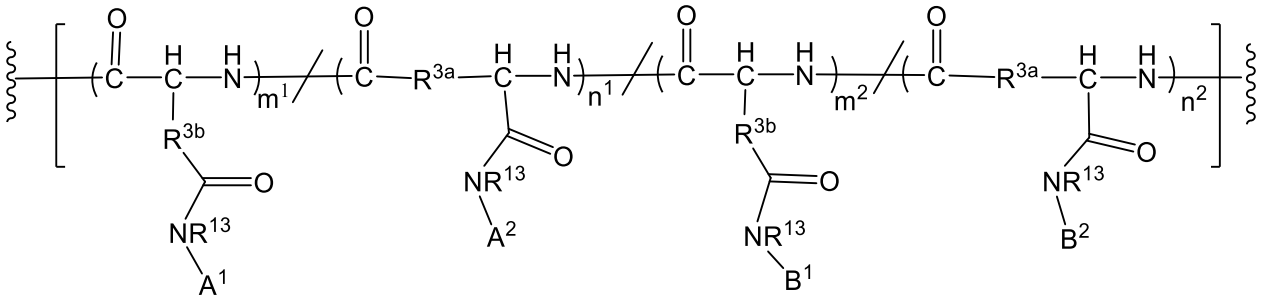
CLAIM(S):

1. A polymer comprising a structure of Formula 1:



wherein:

each of m^1 and n^1 is an integer from 0 to 1000;

each of m^2 and n^2 is an integer from 0 to 1000, provided that the sum of $m^2 + n^2$ is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^{3a} and R^{3b} are each independently a methylene or ethylene group;

each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

A^1 and A^2 are each independently a group of formula

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2_2$;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2_2]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]r_2R^2}; or

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2_2]$_2$}$_2$,

B^1 and B^2 are each independently

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-$(CH_2)_{s1}$-R^4-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-$(CH_2)_{s2}$-R^4-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$$(CH_2)_{s3}$-$R^4$-$R^5$};

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-$(CH_2)_{s4}$-R^4-R^5]$_2$}$_2$;

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-CH_2-CHOH-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-CH_2-CHOH-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$-CH_2-CHOH-R^5};

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-CH_2-CHOH-R^5]$_2$}$_2$;

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-$(CH_2)_{s1}$-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-$(CH_2)_{s2}$-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$$(CH_2)_{s3}$-$R^5$};

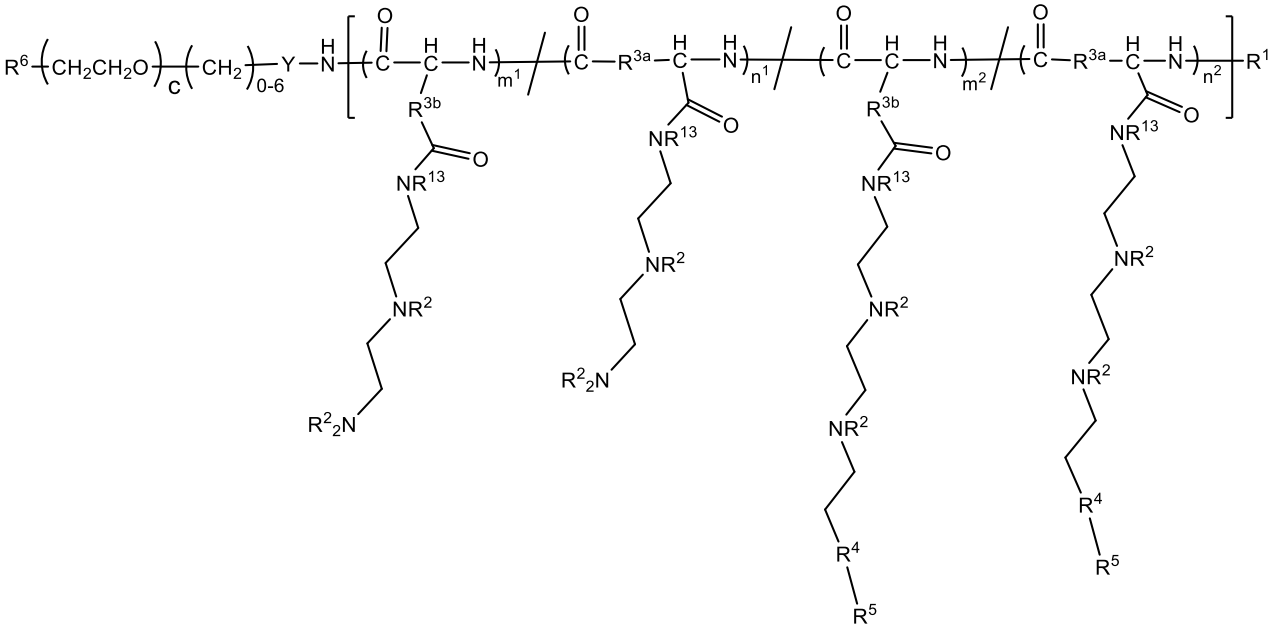
—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-$(CH_2)_{s4}$-R^5]$_2$}$_2$;

—$(CH_2)_{p1}$—[N{$(CH_2)_{s1}$-R^4-R^5}—$(CH_2)_{q1}$—]$_{r1}$$NR^2_2$; or

—$(CH_2)_{p1}$—[N{$(CH_2)_{s1}$-R^5}—$(CH_2)_{q1}$—]$_{r1}$$NR^2_2$,

wherein p1 to p4, q1 to q6, r1 and r2, and s1 to s4 are each independently an integer of 1 to 5; each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group; each instance of R^4 is independently -C(O)O-, -C(O)NH-, or -S(O)(O)-; and each instance of R^5 is independently an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 1 to 8 secondary or tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety.

2. The polymer of claim 1 having the structure of Formula 1A:



wherein

c is an integer from 0 to 50;

Y is optionally present and is a cleavable linker;

each of m^1 and n^1 is an integer from 0 to 1000;

each of m^2 and n^2 is an integer from 0 to 1000, provided that the sum of m^2 + n^2 is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^1 is hydrogen, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, or a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more substituents;

each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

R^{3a} and R^{3a} are each independently a methylene or ethylene group;

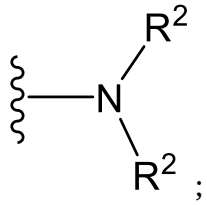
each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

each instance of R^4 is —C(O)O—, —C(O)NH—, or —S(O)(O)—;

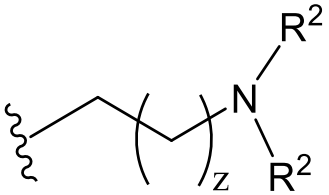
each instance of R^5 is independently an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 1 to 8 secondary or tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety; and

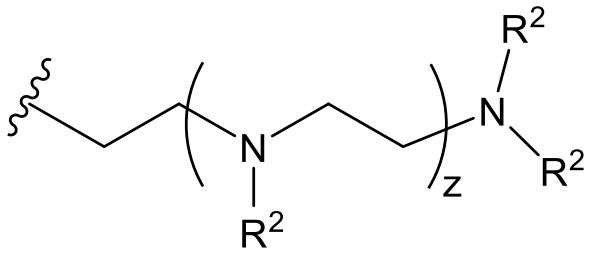
R^6 is hydrogen, an amino group, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more amines; or a tissue-specific or cell-specific targeting moiety.

3. The polymer of claim 1 or 2, wherein each R^5 is independently:

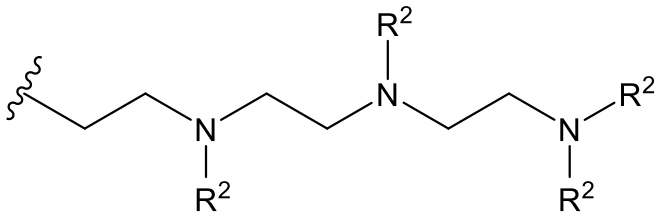


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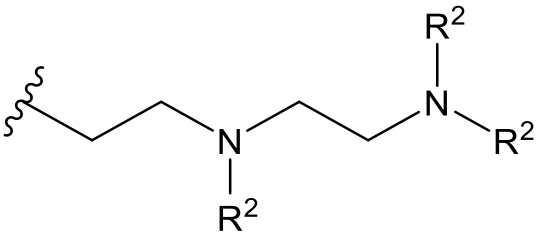




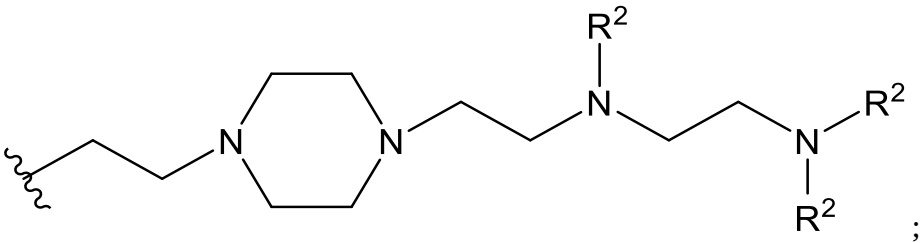
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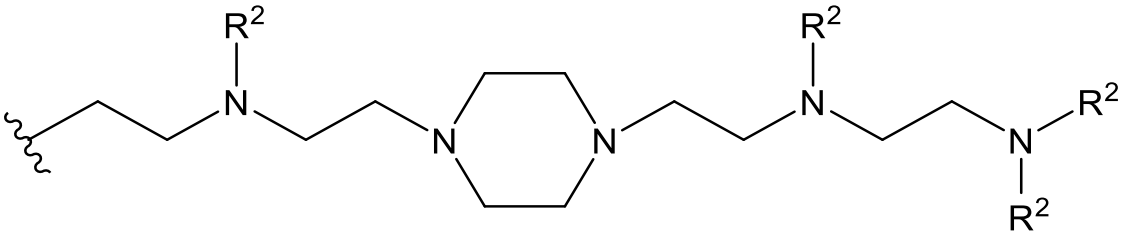
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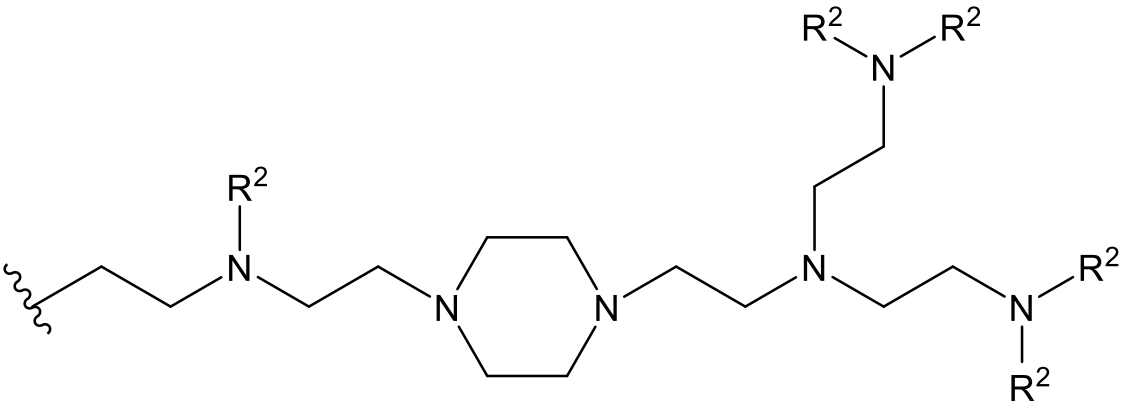
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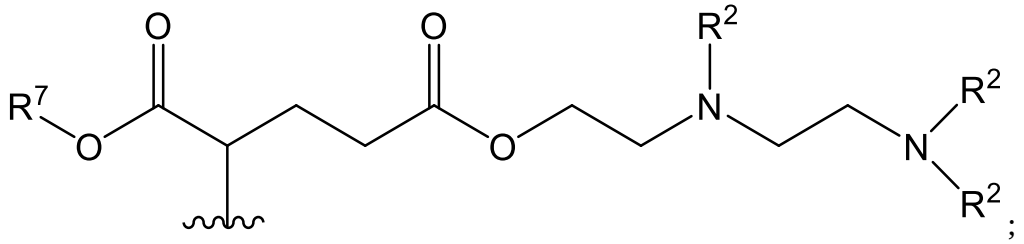
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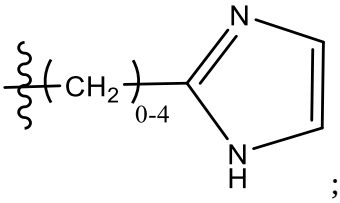
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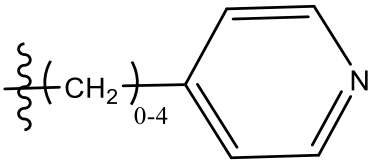
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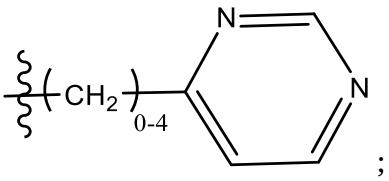
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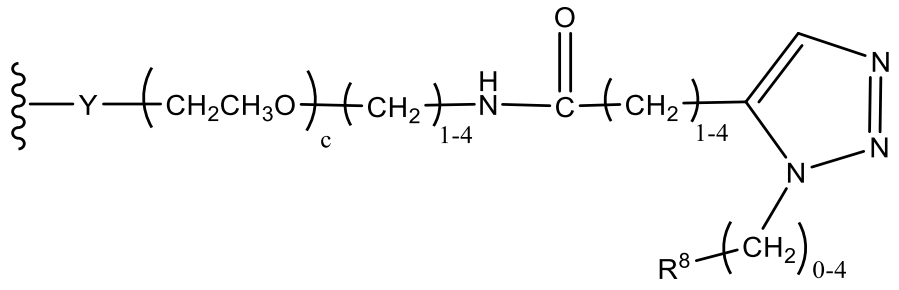
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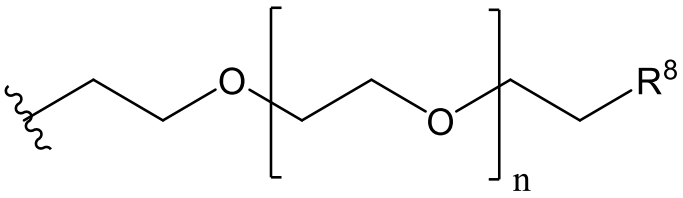
;



;



; and



,

wherein

each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

R^7 is a C_1-C_{50} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group optionally substituted with one or more amines; C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group

z is an integer from 1 to 5;

c is an integer from 0 to 50;

Y is optionally present and is a cleavable linker;

n is an integer from 0 to 50; and

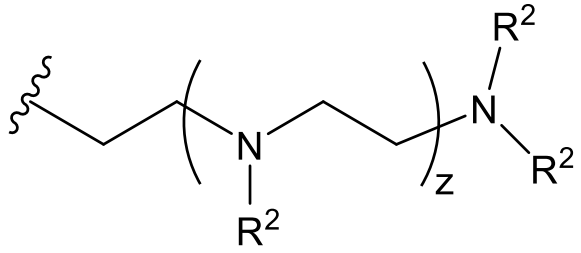
R^8 is a tissue-specific or cell-specific targeting moiety.

4. The polymer of any of claims 1-3, wherein each of A^1 and A^2 is a group of formula —$(CH_2)_{p1}$—[NH—$(CH_2)_{q1}$—]$_{r1}NH_2$, and each of B^1 and B^2 is a group of formula—$(CH_2)_{p1}$—[NH—$(CH_2)_{q1}$—]$_{r1}$NH-$(CH_2)_2$-R^4-R^5.

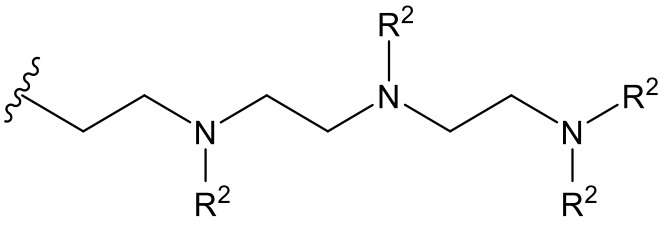
5. The polymer of any of claims 1-4, wherein each of A^1 and A^2 is a group of formula –$(CH_2)_2$-NH-$(CH_2)_2$-NH_2, and each of B^1 and B^2 is a group of formula–$(CH_2)_2$-NH-$(CH_2)_2$-NH-$(CH_2)_2$-R^4-R^5.

6. The polymer of any of claims 1-5, wherein R^4 is –C(O)-O-.

7. The polymer of any of claims 1-6, wherein R^5 is



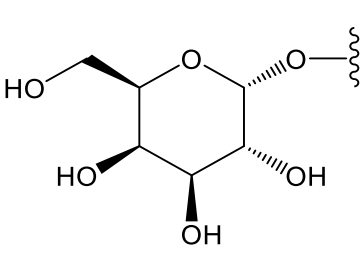
or



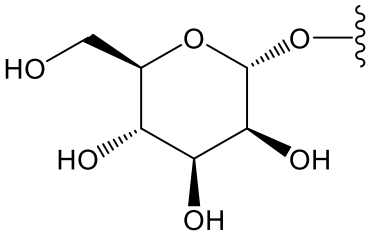
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8. A polymer of any of claims 1-7, wherein the ratio of $(m^1+n^1)/(m^2+n^2)$ is about 20 or less, and, optionally, about 0.2 or more.

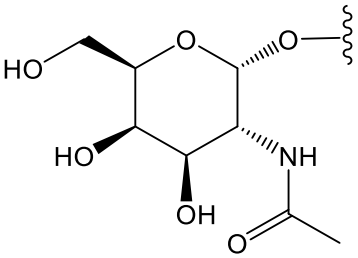
9. The polymer of any one of claims 1-6 or 8, wherein the tissue-specific or cell-specific targeting moiety is:



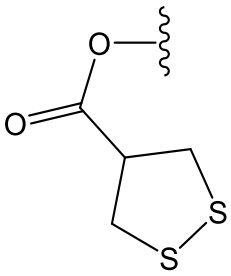
alpha-d-galactose ;



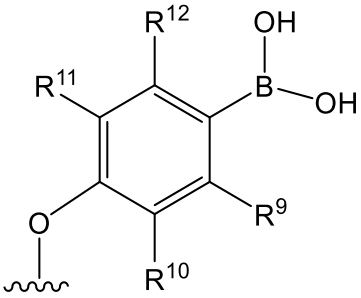
alpha-d-mannose ;



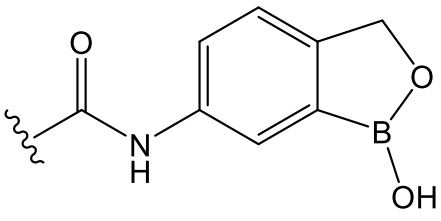
N-acetylgalactosamine ;



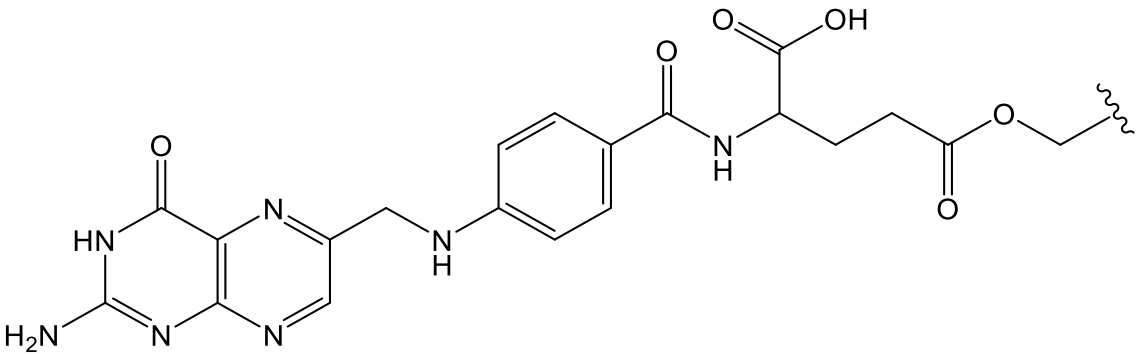
Asparagusic acid ;



Phenylboronic acid ;



; or

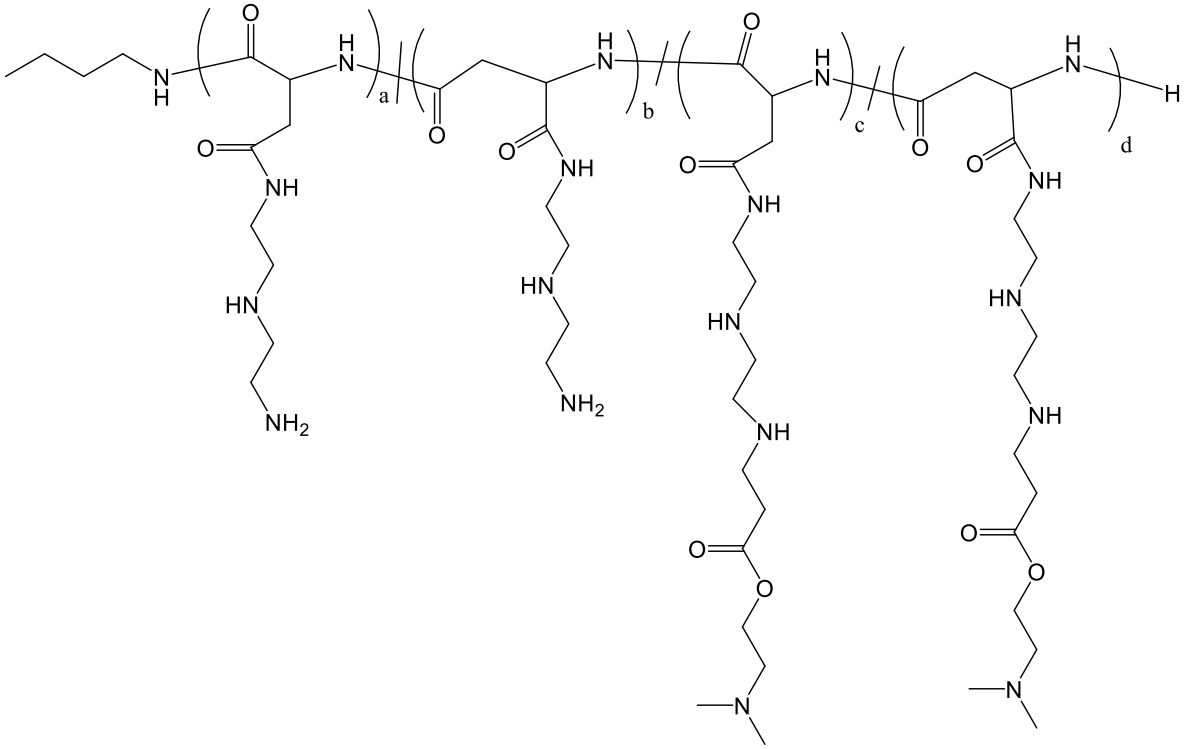


folic acid ,

wherein each of R^9, R^{10}, R^{11}, and R^{12} is independently hydrogen, halogen, C_1-C_4 alkyl, or C_1-C_4 alkoxy, optionally substituted with one or more amino groups.

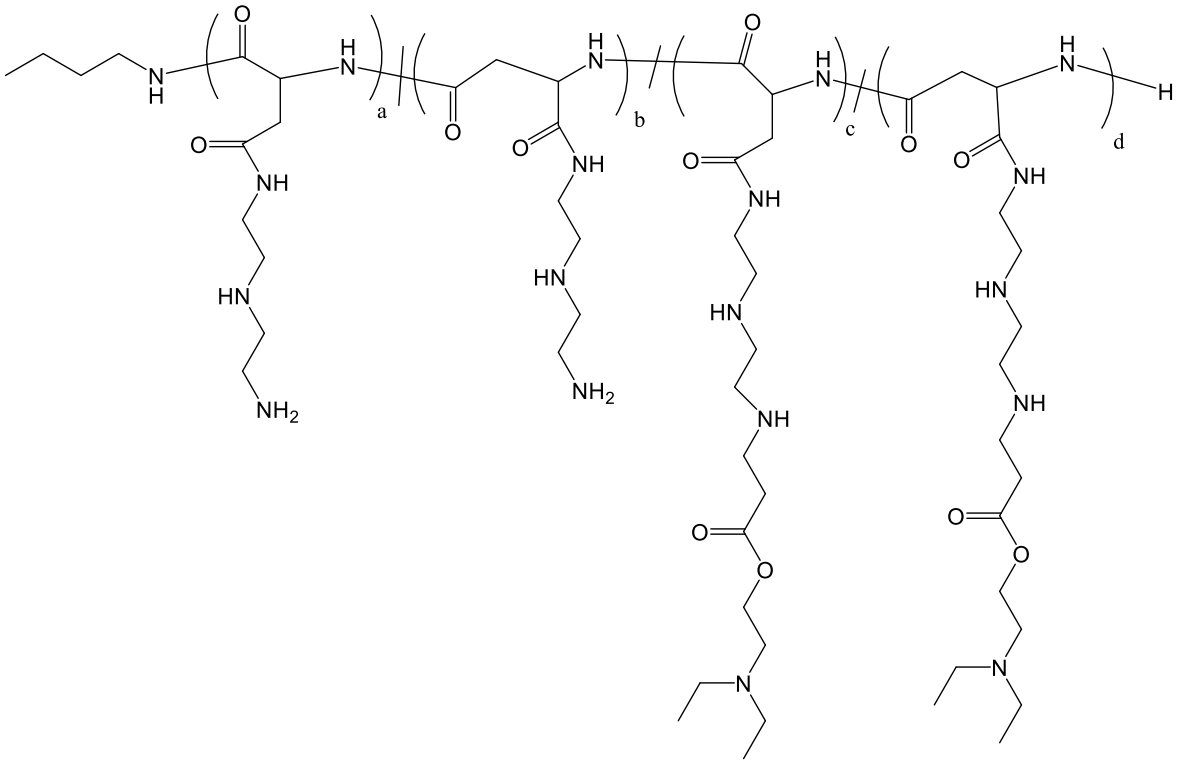
10. The polymer of any of claims 1-9, wherein the polymer is a cationic polymer.

11. The polymer of claim 1 having the formula:



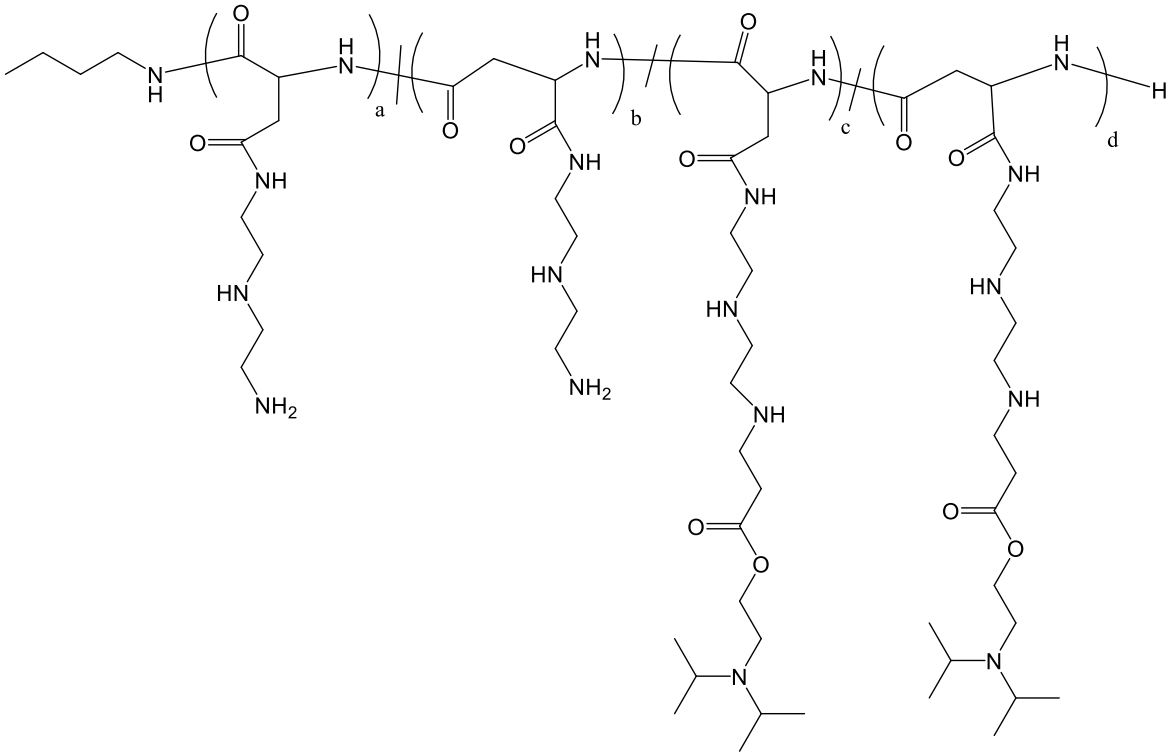
Polymer 1

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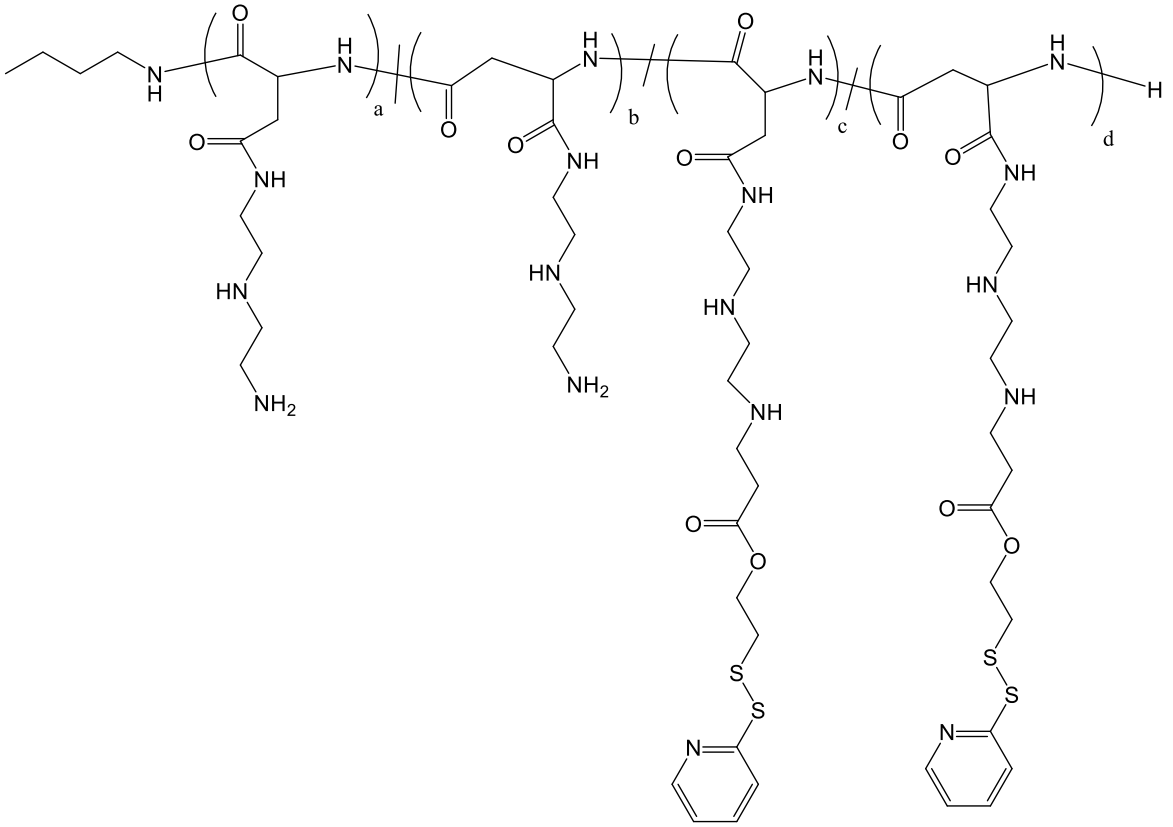
Polymer 2

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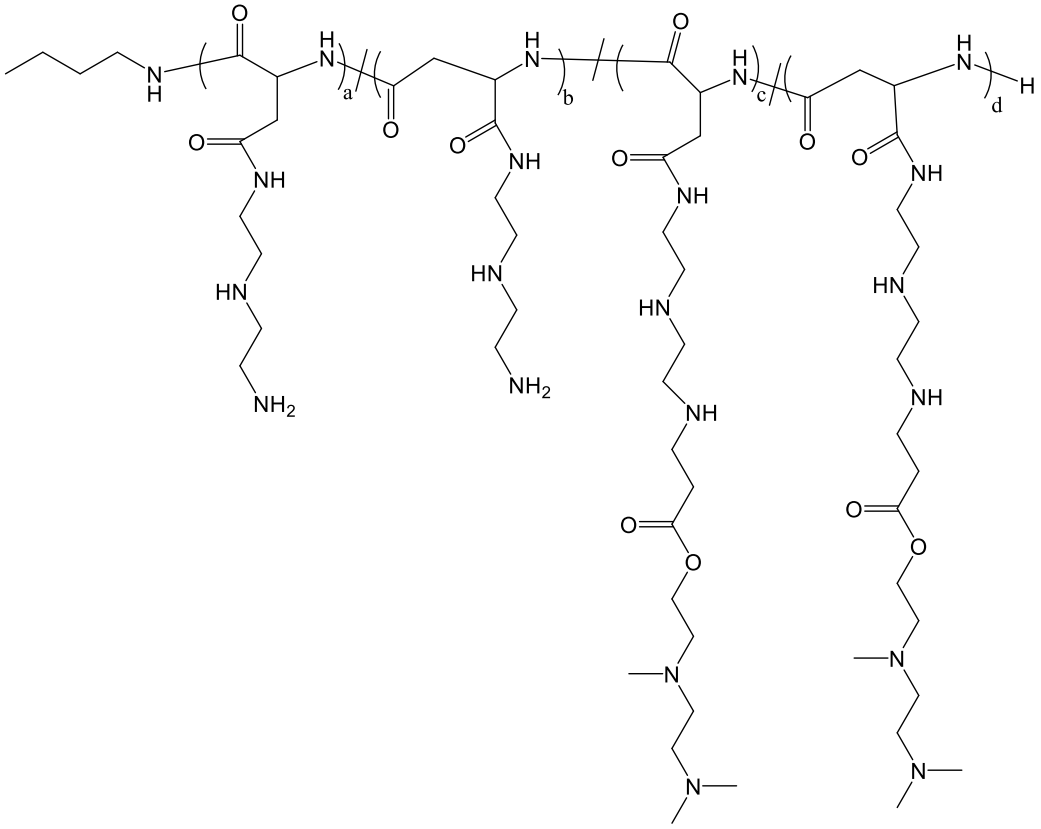
Polymer 3

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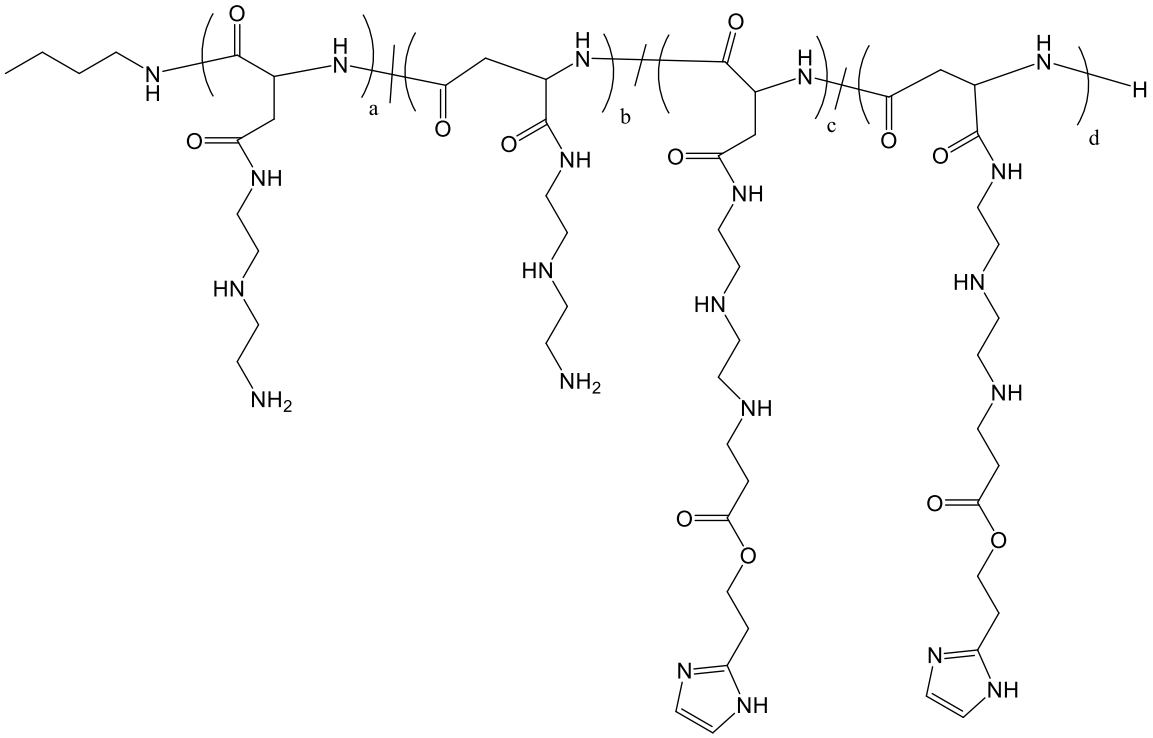
Polymer 4

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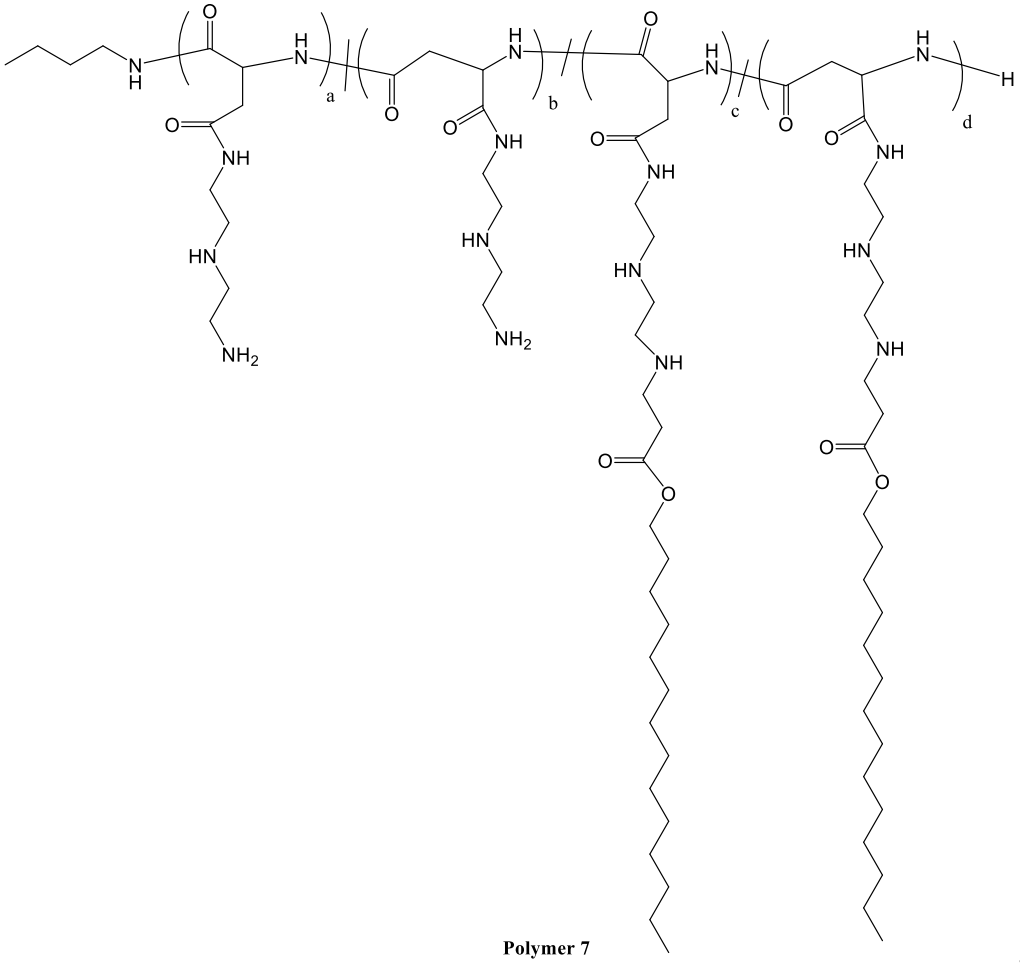
Polymer 5

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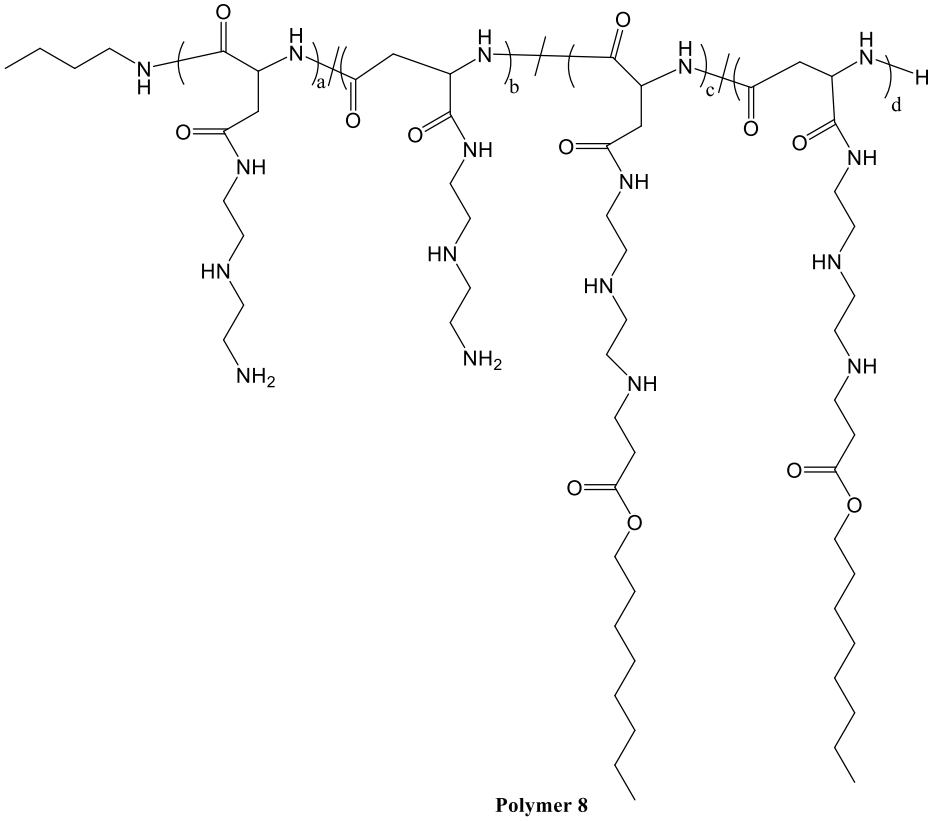
Polymer 6

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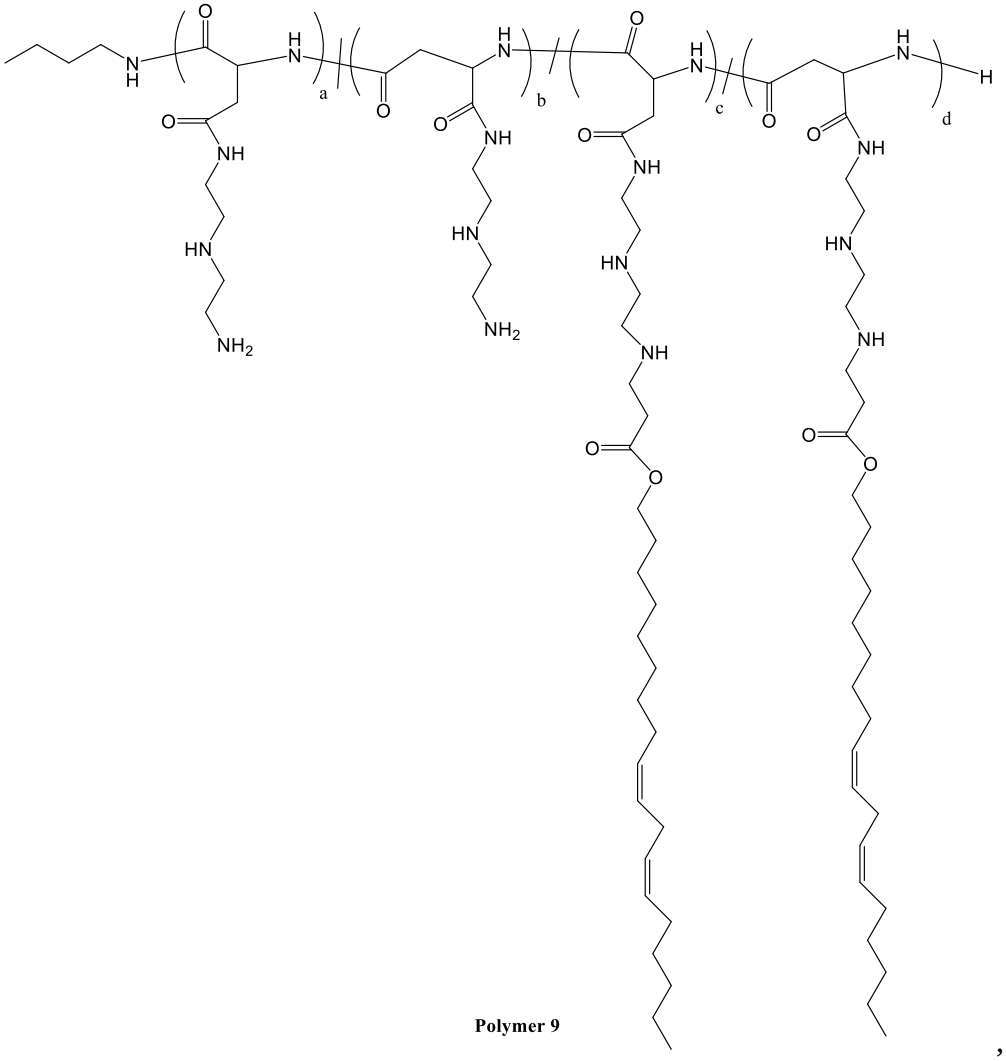
Polymer 7

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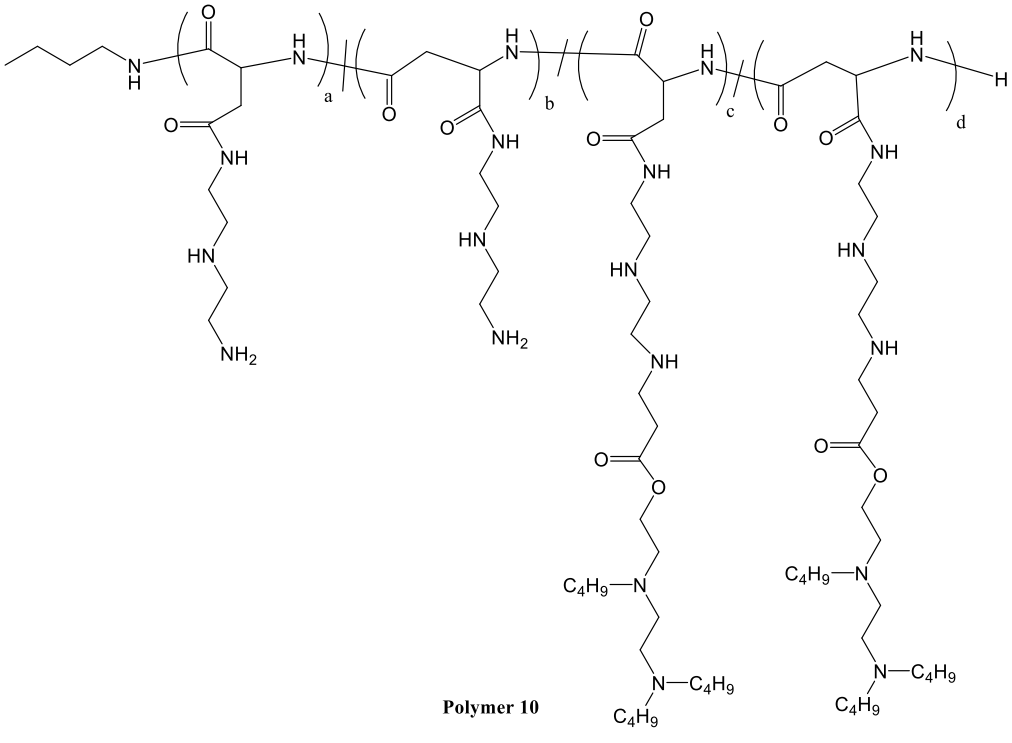
Polymer 8

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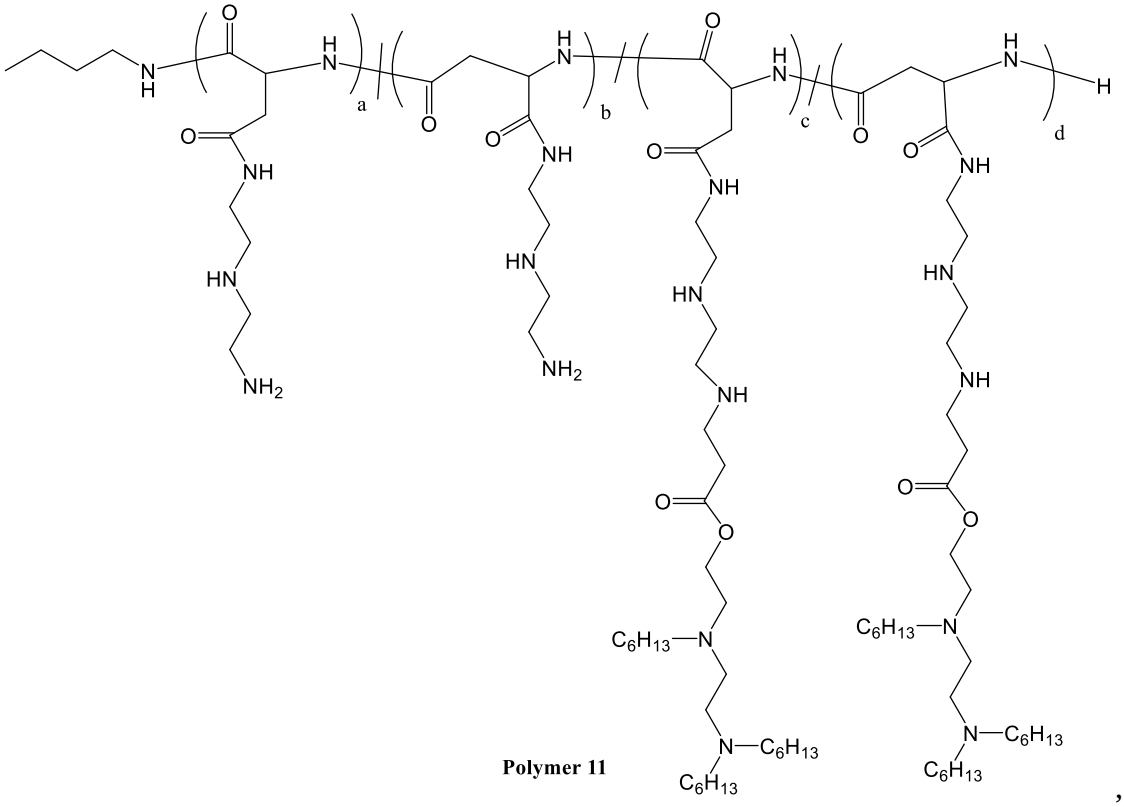
Polymer 9

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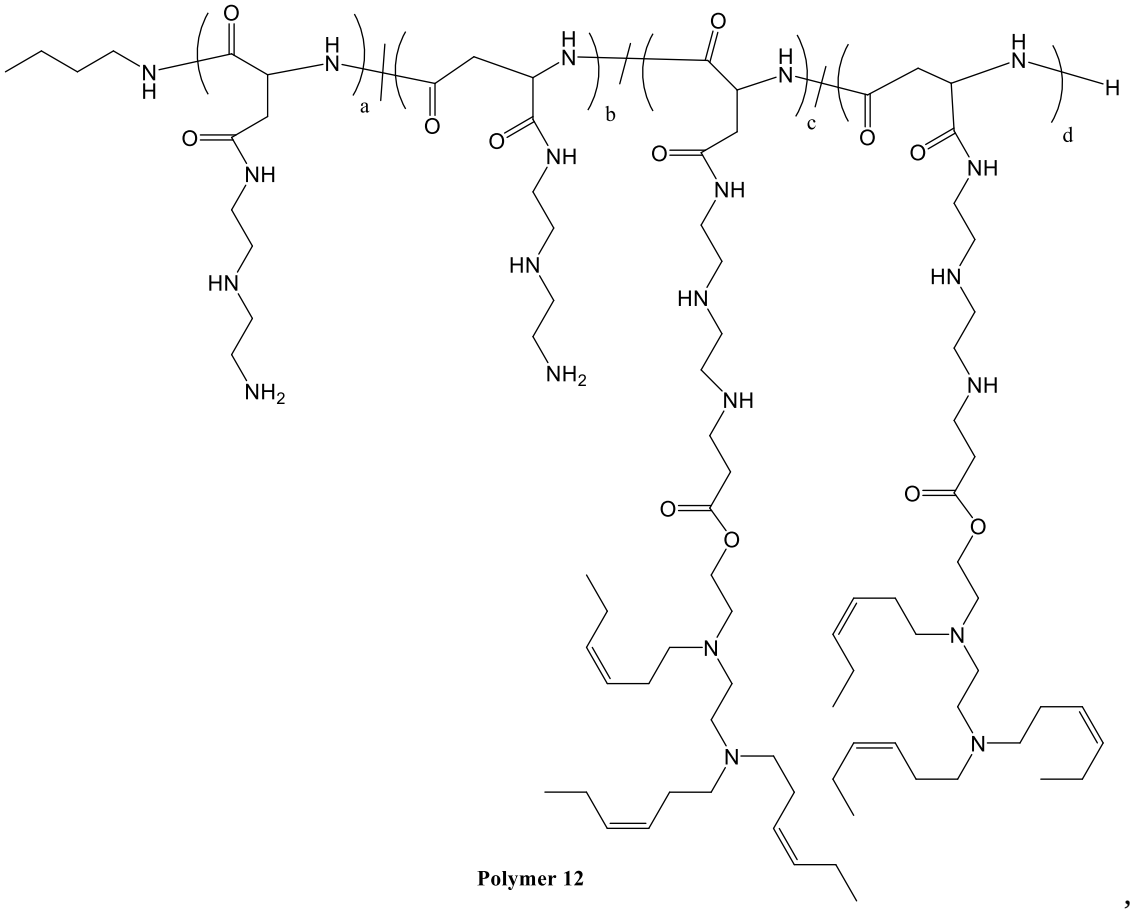
Polymer 10

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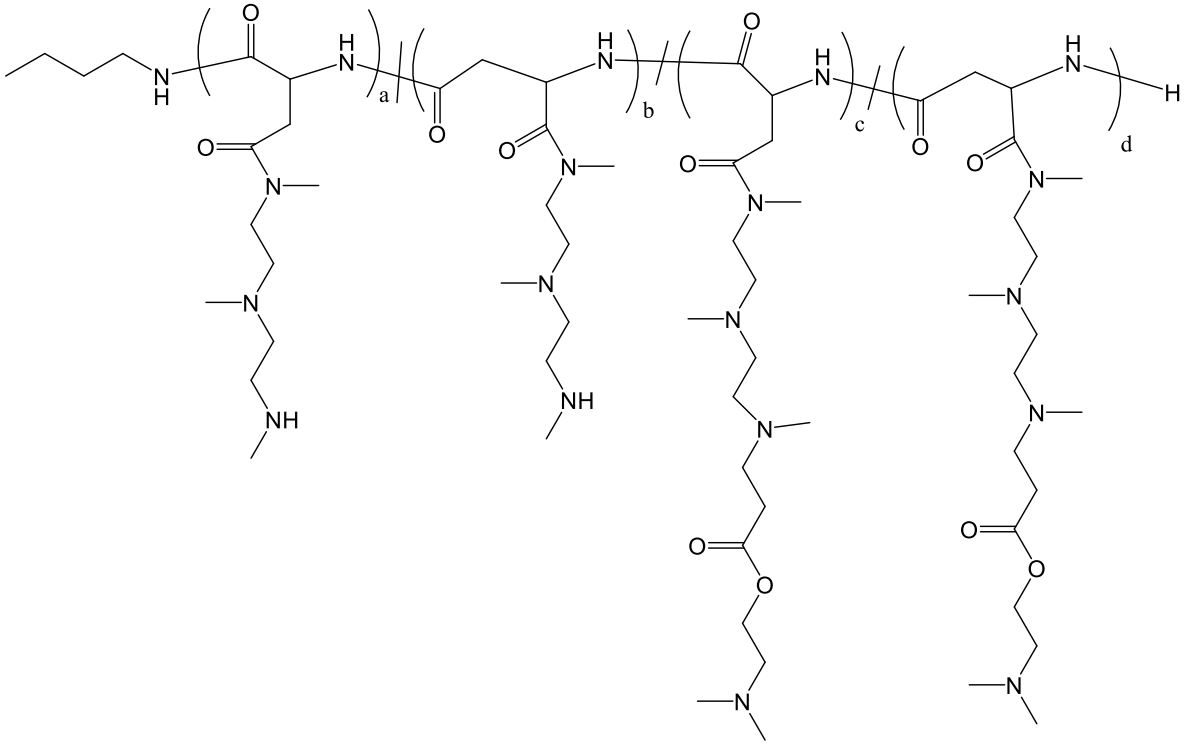
Polymer 11

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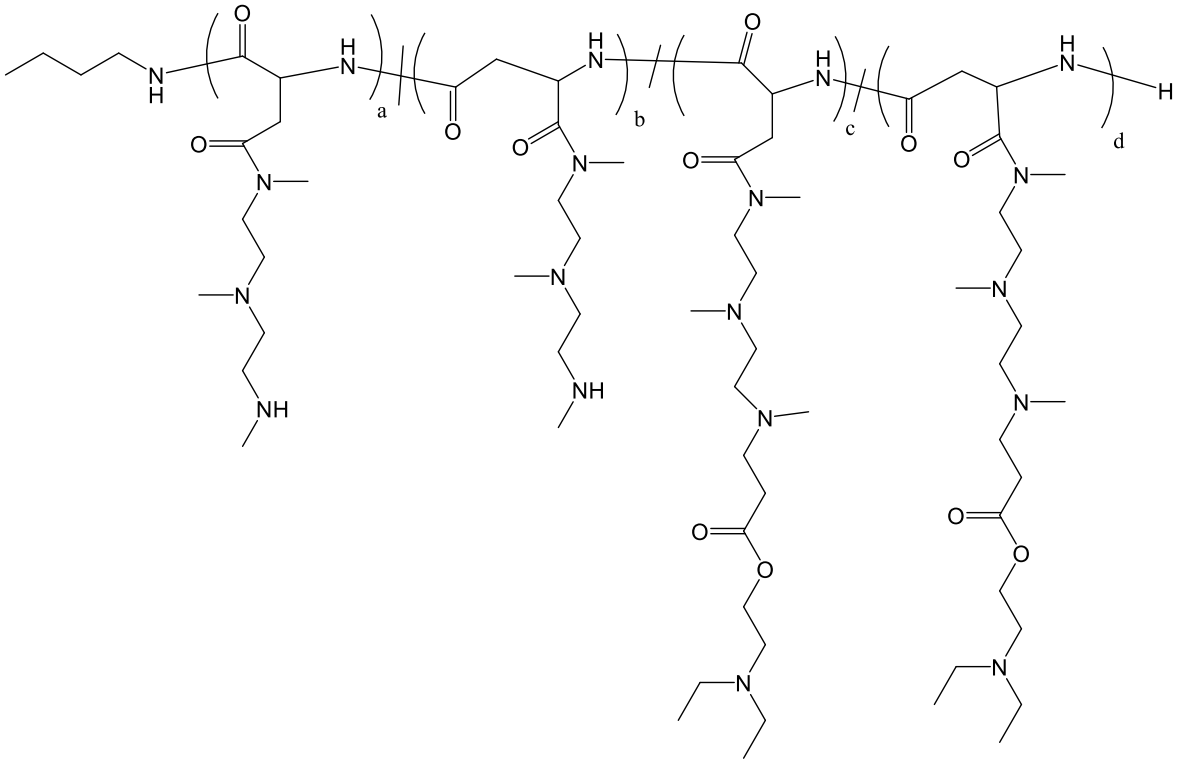
Polymer 12

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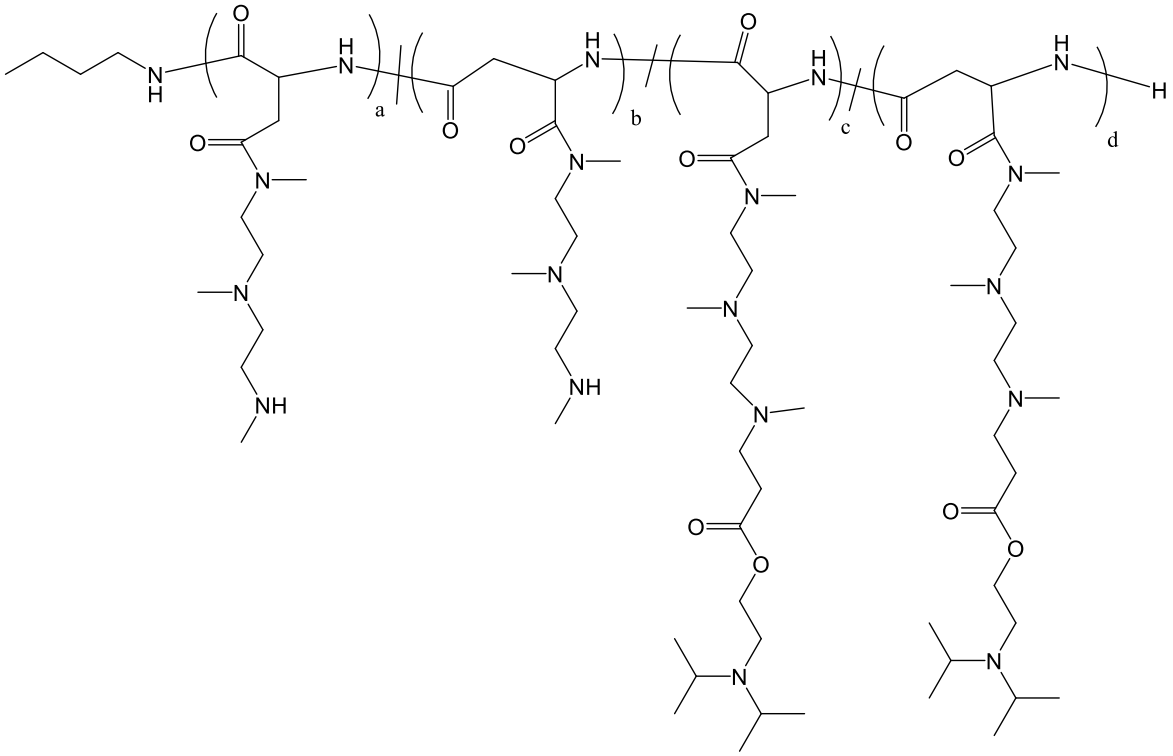
Polymer 13

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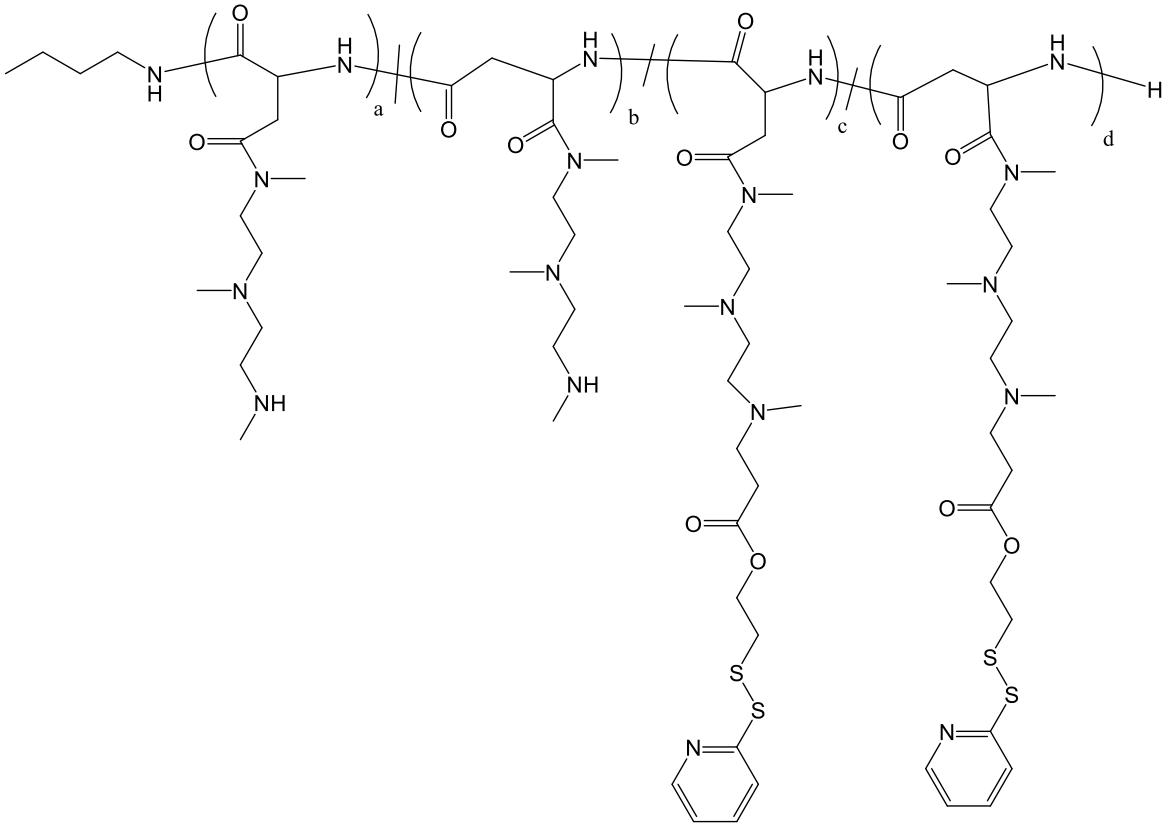
Polymer 14

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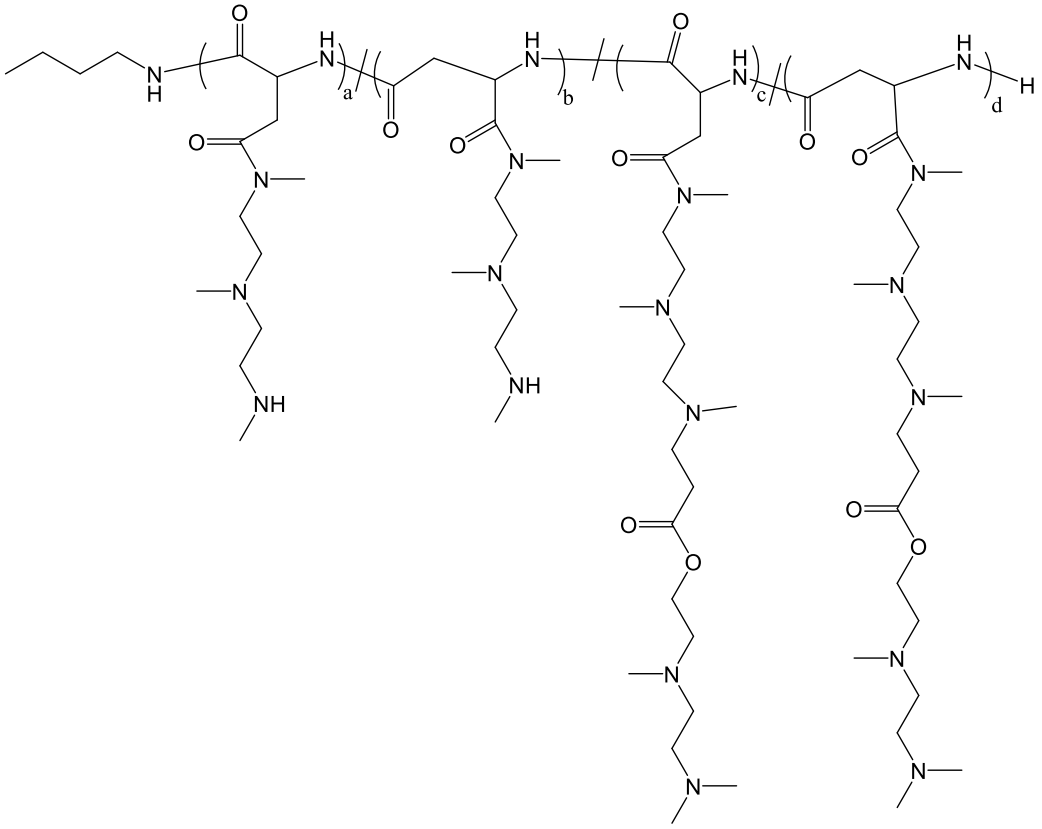
Polymer 15

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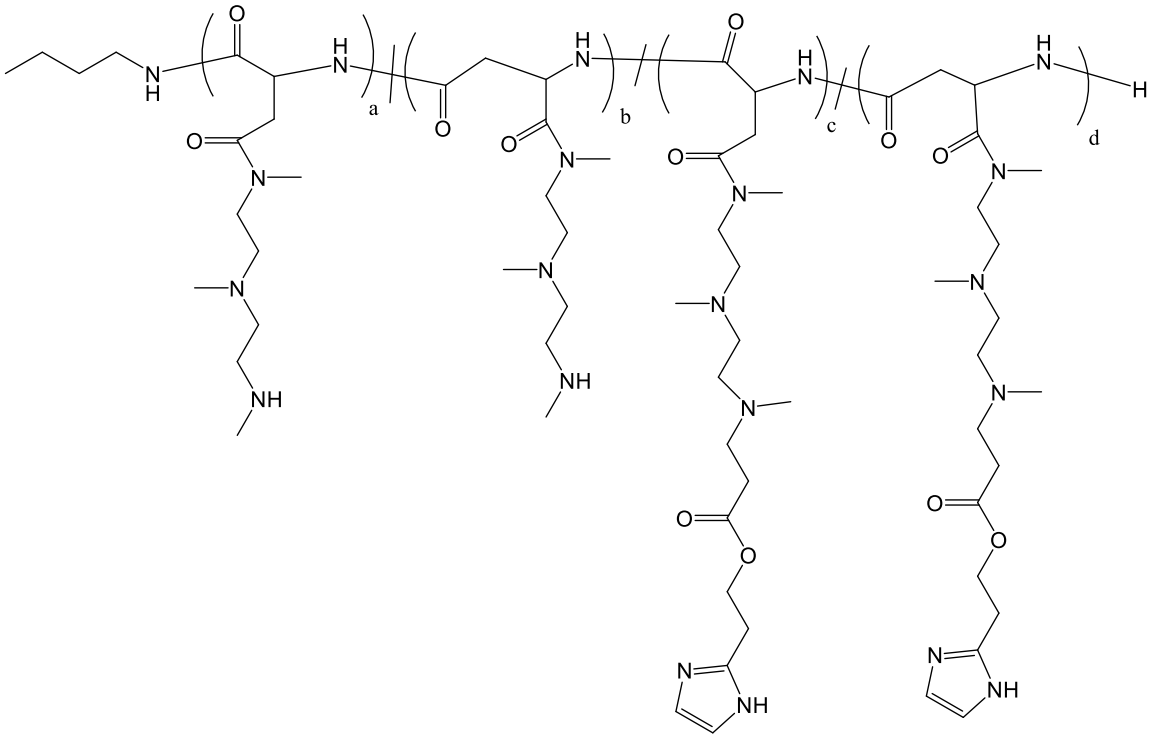
Polymer 16

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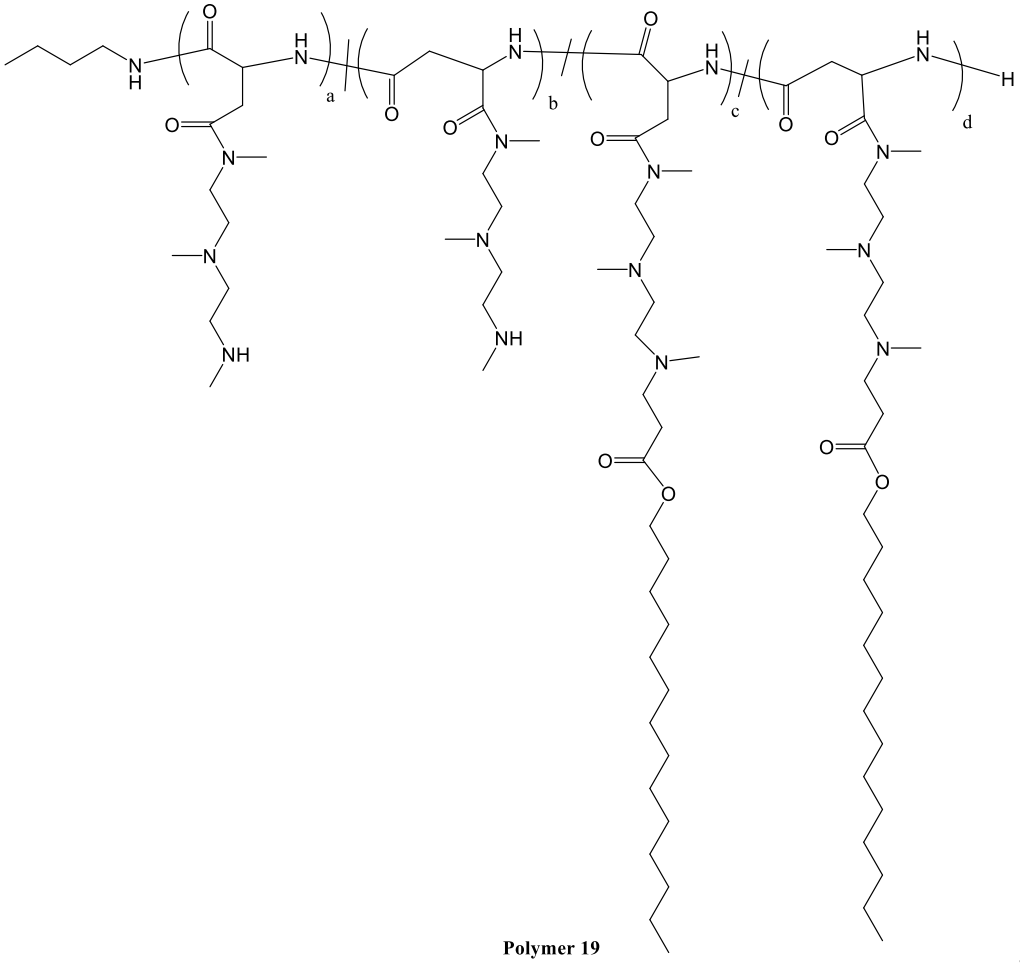
Polymer 17

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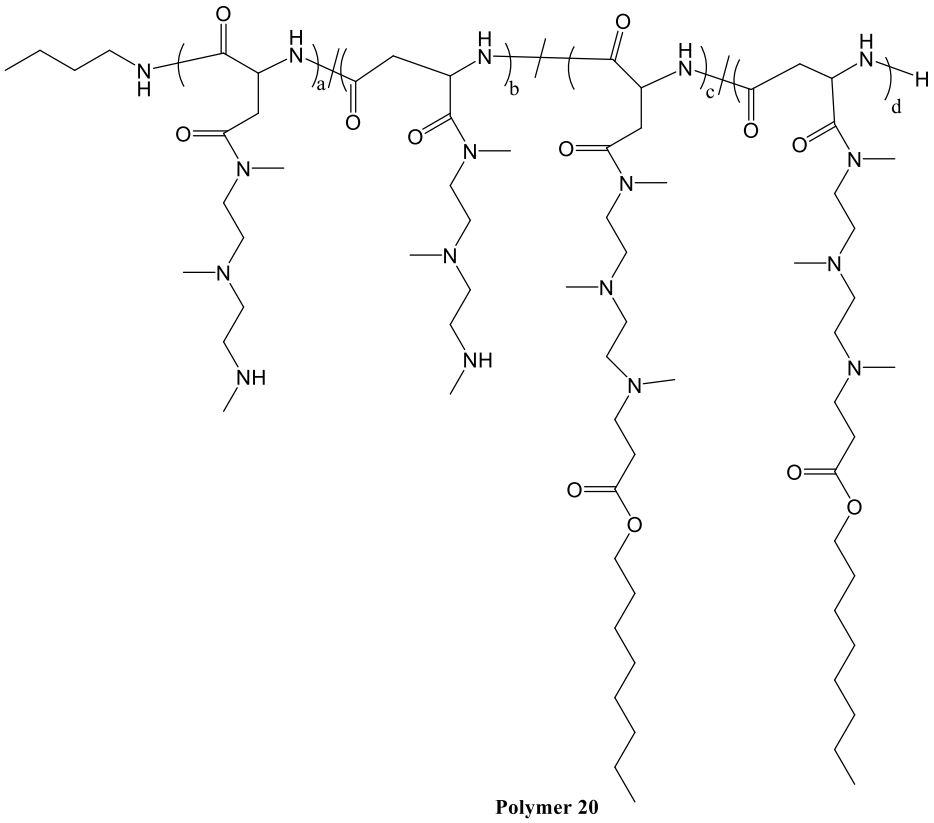
Polymer 18

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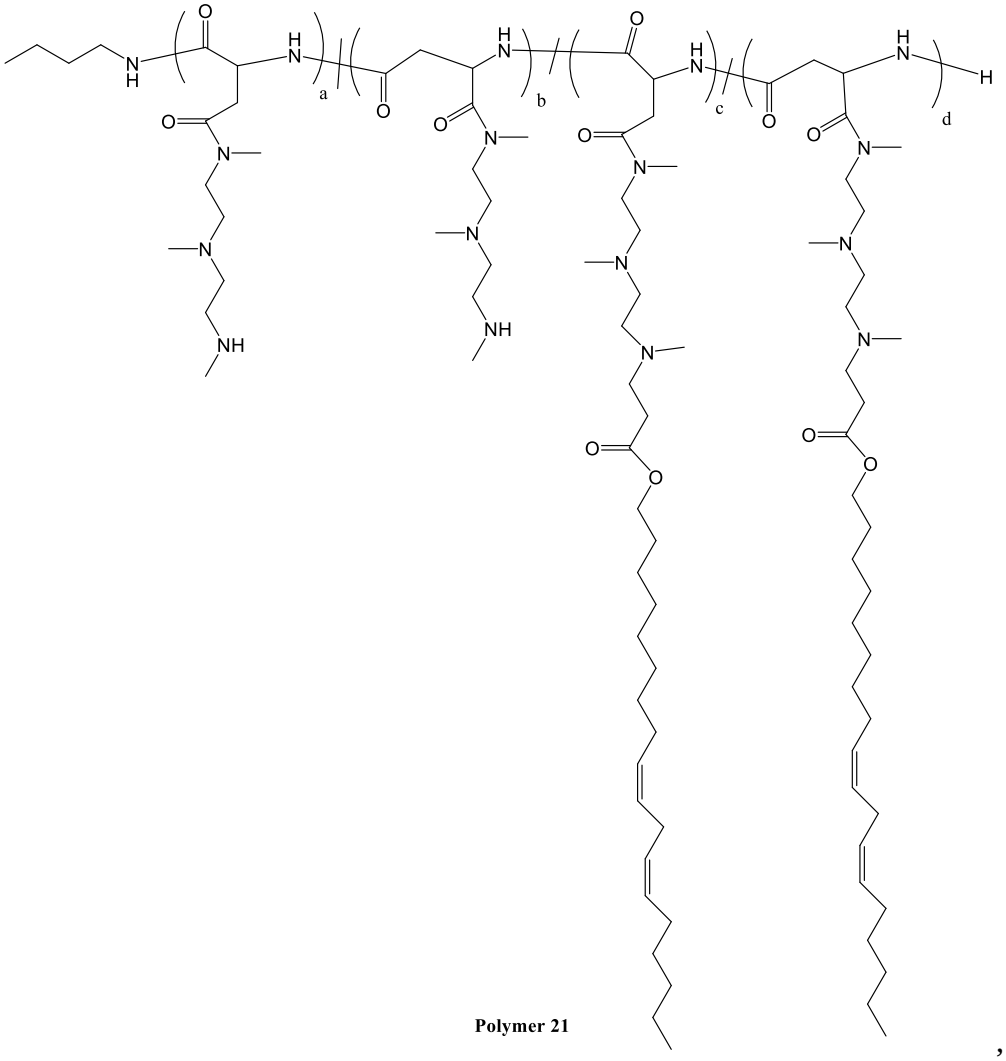
Polymer 19

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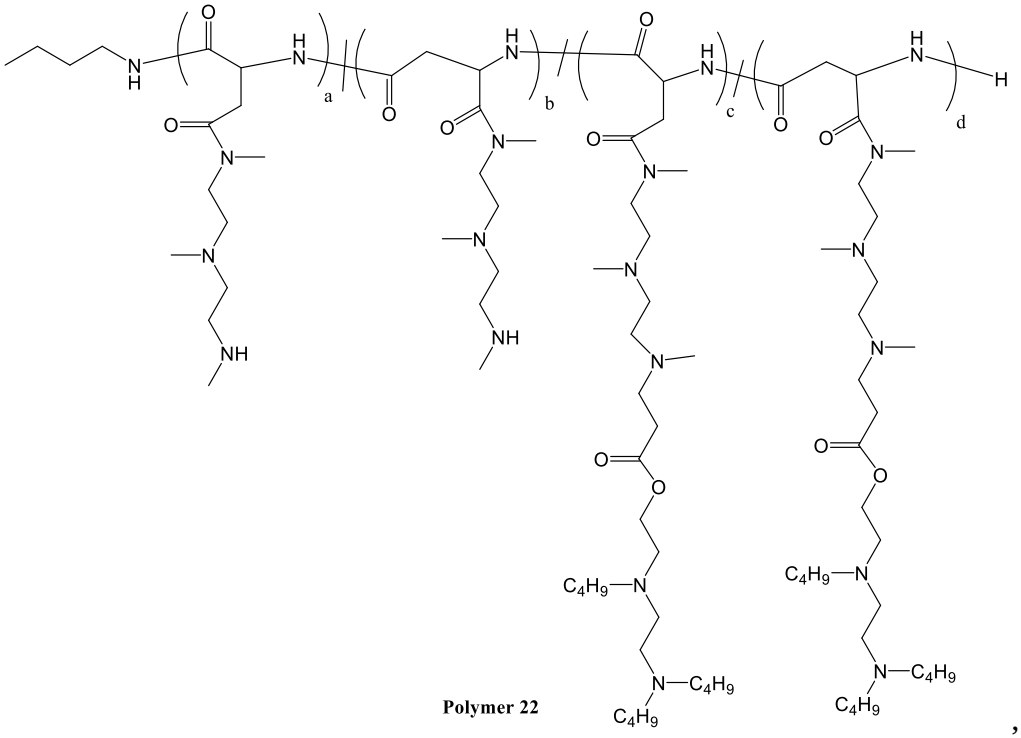
Polymer 20

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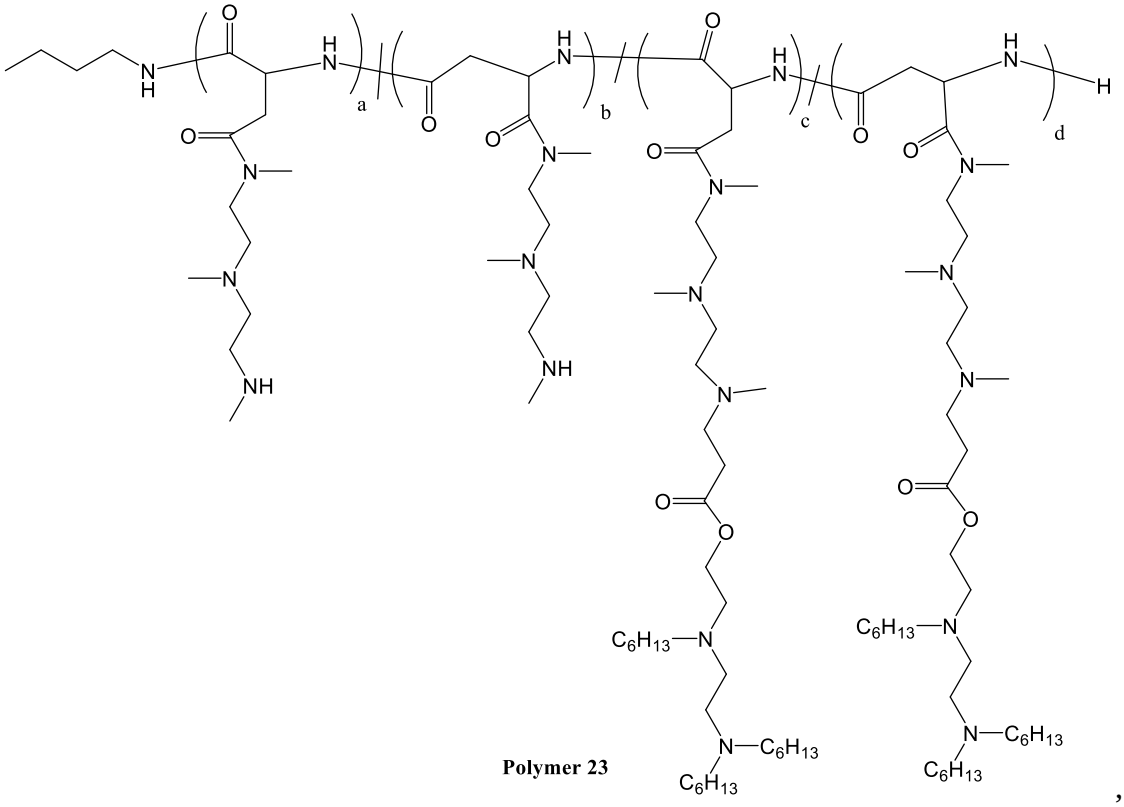
Polymer 21

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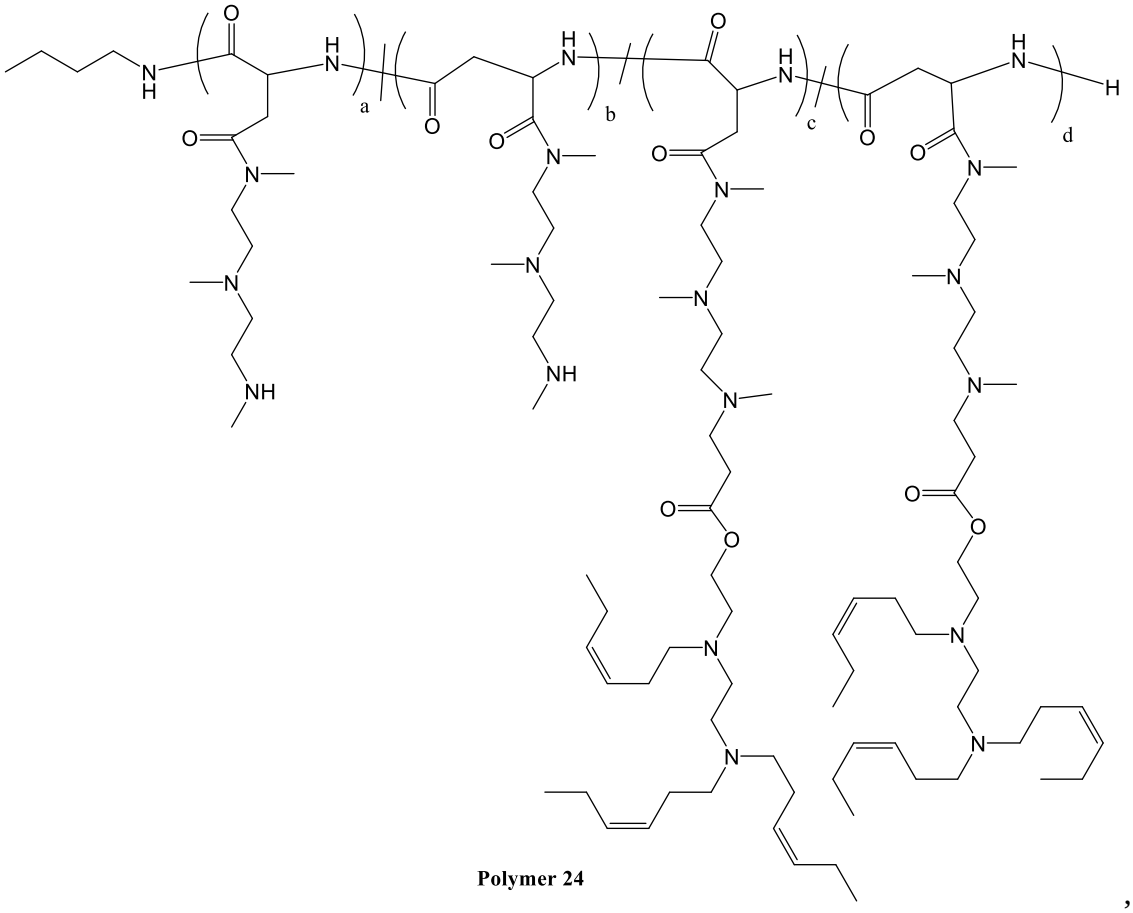
Polymer 22

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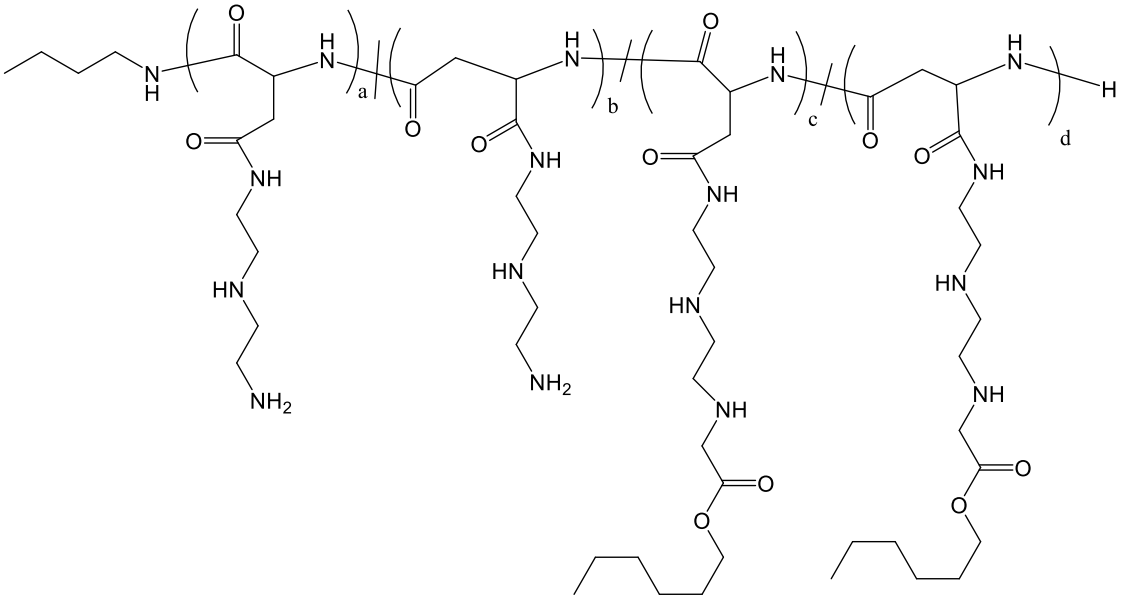
Polymer 23

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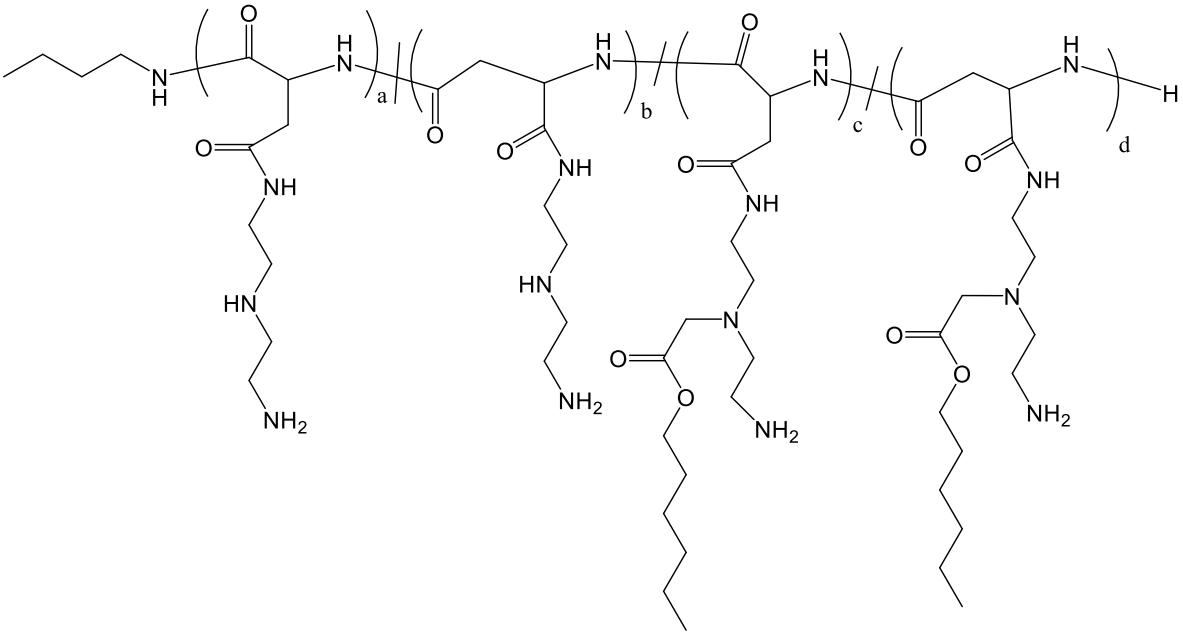
Polymer 24

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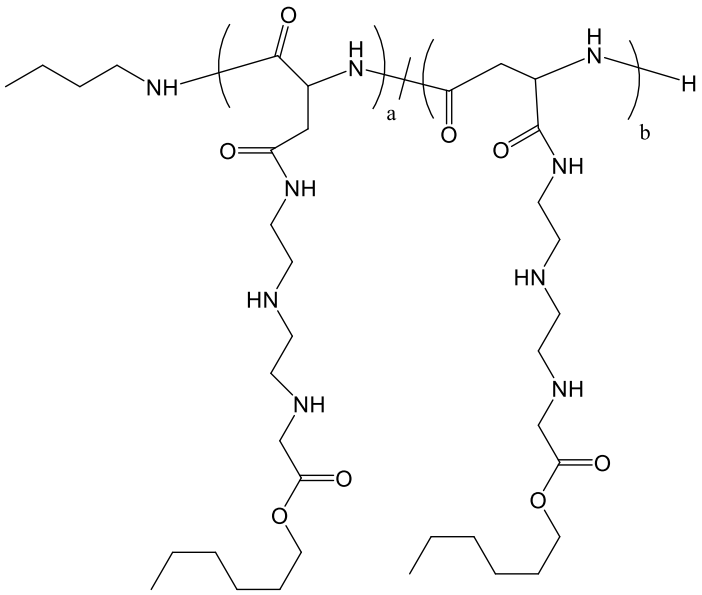
Polymer 28

, or



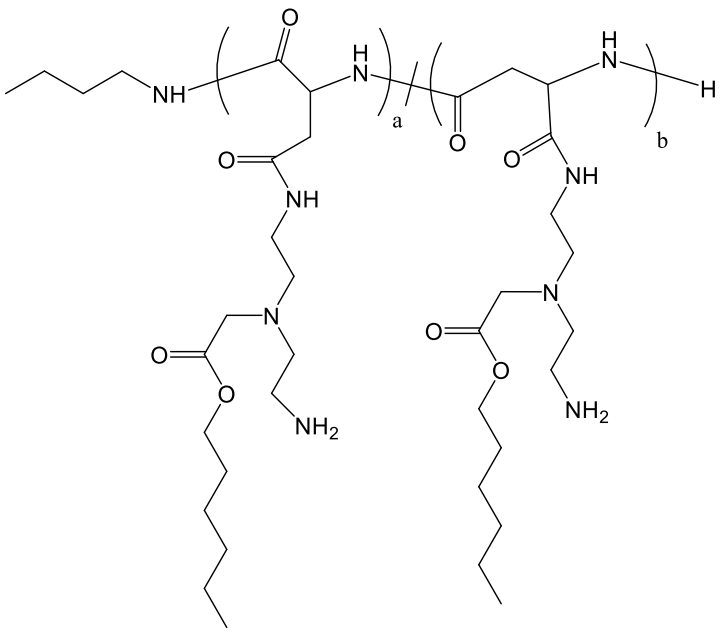
Polymer 29

,wherein (a+b) is from about 0 to about 75 and (c+d) is from about 5 to about 80, or



Polymer 37

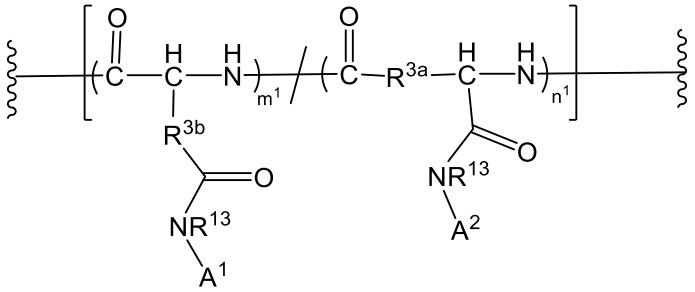
, or



Polymer 38

wherein (a+b) is from about 5 to about 160.

12. A method of preparing a polymer of any one of claims 1-11, the method comprising modifying at least a portion of groups A^1 and/or A^2 of a polymer comprising a structure of Formula 3:



wherein:

each of m^1 and n^1 is an integer from 0 to 1000, provided that $m^1 + n^1$ is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^{3a} and R^{3b} are each independently a methylene or ethylene group;

each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

A^1 and A^2 are each independently a group of formula

$—(CH_2)_{p1}—[NR^2—(CH_2)_{q1}—]_{r1}NR^2_2$;

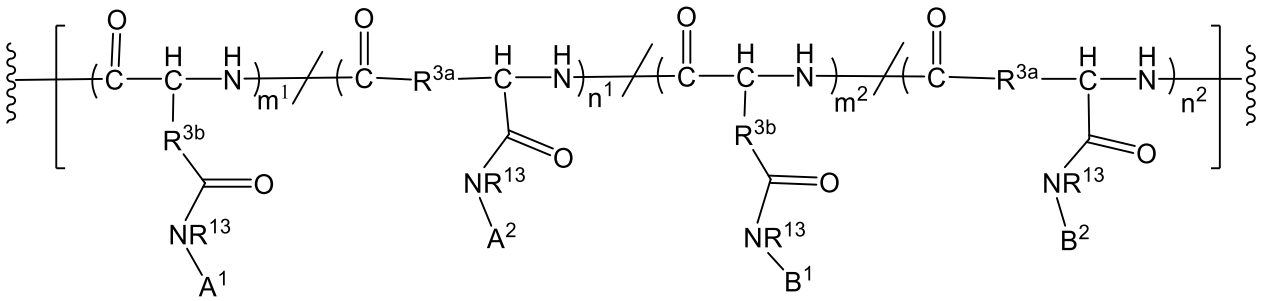
$—(CH_2)_{p2}—N[—(CH_2)_{q2}—NR^2_2]_2$;

$—(CH_2)_{p3}—N\{[—(CH_2)_{q3}—NR^2_2][—(CH_2)_{q4}—NR^2—]r_2R^2\}$; or

$—(CH_2)_{p4}—N\{—(CH_2)_{q5}—N[—(CH_2)_{q6}—NR^2_2]_2\}_2$,

wherein p1 to p4, q1 to q6, and r1 and r2 are each independently an integer of 1 to 5; and each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group,

to produce a polymer comprising a structure of Formula 1:



wherein:

each of m^1 and n^1 is an integer from 0 to 1000;

each of m^2 and n^2 is an integer from 0 to 1000, provided that the sum of $m^2 + n^2$ is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^{3a} and R^{3b} are each independently a methylene or ethylene group;

each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

A^1 and A^2 are each independently a group of formula

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2_2$;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2_2]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}R^2$}; or

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2_2]$_2$}$_2$,

B^1 and B^2 are each independently

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-$(CH_2)_{s1}$-R^4-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-$(CH_2)_{s2}$-R^4-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$$(CH_2)_{s3}$-$R^4$-$R^5$};

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-$(CH_2)_{s4}$-R^4-R^5]$_2$}$_2$;

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-CH_2-CHOH-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-CH_2-CHOH-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$-CH_2-CHOH-R^5};

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-CH_2-CHOH-R^5]$_2$}$_2$;

—$(CH_2)_{p1}$—[NR^2—$(CH_2)_{q1}$—]$_{r1}NR^2$-$(CH_2)_{s1}$-R^5;

—$(CH_2)_{p2}$—N[—$(CH_2)_{q2}$—NR^2-$(CH_2)_{s2}$-R^5]$_2$;

—$(CH_2)_{p3}$—N{[—$(CH_2)_{q3}$—NR^2_2][—$(CH_2)_{q4}$—NR^2—]$_{r2}$$(CH_2)_{s3}$-$R^5$};

—$(CH_2)_{p4}$—N{—$(CH_2)_{q5}$—N[—$(CH_2)_{q6}$—NR^2-$(CH_2)_{s4}$-R^5]$_2$}$_2$;

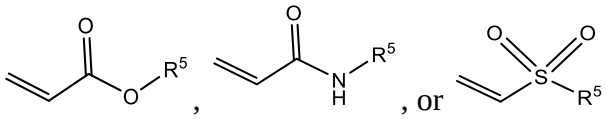
—$(CH_2)_{p1}$—[N{$(CH_2)_{s1}$-R^4-R^5}—$(CH_2)_{q1}$—]$_{r1}NR^2_2$; or

—$(CH_2)_{p1}$—[N{$(CH_2)_{s1}$-R^5}—$(CH_2)_{q1}$—]$_{r1}NR^2_2$,

wherein p1 to p4, q1 to q6, r1 and r2, and s1 to s4 are each independently an integer of 1 to 5; each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group; each instance of R^4 is independently -C(O)O-, -C(O)NH-, or -S(O)(O)-; and each instance of R^5 is independently an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 1 to 8 secondary or tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety.

13. The method of claim 12, wherein group A^1 and/or A^2 of the polymer comprising a structure of Formula 3 are modified by a Michael addition reaction between the polymer comprising the structure of Formula 3 and an acrylate, an acrylamide, a vinyl sulfone, or a combination thereof.

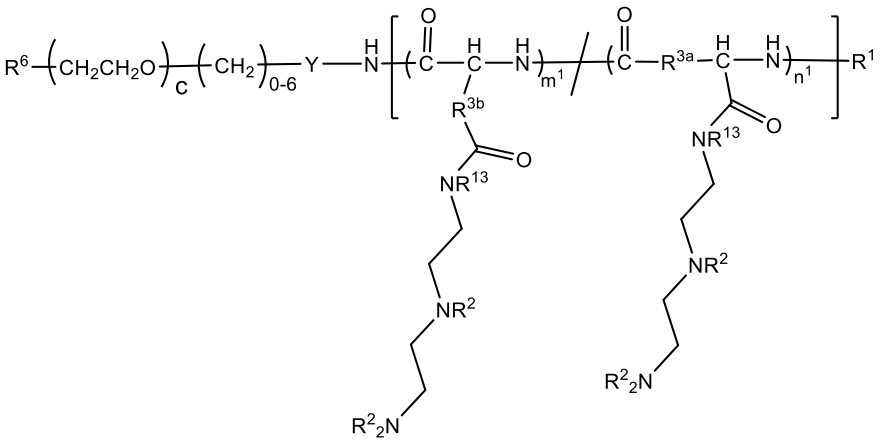
14. The method of claim 13, wherein the acrylate, acrylamide, or vinyl sulfone is of the formula:



, , or

wherein R^5 is an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 1 to 8 secondary or tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety.

15. The method of any one of claims 12-14, wherein the polymer comprising the structure of Formula 3 is a polymer of Formula 3A:



wherein,

c is an integer from 0 to 50;

Y is optionally present and is a cleavable linker;

each of m^1 and n^1 is an integer from 0 to 1000; provided that the sum of $m^1 + n^1$ is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^1 is hydrogen, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, or a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more substituents;

each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

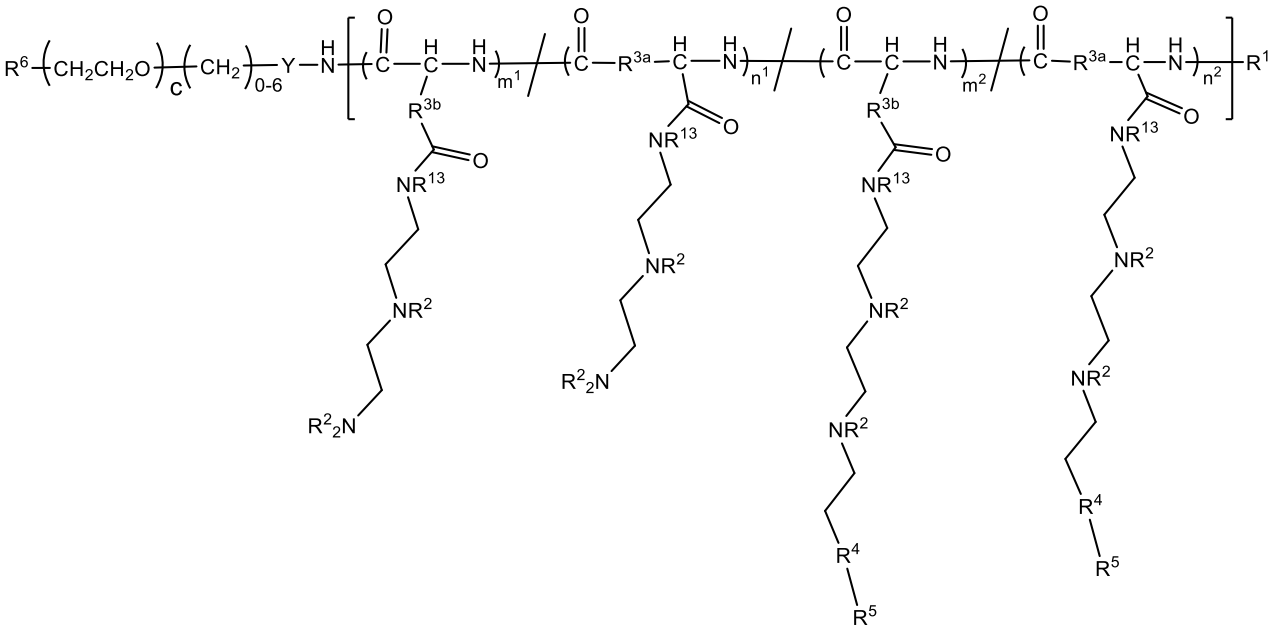
R^{3a} and R^{3a} are each independently a methylene or ethylene group; and

R^6 is hydrogen, an amino group, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more amines; or a tissue-specific or cell-specific targeting moiety;

each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

and

the polymer comprising a structure of Formula 1 is a polymer of Formula 1A:



wherein

c is an integer from 0 to 50;

Y is optionally present and is a cleavable linker;

each of m^1 and n^1 is an integer from 0 to 1000;

each of m^2 and n^2 is an integer from 0 to 1000, provided that the sum of $m^2 + n^2$ is greater than 5;

the symbol "/" indicates that the units separated thereby are linked randomly or in any order;

R^1 is hydrogen, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, or a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more substituents;

each instance of R^2 is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group;

R^{3a} and R^{3a} are each independently a methylene or ethylene group;

each instance of R^4 is —C(O)O—, —C(O)NH—, or —S(O)(O)—;

each instance of R^5 is independently an alkyl group, cycloalkyl group, alkenyl group, cycloalkenyl group, aryl group, heteroalkyl group, heterocyclic group, or combination thereof optionally comprising from 1 to 8 secondary or tertiary amines or a substituent comprising a tissue-specific or cell-specific targeting moiety;

R^6 is hydrogen, an amino group, an aryl group, a heterocyclic group, a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group, a C_1-C_{12} linear or branched alkyl group optionally substituted with one or more amines; or a tissue-specific or cell-specific targeting moiety; and

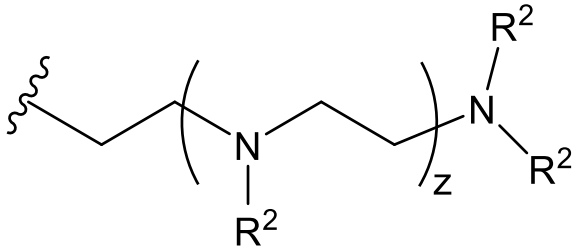
each instance of R^{13} is independently hydrogen or a C_1-C_{12} alkyl group, alkenyl group, cycloalkyl group, or cycloalkenyl group.

16. The method of any of claims 12-15, wherein each of A1 and A2 is a group of formula —$(CH_2)_{p1}$—[NH—$(CH_2)_{q1}$—]$_{r1}$$NH_2$, and each of B^1 and B^2 is a group of formula—$(CH_2)_{p1}$—[NH—$(CH_2)_{q1}$—]$_{r1}$NH-$(CH_2)_2$-R^4-R^5

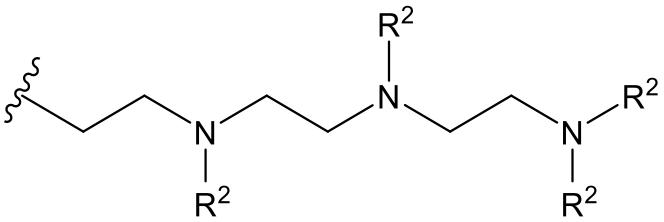
17. The method of any of claims 12-16, wherein each of A^1 and A^2 is a group of formula –$(CH_2)_2$-NH-$(CH_2)_2$-NH_2, and each of B^1 and B^2 is a group of formula–$(CH_2)_2$-NH-$(CH_2)_2$-NH-$(CH_2)_2$-R^4-R^5.

18. The method of any one of claims 12-17, wherein R^4 is –C(O)-O-.

19. The method of any one of claims 12-18, wherein R^5 is



or



.

20. The method of any of claims 12-19, wherein a sufficient number of A^1 and/or A^2 groups of the polymer comprising the structure of Formula 3 are modified to provide a polymer comprising a structure of Formula 1 in which the ratio of $(m^1+n^1)/(m^2+n^2)$ is about 20 or less, and, optionally, about 0.2 or more.

21. A composition comprising a polymer of any one of claims 1-11 and a nucleic acid and/or polypeptide.

22. The composition of claim 21, wherein the composition comprises a guide nucleic acid and/or donor nucleic acid.

23. The composition of claim 21 or 22, wherein the composition comprises an endonuclease.

24. The composition of claim 23, wherein the composition comprises an RNA-guided endonuclease or nucleic acid encoding same.

25. The composition of claim 24, wherein the RNA-guided endonuclease is Cas9, Cpf1, or a combination thereof.

26. The composition of any one of claims 21-25, wherein the composition comprises a DNA recombinase.

27. The composition of claim 26, wherein the DNA recombinase is Cre recombinase.

28. The composition of any one of claims 21-27, wherein the composition comprises a zinc finger nuclease.

29. The composition of any one of claims 21-28, wherein the composition comprises a transcription activator-like effector nuclease.

30. The composition of any one of claims 21-29, wherein the composition comprises an siRNA or dsRNA.

31. The composition of any one of claims 21-29, wherein the composition comprises a nanoparticle comprising the polymer of any of claims 1-9 and the nucleic acid or polypeptide.

32. The composition of any one of claims 21-30, wherein the composition comprises a second polymer that comprises polyethylene oxide.

33. A method of delivering a nucleic acid and/or polypeptide to a cell *in vitro*, the method comprising administering the composition of any one of claims 21-32 to the cell.

34. The composition of any one of claims 21-32 for use in therapy, wherein the nucleic acid and/or polypeptide are to be delivered by the composition to a cell ~~The method of claim 33, wherein the cell is~~ in a subject ~~and the composition is administered to the subject~~.

35. The composition for use according to claim 34, wherein the subject is a human.

~~35~~36. The ~~method of claim 33 or 34~~composition for use according to claim 34 or 35, wherein the polymer comprises a tissue-specific targeting moiety that localizes the polymer to tissues of the peripheral nervous system, the central nervous system, liver, muscle, lung, bone, or the eye of the subject.

~~36~~37. The ~~method of claim 35~~composition for use according to claim 34 or 35, wherein the polymer comprises a targeting moiety that preferentially binds to tumor cells.

~~37. The method of any of claims 33-36, wherein the composition comprises one or more of an RNA-guided endonuclease or nucleic acid encoding same, a guide nucleic acid, and a donor nucleic acid, and the composition facilitates editing of a target gene in the cell.~~

~~38. The method of any of claims 33-37, wherein the cell is in a host, optionally a human, and the composition is delivered to the cell by administering the composition to the host.~~