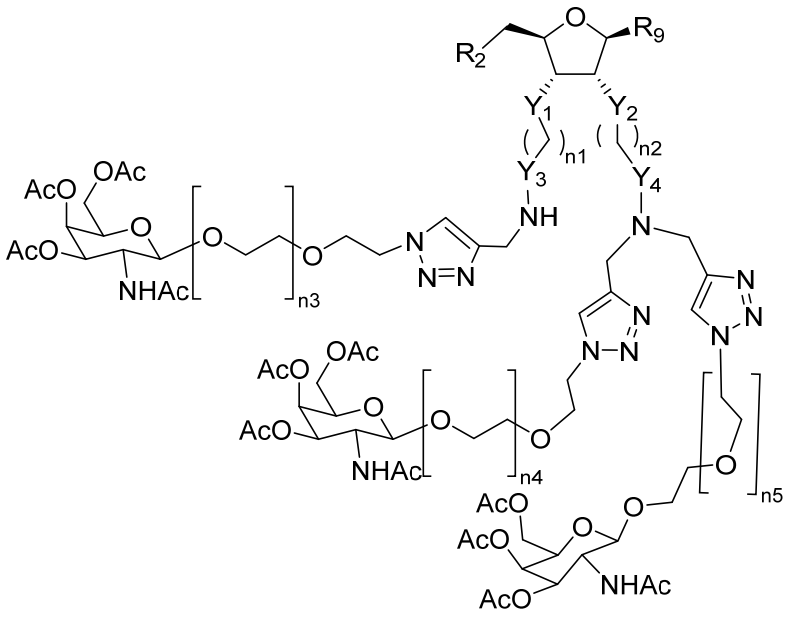
Claims

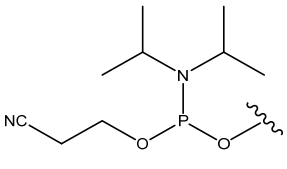
1. A compound of Formula (IX-a), or a salt, solvate, or hydrate thereof:



Formula (IX-a)

wherein:

R^9 is H, adenine, guanine, thymine, cytosine, or uracil, or adenine, guanine, thymine, cytosine, or uracil, each comprising a Protecting Group (PG), a modified nucleobase, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, or a nucleobase isostere;

R^2 is H, OH, O-Protecting Group (PG), , a linker, an azide, a carboxylic acid, or an amine;

Y_1 is O, optionally substituted NH, CH_2, or CH_2O;

Y_2 is O, optionally substituted NH, CH_2, or CH_2O;

Y_3 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

Y_4 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

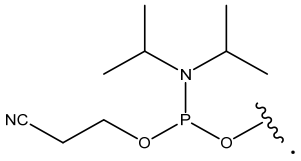
n_2 is 0, 1, 2, 3, 4, 5, or 6; and

each n_1, n_3, n_4 and n_5 is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

2. The compound of claim 1, wherein R^9 is uracil comprising a protecting group.

3. The compound of claim 1 or 2, wherein R^9 is uracil comprising a benzoyl protecting group.

4. The compound of any one of claims 1-3, wherein R^2 is O-Protecting Group (PG).

5. The compound of any one of claims 1-4, wherein R^2 is 

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6. The compound of any one of claims 1-5, wherein Y_1 is O.

7. The compound of any one of claims 1-6, wherein Y_2 is O.

8. The compound of any one of claims 1-7, wherein both Y_1 and Y_2 are O.

9. The compound of any one of claims 1-8, wherein Y_3 is CO.

10. The compound of any one of claims 1-9, wherein Y_4 is CO.

11. The compound of any one of claims 1-10, wherein Y_3 and Y_4 are CO.

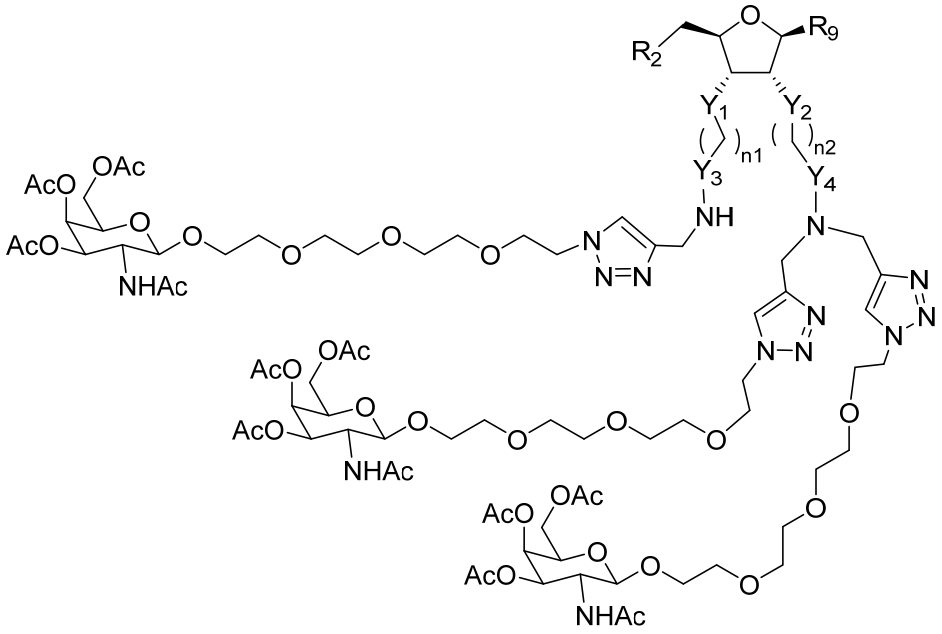
12. The compound of any one of claims 1-11, wherein Y_1 and Y_2 are O, and Y_3 and Y_4 are CO.

13. The compound of any one of claims 1-12, wherein n_3 is 3.

14. The compound of any one of claims 1-13, wherein n_4 is 3.

15. The compound of any one of claims 1-14, wherein n_5 is 3.

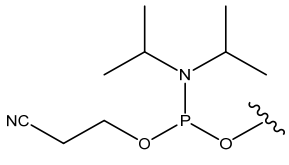
16. The compound of claim 1, wherein the compound is of Formula (IX-b):



Formula (IX-b)

wherein:

R^9 is H, adenine, guanine, thymine, cytosine, or uracil, or adenine, guanine, thymine, cytosine, or uracil, each comprising a Protecting Group (PG), a modified nucleobase, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, or a nucleobase isostere;

R^2 is H, OH, O-Protecting Group (PG), , a linker, an azide, a carboxylic acid, or an amine;

Y_1 is O, optionally substituted NH, CH_2, or CH_2O;

Y_2 is O, optionally substituted NH, CH_2, or CH_2O;

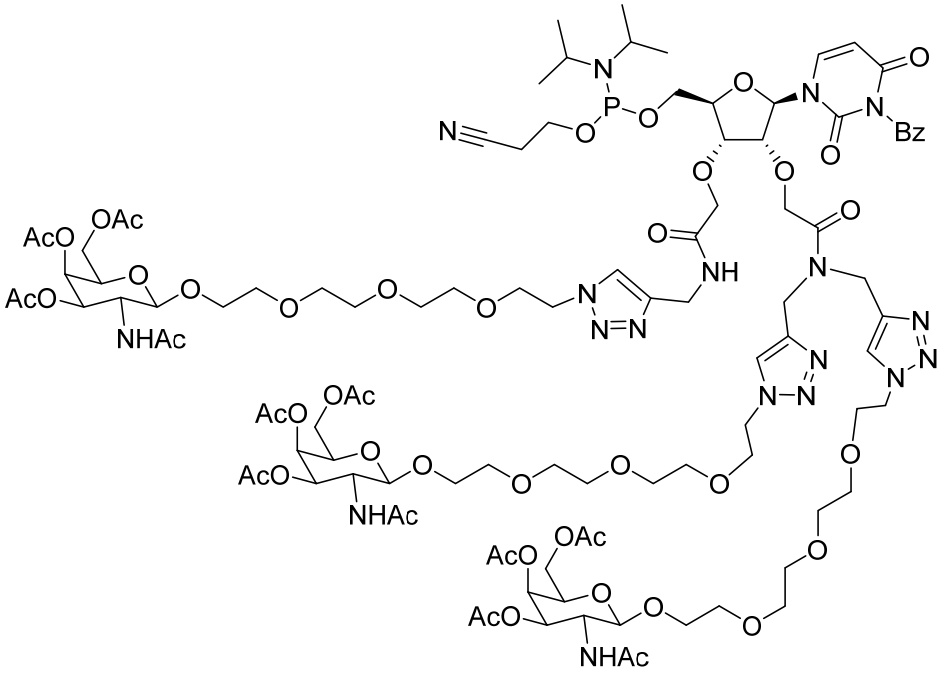
Y_3 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

Y_4 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

n_2 is 0, 1, 2, 3, 4, 5, or 6; and

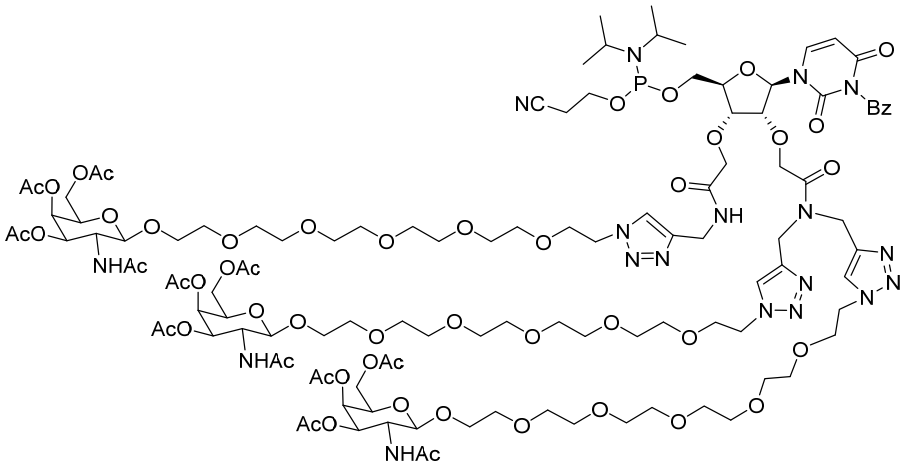
n_1 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

17. The compound of claim 1, wherein the compound is of the formula:



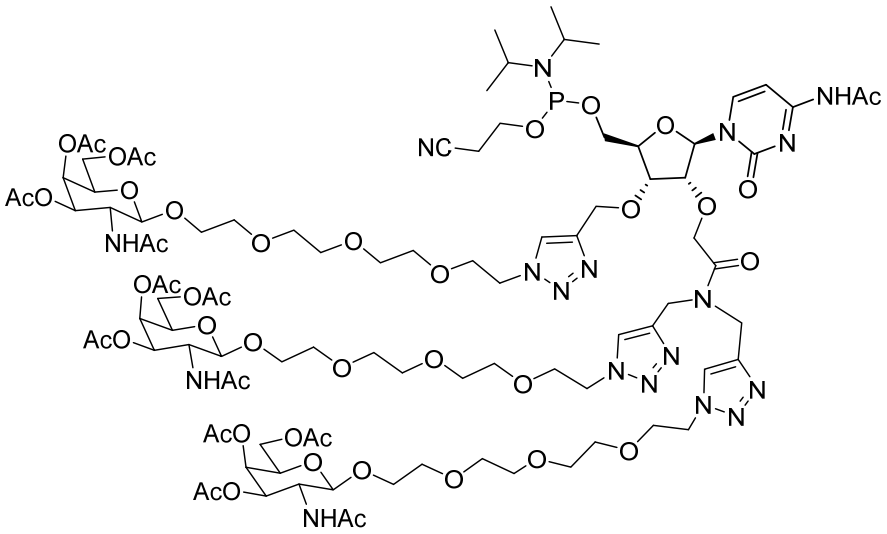
or a salt, solvate, or hydrate thereof.

18. The compound of claim 1, wherein the compound is of the formula:



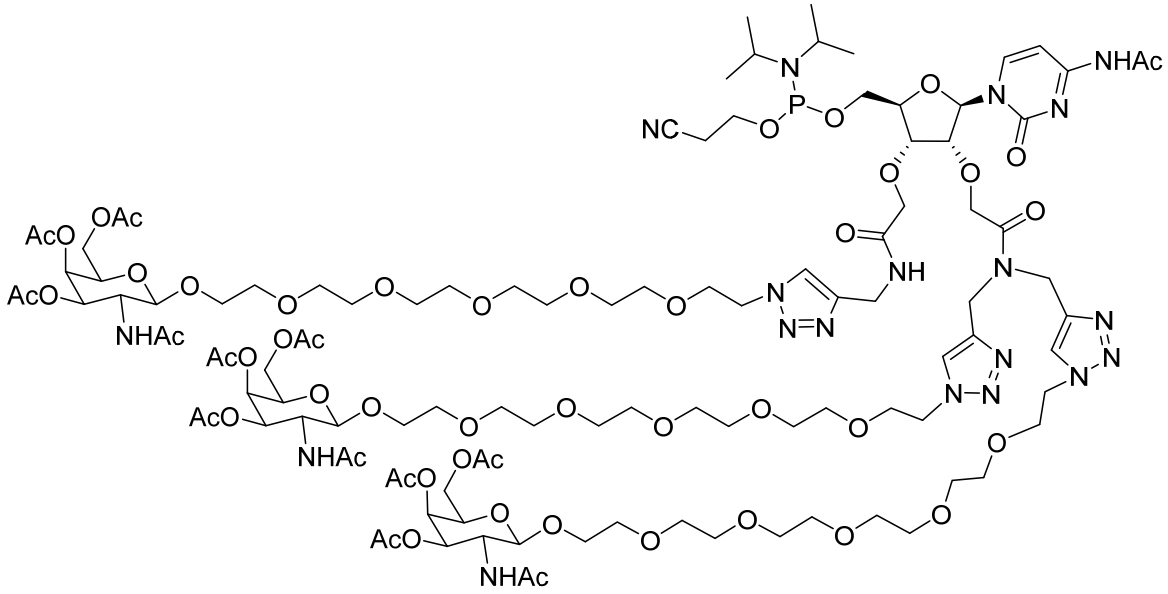
or a salt, solvate, or hydrate thereof.

19. The compound of claim 1, wherein the compound is of the formula:



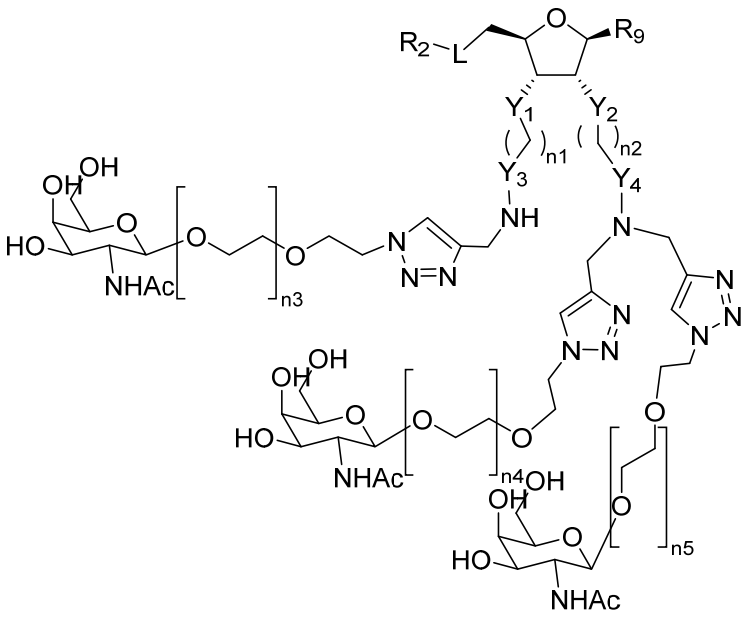
or a salt, solvate, or hydrate thereof.

20. The compound of claim 1, wherein the compound is of the formula:



or a salt, solvate, or hydrate thereof.

21. A compound of Formula (XV-a), or a salt, solvate, or hydrate thereof:



Formula (XV-a)

wherein:

R^9 is H, adenine, guanine, thymine, cytosine, or uracil, or adenine, guanine, thymine, cytosine, or uracil, each comprising a Protecting Group (PG), a modified nucleobase, optionally substituted alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, or a nucleobase isostere;

L is a bond, a phosphodiester bond, a phosphorothioate bond, a triazole, a tetrazole, an amide, a reverse-amide, a carbamate, a carbonate, urea, alkyl, or heteroalkyl;

R^2 is an oligonucleotide sequence;

Y_1 is O, CH_2, CH_2O, or optionally substituted NH;

Y_2 is O, CH_2, CH_2O, or optionally substituted NH;

Y_3 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

Y_4 is CO, SO_2, P(O)O, CH_2-O-C(O), CH_2-NH-C(O), CH_2-NH-SO_2, or CH_2;

n_2 is 0, 1, 2, 3, 4, 5, or 6; and

each n_1, n_3, n_4 and n_5 is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

22. The compound of claim 21, wherein Y_1 is O.

23. The compound of claim 21 or 22, wherein Y_2 is O.

24. The compound of any one of claims 21-23, wherein both Y_1 and Y_2 are O.

25. The compound of any one of claims 21-24, wherein Y_3 is CO.

26. The compound of any one of claims 21-25, wherein Y_4 is CO.

27. The compound of any one of claims 21-26, wherein both Y_3 and Y_4 are CO.

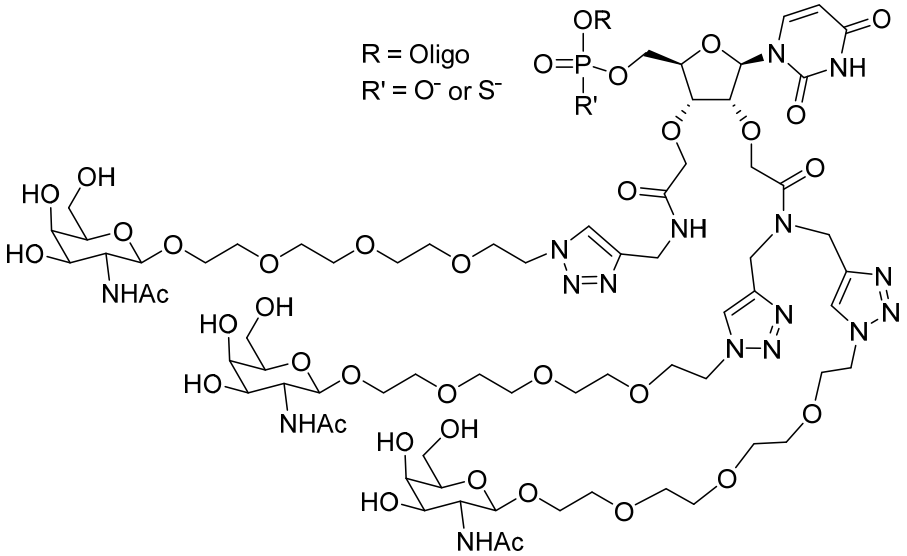
28. The compound of any one of claims 21-27, wherein Y_1 and Y_2 are O, and Y_3 and Y_4 are CO.

29. The compound of any one of claims 21-28, wherein n_3 is 3.

30. The compound of any one of claims 21-29, wherein n_4 is 3.

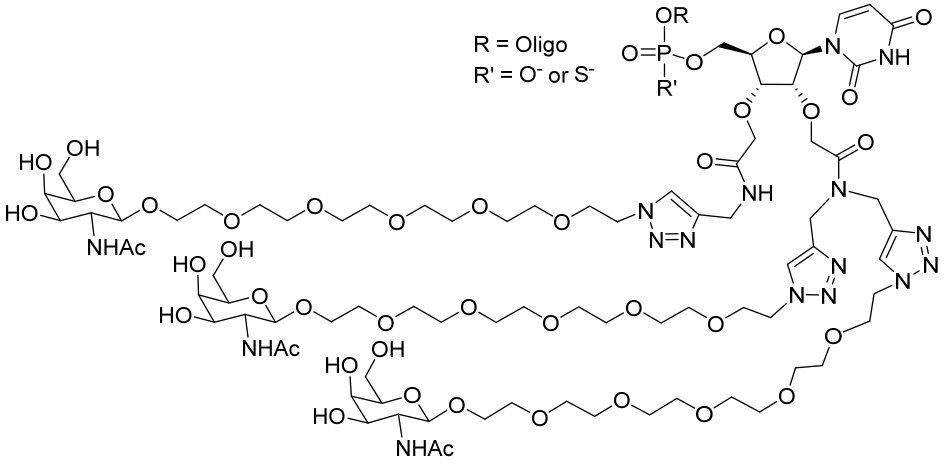
31. The compound of any one of claims 21-30, wherein n_5 is 3.

32. The compound of claim 21, wherein the compound is of the formula:



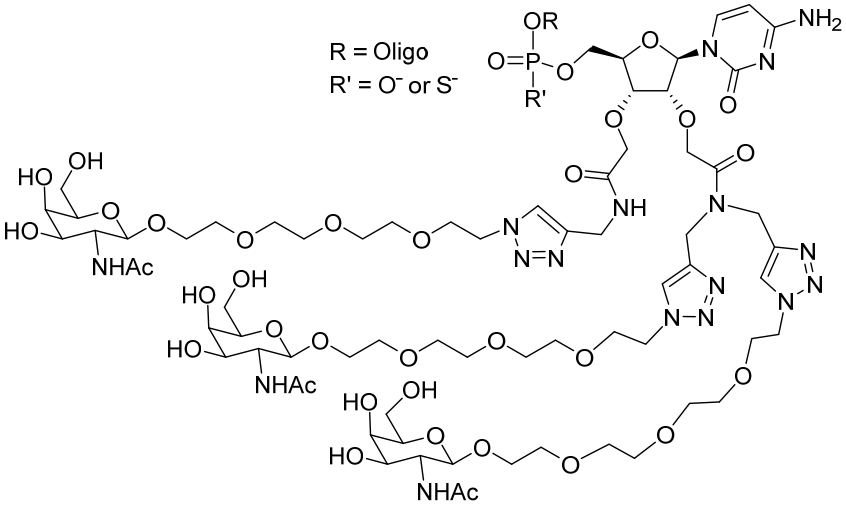
or a salt, solvate, or hydrate thereof.

33. The compound of claim 21, wherein the compound is of the formula:



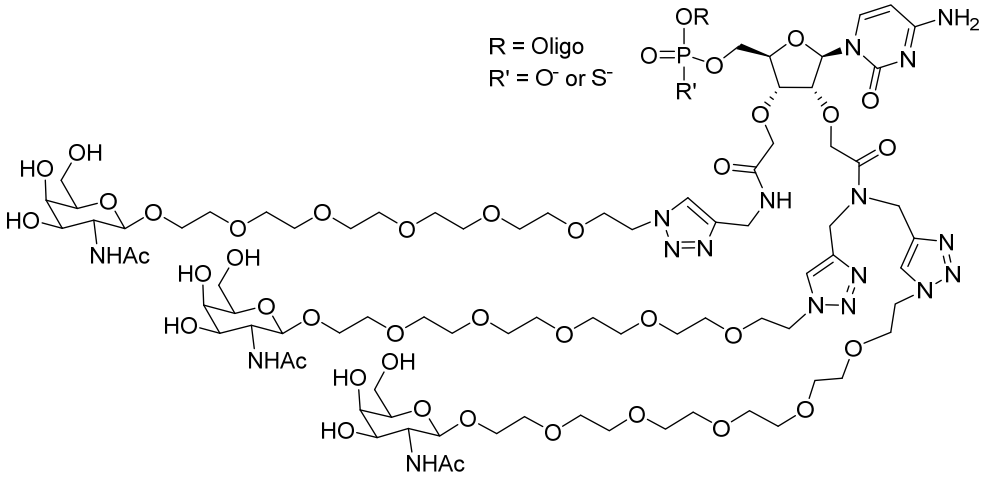
or a salt, solvate, or hydrate thereof.

34. The compound of claim 21, wherein the compound is of the formula:



or a salt, solvate, or hydrate thereof.

35. The compound of claim 21, wherein the compound is of the formula:



or a salt, solvate, or hydrate thereof.

36. The compound of any one of claims 21-35, wherein the oligonucleotide comprises an siRNA, an miRNA, an ADAR recruiting molecule, an ADAR targeting molecule, a guide RNA, or an antisense nucleic acid.

37. The compound of any one of claims 1-36, or salt, solvate, or hydrate thereof, for use as a reagent in a chemical reaction.

38. A composition comprising a compound of any one of claims 1-36, and a pharmaceutically acceptable carrier.

39. A compound of any one of claims 1-36, or a composition of claim 38, for use in modulating protein function in a subject.

40. A compound of any one of claims 1-36, or a composition of claim 38 for use in a method for treating or ameliorating a disease, disorder, or symptom thereof in a subject.

41. Use of a compound of any one of claims 1-36, or a composition of claim 38 in the preparation of a medicament for treating a liver disease, disorder, or symptom thereof.

42. A method for making a compound, or a salt, solvate, or hydrate thereof, of any of claims 1-36 comprising one or more compounds and chemical transformations described herein, including Examples 1-23.