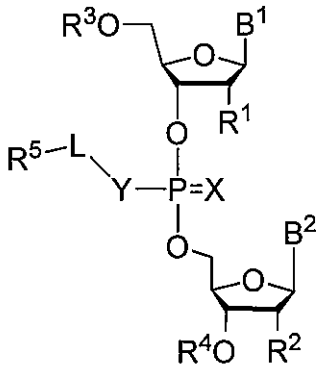
CLAIMS

1. A compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt, wherein:

each of B^1 and B^2 is independently a purinyl nucleobase or pyrimidinyl nucleobase, wherein at least one of B^1 or B^2 is a purinyl nucleobase;

X is O or S;

Y is O, S, or NR^6;

L is absent, C_1-C_6 alkyl or C_1-C_6 heteroalkyl, wherein each C_1-C_6 alkyl and C_1-C_6 heteroalkyl is optionally substituted with R^7;

each of R^1 and R^2 is independently hydrogen, halo, -CN, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), or OR^8, provided that at least one of R^1 and R^2 is halo, O-C_1-C_{20}-alkenyl, or O-C_1-C_{20}-alkynyl or R^1 is hydrogen;

each of R^3 and R^4 is independently hydrogen or C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl).

R^5 is hydrogen, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), C_1-C_{20} heteroalkyl (e.g., C_1-C_6 heteroalkyl), cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_{20} alkyl, C_1-C_{20} heteroalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1-5 R^9;

R^6 is hydrogen or C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl);

R^7 is halo, -CN, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), OR^8, oxo, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_{20} alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1-5 R^{10};

R^8 is hydrogen, C_1-C_{20} alkynyl (e.g., C_1-C_6 alkynyl), C_1-C_{20} alkenyl (e.g., C_1-C_6 alkenyl), cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_{20} alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl is optionally substituted with 1-5 R^{10};

each R^9 is independently C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), C(O)-aryl, C(O)-heteroaryl, OC(O)-aryl, or OC(O)-heteroaryl, wherein each C_1-C_{20} alkyl, C(O)-aryl, C(O)-heteroaryl, OC(O)-aryl, or OC(O)-heteroaryl is optionally substituted by 1-5 R^{10}; and

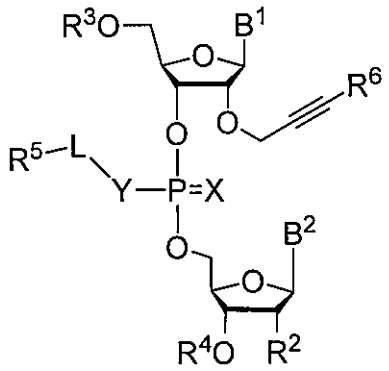
each R^{10} is independently C_1-C_{20} alkyl, halo, -CN, OH, O-C_1-C_{20} alkyl, O-C_1-C_{20} heteroalkyl, O-aryl, or O-heteroaryl.

2. The compound of claim 1, wherein each of B^1 or B^2 is independently modified or unmodified adenosinyl, modified or unmodified guanosinyl, modified or unmodified cytosinyl, modified or unmodified thyminyl, or modified or unmodified uracilyl.

3. The compound of claim 2, wherein each of R^1 and R^2 is independently hydrogen, fluorine, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), C_1-C_{20} alkenyl (e.g., C_1-C_6 alkenyl), or O-C_1-C_{20} alkynyl (e.g., C_1-C_6 alkynyl).

4. The compound of claim 3, wherein each of R^1 and R^2 is independently fluorine.

5. The compound of claim 1, wherein the compound is a compound of Formula (II):

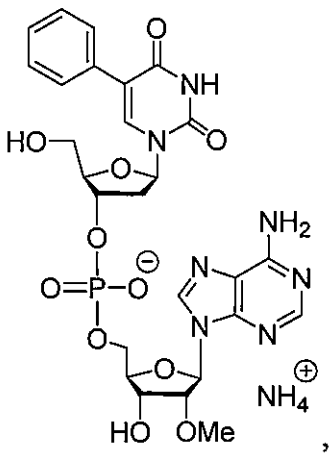
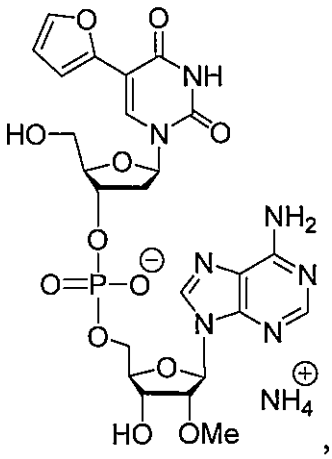
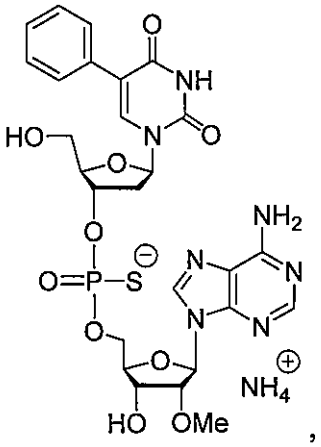
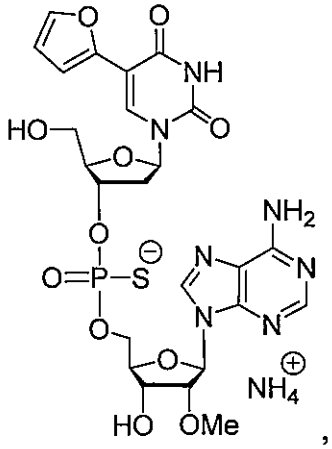
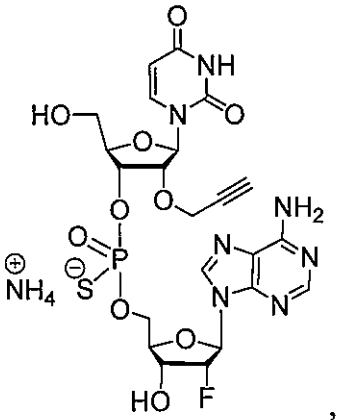
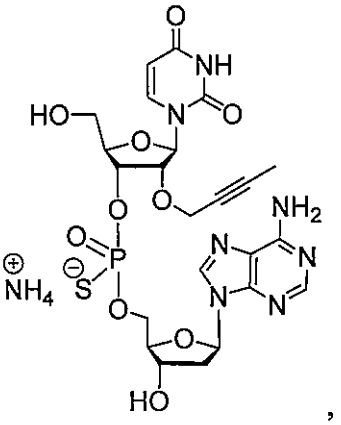
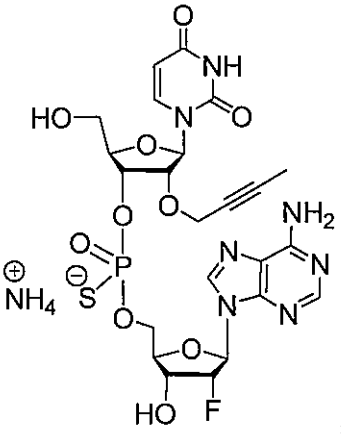
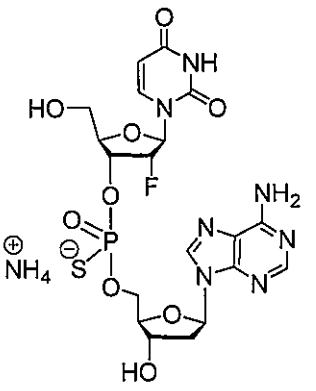
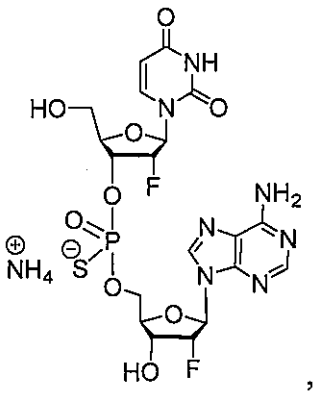


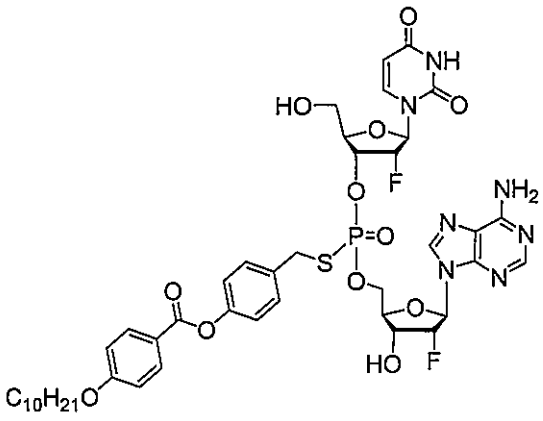
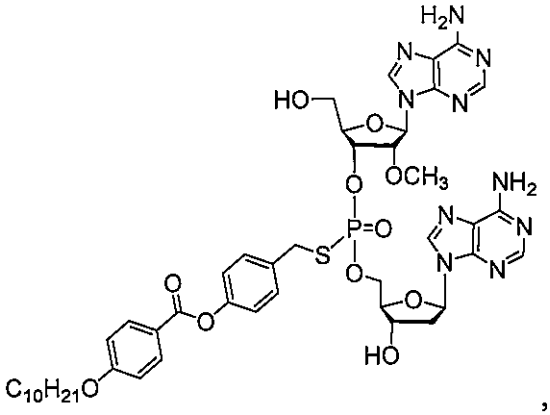
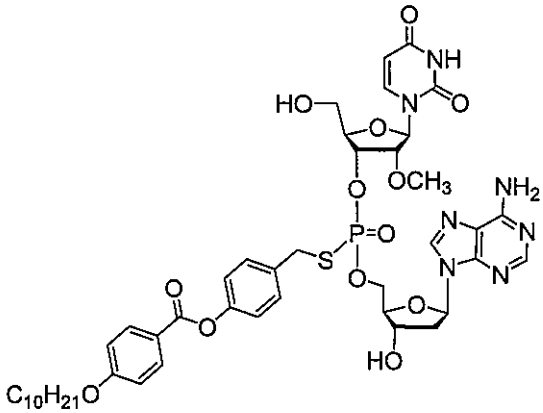
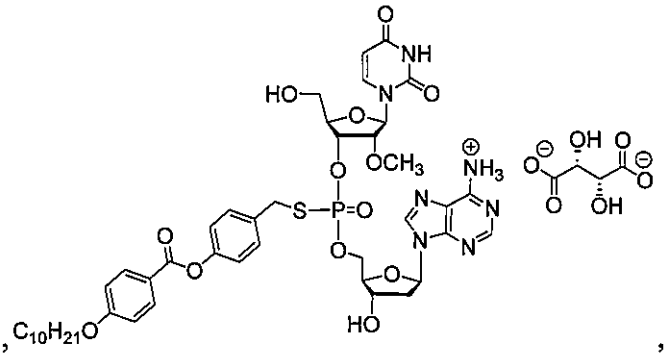
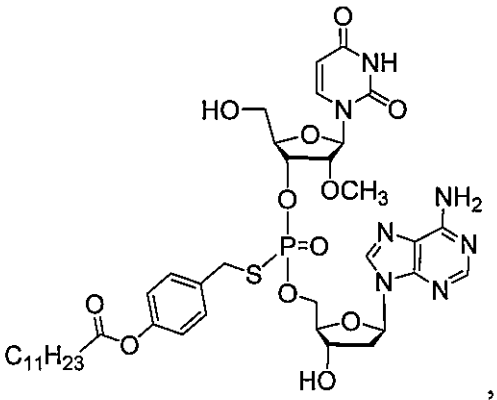
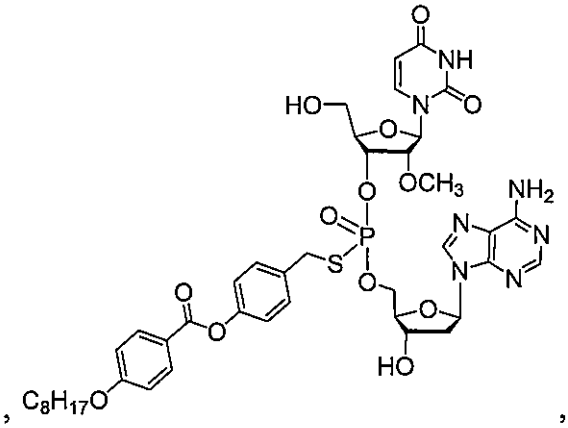
Formula (II)

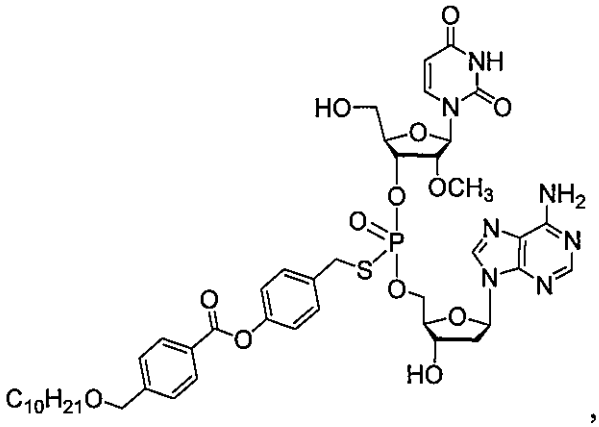
6. The compound of claim 5, wherein R^6 is hydrogen, C_1-C_{20} alkyl (e.g., C_1-C_6 substituted or unsubstituted alkyl), cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_{20} alkyl,

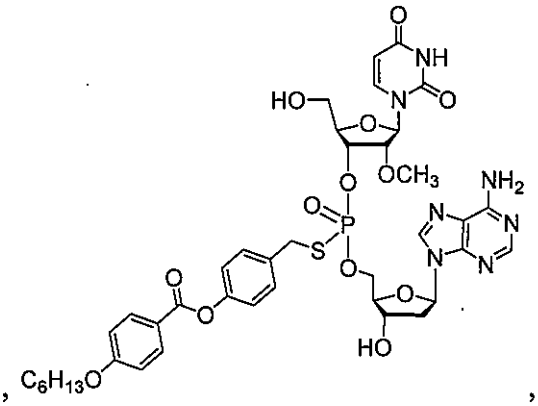
C_1-C_{20} heteroalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1-5 R^9.

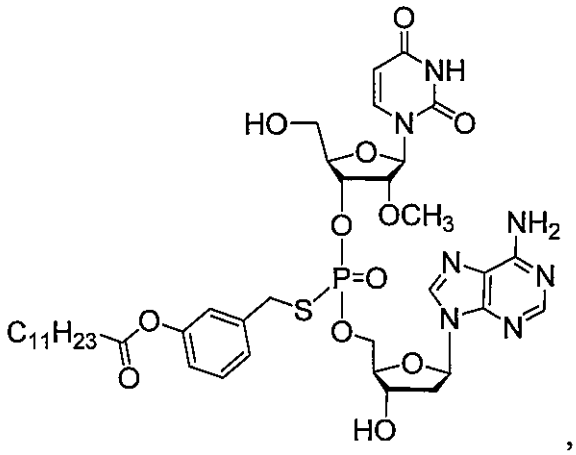
7. The compound of claim 1, wherein the compound is:

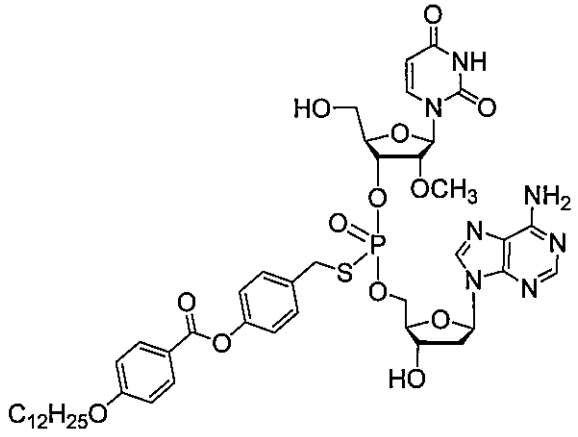

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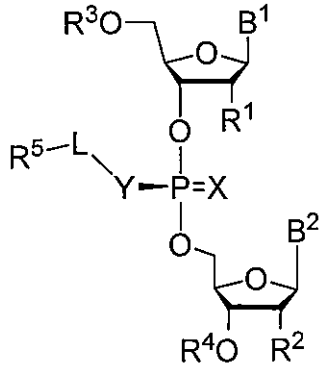
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, or


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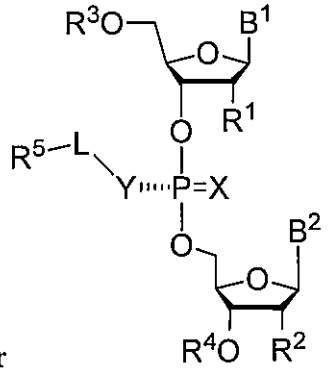
or a pharmaceutically acceptable salt thereof.

8. A composition comprising a compound of Formula (III-a) or (III-b):



(III-a)

or



(III-b)

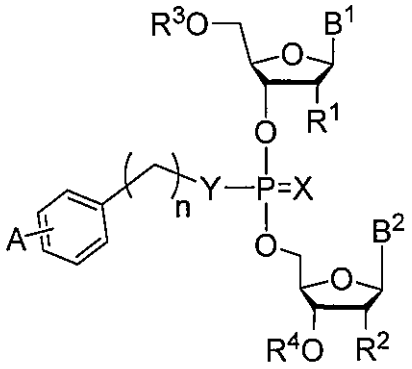
,

or pharmaceutically acceptable salts thereof, wherein the composition is a mixture of a compound of Formula (III-a) or (III-b).

9. The composition of claim 8, wherein the composition comprises an optically enriched mixture of a compound of Formula (III-a) or (III-b).

10. The composition of claim 8, wherein the composition comprises a compound of Formula (III-a) or (III-b) in an enantiomeric excess of 90%.

11. The compound of claim 1, wherein the compound is of Formula (IV):



Formula (IV)

or a pharmaceutically acceptable salt thereof, wherein:

each of B^1 and B^2 is independently a purinyl nucleobase or pyrimidinyl nucleobase, wherein at least one of B^1 or B^2 is a purinyl nucleobase;

X is O or S;

Y is O, S, or NR^5;

n is 1, 2, or 3;

each of R^1 and R^2 is independently hydrogen, -CN, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), or OR^6;

each of R^3 and R^4 is independently hydrogen or C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl);

R^5 is hydrogen or C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl);

R^6 is hydrogen, C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), C_1-C_{20} heteroalkyl (e.g., C_1-C_6 heteroalkyl), cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein each C_1-C_{20} alkyl, C_1-C_{20} heteroalkyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl is optionally substituted with 1-5 R^7;

each R^7 is independently C_1-C_{20} alkyl (e.g., C_1-C_6 alkyl), C(O)-aryl, C(O)-heteroaryl, OC(O)-aryl, or OC(O)-heteroaryl, wherein each C_1-C_{20} alkyl, C(O)-aryl, C(O)-heteroaryl, OC(O)-aryl, or OC(O)-heteroaryl is optionally substituted by 1-5 R^8;

each R^8 is independently C_1-C_{20} alkyl, halo, -CN, OH, O-C_1-C_{20} alkyl, O-C_1-C_{20} heteroalkyl, O-aryl, or O-heteroaryl; and

A is OC(O)-C_6-C_{20} alkyl or OC(O)-aryl, wherein aryl is optionally substituted with C_6-C_{20} alkyl, O-C_6-C_{20} alkyl or C_1-C_6-O-C_6-C_{20} alkyl.

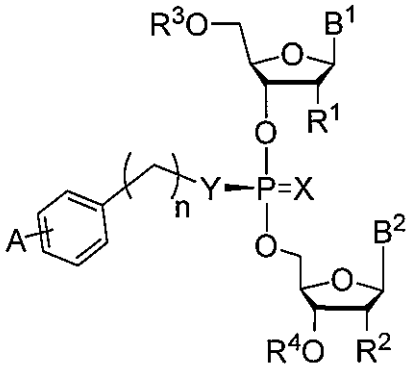
12. The compound of claim 11, wherein each of R^1 and R^2 is independently hydrogen or O-C_1-C_{20} alkyl.

13. The compound of claim 11, wherein A is OC(O)-C_6-C_{20} alkyl or OC(O)-aryl, wherein aryl is substituted with C_6-C_{20} alkyl, O-C_6-C_{20} alkyl or C_1-C_6-O-C_6-C_{20} alkyl.

14. The compound of claim 11, wherein each of R^3 and R^4 is independently hydrogen.

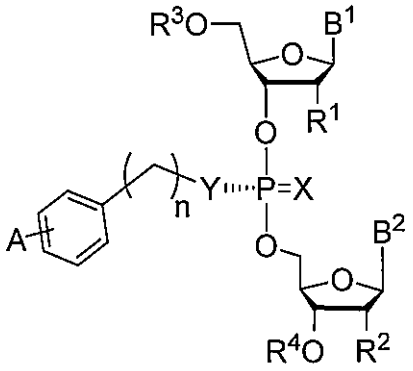
15. The compound of claim 13, wherein R^1 is O-C_1-C_{20} alkyl and R^2 is hydrogen.

16. The composition of claim 8, wherein the composition comprises compounds of Formula (V-a) or (V-b):



(V-a)

or



(V-b)

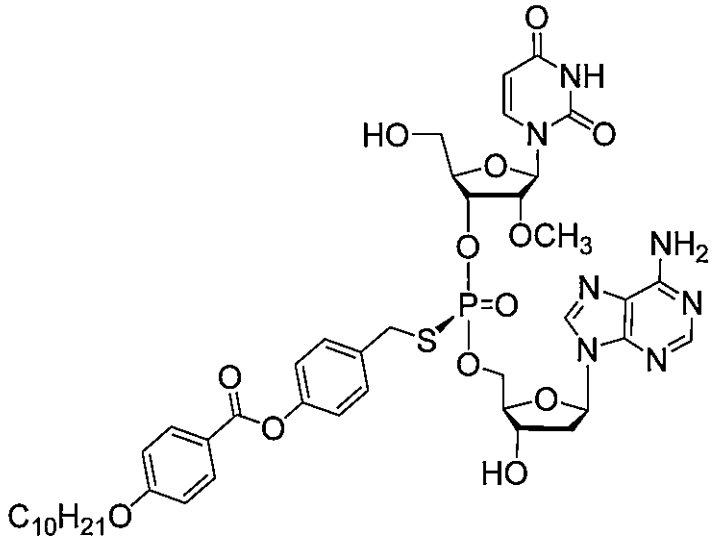
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or pharmaceutically acceptable salts thereof, wherein the composition is a mixture of a compound of Formula (V-a) or (V-b).

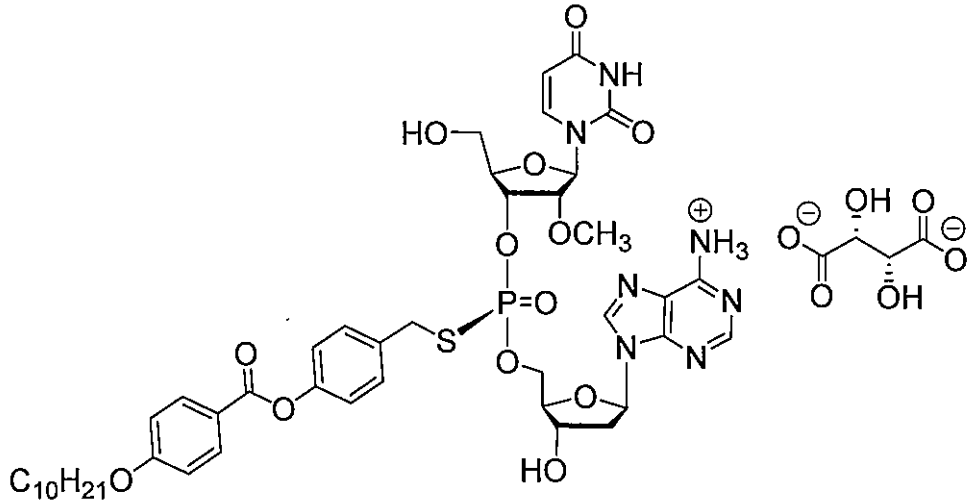
17. The composition of claim 16, wherein the composition is an optically enriched mixture of a compound of Formula (V-a) or (V-b).

18. The composition of claim 16, wherein the composition comprises a compound of Formula (V-a) or (V-b) in an enantiomeric excess of 90%.

19. The composition of claim 16, wherein the composition comprises:



, or



,

or a pharmaceutically acceptable salt thereof.

20. Use of a compound of claim 1 or a composition of claim 8 in the manufacture of a medicament for the treatment of cancer.

21. The use of claim 20, wherein the cancer is a cancer of the breast, bone, brain, cervix, colon, gastrointestinal tract, eye, gall bladder, lymph nodes, blood, lung, liver, skin, mouth, prostate, ovary, penis, pancreas, uterus, testicles, stomach, thymus, thyroid, or other part of the body.

22. The use of claim 20, wherein the cancer is a cancer of the liver.

23. The use of claim 20, wherein the medicament further comprises an additional agent.

24. The use of claim 23, wherein the additional agent comprises methotrexate, 5-fluorouracil, doxorubicin, vincristine, bleomycin, vinblastine, dacarbazine, toposide, cisplatin, epirubicin, or sorafenib tosylate.

25. Use of a compound of claim 1 or a composition of claim 8 in the manufacture of a medicament for immune-modulation.