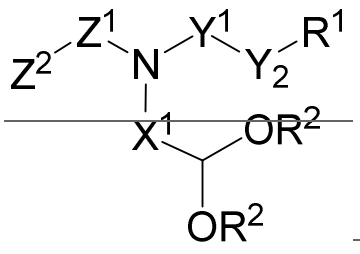
What is claimed is:

1. A compound of Formula (I)

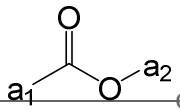
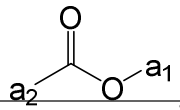


(I)

wherein, independently for each occurrence,

X^1 is C_{5-11} alkylene,

Y^1 is C_{3-11} alkylene,

Y^2 is  or  , wherein a_1 is a bond to Y^1, and a_2 is a bond to R^1,

Z^1 is C_{2-4} alkylene,

Z^2 is selected from -OH, $-NH_2$, $-OC(=O)R^3$, $-OC(=O)NHR^3$, $-NHC(=O)NHR^3$, and $-NHS(=O)_2R^3$,

R^1 is C_{4-12} alkyl or C_{3-12} alkenyl,

each R^2 is independently C_{4-12} alkyl, and

R^3 is C_{1-3} alkyl,

or a salt thereof.

2. The compound of claim 1, wherein the salt is a pharmaceutically acceptable salt.

3. The compound of claim 1 or 2, wherein X^1 is linear C_{5-11} alkylene.

4. The compound of any one of the preceding claims, wherein X^1 is linear C_{6-10} alkylene.

5. The compound of any one of the preceding claims, wherein X^1 is linear C_6 alkylene, linear C_7 alkylene, linear C_8 alkylene, or linear C_9 alkylene.

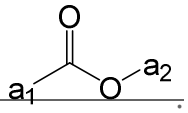
6. The compound of any one of the preceding claims, wherein Y^1 is linear C_{4-9} alkylene.

7. The compound of any one of the preceding claims, wherein Y^1 linear C_{6-8} alkylene.

8. The compound of any one of the preceding claims, wherein Y^1 is linear C_7 alkylene.

9. The compound of any one of the preceding claims, wherein R^1 is C_{4-12} alkenyl.

10. The compound of any one of the preceding claims, wherein R^1 is C_9 alkenyl.

11. The compound of any one of the preceding claims, wherein Y^2 is 

.

12. The compound of any one of the preceding claims, wherein Y^1, Y^2, and R^1 are selected to form a linear chain of 16-21 atoms.

13. The compound of any one of the preceding claims, wherein Y^1, Y^2, and R^1 are selected to form a linear chain of 16-18 atoms.

14. The compound of any one of the preceding claims, wherein Z^1 is linear C_{2-4} alkylene.

15. The compound of any one of the preceding claims, wherein Z^1 is C_2 alkylene or C_3 alkylene.

16. The compound of any one of the preceding claims, wherein Z^2 is -OH.

17. The compound of any one of claims 1-15, wherein Z^2 is $-NH_2$.

18. The compound of any one of claims 1-15, wherein Z^2 is $-OC(=O)R^3$, $-OC(=O)NHR^3$, $-NHC(=O)NHR^3$, or $-NHS(=O)_2R^3$.

19. The compound of claim 18, wherein R^3 is methyl.

~~20. The compound of any one of the preceding claims, wherein R^1 is linear C_{4-12} alkyl.~~

~~21. The compound of any one of the preceding claims, wherein R^1 is linear C_{8-10} alkyl.~~

~~22. The compound of any one of the preceding claims, wherein R^1 is linear C_9 alkyl.~~

~~23. The compound of any one of claims 1-19, wherein R^1 is branched C_{6-12} alkyl.~~

~~24. The compound of claim 23, wherein R^1 is branched C_8 alkyl, branched C_9 alkyl, or branched C_{10} alkyl.~~

~~25. The compound of any one of the preceding claims, wherein each R^2, independently, is linear C_{5-12} alkyl.~~

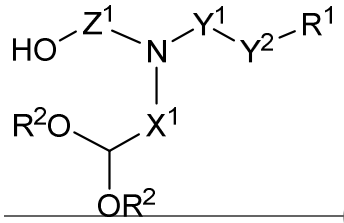
~~26. The compound of any one of the preceding claims, wherein each R^2, independently, is linear C_{6-8} alkyl.~~

~~27. The compound of any one of claims 1-24, wherein each R^2, independently, is branched C_{5-12} alkyl.~~

~~28. The compound of claim 27, wherein each R^2, independently, is branched C_{6-8} alkyl.~~

~~29. The compound of any one of the preceding claims, wherein X^1 and one of the R^2 moieties are selected to form a linear chain of 16-18 atoms, including the carbon and oxygen atoms of the acetal.~~

30. The compound of claim 1, wherein the compound is a compound of Formula (II)

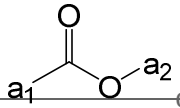
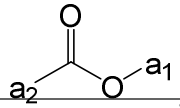


(II)

wherein, independently for each occurrence,

X^1 is C_{5-11} alkylene,

Y^1 is C_{3-10} alkylene,

Y^2 is  or  , wherein a_1 is a bond to Y^1, and a_2 is a bond to R^1,

Z^1 is C_{2-4} alkylene,

R^1 is C_{4-12} alkyl or C_{3-12} alkenyl,

each R^2 is independently C_{4-12} alkyl,

or a salt thereof.

31. The compound of claim 30, wherein the salt is a pharmaceutically acceptable salt.

32. The compound of claim 30 or 31, wherein X^1 is linear C_{5-11} alkylene.

33. The compound of claim 32, wherein X^1 is linear C_{6-8} alkylene.

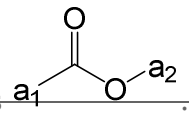
34. The compound of claim 33, wherein X^1 is linear C_7 alkylene.

35. The compound of any one of claims 30-34, wherein Y^1 is linear C_{4-9} alkylene.

36. The compound of any one of claims 30-35, wherein Y^1 is linear C_{5-9} alkylene.

37. The compound of any one of claims 30-36, wherein Y^1 is linear C_{6-8} alkylene.

38. The compound of any one of claims 30-37, wherein Y^1 is linear C_7 alkylene.

39. The compound of any one of claims 30-38, wherein Y^2 is  .

40. The compound of any one of claims 30-39, wherein R^1 is C_{4-12} alkenyl.

41. The compound of any one of claims 30-40, wherein R^1 is C_9 alkenyl.

42. The compound of any one of claims 30-41, wherein Y^1, Y^2, and R^1 are selected to form a linear chain of 16-21 atoms.

43. The compound of any one of claims 30-42, wherein Y^1, Y^2, and R^1 are selected to form a linear chain of 16-18 atoms.

44. The compound of any one of claims 30-43, wherein Z^1 is linear C_{2-4} alkylene.

45. The compound of any one of claims 30-44, wherein Z^1 is C_2 alkylene.

46. The compound of any one of claims 30-39 and 42-45, wherein R^1 is linear C_{4-12} alkyl.

47. The compound of any one of claims 30-39 and 42-46, wherein R^1 is linear C_{8-10} alkyl.

48. The compound of any one of claims 30-39 and 42-47, wherein R^1 is linear C_9 alkyl.

49. The compound of any one of claims 30-48, wherein each R^2 is C_{5-12} alkyl.

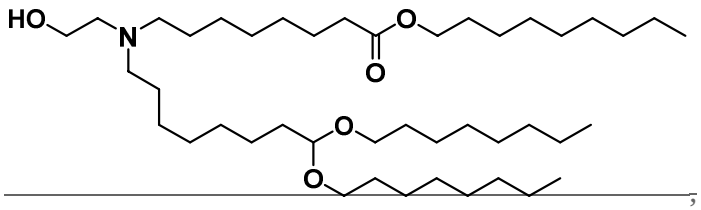
50. The compound of any one of claims 30-49, wherein each R^2 is linear C_{5-12} alkyl.

51. The compound of any one of claims 30-50, wherein each R^2 is linear C_{6-10} alkyl.

52. The compound of any one of claims 30-51, wherein each R^2 is linear C_{6-8} alkyl.

~~53. The compound of any one of claims 30-52, wherein X^1 and one of the R^2 moieties are selected to form a linear chain of 16-18 atoms, including the carbon and oxygen atoms of the acetal.~~

~~54. The compound of claim 1, wherein the compound is selected from:~~



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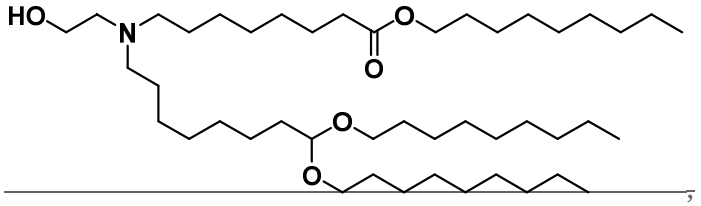

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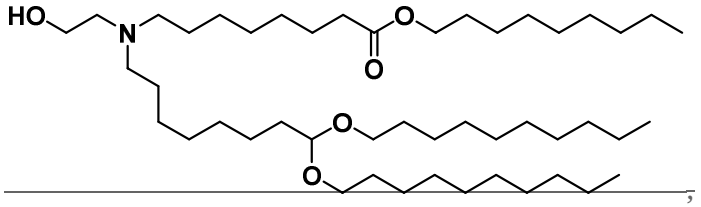

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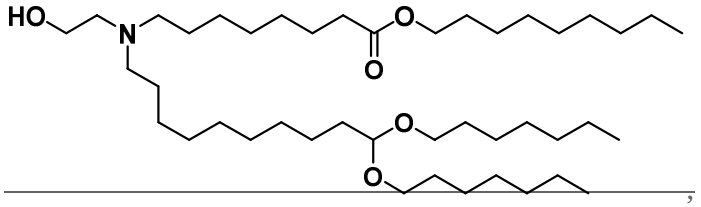

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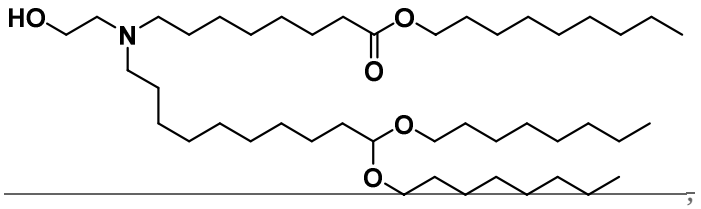

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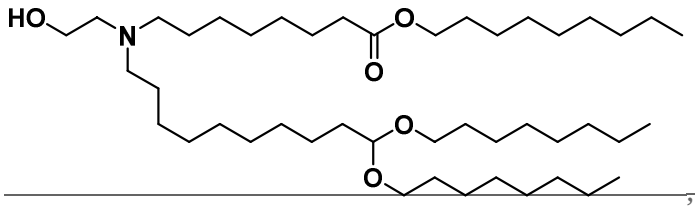

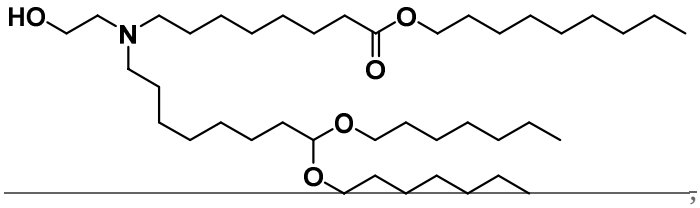

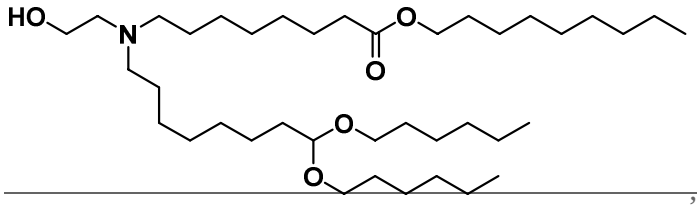

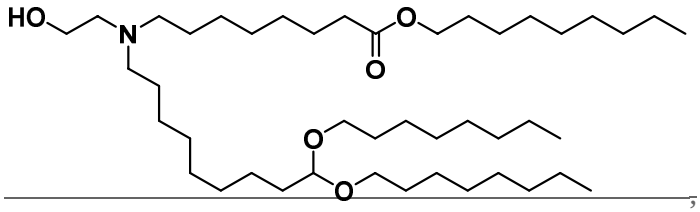

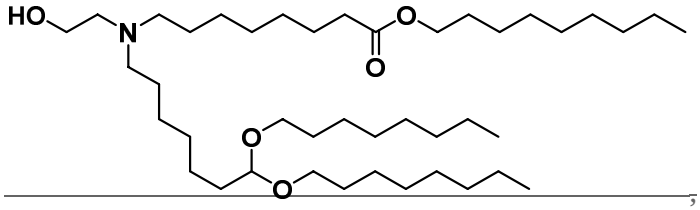

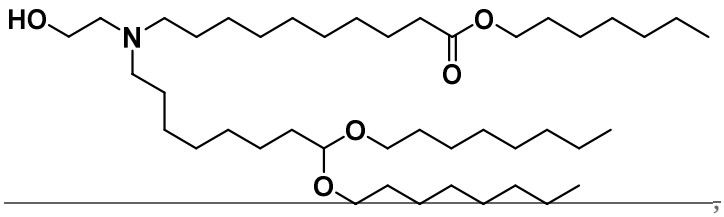

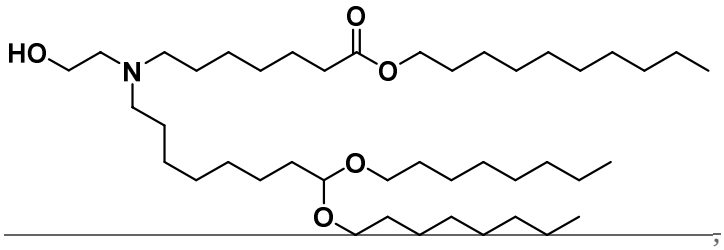

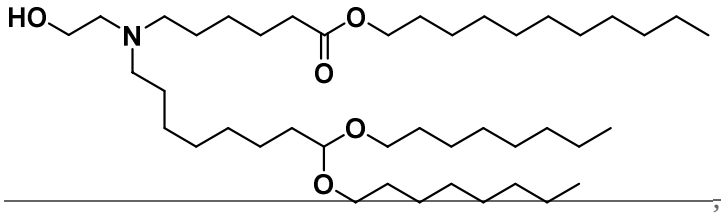

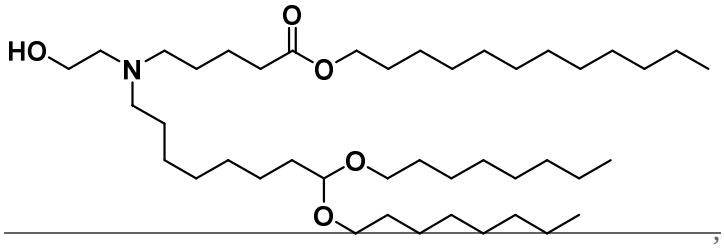

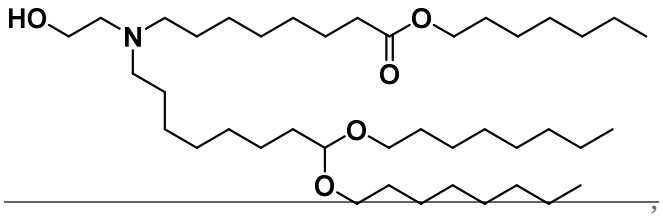

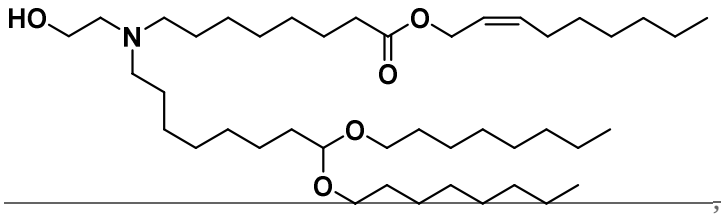

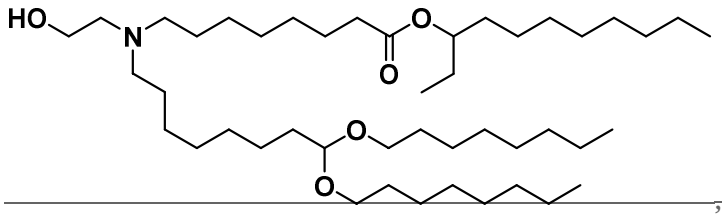

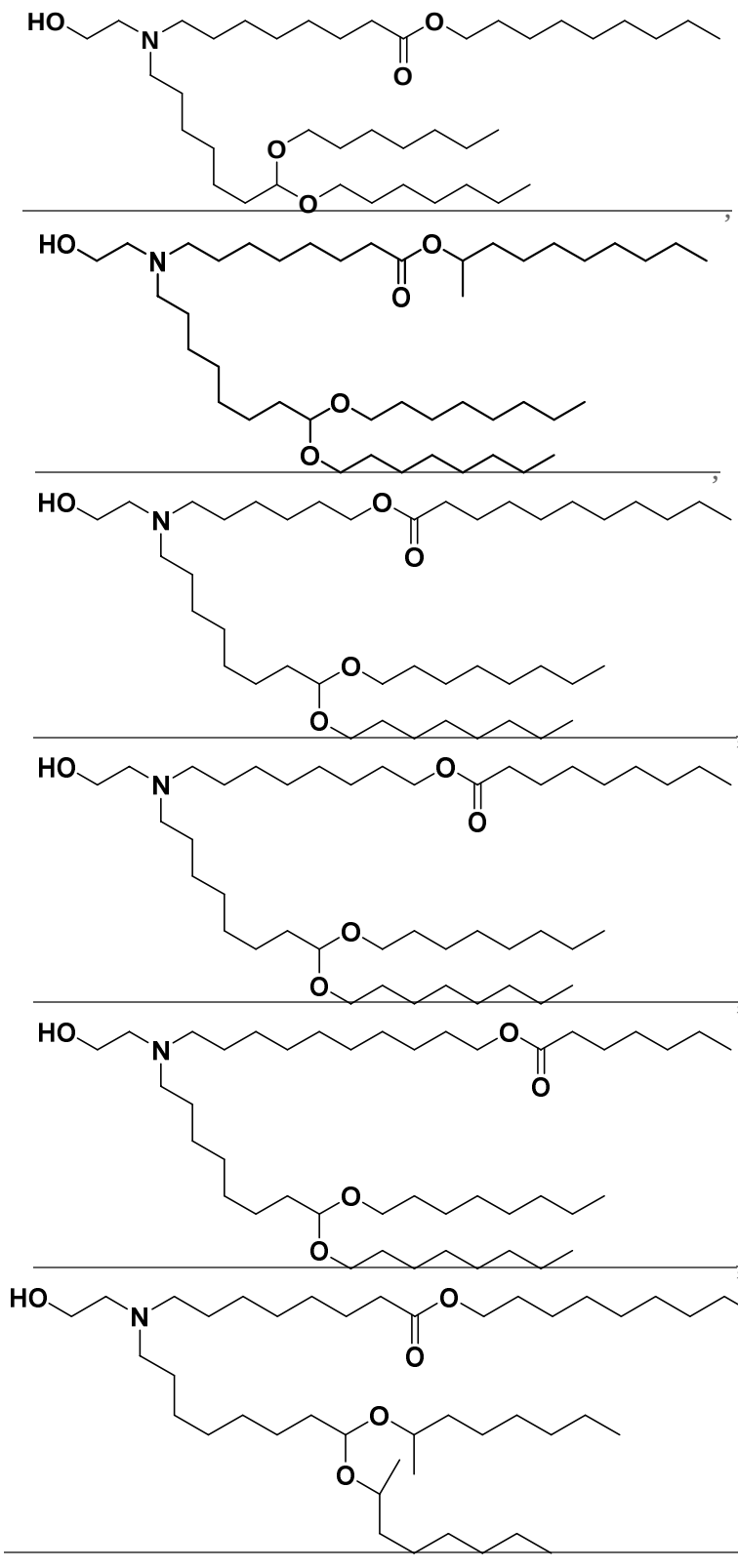

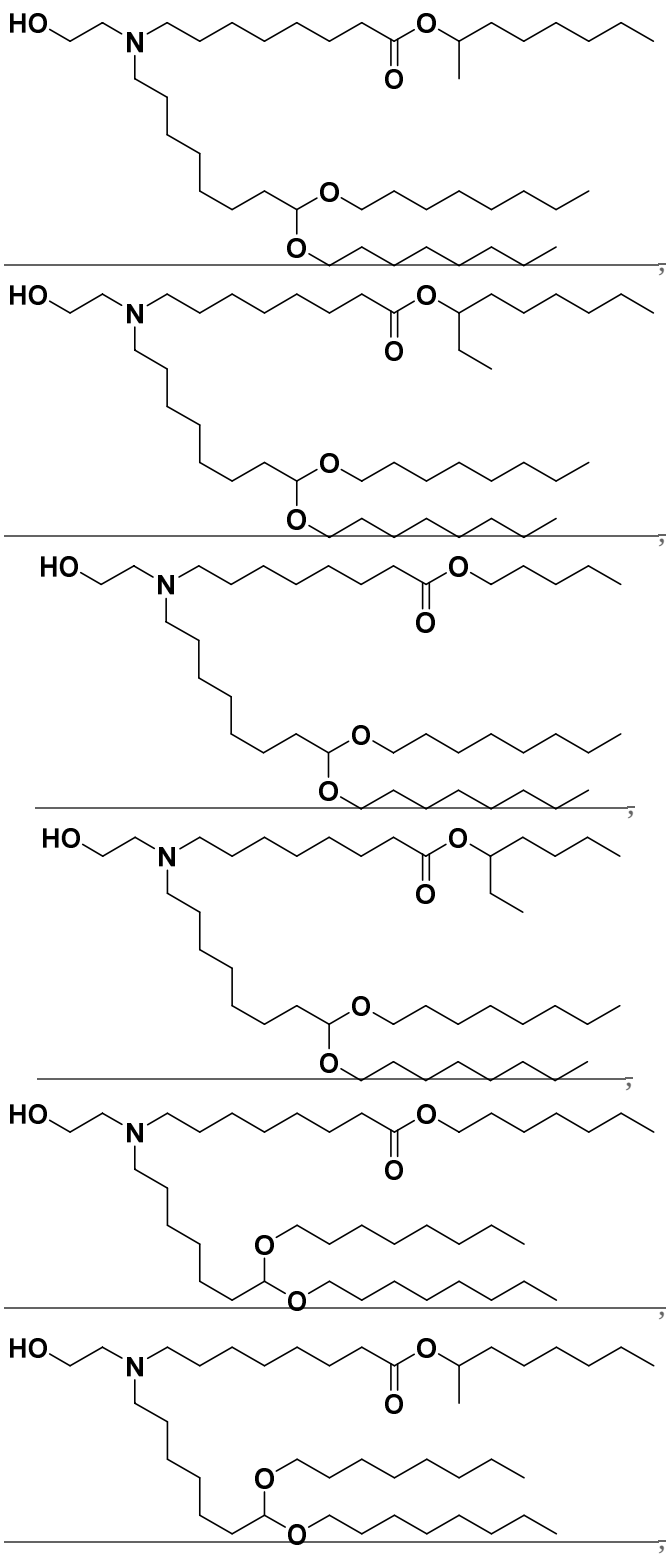

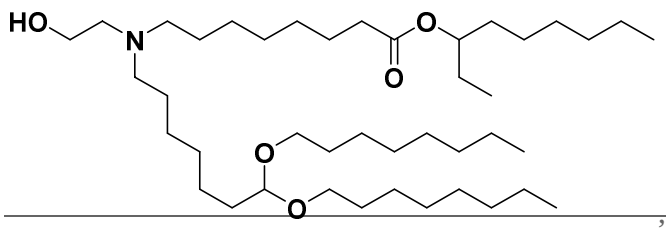

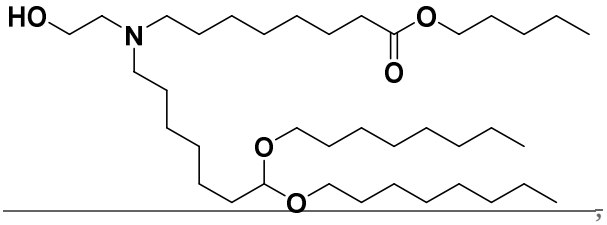

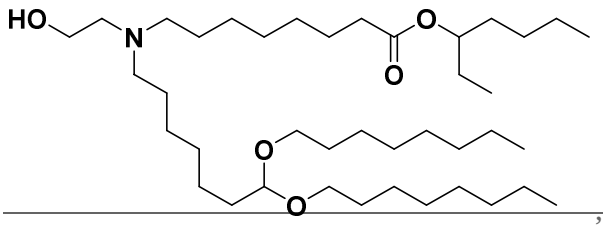

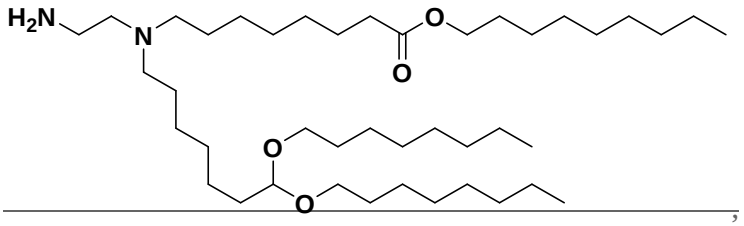

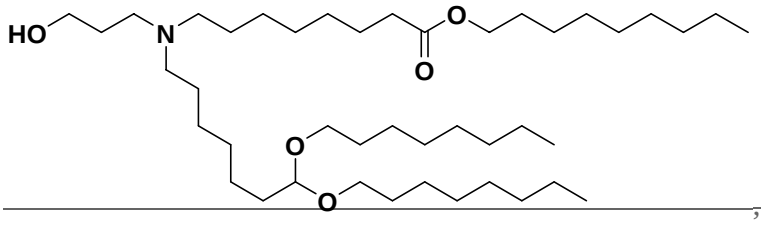

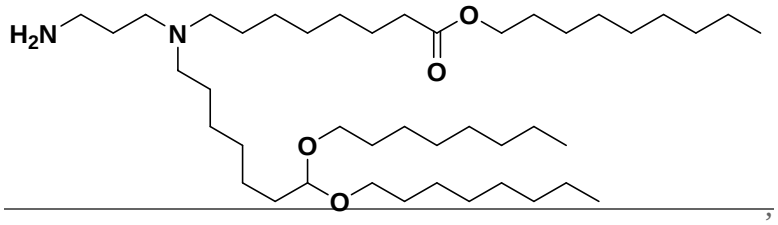

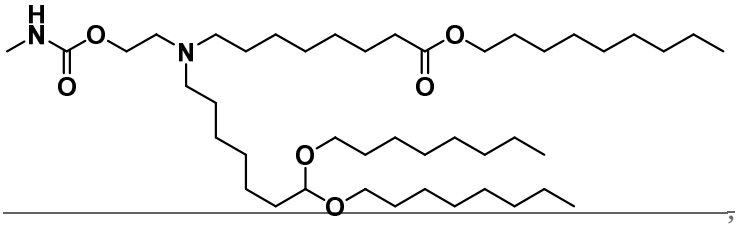

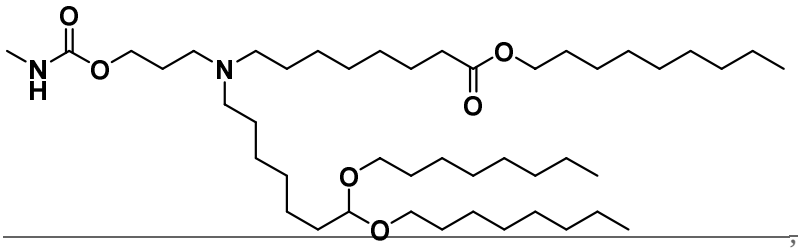

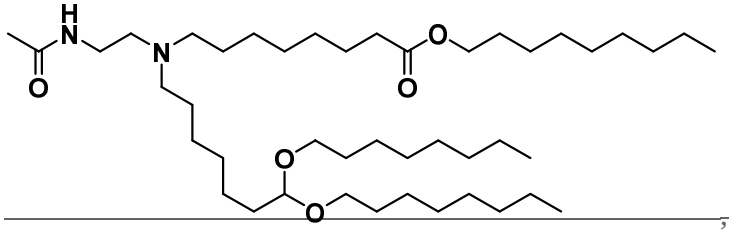

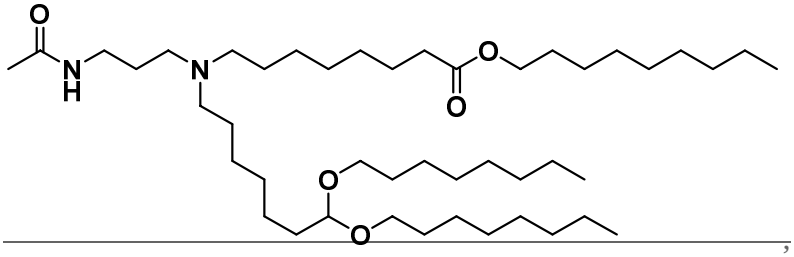

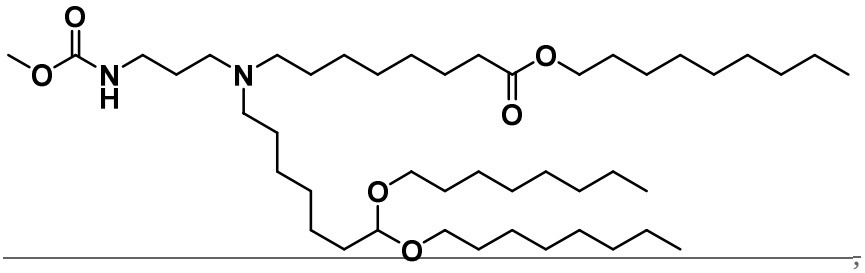

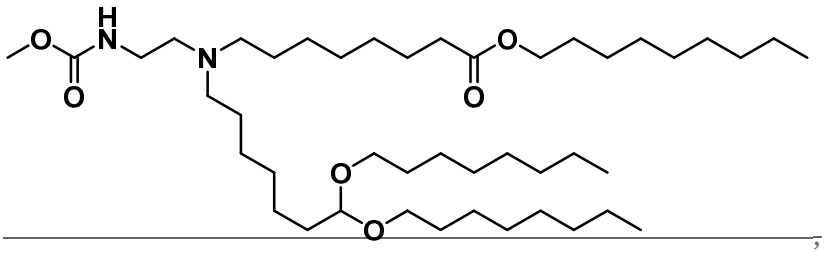

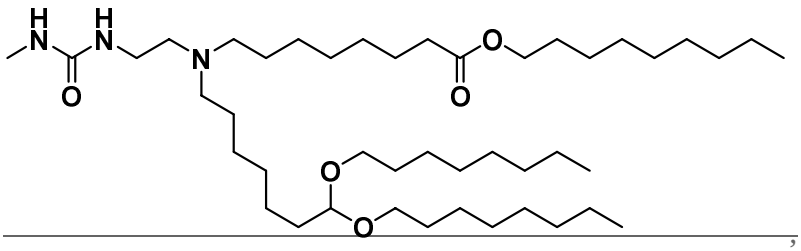

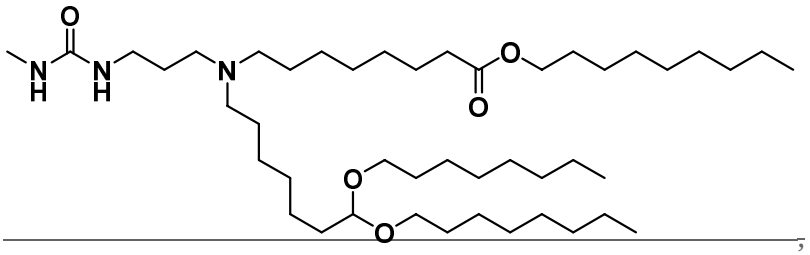

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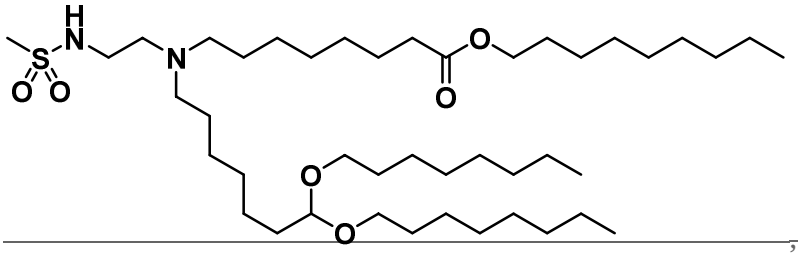

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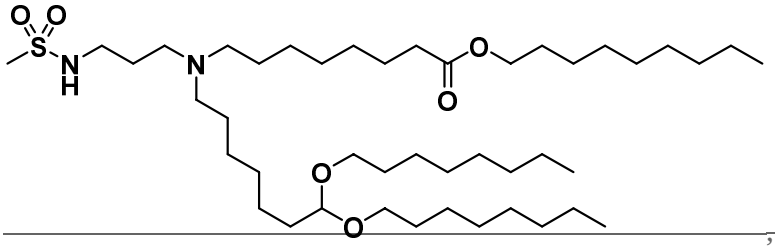

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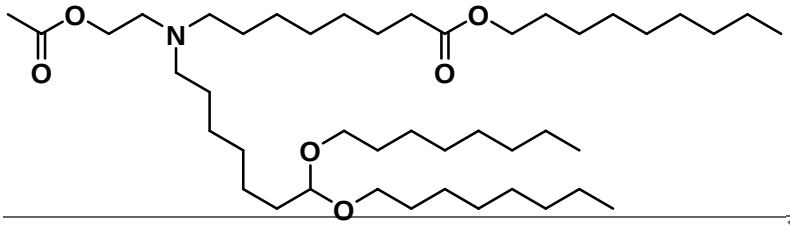

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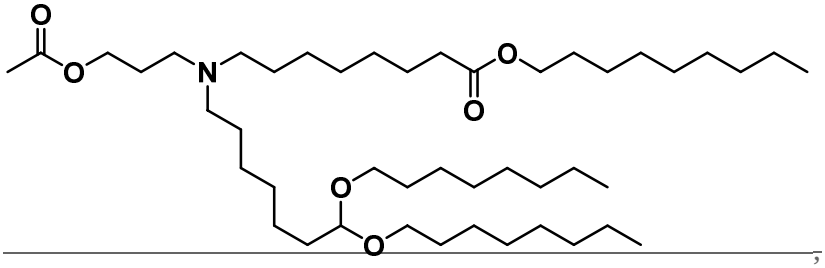


,

or a salt thereof.

55. The compound of claim 55, wherein the salt is a pharmaceutically acceptable salt.

56. The compound of any one of the preceding claims, wherein the pKa of the protonated form of the compound is from about 5.1 to about 8.0.

~~57. The compound of any one of the preceding claims, wherein the pKa of the protonated form of the compound is from about 5.7 to about 6.4.~~

~~58. The compound of any one of the preceding claims, wherein the pKa of the protonated form of the compound is from about 5.8 to about 6.2.~~

~~59. The compound of any one of claims 1-56, wherein the pKa of the protonated form of the compound is from about 5.5 to about 6.0.~~

~~60. The compound of claim 59, wherein the pKa of the protonated form of the compound is from about 6.1 to about 6.3.~~

~~61. A composition comprising a compound of any one of the preceding claims and a lipid component.~~

~~62. The composition of claim 61, wherein the composition comprises about 50% of the compound of any one of the preceding claims and a lipid component.~~

~~63. The composition of claim 61 or 62, wherein the composition is a LNP composition.~~

~~64. The composition of any one of claims 61-63, wherein the lipid component comprises a helper lipid and a PEG lipid.~~

~~65. The composition of any one of claims 61-64, wherein the lipid component comprises a helper lipid, a PEG lipid, and a neutral lipid.~~

~~66. The composition of any one of claims 61-65, further comprising a cryoprotectant.~~

~~67. The composition of any one of claims 61-66, further comprising a buffer.~~

~~68. The composition of any one of claims 61-67, further comprising a nucleic acid component.~~

~~69. The composition of claim 68, wherein the nucleic acid component is an RNA or DNA component.~~

~~70. The composition of claim 68 or 69, wherein the composition has an N/P ratio of about 3-10.~~

~~71. The composition of claim 70, wherein the N/P ratio is about 6 ± 1.~~

~~72. The composition of claim 70, wherein the N/P ratio is about 6 ± 0.5.~~

~~73. The composition of claim 70, wherein the N/P ratio is about 6.~~

~~74. The composition of any one of claims 61-73, comprising a RNA component, wherein the RNA component comprises a mRNA.~~

~~75. The composition of claim 74, wherein the RNA component comprises a RNA-guided DNA-binding agent, such as a Cas nuclease mRNA.~~

~~76. The composition of claim 74 or 75, wherein the RNA component comprises a Class 2 Cas nuclease mRNA.~~

~~77. The composition of any one of claims 74-76, wherein the RNA component comprises a Cas9 nuclease mRNA.~~

~~78. The composition of any one of claims 74-77, wherein the mRNA is a modified mRNA.~~

~~79. The composition of any one of claims 74-78, wherein the RNA component comprises a gRNA nucleic acid.~~

~~80. The composition of claim 79, wherein the gRNA nucleic acid is a gRNA.~~

~~81. The composition of any one of claims 74-78, wherein the RNA component comprises a Class 2 Cas nuclease mRNA and a gRNA.~~

~~82. The composition of any one of claims 79-81, wherein the gRNA nucleic acid is or encodes a dual-guide RNA (dgRNA).~~

~~83. The composition of any one of claims 79-81, wherein the gRNA nucleic acid is or encodes a single-guide RNA (sgRNA).~~

~~84. The composition of any one of claims 79-83, wherein the gRNA is a modified gRNA.~~

~~85. The composition of claim 84, wherein the modified gRNA comprises a modification at one or more of the first five nucleotides at a 5' end.~~

~~86. The composition of claims 84 or 85, wherein the modified gRNA comprises a modification at one or more of the last five nucleotides at a 3' end.~~

~~87. The composition of any one of claims 61-86, further comprising at least one template nucleic acid.~~

~~88. A method of gene editing, comprising contacting a cell with a composition of any one of claims 61-87.~~

~~89. A method of cleaving a DNA, comprising contacting a cell with a composition of any one of claims 61-87.~~

~~90. The method of claim 89, wherein the contacting step results in a single stranded DNA nick.~~

~~91. The method of claim 89, wherein the contacting step results in a double-stranded DNA break.~~

~~92. The method of claim 88, wherein the composition comprises a Class 2 Cas mRNA and a guide RNA nucleic acid.~~

93. The method of claims 88 or 92, further comprising introducing at least one template nucleic acid into the cell.

94. The method of claim 93, comprising contacting the cell with a composition comprising a template nucleic acid.

95. The method of any one of claims 88-94, wherein the method comprises administering the composition to an animal.

96. The method of any one of claims 88-95, wherein the method comprises administering the composition to a human.

97. The method of any one of claims 88-94, wherein the method comprises administering the composition to a cell.

98. The method of claim 97, wherein the cell is a eukaryotic cell.

99. The method of claim 88, wherein the method comprises administering the mRNA formulated in a first LNP composition and a second LNP composition comprising one or more of an mRNA, a gRNA, a gRNA nucleic acid, and a template nucleic acid.

100. The method of claim 99, wherein the first and second LNP compositions are administered simultaneously.

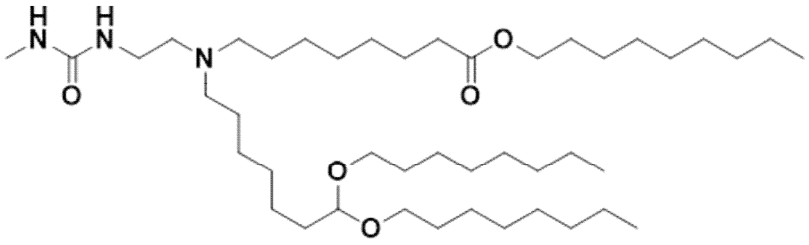
101. The method of claim 99, wherein the first and second LNP compositions are administered sequentially.

102. The method of claim 99, wherein the method comprises administering the mRNA and the guide RNA nucleic acid formulated in a single LNP composition.

103. The method of any one of claims 88-102, wherein the gene editing results in a gene knockout.

~~104. The method of any one of claims 88-102, wherein the gene editing results in a gene correction.~~

1. A compound of the formula:



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