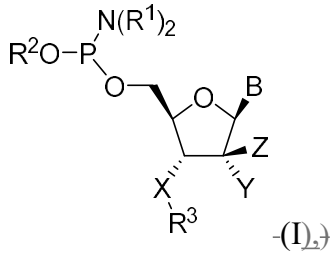
Claims

~~WHAT IS CLAIMED IS:~~

1. ~~1.~~ A compound represented by Formula (I):



~~(~~I~~),~~

wherein

X is ~~O or~~ NH;

Y is OCF_3, ~~selected from the group consisting of O PG,~~ $O(CR^4_2)_aCR^4_3$, $O(CR^4_2)_bOCR^4_3$, ~~or~~ ~~and~~ $O(CR^4_2)_b$ ~~–~~ $CR^4{=}CR^4_2$;

Z is H;

~~PG is a protecting group;~~

B is adenine (A), guanine (G), thymine (T), cytosine (C), uracil (U), 5-methylcytosine (5-me-C), ~~a natural or an unmodified nucleobase or a modified nucleobase~~ or a protected version of A, G, T, C, U, or 5-me-C ~~thereof~~;

each R^1 is independently $C_{1\text{-}6}$ alkyl or cycloalkyl;

R^2 is CH_2CH_2CN or $C_{1\text{-}6}$ alkyl;

or one R^1 and R^2 together form an optionally substituted $C_{1\text{-}6}$ cycloalkyl;

R^3 is H or PG;

PG is a protecting group;

R^4 is independently in each instance H or F;

a is 1 or ~~an integer of 0~~ 2; and

b is 1, 2, or ~~an integer of 1~~ 3. ~~,~~

The compound of claim 1, wherein Y is ~~when X is O, then Y is –O(CR$^4_2$)$_a$CR$^4_3$, –O(CR$^4_2$)$_b$OCR$^4_3$ or –O(CR$^4_2$)$_b$-CR^4=CR$^4_2$.~~

2. ~~2. The compound of claim 1, wherein X is NH and Y is O-PG,~~ OEt or O-$CH_2CH_2OCH_3$. ~~methoxyethoxy.~~

3. ~~3.~~ The compound of claim 1, ~~1 or 2,~~ wherein R^1 is $C_{2\text{-}3}$ alkyl.

4. ~~4.~~ The compound of claim 1, ~~1 or 2,~~ wherein R^1 is isopropyl.

5. ~~5.~~ The compound of claim 1, ~~any of claims 1-4,~~ wherein R^3 is a trityl protecting group.

6. ~~6.~~ The compound of claim 1, ~~any of claims 1-4,~~ wherein R^3 is monomethoxytrityl (MMTr) or tritolyl ~~when X is NH and 4,4′-dimethoxytrityl (DMTr) or tritolyl when X is O~~.

7. ~~7.~~ The compound of claim 1, ~~any of claims 1-6,~~ wherein B is ~~selected from~~ adenine (A), guanine (G), ~~thymine (T),~~ cytosine (C), ~~uracil (U) and 5-methylcytosine (5-me-C),~~ or a protected version of A, G, or C. ~~thereof.~~

8. ~~8.~~ The compound of claim 1, ~~any of claims 1-6,~~ wherein B is ~~selected from~~ 6-*N*-benzoyladenosine (A^{Bz}), 4-*N*-Benzoylcytidine (C^{Bz}), or~~and~~ 2-*N*-isobutyrylguanosine (G^{iBu}).~~_____~~

9. The compound of claim 1, wherein Y is –O–$CF_2CH_2OCH_3$.

10. The compound of claim 1, wherein Y is –O–$CH_2CH_2OCF_3$.

11. The compound of claim 1, wherein Y is –O(CR$^4_2$)$_b$–CR^4=CR$^4_2$.

12. The compound of claim 1, wherein Y is –O–CF_3.

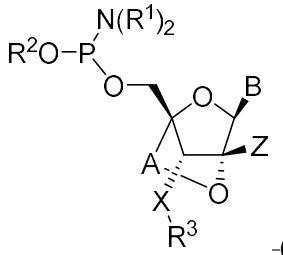
13. The compound of claim 1, ~~9.~~ wherein Y is –O–$CH_2CH_2OCH_3$.

14. A composition comprising the compound ~~any~~ of claim 1~~claims 1–8~~ and one or more reactants or solvents or impurities.

~~10. The composition of claim 9, wherein the amount of impurities is less than 1%.~~

15. ~~11.~~ A method of making an oligonucleotide comprising a modified nucleoside comprising reacting the compound of claim 1 with a monomer~~any of claims 1–8~~ to form the oligonucleotide.

16. ~~12.~~ A compound represented by Formula (II):



~~-~~(II),

wherein

X is ~~O or~~ NH;

Z is H;

B is adenine (A), guanine (G), cytosine (C), uracil (U),~~a natural or an unmodified nucleobase or a modified nucleobase~~ or a protected version of A, G, C, or U~~thereof~~;

R^1 is independently a $C_{1\text{-}6}$ alkyl or cycloalkyl;

R^2 is CH_2CH_2CN or a $C_{1\text{-}6}$ alkyl;

or one R^1 and R^2 together form an optionally substituted $C_{1\text{-}6}$ cycloalkyl;

R^3 is H or a protecting group;

A is –(CR'R')$_{1-2}$–; and

R' is independently in each instance H or Me.

~~13.~~ The compound of claim 16, ~~12, wherein X is NH and Z is H.~~

17. ~~14. The compound of claim 12 or 13,~~ wherein R^1 is a C_{2-3} alkyl.

18. ~~15.~~ The compound of claim 16, ~~12 or 13,~~ wherein R^1 is isopropyl.

19. ~~16.~~ The compound of claim 16, ~~any of claims 12-15,~~ wherein R^3 is a trityl protecting group.

20. ~~17.~~ The compound of claim 16, ~~any of claims 12-15,~~ wherein R^3 is monomethoxytrityl (MMTr) or tritolyl. ~~when X is NH and 4,4′-dimethoxytrityl (DMTr) or tritolyl when X is O.~~

21. ~~18.~~ The compound of claim 16, ~~any of claims 12-17,~~ wherein B is ~~selected from~~ adenine (A), guanine (G), ~~thymine (T), cytosine (C), uracil (U) and 5-methylcytosine (5-me-C),~~ or a protected version of A or G. ~~thereof.~~

22. ~~19.~~ The compound of claim 16, ~~any of claims 11-17,~~ wherein B is ~~selected from~~ 6-*N*-benzoyladenosine (A^{Bz}), 4-*N*-Benzoylcytidine (C^{Bz}), or ~~and~~ 2-*N*-isobutyrylguanosine (G^{iBu}).

23. ~~20.~~ A composition comprising the compound of claim 16 ~~any of claims 12-19~~ and one or more reactants or solvents or impurities.

~~21. The composition of claim 20, wherein the compound has a purity of 99%, or more.~~

~~22.~~ A method of making an oligonucleotide comprising a modified nucleoside, the ~~said~~ method comprising reacting the compound of claim 16 with a monomer ~~any of claims 12-19~~ to form the oligonucleotide.

~~23. A method of making a compound represented by Formula (I):~~

~~R^5 (I)~~

~~wherein~~

~~B is a natural or an unmodified nucleobase or a modified nucleobase or a protected version thereof;~~

~~Z is H;~~

~~Y is $-O(CR^4_2)_b-CR^4=CR^4_2$, wherein R^4 is independently in each instance H or F, and b is an integer of 1-3;~~

~~X is NH;~~

~~R^3 is H or PG, wherein PG is a protecting group;~~

~~each R^1 is independently C_{1-6} alkyl or cycloalkyl;~~

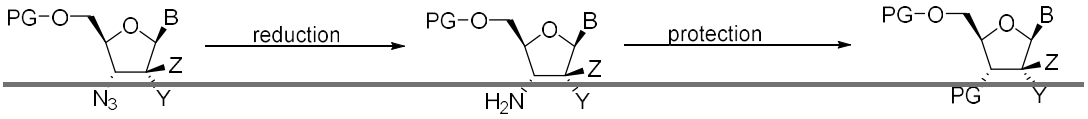
~~R^2 is CH_2CH_2CN or C_{1-6} alkyl;~~

~~or one R^1 and R^2 together form an optionally substituted C_{1-6} cycloalkyl,~~

~~said method comprising reducing compound 1 prior to protecting compound 2 to form compound 3~~

~~Compound 1 Compound 2 Compound 3~~

~~24. A method of making a compound represented by any of claims 1-10 said method comprising reducing compound 1 prior to protecting compound 2 to form compound 3~~



24. Compound 1 Compound 2 Compound 3