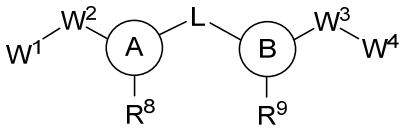
CLAIMS

1. A compound of Formula (I′), or a salt thereof:



(I′),

wherein:

A is a substituted tetrahydrofuranyl ring, substituted tetrahydropyranyl ring, or a modified sugar;

B is a substituted tetrahydrofuranyl ring, substituted tetrahydropyranyl ring, or a modified sugar;

W^1 and W^4 are independently a modified or unmodified nucleoside, oligonucleotide, ligand, lipophilic moiety, or protecting group;

R^8 and R^9 are independently substituted or unsubstituted heteroaryl;

L is a linker, ligand, lipophilic moiety, $-Z^1-Y-Z^2-$, or combination thereof;

W^2 and W^3 are independently a bond, linker, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted carbocyclylene, substituted or unsubstituted heterocyclylene, substituted or unsubstituted arylene, substituted or unsubstituted heteroarylene, -O-, $-OP(O)O_2-$, $-N(R^A)-$, -S-, -C(=O)-, -C(=O)O-, $-C(=O)NR^A-$, $-NR^AC(=O)-$, $-NR^AC(=O)R^A-$, $-C(=O)R^A-$, $-NR^AC(=O)O-$, $-NR^AC(=O)N(R^A)-$, -OC(=O)-, -OC(=O)O-, $-OC(=O)N(R^A)-$, $-S(O)_2NR^A-$, $-NR^ASO_2-$, or a combination thereof;

each R^A is independently hydrogen, substituted or unsubstituted acyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom, or two R^A groups are joined to form with the atoms to which they are attached a substituted or unsubstituted heterocyclyl ring, or a substituted or unsubstituted heteroaryl ring;

Z^1 and Z^2 are independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted carbocyclylene, substituted or unsubstituted heterocyclylene, substituted or unsubstituted arylene, substituted or unsubstituted heteroarylene, -O-, $-OP(O)O_2-$, $-N(R^B)-$, -S-, -C(=O)-, -C(=O)O-, $-C(=O)NR^B-$,

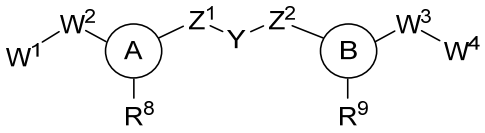
-$NR^BC(=O)$-, -$NR^BC(=O)R^B$-, -$C(=O)R^B$-, -$NR^BC(=O)O$-, -$NR^BC(=O)N(R^B)$-, -OC(=O)-, -OC(=O)O-, -$OC(=O)N(R^B)$-, -$S(O)_2NR^B$-, -NR^BSO_2-, or a combination thereof;

each R^B is independently hydrogen, substituted or unsubstituted acyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, a nitrogen protecting group when attached to a nitrogen atom, an oxygen protecting group when attached to an oxygen atom, or a sulfur protecting group when attached to a sulfur atom, or two R^B groups are joined to form a substituted or unsubstituted heterocyclyl ring, or a substituted or unsubstituted heteroaryl ring;

Y is substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted carbocyclylene, substituted or unsubstituted heterocyclylene, substituted or unsubstituted arylene, substituted or unsubstituted heteroarylene, -O-, -$OP(O)O_2$-, -$N(R^C)$-, -S-, -C(=O)-, -C(=O)O-, -$C(=O)NR^C$-, -$NR^CC(=O)$-, -$NR^CC(=O)R^C$-, -$C(=O)R^C$-, -$NR^CC(=O)O$-, -$NR^CC(=O)N(R^C)$-, -OC(=O)-, -OC(=O)O-, -$OC(=O)N(R^C)$-, -$S(O)_2NR^C$-, -NR^CSO_2-, or a combination thereof; and

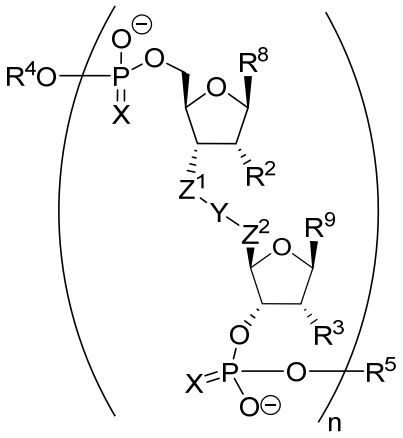
each R^C is independently hydrogen, substituted or unsubstituted acyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or a nitrogen protecting group, or two R^C groups are joined to form a substituted or unsubstituted heterocyclyl ring, or a substituted or unsubstituted heteroaryl ring.

2. The compound of claim 1, or a salt thereof, which has Formula (VIII):



(VIII).

3. The compound of claim 1 or 2, wherein the compound is of the Formula (II-a):



Formula (II-a),

wherein:

each Y is independently substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted carbocyclylene, substituted or unsubstituted heterocyclylene, substituted or unsubstituted arylene, substituted or unsubstituted heteroarylene, -O-, -OP(O)O_2-, -N(R^C)-, -S-, -C(=O)-, -C(=O)O-, -C(=O)NR^C-, -NR^CC(=O)-, -NR^CC(=O)R^C-, -C(=O)R^C-, -NR^CC(=O)O-, -NR^CC(=O)N(R^C)-, -OC(=O)-, -OC(=O)O-, -OC(=O)N(R^C)-, -S(O)$_2$NR^C-, -NR^CSO_2-, or a combination thereof;

each R^C is independently hydrogen, substituted or unsubstituted acyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted carbocyclyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, a nitrogen protecting group, or two R^C groups are joined to form a substituted or unsubstituted heterocyclyl ring, or a substituted or unsubstituted heteroaryl ring;

each R^2 is independently –H, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, –OR^6, -N(R^6), or -SR^6;

each R^3 is independently –H, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, –OR^7, -N(R^7), or -SR^7;

R^4 and R^5 are independently an oligonucleotide or a protecting group, or R^4 and R^5 are joined together to form a single oligonucleotide;

each R^6 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^7 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^8 is independently substituted or unsubstituted heteroaryl;

each R^9 is independently substituted or unsubstituted heteroaryl;

each X is independently O or S;

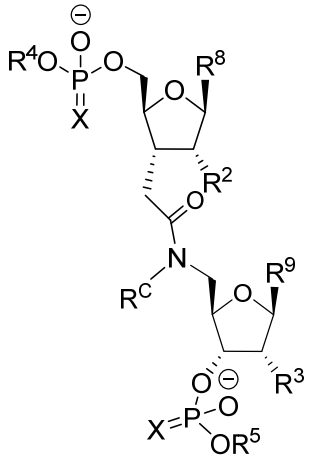
each instance of Z^1 and Z^2 is independently a bond, C_1-C_6 alkylene, or C_2-C_6 alkenylene; and

n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

or a salt thereof.

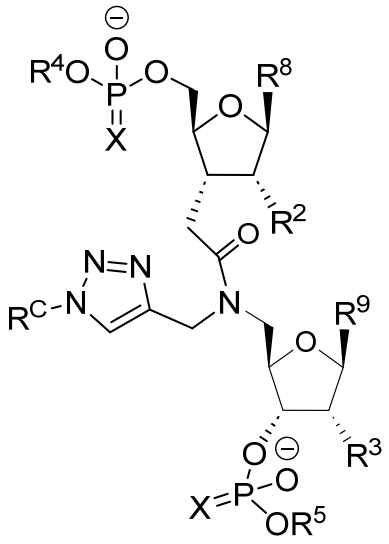
4. A compound comprising:

an oligonucleotide of Formula (IX):



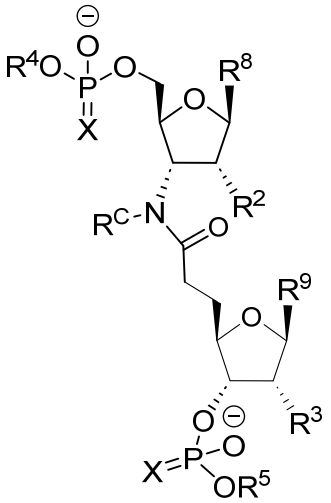
Formula (IX),

an oligonucleotide of Formula (X):



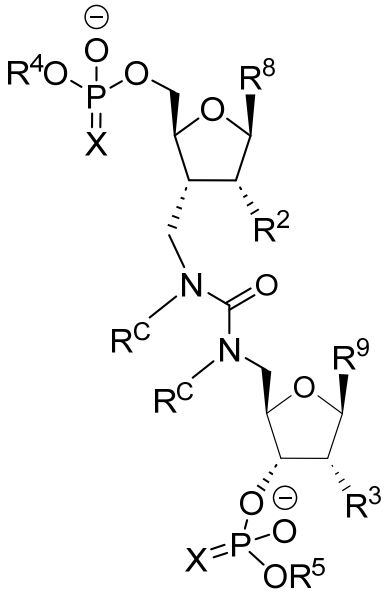
Formula (X),

an oligonucleotide of Formula (XI):



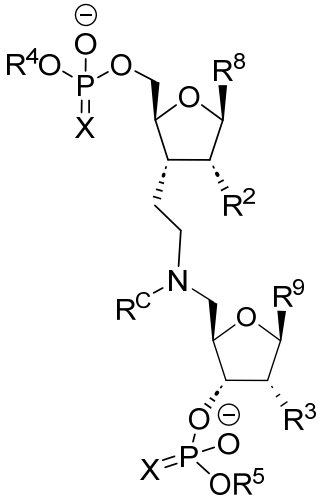
Formula (XI),

an oligonucleotide of Formula (XII):



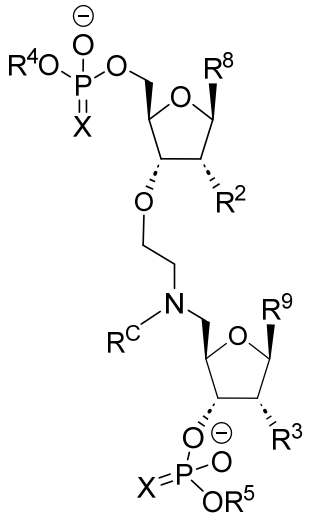
Formula (XII),

an oligonucleotide of Formula (XIII):



Formula (XIII), or

an oligonucleotide of Formula (XIV):



Formula (XIV),

wherein:

R^C is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

each R^2 is independently hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, $–OR^6$, $-N(R^6)$, or $-SR^6$;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, $–OR^7$, $-N(R^7)$, or $-SR^7$;

R^4 and R^5 are independently an oligonucleotide or a protecting group, or R^4 and R^5 are joined together to form a single oligonucleotide;

each R^6 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^7 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^8 is independently a substituted or unsubstituted heteroaryl ring;

each R^9 is independently a substituted or unsubstituted heteroaryl ring; and

each X is independently O or S;

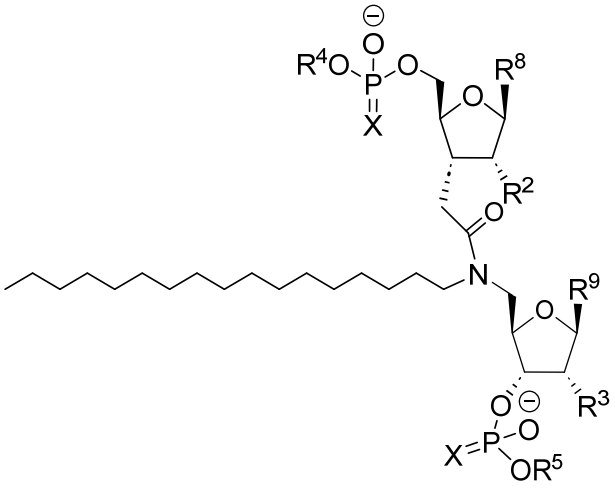
or a salt or prodrug thereof.

5. The compound of any one of claims 1-4, wherein each instance of R^C is independently substituted or unsubstituted C_8-C_{40} alkyl.

6. The compound of any one of claims 1-5, wherein each instance of R^C is independently substituted with one or more of a hydroxyl, amine, carboxylic acid, azide, or alkyne.

7. The compound of any one of claims 1-6, wherein each instance of R^C independently comprises at least one substituent selected from the group consisting of hexanoic acid, heptanoic acid, octanoic acid, nonanoic acid, decanoic acid, undecanoic acid, dodecanoic acid, tridecanoic acid, tetradecanoic acid, pentadecanoic acid, hexadecanoic acid, heptadecanoic acid, octadecanoic acid, oleic acid, linoleic acid, and arachidonic acid.

8. A compound comprising an oligonucleotide of Formula (IX-a):



Formula (IX-a)

wherein:

each R^2 is independently hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, $–OR^6$, $-N(R^6)$, or $-SR^6$;

each R^3 is independently hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, $–OR^7$, $-N(R^7)$, or $-SR^7$;

R^4 and R^5 are independently an oligonucleotide or a protecting group, or R^4 and R^5 are joined together to form a single oligonucleotide;

each R^6 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^7 is independently hydrogen, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

each R^8 is independently a substituted or unsubstituted heteroaryl ring;

each R^9 is independently a substituted or unsubstituted heteroaryl ring; and

each X is independently O or S;

or a salt or prodrug thereof.

9. The compound of any one of claims 3-8, wherein at least one instance of R^2 is –F or $–OR^6$, and wherein R^6 is methyl.

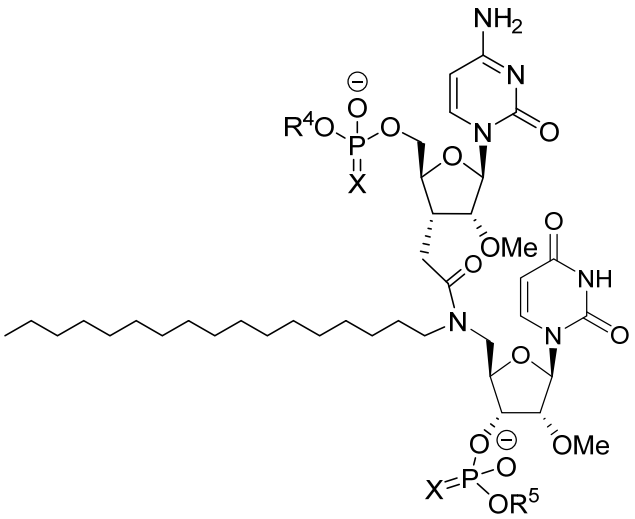
10. The compound of any one of claims 3-9, wherein at least one instance of R^3 is –F or –OR^7, and wherein R^7 is methyl.

11. The compound of any one of claims 1-10, wherein at least one instance of R^8 is uracil, cytosine, adenine, guanine, inosine, or thymine.

12. The compound of any one of claims 1-11, wherein at least one instance of R^9 is uracil, cytosine, adenine, guanine, inosine, or thymine.

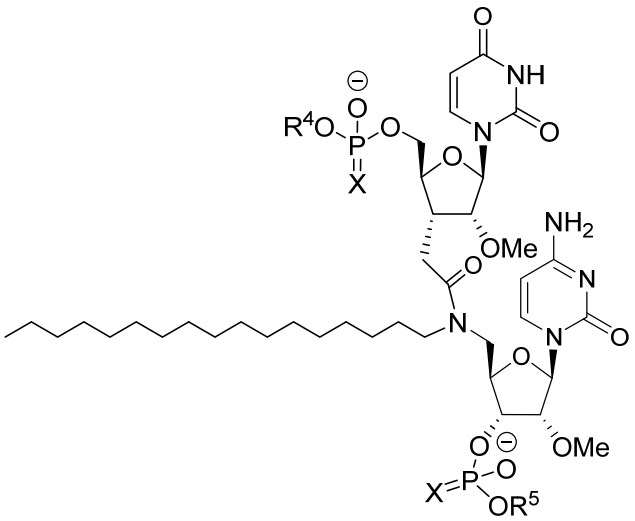
13. A compound comprising:

an oligonucleotide of Formula (IX-c):



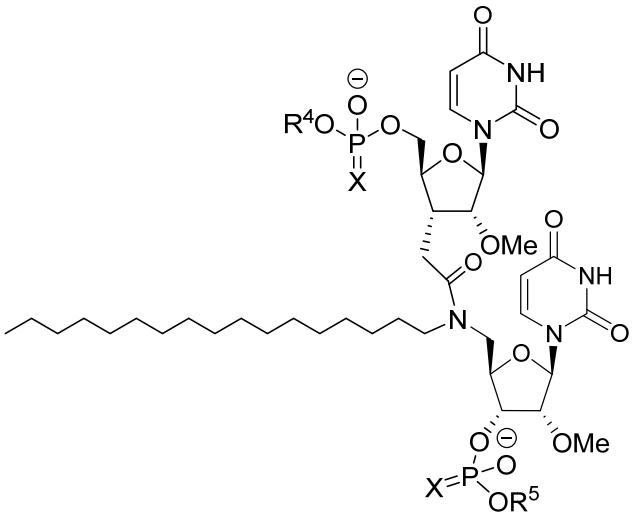
Formula (IX-c),

an oligonucleotide of Formula (IX-d):



Formula (IX-d), or

an oligonucleotide of Formula (IX-e):



Formula (IX-e),

wherein:

R^4 and R^5 are independently an oligonucleotide or a protecting group, or R^4 and R^5 are joined together to form a single oligonucleotide; and

each X is independently O or S;

or a salt or prodrug thereof.

14. The compound of any one of claims 3-13, wherein:

R^4 and R^5 are each independently an oligonucleotide;

R^4 is an oligonucleotide; and R^5 is a protecting group;

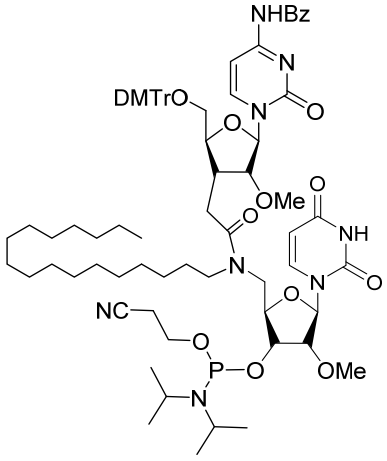
R^4 is a protecting group; and R^5 is an oligonucleotide; or

R^4 and R^5 are each independently a protecting group.

15. The compound of any one of claims 3-14, wherein at least one X is S.

16. The compound of any one of claims 1-15, wherein at least one oligonucleotide comprises at least one siRNA, an miRNA, an ADAR recruiting molecule, an ADAR targeting molecule, a guide RNA, and/or an antisense nucleic acid.

17. A compound of the formula:



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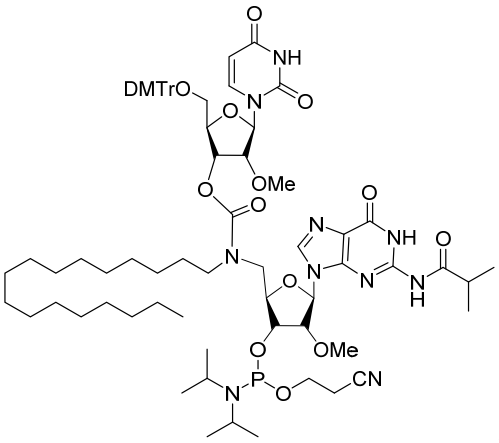

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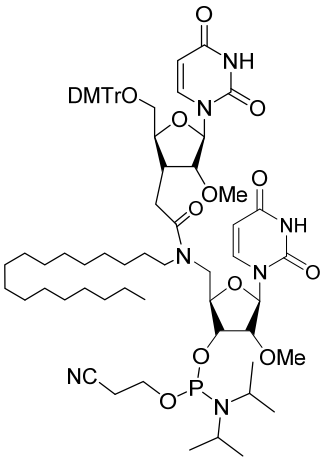

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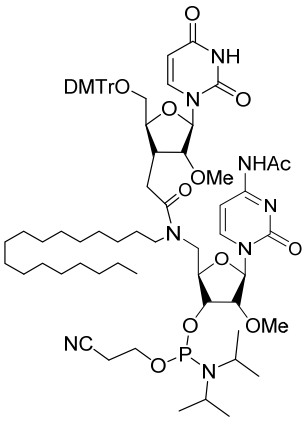

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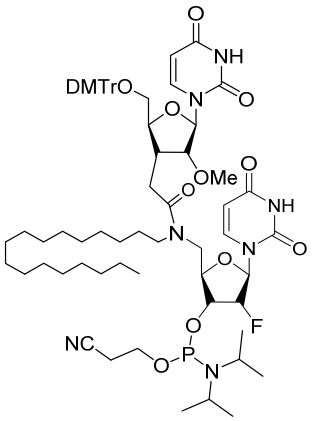

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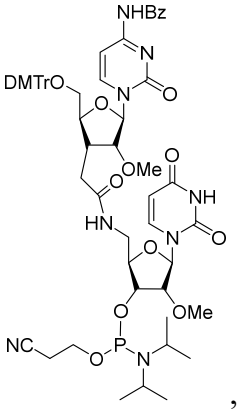

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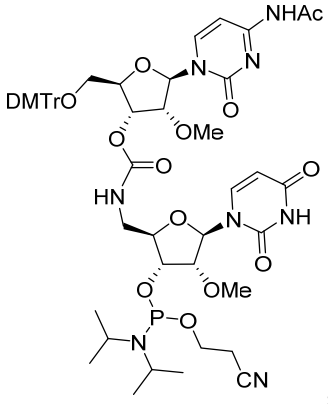

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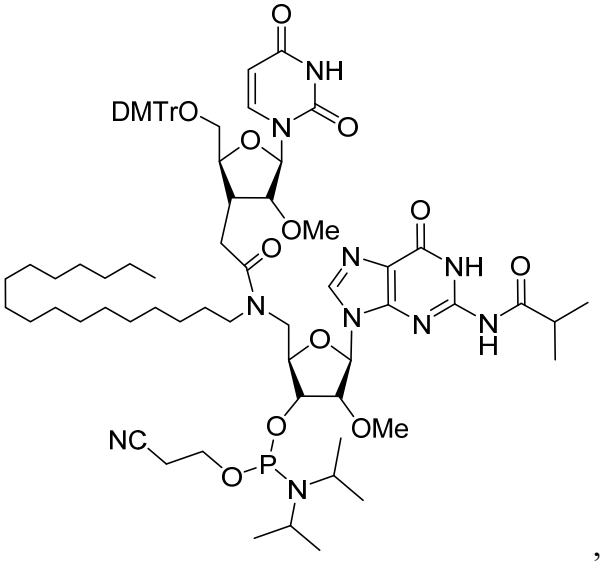

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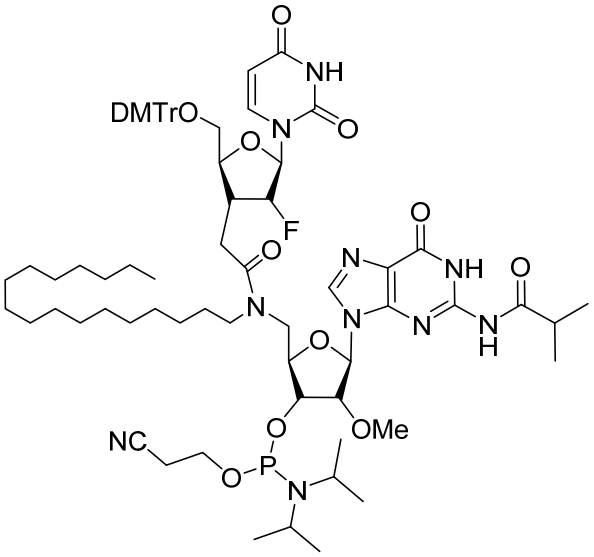

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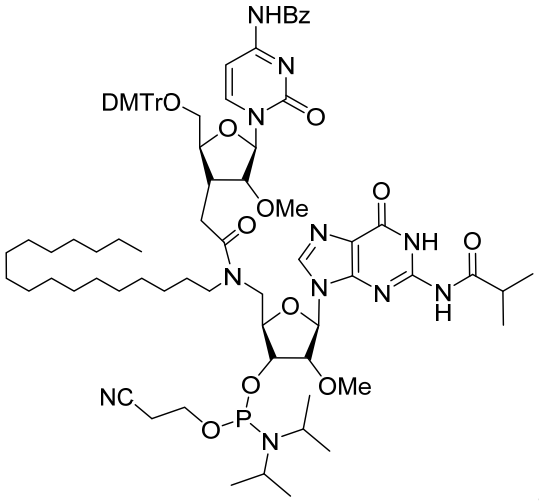

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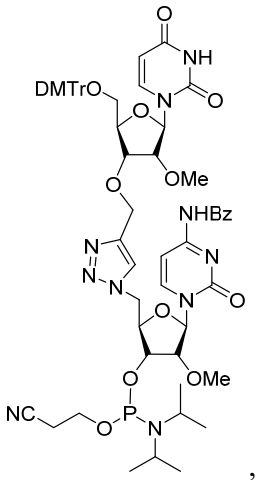
or a salt thereof.

18. A compound of the formula:



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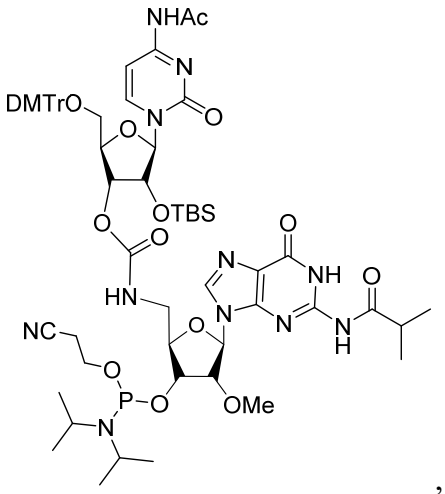

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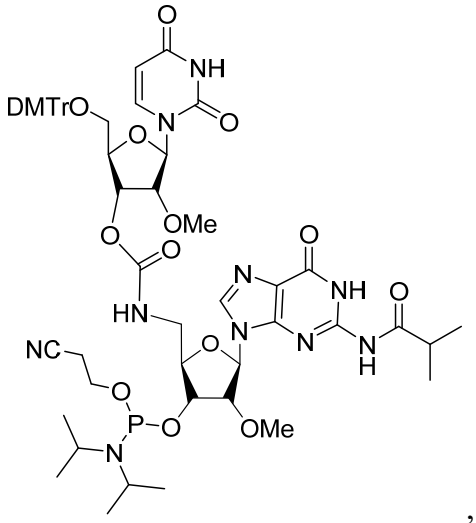

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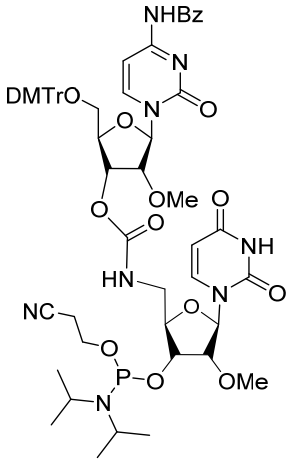

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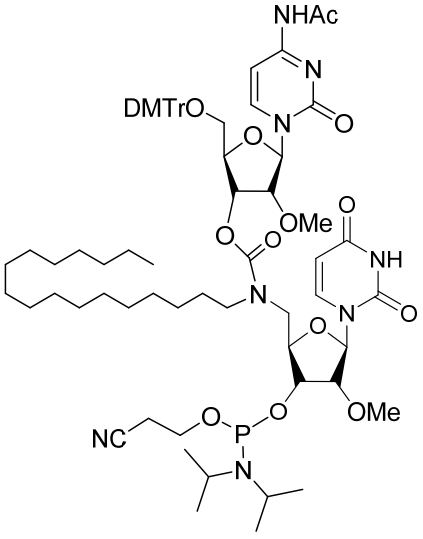

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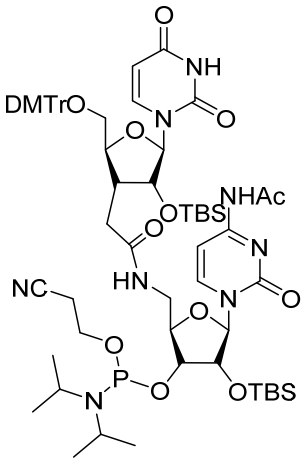

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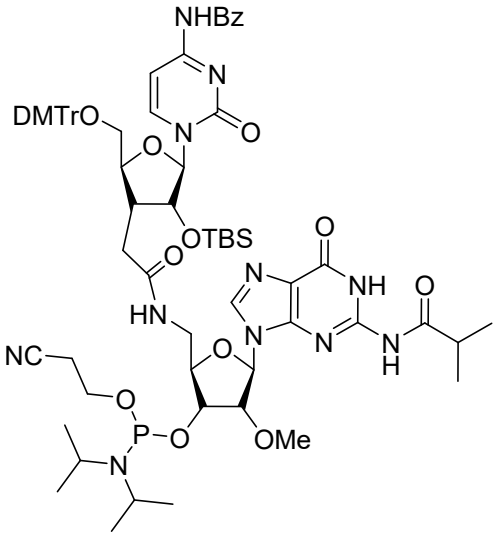
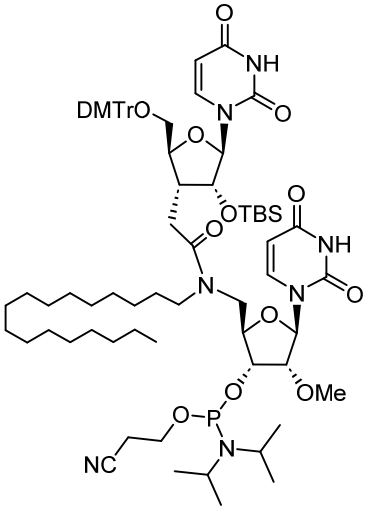
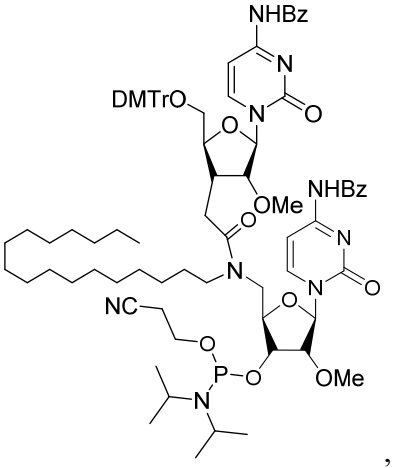
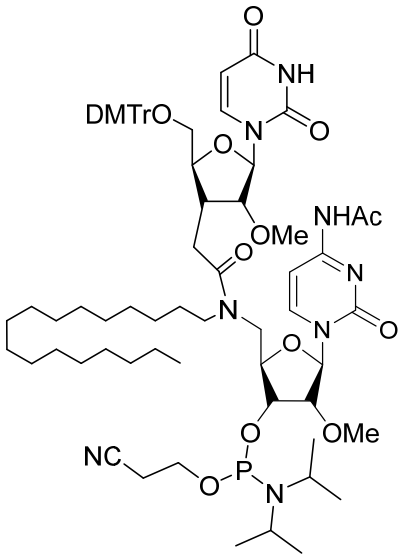
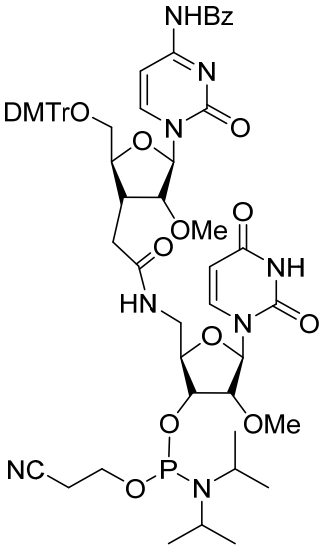
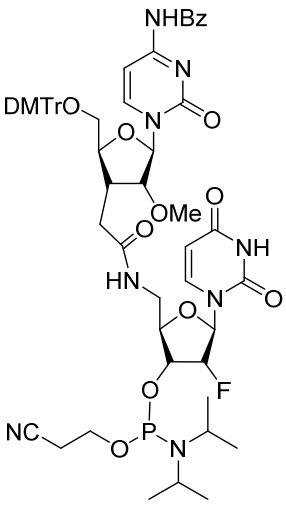
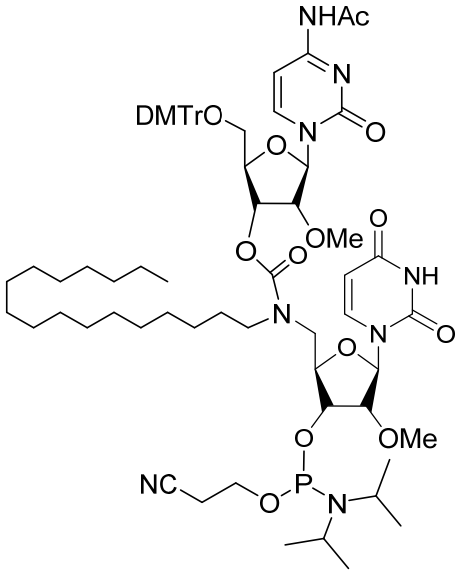

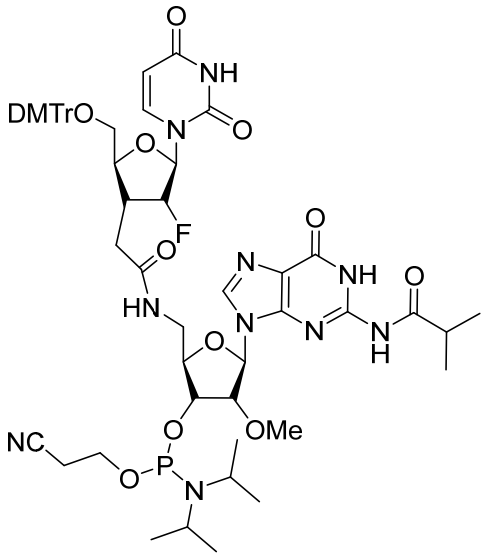
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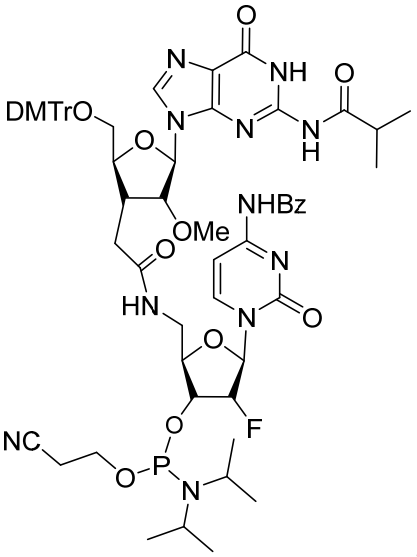
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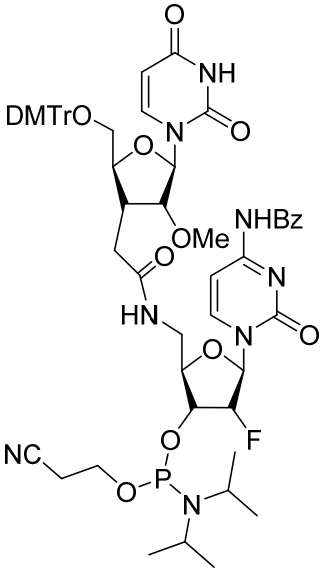
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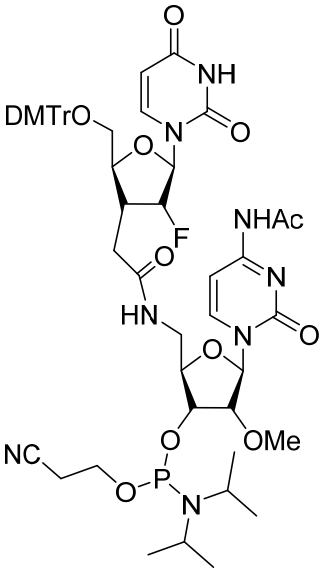
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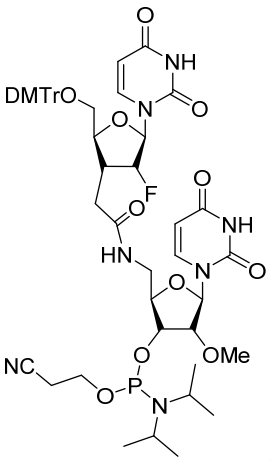
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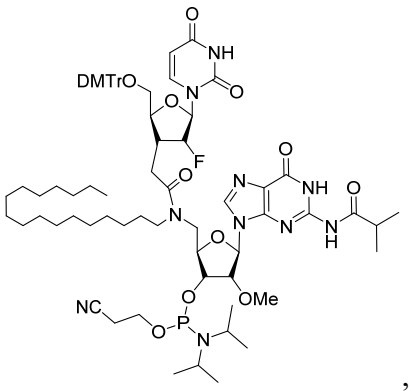
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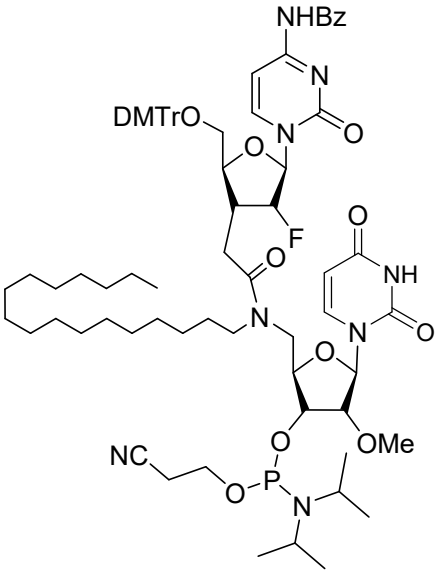
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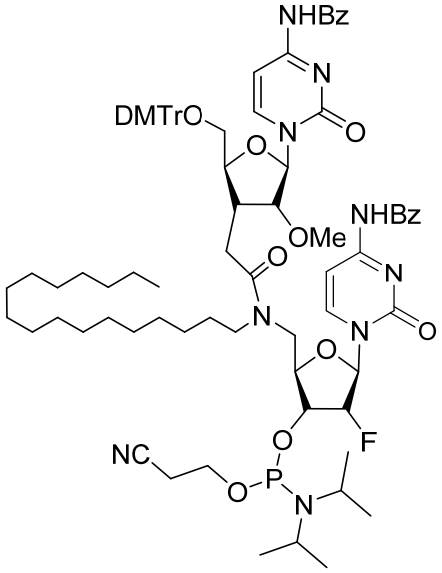
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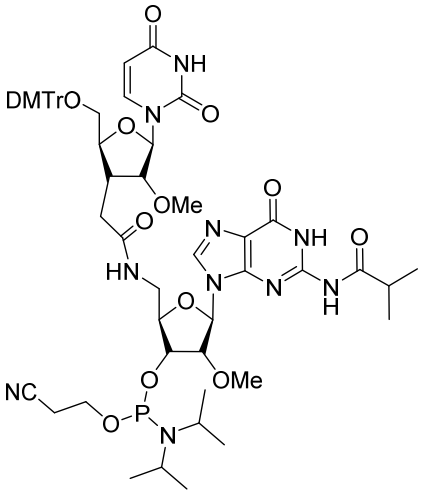
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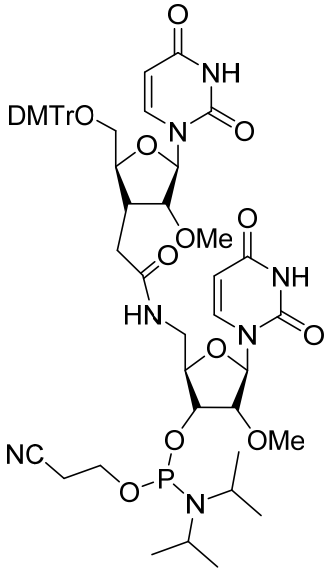
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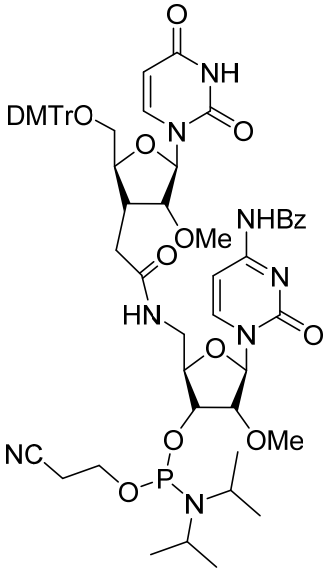
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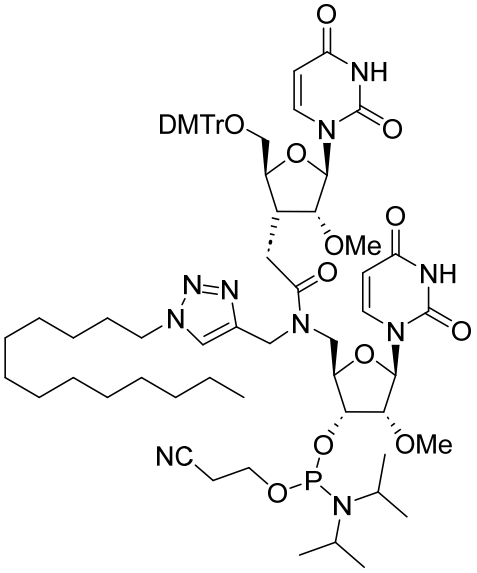
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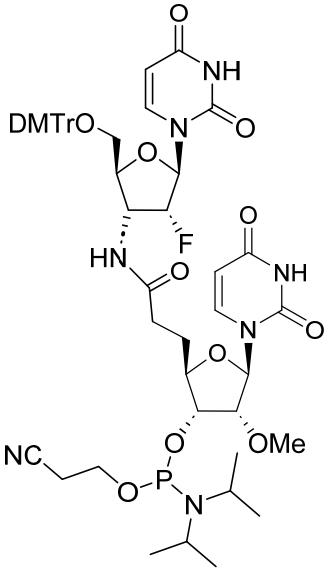
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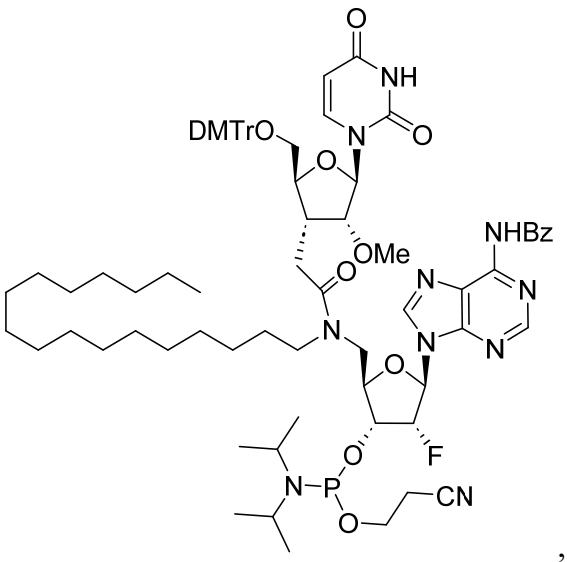
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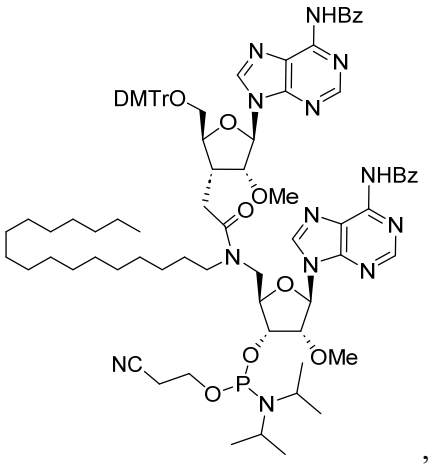
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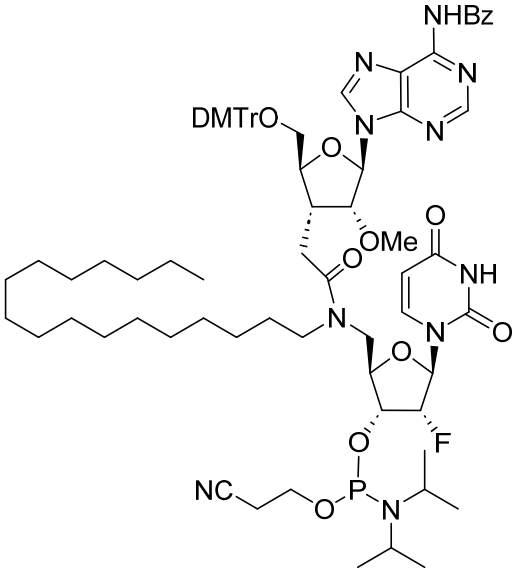
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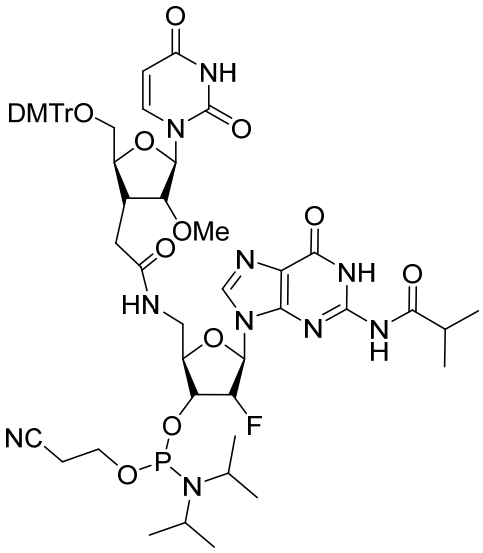
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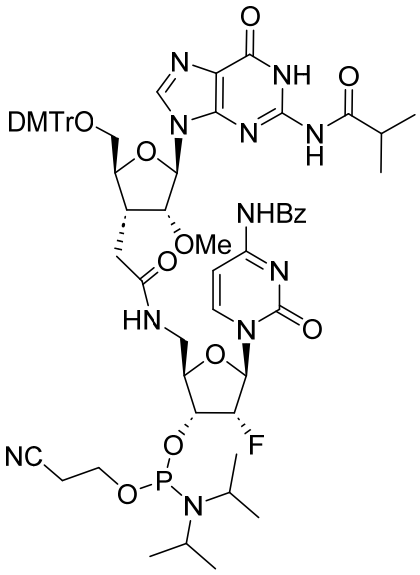
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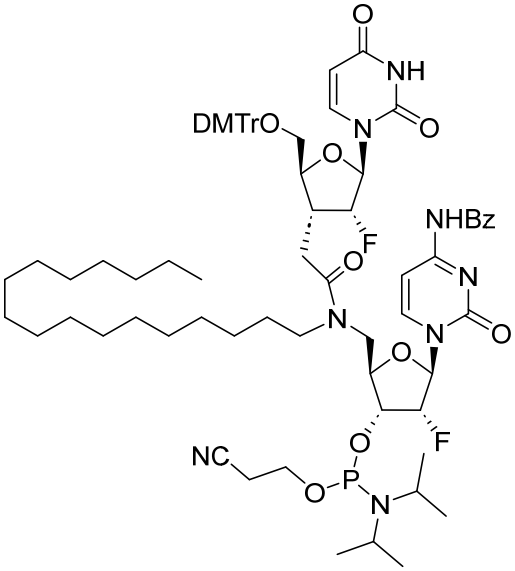
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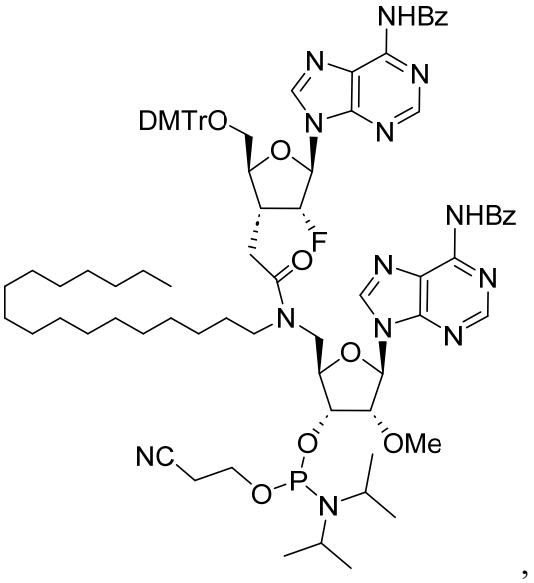
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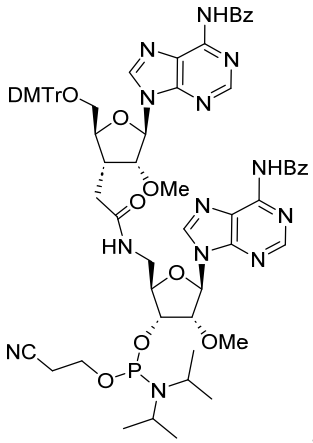
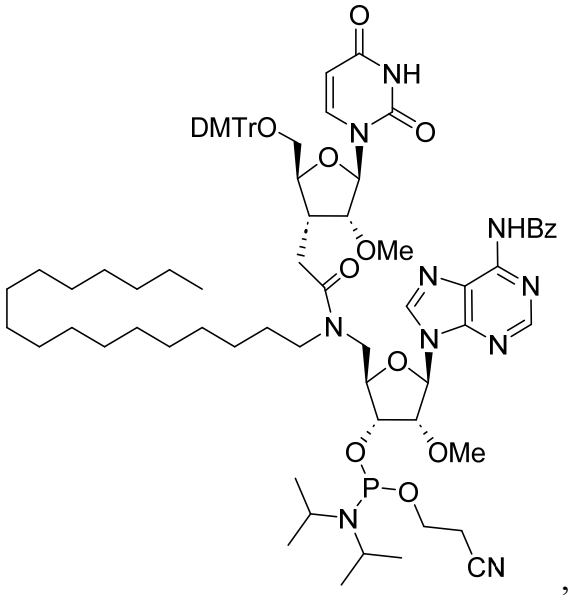
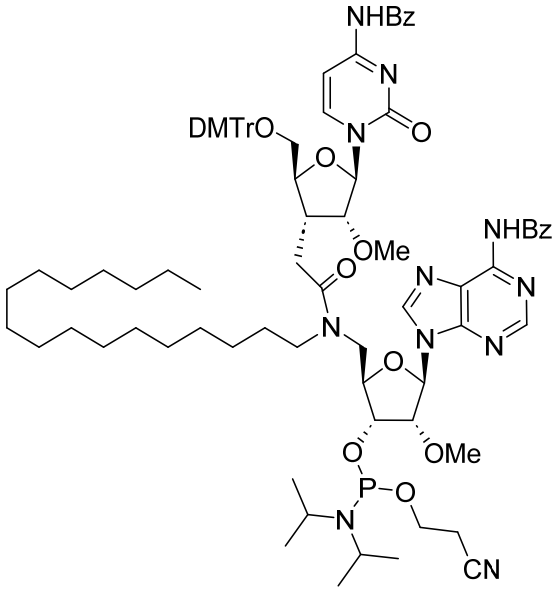
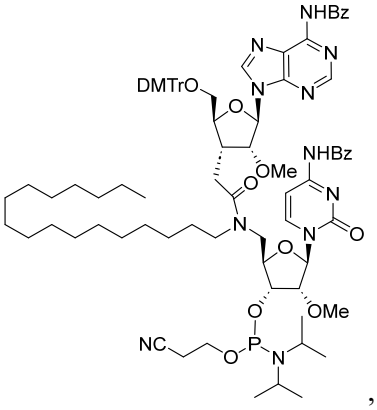
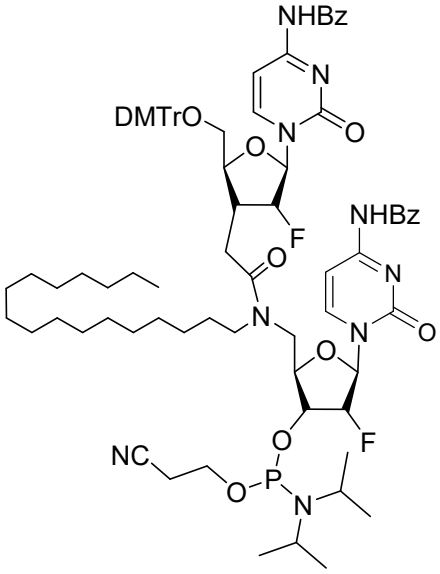
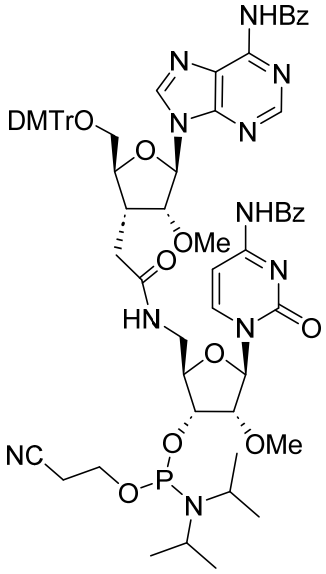
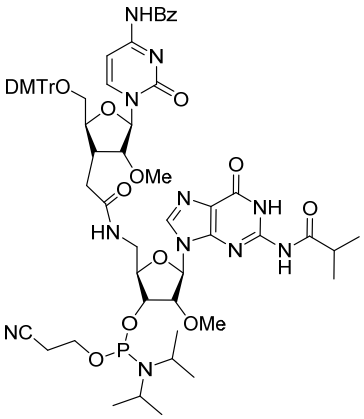

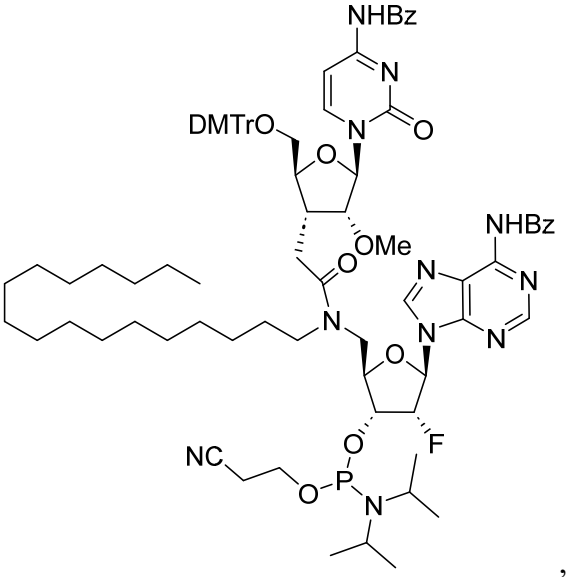
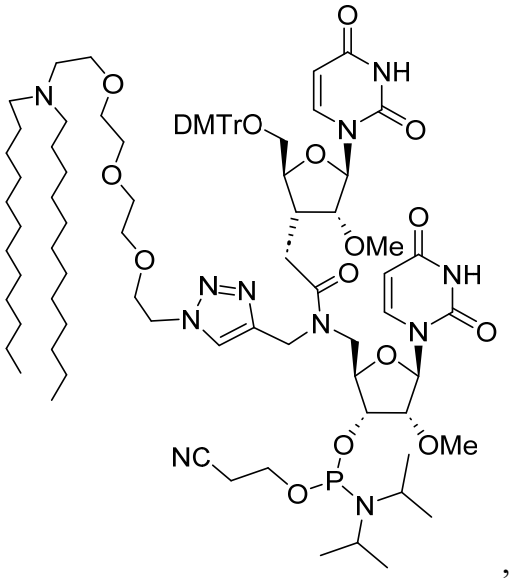
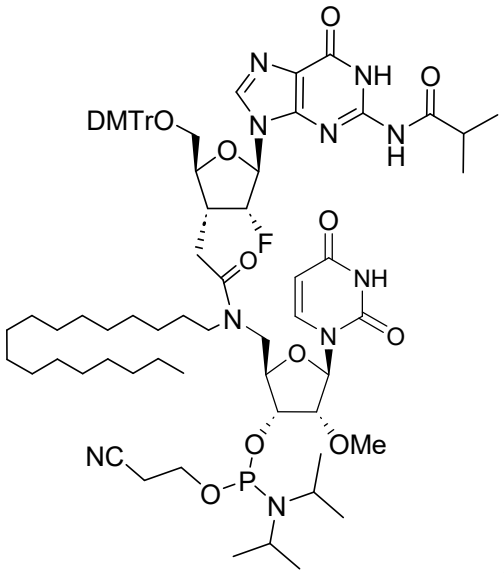
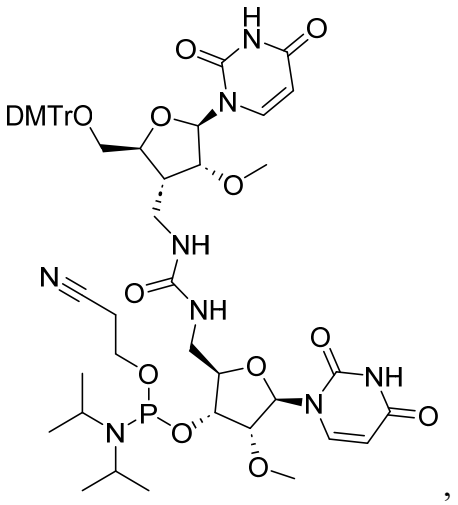
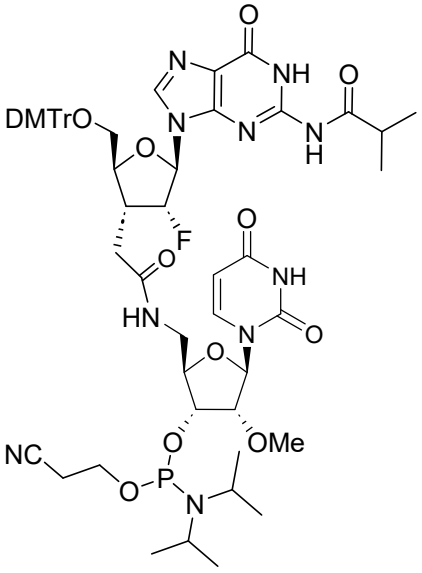
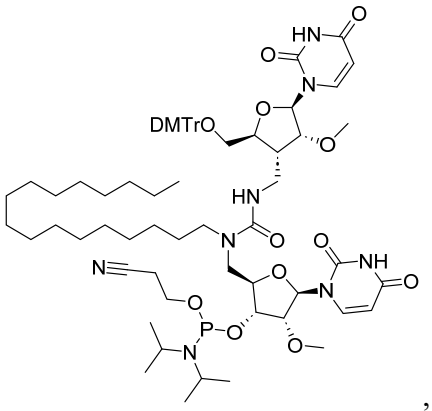

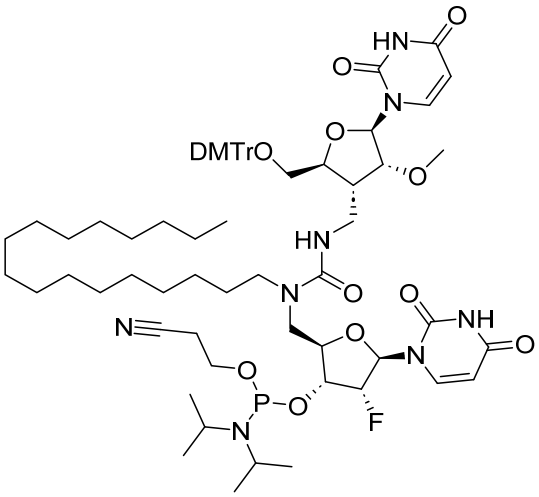
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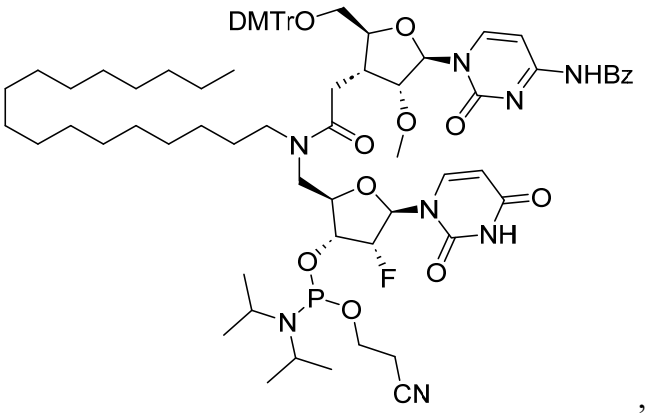
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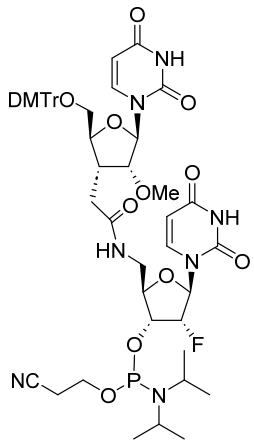
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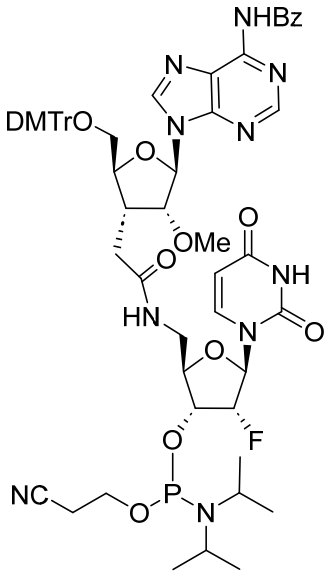
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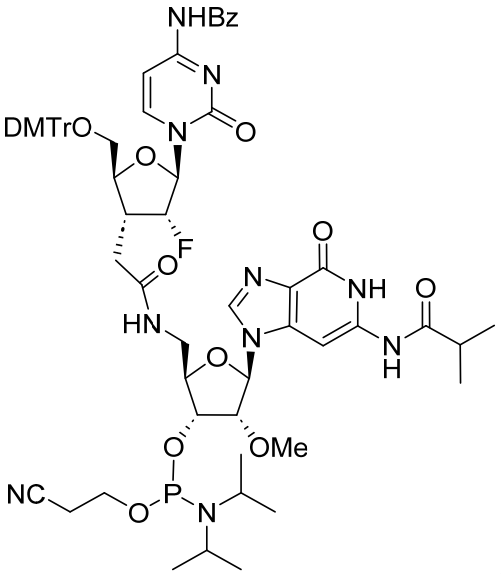
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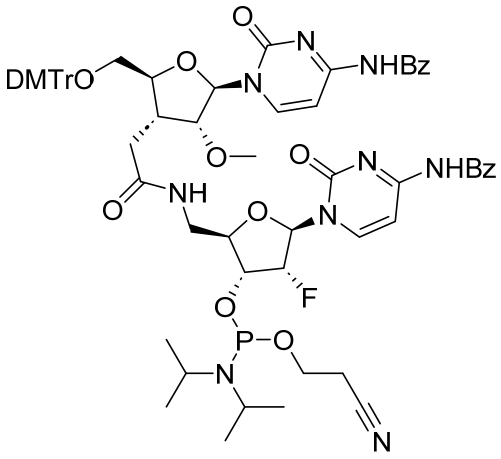
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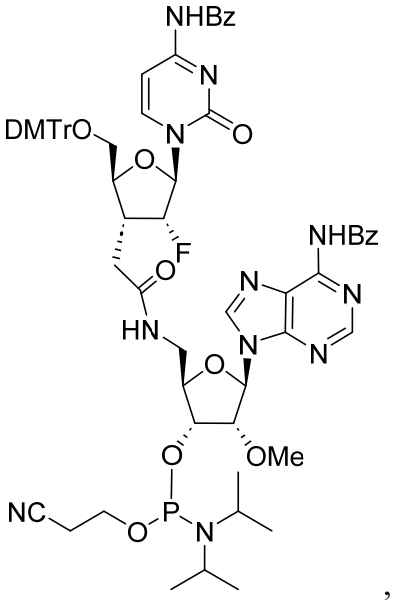
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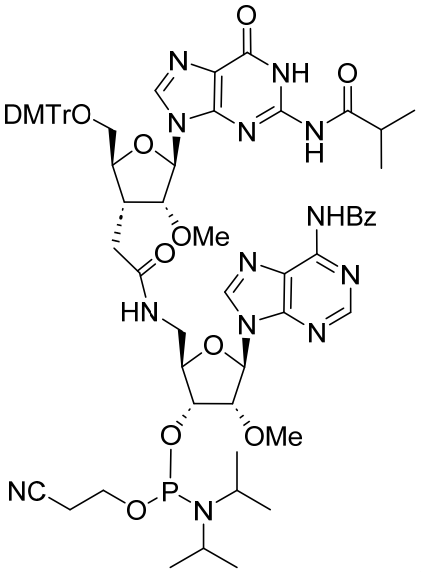
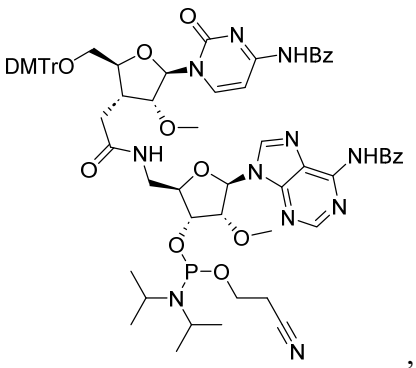
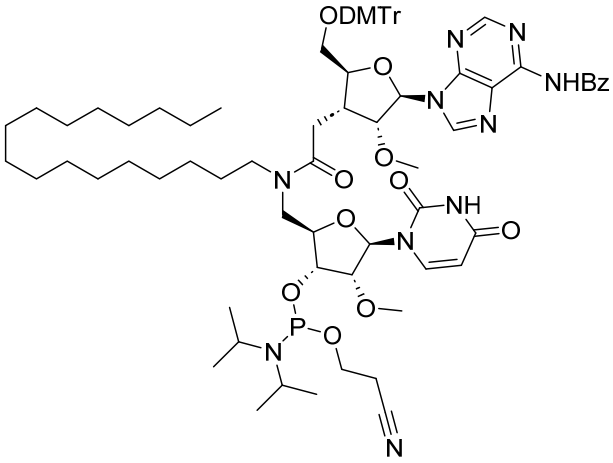
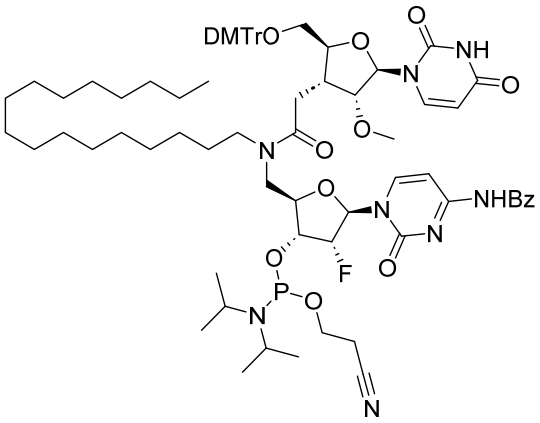
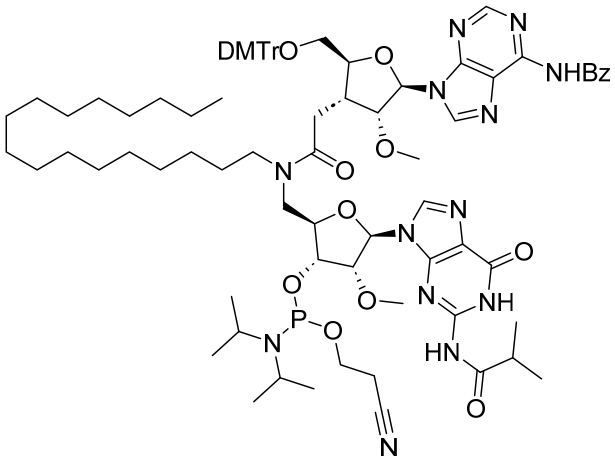
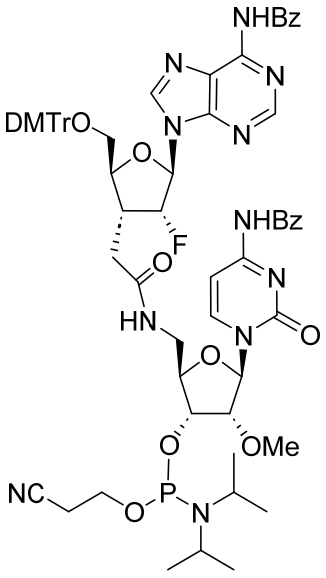

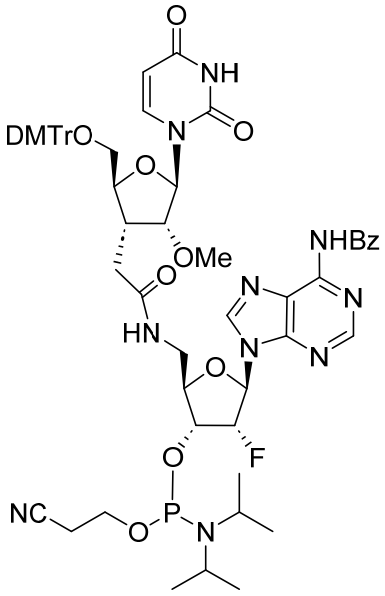
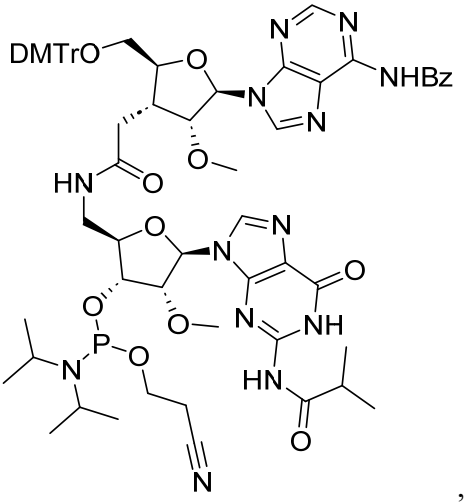
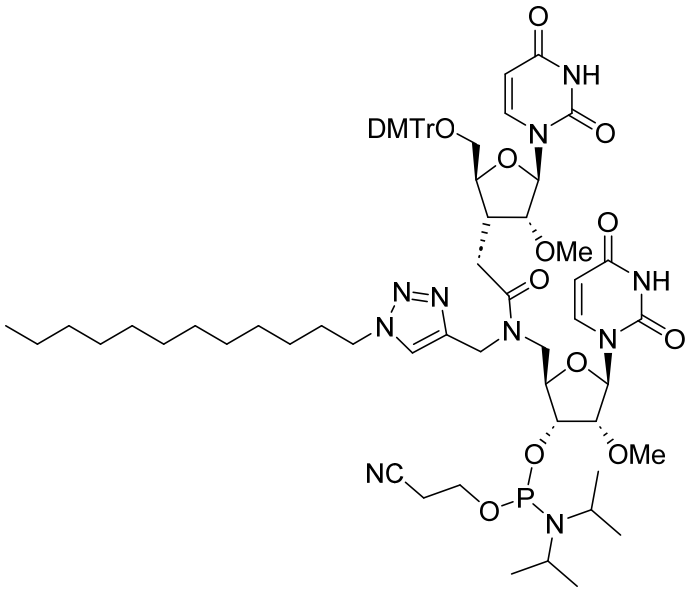
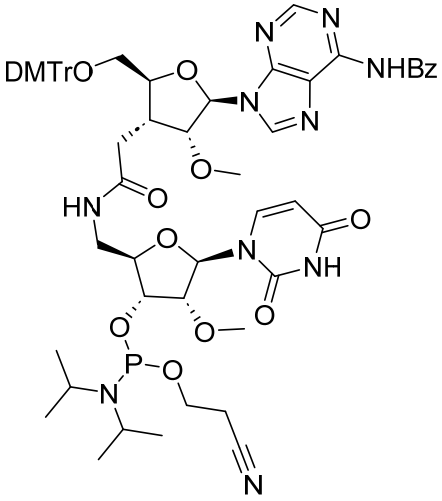
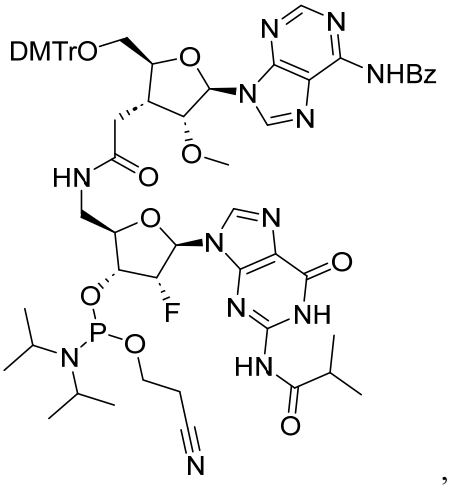
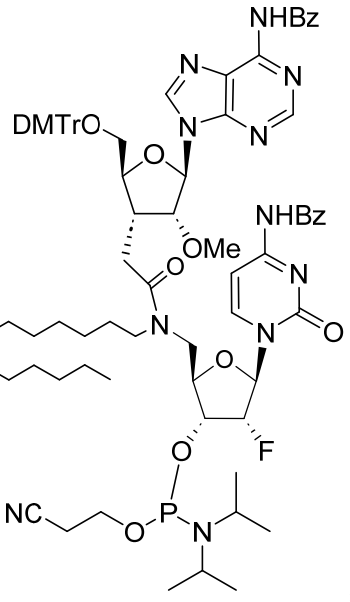

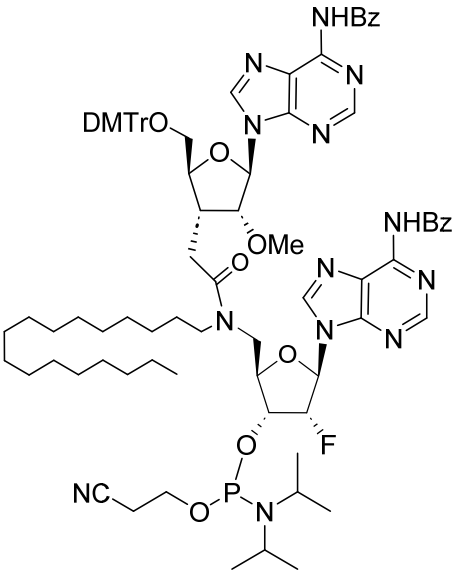
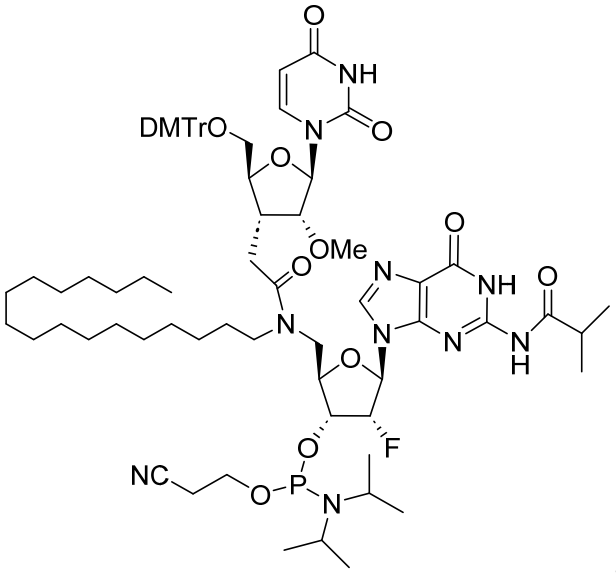
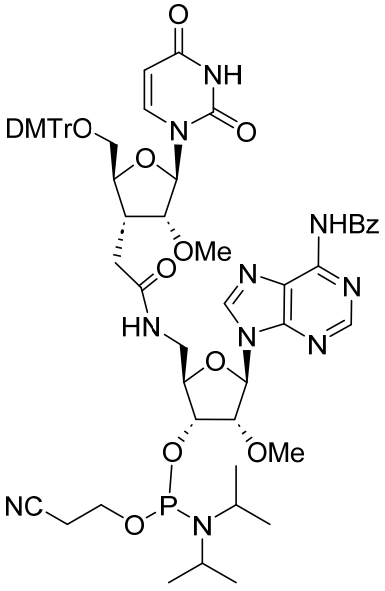
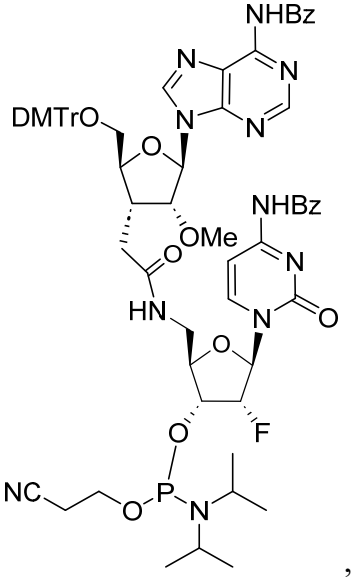
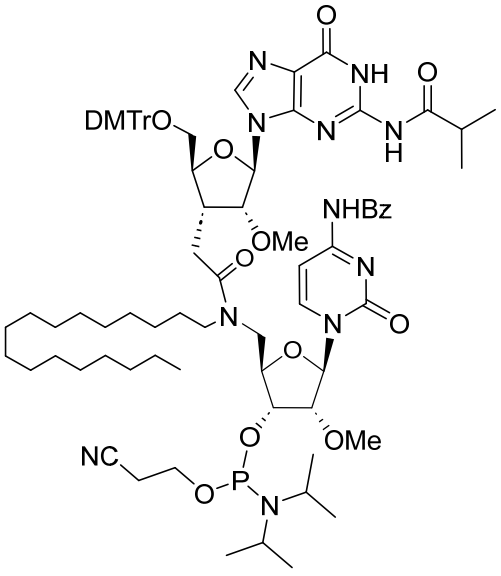
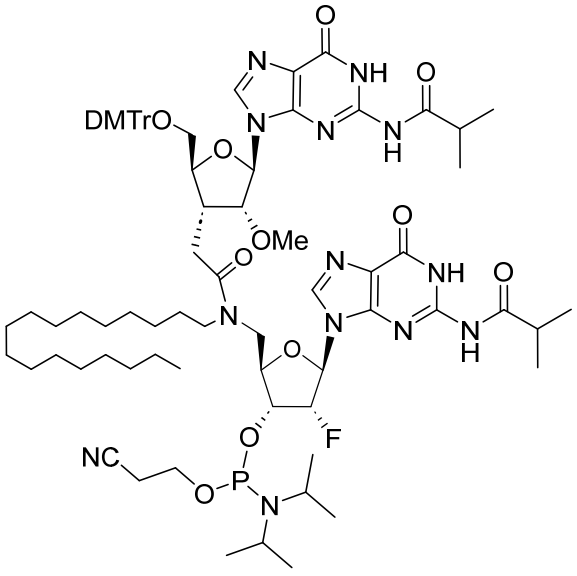

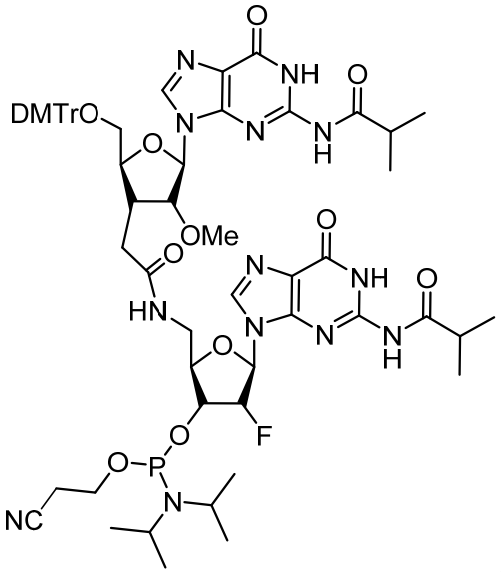
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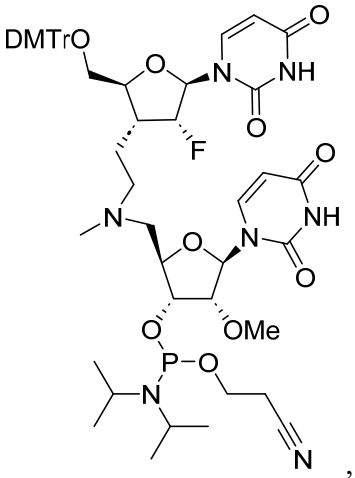
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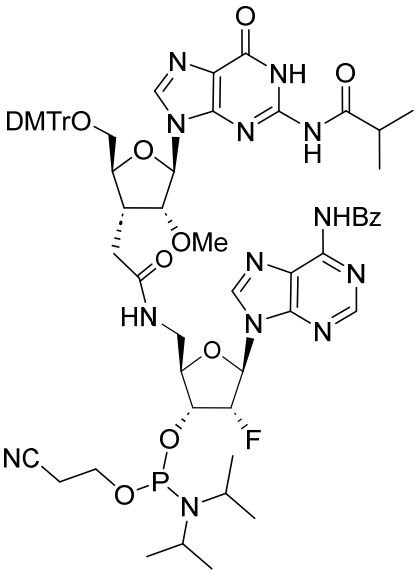
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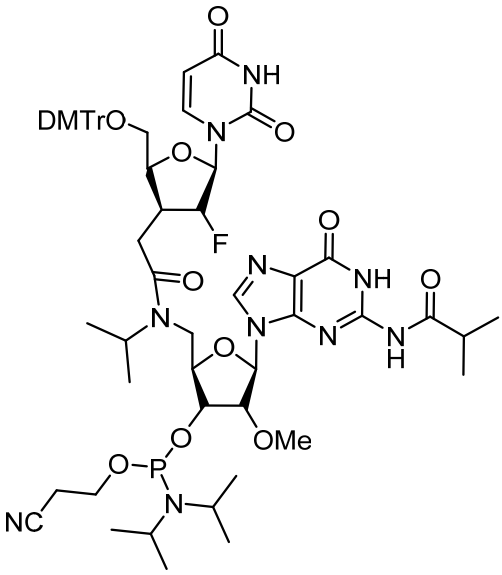
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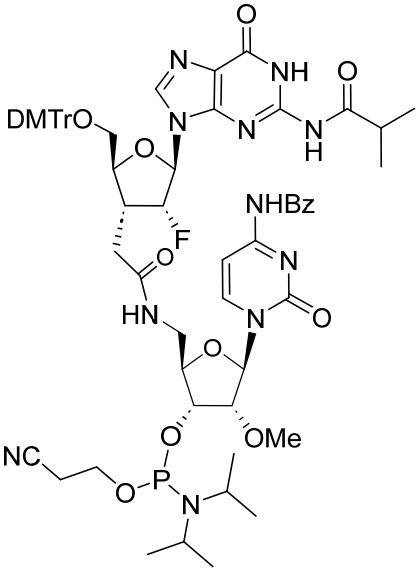
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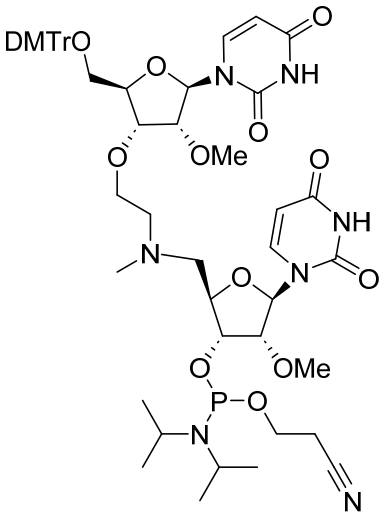
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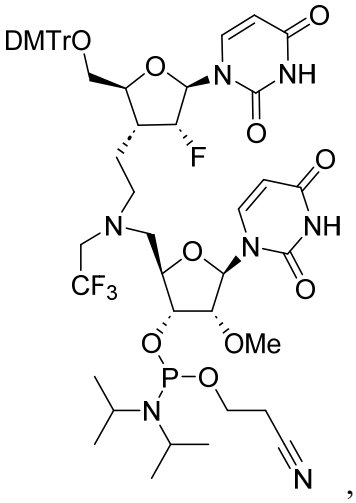
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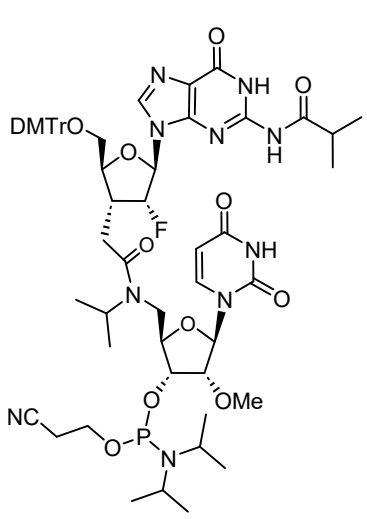
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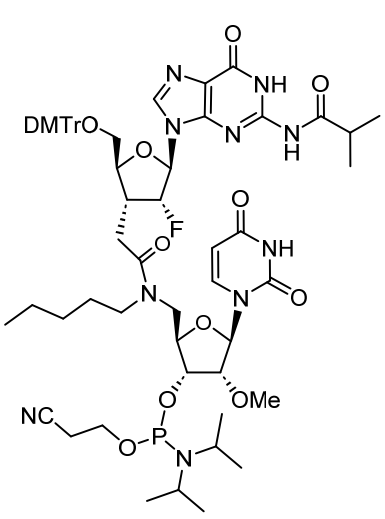
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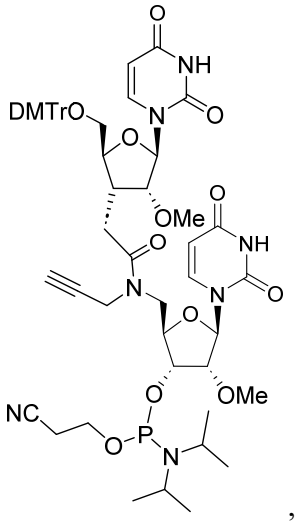
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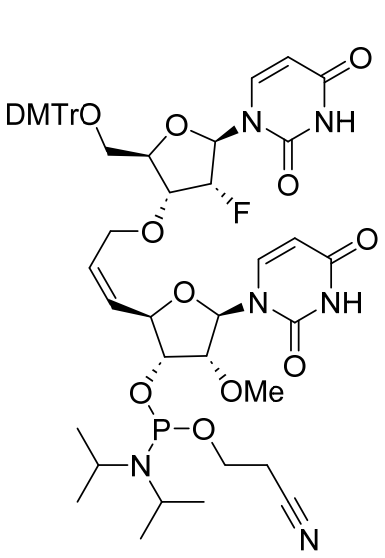
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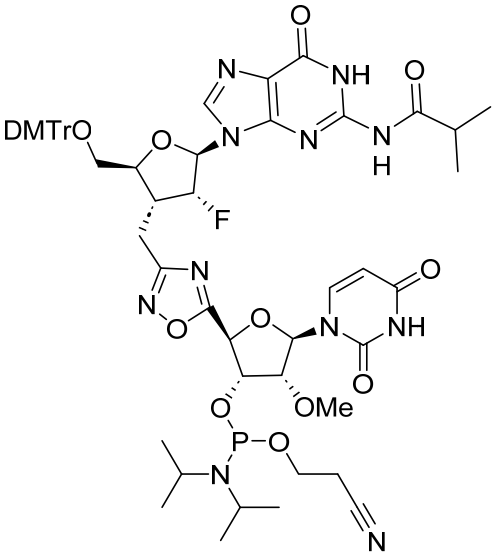
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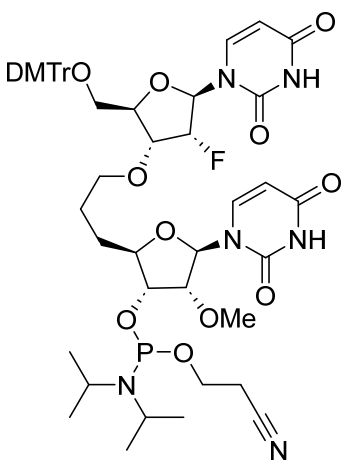
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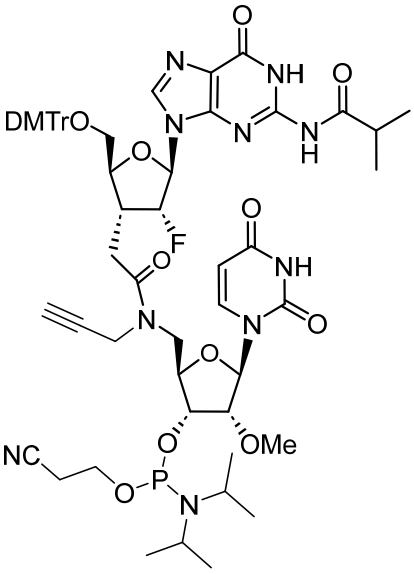
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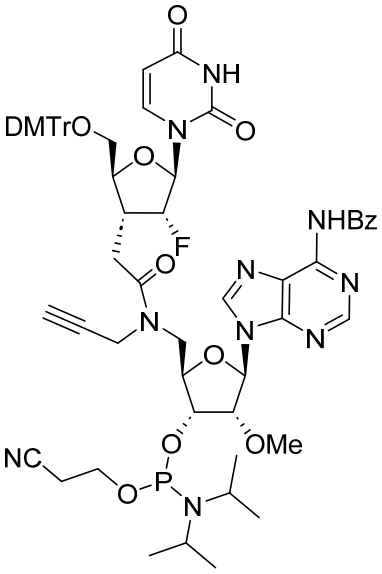
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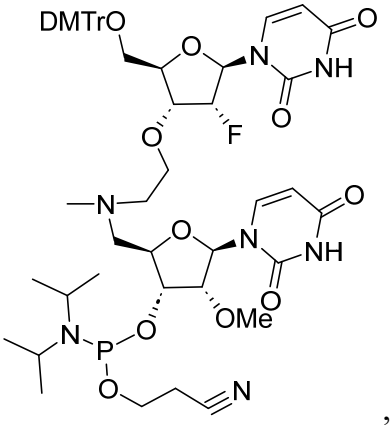
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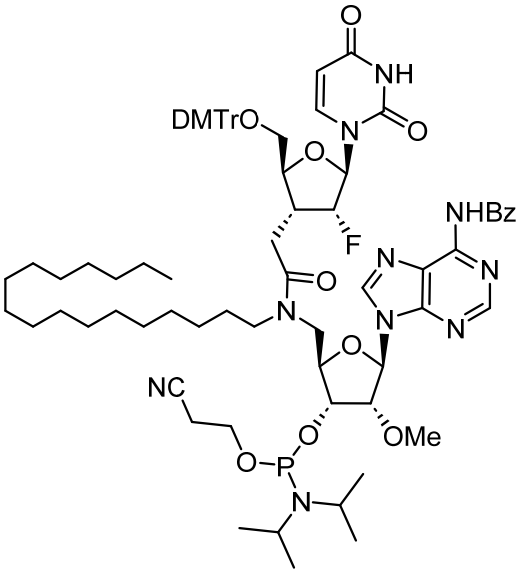
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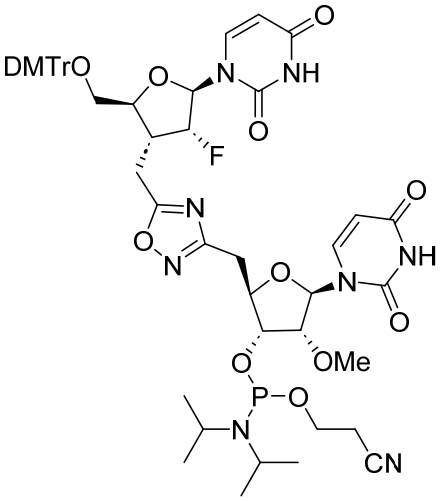
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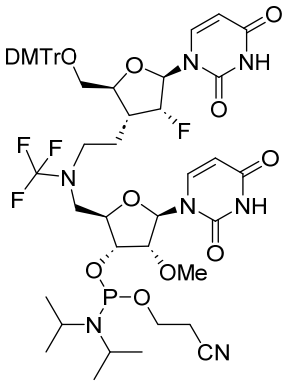
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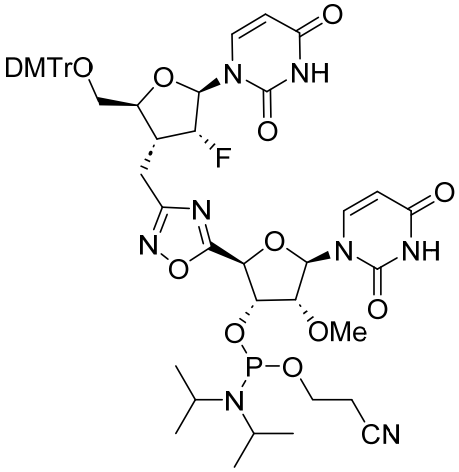
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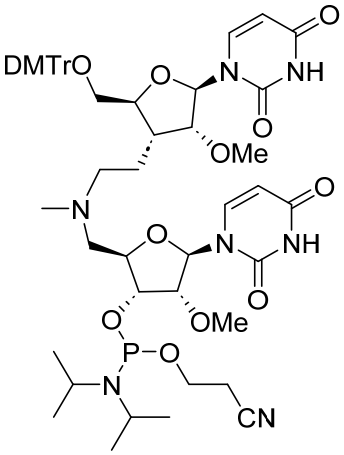
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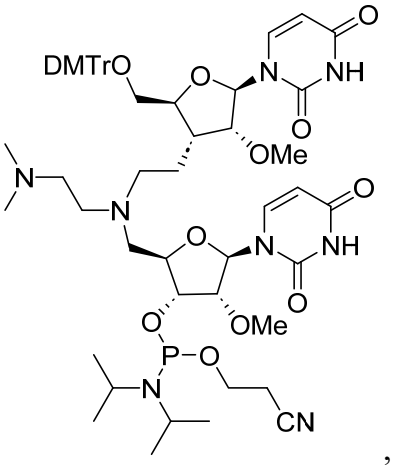

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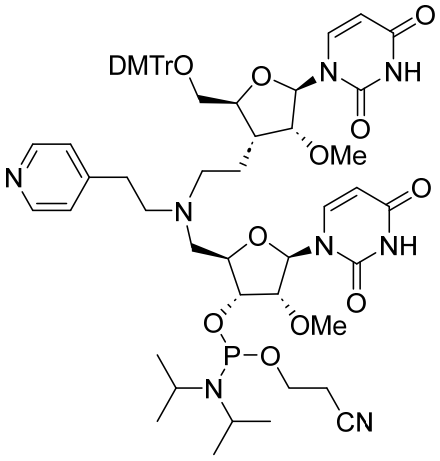

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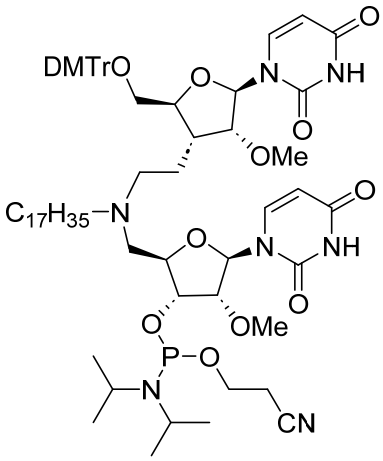

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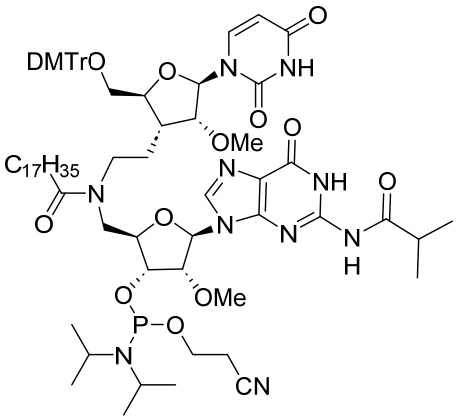

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or a salt thereof.

19. A composition comprising a compound of any one of claims 1-18, and a pharmaceutically acceptable excipient.

20. Use of the compound of any one of claims 1-18 or the composition of claim 19 in the manufacture of a medicament for the treatment of a central nervous system (CNS) disease, disorder, or a symptom thereof.