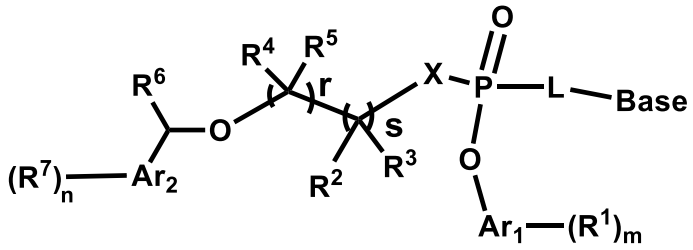
WHAT IS CLAIMED IS:

1. A compound represented by Formula (I), a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing,

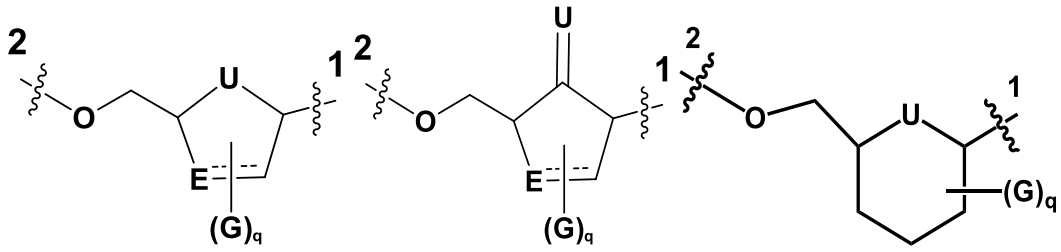


Formula (I)

wherein

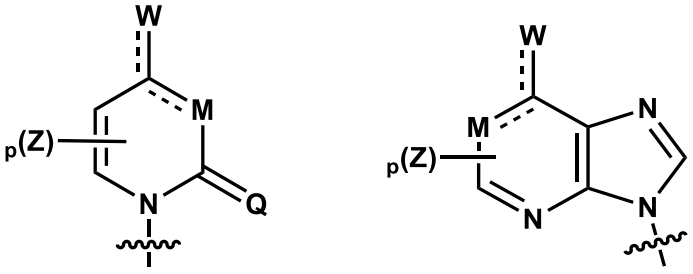
L is selected from the group consisting of substituted or unsubstituted C_{1-12} alkylene, C_{2-12} alkenylene, C_{2-12} alkynylene, and the alkylene, alkenylene or alkynylene is optionally interrupted by one or more -O-, -NR^8- or -S-; or

L represents a group of Formula (c), Formula (d) or Formula (e), wherein ---- represents a single bond or a double bond, position 1 is attached to the Base, and position 2 is attached to the phosphorus atom (P):



Formula (c) Formula (d) Formula (e) ;

Base represents a group of Formula (a) or Formula (b):



Formula (a) Formula (b) ; ------ represents a single bond or a double bond;

M represents N or NR^8;

W represents H, NR^8R^9, NR^8, CH_2, O or S;

Q represents O, S, NR^8 or CH_2;

each Z, at each occurrence, independently represents hydrogen, halogen, hydroxy, cyano, nitro, azido, NR^8R^9, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, or substituted or unsubstituted C_{3-8} cycloalkyl, preferably, each Z, at each occurrence, independently represents hydrogen, halogen, NR^8R^9 or C_{1-6} alkyl, and if there are multiple Z groups, they each may be the same or different;

p represents 0, 1, 2, 3, 4 or 5;

provided that when M is attached by a double bond, W is attached by a single bond; and when M is attached by a single bond, W is attached by a double bond;

U represents O, S, NR^8 or $CR^{10}R^{11}$;

E represents CR^{10}, $CR^{10}R^{11}$ or S, provided that when E is attached by a double bond, it is CR^{10};

each G, at each occurrence, independently represents hydrogen, halogen, hydroxyl, cyano, nitro, azido, NR^8R^9, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, or substituted or unsubstituted C_{3-8} cycloalkyl, preferably, each G, at each occurrence, independently represents hydrogen, halogen, hydroxyl, azido or C_{1-6} alkyl, and if there are multiple G groups, they each may be the same or different;

q represents an integer of from 0 to 5, and preferably, q represents 0, 1, 2, 3 or 4;

Ar_1 represents C_{6-14} aryl, and preferably, Ar_1 represents phenyl, 1-naphthyl or 2-naphthyl;

each R^1, at each occurrence, represents hydrogen, halogen, -OH, -CN, $-NO_2$, $-NR^8R^9$, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, substituted or unsubstituted C_{1-6} haloalkyl, substituted or unsubstituted C_{1-6} alkylthio, substituted or unsubstituted C_{2-10} alkenyl, or substituted or unsubstituted C_{2-10} alkynyl, preferably, each R^1, at each occurrence, independently represents hydrogen, halogen, C_{1-6} alkyl or C_{1-6} alkoxy, more preferably, each R^1, at each occurrence, independently represents hydrogen, fluoro, chloro, bromo, methyl, ethyl or propyl, and if there are multiple R^1 groups, they each may be the same or different;

m represents an integer of from 0 to 7, and preferably, m represents 0, 1, 2, 3 or 4;

X represents $-NR^8-$, preferably, X represents NH or N-C_{1-6} alkyl (e.g., N-methyl), and more preferably, X represents NH;

R^2 and R^3, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{1-6} alkoxy; or R^2 and R^3 together with the carbon atom to which they are attached, form substituted or unsubstituted C_{3-8} cycloalkyl, or substituted or unsubstituted 3- to 10-membered heterocycloalkyl, and preferably, R^2 and R^3, at each occurrence, each independently represent hydrogen or C_{1-6} alkyl (e.g., methyl, ethyl or propyl); or R^2 and R^3 together with the carbon atom to which they are attached, form cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

R^4 and R^5, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{1-6} alkoxy; or R^4 and R^5 together with the carbon atom to which they are attached, form substituted or unsubstituted C_{3-8} cycloalkyl, or substituted or unsubstituted 3- to 10-membered heterocycloalkyl, and preferably, R^4 and R^5, at each occurrence, each independently represent hydrogen or C_{1-6} alkyl (e.g., methyl, ethyl or propyl); or

R^3 and R^4 are linked to each other, together with the carbon atoms to which they each are attached, form substituted or unsubstituted C_{3-8} cycloalkyl, or substituted or unsubstituted 3- to 10-membered heterocycloalkyl;

R^6 represents hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{1-6} alkoxy, preferably, R^6 represents hydrogen or C_{1-6} alkyl, and more preferably, R^6 represents hydrogen, methyl, ethyl or propyl;

each R^7, at each occurrence, independently represents hydrogen, halogen, -OH, -CN, $-NO_2$, $-NR^8R^9$, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} haloalkyl,

substituted or unsubstituted C_{1-6} alkylthio, substituted or unsubstituted C_{2-10} alkynyl, or substituted or unsubstituted C_{1-6} alkoxy, preferably, each R^7, at each occurrence, independently represents hydrogen, fluoro, chloro, bromo, methyl, ethyl, propyl, *t*-butyl or methoxy, and if there are multiple R^7groups, they each may be the same or different; or

R^6 and R^7 are linked to each other, together with the carbon atoms therebetween, form substituted or unsubstituted C_{3-8} carbocyclyl or 3- to 10-membered heterocyclyl;

n represents an integer of from 0 to 7, and preferably, n represents 0, 1, 2, 3 or 4;

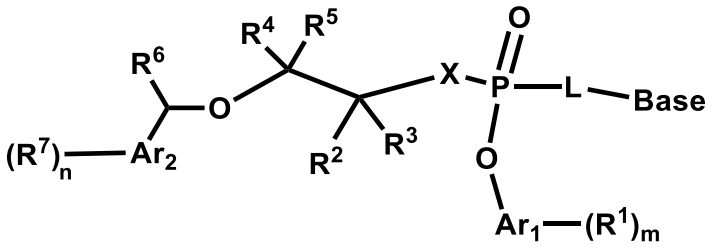
Ar_2 represents C_{6-14} aryl or 5- to 14-membered heteroaryl, and preferably, Ar_2 represents phenyl, 1-naphthyl, 2-naphthyl or 5- to 6-membered heteroaryl (e.g., thienyl, pyridyl or pyrazolyl);

r and s each independently represent 1, 2 or 3;

R^8 and R^9, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{3-8} cycloalkyl, if there are multiple R^8 and R^9 groups, they each may be the same or different, and preferably, R^8 represents hydrogen, C_{1-6} alkyl or C_{3-8} cycloalkyl, and R^9 represents hydrogen; and

R^{10} and R^{11}, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{3-8} cycloalkyl, or R^{10} and R^{11} together form C_{1-6} alkylene, and if there are multiple R^{10} and R^{11} groups, they each may be the same or different.

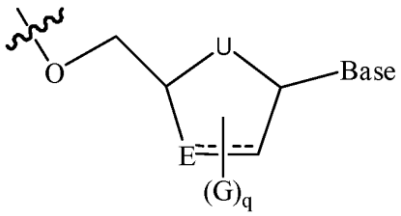
2. The compound of claim 1, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein the compound is a compound of Formula (Ia)

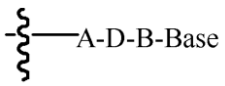


Formula (Ia)

wherein

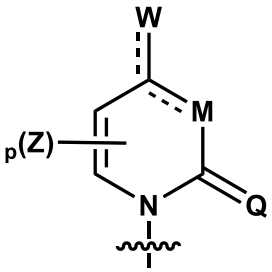
L-Base represents a group of Formula (f) or Formula (g):

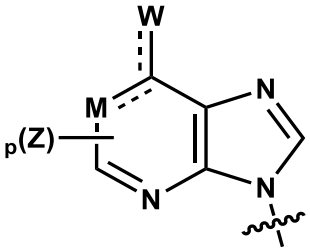




Formula (f) Formula (g) ;

Base represents a group of Formula (a) or Formula (b):





Formula (a) Formula (b) ;

wherein

------ represents a single bond or a double bond;

M represents N or NR^8;

W represents NR^8R^9 or O;

Q represents O or S;

each Z, at each occurrence, independently represents hydrogen, halogen, NR^8R^9, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, or substituted or unsubstituted C_{3-8} cycloalkyl, and if there are multiple Z groups, they each may be the same or different;

p represents an integer of from 0 to 2;

provided that when M is attached by a double bond, W is attached by a single bond, M represents N, and W represents NR^8R^9; and when M is attached by a single bond, W is attached by a double bond, M represents NR^8, and W represents O;

U represents O, S or $CR^{10}R^{11}$;

E represents CR^{10}, $CR^{10}R^{11}$ or S, provided that when E is attached by a double bond, it is CR^{10};

each G, at each occurrence, independently represents hydrogen, halogen, hydroxy, azido, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, or substituted or unsubstituted C_{3-8} cycloalkyl, and if there are multiple G groups, they each may be the same or different;

q represents an integer of from 0 to 4;

A represents substituted or unsubstituted C_{1-6} alkylene, and preferably, A represents C_{1-3} alkylene;

B represents substituted or unsubstituted C_{1-6} alkylene, and preferably, B represents C_{1-3} alkylene that is unsubstituted or substituted by C_{1-3} alkyl;

D represents O, S or NR^8, and preferably, D represents O;

Ar_1 represents C_{6-10} aryl;

each R^1, at each occurrence, independently represents hydrogen, halogen, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{1-6} alkoxy, substituted or unsubstituted C_{2-10} alkenyl group, or substituted or unsubstituted C_{2-10} alkynyl, and if there are multiple R^1 groups, they each may be the same or different;

m represents an integer of from 0 to 7;

X represents -NR^8-;

R^2 and R^3 each independently represent hydrogen, or substituted or unsubstituted C_{1-6} alkyl; or R^2 and R^3 together with the carbon atom to which they are attached, form substituted or unsubstituted C_{3-8} cycloalkyl, or substituted or unsubstituted C_{3-8} heterocycloalkyl;

R^4 and R^5 each independently represent hydrogen, or substituted or unsubstituted C_{1-6} alkyl; or R^4 and R^5 together with the carbon atom to which they are attached, form substituted or unsubstituted C_{3-8} cycloalkyl, or substituted or unsubstituted C_{3-8} heterocycloalkyl; or

R^3 and R^4 are linked to each other, together with the carbon atoms to which they each are attached, form substituted or unsubstituted C_{4-8} cycloalkyl, or substituted or unsubstituted C_{4-8} heterocycloalkyl;

R^6 represents hydrogen, substituted or unsubstituted C_{1-6} alkyl or substituted or unsubstituted C_{1-6} alkoxy;

each R^7, at each occurrence, independently represents hydrogen, halogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{1-6} alkoxy, and if there are multiple R^7 groups, they each may be the same or different; or

R^6 and R^7 are linked to each other, together with the carbon atoms therebetween, form substituted or unsubstituted C_{4-8} carbocyclyl or C_{4-8} heterocyclyl;

n represents an integer of from 0 to 7;

Ar_2 represents C_{6-10} aryl or C_{3-10} heteroaryl;

R^8 and R^9, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{3-8} cycloalkyl, and if there are multiple R^8 and R^9 groups, they each may be the same or different, and

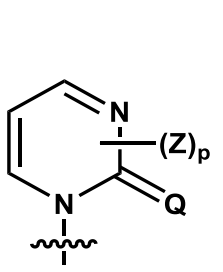
R^{10} and R^{11}, at each occurrence, each independently represent hydrogen, substituted or unsubstituted C_{1-6} alkyl, or substituted or unsubstituted C_{3-8} cycloalkyl, or R^{10} and R^{11} together form C_{1-6} alkylene, and if there are multiple R^{10} and R^{11} groups, they each may be the same or different.

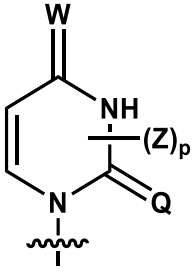
3. The compound of claim 1, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing,

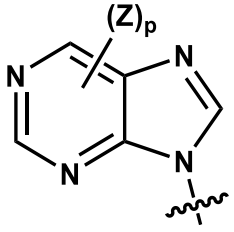
wherein

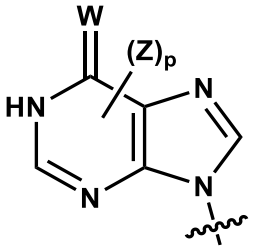
r and s are both 1;

Base is selected from the group consisting of:





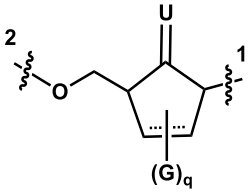


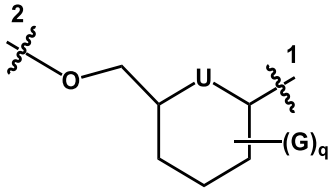
and


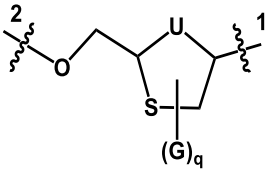
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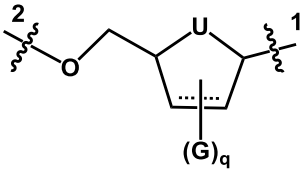
L is selected from the group consisting of C_{1-6} alkylene, C_{2-6} alkenylene and C_{2-6} alkynylene, which are optionally substituted by one or more G groups, and the alkylene, alkenylene or alkynylene is optionally interrupted by one or more -O-, -NR^8- or -S-; or

L is selected from the group consisting of:









wherein

---- represents a single bond or a double bond, position 1 is attached to the Base, and position 2 is attached to the phosphorus atom (P);

X is NR^8;

U, W and Q, at each occurrence, are each independently selected from the group consisting of CH_2, O, S and NR^8;

G and Z, at each occurrence, are each independently selected from the group consisting of halogen, -OH, -CN, $-NO_2$, $-NR^8R^9$, $-N_3$, C_{1-6} alkyl and C_{3-6} cycloalkyl;

p and q, at each occurrence, are each independently 0, 1, 2, 3, 4 or 5, provided that p is not greater than the number of substitutable positions on the corresponding group and q is not greater than the number of substitutable positions on the corresponding group; when p is greater than 1, each Z may be the same or different; and when q is greater than 1, each G may be the same or different;

Ar_1 is C_{6-14} aryl;

Ar_2 is selected from the group consisting of C_{6-14} aryl and 5- to 14-membered heteroaryl;

m and n are each independently selected from the group consisting of 1, 2, 3, 4 or 5, preferably 1 or 2;

R^1 and R^7 are each independently selected from the group consisting of hydrogen, halogen, -OH, -CN, $-NO_2$, $-NR^8R^9$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} alkylthio and C_{2-6} alkynyl;

R^8 and R^9, at each occurrence, each independently represent hydrogen, C_{1-6} alkyl and C_{3-6} cycloalkyl;

R^2 and R^3 are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{1-6} alkoxy, the alkyl andalkoxy are each optionally substituted by one or more substituents selected from the group consisting of halogen, -OH, -CN and $-NO_2$; or

R^2 and R^3 together with the carbon atom to which they are attached, form C_{3-6} cycloalkyl or 3- to 10-membered heterocycloalkyl;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{1-6} alkoxy, and the alkyl, and alkoxy are each optionally substituted by one or more substituents selected from the group consisting of halogen, -OH, -CN and $-NO_2$; or

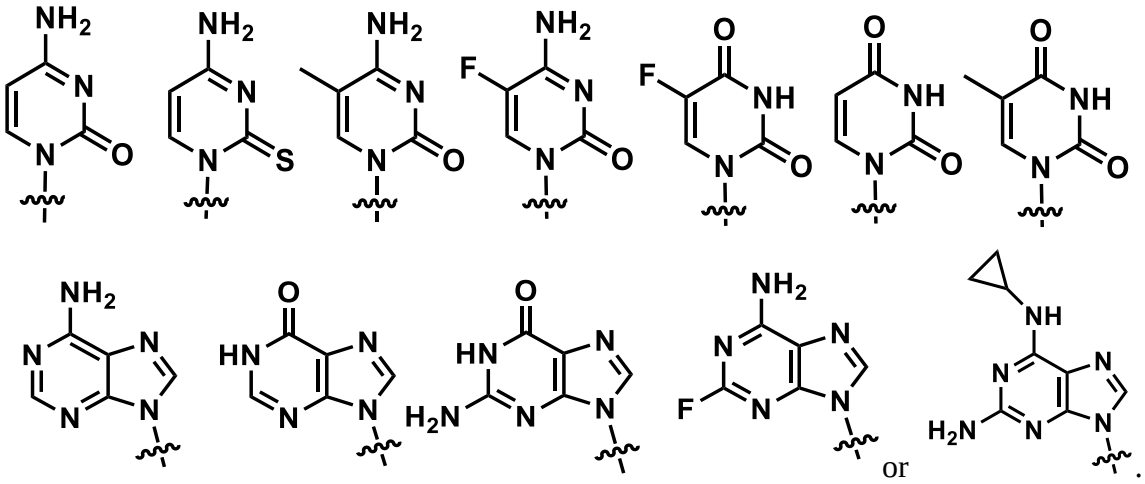
R^4 and R^5 together with the carbon atom to which they are attached, form C_{3-6} cycloalkyl or 3- to 10-membered heterocycloalkyl; or

R^3 and R^4 together with the carbon atoms to which they are attached, form C_{3-6} cycloalkyl or 3- to 10-membered heterocycloalkyl; and

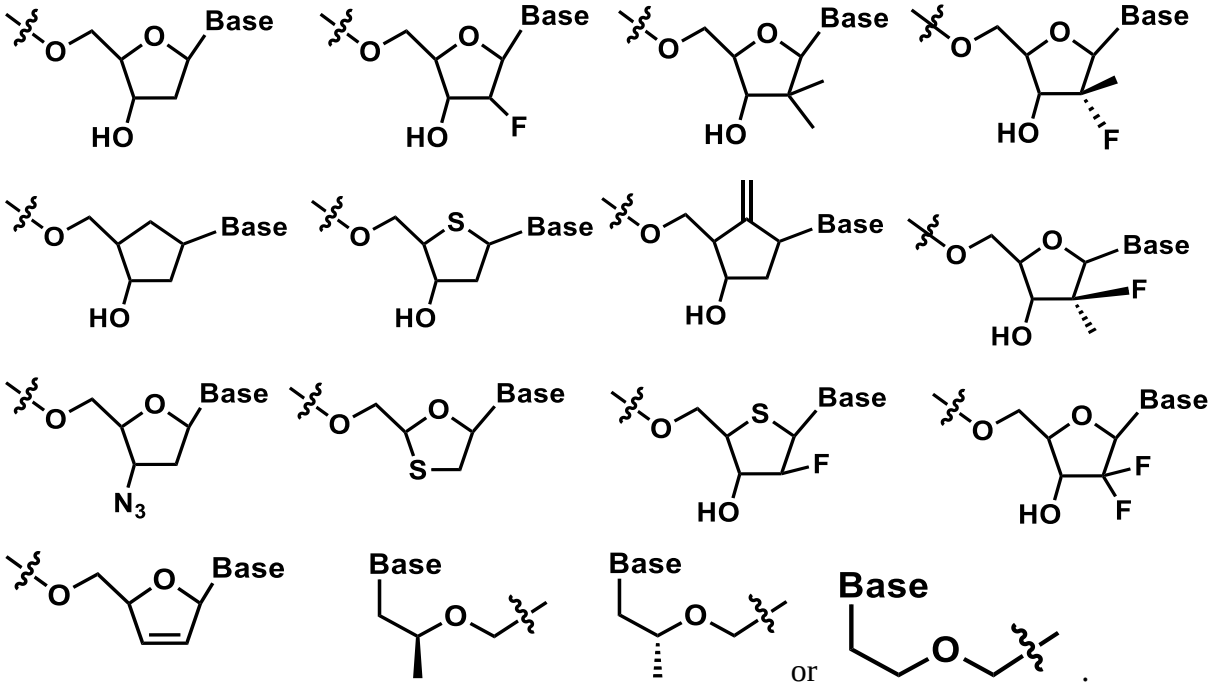
R^6 is selected from the group consisting of hydrogen, C_{1-6} alkyl and C_{1-6} alkoxy, the alkyl and alkoxy are each optionally substituted by one or more substituents selected from the group consisting of halogen, -OH, -CN and $-NO_2$; or

R^6 and R^7 together with the carbon atom to which they are attached, form C_{3-6} cycloalkyl or 3- to 10-membered heterocycloalkyl fused to Ar_2; and preferably, R^6 and R^7 together with the carbon atom to which they are attached, form C_{4-6} cycloalkyl or 4- to 10-membered heterocycloalkyl fused to Ar_2.

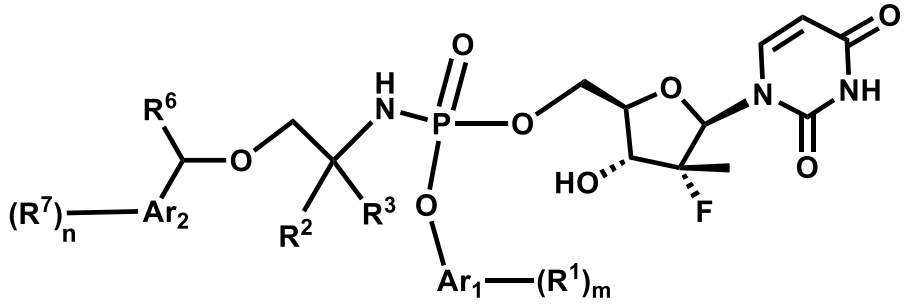
4. The compound of any one of claims 1 to 3, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein Base represents a group of the formula



5. The compound of any one of claims 1 to 4, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein L-Base represents a group of the formula

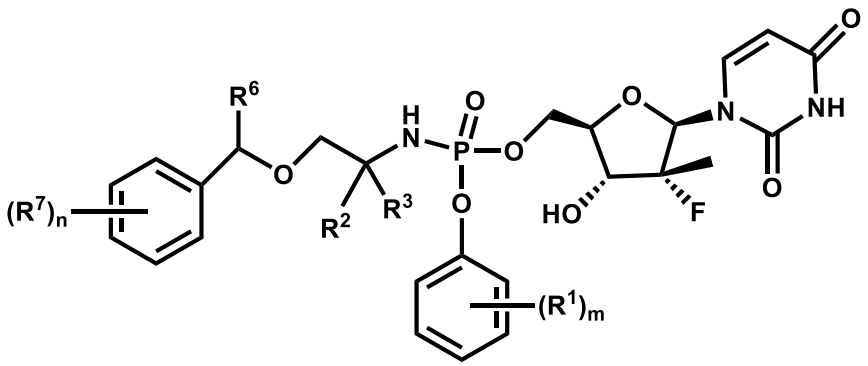


6. The compound of any one of claims 1 to 5, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein the compound is a compound of Formula (II)



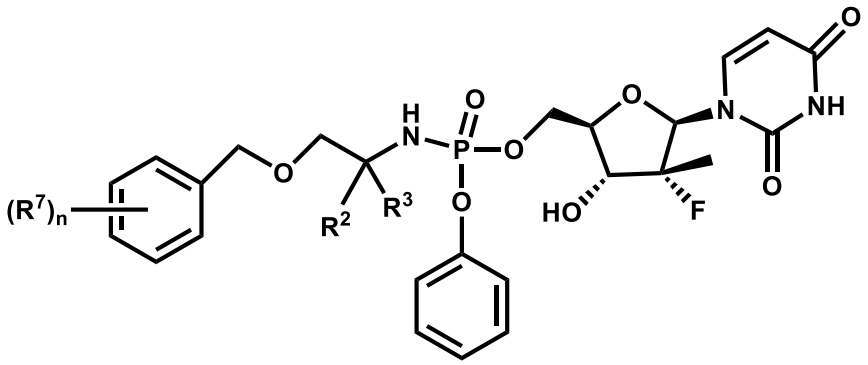
Formula (II)

wherein R^1, R^2, R^3, R^6, R^7, m, n, Ar_1 and Ar_2 are as defined in any one of claims 1 to 5; preferably, the compound is a compound of Formula (IIa)



Formula (IIa)

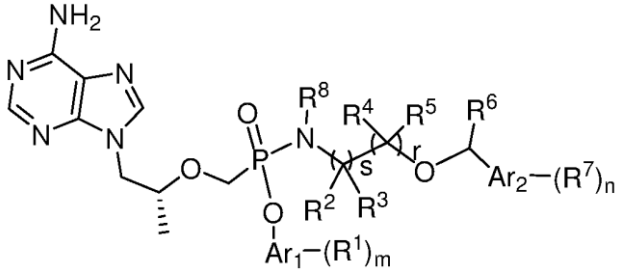
wherein R^1, R^2, R^3, R^6, R^7, m and n are as defined in any one of claims 1 to 5; and more preferably, the compound is a compound of Formula (IIb)



Formula (IIb)

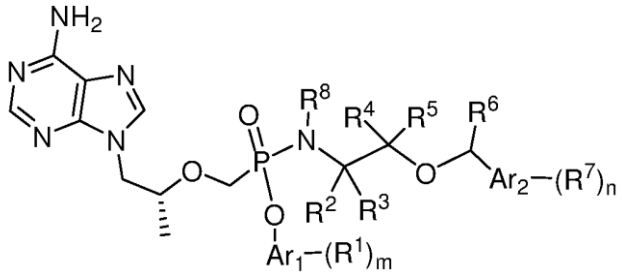
wherein R^2, R^3, R^7 and n are as defined in any one of claims 1 to 5.

7. The compound of claim 1, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein the compound is a compound of Formula (III)



Formula (III)

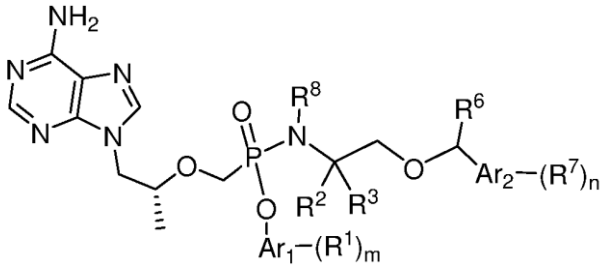
wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, m, n, s, r, Ar_1 and Ar_2 are as defined in claim 1; preferably, the compound is a compound of Formula (IIIa)



Formula (IIIa)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, m, n, Ar_1 and Ar_2 are as defined in claim 1;

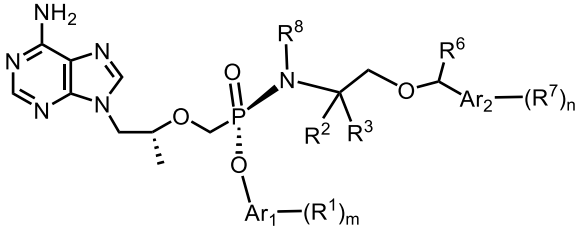
more preferably, the compound is a compound of Formula (IIIb)



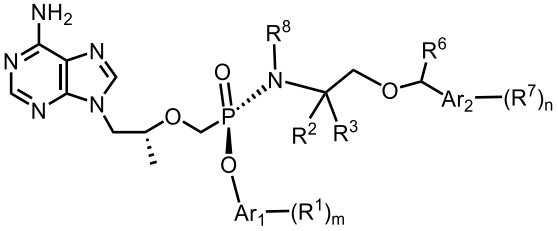
Formula (IIIb)

wherein R^1, R^2, R^3, R^6, R^7, R^8, m, n, Ar_1 and Ar_2 are as defined in claim 1; and

for example, the compound is a compound of Formula (IIIc-1) or Formula (IIIc-2),



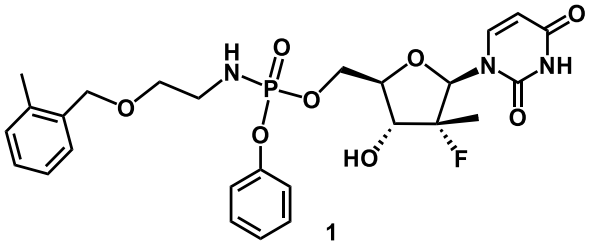
Formula (IIIc-1)



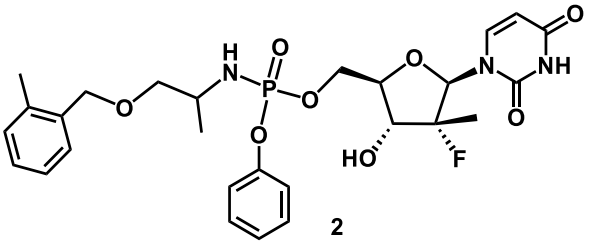
Formula (IIIc-2)

wherein R^1, R^2, R^3, R^6, R^7, R^8, m, n, Ar_1 and Ar_2 are as defined in claim 1.

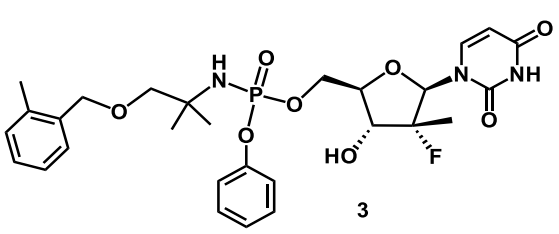
8. The compound of any one of claims 1 to 7, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein the compound is



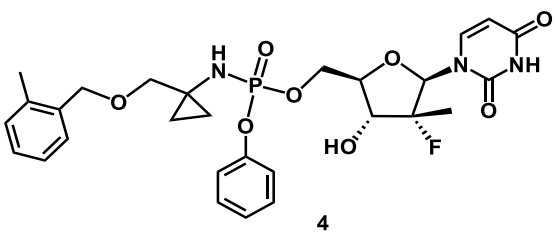
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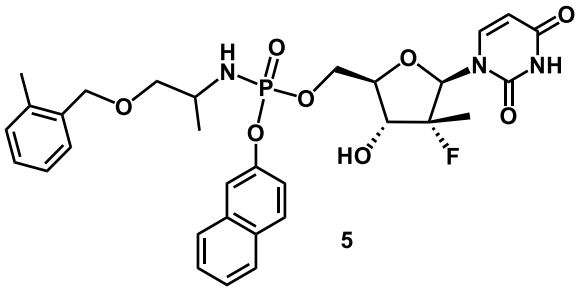
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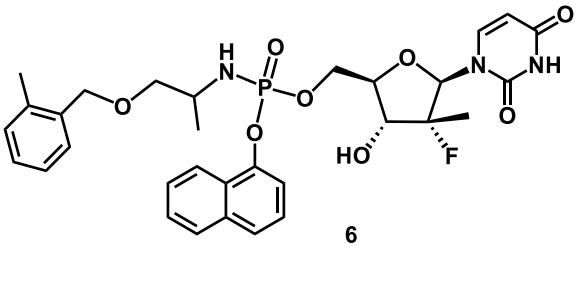
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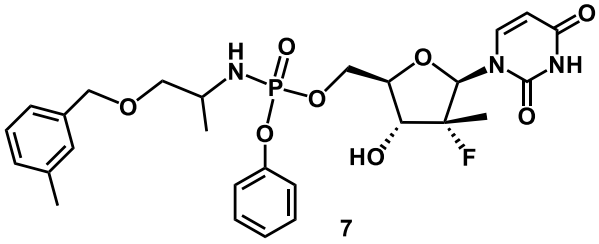
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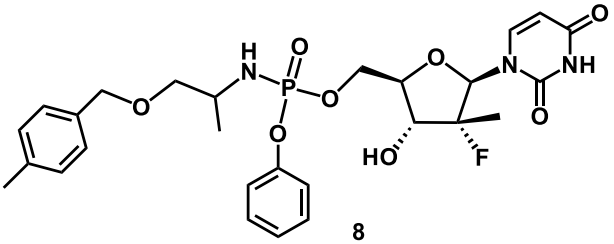
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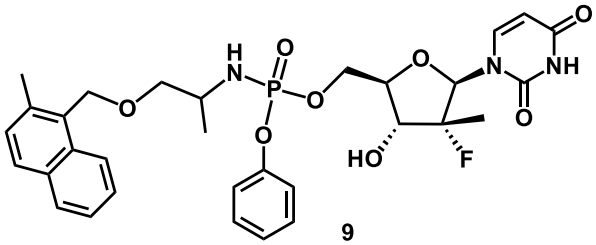
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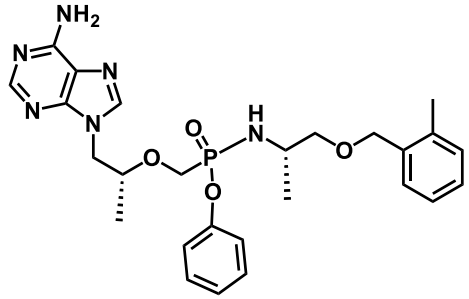
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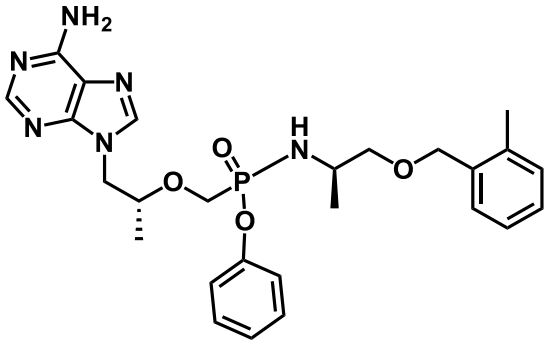
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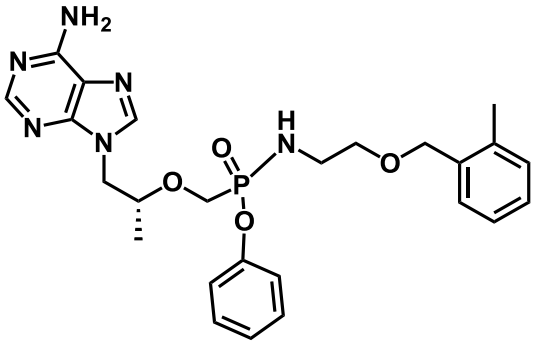
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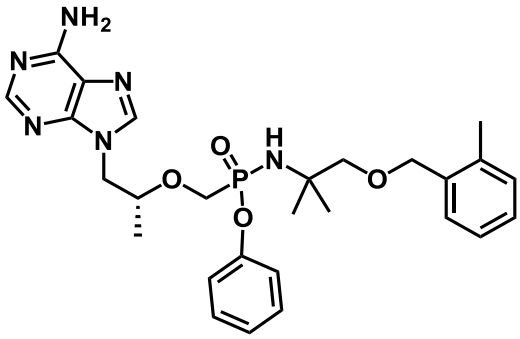
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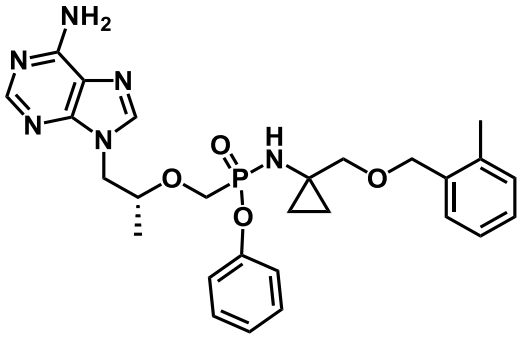
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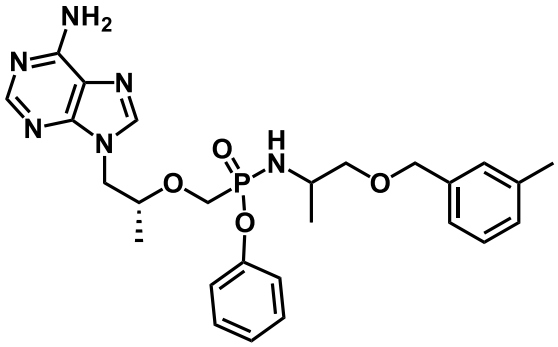
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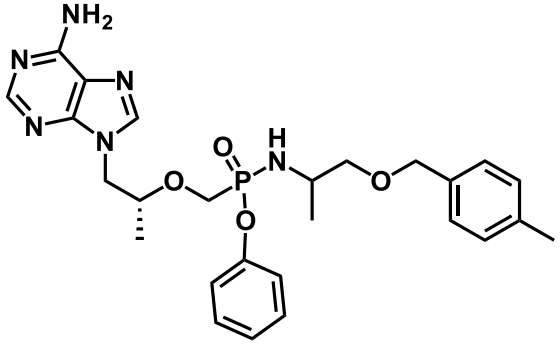
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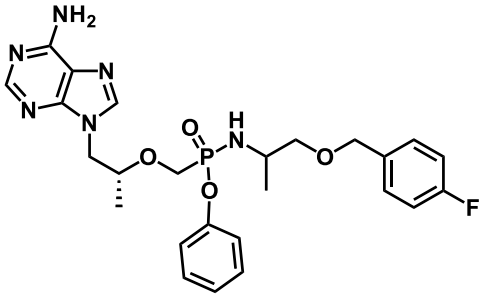
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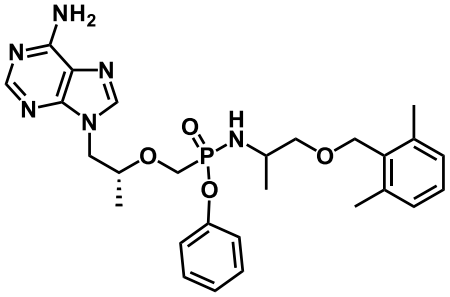
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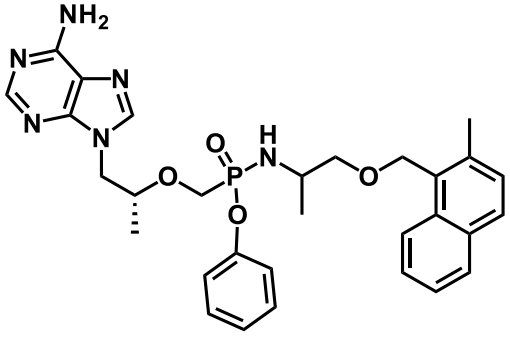
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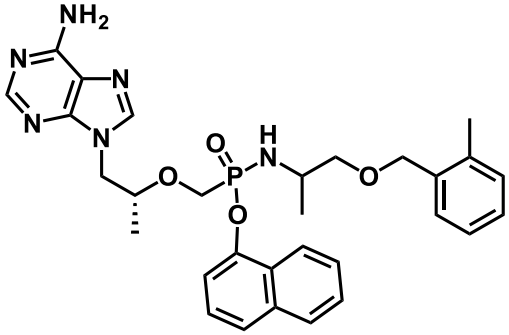
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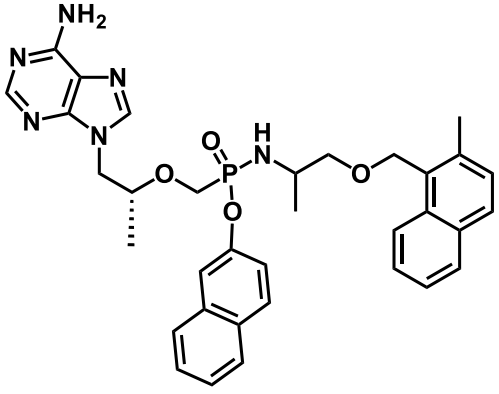
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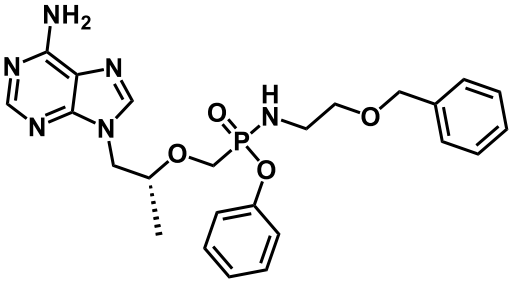
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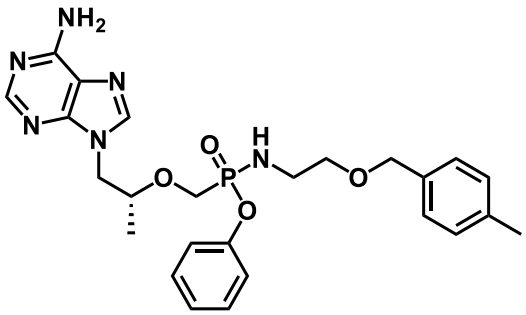
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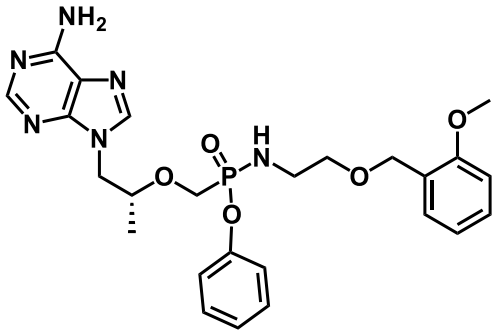
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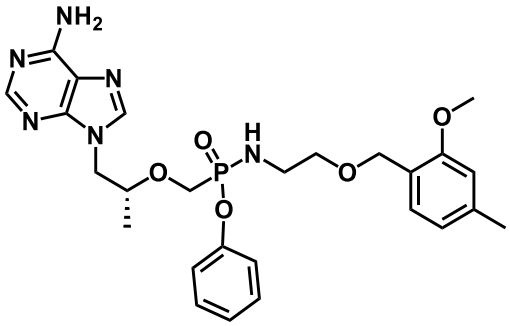
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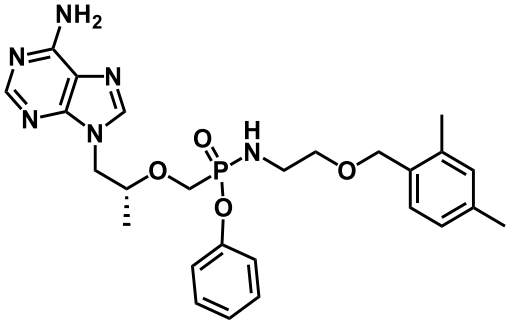
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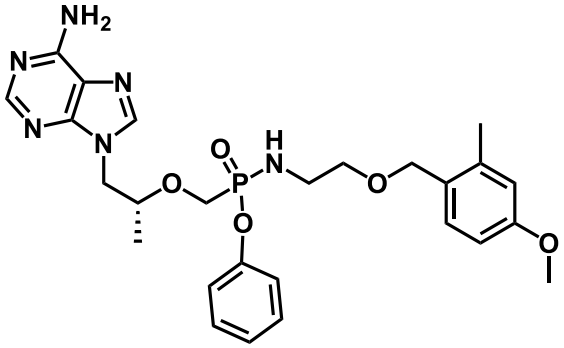
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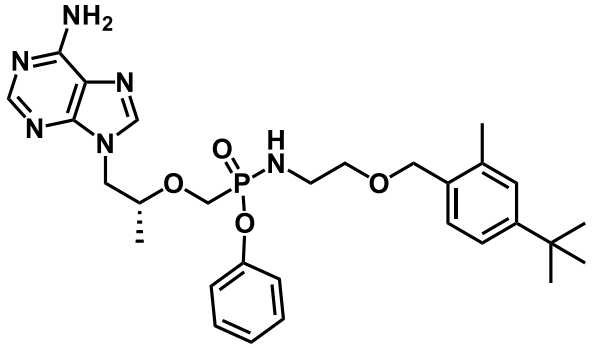
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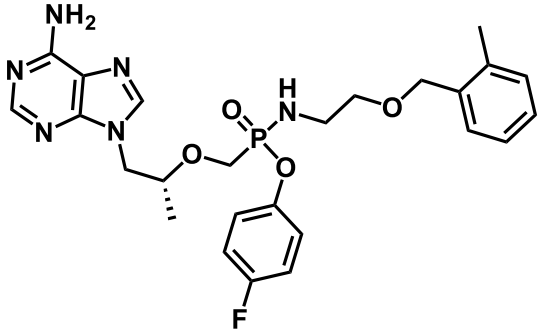
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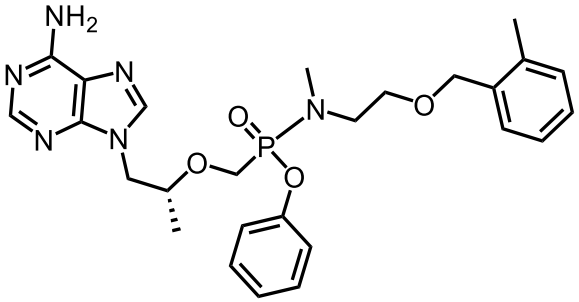
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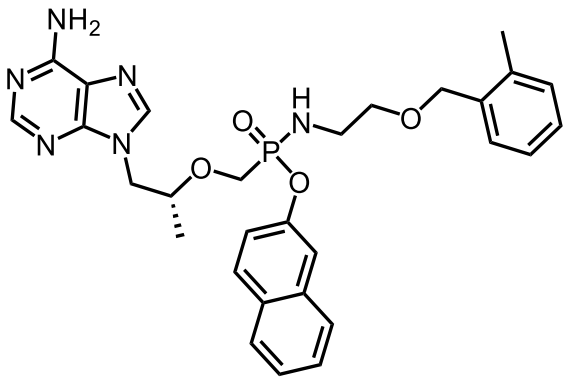
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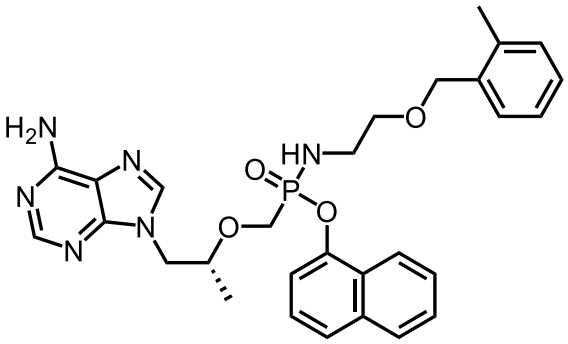
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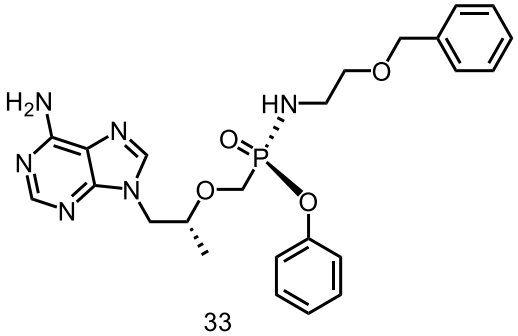
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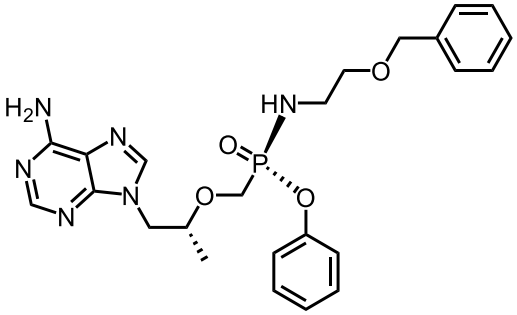
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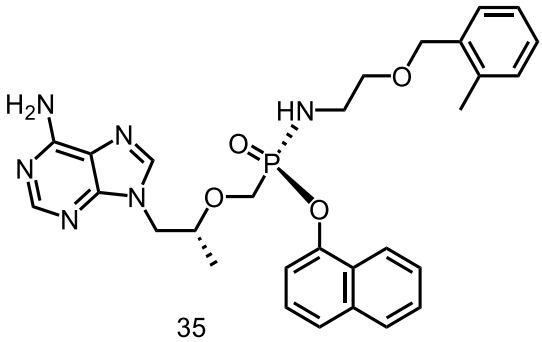
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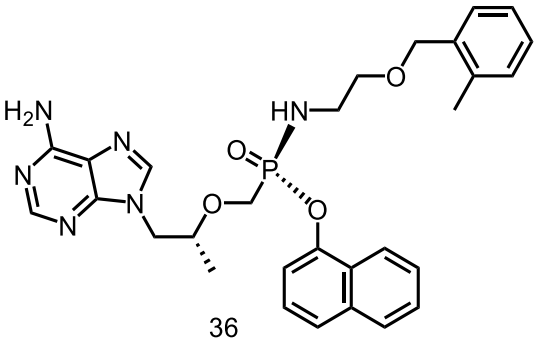
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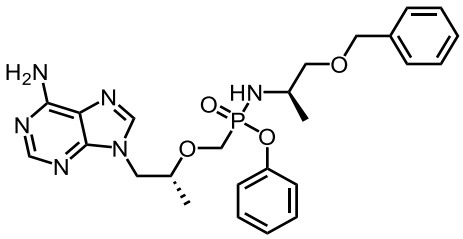
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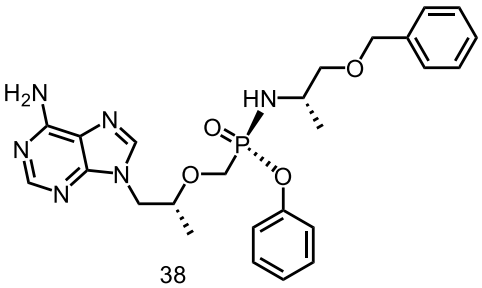
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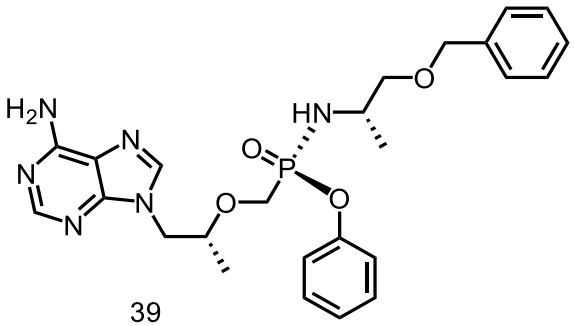
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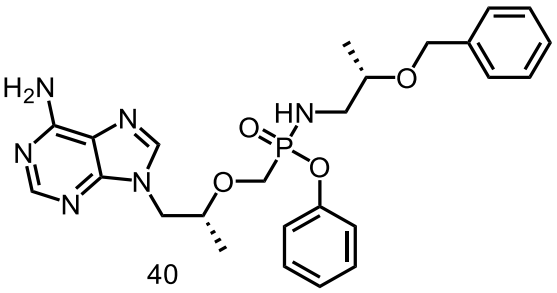
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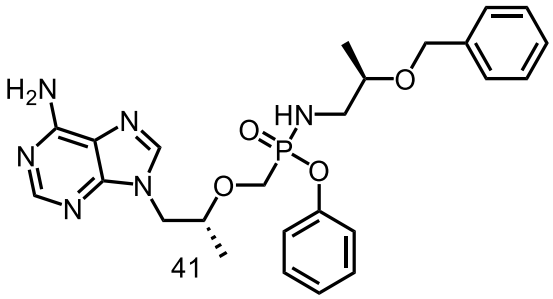
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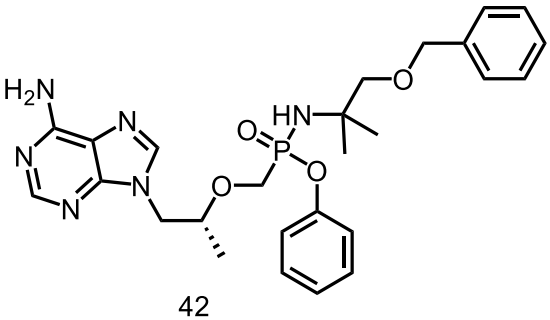
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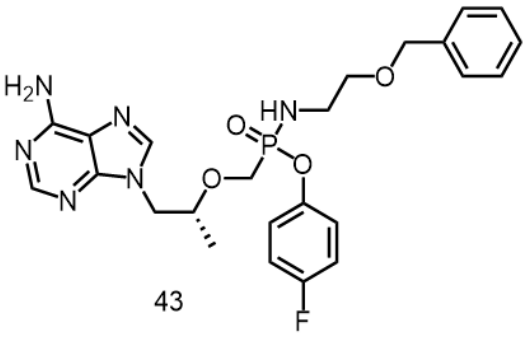
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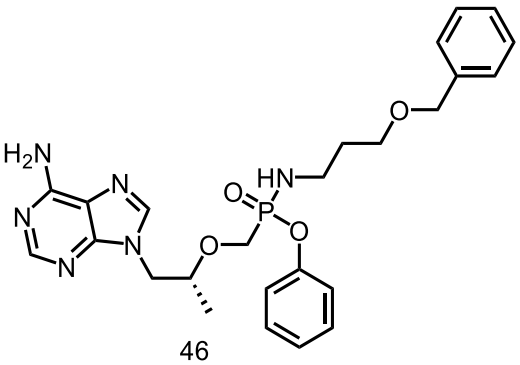
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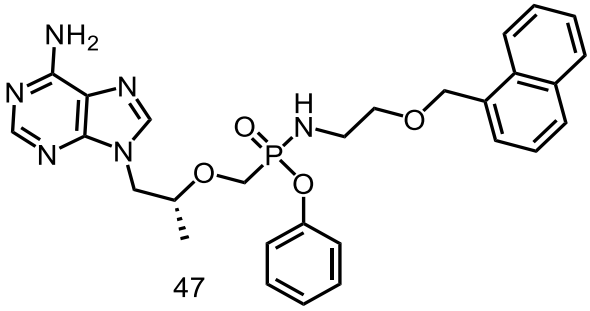
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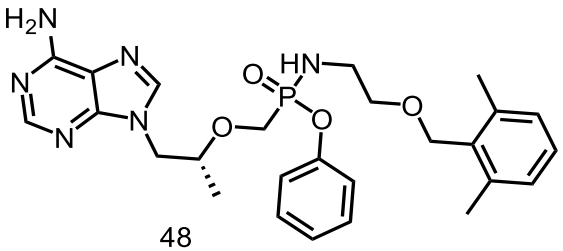
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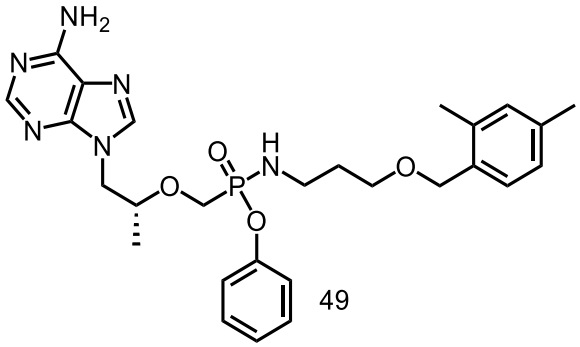
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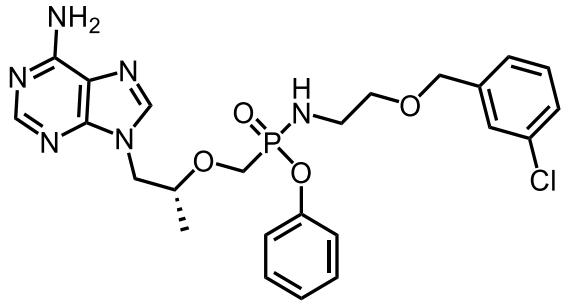
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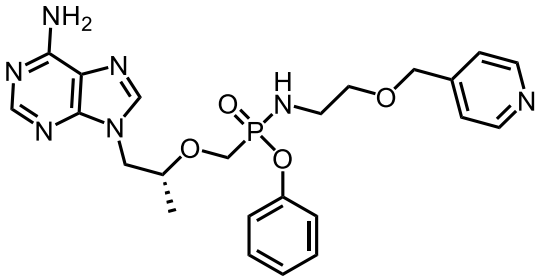
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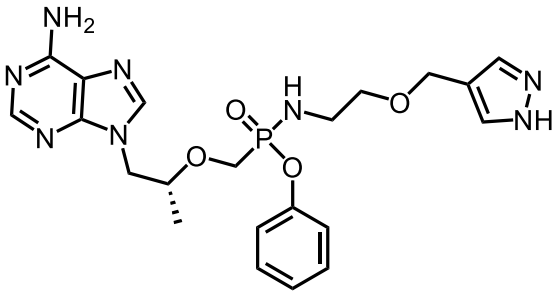
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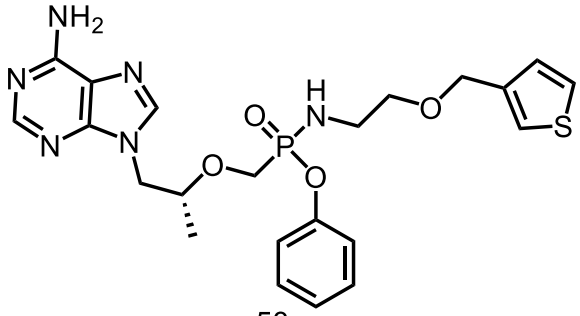


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or



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9. A pharmaceutical composition comprising the compound of any one of claims 1 to 8, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, preferably further comprising a pharmaceutically acceptable adjuvant, and more preferably further comprising additional active ingredient(s) that can be co-administered with the compound of any one of claims 1 to 8, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomers thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, wherein the additional active ingredient(s) is(are) preferably selected from the group consisting of interferons, ribavirin or analogues thereof, HCV NS3 protease inhibitors, α-glucosidase 1 inhibitors, hepatoprotective agents, non-nucleoside inhibitors of HCV NS5B polymerase, HCV NS5A inhibitors, TLR-7 agonists, cyclophilin inhibitors, HCV IRES inhibitors, pharmacokinetic enhancers, and other drugs or therapeutic agents for the treatment of HCV, or a combination thereof, and the pharmaceutical composition is in the form of a solid formulation, a semisolid formulation, or a liquid formulation.

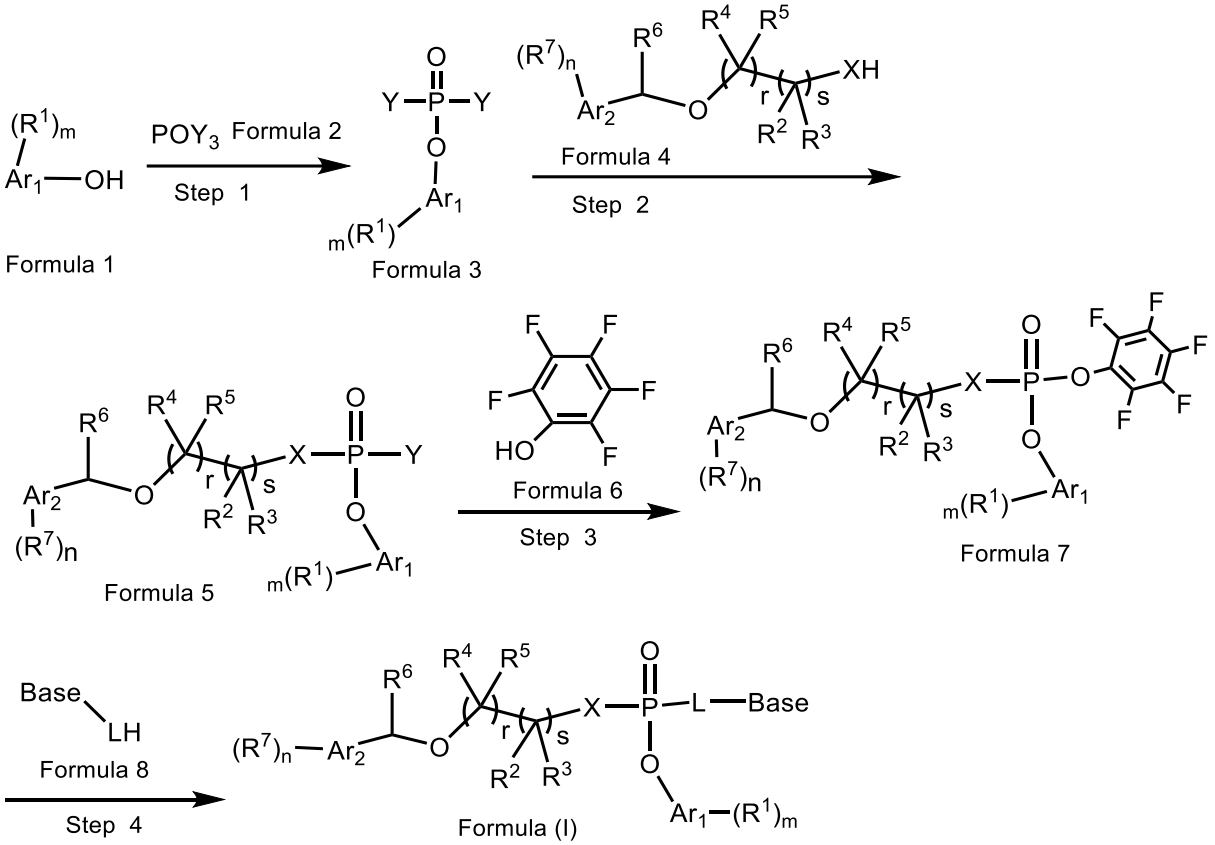
10. The composition of claim 9, wherein the composition comprises the compound of any one of claims 1 to 8, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the

foregoing in an amount of 0.01-1000 mg, suitably 0.5-800 mg, preferably 1-400 mg, more preferably 5-200 mg, particularly preferably 10-100 mg, and most preferably 15-50 mg.

11. Use of the compound of any one of claims 1 to 8, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, or the pharmaceutical composition of claim 9 or 10 in the manufacture of a medicament for the prevention or treatment of viral hepatitis type B.

12. A method for preparing the compound of any one of claims 1 to 8, a pharmaceutically acceptable salt, ester, solvate, R or S enantiomer, or diastereomer thereof, any crystalline form or racemate of the foregoing, or a mixture of the foregoing, comprising the following steps:

Scheme 1



Step 1: reacting a phosphorus oxyhalide of Formula 2 with a compound of Formula 1 to obtain a compound of Formula 3;

Step 2: reacting the compound of Formula 3 with a compound of Formula 4 to obtain a compound of Formula 5;

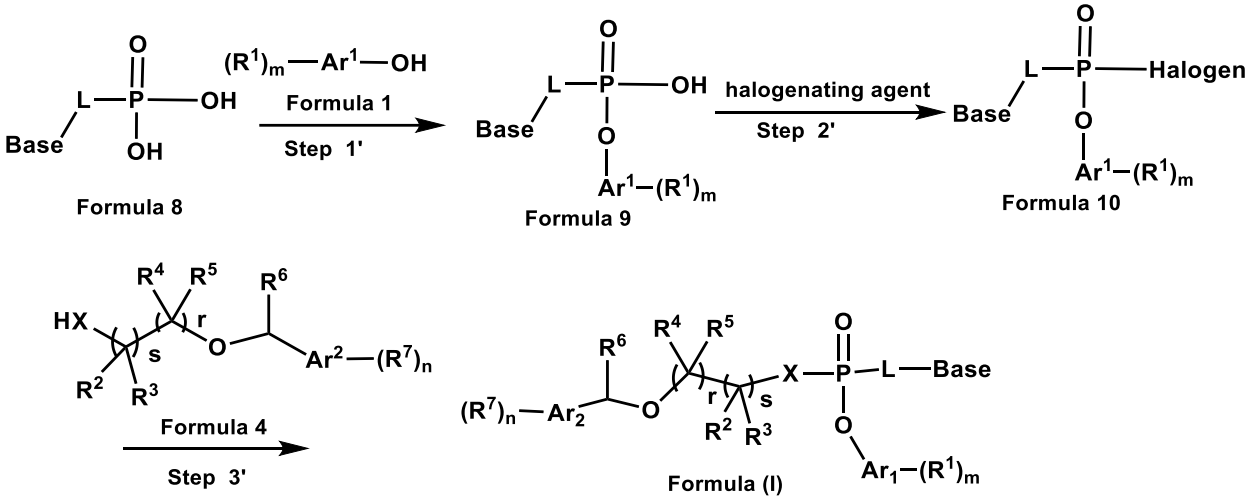
Step 3: reacting the compound of Formula 5 with pentafluorophenol of Formula 6 to obtain a compound of Formula 7; and

Step 4: reacting the compound of Formula 7 with a compound of Formula 8 to obtain a compound of Formula (I);

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, m, n, s, r, X, Ar_1, Ar_2, L and Base are as defined in any one of claims 1 to 5; and each Y is the same or different, and is each independently selected from halogen;

or

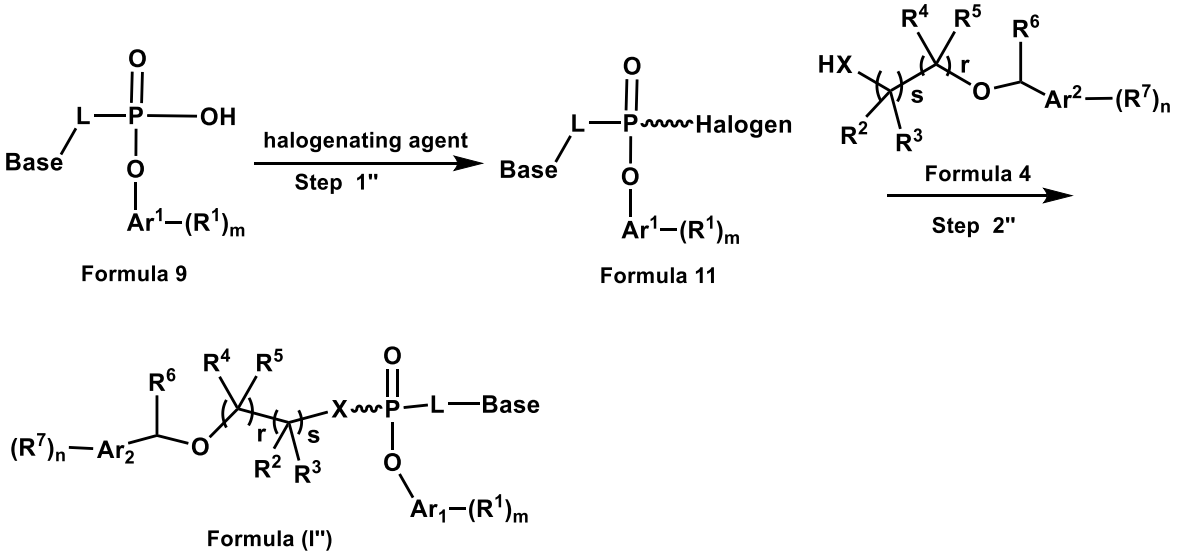
Scheme 2



wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, m, n, s, r, X, Ar_1, Ar_2, L and Base are as defined in any one of claims 1 to 5;

or

Scheme 3



wherein

represents either a solid wedge ( ) or dashed wedge ( ) chemical bond; and

R^1, R^2, R^3, R^4, R^5, R^6, R^7, m, n, s, r, X, Ar_1, Ar_2, L and Base are as defined in any one of claims 1 to 5.