Claims:

1. A composition comprising a first RNAi agent and a second RNAi agent, wherein:

(a) the first RNAi agent comprising: an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:100, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:171, SEQ ID NO:179 and SEQ ID NO:180, and a sense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:229, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:273, SEQ ID NO:302 and SEQ ID NO:319; and

(b) the second RNAi agent comprising: an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:140, SEQ ID NO:137, SEQ ID NO:102, SEQ ID NO:162 and SEQ ID NO:188, and a sense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:248, SEQ ID NO:294, SEQ ID NO:262, SEQ ID NO:271, SEQ ID NO:274, and SEQ ID NO:328.

2. The composition of claim 1, wherein the first RNAi agent or the second RNAi agent comprises at least one modified nucleotide or at least one modified inter-nucleoside linkage.

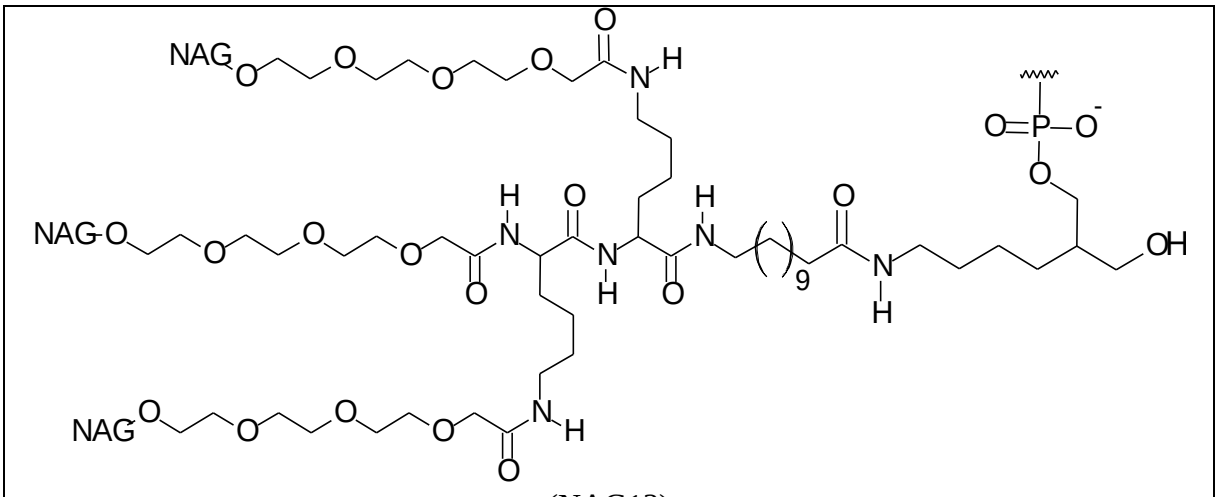
3. The composition of claim 1 or 2, wherein substantially all of the nucleotides in the first RNAi agent or the second RNAi agent are modified nucleotides.

4. The composition of any one of claims 1-3, wherein the first RNAi agent or the second RNAi agent further comprises a targeting ligand that is conjugated to the first RNAi agent or the second RNAi agent.

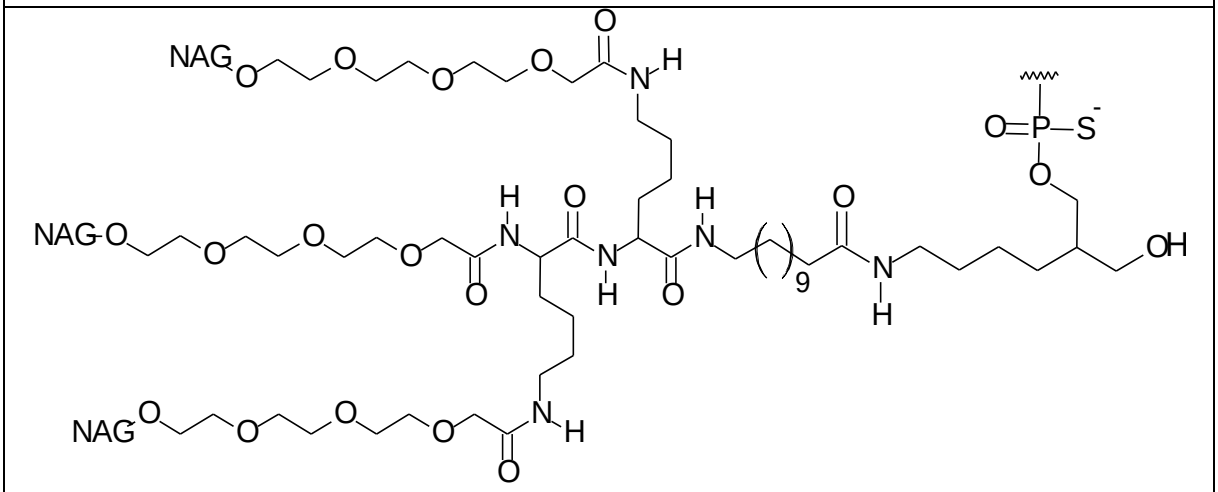
5. The composition of claim 4, wherein the targeting ligand comprises N-acetyl-galactosamine.

6. The composition of claim 5, wherein the targeting ligand comprises an N-acetyl-galactosamine trimer or an N-acetyl-galactosamine tetramer.

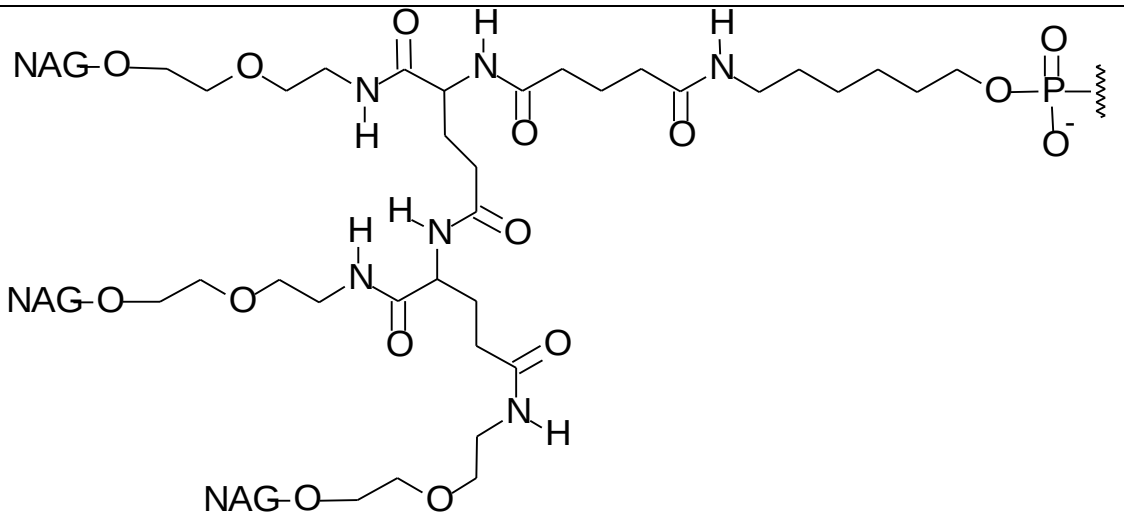
7. The composition of claim 6, wherein the targeting ligand is selected from the group consisting of:



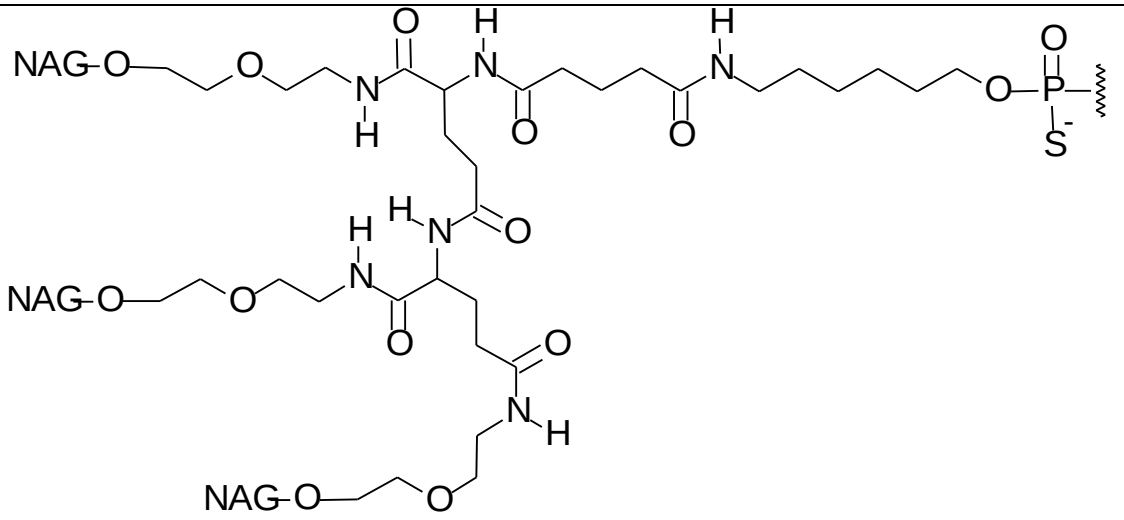
(NAG13)



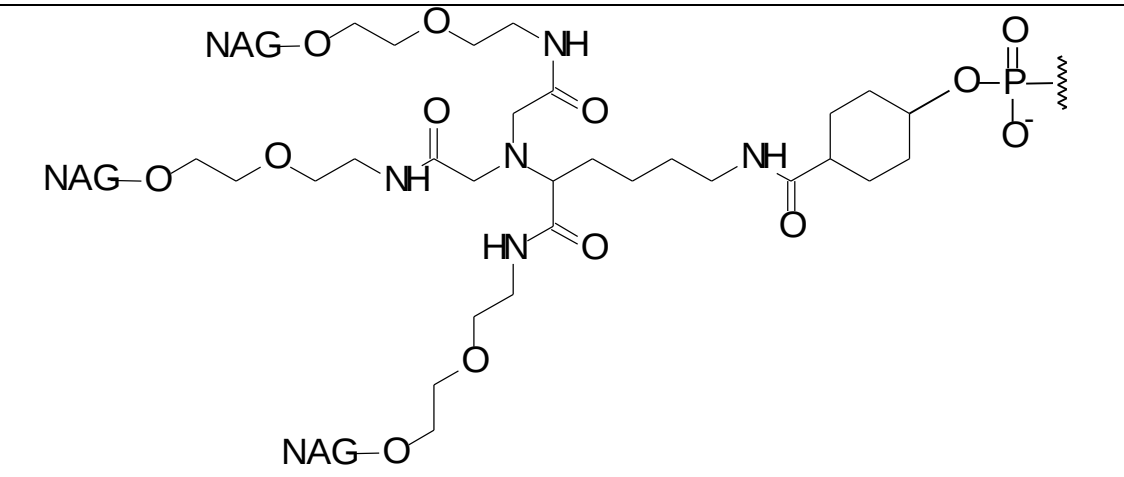
(NAG13)s



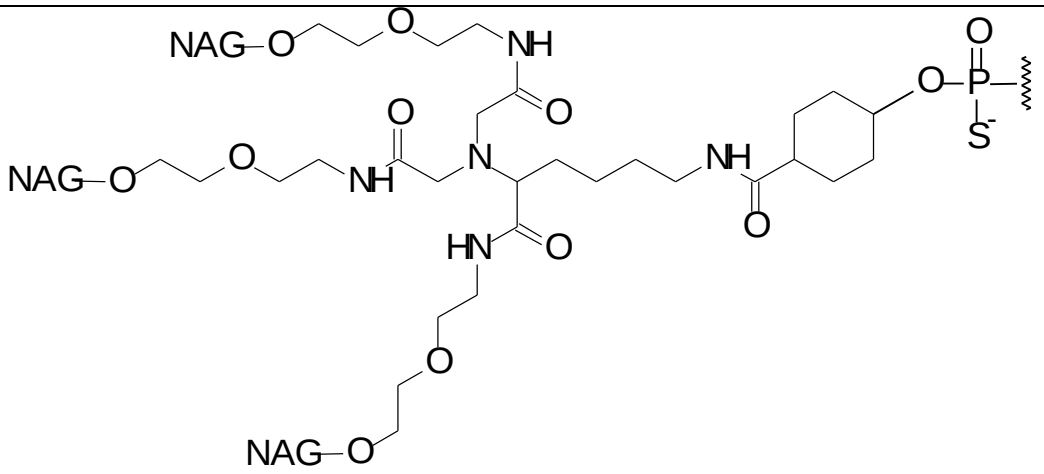
(NAG18)



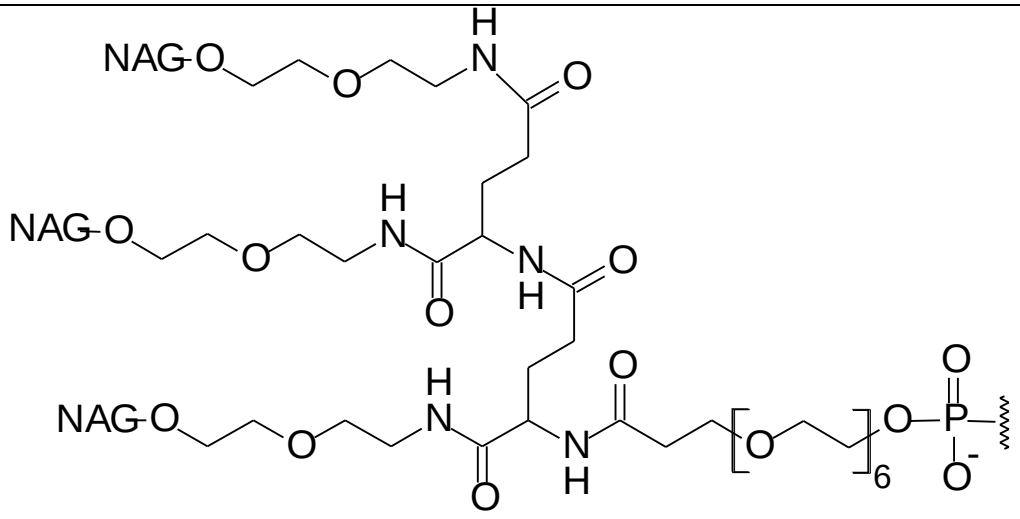
(NAG18)s



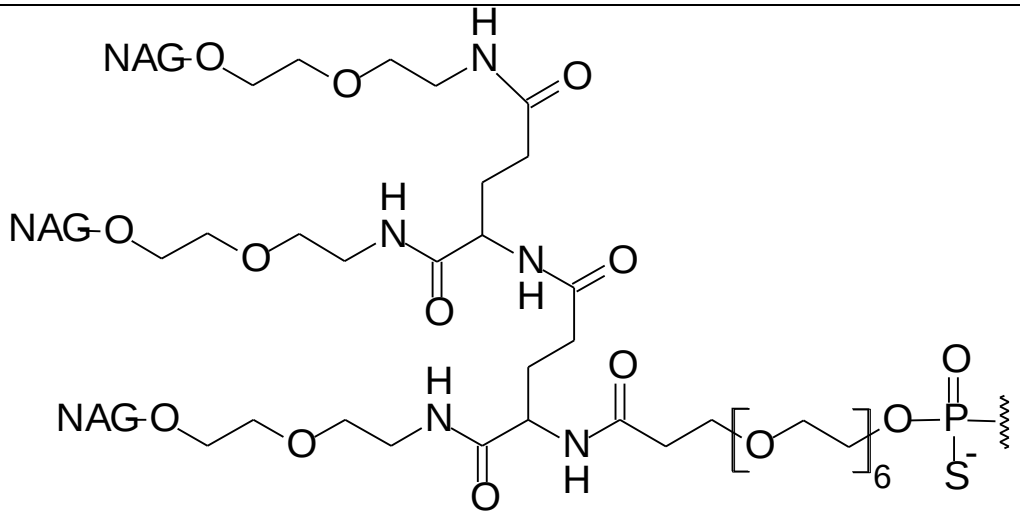
(NAG24)



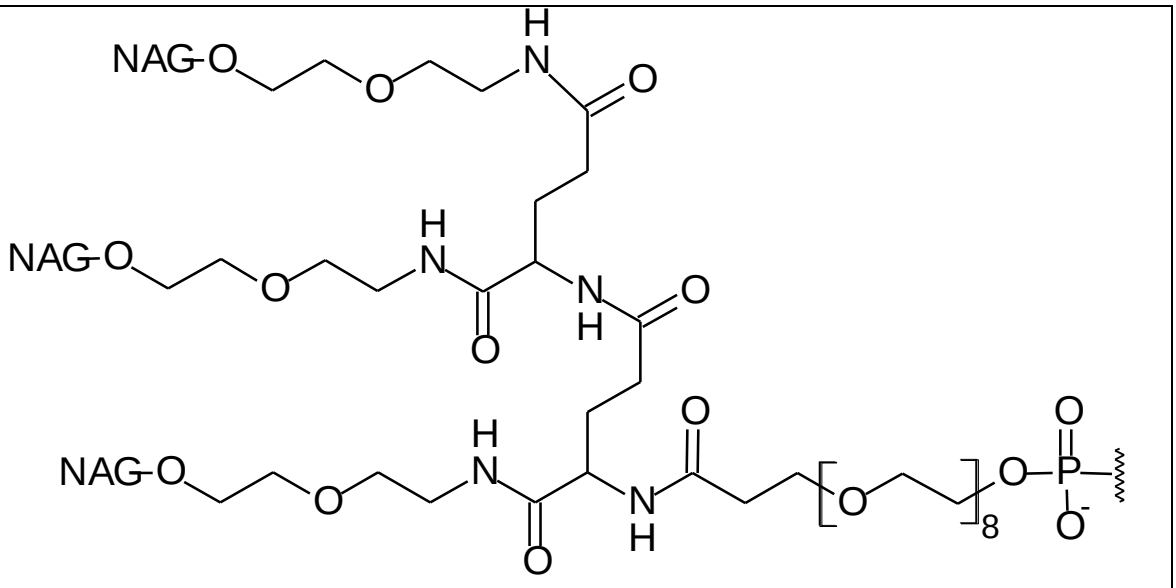
(NAG24)s



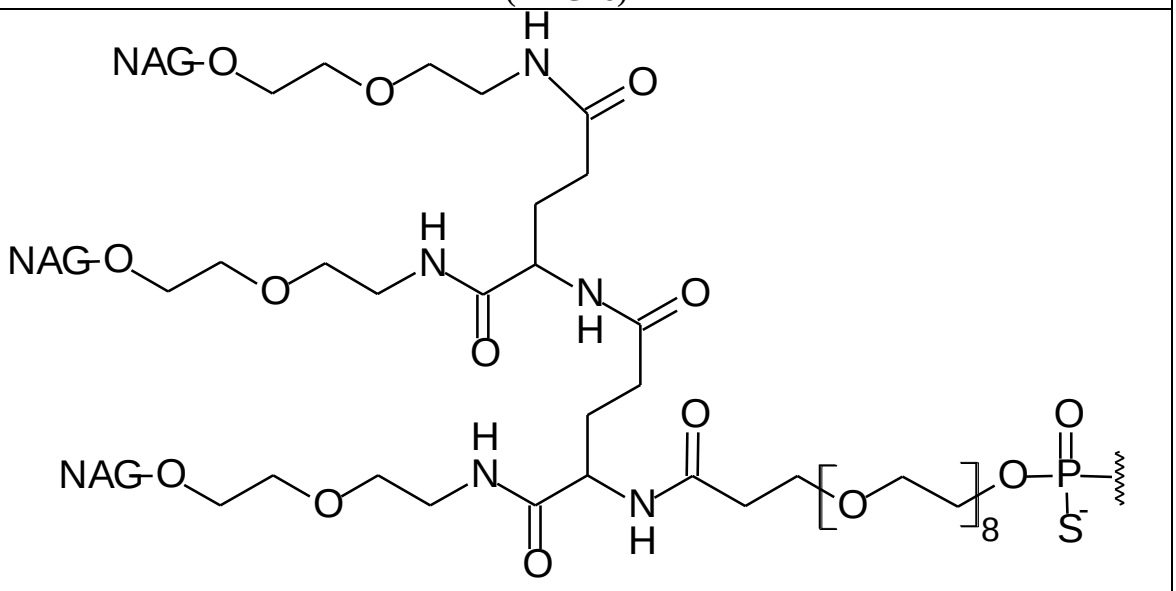
(NAG25)



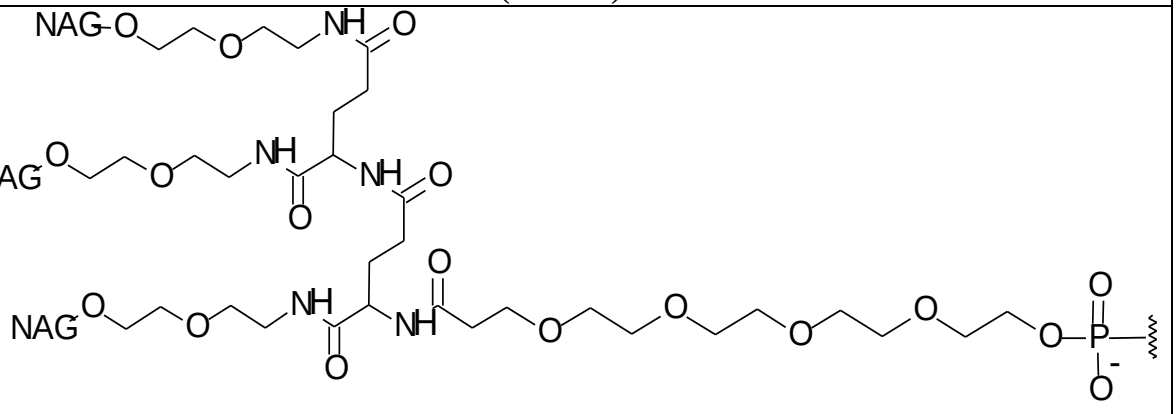
(NAG25)s



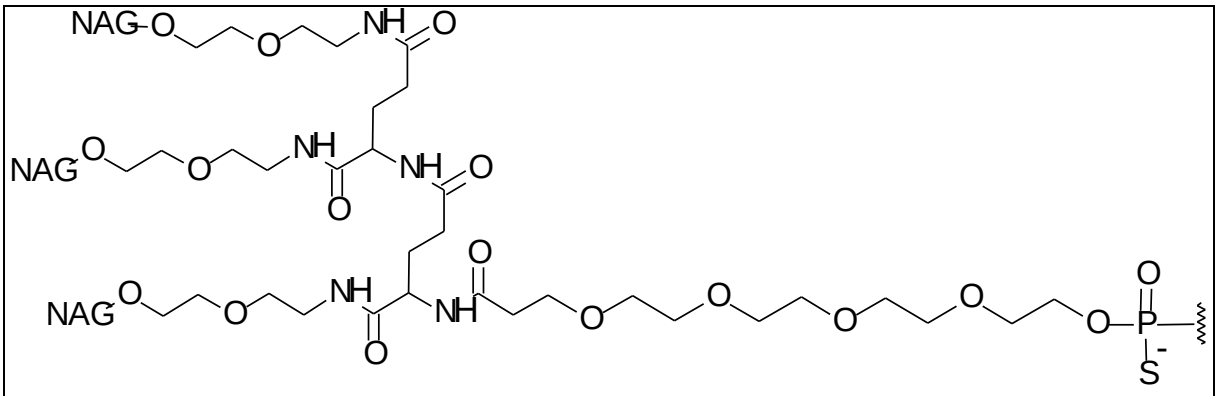
(NAG26)



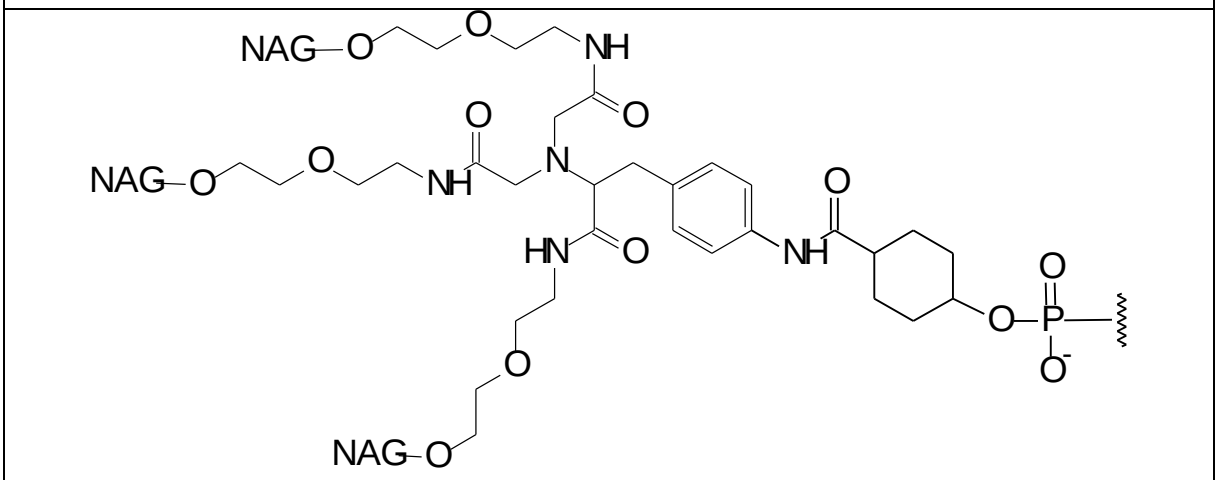
(NAG26)s



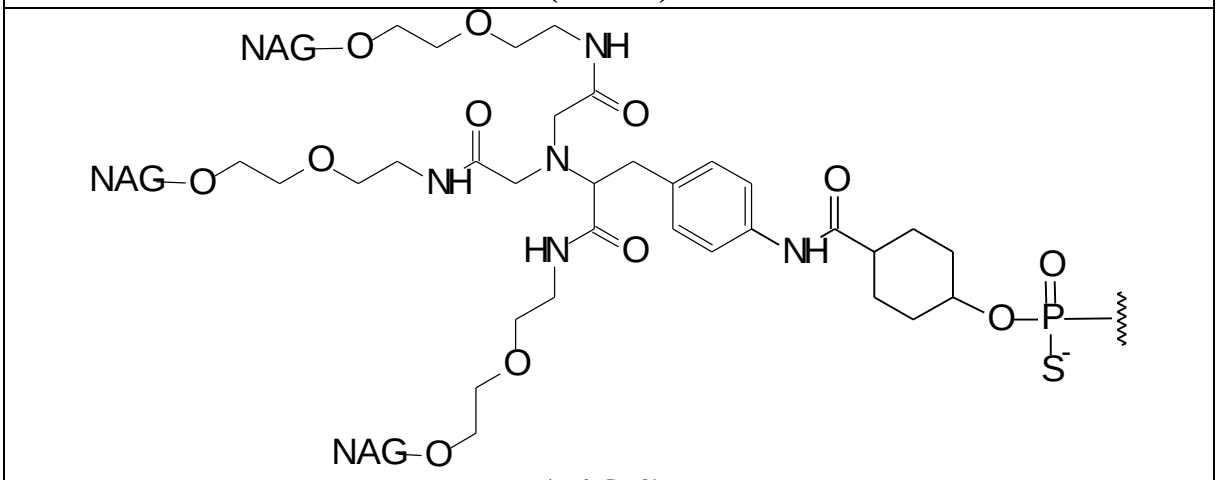
(NAG27)



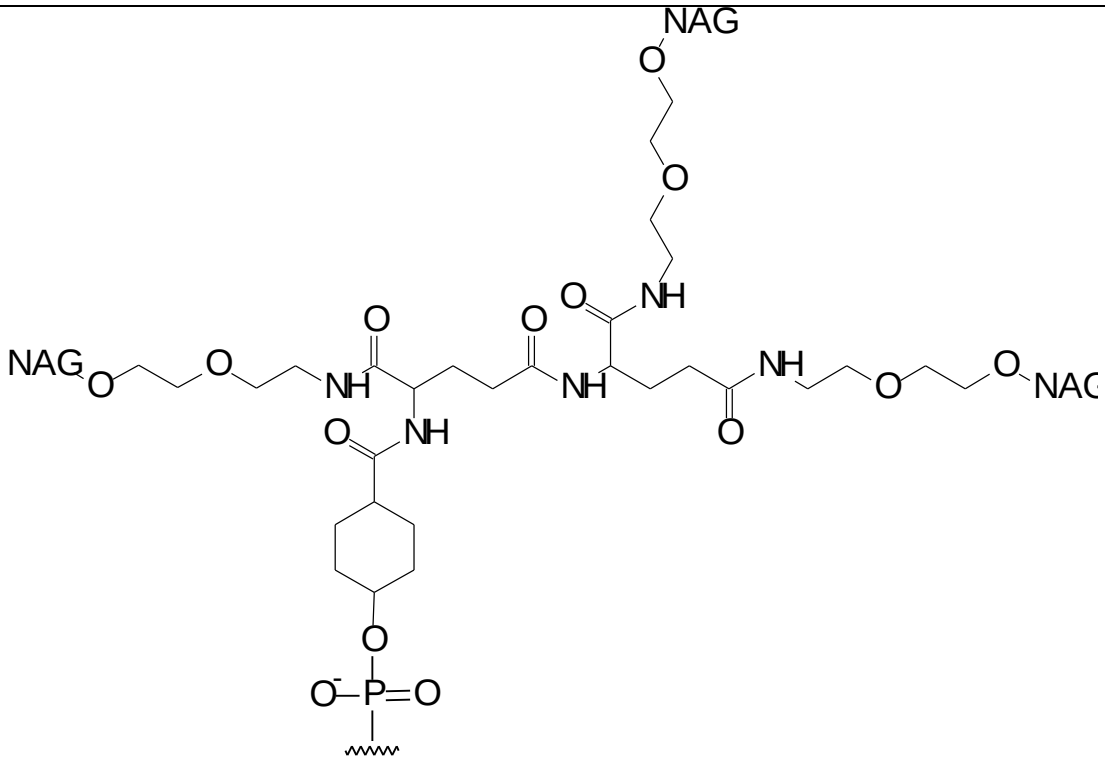
(NAG27)s



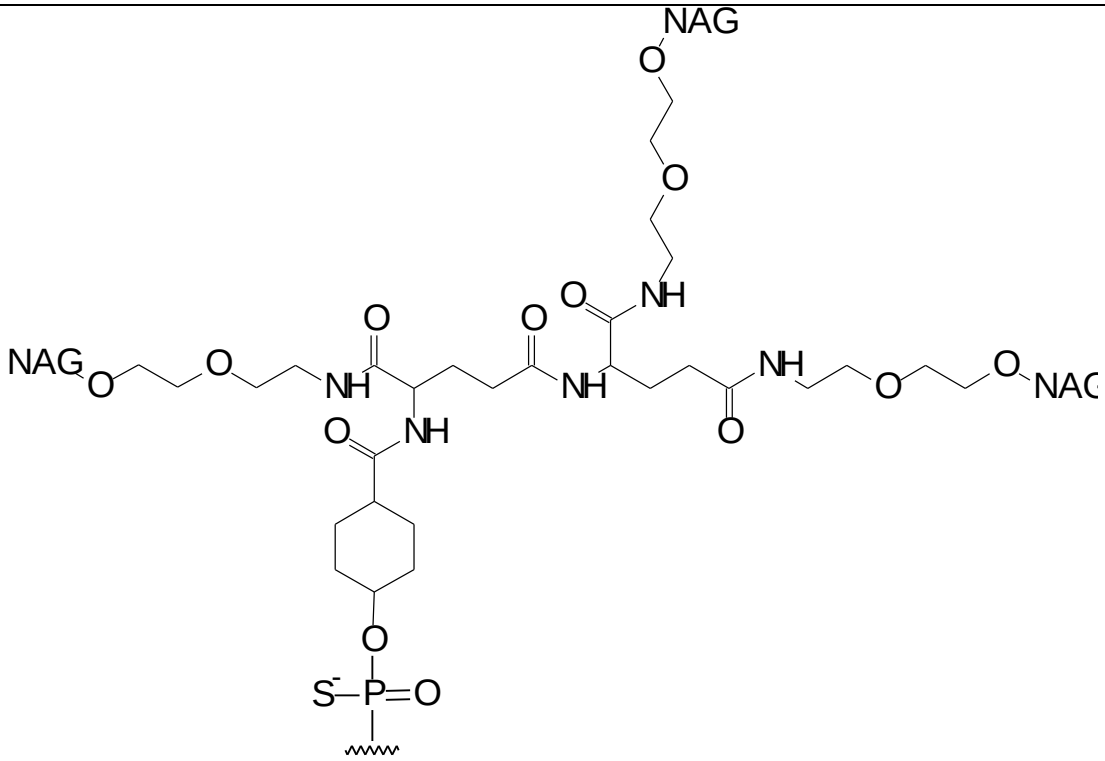
(NAG28)



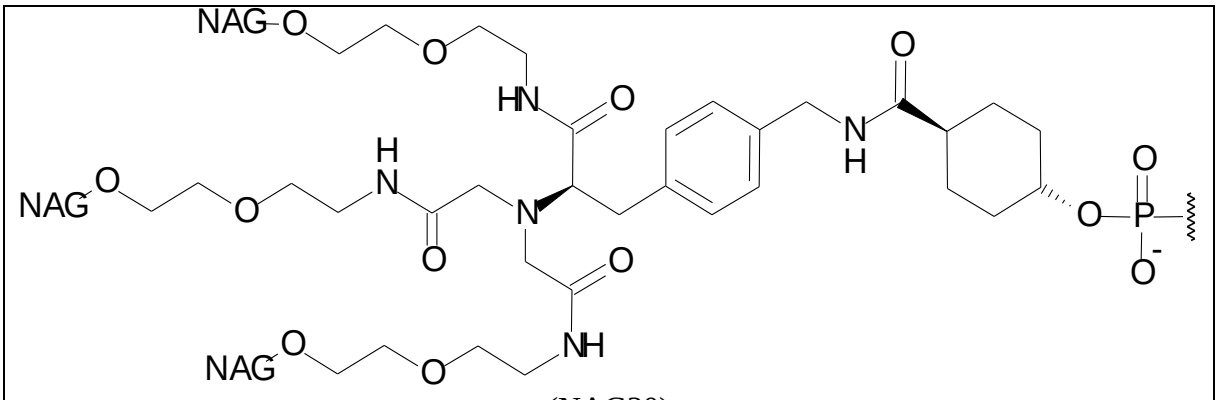
(NAG28)s



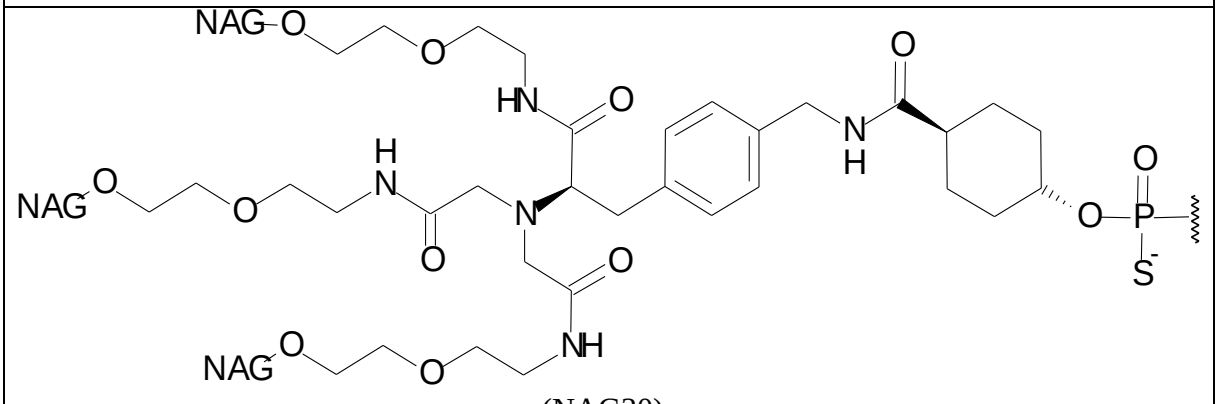
(NAG29)



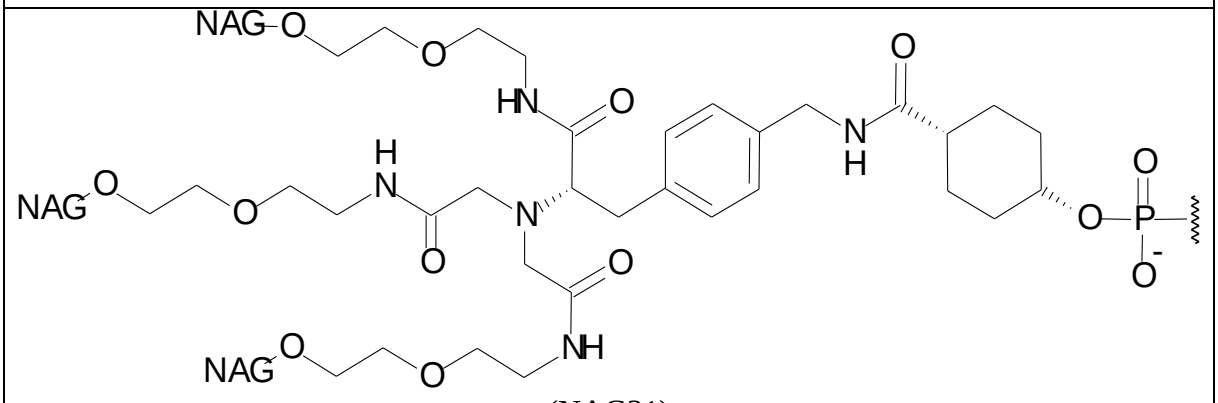
(NAG29)s



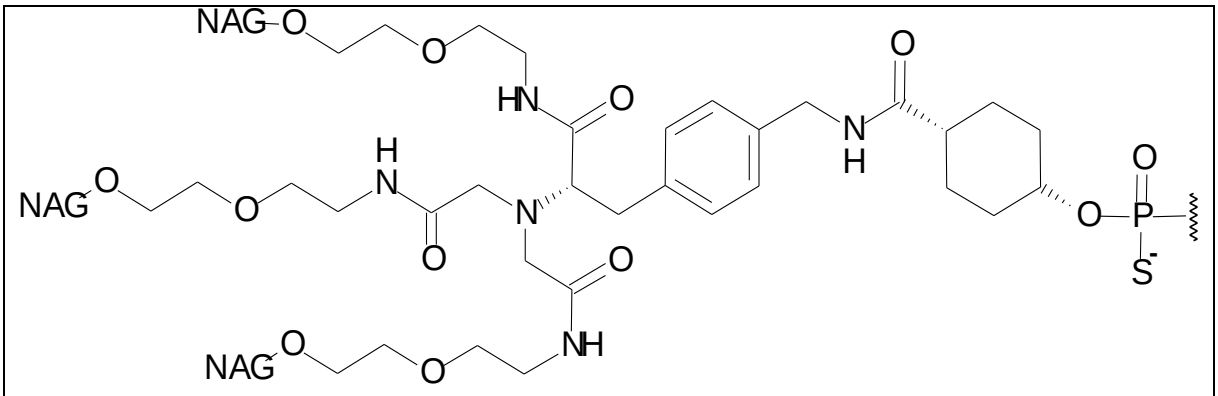
(NAG30)



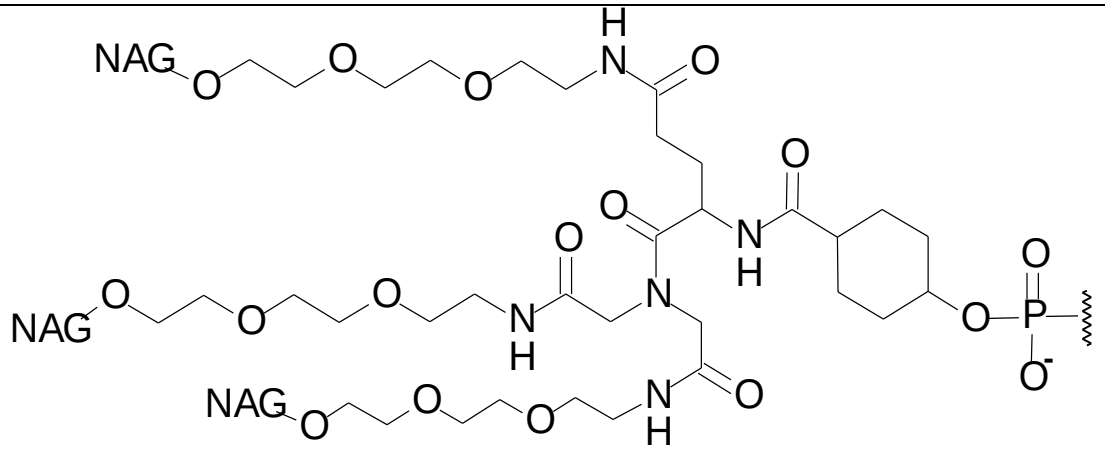
(NAG30)s



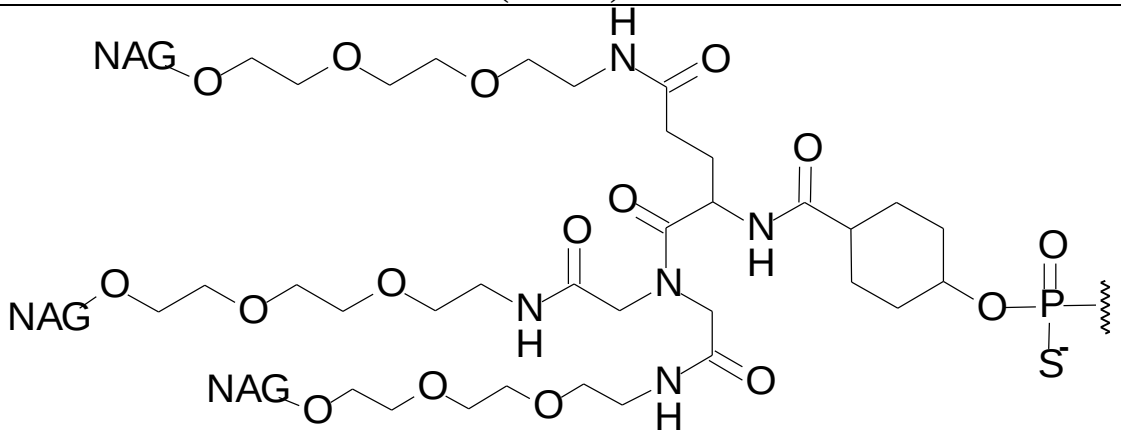
(NAG31)



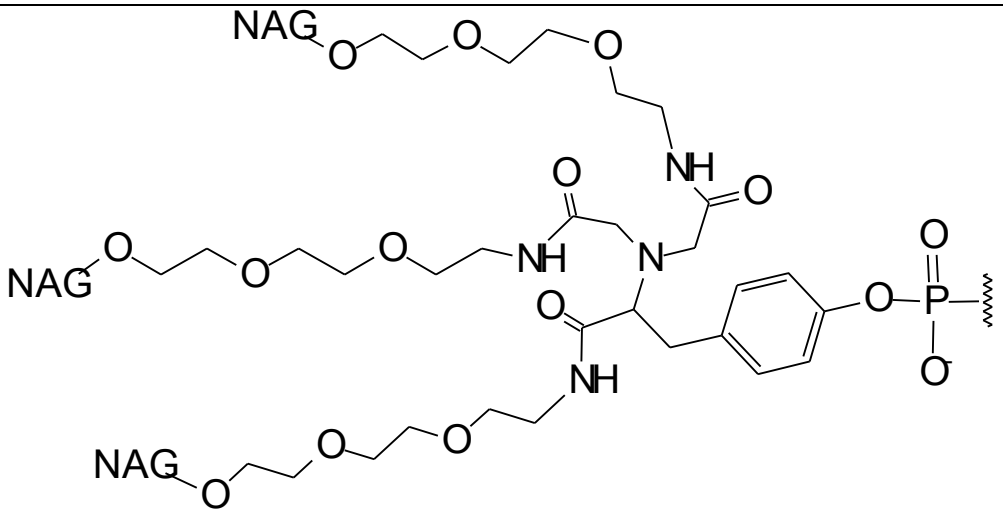
(NAG31)s



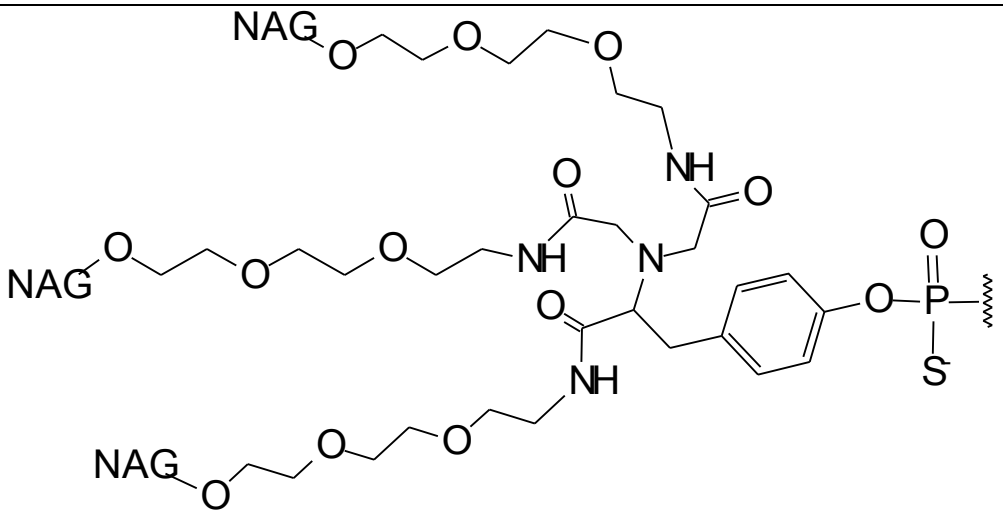
(NAG32)



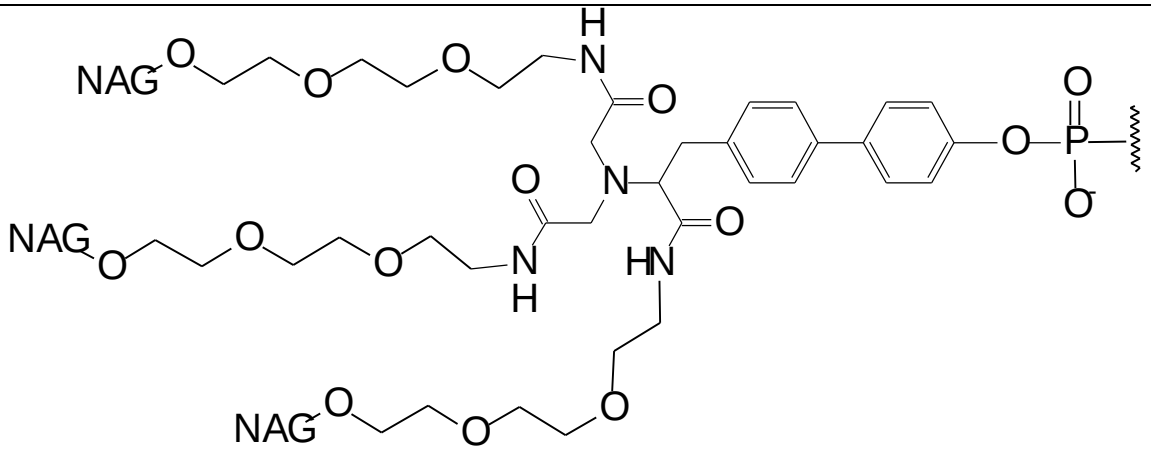
(NAG32)s



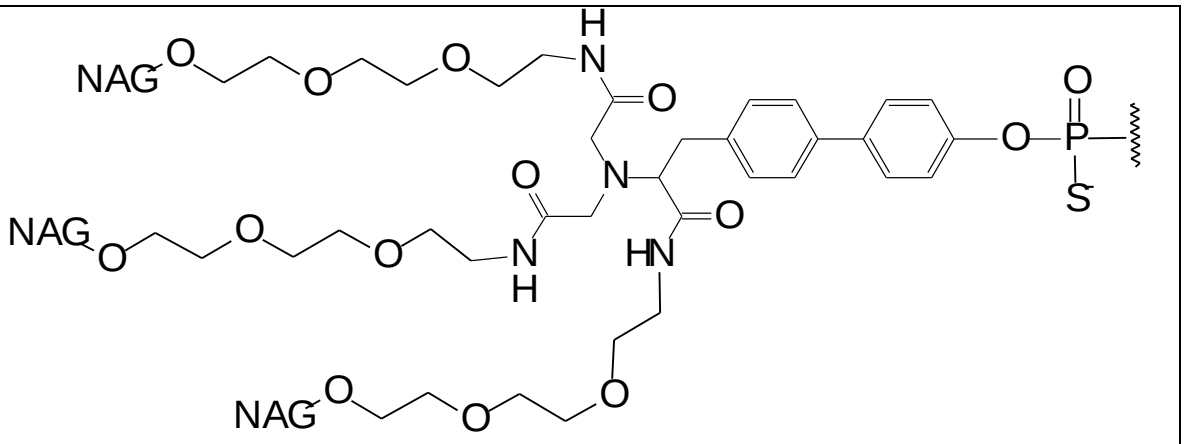
(NAG33)



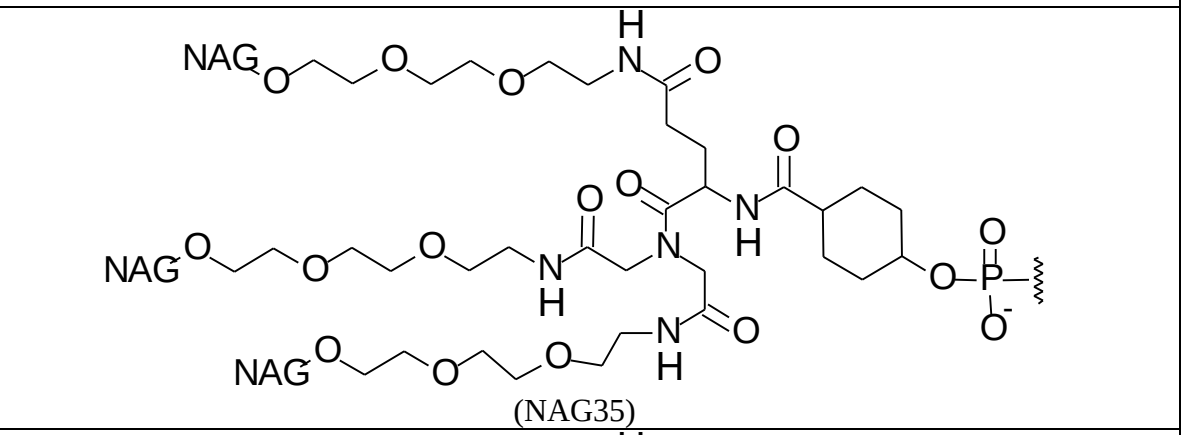
(NAG33)s



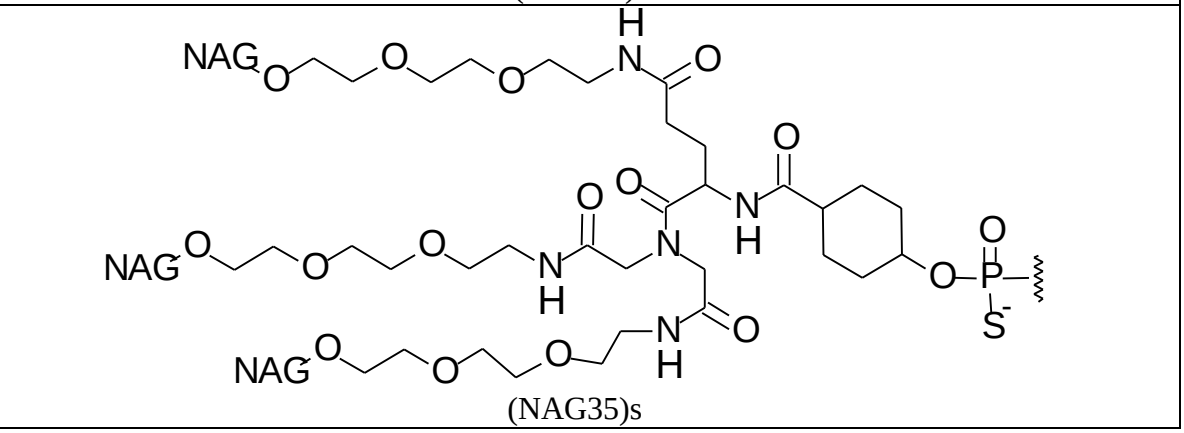
(NAG34)



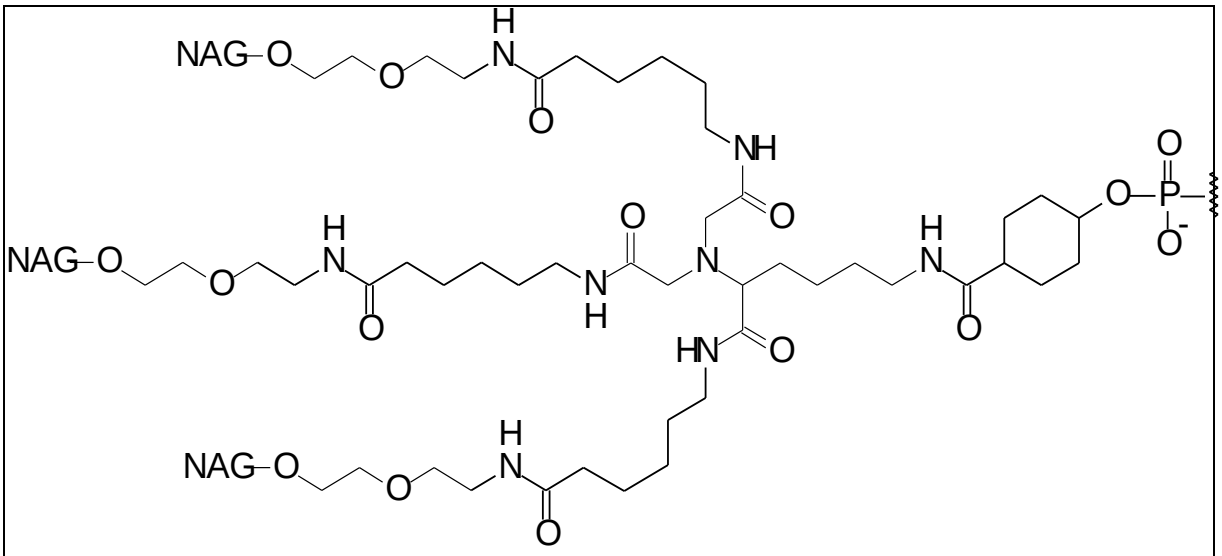
(NAG34)s



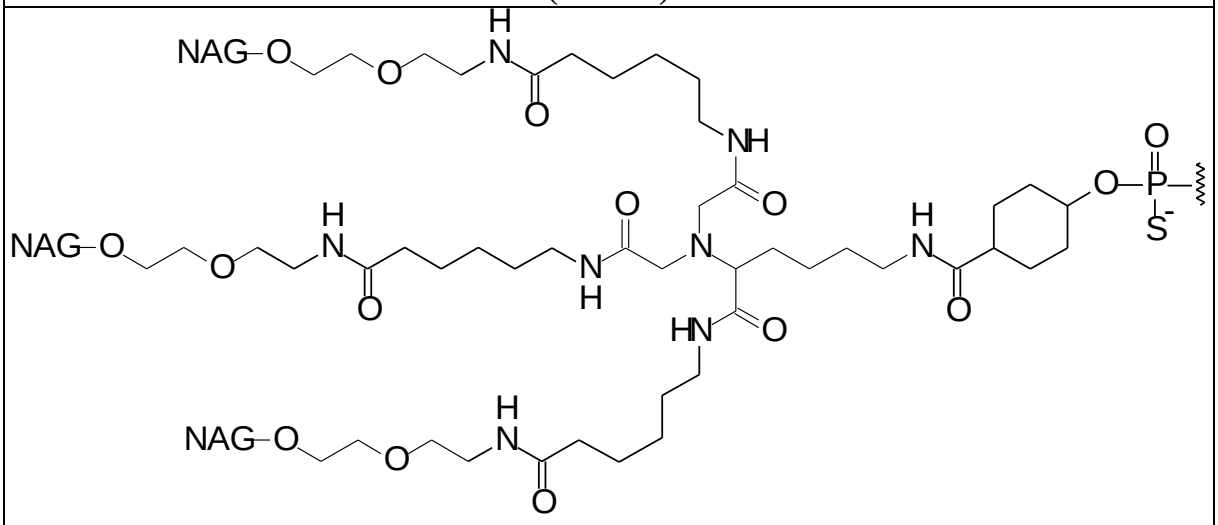
(NAG35)



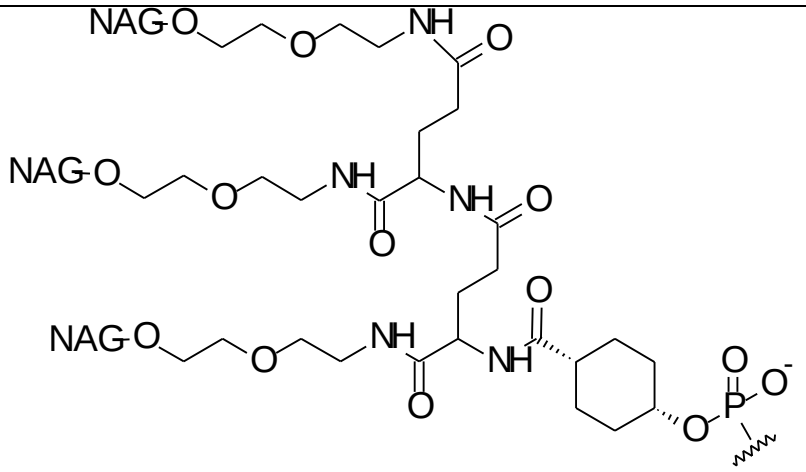
(NAG35)s



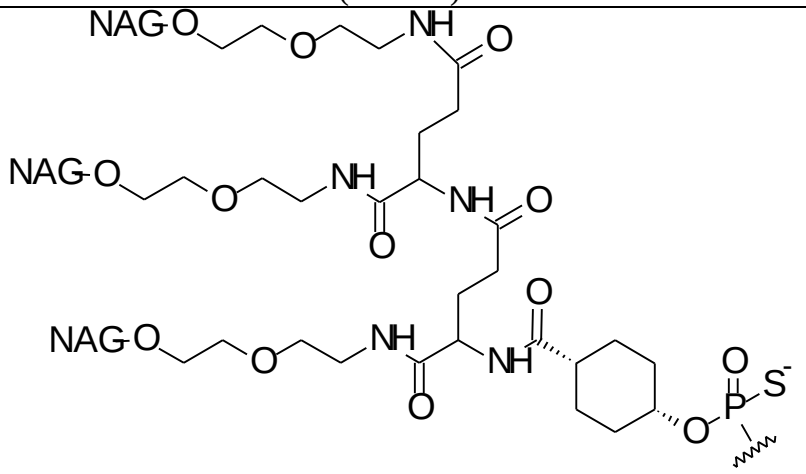
(NAG36)



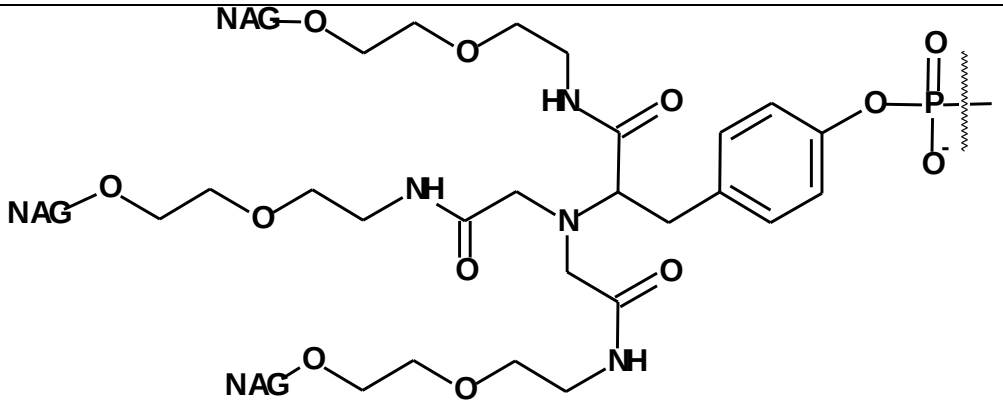
(NAG36)s



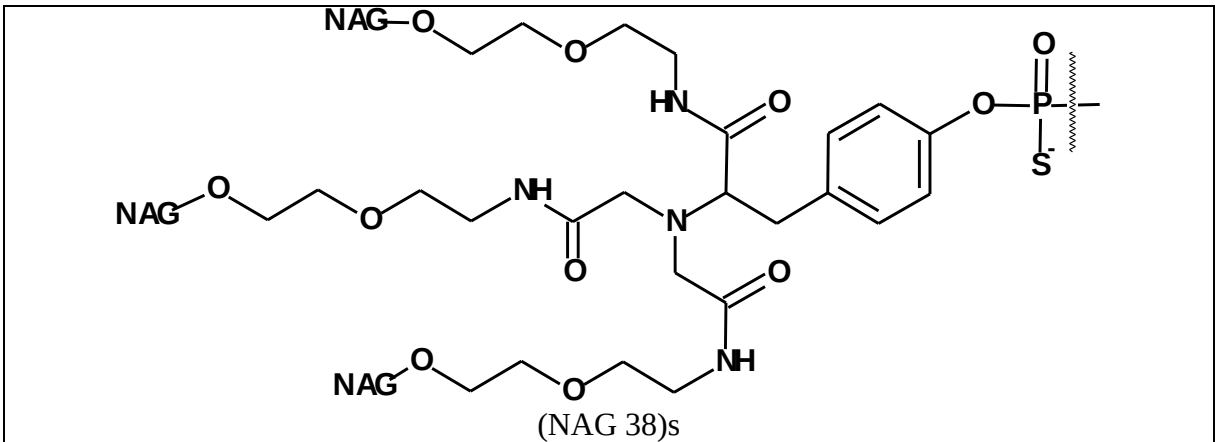
(NAG37)



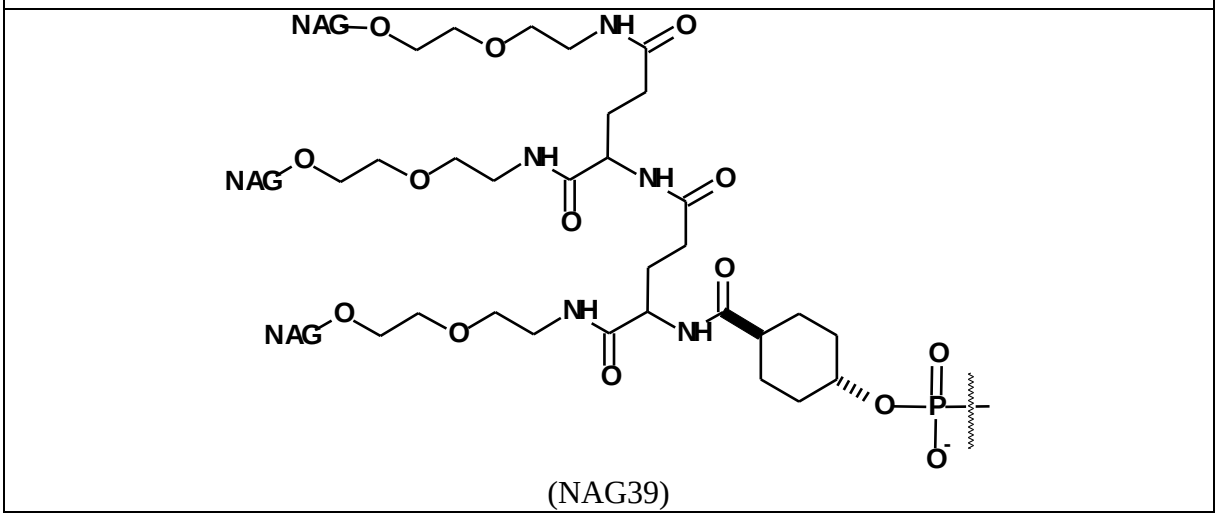
(NAG37)s



(NAG 38)

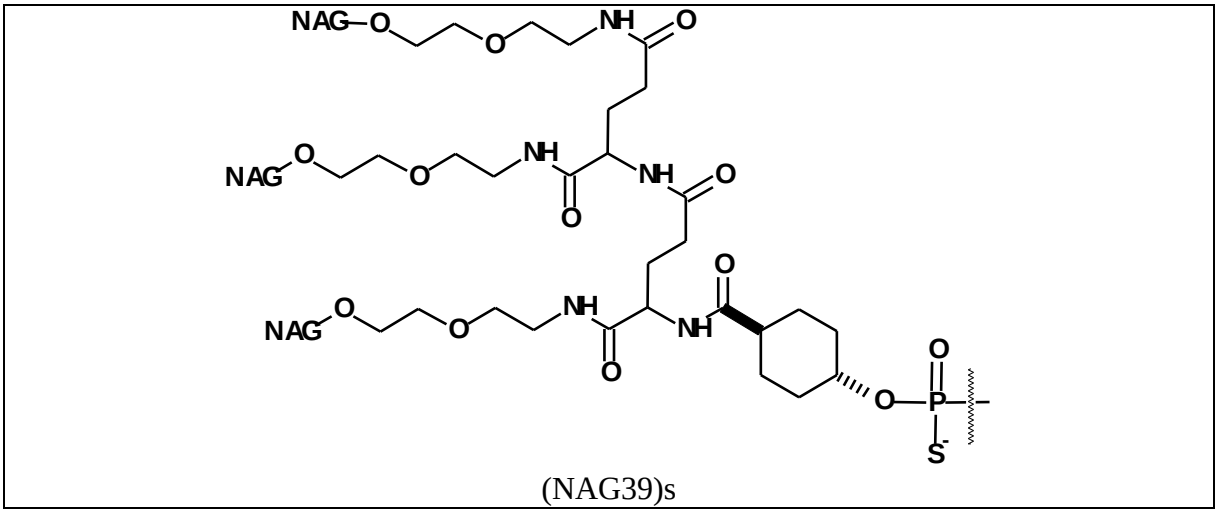


(NAG 38)s



(NAG39)

and



(NAG39)s

8. The composition of claim 7, wherein the targeting ligand is (NAG25), (NAG25)s, (NAG31), (NAG31)s, (NAG37), or (NAG37)s.

9. The composition of any one of claims 4-8, wherein the targeting ligand is conjugated to the sense strand of the first RNAi agent or the sense strand of the second RNAi agent.

10. The composition of any one of claims 4-8, wherein the targeting ligand is conjugated to the antisense strand of the first RNAi agent or the antisense strand of the second RNAi agent.

11. The composition of claim 9, wherein the targeting ligand is conjugated to the 5' terminus of the sense strand of the first RNAi agent or the 5' terminus of the sense strand of the second RNAi agent.

12. The composition of claim 9, wherein the targeting ligand is conjugated to the 3' terminus of the sense strand of the first RNAi agent or the 3' terminus of the sense strand of the second RNAi agent.

13. The composition of claim 10, wherein the targeting ligand is conjugated to the 3' terminus of the antisense strand of the first RNAi agent or the 3' terminus of the antisense strand of the second RNAi agent.

14. The composition of any one of claims 1-13, wherein the sense strand of the first RNAi agent or the sense strand of the second RNAi agent further comprises one or more inverted abasic nucleosides.

15. The composition of any one of claims 1-14, wherein the composition comprises two or more RNAi agents independently selected from the group consisting of: AD04571 (SEQ ID NO: 101 and SEQ ID NO: 230), AD04872 (SEQ ID NO: 126 and SEQ ID NO:252), AD04873 (SEQ ID NO: 127 and SEQ ID NO:252), AD04874 (SEQ ID NO: 128 and SEQ ID NO:253), AD04982 (SEQ ID NO: 137 and SEQ ID NO:248), AD05070 (SEQ ID NO:140 and SEQ ID NO:262),

AD05148 (SEQ ID NO:140 and SEQ ID NO:271), AD05164 (SEQ ID NO:126 and SEQ ID NO:273) and AD05165 (SEQ ID NO:140 and SEQ ID NO:274).

16. The composition of any one of claims 1-15, wherein the ratio of the first RNAi agent to the second RNAi agent by weight is in the range of 1:1 to 5:1.

17. The composition of claim 16, wherein the ratio of the first RNAi agent to the second RNAi agent by weight is 2:1 or 3:1.

18. The composition of any one of claims 1-17, wherein the first RNAi agent comprises an antisense strand comprising SEQ ID NO: 126 and a sense strand comprising SEQ ID NO: 252, and the second RNAi agent comprises an antisense strand comprising SEQ ID NO: 140 and a sense strand comprising SEQ ID NO: 262.

19. The composition of any one of claims 1-17, wherein the first RNAi agent comprises an antisense strand comprising SEQ ID NO: 126 and a sense strand comprising SEQ ID NO: 252, the second RNAi agent comprises an antisense strand comprising SEQ ID NO:102 and a sense strand comprising SEQ ID NO: 248.

20. The composition of any one of claims 1-17, wherein the first RNAi agent comprises an antisense strand comprising SEQ ID NO: 126 and a sense strand comprising SEQ ID NO: 252, the second RNAi agent comprises an antisense strand comprising SEQ ID NO:137 and a sense strand comprising SEQ ID NO: 248.

21. The composition of any one of claims 1-14, wherein the two or more RNAi agents are each independently conjugated to a targeting ligand comprising N-acetyl-galactosamine.

22. The composition of any one of claims 1-17, wherein the sense strand of the first RNAi agent and the sense strand of the second RNAi agent each comprise one or more inverted abasic nucleosides.

23. A pharmaceutical composition comprising the composition of any one of claims 1-22 and a pharmaceutically acceptable excipient, carrier, or diluent.

24. A kit comprising the pharmaceutical composition of claim 23.

25. The kit of claim 24 further comprising a syringe or a vial.

26. Use of an effective amount of the composition according to any one of claims 1-22 in the manufacture of a medicament for reducing or inhibiting the expression of at least one Hepatitis B Virus gene in a subject in need thereof, wherein the medicament is to be administered to the subject.

27. The use of claim 26, wherein the composition is to be administered in the amount of 0.25-5 mg/kg.

28. The use of claim 26 or 27, wherein the composition is formulated for subcutaneous or intravenous injection.

29. The use of any one of claims 26-28, wherein one or more additional therapeutics are to be administered to the subject.

30. The use of claim 29, wherein the additional therapeutic is lamivudine, tenofovir, tenofovir alafenamide, tenofovir disoproxil, or entecavir.

31. Use of an effective amount of the composition according to any one of claims 1-22 in the manufacture of a medicament for the treatment of a disease or disorder associated with Hepatitis B Virus infection in a subject in need thereof, wherein the medicament is to be administered to the subject.

32. The use of claim 31, wherein the composition is to be administered in the amount of 0.25-5 mg/kg.

33. The use of claim 31 or 32, wherein the composition is formulated for subcutaneous or intravenous injection.

34. The use of any one of claims 31-33, wherein the subject has an infection caused by the Hepatitis B Virus.

35. The use of any one of claims 31-34, wherein one or more additional therapeutics are to be administered to the subject.

36. The use of claim 35, wherein the additional therapeutic is lamivudine, tenofovir, tenofovir alafenamide, tenofovir disoproxil, or entecavir.

37. A combination of at least two RNAi agents comprising a first RNAi agent and a second RNAi agent, wherein:

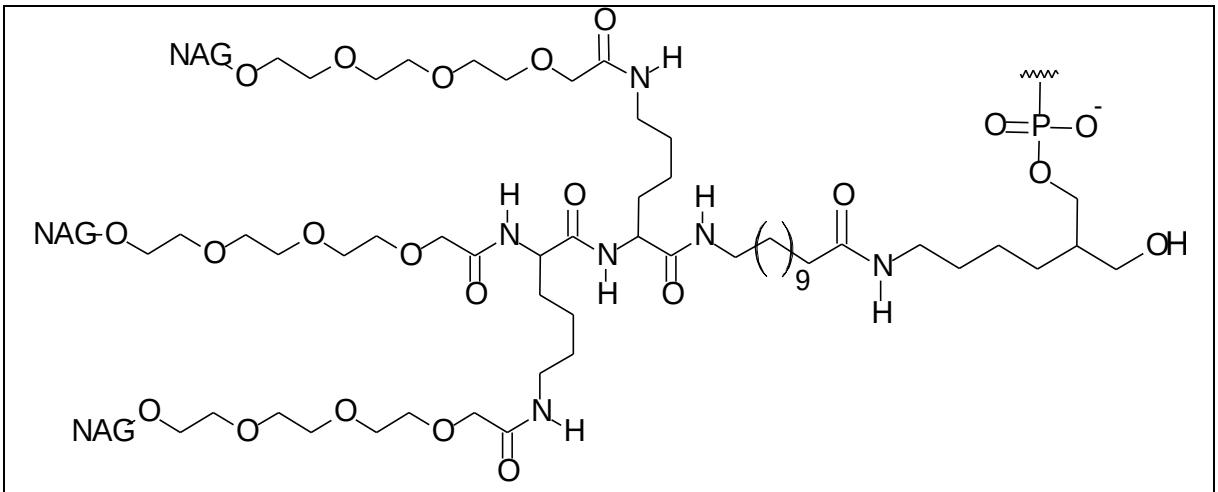
(a) the first RNAi agent comprising: an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:100, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:171, SEQ ID NO:179, and SEQ ID NO:180, and a sense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:229, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:273, SEQ ID NO:302, and SEQ ID NO:319; and

(b) the second RNAi agent comprising: an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:140, SEQ ID NO:102, SEQ ID NO:137, SEQ ID NO:162 and SEQ ID NO:188, and a sense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:248, SEQ ID NO:294, SEQ ID NO:262, SEQ ID NO:271, SEQ ID NO:274, and SEQ ID NO:328.

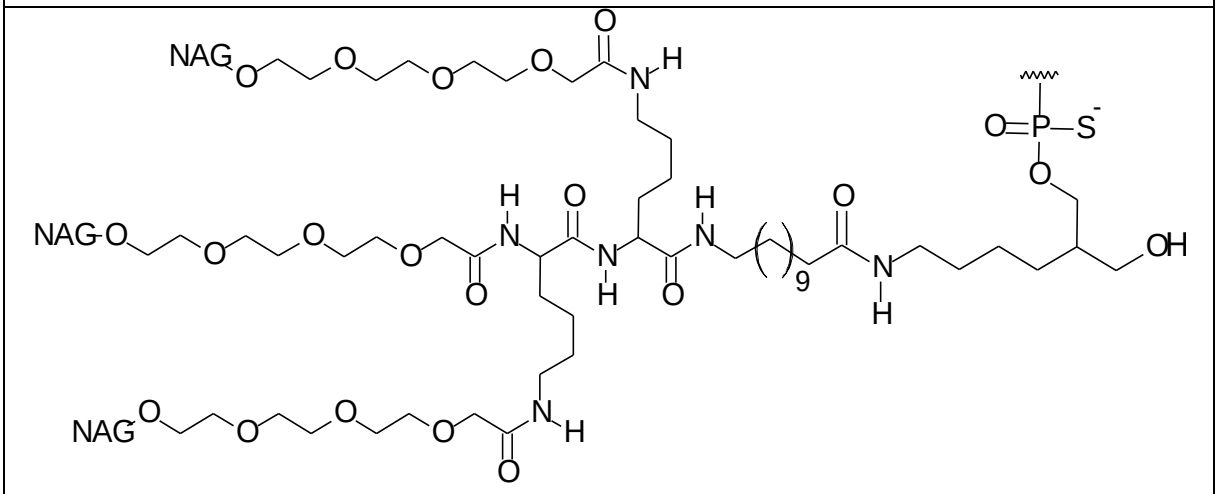
38. The combination of claim 37, wherein the first or the second RNAi agent comprises at least one modified nucleotide or at least one modified inter-nucleoside linkage.

39. The combination of claim 37 or 38, wherein the first or the second RNAi agent further comprises a targeting ligand that is conjugated to the first or the second RNAi agent.

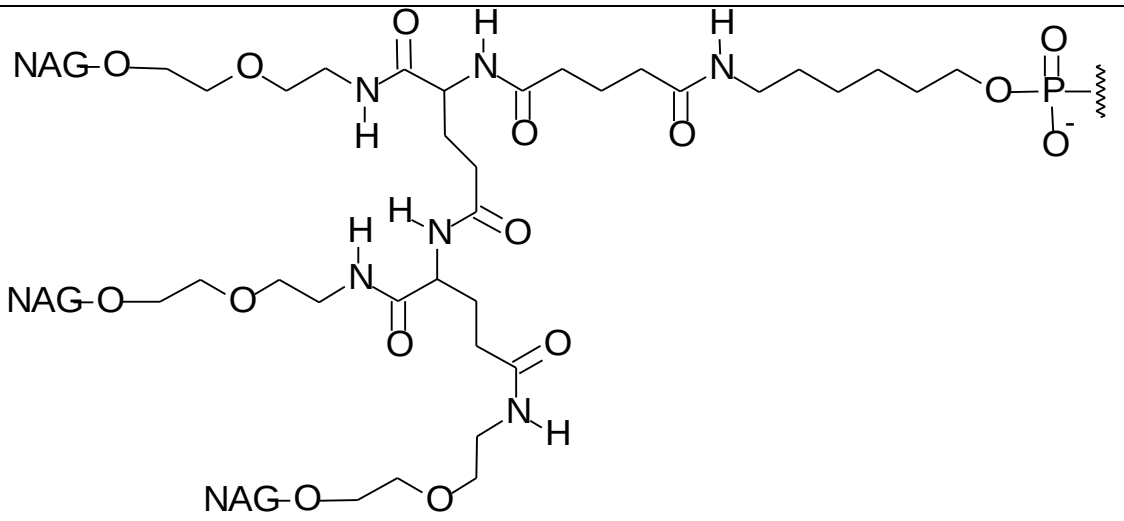
40. The combination of claim 39, wherein the targeting ligand is selected from the group consisting of:



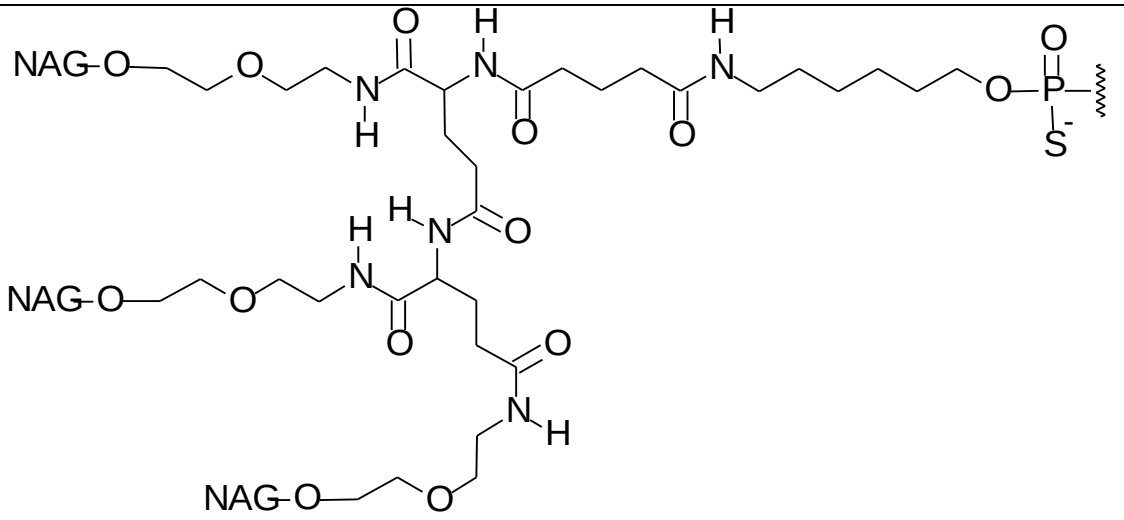
(NAG13)



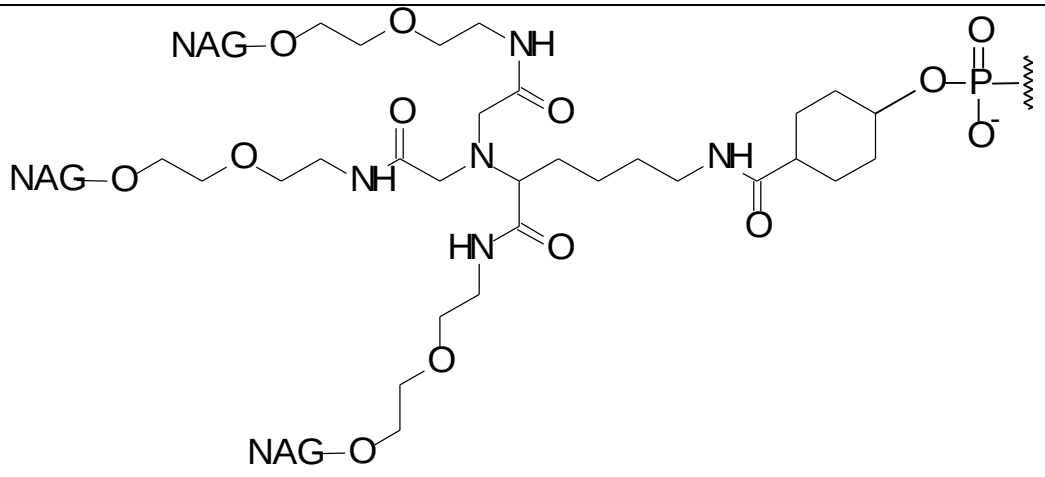
(NAG13)s



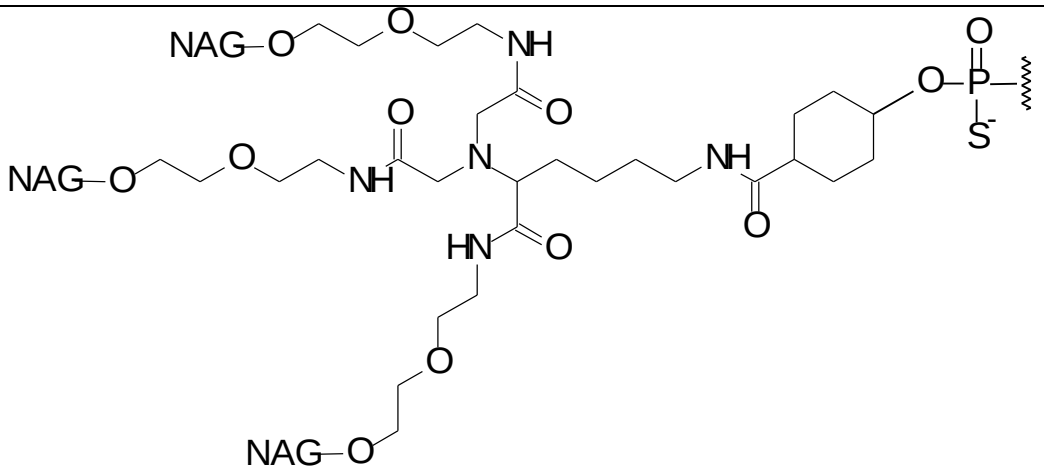
(NAG18)



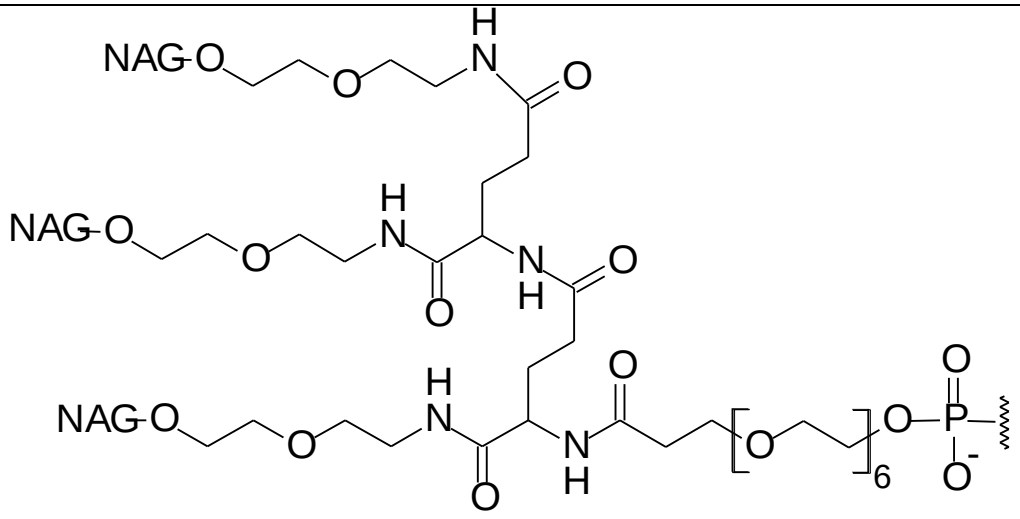
(NAG18)s



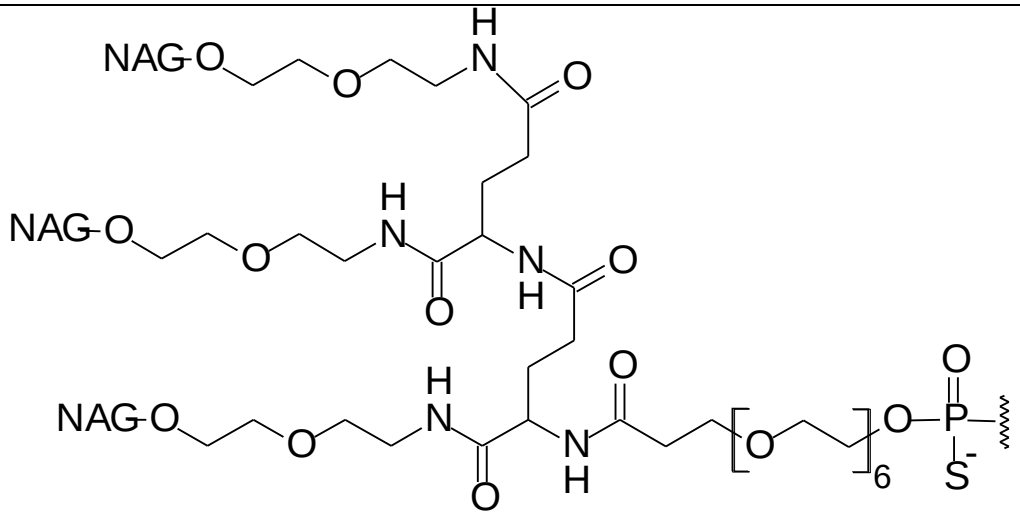
(NAG24)



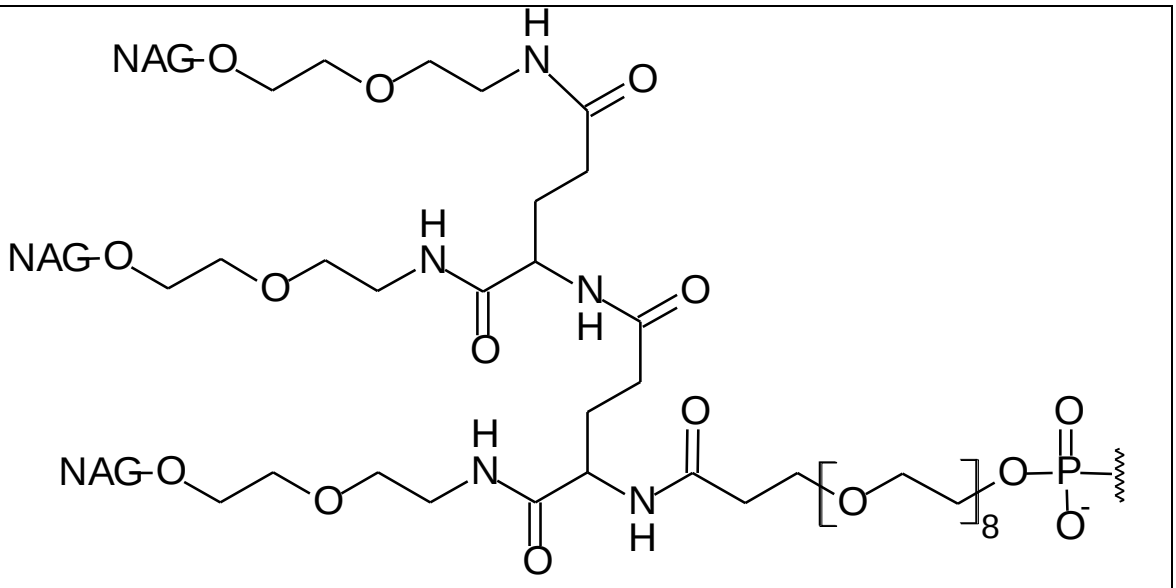
(NAG24)s



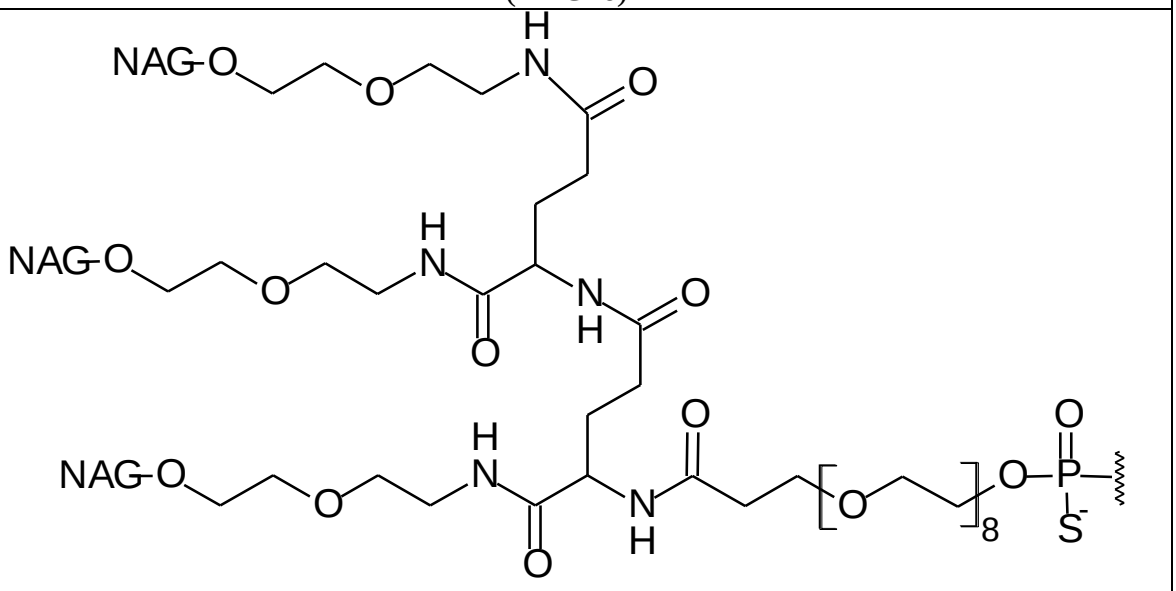
(NAG25)



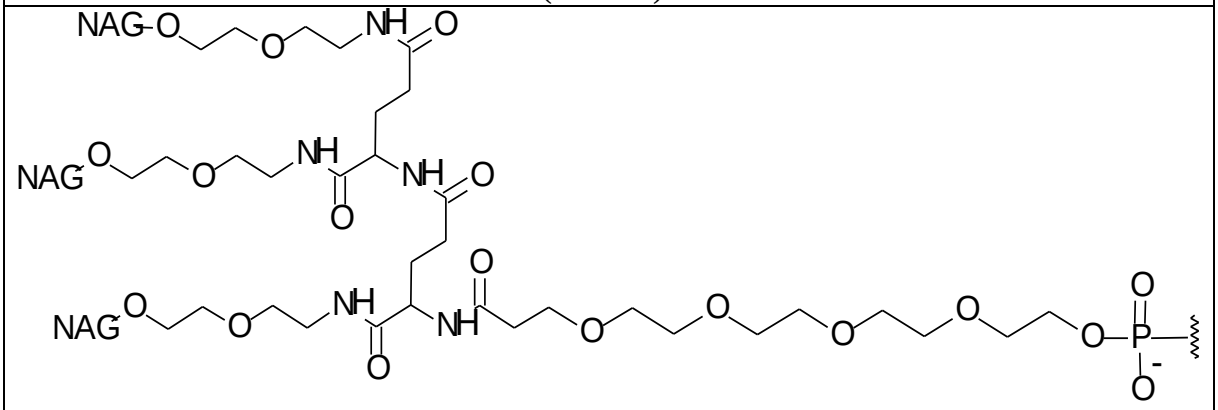
(NAG25)s



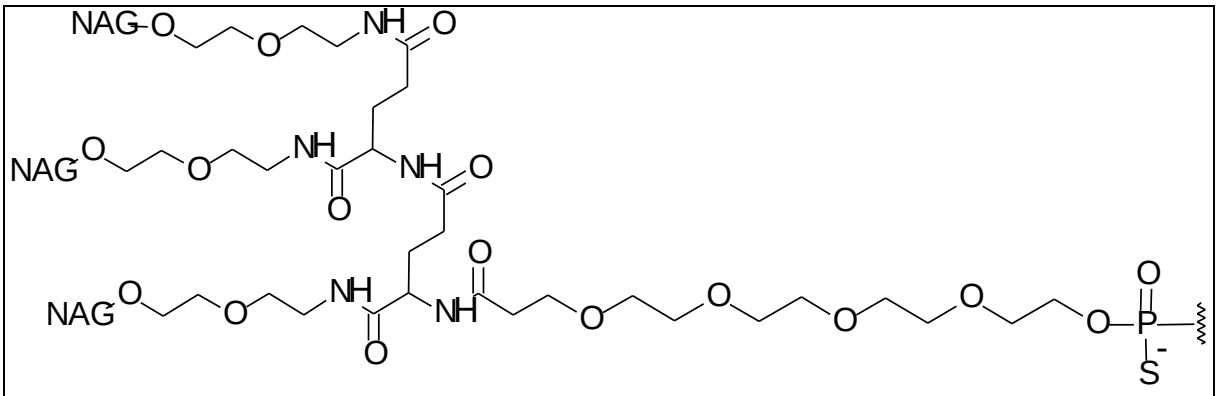
(NAG26)



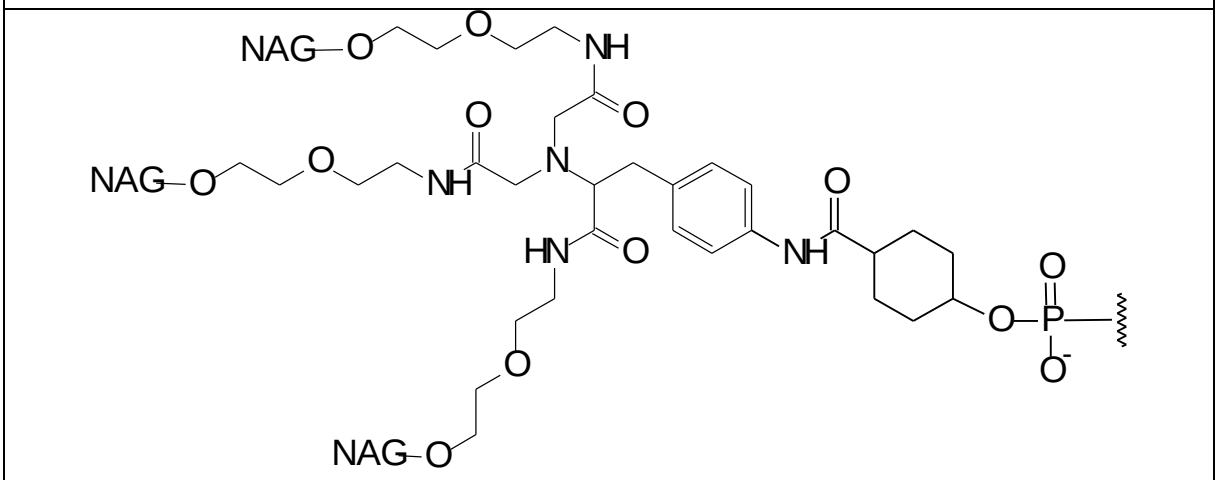
(NAG26)s



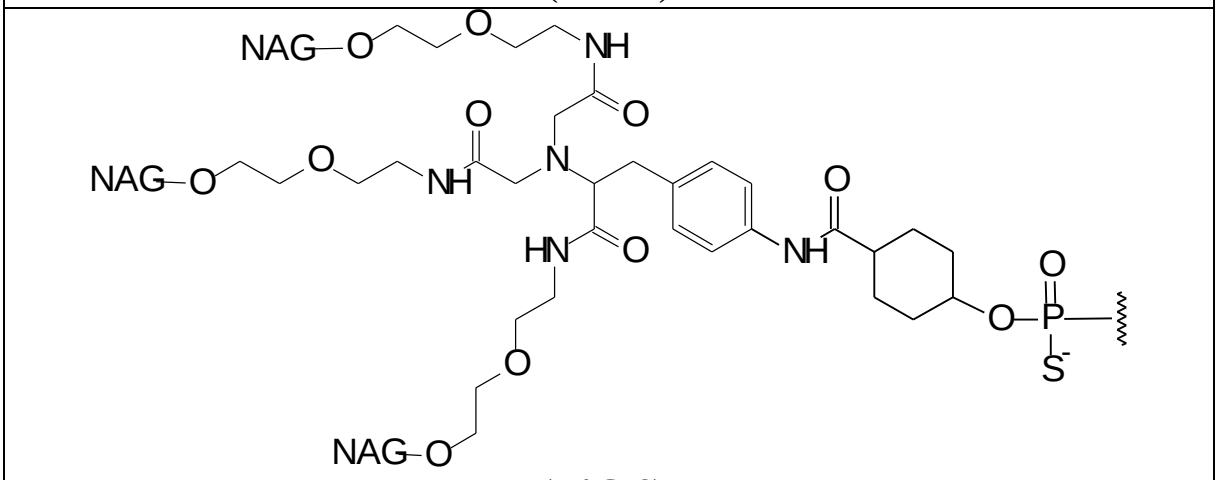
(NAG27)



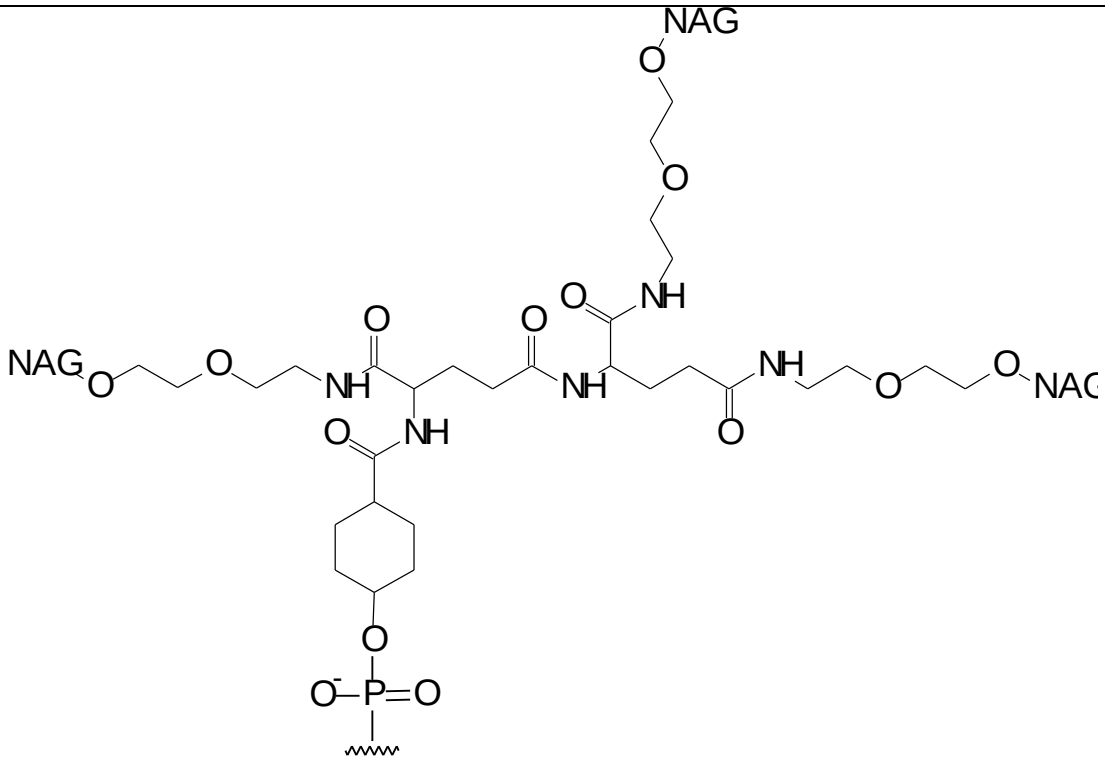
(NAG27)s



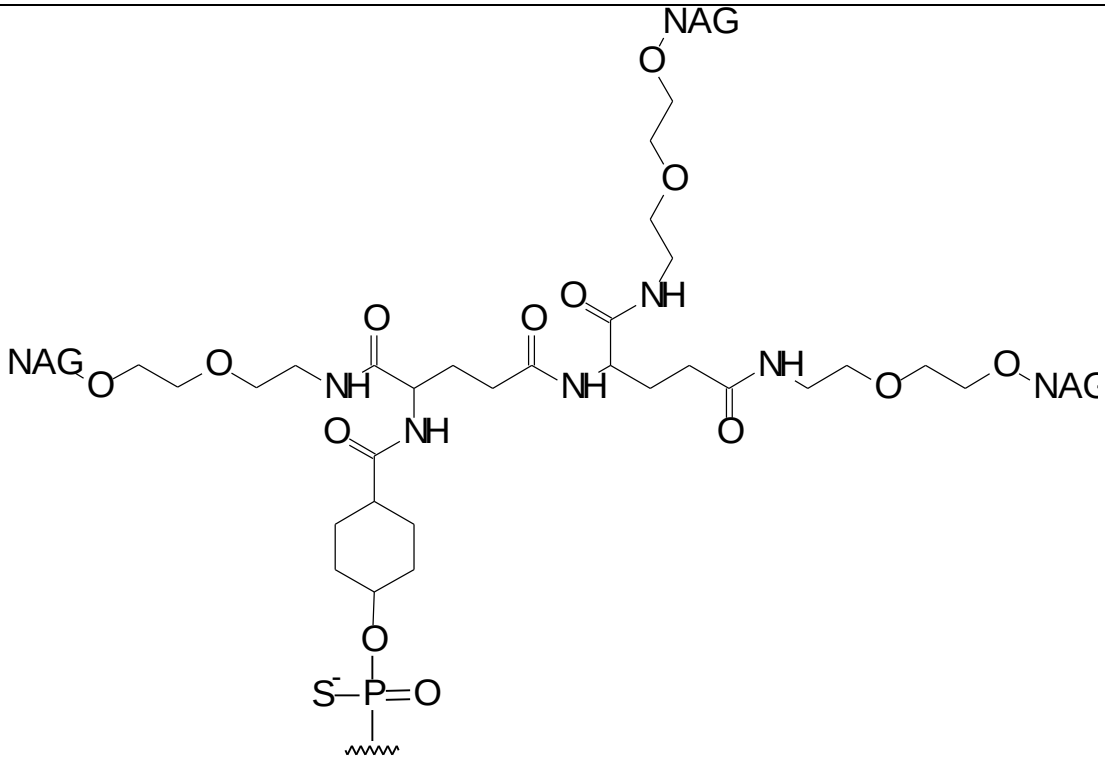
(NAG28)



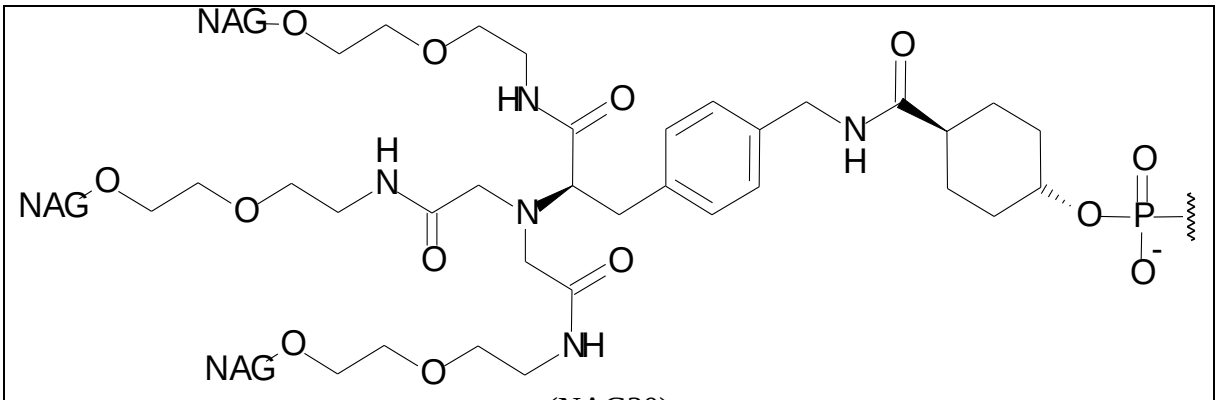
(NAG28)s



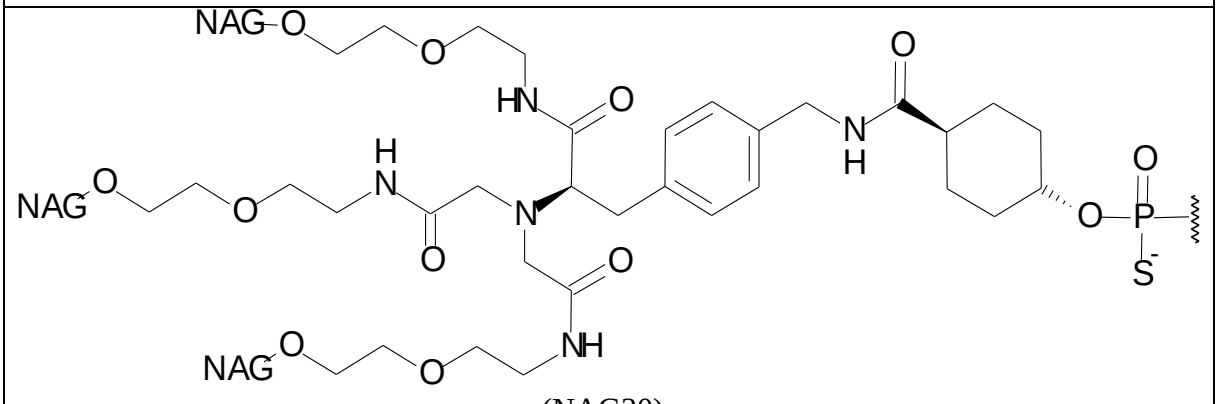
(NAG29)



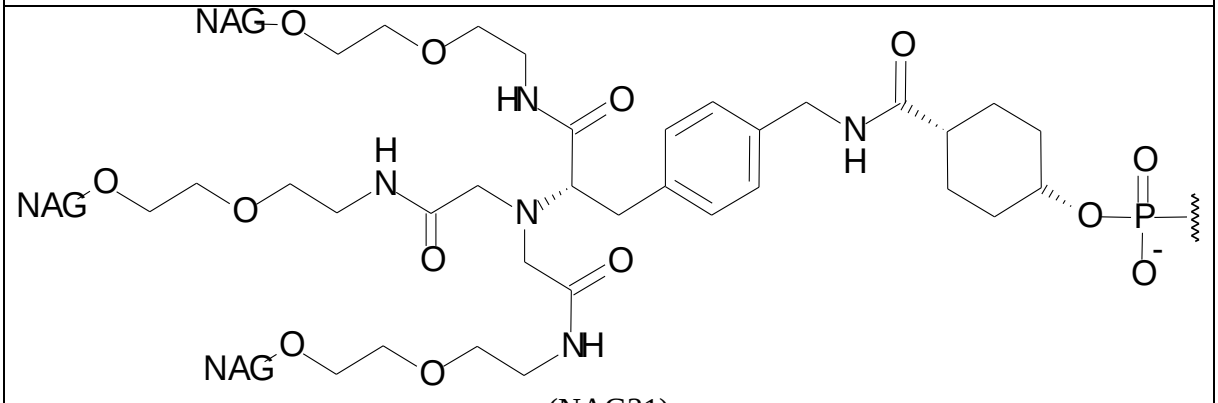
(NAG29)s



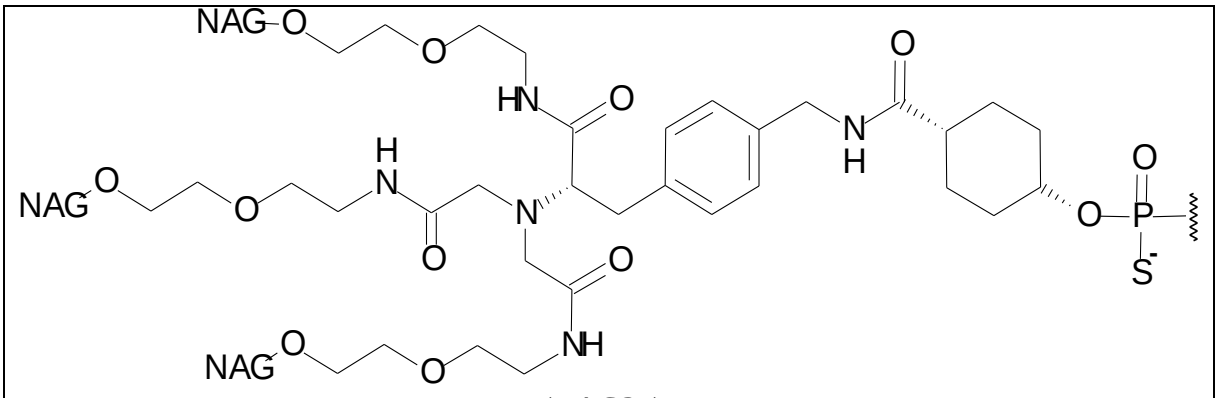
(NAG30)



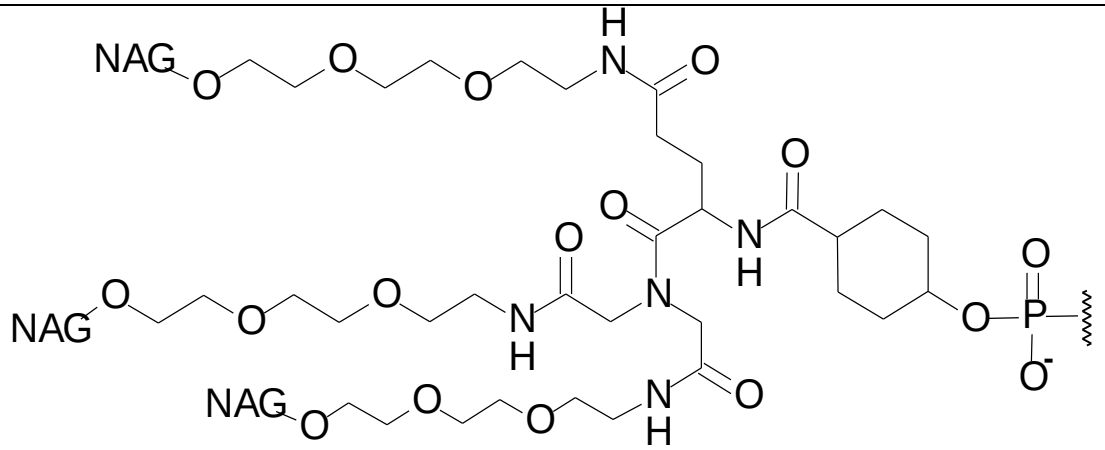
(NAG30)s



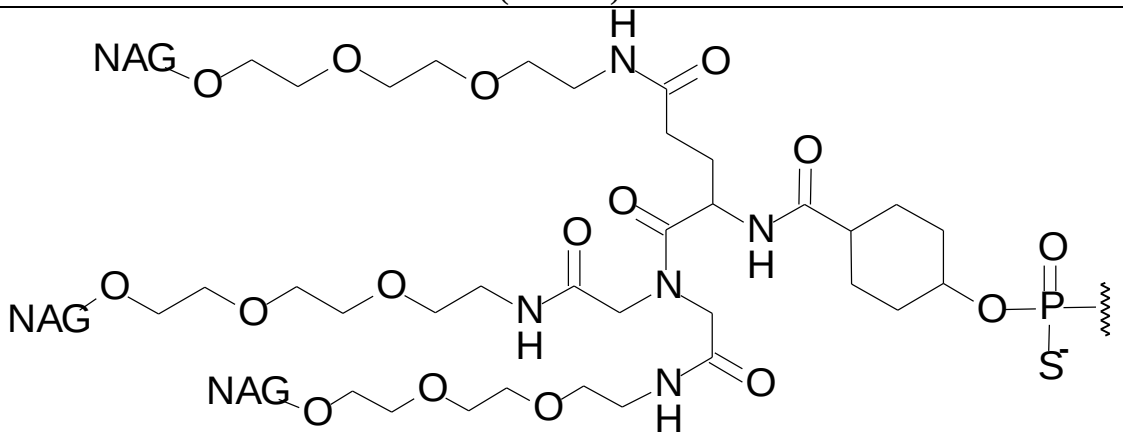
(NAG31)



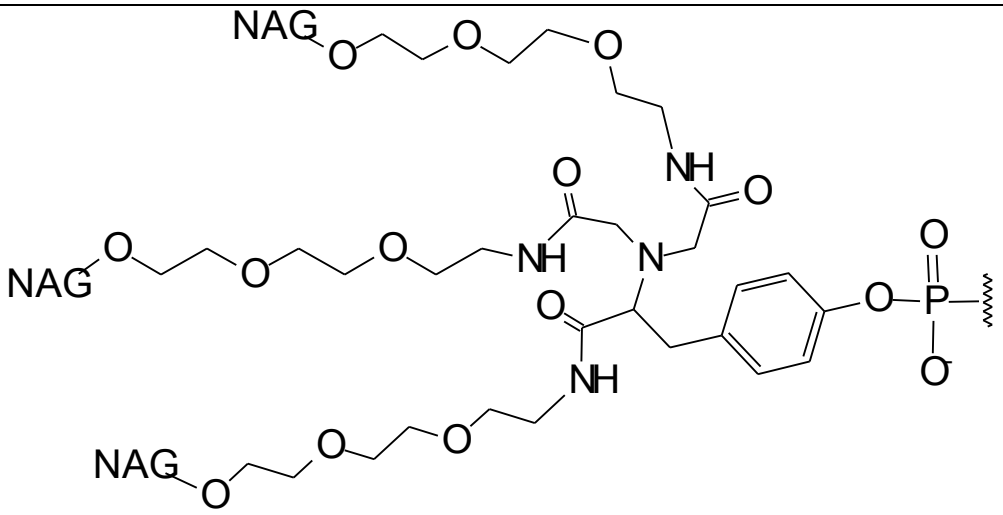
(NAG31)s



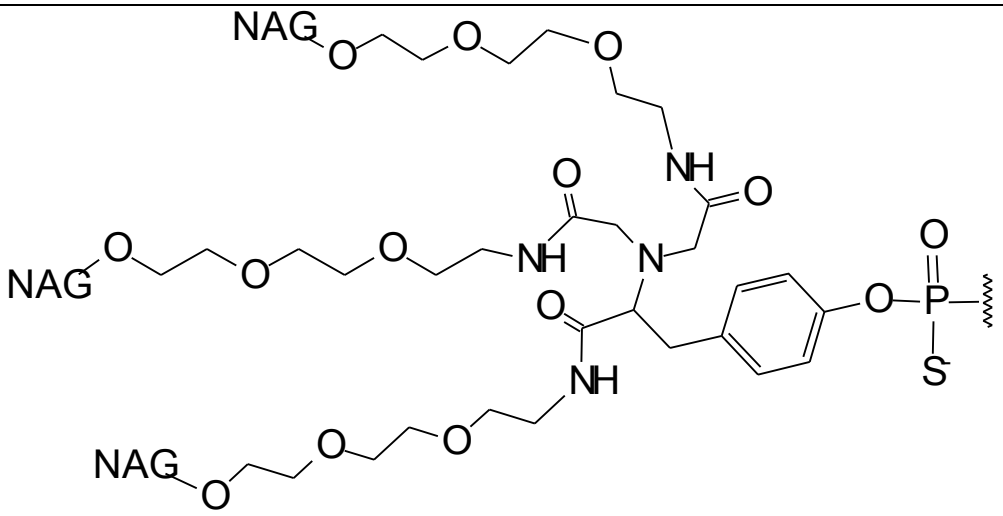
(NAG32)



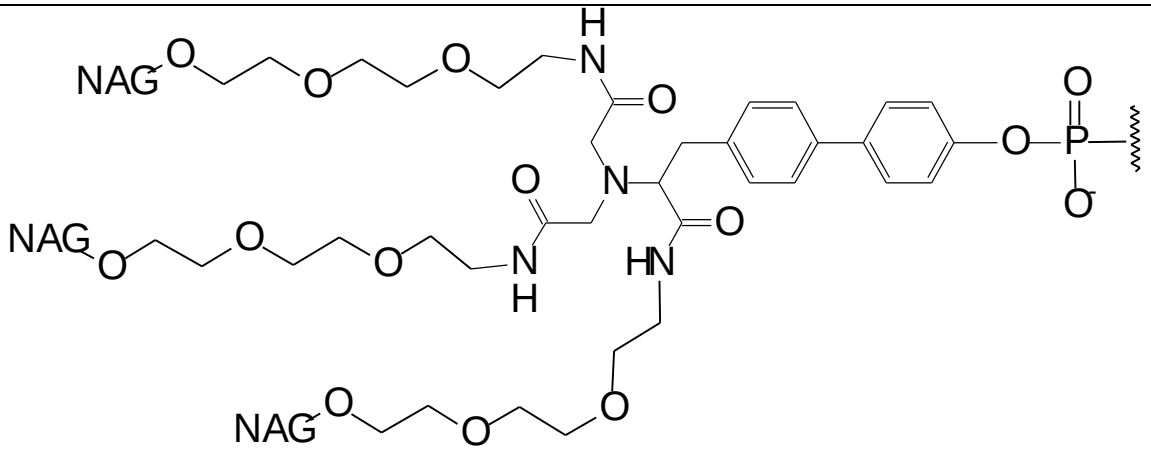
(NAG32)s



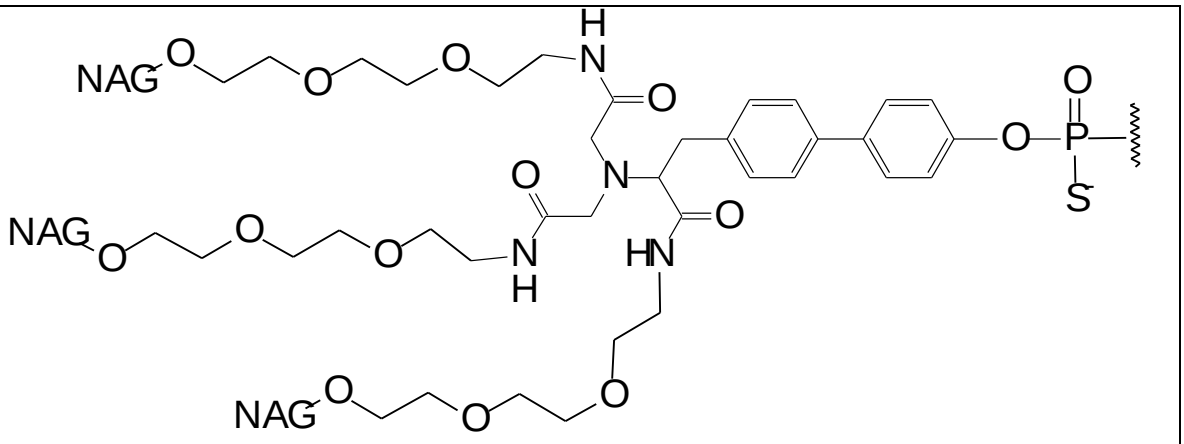
(NAG33)



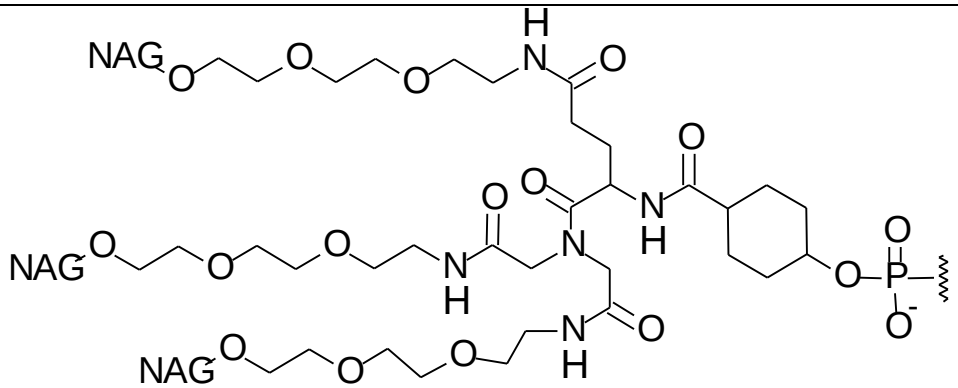
(NAG33)s



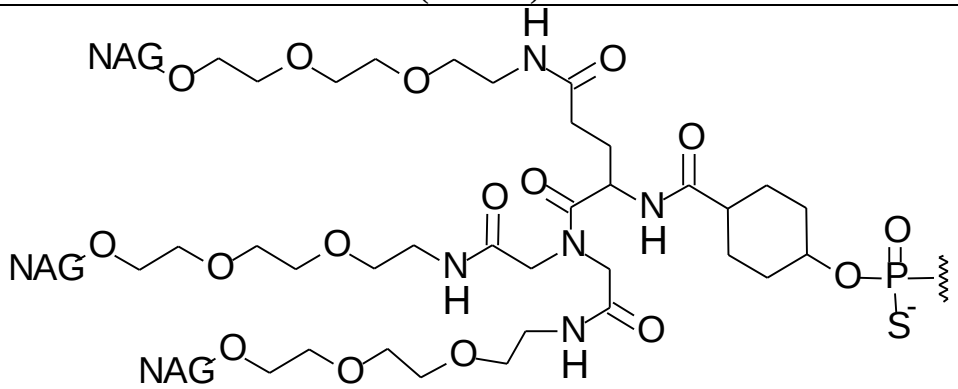
(NAG34)



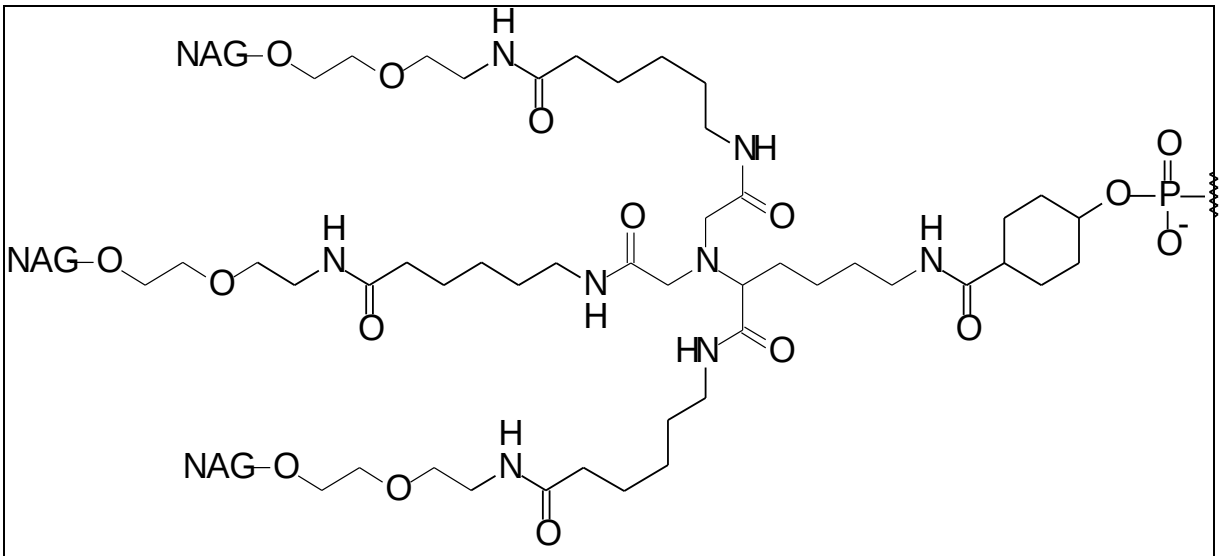
(NAG34)s



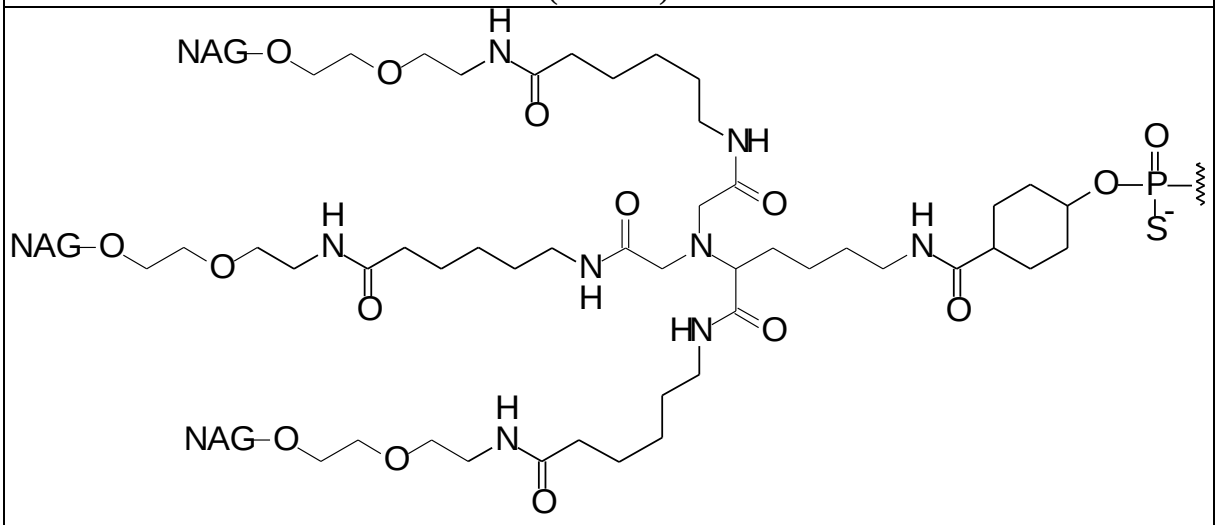
(NAG35)



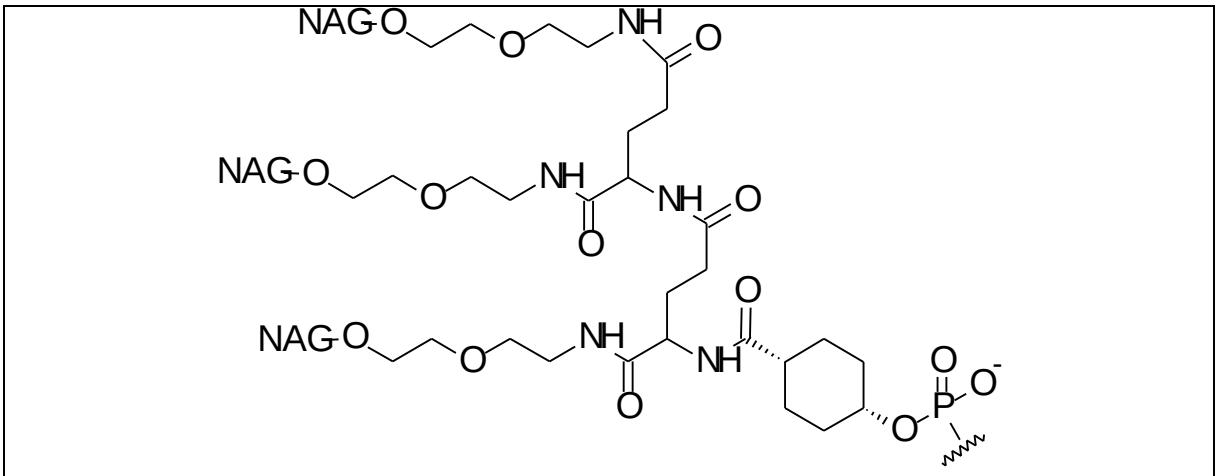
(NAG35)s



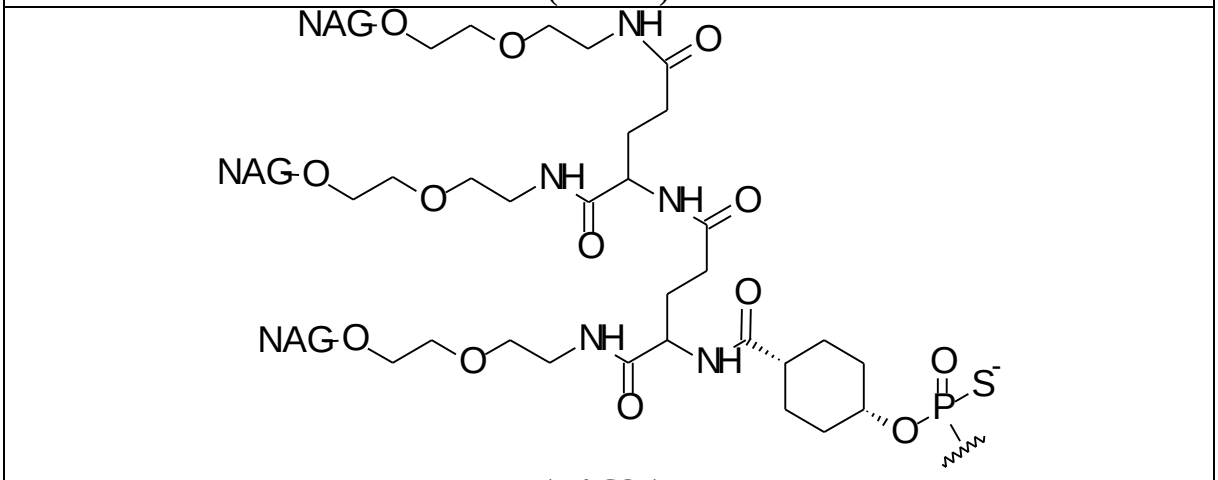
(NAG36)



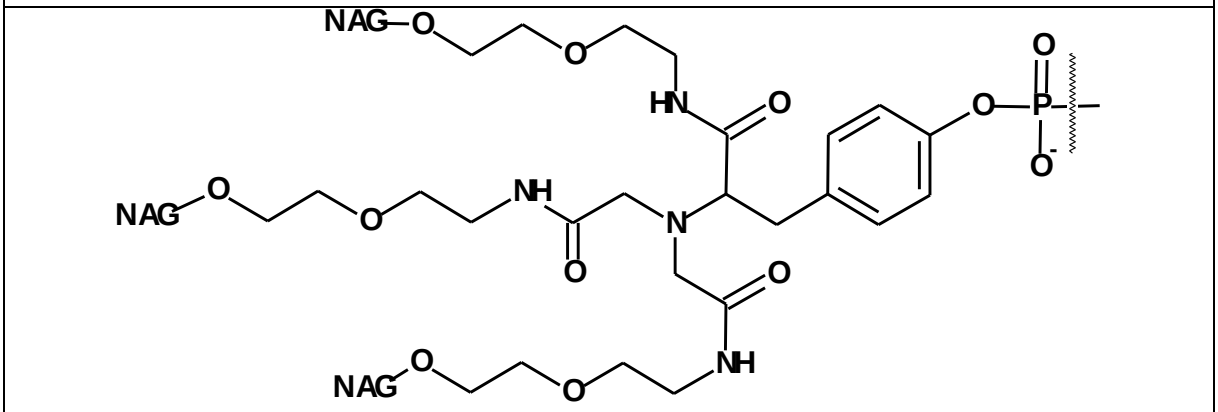
(NAG36)s



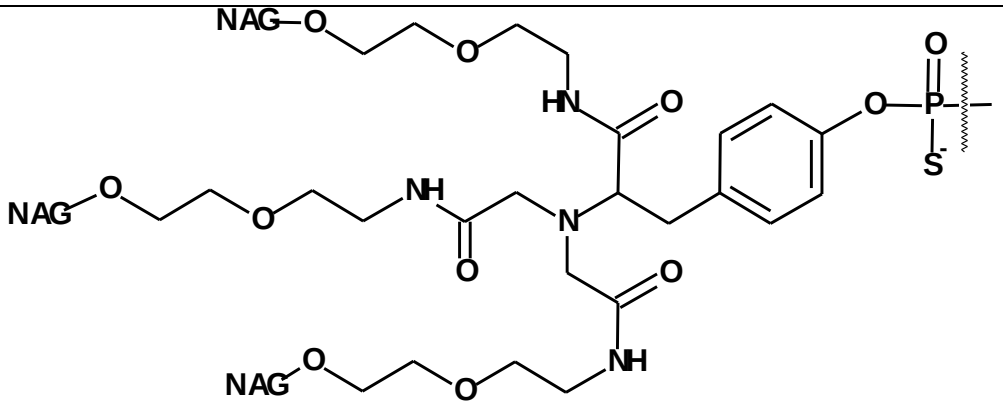
(NAG37)



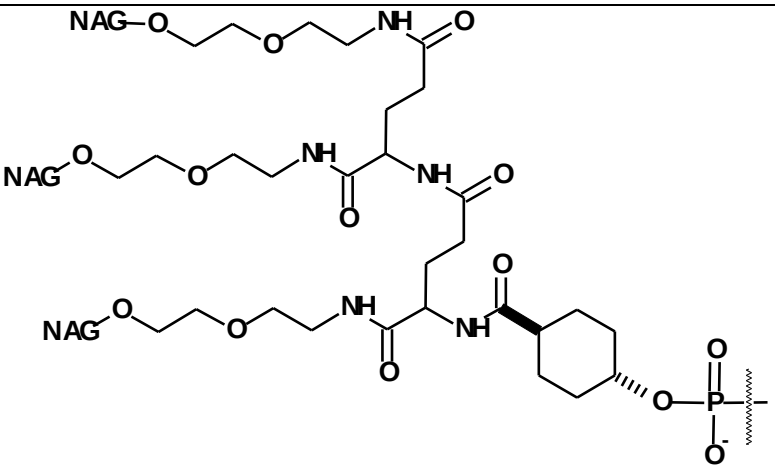
(NAG37)s



(NAG 38)

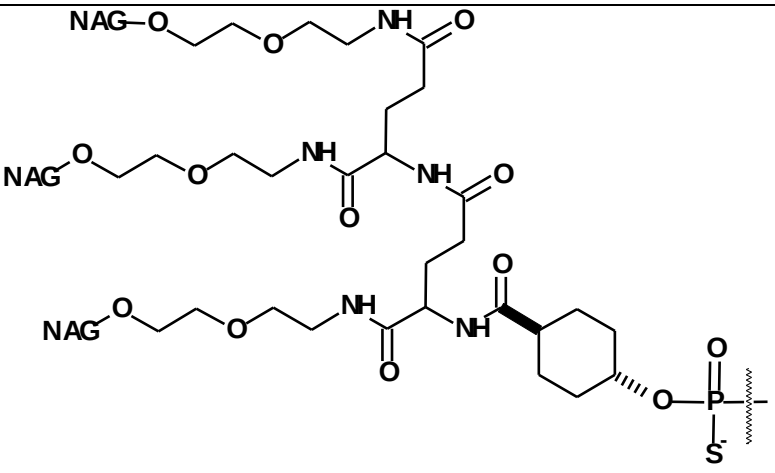


(NAG 38)s



(NAG39)

and



(NAG39)s

41. The combination of claim 39 or 40, wherein the targeting ligand is conjugated to the 3’ or 5’ terminus of the sense strand of the first or the second RNAi agent.

42. The combination of any one of claims 37-41, wherein the sense strand in the first or the second RNAi agents further comprises one or more inverted abasic nucleosides.

43. The combination of any one of claims 37-42 further comprising a pharmaceutically acceptable excipient, carrier, or diluent.

44. The combination of any one of claims 37-43, wherein the ratio of the first RNAi agent to the second RNAi agent by weight is in the range of 1:1 to 5:1.

45. The combination of any one of claims 37-44, wherein the first and the second RNA agents are formulated in a single pharmaceutical composition.

46. The combination of any one of claims 37-44, wherein the first and the second RNA agents are formulated in separate pharmaceutical compositions.

47. The combination of any one of claims 37-46, wherein the first and the second RNA agents are formulated for subcutaneous or intravenous injection.

48. A cell, tissue or non-human organism comprising the combination according to any one of claims 37-42.

49. A method of preparing a combination comprising at least two RNAi agents comprising a first RNAi agent and a second RNAi agent, the method comprising conjugating a first targeting group to a reactive group at the 5’- or 3’- terminus of the first RNAi agent, and conjugating targeting group to a reactive group at the 5’- or 3’- terminus of the second RNAi agent, wherein:

the first RNAi agent comprises: (a) an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:100, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:171, SEQ ID NO:179 and SEQ ID NO:180; and (b) a sense strand

comprising a nucleotide sequence of any one of the following: SEQ ID NO:229, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:273, SEQ ID NO:302 and SEQ ID NO:319;

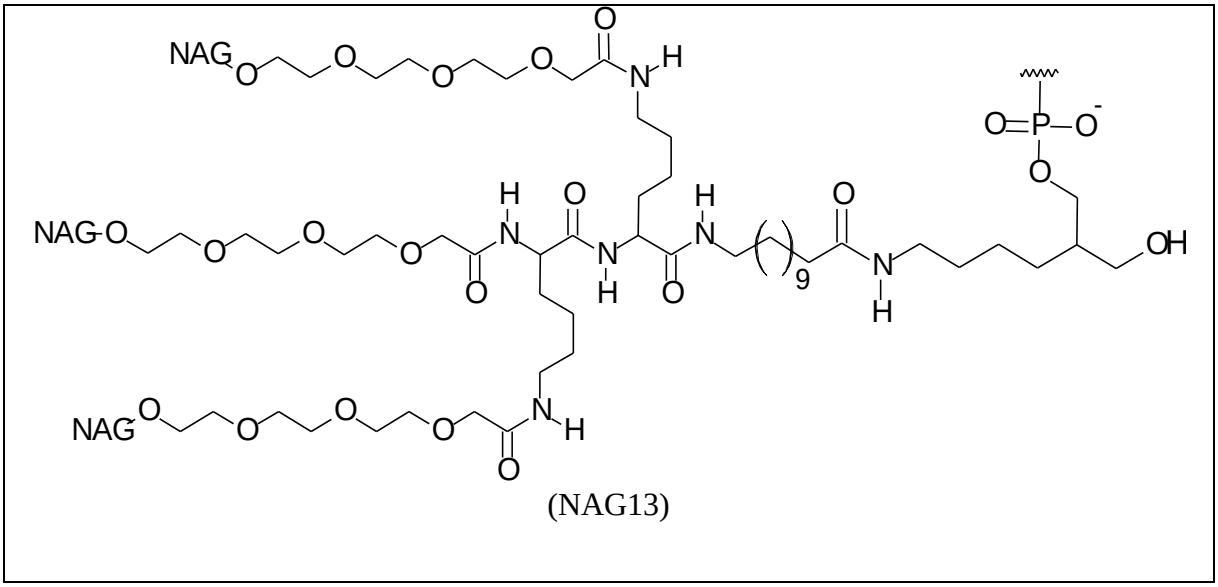
the second RNAi agent comprises: (a) an antisense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:140, SEQ ID NO:137, SEQ ID NO:102, SEQ ID NO:162 and SEQ ID NO:188; and (b) a sense strand comprising a nucleotide sequence of any one of the following: SEQ ID NO:248, SEQ ID NO:294, SEQ ID NO:262, SEQ ID NO:271, SEQ ID NO:274, and SEQ ID NO:328;

the reactive group at the 5'- or 3'- terminus of the first RNAi agent or the 5'- or 3'- terminus of the second RNAi agent is selected from the group consisting of amine, alkyne, alkyl, abasic nucleoside, ribitol and PEG; and

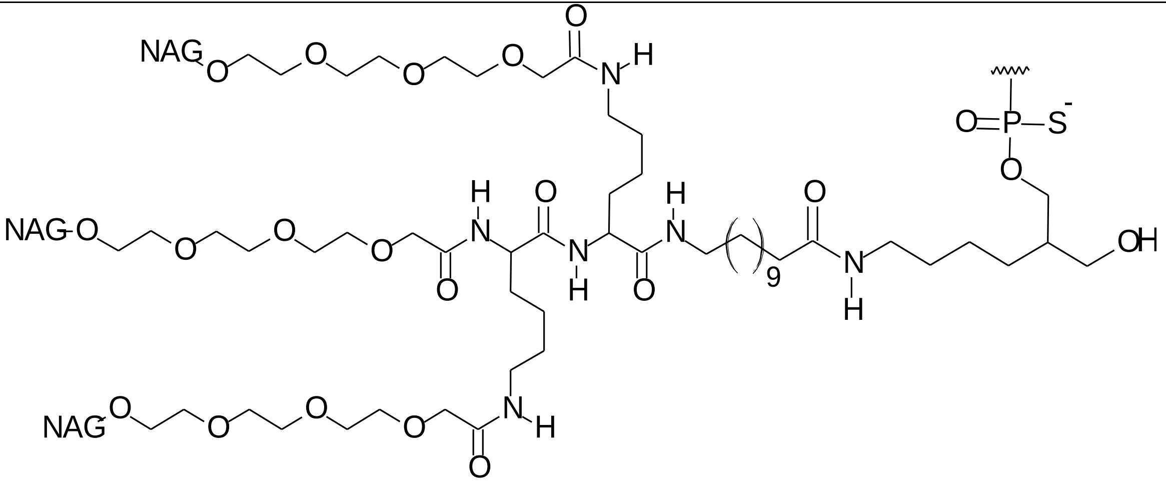
the first targeting group or the second targeting group comprises N-acetyl-galactosamine.

50. The method of claim 49, wherein the reactive group at the 5'- or 3'- terminus of the first RNAi agent or the 5'- or 3'- terminus of the second RNAi agent is an amine.

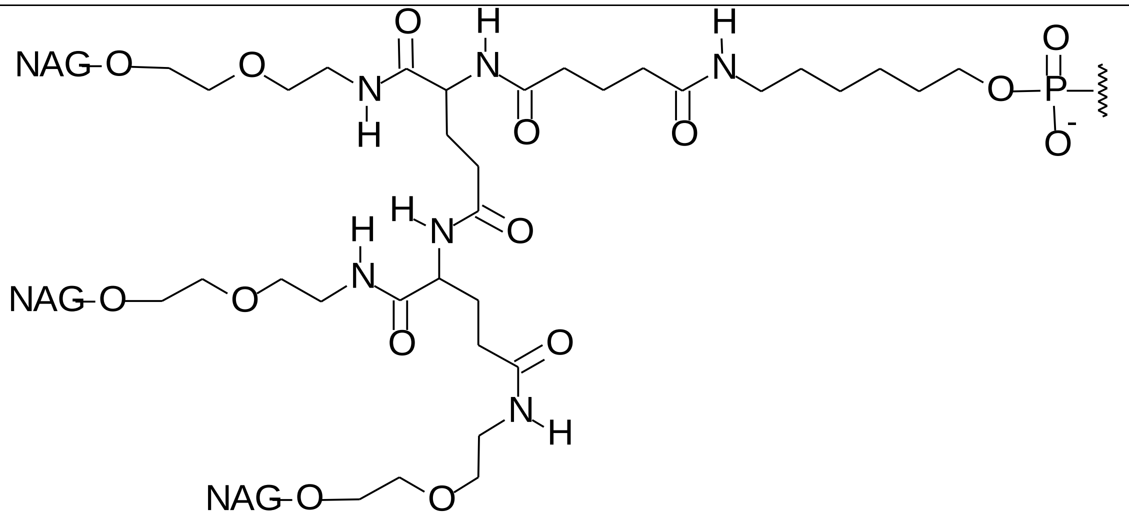
51. The method of claim 49 or 50, wherein the first targeting group or the second targeting group is selected from the group consisting of:



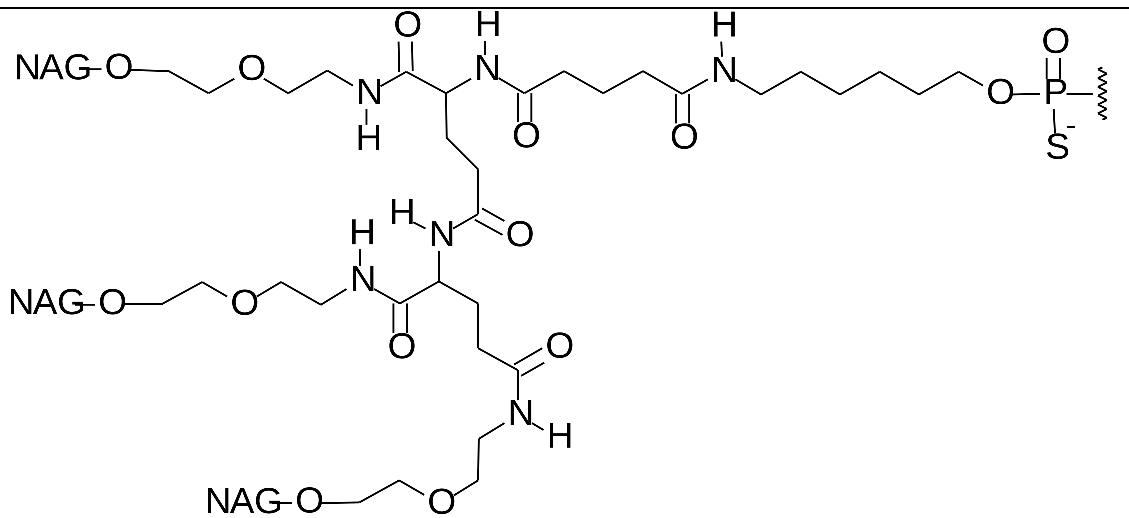
(NAG13)



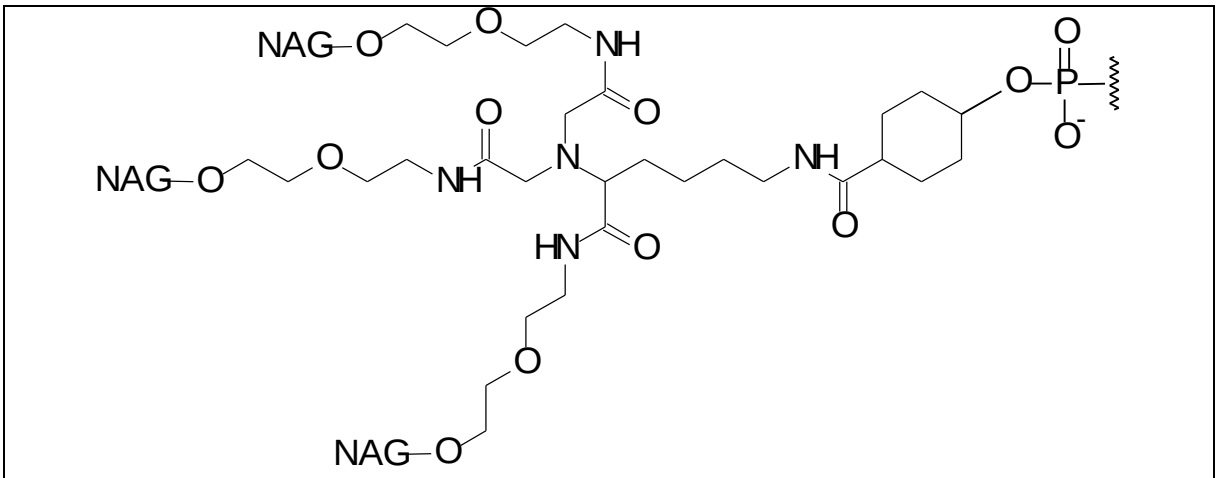
(NAG13)s



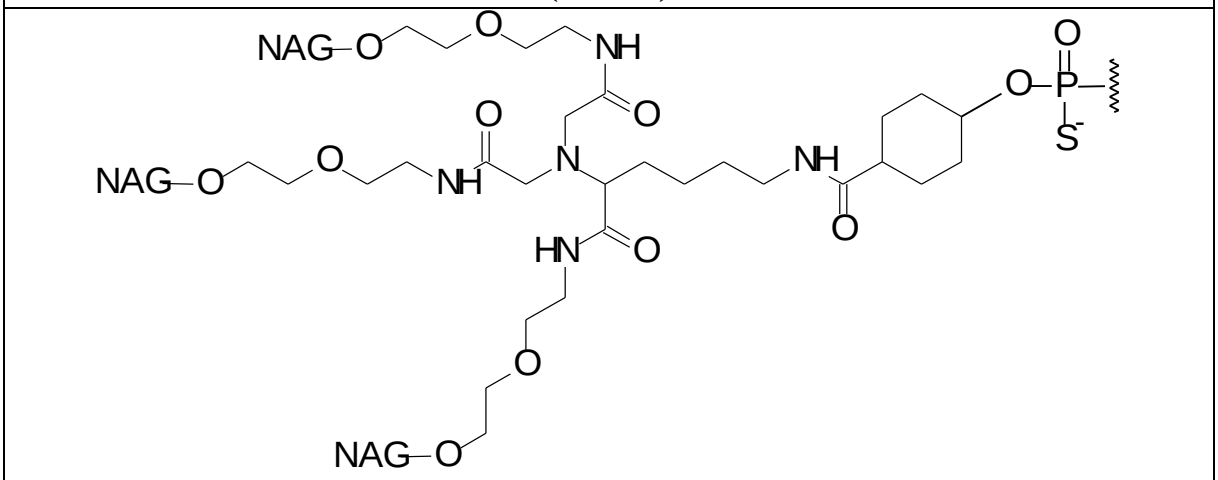
(NAG18)



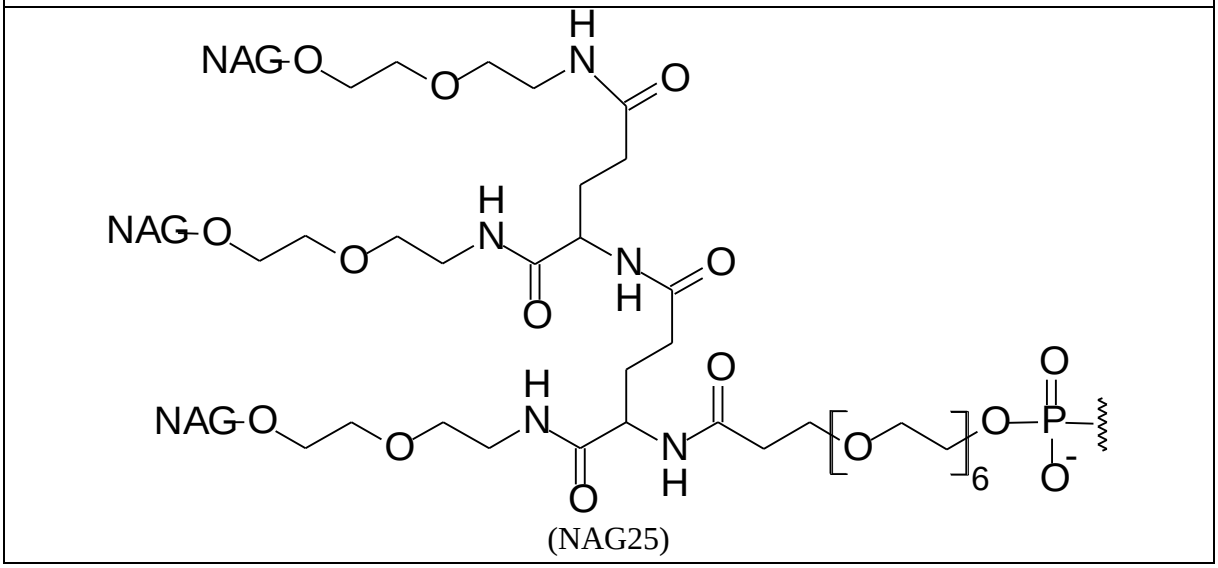
(NAG18)s



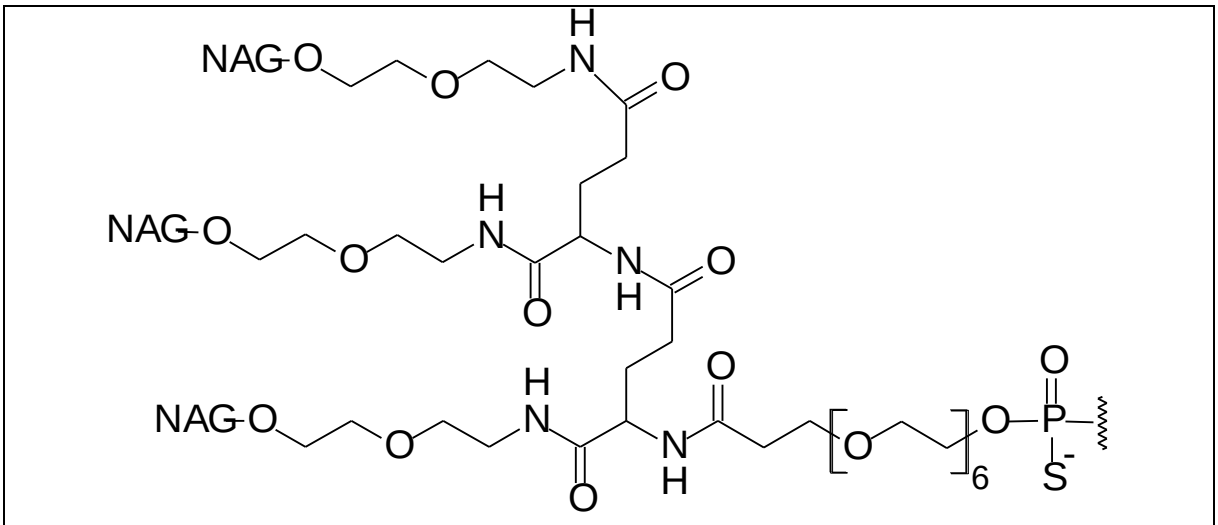
(NAG24)



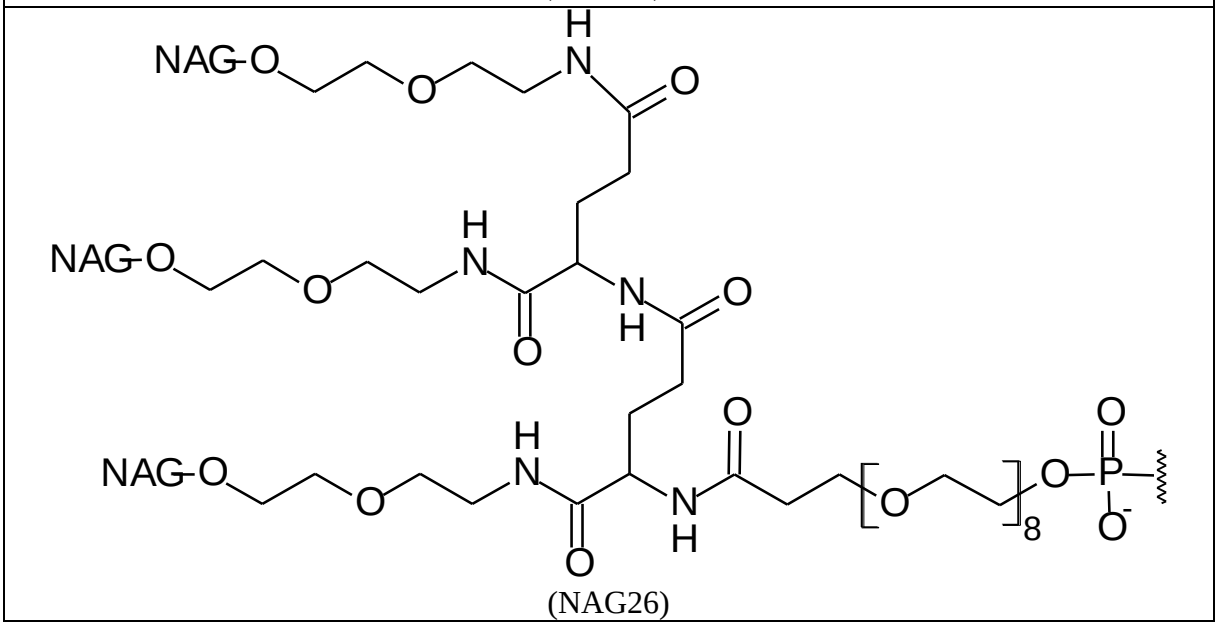
(NAG24)s



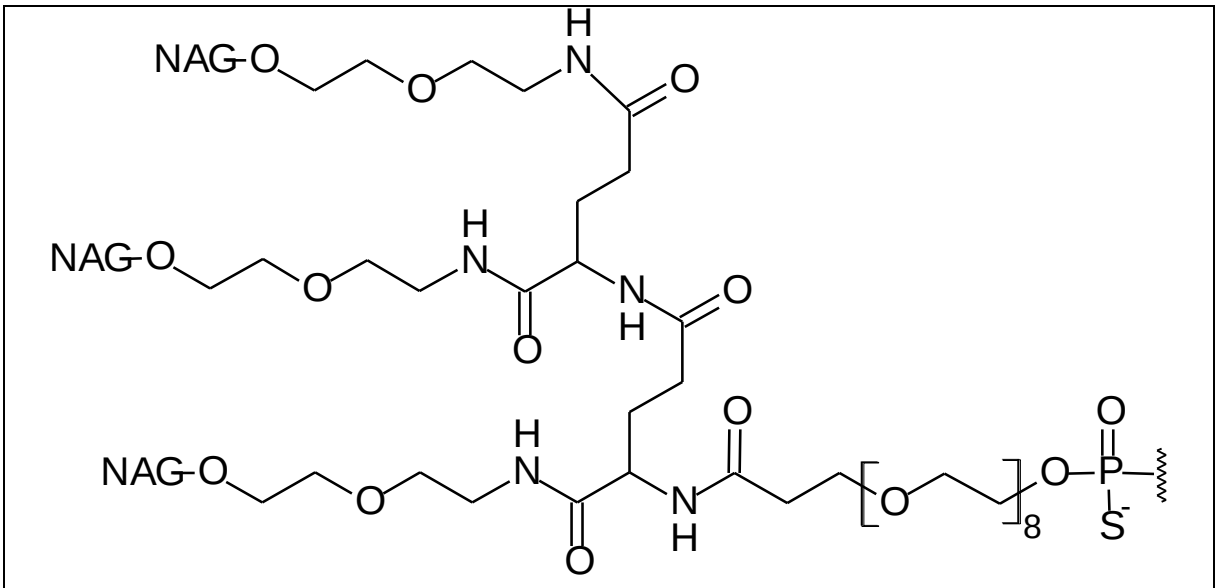
(NAG25)



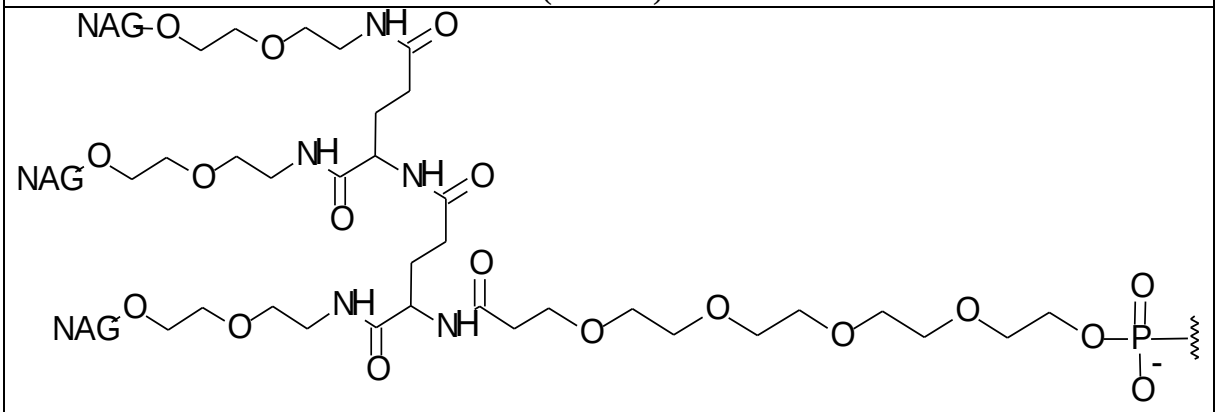
(NAG25)s



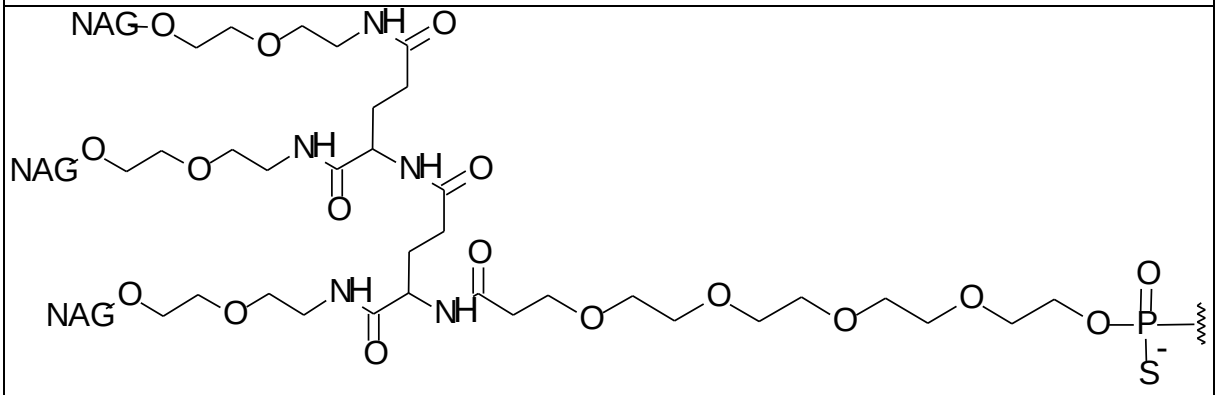
(NAG26)



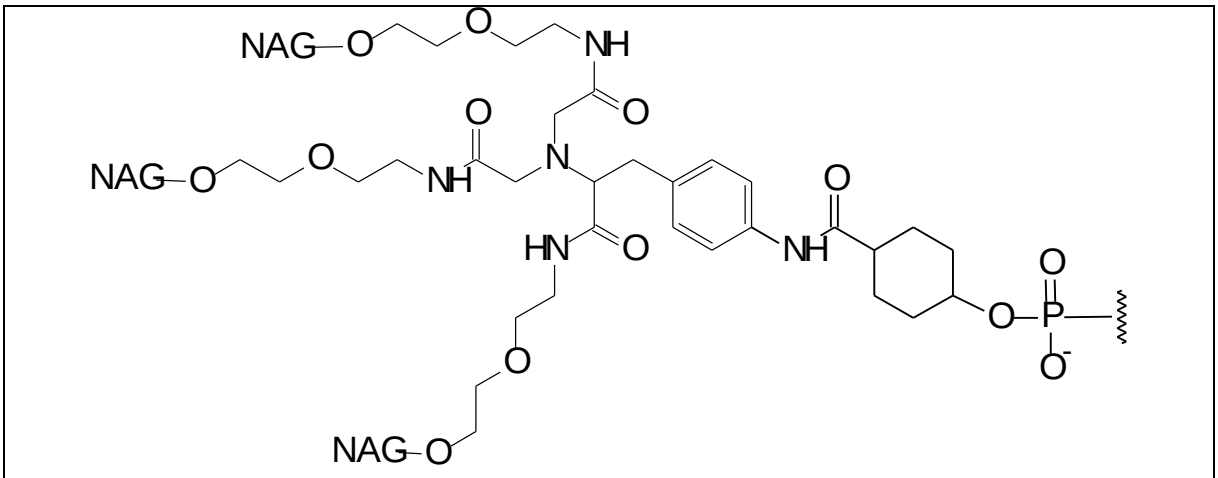
(NAG26)s



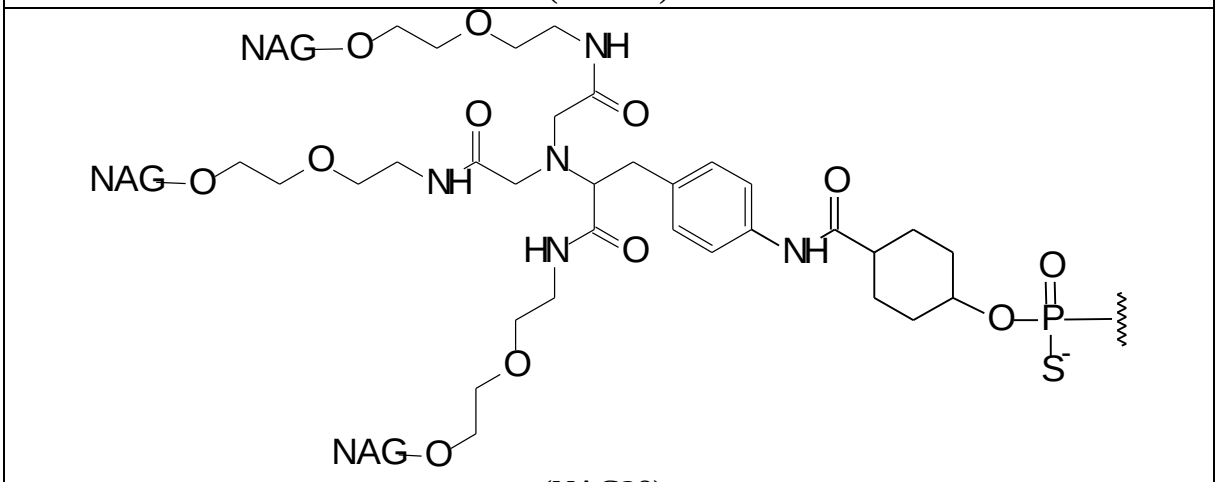
(NAG27)



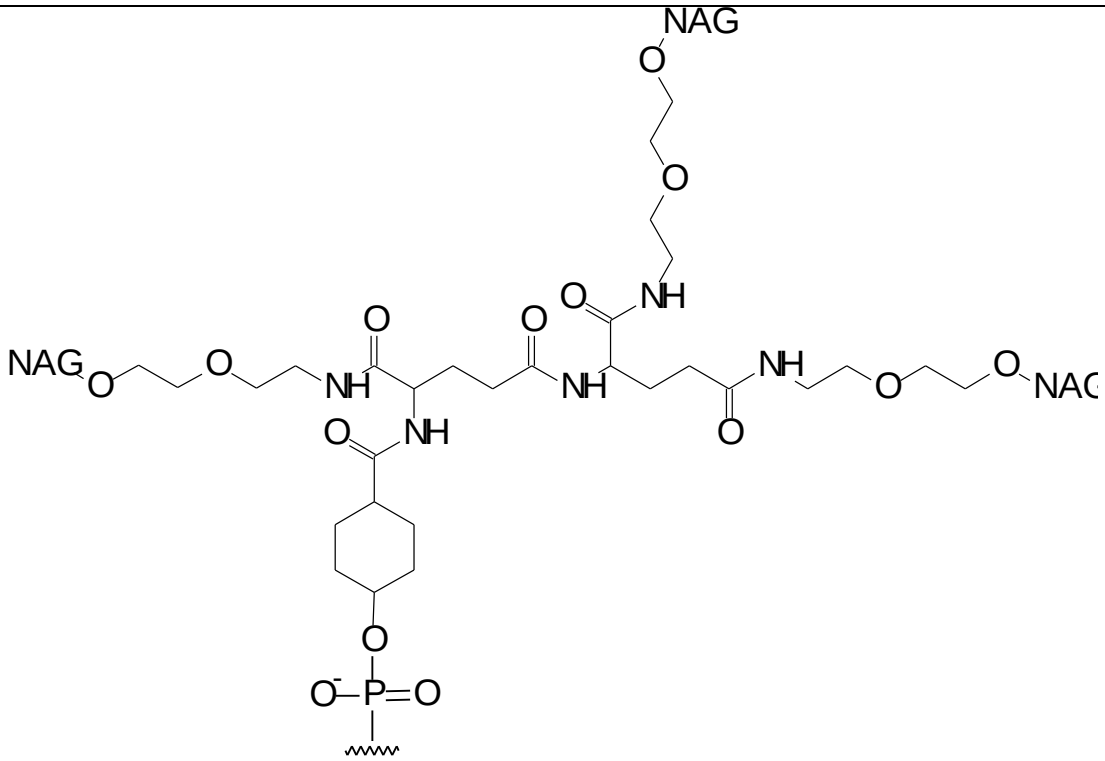
(NAG27)s



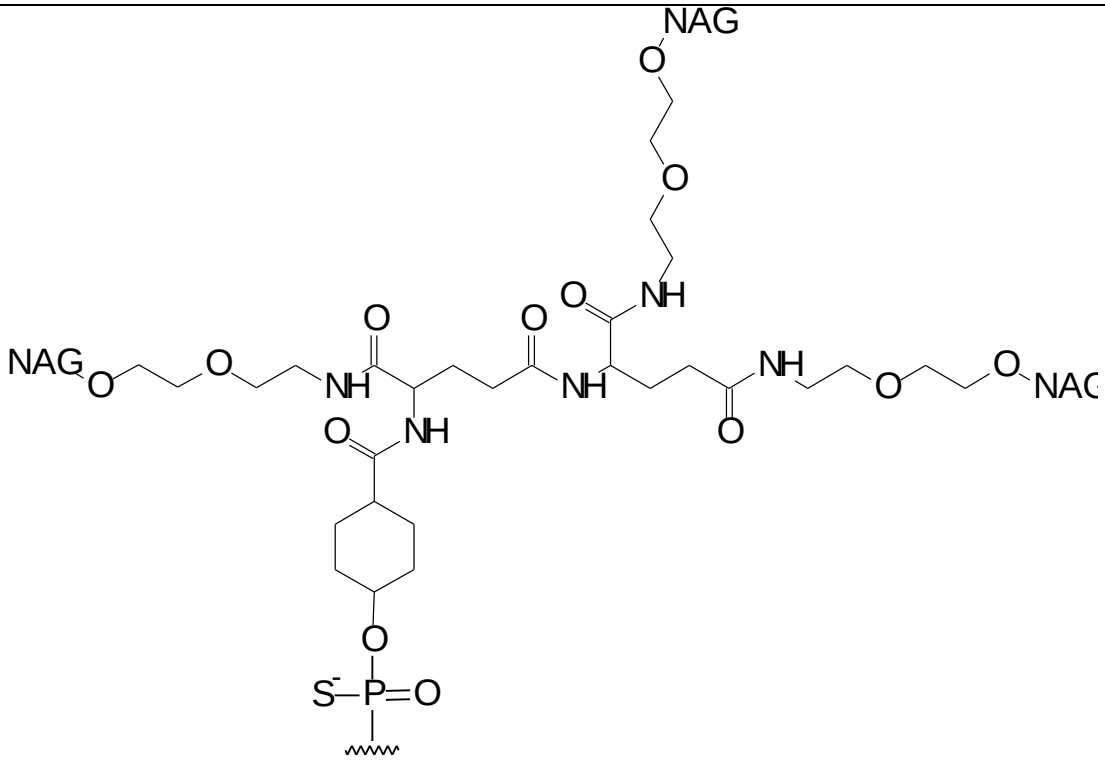
(NAG28)



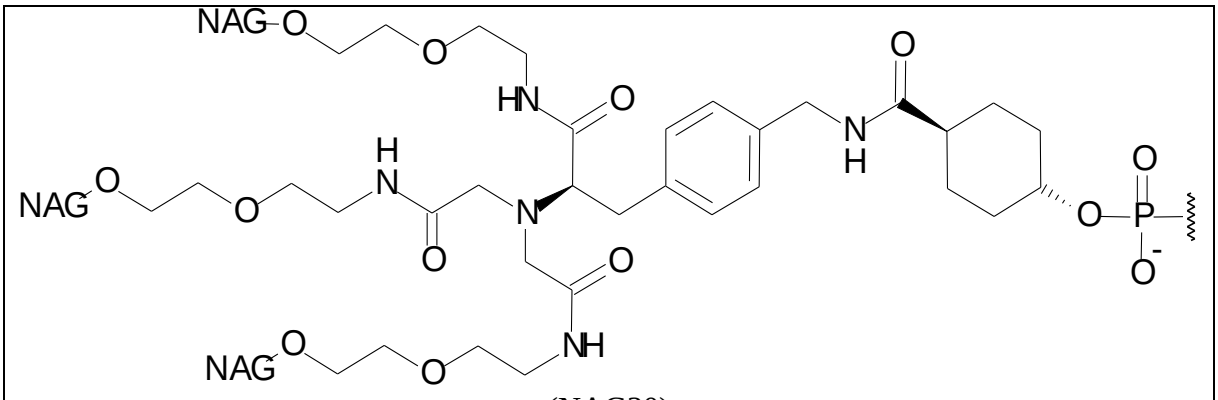
(NAG28)s



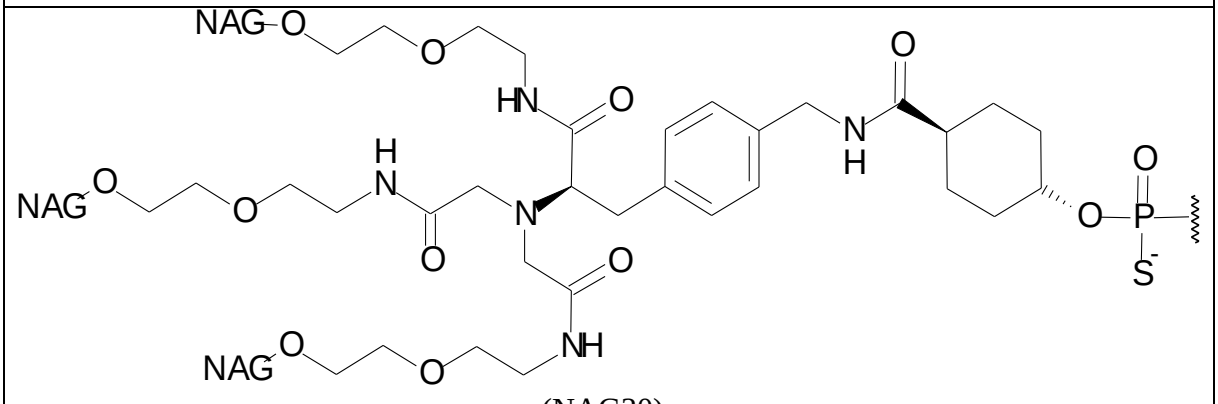
(NAG29)



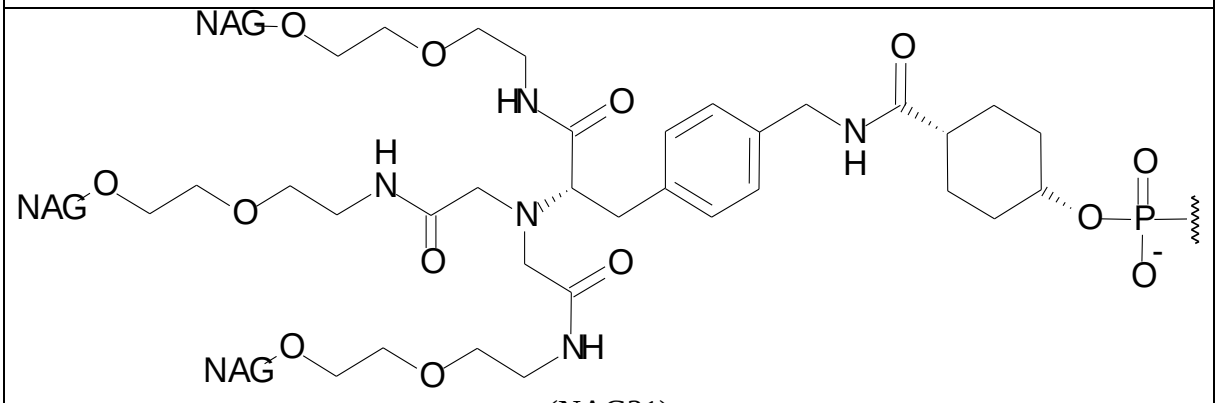
(NAG29)s



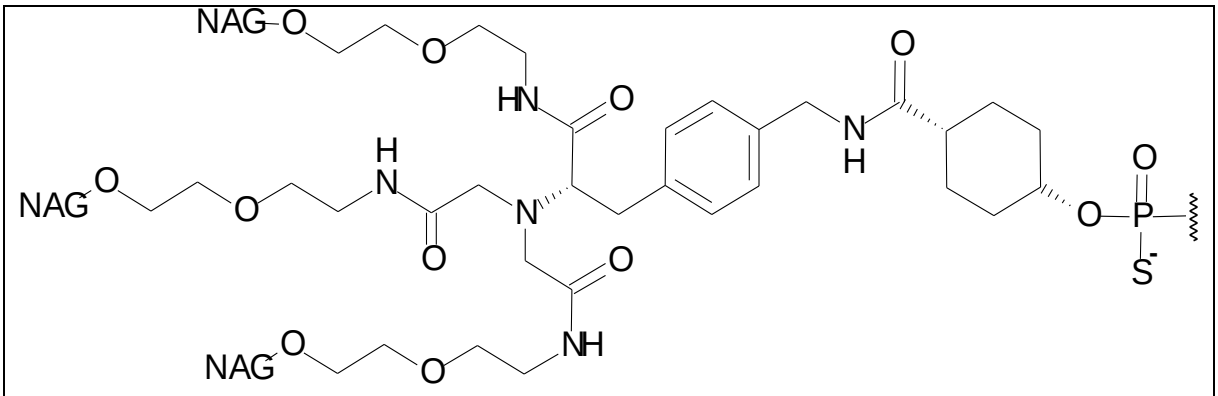
(NAG30)



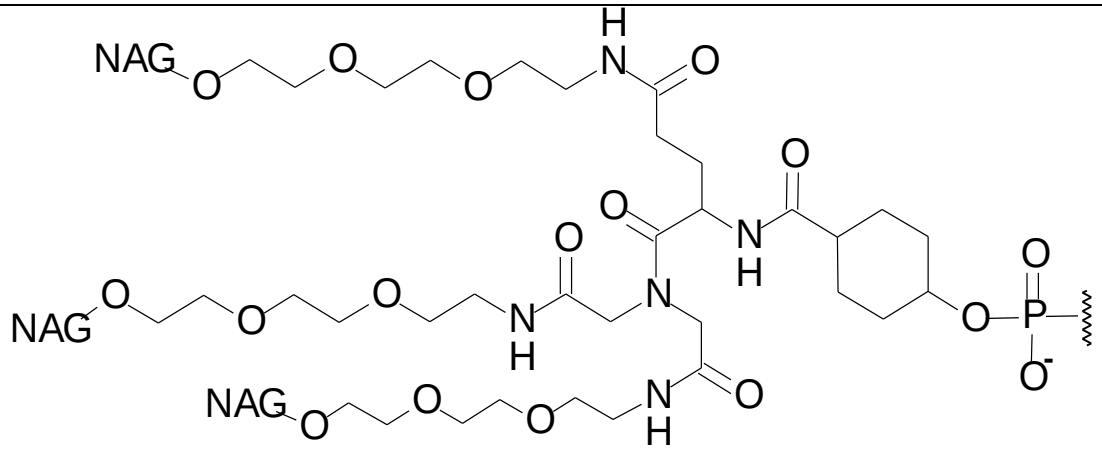
(NAG30)s



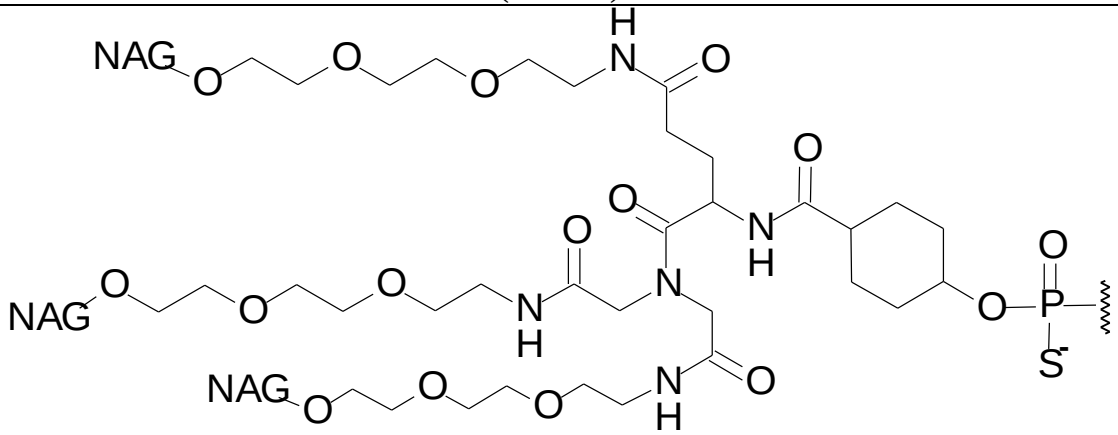
(NAG31)



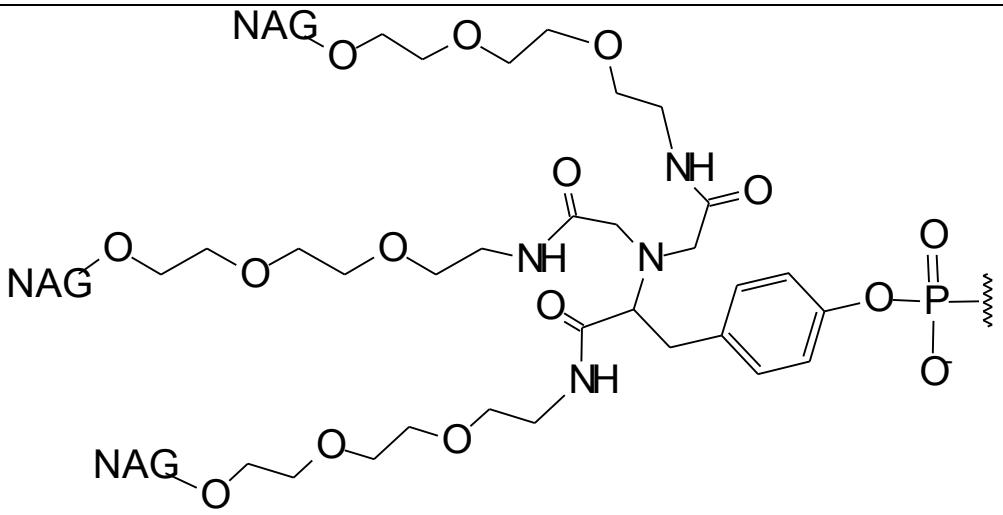
(NAG31)s



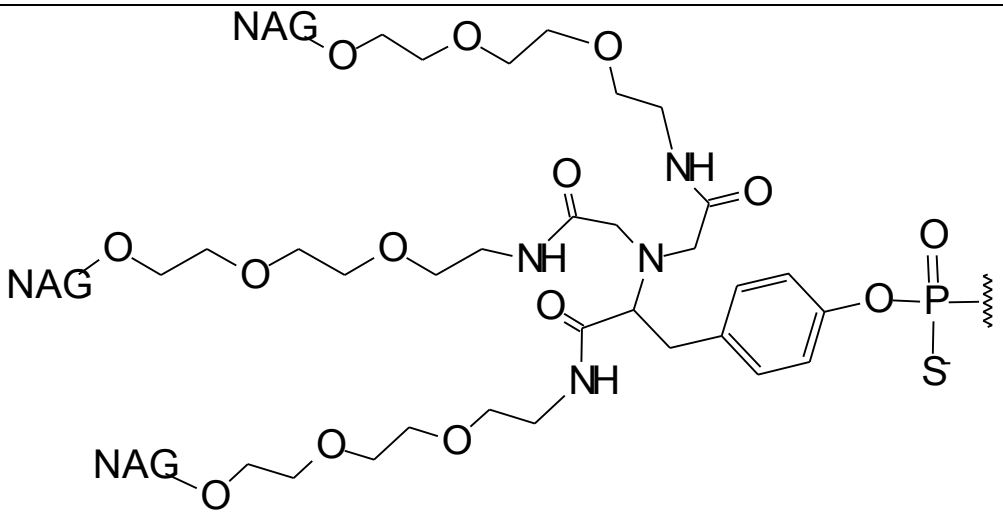
(NAG32)



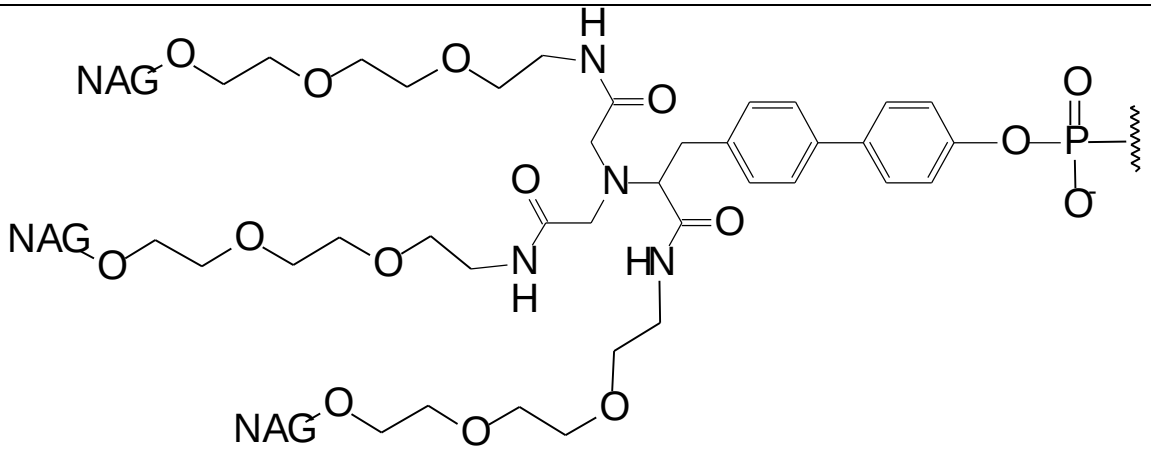
(NAG32)s



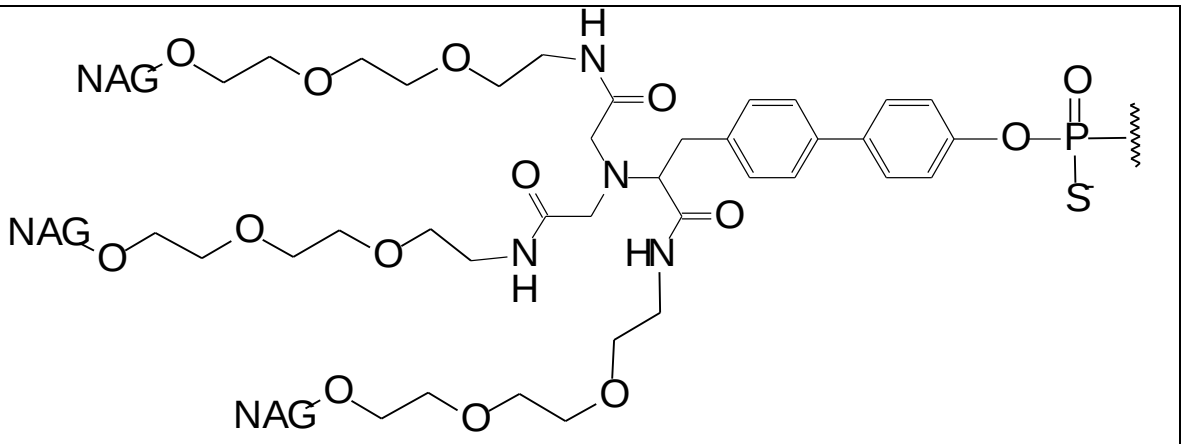
(NAG33)



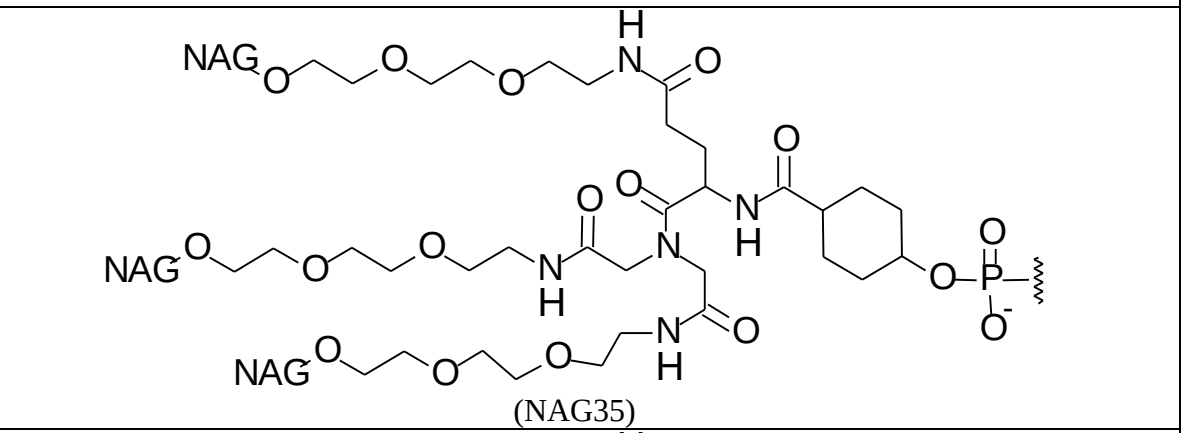
(NAG33)s



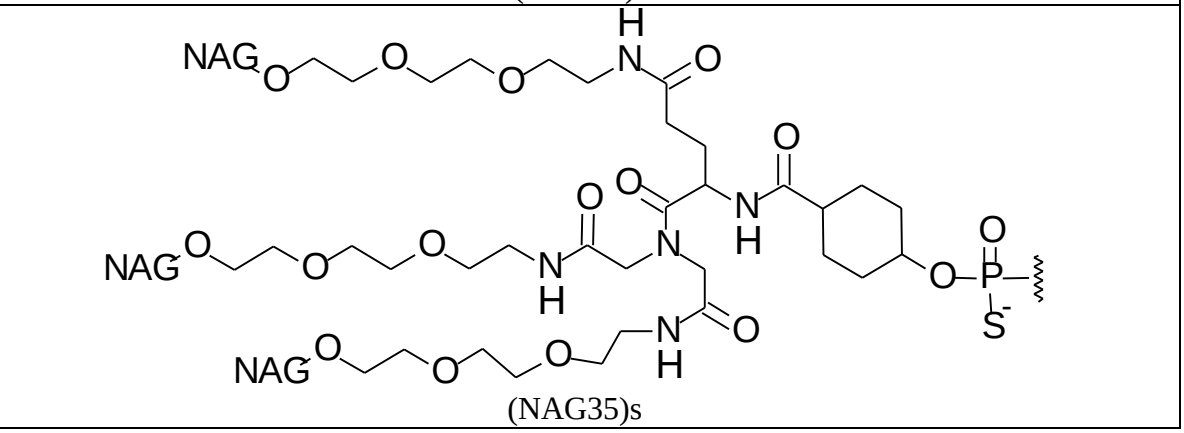
(NAG34)



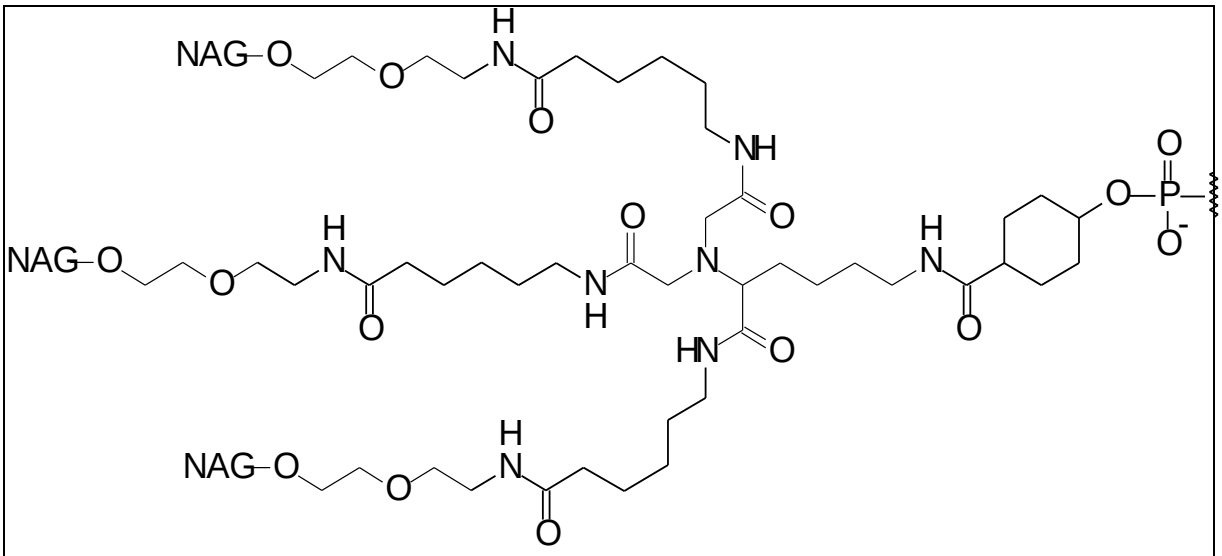
(NAG34)s



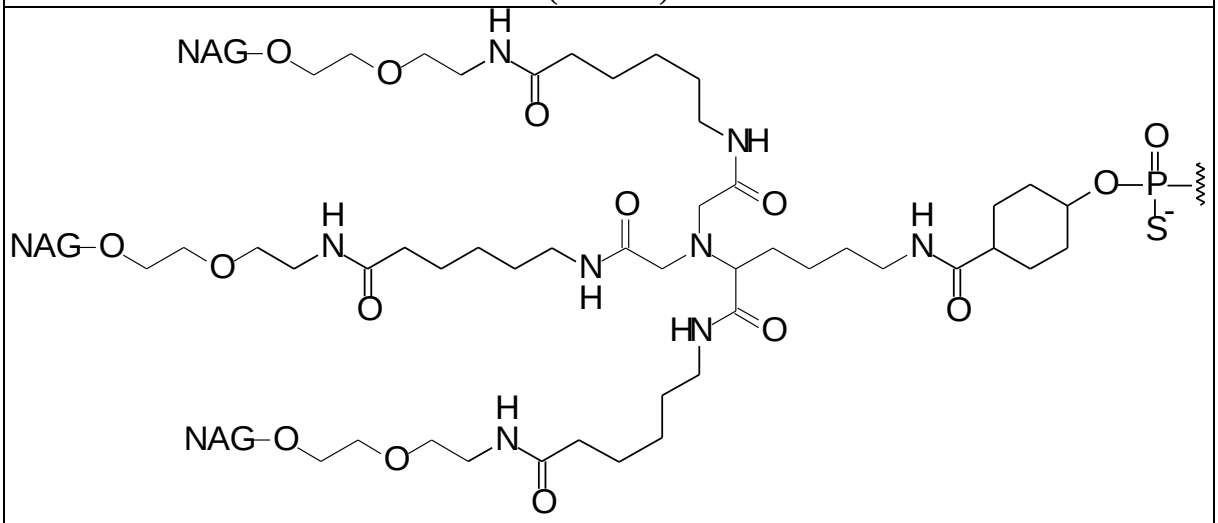
(NAG35)



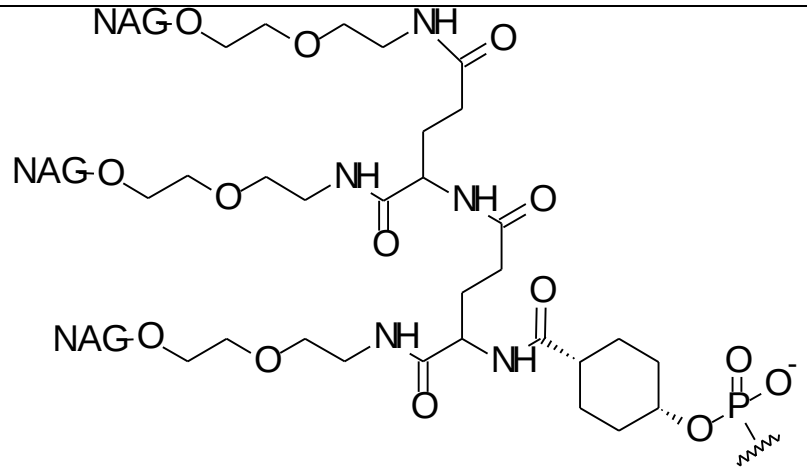
(NAG35)s



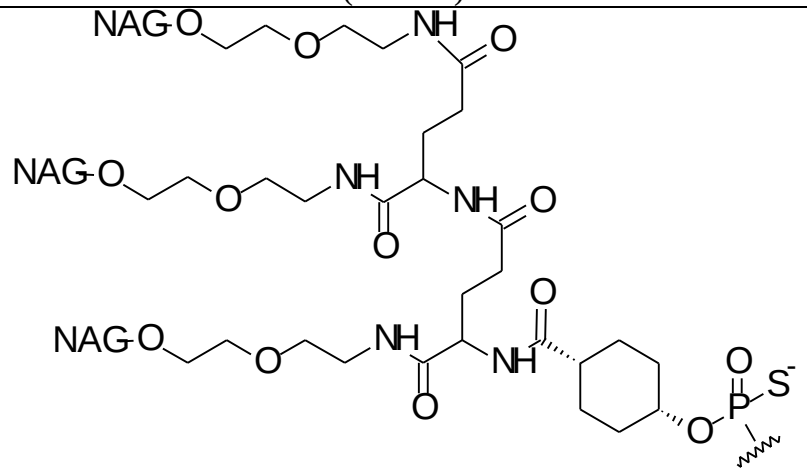
(NAG36)



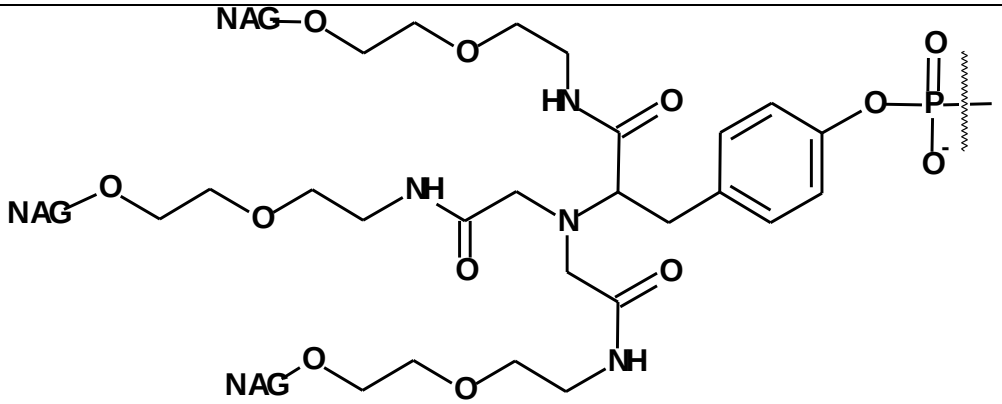
(NAG36)s



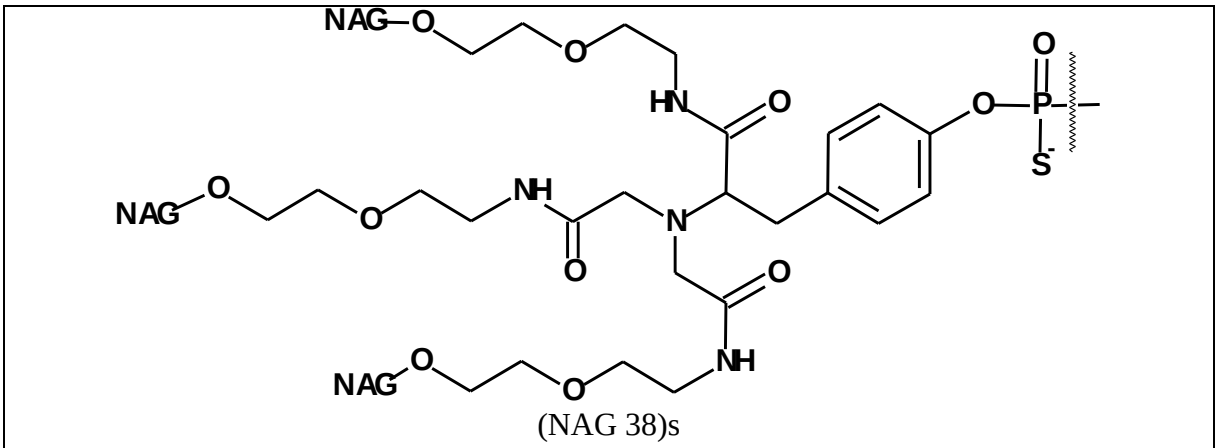
(NAG37)



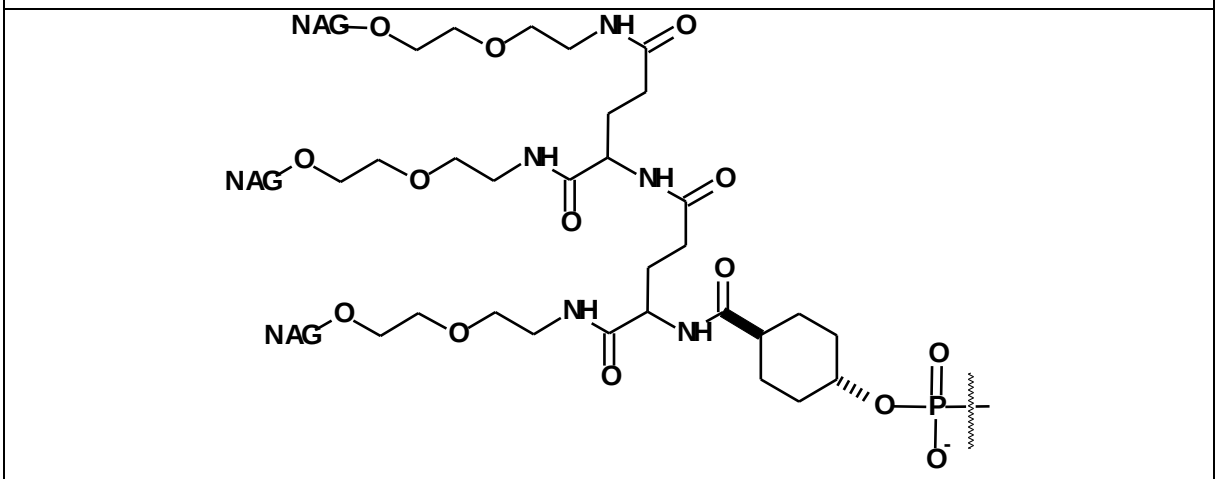
(NAG37)s



(NAG 38)

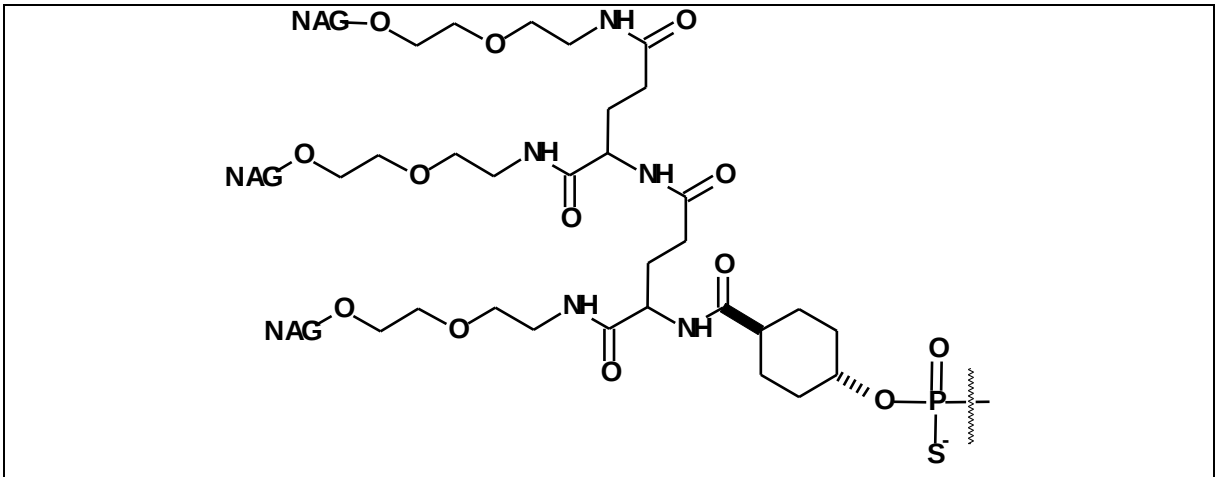


(NAG 38)s



(NAG39)

and



(NAG39)s

52. The method of any one of claims 49-51, wherein the sense strand of the first RNAi agent or the sense strand of the second RNAi agent further comprises one or more inverted abasic nucleosides.