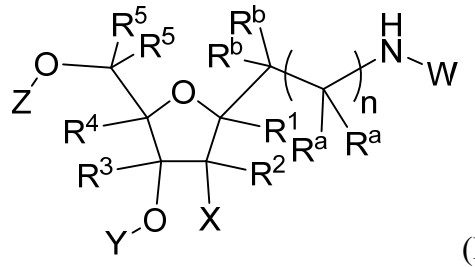
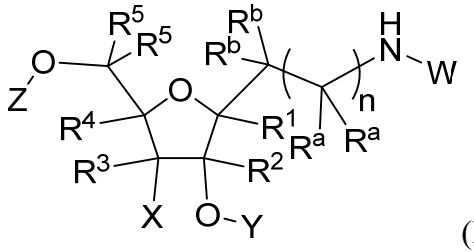
CLAIMS

1. A compound of Formula (I) or (II):



(I);



(II);

or a pharmaceutically acceptable salt thereof, wherein:

W is H, C_1-C_6 alkyl optionally substituted with one or more halogen, or an amino substitution group;

X is H, halogen, or -OR^X;

R^X is H, C_1-C_6 alkyl, or -(C_1-C_6 alkyl)-(C_6-C_{10} aryl), wherein the C_1-C_6 alkyl or -(C_1-C_6 alkyl)-(C_6-C_{10} aryl) is optionally substituted with one or more R^{Xa};

each R^{Xa} independently is halogen, C_1-C_6 alkyl, or -O-(C_1-C_6 alkyl), wherein the C_1-C_6 alkyl or -O-(C_1-C_6 alkyl) is optionally substituted with one or more halogen;

Y is H, C_1-C_6 alkyl optionally substituted with one or more halogen, -$P(R^Y)_2$, -$P(OR^Y)(N(R^Y)_2)$, -$P(=O)(OR^Y)R^Y$, -$P(=S)(OR^Y)R^Y$, -$P(=O)(SR^Y)R^Y$, -$P(=S)(SR^Y)R^Y$, -$P(=O)(OR^Y)_2$, -$P(=S)(OR^Y)_2$, -$P(=O)(SR^Y)_2$, -$P(=S)(SR^Y)_2$, or a hydroxy protecting group;

each R^Y independently is H or C_1-C_6 alkyl optionally substituted with one or more halogen or cyano;

Z is H, or C_1-C_6 alkyl optionally substituted with one or more halogen, -$P(R^Z)_2$, -$P(OR^Z)(N(R^Z)_2)$, -$P(=O)(OR^Z)R^Z$, -$P(=S)(OR^Z)R^Z$, -$P(=O)(SR^Z)R^Z$, -$P(=S)(SR^Z)R^Z$, -$P(=O)(OR^Z)_2$, -$P(=S)(OR^Z)_2$, -$P(=O)(SR^Z)_2$, -$P(=S)(SR^Z)_2$, or a hydroxy protecting group;

each R^Z independently is H or C_1-C_6 alkyl optionally substituted with one or more halogen or cyano;

or Y and Z in Formula (I), together form -$Si(R^L)_2$-O-$Si(R^L)_2$-, wherein each R^L independently is H or C_1-C_6 alkyl;

each R^a independently is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen; or two R^a on two adjacent carbon atoms, together with the two adjacent carbon atoms, form a double bond;

each R^b independently is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen;

R^1 is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen;

R^2 is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen;

R^3 is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen;

R^4 is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen;

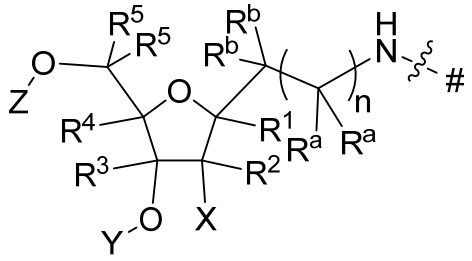
each R^5 independently is H, halogen, or C_1-C_6 alkyl optionally substituted with one or more halogen; and

n is an integer ranging from about 0 to about 10.

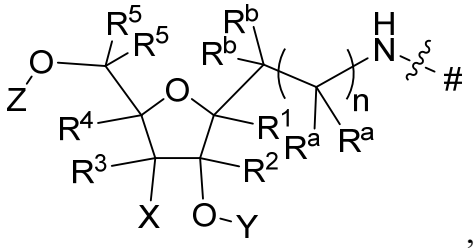
2. A scaffold or a pharmaceutically acceptable salt thereof, wherein the scaffold comprises:

(i) a Ligand; and

(ii) a Linker Unit, wherein the Linker Unit is:



or



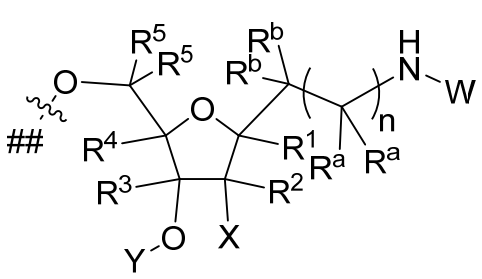
,

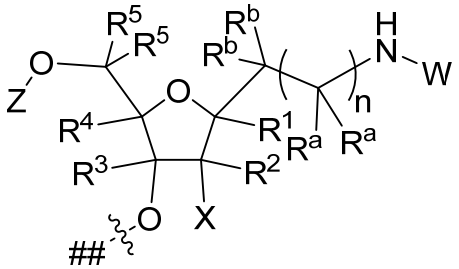
wherein R^1, R^2, R^3, R^4, R^5, X, Y, Z, R^a, R^b, and n are defined in claim 1, and # indicate an attachment to the Ligand.

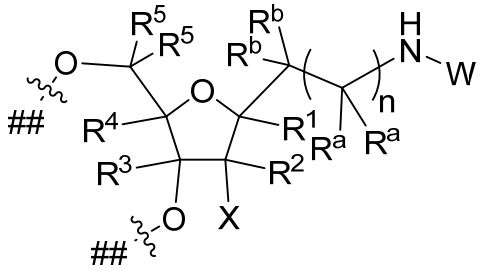
3. A scaffold or a pharmaceutically acceptable salt thereof, wherein the scaffold comprises:

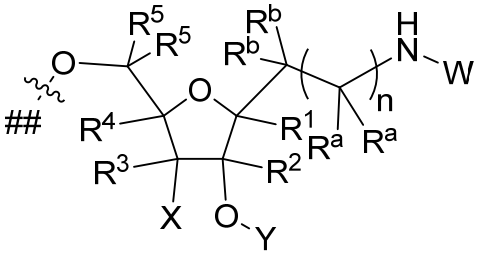
(i) one or more Nucleic Acid Agent; and

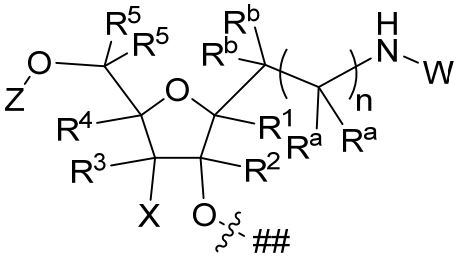
(ii) one or more Linker Unit, wherein each Linker Unit independently is:

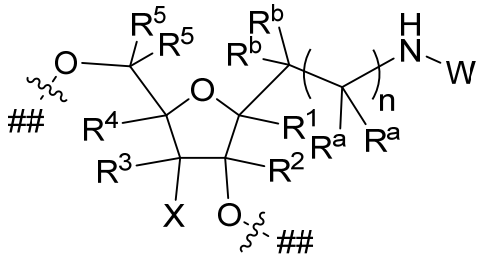


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, or


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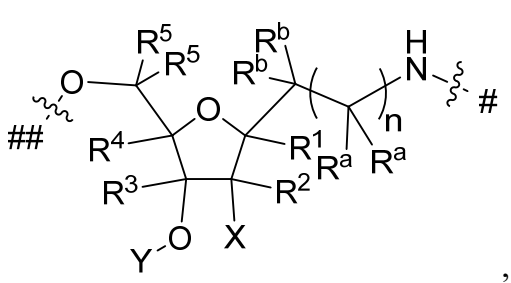
wherein variables R^1, R^2, R^3, R^4, R^5, W, X, Y, Z, R^a, R^b, and n are defined in claim 1, and ## indicates an attachment to the Nucleic Acid Agent.

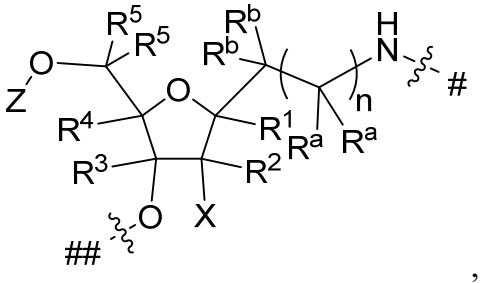
4. A conjugate or a pharmaceutically acceptable salt thereof, wherein the conjugate comprises:

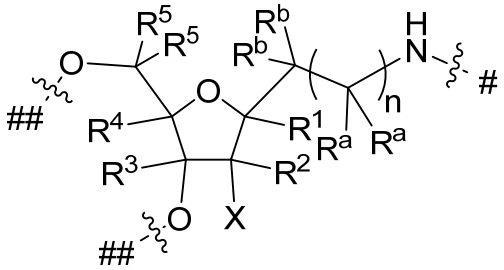
(i) one or more Nucleic Acid Agent;

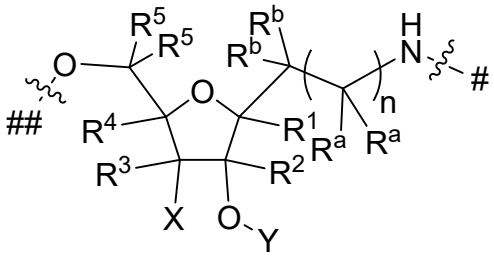
(ii) one or more Ligand; and

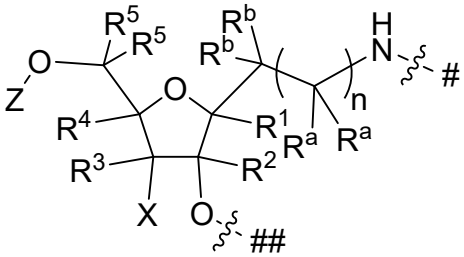
(iii) one or more Linker Unit, wherein each Linker Unit independently is:

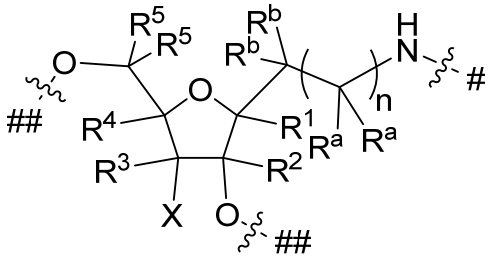


,


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,


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, or


,

wherein variables R^1, R^2, R^3, R^4, R^5, X, Y, Z, R^a, R^b, and n are described in claim 1, # indicate an attachment to the Ligand, and ## indicates an attachment to the Nucleic Acid Agent.

5. The compound, scaffold, or conjugate of any one of the previous claims, wherein W is H.

6. The compound, scaffold, or conjugate of any one of the previous claims, wherein W is C_1-C_6 alkyl optionally substituted with one or more halogen.

7. The compound, scaffold, or conjugate of any one of the previous claims, wherein W is an amino substitution group.

8. The compound, scaffold, or conjugate of any one of the previous claims, wherein W is fluorenylmethyloxycarbonyl (Fmoc), tert-butyloxycarbonyl (BOC), benzyloxycarbonyl (Cbz), optionally substituted acyl, trifluoroacetyl (TFA), benzyl, triphenylmethyl (Tr), 4,4′-dimethoxytrityl (DMTr), or toluenesulfonyl (Ts).

9. The compound, scaffold, or conjugate of any one of the previous claims, wherein X is H.

10. The compound, scaffold, or conjugate of any one of the previous claims, wherein X is halogen.

11. The compound, scaffold, or conjugate of any one of the previous claims, wherein X is $-OR^X$.

12. The compound, scaffold, or conjugate of any one of the previous claims, wherein Y is H.

13. The compound, scaffold, or conjugate of any one of the previous claims, wherein Y is C_1-C_6 alkyl optionally substituted with one or more halogen.

14. The compound, scaffold, or conjugate of any one of the previous claims, wherein Y is $-P(R^Y)_2$, $-P(OR^Y)(N(R^Y)_2)$, $-P(=O)(OR^Y)R^Y$, $-P(=S)(OR^Y)R^Y$, $-P(=O)(SR^Y)R^Y$, $-P(=S)(SR^Y)R^Y$, $-P(=O)(OR^Y)_2$, $-P(=S)(OR^Y)_2$, $-P(=O)(SR^Y)_2$, $-P(=S)(SR^Y)_2$.

15. The compound, scaffold, or conjugate of any one of the previous claims, wherein Y is a hydroxy protecting group.

16. The compound, scaffold, or conjugate of any one of the previous claims, wherein Z is H.

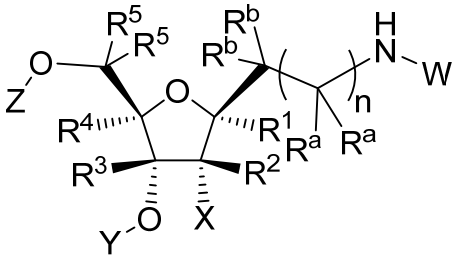
17. The compound, scaffold, or conjugate of any one of the previous claims, wherein Z is C_1-C_6 alkyl optionally substituted with one or more halogen.

18. The compound, scaffold, or conjugate of any one of the previous claims, wherein Z is $-P(R^Z)_2$, $-P(OR^Z)(N(R^Z)_2)$, $-P(=O)(OR^Z)R^Z$, $-P(=S)(OR^Z)R^Z$, $-P(=O)(SR^Z)R^Z$, $-P(=S)(SR^Z)R^Z$, $-P(=O)(OR^Z)_2$, $-P(=S)(OR^Z)_2$, $-P(=O)(SR^Z)_2$, $-P(=S)(SR^Z)_2$.

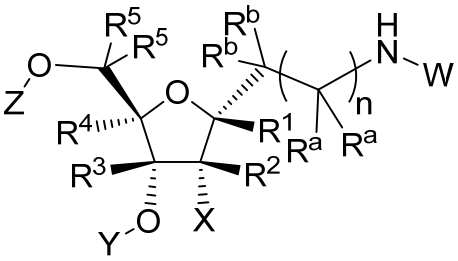
19. The compound, scaffold, or conjugate of any one of the previous claims, wherein Z is a hydroxy protecting group.

20. The compound, scaffold, or conjugate of any one of the previous claims, wherein Y and Z in Formula (I) together form $-Si(R^L)_2-O-Si(R^L)_2-$.

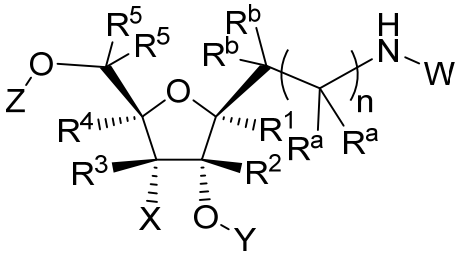
21. The compound of any one of the preceding claims, wherein the compound is of Formula (I'-1), (I'-2), (II'-1), or (II'-2):



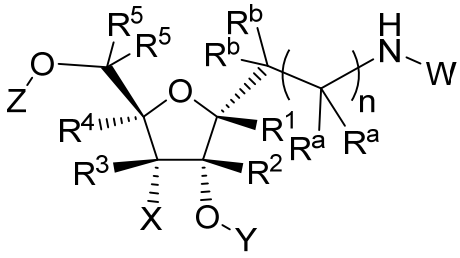
(I'-1);



(I'-2);



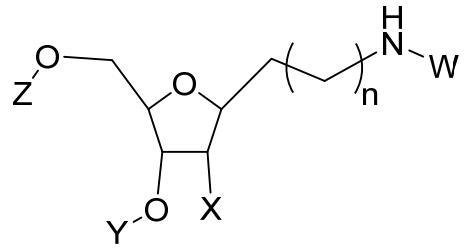
(II'-1); or



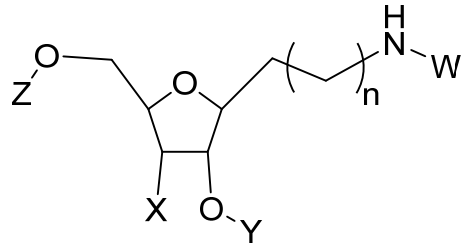
(II'-2);

or a pharmaceutically acceptable salt thereof.

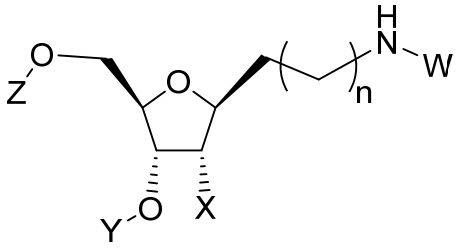
22. The compound of any one of the preceding claims, wherein the compound is of Formula (I-A), (II-A), (I-A'-1), (I-A'-2), (II-A'-1), or (II-A'-2):



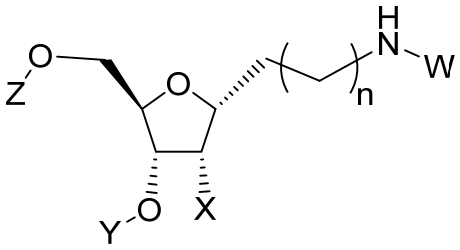
(I-A);



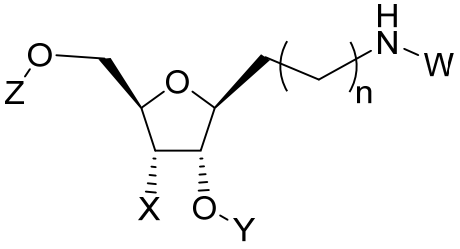
(II-A);



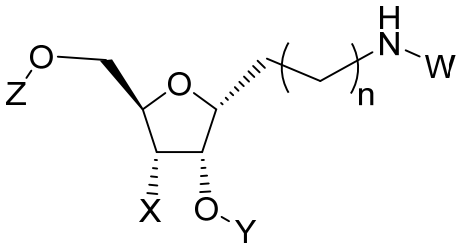
(I-A'-1);



(I-A'-2);



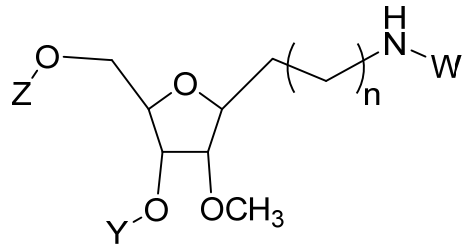
(II-A'-1); or



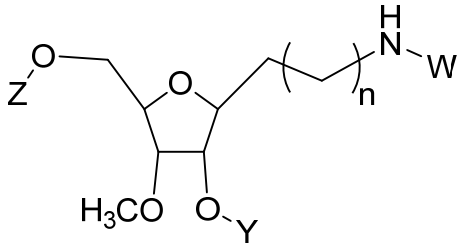
(II-A'-2);

or a pharmaceutically acceptable salt thereof.

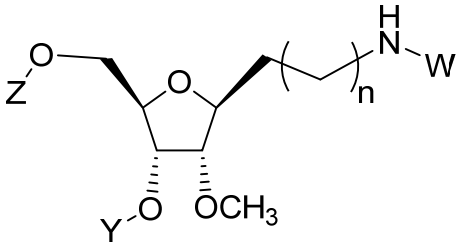
23. The compound of any one of the preceding claims, wherein the compound is of Formula (I-B), (II-B), (I-B'-1), (I-B'-2), (II-B'-1), or (II-B'-2):



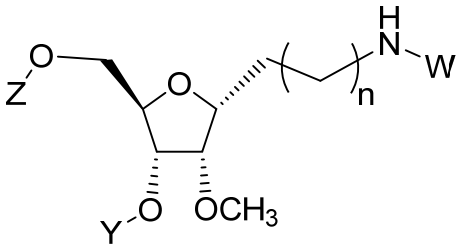
(I-B);



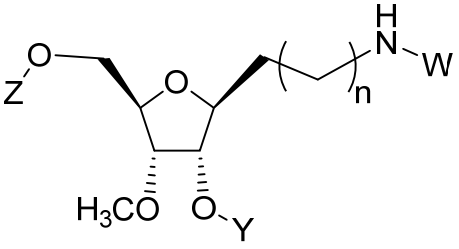
(II-B);



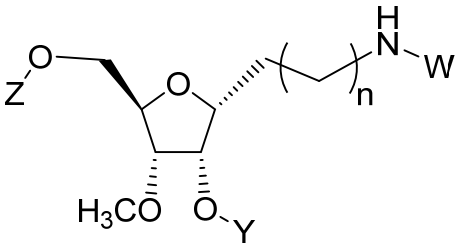
(I-B'-1);



(I-B'-2);



(II-B'-1); or



(II-B'-2);

or a pharmaceutically acceptable salt thereof.

24. The compound of any one of the preceding claims, wherein the compound is selected from the compounds described in Table L and pharmaceutically acceptable salts thereof.

25. The scaffold of any one of the preceding claims, wherein the scaffold is (Linker Unit)$_p$-((Nucleic Acid Agent)-(Linker Unit)$_s$)$_r$-(Nucleic Acid Agent)$_q$, wherein:

each Linker Unit is independent from another Linker Unit, and each Nucleic Acid Agent is independent from another Nucleic Acid Agent;

each r independently is an integer ranging from 0 to 10;

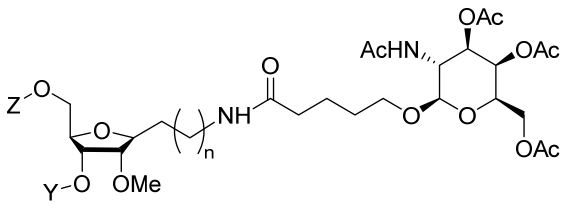
each s independently is an integer ranging from 0 to 10;

p is an integer ranging from 0 to 10;

q is 0 or 1; and

the scaffold comprises at least one Linker Unit and at least one Nucleic Acid Agent.

26. The scaffold of any one of the preceding claims, wherein the scaffold is



or a pharmaceutically acceptable salt thereof, wherein:

Y is -P(R^Y)$_2$, -P(OR^Y)($N(R^Y)_2$), -P(=O)(OR^Y)R^Y, -P(=S)(OR^Y)R^Y, -P(=O)(SR^Y)R^Y, -P(=S)(SR^Y)R^Y, -P(=O)(OR^Y)$_2$, -P(=S)(OR^Y)$_2$, -P(=O)(SR^Y)$_2$, -P(=S)(SR^Y)$_2$, or a hydroxy protecting group;

each R^Y independently is H or C_1-C_6 alkyl optionally substituted with one or more halogen or cyano;

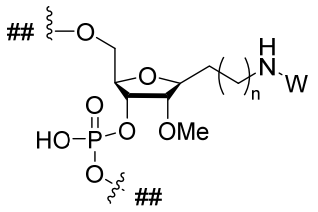
Z is -P(R^Z)$_2$, -P(OR^Z)($N(R^Z)_2$), -P(=O)(OR^Z)R^Z, -P(=S)(OR^Z)R^Z, -P(=O)(SR^Z)R^Z, -P(=S)(SR^Z)R^Z, -P(=O)(OR^Z)$_2$, -P(=S)(OR^Z)$_2$, -P(=O)(SR^Z)$_2$, -P(=S)(SR^Z)$_2$, or a hydroxy protecting group;

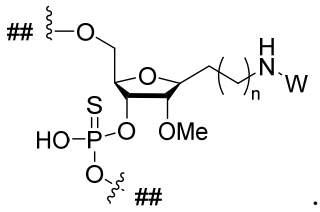
each R^Z independently is H or C_1-C_6 alkyl optionally substituted with one or more halogen or cyano; and

n is an integer ranging from about 0 to about 10.

27. The scaffold of any one of the preceding claims, wherein the scaffold is selected from the scaffolds in Table S1.

28. The scaffold of any one of the preceding claims, wherein the scaffold is



or


;

or a pharmaceutically acceptable salt thereof, wherein:

W is an amino substitution group; and

n is an integer ranging from about 0 to about 10.

29. The scaffold of any one of the preceding claims, wherein the scaffold is selected from the scaffolds in Table S2.

30. The conjugate of any one of the preceding claims, wherein the conjugate is (Linker Unit-(Ligand)$_{0\text{-}1}$)$_p$-((Nucleic Acid Agent)-(Linker Unit-(Ligand)$_{0\text{-}1}$)$_s$)$_r$-(Nucleic Acid Agent)$_q$, wherein:

each Linker Unit is independent from another Linker Unit, each Nucleic Acid Agent is independent from another Nucleic Acid Agent, and each Ligand is independent from another Ligand;

each r independently is an integer ranging from 0 to 10;

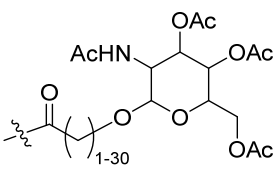
each s independently is an integer ranging from 0 to 10;

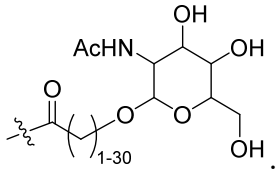
p is an integer ranging from 0 to 10;

q is 0 or 1; and

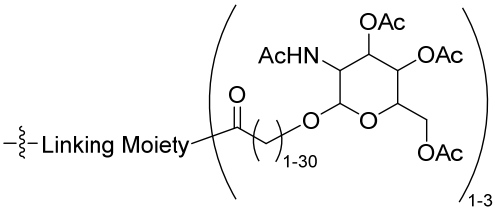
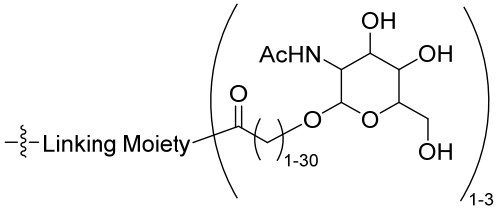
the conjugate comprises at least one Linker Unit, at least one Nucleic Acid Agent, and at least one Ligand.

31. The conjugate of any one of the preceding claims, wherein the conjugate is selected from the conjugates in Table C.

32. The scaffold or conjugate of any one of the preceding claims, wherein the ligand comprises 

or 

.

33. The scaffold or conjugate of any one of the preceding claims, wherein the ligand comprises  or .

34. The scaffold or conjugate of any one of the preceding claims, wherein the ligand comprises a lipid, a peptide moiety, or an antibody moiety.

35. The scaffold or conjugate of any one of the preceding claims, wherein the Nucleic Acid Agent comprises an oligonucleotide.

36. A pharmaceutical composition comprising the compound, scaffold, or conjugate of the any one of the preceding claims.

37. The conjugate of any one of the preceding claims for use as a medicament.

38. Use of the conjugate of any one of the preceding claims in the manufacture of a medicament for modulating the expression of a target gene in a subject in need thereof, for delivering a Nucleic Acid Agent to a subject in need thereof, or for treating or preventing a disease in a subject in need thereof.