

**AMINO ACID-, PEPTIDE- AND POLYPEPTIDE-LIPIDS,
ISOMERS, COMPOSITIONS, AND USES THEREOF DERIVATIVES
FUNCTIONALIZED ON THE N-TERMINAL CAPABLE OF FORMING DRUG
ENCAPSULATING MICROSPHERES**

Related Applications

[0001] The present application claims priority under 35 U.S.C. § 119(e) to U.S. provisional patent application, U.S.S.N. 61/552,423, filed October 27, 2011, which is incorporated herein by reference.

Government Support

[0002] This invention was made with government support under Grant No. R37 EB000244 awarded by the National Institutes of Health. The government has certain rights in this invention.

Background of the Invention

[0003] The ability to silence genes via RNA interference (RNAi) was reported by Mello and Fire in 1998. See Fire *et al.*, *Nature* (1998) 391:806-811. Since then, scientists have rushed to take advantage of the enormous therapeutic potential driven by targeted gene knockdown. This is evidenced by the fact that the first report of small interfering RNA (siRNA) mediated RNAi in human beings was reported only twelve years after the phenomenon was described in *Caenorhabditis elegans*. See Davis *et al.*, *Nature* (2010) 464:1067-1070. It is well understood that development of genetic drugs is slowed by the inability to deliver nucleic acids effectively *in vivo*. When unprotected, genetic material injected into the bloodstream can be degraded by DNAases and RNAases, or, if not degraded, the genetic material can stimulate an immune response. See, *e.g.*, Whitehead *et al.*, *Nature Reviews Drug Discovery* (2009) 8:129-138; Robbins *et al.*, *Oligonucleotides* (2009) 19:89-102. Intact siRNA must then enter the cytosol, where the antisense strand is incorporated into the RNA-induced silencing complex (RISC) (Whitehead *supra*). The RISC associates with and degrades complementary mRNA sequences, thereby preventing translation of the target mRNA into protein, *i.e.*, “silencing” the gene.

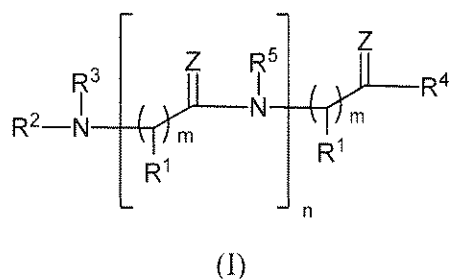
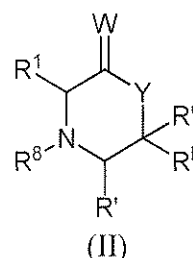
[0004] To overcome difficulties in delivery, nucleotides have been complexed with a wide variety of delivery systems, including polymers, lipids, inorganic nanoparticles and viruses. See, *e.g.*, Peer *et al.* *Nature Nanotechnology*, (2007) 2:751-760. However, despite promising data from ongoing clinical trials for the treatment of respiratory syncytial virus and liver cancers (see, *e.g.*, Zamora *et al.*, *Am. J. Respir. Crit. Care Med.* (2011) 183:531-538),

the clinical use of siRNA continues to require development of safer and more effective delivery systems. Toward this end, numerous lipid-like molecules have been developed including poly β -amino esters and amino alcohol lipids. See, e.g., PCT Application Publication Nos. WO 2002/031025; WO 2004/106411; WO 2008/011561; WO 2007/143659; WO 2006/138380; and WO 2010/053572. Amino acid, peptide, polypeptide-lipids (APPL) have also been studied for a variety of applications, including use as therapeutics, biosurfactants, and nucleotide delivery systems. See, e.g., Giuliani *et al.*, *Cellular and Molecular Life Sciences* (2011) 68:2255-2266; Ikeda *et al.*, *Current Medicinal Chemistry* (2007) 14: 111263-1275; Sen, *Advances in Experimental Medicine and Biology* (2010) 672:316-323; and Damen *et al.*, *Journal of Controlled Release* (2010) 145:33-39. However, there continues to remain a need to investigate and develop new APPL systems with improved properties, such as new and improved APPL nucleotide delivery systems.

Summary of the Invention

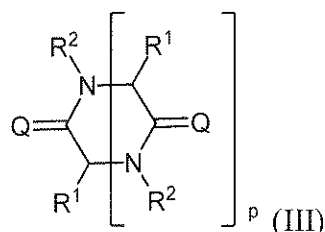
[0005] Described herein are inventive compounds and compositions characterized, in certain embodiments, by conjugation of various groups, such as lipophilic groups, to an amino or amide group of an amino acid, a linear or cyclic peptide, a linear or cyclic polypeptide, or structural isomer thereof, to provide compounds of the present invention, collectively referred to herein as “APPLs”. Such APPLs are deemed useful for a variety of applications, such as, for example, improved nucleotide delivery. The subject matter is as defined in the independent claims 1, 142, 3621, 5240, 6042, 78, 80, and 8243, and their dependent claims.

[0006] Exemplary APPLs include, but are not limited to, compounds of Formula (I), (II), (III), (IV), (V), and (VI), and salts thereof, as described herein:



Claims

1. A compound of Formula (III):



or salt thereof;

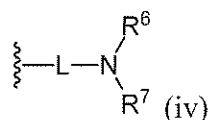
wherein:

p is 1;

Q is O;

each instance of R^1 is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, or a group of formula (iv);

provided at least one instance of R^1 is a group of formula:

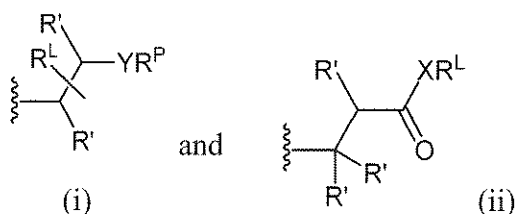


L is independently an optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted heteroalkylene, optionally substituted heteroalkenylene, or optionally substituted heteroalkynylene;

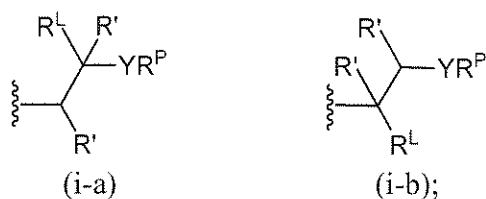
R^6 and R^7 are each independently hydrogen, a nitrogen protecting group, or a group of formula (i) or (ii);

each instance of R^2 is independently hydrogen, a nitrogen protecting group, or a group of the formula (i) or (ii);

formula (i) and (ii) are:



wherein each instance of formula (i) is independently formula (i-a) or formula (i-b):



each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, or NR^{X} , wherein R^{X} is hydrogen, optionally substituted alkyl, or a nitrogen protecting group;

Y is O;

R^{P} is independently hydrogen or an oxygen protecting group; and

R^{L} is independently optionally substituted C_{6-20} alkyl, optionally substituted C_{6-20} alkenyl, optionally substituted C_{6-20} alkynyl, optionally substituted hetero C_{6-20} alkyl, optionally substituted hetero C_{6-20} alkenyl, or optionally substituted hetero C_{6-20} alkynyl; wherein:

optionally substituted refers to a carbon atom of a group which is unsubstituted or independently substituted with halogen, $-\text{CN}$, $-\text{NO}_2$, $-\text{N}_3$, $-\text{SO}_2\text{H}$, $-\text{SO}_3\text{H}$, $-\text{OH}$, $-\text{OR}^{\text{aa}}$, $-\text{ON}(\text{R}^{\text{bb}})_2$, $-\text{N}(\text{R}^{\text{bb}})_2$, $-\text{N}(\text{R}^{\text{bb}})_3^+\text{X}^-$, $-\text{N}(\text{OR}^{\text{cc}})\text{R}^{\text{bb}}$, $-\text{SeH}$, $-\text{SeR}^{\text{aa}}$, $-\text{SH}$, $-\text{SR}^{\text{aa}}$, $-\text{SSR}^{\text{cc}}$, $-\text{C}(=\text{O})\text{R}^{\text{aa}}$, $-\text{CO}_2\text{H}$, $-\text{CHO}$, $-\text{C}(\text{OR}^{\text{cc}})_2$, $-\text{CO}_2\text{R}^{\text{aa}}$, $-\text{OC}(=\text{O})\text{R}^{\text{aa}}$, $-\text{OCO}_2\text{R}^{\text{aa}}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{OC}(=\text{O})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{NR}^{\text{bb}}\text{C}(=\text{O})\text{R}^{\text{aa}}$, $-\text{NR}^{\text{bb}}\text{CO}_2\text{R}^{\text{aa}}$, $-\text{NR}^{\text{bb}}\text{C}(=\text{O})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{C}(=\text{NR}^{\text{bb}})\text{R}^{\text{aa}}$, $-\text{C}(=\text{NR}^{\text{bb}})\text{OR}^{\text{aa}}$, $-\text{OC}(=\text{NR}^{\text{bb}})\text{R}^{\text{aa}}$, $-\text{OC}(=\text{NR}^{\text{bb}})\text{OR}^{\text{aa}}$, $-\text{C}(=\text{NR}^{\text{bb}})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{OC}(=\text{NR}^{\text{bb}})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{NR}^{\text{bb}}\text{C}(=\text{NR}^{\text{bb}})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{C}(=\text{O})\text{NR}^{\text{bb}}\text{SO}_2\text{R}^{\text{aa}}$, $-\text{NR}^{\text{bb}}\text{SO}_2\text{R}^{\text{aa}}$, $-\text{SO}_2\text{N}(\text{R}^{\text{bb}})_2$, $-\text{SO}_2\text{R}^{\text{aa}}$, $-\text{SO}_2\text{OR}^{\text{aa}}$, $-\text{OSO}_2\text{R}^{\text{aa}}$, $-\text{S}(=\text{O})\text{R}^{\text{aa}}$, $-\text{OS}(=\text{O})\text{R}^{\text{aa}}$, $-\text{Si}(\text{R}^{\text{aa}})_3$, $-\text{OSi}(\text{R}^{\text{aa}})_3$, $-\text{C}(=\text{S})\text{N}(\text{R}^{\text{bb}})_2$, $-\text{C}(=\text{O})\text{SR}^{\text{aa}}$, $-\text{C}(=\text{S})\text{SR}^{\text{aa}}$, $-\text{SC}(=\text{S})\text{SR}^{\text{aa}}$, $-\text{SC}(=\text{O})\text{SR}^{\text{aa}}$, $-\text{OC}(=\text{O})\text{SR}^{\text{aa}}$, $-\text{SC}(=\text{O})\text{OR}^{\text{aa}}$, $-\text{SC}(=\text{O})\text{R}^{\text{aa}}$, $-\text{P}(=\text{O})_2\text{R}^{\text{aa}}$, $-\text{OP}(=\text{O})_2\text{R}^{\text{aa}}$, $-\text{P}(=\text{O})(\text{R}^{\text{aa}})_2$, $-\text{OP}(=\text{O})(\text{R}^{\text{aa}})_2$, $-\text{OP}(=\text{O})(\text{OR}^{\text{cc}})_2$, $-\text{P}(=\text{O})_2\text{N}(\text{R}^{\text{bb}})_2$, $-\text{OP}(=\text{O})_2\text{N}(\text{R}^{\text{bb}})_2$, $-\text{P}(=\text{O})(\text{NR}^{\text{bb}})_2$, $-\text{OP}(=\text{O})(\text{NR}^{\text{bb}})_2$, $-\text{NR}^{\text{bb}}\text{P}(=\text{O})(\text{OR}^{\text{cc}})_2$, $-\text{NR}^{\text{bb}}\text{P}(=\text{O})(\text{NR}^{\text{bb}})_2$, $-\text{P}(\text{R}^{\text{cc}})_2$, $-\text{P}(\text{R}^{\text{cc}})_3$, $-\text{OP}(\text{R}^{\text{cc}})_2$, $-\text{OP}(\text{R}^{\text{cc}})_3$, $-\text{B}(\text{R}^{\text{aa}})_2$, $-\text{B}(\text{OR}^{\text{cc}})_2$, $-\text{BR}^{\text{aa}}(\text{OR}^{\text{cc}})$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-14} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group $=\text{O}$, $=\text{S}$, $=\text{NN}(\text{R}^{\text{bb}})_2$, $=\text{NNR}^{\text{bb}}\text{C}(=\text{O})\text{R}^{\text{aa}}$, $=\text{NNR}^{\text{bb}}\text{C}(=\text{O})\text{OR}^{\text{aa}}$, $=\text{NNR}^{\text{bb}}\text{S}(=\text{O})_2\text{R}^{\text{aa}}$, $=\text{NR}^{\text{bb}}$, or $=\text{NOR}^{\text{cc}}$;

refers to a nitrogen atom of a group which is unsubstituted or independently substituted with OH , $-\text{OR}^{\text{aa}}$, $-\text{N}(\text{R}^{\text{cc}})_2$, $-\text{CN}$, $-\text{C}(=\text{O})\text{R}^{\text{aa}}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{\text{cc}})_2$, $-\text{CO}_2\text{R}^{\text{aa}}$, $-\text{SO}_2\text{R}^{\text{aa}}$, $-\text{C}(=\text{NR}^{\text{bb}})\text{R}^{\text{aa}}$, $-\text{C}(=\text{NR}^{\text{cc}})\text{OR}^{\text{aa}}$, $-\text{C}(=\text{NR}^{\text{cc}})\text{N}(\text{R}^{\text{cc}})_2$, $-\text{SO}_2\text{N}(\text{R}^{\text{cc}})_2$, $-\text{SO}_2\text{R}^{\text{cc}}$, $-\text{SO}_2\text{OR}^{\text{cc}}$, $-\text{SOR}^{\text{aa}}$, $-\text{C}(=\text{S})\text{N}(\text{R}^{\text{cc}})_2$, $-\text{C}(=\text{O})\text{SR}^{\text{cc}}$, $-\text{C}(=\text{S})\text{SR}^{\text{cc}}$, $-\text{P}(=\text{O})_2\text{R}^{\text{aa}}$, $-\text{P}(=\text{O})(\text{R}^{\text{aa}})_2$, $-\text{P}(=\text{O})_2\text{N}(\text{R}^{\text{cc}})_2$, $-\text{P}(=\text{O})(\text{NR}^{\text{cc}})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{cc} groups attached to an N atom are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring,

wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{aa} is, independently, selected from C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{aa} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{bb} is, independently, selected from hydrogen, $-OH$, $-OR^{aa}$, $-N(R^{cc})_2$, $-CN$, $-C(=O)R^{aa}$, $-C(=O)N(R^{cc})_2$, $-CO_2R^{aa}$, $-SO_2R^{aa}$, $-C(=NR^{cc})OR^{aa}$, $-C(=NR^{cc})N(R^{cc})_2$, $-SO_2N(R^{cc})_2$, $-SO_2R^{cc}$, $-SO_2OR^{cc}$, $-SOR^{aa}$, $-C(=S)N(R^{cc})_2$, $-C(=O)SR^{cc}$, $-C(=S)SR^{cc}$, $-P(=O)_2R^{aa}$, $-P(=O)(R^{aa})_2$, $-P(=O)_2N(R^{cc})_2$, $-P(=O)(NR^{cc})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{bb} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{cc} is, independently, selected from hydrogen, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{cc} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{dd} is, independently, selected from halogen, $-CN$, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, $-OH$, $-OR^{ee}$, $-ON(R^{ff})_2$, $-N(R^{ff})_2$, $-N(R^{ff})_3^+X^-$, $-N(OR^{ee})R^{ff}$, $-SH$, $-SR^{ee}$, $-SSR^{ee}$, $-C(=O)R^{ee}$, $-CO_2H$, $-CO_2R^{ee}$, $-OC(=O)R^{ee}$, $-OCO_2R^{ee}$, $-C(=O)N(R^{ff})_2$, $-OC(=O)N(R^{ff})_2$, $-NR^{ff}C(=O)R^{ee}$, $-NR^{ff}CO_2R^{ee}$, $-NR^{ff}C(=O)N(R^{ff})_2$, $-C(=NR^{ff})OR^{ee}$, $-OC(=NR^{ff})R^{ee}$, $-OC(=NR^{ff})OR^{ee}$, $-C(=NR^{ff})N(R^{ff})_2$, $-OC(=NR^{ff})N(R^{ff})_2$, $-NR^{ff}C(=NR^{ff})N(R^{ff})_2$, $-NR^{ff}SO_2R^{ee}$, $-SO_2N(R^{ff})_2$, $-SO_2R^{ee}$, $-SO_2OR^{ee}$, $-OSO_2R^{ee}$, $-S(=O)R^{ee}$, $-Si(R^{ee})_3$, $-OSi(R^{ee})_3$, $-C(=S)N(R^{ff})_2$, $-C(=O)SR^{ee}$, $-C(=S)SR^{ee}$, $-SC(=S)SR^{ee}$, $-P(=O)_2R^{ee}$, $-P(=O)(R^{ee})_2$, $-OP(=O)(R^{ee})_2$, $-OP(=O)(OR^{ee})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–10 membered heterocyclyl, C_{6-10} aryl, 5–10 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{eg} groups, or two geminal R^{dd} substituents can be joined to form $=O$ or $=S$;

each instance of R^{cc} is, independently, selected from C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, C_{6-10} aryl, 3–10 membered heterocyclyl, and 3–10 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups;

each instance of R^{ff} is, independently, selected from hydrogen, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–10 membered heterocyclyl, C_{6-10} aryl and 5–10 membered heteroaryl, or two R^{ff} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups; and

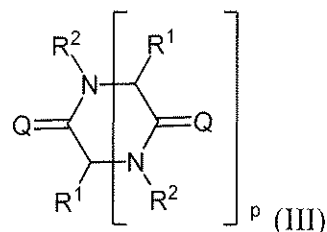
each instance of R^{gg} is, independently, halogen, $-CN$, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, $-OH$, $-OC_{1-50}$ alkyl, $-ON(C_{1-50} \text{ alkyl})_2$, $-N(C_{1-50} \text{ alkyl})_2$, $-N(C_{1-50} \text{ alkyl})_3^+X^-$, $-NH(C_{1-50} \text{ alkyl})_2^+X^-$, $-NH_2(C_{1-50} \text{ alkyl})^+X^-$, $-NH_3^+X^-$, $-N(OC_{1-50} \text{ alkyl})(C_{1-50} \text{ alkyl})$, $-N(OH)(C_{1-50} \text{ alkyl})$, $-NH(OH)$, $-SH$, $-SC_{1-50} \text{ alkyl}$, $-SS(C_{1-50} \text{ alkyl})$, $-C(=O)(C_{1-50} \text{ alkyl})$, $-CO_2H$, $-CO_2(C_{1-50} \text{ alkyl})$, $-OC(=O)(C_{1-50} \text{ alkyl})$, $-OCO_2(C_{1-50} \text{ alkyl})$, $-C(=O)NH_2$, $-C(=O)N(C_{1-50} \text{ alkyl})_2$, $-OC(=O)NH(C_{1-50} \text{ alkyl})$, $-NHC(=O)(C_{1-50} \text{ alkyl})$, $-N(C_{1-50} \text{ alkyl})C(=O)(C_{1-50} \text{ alkyl})$, $-NHCO_2(C_{1-50} \text{ alkyl})$, $-NHC(=O)N(C_{1-50} \text{ alkyl})_2$, $-NHC(=O)NH(C_{1-50} \text{ alkyl})$, $-NHC(=O)NH_2$, $-C(=NH)O(C_{1-50} \text{ alkyl})$, $-OC(=NH)(C_{1-50} \text{ alkyl})$, $-OC(=NH)OC_{1-50} \text{ alkyl}$, $-C(=NH)N(C_{1-50} \text{ alkyl})_2$, $-C(=NH)NH(C_{1-50} \text{ alkyl})$, $-C(=NH)NH_2$, $-OC(=NH)N(C_{1-50} \text{ alkyl})_2$, $-OC(NH)NH(C_{1-50} \text{ alkyl})$, $-OC(NH)NH_2$, $-NHC(NH)N(C_{1-50} \text{ alkyl})_2$, $-NHC(=NH)NH_2$, $-NHSO_2(C_{1-50} \text{ alkyl})$, $-SO_2N(C_{1-50} \text{ alkyl})_2$, $-SO_2NH(C_{1-50} \text{ alkyl})$, $-SO_2NH_2$, $-SO_2C_{1-50} \text{ alkyl}$, $-SO_2OC_{1-50} \text{ alkyl}$, $-OSO_2C_{1-6} \text{ alkyl}$, $-SOC_{1-6} \text{ alkyl}$, $-Si(C_{1-50} \text{ alkyl})_3$, $-OSi(C_{1-6} \text{ alkyl})_3$, $-C(=S)N(C_{1-50} \text{ alkyl})_2$, $C(=S)NH(C_{1-50} \text{ alkyl})$, $C(=S)NH_2$, $-C(=O)S(C_{1-6} \text{ alkyl})$, $-C(=S)SC_{1-6} \text{ alkyl}$, $-SC(=S)SC_{1-6} \text{ alkyl}$, $-P(=O)_2(C_{1-50} \text{ alkyl})$, $-P(=O)(C_{1-50} \text{ alkyl})_2$, $-OP(=O)(C_{1-50} \text{ alkyl})_2$, $-OP(=O)(OC_{1-50} \text{ alkyl})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, C_{6-10} aryl, 3–10 membered heterocyclyl, 5–10 membered heteroaryl; or two geminal R^{gg} substituents can be joined to form $=O$ or $=S$;

X^- is a counterion;

a nitrogen protecting group is $-OH$, $-OR^{aa}$, $-N(R^{cc})_2$, $-C(=O)R^{aa}$, $-C(=O)N(R^{cc})_2$, $-CO_2R^{aa}$, $-SO_2R^{aa}$, $-C(=NR^{cc})R^{aa}$, $-C(=NR^{cc})OR^{aa}$, $-C(=NR^{cc})N(R^{cc})_2$, $-SO_2N(R^{cc})_2$, $-SO_2R^{cc}$, $-SO_2OR^{cc}$, $-SOR^{aa}$, $-C(=S)N(R^{cc})_2$, $-C(=O)SR^{cc}$, $-C(=S)SR^{cc}$, C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl groups, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aralkyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; and

an oxygen protecting group is $-R^{aa}$, $-N(R^{bb})_2$, $-C(=O)SR^{aa}$, $-C(=O)R^{aa}$, $-CO_2R^{aa}$, $-C(=O)N(R^{bb})_2$, $-C(=NR^{bb})R^{aa}$, $-C(=NR^{bb})OR^{aa}$, $-C(=NR^{bb})N(R^{bb})_2$, $-S(=O)R^{aa}$, $-SO_2R^{aa}$, $-Si(R^{aa})_3$, $-P(R^{cc})_2$, $-P(R^{cc})_3$, $-P(=O)_2R^{aa}$, $-P(=O)(R^{aa})_2$, $-P(=O)(OR^{cc})_2$, $-P(=O)_2N(R^{bb})_2$, and $-P(=O)(NR^{bb})_2$.

2. A compound of Formula (III):



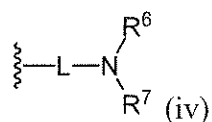
or salt thereof;

wherein:

p is 1;

Q is O;

each instance of R^1 is independently a group of formula:

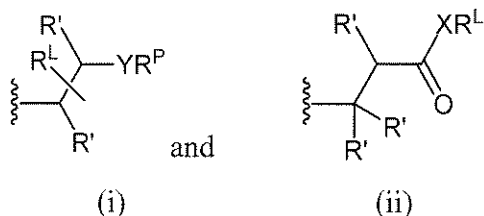


wherein L is independently an optionally substituted alkylene, and

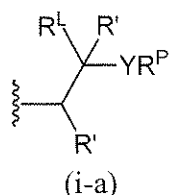
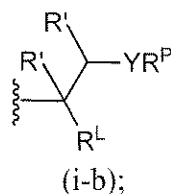
R^6 and R^7 are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group, or a group of formula (i) or (ii);

each instance of R^2 is independently hydrogen, or a group of the formula (i) or (ii);
and

Formulae (i) and (ii) are:



wherein each instance of formula (i) is independently formula (i-a) or formula (i-b):



each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O , S , NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is independently O , S , NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is independently optionally substituted C_{6-20} alkyl, optionally substituted C_{6-20} alkenyl, optionally substituted C_{6-20} alkynyl, optionally substituted hetero C_{6-20} alkyl, optionally substituted hetero C_{6-20} alkenyl, or optionally substituted hetero C_{6-20} alkynyl; wherein:

optionally substituted refers to a carbon atom of a group which is unsubstituted or independently substituted with halogen, $-CN$, $-NO_2$, $-N_3$, $-SO_2H$, $-SO_3H$, $-OH$, $-OR^{aa}$, $-ON(R^{bb})_2$, $-N(R^{bb})_2$, $-N(R^{bb})_3^+X^-$, $-N(OR^{cc})R^{bb}$, $-SeH$, $-SeR^{aa}$, $-SH$, $-SR^{aa}$, $-SSR^{cc}$, $-C(=O)R^{aa}$, $-CO_2H$, $-CHO$, $-C(OR^{cc})_2$, $-CO_2R^{aa}$, $-OC(=O)R^{aa}$, $-OCO_2R^{aa}$, $-C(=O)N(R^{bb})_2$, $-OC(=O)N(R^{bb})_2$, $-NR^{bb}C(=O)R^{aa}$, $-NR^{bb}CO_2R^{aa}$, $-NR^{bb}C(=O)N(R^{bb})_2$, $-C(=NR^{bb})R^{aa}$, $-C(=NR^{bb})OR^{aa}$, $-OC(=NR^{bb})R^{aa}$, $-OC(=NR^{bb})OR^{aa}$, $-C(=NR^{bb})N(R^{bb})_2$, $-OC(=NR^{bb})N(R^{bb})_2$, $-NR^{bb}C(=NR^{bb})N(R^{bb})_2$, $-C(=O)NR^{bb}SO_2R^{aa}$, $-NR^{bb}SO_2R^{aa}$, $-SO_2N(R^{bb})_2$, $-SO_2R^{aa}$, $-SO_2OR^{aa}$, $-OSO_2R^{aa}$, $-S(=O)R^{aa}$, $-OS(=O)R^{aa}$, $-Si(R^{aa})_3$, $-OSi(R^{aa})_3$, $-C(=S)N(R^{bb})_2$, $-C(=O)SR^{aa}$, $-C(=S)SR^{aa}$, $-SC(=S)SR^{aa}$, $-SC(=O)SR^{aa}$, $-OC(=O)SR^{aa}$, $-SC(=O)OR^{aa}$, $-SC(=O)R^{aa}$, $-P(=O)_2R^{aa}$, $-OP(=O)_2R^{aa}$, $-P(=O)(R^{aa})_2$, $-OP(=O)(R^{aa})_2$, $-OP(=O)(OR^{cc})_2$, $-$

$P(=O)_2N(R^{bb})_2$, $-OP(=O)_2N(R^{bb})_2$, $-P(=O)(NR^{bb})_2$, $-OP(=O)(NR^{bb})_2$, $-NR^{bb}P(=O)(OR^{cc})_2$, $-NR^{bb}P(=O)(NR^{bb})_2$, $-P(R^{cc})_2$, $-P(R^{cc})_3$, $-OP(R^{cc})_2$, $-OP(R^{cc})_3$, $-B(R^{aa})_2$, $-B(OR^{cc})_2$, $-BR^{aa}(OR^{cc})$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-14} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group $=O$, $=S$, $=NN(R^{bb})_2$, $=NNR^{bb}C(=O)R^{aa}$, $=NNR^{bb}C(=O)OR^{aa}$, $=NNR^{bb}S(=O)_2R^{aa}$, $=NR^{bb}$, or $=NOR^{cc}$;

refers to a nitrogen atom of a group which is unsubstituted or independently substituted with OH , $-OR^{aa}$, $-N(R^{cc})_2$, $-CN$, $-C(=O)R^{aa}$, $-C(=O)N(R^{cc})_2$, $-CO_2R^{aa}$, $-SO_2R^{aa}$, $-C(=NR^{bb})R^{aa}$, $-C(=NR^{cc})OR^{aa}$, $-C(=NR^{cc})N(R^{cc})_2$, $-SO_2N(R^{cc})_2$, $-SO_2R^{cc}$, $-SO_2OR^{cc}$, $-SOR^{aa}$, $-C(=S)N(R^{cc})_2$, $-C(=O)SR^{cc}$, $-C(=S)SR^{cc}$, $-P(=O)_2R^{aa}$, $-P(=O)(R^{aa})_2$, $-P(=O)_2N(R^{cc})_2$, $-P(=O)(NR^{cc})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{cc} groups attached to an N atom are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{aa} is, independently, selected from C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{aa} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{bb} is, independently, selected from hydrogen, $-OH$, $-OR^{aa}$, $-N(R^{cc})_2$, $-CN$, $-C(=O)R^{aa}$, $-C(=O)N(R^{cc})_2$, $-CO_2R^{aa}$, $-SO_2R^{aa}$, $-C(=NR^{cc})OR^{aa}$, $-C(=NR^{cc})N(R^{cc})_2$, $-SO_2N(R^{cc})_2$, $-SO_2R^{cc}$, $-SO_2OR^{cc}$, $-SOR^{aa}$, $-C(=S)N(R^{cc})_2$, $-C(=O)SR^{cc}$, $-C(=S)SR^{cc}$, $-P(=O)_2R^{aa}$, $-P(=O)(R^{aa})_2$, $-P(=O)_2N(R^{cc})_2$, $-P(=O)(NR^{cc})_2$, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{bb} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{cc} is, independently, selected from hydrogen, C_{1-50} alkyl, C_{2-50} alkenyl, C_{2-50} alkynyl, C_{3-10} carbocyclyl, 3–14 membered heterocyclyl, C_{6-14} aryl, and 5–14 membered heteroaryl, or two R^{cc} groups are joined to form a 3–14 membered heterocyclyl or

5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{dd} is, independently, selected from halogen, –CN, –NO₂, –N₃, –SO₂H, –SO₃H, –OH, –OR^{ee}, –ON(R^{ff})₂, –N(R^{ff})₂, –N(R^{ff})₃⁺X[–], –N(OR^{ee})R^{ff}, –SH, –SR^{ee}, –SSR^{ee}, –C(=O)R^{ee}, –CO₂H, –CO₂R^{ee}, –OC(=O)R^{ee}, –OCO₂R^{ee}, –C(=O)N(R^{ff})₂, –OC(=O)N(R^{ff})₂, –NR^{ff}C(=O)R^{ee}, –NR^{ff}CO₂R^{ee}, –NR^{ff}C(=O)N(R^{ff})₂, –C(=NR^{ff})OR^{ee}, –OC(=NR^{ff})R^{ee}, –OC(=NR^{ff})OR^{ee}, –C(=NR^{ff})N(R^{ff})₂, –OC(=NR^{ff})N(R^{ff})₂, –NR^{ff}C(=NR^{ff})N(R^{ff})₂, –NR^{ff}SO₂R^{ee}, –SO₂N(R^{ff})₂, –SO₂R^{ee}, –SO₂OR^{ee}, –OSO₂R^{ee}, –S(=O)R^{ee}, –Si(R^{ee})₃, –OSi(R^{ee})₃, –C(=S)N(R^{ff})₂, –C(=O)SR^{ee}, –C(=S)SR^{ee}, –SC(=S)SR^{ee}, –P(=O)₂R^{ee}, –P(=O)(R^{ee})₂, –OP(=O)(R^{ee})₂, –OP(=O)(OR^{ee})₂, C_{1–50} alkyl, C_{2–50} alkenyl, C_{2–50} alkynyl, C_{3–10} carbocyclyl, 3–10 membered heterocyclyl, C_{6–10} aryl, 5–10 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups, or two geminal R^{dd} substituents can be joined to form =O or =S;

each instance of R^{ee} is, independently, selected from C_{1–50} alkyl, C_{2–50} alkenyl, C_{2–50} alkynyl, C_{3–10} carbocyclyl, C_{6–10} aryl, 3–10 membered heterocyclyl, and 3–10 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups;

each instance of R^{ff} is, independently, selected from hydrogen, C_{1–50} alkyl, C_{2–50} alkenyl, C_{2–50} alkynyl, C_{3–10} carbocyclyl, 3–10 membered heterocyclyl, C_{6–10} aryl and 5–10 membered heteroaryl, or two R^{ff} groups are joined to form a 3–14 membered heterocyclyl or 5–14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{gg} groups; and

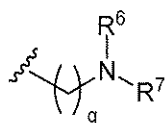
each instance of R^{gg} is, independently, halogen, –CN, –NO₂, –N₃, –SO₂H, –SO₃H, –OH, –OC_{1–50} alkyl, –ON(C_{1–50} alkyl)₂, –N(C_{1–50} alkyl)₂, –N(C_{1–50} alkyl)₃⁺X[–], –NH(C_{1–50} alkyl)₂⁺X[–], –NH₂(C_{1–50} alkyl)⁺X[–], –NH₃⁺X[–], –N(OC_{1–50} alkyl)(C_{1–50} alkyl), –N(OH)(C_{1–50} alkyl), –NH(OH), –SH, –SC_{1–50} alkyl, –SS(C_{1–50} alkyl), –C(=O)(C_{1–50} alkyl), –CO₂H, –CO₂(C_{1–50} alkyl), –OC(=O)(C_{1–50} alkyl), –OCO₂(C_{1–50} alkyl), –C(=O)NH₂, –C(=O)N(C_{1–50} alkyl)₂, –OC(=O)NH(C_{1–50} alkyl), –NHC(=O)(C_{1–50} alkyl), –N(C_{1–50} alkyl)C(=O)(C_{1–50} alkyl), –NHCO₂(C_{1–50} alkyl), –NHC(=O)N(C_{1–50} alkyl)₂, –NHC(=O)NH(C_{1–50} alkyl), –NHC(=O)NH₂, –C(=NH)O(C_{1–50} alkyl), –OC(=NH)(C_{1–50} alkyl), –OC(=NH)OC_{1–50} alkyl, –C(=NH)N(C_{1–50} alkyl)₂, –C(=NH)NH(C_{1–50} alkyl), –C(=NH)NH₂, –OC(=NH)N(C_{1–50}

alkyl)₂, -OC(NH)NH(C₁₋₅₀ alkyl), -OC(NH)NH₂, -NHC(NH)N(C₁₋₅₀ alkyl)₂, -NHC(=NH)NH₂, -NH₂SO₂(C₁₋₅₀ alkyl), -SO₂N(C₁₋₅₀ alkyl)₂, -SO₂NH(C₁₋₅₀ alkyl), -SO₂NH₂, -SO₂C₁₋₅₀ alkyl, -SO₂OC₁₋₅₀ alkyl, -OSO₂C₁₋₆ alkyl, -SOC₁₋₆ alkyl, -Si(C₁₋₅₀ alkyl)₃, -OSi(C₁₋₆ alkyl)₃ -C(=S)N(C₁₋₅₀ alkyl)₂, C(=S)NH(C₁₋₅₀ alkyl), C(=S)NH₂, -C(=O)S(C₁₋₆ alkyl), -C(=S)SC₁₋₆ alkyl, -SC(=S)SC₁₋₆ alkyl, -P(=O)₂(C₁₋₅₀ alkyl), -P(=O)(C₁₋₅₀ alkyl)₂, -OP(=O)(C₁₋₅₀ alkyl)₂, -OP(=O)(OC₁₋₅₀ alkyl)₂, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, C₂₋₅₀ alkynyl, C₃₋₁₀ carbocyclyl, C₆₋₁₀ aryl, 3-10 membered heterocyclyl, 5-10 membered heteroaryl; or two geminal R^{gg} substituents can be joined to form =O or =S;

X⁻ is a counterion;

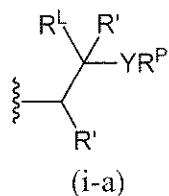
a nitrogen protecting group is -OH, -OR^{aa}, -N(R^{cc})₂, -C(=O)R^{aa}, -C(=O)N(R^{cc})₂, -CO₂R^{aa}, -SO₂R^{aa}, -C(=NR^{cc})R^{aa}, -C(=NR^{cc})OR^{aa}, -C(=NR^{cc})N(R^{cc})₂, -SO₂N(R^{cc})₂, -SO₂R^{cc}, -SO₂OR^{cc}, -SOR^{aa}, -C(=S)N(R^{cc})₂, -C(=O)SR^{cc}, -C(=S)SR^{cc}, C₁₋₁₀ alkyl, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl, C₃₋₁₀ carbocyclyl, 3-14 membered heterocyclyl, C₆₋₁₄ aryl, and 5-14 membered heteroaryl groups, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aralkyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; and an oxygen protecting group is -R^{aa}, -N(R^{bb})₂, -C(=O)SR^{aa}, -C(=O)R^{aa}, -CO₂R^{aa}, -C(=O)N(R^{bb})₂, -C(=NR^{bb})R^{aa}, -C(=NR^{bb})OR^{aa}, -C(=NR^{bb})N(R^{bb})₂, -S(=O)R^{aa}, -SO₂R^{aa}, -Si(R^{aa})₃, -P(R^{cc})₂, -P(R^{cc})₃, -P(=O)₂R^{aa}, -P(=O)(R^{aa})₂, -P(=O)(OR^{cc})₂, -P(=O)₂N(R^{bb})₂, and -P(=O)(NR^{bb})₂.

3. The compound of claim 1 or 2, or salt thereof, wherein at least one instance of R² is hydrogen.
4. The compound of claim 1 or 3, or salt thereof, wherein each R¹ is a group of formula (iv).
5. The compound of any one of claims 1 and 3-4, or salt thereof, wherein L is an optionally substituted alkylene.
6. The compound of any one of claims 1 and 3-5, or salt thereof, wherein the group of formula (iv) is of formula:

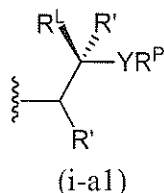


wherein q is an integer between 1 and 50, inclusive.

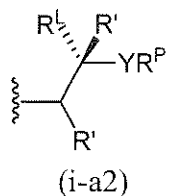
7. The compound of any one of claims 1-6, or salt thereof, wherein the group of formula (i) is a group of formula (i-a):



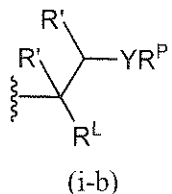
8. The compound of claim 7, or salt thereof, wherein the group of formula (i-a) is a group of formula (i-a1):



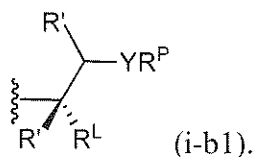
9. The compound of claim 7, or salt thereof, wherein the group of formula (i-a) is a group of formula (i-a2):



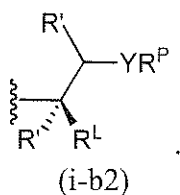
10. The compound of any one of claims 1-6, or salt thereof, wherein the group of formula (i) is a group of formula (i-b):



11. The compound of claim 10, or salt thereof, wherein the group of formula (i-b) is a group of formula (i-b1):



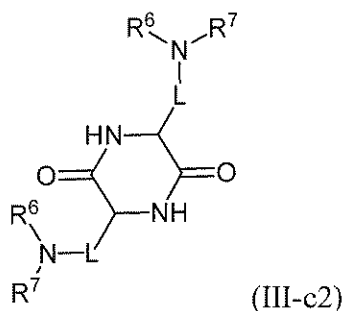
12. The compound of claim 10, or salt thereof, wherein the group of formula (i-b) is a group of formula (i-b2):



13. The compound of any one of claims 1-12, or salt thereof, wherein R^L is optionally substituted C_{6-20} alkyl.

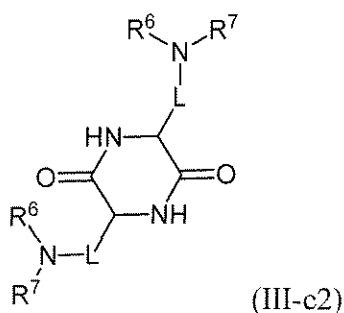
14. The compound of claim 13, or salt thereof, wherein R^L is unsubstituted C_{6-20} alkyl.

15. The compound of any one of claims 1-14, wherein the compound is of formula:



wherein R^6 is a group of formula (i) and R^7 is a group of formula (i).

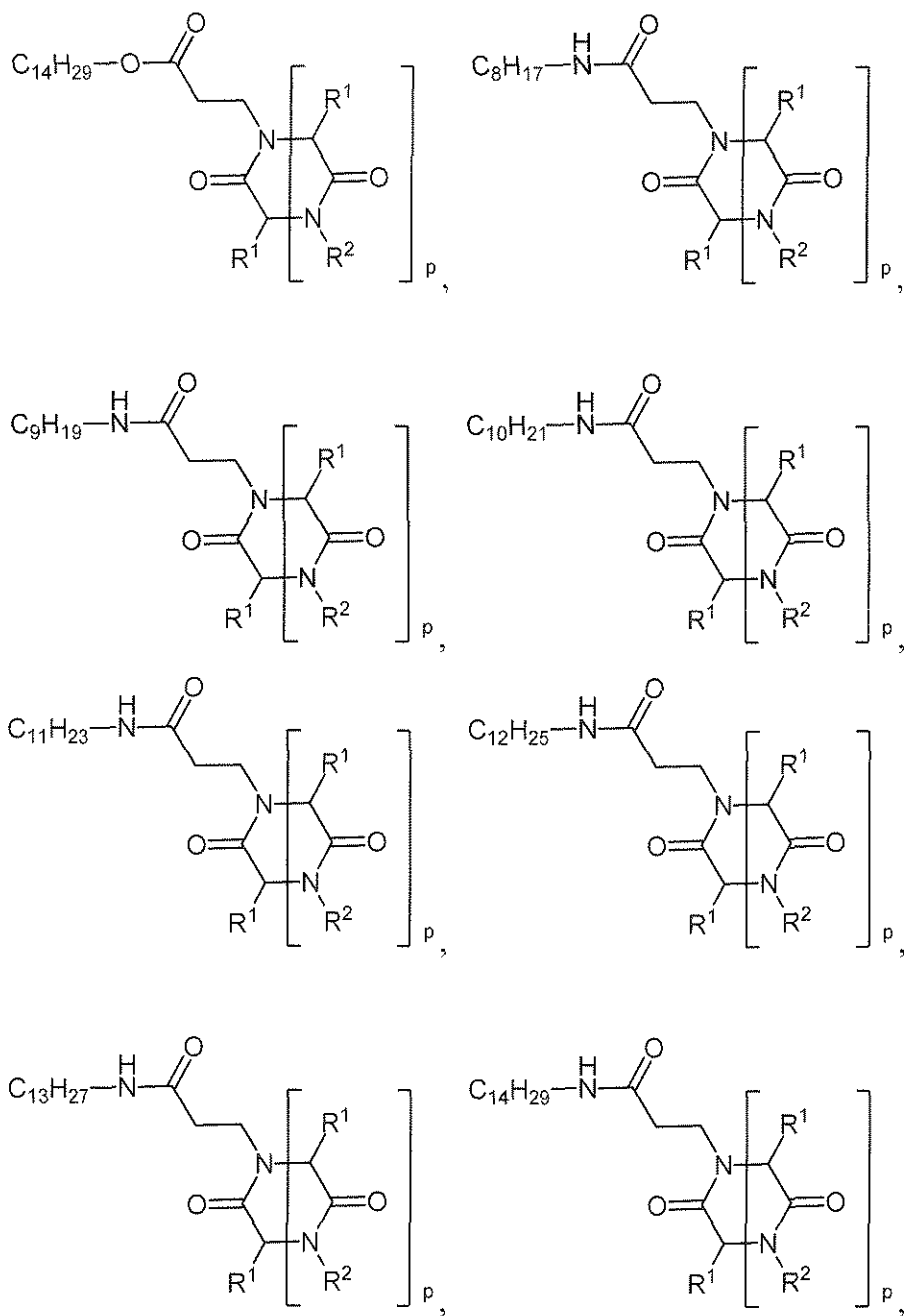
16. The compound of any one of claims 1-15, wherein the compound is of formula:



wherein R^6 is a group of formula (ii) and R^7 is a group of formula (ii).

17. The compound of claim 1, wherein the compound is selected from the group consisting of:



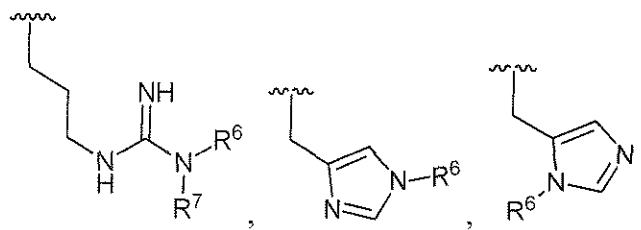


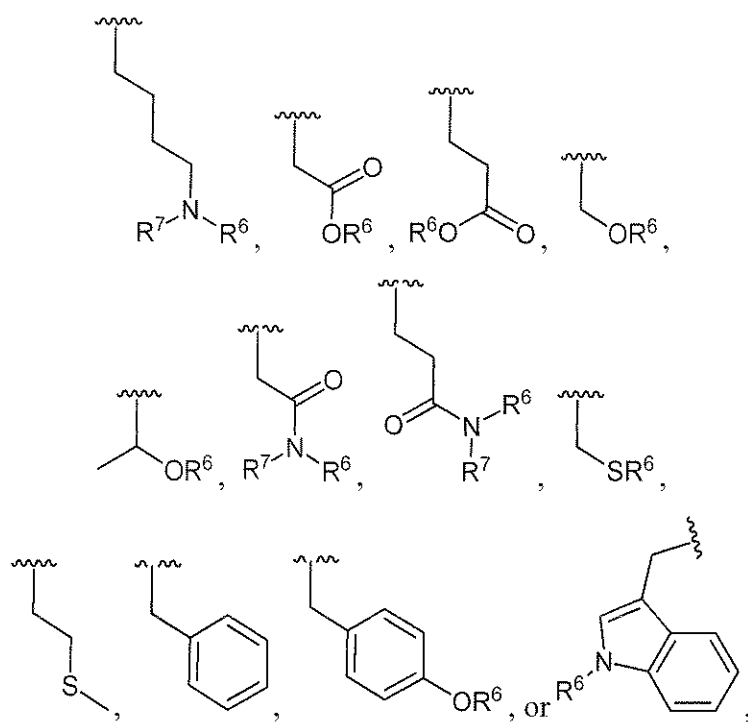
and salts thereof,

wherein:

p is 1; and

R¹ is -H, -CH₃, -CH(CH₃)₂, -CH(CH₃)(CH₂CH₃), -CH₂CH(CH₃)₂,





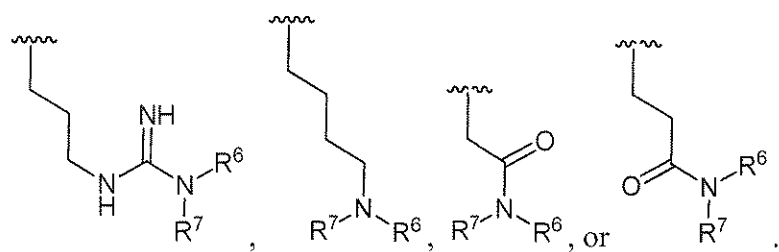
wherein:

R^6 and R^7 are each independently hydrogen, or a group of formula (i) or (ii);

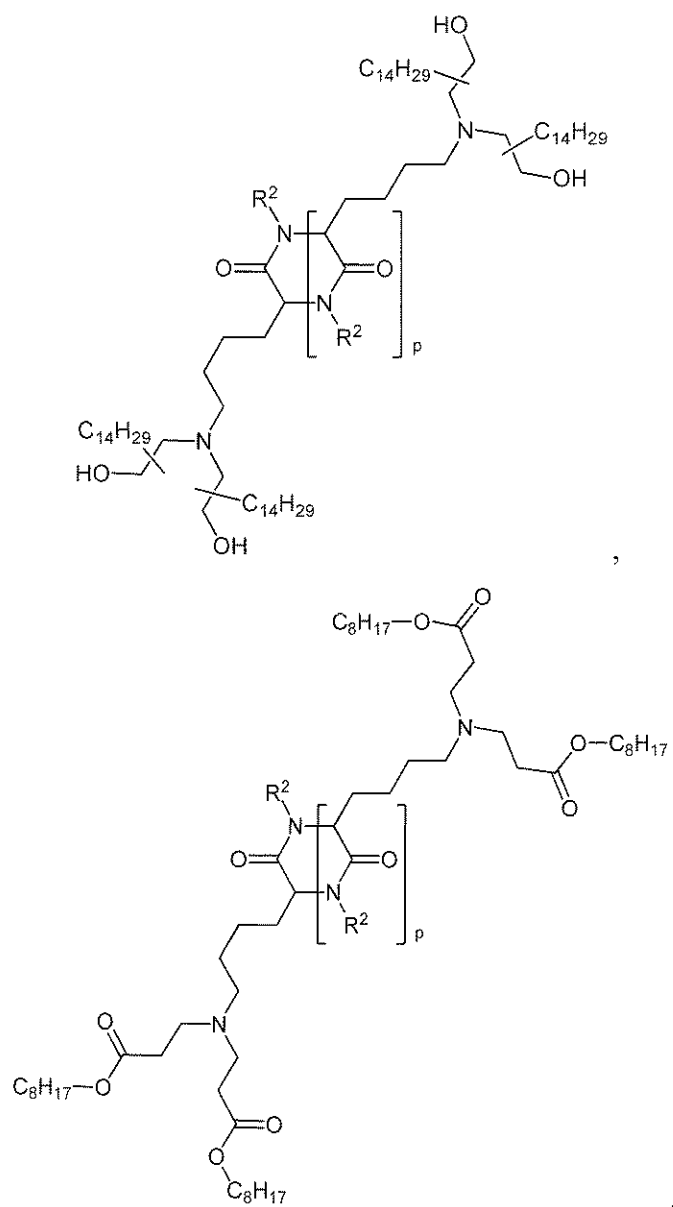
provided that at least one instance of R^6 and R^7 is a group of the formula (i) or (ii);

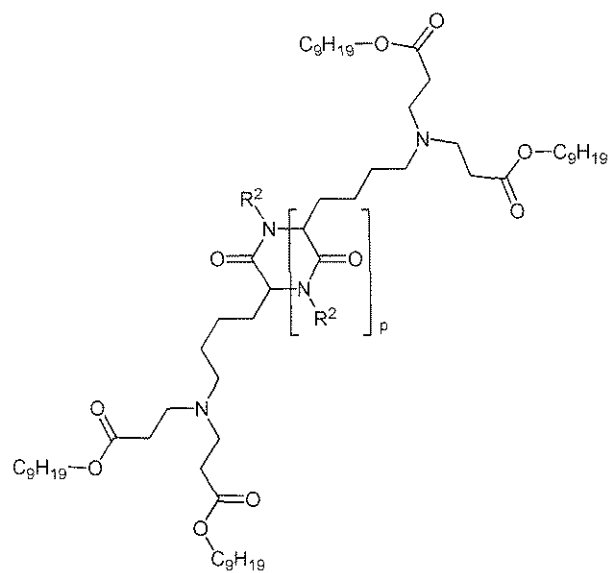
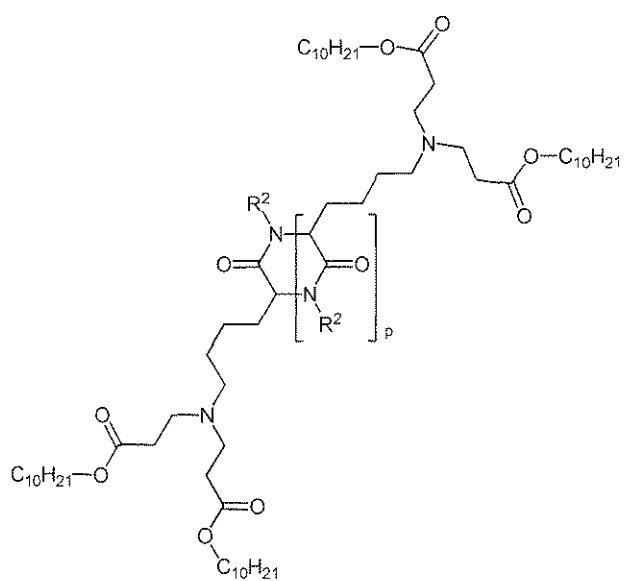
and

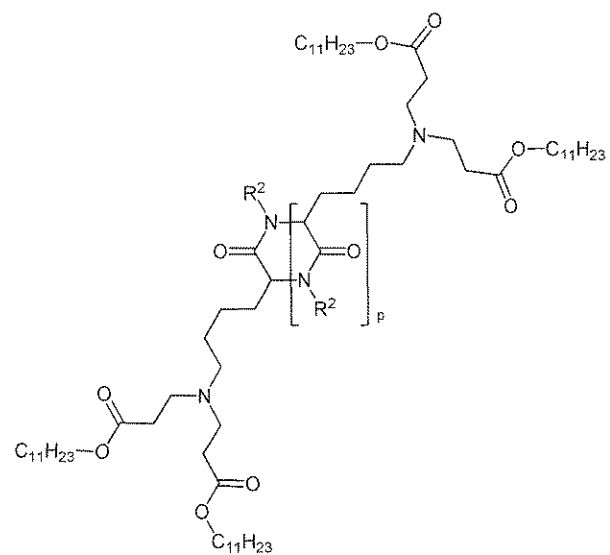
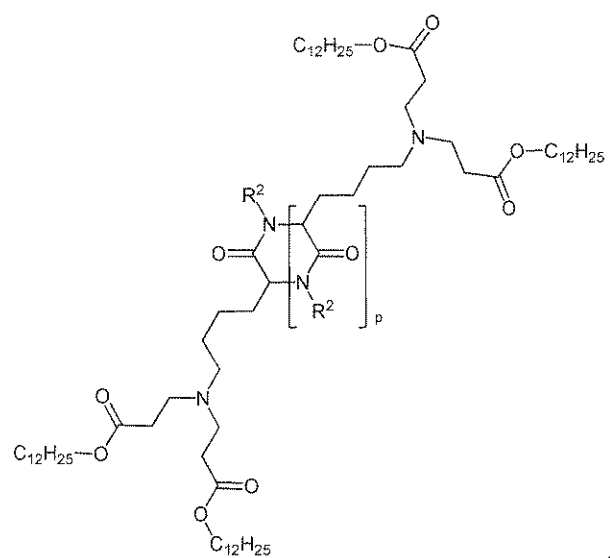
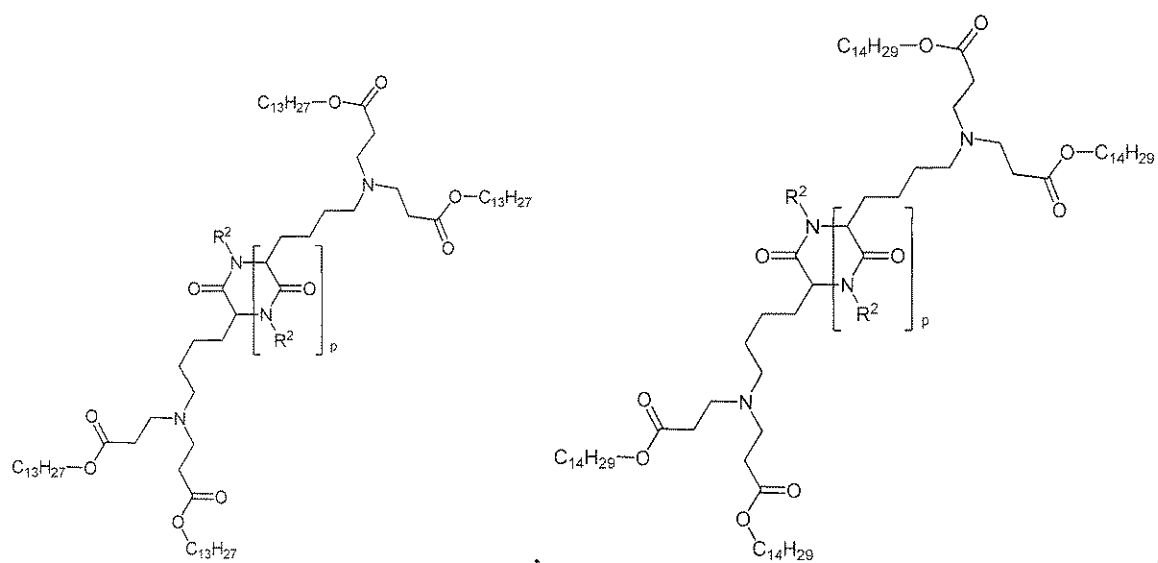
provided at least one R^1 is a group of formula:



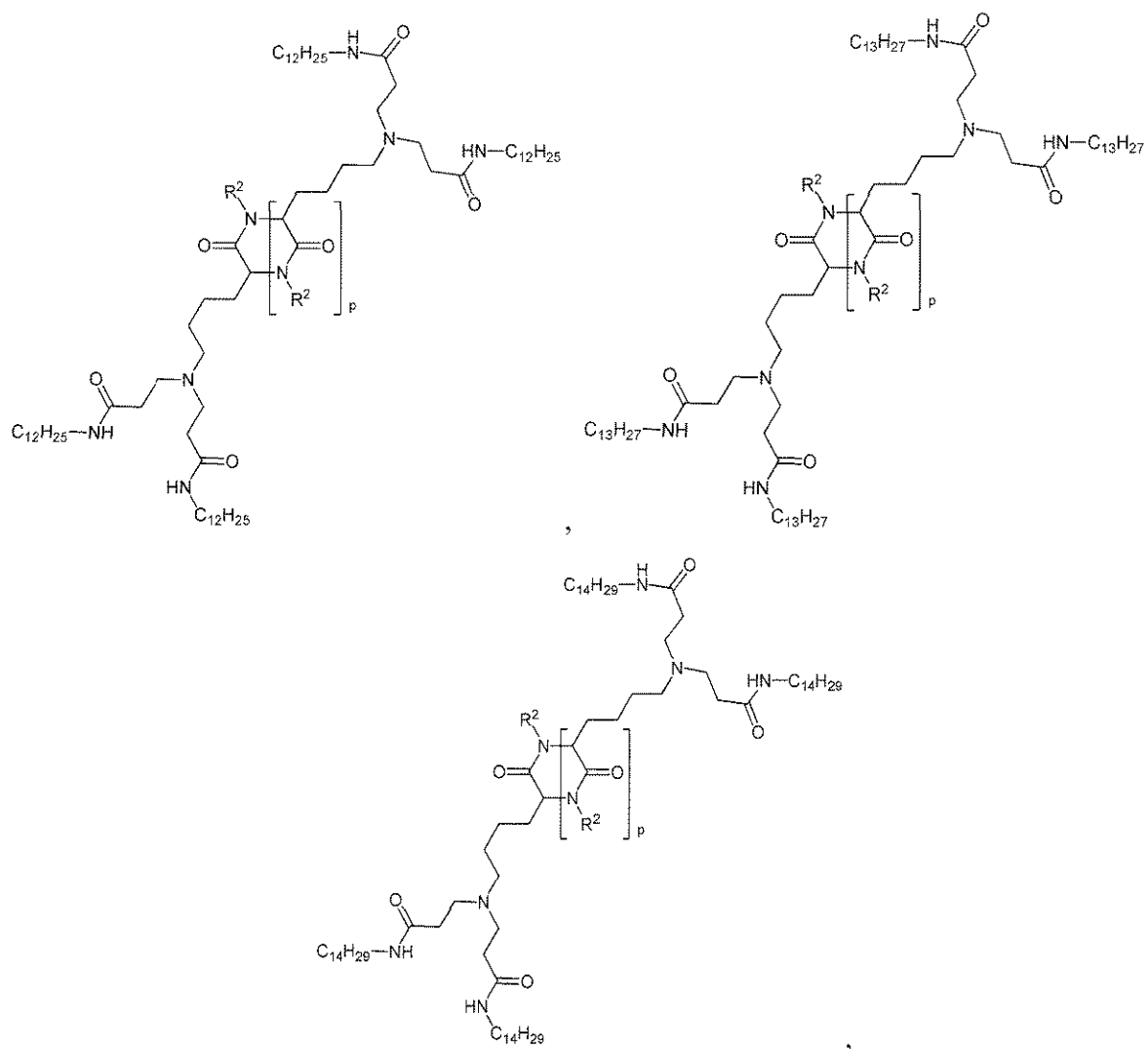
18. The compound of claim 1, wherein the compound is selected from the group consisting of:





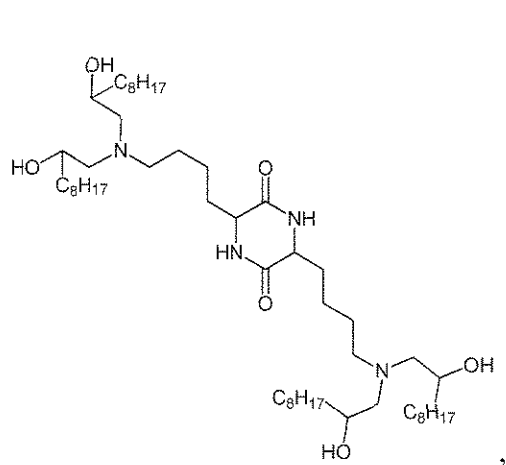
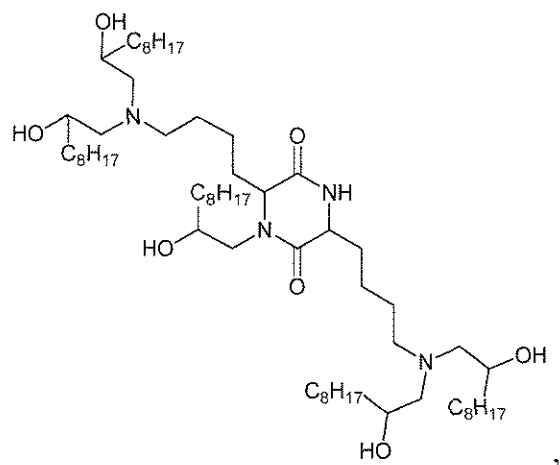
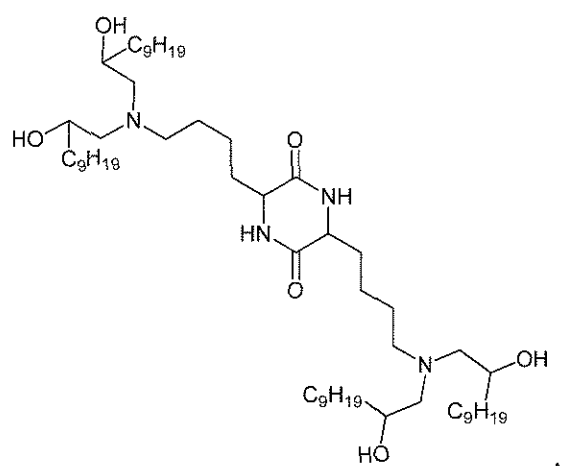
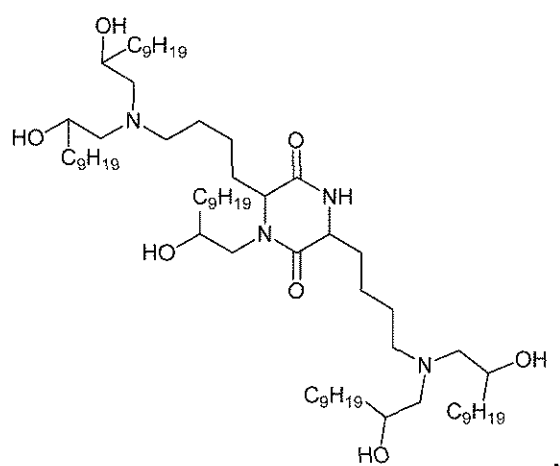
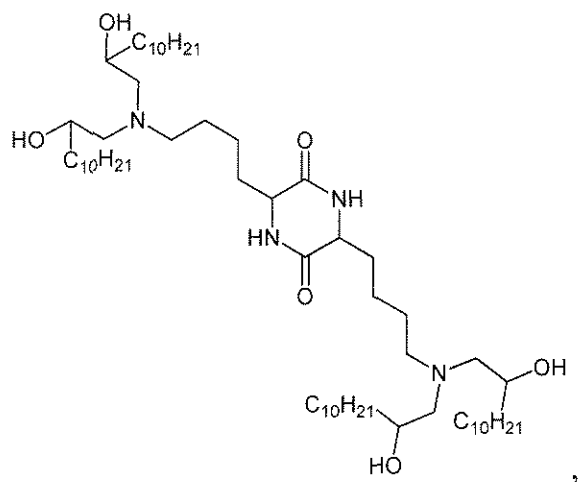
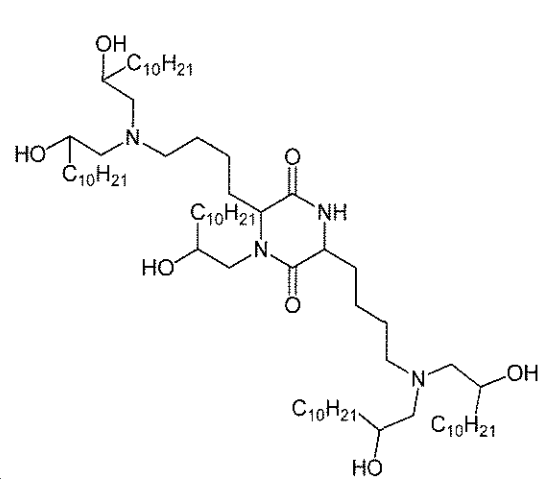


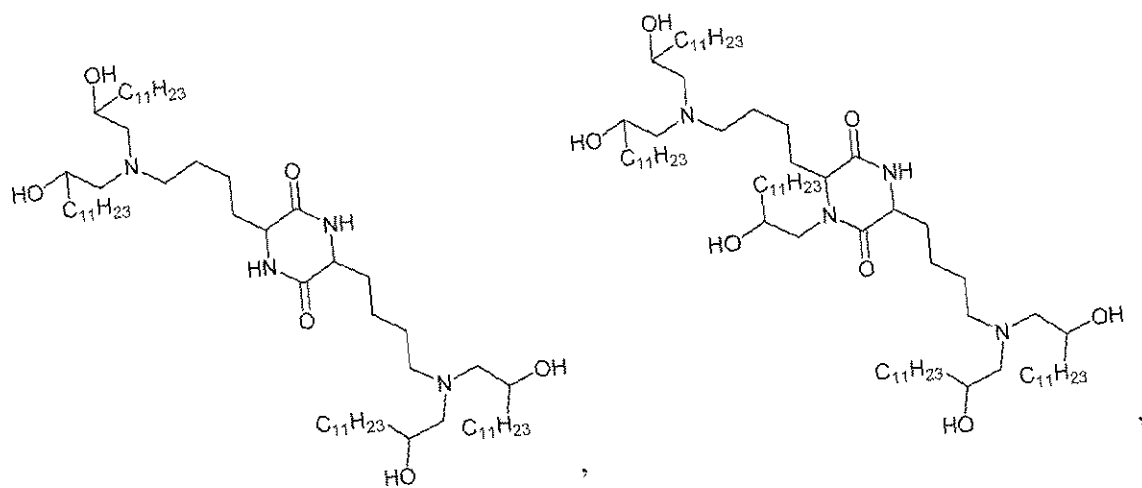
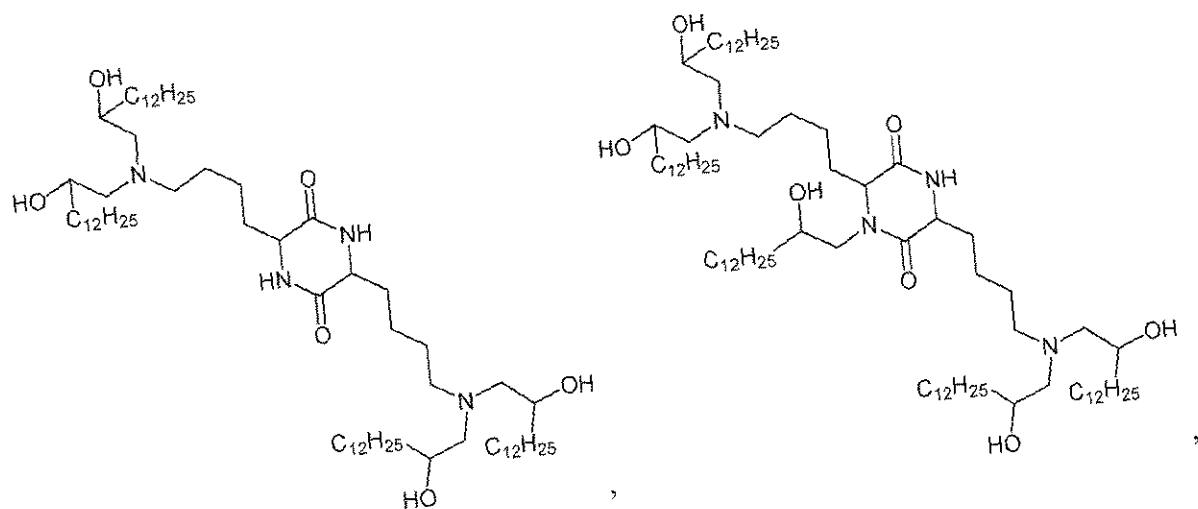
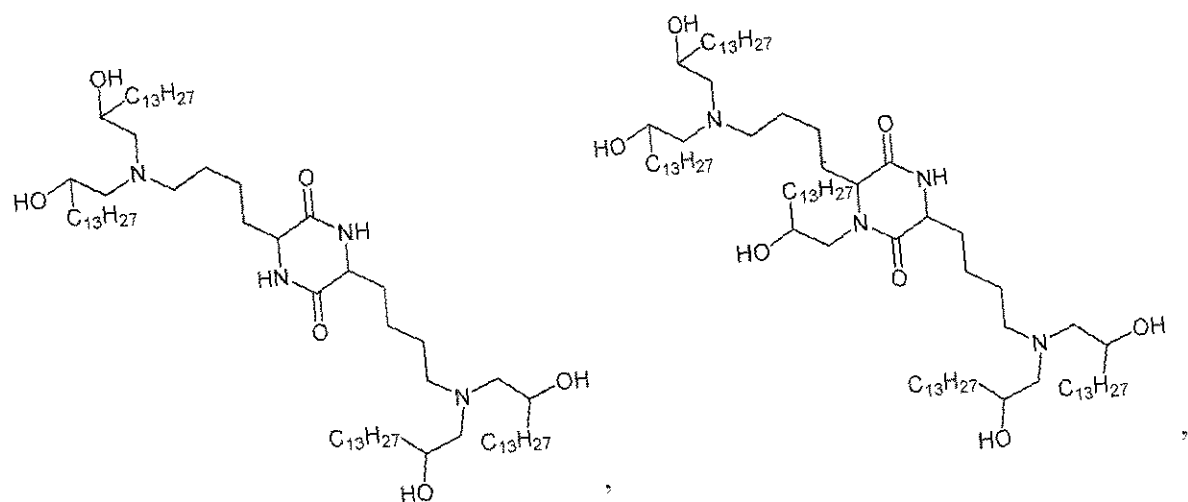


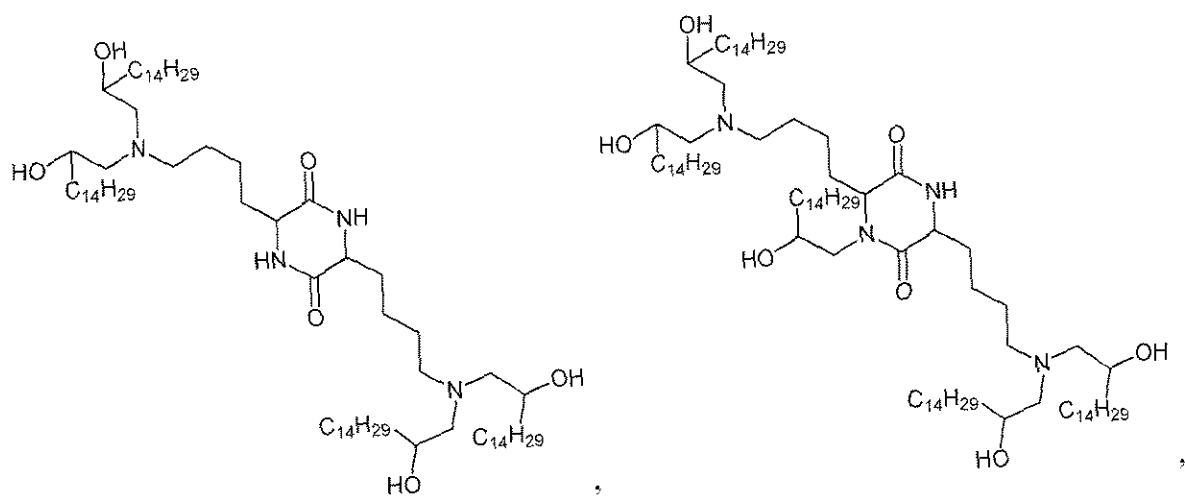
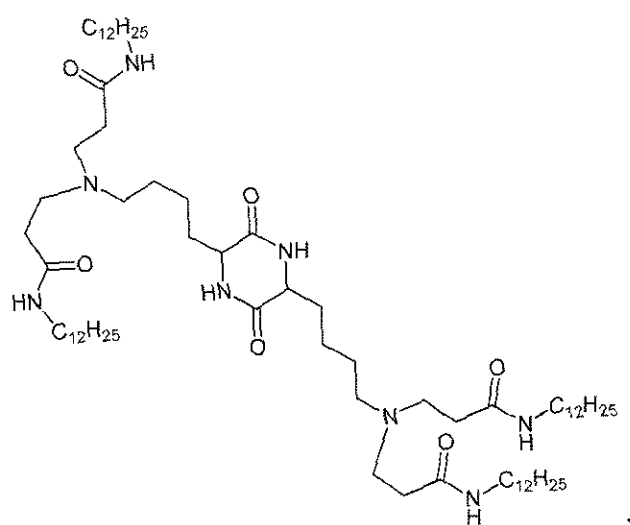
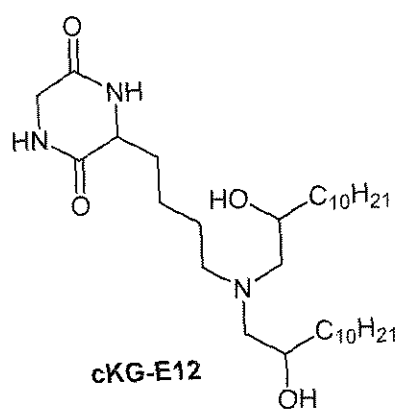
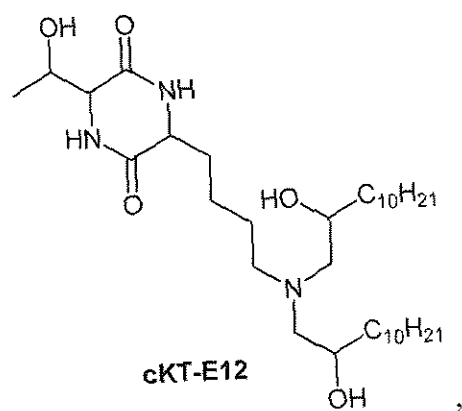


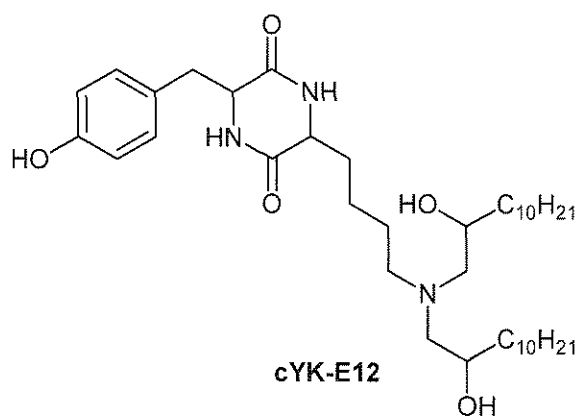
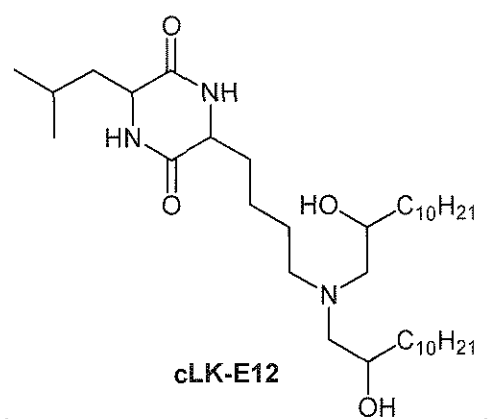
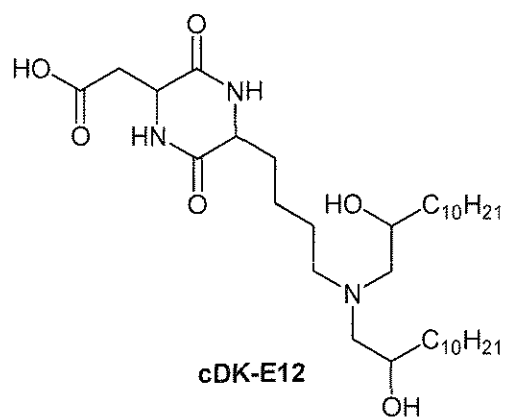
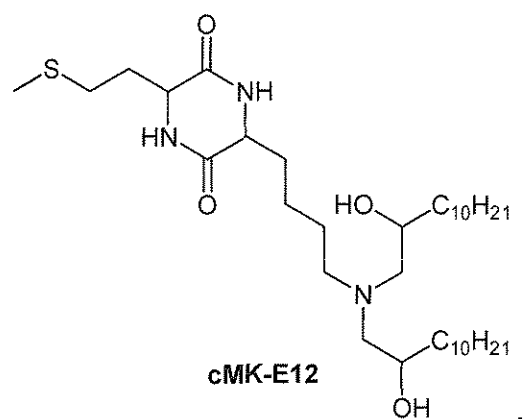
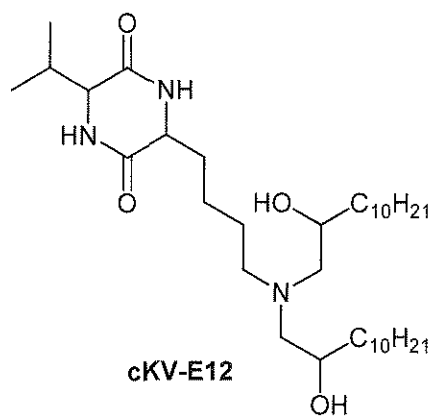
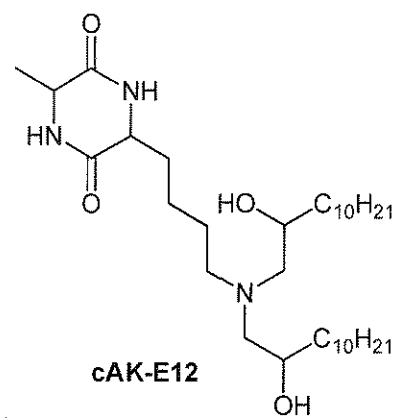
and salts thereof, wherein p is 1.

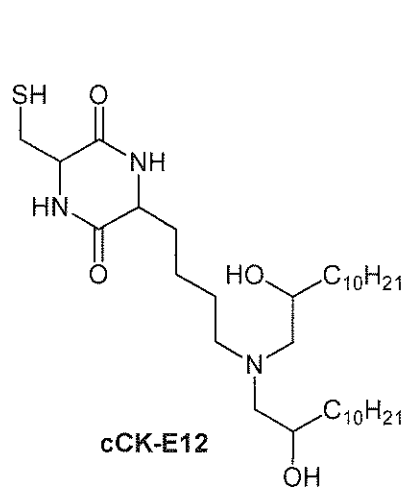
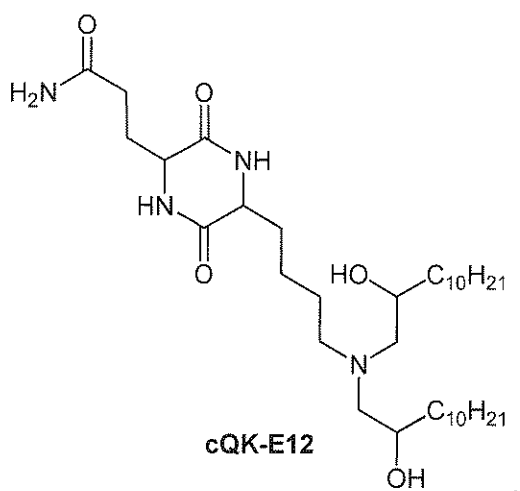
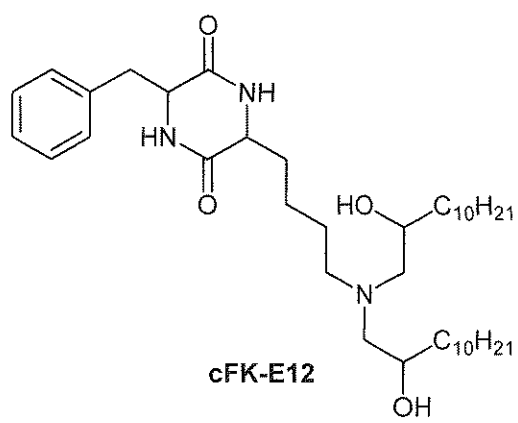
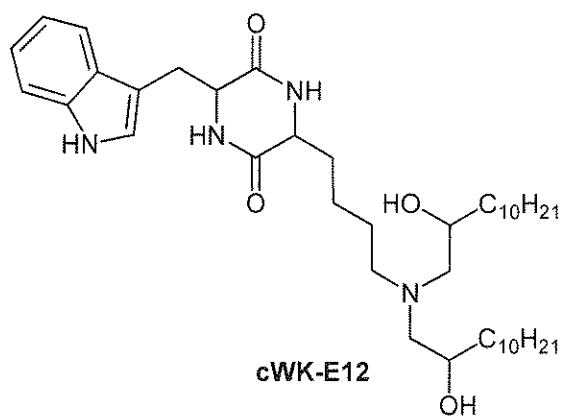
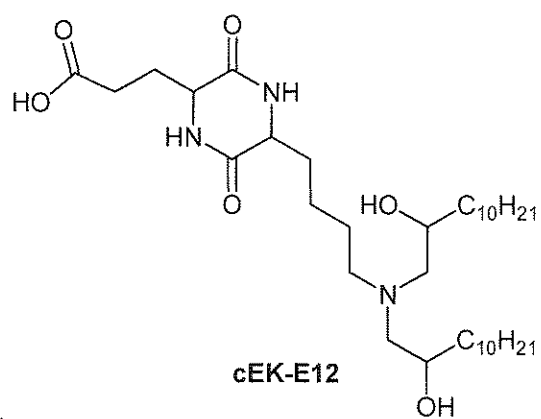
19. The compound of claim 1, wherein the compound is selected from the group consisting of:

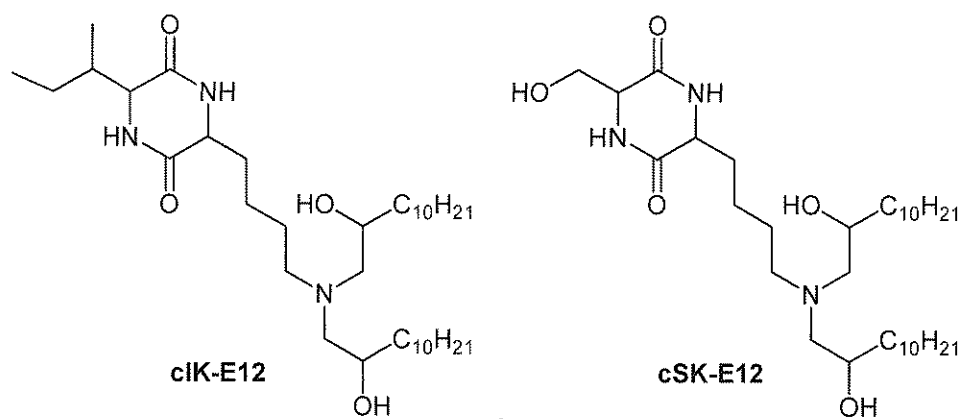






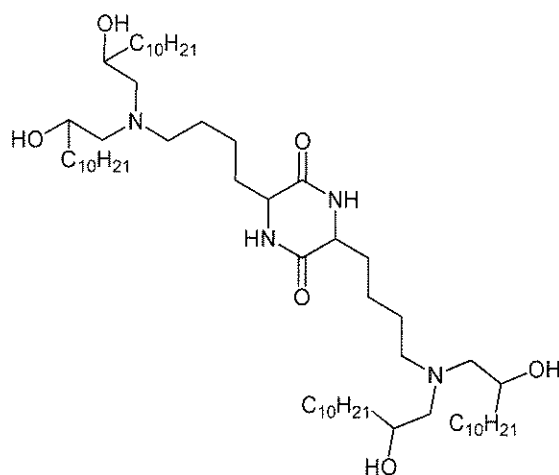






and salts thereof.

20. The compound of claim 19, wherein the compound is:



or salt thereof.

21. A composition comprising a compound of any one of claims 1-20, or salt thereof, and an excipient.

22. The composition of claim 21, wherein the composition is a pharmaceutical composition, a cosmetic composition, a nutraceutical composition, or a composition with non-medical application.

23. The composition of claim 22, wherein the composition with non-medical application is an emulsion or emulsifier useful as a food component, for extinguishing fires, for disinfecting surfaces, or for oil cleanup.

24. The composition of claim 22, wherein the composition is a pharmaceutical composition.

25. The composition of any one of claims 21-24, wherein the composition further comprises cholesterol.

26. The composition of any one of claims 21-25, wherein the composition further comprises a PEGylated lipid.

27. The composition of any one of claims 21-26, wherein the composition further comprises a phospholipid

28. The composition of any one of claims 21-27, wherein the composition further comprises an apolipoprotein.

29. The composition of any one of claims 21-28, wherein the composition further comprises an agent.

30. The composition of claim 29, wherein the agent is an organic molecule, inorganic molecule, nucleic acid, protein, peptide, polynucleotide, targeting agent, an isotopically labeled chemical compound, vaccine, an immunological agent, or an agent useful in bioprocessing;
wherein:

a targeting agent is an agent that targets a particular cell, and is selected from the group consisting of glycoproteins, lipids, antibodies, fragments of antibodies, low-density lipoproteins, transferrin, gp120 envelope protein of the human immunodeficiency virus, carbohydrates, receptor ligands, sialic acid, and aptamers;

an immunological agent is an agent useful in the treatment of cancer and/or autoimmune disorders; and

an agent useful in bioprocessing is an agent useful in maintaining a cell's health and/or growth, and/or in the cell's bioprocessing of a commercially useful chemical or fuel.

31. The composition of claim 30, wherein the agent is a polynucleotide, and the polynucleotide is DNA.

32. The composition of claim 30, wherein the agent is a polynucleotide, and the polynucleotide is RNA.
33. The composition of claim 32, wherein the RNA is RNAi, dsRNA, siRNA, shRNA, miRNA, or antisense RNA.
34. The composition of claim 30, wherein the agent is a polynucleotide, and the polynucleotide encodes a protein or peptide.
35. The composition of claim 29, wherein the agent and the compound, or salt thereof, are not covalently attached.
36. The composition of any one of claims 21-35, wherein the composition is in the form of a particle.
37. The composition of claim 36, wherein the particle is a nanoparticle or microparticle.
38. The composition of claim 36, wherein the particle is a micelle, liposome, or lipoplex.
39. The composition of claim 36, wherein the particle encapsulates an agent.
40. A method of screening a compound library, the method comprising:
providing a plurality of different compounds of any one of claims 1-20, or salts thereof; and
performing at least one assay with the compound library to determine the presence or absence of a desired property.
41. The method of claim 40, wherein the desired property is solubility in water, solubility at different pH, ability to bind polynucleotides, ability to bind heparin, ability to bind small molecules, ability to bind protein, ability to form microparticles, ability to increase transfection efficiency, ability to support cell growth, ability to support cell attachment, ability to support tissue growth, and/or intracellular delivery of the compound, or salt thereof, and/or an agent complexed or attached thereto to aid in bioprocessing;

wherein the agent used to aid in bioprocessing is an agent useful in maintaining a cell's health and/or growth, and/or in the cell's bioprocessing of a commercially useful chemical or fuel.

42. Use of a composition of any one of claims 21-39 in the manufacture of a medicament for treating a disease, disorder, or condition from which a subject suffers, wherein the disease, disorder, or condition is selected from the group consisting of proliferative disorders, inflammatory disorders, autoimmune disorders, painful conditions, liver diseases, and familial amyloid neuropathies.

43. An *in vitro* method of delivering a polynucleotide to a biological cell, comprising:
providing a composition of any one of claims 21-39 and a polynucleotide; and
exposing the composition to the biological cell under conditions sufficient to facilitate delivery of the polynucleotide into the interior of the biological cell.

44. The method of claim 43, wherein the polynucleotide is DNA.

45. The method of claim 43, wherein the polynucleotide is RNA.

46. The method of claim 45, wherein the RNA is RNAi, dsRNA, siRNA, shRNA, miRNA, or antisense RNA.

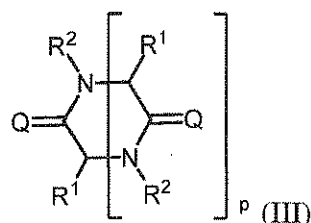
47. The method of claim 43, wherein the polynucleotide encodes a protein or peptide.

48. The method of claim 43, wherein upon delivery of the RNA into the cell, the RNA is able to interfere with the expression of a specific gene in the biological cell.

Claims

What is claimed is:

1. A compound of Formula (III):



or salt thereof;

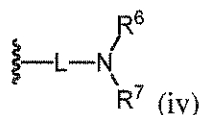
wherein:

p is an integer of between 1 and 9, inclusive;

each instance of Q is independently O, S, or NR^Q, wherein R^Q is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), (iii);

each instance of R¹ is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, halogen, -OR^{A1}, -N(R^{A1})₂, -SR^{A1}; wherein each occurrence of R^{A1} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an optionally substituted heterocyclic or optionally substituted heteroaryl ring;

or at least one instance of R¹ is a group of formula:



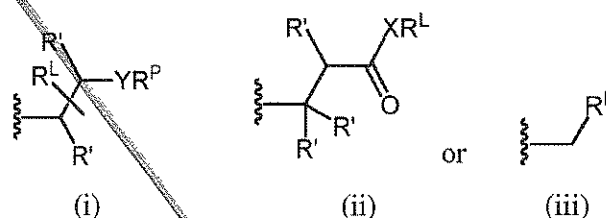
wherein L is an optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted heteroalkylene, optionally substituted heteroalkenylene, optionally substituted heteroalkynylene, optionally substituted

carbocyclylene, optionally substituted heterocyclylene, optionally substituted arylene, or optionally substituted heteroarylene, and

R^6 and R^7 are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group;

each instance of R^2 is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii); and

Formulae (i), (ii), and (iii) are:



wherein:

each instance of R^1 is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

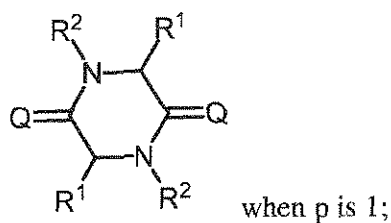
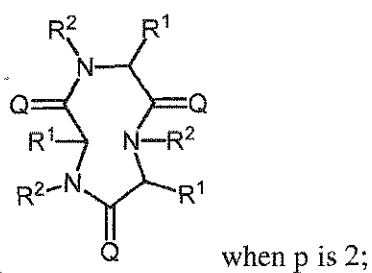
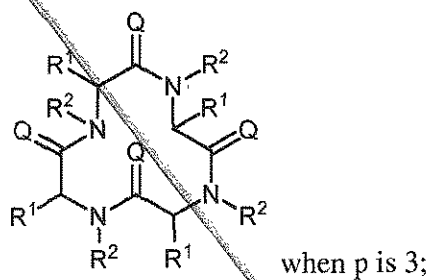
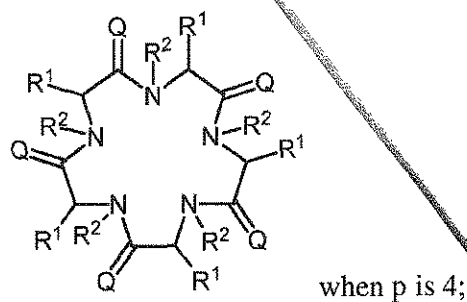
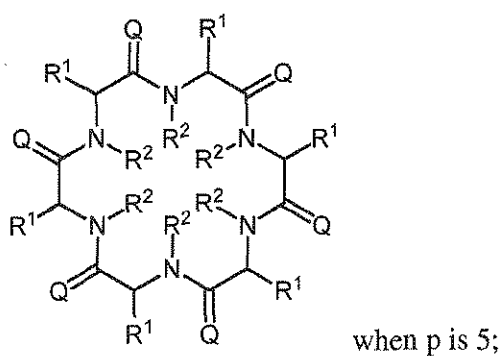
Y is O, S, NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

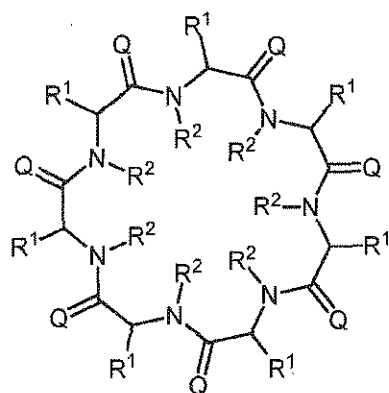
R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C_{1-50} alkyl, optionally substituted C_{2-50} alkenyl, optionally substituted C_{2-50} alkynyl, optionally substituted hetero C_{1-50} alkyl, optionally substituted hetero C_{2-50} alkenyl, optionally substituted hetero C_{2-50} alkynyl, or a polymer;

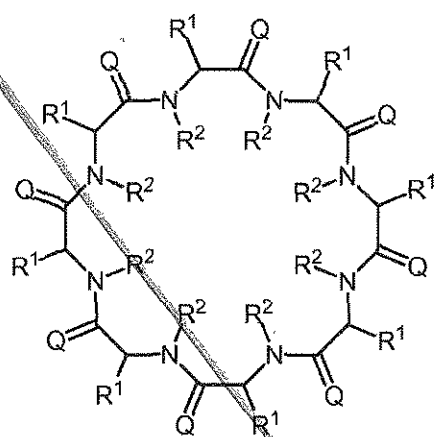
provided that at least one instance of R^Q , R^2 , R^6 , or R^7 is a group of the formula (i), (ii), or (iii).

2. The compound of claim 1, wherein the compound is of Formula:

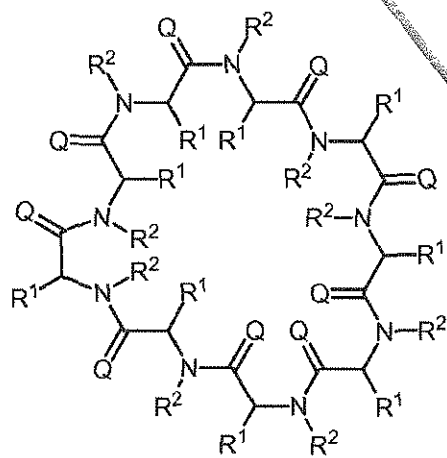




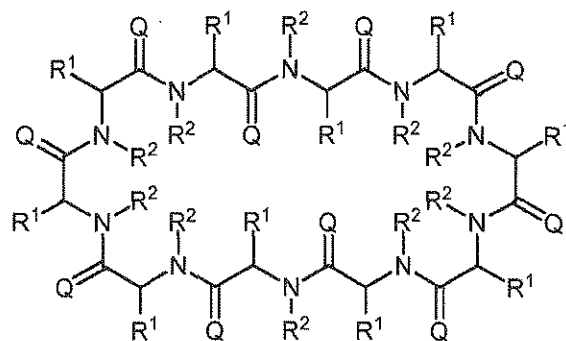
when p is 6;



when p is 7;



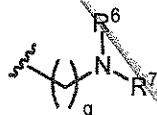
when p is 8; or



when p is 9,

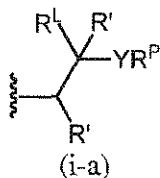
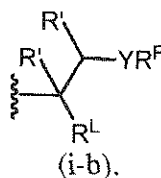
or a salt thereof.

3. The compound of claim 1, wherein each instance of Q is O.
4. The compound of claim 1, wherein at least one instance of R^2 is H.
5. The compound of claim 1, wherein R^1 is a group of formula (iv).
6. The compound of claim 1, wherein L is an optionally substituted alkylene.
7. The compound of claim 1, wherein the group of formula (iv) is of formula:

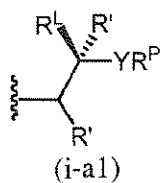
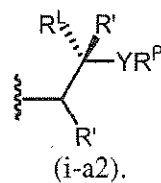


wherein q is an integer between 1 and 50, inclusive.

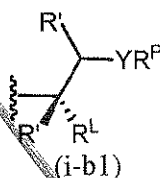
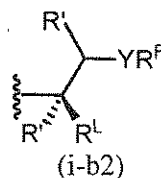
8. The compound of claim 1, wherein the group of formula (i) represents a group of formula (i-a) or a group of formula (i-b):



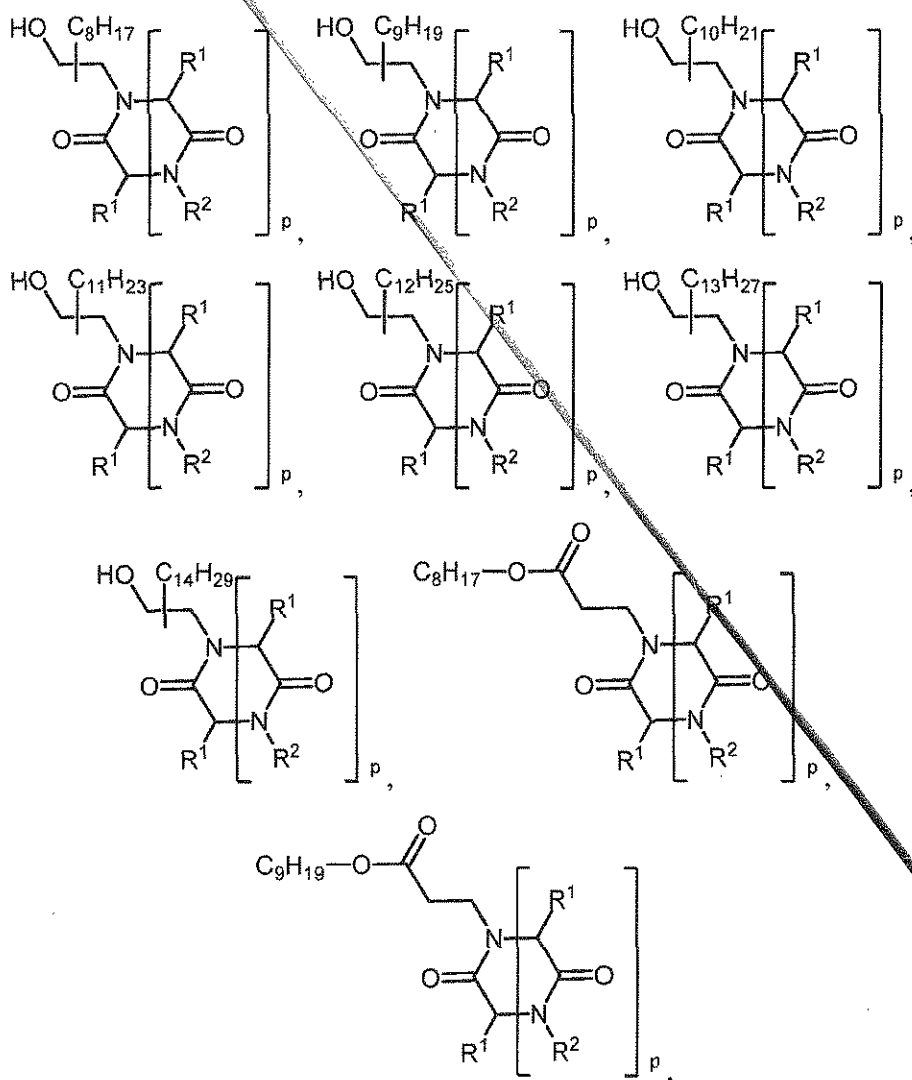
9. The compound of claim 8, wherein the group of formula (i-a) is a group of formula (i-a1) or a group of formula (i-a2):

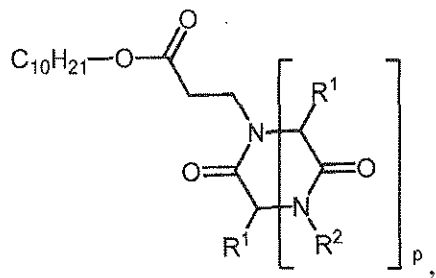
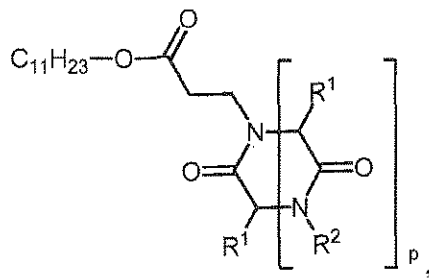
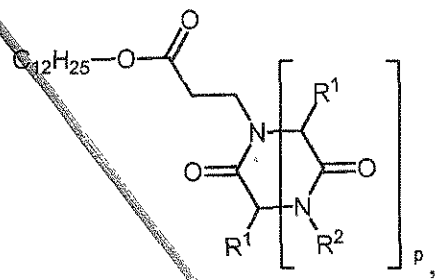
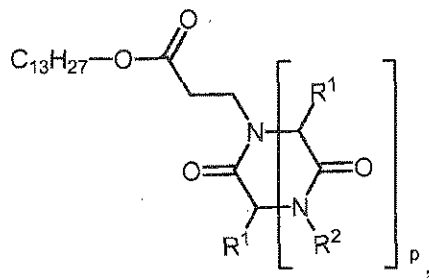
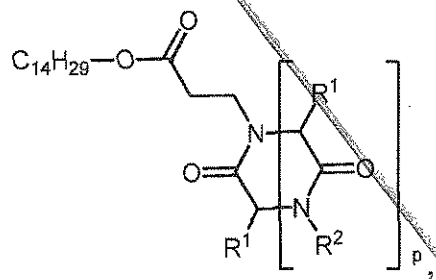
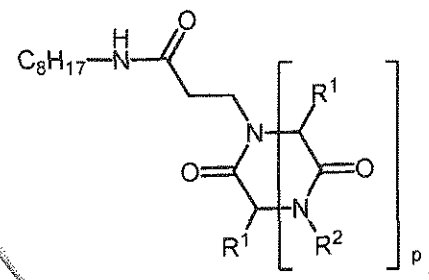
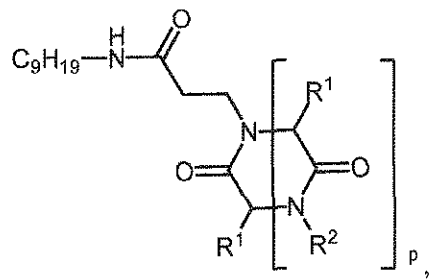
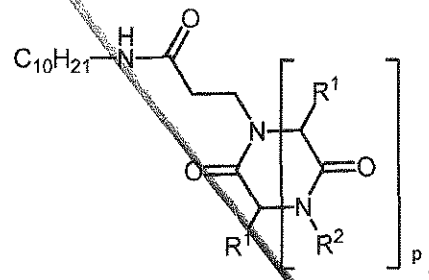
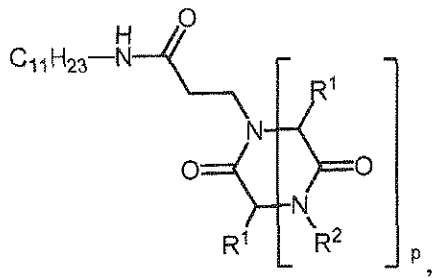
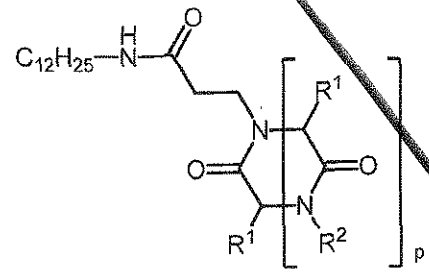


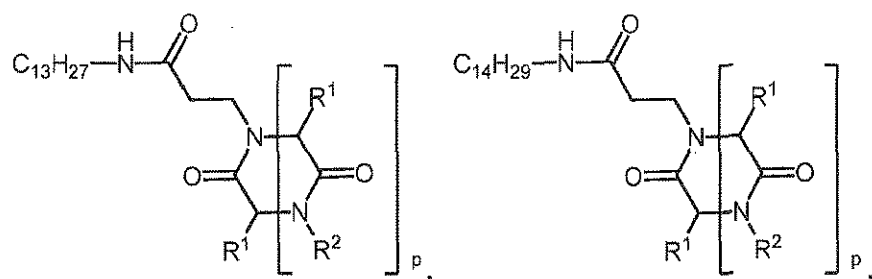
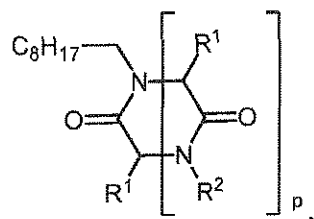
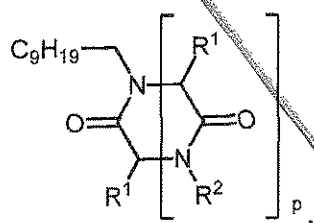
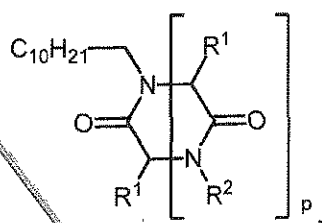
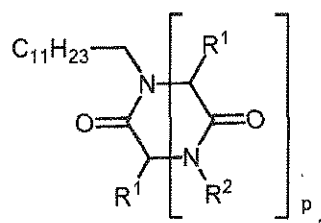
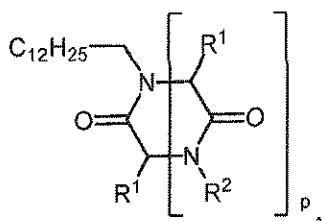
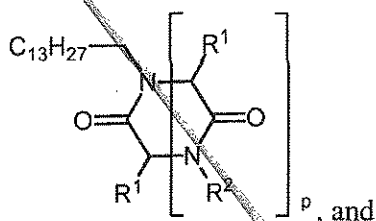
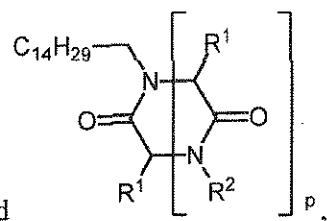
10. The compound of claim 8, wherein the group of formula (i-b) is a group of formula (i-b1) or a group of formula (i-b2):



11. The compound of claim 1, wherein the compound is selected from the group consisting of:



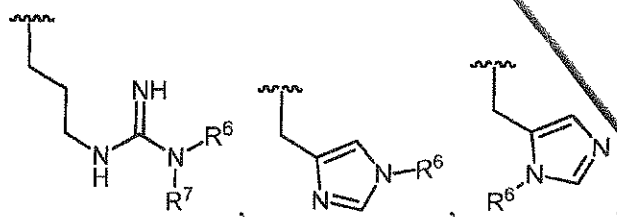
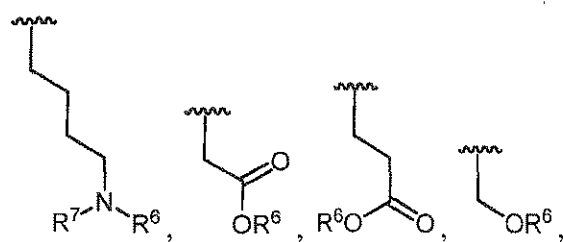


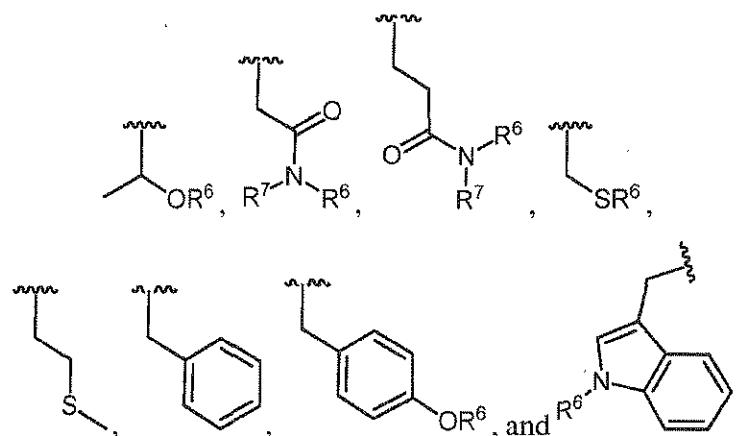


and salts thereof,

wherein R^1 is selected from the group consisting of:

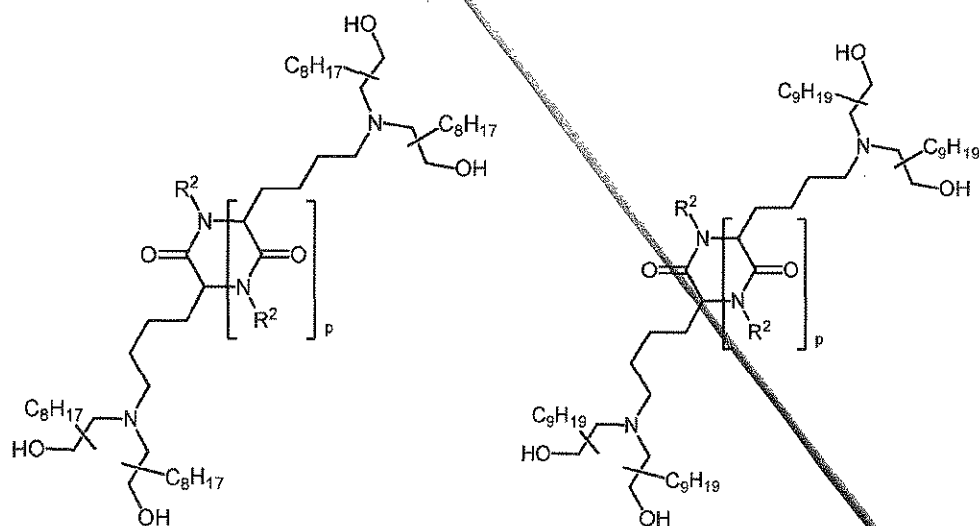
$-\text{H}$, $-\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$,

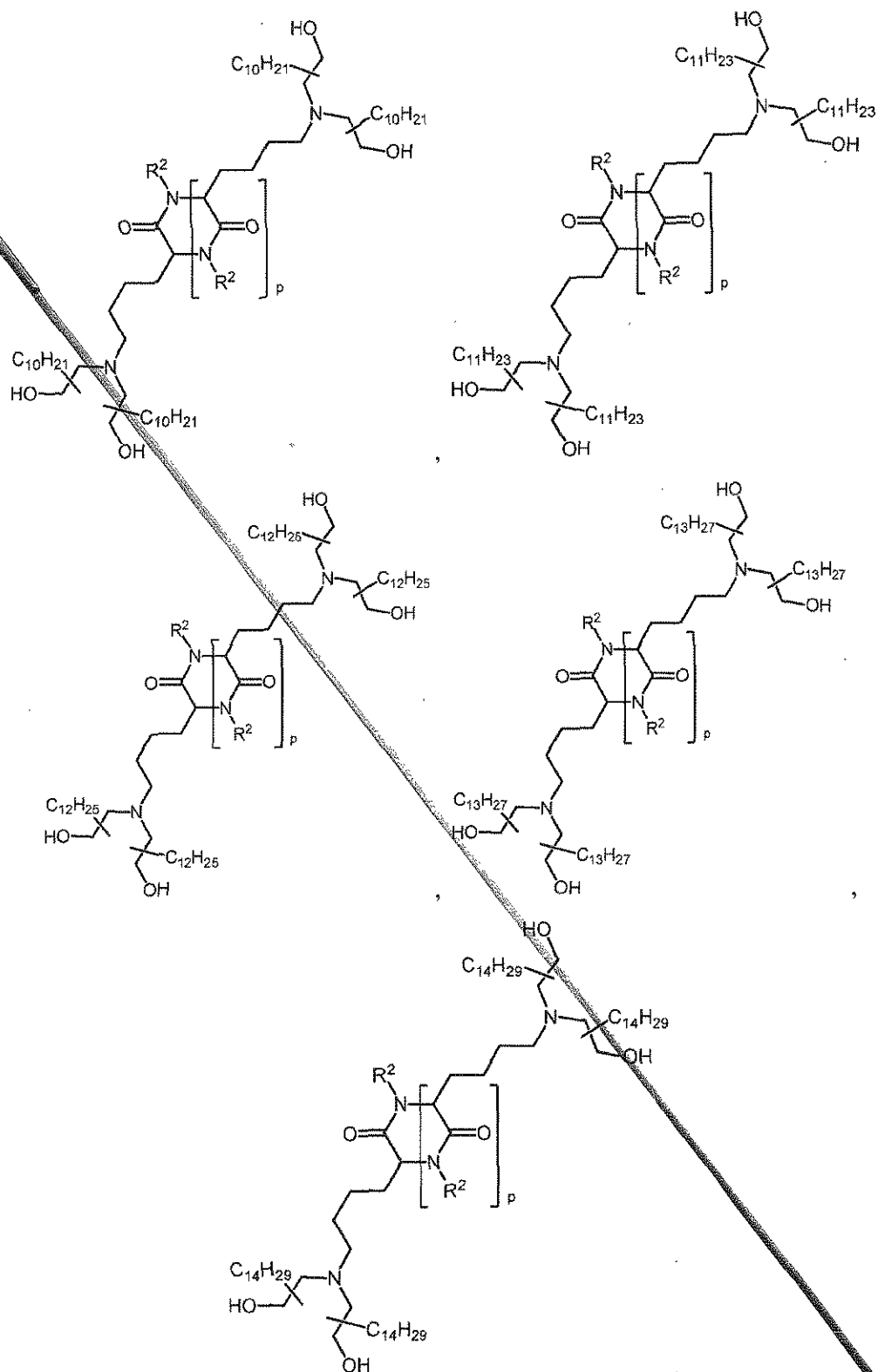


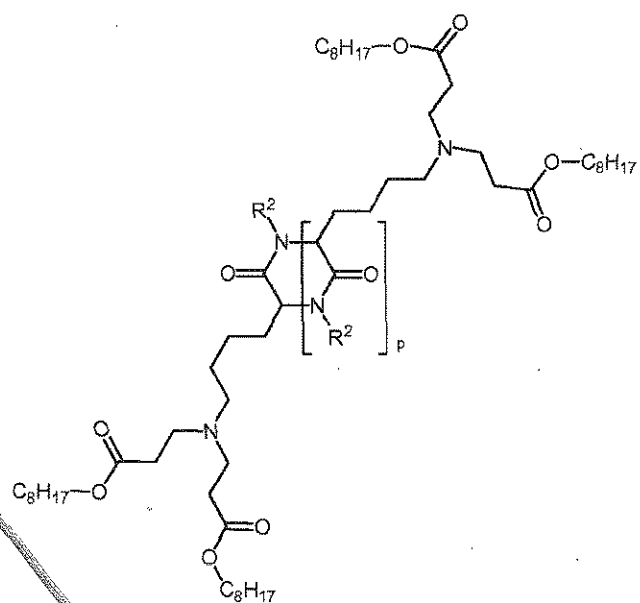
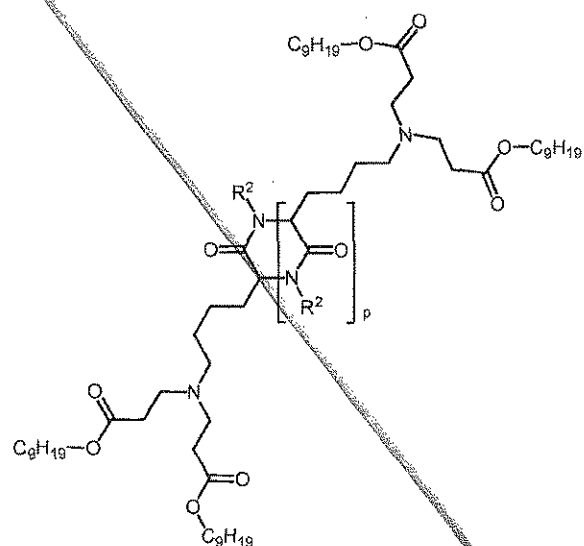
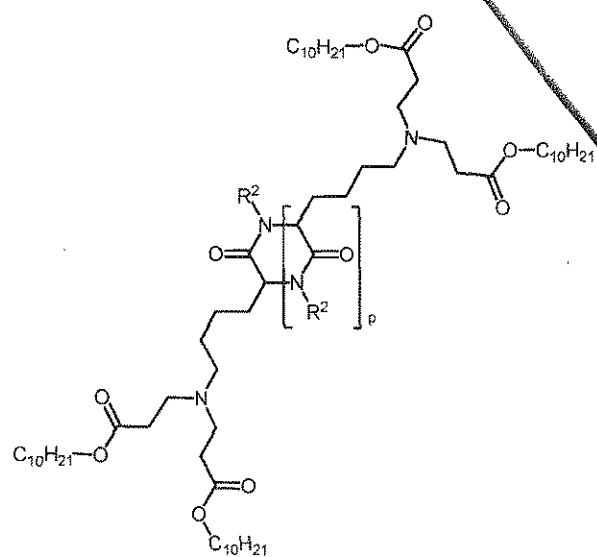


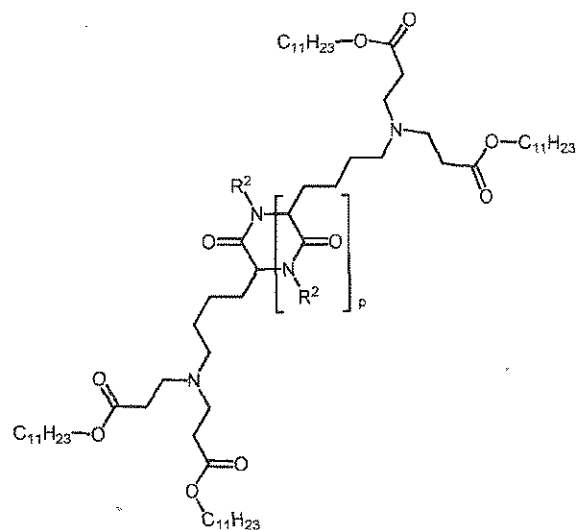
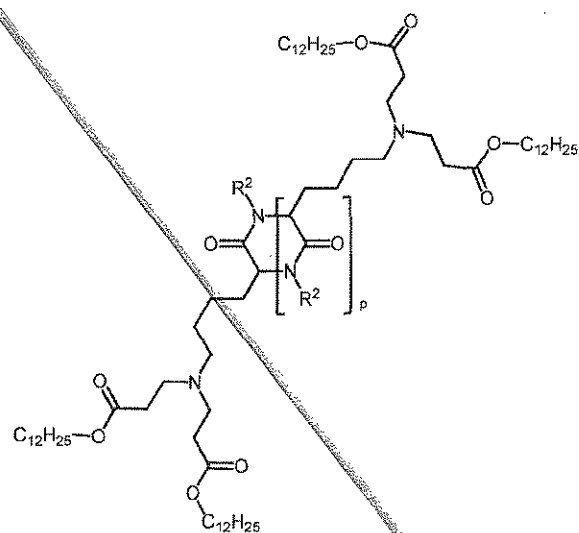
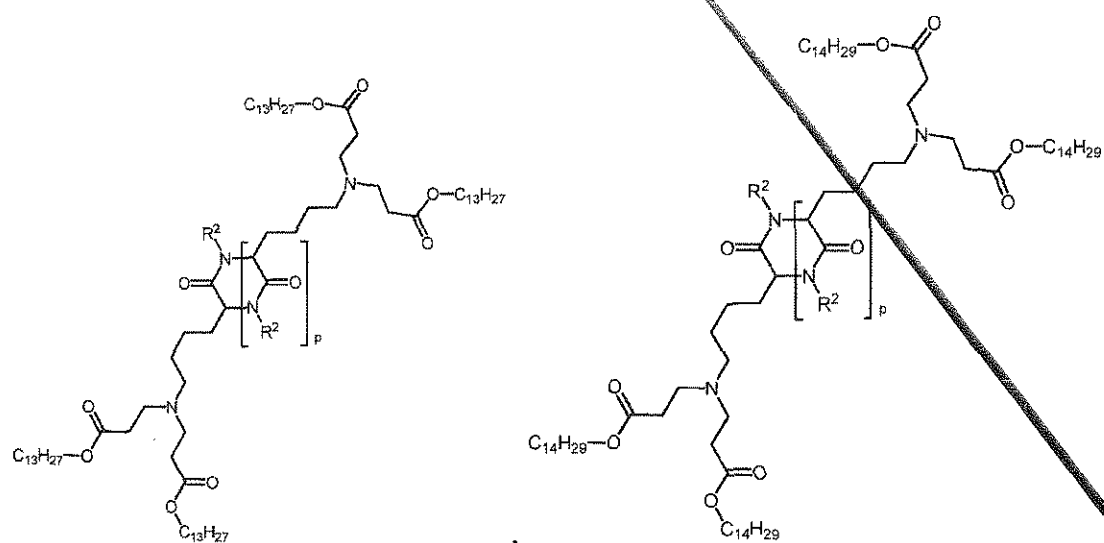
wherein R^6 and R^7 are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, and a sulfur protecting group when attached to a sulfur atom, or a group of formula (i), (ii), or (iii).

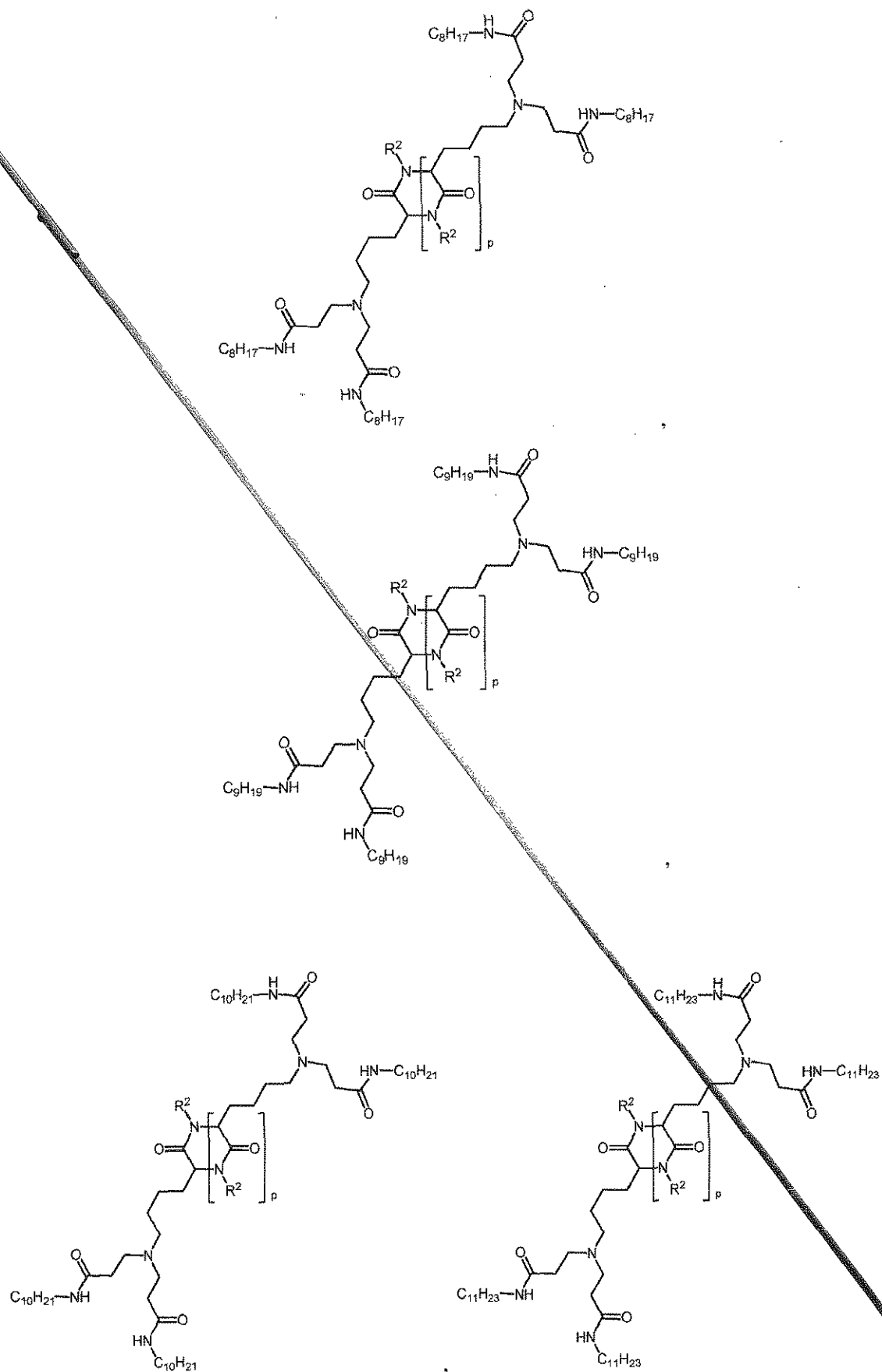
12. The compound of claim 1, wherein the compound is selected from the group consisting of:

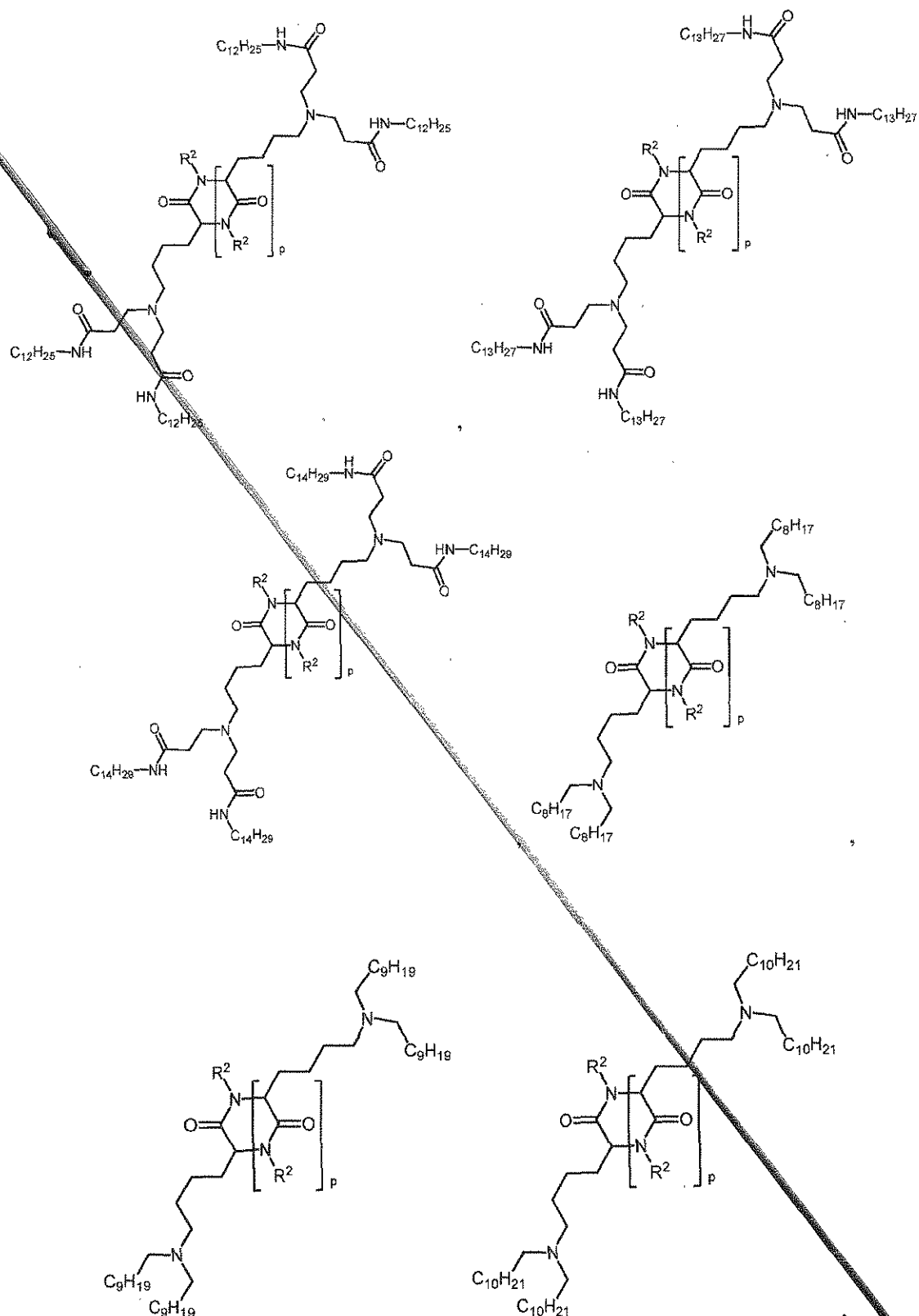


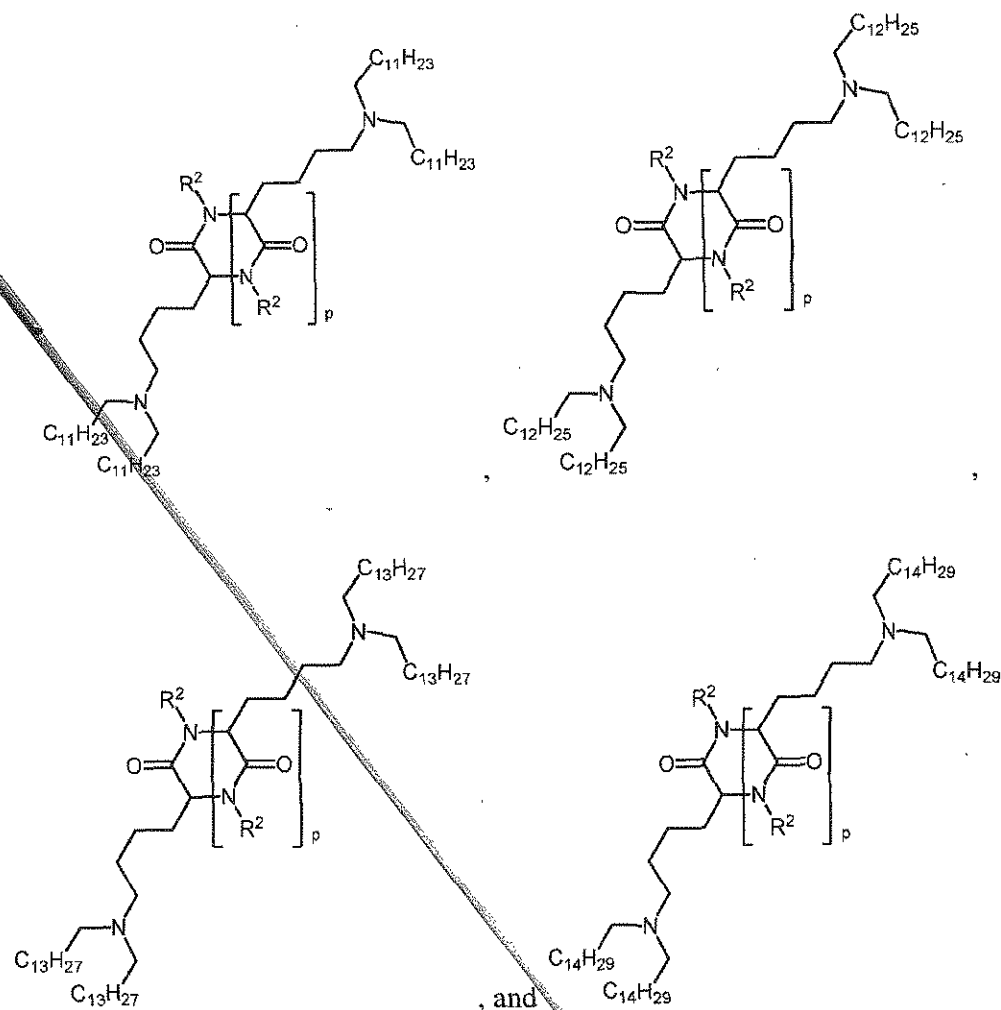






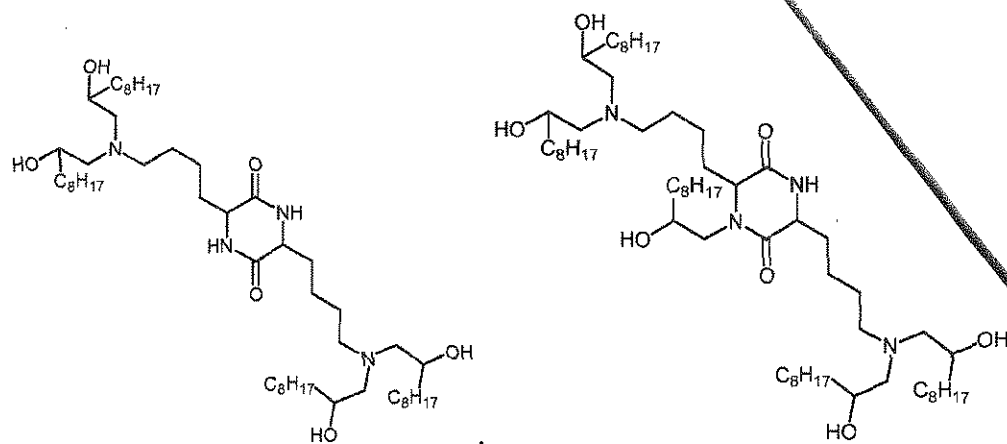


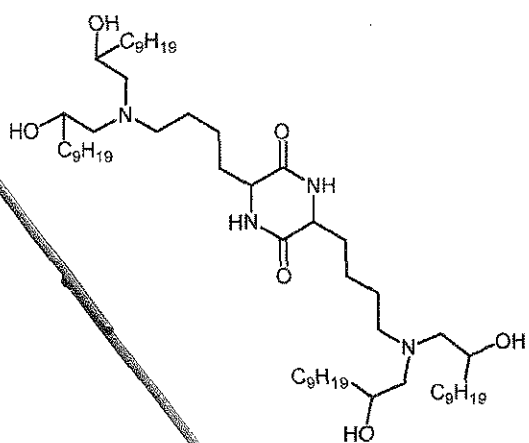
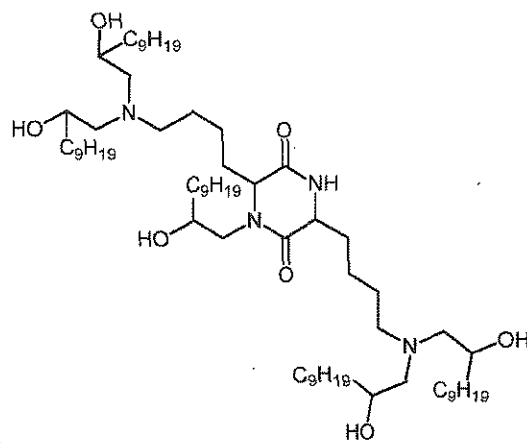
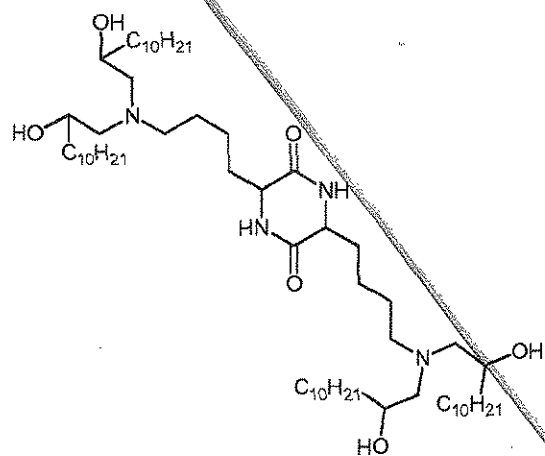
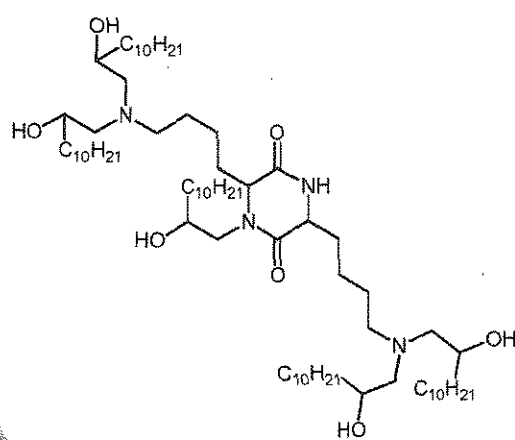
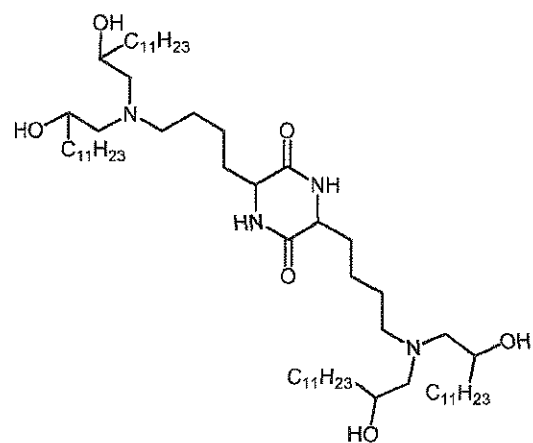
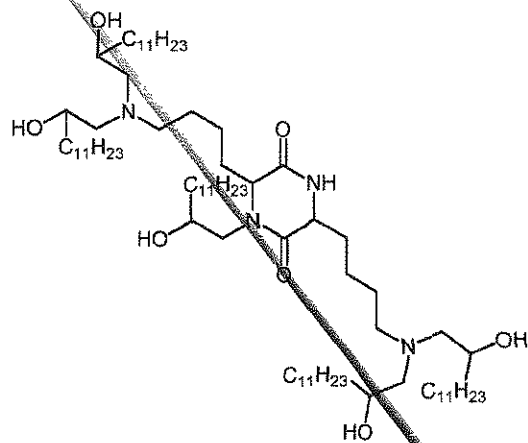


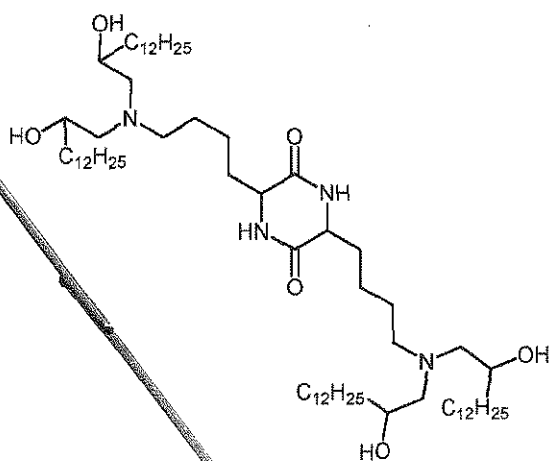
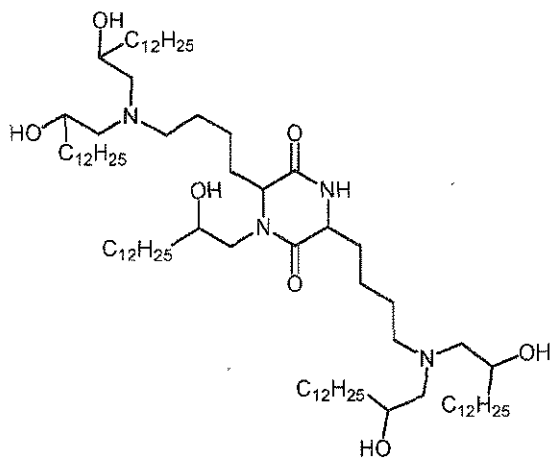
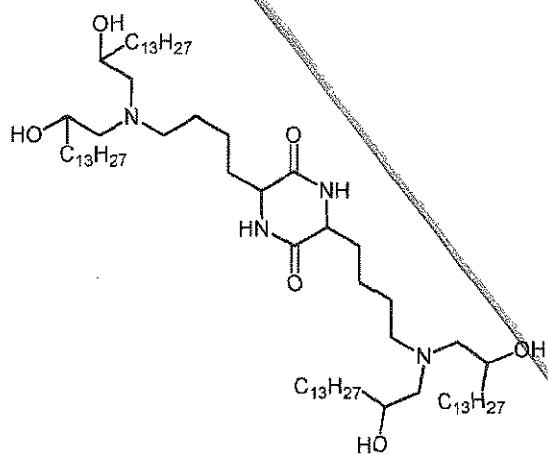
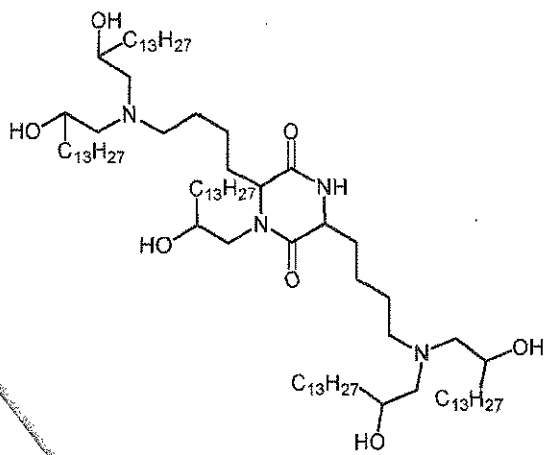
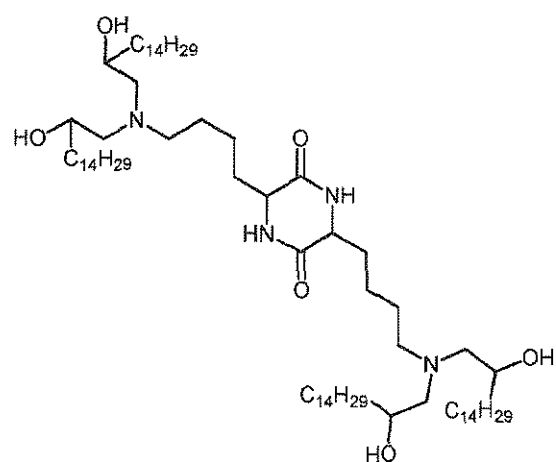
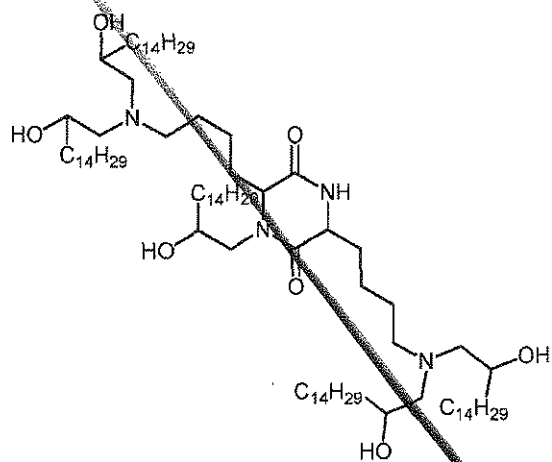


and salts thereof.

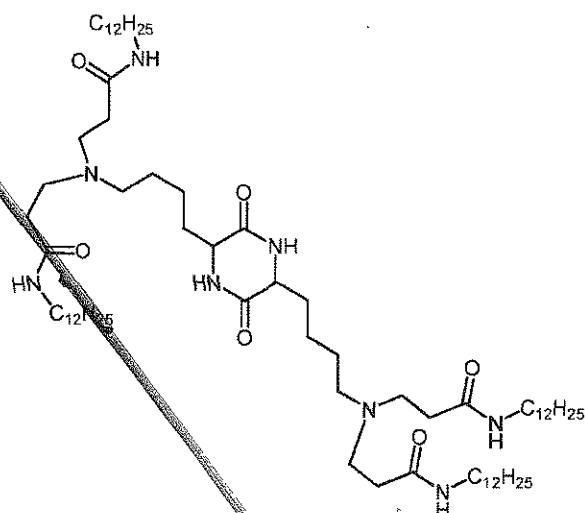
13. The compound of claim 1, wherein the compound is selected from the group consisting of:



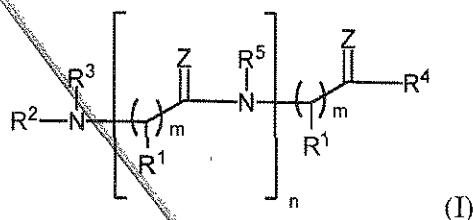




and



14. A compound of Formula (I):



wherein:

each instance of m is independently 1, 2, or 3;

each instance of Z is independently O, S, or NR^Z, wherein R^Z is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii);

each instance of R^{A1} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, halogen, $-OR^{A1}$, $-N(R^{A1})_2$, or $-SR^{A1}$; wherein each occurrence of R^{A1} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached

to an sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an optionally substituted heterocyclic or optionally substituted heteroaryl ring;

R^2 is a group of formula (i), (ii), or (iii);

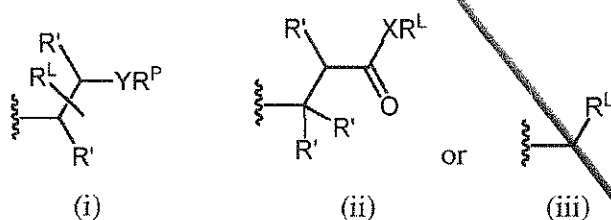
R^3 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii);

or R^3 and an R^1 group are joined to form an optionally substituted 5-6 membered heterocyclic ring;

R^4 is $-OR^{A4}$, $-N(R^{A4})_2$, or $-SR^{A4}$; wherein each occurrence of R^{A4} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A4} groups are joined to form an optionally substituted heterocyclic or optionally substituted heteroaryl ring;

R^5 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group; and

Formulae (i), (ii), and (iii) are:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

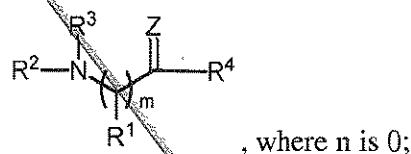
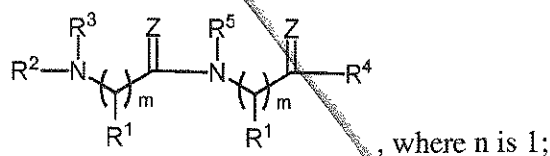
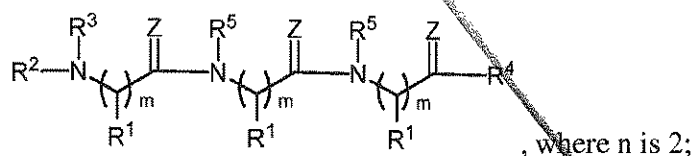
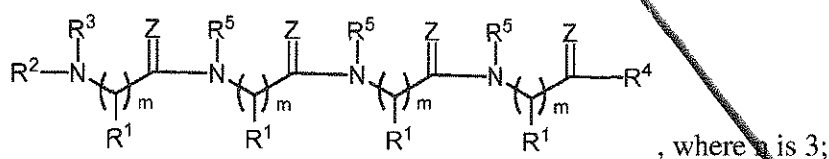
X is O, S, NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

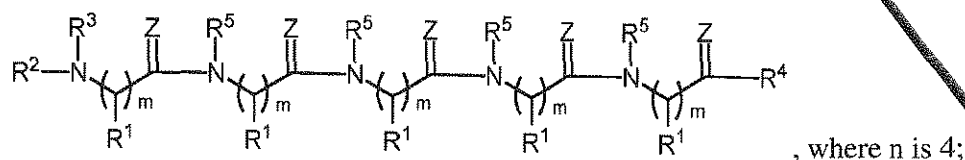
R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer.

15. The compound of claim 14 of formula:

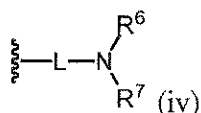


or



or salt thereof.

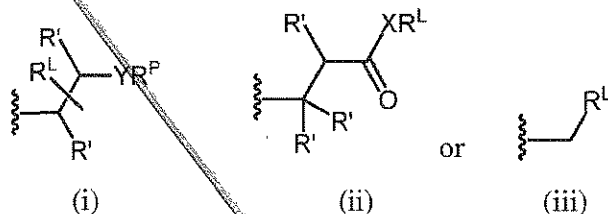
16. The compound of claim 14, wherein at least one instance of R¹ is a group of formula:



wherein L is an optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted heteroalkylene, optionally substituted heteroalkenylene, optionally substituted heteroalkynylene, optionally substituted carbocyclylene, optionally substituted heterocyclylene, optionally substituted arylene, or optionally substituted heteroarylene, and

R⁶ and R⁷ are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group;

provided at least one instance of R^6 and R^7 is a group of formula:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X, wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

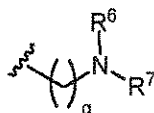
Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^1 is optionally substituted C_{1-50} alkyl, optionally substituted C_{2-50} alkenyl, optionally substituted C_{2-50} alkynyl, optionally substituted hetero C_{1-50} alkyl, optionally substituted hetero C_{2-50} alkenyl, optionally substituted hetero C_{2-50} alkynyl, or a polymer.

17. The compound of claim 16, wherein L is an optionally substituted alkylene.

18. The compound of claim 16, wherein the group of formula (iv) is of the formula:



wherein q is an integer between 1 and 50, inclusive.

19. The compound of claim 16, wherein each instance of R^1 is a group of formula (iv).

20. The compound of claim 14, wherein each instance of Z is O.

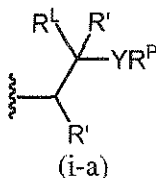
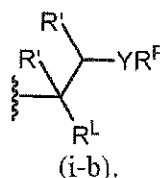
21. The compound of claim 14, wherein each instance of m is 1.

22. The compound of claim 14, wherein each instance of R^5 is hydrogen.

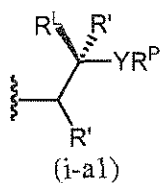
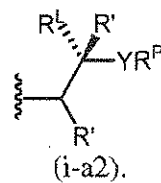
23. The compound of claim 14, wherein R^2 is a group of the formula (i), (ii), or (iii), and R^3 is hydrogen.

24. The compound of claim 14, wherein R^2 and R^3 are the same group selected from formula (i), (ii), or (iii).

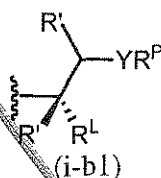
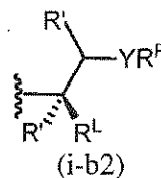
25. The compound of claim 14, wherein the group of formula (i) represents a group of formula (i-a) or a group of formula (i-b):



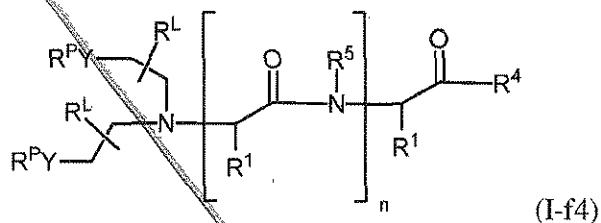
26. The compound of claim 25, wherein the group of formula (i-a) is a group of formula (i-a1) or a group of formula (i-a2):



27. The compound of claim 25, wherein the group of formula (i-b) is a group of formula (i-b1) or a group of formula (i-b2):

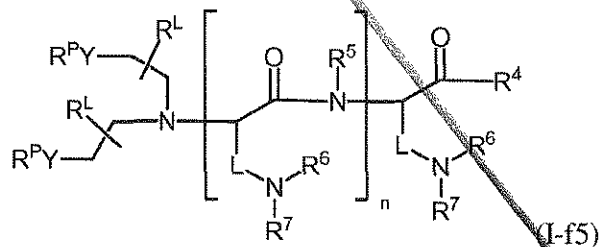


28. The compound of claim 14, wherein the compound is of Formula (I-f4):



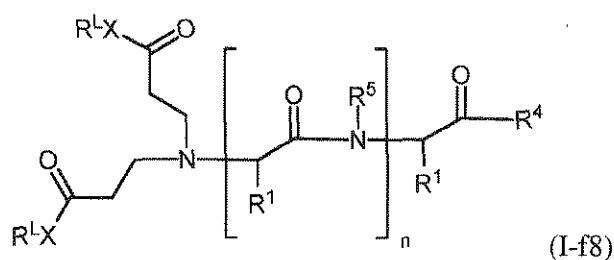
or salt thereof.

29. The compound of claim 14, wherein the compound is of Formula (I-f5):



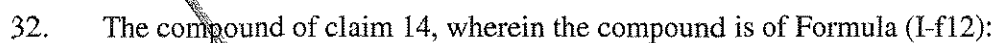
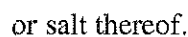
or salt thereof.

30. The compound of claim 14, wherein the compound is of Formula (I-f8):

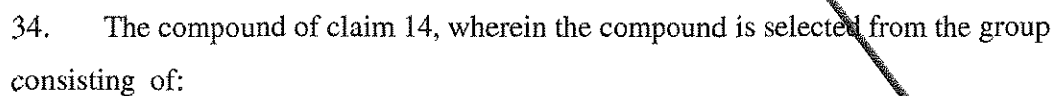
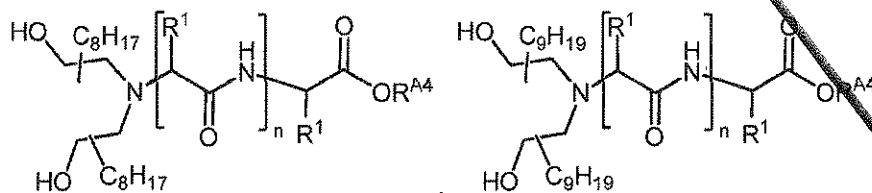


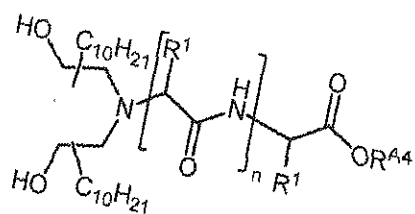
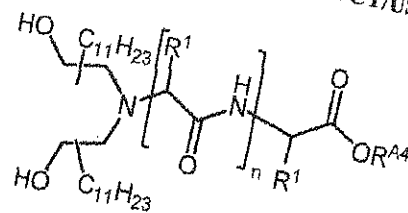
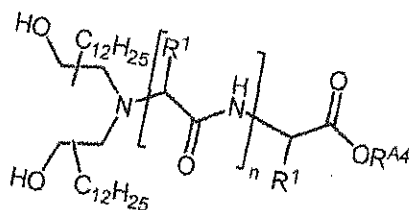
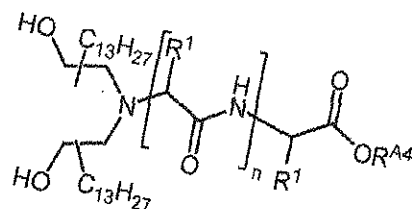
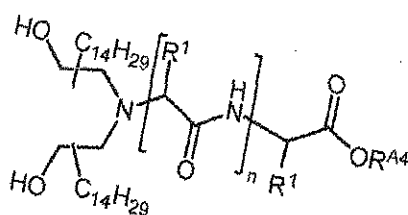
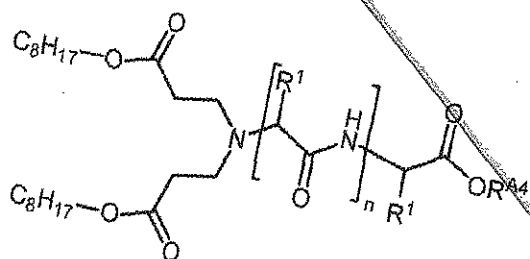
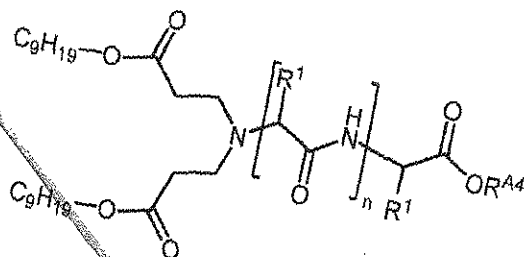
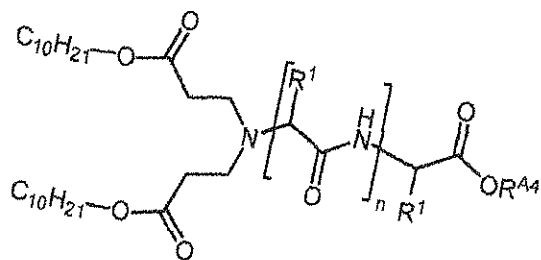
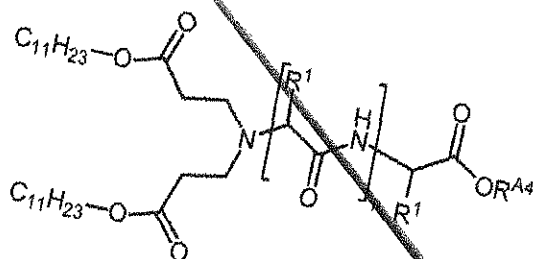
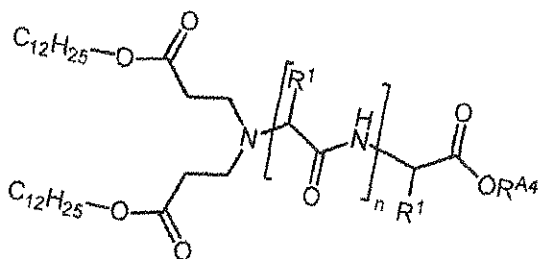
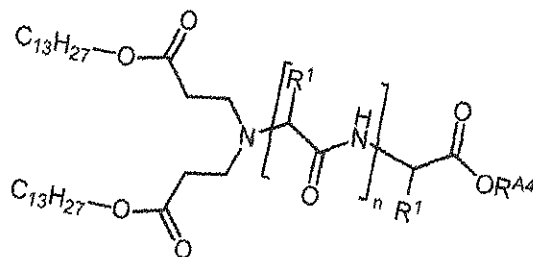
or salt thereof.

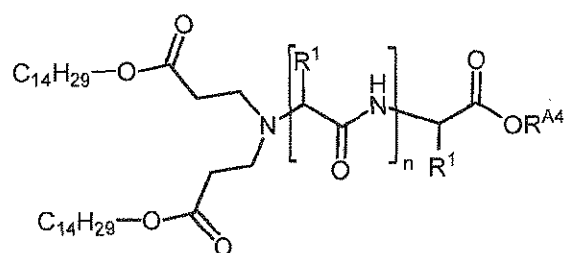
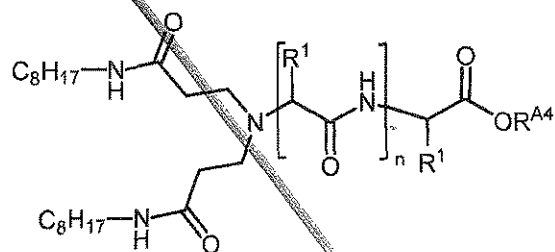
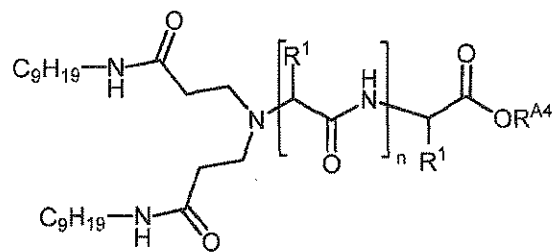
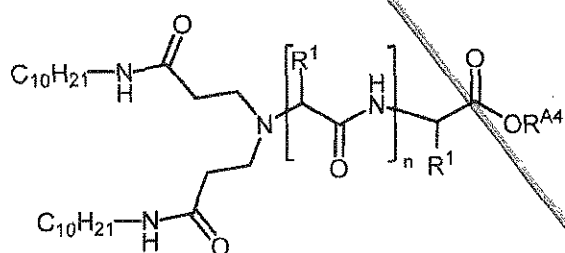
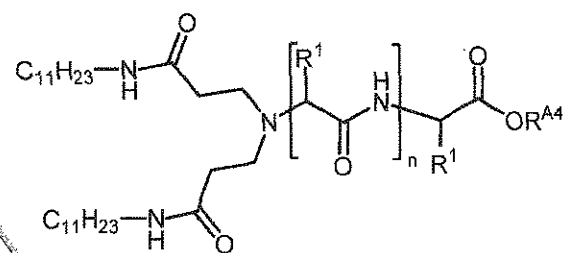
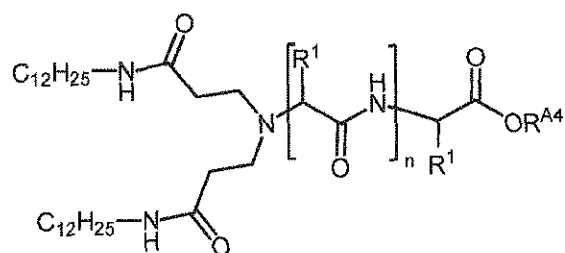
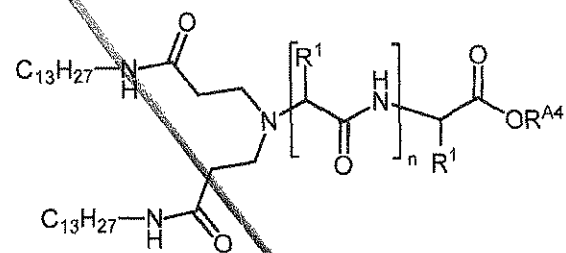
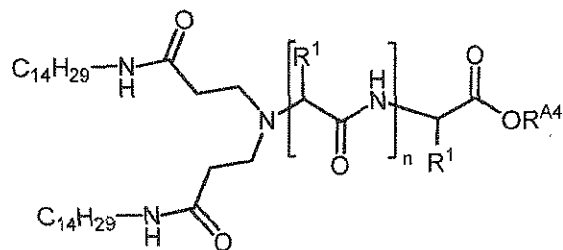
or salt thereof.

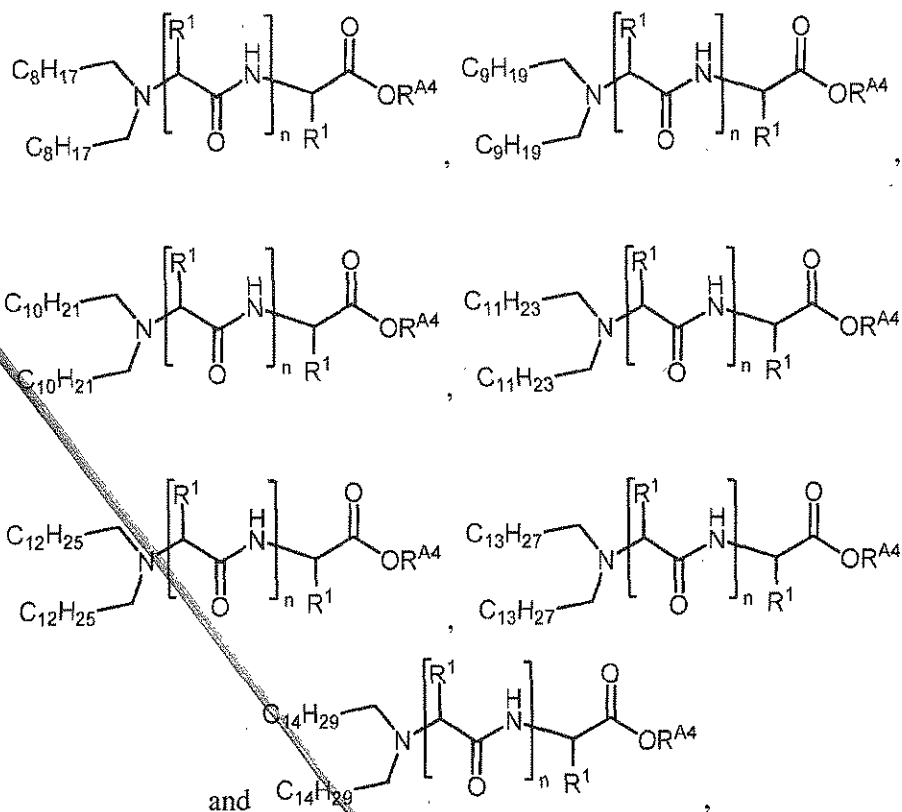


or salt thereof.





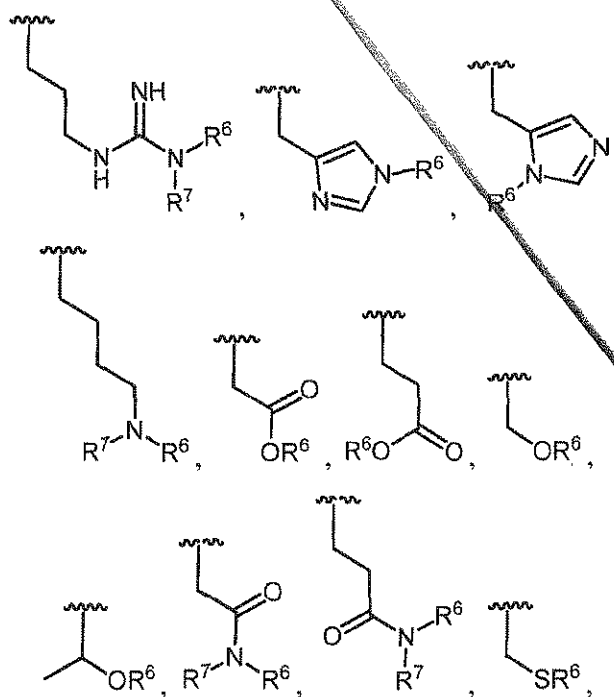


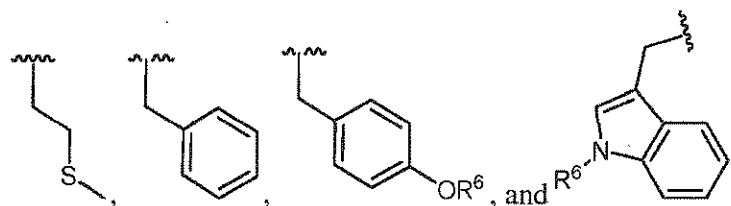


and salts thereof,

wherein R^1 is selected from the group consisting of:

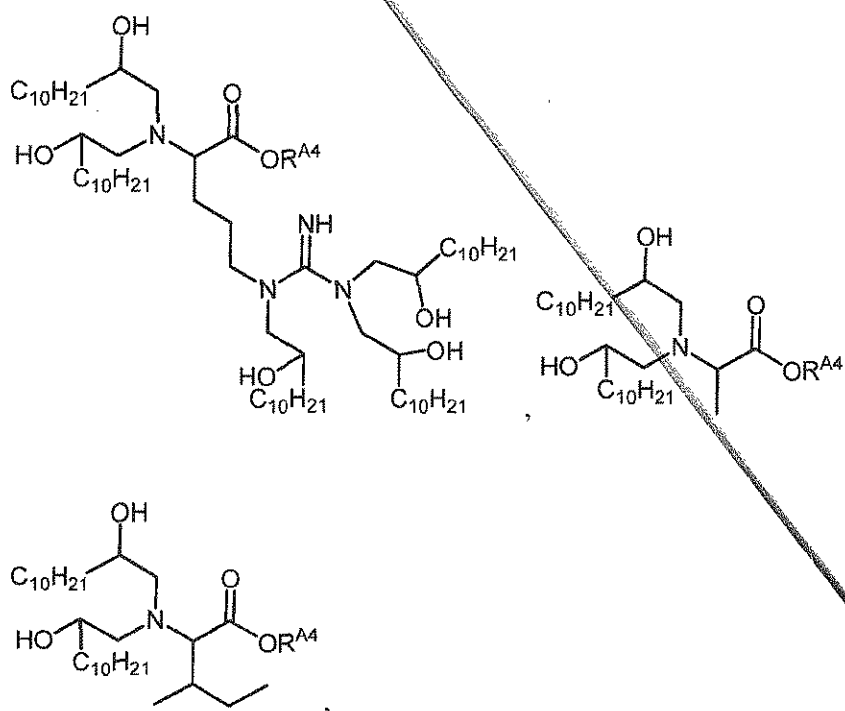
$-\text{H}$, $-\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$,

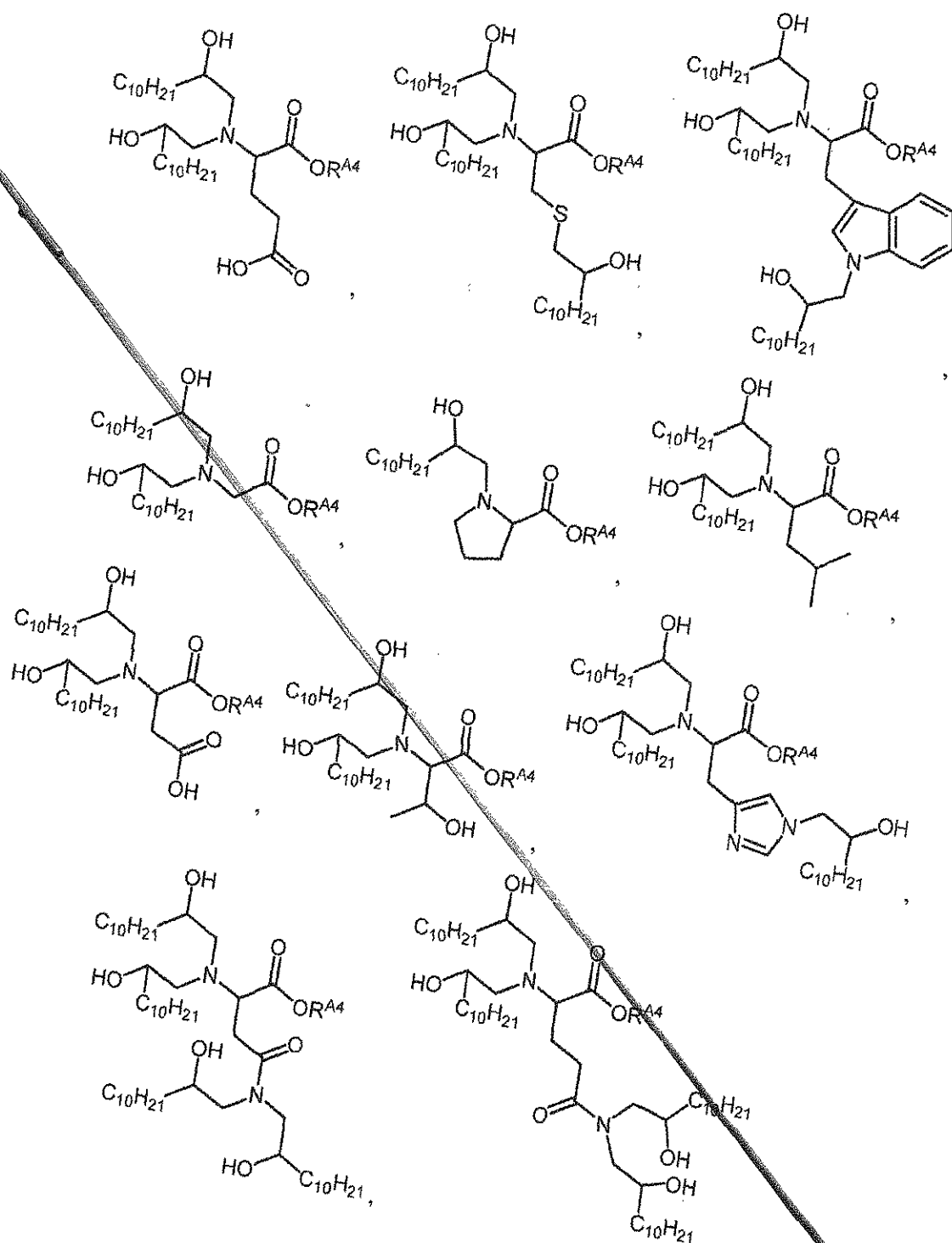


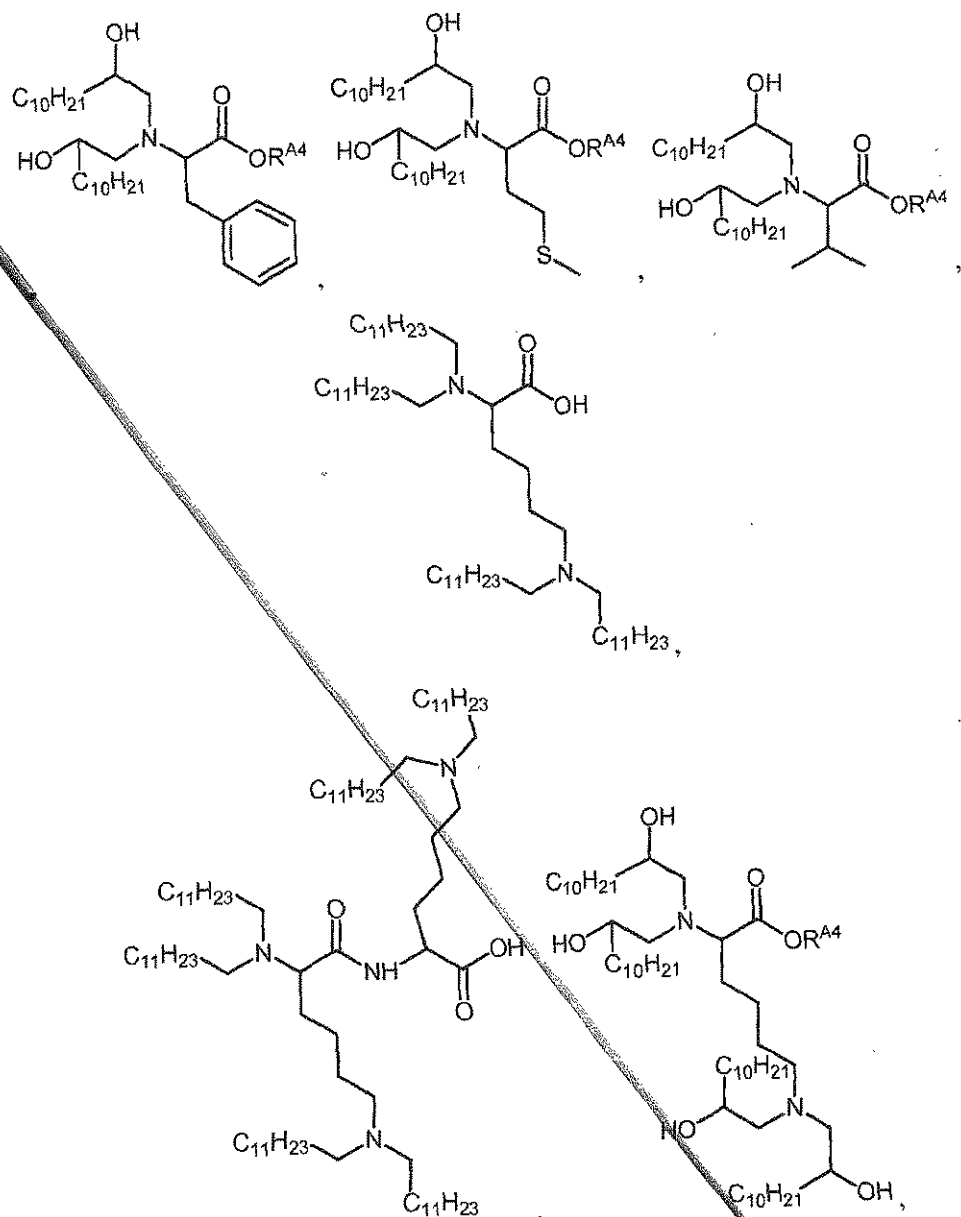


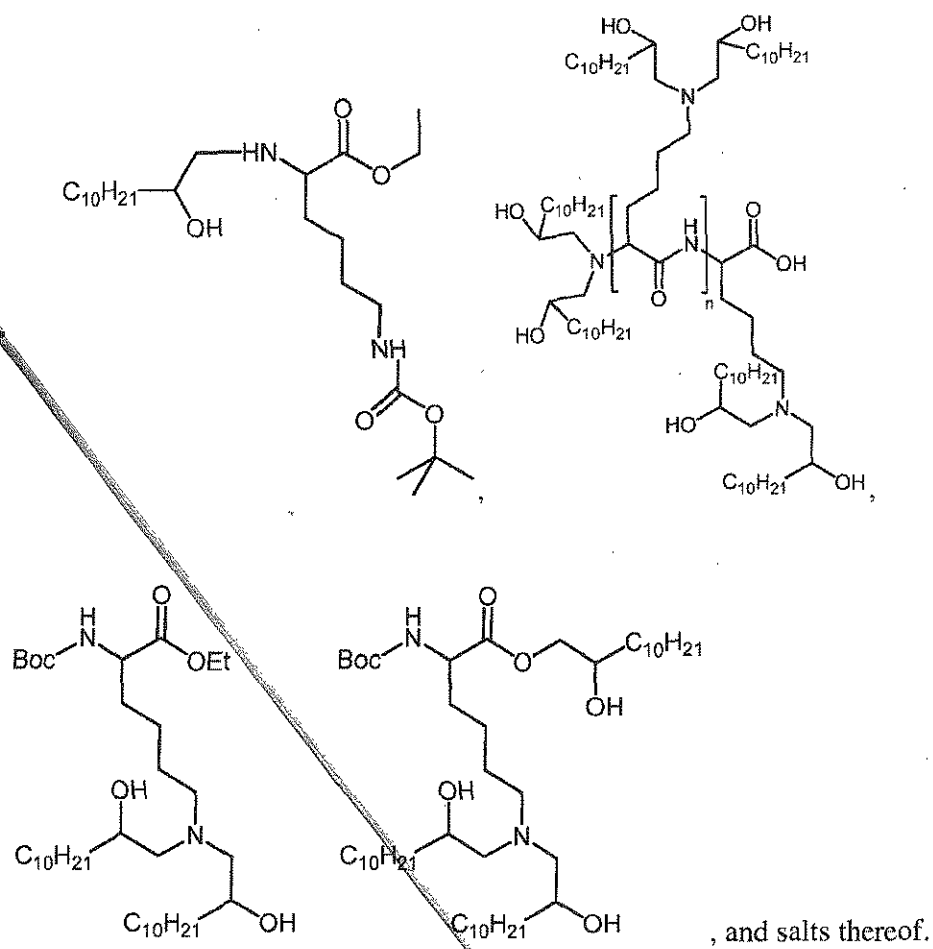
wherein R^6 and R^7 are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, and a sulfur protecting group when attached to a sulfur atom, or a group of formula (i), (ii), or (iii).

35. The compound of claim 14, wherein the compound is selected from the group consisting of:

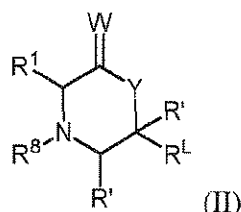








36. A compound of Formula (II):



or salt thereof;

wherein:

each instance of R^1 is independently hydrogen or optionally substituted alkyl;

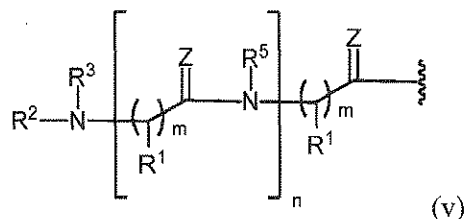
each instance of R^1 is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, halogen,

$-OR^{A1}$, $-N(R^{A1})_2$, or $-SR^{A1}$, wherein each occurrence of R^{A1} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an optionally substituted heterocyclic or optionally substituted heteroaryl ring;

each instance of W is independently O, S, or NR^W , wherein R^W is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii);

each instance of Y is independently O, S, or NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^8 is hydrogen, a group of the formula (i), (ii), or (iii), or a group of the formula (v):



wherein:

n is 0 or is an integer between 1 and 100,000, inclusive;

each instance of m is independently 1, 2, or 3;

each instance of Z is independently O, S, or NR^Z , wherein R^Z is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii);

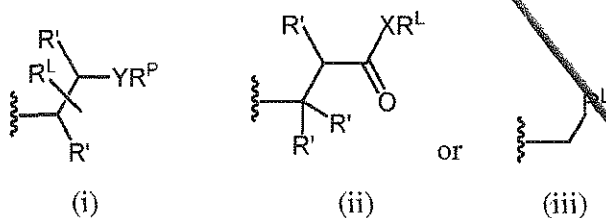
R^2 is a group of formula (i), (ii), or (iii);

R^3 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of the formula (i), (ii), or (iii);

or R^3 and an R^1 group are joined to form an optionally substituted 5-6 membered heterocyclic ring;

R^5 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Formulae (i), (ii), and (iii) are:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

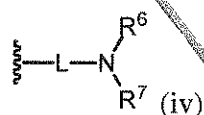
R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer;

or R⁸ and an R¹ group are joined to form an optionally substituted 5-6 membered heterocyclic ring.

37. The compound of claim 36, wherein W is O.

38. The compound of claim 36, wherein Y is O.

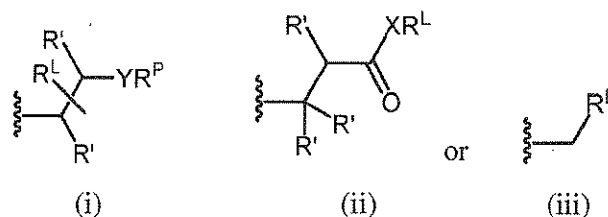
39. The compound of claim 36, wherein at least one instance of R¹ is a group of formula:



wherein L is an optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted heteroalkylene, optionally substituted heteroalkenylene, optionally substituted heteroalkynylene, optionally substituted carbocyclylene, optionally substituted heterocyclylene, optionally substituted arylene, or optionally substituted heteroarylene, and

R⁶ and R⁷ are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group;

provided at least one instance of R⁶ and R⁷ is a group of formula:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;
 X is O, S, NR^X, wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

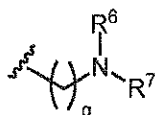
Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer.

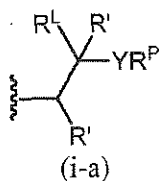
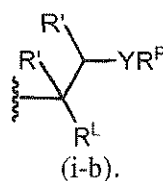
40. The compound of claim 39, wherein L is an optionally substituted alkylene.

41. The compound of claim 39, wherein the group of formula (iv) is of formula:

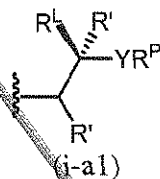
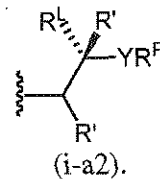


wherein q is an integer between 1 and 50, inclusive.

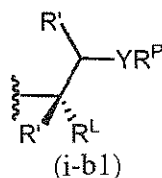
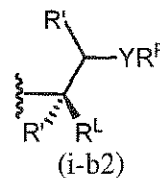
42. The compound of claim 36, wherein the group of formula (i) represents a group of formula (i-a) or a group of formula (i-b):



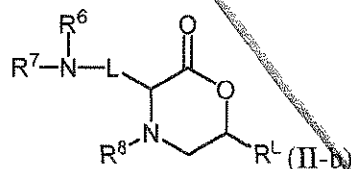
43. The compound of claim 42, wherein the group of formula (i-a) is a group of formula (i-a1) or a group of formula (i-a2):



44. The compound of claim 42, wherein the group of formula (i-b) is a group of formula (i-b1) or a group of formula (i-b2):

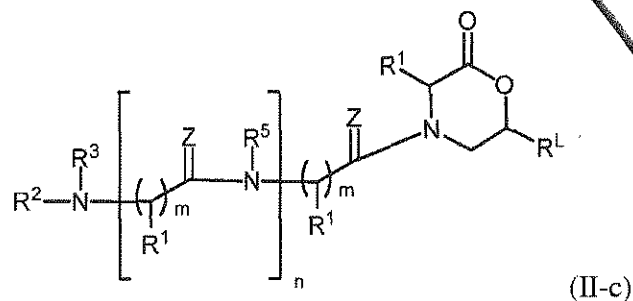


45. The compound of claim 36, wherein the compound is of Formula (II-b):



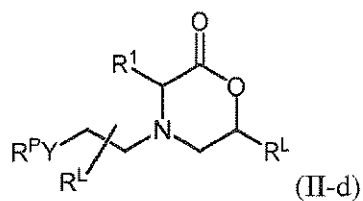
or salt thereof.

46. The compound of claim 36, wherein the compound is of Formula (II-c):



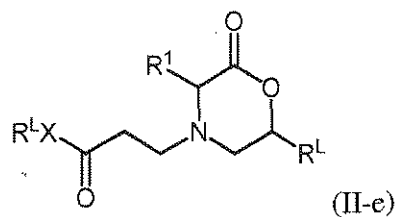
or salt thereof.

47. The compound of claim 36, wherein the compound is of Formula (II-d):



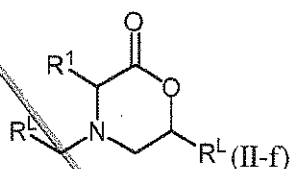
or salt thereof.

48. The compound of claim 36, wherein the compound is of Formula (II-d):



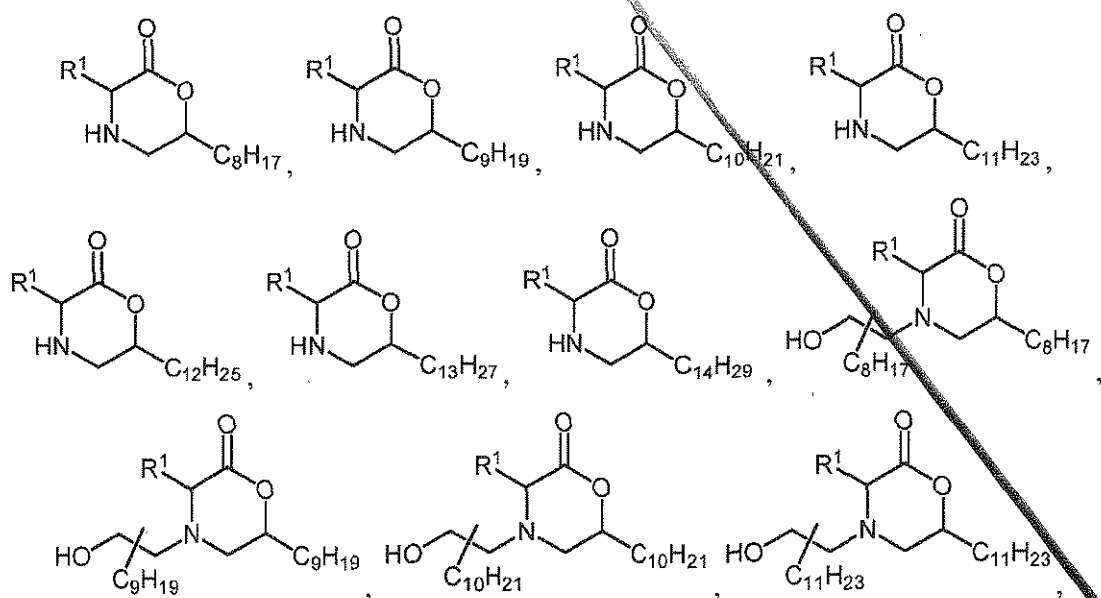
or salt thereof.

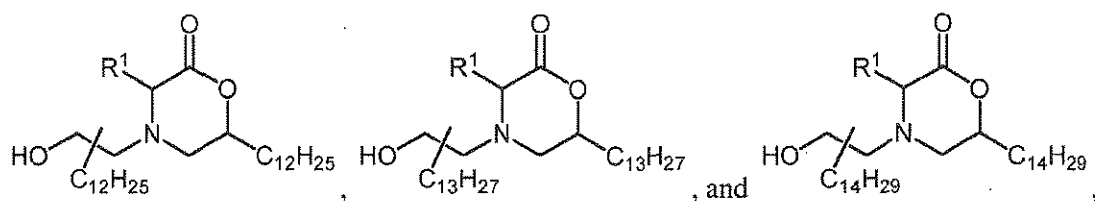
49. The compound of claim 36, wherein the compound is of Formula (II-f):



or salt thereof.

50. The compound of claim 36, wherein the compound is selected from the group consisting of:

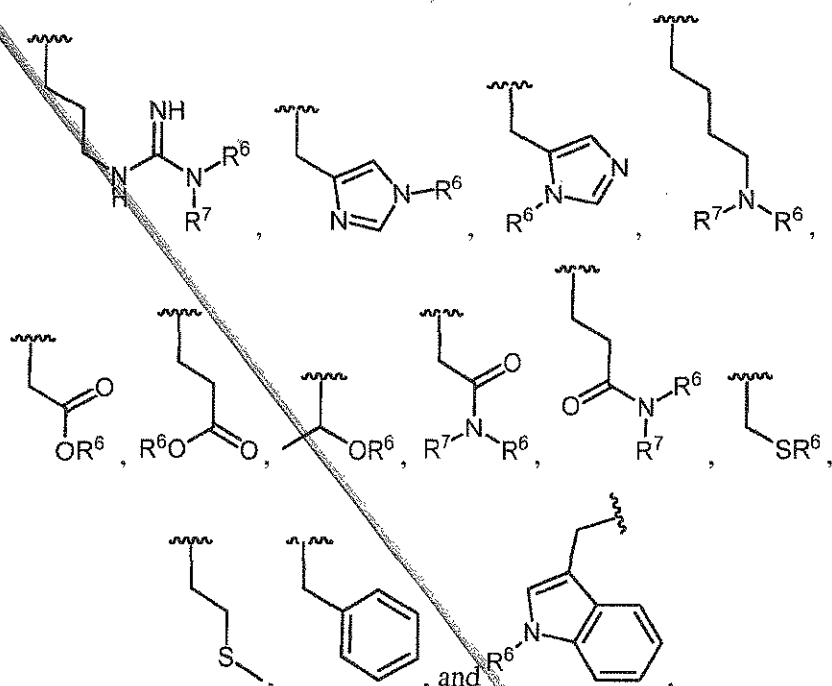




and salts thereof,

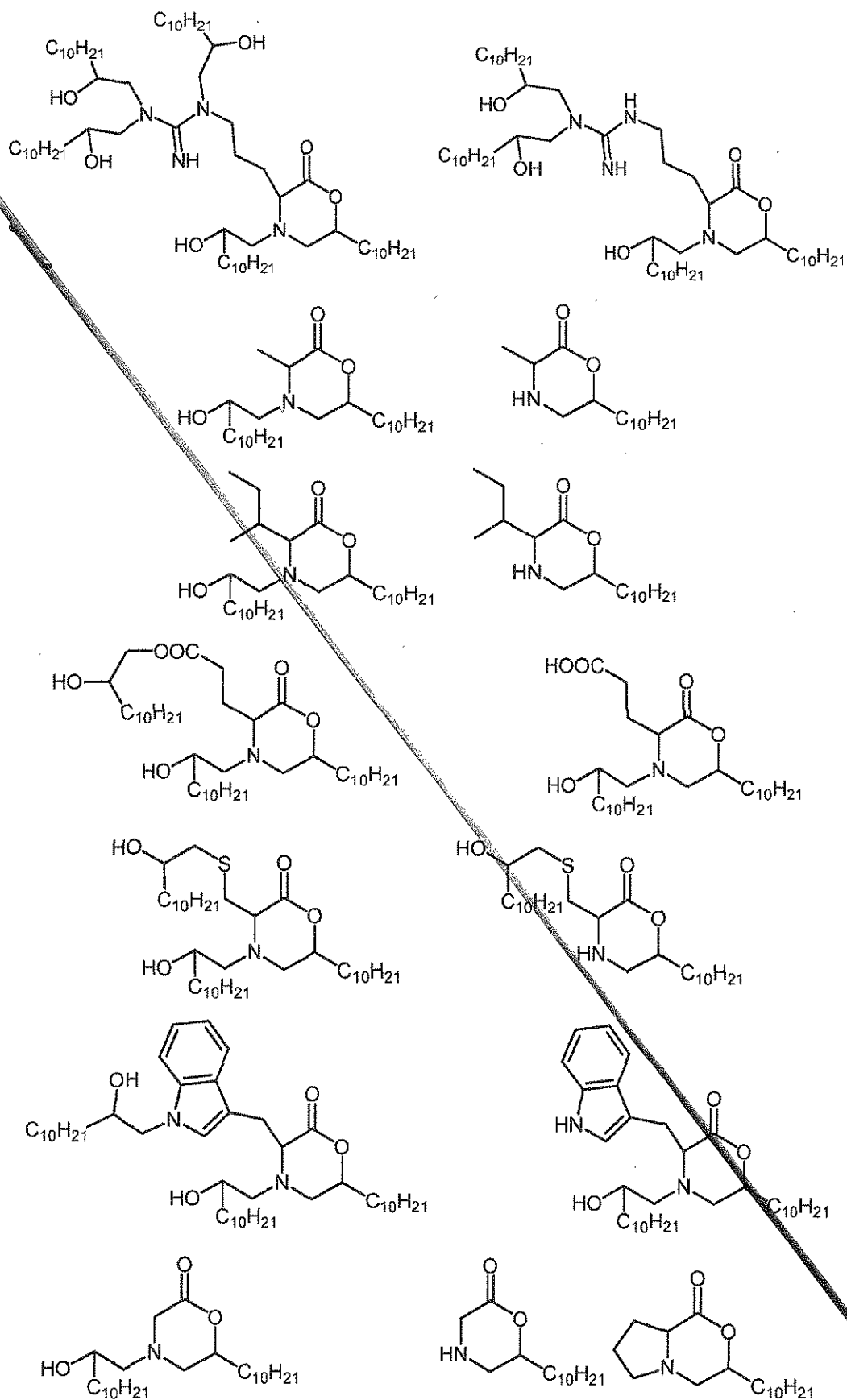
wherein R^1 is selected from the group consisting of:

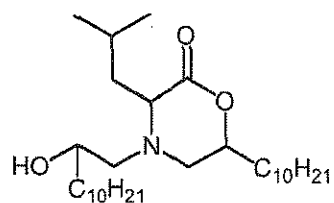
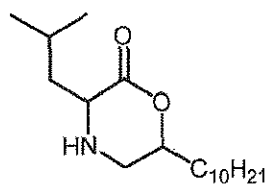
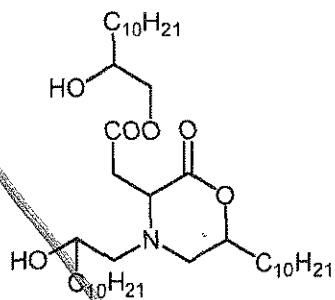
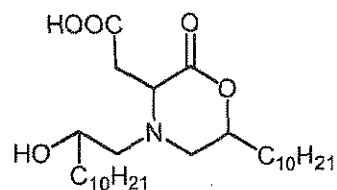
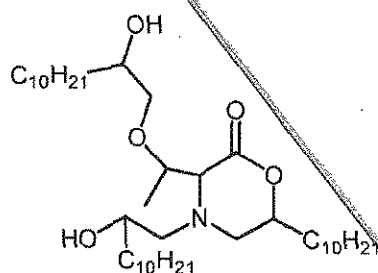
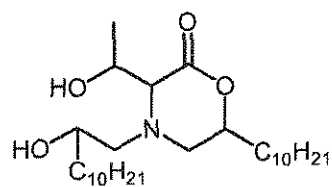
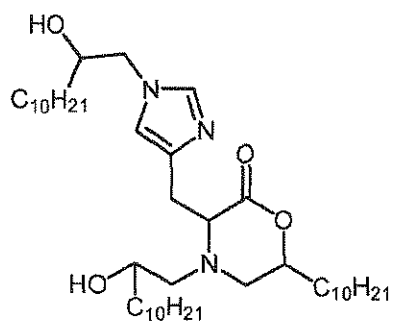
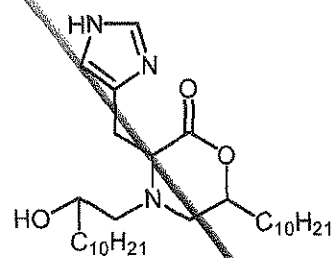
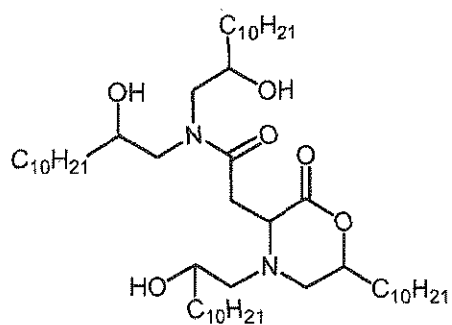
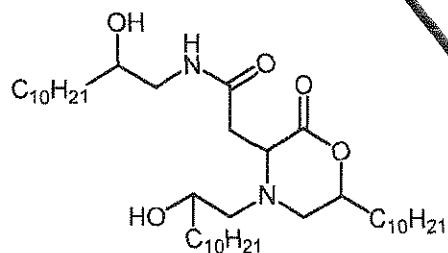
$-\text{H}$, $-\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$, $-\text{CH}_2\text{CH}(\text{CH}_3)_2$,

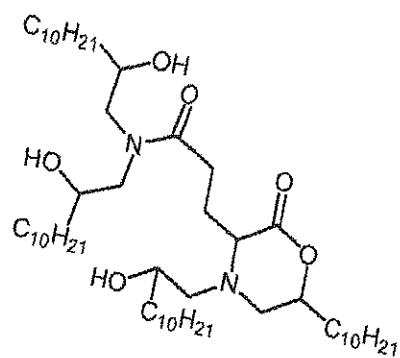
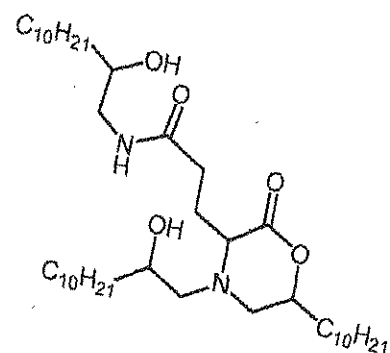
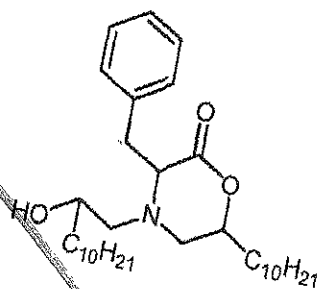
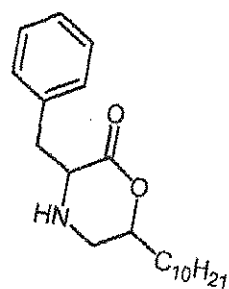
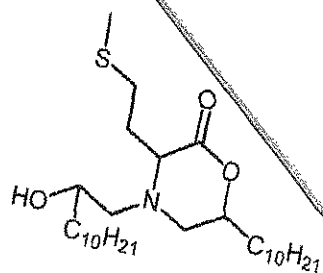
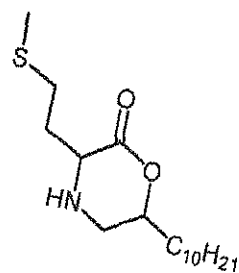
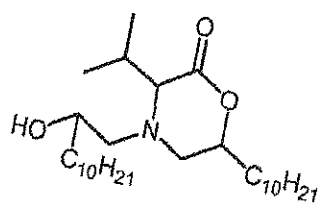
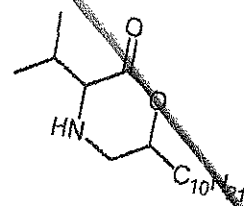
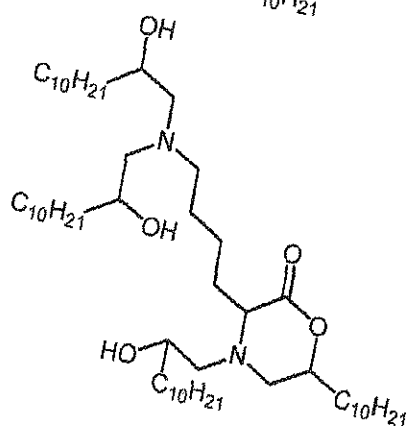
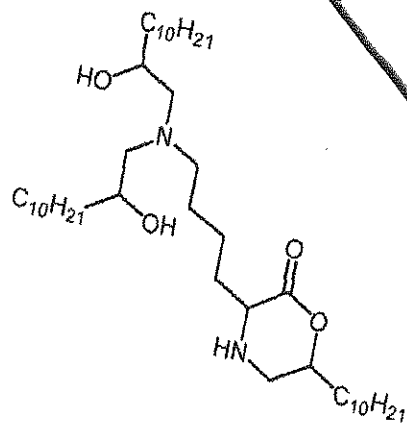


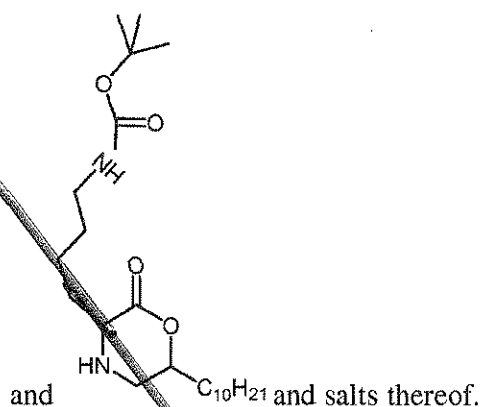
wherein R^6 and R^7 are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, and a sulfur protecting group when attached to a sulfur atom, or a group of formula (i), (ii), or (iii).

51. The compound of claim 36, wherein the compound is selected from the group consisting of:

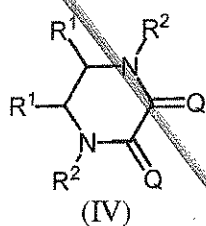
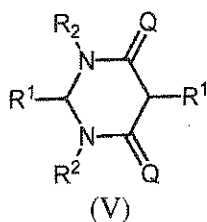
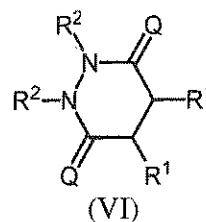








52. A compound of Formula (IV), (V), or (VI):



or salt thereof;

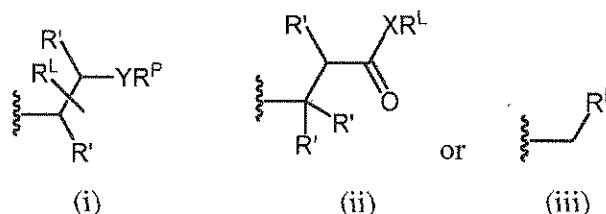
wherein:

each instance of Q is independently Q, S, or NR^Q , wherein R^Q is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of formula (i), (ii), (iii);

each instance of R^1 is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, halogen, $-OR^{A1}$, $-N(R^{A1})_2$, or $-SR^{A1}$, wherein each occurrence of R^{A1} is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to an sulfur atom, a nitrogen protecting group when attached to a nitrogen atom, or two R^{A1} groups are joined to form an optionally substituted heterocyclic or optionally substituted heteroaryl ring;

each instance of R^2 is independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, a nitrogen protecting group, or a group of formula (i), (ii), or (iii); and

Formulae (i), (ii), and (iii) are:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

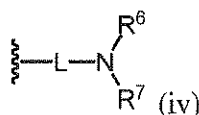
Y is O, S, NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C_{1-50} alkyl, optionally substituted C_{2-50} alkenyl, optionally substituted C_{2-50} alkynyl, optionally substituted hetero C_{1-50} alkyl, optionally substituted hetero C_{2-50} alkenyl, optionally substituted hetero C_{2-50} alkynyl, or a polymer;

provided that at least one instance of R^Q , R^2 , R^6 , or R^7 is a group of the formula (i), (ii), or (iii).

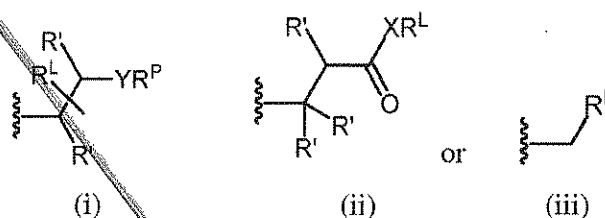
53. The compound of claim 52, wherein at least one instance of R^1 is a group of formula:



wherein L is an optionally substituted alkylene, optionally substituted alkenylene, optionally substituted alkynylene, optionally substituted heteroalkylene, optionally substituted heteroalkenylene, optionally substituted heteroalkynylene, optionally substituted carbocyclylene, optionally substituted heterocyclylene, optionally substituted arylene, or optionally substituted heteroarylene, and

R^6 and R^7 are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, and a nitrogen protecting group;

provided at least one instance of R^6 and R^7 is a group of formula:



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X , wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

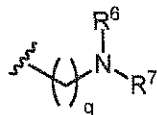
Y is O, S, NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C_{1-50} alkyl, optionally substituted C_{2-50} alkenyl, optionally substituted C_{2-50} alkynyl, optionally substituted hetero C_{1-50} alkyl, optionally substituted hetero C_{2-50} alkenyl, optionally substituted hetero C_{2-50} alkynyl, or a polymer.

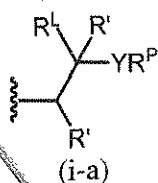
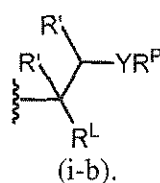
54. The compound of claim 53, wherein L is an optionally substituted alkylene.

55. The compound of claim 53, wherein the group of formula (iv) is of the formula:

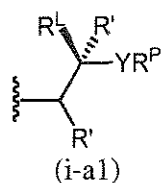
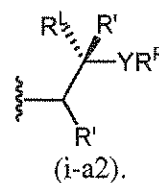


wherein q is an integer between 1 and 50, inclusive.

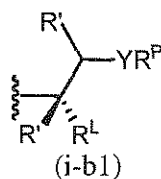
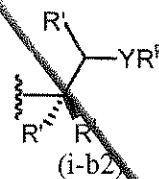
56. The compound of claim 52, wherein the group of formula (i) represents a group of formula (i-a) or a group of formula (i-b):



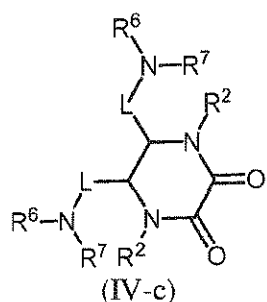
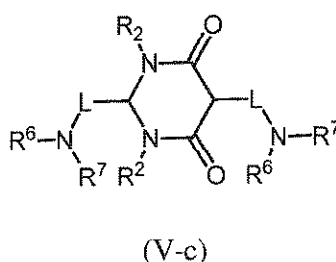
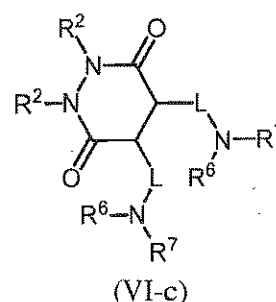
57. The compound of claim 56, wherein the group of formula (i-a) is a group of formula (i-a1) or a group of formula (i-a2):



58. The compound of claim 56, wherein the group of formula (i-b) is a group of formula (i-b1) or a group of formula (i-b2):

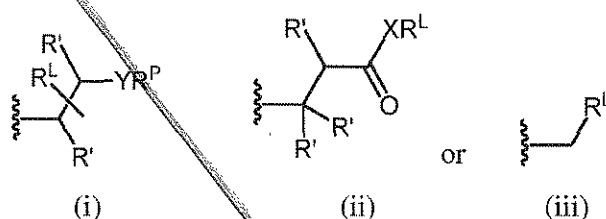


59. The compound of claim 52, wherein the compound is of Formula (IV-c), (V-c), or (VI-c):



or salt thereof.

60. A composition comprising an APPL, or salt thereof, and an excipient;
wherein the APPL is an amino acid, a linear or cyclic peptide, or a linear or cyclic polypeptide, or structural isomer thereof, wherein an amino or amide group of the APPL is conjugated to a group of formula (i), (ii), or (iii):



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X, wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer.

61. The composition of claim 60, wherein the group is attached to an amino group present on the APPL scaffold.

62. The composition of claim 60, wherein the composition is a pharmaceutical composition, a cosmetic composition, a nutraceutical composition, or a composition with non-medical application.

63. The composition of claim 62, wherein the composition with non-medical application is an emulsion or emulsifier useful as a food component, for extinguishing fires, for disinfecting surfaces, or for oil cleanup.

64. The composition of claim 60, wherein the composition is a pharmaceutical composition.

65. The composition of claim 64, wherein the composition further comprises cholesterol.

66. The composition of claim 64, wherein the composition further comprises a PEGylated lipid.

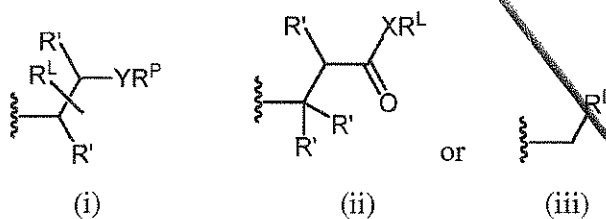
67. The composition of claim 64, wherein the composition further comprises a phospholipid

68. The composition of claim 64, wherein the composition further comprises an apolipoprotein.

69. The composition of claim 60, wherein the composition further comprises an agent.

70. The composition of claim 69, wherein the agent is an organic molecule, inorganic molecule, nucleic acid, protein, peptide, polynucleotide, targeting agent, an isotopically labeled chemical compound, vaccine, an immunological agent, or an agent useful in bioprocessing.

71. The composition of claim 69, wherein the agent is a polynucleotide, and the polynucleotide is DNA or RNA.
72. The composition of claim 71, wherein the RNA is RNAi, dsRNA, siRNA, shRNA, miRNA, or antisense RNA.
73. The composition of claim 69, wherein the agent and the APPL are not covalently attached.
74. The composition of claim 60, wherein the composition is in the form of a particle.
75. The composition of claim 74, wherein the particle is a nanoparticle or microparticle.
76. The composition of claim 74, wherein the particle is a micelle, liposome, or lipoplex.
77. The composition of claim 74, wherein the particle encapsulates an agent.
78. A method of screening a compound library, the method comprising:
 providing a plurality of different APPLs, or salts thereof; and
 performing at least one assay with the compound library to determine the presence or absence of a desired property;
 wherein the APPL is an amino acid, a linear or cyclic peptide, or a linear or cyclic polypeptide, or structural isomer thereof, wherein an amino or amide group of the APPL is conjugated to a group of formula (i), (ii), or (iii):



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;
 X is O, S, NR^x, wherein R^x is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl,

optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y , wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

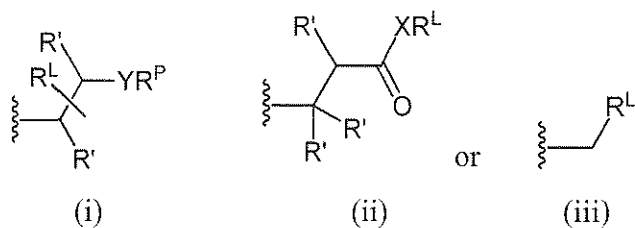
R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C_{1-50} alkyl, optionally substituted C_{2-50} alkenyl, optionally substituted C_{2-50} alkynyl, optionally substituted hetero C_{1-50} alkyl, optionally substituted hetero C_{2-50} alkenyl, optionally substituted hetero C_{2-50} alkynyl, or a polymer.

79. The method of claim 78, wherein the desired property is solubility in water, solubility at different pH, ability to bind polynucleotides, ability to bind heparin, ability to bind small molecules, ability to bind protein, ability to form microparticles, ability to increase transfection efficiency, ability to support cell growth, ability to support cell attachment, ability to support tissue growth, and/or intracellular delivery of the APPL and/or an agent complexed or attached thereto to aid in bioprocessing.

80. Use of a composition comprising an APPL, or salt thereof for treating disease, disorder, or condition from which a subject suffers;

wherein the APPL is an amino acid, a linear or cyclic peptide, or a linear or cyclic polypeptide, or structural isomer thereof, wherein an amino or amide group of the APPL is conjugated to a group of formula (i), (ii), or (iii):



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X, wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

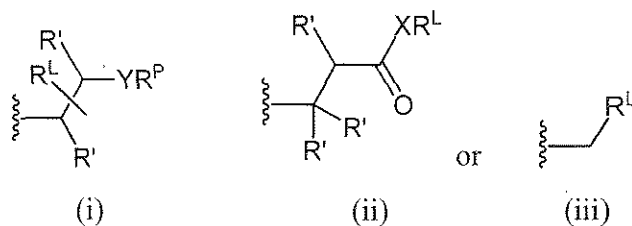
R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer;

wherein the disease, disorder, or condition is selected from the group consisting of proliferative disorders, inflammatory disorders, autoimmune disorders, painful conditions, liver diseases, and familial amyloid neuropathies.

81. An in vitro method of delivering a polynucleotide to a biological cell, comprising:
providing a composition comprising an APPL, or salt thereof, and a polynucleotide;
and

exposing the composition to the biological cell under conditions sufficient to facilitate delivery of the polynucleotide into the interior of the biological cell;

wherein the APPL is an amino acid, a linear or cyclic peptide, or a linear or cyclic polypeptide, or structural isomer thereof, wherein an amino or amide group of the APPL is conjugated to a group of formula (i), (ii), or (iii):



wherein:

each instance of R' is independently hydrogen or optionally substituted alkyl;

X is O, S, NR^X, wherein R^X is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

Y is O, S, NR^Y, wherein R^Y is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, or a nitrogen protecting group;

R^P is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted heteroaryl, an oxygen protecting group when attached to an oxygen atom, a sulfur protecting group when attached to a sulfur atom, or a nitrogen protecting group when attached to a nitrogen atom; and

R^L is optionally substituted C₁₋₅₀ alkyl, optionally substituted C₂₋₅₀ alkenyl, optionally substituted C₂₋₅₀ alkynyl, optionally substituted heteroC₁₋₅₀ alkyl, optionally substituted heteroC₂₋₅₀ alkenyl, optionally substituted heteroC₂₋₅₀ alkynyl, or a polymer.

82. The method of claim 81, wherein the polynucleotide is DNA or RNA.

83. The method of claim 82, wherein the RNA is RNAi, dsRNA, siRNA, shRNA, miRNA, or antisense RNA.

84. The method of claim 83, wherein upon delivery of the RNA into the cell, the RNA is able to interfere with the expression of a specific gene in the biological cell.