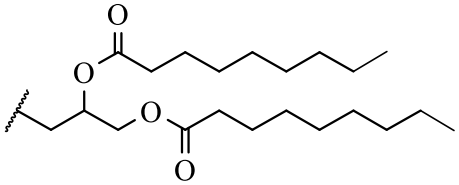

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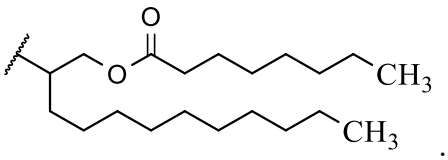
In an embodiment of the present disclosure,  is ,


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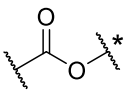
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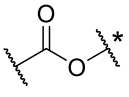
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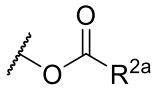
In an embodiment of the present disclosure, R^1 is C_{1-3} alkyl substituted with one or more hydroxyl groups;

X and Y are independently C_{3-8} alkylene, preferably a C_{4-6} alkylene, such as a C_5 alkylene;

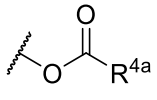
Z^1 is , and the asterisk (*) indicates an attachment to W^1;

Z^2 is , and the asterisk (*) indicates an attachment to W^2;

W^1 and W^2 are independently C_{1-3} alkylene, such as methylene;

R^2 is , and R^{2a} is C_{3-12} alkyl; R^{2a} is preferably a C_{5-9} alkyl, such as a C_7 alkyl;

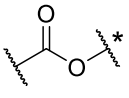
R^3 is C_{5-15} alkyl; R^3 is preferably a C_{8-12} alkyl, such as a C_{10} alkyl;

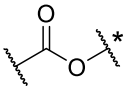
R^4 is ; R^{4a} is C_{3-12} alkyl; R^{4a} is preferably a C_{5-9} alkyl, such as a C_7 alkyl;

R^5 is C_{5-15} alkyl; R^5 is preferably a C_{8-12} alkyl, such as a C_{10} alkyl.

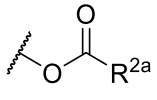
In an embodiment of the present disclosure, R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

X and Y are independently C_{1-12} alkylene;

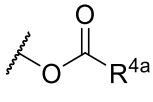
Z^1 is , and the asterisk (*) indicates an attachment to W^1;

Z^2 is , and the asterisk (*) indicates an attachment to W^2;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is , and R^{2a} is C_{1-15} alkyl or C_{1-15} alkenyl;

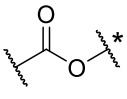
R^3 is C_{1-15} alkyl;

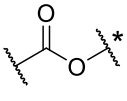
R^4 is C_{1-15} alkyl or ; R^{4a} is C_{1-15} alkyl or C_{1-15} alkenyl;

R^5 is C_{1-15} alkyl.

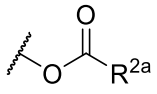
In an embodiment of the present disclosure, R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

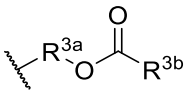
X and Y are independently C_{1-12} alkylene;

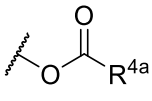
Z^1 is , and the asterisk (*) indicates an attachment to W^1;

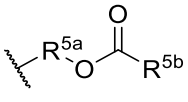
Z^2 is , and the asterisk (*) indicates an attachment to W^2;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

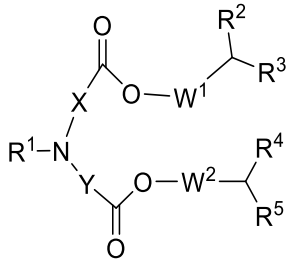
R^2 is , and R^{2a} is C_{1-15} alkyl or C_{1-15} alkenyl;

R^3 is C_{1-15} alkyl or , R^{3a} is C_{1-6} alkylene, and R^{3b} is C_{1-15} alkyl;

R^4 is C_{1-15} alkyl or ; R^{4a} is C_{1-15} alkyl or C_{1-15} alkenyl;

R^5 is C_{1-15} alkyl or , R^{5a} is C_{1-6} alkylene, and R^{5b} is C_{1-15} alkyl.

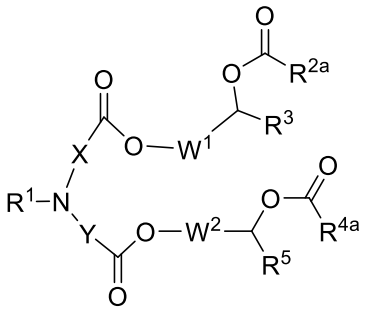
In an embodiment of the present disclosure, the compound I has the following structure:



I-A ;

wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, X, and Y are as described in any one of the preceding embodiments;

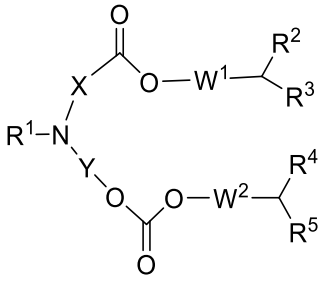
Preferably, the compound I has the following structure:



I-A-1

wherein definitions of R^1, R^{2a}, R^3, R^{4a}, R^5, W^1, W^2, X, and Y are as described in any one of the preceding embodiments.

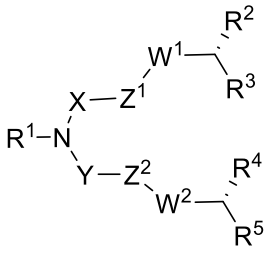
In an embodiment of the present disclosure, the compound I has the following structure:



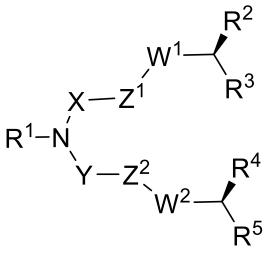
I-B ;

wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, X, and Y are as described in any one of the preceding embodiments.

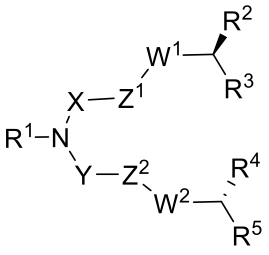
In an embodiment of the present disclosure, the compound I has any one of the following structures:



I-C ,



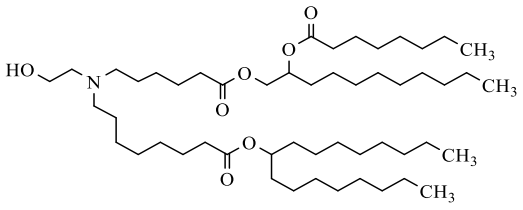
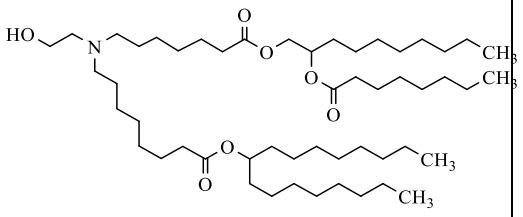
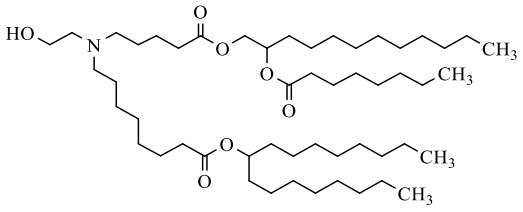
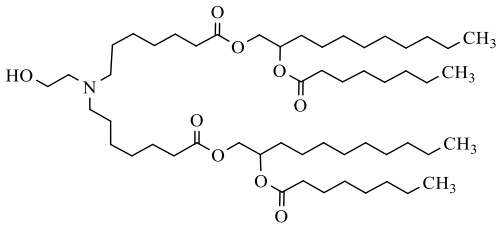
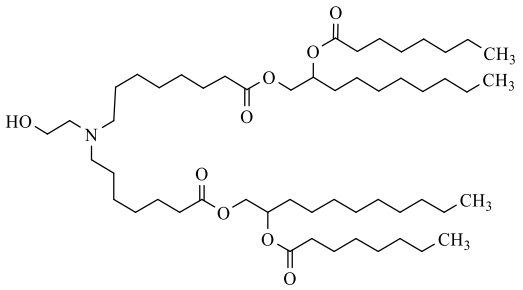
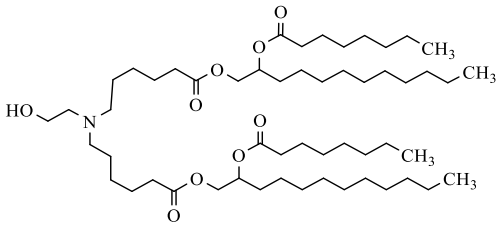
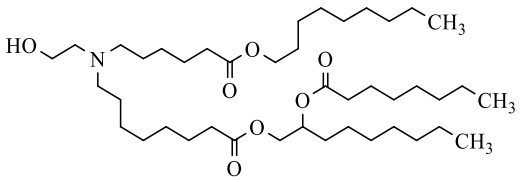
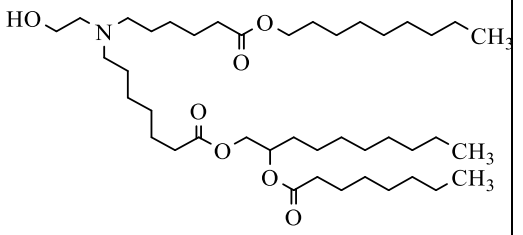
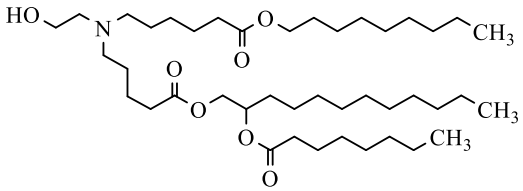
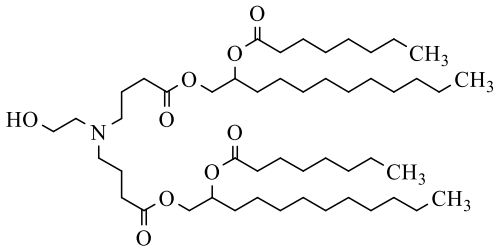
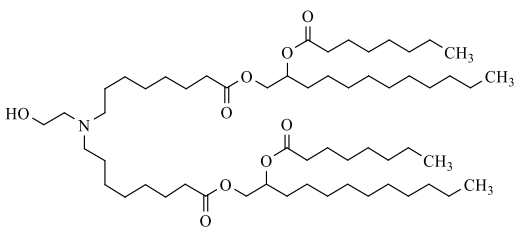
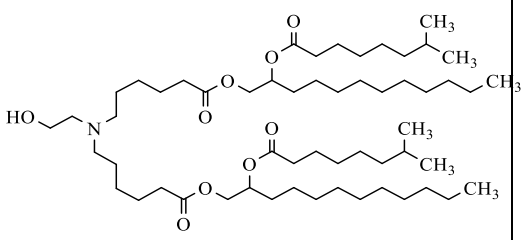
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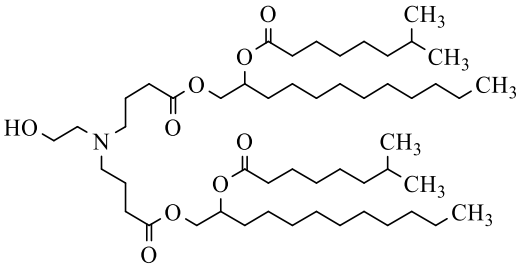
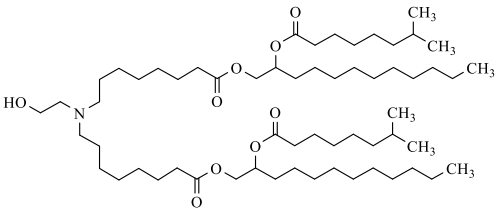
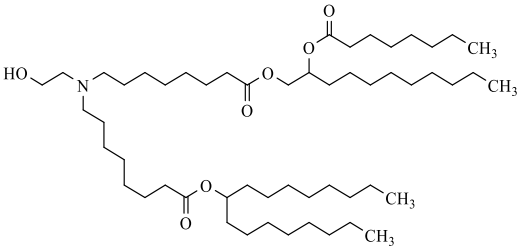
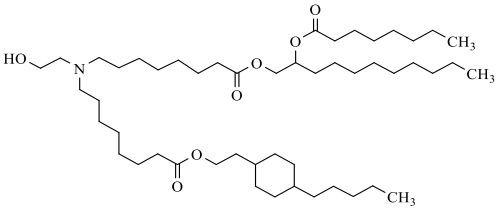
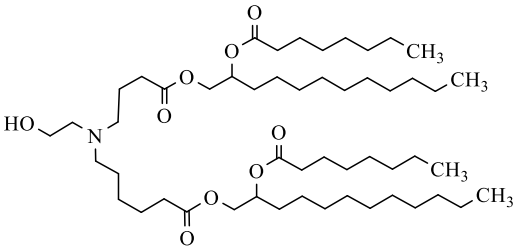
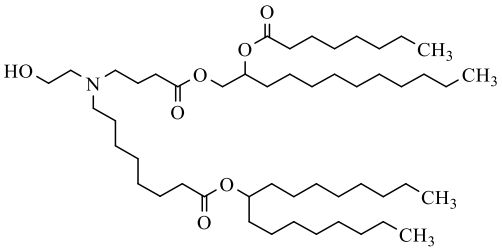
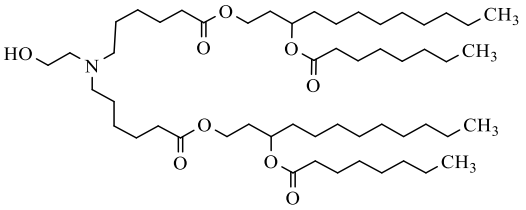
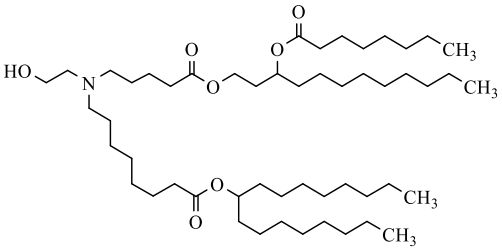
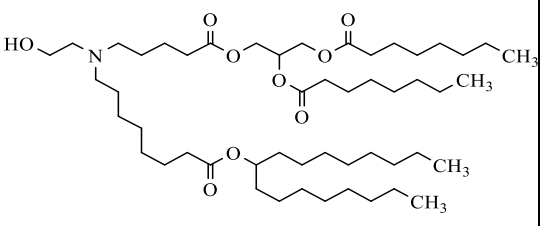
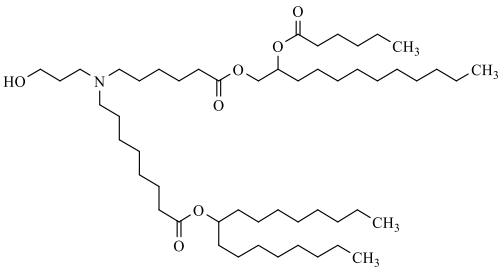


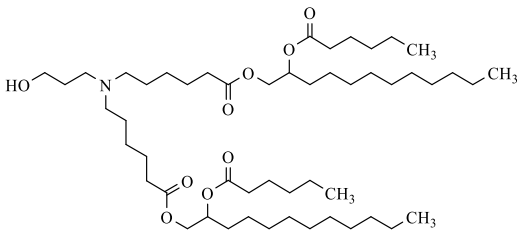
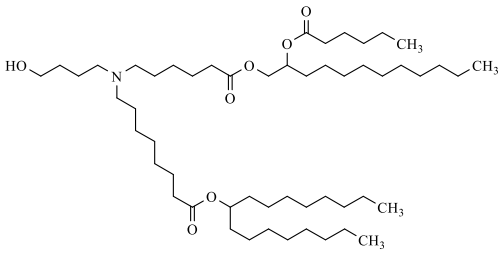
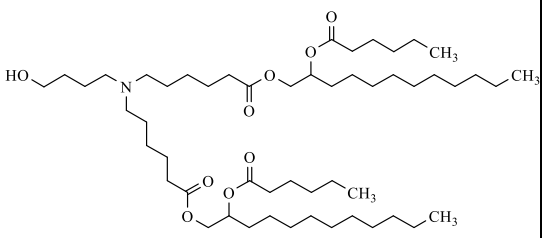
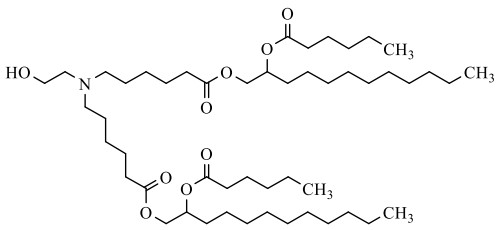
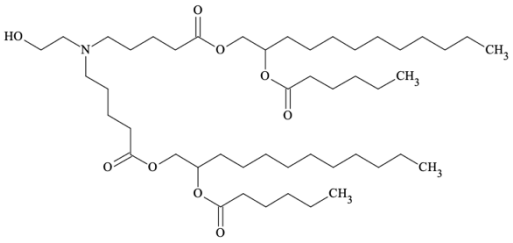
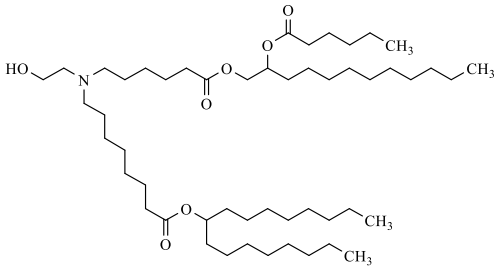
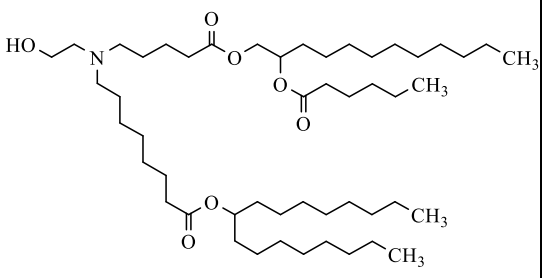
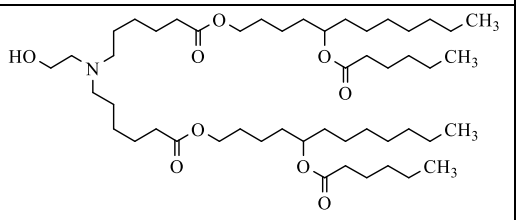
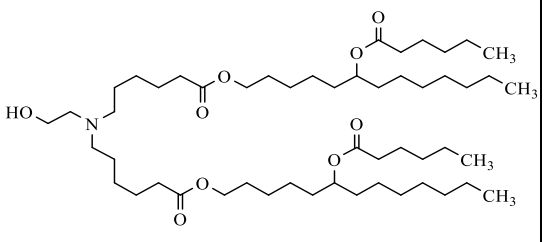
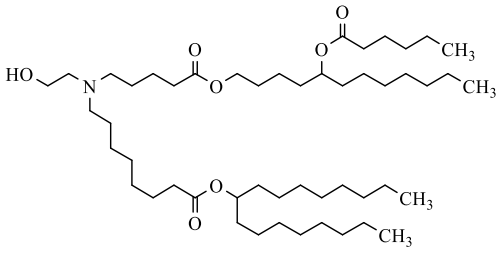
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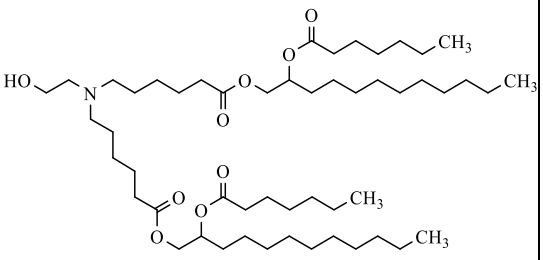
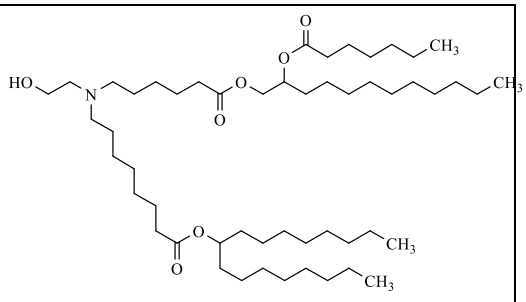
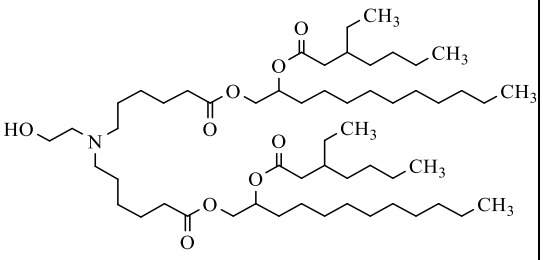
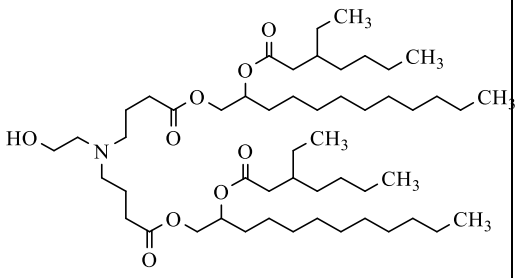
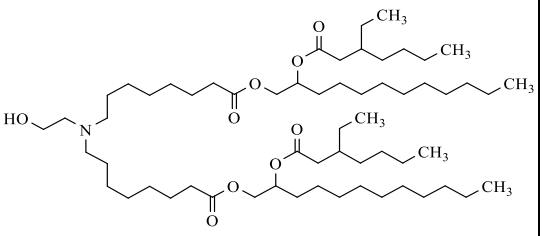
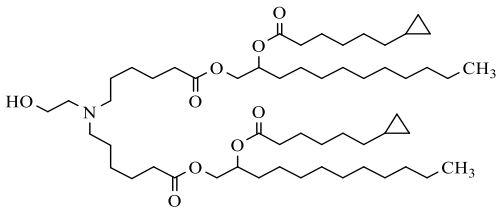
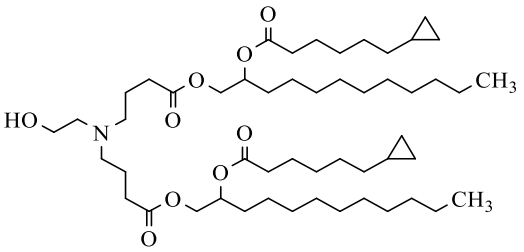
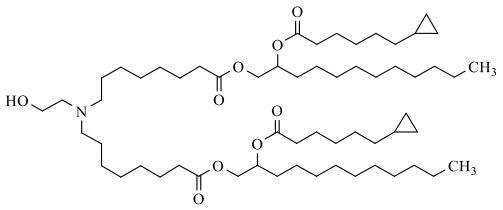
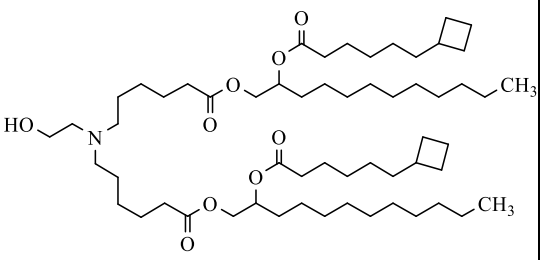
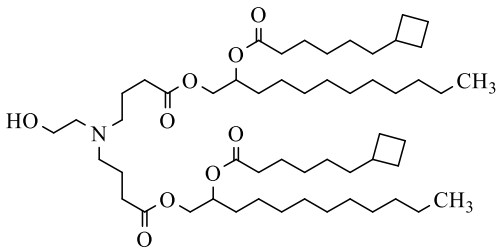
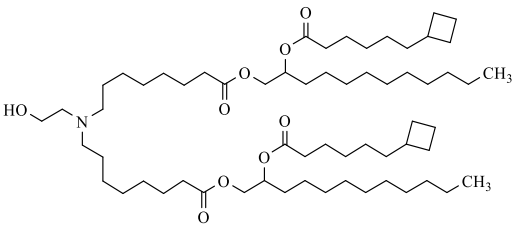
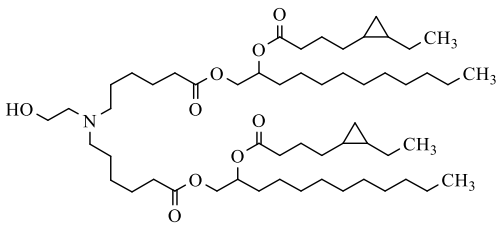
wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, Z^1, Z^2, X, and Y are as described in any one of the preceding embodiments.

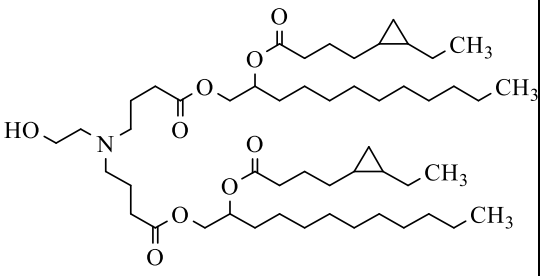
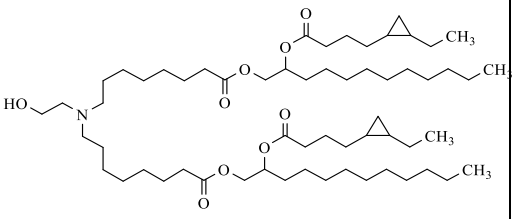
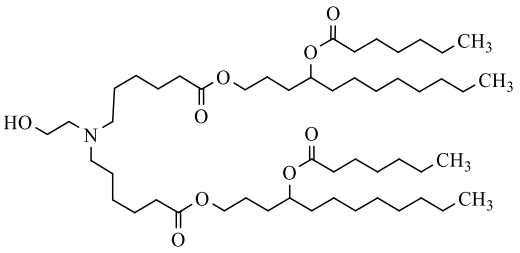
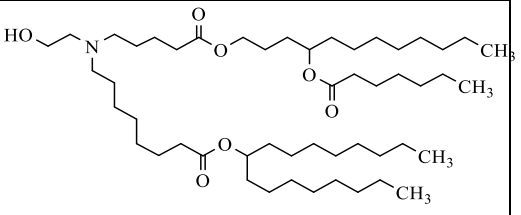
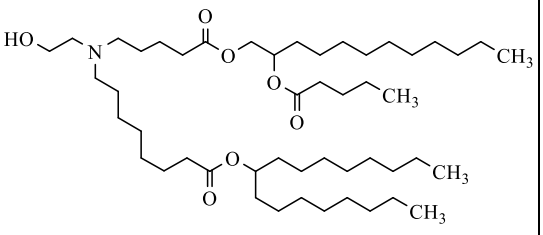
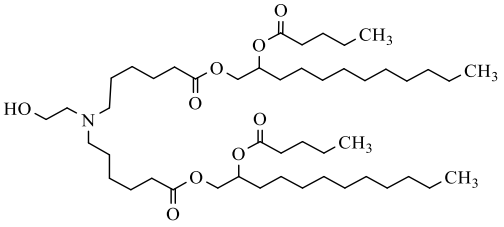
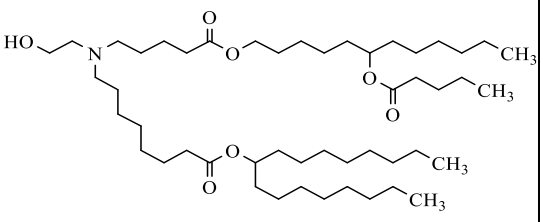
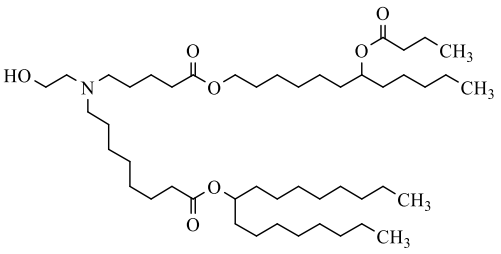
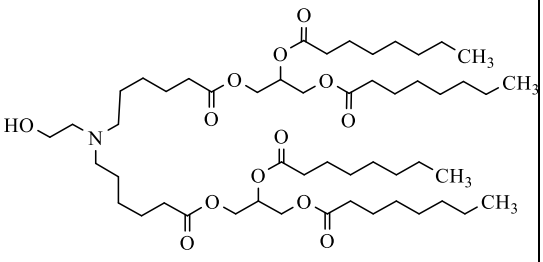
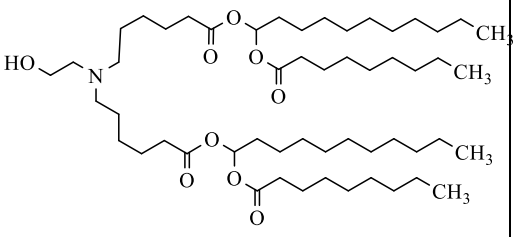
In an embodiment of the present disclosure, the compound I has any one of the following structures:

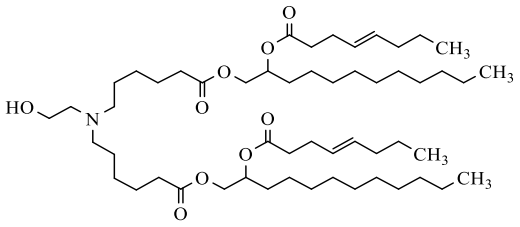
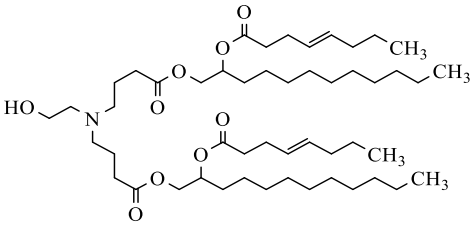
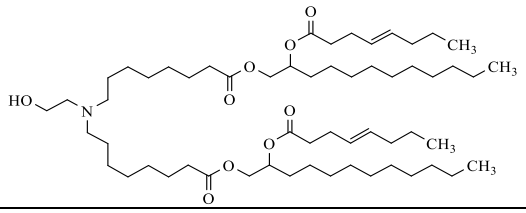
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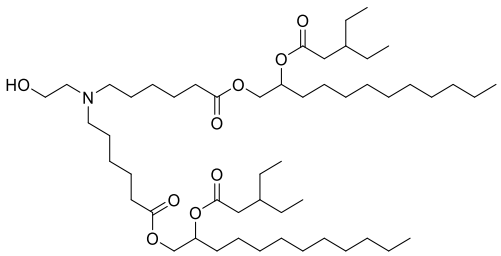
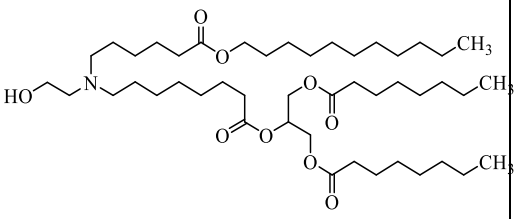
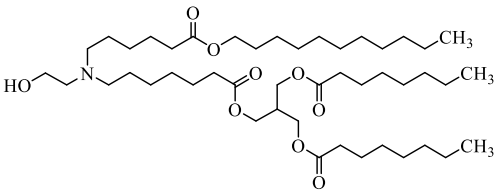
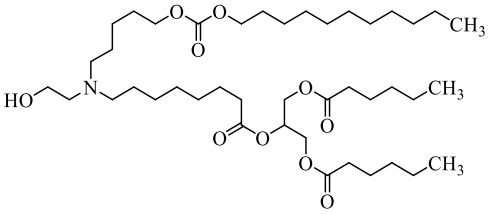
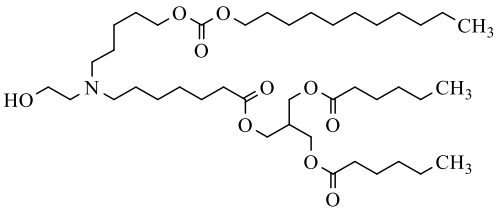
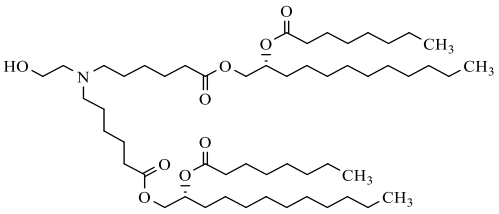
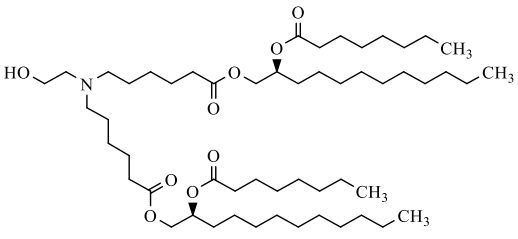
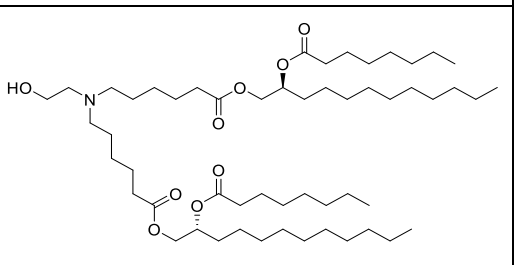
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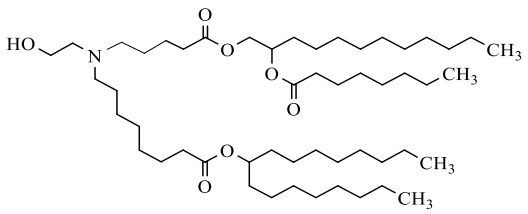
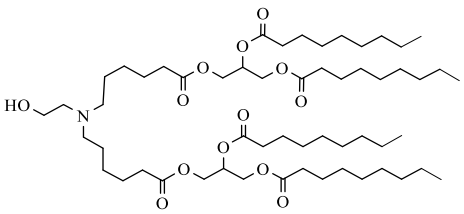
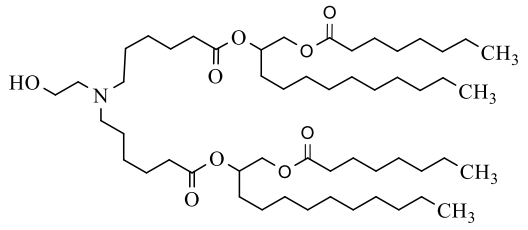
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In an embodiment of the present disclosure, the compound I has any one of the following structures:

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The present disclosure also provides use of the compound I or the pharmaceutically acceptable salt thereof in preparing a delivery carrier for a nucleic acid prophylactic agent and/or therapeutic agent;

The nucleic acid therapeutic agent and/or prophylactic agent is preferably one or more of single-stranded deoxyribonucleic acid (DNA), double-stranded DNA, small interfering RNA (siRNA), asymmetric double-stranded small interfering RNA (aiRNA), microRNA (miRNA), small hairpin RNA (shRNA), circular RNA (circRNA), transfer RNA (tRNA), or messenger RNA (mRNA), preferably mRNA, such as firefly luciferase (Fluc) mRNA, SARS-CoV-2 spike protein (Spike) mRNA, varicella-zoster virus (VZV) mRNA, respiratory syncytial virus (RSV) mRNA, or influenza virus (Flu) mRNA.

The present disclosure also provides a composition, comprising a substance Z, and the substance Z is the compound I or the pharmaceutically acceptable salt thereof as described above.

The present disclosure also provides a lipid carrier, comprising a substance Z, and the substance Z is the compound I or the pharmaceutically acceptable salt thereof as described above.

In an embodiment of the present disclosure, the lipid carrier further comprises a diluent. The diluent may be a phosphate buffer or a Tris buffer, etc.

In an embodiment of the present disclosure, the lipid carrier further comprises a phospholipid.

In an embodiment of the present disclosure, the phospholipid may be a conventional phospholipid in the art, which is an amphoteric auxiliary molecule that facilitates the fusion of

lipid particles with cell membranes. The phospholipid may be a phospholipid molecule having a charged polar end and a fatty chain non-polar end, such as distearoylphosphatidylcholine (DSPC), dimyristoylphosphocholine (DMPC), dioleoylphosphocholine (DOPC), palmitoylphosphocholine (DPPC), 1,2-distearoylphosphocholine (DSPC), heneicosanoylphosphocholine (DUPC), or palmitoylphosphocholine (POPC), etc.

In an embodiment of the present disclosure, the lipid carrier further comprises a PEG lipid (polyethylene glycol-modified lipid).

In an embodiment of the present disclosure, the PEG lipid may be a lipid molecule modified with a polyethylene glycol hydrophilic end. The PEG lipid is preferably one or more selected from a PEG-modified phosphatidylethanolamine, a PEG-modified phosphatidic acid, a PEG-modified ceramide, a PEG-modified dialkylamine, a PEG-modified diacylglycerol, and a PEG-modified dialkylglycerol, such as PEG-modified dimyristoylglycerol (DMG-PEG2000), etc.

In an embodiment of the present disclosure, the lipid carrier further comprises a sterol.

In an embodiment of the present disclosure, the sterol may be a conventional sterol in the art, and the sterol includes an animal sterol, a plant sterol, or a fungal sterol. The sterol is one or more selected from cholesterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, tomatine, ursolic acid, and α-tocopherol, such as cholesterol, etc.

In an embodiment of the present disclosure, in the lipid carrier, a molar ratio of the substance Z to the sterol is 0.5-5:1, preferably 0.5-3:1, such as 1.3:1.

In an embodiment of the present disclosure, in the lipid carrier, a molar ratio of the substance Z to the phospholipid is 1-15:1, preferably 2-8:1, such as 3-6:1.

In an embodiment of the present disclosure, in the lipid carrier, a molar ratio of the substance Z to the phospholipid is 1-15:1, preferably 1-10:1, such as 5:1.

In an embodiment of the present disclosure, in the lipid carrier, a molar ratio of the substance Z to the PEG lipid is 10-100:1, preferably 10-50:1, such as 33.3:1.

In the present disclosure, the molar content means the percentage of a certain substance in the total amount of substances of the lipid carrier, and the sum of the molar contents of the components in the lipid carrier does not exceed 100 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the substance Z is 30 mol% to 70 mol%, such as 50 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the substance Z is 35 mol%, 40 mol%, 45 mol%, 50 mol%, 55 mol%, or 60 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the phospholipid is 5 mol% to 20 mol%, such as 10 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the phospholipid is 0 mol% to 30 mol%, such as 0 mol%, 5 mol%, 10 mol%, 15 mol%, or 20 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the sterol is 20 mol% to 60 mol%, such as 38.5 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the sterol is 28.5 mol%, 33.5 mol%, 37.0 mol%, 38.0 mol%, 38.5 mol%, 39.0 mol%, 39.5 mol%, 43.5 mol%, 48.5 mol%, or 53.5 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the molar content of the PEG lipid is about 0.2 mol% to 5 mol%, such as 1.5 mol%.

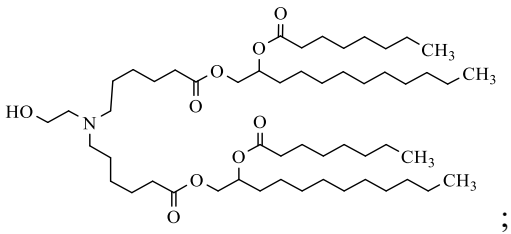
In an embodiment of the present disclosure, in the lipid carrier, the molar content of the PEG lipid is 0.5 mol%, 1.0 mol%, 1.5 mol%, 2.0 mol%, or 3.0 mol%.

In an embodiment of the present disclosure, in the lipid carrier, the lipid carrier consists of the substance Z, the diluent, the phospholipid, the PEG lipid, and the sterol.

In an embodiment of the present disclosure, the lipid carrier has any one of the following formulations:

Formulation	Substance Z : Phospholipid : Sterol : PEG Lipid
1	35 : 10 : 53.5 : 1.5
2	40 : 10 : 48.5 : 1.5
3	45 : 10 : 43.5 : 1.5
4	50 : 10 : 38.5 : 1.5
5	55 : 10 : 33.5 : 1.5
6	60 : 10 : 28.5 : 1.5
7	50 : 0 : 48.5 : 1.5
8	50 : 5 : 43.5 : 1.5
9	50 : 15 : 33.5 : 1.5
10	50 : 20 : 28.5 : 1.5
11	50 : 10 : 39.5 : 0.5
12	50 : 10 : 39.0 : 1.0
13	50 : 10 : 38.0 : 2.0
14	50 : 10 : 37.0 : 3.0

; wherein the substance Z is preferably compound 6 or a pharmaceutically acceptable salt thereof (compound 6 has the following structure);



;

the phospholipid is preferably DSPC; the sterol is preferably cholesterol; the PEG lipid is preferably DMG-PEG2000;

Preferably, the lipid carrier has any one of the following formulations:

Formulation	Compound 6 or Pharmaceutically Acceptable Salt thereof : DSPC : Cholesterol : DMG-PEG2000
1	35 : 10 : 53.5 : 1.5
2	40 : 10 : 48.5 : 1.5
3	45 : 10 : 43.5 : 1.5
4	50 : 10 : 38.5 : 1.5
5	55 : 10 : 33.5 : 1.5
6	60 : 10 : 28.5 : 1.5
7	50 : 0 : 48.5 : 1.5
8	50 : 5 : 43.5 : 1.5
9	50 : 15 : 33.5 : 1.5
10	50 : 20 : 28.5 : 1.5
11	50 : 10 : 39.5 : 0.5
12	50 : 10 : 39.0 : 1.0
13	50 : 10 : 38.0 : 2.0
14	50 : 10 : 37.0 : 3.0

.

The present disclosure also provides use of the lipid carrier in preparing a delivery carrier for a nucleic acid prophylactic agent and/or therapeutic agent;

The nucleic acid therapeutic agent and/or prophylactic agent is preferably one or more of single-stranded deoxyribonucleic acid (DNA), double-stranded DNA, small interfering RNA (siRNA), asymmetric double-stranded small interfering RNA (aiRNA), microRNA (miRNA), small hairpin RNA (shRNA), circular RNA (circRNA), transfer RNA (tRNA), or messenger RNA (mRNA), preferably mRNA, such as firefly luciferase (Fluc) mRNA, SARS-CoV-2 spike protein (Spike) mRNA, varicella-zoster virus (VZV) mRNA, respiratory syncytial virus (RSV)

mRNA, or influenza virus (Flu) mRNA.

The present disclosure also provides a lipid nanoparticle, comprising a nucleic acid prophylactic agent and/or therapeutic agent and the aforementioned lipid carrier;

The nucleic acid therapeutic agent and/or prophylactic agent is preferably one or more of single-stranded deoxyribonucleic acid (DNA), double-stranded DNA, small interfering RNA (siRNA), asymmetric double-stranded small interfering RNA (aiRNA), microRNA (miRNA), small hairpin RNA (shRNA), circular RNA (circRNA), transfer RNA (tRNA), or messenger RNA (mRNA), preferably mRNA, such as firefly luciferase (Fluc) mRNA, SARS-CoV-2 spike protein (Spike) mRNA, varicella-zoster virus (VZV) mRNA, respiratory syncytial virus (RSV) mRNA, or influenza virus (Flu) mRNA.

In an embodiment of the present disclosure, a nitrogen-to-phosphorus ratio in the lipid nanoparticle may be (2-30):1, and the nitrogen-to-phosphorus ratio refers to a ratio of the number of moles of ionizable nitrogen atoms in one or more ionizable lipid compounds to the number of moles of phosphate ester groups in the RNA, which in the present application is a ratio of the number of moles of ionizable nitrogen atoms in the ionizable lipid nanoparticle to the number of moles of phosphate ester groups in the mRNA in the pharmaceutical composition. Preferably, the nitrogen-to-phosphorus ratio is (2-20):1, more preferably (3-20):1, such as (3-16):1.

In an embodiment of the present disclosure, in the lipid nanoparticle, the nitrogen-to-phosphorus ratio is 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, or 9:1.

In an embodiment of the present disclosure, the lipid nanoparticle has a particle size (average particle size) of 10-200 nm, preferably 40-150 nm, further preferably 50-130 nm, such as 57.29 nm, 61.55 nm, 69.72 nm, 70.08 nm, 76.03 nm, 89.89 nm, 97.55 nm, 107.37 nm, or 119.10 nm.

In an embodiment of the present disclosure, the lipid nanoparticle has a particle size of 63.36 nm, 56.53 nm, 71.25 nm, 57.66 nm, 60.92 nm, 55.68 nm, 56.19 nm, 55.52 nm, 67.96 nm, 69.51 nm, or 79.13 nm.

In an embodiment of the present disclosure, the lipid nanoparticle has a particle size of 57.29 nm, 61.55 nm, 69.72 nm, 70.08 nm, 76.03 nm, 89.89 nm, 97.55 nm, 107.37 nm, 119.10 nm, 63.36 nm, 56.53 nm, 71.25 nm, 57.66 nm, 60.92 nm, 55.68 nm, 56.19 nm, 55.52 nm, 67.96 nm, 69.51 nm, or 79.13 nm.

In an embodiment of the present disclosure, the lipid nanoparticle has a polydispersity index of 0.001-0.3, such as 0.035, 0.074, 0.090, 0.097, 0.118, 0.166, or 0.269.

In an embodiment of the present disclosure, the lipid nanoparticle has a polydispersity index of 0.065, 0.074, 0.062, 0.106, 0.089, 0.108, 0.090, 0.078, 0.085, 0.063, or 0.084.

In an embodiment of the present disclosure, the lipid nanoparticle has a polydispersity index of 0.035, 0.074, 0.090, 0.097, 0.118, 0.166, 0.269, 0.065, 0.074, 0.062, 0.106, 0.089, 0.108, 0.090, 0.078, 0.085, 0.063, or 0.084.

In an embodiment of the present disclosure, the lipid nanoparticle has an encapsulation efficiency of 90%-100%, such as 96.73%, 98.07%, 96.90%, 97.71%, 96.36%, 95.02%, 92.94%, 94.44%, 95.23%, or 94.63%.

In an embodiment of the present disclosure, the lipid nanoparticle has an encapsulation efficiency of 95.83%, 94.95%, 96.00%, 96.62%, 94.28%, 96.56%, 96.04%, 95.94%, 98.33%, 95.38%, or 96.78%.

In an embodiment of the present disclosure, the lipid nanoparticle has an encapsulation efficiency of 96.73%, 98.07%, 96.90%, 97.71%, 96.36%, 95.02%, 92.94%, 94.44%, 95.23%, 94.63%, 95.83%, 94.95%, 96.00%, 96.62%, 94.28%, 96.56%, 96.04%, 95.94%, 98.33%, 95.38%, or 96.78%.

In an embodiment of the present disclosure, in the lipid nanoparticle, the lipid carrier encapsulates the nucleic acid prophylactic agent and/or therapeutic agent.

On the basis of conforming to common knowledge in the art, the above preferred conditions can be arbitrarily combined to obtain various preferred examples of the present disclosure.

The reagents and raw materials used in the present disclosure are commercially available.

The advantageous effects of the present disclosure lie in that: the LNP formulation prepared with the nitrogen-containing chain compound of the present disclosure has relatively uniform nanoparticle size, higher encapsulation efficiency, and higher expression activity *in vivo*.

Unless otherwise specified, the terms of the present disclosure may have the following definitions:

Those skilled in the art can understand that, according to conventions used in the art, "" used in the structural formulae describing groups in the present disclosure means that the

corresponding group is attached to other fragments or groups in the compound through this site.

As used herein, the substituents used may be appended with a single dash "-", indicating that the named substituent is attached to the parent moiety through a single bond.

When one of the variables is selected from a chemical bond, it means that the two groups attached thereby are directly attached.

When any variable appears multiple times in the definition of a compound, the definition of the variable at each occurrence is independent of the definitions at the other occurrences, and their meanings are independent of and do not affect each other.

The term "or more" refers to 2, 3, or 4.

The term "alkyl" refers to a straight-chain or branched-chain alkyl having the specified number of carbon atoms (for example, C_1-C_6). Examples of the alkyl include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, a tert-butyl, isobutyl, sec-butyl, and the like.

The term "alkylene" refers to a straight-chain divalent hydrocarbon group or a branched-chain divalent hydrocarbon group having the specified number of carbon atoms (for example, C_1-C_6). Examples of the alkylene include, but are not limited to, methylene, ethylene, propylene, 1-methylpropylene, butylene, and the like.

The term "alkenyl" refers to a straight-chain or branched-chain hydrocarbon group having one or more double bonds and a specified number of carbon atoms (for example, C_2-C_4). The one or more carbon-carbon double bonds can be internal or terminal.

The term "cycloalkyl" refers to a saturated cyclic group having the specified number of ring carbon atoms (for example, C_3-C_8) and whose ring atoms consist solely of carbon atoms. Examples of the cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like.

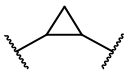
The term "pharmaceutically acceptable salt" refers to a salt prepared from a compound of the present disclosure and a relatively non-toxic, pharmaceutically acceptable acid or base. When the compound of the present disclosure contains a relatively acidic functional group, a base addition salt can be obtained by contacting the neutral form of such a compound with a sufficient amount of a pharmaceutically acceptable base in a pure solution or a suitable inert solvent. When the compound of the present disclosure contains a relatively basic functional group, an acid addition salt can be obtained by contacting the neutral form of such a compound with a sufficient amount of a pharmaceutically acceptable acid in a pure solution or a suitable

inert solvent.

The term "treating" or "treatment" refers to a therapeutic treatment. When referring to a specific disorder, treatment means: (1) alleviating one or more biological manifestations of a disease or disorder, (2) interfering with (a) one or more points in a biological cascade that causes or gives rise to the disorder or (b) one or more biological manifestations of the disorder, (3) ameliorating one or more symptoms, effects or side effects associated with the disorder, or one or more symptoms, effects or side effects associated with the disorder or its treatment, or (4) slowing the progression of the disorder or one or more biological manifestations of the disorder.

The term "preventing" or "prevention" refers to maintaining health in a subject for a certain period of time relative to the disease or disorder mentioned herein. It should be understood that the period of time depends on the amount of the pharmaceutical compound that has been administered and the individual factors of the subject discussed elsewhere in this specification. It should be understood that prevention may not be effective in all subjects treated with a compound according to the present invention. However, the term requires preferably effectively preventing a statistically significant portion of a cohort or population of subjects from suffering from the disease or disorder referred to herein or its accompanying symptoms. Preferably, in this case, a group or population of subjects is envisaged that would normally develop the disease or disorder referred to herein without taking the preventive measures according to the present invention. Those skilled in the art can immediately determine whether a portion is statistically significant using various well-known statistical evaluation tools discussed elsewhere in this specification.

When any variable is used to connect two or more groups, those skilled in the art can understand that the actual meaning of the variable is an implementable embodiment obtained on the basis of the definition of the variable in the claims and/or the specification, without modification or by losing one or more hydrogens on the basis of the aforementioned definition; for example, in the present application, a certain definition of R^{2a} is "-C_{1-12} alkylene-C_{3-10} cycloalkyl-R^{2aa}", wherein the "C_{1-12} alkylene" is used to connect two groups, its definition "C_{1-12} alkylene" itself is an implementable embodiment, examples of which include but are not limited to methylene, ethylene, and the like; and the "C_{3-10} cycloalkyl" is used to connect "C_{1-12} alkylene" and R^{2aa}, when R^{2aa} is not hydrogen, the actual meaning of "C_3-C_{10} cycloalkyl" here is a structure obtained by losing one hydrogen from "C_3-C_{10} cycloalkyl", i.e., "C_3-C_{10}

cycloalkylene", such as  ; when R^{2aa} is hydrogen, the definition of "C_3-C_{10} cycloalkyl" here itself is an implementable embodiment, examples of which include but are not limited to  ,  , and the like.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 2, Compound 3 and Compound 6;

FIG. 2 shows the chemiluminescence intensity at the administration site of mice after intramuscular administration of Compound 2, Compound 3 and Compound 6;

FIG. 3 shows the chemiluminescence intensity in the liver region of mice after intramuscular administration of Compound 2, Compound 3 and Compound 6;

FIG. 4 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 8 and Compound 9;

FIG. 5 shows the chemiluminescence intensity at the administration site of mice after intramuscular administration of Compound 8 and Compound 9;

FIG. 6 shows the chemiluminescence intensity in the liver region of mice after intramuscular administration of Compound 8 and Compound 9;

FIG. 7 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of SM102, Compound 5 and Compound 28;

FIG. 8 shows the chemiluminescence intensity at the administration site of mice after intramuscular administration of Compound 5 and Compound 28;

FIG. 9 shows the chemiluminescence intensity in the liver region of mice after intramuscular administration of Compound 5 and Compound 28;

FIG. 10 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 23, Compound 24, Compound 25, Compound 26, Compound 27, Compound 29 and Compound 34;

FIG. 11 shows the chemiluminescence intensity at the administration site of mice after intramuscular administration of SM102, Compound 23, Compound 24, Compound 25, Compound 26, Compound 27, Compound 29 and Compound 34;

FIG. 12 shows the chemiluminescence intensity in the liver region of mice after intramuscular administration of SM102, Compound 23, Compound 24, Compound 25, Compound 26, Compound 27, Compound 29 and Compound 34;

FIG. 13 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 1, Compound 7, Compound 21, Compound 32, Compound 48, Compound 55 and Compound 57;

FIG. 14 shows the *in vivo* VZV antigen protein expression in mice after tail vein injection of each VZV mRNA LNP in Example 16 (3 hours after administration, n=5);

FIG. 15 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 11, Compound 19, Compound 20, Compound 22, Compound 30, Compound 31, Compound 52, Compound 58 and Compound 60;

FIG. 16 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 33, Compound 35, Compound 36, Compound 37, Compound 47, Compound 49, Compound 50, Compound 62, Compound 63, Compound 64, Compound 65, Compound 66, Compound 67 and Compound 68;

FIG. 17 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of LNP1, LNP2, LNP3, LNP4, LNP5, LNP6, LNP7, LNP8, LNP9, LNP10, LNP11, LNP12, LNP13 and LNP14 under different lipid formulations;

FIG. 18 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of NP3, NP4, NP5, NP6, NP7, NP8 and NP9 under different nitrogen-to-phosphorus ratios;

FIG. 19 shows the chemiluminescence intensity in the liver region of mice after tail vein administration of Compound 10, Compound 12, Compound 13, Compound 14, Compound 15, Compound 16, Compound 17 and Compound 61.

DETAILED DESCRIPTION

The present disclosure is further illustrated below by way of examples, but the present disclosure is not thereby limited to the scope of the described examples. In the following examples, experimental methods without specified conditions are carried out according to conventional methods and conditions, or according to the product instructions.

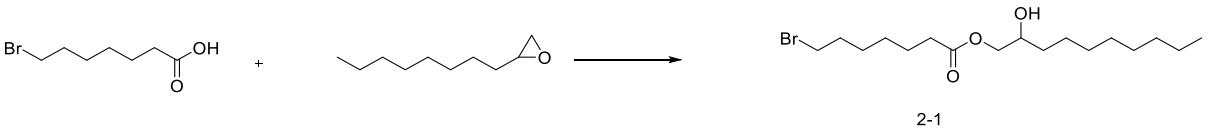
In the examples of the present application, RT in LCMS stands for "retention time", and its

unit is "minutes".

Preparation Example 1: Preparation of Compound 2

Step 1: Preparation of 2-1

Reaction scheme:



2-1

Material ratio:

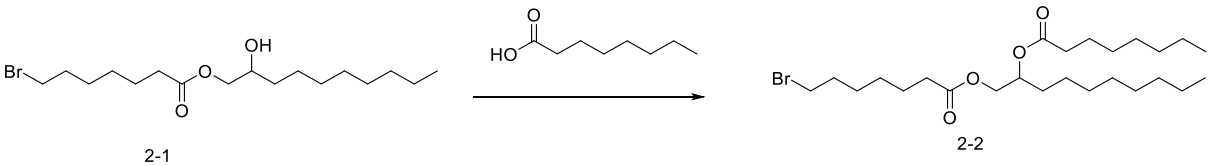
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
epoxydecane	156	1 eq	4.2 g	27
7-bromoheptanoic acid	209	1.1 eq	6.2 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To a 250 mL reaction flask, 7-bromoheptanoic acid, epoxydecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 7.4 g of a colorless oily substance was obtained.

Step 2: Preparation of 2-2

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-1	365.35	1 eq	6.4 g	17.5
octanoic acid	144	1.1 eq	2.8 g	19.2
EDCI	192	2 eq	6.7 g	35
DMAP	122	0.2 eq	420 mg	3.5
dichloromethane	-	-	80 mL	-

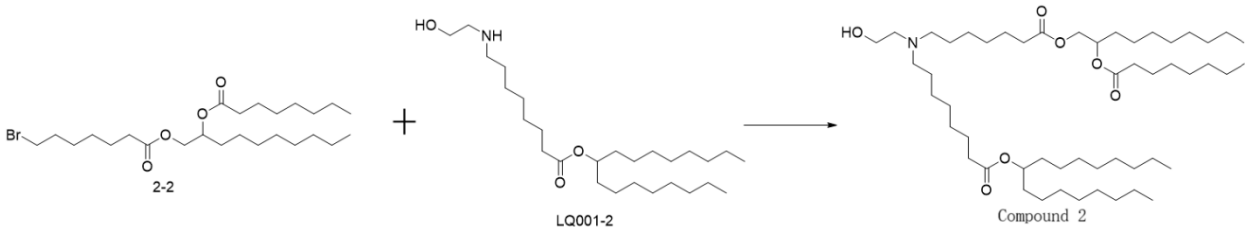
Procedure:

To the reaction flask, 2-1, octanoic acid, EDCI, DMAP, and dichloromethane were added,

and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed twice with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 6 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 2

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-2	491.55	1.1 eq	4.2 g	8.55
LQ001-2	441.74	1 eq	3.4 g	7.77
K_2CO_3	138	1.5 eq	1.6 g	11.6
KI	166	1.5 eq	1.9 g	11.6
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 2-2, LQ001-2, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 3 g of a colorless oily substance was obtained.

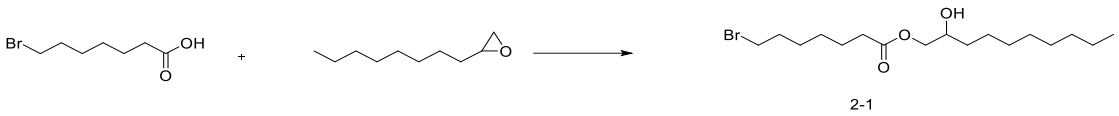
^{1}H NMR (600 MHz, Chloroform-d) δ 5.08 (qd, J = 6.9, 3.3 Hz, 1H), 4.85 (p, J = 6.2 Hz, 1H), 4.21 (dd, J = 11.8, 3.3 Hz, 1H), 4.01 (dd, J = 11.8, 6.8 Hz, 1H), 3.69 – 3.59 (m, 2H), 2.66 (d, J = 75.2 Hz, 4H), 2.28 (dt, J = 14.1, 7.5 Hz, 6H), 1.65 – 1.45 (m, 16H), 1.36 – 1.20 (m, 56H), 0.91 – 0.84 (m, 12H).

MS (ES+) m/z: 852.7$(M+H)^+$.

Compound 2 may also be prepared by the following method:

Step 1: Preparation of 2-1

Reaction scheme:



2-1

Material ratio:

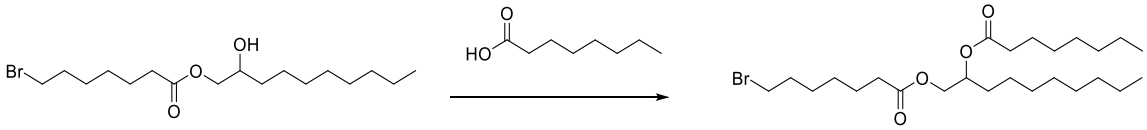
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
7-bromoheptanoic acid	209	1 eq	21 g	100
1,2-epoxydecane	156	1 eq	15.6 g	100
ferric chloride	162	0.05 eq	800 mg	5
pyridine	79	0.025 eq	200 mL	2.5

Procedure:

To the reaction flask, 7-bromoheptanoic acid, 1,2-epoxydecane, ferric chloride, and pyridine were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.4, TLC (PE:EA=4:1). The reaction mixture was diluted with 200 mL of ethyl acetate, washed once with 200 mL of a saturated aqueous sodium bicarbonate solution, and washed once again with 200 mL of a saturated aqueous sodium chloride solution, and the organic phase was taken, dried over anhydrous magnesium sulfate, filtered, and then concentrated. After purification by column chromatography, 17 g of oily substance was obtained.

Step 2: Preparation of 2-2

Reaction scheme:



2-1 2-2

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-1	365.35	1 eq	7.3 g	20
n-octanoic acid	144.21	1 eq	2.9 g	20
EDCI	192	1.5 eq	5.7 g	30
DMAP	122	0.15 eq	370 mg	3
DCM	-	-	100 mL	-

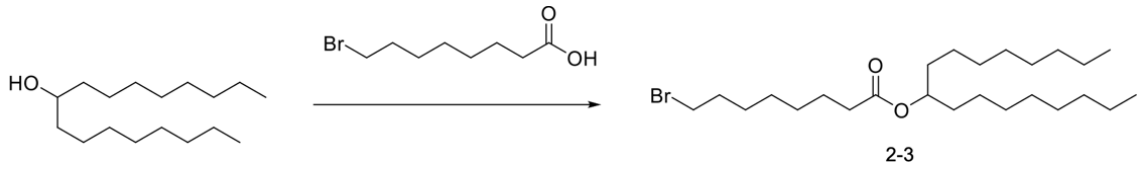
Procedure:

To the reaction flask, 2-1, n-octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was washed once with 100 mL of a saturated aqueous sodium bicarbonate solution, and washed once again with 100 mL of a saturated aqueous

sodium chloride solution, and the organic phase was taken, dried over anhydrous magnesium sulfate, filtered, and then concentrated. After purification by column chromatography, 6.5 g of oily substance was obtained.

Step 3: Preparation of 2-3

Reaction scheme:



Material ratio:

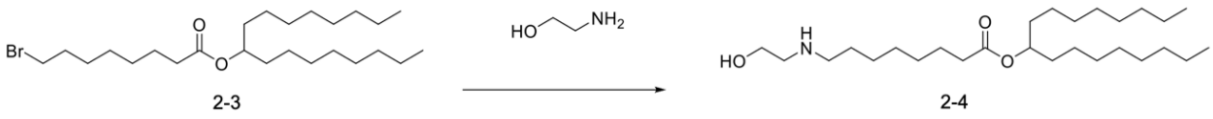
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
8-bromooctanoic acid	223	1 eq	7 g	30
9-heptadecanol	256	1 eq	7.7 g	30
EDCI	192	1.5 eq	5.8 g	45
DMAP	122	0.15 eq	400 mg	4.5
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 8-bromooctanoic acid, 9-heptadecanol, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.5, TLC (PE:EA=10:1). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 10.8 g of oily substance was obtained.

Step 4: Preparation of 2-4

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-3	461	1eq	9.2 g	20
ethanolamine	61	1eq	6.1 g	100
acetonitrile	-	-	80 mL	-

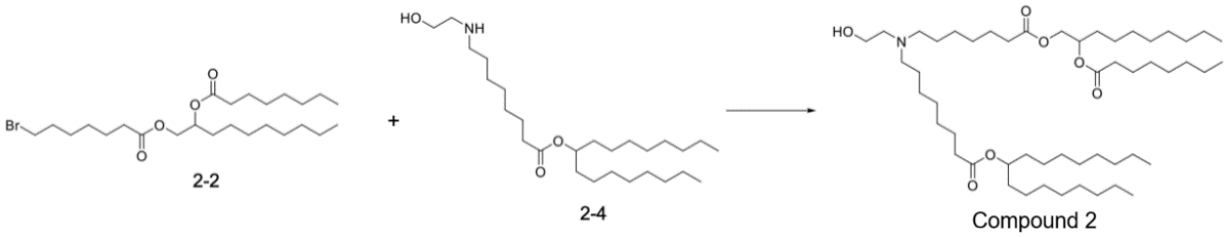
Procedure:

To the reaction flask, 2-3, ethanolamine, and acetonitrile were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value

was 0.3. The reaction mixture was diluted with 200 mL of ethyl acetate, and washed twice with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 5.6 g of a colorless oily substance was obtained.

Step 5: Preparation of Compound 2

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-2	491.55	1 eq	2.9 g	6
2-4	441.74	1.2 eq	2.2 g	5
potassium carbonate	138	1.5 eq	1 g	7.5
potassium iodide	166	0.5 eq	420 mg	2.5
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 2-2, 2-4, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 2.2 g of a colorless oily substance was obtained.

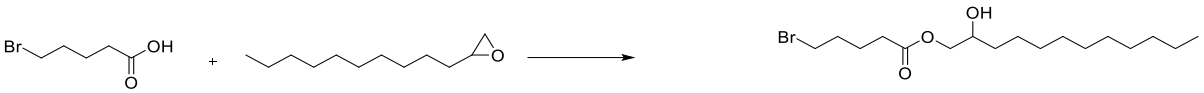
^{1}H NMR (600 MHz, Chloroform-d) δ 5.08 (qd, J = 6.9, 3.3 Hz, 1H), 4.85 (p, J = 6.2 Hz, 1H), 4.21 (dd, J = 11.8, 3.3 Hz, 1H), 4.01 (dd, J = 11.8, 6.8 Hz, 1H), 3.69 – 3.59 (m, 2H), 2.66 (d, J = 75.2 Hz, 4H), 2.28 (dt, J = 14.1, 7.5 Hz, 6H), 1.65 – 1.45 (m, 16H), 1.36 – 1.20 (m, 56H), 0.91 – 0.84 (m, 12H).

MS (ES+) m/z: 852(M).

Preparation Example 2: Preparation of Compound 3

Step 1: Preparation of 3-1

Reaction scheme:



3-1

Material ratio:

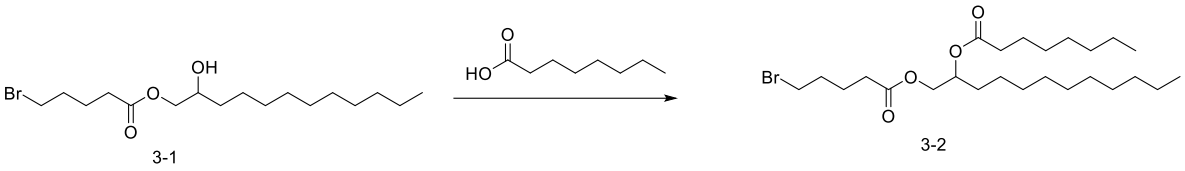
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1 eq	5 g	27
5-bromovaleric acid	181	1.1 eq	5.4 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To a 250 mL reaction flask, 5-bromovaleric acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 6.4 g of a colorless oily substance was obtained.

Step 2: Preparation of 3-2

Reaction scheme:



3-1 3-2

Material ratio:

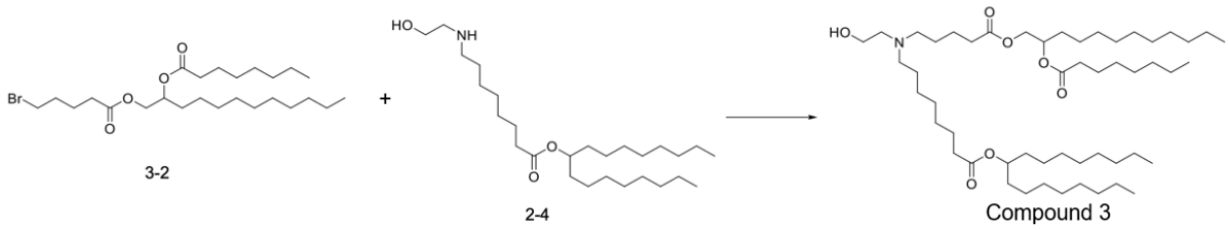
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-1	365.35	1 eq	6.4 g	17.5
octanoic acid	144	1.1 eq	2.8 g	19.2
EDCI	192	2 eq	6.7 g	35
DMAP	122	0.2 eq	420 mg	3.5
dichloromethane	-	-	80 mL	-

Procedure:

To the reaction flask, 3-1, octanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed twice with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 6.5 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 3

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-2	491.55	1.1 eq	4.2 g	8.55
2-4	441.74	1 eq	3.4 g	7.77
K_2CO_3	138	1.5 eq	1.6 g	11.6
KI	166	1.5 eq	1.9 g	11.6
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 3-2, 2-4, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 3.6 g of a colorless oily substance was obtained.

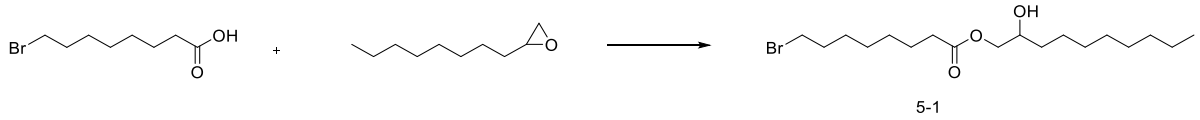
^{1}H NMR (600 MHz, Chloroform-d) δ 5.08 (qd, J = 7.3, 3.2 Hz, 1H), 4.86 (p, J = 6.2 Hz, 1H), 4.27 – 4.21 (m, 1H), 3.99 (dd, J = 11.8, 7.0 Hz, 1H), 3.68 (d, J = 6.3 Hz, 2H), 2.80 – 2.59 (m, 6H), 2.30 (ddt, J = 23.3, 15.5, 7.0 Hz, 6H), 1.65 – 1.47 (m, 16H), 1.35 – 1.21 (m, 54H), 0.87 (t, J = 7.0 Hz, 12H).

MS (ES+) m/z): 852.7$(M+H)^+$.

Preparation Example 3: Preparation of Compound 5

Step 1: Preparation of 5-1

Reaction scheme:



Material ratio:

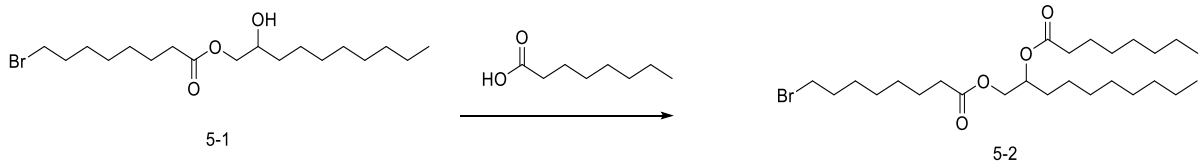
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
epoxydecane	156	1 eq	4.2 g	27
8-bromooctanoic acid	223	1.1 eq	6.7 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To a 250 mL reaction flask, 8-bromooctanoic acid, epoxydecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 6.9 g of a colorless oily substance was obtained.

Step 2: Preparation of 5-2

Reaction scheme:



Material ratio:

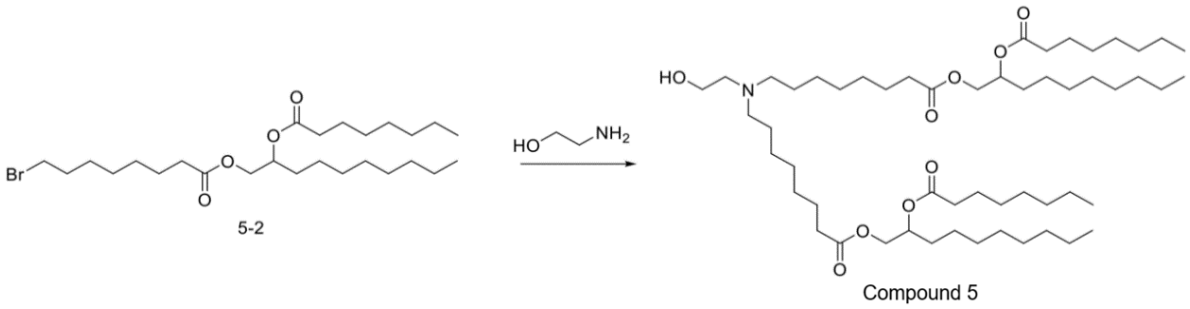
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-1	379.38	1 eq	6.6 g	17.5
octanoic acid	144	1.1 eq	2.8 g	19.2
EDCI	192	2 eq	6.7 g	35
DMAP	122	0.2 eq	420 mg	3.5
dichloromethane	-	-	80 mL	-

Procedure:

To the reaction flask, 5-1, octanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed twice with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 6 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 5

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-2	505.58	2.2 eq	4.3 g	8.55
ethanolamine	61	1 eq	230 mg	3.9
K_2CO_3	138	2 eq	1.1 g	7.8
KI	166	2 eq	1.3 g	7.8
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 5-2, ethanolamine, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 2.5 g of a colorless oily substance was obtained.

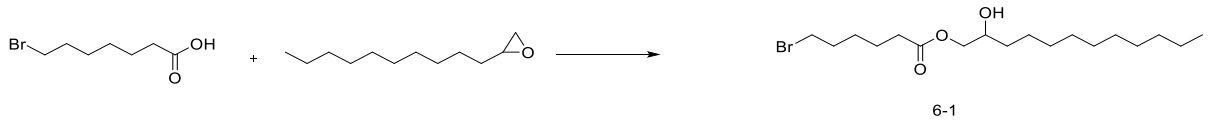
^{1}H NMR (600 MHz, Chloroform-d) δ 5.07 (qd, J = 6.7, 3.2 Hz, 2H), 4.21 (dd, J = 11.8, 3.4 Hz, 2H), 4.01 (dd, J = 11.8, 6.8 Hz, 2H), 2.67 (t, J = 5.6 Hz, 2H), 2.54 (t, J = 7.8 Hz, 4H), 2.29 (t, J = 7.3 Hz, 8H), 1.64 – 1.52 (m, 12H), 1.49 (t, J = 7.9 Hz, 4H), 1.34 – 1.20 (m, 54H), 0.87 (td, J = 7.0, 2.0 Hz, 12H).

MS (ES+) m/z): 910.7$(M+H)^+$.

Preparation Example 4: Preparation of Compound 6

Step 1: Preparation of 6-1

Reaction scheme:



Material ratio:

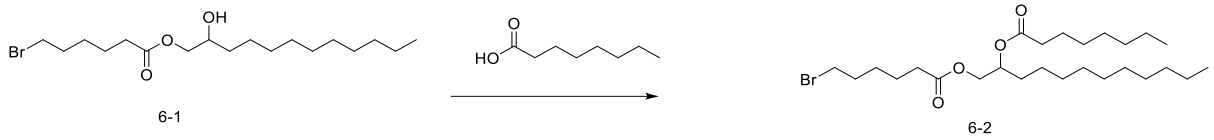
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1 eq	5 g	27
6-bromohexanoic acid	209	1.1 eq	5.85 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To a 250 mL reaction flask, 6-bromohexanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 6.8 g of a colorless oily substance was obtained.

Step 2: Preparation of 6-2

Reaction scheme:



Material ratio:

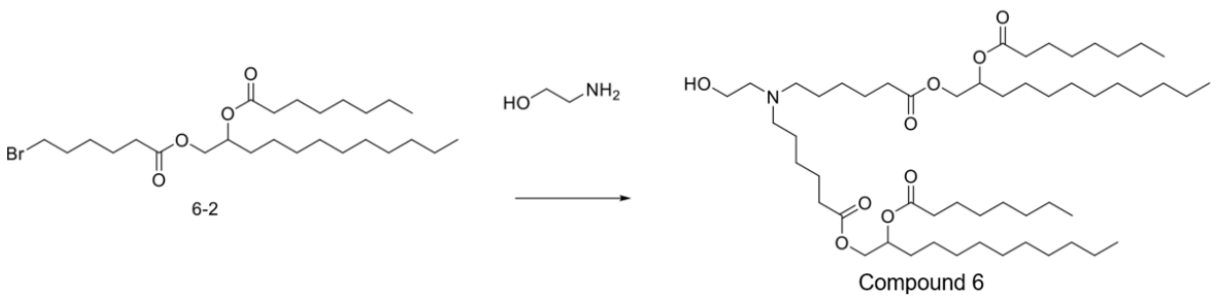
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-1	379.38	1 eq	6.6 g	17.5
octanoic acid	144	1.1 eq	2.8 g	19.2
EDCI	192	2 eq	6.7 g	35
DMAP	122	0.2 eq	420 mg	3.5
dichloromethane	-	-	80 mL	-

Procedure:

To the reaction flask, 6-1, octanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed twice with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 6.5 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 6

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-2	505.58	2.2 eq	4.3 g	8.55
ethanolamine	61	1 eq	230 mg	3.9
K_2CO_3	138	2 eq	1.1 g	7.8
KI	166	2 eq	1.3 g	7.8
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 6-2, ethanolamine, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 2.8 g of a colorless oily substance was obtained.

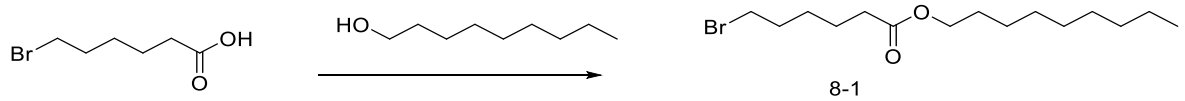
^{1}H NMR (600 MHz, Chloroform-d) δ 5.10 – 5.05 (m, 2H), 4.22 (dd, J = 11.8, 3.3 Hz, 2H), 4.01 (dd, J = 11.8, 6.8 Hz, 2H), 3.61 (d, J = 5.1 Hz, 2H), 2.73 – 2.49 (m, 6H), 2.30 (td, J = 7.5, 5.1 Hz, 8H), 1.65 – 1.50 (m, 16H), 1.33 – 1.23 (m, 52H), 0.91 – 0.85 (m, 12H).

MS (ES+) m/z): 910.7$(M+H)^+$.

Preparation Example 5: Preparation of Compound 8

Step 1: Preparation of 8-1

Reaction scheme:



8-1

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-nonanol	144	1 eq	7.2 g	50
6-bromohexanoic acid	195	1.1 eq	10.7 g	55
EDCI	192	2 eq	19.2 g	100
DMAP	122	0.2 eq	1.2 g	10
dichloromethane	-	-	200 mL	-

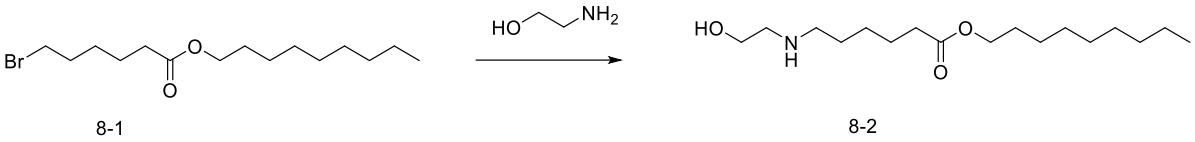
Procedure:

To the reaction flask, 1-nonanol, 6-bromohexanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed twice with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by

column chromatography, 13 g of a colorless oily substance was obtained.

Step 2: Preparation of 8-2

Reaction scheme:



8-1 8-2

Material ratio:

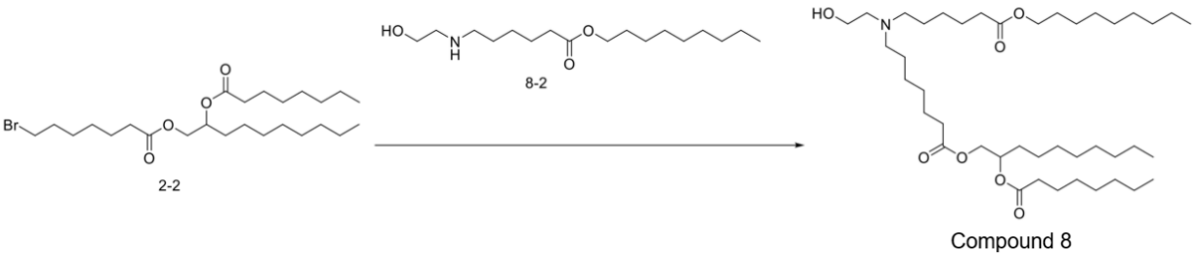
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
8-1	321.3	1 eq	13 g	40.5
ethanolamine	61	10 eq	24.7 g	405
acetonitrile	-	-	200 mL	-

Procedure:

To the reaction flask, 8-1, ethanolamine, and acetonitrile were added, and the mixture was heated to 30 ℃ and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.1). The reaction mixture was concentrated and then diluted with 200 mL of ethyl acetate, and then washed twice with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 8 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 8

Reaction scheme:



Compound 8

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-2	491.55	1.1 eq	4.2 g	8.55
8-2	301.47	1 eq	2.34 g	7.77
K_2CO_3	138	1.5 eq	1.6 g	11.6
KI	166	1.5 eq	1.9 g	11.6
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 2-2, 8-2, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 2.6 g of a colorless oily substance was obtained.

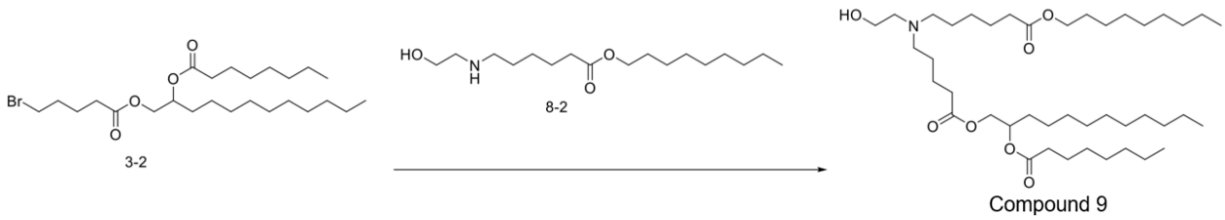
^{1}H NMR (600 MHz, Chloroform-d) δ 5.07 (qd, J = 6.9, 3.3 Hz, 1H), 4.21 (dd, J = 11.8, 3.3 Hz, 1H), 4.06 – 3.99 (m, 3H), 3.53 (t, J = 5.3 Hz, 2H), 2.58 (t, J = 5.3 Hz, 2H), 2.49 – 2.43 (m, 4H), 2.29 (t, J = 7.5 Hz, 6H), 1.66 – 1.52 (m, 10H), 1.45 (dp, J = 14.3, 7.5 Hz, 4H), 1.35 – 1.22 (m, 38H), 0.87 (td, J = 7.0, 2.2 Hz, 9H).

MS (ES+) m/z): 712.6$(M+H)^+$.

Preparation Example 6: Preparation of Compound 9

Step 1: Preparation of Compound 9

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-2	491.55	1.1 eq	4.2 g	8.55
8-2	301.47	1 eq	2.34 g	7.77
K_2CO_3	138	1.5 eq	1.6 g	11.6
KI	166	1.5 eq	1.9 g	11.6
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 3-2, 8-2, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was filtered and then concentrated. After purification by column chromatography, 2.4 g of a colorless oily substance was obtained.

^{1}H NMR (600 MHz, Chloroform-d) δ 5.08 (qd, J = 7.0, 3.2 Hz, 1H), 4.22 (dd, J = 11.8, 3.3 Hz, 1H), 4.07 – 3.99 (m, 3H), 3.53 (t, J = 5.3 Hz, 2H), 2.57 (t, J = 5.4 Hz, 2H), 2.46 (q, J = 8.3 Hz, 4H), 2.33 – 2.27 (m, 6H), 1.65 – 1.53 (m, 10H), 1.50 – 1.43 (m, 4H), 1.34 – 1.22 (m, 38H),

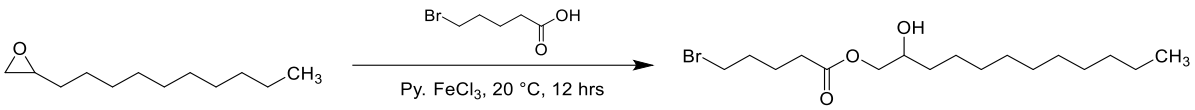
0.87 (t, J = 6.8 Hz, 9H).

MS (ES+) m/z): 712.6$(M+H)^+$.

Preparation Example 7: Preparation of Compound 27

Step 1: Synthesis of 2-hydroxydodecane 5-bromopentanoate

Reaction scheme:



Material ratio:

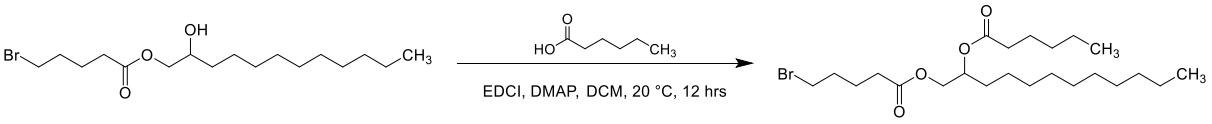
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1.0 eq	10.0 g	54.3 mmol
5-bromovaleric acid	181	1.025 eq	10.3 g	57.0 mmol
ferric chloride	162	0.025 eq	220 mg	1.36 mmol
pyridine	79	0.028 eq	110 mg	1.52 mmol

Procedure:

To the reaction flask, 1,2-epoxydodecane (10.0 g, 54.3 mmol), 5-bromovaleric acid (10.3 g, 57.0 mmol), ferric chloride (220 mg, 1.36 mmol), and pyridine (120 mg, 1.52 mmol) were added sequentially, and finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 2-hydroxydodecane 5-bromopentanoate as a colorless liquid was obtained (13.1 g, 66.1% yield).

Step 2: Synthesis of 1-((5-bromopentanoyl)oxy)dodecan-2-yl hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxydodecane 5-bromopentanoate	365	1.0 eq	5.0 g	13.7 mmol
n-hexanoic acid	116	1.3 eq	2.1 g	17.8 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	3.94 g	20.5 mmol
4-dimethylaminopyridine	122	1.1 eq	167 mg	1.4 mmol
dichloromethane	-	-	50 mL	-

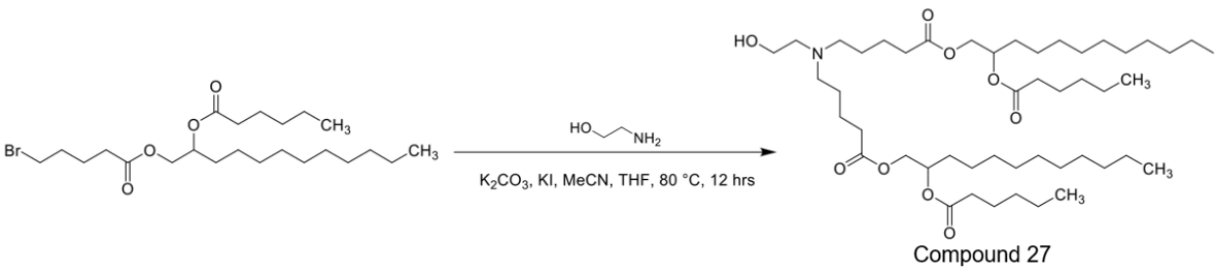
Procedure:

2-hydroxydodecane 5-bromopentanoate (5.00 g, 13.69 mmol) was dissolved in

dichloromethane (50 mL), and n-hexanoic acid (2.07 g, 17.8 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (3.94 g, 20.5 mmol), and 4-dimethylaminopyridine (167 mg, 1.37 mmol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-((5-bromopentanoyl)oxy)dodecan-2-yl hexanoate as a colorless liquid (4.00 g, 63.1% yield).

Step 3: Synthesis of 1-({5-[(5-{[2-(hexanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]pentanoyl}oxy) dodecan-2-yl hexanoate

Reaction scheme:



Compound 27

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-((5-bromopentanoyl)oxy)dodecan -2-yl hexanoate	462	1.0 eq	2.0 g	4.3 mmol
ethanolamine	61	0.46 eq	121 mg	2.0 mmol
potassium carbonate	138	3.5 eq	2.1 g	15.1 mmol
potassium iodide	166	1.2 eq	860 mg	5.2 mmol
acetonitrile	-	-	10 mL	-
tetrahydrofuran	-	-	10 mL	-

Procedure:

1-((5-bromopentanoyl)oxy)dodecan-2-yl hexanoate (2.00 g, 4.32 mmol) was dissolved in acetonitrile (10 mL), and ethanolamine (121 mg, 1.98 mmol), potassium carbonate (2.09 g, 15.1 mmol), potassium iodide (860 mg, 5.18 mmol), and tetrahydrofuran (10 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({5-[(5-{[2-(hexanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]pentanoyl}oxy) dodecan-2-yl hexanoate as a pale yellow liquid was obtained (700 mg, 19.6% yield).

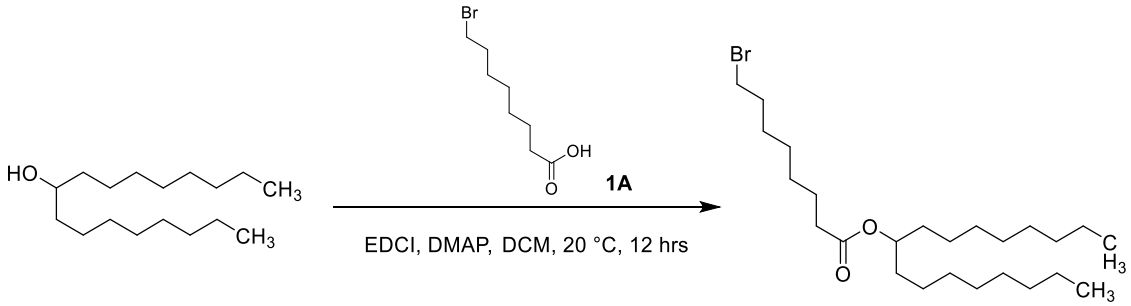
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.10 (dq, J1 = 3.2, J2 = 6.6 Hz, 2H), 4.26 (dd, J1 = 3.2, J2 = 11.8 Hz, 2H), 4.00 (dd, J1 = 7.0, J2 = 11.8 Hz, 2H), 3.85 - 3.77 (m, 1H), 3.71 (br d, J = 2.8 Hz, 2H), 3.58 - 3.52 (m, 1H), 3.38 (t, J = 5.6 Hz, 1H), 2.70 (br s, 5H), 2.42 (t, J = 6.2 Hz, 1H), 2.37 - 2.29 (m, 8H), 1.86 - 1.81 (m, 1H), 1.63 (br t, J = 7.0 Hz, 10H), 1.56 (br d, J = 5.8 Hz, 2H), 1.34 - 1.24 (m, 40H), 0.93 - 0.86 (m, 12H) ppm.

LCMS: RT = 1.985, m/z 826.6 $[M+H]^+$.

Preparation Example 8: Preparation of Compound 24

Step 1: Synthesis of heptadecan-9-yl 8-bromooctanoate

Reaction scheme:



Material ratio:

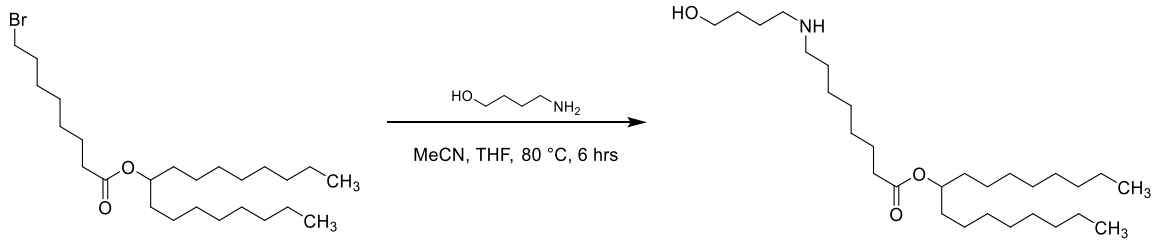
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-ol	256	1.0 eq	6.00 g	23.4 mmol
8-bromooctanoic acid	222	1.3 eq	6.79 g	30.4 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	6.73 g	35.1 mmol
4-dimethylaminopyridine	122	0.1 eq	286 mg	2.34 mmol
dichloromethane	-	-	60 mL	-

Procedure:

Heptadecan-9-ol (6.00 g, 23.4 mmol) was dissolved in dichloromethane (60 mL), and 8-bromooctanoic acid (6.79 g, 30.4 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (6.73 g, 35.1 mmol), and 4-dimethylaminopyridine (286 mg, 2.34 mmol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain heptadecan-9-yl 8-bromooctanoate as colorless (8.40 g, 77.8% yield).

Step 2: Synthesis of heptadecan-9-yl 8-((4-hydroxybutyl)amino)octanoate

Reaction scheme:



Material ratio:

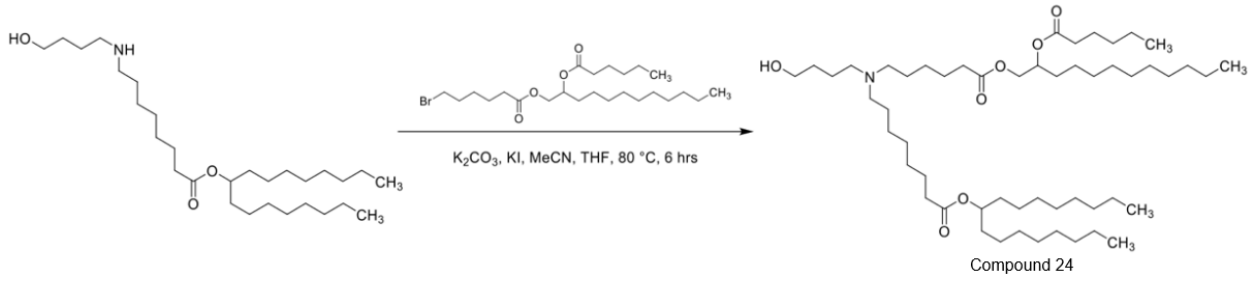
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-bromooctanoate	461	1.0 eq	1.00 g	2.17 mmol
4-amino-1-butanol	89	10 eq	1.93 g	21.7 mmol
acetonitrile	-	-	10 mL	-

Procedure:

Heptadecan-9-yl 8-bromooctanoate (1.00 g, 2.17 mmol) was dissolved in acetonitrile (10 mL), and then 4-amino-1-butanol (1.93 g, 21.7 mmol) was added. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated, washed with water, and extracted. The crude product was subjected to column chromatography to obtain heptadecan-9-yl 8-((4-hydroxybutyl)amino)octanoate as a colorless liquid (1.00 g, 98.3% yield).

Step 3: Synthesis of heptadecan-9-yl 8-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(4-hydroxybutyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-[(4-hydroxybutyl)amino] octanoate	469	1.0 eq	600 mg	1.28 mmol
2-(hexanoyloxy)dodecyl 6-bromohexanoate	477	1.3 eq	792 mg	1.66 mmol
potassium carbonate	138	3.5 eq	617 mg	4.47 mmol
potassium iodide	166	1.2 eq	254 mg	1.53 mmol
acetonitrile	-	-	6.00 mL	-
tetrahydrofuran	-	-	6.00 mL	-

Procedure:

Heptadecan-9-yl 8-[(4-hydroxybutyl)amino]octanoate (600 mg, 1.28 mmol) was dissolved in acetonitrile (6.00 mL), and 2-(hexanoyloxy)dodecyl 6-bromohexanoate (792 mg, 1.66 mmol), potassium carbonate (617 mg, 4.47 mmol), potassium iodide (254 mg, 1.53 mmol), and tetrahydrofuran (6.00 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(4-hydroxybutyl)amino]octanoate as a colorless liquid was obtained (500 mg, 43.3% yield).

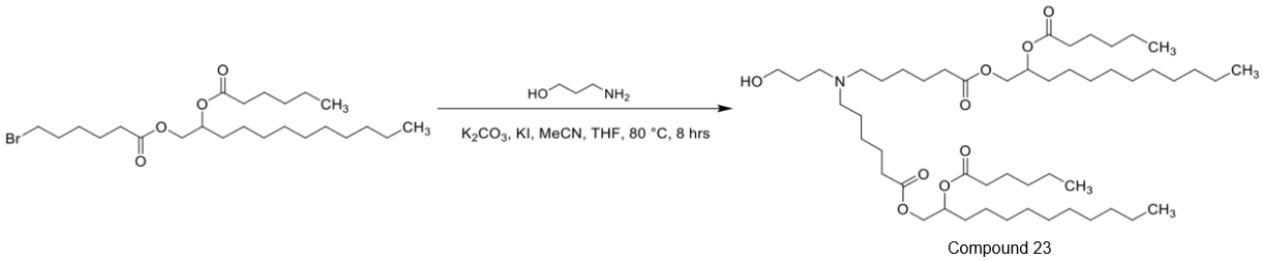
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 6.67 - 6.14 (m, 1H), 5.09 (dq, J_1 = 3.4, J_2 = 6.6 Hz, 1H), 4.87 (t, J = 6.2 Hz, 1H), 4.23 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 1H), 4.03 (dd, J_1 = 6.8, J_2 =11.8 Hz, 1H), 3.64 - 3.49 (m, 2H), 2.50 - 2.36 (m, 6H), 2.35 - 2.22 (m, 6H), 1.66 - 1.42 (m, 22H), 1.34 - 1.23 (m, 50H), 0.95 - 0.78 (m, 12H) ppm.

LCMS: RT = 2.124, m/z 866.7 $[M+H]^+$.

Preparation Example 9: Preparation of Compound 23

Step 1: Synthesis of 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(3-hydroxypropyl)amino]hexanoate

Reaction scheme:



Compound 23

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(hexanoyloxy)dodecyl 6-bromohexanoate	476	1.0 eq	2.00 g	4.19 mmol
3-aminopropanol	75	0.45 eq	142 mg	1.88 mmol
potassium carbonate	138	3.5 eq	2.03 g	14.7 mmol
potassium iodide	166	1.2 eq	834 mg	5.03 mmol
tetrahydrofuran	-	-	10 mL	-
acetonitrile	-	-	10 mL	-

Procedure:

2-(hexanoyloxy)dodecyl 6-bromohexanoate (2.00 g, 4.19 mmol) was dissolved in acetonitrile (10 mL), and then 3-aminopropanol (142 mg, 1.88 mmol), potassium carbonate (2.03 g, 14.7 mmol), potassium iodide (834 mg, 5.03 mmol), and tetrahydrofuran (10 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 8 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(3-hydroxypropyl)amino]hexanoate as a pale yellow liquid was obtained (800 mg, 22.0% yield).

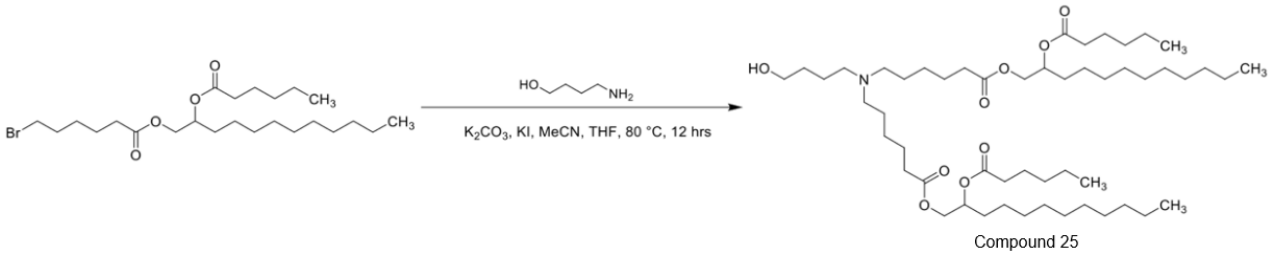
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.13 - 5.05 (m, 2H), 4.23 (dd, J_1 = 2.8, J_2 = 11.8 Hz, 2H), 4.03 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 2H), 3.79 (br t, J = 4.8 Hz, 2H), 2.67 (br s, 2H), 2.51 - 2.40 (m, 4H), 2.31 (dt, J_1 = 3.6, J_2 = 7.2 Hz, 8H), 1.72 - 1.47 (m, 20H), 1.35 - 1.25 (m, 42H), 0.89 (q, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 5.629, m/z 868.5 $[M+H]^+$.

Preparation Example 10: Preparation of Compound 25

Step 1: Synthesis of 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(4-hydroxybutyl)amino]hexanoate

Reaction scheme:



Compound 25

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(hexanoyloxy)dodecyl 6-bromohexanoate	476	1.0 eq	2.00 g	4.19 mmol
4-aminobutanol	89	0.45 eq	168 mg	1.88 mmol
potassium carbonate	138	3.5 eq	2.03 g	14.7 mmol
potassium iodide	166	1.2 eq	834 mg	5.03 mmol
tetrahydrofuran	-	-	10 mL	-
acetonitrile	-	-	10 mL	-

Procedure:

2-(hexanoyloxy)dodecyl 6-bromohexanoate (2.00 g, 4.19 mmol) was dissolved in acetonitrile (10 mL), and 4-aminobutanol (168 mg, 1.88 mmol), potassium carbonate (2.03 g,

14.7 mmol), potassium iodide (834 mg, 5.03 mmol), and tetrahydrofuran (10 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(4-hydroxybutyl)amino]hexanoate as a pale yellow liquid was obtained (800 mg, 21.7% yield).

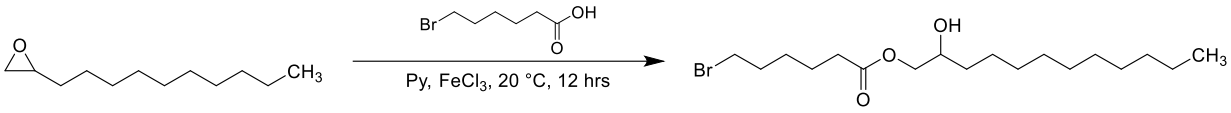
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.14 - 5.04 (m, 2H), 4.23 (dd, J_1 = 3.2, J_2 = 11.8 Hz, 2H), 4.02 (dd J_1 = 6.8, J_2 = 11.8 Hz, 2H), 3.58 (br s, 2H), 2.54 (br s, 6H), 2.31 (dt, J_1 = 4.2, J_2 = 7.2 Hz, 8H), 1.73 - 1.52 (m, 20H), 1.36 - 1.23 (m, 44H), 0.89 (q, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 5.781, m/z 882.5 $[M+H]^+$

Preparation Example 11: Preparation of Compound 26

Step 1: Synthesis of 2-hydroxydodecane 6-bromohexanoate

Reaction scheme:



Material ratio:

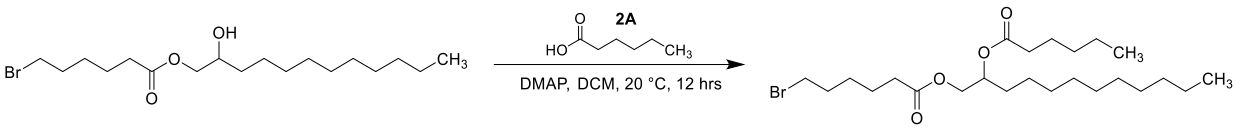
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1.0 eq	10.0 g	54.3 mmol
6-bromohexanoic acid	181	1.1 eq	11.6 g	59.7 mmol
ferric chloride	162	0.025 eq	220 mg	1.36 mmol
pyridine	79	0.028 eq	120 mg	1.52 mmol

Procedure:

To the reaction flask, 1,2-epoxydodecane (10.0 g, 54.3 mmol), 6-bromohexanoic acid (11.6 g, 59.7 mmol), ferric chloride (220 mg, 1.36 mmol), and pyridine (120 mg, 1.52 mmol) were added sequentially, and finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, the reaction mixture was concentrated to remove pyridine, and after purification by column chromatography, 2-hydroxydodecyl 6-bromohexanoate as a colorless liquid was obtained (14.5 g, 70.5% yield).

Step 2: Synthesis of 2-(hexanoyloxy)dodecane 6-bromohexanoate

Reaction scheme:



Material ratio:

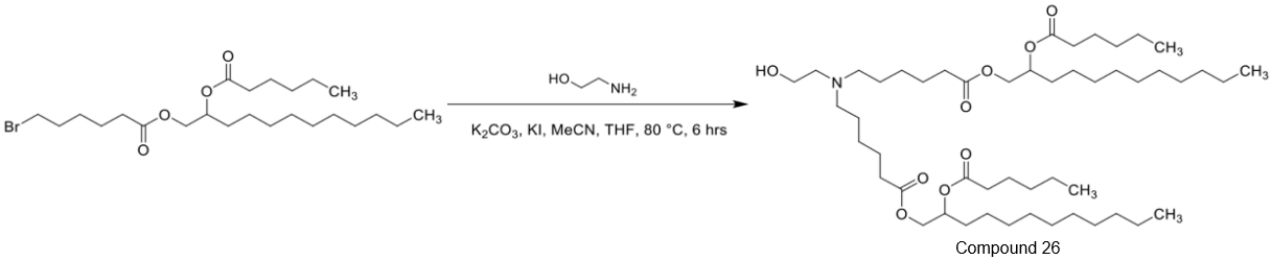
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxydodecane 6-bromohexanoate	378	1.0 eq	11.0 g	29.0 mmol
n-hexanoic acid	116	1.3 eq	4.38 g	37.7 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	8.34 g	43.5 mmol
4-dimethylaminopyridine	122	0.1 eq	354 mg	2.90 mmol
dichloromethane	-	-	100 mL	-

Procedure:

2-hydroxydodecane 6-bromohexanoate (11 g, 29.0 mmol) was dissolved in dichloromethane (100 mL), and n-hexanoic acid (4.38 g, 37.7 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (8.34 g, 43.5 mmol), and 4-dimethylaminopyridine (354 mg, 2.90 mmol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(hexanoyloxy)dodecane 6-bromohexanoate as a colorless liquid (12.5 g, 90.3% yield).

Step 3: Synthesis of 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(hexanoyloxy)dodecyl 6-bromohexanoate	476	2.1 eq	2.50 g	5.24 mmol
ethanolamine	61	1.0 eq	150 mg	2.46 mmol
potassium carbonate	138	3.5 eq	1.19 g	8.59 mmol
potassium iodide	166	1.2 eq	938 mg	5.65 mmol
tetrahydrofuran	-	-	10 mL	-
acetonitrile	-	-	10 mL	-

Procedure:

2-(hexanoyloxy)dodecyl 6-bromohexanoate (2.50 g, 5.24 mmol) was dissolved in acetonitrile (10 mL), and ethanolamine (150 mg, 2.46 mmol), potassium carbonate (1.19 g, 8.59 mmol), potassium iodide (938 mg, 5.65 mmol), and tetrahydrofuran (10 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 6 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(hexanoyloxy)dodecyl 6-[(6-{[2-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate as a pale yellow liquid was obtained (1.10 g, 52.4% yield).

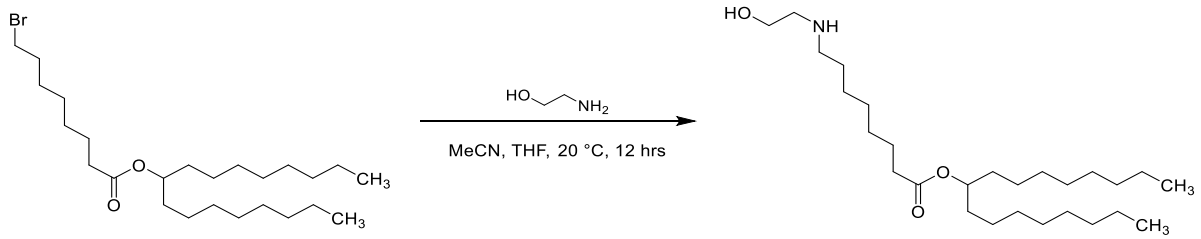
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (br dd, J_1 = 3.0, J_2 = 6.3 Hz, 2H), 4.24 (dd, J_1 = 3.2, J_2 = 11.8 Hz, 2H), 4.02 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 2H), 3.62 (br s, 2H), 2.69 (br s, 2H), 2.58 (br s, 4H), 2.31 (dt, J_1 = 3.8, J_2 = 7.4 Hz, 8H), 1.68 - 1.52 (m, 16H), 1.36 - 1.24 (m, 44H), 0.89 (q, J = 7.0 Hz, 12H) ppm.

LCMS: RT = 2.013, m/z 854.6 $[M+H]^+$

Preparation Example 12: Preparation of Compound 28

Step 1: Synthesis of heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate

Reaction scheme:



Material ratio:

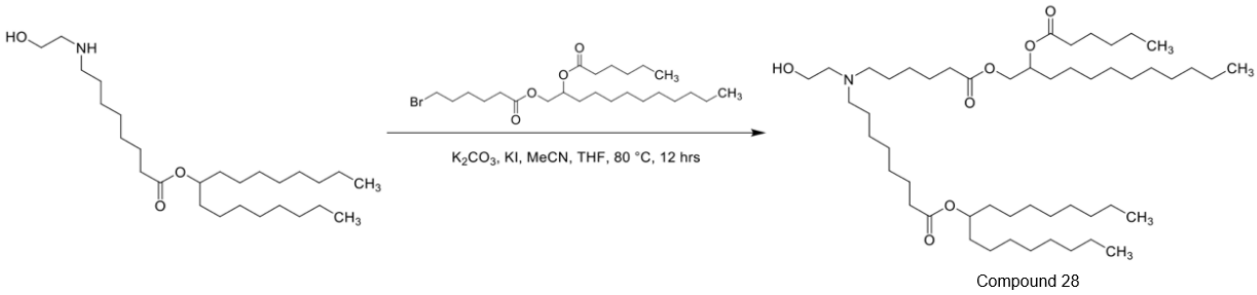
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-bromooctanoate	460	1.0 eq	6.00 g	13.0 mmol
ethanolamine	61	10 eq	7.94 g	130 mmol
acetonitrile	-	-	60 mL	-
tetrahydrofuran	-	-	20 mL	-

Procedure:

Heptadecan-9-yl 8-bromooctanoate (6.00 g, 13.0 mmol) was dissolved in acetonitrile (60 mL), and then ethanolamine (7.94 g, 130 mmol) and tetrahydrofuran (20 mL) were added. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated, washed with water, and extracted. The crude product was subjected to column chromatography to obtain heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate as a colorless liquid (3.40 g, 59.2% yield).

Step 2: Synthesis of heptadecan-9-yl 8-((6-((2-(hexanoyloxy)dodecyl)oxy)-6-oxohexyl)(2-hydroxyethyl)amino)octanoate

Reaction scheme:



Compound 28

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate	441	1.0 eq	1.50 g	3.40 mmol
2-(hexanoyloxy)dodecane 6-bromohexanoate	476	1.1 eq	1.78 g	3.74 mmol
potassium carbonate	138	3.5 eq	1.64 g	11.9 mmol
potassium iodide	166	1.2 eq	676 mg	4.07 mmol
tetrahydrofuran	-	-	8 mL	-
acetonitrile	-	-	8 mL	-

Procedure:

Heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate (1.50 g, 3.40 mmol) was dissolved in acetonitrile (8 mL), and then 2-(hexanoyloxy)dodecane 6-bromohexanoate (1.78 g, 3.74 mmol), potassium carbonate (1.64 g, 11.9 mmol), potassium iodide (676 mg, 4.07 mmol), and

tetrahydrofuran (8 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-((6-((2-(hexanoyloxy)dodecyl)oxy)-6-oxohexyl)(2-hydroxyethyl)amino)octanoate as a pale yellow liquid was obtained (1.22 g, 42.8% yield).

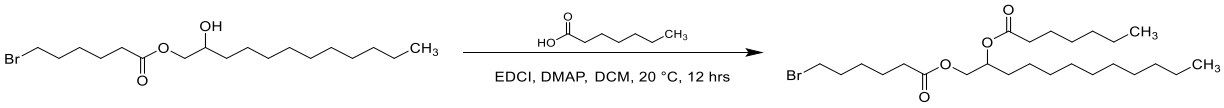
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (dq, J_1 = 3.4, J_2 = 6.6 Hz, 1H), 4.87 (quin, J = 6.2 Hz, 1H), 4.23 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 1H), 4.03 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 1H), 3.52 (t, J = 5.2 Hz, 2H), 3.21 - 2.75 (m, 1H), 2.57 (t, J = 5.2 Hz, 2H), 2.48 - 2.39 (m, 4H), 2.36 - 2.24 (m, 6H), 1.68 - 1.55 (m, 8H), 1.54 - 1.42 (m, 8H), 1.35 - 1.22 (m, 52H), 1.00 - 0.79 (m, 12H) ppm.

LCMS: RT = 5.920, m/z 838.6 $[M+H]^+$.

Preparation Example 13: Preparation of Compound 34

Step 1: Synthesis of 1-((6-bromohexanoyl)oxy)dodecan-2-yl heptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxydodecane 6-bromohexanoate	378	1.0 eq	3.50 g	9.23 mmol
n-heptanoic acid	130	1.3 eq	1.56 g	12.0 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	2.65 g	13.8 mmol
4-dimethylaminopyridine	122	0.1 eq	113 mg	923 umol
dichloromethane	-	-	35 mL	-

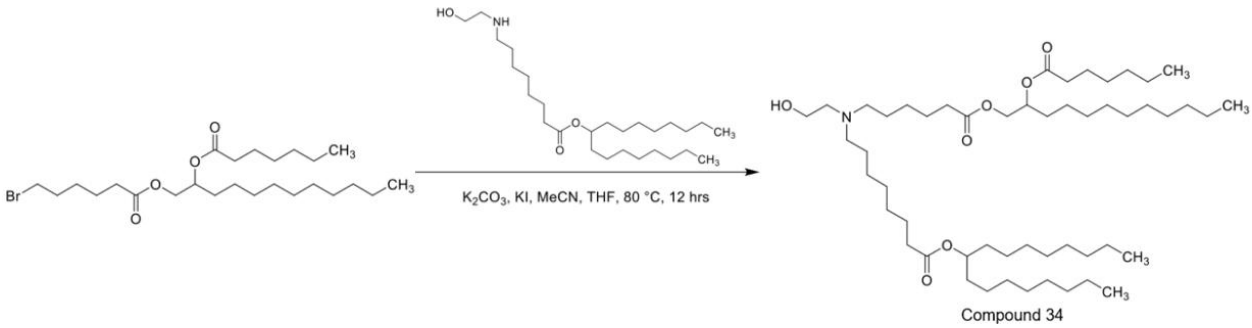
Procedure:

2-hydroxydodecane 6-bromohexanoate (3.50 g, 9.23 mmol) was dissolved in dichloromethane (35 mL), and n-heptanoic acid (1.56 g, 12.0 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.65 g, 13.8 mmol), and 4-dimethylaminopyridine (113 mg, 923 umol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated, washed with water, and extracted. The crude product was subjected to column chromatography to obtain

1-((6-bromohexanoyl)oxy)dodecan-2-yl heptanoate as a colorless liquid (3.60 g, 79.4% yield).

Step 2: Synthesis of heptadecan-9-yl 8-((6-((2-(heptanoyloxy)dodecyl)oxy)-6-oxohexyl)(2-hydroxyethyl)amino)octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-((6-bromohexanoyl)oxy)dodecan-2-yl heptanoate	441	1.0 eq	1.50 g	3.40 mmol
heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate	490	1.1 eq	1.84 g	3.74 mmol
potassium carbonate	138	3.5 eq	1.64 g	11.9 mmol
potassium iodide	166	1.2 eq	676 mg	4.07 mmol
acetonitrile	-	-	8 mL	-
tetrahydrofuran	-	-	8 mL	-

Procedure:

1-((6-bromohexanoyl)oxy)dodecan-2-yl heptanoate (1.50 g, 3.40 mmol) was dissolved in acetonitrile (8 mL), and heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate (1.84 g, 3.74 mmol), potassium carbonate (1.64 g, 11.9 mmol), potassium iodide (676 mg, 4.07 mmol), and tetrahydrofuran (8 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-((6-((2-(heptanoyloxy)dodecyl)oxy)-6-oxohexyl)(2-hydroxyethyl)amino)octanoate as a pale yellow liquid was obtained (900 mg, 31.1% yield).

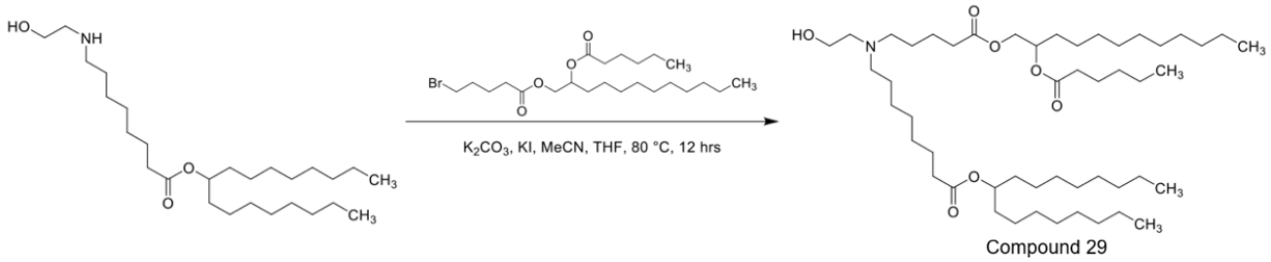
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.13 - 5.05 (m, 1H), 4.86 (quin, J = 6.2 Hz, 1H), 4.23 (dd, J_1 = 3.2, J_2 = 11.8 Hz, 1H), 4.02 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 1H), 3.56 (br t, J = 5.2 Hz, 2H), 2.61 (br t, J = 5.0 Hz, 2H), 2.53 - 2.44 (m, 4H), 2.35 - 2.25 (m, 6H), 1.66 - 1.45 (m, 16H), 1.36 - 1.23 (m, 54H), 0.97 - 0.79 (m, 12H) ppm.

LCMS: RT = 7.550, m/z 852.6 $[M+H]^+$.

Preparation Example 14: Preparation of Compound 29

Step 1: Synthesis of heptadecan-9-yl 8-((5-((2-(hexanoyloxy)dodecyl)oxy)-5-oxopentyl)(2-hydroxyethyl)amino)octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate	441	1.0 eq	1.50 g	3.40 mmol
1-((5-bromopentanoyl)oxy)dodecan-2-yl hexanoate	462	1.1 eq	1.73 g	3.74 mmol
potassium carbonate	138	3.5 eq	1.68 g	11.9 mmol
potassium iodide	166	1.2 eq	676 mg	4.07mmol
tetrahydrofuran	-	-	8 mL	-
acetonitrile	-	-	8 mL	-

Procedure:

Heptadecan-9-yl 8-((2-hydroxyethyl)amino)octanoate (1.50 g, 3.40 mmol) was dissolved in acetonitrile (8 mL), and then 1-((5-bromopentanoyl)oxy)dodecan-2-yl hexanoate (1.73 g, 3.74 mmol), potassium carbonate (1.68 g, 11.9 mmol), potassium iodide (676 mg, 4.07 mmol), and tetrahydrofuran (8 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-((5-((2-(hexanoyloxy)dodecyl)oxy)-5-oxopentyl)(2-hydroxyethyl)amino)octanoate as a pale yellow liquid was obtained (1.66 g, 59.3% yield).

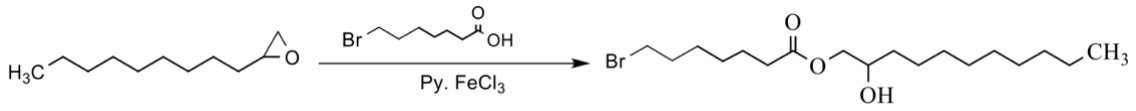
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.10 (dq, J_1 = 3.2, J_2 = 6.6 Hz, 1H), 4.87 (t, J = 6.2 Hz, 1H), 4.25 (dd, J_1 = 3.2, J_2 = 11.8 Hz, 1H), 4.02 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 1H), 3.59 (br t, J = 4.8 Hz, 2H), 2.65 (br s, 2H), 2.57 - 2.48 (m, 4H), 2.36 - 2.26 (m, 6H), 1.68 - 1.44 (m, 18H), 1.34 - 1.25 (m, 48H), 0.93 - 0.85 (m, 12H) ppm.

LCMS: RT = 2.184, m/z 824.7 $[M+H]^+$.

Preparation Example 15: Preparation of Compound 4

Step 1: Synthesis of 2-hydroxyundecyl 7-bromoheptanoate

Reaction scheme:



Material ratio:

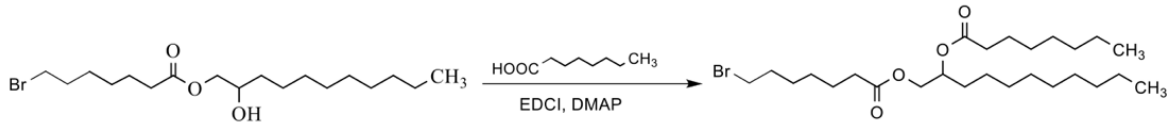
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-nonyloxirane	170	1.0 eq	4.00 g	23.4 mmol
7-bromoheptanoic acid	208	1.05 eq	5.16 g	24.6 mmol
ferric chloride	162	0.025 eq	95.2 mg	0.587 mmol
pyridine	79	0.025 eq	46.4 mg	0.587 mmol

Procedure:

To the reaction flask, 2-nonyloxirane (4.00 g, 23.4 mmol), 7-bromoheptanoic acid (5.16 g, 24.6 mmol), ferric chloride (95.2 mg, 587 μmol), and pyridine (46.4 mg, 587 μmol) were added sequentially, and finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 2-hydroxyundecyl 7-bromoheptanoate as a colorless liquid was obtained (6.30 g, 70.3% yield).

Step 2: Synthesis of 1-[(7-bromoheptanoyl)oxy]undecan-2-yl octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxyundecyl 7-bromoheptanoate	378	1.0 eq	3.00 g	7.91 mmol
n-octanoic acid	144	1.2 eq	1.37 g	9.49 mmol
1-(3-dimethylaminopropyl)-3 -ethylcarbodiimide hydrochloride	192	1.5 eq	2.27 g	11.8 mmol
4-dimethylaminopyridine	122	0.1 eq	96.6 mg	0.79 mmol
dichloromethane	-	-	30.0 mL	-

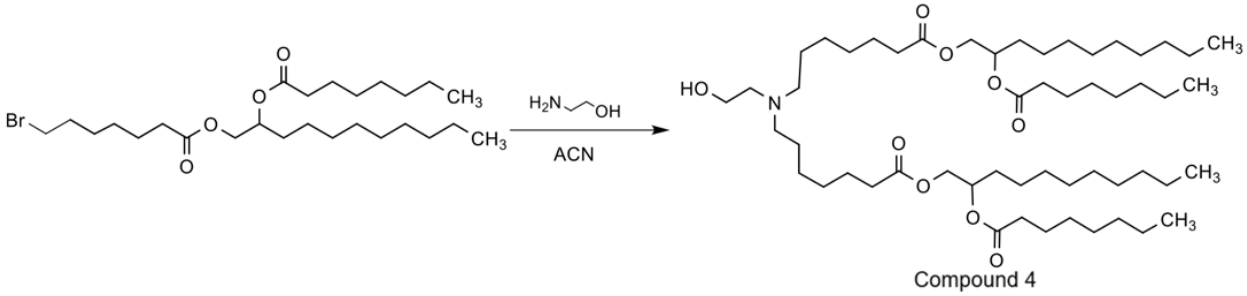
Procedure:

2-hydroxyundecyl 7-bromoheptanoate (3.00 g, 7.91 mmol) was dissolved in dichloromethane (3.00 mL), and n-octanoic acid (1.37 g, 9.49 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.27 g, 11.8 mmol), and

4-dimethylaminopyridine (96.6 mg, 790 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(7-bromoheptanoyl)oxy]undecan-2-yl octanoate as a colorless liquid (2.95 g, 73.7% yield).

Step 3: Synthesis of 1-({7-[(2-hydroxyethyl)(7-{[2-(octanoyloxy)undecyl]oxy}-7-oxoheptyl)amino]heptanoyl}oxy)undecan-2-yl octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(7-bromoheptanoyl)oxy] undecan-2-yl octanoate	504	1.0 eq	1.30 g	2.57 mmol
ethanolamine	61	0.45 eq	70.6 mg	1.16 mmol
potassium carbonate	138	3.5 eq	1.24 g	9.00 mmol
potassium iodide	166	1.2 eq	512 mg	3.09 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	3.00 mL	-

Procedure:

1-[(7-bromoheptanoyl)oxy]undecan-2-yl octanoate (1.30 g, 2.57 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (70.6 mg, 1.16 mmol), potassium carbonate (1.24 g, 9.00 mmol), potassium iodide (512 mg, 3.09 mmol), and tetrahydrofuran (3.00 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({7-[(2-hydroxyethyl)(7-{[2-(octanoyloxy)undecyl]oxy}-7-oxoheptyl)amino]heptanoyl}oxy)undecan-2-yl octanoate as a colorless liquid was obtained (546 mg, 21.8% yield).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (dq, J_1 = 3.4, J_2 = 6.6 Hz, 2H), 4.22 (dd,

J_1 = 3.4, J_2 = 11.8 Hz, 2H), 4.03 (dd, J_1 = 6.8, J_2 = 11.8 Hz, 2H), 3.56 (t, J = 5.4 Hz, 2H), 2.62 (br t, J = 5.2 Hz, 2H), 2.55 - 2.42 (m, 4H), 2.30 (t, J = 7.6 Hz, 8H), 1.70 - 1.54 (m, 12H), 1.47 (td, J = 7.4, 14.2 Hz, 4H), 1.35 - 1.18 (m, 52H), 0.95 - 0.77 (m, 12H) ppm.

LCMS: RT = 2.130, m/z 910.6 $[M+H]^+$.

Preparation Example 16: Preparation of Compound 1

Step 1: Synthesis of 2-nonyloxirane

Reaction scheme:



Material ratio:

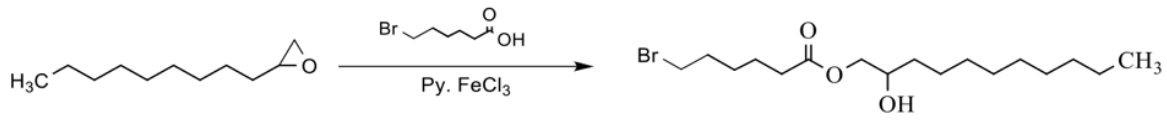
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
undec-1-ene	154	1.00 eq	10.0 g	64.8 mmol
3-chloroperoxybenzoic acid	172	1.20 eq	15.7 g	77.7 mmol
dichloromethane	-	-	140 mL	-

Procedure:

To the reaction flask, undec-1-ene (10.0 g, 64.8 mmol) and dichloromethane (140 mL) were added sequentially. 3-chloroperoxybenzoic acid (15.7 g, 77.7 mmol) was slowly added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction mixture was quenched and extracted; after purification by column chromatography, 2-nonyloxirane as a colorless liquid was obtained (11.0 g, 99.6% yield).

Step 2: Synthesis of 2-hydroxyundecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-nonyloxirane	170	1.00 eq	4.00 g	23.4 mmol
6-bromohexanoic acid	193	1.05 eq	4.81 g	24.6 mmol
ferric chloride	162	0.025 eq	95.2 mg	0.587 mmol
pyridine	79	0.025 eq	46.4 mg	0.587 mmol

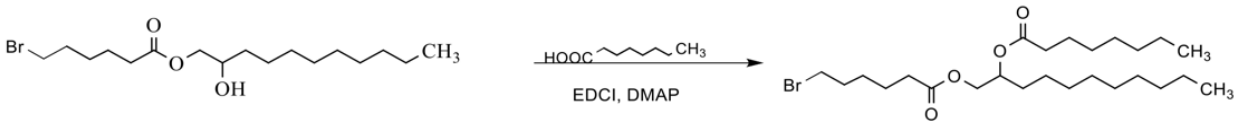
Procedure:

To the reaction flask, 2-nonyloxirane (4.00 g, 23.4 mmol), 6-bromohexanoic acid (4.81 g,

24.6 mmol), ferric chloride (95.2 mg, 587 μmol), and pyridine (46.4 mg, 587 μmol) were added sequentially, and finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 2-hydroxyundecyl 6-bromohexanoate as a colorless liquid was obtained (6.50 g, 75.5% yield).

Step 3: Synthesis of 1-[(6-bromohexanoyl)oxy]undecan-2-yl octanoate

Reaction scheme:



Material ratio:

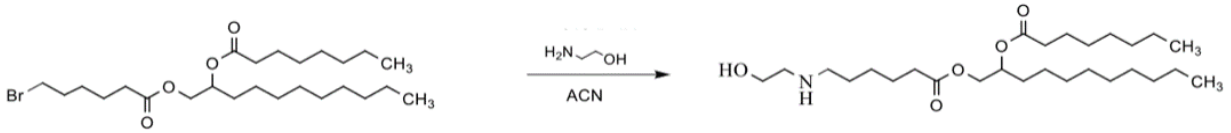
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxyundecyl 6-bromohexanoate	364	1.00 eq	3.00 g	8.21 mmol
n-octanoic acid	144	1.20 eq	1.42 g	9.85 mmol
1-(3-dimethylaminopropyl)-3 -ethylcarbodiimide hydrochloride	192	1.50 eq	2.36 g	12.3 mmol
4-dimethylaminopyridine	122	0.10 eq	100 mg	0.821 mmol
dichloromethane	-	-	30.0 mL	-

Procedure:

2-hydroxyundecyl 6-bromohexanoate (3.00 g, 8.21 mmol) was dissolved in dichloromethane (30.0 mL), and n-octanoic acid (1.42 g, 9.85 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.36 g, 12.3 mmol), and 4-dimethylaminopyridine (100 mg, 821 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(6-bromohexanoyl)oxy]undecan-2-yl octanoate as a colorless liquid (2.74 g, 67.8% yield).

Step 4: Synthesis of 1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy)undecan-2-yl octanoate

Reaction scheme:



Material ratio:

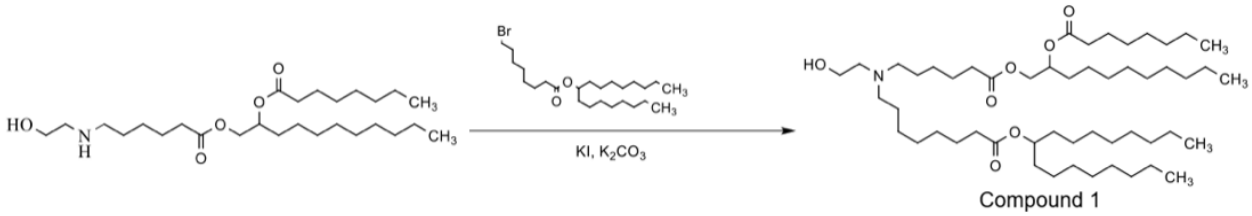
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy] undecan-2-yl octanoate	490	1.00 eq	1.00 g	2.03 mmol
ethanolamine	61	10.0 eq	1.24 g	20.3 mmol
acetonitrile	-	-	22.0 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]undecan-2-yl octanoate (1.00 g, 2.03 mmol) was dissolved in acetonitrile (22.0 mL), and ethanolamine (1.24 g, 20.3 mmol) was added sequentially. Finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy)undecan-2-yl octanoate as a colorless liquid was obtained (840 mg, 93.0% yield).

Step 5: Synthesis of heptadecan-9-yl 8-[(2-hydroxyethyl)(6-{[2-(octanoyloxy)undecyl]oxy}-6-oxohexyl)amino]octanoate

Reaction scheme:



Compound 1

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy) undecan-2-yl octanoate	471	1.00 eq	740 mg	1.57 mmol
heptadecan-9-yl 8-bromooctanoate	460	1.20 eq	868 mg	1.88 mmol
potassium carbonate	138	3.5 eq	758 mg	5.49 mmol
potassium iodide	166	1.2 eq	312 mg	1.88 mmol
acetonitrile	-	-	7.00 mL	-
tetrahydrofuran	-	-	7.00 mL	-

Procedure:

2-(octyloxy)undecyl 5-[(2-hydroxyethyl)amino]pentanoate (740 mg, 1.57 mmol) was dissolved in acetonitrile (7.00 mL), and heptadecan-9-yl 8-bromooctanoate (868 mg, 1.88 mmol), potassium carbonate (758 mg, 5.49 mmol), potassium iodide (312 mg, 1.88 mmol), and tetrahydrofuran (7.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the

mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(2-hydroxyethyl)(6-{[2-(octanoyloxy)undecyl]oxy}-6-oxohexyl)amino]octanoate as a colorless liquid was obtained (700 mg, 19.6% yield).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.16 - 5.01 (m, 1H), 4.87 (t, J = 6.2 Hz, 1H), 4.23 (dd, J_1 = 3.4, J_2 =11.8 Hz, 1H), 4.02 (dd, J_1 = 6.8, J_2 =11.8 Hz, 1H), 3.58 (t, J = 5.2 Hz, 2H), 2.63 (br t, J = 5.2 Hz, 2H), 2.57 - 2.43 (m, 4H), 2.34 - 2.23 (m, 6H), 1.65 - 1.42 (m, 16H), 1.34 - 1.16 (m, 54H), 0.88 (t, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 2.187, m/z 852.7 $[M+H]^+$.

Preparation Example 17: Preparation of Compound 7

Step 1: Synthesis of 2-heptyloxirane

Reaction scheme:



Material ratio:

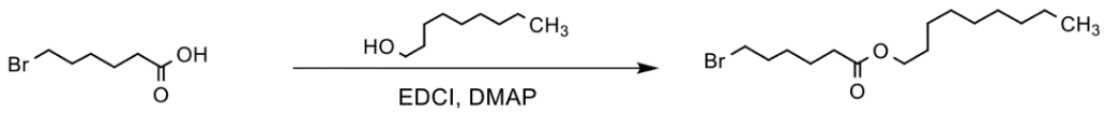
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
non-1-ene	126	1.00 eq	4.00 g	31.6 mmol
3-chloroperoxybenzoic acid	172	1.20 eq	7.72 g	38.0 mmol
dichloromethane			51.0 mL	

Procedure:

To the reaction flask, undec-1-ene (4.00 g, 31.6 mmol) and dichloromethane (51.0 mL) were added sequentially. 3-chloroperoxybenzoic acid (7.72 g, 38.0 mmol) was slowly added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction mixture was quenched and extracted; after purification by column chromatography, 2-heptyloxirane was obtained as a colorless liquid (3.95 g, 87.6% yield).

Step 2: Synthesis of nonyl 6-bromohexanoate

Reaction scheme:



Material ratio:

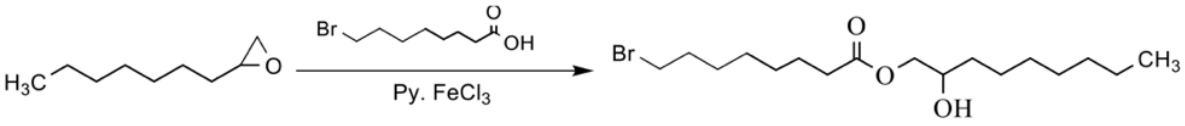
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-bromohexanoic acid	193	1.20 eq	6.49 g	33.2 mmol
nonan-1-ol	144	1.00 eq	4.00 g	27.7 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.50 eq	7.97 g	41.5 mmol
4-dimethylaminopyridine	122	0.10 eq	338 mg	2.77 mmol
dichloromethane	-	-	30.0 mL	-

Procedure:

Nonan-1-ol (4 g, 27.7 mmol) was dissolved in dichloromethane (40.0 mL), and 6-bromohexanoic acid (6.49 g, 33.2 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.97 g, 41.5 mmol), and 4-dimethylaminopyridine (338 mg, 2.77 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain nonyl 6-bromohexanoate as a colorless liquid (8.50 g, 95.4% yield).

Step 3: Synthesis of 2-hydroxynonyl 8-bromooctanoate

Reaction scheme:



Material ratio:

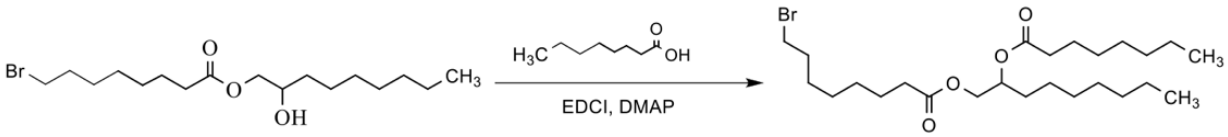
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-heptyloxirane	142	1.00 eq	3.34 g	23.4 mmol
8-bromooctanoic acid	222	1.05 eq	5.50 g	24.6 mmol
ferric chloride	162	0.025 eq	95.2 mg	0.587 mmol
pyridine	79	0.028 eq	52.0 mg	0.657 mmol

Procedure:

To the reaction flask, 2-heptyloxirane (3.34 g, 23.4 mmol), 8-bromooctanoic acid (5.50 g, 24.6 mmol), ferric chloride (95.2 mg, 587 μmol), and pyridine (52.0 mg, 657 μmol) were added sequentially, and finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 2-hydroxynonyl 8-bromooctanoate as a colorless liquid was obtained (6.50 g, 75.7% yield).

Step 4: Synthesis of 2-(octanoyloxy)nonyl 8-bromooctanoate

Reaction scheme:



Material ratio:

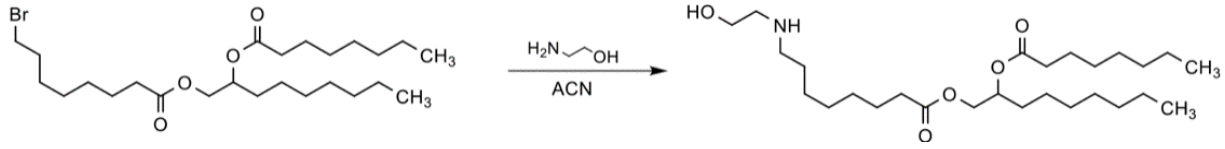
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxynonyl 8-bromooctanoate	364	1.00 eq	3.00 g	8.21 mmol
n-octanoic acid	144	1.20 eq	1.42 g	9.85 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.50 eq	2.36 g	12.3 mmol
4-dimethylaminopyridine	122	0.10 eq	100 mg	0.821 mmol
dichloromethane	-	-	30.0 mL	-

Procedure:

2-hydroxynonyl 8-bromooctanoate (3.00 g, 8.21 mmol) was dissolved in dichloromethane (30.0 mL), and n-octanoic acid (1.42 g, 9.85 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.36 g, 12.3 mmol), and 4-dimethylaminopyridine (100 mg, 821 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(octanoyloxy)nonyl 8-bromooctanoate as a colorless liquid (3.00 g, 74.3% yield).

Step 5: Synthesis of 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(octanoyloxy)nonyl 8-bromooctanoate	490	1.00 eq	1.20 g	2.44 mmol
ethanolamine	61	10.0 eq	1.49 g	24.4 mmol
acetonitrile	-	-	22.0 mL	-

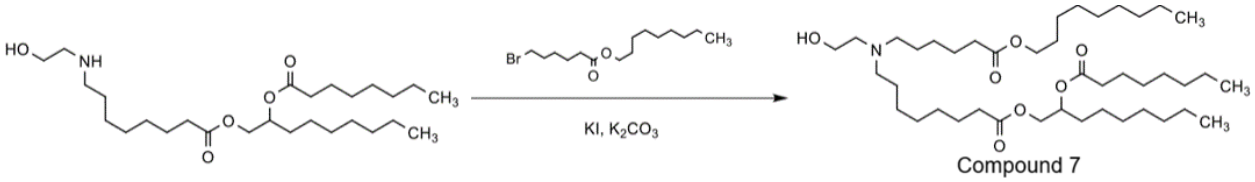
Procedure:

2-(octanoyloxy)nonyl 8-bromooctanoate (1.20 g, 2.44 mmol) was dissolved in acetonitrile (22.0 mL), and ethanolamine (1.49 g, 24.4 mmol) was added sequentially. Finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction

was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)amino]octanoate as a colorless liquid was obtained (800 mg, 69.4% yield).

Step 6: Synthesis of 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)[6-(nonyloxy)-6-oxohexyl]amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)amino]octanoate	471	1.00 eq	700 mg	1.48 mmol
nonyl 6-bromohexanoate	460	1.20 eq	572 mg	1.78 mmol
potassium carbonate	138	3.5 eq	717 mg	5.19 mmol
potassium iodide	166	1.2 eq	295 mg	1.78 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	10.0 mL	-

Procedure:

2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)amino]octanoate (700 mg, 1.48 mmol) was dissolved in acetonitrile (10.0 mL), and nonyl 6-bromohexanoate (572 mg, 1.78 mmol), potassium carbonate (717 mg, 5.19 mmol), potassium iodide (295 mg, 1.78 mmol), and tetrahydrofuran (10.0 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)[6-(nonyloxy)-6-oxohexyl]amino]octanoate as a colorless liquid was obtained (780 mg, 69.2% yield).

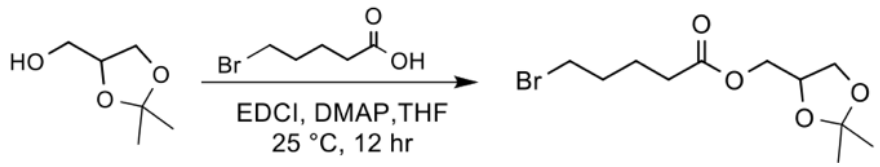
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.19 - 5.01 (m, 1H), 4.22 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 1H), 4.10 - 3.99 (m, 3H), 3.63 (br s, 2H), 2.70 (br s, 2H), 2.58 (br s, 4H), 2.31 (dt, J_1 = 2.4, J_2 = 7.4 Hz, 6H), 1.72 - 1.51 (m, 14H), 1.37 - 1.18 (m, 38H), 0.97 - 0.75 (m, 9H) ppm.

LCMS: RT = 1.810, m/z 712.5 $[M+H]^+$.

Preparation Example 18: Preparation of Compound 21

Step 1: Synthesis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl 5-bromopentanoate

Reaction scheme:



Material ratio:

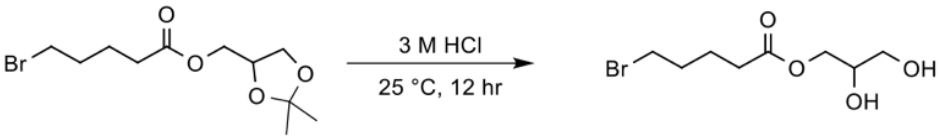
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2,2-dimethyl-1,3-dioxolan-4-yl)methanol	132	1.0 eq	3.32 g	25.1 mmol
5-bromovaleric acid	179	1.1 eq	5.00 g	27.6 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	7.22 g	37.7mmol
4-dimethylaminopyridine	122	0.1 eq	306 mg	2.5 mmol
tetrahydrofuran	-	-	35 mL	-

Procedure:

(2,2-dimethyl-1,3-dioxolan-4-yl)methanol (3.32 g, 25.1 mmol) and 5-bromovaleric acid (5.00 g, 27.6 mmol) were dissolved in tetrahydrofuran (35 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.22 g, 37.7 mmol) and 4-dimethylaminopyridine (306 mg, 2.51 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. 50 mL of water was added, and the mixture was extracted twice with dichloromethane, 50 mL each time. The organic phase was concentrated, and after purification by column chromatography, (2,2-dimethyl-1,3-dioxolan-4-yl)methyl 5-bromopentanoate as a bright yellow liquid was obtained (6.31 g, 85.1% yield).

Step 2: Synthesis of 2,3-dihydroxypropyl 5-bromopentanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2,2-dimethyl-1,3-dioxolan-4-yl) methyl 5-bromopentanoate	294	1.0 eq	5.80 g	19.7 mmol
3 M hydrochloric acid	35.9	0.88 eq	634 mg	17.4 mmol
tetrahydrofuran	-	-	58 mL	-

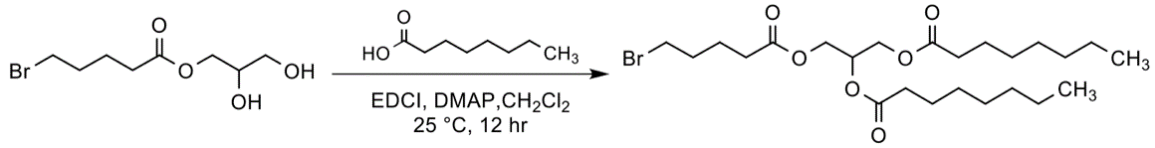
Procedure:

(2,2-dimethyl-1,3-dioxolan-4-yl)methyl 5-bromopentanoate (5.80 g, 19.7 mmol) was dissolved in tetrahydrofuran (58 mL), and hydrochloric acid (5.80 mL, 17.4 mmol) was added.

The mixture was reacted at 25 ℃ for 12 hours. TLC monitored the generation of a new spot. 10 mL of an aqueous sodium bicarbonate solution was added, and the mixture was extracted twice with ethyl acetate, 20 mL each time. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 2,3-dihydroxypropyl 5-bromopentanoate as a yellow liquid (3.50 g, 69.8% yield).

Step 3: Synthesis of 1-[(5-bromopentanoyl)oxy]-3-(octanoyloxy)propan-2-yl octanoate

Reaction scheme:



Material ratio:

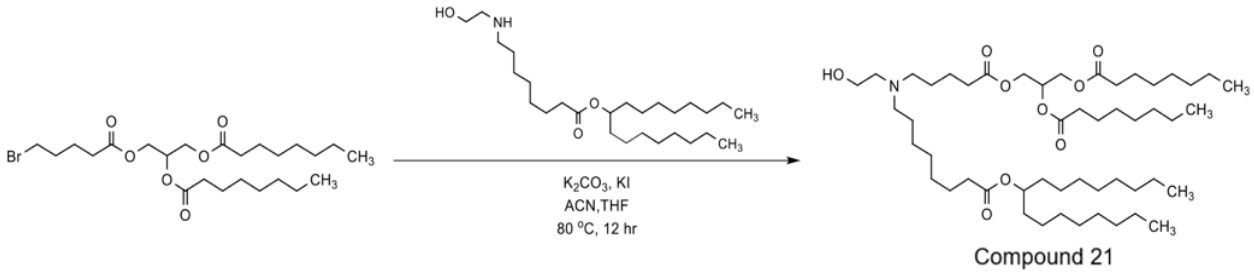
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2,3-dihydroxypropyl 5-bromopentanoate	254	1.0 eq	3.50 g	13.7 mmol
octanoic acid	144	2.5 eq	4.95 g	34.3 mmol
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	3.0 eq	7.89 g	41.2 mmol
4-dimethylaminopyridine	122	0.2 eq	335 mg	2.74 mmol
dichloromethane	-	-	70 mL	-

Procedure:

2,3-dihydroxypropyl 5-bromopentanoate (3.50 g, 13.7 mmol) and octanoic acid (4.95 g, 34.3 mmol) were dissolved in dichloromethane (70 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.89 g, 41.16 mmol) and 4-dimethylaminopyridine (335 mg, 2.74 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 10 mL of water was added, and the mixture was extracted twice with dichloromethane, 10 mL each time. The organic phase was concentrated. After purification by column chromatography, 1-[(5-bromopentanoyl)oxy]-3-(octanoyloxy)propan-2-yl octanoate as a colorless liquid was obtained (6.14 g, 88.1% yield).

Step 4: Synthesis of heptadecan-9-yl 8-({5-[2,3-bis(octanoyloxy)propoxy]-5-oxopentyl}(2-hydroxyethyl)amino)octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(5-bromopentanoyl)oxy]-3-(octanoyloxy) propan-2-yl octanoate	441	1.0 eq	1.00 g	2.26 mmol
heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate	506	1.1 eq	1.26 g	2.49 mmol
potassium carbonate	138	3.5 eq	1.10 g	7.92 mmol
potassium iodide	166	1.2 eq	450 mg	2.72 mmol
acetonitrile	-	-	5 mL	-
tetrahydrofuran	-	-	5 mL	-

Procedure:

1-[(5-bromopentanoyl)oxy]-3-(octanoyloxy)propan-2-yl octanoate (1.00 g, 2.26 mmol) was dissolved in acetonitrile (5.0 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (1.26 g, 2.49 mmol), potassium carbonate (1.10 g, 7.92 mmol), potassium iodide (450 mg, 2.72 mmol), and tetrahydrofuran (5 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl

8-({5-[2,3-bis(octanoyloxy)propoxy]-5-oxopentyl}(2-hydroxyethyl)amino)octanoate as a bright yellow liquid was obtained (230 mg, 10.4% yield).

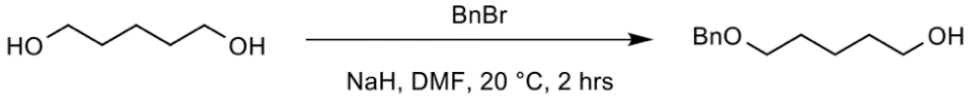
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.34 - 5.25 (m, 1H), 4.88 (quin, J = 6.2 Hz, 1H), 4.37 - 4.28 (m, 2H), 4.17 (dd, J_1 = 6.0, J_2 = 12.0 Hz, 2H), 3.59 - 3.51 (m, 2H), 2.60 (br s, 2H), 2.47 (br d, J = 1.0 Hz, 4H), 2.38 - 2.27 (m, 8H), 1.68 - 1.59 (m, 10H), 1.55 - 1.42 (m, 9H), 1.37 - 1.23 (m, 48H), 0.94 - 0.85 (m, 12H) ppm.

LCMS: RT = 2.062, m/z 868.6 $[M+H]^+$.

Preparation Example 19: Preparation of Compound 32

Step 1: Synthesis of 5-(benzyloxy)pentan-1-ol

Reaction scheme:



Material ratio:

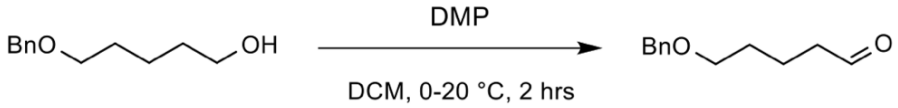
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
pentanediol	104	1.0 eq	15.0 g	144 mmol
benzyl bromide	170	1.0 eq	24.6g	144 mmol
sodium hydride	24	1.2 eq	6.91 g	173 mmol
N,N-dimethylformamide	-	-	300 mL	-

Procedure:

Pentanediol (15.0 g, 144 mmol) and sodium hydride (6.91 g, 173 mmol, 60%) were dissolved in N,N-dimethylformamide (150 mL), and the mixture was stirred at 20 ℃ for 0.5 hours under nitrogen protection. A solution of benzyl bromide (24.6 g, 144 mmol) in N,N-dimethylformamide (150 mL) was slowly added dropwise at 0 ℃, and finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was washed with water, extracted, and concentrated. The crude product was subjected to column chromatography to obtain 5-(benzyloxy)pentan-1-ol as a colorless liquid (14.8 g, 52.9% yield).

Step 2: Synthesis of 5-(benzyloxy)pentanal

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-(benzyloxy)pentan-1-ol	194	1.0 eq	14.8 g	76.2 mmol
Dess-Martin	424	1.2 eq	38.8 g	91.4 mmol
dichloromethane	-	-	150 mL	-

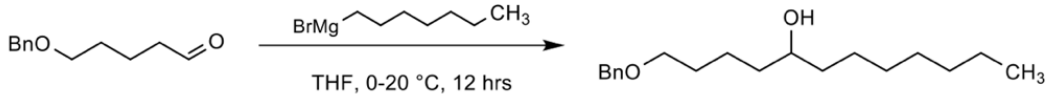
Procedure:

5-(benzyloxy)pentan-1-ol (14.5 g, 76.2 mmol) was dissolved in dichloromethane (150 mL), and Dess-Martin (38.8 g, 91.4 mmol) was added at 0 ℃. Finally, the mixture was reacted at 20 ℃ for 2 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction mixture was slowly poured into a saturated aqueous sodium bicarbonate solution to quench at 0 ℃, washed with water, extracted, and concentrated. The crude product was subjected to column chromatography to obtain 5-(benzyloxy)pentanal as a colorless liquid (10.1

g, 57.5% yield).

Step 3: Synthesis of 1-(benzyloxy)dodecan-5-ol

Reaction scheme:



Material ratio:

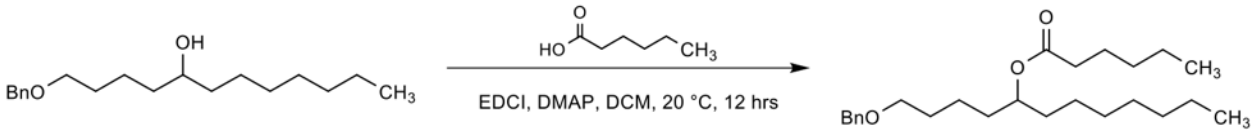
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-(benzyloxy)pentanal	192	1.0 eq	10.0 g	52.0 mmol
heptylmagnesium bromide	202	1.05 eq	11.1 g	54.6 mmol
tetrahydrofuran	-	-	100 mL	-

Procedure:

5-(benzyloxy)pentanal (10.0 g, 52.0 mmol) was dissolved in tetrahydrofuran (100 mL), and a tetrahydrofuran solution of heptylmagnesium bromide (11.1 g, 54.6 mmol) was slowly added dropwise at 0 ℃. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-5-ol as a colorless liquid (10.0 g, 59.2% yield).

Step 4: Synthesis of 1-(benzyloxy)dodecan-5-yl hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-5-ol	292	1.0 eq	10.0 g	34.2 mmol
n-hexanoic acid	116	1.3 eq	5.16 g	44.5 mmol
1-(3-dimethylaminopropyl)-3 -ethylcarbodiimide hydrochloride	191	1.5 eq	9.83 g	51.3 mmol
4-dimethylaminopyridine	122	0.1 eq	418 mg	3.42 mmol
dichloromethane	-	-	100 mL	-

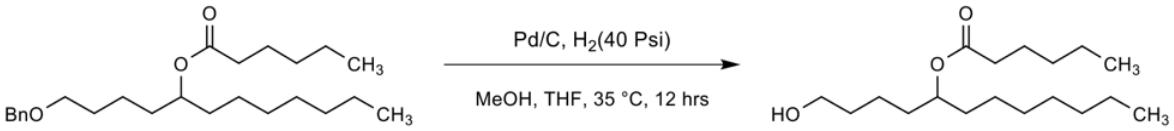
Procedure:

1-(benzyloxy)dodecan-5-ol (10.0 g, 34.2 mmol) was dissolved in dichloromethane (100 mL), and n-hexanoic acid (5.16 g, 44.5 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (9.83 g, 51.3 mmol), and 4-dimethylaminopyridine (418 mg, 3.42 mmol) were

added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-5-yl hexanoate as a colorless liquid (9.00 g, 67.4% yield).

Step 5: Synthesis of 1-hydroxydodecan-5-yl hexanoate

Reaction scheme:



Material ratio:

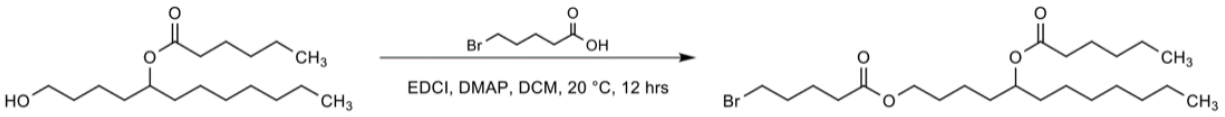
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-5-yl hexanoate	390	1.0 eq	9.00 g	23.0 mmol
palladium/carbon	106	0.1 eq	2.50 g	2.40 mmol
hydrogen	-	(40 Psi)	-	-
methanol		-	90 mL	-

Procedure:

1-(benzyloxy)dodecan-5-yl hexanoate (9.00 g, 23.0 mmol) was dissolved in methanol (90 mL), and palladium/carbon (2.50 g, 2.40 mmol) was added under a nitrogen atmosphere. Finally, the mixture was reacted at 35 ℃ for 12 hours under a hydrogen (40 Psi) atmosphere. TLC monitored that the reaction was complete, and the reaction mixture was filtered and concentrated. The crude product was subjected to column chromatography to obtain 1-hydroxydodecan-5-yl hexanoate as a colorless liquid (7.20 g, 92.9% yield).

Step 6: Synthesis of 1-[(5-bromopentanoyl)oxy]dodecan-5-yl hexanoate

Reaction scheme:



Material ratio:

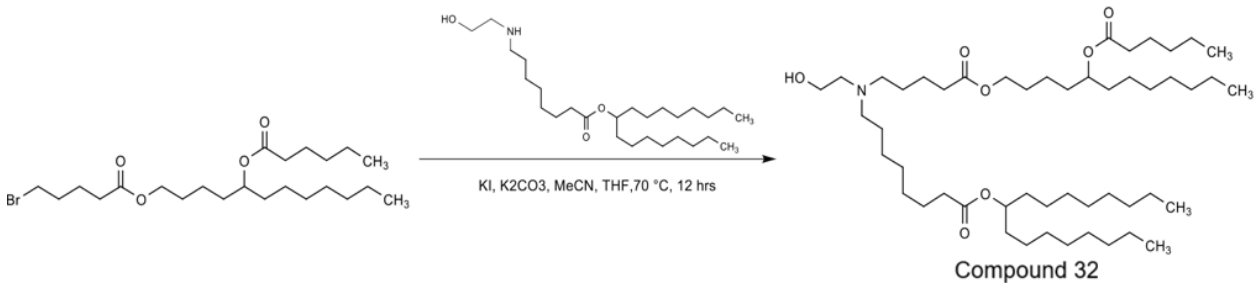
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-5-yl hexanoate	300	1.0 eq	2.00 g	6.66 mmol
5-bromovaleric acid	180	1.3 eq	1.57 g	8.65 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.91 g	9.98 mmol
4-dimethylaminopyridine	122	0.1 eq	81.3 mg	666 umol
dichloromethane	-	-	20 mL	-

Procedure:

1-hydroxydodecan-5-yl hexanoate (2.00 g, 6.66 mmol) was dissolved in dichloromethane (20 mL), and 5-bromovaleric acid (1.57 g, 8.65 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.91 g, 9.98 mmol), and 4-dimethylaminopyridine (81.3 mg, 666 umol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(5-bromopentanoyl)oxy]dodecan-5-yl hexanoate as a colorless liquid (2.10 g, 68.1% yield).

Step 7: Synthesis of heptadecan-9-yl 8-[(5-{[5-(hexanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate

Reaction scheme:



Compound 32

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate	441	1.0 eq	1.50 g	3.40 mmol
1-[(5-bromopentanoyl)oxy]dodecan-5-yl hexanoate	462	1.05 eq	1.65 g	3.57 mmol
potassium carbonate	138	3.5 eq	1.64 g	11.9 mmol
potassium iodide	166	1.2 eq	676 mg	4.07 mmol
acetonitrile	-	-	12 mL	-
tetrahydrofuran	-	-	3 mL	-

Procedure:

The reaction was run in parallel in 1.33 batches. 1-[(5-bromopentanoyl)oxy]dodecan-5-yl hexanoate (1.65 g, 3.57 mmol) was dissolved in acetonitrile (12 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (1.50 g, 3.40 mmol), potassium carbonate (1.64 g, 11.9 mmol), potassium iodide (676 mg, 4.07 mmol), and tetrahydrofuran (3 mL) were added sequentially. Finally, the mixture was reacted at 70 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(5-{[5-(hexanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate as a pale yellow liquid was obtained (800 mg, 21.6% yield).

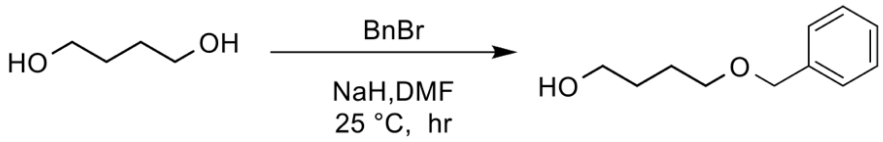
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 4.87 (sex, J = 6.0 Hz, 2H), 4.05 (t, J = 6.6 Hz, 2H), 3.60 (t, J = 5.0 Hz, 2H), 2.66 (br t, J = 5.0 Hz, 2H), 2.61 - 2.49 (m, 4H), 2.35 - 2.25 (m, 6H), 1.67 - 1.58 (m, 8H), 1.57 - 1.45 (m, 12H), 1.38 - 1.29 (m, 14H), 1.26 (br s, 32H), 0.99 - 0.78 (m, 12H) ppm.

LCMS: RT = 2.135, m/z 824.6 $[M+H]^+$.

Preparation Example 20: Preparation of Compound 48

Step 1: Synthesis of 4-(benzyloxy)butan-1-ol

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
butane-1,4-diol	90	1.0 eq	5.00 g	55.5 mmol
benzyl bromide	169	1.0 eq	9.49 g	55.5 mmol
sodium hydride	24	1.5 eq	3.33 g	83.2 mmol
N,N-dimethylformamide	-	-	100 mL	-

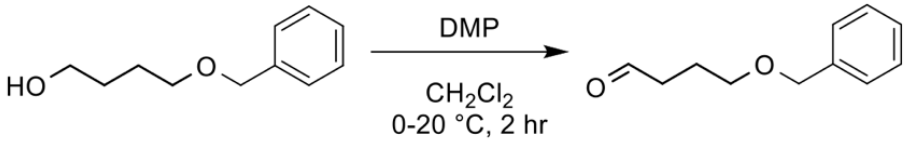
Procedure:

Butane-1,4-diol (5.00 g, 55.5 mmol) was dissolved in N,N-dimethylformamide (100 mL), sodium hydride (3.33 g, 83.2 mmol) was added at 25 ℃, and the mixture was reacted at 25 ℃ for half an hour. Benzyl bromide (9.49 g, 55.5 mmol) was added to the reaction mixture, and the mixture was reacted at 25 ℃ for half an hour under nitrogen protection. TLC monitored that the reaction was complete. 1000 mL of water was added, and the mixture was extracted twice with ethyl acetate, 500 mL each time. The organic phase was concentrated, and after purification by

column chromatography, 4-(benzyloxy)butan-1-ol as a colorless liquid was obtained (9.60 g, 96.0% yield).

Step 2: Synthesis of 4-(benzyloxy)butanal

Reaction scheme:



Material ratio:

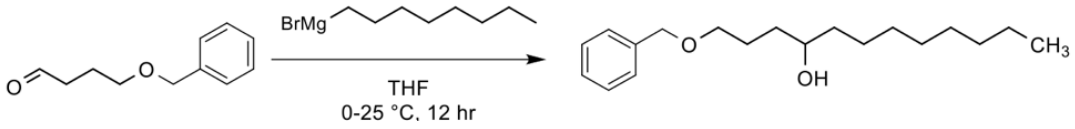
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
4-(benzyloxy)butan-1-ol	180	1.0 eq	9.60 g	53.3 mmol
Dess-Martin periodinane	423	1.2 eq	27.1 mg	63.9 mmol
dichloromethane	-	-	150 mL	-

Procedure:

4-(benzyloxy)butan-1-ol (9.60 g, 53.3 mmol) was dissolved in dichloromethane (150 mL), Dess-Martin periodinane (27.1 g, 63.9 mmol) was added at 0 ℃, and the mixture was reacted at 20 ℃ for 2 hours. TLC monitored the generation of a new spot. 100 mL of an aqueous sodium bicarbonate solution was added, and the mixture was extracted twice with dichloromethane, 200 mL each time. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 4-(benzyloxy)butanal as a colorless liquid (6.32 g, 66.5% yield).

Step 3: Synthesis of 1-(benzyloxy)dodecan-4-ol

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
4-(benzyloxy)butanal	178	1.0 eq	6.32 g	35.5 mmol
bromo(octyl)magnesium	216	1.2 eq	9.25 g	42.6 mmol
tetrahydrofuran	-	-	64 mL	-

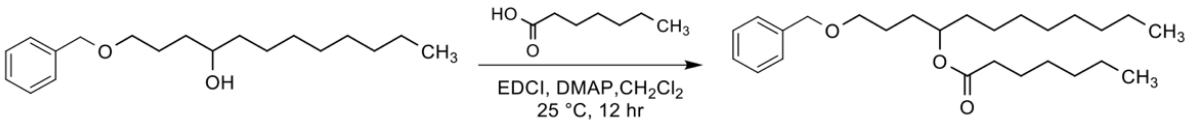
Procedure:

4-(benzyloxy)butanal (6.32 g, 35.5 mmol) was dissolved in tetrahydrofuran (64 mL), bromo(octyl)magnesium (9.25 g, 42.6 mmol) was added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 10 mL of a saturated aqueous ammonium chloride solution was added, and the mixture was extracted twice with ethyl acetate, 20 mL each time. The organic phase was concentrated.

After purification by column chromatography, 1-(benzyloxy)dodecan-4-ol as a colorless liquid was obtained (7.14 g, 68.1% yield).

Step 4: Synthesis of 1-(benzyloxy)dodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

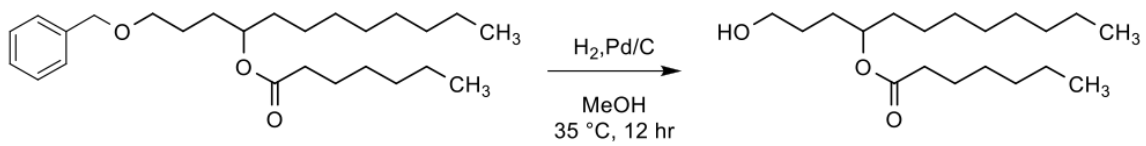
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-4-ol	292	1.0 eq	7.14 g	24.4 mmol
heptanoic acid	130	1.5 eq	4.77 g	36.6 mmol
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	7.02 g	36.6 mmol
4-dimethylaminopyridine	122	0.1 eq	298 mg	2.44 mmol
dichloromethane	-	-	140 mL	-

Procedure:

1-(benzyloxy)dodecan-4-ol (7.14 g, 24.4 mmol) and heptanoic acid (4.77 g, 36.6 mmol) were dissolved in dichloromethane (140 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.02 g, 36.6 mmol) and 4-dimethylaminopyridine (298 mg, 24.4 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 100 mL of water was added, and the mixture was extracted twice with dichloromethane, 100 mL each time. The organic phase was concentrated. After purification by column chromatography, 1-(benzyloxy)dodecan-4-yl heptanoate as a colorless liquid was obtained (7.13 g, 72.1% yield).

Step 5: Synthesis of 1-hydroxydodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

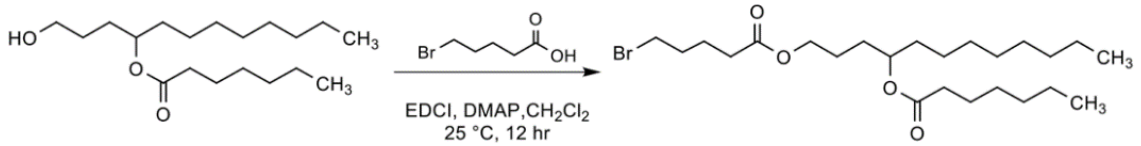
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-4-yl heptanoate	404	1.0 eq	7.13 g	17.6 mmol
palladium on carbon	105	0.2 eq	3.75 g	3.52 mmol
methanol	-	-	74 mL	-

Procedure:

1-(benzyloxy)dodecan-4-yl heptanoate (7.13 g, 17.6 mmol) was dissolved in methanol (74 mL), palladium on carbon (3.75 g, 3.52 mmol) was added, and the mixture was reacted at 35 ℃ and 40 Psi for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. The crude product was subjected to column chromatography to obtain 1-hydroxydodecan-4-yl heptanoate as a colorless liquid (5.07 g, 91.4% yield).

Step 6: Synthesis of 1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-4-yl heptanoate	314	1.0 eq	5.07 g	16.1 mmol
5-bromovaleric acid	179	1.1 eq	3.21 g	17.7 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	4.64 g	24.2 mmol
4-dimethylaminopyridine	122	0.1 eq	196 mg	1.61 mmol
dichloromethane	-	-	100 mL	-

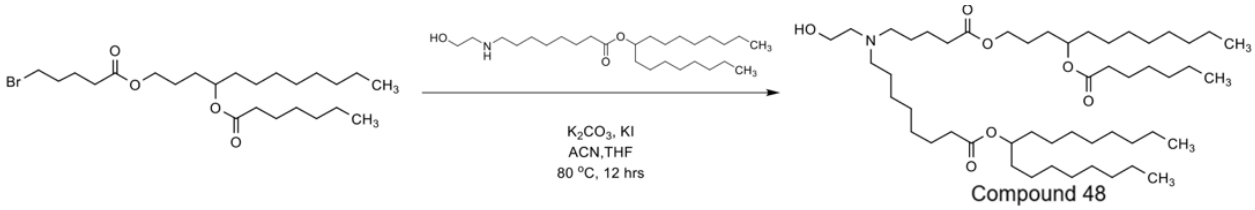
Procedure:

1-hydroxydodecan-4-yl heptanoate (5.07 g, 16.1 mmol) and 5-bromovaleric acid (3.21 g, 17.7 mmol) were dissolved in dichloromethane (100 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (4.64 g, 24.2 mmol) and 4-dimethylaminopyridine (196 mg, 1.61 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 100 mL of water was added, and the mixture was extracted twice with dichloromethane, 100 mL each time. The organic phase was concentrated. After purification by

column chromatography, 1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate as a bright yellow liquid was obtained (4.20 g, 54.5% yield).

Step 7: Synthesis of heptadecan-9-yl 8-[(5-{[4-(heptanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(5-bromopentanoyl)oxy] dodecan-4-yl heptanoate	476	1.1 eq	594 mg	1.25 mmol
heptadecan-9-yl 8-[(2-hydroxyethyl)amino] octanoate	441	1.0 eq	500 mg	1.13 mmol
potassium carbonate	138	3.5 eq	547 mg	3.96 mmol
potassium iodide	166	1.2 eq	225 mg	1.36 mmol
acetonitrile	-	-	3 mL	-
tetrahydrofuran	-	-	2 mL	-

Procedure:

1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate (594 mg, 1.25 mmol) was dissolved in acetonitrile (3.0 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (500 mg, 1.13 mmol), potassium carbonate (547 mg, 3.96 mmol), potassium iodide (225 mg, 1.36 mmol), and tetrahydrofuran (2 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(5-{[4-(heptanoyloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate as a bright yellow liquid was obtained (670 mg, 66.4% yield).

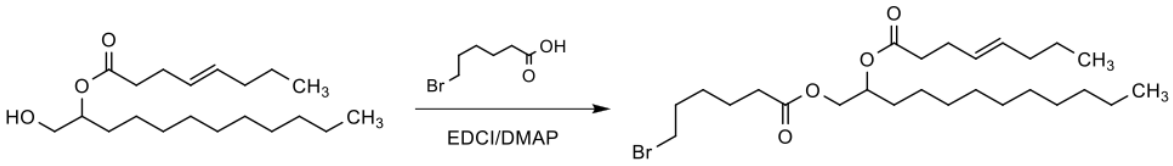
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 4.89 (td, J = 6.2, 12.8 Hz, 2H), 4.15 - 4.00 (m, 2H), 3.57 (t, J = 5.2 Hz, 2H), 2.63 (br t, J = 5.2 Hz, 2H), 2.51 (td, J_1 = 7.4, J_2 = 12.0 Hz, 4H), 2.35 - 2.26 (m, 6H), 1.69 - 1.57 (m, 11H), 1.56 - 1.45 (m, 10H), 1.35 - 1.22 (m, 48H), 0.97 - 0.83 (m, 12H) ppm.

LCMS: RT = 2.183, m/z 839.3 $[M+H]^+$.

Preparation Example 21: Preparation of Compound 55

Step 1: Synthesis of 1-[(6-bromohexanoyl)oxy]dodecan-2-yl (4E)-oct-4-enoate

Reaction scheme:



Material ratio:

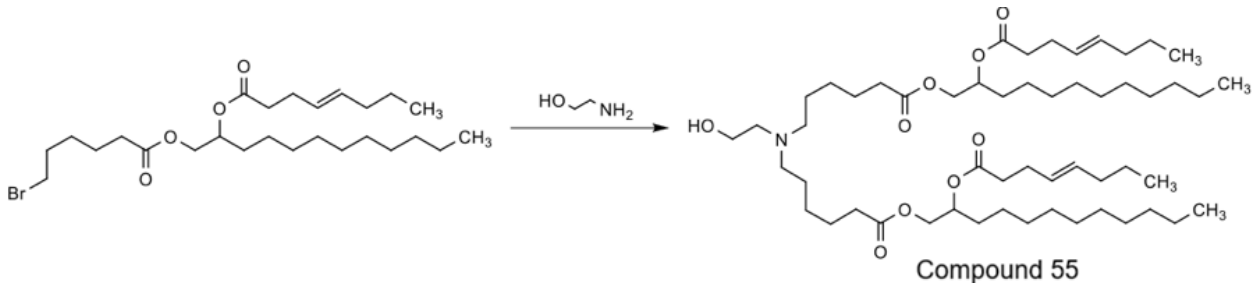
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl (4E)-oct-4-enoate	326	1.0 eq	3.00 g	9.19 mmol
6-bromohexanoic acid	193	1.2 eq	2.15 g	11.0 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	2.64 g	13.7 mmol
4-dimethylaminopyridine	122	0.1 eq	112 mg	0.918 mmol
dichloromethane	-	-	30.0 mL	-

Procedure:

To the reaction flask, dichloromethane (30.0 mL), 1-hydroxydodecan-2-yl (4E)-oct-4-enoate (3.00 g, 9.19 mmol), 6-bromohexanoic acid (2.15 g, 11.0 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.64 g, 13.7 mmol), and 4-dimethylaminopyridine (112 mg, 918 μmol) were added sequentially, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 1-[(6-bromohexanoyl)oxy]dodecan-2-yl (4E)-oct-4-enoate as a colorless liquid was obtained (3.27 g, 70.6% yield).

Step 2: Synthesis of 1-({6-[(2-hydroxyethyl)[6-({2-[(4E)-oct-4-enoyloxy]dodecyl}oxy)-6-oxohexyl]amino]hexanoyl}oxy)dodecan-2-yl (4E)-oct-4-enoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]dodecan-2-yl (4E)-oct-4-enoate	502	1.0 eq	1.00 g	1.99 mmol
ethanolamine	61	0.45 eq	58.2 mg	0.953 mmol
potassium carbonate	138	3.5 eq	960 mg	6.95 mmol
potassium iodide	166	1.2 eq	395 mg	2.38 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]dodecan-2-yl (4E)-oct-4-enoate (1.00 g, 1.99 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (58.2 mg, 953 μmol), potassium carbonate (960 mg, 6.95 mmol), potassium iodide (395 mg, 2.38 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({6-[(2-hydroxyethyl)[6-({2-[(4E)-oct-4-enoyloxy]dodecyl}oxy)-6-oxohexyl]amino]hexanoyl }oxy)dodecan-2-yl (4E)-oct-4-enoate as a colorless liquid was obtained (669 mg, 31.7% yield).

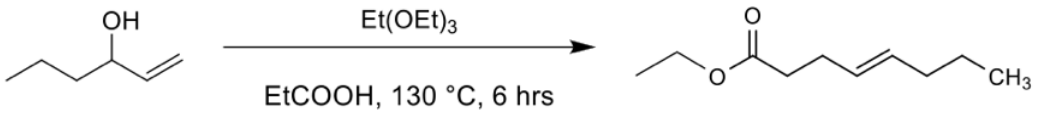
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.62 - 5.29 (m, 4H), 5.17 - 4.85 (m, 2H), 4.23 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 2H), 4.03 (dd, J_1 = 6.4, J_2 = 11.8 Hz, 2H), 3.58 (br s, 2H), 2.64 (br s, 2H), 2.52 (br t, J = 6.4 Hz, 4H), 2.40 - 2.27 (m, 12H), 1.96 (q, J = 6.8 Hz, 4H), 1.67 - 1.47 (m, 12H), 1.37 - 1.18 (m, 40H), 0.99 - 0.75 (m, 12H) ppm.

LCMS: RT = 2.070, m/z 906.5 $[M+H]^+$.

Preparation Example 22: Preparation of Compound 57

Step 1: Synthesis of ethyl 4-oct-4-enoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hexen-3-ol	100	1.00 eq	15.0 g	150 mmol
triethyl orthoacetate	162	3.00 eq	72.9 g	449 mmol
propionic acid	74	0.1 eq	1.11 g	15.0 mmol

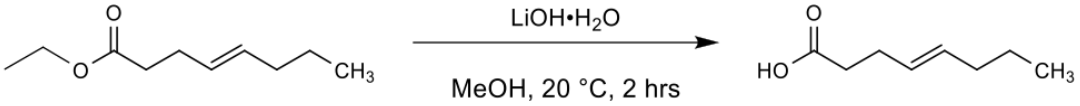
Procedure:

1-hexen-3-ol (15.0 g, 150 mmol) was dissolved in triethyl orthoacetate (72.9 g, 449 mmol),

and propionic acid (1.11 g, 15.0 mmol) was added. Finally, the mixture was reacted at 130 ℃ for 6 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain ethyl 4-oct-4-enoate as a colorless liquid (24.1 g, 70.9% yield).

Step 2: Synthesis of oct-4-enoic acid

Reaction scheme:



Material ratio:

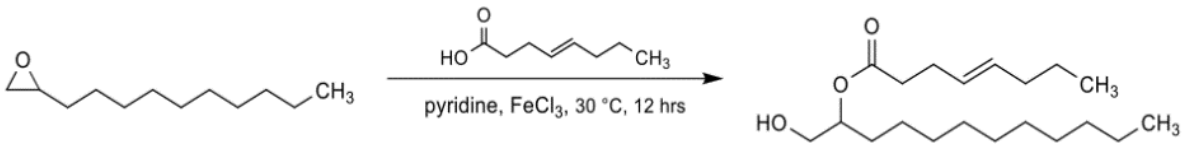
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
ethyl 4-oct-4-enoate	170	1.00 eq	22.0 g	129 mmol
lithium hydroxide monohydrate	42	3.00 eq	16.3 g	388 mmol
methanol	-	-	220 mL	-

Procedure:

Ethyl 4-oct-4-enoate (22.0 g, 129 mmol) was dissolved in methanol (220 mL), and lithium hydroxide monohydrate (16.3 g, 388 mmol) was added. Finally, the mixture was reacted at 20 ℃ for 2 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction mixture was acidified, washed with water, extracted, and concentrated. The crude product was subjected to column chromatography to obtain oct-4-enoic acid as a colorless liquid (16.5 g, 81.6% yield).

Step 3: Synthesis of 1-hydroxydodecan-2-yl oct-4-enoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1.0 eq	20.0 g	108 mmol
oct-4-enoic acid	142	1.05 eq	16.2 g	113 mmol
pyridine	79	0.07 eq	600 mg	7.60 mmol
ferric chloride	160	0.025 eq	440 mg	2.71 mmol

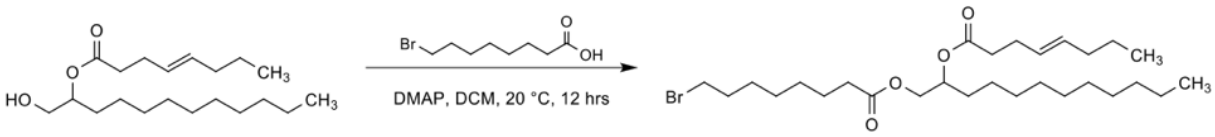
Procedure:

1,2-epoxydodecane (20.0 g, 108 mmol), oct-4-enoic acid (16.2 mg, 113 mmol), pyridine (600 mg, 7.60 mmol), and ferric chloride (440 mg, 2.71 mmol) were added sequentially to the

reaction flask, and finally, the mixture was reacted at 30 ℃ for 12 hours. TLC monitored that the reaction was complete. The mixture was extracted three times with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated to obtain a crude product. The crude product was purified by column chromatography to obtain 1-hydroxydodecan-2-yl oct-4-enoate as a white solid (18.9 g, 53.3% yield).

Step 4: Synthesis of 1-[(8-bromooctanoyl)oxy]dodecan-2-yl oct-4-enoate

Reaction scheme:



Material ratio:

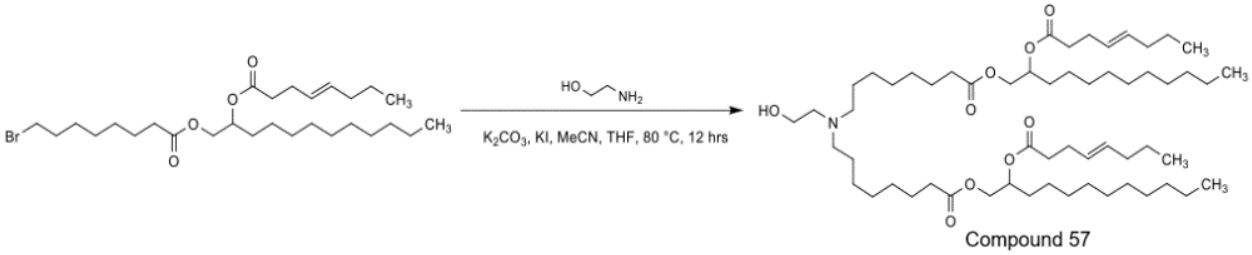
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl oct-4-enoate	326	1.0 eq	2.00 g	6.13 mmol
8-bromooctanoic acid	222	1.3 eq	1.78 g	7.96 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.76 g	9.19 mmol
4-dimethylaminopyridine	122	0.1 eq	74.8 mg	613 umol
dichloromethane	-	-	20 mL	-

Procedure:

1-hydroxydodecan-2-yl oct-4-enoate (2.00 g, 6.13 mmol) was dissolved in dichloromethane (20 mL), and 8-bromooctanoic acid (1.78 g, 7.96 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.76 g, 9.19 mmol), and 4-dimethylaminopyridine (74.8 mg, 613 umol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(8-bromooctanoyl)oxy]dodecan-2-yl oct-4-enoate as a colorless liquid (2.20 g, 67.6% yield).

Step 5: Synthesis of 1-({8-[(2-hydroxyethyl)(8-{[2-(oct-4-enoyloxy)dodecyl]oxy}-8-oxooctyl)amino]octanoyl}oxy) dodecan-2-yl oct-4-enoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(8-bromooctanoyl)oxy]dodecan-2-yl oct-4-enoate	532	1.0 eq	1.50 g	2.28 mmol
ethanolamine	61	0.49 eq	84.5 mg	1.38mmol
potassium carbonate	138	3.5 eq	1.36 g	9.88 mmol
potassium iodide	166	1.2 eq	562 mg	3.39 mmol
acetonitrile	-	-	10 mL	-
tetrahydrofuran	-	-	5 mL	-

Procedure:

1-[(8-bromooctanoyl)oxy]dodecan-2-yl oct-4-enoate (1.50 g, 2.28 mmol) was dissolved in acetonitrile (10 mL), and ethanolamine (84.5 mg, 1.38 mmol), potassium carbonate (1.36 g, 9.88 mmol), potassium iodide (562 mg, 3.39 mmol), and tetrahydrofuran (5 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. The crude product was purified by column chromatography to obtain 1-({8-[(2-hydroxyethyl)(8-{[2-(oct-4-enoyloxy)dodecyl]oxy}-8-oxooctyl)amino]octanoyl}oxy) dodecan-2-yl oct-4-enoate as a pale yellow liquid (800 mg, 26.8% yield).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.58 - 5.32 (m, 4H), 5.11 - 5.04 (m, 2H), 4.22 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 2H), 4.03 (dd, J_1 = 6.6, J_2 = 11.8 Hz, 2H), 3.56 (t, J = 5.2 Hz, 2H), 2.61 (br t, J = 5.0 Hz, 2H), 2.48 (br t, J = 7.4 Hz, 4H), 2.40 - 2.35 (m, 4H), 2.30 (br t, J = 7.4 Hz, 8H), 1.95 (q, J = 6.6 Hz, 4H), 1.65 - 1.54 (m, 8H), 1.50 - 1.43 (m, 4H), 1.41 - 1.25 (m, 48H), 0.91 - 0.85 (m, 12H) ppm.

LCMS: RT = 2.132, m/z 962.7 $[M+H]^+$.

Preparation Example 23: Preparation of Compound 11

Step 1: Preparation of 11-1

Reaction scheme:



11-1

Material ratio:

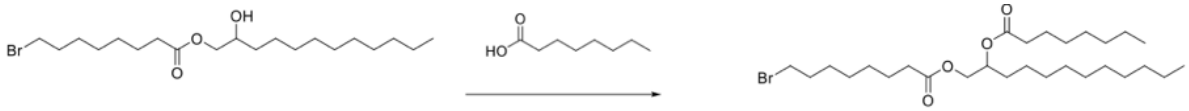
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1 eq	5 g	27
8-bromooctanoic acid	223	1.1 eq	6.7 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To the reaction flask, 8-bromooctanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 7.5 g of a colorless oily substance was obtained.

Step 2: Preparation of 11-2

Reaction scheme:



11-1 11-2

Material ratio:

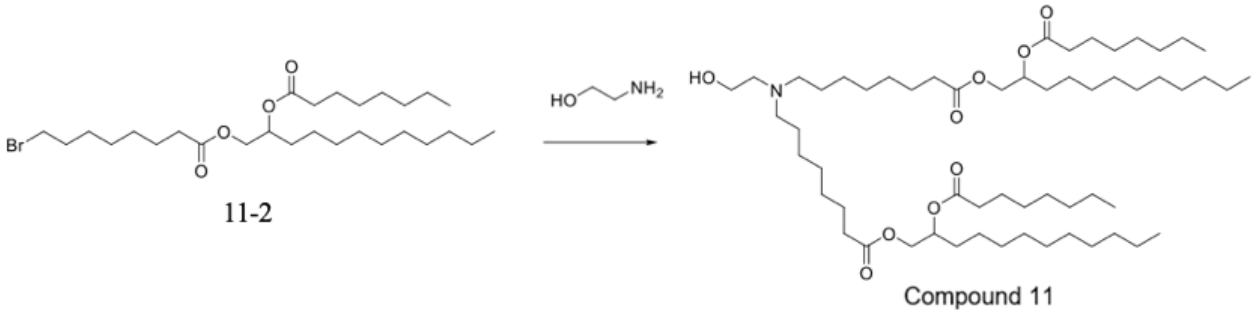
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
11-1	407.43	1 eq	7.1 g	17.5
octanoic acid	144	1.1 eq	2.8 g	19.2
EDCI	192	1.5 eq	5 g	26
DMAP	122	0.15 eq	320 mg	2.6
dichloromethane	-	-	80 mL	-

Procedure:

To the reaction flask, 11-1, octanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 6 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 11

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
11-2	533.63	2.2 eq	4.56 g	8.55
ethanolamine	61	1 eq	237 mg	3.9
K_2CO_3	138	3 eq	1.6 g	11.6
KI	166	2 eq	1.3 g	7.8
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 11-2, ethanolamine, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was concentrated, then diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 1.8 g of a colorless oily substance was obtained.

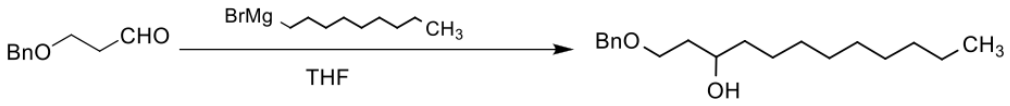
^{1}H NMR (600 MHz, Chloroform-d) δ 5.07 (qd, J = 6.9, 3.3 Hz, 1H), 4.20 (dd, J = 11.8, 3.3 Hz, 1H), 4.01 (dd, J = 11.8, 6.8 Hz, 1H), 3.57 (t, J = 5.3 Hz, 1H), 2.63 (t, J = 5.3 Hz, 1H), 2.51 (t, J = 7.6 Hz, 2H), 2.29 (td, J = 7.5, 1.9 Hz, 4H), 1.63 – 1.51 (m, 6H), 1.47 (p, J = 7.4 Hz, 2H), 1.32 – 1.22 (m, 30H), 0.87 (t, J = 6.8 Hz, 6H).

MS (ES+) m/z: 967.63$(M+H)^+$.

Preparation Example 24: Preparation of Compound 19

Step 1: Synthesis of 1-(benzyloxy)dodecan-3-ol

Reaction scheme:



Material ratio:

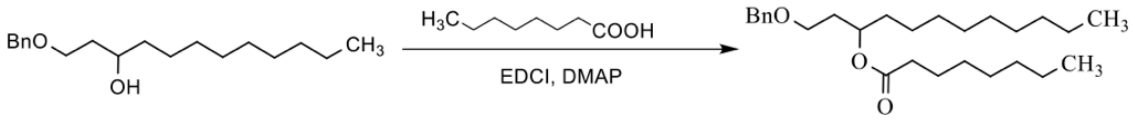
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-(benzyloxy)propanal	164	1.00 eq	6.00 g	36.5 mmol
nonylmagnesium bromide	230	1.20 eq	10.1 g	43.8 mmol
tetrahydrofuran	-	-	60.0 mL	-

Procedure:

3-(benzyloxy)propanal (6.00 g, 36.5 mmol) was dissolved in tetrahydrofuran (60.0 mL), and a tetrahydrofuran solution of nonylmagnesium bromide (10.1 g, 43.8 mmol) was slowly added dropwise at 0 ℃. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-3-ol as a colorless liquid (5.87 g).

Step 2: Synthesis of 1-(benzyloxy)dodecan-3-yl octanoate

Reaction scheme:



Material ratio:

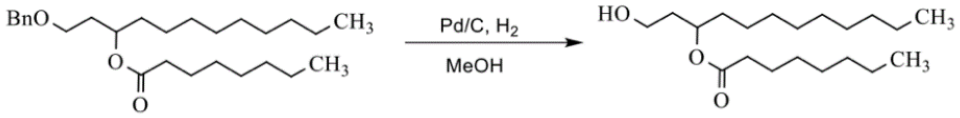
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-3-ol	292	1.00 eq	5.87 g	20.0 mmol
n-octanoic acid	144	1.20 eq	3.47 g	24.0 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.50 eq	5.77 g	30.1 mmol
4-dimethylaminopyridine	122	0.10 eq	245 mg	2.01 mmol
dichloromethane	-	-	58.0 mL	-

Procedure:

1-(benzyloxy)dodecan-3-ol (5.87 g, 20.0 mmol) and n-octanoic acid (3.47 g, 24.0 mmol) were dissolved in dichloromethane (58.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (5.77 g, 30.1 mmol) and 4-dimethylaminopyridine (245 mg, 2.01 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-3-yl octanoate as a colorless liquid (6.00 g).

Step 3: Synthesis of 1-hydroxydodecan-3-yl octanoate

Reaction scheme:



Material ratio:

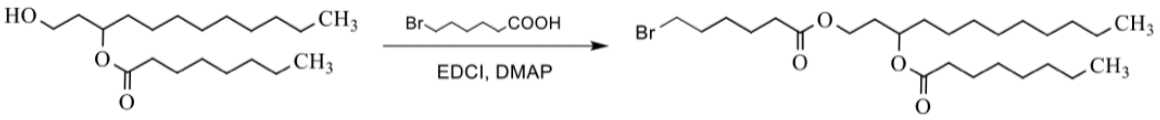
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-3-yl octanoate	418	1.0 eq	6.00 g	14.3 mmol
palladium/carbon	106	0.20 eq	3.05 g	2.87 mmol
hydrogen	-	(40 Psi)	-	-
methanol	-	-	60.0 mL	-

Procedure:

1-(benzyloxy)dodecan-3-yl octanoate (6.00 g, 14.3 mmol) was dissolved in methanol (60.0 mL), palladium/carbon (3.05 g, 2.87 mmol) was added under an argon atmosphere, and finally, the mixture was reacted at 35 ℃ for 12 hours under a hydrogen (40 Psi) atmosphere. TLC monitored that the reaction was complete, and the reaction mixture was filtered and concentrated. Spin drying gave 1-hydroxydodecan-3-yl octanoate as a colorless liquid (4.60 g).

Step 4: Synthesis of 1-[(6-bromohexanoyl)oxy]dodecan-3-yl octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-3-yl octanoate	328	1.00 eq	2.00 g	6.09 mmol
6-bromohexanoic acid	193	1.20 eq	1.42 g	7.31 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.75 g	9.13 mmol
4-dimethylaminopyridine	122	0.1 eq	74.3 mg	0.608 mmol
dichloromethane	-	-	15.0 mL	-

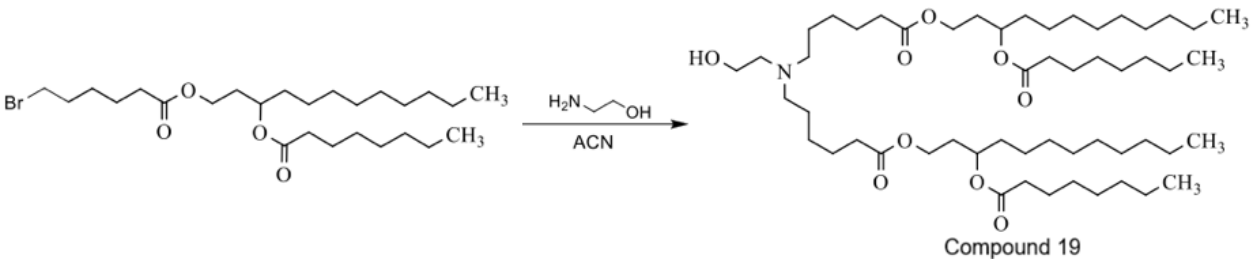
Procedure:

1-hydroxydodecan-3-yl octanoate (2.00 g, 6.09 mmol) was dissolved in dichloromethane (15.0 mL), and 6-bromohexanoic acid (1.42 g, 7.31 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.75 g, 9.13 mmol), and 4-dimethylaminopyridine (74.3 mg, 608 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction

was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(6-bromohexanoyl)oxy]dodecan-3-yl octanoate as a colorless liquid (2.78 g).

Step 5: Synthesis of 1-({6-[(2-hydroxyethyl)(6-{[3-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-3-yl octanoate

Reaction scheme:



Compound 19

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]dodecan-3-yl octanoate	504	2.00 eq	1.00 g	1.98 mmol
ethanolamine	61	0.98 eq	57.9 mg	0.949 mmol
potassium carbonate	138	3.50 eq	0.478 g	3.46 mmol
potassium iodide	166	1.20 eq	197 mg	1.19 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]dodecan-3-yl octanoate (1.00 g, 1.98 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (57.9 mg, 949 μmol), potassium carbonate (478 mg, 3.46 mmol), potassium iodide (197 mg, 1.19 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({6-[(2-hydroxyethyl)(6-{[3-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-3-yl octanoate as a colorless liquid was obtained (603 mg).

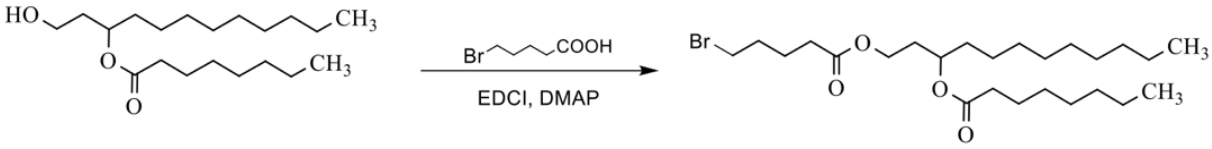
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.08 - 4.88 (m, 2H), 4.17 - 3.98 (m, 4H), 3.58 (br s, 2H), 2.64 (br s, 2H), 2.52 (br s, 4H), 2.30 (q, J = 7.4 Hz, 8H), 1.94 - 1.80 (m, 4H), 1.69 - 1.49 (m, 16H), 1.34 - 1.18 (m, 48H), 0.89 (t, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 2.169, m/z 910.6 $[M+H]^+$.

Preparation Example 25: Preparation of Compound 20

Step 1: Synthesis of 1-[(5-bromopentanoyl)oxy]dodecan-3-yl octanoate

Reaction scheme:



Material ratio:

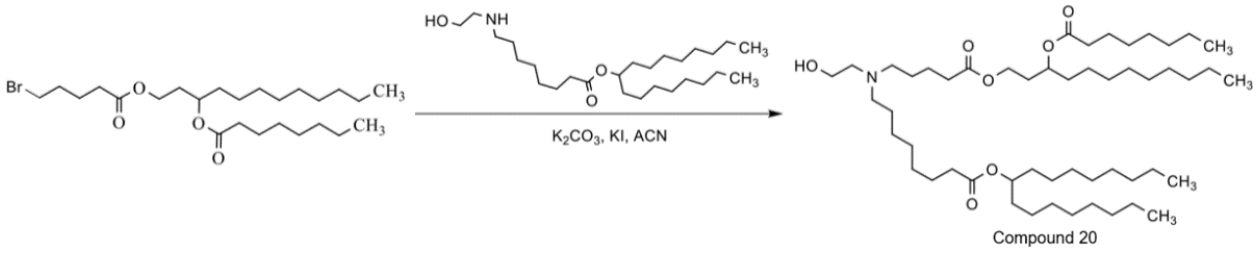
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-3-yl octanoate	328	1.00 eq	1.00 g	3.04 mmol
5-bromovaleric acid	179	1.20 eq	0.661 g	3.65 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.50 eq	0.875 g	4.57 mmol
4-dimethylaminopyridine	122	0.10 eq	37.1 mg	0.304 mmol
dichloromethane	-	-	10.0 mL	-

Procedure:

1-hydroxydodecan-3-yl octanoate (1.00 g, 3.04 mmol) and 5-bromovaleric acid (661 mg, 3.65 mmol) were dissolved in dichloromethane (10.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (875 mg, 4.57 mmol) and 4-dimethylaminopyridine (37.1 mg, 304 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(5-bromopentanoyl)oxy]dodecan-3-yl octanoate as a colorless liquid (1.40 g).

Step 2: Synthesis of heptadecan-9-yl 8-[(2-hydroxyethyl)(5-{[3-(octanoyloxy)dodecyl]oxy}-5-oxopentyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(5-bromopentanoyl)oxy] dodecan-3-yl octanoate	490	1.05 eq	1.17 g	2.8 mmol
heptadecan-9-yl 8-[(2-hydroxyethyl)amino] octanoate	441	1.00 eq	1.00 g	2.26 mmol
potassium carbonate	138	3.50 eq	1.10 g	7.92 mmol
potassium iodide	166	1.20 eq	450 mg	2.72 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

1-[(5-bromopentanoyl)oxy]dodecan-3-yl octanoate (1.17 g, 2.38 mmol) was dissolved in acetonitrile (10.0 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (1.00 g, 2.26 mmol), potassium carbonate (1.10 g, 7.92 mmol), potassium iodide (450 mg, 2.72 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(2-hydroxyethyl)(5-{[3-(octanoyloxy)dodecyl]oxy}-5-oxopentyl)amino]octanoate as a colorless liquid was obtained (1.50 g).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.06 - 4.92 (m, 1H), 4.87 (quin, J = 6.2 Hz, 1H), 4.18 - 4.01 (m, 2H), 3.56 (br t, J = 5.0 Hz, 2H), 2.62 (br s, 2H), 2.56 - 2.43 (m, 4H), 2.37 - 2.24 (m, 6H), 1.94 - 1.80 (m, 2H), 1.64 - 1.44 (m, 16H), 1.33 - 1.15 (m, 52H), 0.88 (t, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 2.325, m/z 874.6 $[M+23]^+$.

Preparation Example 26: Preparation of Compound 22

Step 1: Preparation of 22-1

Reaction scheme:



22-1

Material ratio:

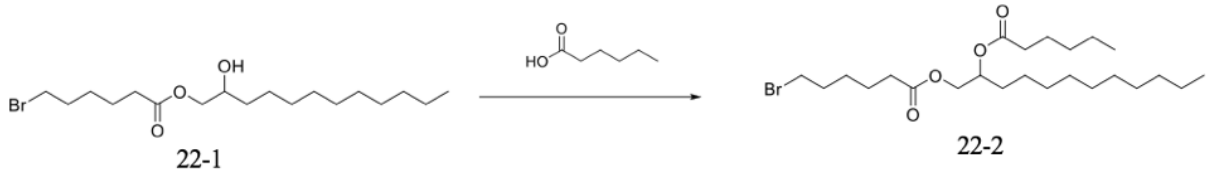
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1,2-epoxydodecane	184	1 eq	5 g	27
6-bromohexanoic acid	195	1.1 eq	5.85 g	30
ferric chloride	162	0.025 eq	220 mg	1.35
pyridine	79	0.0125 eq	53 mg	0.68

Procedure:

To the reaction flask, 6-bromohexanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added. After the addition was completed, the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) showed that the reaction was complete (the product rf value was 0.5). After purification by column chromatography, 7 g of a colorless oily substance was obtained.

Step 2: Preparation of 22-2

Reaction scheme:



22-1 22-2

Material ratio:

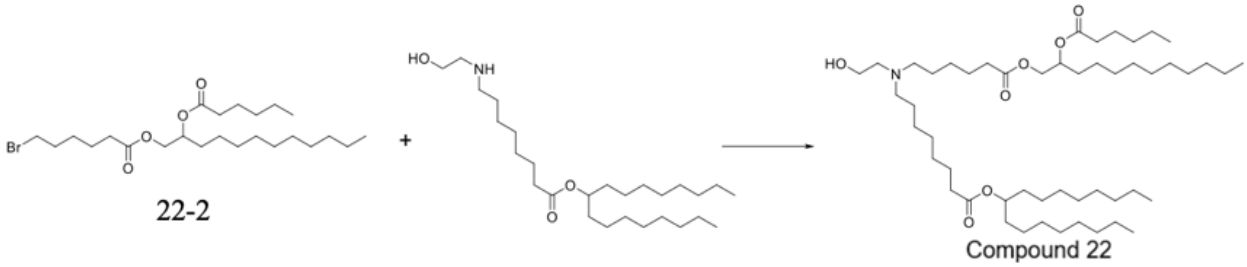
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
22-1	379.38	1 eq	6.6 g	17.5
hexanoic acid	116	1.1 eq	2.2 g	19.2
EDCI	192	1.5 eq	5 g	26
DMAP	122	0.15 eq	320 mg	2.6
dichloromethane	-	-	80 mL	-

Procedure:

To the reaction flask, 22-1, hexanoic acid, EDCI, DMAP, and dichloromethane were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) showed that the reaction was complete (the product rf value was 0.6). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 5.6 g of a colorless oily substance was obtained.

Step 3: Preparation of Compound 22

Reaction scheme:



22-2 Compound 22

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
22-2	477.52	1.1 eq	4.1 g	8.55
LQ001-2	441.74	1 eq	3.4 g	7.8
K_2CO_3	138	1.5 eq	1.6 g	11.6
KI	166	1 eq	1.3 g	7.8
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 22-2, LQ001-2, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) showed that the reaction was complete (the product rf value was 0.5). The reaction mixture was concentrated, then diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 2.5 g of a colorless oily substance was obtained.

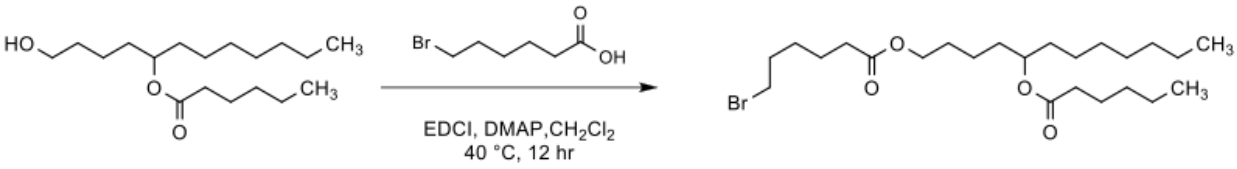
^{1}H NMR (600 MHz, Chloroform-d) δ 5.08 (qd, J = 6.9, 3.2 Hz, 1H), 4.85 (p, J = 6.2 Hz, 1H), 4.22 (dd, J = 11.8, 3.3 Hz, 1H), 4.01 (dd, J = 11.8, 6.8 Hz, 1H), 3.57 (t, J = 5.3 Hz, 2H), 2.62 (t, J = 5.3 Hz, 2H), 2.50 (q, J = 7.5 Hz, 4H), 2.32 – 2.24 (m, 6H), 1.62 (p, J = 7.4 Hz, 6H), 1.57 – 1.43 (m, 10H), 1.33 – 1.22 (m, 52H), 0.88 (dt, J = 13.6, 6.8 Hz, 12H).

MS (ES+) m/z): 839.38$(M+H)^+$.

Preparation Example 27: Preparation of Compound 30

Step 1: Synthesis of 5-(hexanoyloxy)dodecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

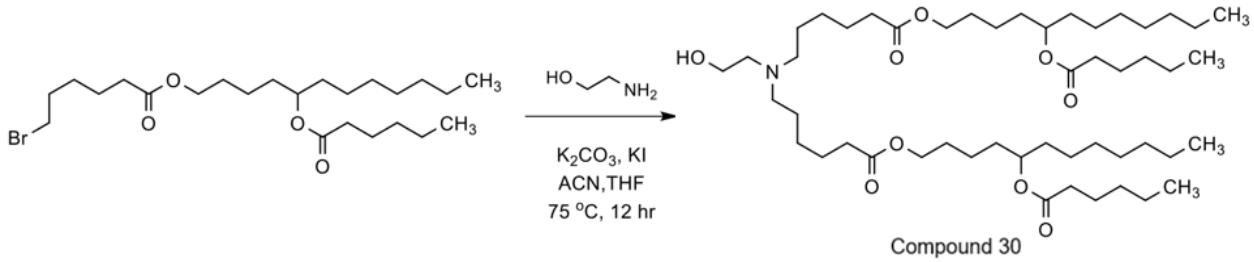
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-5-yl hexanoate	300	1.0 eq	2.00 g	6.66 mmol
6-bromohexanoic acid	195	1.3 eq	1.69 g	8.65 mmol
1-(3-dimethylaminopropyl) -3-ethylcarbodiimide hydrochloride	192	1.5 eq	1.91 g	9.98 mmol
4-dimethylaminopyridine	122	0.1 eq	81.3 mg	0.665 mmol
dichloromethane	-	-	20 mL	-

Procedure:

1-hydroxydodecan-5-yl hexanoate (2.00 g, 6.66 mmol) and 6-bromohexanoic acid (1.69 g, 8.65 mmol) were dissolved in dichloromethane (20 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.91 g, 9.98 mmol) and 4-dimethylaminopyridine (8.3 mg, 0.665 mmol) were added sequentially. Finally, the mixture was reacted at 45 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. The organic phase was concentrated, washed twice with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, 5-(hexanoyloxy)dodecyl 6-bromohexanoate as a colorless liquid was obtained (2.30 g).

Step 2: Synthesis of 5-(hexanoyloxy)dodecyl 6-[(6-{[5-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-(hexanoyloxy)dodecyl 6-bromohexanoate	476	1.0 eq	1.00 g	2.09 mmol
2-aminoethan-1-ol	61	0.45 eq	57.5 mg	0.942 mmol
potassium carbonate	138	3.0 eq	868 mg	6.28 mmol
potassium iodide	166	1.5 eq	521 mg	3.14 mmol
acetonitrile	-	-	6 mL	-
tetrahydrofuran	-	-	4 mL	-

Procedure:

5-(hexanoyloxy)dodecyl 6-bromohexanoate (1.00 g, 2.09 mmol) was dissolved in acetonitrile (6.0 mL), and 2-aminoethan-1-ol (57.5 mg, 0.942 mmol), potassium carbonate (868 mg, 6.28 mmol), potassium iodide (521 mg, 3.14 mmol), and tetrahydrofuran (4 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 5-(hexanoyloxy)dodecyl 6-[(6-{[5-(hexanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate as a bright yellow liquid was obtained (550 mg).

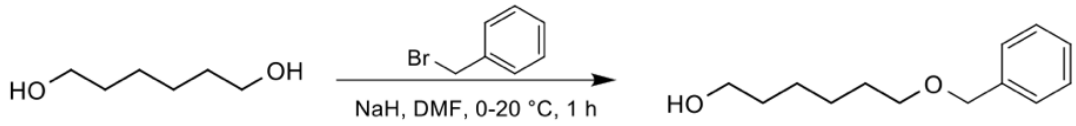
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 4.90 (quin, J = 6.0 Hz, 2H), 4.07 (t, J = 6.4 Hz, 4H), 3.67 (br s, 2H), 2.73 (br d, J = 1.2 Hz, 2H), 2.62 (br d, J = 5.6 Hz, 3H), 2.31 (q, J = 7.6 Hz, 8H), 1.73 - 1.48 (m, 28H), 1.42 - 1.23 (m, 36H), 0.97 - 0.86 (m, 12H) ppm.

LCMS: RT = 1.960, m/z 854.6 $[M+H]^+$.

Preparation Example 28: Preparation of Compound 31

Step 1: Synthesis of 6-(benzyloxy)hexan-1-ol

Reaction scheme:



Material ratio:

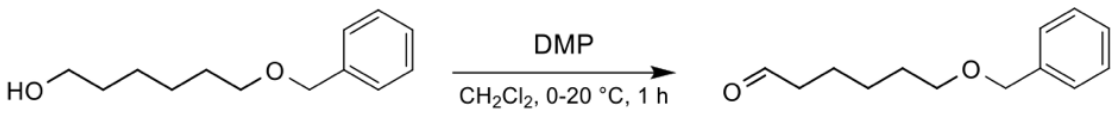
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
hexane-1,6-diol	118	1.0 eq	5.00 g	42.3 mmol
(bromomethyl)benzene	169	5.0 eq	7.24 g	42.3 mmol
sodium cyanide	24	1.5 eq	2.54 g	63.4 mmol
N,N-dimethylformamide	-	-	100 mL	-

Procedure:

In the reaction flask, hexane-1,6-diol (5.00 g, 42.3 mmol) was dissolved in N,N-dimethylformamide (100 mL), and the temperature was lowered to 0 ℃. Sodium hydride (2.54 g, 63.4 mmol) was added in batches, and the mixture was reacted at 20 ℃ for 30 minutes, then (bromomethyl)benzene (7.24 g, 42.3 mmol) was added, and finally, the mixture was reacted at 20 ℃ for 30 minutes. TLC monitored that the reaction was complete. Water (200 mL) was added to the reaction to quench the reaction. The mixture was extracted three times with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated to obtain a crude product. The crude product was purified by column chromatography to obtain 6-(benzyloxy)hexan-1-ol as a colorless liquid (4.00 g).

Step 2: Synthesis of 6-(benzyloxy)hexanal

Reaction scheme:



Material ratio:

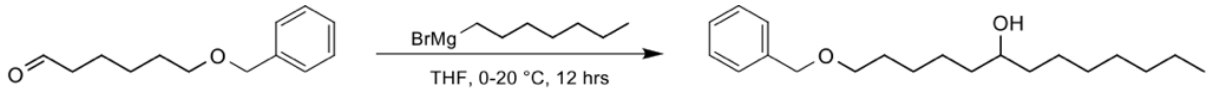
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-(benzyloxy)hexan-1-ol	208	1.0 eq	4.00 g	19.2 mmol
Dess-Martin periodinane	423	1.2 eq	9.77 g	23.0 mmol
dichloromethane	-	-	40 mL	-

Procedure:

In the reaction flask, 6-(benzyloxy)hexan-1-ol (4.00 g, 19.2 mmol) was dissolved in dichloromethane (40 mL), and the temperature was lowered to 0 ℃. Dess-Martin periodinane (9.77 g, 23.0 mmol) was added in batches, and the mixture was reacted at 20 ℃ for 1 hour. TLC monitored that the reaction was complete. A saturated sodium carbonate solution (100 mL) was added to the reaction to quench the reaction. The mixture was extracted three times with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated to obtain a crude product. The crude product was purified by column chromatography to obtain 6-(benzyloxy)hexanal as a colorless liquid (3.00 g).

Step 3: Synthesis of 1-(benzyloxy)tridecan-6-ol

Reaction scheme:



Material ratio:

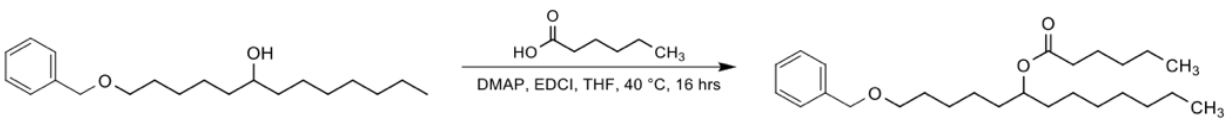
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-(benzyloxy)hexanal	206	1.0 eq	3.00 g	14.5 mmol
n-heptylmagnesium bromide	203	1.2 eq	3.55 g	17.4 mmol
tetrahydrofuran	-	-	30 mL	-

Procedure:

6-(benzyloxy)hexanal (3.00 g, 14.5 mmol) was dissolved in tetrahydrofuran (30 mL), and a tetrahydrofuran solution of n-heptylmagnesium bromide (3.55 g, 17.4 mmol) was slowly added dropwise. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)tridecan-6-ol as a colorless liquid (2.90 g).

Step 4: Synthesis of 1-(benzyloxy)tridecan-6-yl hexanoate

Reaction scheme:



Material ratio:

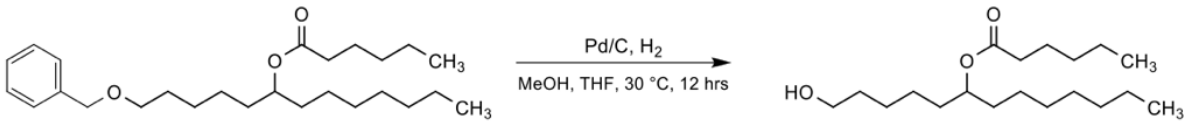
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)tridecan-6-ol	306	1.0 eq	2.90 g	9.46 mmol
hexanoic acid	116	1.5 eq	1.65 g	14.1 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	2.72 g	14.1 mmol
4-dimethylaminopyridine	122	0.2 eq	231 mg	1.89 mmol
tetrahydrofuran	-	-	30 mL	-

Procedure:

In the reaction flask, 1-(benzyloxy)tridecan-6-ol (2.90 g, 9.46 mmol) was dissolved in tetrahydrofuran (30 mL), and hexanoic acid (1.65 g, 14.1 mmol), 4-dimethylaminopyridine (231 mg, 1.89 mmol), and 1-ethyl-(3-dimethylaminopropyl)carbodiimide hydrochloride (2.72 g, 14.1 mmol) were added sequentially. Finally, the mixture was reacted at 40 ℃ for 16 hours. TLC monitored that the reaction was complete. The mixture was extracted three times with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated to obtain a crude product. The crude product was purified by column chromatography to obtain 1-(benzyloxy)tridecan-6-yl hexanoate as a colorless liquid (3.10 g).

Step 5: Synthesis of 1-hydroxytridecan-6-yl hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)tridecan-6-yl hexanoate	404	1.0 eq	3.10 g	7.66 mmol
wet palladium on carbon	-	0.06 eq	500 mg	469 μmol
tetrahydrofuran	-	-	10 mL	-
methanol	-	-	30 mL	-

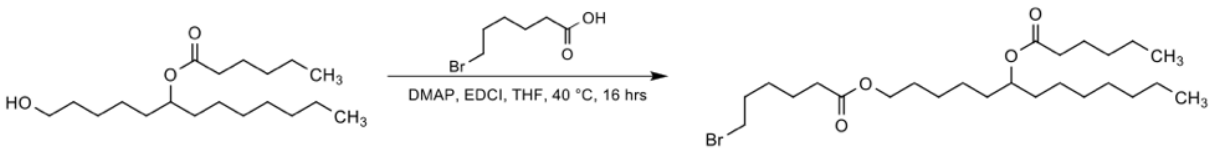
Procedure:

1-hydroxytridecan-6-yl hexanoate (3.10 g, 7.66 mmol) was dissolved in methanol (30 mL) and tetrahydrofuran (10 mL), palladium/carbon (500 mg, 469 μmol) was added under a nitrogen atmosphere, and finally, the mixture was reacted at 30 ℃ for 12 hours under a hydrogen (40 Psi) atmosphere. TLC monitored that the reaction was complete, and the reaction mixture was filtered and concentrated. The crude product was subjected to column chromatography to obtain

1-hydroxytridecan-6-yl hexanoate as a colorless liquid (2.10 g).

Step 6: Synthesis of 6-(hexanoyloxy)tridecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

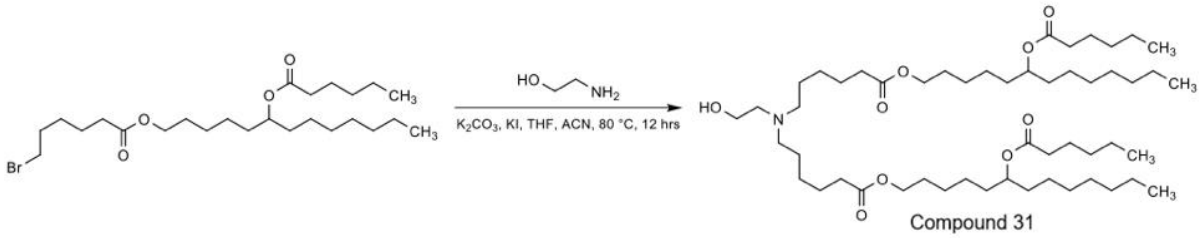
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxytridecan-6-yl hexanoate	314	1.0 eq	2.10 g	6.68 mmol
6-bromohexanoic acid	195	1.5 eq	1.95 g	10.0 mmol
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	1.92 g	10.0 mmol
4-dimethylaminopyridine	122	0.2 eq	163 mg	1.34 mmol
tetrahydrofuran	-	-	22 mL	-

Procedure:

In the reaction flask, 1-hydroxytridecan-6-yl hexanoate (2.10 g, 6.68 mmol) was dissolved in tetrahydrofuran (22 mL), and hexanoic acid (1.95 g, 10.0 mmol), 4-dimethylaminopyridine (163 mg, 1.34 mmol), and 1-ethyl-(3-dimethylaminopropyl)carbodiimide hydrochloride (1.92 g, 10.0 mmol) were added sequentially. Finally, the mixture was reacted at 40 ℃ for 16 hours. TLC monitored that the reaction was complete. The mixture was extracted three times with ethyl acetate, dried over anhydrous sodium sulfate, and concentrated to obtain a crude product. The crude product was purified by column chromatography to obtain 1-(benzyloxy)tridecan-6-yl hexanoate as a colorless liquid (3.00 g).

Step 7: Synthesis of 6-(hexanoyloxy)tridecyl 6-[(6-{[6-(hexanoyloxy)tridecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)tridecan-6-yl hexanoate	491	1.0 eq	2.50 g	5.09 mmol
ethanolamine	61	2.0 eq	124 mg	2.03 mmol
potassium carbonate	138	3.0 eq	2.11 g	15.2 mmol
potassium iodide	166	1.2 eq	1.01 g	6.10 mmol
acetonitrile	-	-	15 mL	-
tetrahydrofuran	-	-	15 mL	-

Procedure:

1-(benzyloxy)tridecan-6-yl hexanoate (2.50 g, 2.09 mmol) was dissolved in acetonitrile (15 mL), and then ethanolamine (124 mg, 2.03 mmol), potassium carbonate (2.11 g, 15.2 mmol), potassium iodide (1.01 g, 6.10 mmol), and tetrahydrofuran (15 mL) were added sequentially. Finally, the mixture was reacted at 80 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 6-(hexanoyloxy)tridecyl 6-[(6-{[6-(hexanoyloxy)tridecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoate as a yellow liquid was obtained (1.30 g).

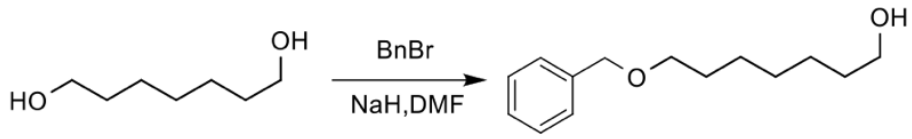
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 4.87 (t, J = 6.2 Hz, 2H), 4.05 (t, J = 6.8 Hz, 4H), 3.72 (br s, 2H), 2.87 - 2.62 (m, 6H), 2.30 (td, J_1 = 7.6, J_2 = 11.4 Hz, 8H), 1.69 - 1.59 (m, 16H), 1.57 - 1.48 (m, 8H), 1.40 - 1.24 (m, 40H), 0.96 - 0.83 (m, 12H) ppm.

LCMS: RT = 2.019, m/z 882.6 $[M+H]^+$.

Preparation Example 29: Preparation of Compound 52

Step 1: Synthesis of 7-(benzyloxy)heptan-1-ol

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
heptane-1,7-diol	132	1.00 eq	5.00 g	37.8 mmol
benzyl bromide	169	1.00 eq	6.47 g	37.8 mmol
sodium hydride	24	1.20 eq	1.82 g	45.3 mmol
N,N-dimethylformamide	-	-	100 mL	-

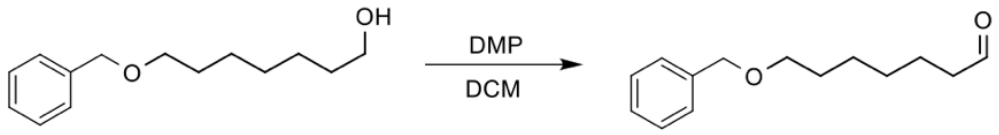
Procedure:

Heptane-1,7-diol (5.00 g, 37.8 mmol) was dissolved in N,N-dimethylformamide (100 mL), sodium hydride (1.82 g, 45.3 mmol) was added at 25 ℃, and the mixture was reacted at 0 ℃ for

half an hour. Benzyl bromide (6.47 g, 37.8 mmol) was added to the reaction mixture at 0 ℃, and the mixture was reacted at 25 ℃ for two hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction was quenched, extracted twice with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, 7-(benzyloxy)heptan-1-ol as a colorless liquid was obtained (4.39 g).

Step 2: Synthesis of 7-(benzyloxy)heptanal

Reaction scheme:



Material ratio:

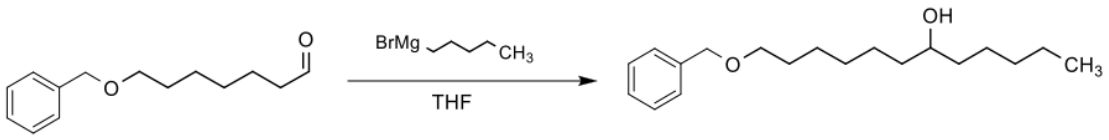
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
7-(benzyloxy)heptan-1-ol	222	1.00 eq	4.39 g	19.7 mmol
Dess-Martin periodinane	423	1.20 eq	16.7 g	39.4 mmol
dichloromethane	-	-	44.0 mL	-

Procedure:

7-(benzyloxy)heptan-1-ol (4.39 g, 19.7 mmol) was dissolved in dichloromethane (44.0 mL), Dess-Martin periodinane (16.7 g, 39.4 mmol) was added at 0 ℃, and the mixture was reacted at 25 ℃ for 2 hours. TLC monitored the generation of a new spot. 200 mL of an aqueous sodium bicarbonate solution was added, and the mixture was extracted with dichloromethane. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 7-(benzyloxy)heptanal as a colorless liquid (2.50 g).

Step 3: Synthesis of 12-(benzyloxy)dodecan-6-ol

Reaction scheme:



Material ratio:

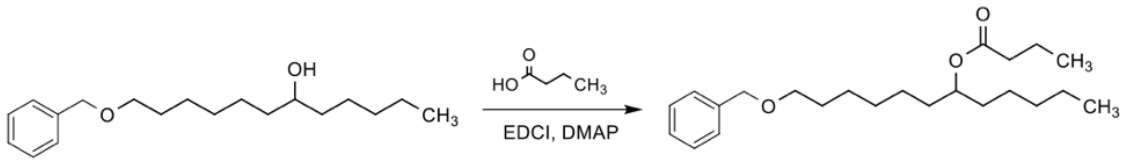
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
7-(benzyloxy)heptanal	220	1.00 eq	2.50 g	11.3 mmol
bromo(pentyl)magnesium	173	1.20 eq	2.39 g	13.6 mmol
tetrahydrofuran	-	-	25.0 mL	-

Procedure:

7-(benzyloxy)heptanal (2.50 g, 11.3 mmol) was dissolved in tetrahydrofuran (25.0 mL), bromo(pentyl)magnesium (2.39 g, 13.6 mmol) was added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 100 mL of a saturated aqueous ammonium chloride solution was added, and the mixture was extracted with ethyl acetate. The organic phase was concentrated. After purification by column chromatography, 12-(benzyloxy)dodecan-6-ol as a colorless liquid was obtained (2.57 g).

Step 4: Synthesis of 12-(benzyloxy)dodecan-6-yl butyrate

Reaction scheme:



Material ratio:

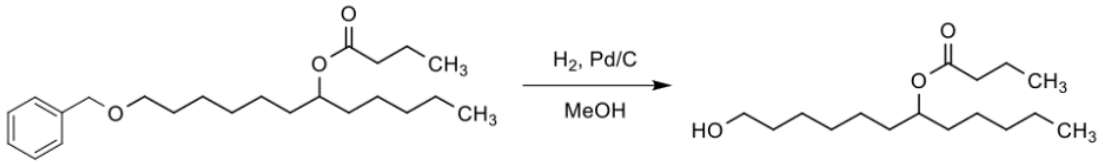
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
12-(benzyloxy)dodecan-6-ol	292	1.00 eq	2.57 g	8.79 mmol
n-butyric acid	88	1.20 eq	929 mg	10.5 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.50 eq	2.53 g	13.1 mmol
4-dimethylaminopyridine	122	0.10 eq	107 mg	878 umol
dichloromethane	-	-	25.0 mL	-

Procedure:

12-(benzyloxy)dodecan-6-ol (2.57 g, 8.79 mmol) and n-butyric acid (929 mg, 10.5 mmol) were dissolved in dichloromethane (25.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.53 g, 13.1 mmol) and 4-dimethylaminopyridine (107 mg, 878 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, 12-(benzyloxy)dodecan-6-yl butyrate as a colorless liquid was obtained (2.25 g).

Step 5: Synthesis of 12-hydroxydodecan-6-yl butyrate

Reaction scheme:



Material ratio:

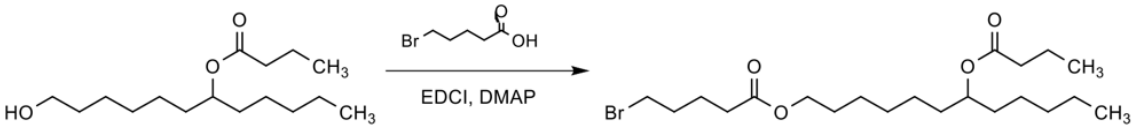
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
12-(benzyloxy)dodecan-6-yl butyrate	362	1.00 eq	2.25 g	6.21 mmol
palladium on carbon	105	0.20 eq	1.32 g	1.24 mmol
methanol	-	-	50.0 mL	-

Procedure:

12-(benzyloxy)dodecan-6-yl butyrate (2.25 g, 6.21 mmol) was dissolved in methanol (50.0 mL), palladium on carbon (1.32 g, 1.24 mmol) was added, and the mixture was reacted at 35 ℃ and 35 Psi for 12 hours under a hydrogen atmosphere. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated to obtain 12-hydroxydodecan-6-yl butyrate as a colorless liquid (1.50 g).

Step 6: Synthesis of 1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
12-hydroxydodecan-6-yl butyrate	272	1.00 eq	1.50 g	5.51 mmol
5-bromovaleric acid	179	1.20 eq	1.20 g	6.61 mmol
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.50 eq	1.58 g	8.26 mmol
4-dimethylaminopyridine	122	0.10 eq	67.7 mg	550 umol
dichloromethane	-	-	15.0 mL	-

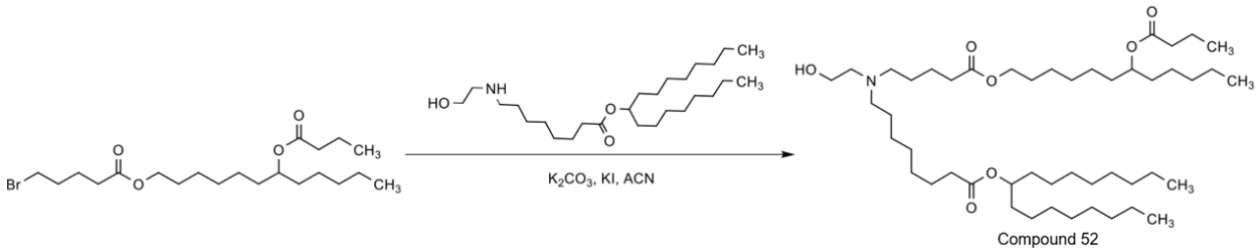
Procedure:

12-hydroxydodecan-6-yl butyrate (1.50 g, 5.51 mmol) and 5-bromovaleric acid (1.20 g, 6.61 mmol) were dissolved in dichloromethane (15.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.58 g, 8.26 mmol) and 4-dimethylaminopyridine (67.7 mg, 550 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a

new spot. The organic phase was concentrated. After purification by column chromatography, 1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate as a colorless liquid was obtained (2.20 g).

Step 7: Synthesis of heptadecan-9-yl 8-[(5-{[7-(butyryloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate	434	1.10 eq	1.08 g	2.49 mmol
heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate	441	1.00 eq	1.00 g	2.26 mmol
potassium carbonate	138	3.50 eq	1.10 g	7.92 mmol
potassium iodide	166	1.20 eq	450 mg	2.72 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

1-[(5-bromopentanoyl)oxy]dodecan-4-yl heptanoate (1.08 g, 2.49 mmol) was dissolved in acetonitrile (10.0 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (1.00 g, 2.26 mmol), potassium carbonate (1.10 g, 7.92 mmol), potassium iodide (450 mg, 2.72 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(5-{[7-(butyryloxy)dodecyl]oxy}-5-oxopentyl)(2-hydroxyethyl)amino]octanoate as a colorless liquid was obtained (1.50 g).

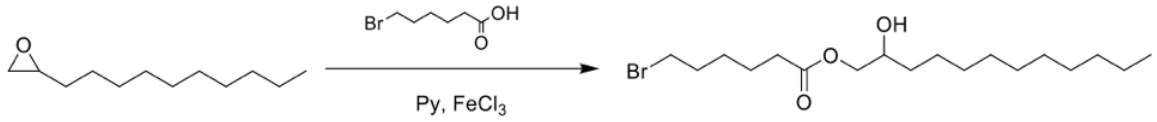
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.03 - 4.76 (m, 2H), 4.20 - 3.92 (m, 2H), 3.70 - 3.43 (m, 2H), 2.70 - 2.58 (m, 2H), 2.57 - 2.43 (m, 4H), 2.40 - 2.19 (m, 6H), 1.69 - 1.58 (m, 8H), 1.52 (br s, 12H), 1.38 - 1.19 (m, 42H), 1.06 - 0.70 (m, 12H) ppm.

LCMS: RT = 2.037, m/z 796.5 $[M+H]^+$.

Preparation Example 30: Preparation of Compound 58

Step 1: Synthesis of 2-hydroxydodecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

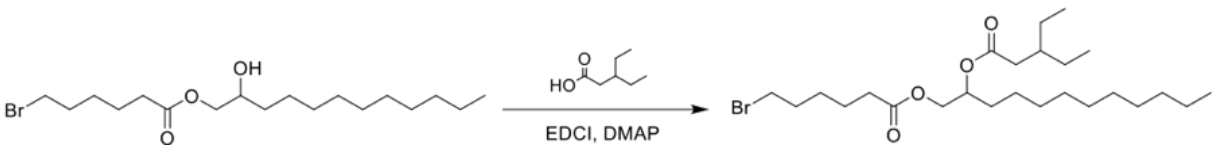
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-decyloxirane	184	1.0 eq	4.00 g	21.7 mmol
6-bromohexanoic acid	193	1.05 eq	4.44 g	22.7 mmol
ferric chloride	162	0.025 eq	95.2 mg	0.587 mmol
pyridine	79	0.025 eq	46.4 mg	0.587 mmol

Procedure:

To the reaction flask, 2-decyloxirane (4.00 g, 21.7 mmol), 6-bromohexanoic acid (4.44 g, 22.7 mmol), ferric chloride (88.0 mg, 542 μmol), and pyridine (42.9 mg, 542 μmol) were added sequentially, and finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. After purification by column chromatography, 2-hydroxydodecyl 6-bromohexanoate as a colorless liquid was obtained (5.60 g).

Step 2: Synthesis of 2-[(3-ethylpentanoyl)oxy]dodecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxydodecyl 6-bromohexanoate	378	1.0 eq	3.00 g	7.91 mmol
3-ethylpentanoic acid	144	1.0 eq	1.37 g	7.91 mmol
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	2.27 g	11.8 mmol
4-dimethylaminopyridine	122	0.1 eq	96.6 mg	0.79 mmol
dichloromethane	-	-	30.0 mL	-

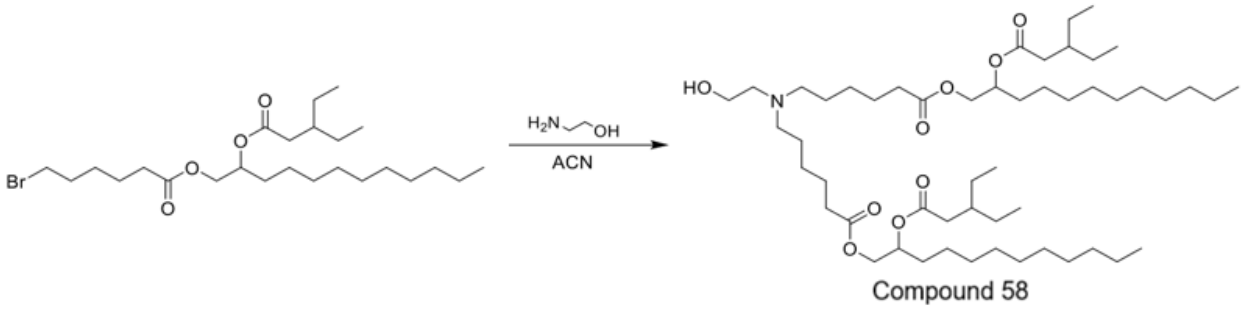
Procedure:

2-hydroxydodecyl 6-bromohexanoate (3.00 g, 7.91 mmol) was dissolved in dichloromethane (30.0 mL), and 3-ethylpentanoic acid (1.03 g, 7.91 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.27 g, 11.8 mmol), and

4-dimethylaminopyridine (96.6 mg, 790 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-[(3-ethylpentanoyl)oxy]dodecyl 6-bromohexanoate as a colorless liquid (2.47 g).

Step 3: Synthesis of 2-[(3-ethylpentanoyl)oxy]dodecyl 6-{[6-({2-[(3-ethylpentanoyl)oxy]dodecyl}oxy)-6-oxohexyl](2-hydroxyethyl)amino}hexanoate

Reaction scheme:



Compound 58

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-[(3-ethylpentanoyl)oxy]dodecyl 6-bromohexanoate	504	1.00 eq	1.30 g	2.03 mmol
ethanolamine	61	0.48 eq	59.6 mg	0.976 mmol
potassium carbonate	138	3.50 eq	984 mg	7.12 mmol
potassium iodide	166	1.20 eq	405 mg	2.44 mmol
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

2-[(3-ethylpentanoyl)oxy]dodecyl 6-bromohexanoate (1.00 g, 2.03 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (59.6 mg, 976 μmol), potassium carbonate (984 mg, 7.12 mmol), potassium iodide (405 mg, 2.44 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-[(3-ethylpentanoyl)oxy]dodecyl 6-{[6-({2-[(3-ethylpentanoyl)oxy]dodecyl}oxy)-6-oxohexyl](2-hydroxyethyl)amino}hexanoate as a colorless liquid was obtained (520 mg).

^{1}H NMR (400 MHz, CHLOROFORM-d)δ = 5.10 (dq, J_1 = 3.4, J_2 = 6.6 Hz, 2H), 4.24 (dd, J_1 = 3.4, J_2 = 11.8 Hz, 2H), 4.02 (dd, J_1 = 7.0, J_2 = 11.8 Hz, 2H), 3.59 (br s, 2H), 2.65 (br s, 2H),

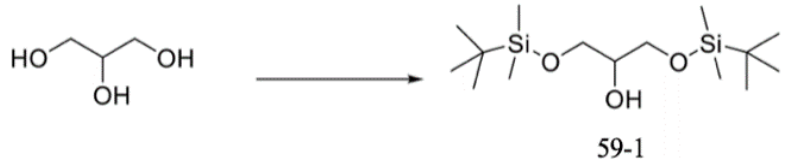
2.53 (br s, 4H), 2.31 (t, J = 7.4 Hz, 4H), 2.25 (d, J = 7.0 Hz, 4H), 1.75 (td, J_1 = 6.4, J_2 = 13.2 Hz, 2H), 1.66 - 1.46 (m, 12H), 1.38 - 1.20 (m, 44H), 0.97 - 0.81 (m, 18H) ppm.

LCMS: RT = 2.069, m/z 882.6 $[M+H]^+$.

Preparation Example 31: Preparation of Compound 59

Step 1: Preparation of 59-1

Reaction scheme:



59-1

Material ratio:

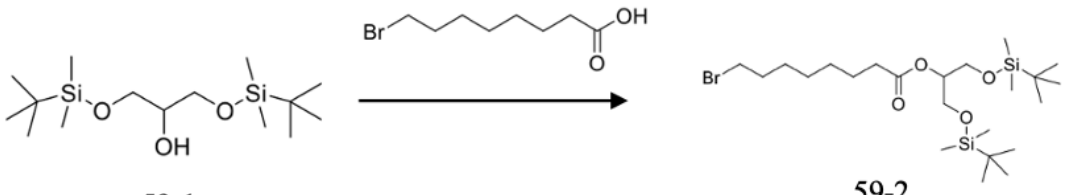
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
glycerol	92	1 eq	9.2 g	100
imidazole	68	2.5 eq	17 g	250
tert-butyldimethylchlorosilane	150.72	2.1 eq	31.7 g	210
tetrahydrofuran	-	-	380 mL	-

Procedure:

To the reaction flask, glycerol, imidazole, and tetrahydrofuran (200 mL) were added. The temperature was lowered to 0-5 ℃, a tetrahydrofuran solution of tert-butyldimethylchlorosilane (180 mL) was added dropwise, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=10:1) product Rf value was 0.3. 500 mL of water was added to the reaction mixture, followed by extraction with 400 mL of ethyl acetate. The organic phase was taken, dried, and then concentrated. After purification by column chromatography, 28 g of a colorless oily substance was obtained.

Step 2: Preparation of 10-2

Reaction scheme:



59-1 59-2

Material ratio:

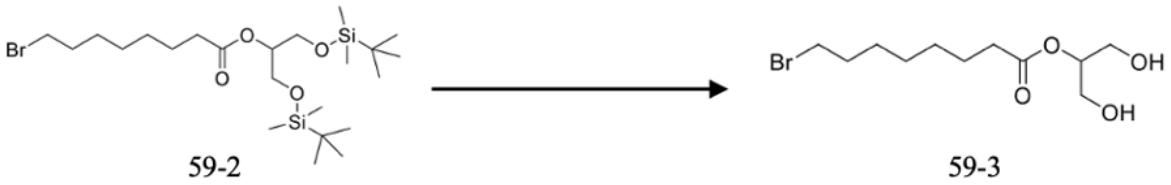
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
59-1	320.62	1 eq	12.8 g	40
8-bromooctanoic acid	223.11	1.1 eq	9.8 g	44
EDCI	192	2 eq	15.4 g	80
DMAP	122	0.2 eq	1 g	8
dichloromethane	-	-	200 mL	-

Procedure:

To the reaction flask, 59-1, 8-bromooctanoic acid, EDCI, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) product Rf value was 0.5. The reaction mixture was washed once with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 13.2 g of a colorless oily substance was obtained.

Step 3: Preparation of 10-3

Reaction scheme:



59-2 59-3

Material ratio:

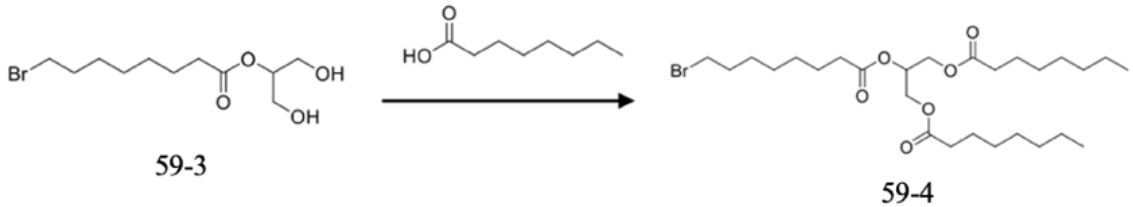
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
59-2	525.72	1 eq	13.2 g	25
1 M tetrabutylammonium fluoride in tetrahydrofuran	-	3 eq	75 mL	75
tetrahydrofuran	-	-	100 mL	-

Procedure:

To the reaction flask, 59-2 and tetrahydrofuran were added, and then a 1 M tetrabutylammonium fluoride in tetrahydrofuran was added. The mixture was stirred and reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. 400 mL of water was added to the reaction mixture, followed by extraction with 400 mL of ethyl acetate. The organic phase was taken, dried, and then concentrated. After purification by column chromatography, 6.5 g of a colorless oily substance was obtained.

Step 4: Preparation of 10-4

Reaction scheme:



59-3 59-4

Material ratio:

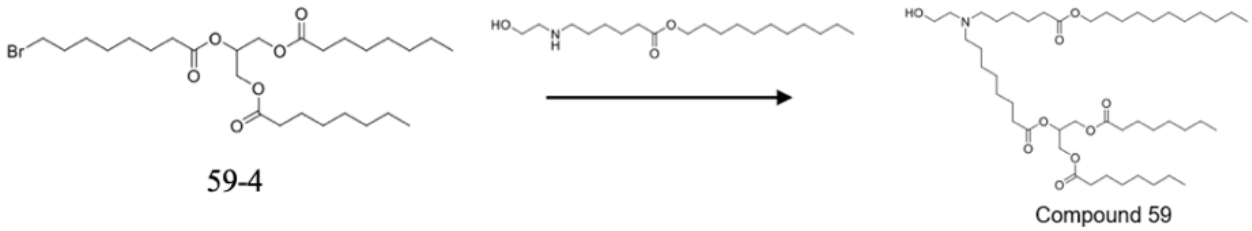
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
59-3	297.19	1 eq	6 g	20
octanoic acid	144.21	2.2 eq	6.3 g	44
EDCI	192	3 eq	11.5 g	60
DMAP	122	0.2 eq	488 mg	4
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 59-3, octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) product Rf value was 0.6. The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 8.2 g of a colorless oily substance was obtained.

Step 5: Preparation of Compound 10

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
59-4	549.59	1.1 eq	4.7 g	8.55
SM102-3	329.53	1 eq	2.56 g	7.77
potassium carbonate	138	1.5 eq	1.6 g	11.6
potassium iodide	166	1.5 eq	1.9 g	11.6
acetonitrile	-	-	40 mL	-

Procedure:

To the reaction flask, 10-4, SM102-3, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was concentrated, then diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 2.8 g of a colorless oily substance was obtained.

^{1}H NMR (600 MHz, Chloroform-d) δ 5.26 (ddd, J = 10.2, 6.0, 4.3 Hz, 1H), 4.28 (ddd, J = 11.9, 4.3, 1.7 Hz, 2H), 4.14 (dd, J = 11.9, 6.0 Hz, 2H), 4.05 (t, J = 6.8 Hz, 2H), 3.53 (t, J = 5.3

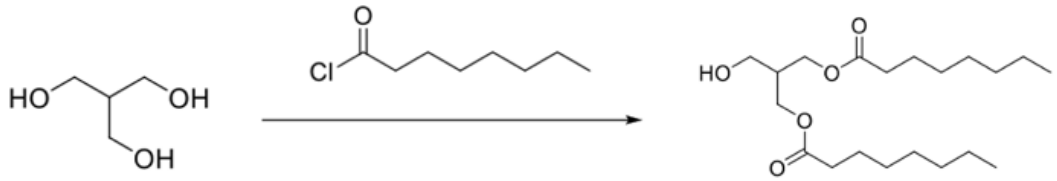
Hz, 2H), 2.59 (t, J = 5.3 Hz, 2H), 2.46 (q, J = 7.6 Hz, 4H), 2.33 – 2.27 (m, 8H), 1.61 (q, J = 8.7, 8.2 Hz, 10H), 1.50 – 1.40 (m, 4H), 1.28 (ddd, J = 22.6, 11.5, 4.6 Hz, 41H), 0.87 (t, J = 6.9 Hz, 9H).

MS (ES+) m/z: 798.7$(M+H)^+$.

Preparation Example 32: Preparation of Compound 60

Step 1: Preparation of 60-1

Reaction scheme:



60-1

Material ratio:

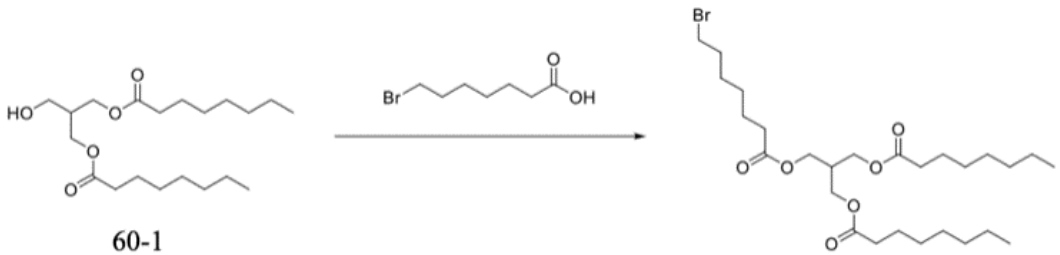
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxymethyl-1,3-propanediol	106.12	1 eq	3 g	28.3
octanoyl chloride	162.66	1.95 eq	9 g	55.12
pyridine	79	4	9 g	113
DMAP	122	0.4	1.4 g	11
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 2-hydroxymethyl-1,3-propanediol, octanoyl chloride, pyridine, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=4:1) product Rf value was 0.4. The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated, and then purified by column chromatography to obtain 8 g of a product.

Step 2: Preparation of 60-2

Reaction scheme:



60-1

60-2

Material ratio:

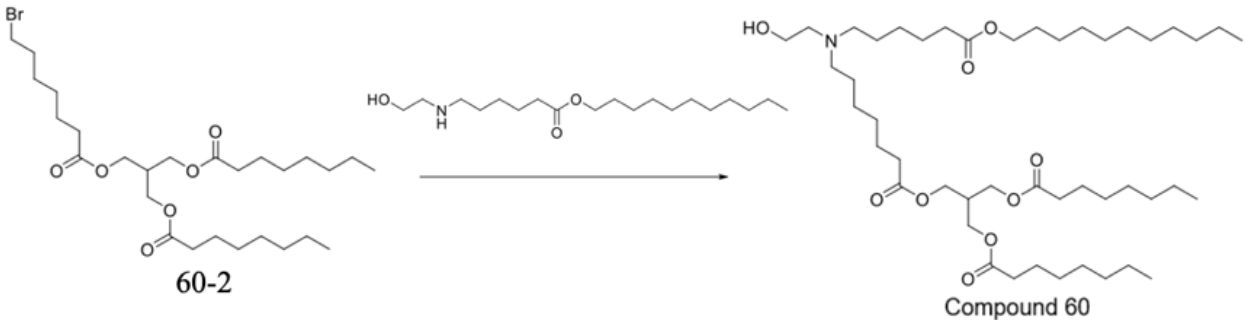
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
60-1	358.52	1 eq	6 g	16.7
7-bromoheptanoic acid	209.08	1.1 eq	3.85 g	18.4
EDCI	192	1.5 eq	4.8 g	25
DMAP	122	0.15 eq	300 mg	2.5
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 60-1, 7-bromoheptanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.5, TLC (PE:EA=10:1). The reaction mixture was washed once with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 5 g of oily substance was obtained.

Step 3: Preparation of Compound 60

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
60-2	549.59	1.1 eq	2.2 g	4
SM102-3	329.53	1 eq	1.2 g	3.7
potassium carbonate	138	1.5 eq	770 mg	5.6
potassium iodide	166	1 eq	660 mg	4
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 60-2, SM102-3, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was stirred and reacted at 65 ℃ for 16 h. The product rR value was 0.6, TLC (DCM:MeOH=10:1). The reaction mixture was diluted with 100 mL of ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 1.2 g of oily substance was obtained.

^{1}H NMR (600 MHz, Chloroform-d) δ 4.12 (d, J = 6.0 Hz, 6H), 4.05 (t, J = 6.8 Hz, 2H),

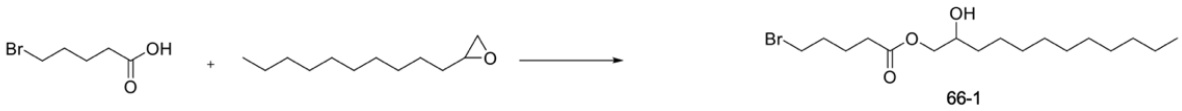
3.55 (t, J = 5.3 Hz, 2H), 2.60 (t, J = 5.4 Hz, 2H), 2.48 (dq, J = 8.2, 4.7 Hz, 4H), 2.39 (p, J = 6.0 Hz, 1H), 2.30 (tt, J = 7.3, 3.3 Hz, 8H), 1.65 – 1.58 (m, 10H), 1.51 – 1.43 (m, 4H), 1.34 – 1.24 (m, 40H), 0.88 (t, J = 7.0 Hz, 9H).

MS (ES+) m/z): 798.7$(M+H)^+$.

Preparation Example 33: Preparation of Compound 66

Step 1: Preparation of 66-1

Reaction scheme:



Material ratio:

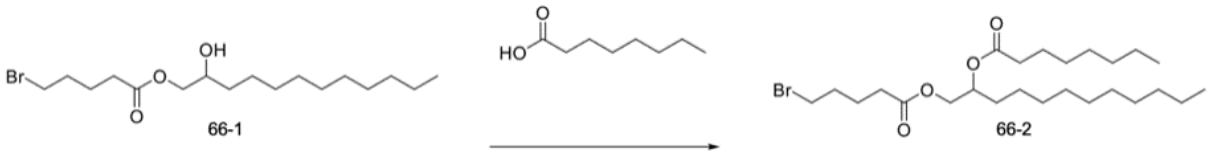
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-bromovaleric acid	181	1 eq	18.1 g	100
1,2-epoxydodecane	184	1 eq	18.4 g	100
ferric chloride	162	0.05 eq	800 mg	5
pyridine	79	0.025 eq	200 mg	2.5

Procedure:

To the reaction flask, 5-bromovaleric acid, 1,2-epoxydodecane, pyridine, and ferric chloride were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.4, TLC (PE:EA=4:1). After purification by column chromatography, 18 g of oily substance was obtained.

Step 2: Preparation of 66-2

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
66-1	365	1 eq	11 g	30
octanoic acid	144	1 eq	4.4 g	30
EDCI	192	1.5 eq	5.8 g	45
DMAP	122	0.15 eq	400 mg	4.5
DCM	-	-	100 mL	-

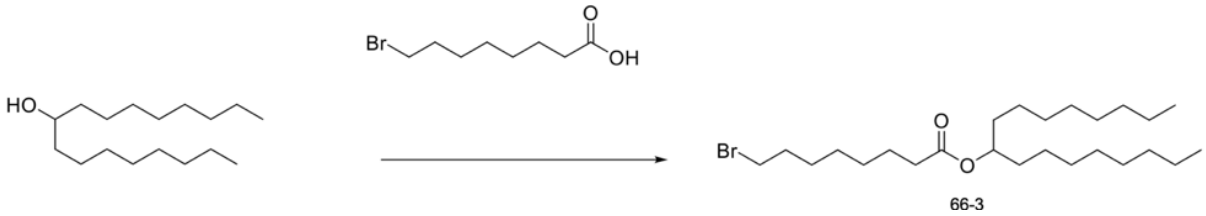
Procedure:

To the reaction flask, 66-1, octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.5, TLC

(PE:EA=10:1). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 8 g of oily substance was obtained.

Step 3: Preparation of 66-3

Reaction scheme:



Material ratio:

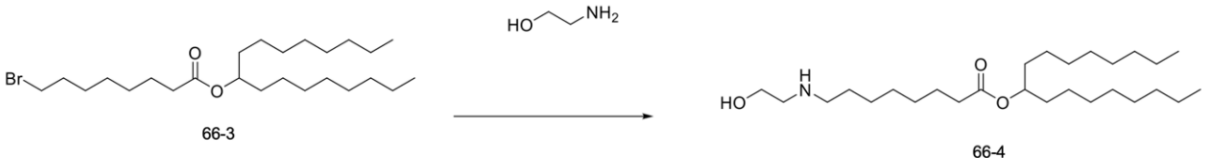
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
8-bromooctanoic acid	223	1 eq	7 g	30
9-heptadecanol	256	1 eq	7.7 g	30
EDCI	192	1.5 eq	5.8 g	45
DMAP	122	0.15 eq	400 mg	4.5
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 8-bromooctanoic acid, 9-heptadecanol, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.5, TLC (PE:EA=10:1). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 10.8 g of oily substance was obtained.

Step 4: Preparation of 66-4

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
66-3	461	1 eq	9.2 g	20
ethanolamine	61	1 eq	6.1 g	100
acetonitrile	-	-	80 mL	-

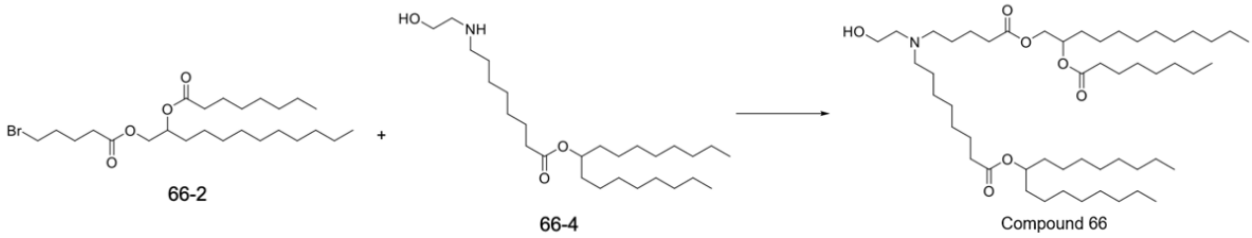
Procedure:

To the reaction flask, 66-3, ethanolamine, and acetonitrile were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value

was 0.3. The reaction mixture was diluted with 200 mL of ethyl acetate, and washed twice with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 5.6 g of a colorless oily substance was obtained.

Step 5: Preparation of Compound 66

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
66-4	441	1 eq	2.2 g	5
66-2	491	1.1 eq	2.7 g	5.5
potassium carbonate	138	1.5 eq	1 g	7.5
potassium iodide	166	0.5 eq	420 mg	2.5
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 66-2, 66-4, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was reacted at 65 ℃ for 16 h. The product rR value was 0.6, TLC (DCM:MeOH=20:1). The reaction mixture was diluted with 100 mL of ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 1.8 g of oily substance was obtained.

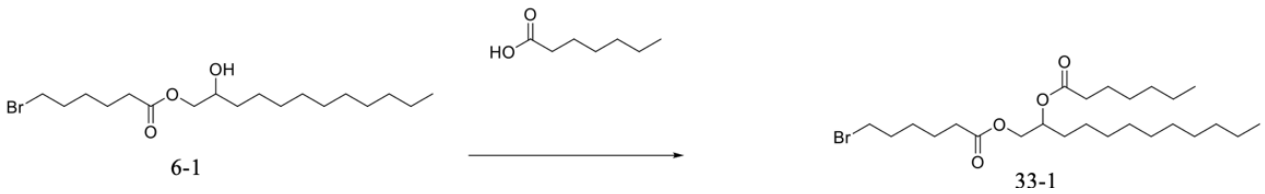
^{1}H NMR (600 MHz, Chloroform-d) δ 5.10 – 5.05 (m, 1H), 4.86 (p, J = 6.2 Hz, 1H), 4.23 (dd, J = 11.8, 3.3 Hz, 1H), 4.01 (dd, J = 11.8, 6.9 Hz, 1H), 3.55 (t, J = 5.3 Hz, 2H), 2.60 (t, J = 5.3 Hz, 2H), 2.48 (dt, J = 16.5, 7.5 Hz, 4H), 2.29 (dq, J = 22.5, 7.4 Hz, 6H), 1.65 – 1.53 (m, 8H), 1.47 (dq, J = 33.8, 8.0, 7.4 Hz, 8H), 1.32 – 1.23 (m, 55H), 0.87 (td, J = 7.3, 6.8, 1.9 Hz, 12H).

MS (ES+) m/z): 853.7$(M+H)^+$.

Preparation Example 34: Preparation of Compound 33

Step 1: Preparation of Compound 33-1

Reaction scheme:



Material ratio:

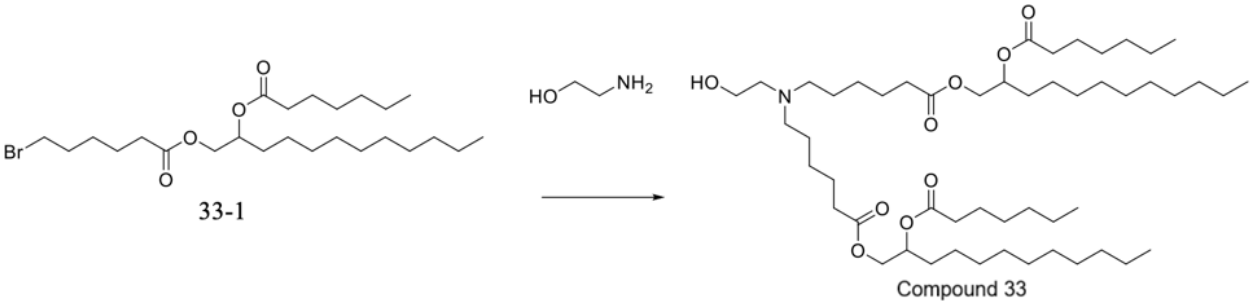
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-1	379.38	1 eq	6.9 g	18.2
n-heptanoic acid	130	1 eq	2.37 g	18.2
EDCI	192	1.5 eq	5.2 g	27
DMAP	122	0.15 eq	330 mg	2.7
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 6-1, n-heptanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.5, TLC (PE:EA=10:1). The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 5.6 g of oily substance was obtained.

Step 2: Preparation of Compound 33

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
33-1	491.55	2.2 eq	2 g	4.19
ethanolamine	61	1 eq	116 mg	1.9
potassium carbonate	138	3 eq	800 mg	5.7
potassium iodide	166	1 eq	320 mg	1.9
acetonitrile	-	-	30 mL	-

Procedure:

To the reaction flask, 33-1, ethanolamine, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was stirred and reacted at 65 ℃ for 16 h. The product rR value was 0.6, TLC (DCM:MeOH=10:1). The reaction mixture was diluted with 100 mL of

ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 1 g of oily substance was obtained.

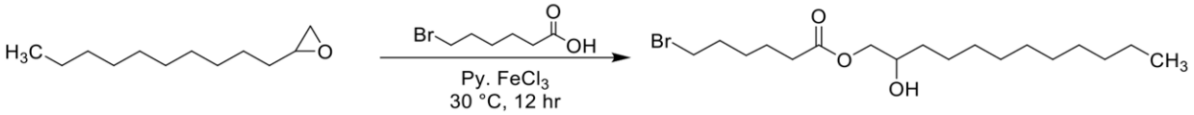
^{1}H NMR (400 MHz, Chloroform-d) δ 5.08 (qd, J = 6.7, 3.3 Hz, 2H), 4.22 (dd, J = 11.8, 3.3 Hz, 2H), 4.02 (dd, J = 11.8, 6.8 Hz, 2H), 3.54 (t, J = 5.3 Hz, 2H), 2.58 (t, J = 5.3 Hz, 2H), 2.46 (t, J = 7.5 Hz, 4H), 2.34 – 2.26 (m, 8H), 1.61 (tdd, J = 16.0, 13.8, 7.9, 4.6 Hz, 12H), 1.46 (p, J = 7.6 Hz, 4H), 1.34 – 1.21 (m, 48H), 0.88 (td, J = 6.9, 2.8 Hz, 12H).

MS (ES+) m/z): 882.6$(M+H)^+$.

Preparation Example 35: Preparation of Compound 35

Step 1: Synthesis of 2-hydroxydodecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

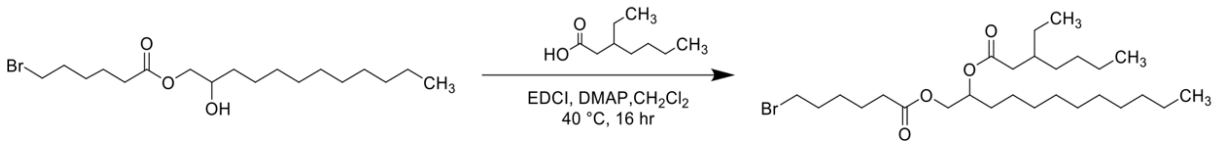
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-decyloxirane	184	1.0 eq	4.00 g	21.7
6-bromohexanoic acid	195	1.05 eq	4.44 g	22.7
pyridine	79.1	0.025 eq	42.9 mg	0.542
ferric chloride	162	0.025 eq	88.0 mg	0.542

Procedure:

6-bromohexanoic acid (4.44 g, 22.7 mmol) was dissolved in 2-decyloxirane (4.00 g, 21.7 mmol), and pyridine (42.9 mg, 0.542 mmol) and ferric chloride (88.0 mg, 0.542 mmol) were added. The mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 2-hydroxydodecyl 6-bromohexanoate as a white solid (5.50 g, 66.8% yield).

Step 2: Synthesis of 1-[(6-bromohexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

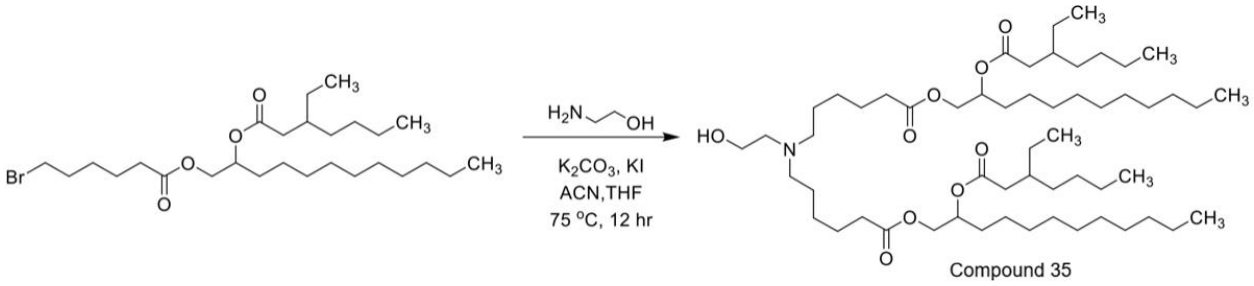
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxydodecyl 6-bromohexanoate	379	1.0 eq	1.20 g	3.16
3-ethylheptanoic acid	158	1.0 eq	500 mg	3.16
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	909 mg	4.74
4-dimethylaminopyridine	122	0.2 eq	77.3 mg	0. 632
tetrahydrofuran	-	-	12 mL	-

Procedure:

2-hydroxydodecyl 6-bromohexanoate (1.20 g, 3.16 mmol) and 3-ethylheptanoic acid (500 mg, 3.16 mmol) were dissolved in tetrahydrofuran (12 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (909 mg, 4.74 mmol) and 4-dimethylaminopyridine (77.3 mg, 0.632 mmol) were added sequentially. Finally, the mixture was reacted at 40 ℃ for 16 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 1-[(6-bromohexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate as a colorless liquid (1.1 g, 66.9% yield).

Step 3: Synthesis of 1-[(6-{[6-({2-[(3-Ethylheptanoyl)oxy]dodecyl}oxy)-6-oxohexyl](2-hydroxyethyl)amino}hexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate	520	1.0 eq	1.10 g	2.12
2-aminoethan-1-ol	61.0	0.48 eq	62.0 mg	1.02
potassium carbonate	138	3.0 eq	877 mg	6.35
potassium iodide	166	1.2 eq	421 mg	2.54
acetonitrile	-	-	6 mL	-
tetrahydrofuran	-	-	6 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate (1.10 g, 2.12 mmol) was dissolved in acetonitrile (6 mL), and 2-aminoethan-1-ol (62.0 mg, 1.02 mmol), potassium carbonate (877 mg, 6.35 mmol), potassium iodide (421 mg, 2.54 mmol), and tetrahydrofuran (6 mL) were added sequentially. Finally, the mixture was reacted at 70 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-[(6-{[6-({2-[(3-ethylheptanoyl)oxy]dodecyl}oxy)-6-oxohexyl](2-hydroxyethyl)amino}hexanoyl)oxy]dodecan-2-yl 3-ethylheptanoate as a yellow liquid was obtained (320 mg, 13.6% yield).

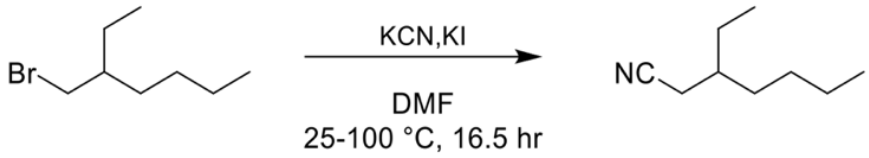
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.15 - 5.05 (m, 2H), 4.23 (dd, J = 3.2, 12.0 Hz, 2H), 4.02 (dd, J = 6.8, 12.0 Hz, 2H), 3.53 (br t, J = 5.2 Hz, 2H), 2.62 - 2.54 (m, 2H), 2.46 (br t, J = 7.2 Hz, 4H), 2.31 (t, J = 7.6 Hz, 4H), 2.25 (d, J = 6.8 Hz, 4H), 1.86 - 1.74 (m, 2H), 1.69 - 1.60 (m, 9H), 1.50 - 1.43 (m, 4H), 1.40 - 1.20 (m, 54H), 0.95 - 0.81 (m, 18H).

LCMS: RT = 2.297, m/z 994.9 $[M+H]^+$.

Preparation Example 36: Preparation of Compound 36

Step 1: Synthesis of 3-ethylheptanenitrile

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-(bromomethyl)heptane	192	1.0 eq	19.0 g	98.3
potassium cyanide	64.9	1.5 eq	9.61 g	147
potassium iodide	165	0.10 eq	1.63 g	9.84
N,N-dimethylformamide	-	-	190 mL	-

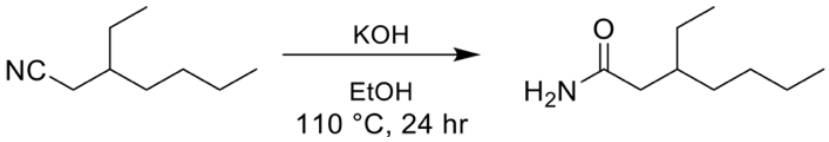
Procedure:

Potassium cyanide (9.61 g, 147 mmol) was dissolved in N,N-dimethylformamide (90 mL), and the mixture was reacted at 25 ℃ for 0.5 hours. At 25 ℃, 3-(bromomethyl)heptane (19.0 g, 98.3 mmol) was dissolved in N,N-dimethylformamide (100 mL) and added dropwise to the reaction mixture. Potassium iodide (1.63 g, 9.84 mmol) was added to the reaction mixture, and the mixture was reacted at 100 ℃ for 16 hours under nitrogen protection. TLC monitored the

generation of a new spot. 1000 mL of water was added, and the mixture was extracted twice with petroleum ether, 500 mL each time. The organic phase was concentrated, and after purification by column chromatography, 3-ethylheptanenitrile as a colorless liquid was obtained (1.67 g, 12.1% yield).

Step 2: Synthesis of 3-ethylheptanamide

Reaction scheme:



Material ratio:

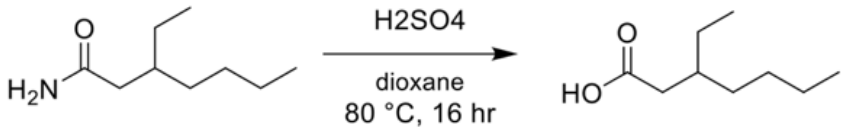
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-ethylheptanenitrile	139	1.0 eq	1.67 g	11.9
potassium hydroxide	55.9	3.0 eq	2.02 g	35.9
ethanol	-	-	16 mL	-

Procedure:

3-ethylheptanenitrile (1.67 g, 11.9 mmol) was dissolved in ethanol (16 mL), and potassium hydroxide (2.02 g, 2.5 M, 35.9 mmol) was added. The mixture was reacted at 110 ℃ for 24 hours under nitrogen protection. TLC monitored the generation of a new spot. The mixture was concentrated to dryness, 10 mL of water was added, and the mixture was extracted twice with dichloromethane, 50 mL each time. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 3-ethylheptanamide as a white solid (680 mg, 36.0% yield).

Step 3: Synthesis of 3-ethylheptanoic acid

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
3-ethylheptanamide	157	1.0 eq	1.30 g	8.27
sulfuric acid	97.9	4.72 eq	3.83 g	39.0
dioxane	-	-	13 mL	-

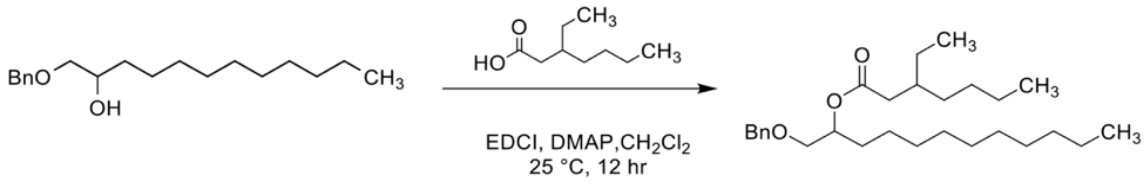
Procedure:

3-ethylheptanamide (1.30 g, 8.27 mmol) was dissolved in dioxane (13 mL), and sulfuric

acid (3.83 g, 3.0 M, 39.0 mmol) was added. The mixture was reacted at 80 ℃ for 16 hours under nitrogen protection. TLC monitored the generation of a new spot. The mixture was concentrated to dryness, extracted twice with dichloromethane, 50 mL each time. The organic phase was concentrated to obtain 3-ethylheptanoic acid as a white solid (1.31 g, 88.6% yield).

Step 4: Synthesis of 1-(benzyloxy)dodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

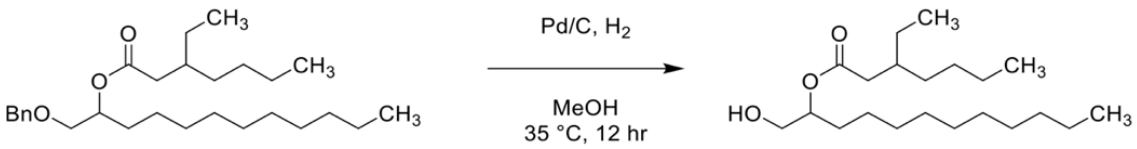
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-ol	292	1.2 eq	2.22 g	7.58
3-ethylheptanoic acid	158	1.0 eq	1.00 g	6.32
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	1.82 g	9.48
4-dimethylaminopyridine	122	0.1 eq	77.2 mg	0.631
dichloromethane	-	-	10 mL	-

Procedure:

1-(benzyloxy)dodecan-2-ol (2.22 g, 7.58 mmol) and 3-ethylheptanoic acid (1.00 g, 6.32 mmol) were dissolved in dichloromethane (10 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.82 g, 9.48 mmol) and 4-dimethylaminopyridine (77.2 mg, 0.631 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-2-yl 3-ethylheptanoate as a colorless liquid (2.15 g, 78.6% yield).

Step 5: Synthesis of 1-hydroxydodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

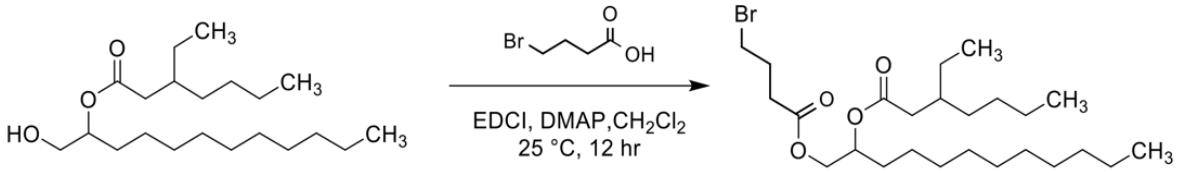
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-yl 3-ethylheptanoate	432	1.0 eq	2.15 g	4.97
Palladium on carbon	105.9	0.2 eq	1.06 g	0.993
Methanol	-	-	21 mL	-

Procedure:

1-(benzyloxy)dodecan-2-yl 3-ethylheptanoate (2.15 g, 4.97 mmol) was dissolved in methanol (21 mL), palladium on carbon (1.06 g, 0.993 mmol) was added, and the mixture was reacted at 35 ℃ and 40 Psi for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-hydroxydodecan-2-yl 3-ethylheptanoate as a colorless liquid was obtained (1.54 g, 90.4% yield).

Step 6: Synthesis of 1-[(4-bromobutanoyl)oxy]dodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 3-ethylheptanoate	342	1.0 eq	750 mg	2.19
4-bromobutanoic acid	167	1.1 eq	402 mg	2.41
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	629 mg	3.28
4-dimethylaminopyridine	122	0.1 eq	26.7 mg	0.218
dichloromethane	-	-	8 mL	-

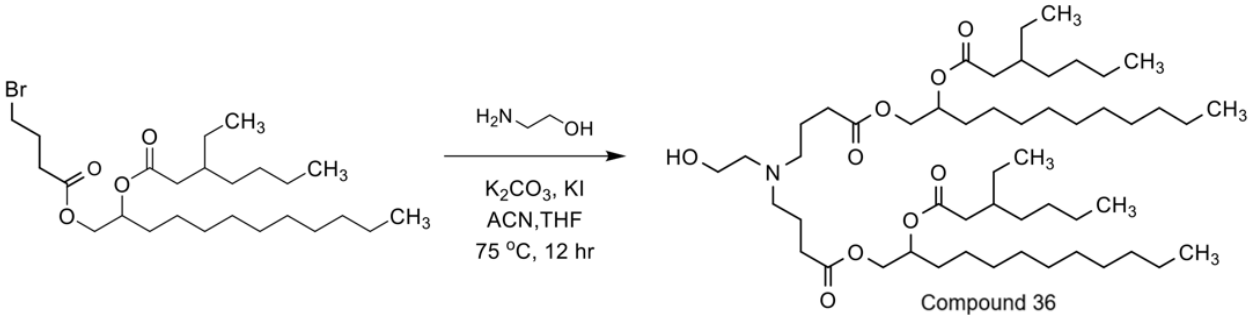
Procedure:

1-hydroxydodecan-2-yl 3-ethylheptanoate (750 mg, 2.19 mmol) and 4-bromobutanoic acid (402 mg, 2.41 mmol) were dissolved in dichloromethane (8 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (629 mg, 3.28 mmol) and 4-dimethylaminopyridine (26.7 mg, 0.218 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 1-[(4-bromobutanoyl)oxy]dodecan-2-yl 3-ethylheptanoate as a

colorless liquid (850 mg, 78.9% yield).

Step 7: Synthesis of 1-[(4-{[4-({2-[(3-ethylheptanoyl)oxy]dodecyl}oxy)-4-oxobutyl](2-hydroxyethyl)amino}butanoyl)oxy]dodecan-2-yl 3-ethylheptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(4-bromobutanoyl)oxy]dodecan-2-yl 3-ethylheptanoate	491	1.0 eq	750 mg	1.53
2-aminoethan-1-ol	61.0	0.45 eq	41.9 mg	0.686
potassium carbonate	138	3.0 eq	632 mg	4.58
potassium iodide	166	1.5 eq	379 mg	2.29
acetonitrile	-	-	7 mL	-
tetrahydrofuran	-	-	3 mL	-

Procedure:

1-[(4-bromobutanoyl)oxy]dodecan-2-yl 3-ethylheptanoate (750 mg, 1.53 mmol) was dissolved in acetonitrile (7 mL), and 2-aminoethan-1-ol (41.9 mg, 0.686 mmol), potassium carbonate (632 mg, 4.58 mmol), potassium iodide (379 mg, 2.29 mmol), and tetrahydrofuran (3 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-[(4-{[4-({2-[(3-ethylheptanoyl)oxy]dodecyl}oxy)-4-oxobutyl](2-hydroxyethyl)amino}butanoyl)oxy]dodecan-2-yl 3-ethylheptanoate as a bright yellow liquid was obtained (340 mg, 24.0% yield).

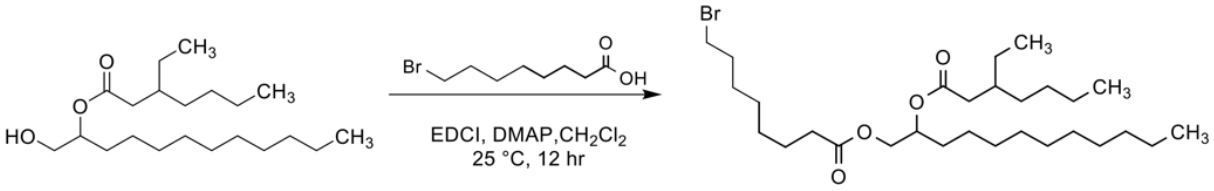
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.20 - 5.00 (m, 2H), 4.24 (dd, J = 3.2, 12.0 Hz, 2H), 4.01 (dd, J = 6.8, 12.0 Hz, 2H), 3.62 - 3.50 (m, 2H), 2.61 (br s, 2H), 2.51 (br t, J = 6.8 Hz, 4H), 2.32 (t, J = 7.2 Hz, 4H), 2.25 (d, J = 6.8 Hz, 4H), 1.84 - 1.74 (m, 6H), 1.59 (br s, 13H), 1.33 - 1.26 (m, 40H), 0.95 - 0.84 (m, 18H).

LCMS: RT = 2.213, m/z 882.7 $[M+H]^+$.

Preparation Example 37: Preparation of Compound 37

Step 1: Synthesis of 2-[(3-ethylheptanoyl)oxy]dodecyl 8-bromooctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 3-ethylheptanoate	342	1.0 eq	750 mg	2.19
8-bromooctanoic acid	222	1.1 eq	537 mg	2.41
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	629 mg	3.28
4-dimethylaminopyridine	122	0.1 eq	26.7 mg	0.218
dichloromethane	-	-	8 mL	-

Procedure:

1-hydroxydodecan-2-yl 3-ethylheptanoate (750 mg, 2.19 mmol) and 8-bromooctanoic acid (537 mg, 2.41 mmol) were dissolved in dichloromethane (8 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (629 mg, 3.28 mmol) and 4-dimethylaminopyridine (26.7 mg, 0.218 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 2-[(3-ethylheptanoyl)oxy]dodecyl 8-bromooctanoate as a colorless liquid (1.15 g, 95.9% yield).

Step 2: Synthesis of 2-[(3-ethylheptanoyl)oxy]dodecyl 8-{[8-({2-[(3-ethylheptanoyl)oxy]dodecyl}oxy)-8-oxooctyl](2-hydroxyethyl)amino}octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-[(3-ethylheptanoyl)oxy]dodecyl 8-bromooctanoate	546	1.0 eq	1.00 g	1.83
2-aminoethan-1-ol	61.0	0.50 eq	55.7 mg	0.913
potassium carbonate	138	3.0 eq	757 mg	5.48
potassium iodide	166	1.5 eq	454 mg	2.74
acetonitrile	-	-	7 mL	-
tetrahydrofuran	-	-	3 mL	-

Procedure:

2-[(3-ethylheptanoyl)oxy]dodecyl 8-bromooctanoate (1.00 g, 1.83 mmol) was dissolved in acetonitrile (7 mL), and 2-aminoethan-1-ol (55.7 mg, 0.913 mmol), potassium carbonate (757 mg, 5.48 mmol), potassium iodide (454 mg, 2.74 mmol), and tetrahydrofuran (3 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-[(3-ethylheptanoyl)oxy]dodecyl 8-{[8-({2-[(3-ethylheptanoyl)oxy]dodecyl}oxy)-8-oxooctyl](2-hydroxyethyl)amino}octanoate as a yellow liquid was obtained (656 mg, 34.6% yield).

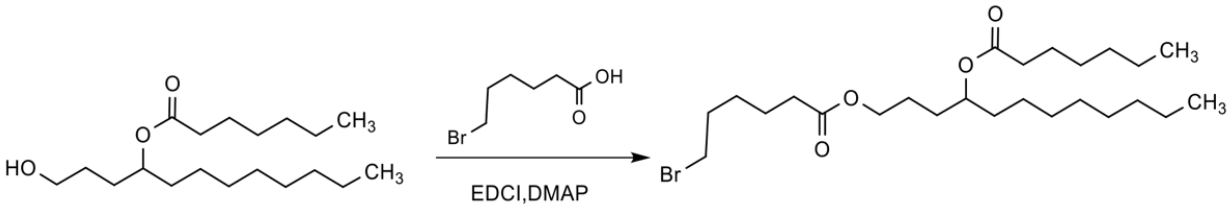
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.16 - 5.03 (m, 2H), 4.23 (dd, J = 3.2, 12.0 Hz, 2H), 4.02 (dd, J = 6.8, 11.6 Hz, 2H), 3.64 - 3.54 (m, 2H), 2.65 (br s, 2H), 2.52 (br s, 3H), 2.30 (t, J = 7.6 Hz, 4H), 2.25 (d, J = 6.8 Hz, 4H), 1.85 - 1.74 (m, 3H), 1.61 (br s, 8H), 1.52 - 1.42 (m, 6H), 1.37 - 1.22 (m, 60H), 0.96 - 0.82 (m, 18H).

LCMS: RT = 2.297, m/z 994.9 $[M+H]^+$.

Preparation Example 38: Preparation of Compound 47

Step 1: Synthesis of 1-[(6-bromohexanoyl)oxy]dodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

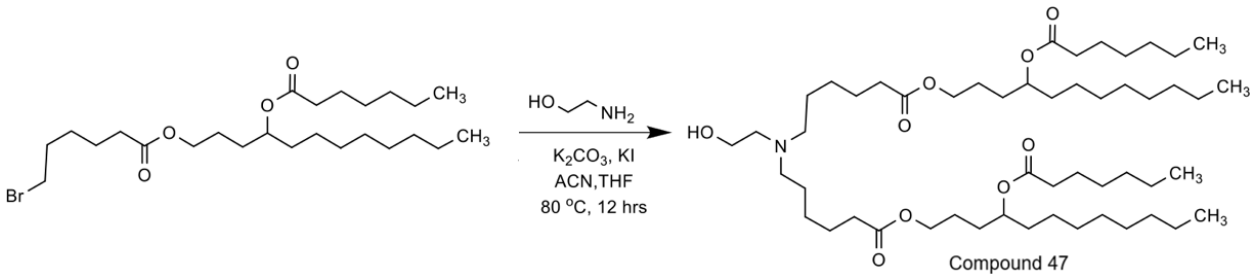
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-4-yl heptanoate	314	1.00 eq	1.60 g	5.09
6-bromohexanoic acid	193	1.20 eq	1.19 g	6.10
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.50 eq	1.46 g	7.63
4-dimethylaminopyridine	122	0.10 eq	62.1 mg	0.508
dichloromethane	-	-	16.0 mL	-

Procedure:

1-hydroxydodecan-4-yl heptanoate (1.60 g, 5.09 mmol) and 6-bromohexanoic acid (1.19 g, 6.10 mmol) were dissolved in dichloromethane (16.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.46 g, 7.63 mmol) and 4-dimethylaminopyridine (62.1 mg, 508 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. 100 mL of water was added, and the mixture was extracted twice with dichloromethane, 100 mL each time. The organic phase was concentrated. After purification by column chromatography, 1-[(6-bromohexanoyl)oxy]dodecan-4-yl heptanoate as a bright yellow liquid was obtained (1.70 g, 67.9% yield).

Step 2: Synthesis of 1-({6-[(6-{[4-(heptanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoyl}oxy)dodecan-4-yl heptanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]dodecan-4-yl heptanoate	490	1.00 eq	1.00 g	2.03
ethanolamine	61	0.48 eq	59.6 mg	0.976
potassium carbonate	138	3.50 eq	984 mg	7.12
potassium iodide	166	1.20 eq	405 mg	2.44
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]dodecan-4-yl heptanoate (1.00 g, 2.03 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (59.6 mg, 976 μmol), potassium carbonate (984 mg, 7.12 mmol), potassium iodide (405 mg, 2.44 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({6-[(6-{[4-(heptanoyloxy)dodecyl]oxy}-6-oxohexyl)(2-hydroxyethyl)amino]hexanoyl}oxy)dodecan-4-yl heptanoate as a colorless liquid was obtained (608 mg, 32.7% yield).

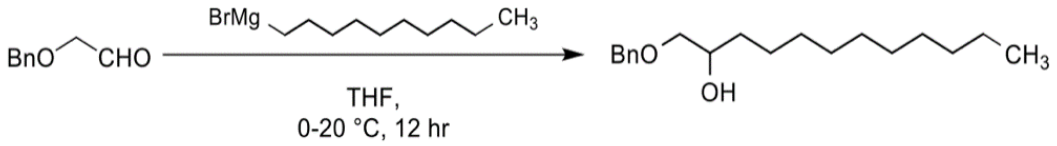
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 4.90 (quin, J = 6.0 Hz, 2H), 4.17 - 3.93 (m, 4H), 3.56 (t, J = 5.2 Hz, 2H), 2.62 (br t, J = 5.2 Hz, 2H), 2.50 (br t, J = 7.4 Hz, 4H), 2.30 (dt, J1 = 4.8, J2 =7.6 Hz, 8H), 1.67 - 1.47 (m, 24H), 1.34 - 1.16 (m, 40H), 0.98 - 0.76 (m, 12H)ppm.

LCMS: RT = 2.059, m/z 882 $[M+H]^+$.

Preparation Example 39: Preparation of Compound 49

Step 1: Synthesis of 1-(benzyloxy)dodecan-2-ol

Reaction scheme:



Material ratio:

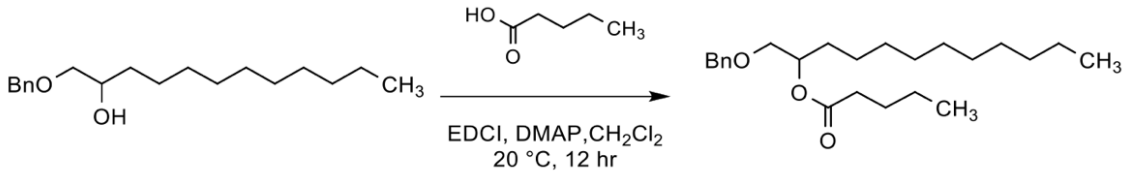
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(benzyloxy)acetaldehyde	150	1.0 eq	5.0 g	33.29
bromo(decyl)magnesium	244	1.2 eq	9.81 g	39.95
tetrahydrofuran	-	-	50 mL	-

Procedure:

2-(benzyloxy)acetaldehyde (5.0 g, 33.29 mmol) was dissolved in tetrahydrofuran (50 mL), and bromo(decyl)magnesium (9.81 g, 0.5 M, 79.91 Ml, 19.06 mmol) was added at 0 ℃. The mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. 50 mL of an aqueous ammonium chloride solution was added, and the mixture was extracted twice with ethyl acetate, 200 mL each time. The organic phase was concentrated, and after purification by column chromatography, 1-(benzyloxy)dodecan-2-ol as a colorless liquid was obtained (7.5 g, 77.0% yield).

Step 2: Synthesis of 1-(benzyloxy)dodecan-2-yl pentanoate

Reaction scheme:



Material ratio:

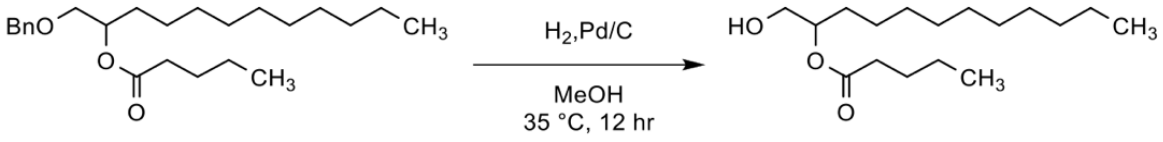
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-ol	292	1.0 eq	4.0 g	13.6
pentanoic acid	102	1.5 eq	2.10 g	20.5
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.5 eq	3.93 g	20.5
4-dimethylaminopyridine	122	0.1 eq	167 mg	1.37
dichloromethane	-	-	40 mL	-

Procedure:

1-(benzyloxy)dodecan-2-ol (4.0 g, 13.6 mmol) and pentanoic acid (2.10 g, 20.5 mmol) were dissolved in dichloromethane (40 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (3.93 g, 20.5 mmol) and 4-dimethylaminopyridine (167 mg, 1.37 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-2-yl pentanoate as a colorless liquid (3.8 g, 73.7% yield).

Step 3: Synthesis of 1-hydroxydodecan-2-yl pentanoate

Reaction scheme:



Material ratio:

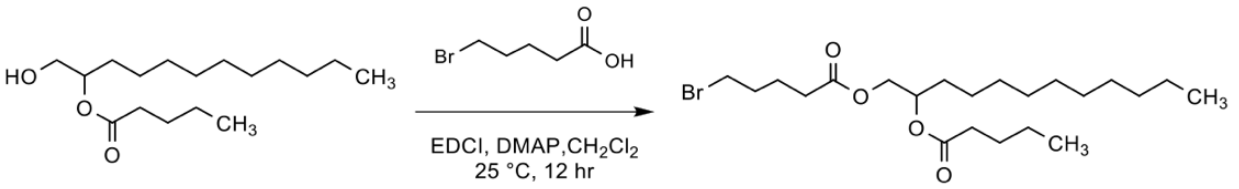
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-yl pentanoate	376	1.0 eq	3.80 g	10.0
palladium on carbon	105.9	0.2 eq	2.15 g	2.02
methanol	-	-	40 mL	-

Procedure:

1-(benzyloxy)dodecan-2-yl pentanoate (3.80 g, 10.0 mmol) was dissolved in methanol (40 mL), palladium on carbon (2.15 g, 2.02 mmol) was added, and the mixture was reacted at 35 ℃ and 40 Psi for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-hydroxydodecan-2-yl pentanoate as a colorless liquid was obtained (2.00 g, 69.1% yield).

Step 4: Synthesis of 2-(pentanoyloxy)dodecyl 5-bromopentanoate

Reaction scheme:



Material ratio:

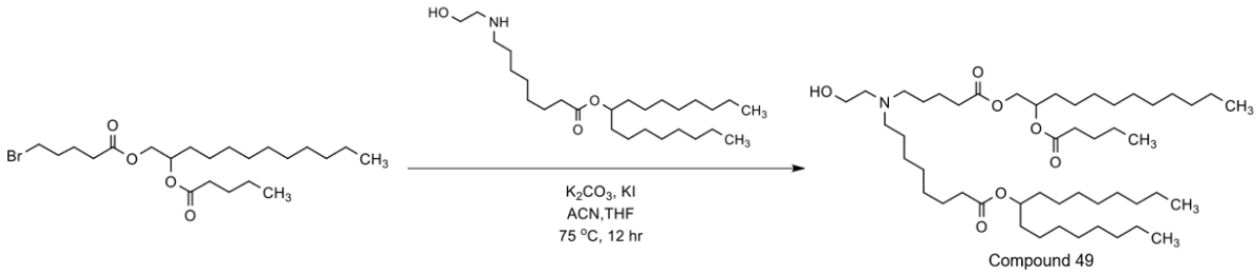
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl pentanoate	286	1.0 eq	1.00 g	3.49
5-bromovaleric acid	181	1.2 eq	758 mg	4.19
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	1.00 g	5.24
4-dimethylaminopyridine	122	0.1 eq	42.6 mg	0.349
dichloromethane	-	-	20 mL	-

Procedure:

1-hydroxydodecan-2-yl pentanoate (1.00 g, 3.49 mmol) and 5-bromovaleric acid (758 mg, 4.19 mmol) were dissolved in dichloromethane (80 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.00 g, 5.24 mmol) and 4-dimethylaminopyridine (42.6 mg, 0.349 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(pentanoyloxy)dodecyl 5-bromopentanoate as a colorless liquid (1.40 g, 89.2% yield).

Step 5: Synthesis of heptadecan-9-yl 8-[(2-hydroxyethyl)(5-oxo-5-{[2-(pentanoyloxy)dodecyl]oxy}pentyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(pentanoyloxy)dodecyl 5-bromopentanoate	449	1.1 eq	1.12 g	2.49
heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate	441	1.0 eq	1.00 g	2.26
potassium carbonate	138	3.5 eq	1.10 g	7.92
potassium iodide	166	1.2 eq	450 mg	2.72
acetonitrile	-	-	8 mL	-
tetrahydrofuran	-	-	2 mL	-

Procedure:

2-(pentanoyloxy)dodecyl 5-bromopentanoate (1.12 g, 2.49 mmol) was dissolved in acetonitrile (8 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (1.00 g, 2.26 mmol), potassium carbonate (1.10 g, 7.92 mmol), potassium iodide (450 mg, 2.72 mmol), and tetrahydrofuran (2 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(2-hydroxyethyl)(5-oxo-5-{[2-(pentanoyloxy)dodecyl]oxy}pentyl)amino]octanoate as a yellow liquid was obtained (1.00 g, 50.2% yield).

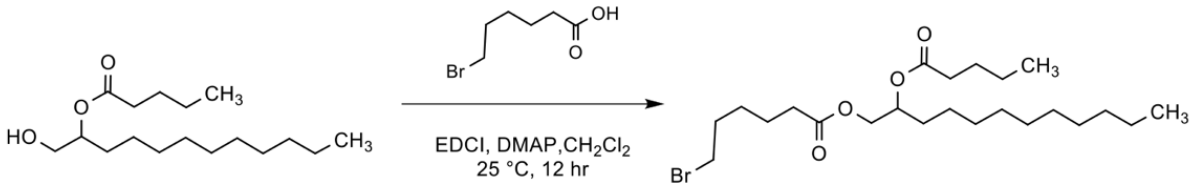
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.11 (dq, J = 3.2, 6.8 Hz, 1H), 4.88 (quin, J = 6.4 Hz, 1H), 4.26 (dd, J = 3.2, 12.0 Hz, 1H), 4.04 (dd, J = 6.8, 12.0 Hz, 1H), 3.58 (br t, J = 5.2 Hz, 2H), 2.63 (br t, J = 5.2 Hz, 2H), 2.56 - 2.47 (m, 4H), 2.32 (dt, J = 7.2, 13.2 Hz, 6H), 1.63 (quin, J = 7.6 Hz, 7H), 1.59 - 1.44 (m, 10H), 1.42 - 1.23 (m, 48H), 0.99 - 0.85 (m, 12H).

LCMS: RT = 2.146, m/z 810.7 $[M+H]^+$.

Preparation Example 40: Preparation of Compound 50

Step 1: Synthesis of 2-(pentanoyloxy)dodecyl 6-bromohexanoate

Reaction scheme:



Material ratio:

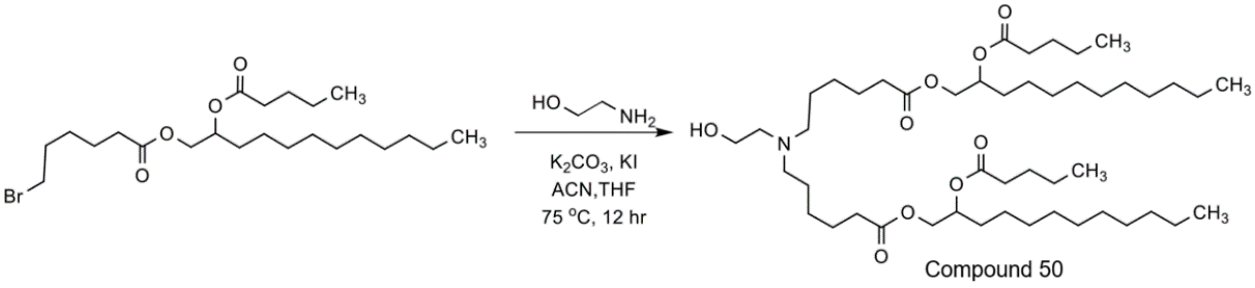
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl pentanoate	286	1.0 eq	1.0 g	3.49
6-bromohexanoic acid	195	1.2 eq	817 mg	4.19
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	1.00 g	5.24
4-dimethylaminopyridine	122	0.1 eq	42.65 mg	0.349 μmol
dichloromethane	-	-	20 mL	-

Procedure:

1-hydroxydodecan-2-yl pentanoate (1.00 g, 3.49 mmol) and 6-bromohexanoic acid (817 mg, 4.19 mmol) were dissolved in dichloromethane (20 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.00 g, 5.24 mmol) and 4-dimethylaminopyridine (42.6 mg, 0.349 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(pentanoyloxy)dodecyl 6-bromohexanoate as a colorless liquid (1.5 g, 92.7% yield).

Step 2: Synthesis of 2-(pentanoyloxy)dodecyl 6-[(2-hydroxyethyl)(6-oxo-6-{[2-(pentanoyloxy)dodecyl]oxy}hexyl)amino]hexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(pentanoyloxy)dodecyl 6-bromohexanoate	463	1.0 eq	1.40 g	3.02
ethanolamine	61.0	0.45 eq	83.0 mg	1.36
potassium carbonate	138	3.5 eq	1.25 g	9.06
potassium iodide	166	1.2 eq	752 mg	4.53
acetonitrile	-	-	10 mL	-
tetrahydrofuran	-	-	4mL	-

Procedure:

2-(pentanoyloxy)dodecyl 6-bromohexanoate (1.40 g, 3.02 mmol) was dissolved in acetonitrile (10 mL), and ethanolamine (83.0 mg, 1.36 mmol), potassium carbonate (1.25 g, 9.06 mmol), potassium iodide (752 mg, 4.53 mmol), and tetrahydrofuran (4 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(pentanoyloxy)dodecyl 6-[(2-hydroxyethyl)(6-oxo-6-{[2-(pentanoyloxy)dodecyl]oxy}hexyl)amino]hexanoate as a yellow liquid was obtained (670 mg, 25.2% yield).

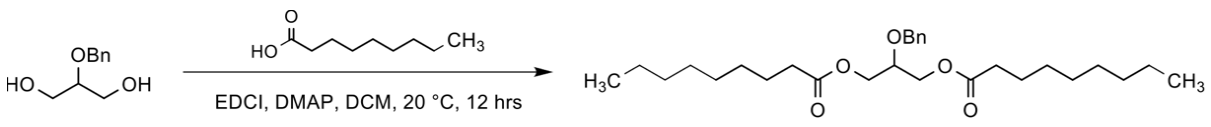
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.17 - 5.05 (m, 2H), 4.25 (dd, J = 3.2, 12.0 Hz, 2H), 4.04 (dd, J = 6.8, 12.0 Hz, 2H), 3.61 (br s, 2H), 2.67 (br s, 2H), 2.56 (br d, J = 6.4 Hz, 4H), 2.33 (t, J = 7.6 Hz, 8H), 1.68 - 1.49 (m, 17H), 1.44 - 1.26 (m, 40H), 0.92 (td, J = 7.2, 16.4 Hz, 12H).

LCMS: RT = 2.013, m/z 826.5 $[M+H]^+$.

Preparation Example 41: Preparation of Compound 67

Step 1: Synthesis of 2-(benzyloxy)-3-(nonanoyloxy)propyl nonanoate

Reaction scheme:



Material ratio:

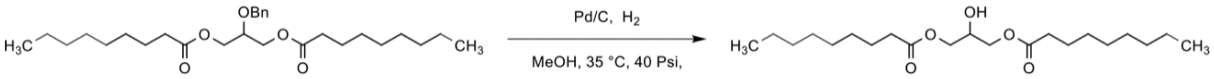
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(benzyloxy)propane-1,3-diol	182	1.0 eq	3.00 g	16.5
nonanoic acid	158	2.3 eq	5.99 g	37.9
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	2.5 eq	7.89 g	41.2
4-dimethylaminopyridine	122	0.2 eq	402 mg	3.29
dichloromethane	-	-	60 mL	-

Procedure:

2-(benzyloxy)propane-1,3-diol (3.00 g, 16.5 mmol) was dissolved in dichloromethane (60 mL), and nonanoic acid (5.99 g, 37.9 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (7.89 g, 41.2 mmol), and 4-dimethylaminopyridine (402 mg, 3.29 mmol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(benzyloxy)-3-(nonanoyloxy)propyl nonanoate as a colorless liquid (6.00 g, 78.8% yield).

Step 2: Synthesis of 2-hydroxy-3-(nonanoyloxy)propyl nonanoate

Reaction scheme:



Material ratio:

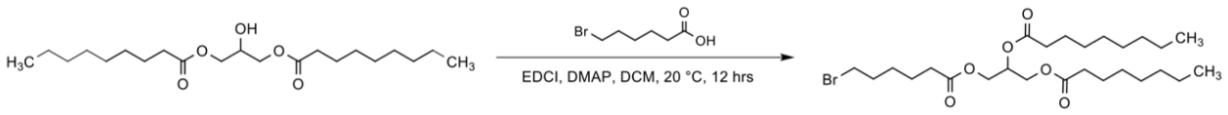
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(benzyloxy)-3-(nonanoyloxy)propyl nonanoate	463	1.0 eq	6.00 g	13.0
palladium/carbon（10%）	106	0.1 eq	1.38 g	1.30
hydrogen	-	(40 Psi)	-	-
methanol	-	-	50 mL	-
tetrahydrofuran	-	-	10 mL	-

Procedure:

2-(benzyloxy)-3-(nonanoyloxy)propyl nonanoate (6.00 g, 13.0 mmol) was dissolved in methanol (50 mL) and tetrahydrofuran (10 mL), palladium/carbon (1.38 g, 1.30 mmol) was added under a nitrogen atmosphere, and finally, the mixture was reacted at 35 ℃ for 12 hours under a hydrogen (40 Psi) atmosphere. TLC monitored that the reaction was complete, and the reaction mixture was filtered and concentrated. The crude product was subjected to column chromatography to obtain 2-hydroxy-3-(nonanoyloxy)propyl nonanoate as a colorless liquid (3.80 g, 78.7% yield).

Step 3: Synthesis of 1-[(6-bromohexanoyl)oxy]-3-(octanoyloxy)propan-2-yl nonanoate

Reaction scheme:



Material ratio:

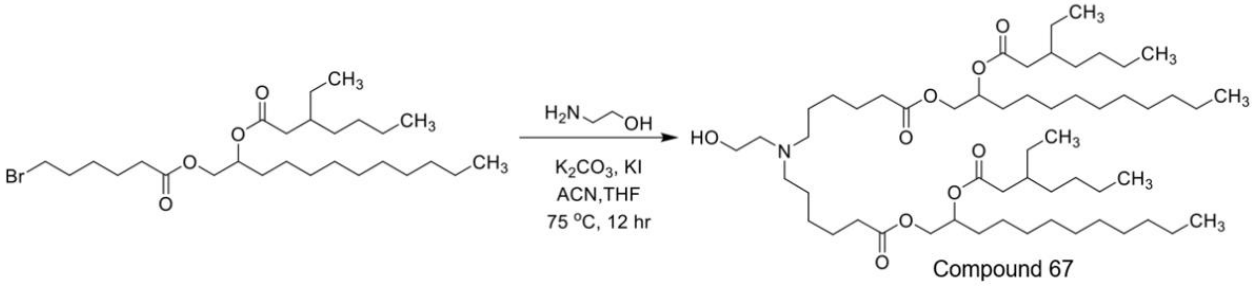
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxy-3-(nonanoyloxy)propyl nonanoate	372	1.0 eq	2.00 g	5.37
6-bromohexanoic acid	194	1.3 eq	1.36 g	6.98
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.54 g	8.05
4-dimethylaminopyridine	122	0.1 eq	65.6 mg	537 μmol
dichloromethane	-	-	20 mL	-

Procedure:

2-hydroxy-3-(nonanoyloxy)propyl nonanoate (2.00 g, 5.37 mmol) was dissolved in dichloromethane (20 mL), and 6-bromohexanoic acid (1.36 g, 6.98 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.54 g, 8.05 mmol), and 4-dimethylaminopyridine (65.6 mg, 537 μmol) were added sequentially. Finally, the mixture was reacted at 20 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(6-bromohexanoyl)oxy]-3-(octanoyloxy)propan-2-yl nonanoate as a colorless liquid (2.50 g, 87.0% yield).

Step 4: Synthesis of 1-{[6-({6-[2,3-bis(nonanoyloxy)propoxy]-6-oxohexyl}(2-hydroxyethyl)amino)hexanoyl]oxy}-3-(nonanoyloxy)propan-2-yl nonanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]-3-(octanoyloxy)propan-2-yl nonanoate	534	2.0 eq	2.50 g	4.67
ethanolamine	75	1.0 eq	175 mg	2.33
potassium carbonate	138	6.5 eq	2.10 g	15.2
potassium iodide	166	2.2 eq	852 mg	5.13
acetonitrile	-	-	25 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]-3-(octanoyloxy)propan-2-yl nonanoate (2.50 g, 4.67 mmol) was dissolved in acetonitrile (25 mL), and ethanolamine (175 mg, 2.33 mmol), potassium carbonate (2.10 g, 15.2 mmol), and potassium iodide (852 mg, 5.13 mmol) were added sequentially. Finally, the mixture was reacted at 70 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-{[6-({6-[2,3-bis(nonanoyloxy)propoxy]-6-oxohexyl}(2-hydroxyethyl)amino)hexanoyl]oxy}-3-(nonanoyloxy)propan-2-yl nonanoate as a pale yellow liquid was obtained (300 mg, 11.1% yield).

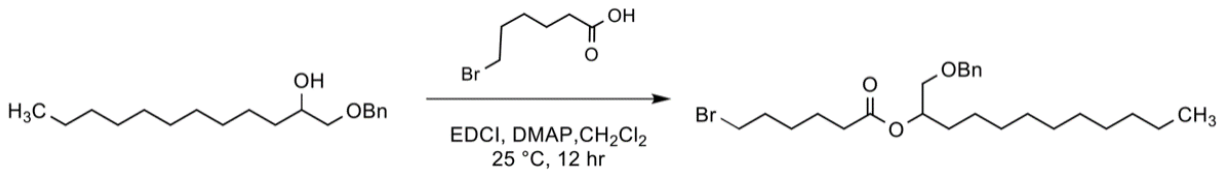
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.31 - 5.23 (m, 2H), 4.32 (dd, J = 4.4, 11.9 Hz, 4H), 4.16 (dd, J = 5.9, 11.9 Hz, 4H), 3.54 (t, J = 5.3 Hz, 2H), 2.59 (t, J = 5.4 Hz, 2H), 2.50 - 2.43 (m, 4H), 2.37 - 2.29 (m, 12H), 1.70 - 1.59 (m, 12H), 1.51 - 1.43 (m, 4H), 1.29 (br d, J = 5.3 Hz, 43H), 1.02 - 0.77 (m, 12H) ppm.

LCMS: RT = 2.135, m/z 824.6 $[M+H]^+$.

Preparation Example 42: Preparation of Compound 68

Step 1: Synthesis of 1-(benzyloxy)dodecan-2-yl 6-bromohexanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-ol	292	1.0 eq	2.50 g	8.55
6-bromohexanoic acid	102	1.2 eq	2.00 g	10.2
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	2.46 g	12.8
4-dimethylaminopyridine	122	0.1 eq	104 mg	0.854
dichloromethane	-	-	40 mL	-

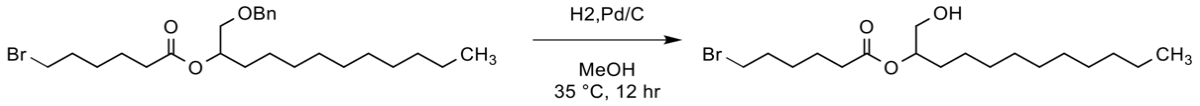
Procedure:

1-(benzyloxy)dodecan-2-ol (2.50 g, 8.55 mmol) and 6-bromohexanoic acid (2.00 g, 10.2 mmol) were dissolved in dichloromethane (40 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.46 g, 12.8 mmol) and 4-dimethylaminopyridine (104 mg, 0.854 mmol) were added sequentially. Finally, the mixture

was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-2-yl 6-bromohexanoate as a colorless liquid (3.18 g, 79.2% yield).

Step 2: Synthesis of 1-hydroxydodecan-2-yl 6-bromohexanoate

Reaction scheme:



Material ratio:

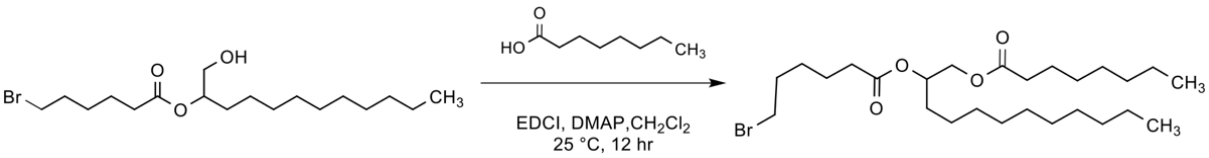
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-yl 6-bromohexanoate	469	1.0 eq	3.18 g	6.77
palladium on carbon	105.9	0.2 eq	1.44 g	1.35
methanol	-	-	32 mL	-

Procedure:

1-(benzyloxy)dodecan-2-yl 6-bromohexanoate (3.18 g, 6.77 mmol) was dissolved in methanol (32 mL), palladium on carbon (1.44 g, 1.35 mmol) was added, and the mixture was reacted at 35 ℃ and 40 Psi for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-hydroxydodecan-2-yl 6-bromohexanoate as a colorless liquid was obtained (1.88 g, 73.1% yield).

Step 3: Synthesis of 2-[(6-bromohexanoyl)oxy]dodecyl octanoate

Reaction scheme:



Material ratio:

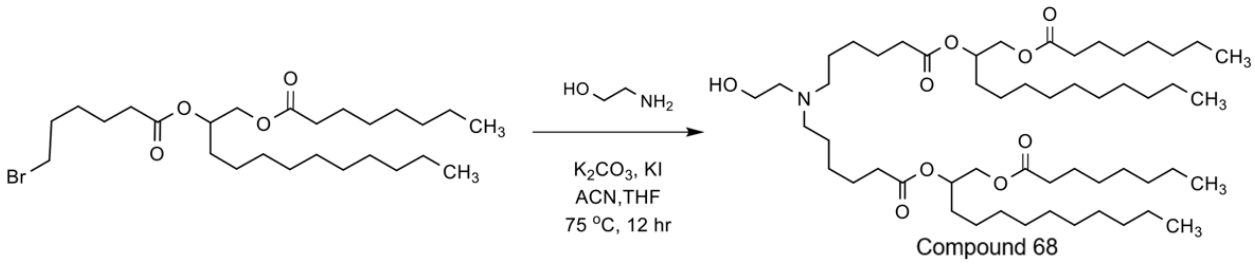
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 6-bromohexanoate	378	1.0 eq	1.88 g	4.96
octanoic acid	144	1.2 eq	857 mg	5.95
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	1.42 g	7.43
4-dimethylaminopyridine	122	0.1 eq	60.5 mg	0.495
dichloromethane	-	-	40 mL	-

Procedure:

1-hydroxydodecan-2-yl 6-bromohexanoate (1.88 g, 4.96 mmol) and octanoic acid (857 mg, 5.95 mmol) were dissolved in dichloromethane (40 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.42 g, 7.43 mmol) and 4-dimethylaminopyridine (60.5 mg, 0.495 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-[(6-bromohexanoyl)oxy]dodecyl octanoate as a colorless liquid (2.28 g, 91.0% yield).

Step 4: Synthesis of 2-({6-[(2-hydroxyethyl)(6-{[1-(octanoyloxy)dodecan-2-yl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecyl octanoate

Reaction scheme:



Compound 68

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-[(6-bromohexanoyl)oxy]dodecyl octanoate	504	1.0 eq	2.00 g	1.78
2-aminoethan-1-ol	61.0	0.45 eq	108 mg	3.96
potassium carbonate	138	3.0 eq	1.64 g	11.8
potassium iodide	166	1.5 eq	985 mg	5.93
acetonitrile	-	-	15 mL	-
tetrahydrofuran	-	-	5mL	-

Procedure:

2-[(6-bromohexanoyl)oxy]dodecyl octanoate (2.00 g, 1.78 mmol) was dissolved in acetonitrile (15 mL), and 2-aminoethan-1-ol (108 mg, 3.96 mmol), potassium carbonate (1.64 g, 11.8 mmol), potassium iodide (985 mg, 5.93 mmol), and tetrahydrofuran (5 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography,

2-({6-[(2-hydroxyethyl)(6-{[1-(octanoyloxy)dodecan-2-yl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecyl octanoate as a yellow liquid was obtained (840 mg, 20.6% yield).

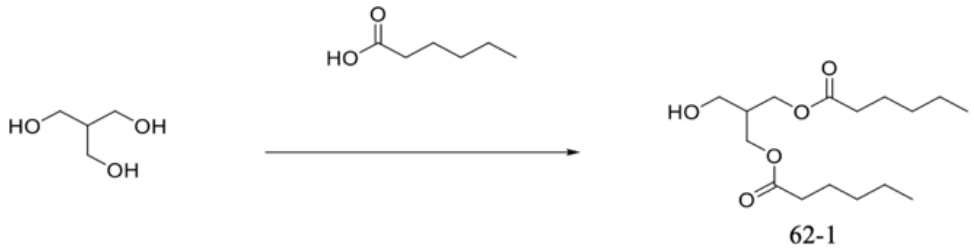
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (dq, J = 3.2, 6.4 Hz, 2H), 4.25 (dd, J = 3.2, 12.0 Hz, 2H), 4.05 (dd, J = 6.4, 12.0 Hz, 2H), 3.64 (br s, 2H), 2.71 (br s, 2H), 2.60 (br s, 4H), 2.33 (dt, J = 4.8, 7.6 Hz, 8H), 1.71 - 1.51 (m, 17H), 1.40 - 1.24 (m, 52H), 0.96 - 0.84 (m, 12H).

LCMS: RT = 2.128, m/z 910.8 $[M+H]^+$.

Preparation Example 43: Preparation of Compound 62

Step 1: Preparation of 62-1

Reaction scheme:



62-1

Material ratio:

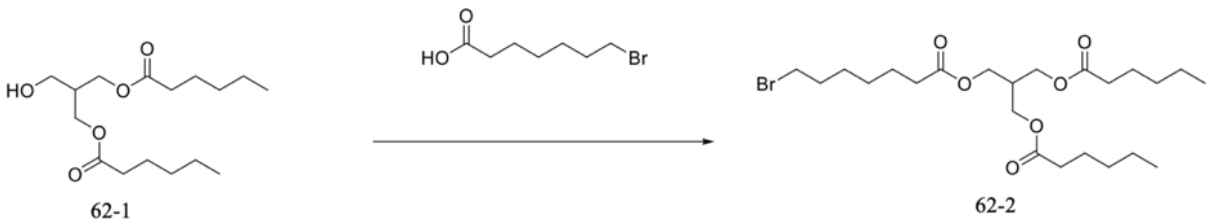
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-hydroxymethyl-1,3-propanediol	106	1 eq	3 g	30
hexanoic acid	116	2 eq	6.5 g	60
EDCI	192	2.5 eq	14 g	75
DMAP	122	0.25 eq	900 mg	7.5
DCM	-	-	200 mL	-

Procedure:

To the reaction flask, 2-hydroxymethyl-1,3-propanediol, hexanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.4, TLC (PE:EA=4:1). The reaction mixture was washed once with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 3.5 g of oily substance was obtained.

Step 2: Preparation of 62-2

Reaction scheme:



62-1 62-2

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
62-1	302	1.2 eq	3.5 g	11.6
7-bromoheptanoic acid	209	1 eq	2 g	9.7
EDCI	192	1.5 eq	3 g	15
DMAP	122	0.5 eq	200 mg	1.5
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 62-1, 7-bromoheptanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was washed once with 60 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, and concentrated. After purification by column chromatography, 4.2 g of oily substance was obtained.

Step 3: Preparation of Compound 62-3

Reaction scheme:



Material ratio:

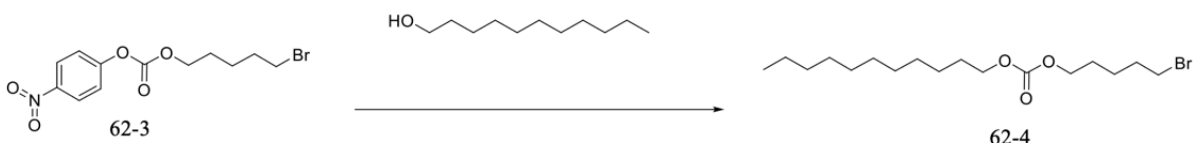
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-bromopentanol	167	1 eq	3.34 g	20
p-nitrophenyl chloroformate	201	1.2 eq	4.8 g	24
pyridine	79	1.5 eq	2.4 g	30
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 5-bromopentanol, p-nitrophenyl chloroformate, pyridine, and DCM were added, and the mixture was reacted at room temperature for 16 h. TLC (PE:EA=4:1), product Rf value was 0.6. After purification by column chromatography, 5.3 g of a colorless oily substance was obtained.

Step 4: Preparation of Compound 62-4

Reaction scheme:



Material ratio:

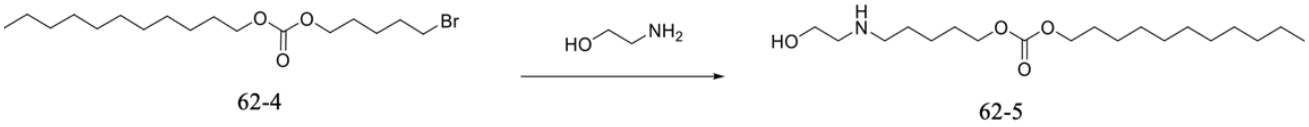
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
62-3	332	1 eq	3.32 g	10
undecanol	172	4 eq	6.88 g	40
pyridine	79	1.2 eq	950 mg	12
DMAP	122	0.2 eq	250 mg	2
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 62-3, undecanol, pyridine, DMAP, and DCM were added, and the mixture was reacted at room temperature for 16 h. TLC (PE:EA=10:1), product Rf value was 0.6. After purification by column chromatography, 2.8 g of a colorless oily substance was obtained.

Step 5: Preparation of Compound 62-5

Reaction scheme:



62-4 62-5

Material ratio:

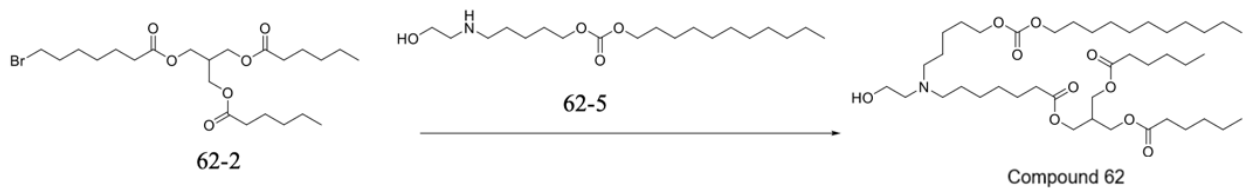
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
62-4	365	1 eq	2.8 g	7.67
ethanolamine	61	10 eq	4.7 g	77
acetonitrile	-	-	60 mL	-

Procedure:

To the reaction flask, 62-4, ethanolamine, and acetonitrile were added, and the mixture was reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.3. After purification by column chromatography, 1.8 g of a colorless oily substance was obtained.

Step 6: Preparation of Compound 62

Reaction scheme:



62-2 Compound 62

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
62-5	345	1 eq	1.8 g	5.2
62-2	493	1.2 eq	3 g	6.3
potassium carbonate	138	1.5 eq	1.1 g	7.8
potassium iodide	166	0.5 eq	430 mg	2.6
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 62-5, 62-2, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was reacted at 65 ℃ for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was diluted with 100 mL of ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 1.5 g of oily substance was obtained.

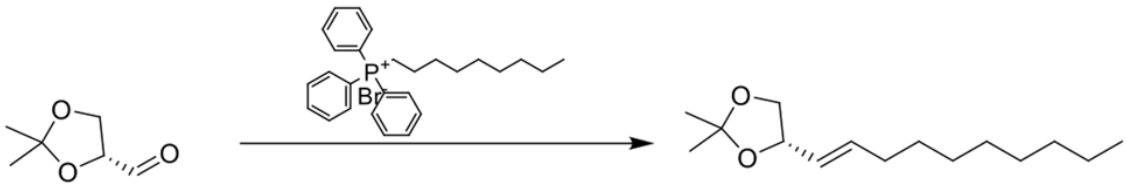
^{1}H NMR (400 MHz, Chloroform-d) δ 4.12 (dd, J = 8.7, 6.4 Hz, 10H), 3.57 (t, J = 5.3 Hz, 2H), 2.63 (t, J = 5.3 Hz, 2H), 2.55 – 2.47 (m, 4H), 2.39 (p, J = 6.0 Hz, 1H), 2.31 (td, J = 7.6, 1.9 Hz, 6H), 1.72 – 1.58 (m, 10H), 1.50 (dp, J = 14.6, 7.3 Hz, 4H), 1.38 – 1.23 (m, 30H), 0.88 (q, J = 6.7 Hz, 9H).

MS (ES+) m/z: 758.6$(M+H)^+$.

Preparation Example 44: Preparation of Compound 63

Step 1: Synthesis of (4S)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4R)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde	130	1.00 eq	5.54 g	40.4
nonyltriphenylphosphonium bromide	469	1.00 eq	19.0 g	40.4
n-butyllithium	64	1.10 eq	2.85 g	44.5
tetrahydrofuran	-	-	190 mL	-

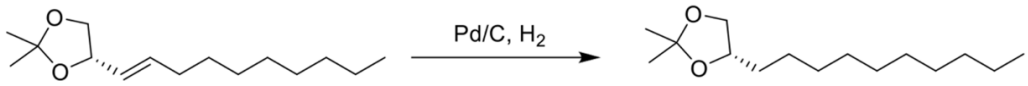
Procedure:

Nonyltriphenylphosphonium bromide (19.0 g, 40.4 mmol) was dissolved in tetrahydrofuran (190 mL), n-butyllithium (2.5 M, 17.8 mL) was added at -20 ℃, and the mixture was reacted at -20 ℃ for half an hour. (4R)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (5.54 g, 40.4 mmol)

was added to the reaction mixture at -20 ℃, and the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction was quenched, extracted twice with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (4S)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane as a colorless liquid was obtained (6.37 g, 65.4% yield).

Step 2: Synthesis of (4S)-4-decyl-2,2-dimethyl-1,3-dioxolane

Reaction scheme:



Material ratio:

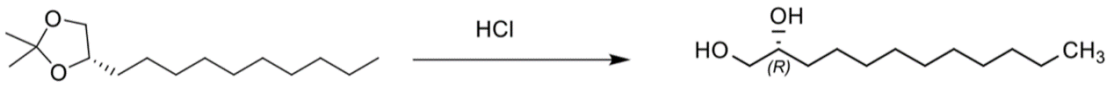
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4S)-4-decyl-2,2-dimethyl-1,3-dioxolane	240	1.00 eq	6.37 g	26.5
palladium on carbon	105	0.10 eq	2.82 g	2.65
methanol	-	-	60.0 mL	-

Procedure:

(4S)-4-decyl-2,2-dimethyl-1,3-dioxolane (6.37 g, 26.5 mmol) was dissolved in methanol (60.0 mL), palladium on carbon (2.82 g, 2.65 mmol) was added, and the mixture was reacted at 25 ℃ and 30 Psi for 12 hours under a hydrogen atmosphere. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated to obtain (4S)-4-decyl-2,2-dimethyl-1,3-dioxolane as a colorless liquid (6.42 g, 100% yield)

Step 3: Synthesis of (2R)-dodecan-1,2-diol

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4S)-4-decyl-2,2-dimethyl-1,3-dioxolane	242	1.00 eq	6.42 g	26.4
hydrochloric acid	36	0.72 eq	6.40 mL	0.72
tetrahydrofuran	-	-	64.0 mL	-

Procedure:

(4S)-4-decyl-2,2-dimethyl-1,3-dioxolane (6.42 g, 26.4 mmol) was dissolved in tetrahydrofuran (64.0 mL), hydrochloric acid (3 M, 6.40 mL) was added, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the

generation of a new spot. After adjusting the pH to neutral, the mixture was extracted with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (2R)-dodecan-1,2-diol as a white solid was obtained (4.43 g, 82.6% yield).

Step 4: Synthesis of (2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol

Reaction scheme:



Material ratio:

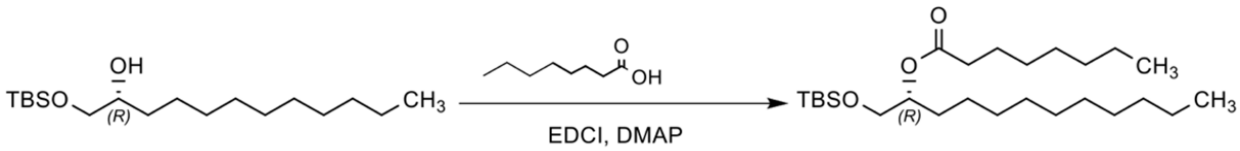
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-dodecan-1,2-diol	202	1.00 eq	2.00 g	9.88
tert-butylchlorodimethylsilane	150	1.05 eq	1.56 g	10.3
imidazole	68	1.05 eq	0.706 g	10.3
tetrahydrofuran	-	-	20.0 mL	-

Procedure:

(2R)-dodecan-1,2-diol (2.00 g, 9.88 mmol) and imidazole (706 mg, 10.3 mmol) were dissolved in tetrahydrofuran (20.0 mL), tert-butylchlorodimethylsilane (1.56 g, 10.3 mmol) was slowly added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol as a colorless liquid was obtained (2.40 g, 76.6% yield).

Step 5: Synthesis of (2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

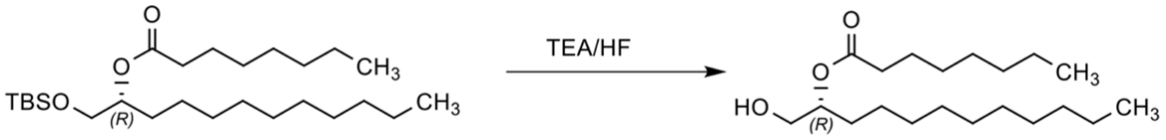
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-[(tert-butyldimethylsilyl)oxy] dodecan-2-ol	316	1.00 eq	2.40 g	7.58
n-octanoic acid	144	1.20 eq	1.31 g	9.10
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.50 eq	2.18 g	11.3
4-dimethylaminopyridine	122	0.10 eq	92.6 mg	758 μmol
dichloromethane	-	-	24.0 mL	-

Procedure:

(2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol (2.40 g, 7.58 mmol) and n-octanoic acid (1.31 g, 9.10 mmol) were dissolved in dichloromethane (24.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.18 g, 11.3 mmol) and 4-dimethylaminopyridine (92.6 mg, 758 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate as a colorless liquid was obtained (3.00 g, 89.3% yield).

Step 6: Synthesis of (2R)-1-hydroxydodecan-2-yl octanoate

Reaction scheme:



Material ratio:

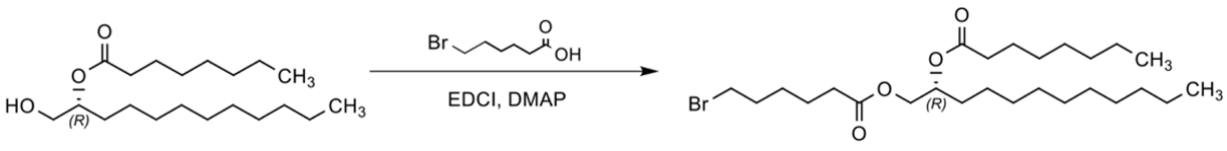
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-[(tert-butyldimethylsilyl)oxy] dodecan-2-yl octanoate	442	1.00 eq	3.00 g	6.78
triethylamine hydrofluoride	161	3.00 eq	3.28 g	20.3
tetrahydrofuran	-	-	30.0 mL	-

Procedure:

(2R)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate (3.00 g, 6.78 mmol) was dissolved in tetrahydrofuran (30.0 mL), triethylamine hydrofluoride (3.28 g, 20.3 mmol) was added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. After adjusting the pH to neutral, the mixture was extracted with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (2R)-1-hydroxydodecan-2-yl octanoate as a colorless liquid was obtained (1.82 g, 81.7% yield).

Step 7: Synthesis of (2R)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

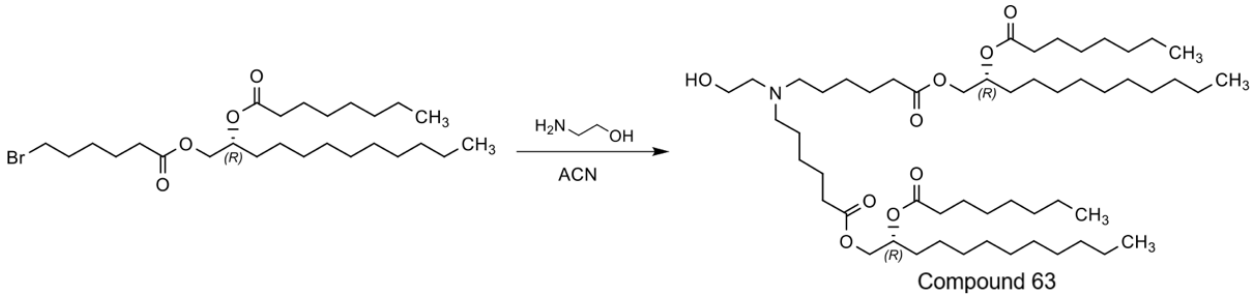
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-hydroxydodecan-2-yl octanoate	328	1.00 eq	1.82 g	5.54
6-bromohexanoic acid	193	1.20 eq	1.30 g	6.65
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.50 eq	1.59 g	8.31
4-dimethylaminopyridine	122	0.10 eq	67.6 mg	553 μmol
dichloromethane	-	-	20.0 mL	-

Procedure:

(2R)-1-hydroxydodecan-2-yl octanoate (1.82 g, 5.54 mmol) and 6-bromohexanoic acid (1.30 g, 6.65 mmol) were dissolved in dichloromethane (20.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.59 g, 8.31 mmol) and 4-dimethylaminopyridine (67.6 mg, 553 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2R)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate as a colorless liquid was obtained (2.49 g, 88.9% yield).

Step 8: Synthesis of (2R)-1-({6-[(2-hydroxyethyl)(6-{[(2R)-2-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-[(6-bromohexanoyl)oxy] dodecan-2-yl octanoate	504	1.00 eq	1.00 g	1.98
ethanolamine	61	0.48 eq	57.9 mg	0.949
potassium carbonate	138	3.50 eq	956 mg	6.92
potassium iodide	166	1.20 eq	394 mg	2.37
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

(2R)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate (1.00 g, 1.98 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (57.9 mg, 949 μmol), potassium carbonate (956 mg, 6.92 mmol), potassium iodide (394 mg, 2.37 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, (2R)-1-({6-[(2-hydroxyethyl)(6-{[(2R)-2-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate as a colorless liquid was obtained (523 mg, 27.4% yield).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (dq, J1 = 3.4, J2 = 6.6 Hz, 2H), 4.23 (dd, J1 = 3.4, J2 = 11.8 Hz, 2H), 4.03 (dd, J1 = 6.8, J2 = 11.8 Hz, 2H), 3.56 (br t, J = 5.2 Hz, 2H), 2.61 (br t, J = 4.8 Hz, 2H), 2.49 (br t, J = 7.2 Hz, 4H), 2.31 (dt, J1 = 2.2, J2 = 7.6 Hz, 8H), 1.65 - 1.55 (m, 12H), 1.51 - 1.43 (m, 4H), 1.34 - 1.17 (m, 52H), 0.98 - 0.78 (m, 12H) ppm.

LCMS: RT = 2.180, m/z 910.8 $[M+H]^+$.

Preparation Example 45: Preparation of Compound 64

Step 1: Synthesis of (4S)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol	132	1.00 eq	5.00 g	37.8
trichloroisocyanuric acid	232	0.40 eq	3.52 g	15.1
1-hydroxy-2,2,6,6-tetramethylpiperidine	157	0.0025 eq	2.85 g	0.0945
sodium acetate	82	1.20 eq	3.72 g	45.4
acetone	-	-	25.0 mL	-
acetone	-	-	15.0 mL	-

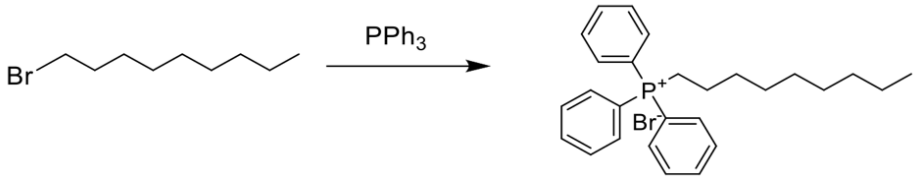
Procedure:

[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (5.00 g, 37.8 mmol) was dissolved in acetone (25.0 mL), trichloroisocyanuric acid (3.52 g, 15.1 mmol) and sodium acetate (3.72 g, 45.4 mmol) were added at 25 ℃, and 1-hydroxy-2,2,6,6-tetramethylpiperidine (14.8 mg, 94.5 μmol) dissolved in acetone (15.0 mL) was slowly added to the reaction mixture. The mixture

was reacted at 59 ℃ for 0.5 hours under nitrogen protection. TLC monitored that the reaction was complete. The mixture was filtered, and the organic phase was concentrated to obtain (4S)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde as a colorless liquid (7.00 g, crude product).

Step 2: Synthesis of nonyltriphenylphosphonium bromide

Reaction scheme:



Material ratio:

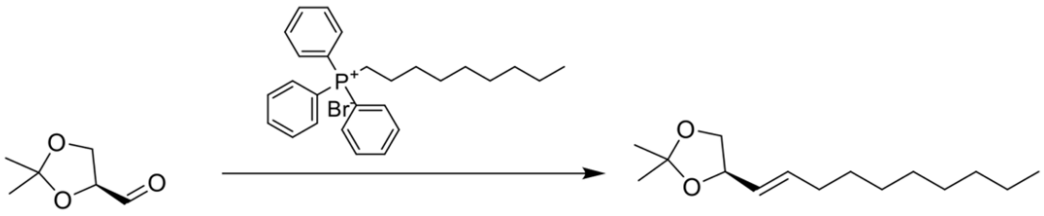
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-bromononane	206	1.00 eq	5.54 g	40.4
triphenylphosphine	262	1.05 eq	19.0 g	40.4
toluene	-	-	200 mL	-

Procedure:

1-bromononane (20.0 g, 96.5 mmol) was dissolved in toluene (200 mL), triphenylphosphine (26.5 g, 101 mmol) was added, and the mixture was reacted at 115 ℃ for 48 hours. TLC monitored that the reaction was complete. The temperature was lowered, and the mixture was diluted with isopropyl ether, and filtered to obtain nonyltriphenylphosphonium bromide as a white solid (28.0 g, 61.7% yield).

Step 3: Synthesis of (4R)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4S)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde	130	1.00 eq	5.54 g	40.4
nonyltriphenylphosphonium bromide	469	1.00 eq	9.96 g	21.2
n-butyllithium	64	1.10 eq	1.36 g	21.2
tetrahydrofuran	-	-	96.0 mL	-

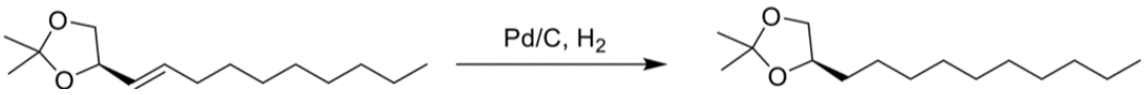
Procedure:

Nonyltriphenylphosphonium bromide (9.96 g, 21.2 mmol) was dissolved in tetrahydrofuran (96.0 mL), n-butyllithium (2.5 M, 8.48 mL) was added at -20 ℃, and the mixture was reacted at

-20 ℃ for half an hour. (4S)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (5.54 g, 40.4 mmol) was added to the reaction mixture at -20 ℃, and the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete. The reaction was quenched, extracted twice with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (4R)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane as a colorless liquid was obtained (2.24 g, 50.5% yield).

Step 4: Synthesis of (4R)-4-decyl-2,2-dimethyl-1,3-dioxolane

Reaction scheme:



Material ratio:

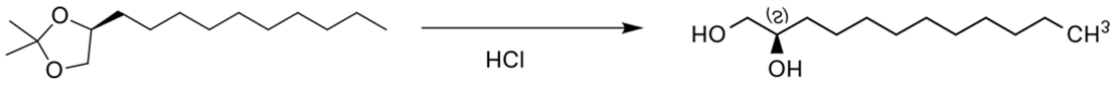
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4R)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane	240	1.00 eq	2.24 g	9.32
palladium on carbon	105	0.10 eq	0.991 g	0.931
methanol	-	-	24.0 mL	-

Procedure:

(4R)-4-[(1E)-dec-1-en-1-yl]-2,2-dimethyl-1,3-dioxolane (2.24 g, 9.32 mmol) was dissolved in methanol (24.0 mL), palladium on carbon (991 mg, 931 μmol) was added, and the mixture was reacted at 25 ℃ and 30 Psi for 12 hours under a hydrogen atmosphere. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated to obtain (4R)-4-decyl-2,2-dimethyl-1,3-dioxolane as a colorless liquid (2.26 g, 100% yield)

Step 5: Synthesis of (2S)-dodecan-1,2-diol

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(4R)-4-decyl-2,2-dimethyl-1,3-dioxolane	242	1.00 eq	2.26 g	9.32
hydrochloric acid	36	0.72 eq	2.25 mL	6.76
tetrahydrofuran	-	-	30.0 mL	-

Procedure:

(4R)-4-decyl-2,2-dimethyl-1,3-dioxolane (2.26 g, 9.32 mmol) was dissolved in tetrahydrofuran (30.0 mL), hydrochloric acid (3 M, 2.25 mL) was added, and finally, the

mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. After adjusting the pH to neutral, the mixture was extracted with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (2S)-dodecan-1,2-diol as a white solid was obtained (1.49 g, 78.9% yield).

Step 6: Synthesis of (2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol

Reaction scheme:



Material ratio:

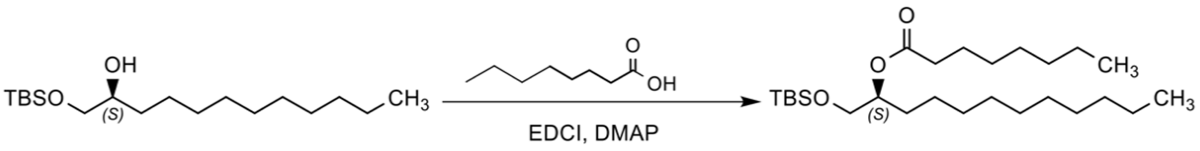
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2S)-dodecan-1,2-diol	202	1.00 eq	1.49 g	7.36
tert-butylchlorodimethylsilane	150	1.05 eq	1.17 g	7.73
imidazole	68	1.05 eq	0.526 g	7.73
tetrahydrofuran	-	-	20.0 mL	-

Procedure:

(2S)-dodecan-1,2-diol (1.49 g, 7.36 mmol) and imidazole (526 mg, 7.73 mmol) were dissolved in tetrahydrofuran (20.0 mL), tert-butylchlorodimethylsilane (1.17 g, 7.73 mmol) was slowly added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol as a colorless liquid was obtained (2.00 g, 85.7% yield).

Step 7: Synthesis of (2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

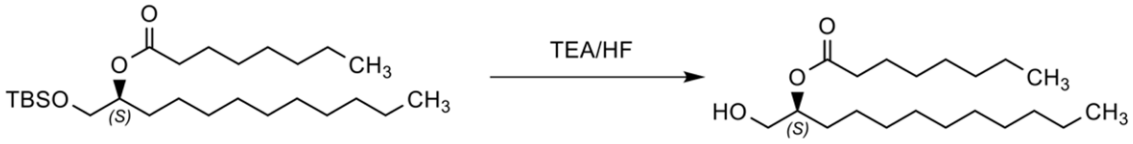
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2S)-1-[(tert-butyldimethylsilyl)oxy] dodecan-2-ol	316	1.00 eq	2.00 g	6.32
n-octanoic acid	144	1.40 eq	1.28 g	8.84
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.80 eq	2.18 g	11.3
4-dimethylaminopyridine	122	0.20 eq	154 mg	1.26
dichloromethane	-	-	20.0 mL	-

Procedure:

(2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-ol (2.00 g, 6.32 mmol) and n-octanoic acid (1.28 g, 8.84 mmol) were dissolved in dichloromethane (20.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.18 g, 11.3 mmol) and 4-dimethylaminopyridine (154 mg, 1.26 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate as a colorless liquid was obtained (2.50 g, 89.3% yield).

Step 8: Synthesis of (2S)-1-hydroxydodecan-2-yl octanoate

Reaction scheme:



Material ratio:

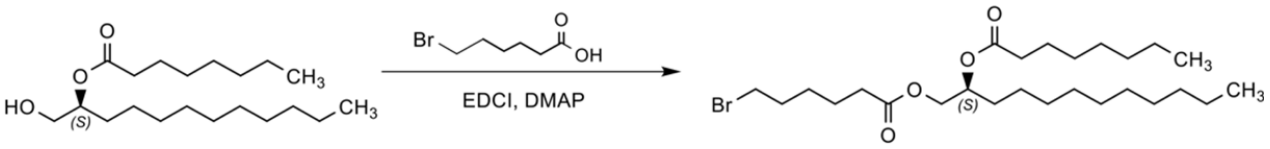
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate	442	1.00 eq	2.50g	5.65
triethylamine hydrofluoride	161	3.00 eq	2.73 g	16.9
tetrahydrofuran	-	-	30.0 mL	-

Procedure:

(2S)-1-[(tert-butyldimethylsilyl)oxy]dodecan-2-yl octanoate (2.50 g, 5.65 mmol) was dissolved in tetrahydrofuran (25.0 mL), triethylamine hydrofluoride (2.73 g, 16.9 mmol) was added at 0 ℃, and finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. After adjusting the pH to neutral, the mixture was extracted with ethyl acetate, and the organic phase was concentrated. After purification by column chromatography, (2S)-1-hydroxydodecan-2-yl octanoate as a colorless liquid was obtained (1.37 g, 73.8% yield).

Step 9: Synthesis of (2S)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

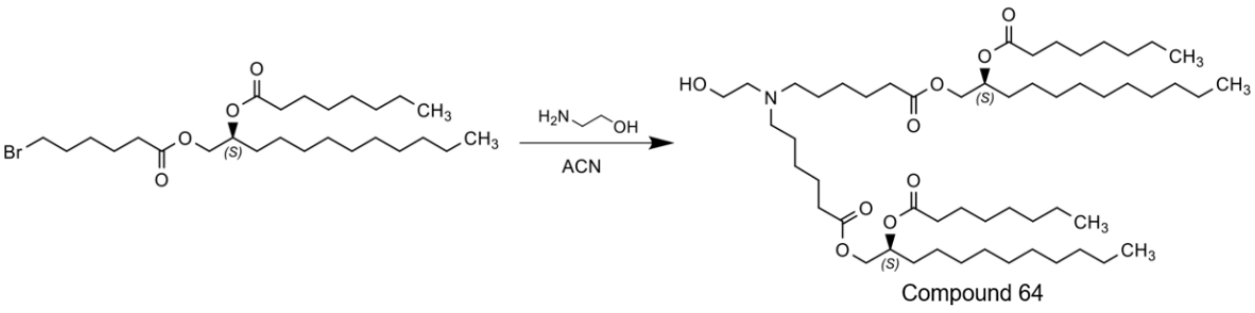
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2S)-1-hydroxydodecan-2-yl octanoate	328	1.00 eq	1.37 g	4.17
6-bromohexanoic acid	193	1.40 eq	1.14 g	5.84
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	192	1.80 eq	1.44 g	7.51
4-dimethylaminopyridine	122	0.20 eq	101 mg	834 μmol
dichloromethane	-	-	20.0 mL	-

Procedure:

(2S)-1-hydroxydodecan-2-yl octanoate (1.37 g, 4.17 mmol) and 6-bromohexanoic acid (1.14 g, 5.84 mmol) were dissolved in dichloromethane (13.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.44 g, 7.51 mmol) and 4-dimethylaminopyridine (101 mg, 834. μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. After purification by column chromatography, (2S)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate as a colorless liquid was obtained (1.94 g, 92.0% yield).

Step 10: Synthesis of (2S)-1-({6-[(2-hydroxyethyl)(6-{[(2S)-2-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2S)-1-[(6-bromohexanoyl)oxy] dodecan-2-yl octanoate	504	1.00 eq	1.00 g	1.98
ethanolamine	61	0.48 eq	57.9 mg	0.949
potassium carbonate	138	3.50 eq	956 mg	6.92
potassium iodide	166	1.20 eq	394 mg	2.37
acetonitrile	-	-	10.0 mL	-
tetrahydrofuran	-	-	5.00 mL	-

Procedure:

(2S)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate (1.00 g, 1.98 mmol) was dissolved in acetonitrile (10.0 mL), and ethanolamine (57.9 mg, 949 μmol), potassium carbonate (956 mg, 6.92 mmol), potassium iodide (394 mg, 2.37 mmol), and tetrahydrofuran (5.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, (2S)-1-({6-[(2-hydroxyethyl)(6-{[(2S)-2-(octanoyloxy)dodecyl]oxy}-6-oxohexyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate as a colorless liquid was obtained (430 mg, 22.3% yield).

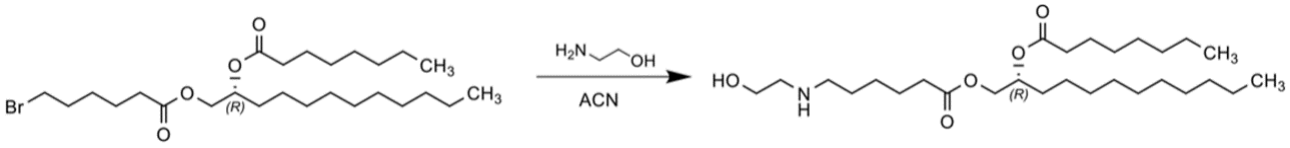
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.09 (br dd, J1 = 3.2, J2 = 6.2 Hz, 2H), 4.23 (dd, J1 = 3.2, J2 = 11.8 Hz, 2H), 4.03 (dd, J1 = 6.8, J2 = 11.8 Hz, 2H), 3.56 (br t, J = 5.2 Hz, 2H), 2.61 (br t, J = 4.8 Hz, 2H), 2.49 (br t, J = 7.2 Hz, 4H), 2.31 (dt, J1 = 2.2, J2 =7.4 Hz, 8H), 1.70 - 1.57 (m, 12H), 1.51 - 1.43 (m, 4H), 1.35 - 1.22 (m, 52H), 0.89 (t, J = 6.6 Hz, 12H) ppm.

LCMS: RT = 2.204, m/z 910.8 $[M+H]^+$.

Preparation Example 46: Preparation of Compound 65

Step 1: Synthesis of (2R)-1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate

Reaction scheme:



Material ratio:

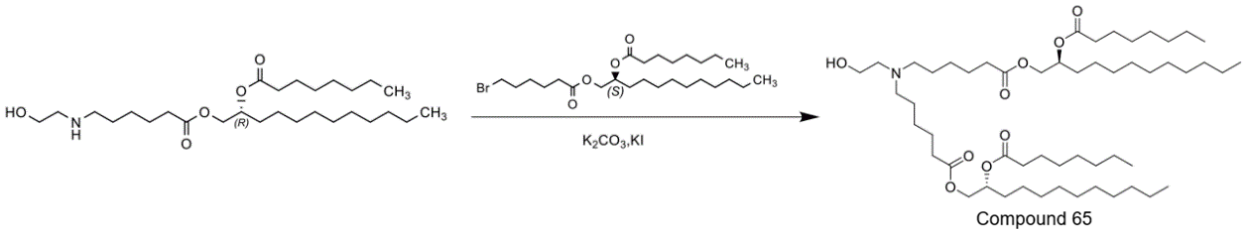
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-[(6-bromohexanoyl) oxy]dodecan-2-yl octanoate	504	1.00 eq	1.15 g	2.27
ethanolamine	61	10.0 eq	1.39 g	22.7
acetonitrile	-	-	11.0 mL	-

Procedure:

(2R)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate (1.15 g, 2.27 mmol) was dissolved in acetonitrile (11.0 mL), and ethanolamine (1.39 g, 22.7 mmol) was added sequentially. Finally, the mixture was reacted at 30 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, (2R)-1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate as a colorless liquid was obtained (740 mg, 66.9% yield).

Step 2: Synthesis of 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)[6-(nonyloxy)-6-oxohexyl]amino]octanoate

Reaction scheme:



Compound 65

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
(2R)-1-({6-[(2-hydroxyethyl)amino] hexanoyl}oxy)dodecan-2-yl octanoate	485	1.00 eq	400 mg	0.823
(2S)-1-[(6-bromohexanoyl) oxy]dodecan-2-yl octanoate	504	1.00 eq	416 mg	0.823
potassium carbonate	138	3.5 eq	398 mg	2.88
potassium iodide	166	1.2 eq	164 mg	0.988
acetonitrile	-	-	4.00 mL	-
tetrahydrofuran	-	-	2.00 mL	-

Procedure:

(2R)-1-({6-[(2-hydroxyethyl)amino]hexanoyl}oxy)dodecan-2-yl octanoate (400 mg, 823 μmol) was dissolved in acetonitrile (4.00 mL), and (2S)-1-[(6-bromohexanoyl)oxy]dodecan-2-yl octanoate (416 mg, 823 μmol), potassium carbonate (398 mg, 2.88 mmol), potassium iodide (164 mg, 988 μmol), and tetrahydrofuran (2.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(octanoyloxy)nonyl 8-[(2-hydroxyethyl)[6-(nonyloxy)-6-oxohexyl]amino]octanoate as a colorless liquid was

obtained (780 mg, 69.2% yield).

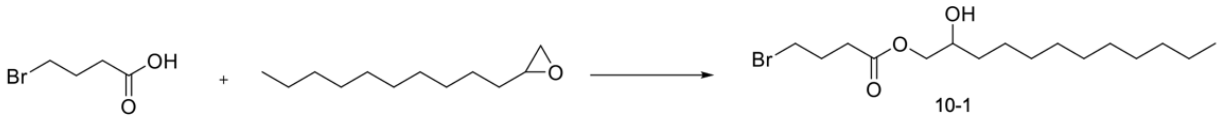
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.18 - 5.00 (m, 2H), 4.23 (dd, J1 = 3.4, J2 = 11.8 Hz, 2H), 4.03 (dd, J1 = 6.8, J2 = 11.8 Hz, 2H), 3.59 (br t, J = 4.8 Hz, 2H), 2.64 (br s, 2H), 2.52 (br t, J = 6.8 Hz, 4H), 2.31 (dt, J1 = 2.8, J2 = 7.6 Hz, 8H), 1.64 - 1.44 (m, 16H), 1.38 - 1.20 (m, 52H), 0.89 (t, J = 6.8 Hz, 12H) ppm.

LCMS: RT = 2.212, m/z 910.7 $[M+H]^+$.

Preparation Example 47: Preparation of Compound 10

Step 1: Preparation of 10-1

Reaction scheme:



Material ratio:

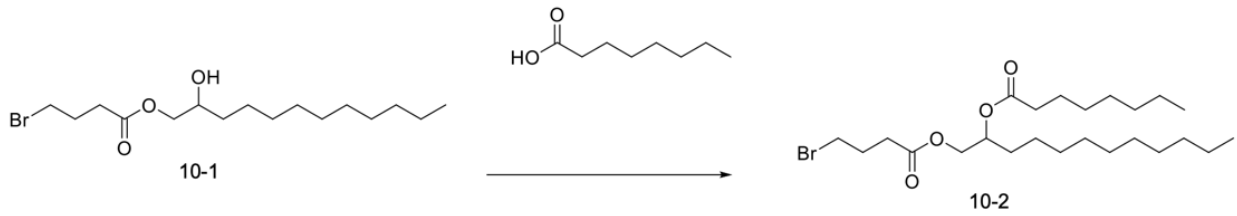
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
4-bromobutanoic acid	167	1 eq	6.68 g	40
1,2-epoxydodecane	184	1 eq	7.36 g	40
ferric chloride	162	0.05 eq	324 mg	2
pyridine	79	0.05 eq	158 mg	2

Procedure:

To the reaction flask, 4-bromobutanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.4, TLC (PE:EA=4:1). The reaction mixture was concentrated, and after purification by column chromatography, 8 g of oily substance was obtained.

Step 2: Preparation of 10-2

Reaction scheme:



Material ratio:

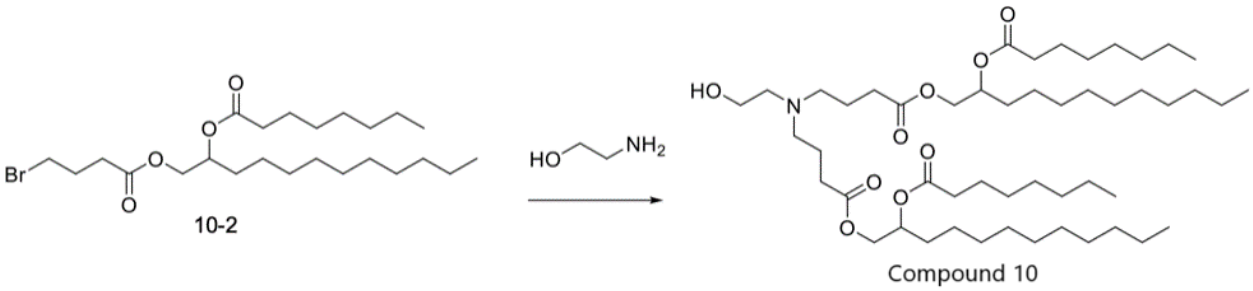
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
10-1	351.33	1 eq	8 g	22.8
octanoic acid	144.21	1.1 eq	3.6 g	25
EDCI	155	1.5 eq	5.3 g	34
DMAP	122	0.15 eq	420 mg	3.4
DCM	-	-	150 mL	-

Procedure:

To the reaction flask, 10-1, octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was concentrated, and after purification by column chromatography, 7.5 g of oily substance was obtained.

Step 3: Preparation of Compound 10

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
10-2	477.5	2.2 eq	3.15 g	6.6
ethanolamine	61	1 eq	183 mg	3
potassium carbonate	138	3 eq	1.24 g	9
potassium iodide	166	1 eq	500 mg	3
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 10-2, ethanolamine, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 1 g of a colorless oily substance was obtained.

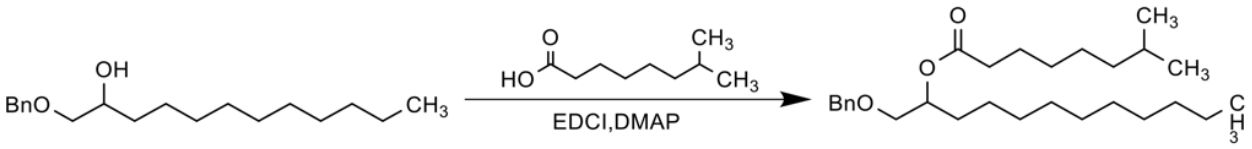
^{1}H NMR (400 MHz, Chloroform-d) δ 5.08 (qd, J = 6.9, 3.3 Hz, 2H), 4.23 (dd, J = 11.8, 3.3 Hz, 2H), 4.01 (dd, J = 11.8, 6.9 Hz, 2H), 3.54 (t, J = 5.2 Hz, 2H), 2.60 (d, J = 6.5 Hz, 2H), 2.49 (t, J = 7.2 Hz, 4H), 2.31 (q, J = 7.2 Hz, 8H), 1.76 (p, J = 7.3 Hz, 4H), 1.65 – 1.52 (m, 12H), 1.27 (d, J = 13.5 Hz, 44H), 0.88 (t, J = 6.7 Hz, 12H).

MS (ES+) m/z: 854.7$(M)^+$.

Preparation Example 48: Preparation of Compound 12

Step 1: Synthesis of 1-(benzyloxy)dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

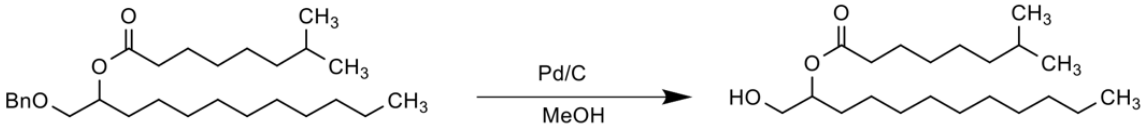
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-ol	292	1.00 eq	5.60 g	19.1
7-methyloctanoic acid	158	1.00 eq	3.03 g	19.1
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.50 eq	5.51 g	28.7
4-dimethylaminopyridine	122	0.10 eq	245 mg	2.01
dichloromethane	-	-	58.0 mL	-

Procedure:

1-(benzyloxy)dodecan-2-ol (5.60 g, 19.1 mmol) and 7-methyloctanoic acid (3.03 g, 19.1 mmol) were dissolved in dichloromethane (50.0 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (5.51 g, 28.7 mmol) and 4-dimethylaminopyridine (245 mg, 2.01 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)dodecan-2-yl 7-methyloctanoate as a colorless liquid (5.75 g, 64.4% yield).

Step 2: Synthesis of 1-hydroxydodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)dodecan-2-yl 7-methyloctanoate	432	1.0 eq	2.87 g	6.63
palladium/carbon	106	0.10 eq	0.233 g	1.91
hydrogen	-	(40 Psi)	-	-
methanol		-	50.0 mL	-

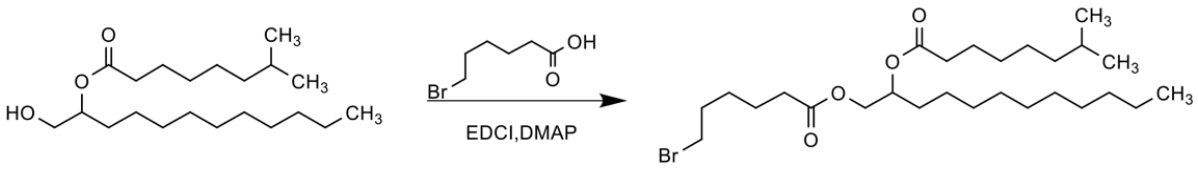
Procedure:

In two parallel batches, 1-(benzyloxy)dodecan-2-yl 7-methyloctanoate (2.87 g, 6.63 mmol) was dissolved in methanol (50.0 mL), palladium/carbon (233 mg, 1.91 mmol) was added under an argon atmosphere, and finally, the mixture was reacted at 25 ℃ for 12 hours under a

hydrogen (40 Psi) atmosphere. TLC monitored that the reaction was complete, and the reaction mixture was filtered and concentrated. Spin drying gave 1-hydroxydodecan-2-yl 7-methyloctanoate as a colorless liquid (3.65 g, 80.3% yield).

Step 3: Synthesis of 1-[(6-bromohexanoyl)oxy]dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

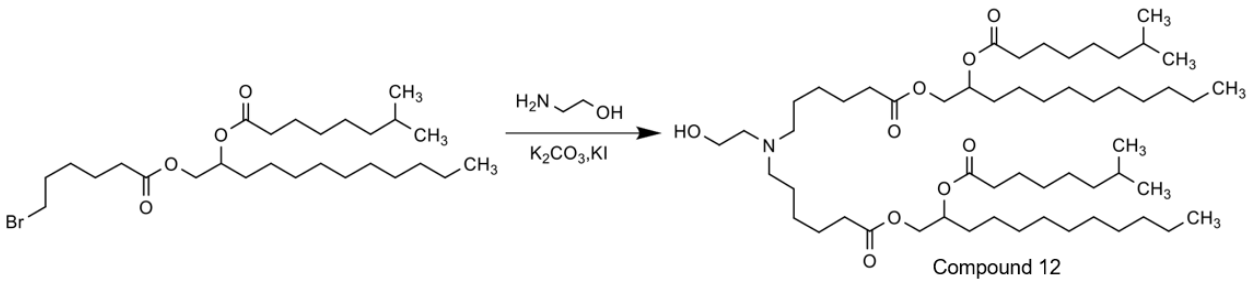
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 7-methyloctanoate	342	1.00 eq	1.20 g	3.50
6-bromohexanoic acid	193	1.40 eq	0.956 g	4.90
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.01 g	5.25
4-dimethylaminopyridine	122	0.1 eq	42.8 mg	0.350
dichloromethane	-	-	12.0 mL	-

Procedure:

1-hydroxydodecan-2-yl 7-methyloctanoate (1.20 g, 3.50 mmol) was dissolved in dichloromethane (12.0 mL), and 6-bromohexanoic acid (956 mg, 4.90 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.01 g, 5.25 mmol), and 4-dimethylaminopyridine (42.8 mg, 350 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(6-bromohexanoyl)oxy]dodecan-2-yl 7-methyloctanoate as a colorless liquid (1.57 g, 86.2% yield).

Step 4: Synthesis of 1-({6-[(2-hydroxyethyl)[6-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-6-oxohexyl]amino]hexanoyl}oxy)dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(6-bromohexanoyl)oxy]dodecan -2-yl 7-methyloctanoate	518	1.00 eq	200 mg	0.384
ethanolamine	61	0.48 eq	11.2 mg	0.184
potassium carbonate	138	3.50 eq	186 mg	1.35
potassium iodide	166	1.20 eq	76.6 mg	0.461
acetonitrile	-	-	2.00 mL	-
tetrahydrofuran	-	-	1.00 mL	-

Procedure:

1-[(6-bromohexanoyl)oxy]dodecan-2-yl 7-methyloctanoate (200 mg, 384 μmol) was dissolved in acetonitrile (2.00 mL), and ethanolamine (11.2 mg, 184 μmol), potassium carbonate (186 mg, 1.35 mmol), potassium iodide (76.6 mg, 461 μmol), and tetrahydrofuran (1.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({6-[(2-hydroxyethyl)[6-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-6-oxohexyl]amino]hexanoyl}oxy)dodecan-2-yl 7-methyloctanoate as a colorless liquid was obtained (98.0 mg, 27.1% yield).

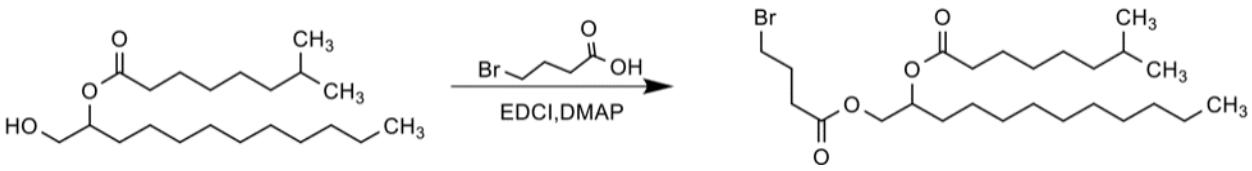
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.17 - 4.91 (m, 2H), 4.24 (dd, J1 = 3.0, J2 = 11.6 Hz, 2H),4.02 (ddd, J1 = 3.2, J2 = 6.8, J3 =11.8 Hz, 2H), 3.63 (br s, 2H), 2.73 - 2.49 (m, 5H), 2.40 - 2.25 (m, 6H), 2.19- 1.97 (m, 4H), 1.63 (br dd, J1 = 7.6, J2 = 15.2 Hz, 12H), 1.41 - 1.09 (m, 42H), 1.01 - 0.75 (m, 30H) ppm.

LCMS: RT = 2.182, m/z 960.8 $[M+23]^+$.

Preparation Example 49: Preparation of Compound 13

Step 1: Synthesis of 1-[(4-bromobutanoyl)oxy]dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

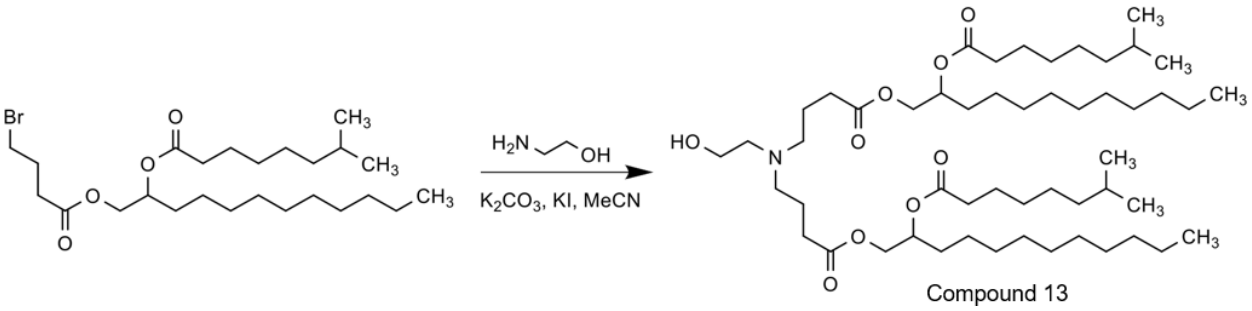
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 7-methyloctanoate	342	1.00 eq	1.20 g	3.50
4-bromobutanoic acid	165	1.40 eq	0.819 g	4.90
1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	191	1.5 eq	1.01 g	5.25
4-dimethylaminopyridine	122	0.1 eq	42.8 mg	0.350
dichloromethane	-	-	12.0 mL	-

Procedure:

1-hydroxydodecan-2-yl 7-methyloctanoate (1.20 g, 3.50 mmol) was dissolved in dichloromethane (12.0 mL), and 4-bromobutanoic acid (819 mg, 4.90 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.01 g, 5.25 mmol), and 4-dimethylaminopyridine (42.8 mg, 350 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(4-bromobutanoyl)oxy]dodecan-2-yl 7-methyloctanoate as a colorless liquid (1.20 g, 69.6% yield).

Step 2: Synthesis of 1-({4-[(2-hydroxyethyl)[4-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-4-oxobutyl]amino]butanoyl}oxy)dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(4-bromobutanoyl)oxy]dodecan-2-yl 7-methyloctanoate	490	1.00 eq	200 mg	0.406
ethanolamine	61	0.48 eq	11.9 mg	0.195
potassium carbonate	138	3.50 eq	196 mg	1.42
potassium iodide	166	1.20 eq	81.0 mg	0.488
acetonitrile	-	-	2.00 mL	-
tetrahydrofuran	-	-	1.00 mL	-

Procedure:

1-[(4-bromobutanoyl)oxy]dodecan-2-yl 7-methyloctanoate (200 mg, 406 μmol) was dissolved in acetonitrile (2.00 mL), and ethanolamine (11.9 mg, 195 μmol), potassium carbonate (196 mg, 1.42 mmol), potassium iodide (81.0 mg, 488 μmol), and tetrahydrofuran (1.00 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({4-[(2-hydroxyethyl)[4-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-4-oxobutyl]amino]butanoyl}oxy)dodecan-2-yl 7-methyloctanoate as a colorless liquid was obtained (84.0 mg, 23.4% yield).

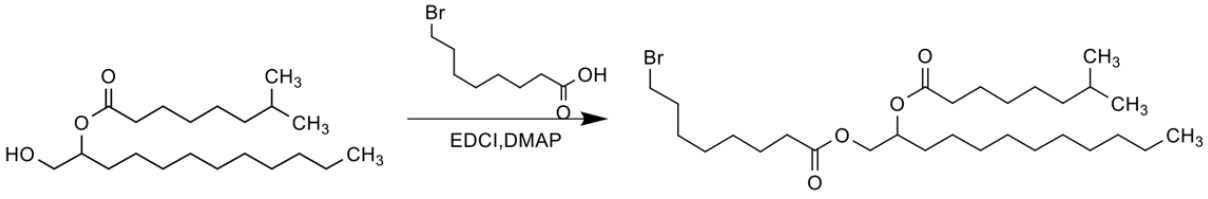
^{1}H NMR (400 MHz, CHLOROFORM-d) δ= 5.23 - 4.92 (m, 2H), 4.25 (dd, J1 = 3.0, J2=11.8 Hz, 2H), 4.09 - 3.92 (m, 2H), 3.56 (br s, 2H), 2.71 - 2.43 (m, 6H), 2.40 - 2.25(m, 6H), 2.20 - 1.99 (m, 4H), 1.88 - 1.70 (m, 4H), 1.68 - 1.60 (m, 2H), 1.42 - 1.07 (m,38H), 1.04 - 0.79 (m, 30H) ppm.

LCMS: RT = 2.143, m/z 882.6 $[M+H]^+$.

Preparation Example 50: Preparation of Compound 14

Step 1: Synthesis of 1-[(8-bromooctanoyl)oxy]dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

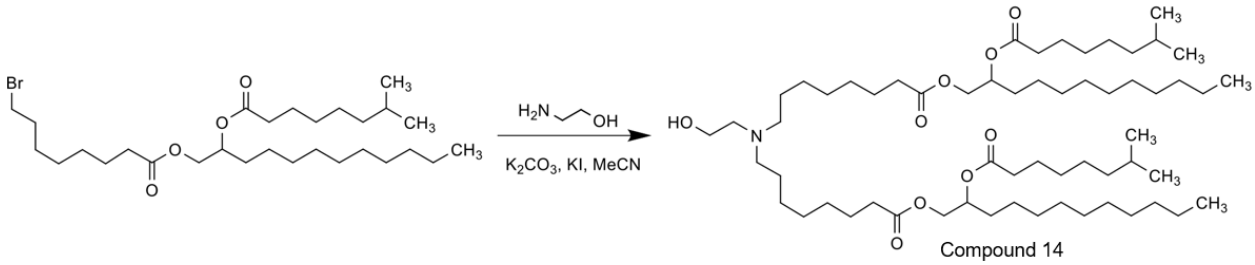
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxydodecan-2-yl 7-methyloctanoate	342	1.00 eq	1.20 g	3.50
8-bromooctanoic acid	222	1.40 eq	1.09 g	4.90
1-(3-dimethylaminopropyl)-3-ethylc arbodiimide hydrochloride	191	1.5 eq	1.01 g	5.25
4-dimethylaminopyridine	122	0.1 eq	42.8 mg	0.350
dichloromethane	-	-	12.0 mL	-

Procedure:

1-hydroxydodecan-2-yl 7-methyloctanoate (1.20 g, 3.50 mmol) was dissolved in dichloromethane (12.0 mL), and 8-bromooctanoic acid (1.09 g, 4.90 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.01 g, 5.25 mmol), and 4-dimethylaminopyridine (42.8 mg, 350 μmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 1-[(8-bromooctanoyl)oxy]dodecan-2-yl 7-methyloctanoate as a colorless liquid (1.87 g, 97.4% yield).

Step 2: Synthesis of 1-({8-[(2-hydroxyethyl)[8-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-8-oxooctyl]amino]octanoyl}oxy)dodecan-2-yl 7-methyloctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-[(8-bromooctanoyl)oxy]dodecan-2-yl 7-methyloctanoate	490	1.00 eq	200 mg	0.365
ethanolamine	61	0.48 eq	10.7 mg	0.175
potassium carbonate	138	3.50 eq	176 mg	1.28
potassium iodide	166	1.20 eq	72.7 mg	0.438
acetonitrile	-	-	2.00 mL	-
tetrahydrofuran	-	-	1.00 mL	-

Procedure:

1-[(8-bromooctanoyl)oxy]dodecan-2-yl 7-methyloctanoate (200 mg, 365 μmol) was dissolved in acetonitrile (2.00 mL), and ethanolamine (10.7 mg, 175 μmol), potassium carbonate (176 mg, 1.28 mmol), potassium iodide (72.7 mg, 438 μmol), and tetrahydrofuran (1.00 mL)

were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-({8-[(2-hydroxyethyl)[8-({2-[(7-methyloctanoyl)oxy]dodecyl}oxy)-8-oxooctyl]amino]octanoyl}oxy)dodecan-2-yl 7-methyloctanoate as a colorless liquid was obtained (112 mg, 30.8% yield).

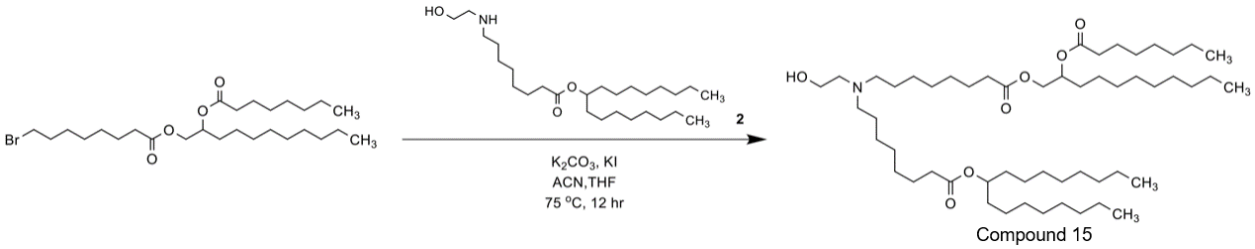
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.21 - 4.94 (m, 2H), 4.35 - 4.14 (m, 2H), 4.03(ddd, J1 = 2.8, J2 = 6.8, J3 = 11.8 Hz, 2H), 3.69 (br s, 2H), 2.79 - 2.51 (m, 5H), 2.37 - 2.25 (m, 6H), 2.19- 1.97 (m, 5H), 1.66 - 1.57 (m, 9H), 1.39 - 1.05 (m, 51H), 1.03 - 0.80 (m, 30H) ppm.

LCMS: RT = 2.209, m/z 995.2 $[M+H]^+$.

Preparation Example 51: Preparation of Compound 15

Step 1: Synthesis of heptadecan-9-yl 8-[(2-hydroxyethyl)(8-{[2-(octanoyloxy)undecyl]oxy}-8-oxooctyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(octanoyloxy)undecyl 8-bromooctanoate	518	1.2 eq	50.0 mg	0.096
heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate	441	1.0 eq	35.4 mg	0.08
potassium carbonate	138	3.5 eq	38.7 mg	0.28
potassium iodide	166	1.2 eq	15.9 mg	0.096
acetonitrile	-	-	0.3 mL	-
tetrahydrofuran	-	-	0.2mL	-

Procedure:

2-(octanoyloxy)undecyl 8-bromooctanoate (50.0 mg, 0.096 mmol) was dissolved in acetonitrile (0.3 mL), and heptadecan-9-yl 8-[(2-hydroxyethyl)amino]octanoate (35.4 mg, 0.08 mmol), potassium carbonate (38.7 mg, 0.28 mmol), potassium iodide (15.9 mg, 0.096 mmol), and tetrahydrofuran (0.2 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃

for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, heptadecan-9-yl 8-[(2-hydroxyethyl)(8-{[2-(octanoyloxy)undecyl]oxy}-8-oxooctyl)amino]octanoate as a colorless liquid was obtained (33 mg, 46.2% yield).

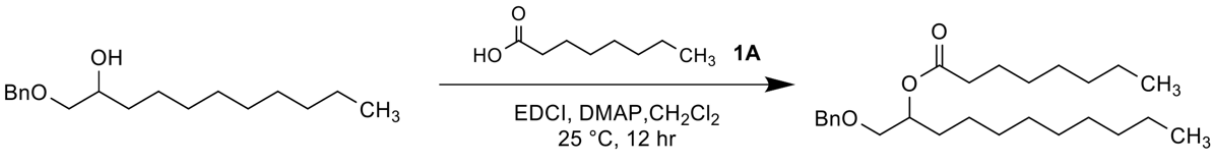
^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.08 (dq, J_1 = 3.2, J_2 = 6.8 Hz, 1H), 4.87 (quin, J = 6.0 Hz, 1H), 4.22 (dd, J_1 = 3.2, J_2 =12.0 Hz, 1H), 4.04 (dd, J_1 = 6.8, J_2 =12.0 Hz, 1H), 3.58 (br t, J = 5.2 Hz, 2H), 2.65 (br t, J = 4.4 Hz, 2H), 2.55 - 2.48 (m, 3H), 2.30 (q, J = 8.0 Hz, 6H), 1.63 (br d, J = 6.8 Hz, 10H), 1.53 - 1.42 (m, 9H), 1.37 - 1.19 (m, 57H), 0.89 (t, J = 6.8 Hz, 12H).

LCMS: RT = 2.222, m/z 880.7 $[M+H]^+$.

Preparation Example 52: Preparation of Compound 16

Step 1: Synthesis of 1-(benzyloxy)undecan-2-yl octanoate

Reaction scheme:



Material ratio:

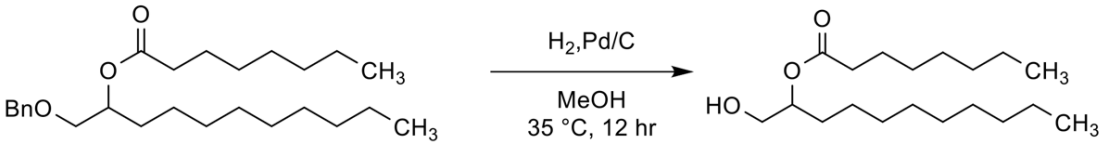
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)undecan-2-ol	278	1.0 eq	2.0 g	7.18
octanoic acid	144	1.2 eq	1.24 g	8.62
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	2.07 g	10.7
4-dimethylaminopyridine	122	0.1 eq	87.7 mg	0.718
dichloromethane	-	-	20 mL	-

Procedure:

1-(benzyloxy)undecan-2-ol (2.0 g, 7.18 mmol) and octanoic acid (1.24 g, 8.62 mmol) were dissolved in dichloromethane (20 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.07 g, 10.7 mmol) and 4-dimethylaminopyridine (87.7 mg, 0.718 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 1-(benzyloxy)undecan-2-yl octanoate as a colorless liquid (1.56 g, 53.6% yield).

Step 2: Synthesis of 1-hydroxyundecan-2-yl octanoate

Reaction scheme:



Material ratio:

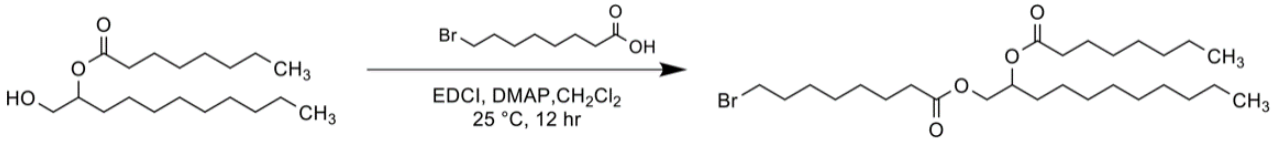
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-(benzyloxy)undecan-2-yl octanoate	404	1.0 eq	1.56 g	3.86
palladium on carbon	105.9	0.2 eq	820 mg	0.771
methanol	-	-	20 mL	-

Procedure:

1-(benzyloxy)undecan-2-yl octanoate (1.56 g, 3.86 mmol) was dissolved in methanol (20 mL), palladium on carbon (820 mg, 0.771 mmol) was added, and the mixture was reacted at 35 ℃ and 40 Psi for 12 hours under nitrogen protection. TLC monitored that the reaction was complete, and the mixture was filtered and concentrated. After purification by column chromatography, 1-hydroxyundecan-2-yl octanoate as a colorless liquid was obtained (600 mg, 49.4% yield).

Step 3: Synthesis of 2-(octanoyloxy)undecyl 8-bromooctanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
1-hydroxyundecan-2-yl octanoate	286	1.0 eq	600 mg	1.91
8-bromooctanoic acid	222	1.2 eq	510 mg	2.29
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	192	1.5 eq	548 mg	2.86
4-dimethylaminopyridine	122	0.1 eq	23.3 mg	0.19
dichloromethane	-	-	10 mL	-

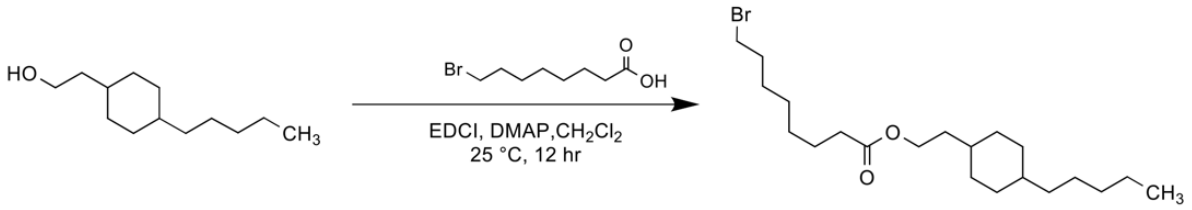
Procedure:

1-hydroxyundecan-2-yl octanoate (600 mg, 1.91 mmol) and 8-bromooctanoic acid (510 mg, 2.29 mmol) were dissolved in dichloromethane (10 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (548 mg, 2.86 mmol) and 4-dimethylaminopyridine (23.3 mg, 0.19 mmol) were added sequentially. Finally, the mixture

was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The reaction mixture was concentrated. The crude product was subjected to column chromatography to obtain 2-(octanoyloxy)undecyl 8-bromooctanoate as a colorless liquid (846 mg, 85.3% yield).

Step 4: Synthesis of 2-(4-pentylcyclohexyl)ethyl 8-bromooctanoate

Reaction scheme:



Material ratio:

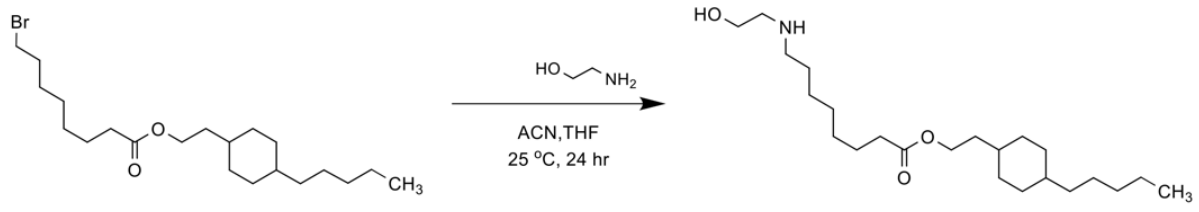
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(4-pentylcyclohexyl)ethan-1-ol	198	1.0 eq	1.0 g	5.04
8-bromooctanoic acid	144	1.2 eq	1.35 g	6.05
1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride	222	1.5 eq	1.45 g	7.56
4-dimethylaminopyridine	122	0.1 eq	61.5 mg	0.504
dichloromethane	-	-	15 mL	-

Procedure:

2-(4-pentylcyclohexyl)ethan-1-ol (1.0 g, 5.04 mmol) and 8-bromooctanoic acid (1.35 g, 6.05 mmol) were dissolved in dichloromethane (15 mL), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.45 g, 1.45 g) and 4-dimethylaminopyridine (61.5 mg, 0.504 mmol) were added sequentially. Finally, the mixture was reacted at 25 ℃ for 12 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 2-(4-pentylcyclohexyl)ethyl 8-bromooctanoate as a colorless liquid (2.0 g, 98.3% yield).

Step 5: Synthesis of 2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)amino]octanoate

Reaction scheme:



Material ratio:

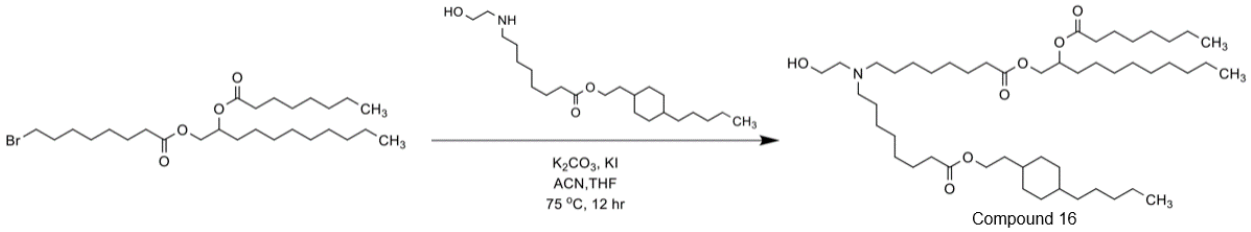
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(4-pentylcyclohexyl)ethyl 8-bromooctanoate	402	1.0 eq	2.00 g	4.96
ethanolamine	61	10.0 eq	3.03 g	49.5
acetonitrile	-	-	20 mL	-

Procedure:

Undecyl 8-bromooctanoate (2.00 g, 4.96 mmol) was dissolved in acetonitrile (20 mL), ethanolamine (3.03 g, 49.5 mmol) was added to the reaction mixture, and the mixture was reacted at 25 ℃ for 24 hours under nitrogen protection. TLC monitored the generation of a new spot. The organic phase was concentrated. The crude product was subjected to column chromatography to obtain 2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)amino]octanoate as a bright yellow liquid (1.23 g, 64.0% yield).

Step 6: Synthesis of 2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)(8-{[2-(octanoyloxy)undecyl]oxy}-8-oxooctyl)amino]octanoate

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
2-(octanoyloxy)undecyl 8-bromooctanoate	518	1.2 eq	50.0 mg	0.096
2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)amino]octanoate	383	1.0 eq	30.7 mg	0.08
potassium carbonate	138	3.5 eq	38.7 mg	0.28
potassium iodide	166	1.2 eq	15.9 mg	0.096
acetonitrile	-	-	0.3 mL	-
tetrahydrofuran	-	-	0.2 mL	-

Procedure:

2-(octanoyloxy)undecyl 8-bromooctanoate (50.0 mg, 0.096 mmol) was dissolved in acetonitrile (0.3 mL), and 2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)amino]octanoate (30.7 mg, 0.08 mmol), potassium carbonate (38.7 mg, 0.28 mmol), potassium iodide (15.9 mg, 0.096 mmol), and tetrahydrofuran (0.2 mL) were added sequentially. Finally, the mixture was reacted at 75 ℃ for 12 hours under nitrogen protection. TLC monitored that the reaction was

complete, and the mixture was filtered and concentrated. After purification by column chromatography, 2-(4-pentylcyclohexyl)ethyl 8-[(2-hydroxyethyl)(8-{[2-(octanoyloxy)undecyl]oxy}-8-oxooctyl)amino]octanoate as a colorless liquid was obtained (33 mg, 50.0% yield).

^{1}H NMR (400 MHz, CHLOROFORM-d) δ = 5.10 (dq, J_1 = 4.0, J_2 =6.8 Hz, 1H), 4.24 (dd, J_1 = 3.6, J_2 = 12.0 Hz, 1H), 4.15 - 4.09 (m, 2H), 4.05 (dd, J_1 = 6.8, J_2 =12.0 Hz, 1H), 3.60 (br s, 2H), 2.73 - 2.60 (m, 2H), 2.54 (br s, 3H), 2.36 - 2.28 (m, 6H), 1.76 (br d, J = 10.8 Hz, 5H), 1.62 (br d, J = 6.0 Hz, 17H), 1.38 - 1.23 (m, 44H), 1.20 - 1.15 (m, 2H), 0.90 (br t, J = 6.8 Hz, 9H) ppm.

LCMS: RT = 2.103, m/z 822.7 $[M+H]^+$.

Preparation Example 53: Preparation of Compound 17

Step 1: Preparation of 17-1

Reaction scheme:



Material ratio:

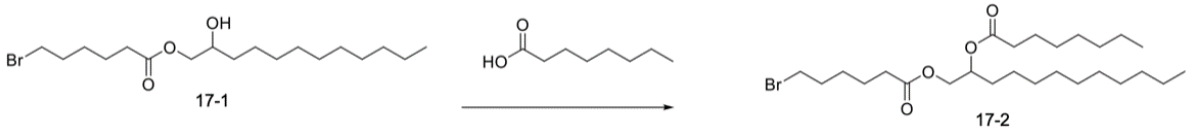
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
6-bromohexanoic acid	195	1 eq	19.5 g	100
1,2-epoxydodecane	184	1 eq	18.4 g	100
ferric chloride	162	0.05 eq	800 mg	5
pyridine	79	0.025 eq	200 mL	2.5

Procedure:

To the reaction flask, 6-bromohexanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.4, TLC (PE:EA=4:1). The reaction mixture was diluted with 200 mL of ethyl acetate, washed once with 200 mL of a saturated aqueous sodium bicarbonate solution, and washed once again with 200 mL of a saturated aqueous sodium chloride solution, and the organic phase was taken, dried over anhydrous magnesium sulfate, filtered, and then concentrated. After purification by column chromatography, 18 g of oily substance was obtained.

Step 2: Preparation of 17-2

Reaction scheme:



Material ratio:

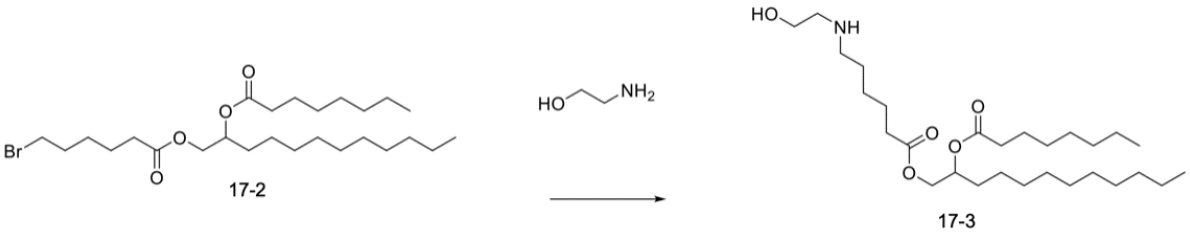
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
17-1	379.38	1 eq	3.45 g	9.1
n-octanoic acid	144.21	1 eq	1.3 g	9.1
EDCI	192	1.5 eq	2.7 g	13.7
DMAP	122	0.15 eq	200 mg	1.4
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 17-1, n-octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was diluted with 100 mL of dichloromethane, washed once with 100 mL of a saturated aqueous sodium bicarbonate solution, and washed once again with 100 mL of a saturated aqueous sodium chloride solution, and the organic phase was taken, dried over anhydrous magnesium sulfate, filtered, and then concentrated. After purification by column chromatography, 4 g of oily substance was obtained.

Step 3: Preparation of 17-3

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
17-2	505.58	1 eq	4 g	7.9
ethanolamine	61	10 eq	4.8 g	79
acetonitrile	-	-	60 mL	-

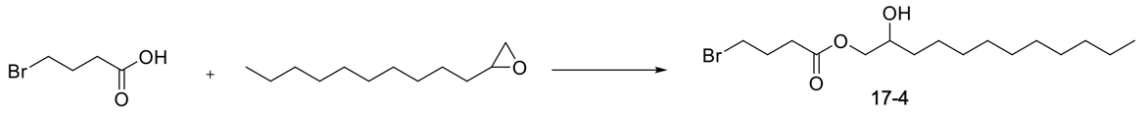
Procedure:

To the reaction flask, 17-2, ethanolamine, and acetonitrile were added, and the mixture was reacted at room temperature for 16 h. The product rR value was 0.3, TLC (DCM:MeOH=10:1). The reaction mixture was diluted with 100 mL of ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and

then concentrated. After purification by column chromatography, 2.8 g of oily substance was obtained.

Step 4: Preparation of 17-4

Reaction scheme:



Material ratio:

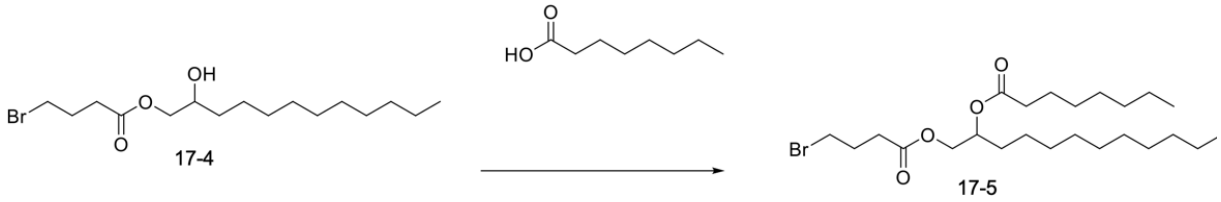
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
4-bromobutanoic acid	167	1 eq	6.68 g	40
1,2-epoxydodecane	184	1 eq	7.36 g	40
ferric chloride	162	0.05 eq	324 mg	2
pyridine	79	0.05 eq	158 mg	2

Procedure:

To the reaction flask, 4-bromobutanoic acid, 1,2-epoxydodecane, ferric chloride, and pyridine were added, and the mixture was reacted at room temperature for 16 h. The product Rf value was 0.4, TLC (PE:EA=4:1). The reaction mixture was concentrated, and after purification by column chromatography, 8 g of oily substance was obtained.

Step 5: Preparation of 17-5

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
17-4	351.33	1 eq	8 g	22.8
octanoic acid	144.21	1.1 eq	3.6 g	25
EDCI	155	1.5 eq	5.3 g	34
DMAP	122	0.15 eq	420 mg	3.4
DCM	-	-	150 mL	-

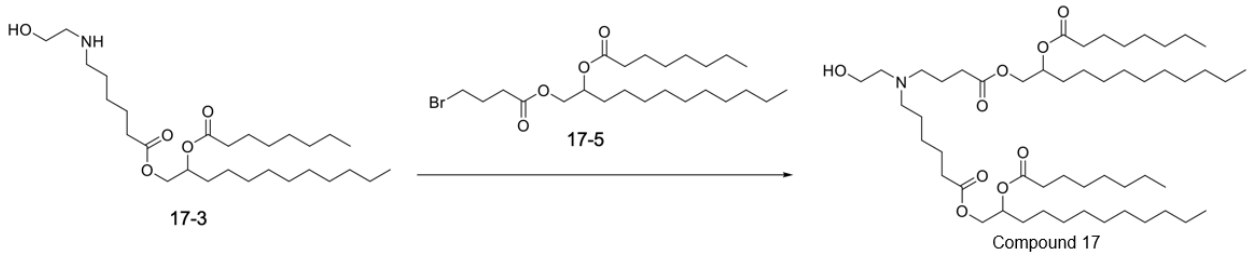
Procedure:

To the reaction flask, 17-4, octanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was concentrated, and after purification by column

chromatography, 7.5 g of oily substance was obtained.

Step 6: Preparation of Compound 17

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
17-3	485.75	1 eq	2.4 g	5
17-5	477.52	1.2 eq	2.9 g	6
potassium carbonate	138	1.5 eq	1 g	7.5
potassium iodide	166	0.5 eq	420 mg	2.5
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 17-3, 17-5, K_2CO_3, KI, and acetonitrile were added, and the mixture was heated to 65°C and stirred for the reaction for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was diluted with 100 mL of ethyl acetate, and washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 2 g of a colorless oily substance was obtained.

^{1}H NMR (400 MHz, Chloroform-d) δ 5.08 (qd, J = 6.7, 3.2 Hz, 2H), 4.22 (ddd, J = 11.9, 5.6, 3.4 Hz, 2H), 4.02 (ddd, J = 11.8, 6.8, 2.1 Hz, 2H), 3.53 (t, J = 5.3 Hz, 2H), 2.58 (t, J = 5.4 Hz, 2H), 2.47 (dt, J = 14.4, 7.2 Hz, 4H), 2.31 (q, J = 7.1 Hz, 8H), 1.76 (p, J = 7.4 Hz, 2H), 1.65 – 1.53 (m, 12H), 1.44 (q, J = 7.6 Hz, 2H), 1.32 – 1.23 (m, 48H), 0.88 (t, J = 6.7 Hz, 12H).

MS (ES+) m/z): 882.7$(M)^+$.

Preparation Example 54: Preparation of Compound 61

Step 1: Preparation of 61-1

Reaction scheme:



Material ratio:

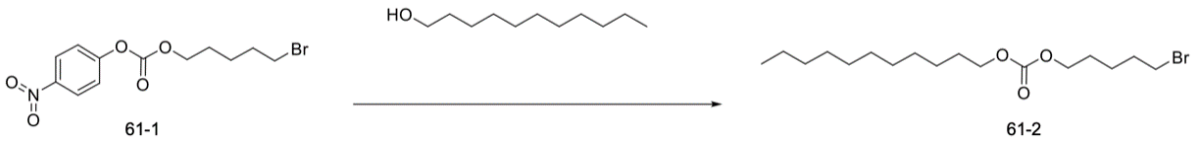
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
5-bromopentanol	167	1 eq	3.34 g	20
p-nitrophenyl chloroformate	201	1.2 eq	4.8 g	24
pyridine	79	1.5 eq	2.4 g	30
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 5-bromopentanol, p-nitrophenyl chloroformate, pyridine, and DCM were added, and the mixture was reacted at room temperature for 16 h. TLC (PE:EA=4:1), product Rf value was 0.6. After purification by column chromatography, 5.3 g of a colorless oily substance was obtained.

Step 2: Preparation of 61-2

Reaction scheme:



Material ratio:

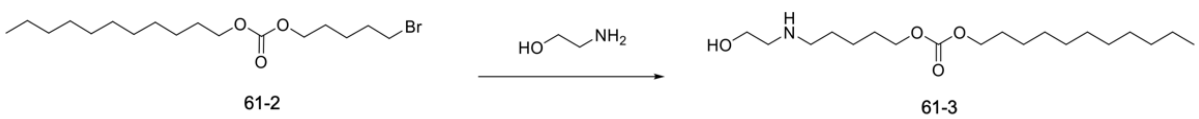
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-1	332	1 eq	3.32 g	10
undecanol	172	4 eq	6.88 g	40
pyridine	79	1.2 eq	950 mg	12
DMAP	122	0.2 eq	250 mg	2
DCM	-	-	60 mL	-

Procedure:

To the reaction flask, 61-1, undecanol, pyridine, DMAP, and DCM were added, and the mixture was reacted at room temperature for 16 h. TLC (PE:EA=10:1), product Rf value was 0.6. After purification by column chromatography, 2.8 g of a colorless oily substance was obtained.

Step 3: Preparation of 61-3

Reaction scheme:



Material ratio:

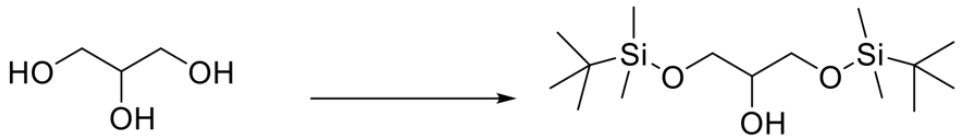
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-2	365	1 eq	2.8 g	7.67
ethanolamine	61	10 eq	4.7 g	77
acetonitrile	-	-	60 mL	-

Procedure:

To the reaction flask, 61-2, ethanolamine, and acetonitrile were added, and the mixture was reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.3. After purification by column chromatography, 1.8 g of a colorless oily substance was obtained.

Step 4: Preparation of 61-4

Reaction scheme:



61-4

Material ratio:

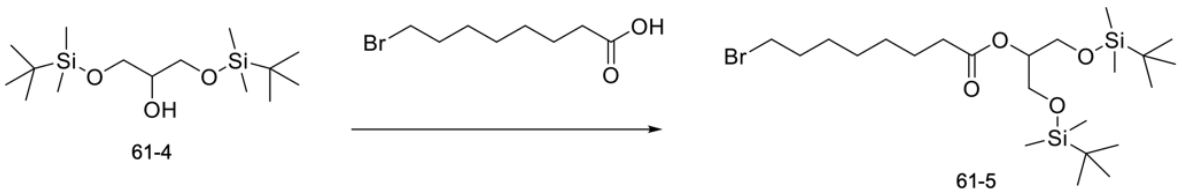
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
glycerol	92	1 eq	9.2 g	100
imidazole	68	2.5 eq	17 g	250
tert-butyldimethylchlorosilane	150.72	2.1 eq	31.7 g	210
tetrahydrofuran	-	-	200 mL	-

Procedure:

To the reaction flask, glycerol, imidazole, and tetrahydrofuran were added. The temperature was lowered to 0-5 ℃, a tetrahydrofuran solution of tert-butyldimethylchlorosilane was added dropwise, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=10:1) product Rf value was 0.3. 500 mL of water was added to the reaction mixture, followed by extraction with 500 mL of ethyl acetate. The organic phase was taken, dried, and then concentrated. After purification by column chromatography, 28 g of a colorless oily substance was obtained.

Step 5: Preparation of 61-5

Reaction scheme:



61-4 61-5

Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-4	320.62	1 eq	12.8 g	40
8-bromooctanoic acid	223.11	1.1 eq	9.8 g	44
EDCI	192	2 eq	15.4 g	80
DMAP	122	0.2 eq	1 g	8
dichloromethane	-	-	200 mL	-

Procedure:

To the reaction flask, 61-4, 8-bromooctanoic acid, EDCI, DMAP, and DCM were added, and the mixture was reacted at room temperature for 2 h. The product Rf value was 0.6, TLC (PE:EA=10:1). The reaction mixture was washed once with 200 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 13.2 g of a colorless oily substance was obtained.

Step 6: Preparation of 61-6

Reaction scheme:



Material ratio:

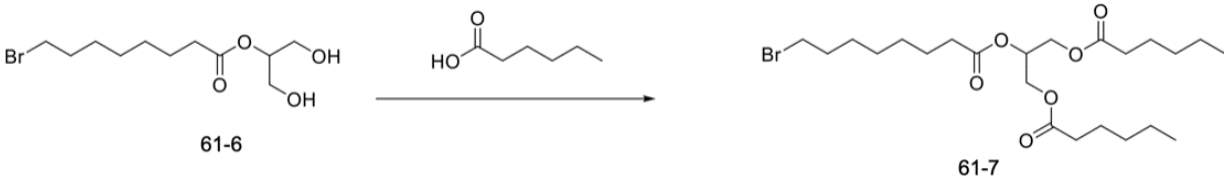
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-5	525.72	1 eq	13.2 g	25
1 M tetrabutylammonium fluoride in tetrahydrofuran	-	3 eq	75 mL	75
tetrahydrofuran	-	-	100 mL	-

Procedure:

To the reaction flask, 61-5 and tetrahydrofuran were added, and then a 1 M tetrabutylammonium fluoride in tetrahydrofuran was added. The mixture was stirred and reacted at room temperature for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. 400 mL of water was added to the reaction mixture, followed by extraction with 400 mL of ethyl acetate. The organic phase was taken, dried, and then concentrated. After purification by column chromatography, 6.5 g of a colorless oily substance was obtained.

Step 7: Preparation of 61-7

Reaction scheme:



Material ratio:

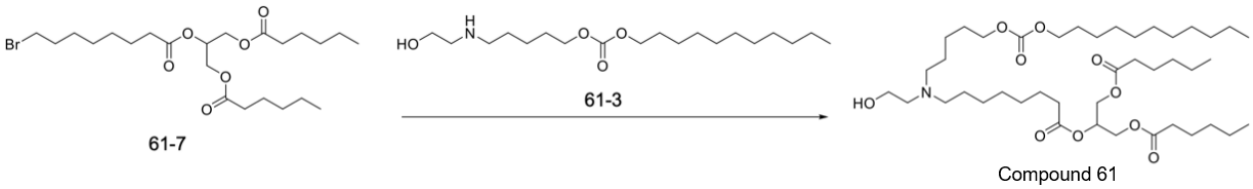
Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-6	297.19	1 eq	6 g	20
hexanoic acid	116	2.2 eq	5.1 g	44
EDCI	192	3 eq	11.5 g	60
DMAP	122	0.2 eq	488 mg	4
DCM	-	-	100 mL	-

Procedure:

To the reaction flask, 61-6, hexanoic acid, EDCI, DMAP, and DCM were added, and the mixture was stirred and reacted at room temperature for 16 h. TLC (PE:EA=20:1) product Rf value was 0.6. The reaction mixture was washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 8.2 g of a colorless oily substance was obtained.

Step 8: Preparation of Compound 61

Reaction scheme:



Material ratio:

Material Name	Molecular Weight	Feed Ratio	Feed Amount	mmol
61-3	345	1 eq	1.8 g	5.2
61-7	493	1.2 eq	3 g	6.3
potassium carbonate	138	1.5 eq	1.1 g	7.8
potassium iodide	166	0.5 eq	430 mg	2.6
acetonitrile	-	-	50 mL	-

Procedure:

To the reaction flask, 61-3, 61-7, potassium carbonate, potassium iodide, and acetonitrile were added, and the mixture was reacted at 65 ℃ for 16 h. TLC (DCM:MeOH=10:1) product Rf value was 0.5. The reaction mixture was diluted with 100 mL of ethyl acetate, and then washed once with 100 mL of water, and the organic phase was taken, dried over anhydrous sodium sulfate, filtered, and then concentrated. After purification by column chromatography, 2.5 g of

oily substance was obtained.

^{1}H NMR (400 MHz, Chloroform-d) δ 5.29 – 5.23 (m, 1H), 4.29 (dd, J = 11.9, 4.3 Hz, 2H), 4.17 – 4.08 (m, 6H), 3.61 (t, J = 5.3 Hz, 2H), 2.68 (t, J = 5.4 Hz, 2H), 2.56 (q, J = 7.2 Hz, 4H), 2.31 (td, J = 7.6, 2.6 Hz, 6H), 1.74 – 1.44 (m, 14H), 1.40 – 1.23 (m, 32H), 0.88 (q, J = 6.8 Hz, 9H).

MS (ES+) m/z): 758.6$(M+H)^+$.

Example 1: Preparation and Detection of Lipid Nanoparticles (LNPs)

This example is used to verify whether the lipid nanoparticle (LNP) formulations prepared from the ionizable lipid compounds disclosed in the present application can effectively encapsulate mRNA and maintain the structural integrity of the mRNA. The prepared ionizable lipid compound, distearoylphosphatidylcholine (DSPC, purchased from Nippon Fine Chemical Co., Ltd., Cat. No.: S01005), cholesterol (purchased from Nippon Fine Chemical Co., Ltd., Cat. No.: O01001), and dimyristoylglycerol-polyethylene glycol 2000 (DMG-PEG2000, purchased from Guobang Pharma, Cat. No.: O02005) were respectively dissolved in an ethanol (manufacturer: Nanjing Chemical Reagent Co., Ltd., purity 99.6%) solution, and then mixed according to a certain molar ratio to prepare solution of mixed lipids in ethanol, in which a total concentration of lipids was 12.5 mM (the unit of measurement "M" appearing in the present application refers to mol/L). Firefly luciferase (Fluc) mRNA was diluted in a 25 mM sodium acetate buffer at pH 5.0 to obtain mRNA solution. By using a microfluidic device, controlling a flow rate to be 12 mL/min, and controlling a volume ratio of the solution of mixed lipids in ethanol to the mRNA solution prepared in the previous step to be 1:3, the lipid nanoparticles were prepared at a nitrogen-to-phosphorus ratio of the ionizable lipid to the mRNA of 3 to 15:1. Ethanol was removed by dialysis in 20 mM Tris-acetate for 12 to 24 hours. Finally, the LNP solution was filtered through a sterile filter with a pore size of 0.22 μm (manufacturer: Millex, Cat. No.: SLGPR33RB), and concentrated by ultrafiltration (manufacturer: Amicon-Ultra, molecular weight cutoff: 10 kDa) to obtain the LNP formulation in which Fluc mRNA was encapsulated by the ionizable lipid described in the present application, DSPC, cholesterol, and DMG-PEG2000. Using a dynamic light scattering method, the particle size and polydispersity index (polymer dispersity index, PDI) of each LNP formulation were measured by a Malvern Zetasizer Ultra instrument (manufacturer: Malvern); the encapsulation efficiency of LNP was measured using a Quant-it Ribogreen RNA quantitative assay kit (manufacturer: ThermoFisher

Scientific, Cat. No.: R11490).

Table 1

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
SM102	SM102: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	73.57	0.102	94.0
Compound 2	compound2: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	61.55	0.073	98.1
Compound 3	compound3: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.72	0.090	96.9
Compound 6	compound6: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	70.08	0.097	97.7

In the art, if a PDI is less than 0.3, it indicates that nanoparticle sizes in the LNP formulation are relatively uniform; the encapsulation efficiency is used to indicate whether the LNP can effectively encapsulate mRNA, and an encapsulation efficiency higher than 70% indicates that the LNP can effectively encapsulate mRNA. The particle sizes of the LNPs prepared by the present application were kept at 60-100 nm, all the PDIs were less than 0.2, and all the encapsulation efficiencies were higher than 90%.

Example 2: *in vivo* Study of LNP Formulations in Animals

In this example, the LNPs prepared in Example 1 were injected at a dose of 5 μg/mouse via tail vein or lower limb intramuscular injection into 6- to 8-week-old female Balb/C mice (Vital River) in vivo (n=3, i.e., 3 mice in each group were used for injection and testing, and the data results presented are the mean values of the measurements of each group). At specific time points after administration (in this example, 4th hour, 24th hour, and 48th hour), D-luciferin potassium salt was injected intraperitoneally, and then luminescence was detected by an IVIS Spectrum small animal *in vivo* imager (manufacturer: PerkinElmer). The total chemiluminescence intensity in *in vivo* expression parts of the mice (such as liver, lower limb administration parts, etc.) was counted. The higher the chemiluminescence intensity, the higher the luciferase expression, that is, the better the corresponding LNP formulation expresses in the mice. The total chemiluminescence intensity is data of the chemiluminescence intensity of a light-emitting part measured by bioluminescence imaging 6 to 15 minutes (min) after intraperitoneal injection of D-luciferin potassium salt. The total chemiluminescence intensity of an *in vivo* expression region was counted by Living Image software (manufacturer:

PerkinElmer). Usually, the reading of the total chemiluminescence intensity detected by the *in vivo* imager in mice not subjected to administration treatment is on the order of 10^5.

Referring to the above mouse *in vivo* experimental method, the LNP formulations in Example 1 were injected into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse via tail vein, and the total chemiluminescence intensity in the liver region was counted. The test results are shown in FIG. 1 and Table 2. The LNP formulations tested in this example all exhibited strong expression in mice, and the AUC ranged from 10^9 to 10^{12}, indicating that the LNP formulations corresponding to the ionizable lipids described in the Preparation Examples can effectively deliver mRNA in vivo for expression. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 2: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 2	9.30E+11
Compound 3	3.00E+12
Compound 6	4.93E+12

Similarly, the LNP formulations prepared in Example 1 were administered at a dose of 5 μg/mouse to 6- to 8-week-old female Balb/C mice by intramuscular injection (into right lower hind limb), and the respective total chemiluminescence intensities in the liver region and the injected muscle site under this administration mode were counted, and the corresponding area under the expression kinetics curve (AUC) from 4 to 48 h was calculated. The test results are shown in FIG. 2, FIG. 3, and Table 3. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 3: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region and at the administration site

Group	Administration site AUC (p/s×h)	Liver AUC (p/s×h)
Compound 2	1.08E+11	2.74E+10
Compound 3	1.33E+11	1.08E+11
Compound 6	2.72E+11	2.88E+11

Example 3: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 8 and Compound 9 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 4. The mRNA in this

example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 4, the particle sizes of the LNP formulations prepared in this example were between 60 and 110 nm, all the PDIs were less than 0.2, and all the encapsulation efficiencies were higher than 90%.

Table 4

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 8	Compound 8: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	89.89	0.118	95.0
Compound 9	Compound 9: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	107.37	0.166	92.9

Example 4: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 3 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 4 and Table 5. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 5: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 8	1.98E+12
Compound 9	1.50E+12

Similarly, the LNP formulations prepared in Example 3 were administered at a dose of 5 μg/mouse to 6- to 8-week-old female Balb/C mice by intramuscular injection (into right lower hind limb), and the respective total chemiluminescence intensities in the liver region and the injected muscle site under this administration mode were counted, and the corresponding area under the expression kinetics curve (AUC) from 4 to 48 h was calculated. The test results are shown in FIG. 5, FIG. 6, and Table 6. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 6: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region and at the administration site

Group	Administration site AUC (p/s×h)	Liver AUC (p/s×h)
Compound 8	1.30E+11	4.22E+10
Compound 9	1.12E+11	3.45E+10

Example 5: Atomization Stability Test

The LNP formulations prepared in Example 1 and Example 3 were atomized and generated by an aerosol needle (Shanghai Yuyan Scientific Instrument Co., Ltd.) (the same group name indicates that the molar percentage and nitrogen-to-phosphorus ratio of the formulation are the same as those in Examples 1 and 3), and the physicochemical characteristics of the samples before and after atomization were tested. The results are shown in Table 7. It can be seen that after atomization, all the samples showed an increase in particle size, an increase in PDI, and a decrease in encapsulation efficiency. It is generally considered in the art that, using the determination method described in the present application, the criteria for relatively good stability of the formulation after atomization are: PDI < 0.3, encapsulation efficiency > 85%. The formulations of Compound 3, Compound 6, Compound 8 and Compound 9 after atomization had relatively good stability, and are expected to improve the stability and efficacy when developed as aerosols.

Table 7

Group	Product characteristics		
	Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
SM102 before atomization	68.40	0.035	96.4
SM102 after atomization	86.79	0.267	82.9
Compound 2 before atomization	61.55	0.073	98.1
Compound 2 after atomization	90.97	0.380	89.9
Compound 3 before atomization	69.72	0.090	96.9
Compound 3 after atomization	83.79	0.255	87.5
Compound 6 before atomization	70.08	0.097	97.7
Compound 6 after atomization	86.59	0.252	86.2
Compound 8 before atomization	89.89	0.118	95.0
Compound 8 after atomization	102.97	0.225	85.4
Compound 9 before atomization	107.37	0.166	92.9
Compound 9 after atomization	119.10	0.275	85.6

Example 6: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 5 and Compound 28 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 8. The mRNA in this

example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 8, the particle sizes of the LNP formulations prepared in this example were between 50 and 100 nm, all the PDIs were less than 0.2, and all the encapsulation efficiencies were higher than 90%.

Table 8

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 5	Compound 5: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	59.75	0.084	95.2
Compound 28	Compound 28: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	57.29	0.077	94.6

Example 7: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 6 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 7 and Table 9, and the LNP formulations prepared in this example all exhibited strong expression in mice. In terms of overall expression trend, Compound 5 and Compound 28 were both slightly better than SM102.

Table 9: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
SM102	2.73E+12
Compound 5	4.00E+12
Compound 28	3.81E+12

Similarly, the LNP formulations prepared in Example 6 were administered at a dose of 5 μg/mouse to 6- to 8-week-old female Balb/C mice by intramuscular injection (into right lower hind limb), and the respective total chemiluminescence intensities in the liver region and the injected muscle site under this administration mode were counted, and the corresponding area under the expression kinetics curve (AUC) from 4 to 48 h was calculated. The test results are shown in FIG. 8, FIG. 9, and Table 10. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 10: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

and at the administration site

Group	Administration site AUC (p/s×h)	Liver AUC (p/s×h)
Compound 5	1.60E+11	1.35E+11
Compound 28	1.47E+11	1.07E+11

Example 8: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compounds 23-27, Compound 29, and Compound 34 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 11. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 11, the particle sizes of the LNP formulations prepared in this example were between 60 and 100 nm, all the PDIs were less than 0.3, and all the encapsulation efficiencies were higher than 90%.

Table 11

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
SM102	SM102: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	73.57	0.102	94.0
Compound 23	Compound 23: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	76.39	0.110	97.4
Compound 24	Compound 24: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.38	0.134	97.6
Compound 25	Compound 25: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	75.20	0.072	96.7
Compound 26	Compound 26: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	72.67	0.099	97.3
Compound 27	Compound 27: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	97.55	0.269	96.7
Compound 29	Compound 29: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	63.76	0.082	97.2
Compound 34	Compound 34: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	64.17	0.062	97.6

Example 9: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 8 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a

dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 10 and Table 12. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 12: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 23	4.22E+12
Compound 24	5.37E+12
Compound 25	3.02E+12
Compound 26	7.92E+12
Compound 29	5.12E+12
Compound 34	4.43E+12

Similarly, the LNP formulations prepared in Example 8 were administered at a dose of 5 μg/mouse to 6- to 8-week-old female Balb/C mice by intramuscular injection (into right lower hind limb), and the respective total chemiluminescence intensities in the liver region and the injected muscle site under this administration mode were counted, and the corresponding area under the expression kinetics curve (AUC) from 4 to 48 h was calculated. The test results are shown in FIG. 11, FIG. 12, and Table 13. It can be seen that the LNP formulations prepared in this example all exhibited strong expression in mice. In terms of overall expression trend, Compounds 23-26, Compound 29, and Compound 34 were all slightly better than SM102, and compound 27 was better than SM102 at the local administration site.

Table 13: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region and at the administration site

Group	Administration site AUC (p/s×h)	Liver AUC (p/s×h)
SM102	1.45E+11	7.20E+10
Compound 23	3.74E+11	2.08E+11
Compound 24	3.07E+11	1.62E+11
Compound 25	3.41E+11	8.68E+10
Compound 26	3.59E+11	1.07E+11
Compound 27	2.02E+11	2.82E+10
Compound 29	2.70E+11	8.88E+10
Compound 34	2.27E+11	1.44E+11

Example 10: Atomization Stability Test

The LNP formulations prepared in Example 6 and Example 8 were atomized and generated by an aerosol needle (Shanghai Yuyan Scientific Instrument Co., Ltd.) (the same group name indicates that the molar percentage and nitrogen-to-phosphorus ratio of the formulation were the

same as those in Examples 6 and 8), and the physicochemical characteristics of the samples before and after atomization were tested. The results are shown in Table 14.

Table 14

Group	Product characteristics		
	Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
SM102 before atomization	69.57	0.085	94.4
SM102 after atomization	95.45	0.316	78.8
Compound 5 before atomization	59.75	0.084	95.2
Compound 5 after atomization	99.47	0.402	77.7
Compound 23 before atomization	76.39	0.110	97.4
Compound 23 after atomization	100.95	0.281	83.7
Compound 24 before atomization	69.38	0.134	97.6
Compound 24 after atomization	95.91	0.339	79.7
Compound 25 before atomization	75.20	0.072	96.7
Compound 25 after atomization	92.04	0.242	85.4
Compound 26 before atomization	72.67	0.099	97.3
Compound 26 after atomization	104.50	0.329	75.3
Compound 27 before atomization	97.55	0.269	96.7
Compound 27 after atomization	97.76	0.374	79.2
Compound 28 before atomization	57.29	0.077	94.6
Compound 28 after atomization	98.79	0.417	78.0
Compound 29 before atomization	63.76	0.082	97.2
Compound 29 after atomization	90.93	0.351	81.3
Compound 34 before atomization	64.17	0.062	97.6
Compound 34 after atomization	87.61	0.308	83.2

It can be seen that after atomization, all the samples showed an increase in particle size, an increase in PDI, and a decrease in encapsulation efficiency. It is generally considered in the art that, using the determination method described in the present application, the criteria for relatively good stability of the formulation after atomization are: PDI < 0.3, encapsulation efficiency > 85%. The stability of the formulation of Compound 25 after atomization was better, which is expected to improve its stability and efficacy when developed as an aerosol.

Example 11: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 4 was selected as an ionizable lipid, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 15. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at

pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 15, the particle sizes of the LNP formulations prepared in this example were between 60 and 70 nm, all the PDIs were less than 0.1, and the encapsulation efficiency was higher than 90%.

Table 15

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 4	Compound 4: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	63.36	0.065	95.8

Example 12: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 11 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in Table 16, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 16 Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 4	3.56E+12

Example 13: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 1, Compound 7, Compound 21, Compound 32, Compound 48, Compound 55, and compound 57 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 17. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 17, the particle sizes of the LNP formulations prepared in this example were between 50 and 80 nm, all the PDIs were less than 0.15, and all the encapsulation efficiencies were higher than 90%.

Table 17

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 1	Compound 1: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	56.53	0.074	95.0
Compound 7	Compound 7: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	71.25	0.062	96.0
Compound 21	Compound 21: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	57.66	0.106	96.6
Compound 32	Compound 32: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	60.92	0.089	94.3
Compound 48	Compound 48: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	55.68	0.108	96.6
Compound 55	Compound 55: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	56.19	0.090	96.0
Compound 57	Compound 57: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	55.52	0.078	95.9

Example 14: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 13 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 13 and Table 18, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 18: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 1	1.96E+12
Compound 7	2.01E+12
Compound 21	9.44E+11
Compound 32	2.37E+12
Compound 48	2.50E+12
Compound 55	1.16E+12
Compound 57	1.93E+12

Example 15: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 2, Compound 3, and compound 6 were selected as ionizable lipids, and LNP formulations (encapsulating VZV mRNA) were prepared by referring to the

method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 19. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 19, the particle sizes of the LNP formulations prepared in this example were between 60 and 80 nm, all the PDIs were less than 0.1, and all the encapsulation efficiencies were higher than 90%.

Table 19

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 2	Compound 2: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	67.96	0.085	98.3
Compound 3	Compound 3: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.51	0.063	95.4
Compound 6	Compound 6: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	79.13	0.084	96.8

Example 16: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the VZV-LNP formulations prepared in Example 15 were injected via tail vein into 6- to 8-week-old female BABL/c mice at a dose of 60 μg/mouse, and whole blood was collected from the mice 3 hours after injection. Serum was isolated from the whole blood by centrifugation at 4 °C and 2000 g for 10 min, and stored at -80 °C for analysis. According to the manufacturer's instructions, Glycoprotein E (VZV) Standard (AcroBiosystems, Cat. No. RAS102-C02) and Biotin-Anti-Glycoprotein E (VZV) Antibody (AcroBiosystems, Cat. No. RAS102-C03) were used for enzyme-linked immunosorbent assay (ELISA) analysis to determine the VZV antigen concentration. The test results are shown in FIG. 14 and Table 20 (VZV antigen concentration in serum (n=5), statistical analysis by ANOVA, **** $p < 0.0001$, ***** $p < 0.0001$, compared with a placebo group). Compared with the placebo group animals, the VZV antigen concentrations of the SM102, Compound 2, Compound 3, and compound 6 group animals all significantly increased, and the VZV antigen concentration of the compound 6 group was better than that of the SM102 group.

Table 20: VZV antigen content in serum of BABL/c mice 3 hours after intravenous administration

Group	Serum antigen content (ng/mL)
Placebo	0.08
SM102	189.23
Compound 2	33.31
Compound 3	170.05
Compound 6	245.49

Example 17: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 11, Compounds 19-20, Compound 22, Compounds 30-31, Compound 52, Compound 58, and Compound 60 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 21. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 21, the particle sizes of the LNP formulations prepared in this example were between 50 and 100 nm, all the PDIs were less than 0.2, and all the encapsulation efficiencies were higher than 90%.

Table 21

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
SM102	SM102: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	82.88	0.174	95.9
Compound 11	Compound 11: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	60.56	0.088	94.8
Compound 19	Compound 19: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	73.84	0.083	94.0
Compound 20	Compound 20: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	65.61	0.075	91.8
Compound 22	Compound 22: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	58.72	0.101	95.4
Compound 30	Compound 30: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.39	0.095	96.4
Compound 31	Compound 31: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	75.09	0.126	97.3
Compound 52	Compound 52: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	76.88	0.112	93.8
Compound 58	Compound 58: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	65.99	0.075	95.6
Compound 60	Compound 60: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	97.60	0.117	93.0

Example 18: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 22 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 15 and Table 22, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 22: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 11	2.48E+12
Compound 19	6.27E+12
compound 20	4.37E+12
Compound 22	2.68E+12
Compound 30	1.33E+12
Compound 31	1.07E+12
Compound 52	5.25E+12
Compound 58	2.89E+12
Compound 60	1.43E+12

Example 19: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 33, Compound 35, Compound 36, Compound 37, Compound 47, Compound 49, Compound 50, and Compounds 62-68 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 23. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 23, the particle sizes of the LNP formulations prepared in this example were between 50 and 115 nm, all the PDIs were less than 0.20, and all the encapsulation efficiencies were higher than 90%.

Table 23

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 33	Compound 33: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	60.98	0.044	96.7
Compound 35	Compound 35: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	57.47	0.100	97.3
Compound 36	Compound 36: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	51.68	0.109	93.7
Compound 37	Compound 37: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	65.48	0.123	95.8
Compound 47	Compound 47: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	70.92	0.117	93.1
Compound 49	Compound 49: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	62.38	0.089	95.1
Compound 50	Compound 50: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	84.28	0.158	93.7
Compound 62	Compound 62: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	112.10	0.196	90.2
Compound 63	Compound 63: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	58.70	0.067	96.6
Compound 64	Compound 64: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	60.53	0.102	96.0
Compound 65	Compound 65: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	67.48	0.072	95.9
Compound 66	Compound 66: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	51.48	0.064	95.6
Compound 67	Compound 67: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	57.18	0.067	39.1
Compound 68	Compound 68: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	65.79	0.101	94.4

Example 20: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 19 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 16 and Table 24, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 24: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 33	4.39E+12
Compound 35	1.56E+12
Compound 36	2.87E+10
Compound 37	1.88E+12
Compound 47	1.25E+12
Compound 49	2.63E+12
Compound 50	1.05E+12
Compound 62	1.82E+11
Compound 63	3.81E+12
Compound 64	2.97E+12
Compound 65	3.92E+12
Compound 66	2.32E+12
Compound 67	4.02E+12
Compound 68	9.62E+11

Example 21: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 6 was selected as an ionizable lipid, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 21. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 25, the particle sizes of the LNP formulations prepared in this example were between 50 and 100 nm, all the PDIs were less than 0.3, and all the encapsulation efficiencies were higher than 90%.

Table 25

Group	Compound 6: DSPC: cholesterol: DMG-PEG [Molar percentage of formulation components (%)]	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
LNP1	35: 10: 53.5: 1.5	6:1	83.66	0.246	94.2
LNP2	40: 10: 48.5: 1.5	6:1	64.73	0.132	93.5
LNP3	45: 10: 43.5: 1.5	6:1	65.84	0.095	95.3
LNP4	50: 10: 38.5: 1.5	6:1	68.45	0.072	95.6
LNP5	55: 10: 33.5: 1.5	6:1	77.16	0.049	95.1
LNP6	60: 10: 28.5: 1.5	6:1	89.98	0.029	95.1
LNP7	50: 0: 48.5: 1.5	6:1	96.87	0.074	97.1
LNP8	50: 5: 43.5: 1.5	6:1	77.45	0.094	96.8
LNP9	50: 15: 33.5: 1.5	6:1	66.49	0.078	95.1
LNP10	50: 20: 28.5: 1.5	6:1	67.76	0.092	94.6
LNP11	50: 10: 39.5: 0.5	6:1	93.29	0.087	94.7
LNP12	50: 10: 39.0: 1.0	6:1	77.10	0.086	95.2
LNP13	50: 10: 38.0: 2.0	6:1	64.95	0.069	96.0
LNP14	50: 10: 37.0: 3.0	6:1	58.39	0.058	97.1

Example 22: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 21 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 17 and Table 26, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 26: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
LNP1	1.27E+12
LNP2	2.26E+12
LNP3	2.80E+12
LNP4	4.45E+12
LNP5	3.59E+12
LNP6	2.17E+12
LNP7	8.26E+12
LNP8	7.62E+12
LNP9	1.23E+12
LNP10	3.08E+11
LNP11	4.61E+12
LNP12	5.13E+12
LNP13	2.08E+12
LNP14	6.88E+11

Example 23: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 6 was selected as an ionizable lipid, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 26. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 27, the particle sizes of the LNP formulations prepared in this example were between 50 and 70 nm, all the PDIs were less than 0.10, and all the encapsulation efficiencies were higher than 95%.

Table 27

Group	Compound 6: DSPC: cholesterol: DMG-PEG [Molar percentage of formulation components (%)]	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
NP3	50: 10: 38.5: 1.5	3:1	69.45	0.034	97.0
NP4	50: 10: 38.5: 1.5	4:1	63.31	0.056	96.8
NP5	50: 10: 38.5: 1.5	5:1	59.09	0.047	97.2
NP6	50: 10: 38.5: 1.5	6:1	58.83	0.050	97.2
NP7	50: 10: 38.5: 1.5	7:1	58.22	0.049	97.2
NP8	50: 10: 38.5: 1.5	8:1	60.97	0.037	96.9
NP9	50: 10: 38.5: 1.5	9:1	56.96	0.038	96.0

Example 24: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 23 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 18 and Table 28, and the LNP formulations prepared in this example all exhibited strong expression in mice.

Table 28: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
NP3	2.82E+12
NP4	3.41E+12
NP5	4.30E+12
NP6	4.90E+12
NP7	5.20E+12
NP8	6.35E+12
NP9	5.95E+12

Example 25: Preparation and Detection of Lipid Nanoparticles (LNPs)

In this example, Compound 10, Compounds 12-17, and Compound 61 were selected as ionizable lipids, and LNP formulations (encapsulating Fluc mRNA) were prepared by referring to the method in Example 1 according to the molar ratios and nitrogen-to-phosphorus ratios in Table 28. The mRNA in this example was diluted in a 25 mM sodium acetate solution at pH 5.0, and a 20 mM Tris-acetate solution at pH 7.5 was used during dialysis. The particle size, PDI, and encapsulation efficiency of all the LNP formulations in this example were determined. As can be seen from Table 29, the particle sizes of the LNP formulations prepared in this example were between 50 and 140 nm, all the PDIs were less than 0.3, and all the encapsulation efficiencies were higher than 90%.

Table 29

Group	Molar percentage of formulation components (%)	N/P ratio	Product characteristics		
			Particle size (nm)	Polydispersity index (PDI)	Encapsulation efficiency (%)
Compound 10	Compound 10: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.23	0.214	97.1
Compound 12	Compound 12: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	59.78	0.101	97.1
Compound 13	Compound 13: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	55.71	0.131	94.9
Compound 14	Compound 14: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	60.83	0.148	96.0
Compound 15	Compound 15: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	56.85	0.119	96.2
Compound 16	Compound 16: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	69.31	0.094	96.8
Compound 17	Compound 17: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	62.09	0.074	97.8
Compound 61	Compound 61: DSPC: cholesterol: DMG-PEG=50: 10: 38.5: 1.5	6:1	134.03	0.149	90.1

Example 26: *in vivo* Study of LNP Formulations in Animals

Referring to the mouse *in vivo* experimental method in Example 2, the LNP formulations prepared in Example 25 were injected via tail vein into 6- to 8-week-old female Balb/C mice at a dose of 5 μg/mouse, and the total chemiluminescence intensity in the liver part of the mice *in vivo* was counted. The test results are shown in FIG. 19 and Table 30, and the LNP formulations prepared in this example all exhibited strong expression in mice.

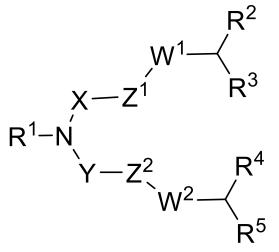
Table 30: Area under the expression kinetics curve (AUC) from 4 to 48 h in the liver region

Group	Liver AUC (p/s*h)
Compound 10	1.86E+11
Compound 12	2.35E+12
Compound 13	5.53E+10
Compound 14	1.75E+12
Compound 15	8.35E+11
Compound 16	1.50E+12
Compound 17	1.19E+12
Compound 61	2.90E+10

Although specific embodiments of the present invention are described above, those skilled in the art should understand that these are merely examples, and various changes or modifications can be made to these embodiments without departing from the principle and essence of the present invention. Therefore, the scope of protection of the present invention is defined by the appended claims.

CLAIMS

1. A compound I or a pharmaceutically acceptable salt thereof,

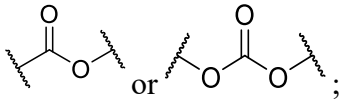


I

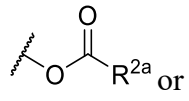
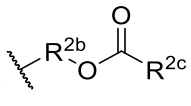
wherein:

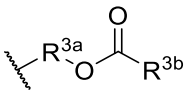
R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

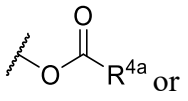
X and Y are independently C_{1-12} alkylene;

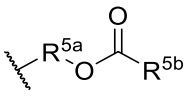
Z^1 and Z^2 are independently  or ;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is  or , R^{2a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-6} alkyl; R^{2b} is C_{1-6} alkylene, and R^{2c} is C_{1-15} alkyl;

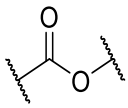
R^3 is C_{1-15} alkyl or , R^{3a} is C_{1-6} alkylene, and R^{3b} is C_{1-15} alkyl;

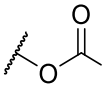
R^4 is H, C_{1-15} alkyl,  or -C_{3-10} cycloalkyl-C_{1-15} alkyl; R^{4a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa}; R^{4aa} is H or C_{1-6} alkyl;

R^5 is C_{1-15} alkyl or , R^{5a} is C_{1-6} alkylene, and R^{5b} is C_{1-15} alkyl.

2. The compound I or the pharmaceutically acceptable salt thereof according to claim 1, satisfying any one of the following schemes:

Scheme (1):

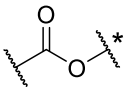
Z^1 and Z^2 are independently ;

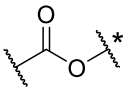
R^2 is , and R^{2a} is C_{1-15} alkyl, C_{1-15} alkenyl, or -C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-6} alkyl;

Scheme (2):

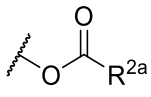
R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

X and Y are independently C_{1-12} alkylene;

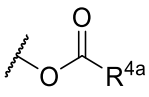
Z^1 is , and the asterisk (*) indicates an attachment to W^1;

Z^2 is , and the asterisk (*) indicates an attachment to W^2;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is , and R^{2a} is C_{1-15} alkyl or C_{1-15} alkenyl;

R^3 is C_{1-15} alkyl;

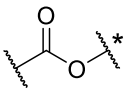
R^4 is C_{1-15} alkyl or ; R^{4a} is C_{1-15} alkyl or C_{1-15} alkenyl;

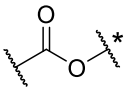
R^5 is C_{1-15} alkyl; and

Scheme (3):

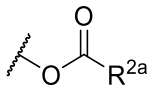
R^1 is C_{1-6} alkyl substituted with one or more hydroxyl groups;

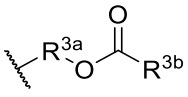
X and Y are independently C_{1-12} alkylene;

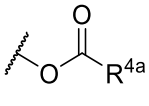
Z^1 is , and the asterisk (*) indicates an attachment to W^1;

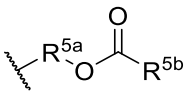
Z^2 is , and the asterisk (*) indicates an attachment to W^2;

W^1 and W^2 are independently a chemical bond or C_{1-6} alkylene;

R^2 is , and R^{2a} is C_{1-15} alkyl or C_{1-15} alkenyl;

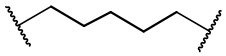
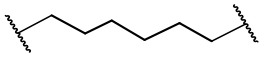
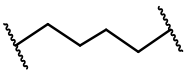
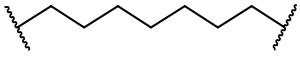
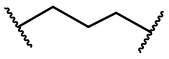
R^3 is C_{1-15} alkyl or , R^{3a} is C_{1-6} alkylene, and R^{3b} is C_{1-15} alkyl;

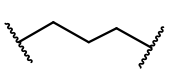
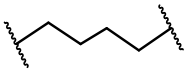
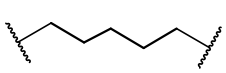
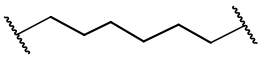
R^4 is C_{1-15} alkyl or ; R^{4a} is C_{1-15} alkyl or C_{1-15} alkenyl;

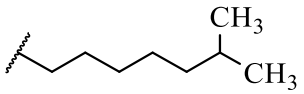
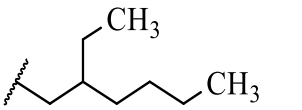
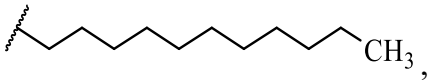
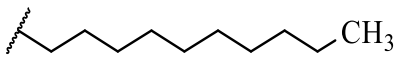
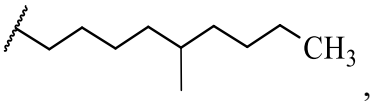
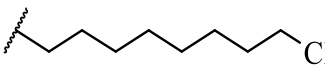
R^5 is C_{1-15} alkyl or , R^{5a} is C_{1-6} alkylene, and R^{5b} is C_{1-15} alkyl.

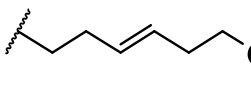
3. The compound I or the pharmaceutically acceptable salt thereof according to claim 2, satisfying one or more of the following conditions:

(1) in R^1, R^{2aa} and R^{4aa}, the "C_{1-6} alkyl" in each of "C_{1-6} alkyl substituted with one or more hydroxyl groups" and "C_{1-6} alkyl" is independently C_{1-4} alkyl, such as methyl, ethyl, n-propyl, or n-butyl;

(2) in X, Y, R^{2a} and R^{4a}, the "C_{1-12} alkylene" in each of "C_{1-12} alkylene", "-C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}", and "-C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa}" is independently C_{3-7} alkylene, such as , , , , or ;

(3) in W^1, W^2, R^{3a} and R^{5a}, each C_{1-6} alkylene is independently methylene, -CH_2CH_2-, , , , or ;

(4) in R^{2a}, R^3, R^{3b}, R^4, R^{4a}, R^5, and R^{5b}, the "C_{1-15} alkyl" in each of "C_{1-15} alkyl" and "-C_{3-10} cycloalkyl-C_{1-15} alkyl" is independently C_{3-12} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , , , or ;

(5) in R^{2a} and R^{4a}, each C_{1-15} alkenyl is independently C_{3-10} alkenyl, such as ;

(6) in R^{2a} and R^{4a}, the "C_{3-6} cycloalkyl" in each of "-C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{2aa}" and "-C_{1-12} alkylene-C_{3-6} cycloalkyl-R^{4aa}" is independently cyclopropyl or cyclobutyl;

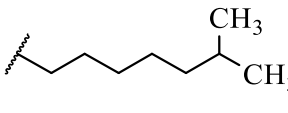
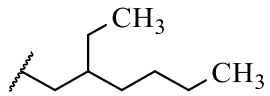
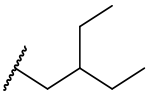
(7) in R^4, the "C_{3-10} cycloalkyl" in "-C_{3-10} cycloalkyl-C_{1-15} alkyl" is C_{3-6} cycloalkyl, such as

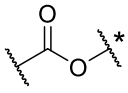
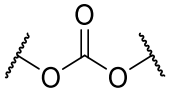
a cyclohexyl.

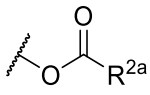
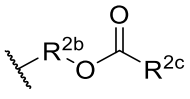
4. The compound I or the pharmaceutically acceptable salt thereof according to claim 1, satisfying one or more of the following conditions:

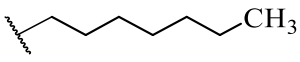
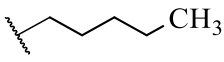
(1) in R^{2b}, the "C_{1-6} alkylene" is C_{1-3} alkylene, such as methylene;

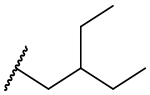
(2) in R^{2c}, the "C_{1-15} alkyl" is C_{3-12} alkyl, such as n-pentyl or n-heptyl;

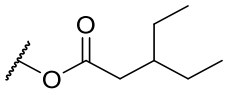
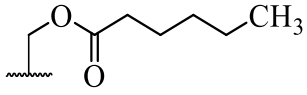
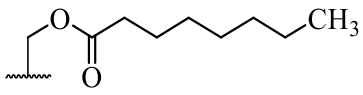
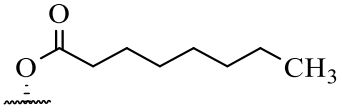
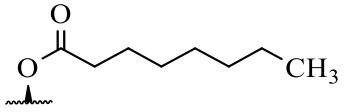
(3) in R^{2a}, the "C_{1-15} alkyl" is C_{3-10} alkyl, such as n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , or ;

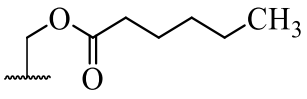
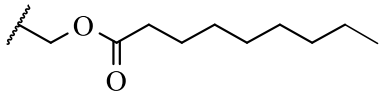
(4) Z^2 is  or , and the asterisk (*) indicates an attachment to W^1;

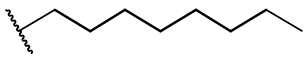
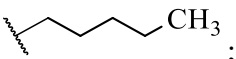
(5) R^2 is  or , and R^{2a} is C_{3-10} alkyl, C_{3-10} alkenyl, or -C_{3-7} alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-3} alkyl; R^{2b} is C_{1-3} alkylene, and R^{2c} is C_{3-10} alkyl;

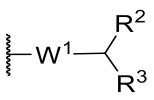
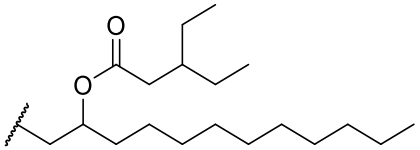
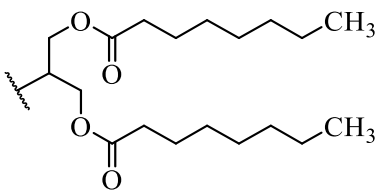
(6) R^{2b} is C_{1-3} alkylene, such as methylene; and R^{2c} is C_{3-10} alkyl, such as  or ;

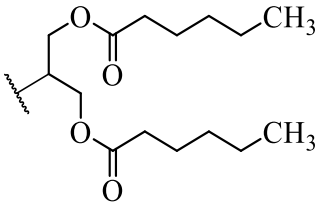
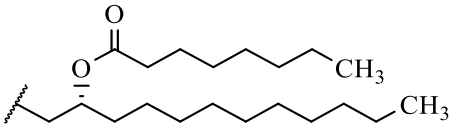
(7) R^{2a} is ;

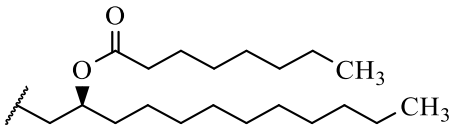
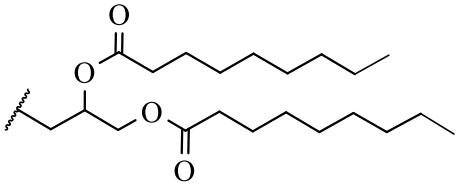
(8) R^2 is ,  or ,  or ;

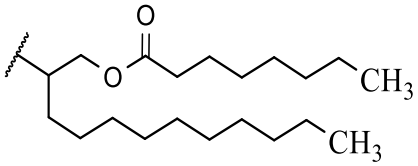
(9) R^3 is  or ;

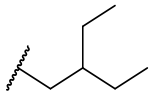
(10) R^{3b} is  or ;

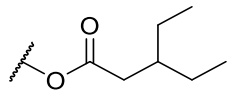
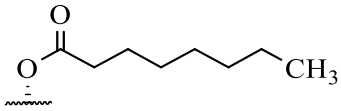
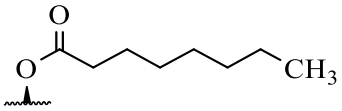
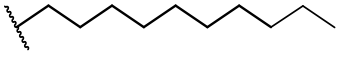
(11)  is , ,


, 
,

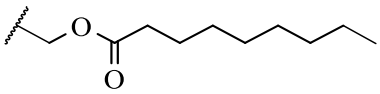

, 
or

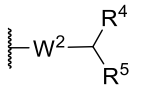
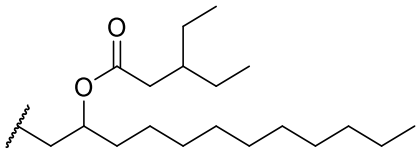
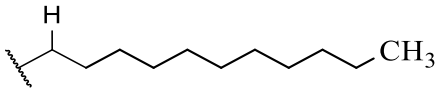

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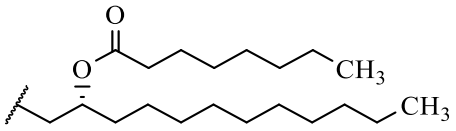
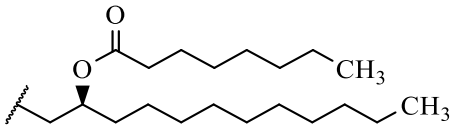
(12) R^{4a} is ;

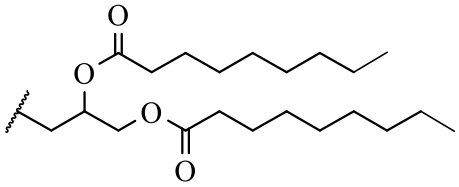
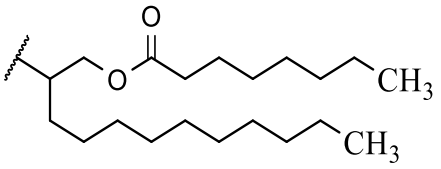
(13) R^4 is , , 
or 
;

(14) R^{5b} is n-octyl;

(15) R^5 is ;

(16)  is , ,

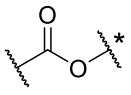

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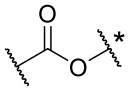

or 
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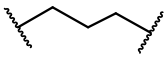
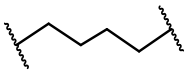
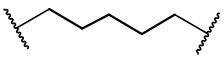
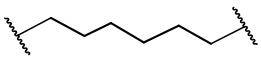
5. The compound I or the pharmaceutically acceptable salt thereof according to claim 2, satisfying one or more of the following conditions:

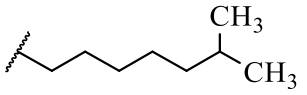
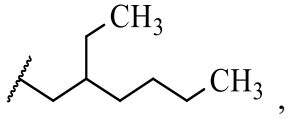
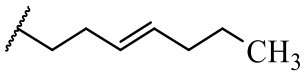
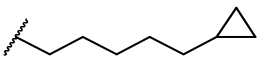
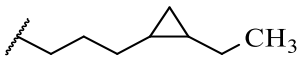
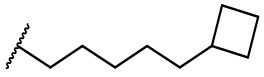
(1) R^1 is C_{1-6} alkyl substituted with one hydroxyl group;

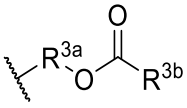
(2) X and Y are independently C_{3-7} alkylene;

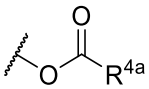
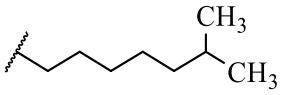
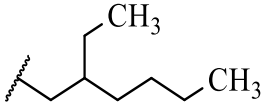
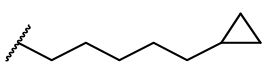
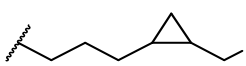
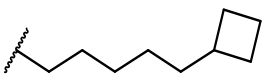
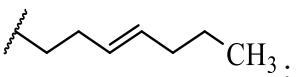
(3) Z^1 is , and the asterisk (*) indicates an attachment to W^1;

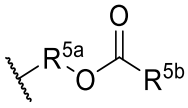
(4) Z^2 is , and the asterisk (*) indicates an attachment to W^2;

(5) W^1 and W^2 are independently a chemical bond, methylene, $-CH_2CH_2-$, , ,  or ;

(6) R^{2a} is C_{3-10} alkyl, C_{3-10} alkenyl, or $-C_{3-7}$ alkylene-C_{3-6} cycloalkyl-R^{2aa}, wherein R^{2aa} is H or C_{1-3} alkyl; preferably, R^{2a} is n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or ;

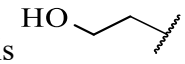
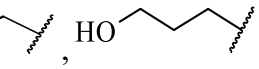
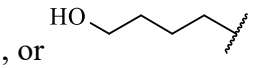
(7) R^3 is C_{4-12} alkyl or , R^{3a} is C_{1-3} alkylene, and R^{3b} is C_{6-12} alkyl; preferably, R^{3a} is methylene; and R^{3b} is n-heptyl;

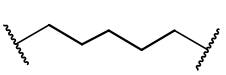
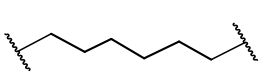
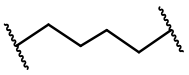
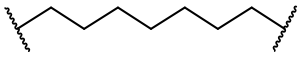
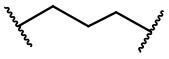
(8) R^4 is H, C_{3-10} alkyl,  or $-C_{3-6}$ cycloalkyl-C_{3-10} alkyl; R^{4a} is C_{3-10} alkyl, C_{3-10} alkenyl, or $-C_{3-7}$ alkylene-C_{3-6} cycloalkyl-R^{4aa}; R^{4aa} is H or C_{1-3} alkyl; preferably, R^{4a} is n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, , , , ,  or ;

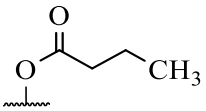
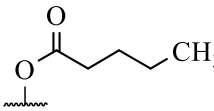
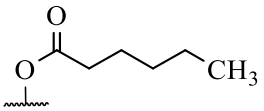
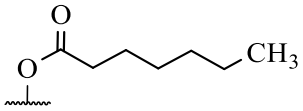
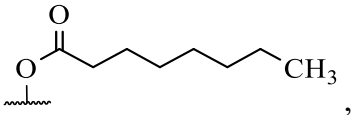
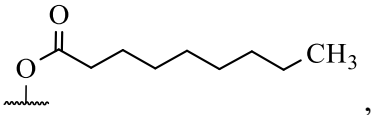
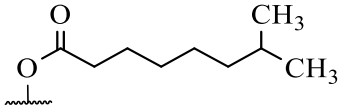
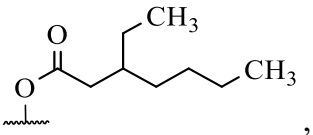
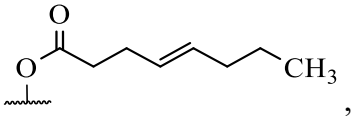
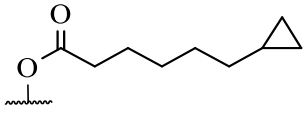
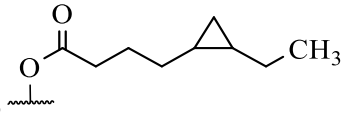
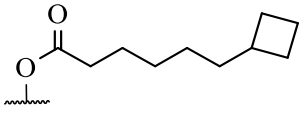
(9) R^5 is C_{6-10} alkyl or , R^{5a} is C_{1-3} alkylene, and R^{5b} is C_{6-10} alkyl; preferably, R^{5a} is methylene; and R^{5b} is n-heptyl.

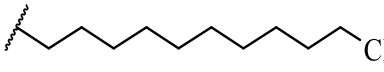
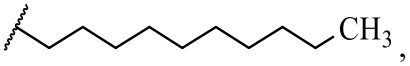
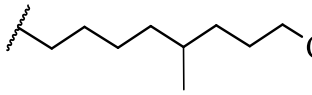
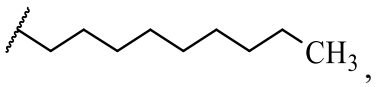
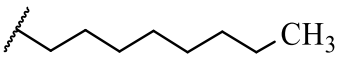
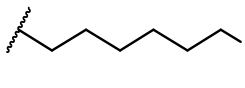
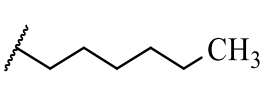
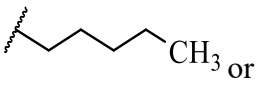
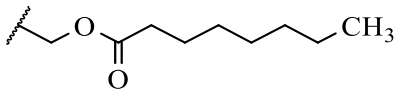
6. The compound I or the pharmaceutically acceptable salt thereof according to claim 2,

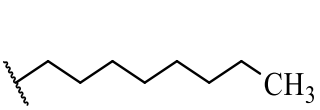
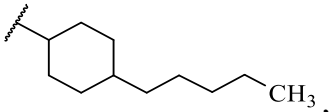
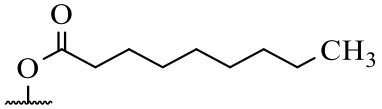
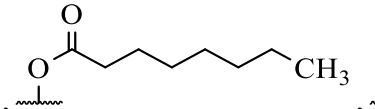
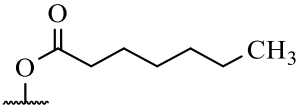
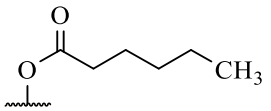
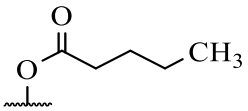
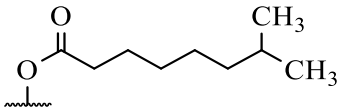
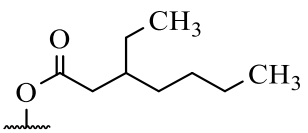
satisfying one or more of the following conditions:

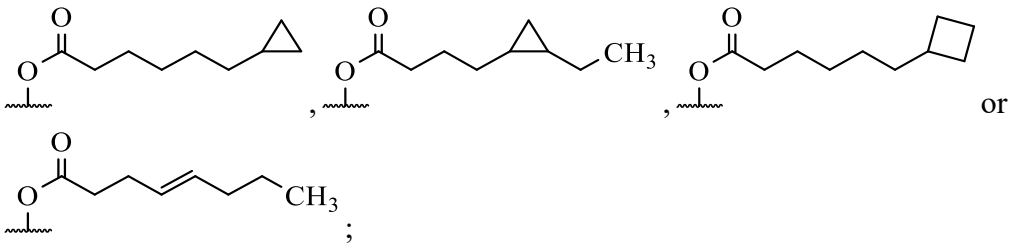
(1) R^1 is , , or ;

(2) X and Y are independently , , ,  or ;

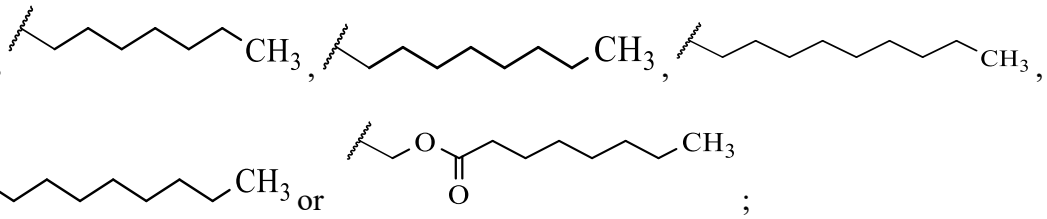
(3) R^2 is , , , , , , , , , ,  or ;

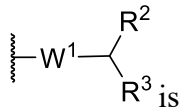
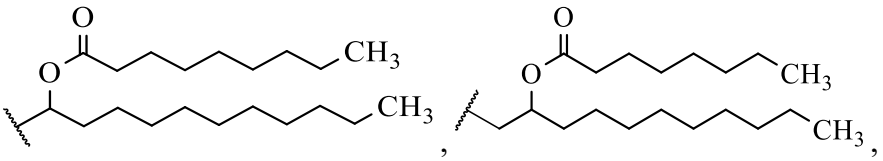
(4) R^3 is , , , , , , ,  or ;

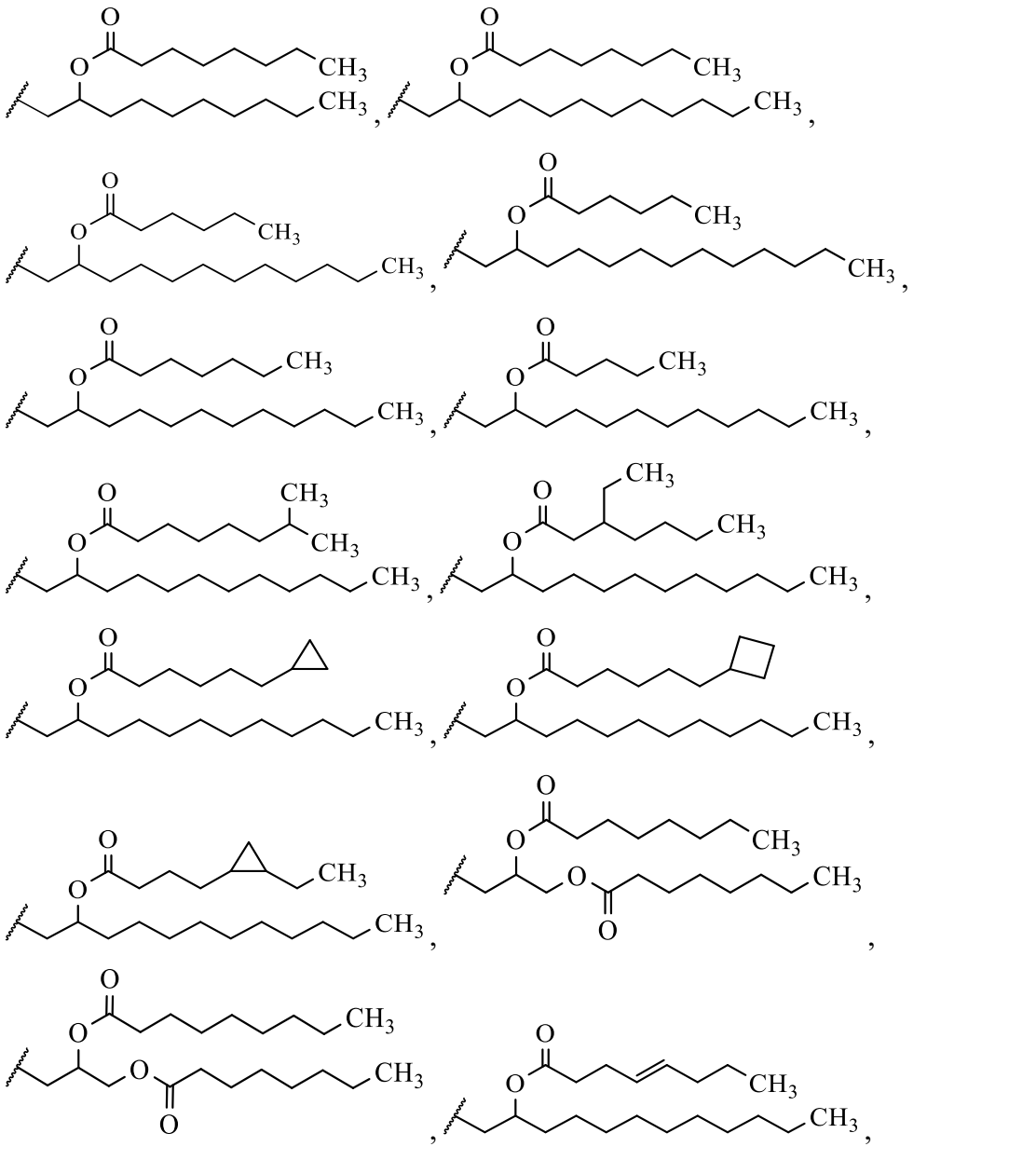
(5) R^4 is H, , , , , , , , , ,

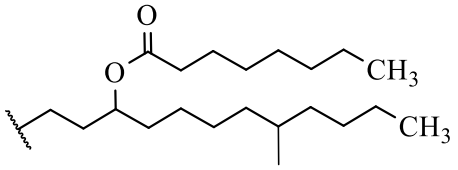
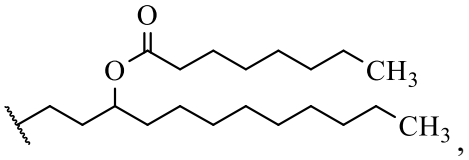
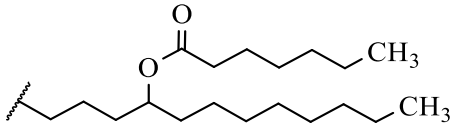
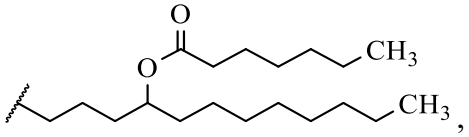
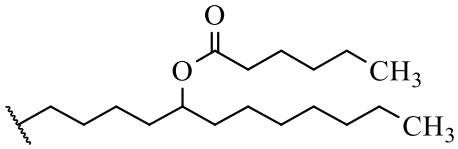
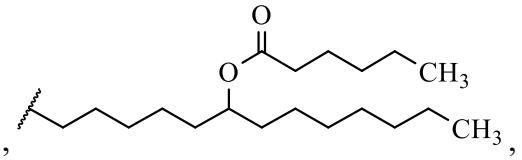
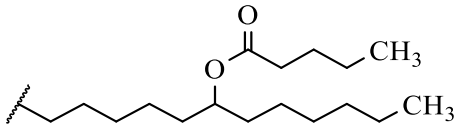
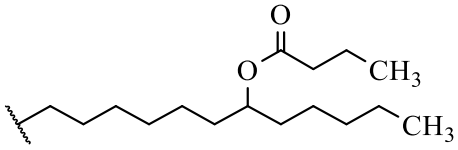

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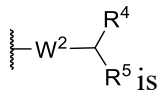
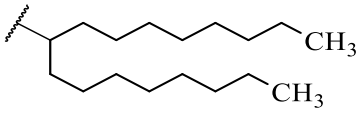
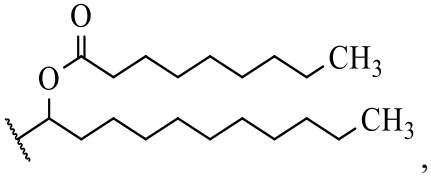
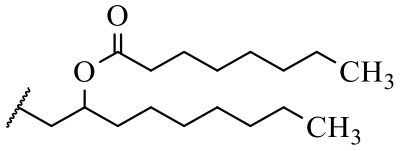
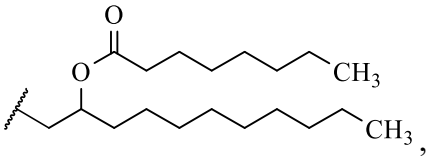
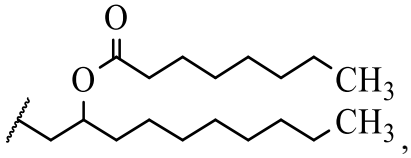
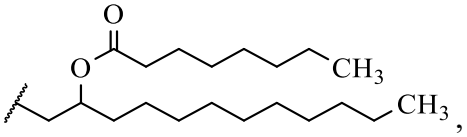
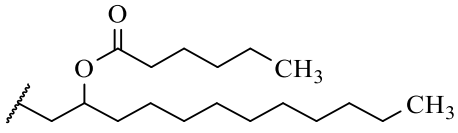
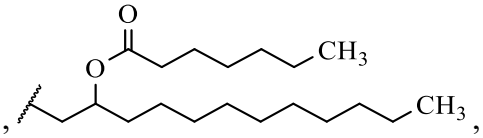
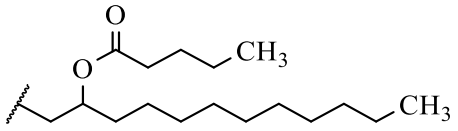
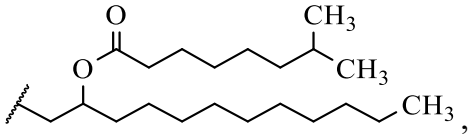
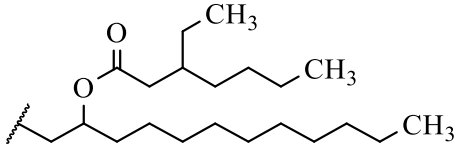
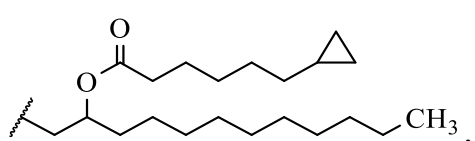
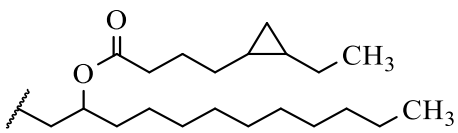
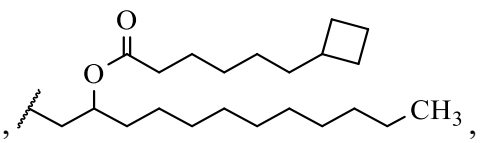
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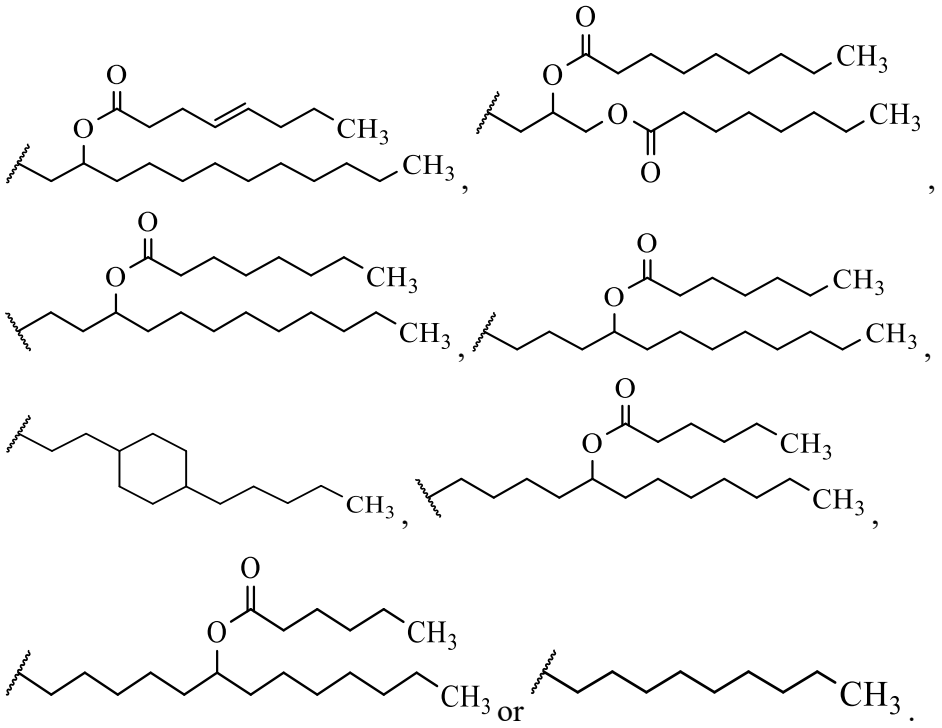
(6) R^5 is 
or
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(7)  is 




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or

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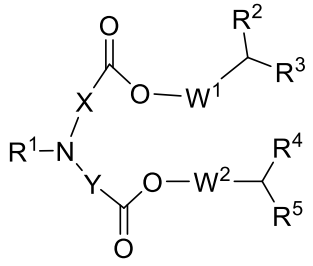
(8)  is

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7. The compound I or the pharmaceutically acceptable salt thereof according to claim 1, wherein the compound I satisfies any one of the following schemes:

Scheme (1):

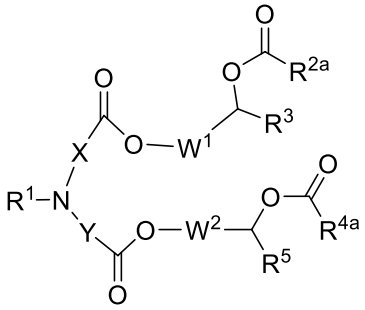
the compound I has the following structure:



I-A ;

wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, X, and Y are as described in any one of claims 1 to 6;

preferably, the compound I has the following structure:

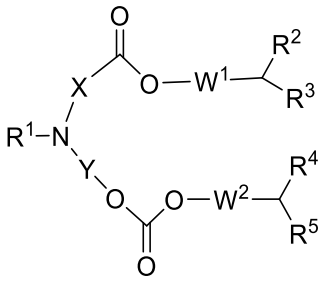


I-A-1 ;

wherein definitions of R^1, R^{2a}, R^3, R^{4a}, R^5, W^1, W^2, X, and Y are as described in any one of claims 1 to 6;

Scheme (2):

the compound I has the following structure:

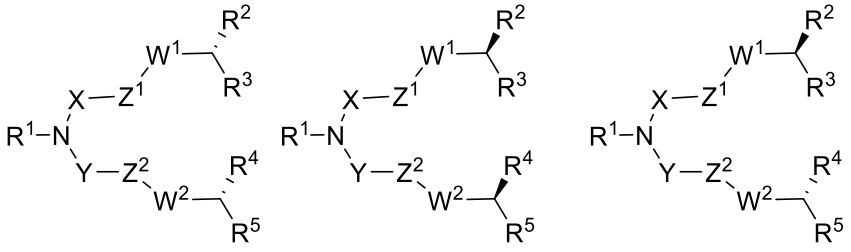


I-B ;

wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, X, and Y are as described in any one of claims 1 to 6; and

Scheme (3):

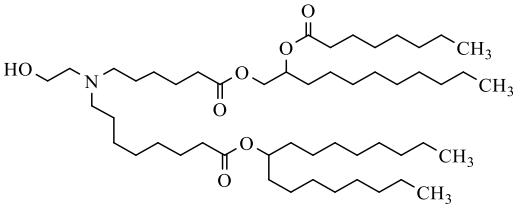
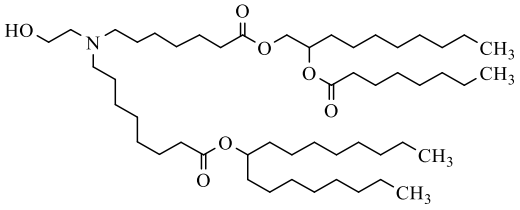
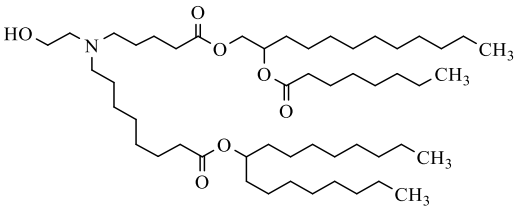
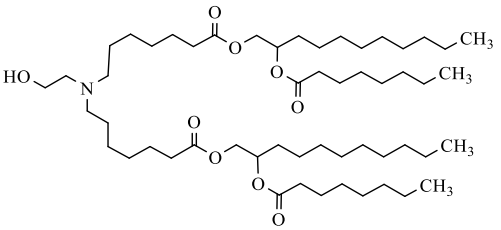
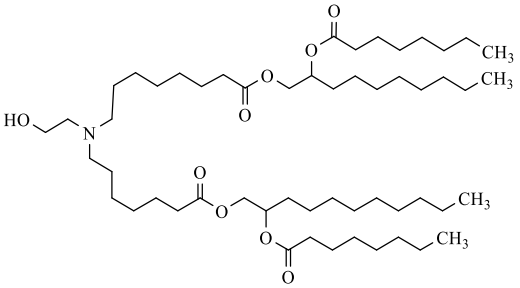
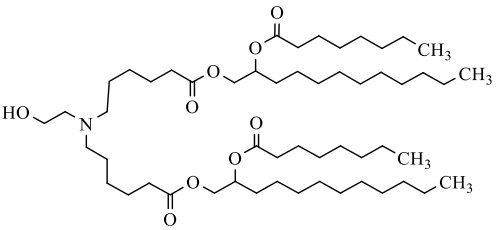
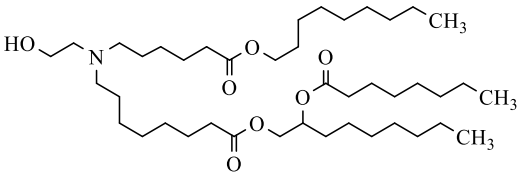
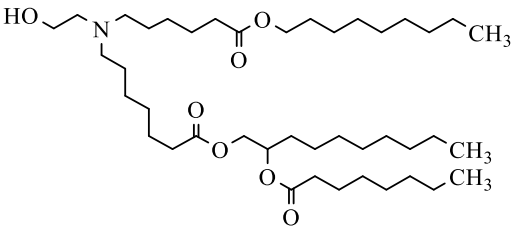
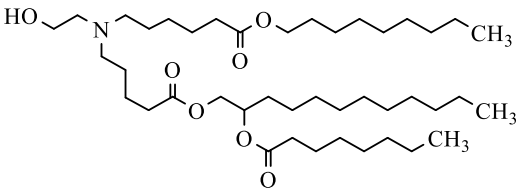
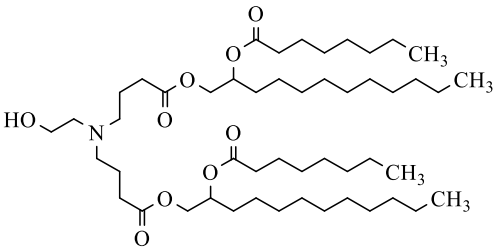
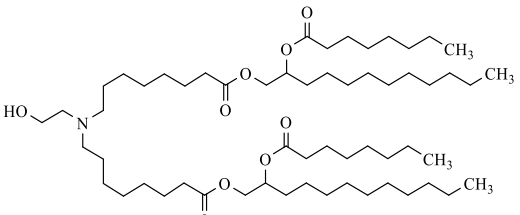
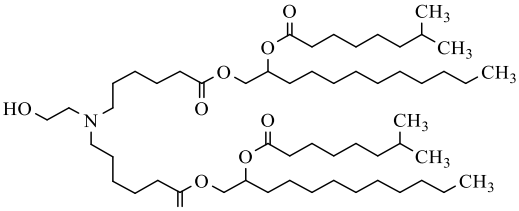
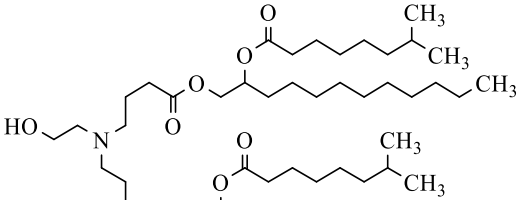
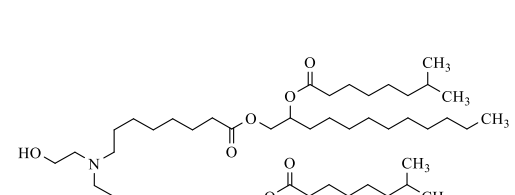
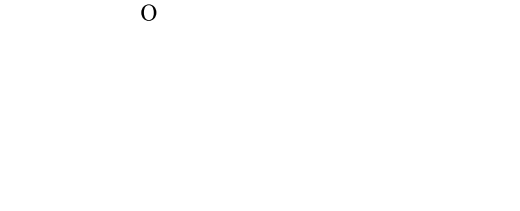
the compound I has any one of the following structures:



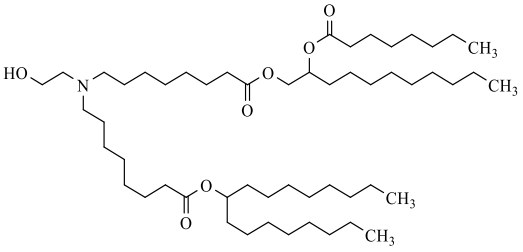
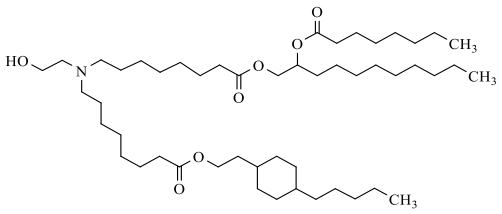
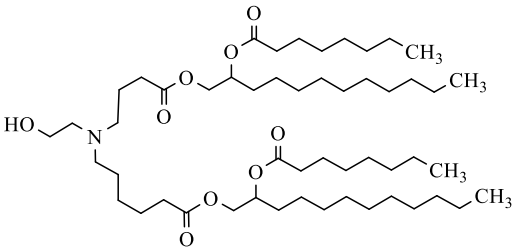
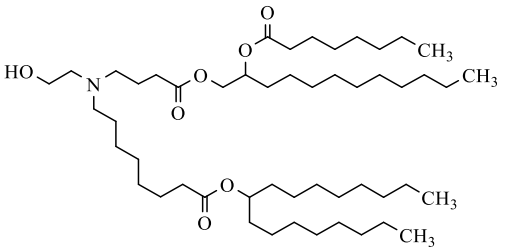
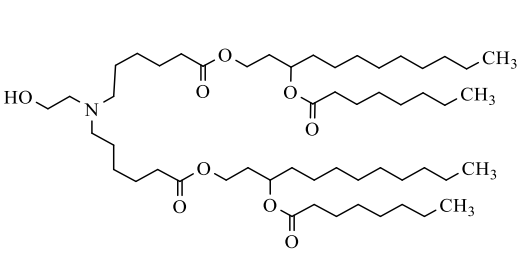
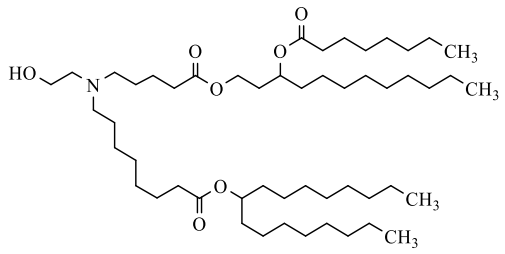
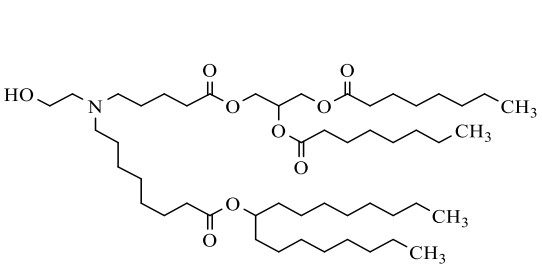
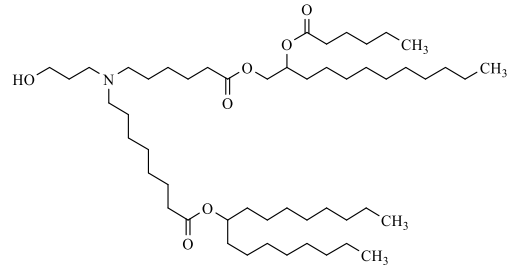
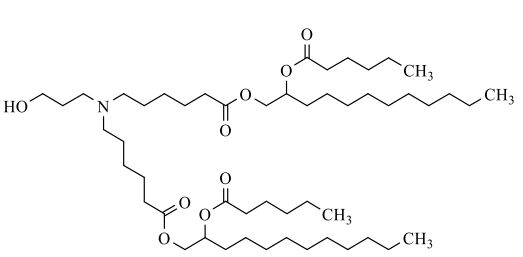
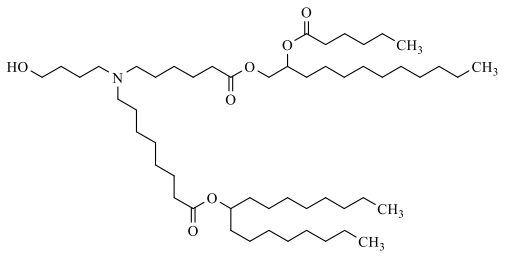
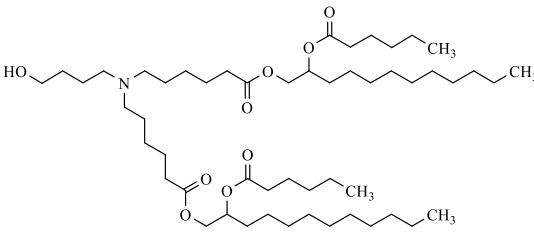
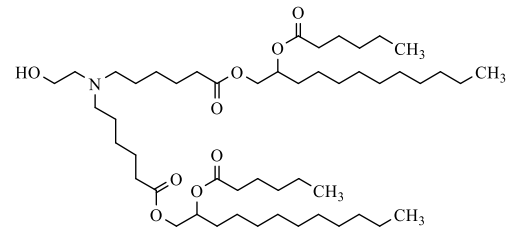
I-C , I-D or I-E ;

wherein definitions of R^1, R^2, R^3, R^4, R^5, W^1, W^2, Z^1, Z^2, X, and Y are as described in any one of claims 1 to 6.

8. The compound I or the pharmaceutically acceptable salt thereof according to claim 1, wherein the compound I has any one of the following structures:

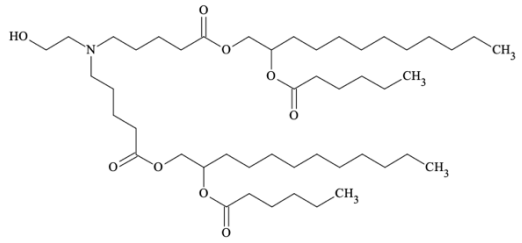
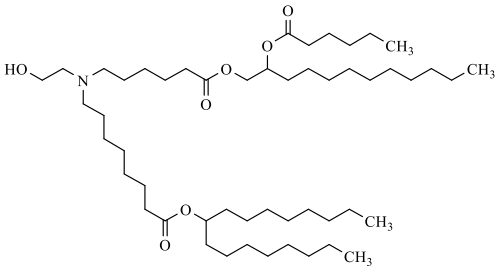
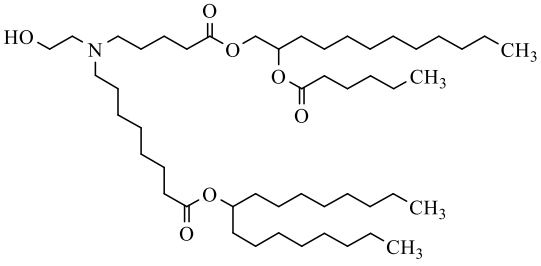
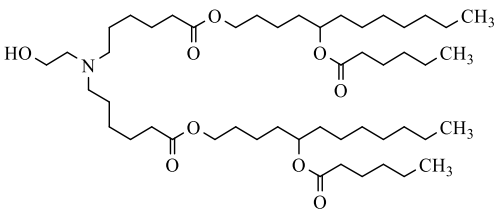
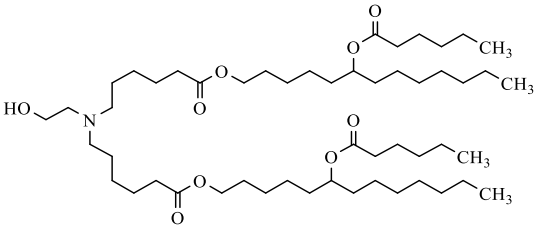
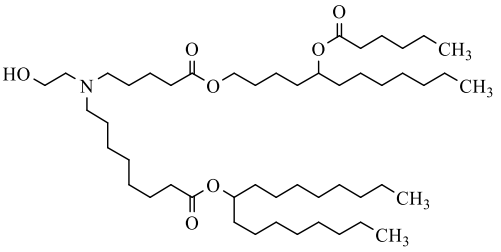
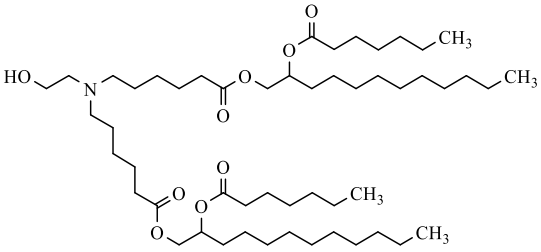
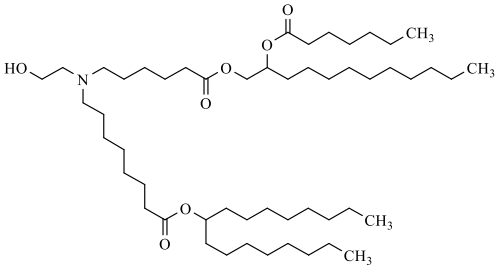
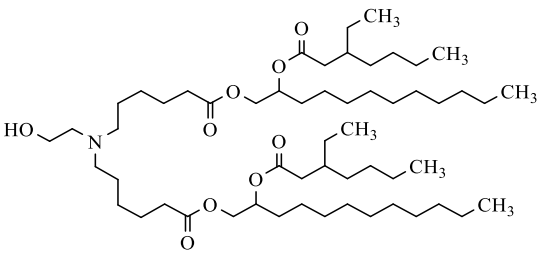
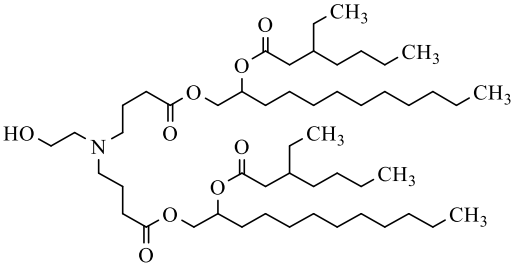
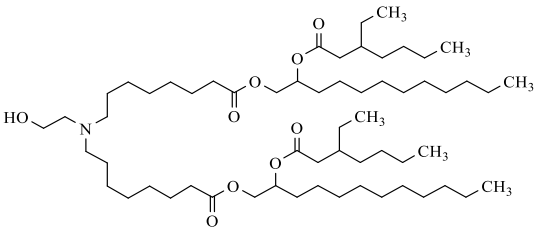
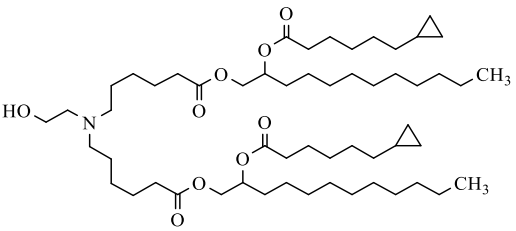

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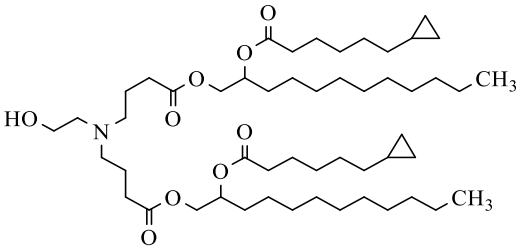
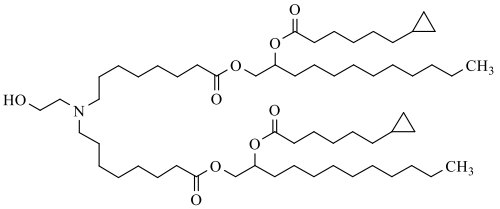
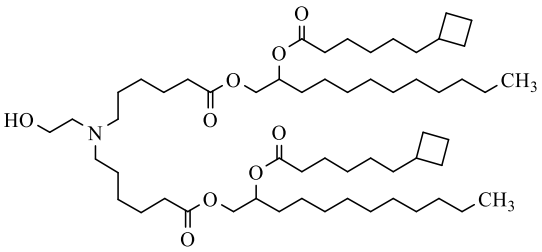
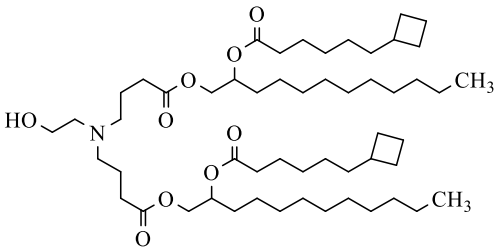
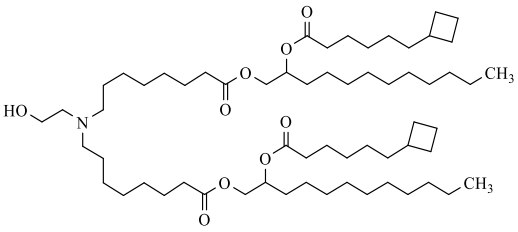
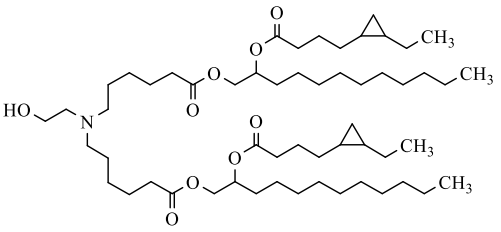
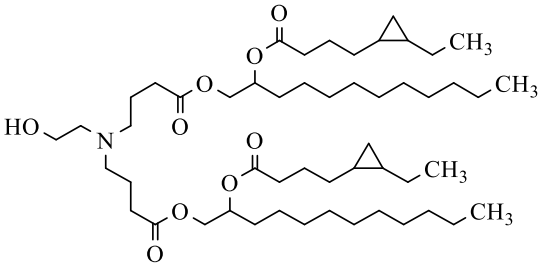
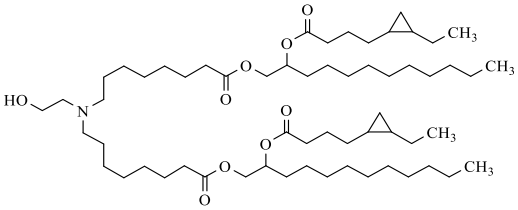
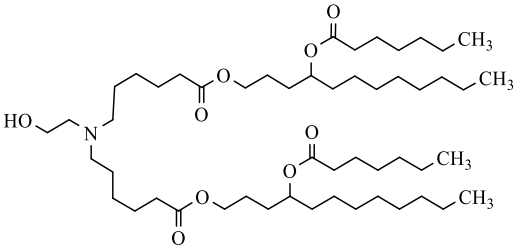
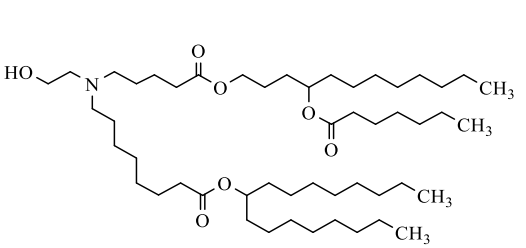
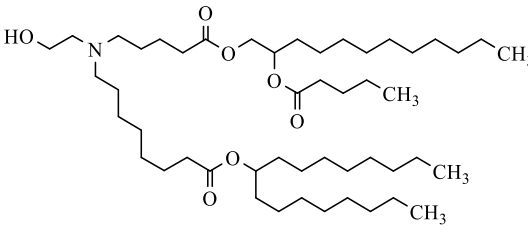
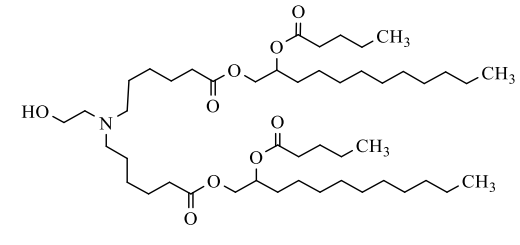
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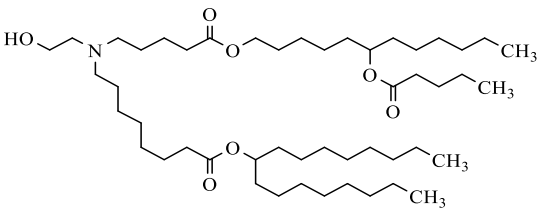
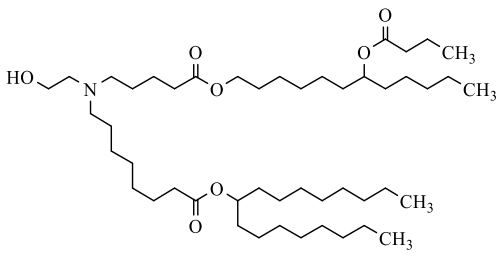
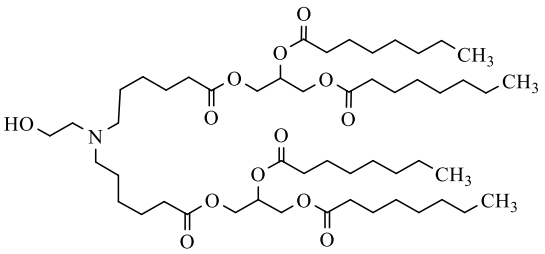
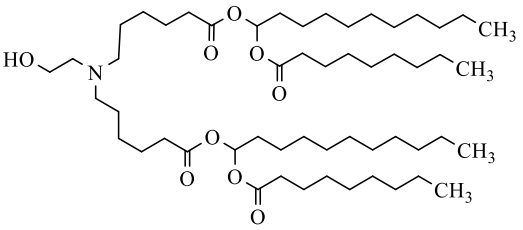
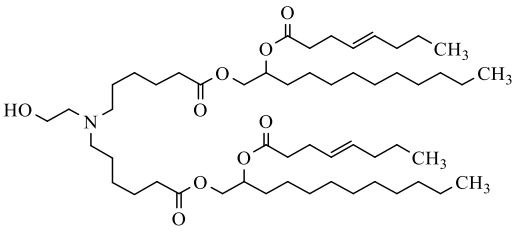
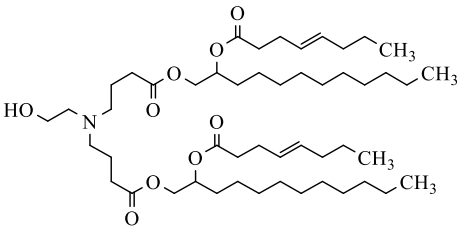
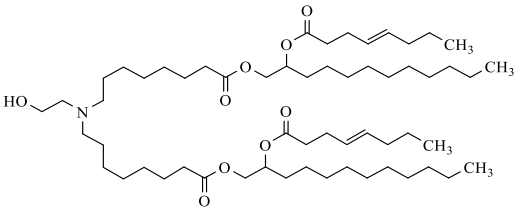
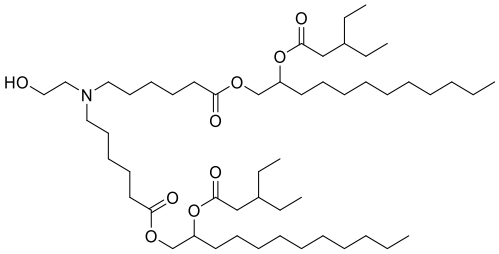
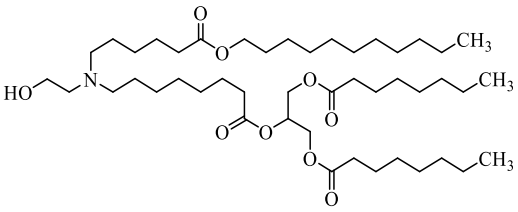
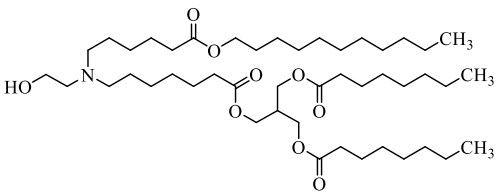
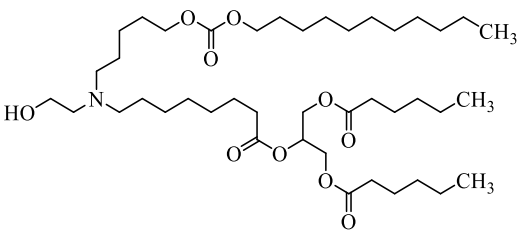
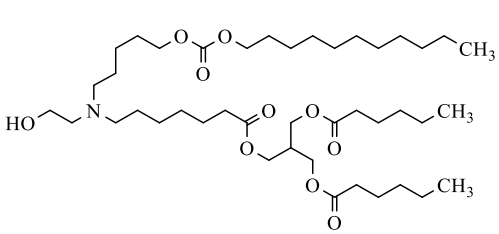
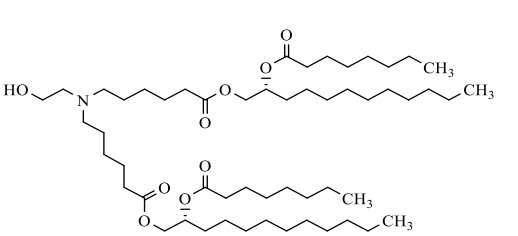
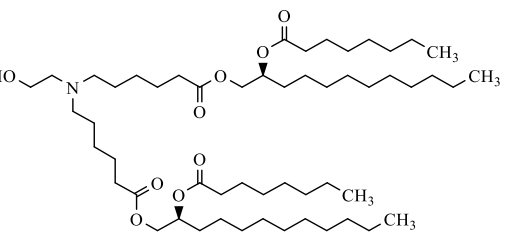
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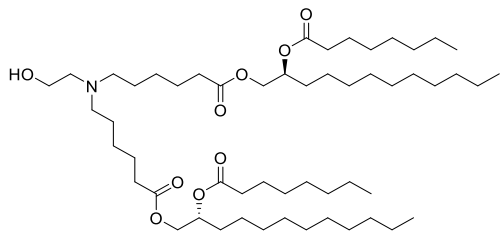
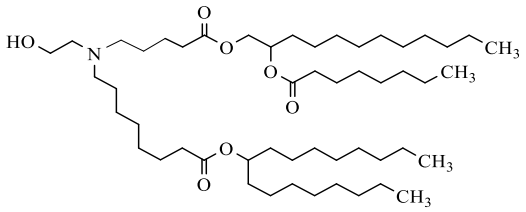
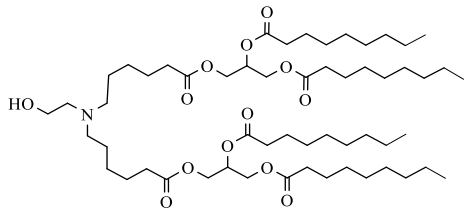
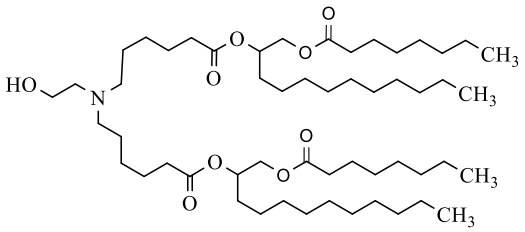
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or


9. A lipid carrier, comprising a substance Z, wherein the substance Z is the compound I or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 8;

preferably, the lipid carrier satisfies one or more of the following conditions:

(1) the lipid carrier further comprises a diluent, such as a phosphate buffer or a Tris buffer;

(2) the lipid carrier further comprises a phospholipid, and the phospholipid is a phospholipid molecule having a charged polar end and a fatty chain non-polar end, such as distearoylphosphatidylcholine, dimyristoylphosphocholine, dioleoylphosphocholine, palmitoylphosphocholine, 1,2-distearoylphosphocholine, heneicosanoylphosphocholine, or palmitoylphosphocholine;

(3) the lipid carrier further comprises a PEG lipid, and the PEG lipid is a lipid molecule modified with a polyethylene glycol hydrophilic end, such as PEG-modified dimyristoylglycerol;

(4) the lipid carrier further comprises a sterol, and the sterol is one or more selected from cholesterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, tomatine, ursolic acid, and α-tocopherol, such as cholesterol;

(5) in the lipid carrier, a molar ratio of the substance Z to the sterol is 0.5-5:1, preferably 0.5-3:1, such as 1.3:1;

(6) in the lipid carrier, a molar ratio of the substance Z to the phospholipid is 1-15:1, preferably 2-8:1, such as 3-6:1;

(7) in the lipid carrier, a molar ratio of the substance Z to the phospholipid is 1-15:1, preferably 1-10:1, such as 5:1;

(8) in the lipid carrier, a molar ratio of the substance Z to the PEG lipid is 10-100:1,

preferably 10-50:1, such as 33.3:1;

(9) in the lipid carrier, a molar content of the substance Z is 30 mol% to 70 mol%, such as 50 mol%;

(10) in the lipid carrier, a molar content of the phospholipid is 5 mol% to 20 mol%, such as 10 mol%;

(11) in the lipid carrier, a molar content of the sterol is 20 mol% to 60 mol%, such as 38.5 mol%;

(12) in the lipid carrier, a molar content of the PEG lipid is about 0.2 mol% to 5 mol%, such as 1.5 mol%;

(13) in the lipid carrier, the lipid carrier consists of the substance Z, the diluent, the phospholipid, the PEG lipid, and the sterol.

10. The lipid carrier according to claim 9, satisfying one or more of the following conditions:

(1) in the lipid carrier, the molar content of the substance Z is 35 mol%, 40 mol%, 45 mol%, 50 mol%, 55 mol%, or 60 mol%;

(2) in the lipid carrier, the molar content of the phospholipid is 0 mol% to 30 mol%, such as 0 mol%, 5 mol%, 10 mol%, 15 mol%, or 20 mol%;

(3) in the lipid carrier, the molar content of the sterol is 28.5 mol%, 33.5 mol%, 37.0 mol%, 38.0 mol%, 38.5 mol%, 39.0 mol%, 39.5 mol%, 43.5 mol%, 48.5 mol%, or 53.5 mol%;

(4) in the lipid carrier, the molar content of the PEG lipid is 0.5 mol%, 1.0 mol%, 1.5 mol%, 2.0 mol%, or 3.0 mol%;

(5) the lipid carrier has any one of the following formulations:

Formulation	Compound 6 or pharmaceutically acceptable salt thereof : DSPC : cholesterol : DMG-PEG2000
1	35 : 10 : 53.5 : 1.5
2	40 : 10 : 48.5 : 1.5
3	45 : 10 : 43.5 : 1.5
4	50 : 10 : 38.5 : 1.5
5	55 : 10 : 33.5 : 1.5
6	60 : 10 : 28.5 : 1.5

7	50 : 0 : 48.5 : 1.5
8	50 : 5 : 43.5 : 1.5
9	50 : 15 : 33.5 : 1.5
10	50 : 20 : 28.5 : 1.5
11	50 : 10 : 39.5 : 0.5
12	50 : 10 : 39.0 : 1.0
13	50 : 10 : 38.0 : 2.0
14	50 : 10 : 37.0 : 3.0

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11. Use of the compound I or the pharmaceutically acceptable salt thereof according to any one of claims 1 to 8, or the lipid carrier according to claim 9 in preparing a delivery carrier for a nucleic acid prophylactic agent and/or therapeutic agent;

wherein the nucleic acid therapeutic agent and/or prophylactic agent is preferably one or more of single-stranded deoxyribonucleic acid, double-stranded DNA, small interfering RNA, asymmetric double-stranded small interfering RNA, microRNA, small hairpin RNA, circular RNA, transfer RNA, or messenger RNA, more preferably mRNA, such as firefly luciferase mRNA, SARS-CoV-2 spike protein mRNA, varicella-zoster virus mRNA, respiratory syncytial virus mRNA, or influenza virus mRNA.

12. A lipid nanoparticle, comprising a nucleic acid prophylactic agent and/or therapeutic agent and the lipid carrier according to claim 9;

wherein the nucleic acid therapeutic agent and/or prophylactic agent is preferably one or more of single-stranded deoxyribonucleic acid, double-stranded DNA, small interfering RNA, asymmetric double-stranded small interfering RNA, microRNA, small hairpin RNA, circular RNA, transfer RNA, or messenger RNA, more preferably mRNA, such as firefly luciferase mRNA, SARS-CoV-2 spike protein mRNA, varicella-zoster virus mRNA, respiratory syncytial virus mRNA, or influenza virus mRNA.

13. The lipid nanoparticle according to claim 12, satisfying one or more of the following conditions:

(1) a nitrogen-to-phosphorus ratio in the lipid nanoparticle is (2-30):1, preferably (2-20):1,

more preferably (3-20):1, such as (3-16):1;

(2) the lipid nanoparticle has a particle size of 10-200 nm, preferably 40-150 nm, more preferably 50-130 nm, such as 57.29 nm, 61.55 nm, 69.72 nm, 70.08 nm, 76.03 nm, 89.89 nm, 97.55 nm, 107.37 nm, or 119.10 nm;

(3) the lipid nanoparticle has a polydispersity index of 0.001-0.3, such as 0.035, 0.074, 0.090, 0.097, 0.118, 0.166, or 0.269;

(4) the lipid nanoparticle has an encapsulation efficiency of 90%-100%, such as 96.73%, 98.07%, 96.90%, 97.71%, 96.36%, 95.02%, 92.94%, 94.44%, 95.23%, or 94.63%;

(5) in the lipid nanoparticle, the lipid carrier encapsulates the nucleic acid prophylactic agent and/or therapeutic agent.

14. The lipid nanoparticle according to claim 12, satisfying one or more of the following conditions:

(1) in the lipid nanoparticle, a nitrogen-to-phosphorus ratio is 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, or 9:1;

(2) the lipid nanoparticle has a particle size of 57.29 nm, 61.55 nm, 69.72 nm, 70.08 nm, 76.03 nm, 89.89 nm, 97.55 nm, 107.37 nm, 119.10 nm, 63.36 nm, 56.53 nm, 71.25 nm, 57.66 nm, 60.92 nm, 55.68 nm, 56.19 nm, 55.52 nm, 67.96 nm, 69.51 nm, or 79.13 nm;

(3) the lipid nanoparticle has a polydispersity index of 0.035, 0.074, 0.090, 0.097, 0.118, 0.166, 0.269, 0.065, 0.074, 0.062, 0.106, 0.089, 0.108, 0.090, 0.078, 0.085, 0.063, or 0.084;

(4) the lipid nanoparticle has an encapsulation efficiency of 96.73%, 98.07%, 96.90%, 97.71%, 96.36%, 95.02%, 92.94%, 94.44%, 95.23%, 94.63%, 95.83%, 94.95%, 96.00%, 96.62%, 94.28%, 96.56%, 96.04%, 95.94%, 98.33%, 95.38%, or 96.78%.