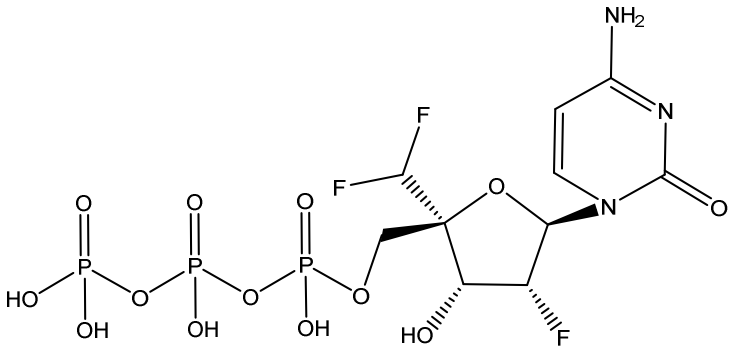
Base is uracil, cytosine, guanine, adenine, thymine, or heterocycloalkyl, each of which may optionally be substituted with one or more hydroxy, C_{1-7}-alkyl, C_{1-7}-alkoxy, halo, nitro or cyano, wherein said heterocycloalkyl is an optionally substituted saturated monocyclic, bicyclic or tricyclic heterocyclic system;

with the proviso that if R^w is H, R^y is H, and R^z is H, then R^x is not H;

and

with the proviso that Formula I is not ((2R,3R,4R,5R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-2-(difluoromethyl)-4-fluoro-3-hydroxytetrahydrofuran-2-yl)methyl tetrahydrogen triphosphate;



or a pharmacologically acceptable salt thereof.

[0006b] The application provides, in another aspect, a compound selected from the list consisting of:

4'-Difluoromethyluridine;

4'-Difluoromethyluridine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl phosphoramidate;

4'-Difluoromethyluridine-5'-(*O*-phenyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiophosphoramidate;

4'-Difluoromethyluridine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl phosphoramidate;

4'-Difluoromethyluridine-5'-(*O*-1-naphthyl-*N*-(S)-1-(isopropoxycarbonyl)ethyl thiophosphoramidate;

3’-Deoxy-3’,3’-difluoro-4’-difluoromethyl-5’-*O*-(2-oxido-4-H-1,3,2-benzodioxaphosphorin-2-yl)-guanosine;

3’-Deoxy-3’,3’-difluoro-4’-difluoromethyl-5’-*O*-(2-sulfide-4-H-1,3,2-benzodioxaphosphorin-2-yl)-guanosine;

3’-Deoxy-3’,3’-difluoro -4’-difluoromethyl-5’-*O*-[bis(4-methoxyphenoxy)phosphinyl] guanosine; and

3’-Deoxy-3’,3’-difluoro -4’-difluoromethyl-5’-*O*-[bis(4-methoxyphenoxy)thiophosphinyl] guanosine.

[0007] The application provides the compounds of Formula I which are useful for the treatment of diseases mediated by Influenza, pharmaceutical compositions comprising such compounds of Formula I, or result in the formation of such compounds of Formula I in vivo during said treatment.

[0007a] The application provides, in another aspect, a compound as defined herein for use as a therapeutically active substance.

[0007b] The application provides, in another aspect, a pharmaceutical composition comprising a compound as defined herein and a therapeutically inert carrier.

[0007c] The application provides, in another aspect, a compound according to Formula I as described herein for use in the treatment or prophylaxis of Influenza infection.

[0007d] The application provides, in another aspect, a compound according to Formula I as described herein for use in the treatment or prophylaxis of Influenza infection.

[0007e] The application provides, in another aspect, a pharmaceutical composition as defined herein for use in the treatment or prophylaxis of Influenza infection.

[0008] The application provides a method for treating an Influenza infection comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Formula I or a compound resulting in the formation of a compound of Formula I in vivo.

[0009] The application provides a composition comprising a compound of Formula I and a pharmaceutically acceptable excipient.

each R^3 is independently H, C_{1-7}-alkyl, halo-C_{1-7}-alkyl, phenyl or phenyl C_{1-7}-alkyl, wherein phenyl and phenyl C_{1-7}-alkyl are optionally substituted with C_{1-7}-alkoxy;

or R^3 and $R^{1''}$ together form CH_2;

each R^4 is independently H, C_{1-7}-alkyl;

or R^{2b} and R^4 together form $(CH_2)_3$;

R^w, R^y, and R^z are each independently H, OH or F;

R^x is H, OH, or F;

or R^3 and R^x together form a bond;

or R^1 and R^x together form a bond;

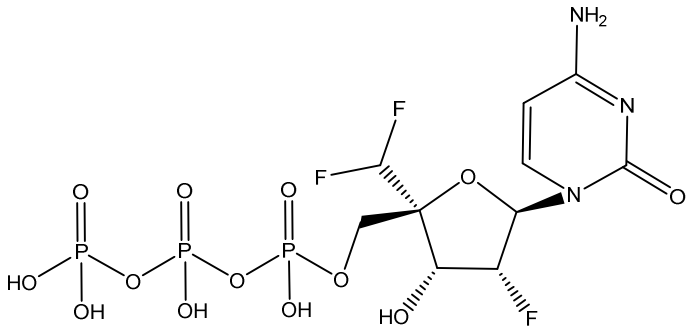
X is O or S;

Base is uracil, cytosine, guanine, adenine, thymine, or heterocycloalkyl, each of which may optionally be substituted with one or more hydroxy, C_{1-7}-alkyl, C_{1-7}-alkoxy, halo, nitro or cyano, wherein said heterocycloalkyl is an optionally substituted saturated monocyclic, bicyclic or tricyclic heterocyclic system;

with the proviso that if R^w is H, R^y is H, and R^z is H, then R^x is not H;

and

with the proviso that Formula I is not ((2R,3R,4R,5R)-5-(4-amino-2-oxopyrimidin-1(2H)-yl)-2-(difluoromethyl)-4-fluoro-3-hydroxytetrahydrofuran-2-yl)methyl tetrahydrogen triphosphate;



or a pharmacologically acceptable salt thereof.

2. The compound of claim 1, wherein R^W is H, R^y is H, R^x is OH, and R^z is OH.

3. The compound of claim 1, wherein R^W is F, R^y is H, R^x is F, and R^z is OH.

4. The compound of claim 1, wherein R^W is OH, R^y is H, R^x is H, and R^z is OH.

5. The compound of claim 1, wherein R^W is F, R^y is H, R^x is H, and R^z is OH.

6. The compound of claim 1, wherein R^W is H, R^y is H, R^x is F, and R^z is OH.

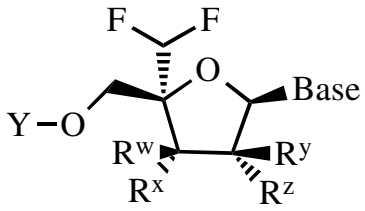
7. The compound of claim 1, wherein R^W is H, R^y is OH, R^x is OH, and R^z is H.

8. The compound of claim 1, wherein R^W is H, R^y is F, R^x is OH, and R^z is F.

26. The pharmaceutical composition of claim 25, in combination with one or more antiviral compounds.

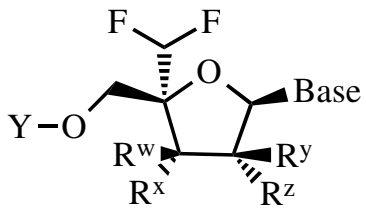
27. The pharmaceutical composition of claim 26, wherein the one or more antiviral compounds comprises one or more anti-Influenza compounds.

28. A compound according to any one of claims 1 to 23 for use in the treatment or prophylaxis of Influenza infection



I .

29. A compound according to any one of claims 1 to 23, for use in the treatment or prophylaxis of Influenza infection



I

30. A pharmaceutical composition according to any one of claims 25 to 27 for use in the treatment or prophylaxis of Influenza infection.