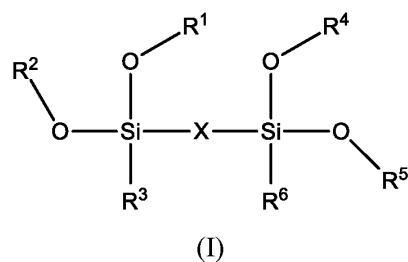


CLAIMS

WHAT IS CLAIMED IS:

1. A compound of formula (I):



wherein:

- R¹ is a C₂-C₃₀ hydrocarbyl;
 - R² is a C₂-C₃₀ hydrocarbyl;
 - R³ is C₁-C₄ alkyl or -O-C₂-C₃₀ hydrocarbyl;
 - R⁴ is a C₂-C₃₀ hydrocarbyl;
 - R⁵ is a C₂-C₃₀ hydrocarbyl;
 - R⁶ is C₁-C₄ alkyl or -O-C₂-C₃₀ hydrocarbyl; and
 - X is a divalent linking group.
2. The compound of claim 1, wherein R¹ is C₂-C₂₀ hydrocarbyl.
 3. The compound of claim 1, wherein R¹ is C₂-C₁₅ hydrocarbyl.
 4. The compound of claim 1, wherein R¹ is C₂-C₁₀ hydrocarbyl.
 5. The compound of claim 1, wherein R¹ is C₅-C₂₀ hydrocarbyl.
 6. The compound of claim 1, wherein R¹ is (C₂-C₂₀)alkyl, (C₂-C₂₀)alkenyl, or (C₂-C₂₀)alkynyl.
 7. The compound of claim 1, wherein R¹ is (C₇-C₁₅)alkyl.

8. The compound of claim 1, wherein R^1 is (C₇-C₁₅)alkenyl.
9. The compound of claim 1, wherein R^1 is (C₇-C₁₅)alkynyl.
10. The compound of claim 1, wherein R^1 is (C₇-C₁₅)alkenyl, having only one double bond.
11. The compound of claim 1, wherein R^1 is (Z)-4-decen-1-yl, 1-tridecyl, (Z)-3-hept-1-yl, or (Z)-5-dodecen-1-yl.
12. The compound of any one of claims 1-11, wherein R^2 is C₂-C₂₀ hydrocarbyl.
13. The compound of any one of claims 1-11, wherein R^2 is C₂-C₁₅ hydrocarbyl.
14. The compound of any one of claims 1-11, wherein R^2 is C₂-C₁₀ hydrocarbyl.
15. The compound of any one of claims 1-11, wherein R^2 is C₅-C₂₀ hydrocarbyl.
16. The compound of any one of claims 1-11, wherein R^2 is (C₂-C₂₀)alkyl, (C₂-C₂₀)alkenyl, or (C₂-C₂₀)alkynyl.
17. The compound of any one of claims 1-11, wherein R^2 is a (C₇-C₁₅)alkyl.
18. The compound of any one of claims 1-11, wherein R^2 is a (C₇-C₁₅)alkenyl.
19. The compound of any one of claims 1-11, wherein R^2 is a (C₇-C₁₅)alkynyl.
20. The compound of any one of claims 1-11, wherein R^2 is a (C₇-C₁₅)alkenyl, having only one double bond.
21. The compound of any one of claims 1-11, wherein R^2 is (Z)-4-decen-1-yl, 1-tridecyl, (Z)-3-hept-1-yl, or (Z)-5-dodecen-1-yl.
22. The compound of any one of claims 1-21, wherein R^3 is C₁-C₄ alkyl.

23. The compound of any one of claims 1-21, wherein R^3 is methyl.
24. The compound of any one of claims 1-21, wherein R^3 is $-O-C_2-C_{20}$ hydrocarbyl.
25. The compound of any one of claims 1-21, wherein R^3 is $-O-C_2-C_{15}$ hydrocarbyl.
26. The compound of any one of claims 1-21, wherein R^3 is $-O-C_2-C_{10}$ hydrocarbyl.
27. The compound of any one of claims 1-21, wherein R^3 is $-O-C_5-C_{20}$ hydrocarbyl.
28. The compound of any one of claims 1-21, wherein R^3 is $-O-(C_2-C_{20})$ alkyl, $-O-(C_2-C_{20})$ alkenyl, or $-O-(C_2-C_{20})$ alkynyl.
29. The compound of any one of claims 1-21, wherein R^3 is a $-O-(C_7-C_{15})$ alkyl.
30. The compound of any one of claims 1-21, wherein R^3 is a $-O-(C_7-C_{15})$ alkenyl.
31. The compound of any one of claims 1-21, wherein R^3 is a $-O-(C_7-C_{15})$ alkynyl.
32. The compound of any one of claims 1-21, wherein R^3 is a $-O-(C_7-C_{15})$ alkenyl, having only one double bond.
33. The compound of any one of claims 1-21, wherein R^3 is (Z)-4-decen-1-yloxy, 1-tridecyloxy, (Z)-3-hept-1-yloxy, or (Z)-5-dodecen-1-yloxy.
34. The compound of any one of claims 1-33, wherein R^4 is C_2-C_{20} hydrocarbyl.
35. The compound of any one of claims 1-33, wherein R^4 is C_2-C_{15} hydrocarbyl.
36. The compound of any one of claims 1-33, wherein R^4 is C_2-C_{10} hydrocarbyl.
37. The compound of any one of claims 1-33, wherein R^4 is C_5-C_{20} hydrocarbyl.

38. The compound of any one of claims 1-33, wherein R^4 is (C_2-C_{20}) alkyl, (C_2-C_{20}) alkenyl, or (C_2-C_{20}) alkynyl.
39. The compound of any one of claims 1-33, wherein R^4 is (C_7-C_{15}) alkyl.
40. The compound of any one of claims 1-33, wherein R^4 is (C_7-C_{15}) alkenyl.
41. The compound of any one of claims 1-33, wherein R^4 is (C_7-C_{15}) alkynyl.
42. The compound of any one of claims 1-33, wherein R^4 is (C_7-C_{15}) alkenyl, having only one double bond.
43. The compound of any one of claims 1-33, wherein R^4 is (Z)-4-decen-1-yl, 1-tridecyl, (Z)-3-hept-1-yl, or (Z)-5-dodecen-1-yl.
44. The compound of any one of claims 1-43, wherein R^5 is C_2-C_{20} hydrocarbyl.
45. The compound of any one of claims 1-43, wherein R^5 is C_2-C_{15} hydrocarbyl.
46. The compound of any one of claims 1-43, wherein R^5 is C_2-C_{10} hydrocarbyl.
47. The compound of any one of claims 1-43, wherein R^5 is C_5-C_{20} hydrocarbyl.
48. The compound of any one of claims 1-43, wherein R^5 is (C_2-C_{20}) alkyl, (C_2-C_{20}) alkenyl, or (C_2-C_{20}) alkynyl.
49. The compound of any one of claims 1-43, wherein R^5 is a (C_7-C_{15}) alkyl.
50. The compound of any one of claims 1-43, wherein R^5 is a (C_7-C_{15}) alkenyl.
51. The compound of any one of claims 1-43, wherein R^5 is a (C_7-C_{15}) alkynyl.
52. The compound of any one of claims 1-43, wherein R^5 is a (C_7-C_{15}) alkenyl, having only one double bond.

53. The compound of any one of claims 1-43, wherein R^5 is (Z)-4-decen-1-yl, 1-tridecyl, (Z)-3-hept-1-yl, or (Z)-5-dodecen-1-yl.
54. The compound of any one of claims 1-53, wherein R^6 is C_1 - C_4 alkyl.
55. The compound of any one of claims 1-53, wherein R^6 is methyl.
56. The compound of any one of claims 1-53, wherein R^6 is $-O$ - C_2 - C_{20} hydrocarbyl.
57. The compound of any one of claims 1-53, wherein R^6 is $-O$ - C_2 - C_{15} hydrocarbyl.
58. The compound of any one of claims 1-53, wherein R^6 is $-O$ - C_2 - C_{10} hydrocarbyl.
59. The compound of any one of claims 1-53, wherein R^6 is $-O$ - C_5 - C_{20} hydrocarbyl.
60. The compound of any one of claims 1-53, wherein R^6 is $-O$ -(C_2 - C_{20})alkyl, $-O$ -(C_2 - C_{20})alkenyl, or $-O$ -(C_2 - C_{20})alkynyl.
61. The compound of any one of claims 1-53, wherein R^6 is a $-O$ -(C_7 - C_{15})alkyl.
62. The compound of any one of claims 1-53, wherein R^6 is a $-O$ -(C_7 - C_{15})alkenyl.
63. The compound of any one of claims 1-53, wherein R^6 is a $-O$ -(C_7 - C_{15})alkynyl.
64. The compound of any one of claims 1-53, wherein R^6 is a $-O$ -(C_7 - C_{15})alkenyl, having only one double bond.
65. The compound of any one of claims 1-53, wherein R^6 is (Z)-4-decen-1-yloxy, 1-tridecyloxy, (Z)-3-hept-1-yloxy, or (Z)-5-dodecen-1-yloxy.
66. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by ($-O$),

(-NR^a-), (a divalent (C₃-C₈)cycloalkyl), or (a divalent 3-12 membered heterocycle), and wherein the chain, the divalent (C₃-C₈)cycloalkyl, or the divalent 3-12 membered heterocycle is optionally substituted with one or more (e.g. 1, 2, 3, or 4) substituents independently selected from the group consisting of (C₁-C₆)alkoxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, (C₁-C₆)alkoxycarbonyl, cyano, nitro, halo, hydroxy, oxo (=O), and carboxy; and wherein each R^a is independently selected from H and (C₁-C₆)alkyl that is optionally substituted with one or more groups independently selected from halo, hydroxy, and (C₁-C₆)alkoxy.

67. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by (-O-), (-NR^a-), (a divalent (C₃-C₈)cycloalkyl), or (a divalent 3-8 membered heterocycle), and wherein the chain, the divalent (C₃-C₈)cycloalkyl, or the divalent 3-8 membered heterocycle is optionally substituted with one or more (e.g. 1, 2, 3, or 4) substituents independently selected from the group consisting of (C₁-C₆)alkoxy, (C₁-C₆)alkanoyl, (C₁-C₆)alkanoyloxy, (C₁-C₆)alkoxycarbonyl, cyano, nitro, halo, hydroxy, oxo (=O), and carboxy; and wherein each R^a is independently selected from H and (C₁-C₆)alkyl.

68. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by (-NR^a-) or (a divalent 3-12 membered heterocycle); and wherein each R^a is independently selected from (C₁-C₆)alkyl that is optionally substituted with one or more groups independently selected from halo, hydroxy, and (C₁-C₆)alkoxy.

69. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by (-NR^a-) or (a divalent 3-8 membered heterocycle); and wherein each R^a is independently selected from (C₁-C₆)alkyl.

70. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is replaced by (-NR^a-); and

wherein each R^a is independently selected from (C₁-C₆)alkyl that is optionally substituted with one or more groups independently selected from halo, hydroxy, and (C₁-C₆)alkoxy.

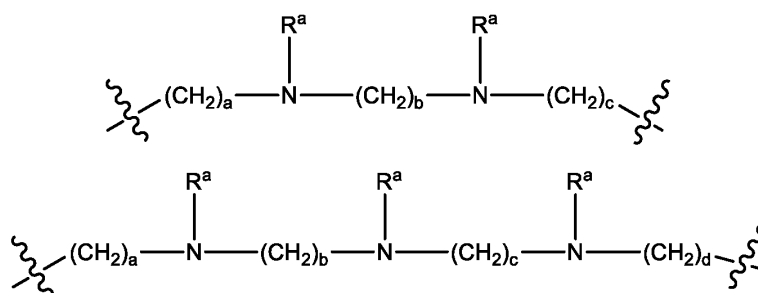
71. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is replaced by (-NR^a-); and wherein each R^a is independently selected from (C₁-C₆)alkyl.

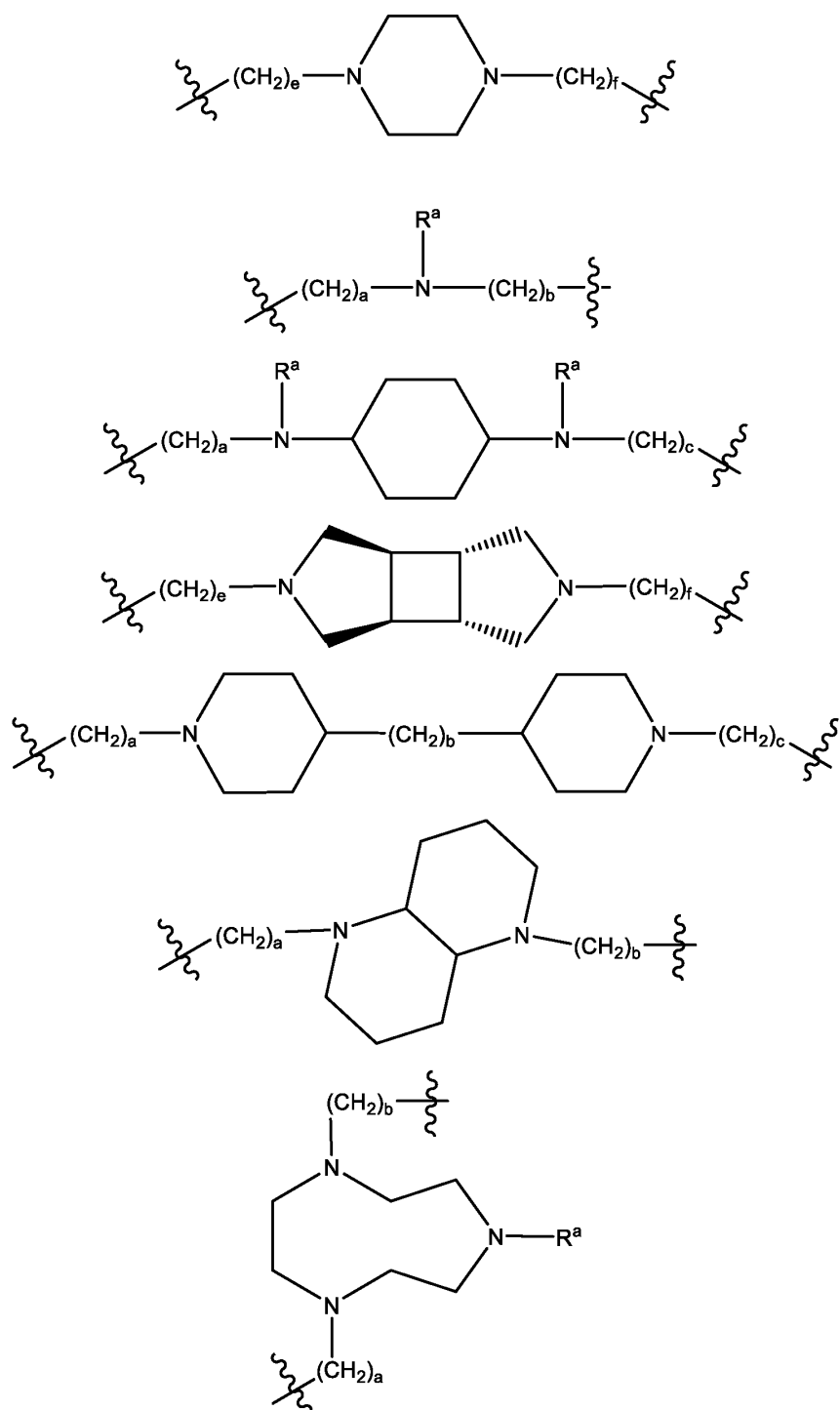
72. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by a divalent 3-12 membered heterocycle.

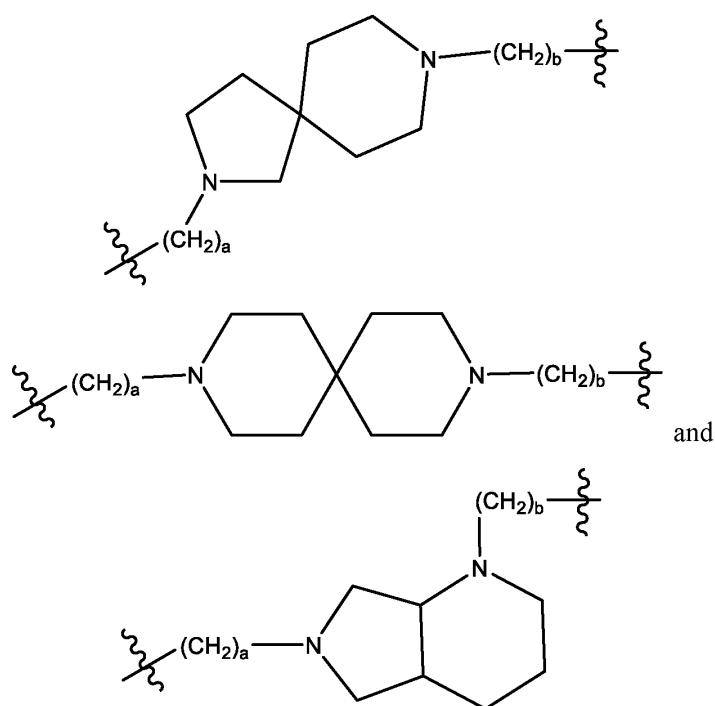
73. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 2 to 25 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by a divalent 3-8 membered heterocycle.

74. The compound of any one of claims 1-65, wherein X is a divalent, branched or unbranched, saturated or unsaturated, hydrocarbon chain, having from 6 to 12 carbon atoms, wherein one or more (e.g. 1, 2, 3, or 4) of the carbon atoms is optionally replaced by a piperazin-1,4-diyl.

75. The compound of any one of claims 1-65, wherein X is selected from the group consisting of:







wherein:

a is 2, 3, 4, or 5;

b is 2, 3, 4, or 5;

c is 2, 3, 4, or 5;

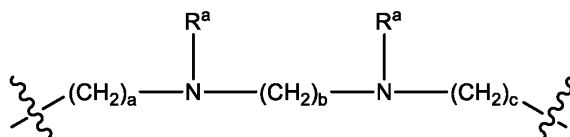
d is 2, 3, 4, or 5;

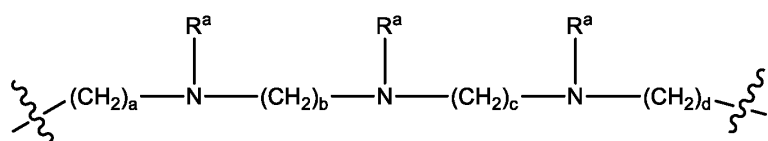
e is 2, 3, 4, 5, 6, 7, or 8;

f is 2, 3, 4, 5, 6, 7, or 8; and

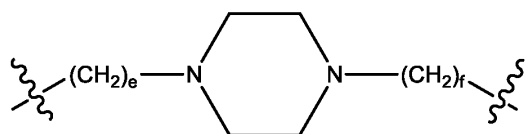
each R^a is independently selected from H and (C₁-C₆)alkyl that is optionally substituted with one or more groups independently selected from halo, hydroxy, and (C₁-C₆)alkoxy.

76. The compound of any one of claims 1-65, wherein X is selected from the group consisting of:





and



wherein:

a is 2, 3, 4, or 5;

b is 2, 3, 4, or 5;

c is 2, 3, 4, or 5;

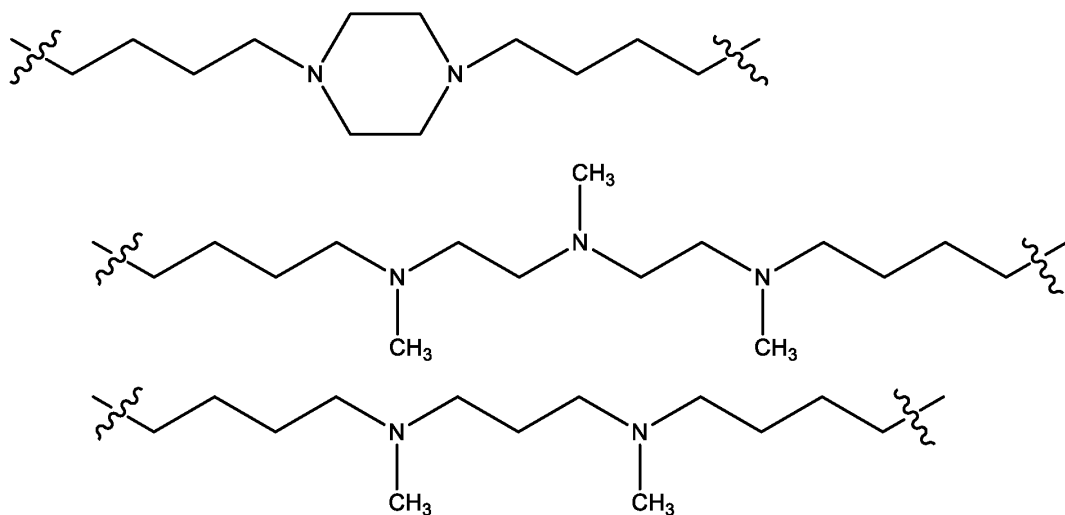
d is 2, 3, 4, or 5;

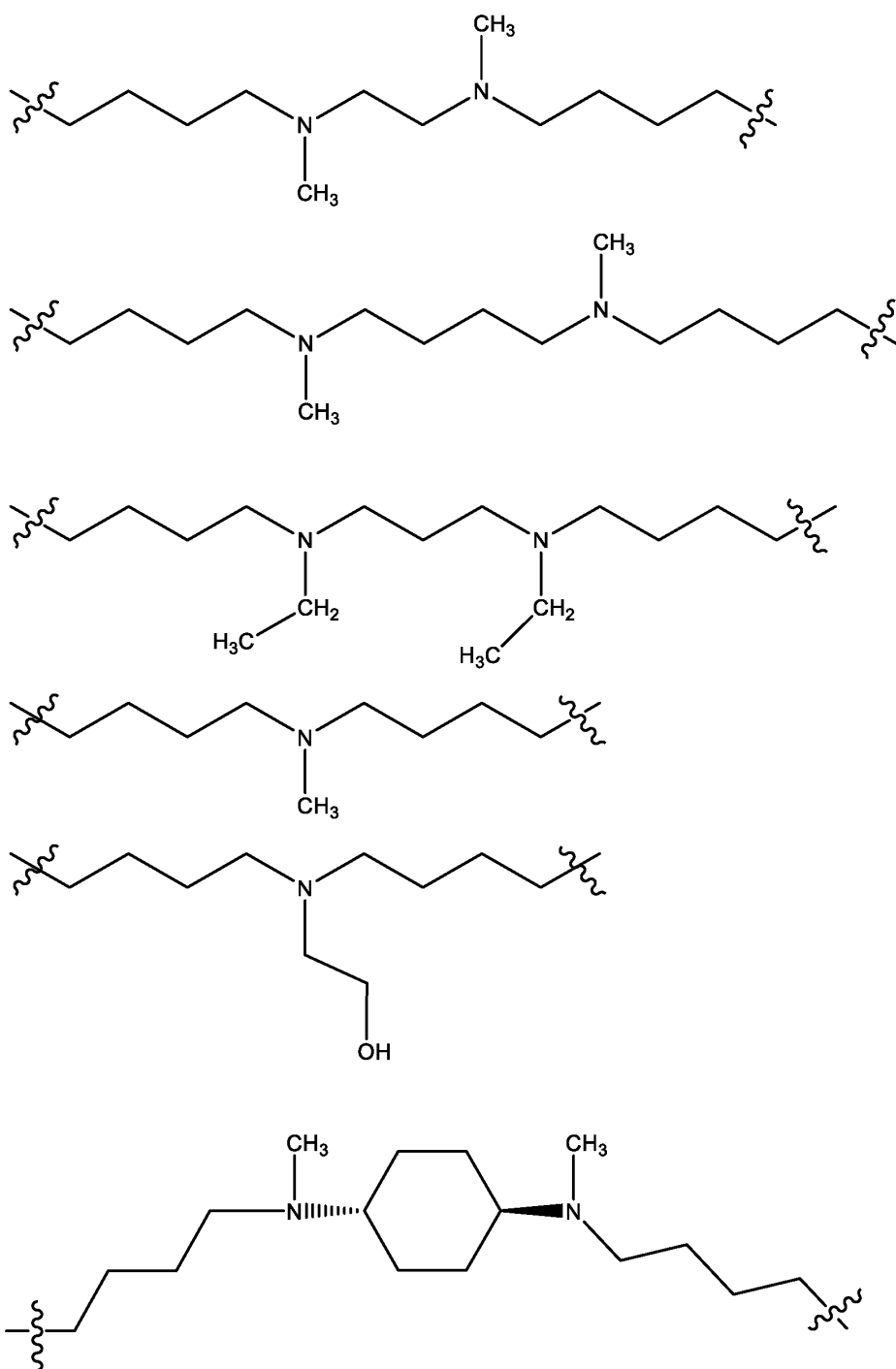
e is 2, 3, 4, 5, 6, 7, or 8;

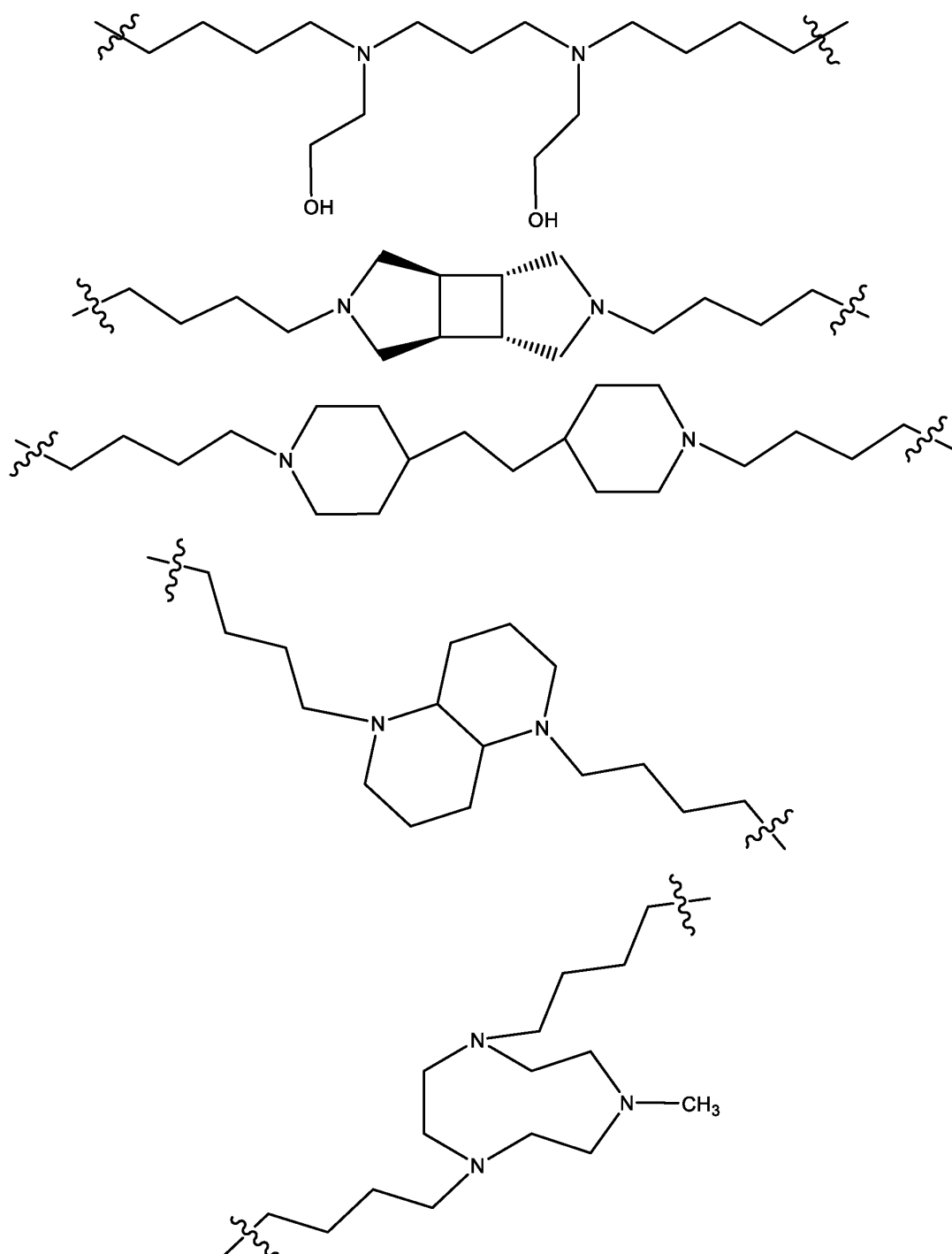
f is 2, 3, 4, 5, 6, 7, or 8; and

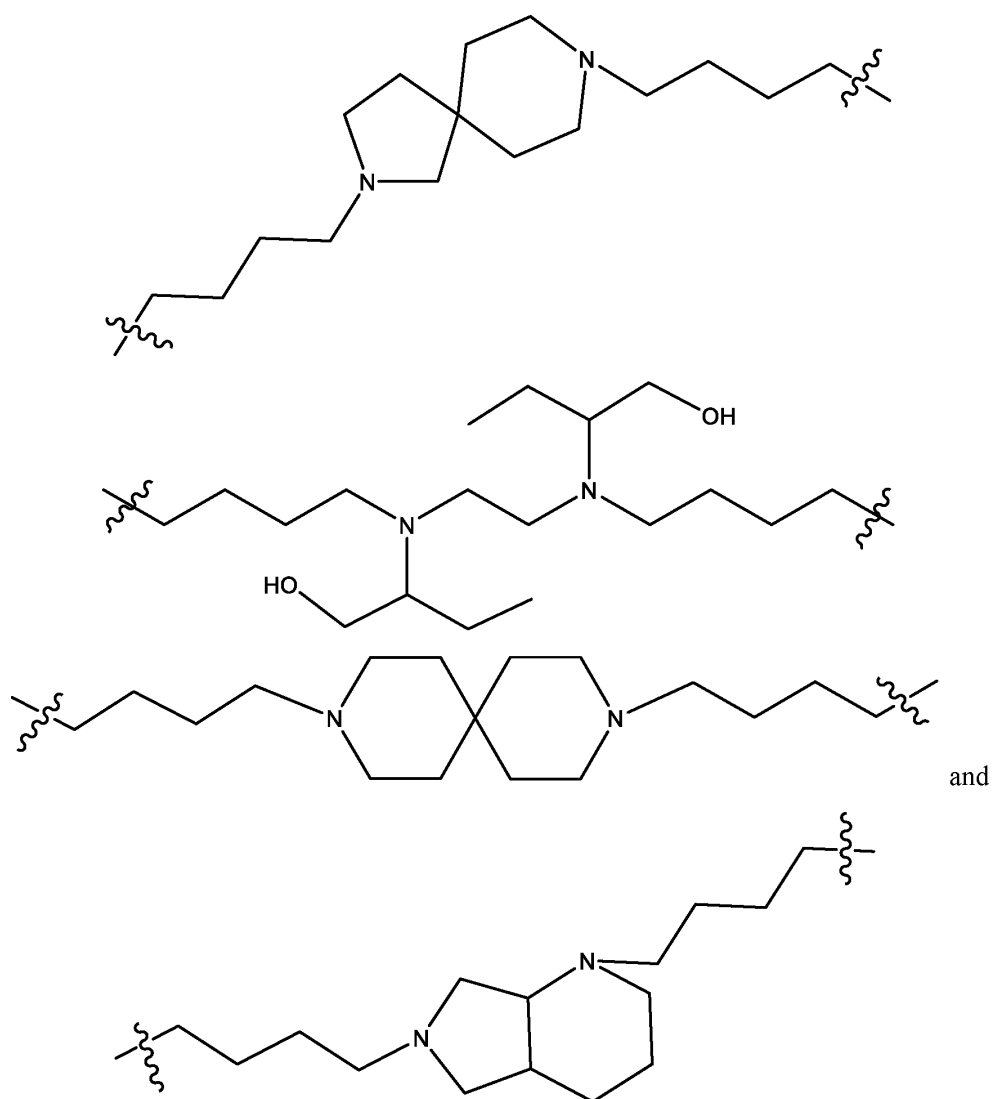
each R^a is independently selected from H and (C₁-C₆)alkyl.

77. The compound of any one of claims 1-65, wherein X is selected from the group consisting of:

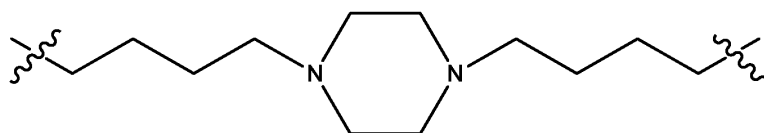


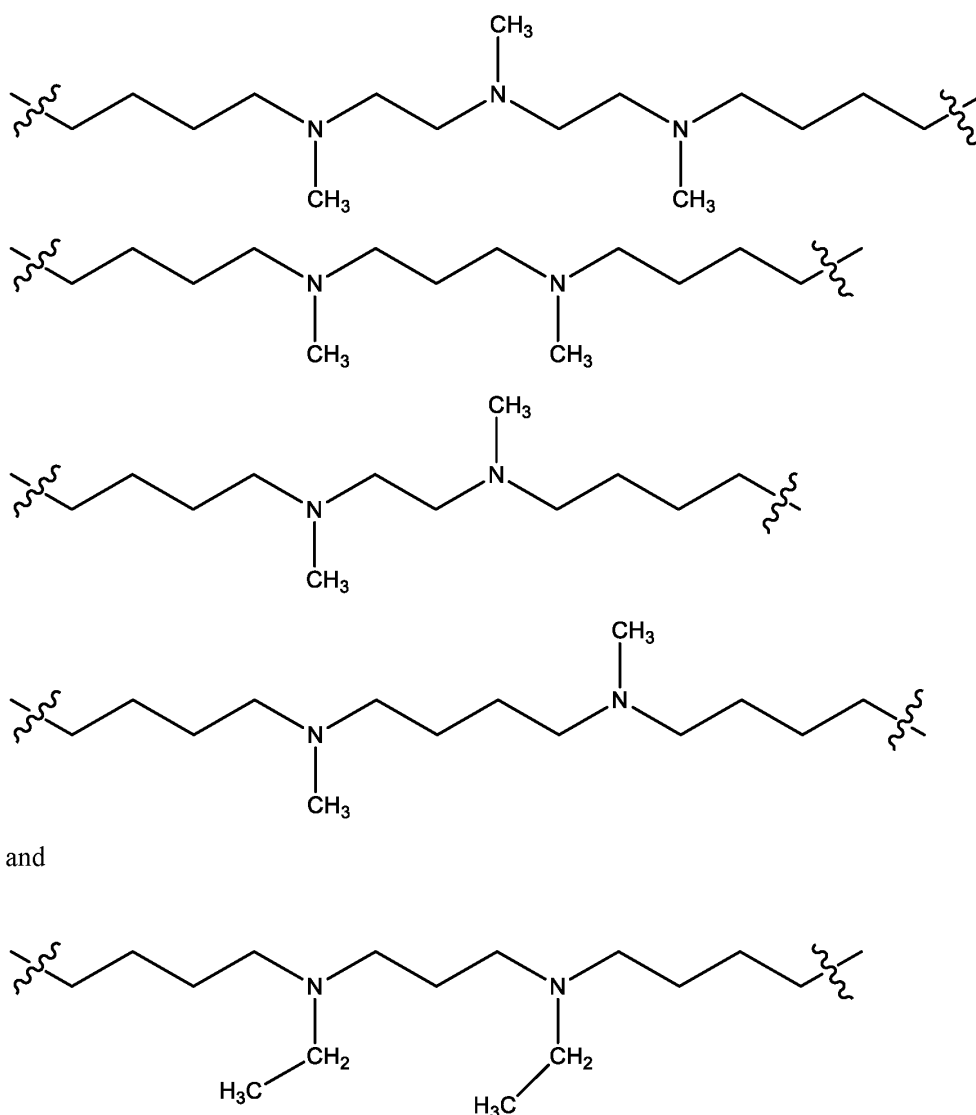






78. The compound of any one of claims 1-65, wherein X is selected from the group consisting of:





79. The compound of claim 1, which is selected from a compound of formula 12-43 as described in the Examples, or a salt thereof.

80. A lipid particle comprising the compound of any one of claims 1-79.

81. The lipid particle of claim 80, wherein the lipid particle further comprises a non-cationic lipid.

82. The lipid particle of claim 80 or 81, wherein the lipid particle further comprises a conjugated lipid that inhibits aggregation of particles.
83. The lipid particle of any one of claims 80-82, wherein the lipid particle further comprises a therapeutic agent.
84. The lipid particle of claim 83, wherein the therapeutic agent is a nucleic acid therapeutic agent.
85. The lipid particle of claim 83, wherein the therapeutic agent is an interfering RNA agent.
86. The lipid particle of claim 85, wherein the therapeutic agent is siRNA.
87. The lipid particle of claim 83, wherein the therapeutic agent is mRNA.
88. The lipid particle of any one of claims 84-87, wherein the nucleic acid therapeutic agent comprises at least one modified nucleotide.
89. The lipid particle of claim 88, wherein the nucleic acid therapeutic agent comprises at least one 2'-O-methyl (2'OMe) nucleotide.
90. The lipid particle of any one of claims 81-89, wherein the non-cationic lipid is cholesterol or a derivative thereof.
91. The lipid particle of any one of claims 81-90, wherein the non-cationic lipid is cholesterol.
92. The lipid particle of any one of claims 81-89, wherein the non-cationic lipid comprises a phospholipid.
93. The lipid particle of any one of claims 81-90, wherein the non-cationic lipid comprises a mixture of a phospholipid and cholesterol.

94. The lipid particle of any one of claims 92-93, wherein the phospholipid is distearoylphosphatidylcholine (DSPC).
95. The lipid particle of any one of claims 82-90, wherein the conjugated lipid is a polyethyleneglycol (PEG)-lipid conjugate.
96. The lipid particle of claim 95, wherein the PEG-lipid conjugate is a PEG-dimyristyloxypropyl (PEG-DMA) conjugate.
97. A composition comprising a compound of any one of claims 1-79.
98. A pharmaceutical composition comprising a lipid particle of any one of claims 80-96, and a pharmaceutically acceptable carrier.
99. A method for the *in vivo* delivery of a therapeutic agent, the method comprising: administering to a mammalian subject a lipid particle of any one of claims 83-96.
100. A lipid particle of any one of claims 83-96 for use in the *in vivo* delivery of a therapeutic agent to a mammal.
101. The use of a lipid particle of any one of claims 83-96 to prepare a medicament for the *in vivo* delivery of a therapeutic agent to a mammal.
102. A method for treating a disease or disorder in a mammalian subject in need thereof, the method comprising:
administering to the mammalian subject a therapeutically effective amount of a lipid particle of any one of claims 83-96.
103. The method of claim 102, wherein the disease or disorder is liver fibrosis.
104. The method of claim 102, wherein the disease or disorder is non-alcoholic steatohepatitis (NASH).

105. The method of claim 102, wherein the disease or disorder is alcoholic steatohepatitis (ASH).

106. The method of claim 102, wherein the disease or disorder is liver fibrosis associated non-alcoholic steatohepatitis (NASH) or alcoholic steatohepatitis (ASH).

107. A method of delivering a therapeutic agent to a hepatic stellate cell (HSC), *in vivo* or *in vitro*, comprising contacting the HSC with the lipid particle of any one of claims 83-96.