METHODS AND COMPOSITIONS FOR TREATING FLAVIVIRUSES AND PESTIVIRUSES

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FIELD OF THE INVENTION

This invention is in the area of pharmaceutical chemistry, and in particular, is a compound, method and composition for the treatment of flaviviruses and pestiviruses. This application claims priority to U.S. provisional application no. 60/207,674, filed on May 26, 2000 and U.S. provisional application no. 60/283,276, filed on April 11, 2001.

BACKGROUND OF THE INVENTION

Pestiviruses and flaviviruses belong to the *Flaviviridae* family of viruses along with hepatitis C virus. The pestivirus genus includes bovine viral diarrhea virus (BVDV), classical swine fever virus (CSFV, also called hog cholera virus) and border disease virus (BDV) of sheep (Moennig, V. et al. *Adv. Vir. Res.* **1992**, *41*, 53-98). Pestivirus infections of domesticated livestock (cattle, pigs and sheep) cause significant economic losses worldwide. BVDV causes mucosal disease in cattle and is of significant economic importance to the livestock industry (Meyers, G. and Thiel, H.-J., *Advances in Virus Research,* **1996**, *47*, 53-118; Moennig V., et al, *Adv. Vir. Res.* **1992**, *41*, 53-98).

Human pestiviruses have not been as extensively characterized as the animal pestiviruses. However, serological surveys indicate considerable pestivirus exposure in humans. Pestivirus infections in man have been implicated in several diseases including congenital brain injury, infantile gastroenteritis and chronic diarrhea in human immunodeficiency virus (HIV) positive patients. M. Giangaspero et al., *Arch. Virol. Suppl.*, **1993**, *7*, 53-62; M. Giangaspero et al., *Int. J. Std. Aids*, **1993**, *4* (5): 300-302.

The flavivirus genus includes more than 68 members separated into groups on the basis of serological relatedness (Calisher et al., *J. Gen. Virol*, **1993**, *70*, 37-43). Clinical symptoms vary and include fever, encephalitis and hemorrhagic fever. *Fields Virology*, Editors: Fields, B. N., Knipe, D. M., and Howley, P. M., Lippincott-Raven Publishers, Philadelphia, PA, **1996**, Chapter 31, 931-959. Flaviviruses of global concern that are associated with human disease include the dengue hemorrhagic fever viruses (DHF), yellow fever virus, shock syndrome and Japanese encephalitis virus. Halstead, S. B., *Rev. Infect.*

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Dis., **1984**, *6*, 251-264; Halstead, S. B., *Science*, 239:476-481, 1988; Monath, T. P., *New Eng. J. Med.*, **1988**, *319*, 641-643.

Examples of antiviral agents that have been identified as active against the flavivirus or pestiviruses include:

(1) interferon and ribavirin (Battaglia, A.M. *et al.*, *Ann. Pharmacother*, **2000**,. *34*, 487-494); Berenguer, M. *et al. Antivir. Ther.*, **1998**, *3* (Suppl. 3), 125-136);

(2) Substrate-based NS3 protease inhibitors (Attwood *et al.*, *Antiviral peptide derivatives*, PCT WO 98/22496, **1998**; Attwood *et al.*, *Antiviral Chemistry and Chemotherapy* **1999**, *10*, 259-273; Attwood *et al., Preparation and use of amino acid derivatives as anti-viral agents,* German Patent Pub. DE 19914474; Tung *et al. Inhibitors of serine proteases, particularly hepatitis C virus NS3 protease*, PCT WO 98/17679), including alphaketoamides and hydrazinoureas, and inhibitors that terminate in an electrophile such as a boronic acid or phosphonate (Llinas-Brunet et al, *Hepatitis C inhibitor peptide analogues,* PCT WO 99/07734).

(3) Non-substrate-based inhibitors such as 2,4,6-trihydroxy-3-nitro-benzamide derivatives (Sudo K. *et al.*, *Biochemical and Biophysical Research Communications*, **1997**, *238*, 643-647; Sudo K. *et al. Antiviral Chemistry and Chemotherapy*, **1998**, *9*, 186), including RD3-4082 and RD3-4078, the former substituted on the amide with a 14 carbon chain and the latter processing a *para*-phenoxyphenyl group;

(4) Thiazolidine derivatives which show relevant inhibition in a reverse-phase HPLC assay with an NS3/4A fusion protein and NS5A/5B substrate (Sudo K. *et al.*, *Antiviral Research*, **1996**, *32*, 9-18), especially compound RD-1-6250, possessing a fused cinnamoyl moiety substituted with a long alkyl chain, RD4 6205 and RD4 6193;

(5) Thiazolidines and benzanilides identified in Kakiuchi N. *et al. J. EBS Letters 421*, 217-220; Takeshita N. *et al. Analytical Biochemistry*, **1997**, *247*, 242-246;

(6) A phenan-threnequinone possessing activity against protease in a SDS-PAGE and autoradiography assay isolated from the fermentation culture broth of *Streptomyces* sp., Sch 68631 (Chu M. *et al., Tetrahedron Letters*, **1996**, *37*, 7229-7232), and Sch 351633, isolated from the fungus *Penicillium griscofuluum,* which demonstrates

activity in a scintillation proximity assay (Chu M. *et al., Bioorganic and Medicinal Chemistry Letters 9*, 1949-1952);

(7) Selective NS3 inhibitors based on the macromolecule elgin c, isolated from leech (Qasim M.A. *et al., Biochemistry*, **1997**, *36*, 1598-1607);

(8) Helicase inhibitors (Diana G.D. *et al., Compounds, compositions and methods for treatment of hepatitis C*, U.S. Pat. No. 5,633,358; Diana G.D. *et al., Piperidine derivatives, pharmaceutical compositions thereof and their use in the treatment of hepatitis C*, PCT WO 97/36554);

(9) Polymerase inhibitors such as nucleotide analogues, gliotoxin (Ferrari R. *et al. Journal of Virology*, **1999**, *73*, 1649-1654), and the natural product cerulenin (Lohmann V. *et al., Virology*, **1998**, *249*, 108-118);

(10) Antisense phosphorothioate oligodeoxynucleotides (S-ODN) complementary to sequence stretches in the 5' non-coding region (NCR) of the virus (Alt M. *et al., Hepatology*, **1995**, *22*, 707-717), or nucleotides 326-348 comprising the 3' end of the NCR and nucleotides 371-388 located in the core coding region of the HCV RNA (Alt M. *et al., Archives of Virology*, **1997**, *142*, 589-599; Galderisi U. *et al., Journal of Cellular Physiology*, **1999**, *181*, 251-257);

(11) Inhibitors of IRES-dependent translation (Ikeda N *et al., Agent for the prevention and treatment of hepatitis C*, Japanese Patent Pub. JP-08268890; Kai Y. *et al. Prevention and treatment of viral diseases*, Japanese Patent Pub. JP-10101591);

(12) Nuclease-resistant ribozymes (Maccjak, D. J. *et al., Hepatology* **1999**, *30*, abstract 995); and

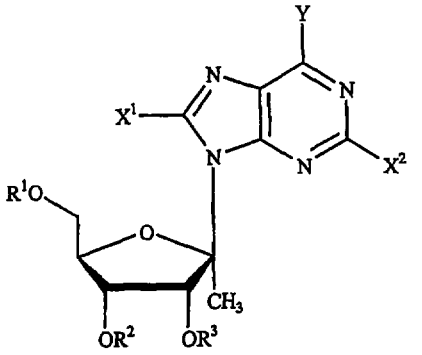
(13) Other miscellaneous compounds including 1-amino-alkylcyclohexanes (U.S. Patent No. 6,034,134 to Gold *et al.*), alkyl lipids (U.S. Pat. No. 5,922,757 to Chojkier *et al.*), vitamin E and other antioxidants (U.S. Pat. No. 5,922,757 to Chojkier *et al.*), squalene, amantadine, bile acids (U.S. Pat. No. 5,846,964 to Ozeki *et al.*), N-(phosphonoacetyl)-L-aspartic acid, (U.S. Pat. No. 5,830,905 to Diana *et al.*), benzenedicarboxamides (U.S. Pat. No. 5,633,388 to Diana *et al.*), polyadenylic acid derivatives (U.S. Pat. No. 5,496,546 to Wang *et al.*), 2',3'-dideoxyinosine (U.S. Pat. No. 5,026,687 to Yarchoan *et al.*), and benzimidazoles (U.S. Pat. No. 5,891,874 to Colacino *et al.*).

In view of the severity of diseases associated with pestiviruses and flaviviruses, and their pervasiveness in animal and man, it is an object of the present invention to provide a compound, method and composition for the treatment of a host infected with flavivirus or pestivirus.

SUMMARY OF THE INVENTION

Compounds, methods and compositions for the treatment of a host infected with a flavivirus or pestivirus infection are described that includes an effective treatment amount of a β-D- or β-L-nucleoside of the Formulas (I) - (XVIII), or a pharmaceutically acceptable salt or prodrug thereof.

In a first principal embodiment, a compound of Formula I, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(I)

wherein:

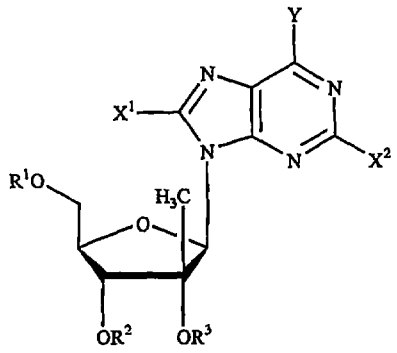
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a second principal embodiment, a compound of Formula II, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(II)

wherein:

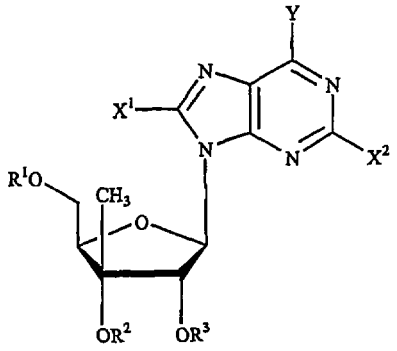
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a third principal embodiment, a compound of Formula III, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(III)

wherein:

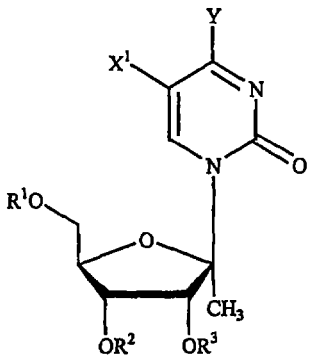
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a fourth principal embodiment, a compound of Formula IV, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(IV)

wherein:

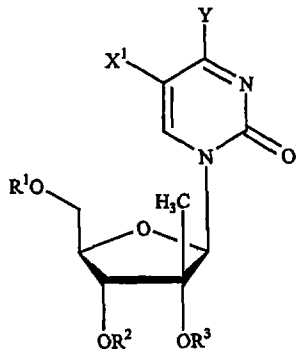
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a fifth principal embodiment, a compound of Formula V, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(V)

wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving

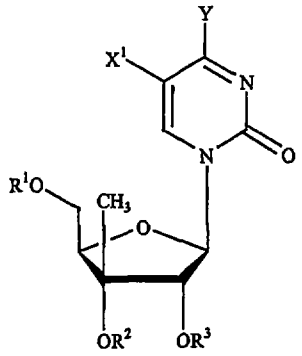
group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a sixth principal embodiment, a compound of Formula VI, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(VI)

wherein:

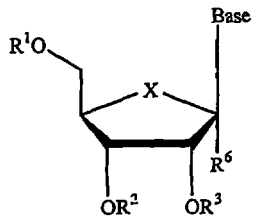
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

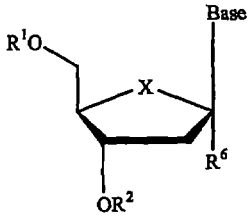
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

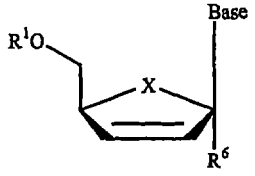
In a seventh principal embodiment, a compound selected from Formulas VII, VIII and IX, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(VII)



(VIII)



(IX)

wherein:

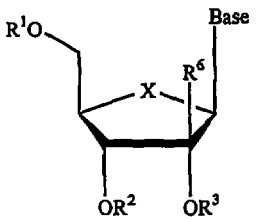
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

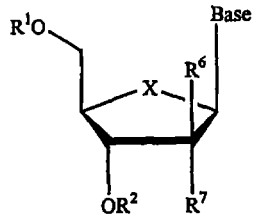
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

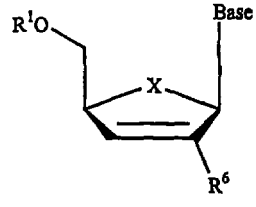
In a eighth principal embodiment, a compound of Formulas X, XI and XII, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(X)



(XI)



(XII)

wherein:

Base is a purine or pyrimidine base as defined herein;

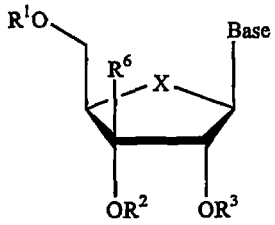
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

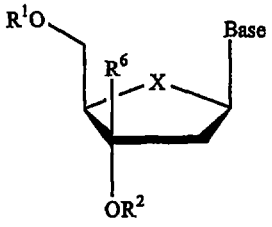
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

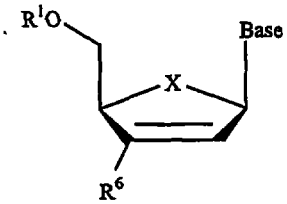
In a ninth principal embodiment a compound selected from Formulas XIII, XIV and XV, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(XIII)



(XIV)



(XV)

wherein:

Base is a purine or pyrimidine base as defined herein;

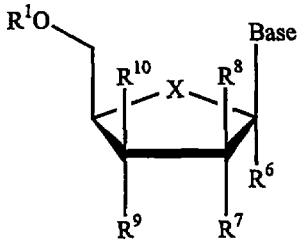
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino

acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

In a tenth principal embodiment the invention provides a compound of Formula XVI, or a pharmaceutically acceptable salt or prodrug thereof:



(XVI)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 or R^2 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

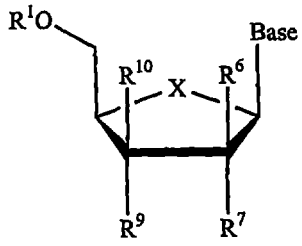
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a pi bond; and

X is O, S, SO_2 or CH_2.

In a eleventh principal embodiment the invention provides a compound of Formula XVII, or a pharmaceutically acceptable salt or prodrug thereof:



(XVII)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 or R^2 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

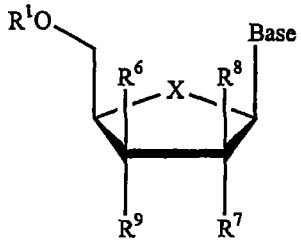
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a pi bond; and

X is O, S, SO_2 or CH_2.

In an twelfth principal embodiment, the invention provides a compound of Formula XVIII, or a pharmaceutically acceptable salt or prodrug thereof:



(XVIII)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 or R^2 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(lower-alkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a pi bond;

X is O, S, SO_2 or CH_2.

The β-D- and β-L-nucleosides of this invention may inhibit flavivirus or pestivirus polymerase activity. These nucleosides can be assessed for their ability to inhibit flavivirus or pestivirus polymerase activity *in vitro* according to standard screening methods.

In one embodiment the efficacy of the anti-flavivirus or pestivirus compound is measured according to the concentration of compound necessary to reduce the plaque number of the virus *in vitro*, according to methods set forth more particularly herein, by 50% (i.e. the compound's EC_{50}). In preferred embodiments the compound exhibits an EC_{50} of less than 15 or preferably, less than 10 micromolar *in vitro*.

In another embodiment, the active compound can be administered in combination or alternation with another anti-flavivirus or pestivirus agent. In combination therapy, effective dosages of two or more agents are administered together, whereas during alternation therapy an effective dosage of each agent is administered serially. The dosages will depend on absorption, inactivation and excretion rates of the drug as well as other factors known to those of skill in the art. It is to be noted that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens and schedules should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions.

HCV is a member of the *Flaviviridae* family; however, now, HCV has been placed in a new monotypic genus, hepacivirus. Therefore, in one embodiment, the flavivirus or pestivirus is not HCV.

Nonlimiting examples of antiviral agents that can be used in combination with the compounds disclosed herein include:

(1) an interferon and/or ribavirin (Battaglia, A.M. *et al.*, Ann. Pharmacother. 34:487-494, 2000); Berenguer, M. *et al.* Antivir. Ther. 3(Suppl. 3):125-136, 1998);

(2) Substrate-based NS3 protease inhibitors (Attwood *et al.*, *Antiviral peptide derivatives*, PCT WO 98/22496, 1998; Attwood *et al.*, *Antiviral Chemistry and Chemotherapy* 10.259-273, 1999; Attwood *et al.*, *Preparation and use of amino acid derivatives as anti-viral agents*, German Patent Publication DE 19914474; Tung *et al.* *Inhibitors of serine proteases, particularly hepatitis C virus NS3 protease*, PCT WO 98/17679), including alphaketoamides and hydrazinoureas, and inhibitors that terminate in an electrophile such as a boronic acid or phosphonate. Llinas-Brunet et al, *Hepatitis C inhibitor peptide analogues*, PCT WO 99/07734.

(3) Non-substrate-based inhibitors such as 2,4,6-trihydroxy-3-nitro-benzamide derivatives(Sudo K. *et al.*, *Biochemical and Biophysical Research Communications*, 238:643-647, 1997; Sudo K. *et al.* *Antiviral Chemistry and Chemotherapy* 9:186, 1998), including RD3-4082 and RD3-4078, the former substituted on the amide with a 14 carbon chain and the latter processing a *para*-phenoxyphenyl group;

(4) Thiazolidine derivatives which show relevant inhibition in a reverse-phase HPLC assay with an NS3/4A fusion protein and NS5A/5B substrate (Sudo K. *et al.*, *Antiviral Research* 32:9-18, 1996), especially compound RD-1-6250, possessing a fused cinnamoyl moiety substituted with a long alkyl chain, RD4 6205 and RD4 6193;

(5) Thiazolidines and benzanilides identified in Kakiuchi N. *et al. J. EBS Letters* 421:217-220; Takeshita N. *et al. Analytical Biochemistry* 247:242-246, 1997;

(6) A phenan-threnequinone possessing activity against protease in a SDS-PAGE and autoradiography assay isolated from the fermentation culture broth of *Streptomyces* sp., Sch 68631 (Chu M. *et al.*, *Tetrahedron Letters* 37:7229-7232, 1996), and Sch 351633, isolated from the fungus *Penicillium griscofuluum*, which demonstrates activity in a scintillation proximity assay (Chu M. *et al.*, *Bioorganic and Medicinal Chemistry Letters* 9:1949-1952);

(7) Selective NS3 inhibitors based on the macromolecule elgin c, isolated from leech (Qasim M.A. *et al.*, *Biochemistry* 36:1598-1607, 1997);

(8) Helicase inhibitors (Diana G.D. *et al.*, *Compounds, compositions and methods for treatment of hepatitis C*, U.S. Patent No. 5,633,358; Diana G.D. *et al.*, *Piperidine derivatives, pharmaceutical compositions thereof and their use in the treatment of hepatitis C*, PCT WO 97/36554);

(9) Polymerase inhibitors such as nucleotide analogues, gliotoxin (Ferrari R. *et al. Journal of Virology* 73:1649-1654, 1999), and the natural product cerulenin (Lohmann V. *et al., Virology* 249:108-118, 1998);

(10) Antisense phosphorothioate oligodeoxynucleotides (S-ODN) complementary to sequence stretches in the 5' non-coding region (NCR) of the virus (Alt M. *et al., Hepatology* 22:707-717, 1995), or nucleotides 326-348 comprising the 3' end of the NCR and nucleotides 371-388 located in the core coding region of the HCV RNA (Alt M. *et al., Archives of Virology* 142:589-599, 1997; Galderisi U. *et al., Journal of Cellular Physiology* 181:251-257, 1999);

(11) Inhibitors of IRES-dependent translation (Ikeda N *et al., Agent for the prevention and treatment of hepatitis C,* Japanese Patent Publication JP-08268890; Kai Y. *et al. Prevention and treatment of viral diseases,* Japanese Patent Publication JP-10101591);

(12) Nuclease-resistant ribozymes. (Maccjak D.J. *et al., Hepatology 30* abstract 995, 1999); and

(13) Other miscellaneous compounds including 1-amino-alkylcyclohexanes (U.S. Patent No. 6,034,134 to Gold *et al.*), alkyl lipids (U.S. Patent No. 5,922,757 to Chojkier *et al.*), vitamin E and other antioxidants (U.S. Patent No. 5,922,757 to Chojkier *et al.*), squalene, amantadine, bile acids (U.S. Patent No. 5,846,964 to Ozeki *et al.*), N-(phosphonoacetyl)-L-aspartic acid, (U.S. Patent No. 5,830,905 to Diana *et al.*), benzenedicarboxamides (U.S. Patent No. 5,633,388 to Diana *et al.*), polyadenylic acid derivatives (U.S. Patent No. 5,496,546 to Wang *et al.*), 2',3'-dideoxyinosine (U.S. Patent No. 5,026,687 to Yarchoan *et al.*), and benzimidazoles (U.S. Patent No. 5,891,874 to Colacino *et al.*).

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 provides the structure of various non-limiting examples of nucleosides of the present invention, as well as other known nucleosides, FIAU and Ribavirin, which are used as comparative examples in the text.

Figure 2 is a line graph of the pharmacokinetics (plasma concentrations) of β-D-2'-CH_3-riboG administered to Cynomolgus Monkeys over time after administration.

Figure 3a and **3b** are line graphs of the pharmacokinetics (plasma concentrations) of β-D-2'-CH_3-riboG administered to Cynomolgus Monkeys either intravenously (**3a**) or orally (**3b**) over time after administration.

Figure 4 depicts line graphs of the results of the cell protection assay of β-D-2'-CH_3-riboG against BVDV.

Figure 5 depicts line graphs of the results of the cell protection assay of ribavirin against BVDV.

Figure 6 are line graphs of the cell protection assay of β-D-2'-CH_3-riboG, β-D-2'-CH_3-riboC, β-D-2'-CH_3-riboU, β-D-2'-CH_3-riboA and ribavirin.

Figure 7 are line graphs of the results of the plaque reduction assay for β-D-2'-CH_3-riboU, β-D-2'-CH_3-riboC and β-D-2'-CH_3-riboG.

Figure 8 is an illustration of plaque reduction based on increasing concentrations of β-D-2'-CH_3-riboU.

Figure 9 is a line graph of the results of the yield reduction assay for β-D-2'-CH_3-riboG, depicting a 4 log reduction at 9 μM.

Figure 10 is an illustration of the yield reduction based on increasing concentrations of β-D-2'-CH_3-riboC.

DETAILED DESCRIPTION OF THE INVENTION

The invention as disclosed herein is a compound, method and composition for the treatment of pestiviruses and flaviviruses in humans and other host animals, that includes the administration of an effective flavivirus or pestivirus treatment amount of an β-D- or β-L-nucleoside as described herein or a pharmaceutically acceptable salt or prodrug thereof, optionally in a pharmaceutically acceptable carrier. The compounds of this invention either possess antiviral (i.e., anti-flavivirus or pestivirus) activity, or are metabolized to a compound that exhibits such activity.

In summary, the present invention includes the following features:

(a) β-D- and β-L-nucleosides, as described herein, and pharmaceutically acceptable salts and prodrugs thereof;

(b) β-D- and β-L-nucleosides as described herein, and pharmaceutically acceptable salts and prodrugs thereof for use in the treatment or prophylaxis of a flavivirus or pestivirus infection, especially in individuals diagnosed as having a flavivirus or pestivirus infection or being at risk for becoming infected by flavivirus or pestivirus;

(c) use of these β-D- and β-L-nucleosides, and pharmaceutically acceptable salts and prodrugs thereof in the manufacture of a medicament for treatment of a flavivirus or pestivirus infection;

(d) pharmaceutical formulations comprising the β-D- and β-L-nucleosides or pharmaceutically acceptable salts or prodrugs thereof together with a pharmaceutically acceptable carrier or diluent;

(e) β-D- and β-L-nucleosides as described herein substantially in the absence of enantiomers of the described nucleoside, or substantially isolated from other chemical entities;

(f) processes for the preparation of β-D- and β-L-nucleosides, as described in more detail below; and

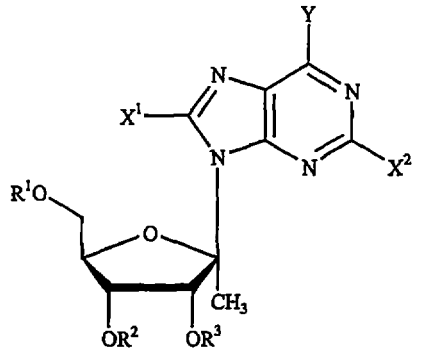
(g) processes for the preparation of β-D- and β-L-nucleosides substantially in the absence of enantiomers of the described nucleoside, or substantially isolated from other chemical entities.

Flaviviruses included within the scope of this invention are discussed generally in *Fields Virology*, Editors: Fields, B. N., Knipe, D. M., and Howley, P. M., Lippincott-Raven Publishers, Philadelphia, PA, Chapter 31, 1996. Specific flaviviruses include, without limitation: Absettarov, Alfuy, Apoi, Aroa, Bagaza, Banzi, Bouboui, Bussuquara, Cacipacore, Carey Island, Dakar bat, Dengue 1, Dengue 2, Dengue 3, Dengue 4, Edge Hill, Entebbe bat, Gadgets Gully, Hanzalova, Hypr, Ilheus, Israel turkey meningoencephalitis, Japanese encephalitis, Jugra, Jutiapa, Kadam, Karshi, Kedougou, Kokobera, Koutango, Kumlinge, Kunjin, Kyasanur Forest disease, Langat, Louping ill, Meaban, Modoc, Montana myotis leukoencephalitis, Murray valley encephalitis, Naranjal, Negishi, Ntaya, Omsk hemorrhagic fever, Phnom-Penh bat, Powassan, Rio Bravo, Rocio, Royal Farm, Russian spring-summer encephalitis, Saboya, St. Louis encephalitis, Sal Vieja, San Perlita, Saumarez Reef, Sepik, Sokuluk, Spondweni, Stratford, Tembusu, Tyuleniy, Uganda S, Usutu, Wesselsbron, West Nile, Yaounde, Yellow fever, and Zika.

Pestiviruses included within the scope of this invention are discussed generally in *Fields Virology*, Editors: Fields, B. N., Knipe, D. M., and Howley, P. M., Lippincott-Raven Publishers, Philadelphia, PA, Chapter 33, 1996. Specific pestiviruses include, without limitation: bovine viral diarrhea virus ("BVDV"), classical swine fever virus ("CSFV," also called hog cholera virus), and border disease virus ("BDV").

I. Active Compound, and Physiologically Acceptable Salts and Prodrugs Thereof

In a first principal embodiment, a compound of Formula I, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(I)

wherein:

R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a preferred subembodiment, a compound of Formula I, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

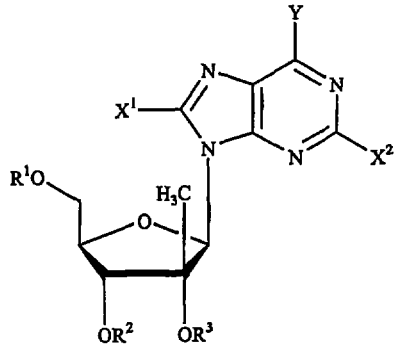
R^1, R^2 and R^3 are independently H or phosphate (preferably H);

X^1 is H;

X^2 is H or NH_2; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

In a second principal embodiment, a compound of Formula II, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(II)

wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a preferred subembodiment, a compound of Formula II, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

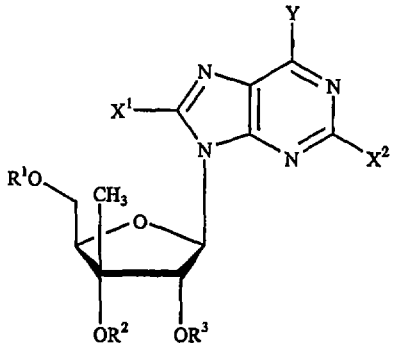
R^1, R^2 and R^3 are independently H or phosphate (preferably H);

X^1 is H;

X^2 is H or NH_2; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

In a third principal embodiment, a compound of Formula III, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(III)

wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

In a preferred subembodiment, a compound of Formula III, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

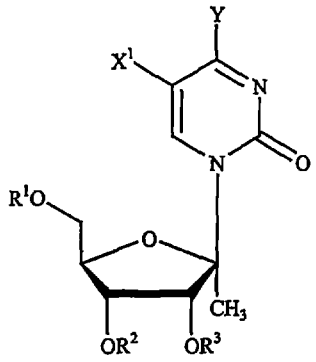
R^1, R^2 and R^3 are independently H or phosphate (preferably H);

X^1 is H;

X^2 is H or NH_2; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

In a fourth principal embodiment, a compound of Formula IV, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(IV)

wherein:

R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

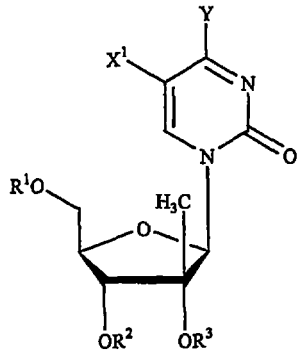
In a preferred subembodiment, a compound of Formula IV, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

R^1, R^2 and R^3 are independently H or phosphate (preferably H);

X^1 is H or CH_3; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

In a fifth principal embodiment, a compound of Formula V, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(V)

wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

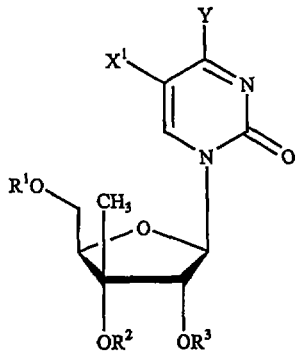
In a preferred subembodiment, a compound of Formula V, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

R^1, R^2 and R^3 are independently H or phosphate (preferably H);

X^1 is H or CH_3; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

In a sixth principal embodiment, a compound of Formula VI, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(VI)

wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^5; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

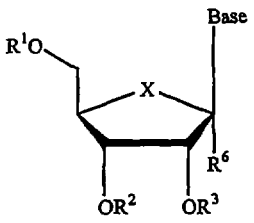
In a preferred subembodiment, a compound of Formula VI, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

R^1, R^2 and R^3 are independently H or phosphate (preferably H);

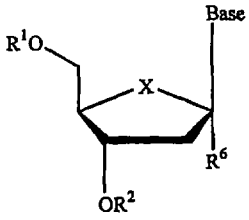
X^1 is H or CH_3; and

Y is hydrogen, bromo, chloro, fluoro, iodo, NH_2 or OH.

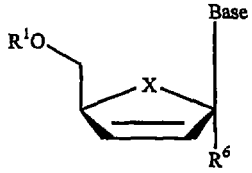
In a seventh principal embodiment, a compound selected from Formulas VII, VIII and IX, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(VII)



(VIII)



(IX)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

In a first preferred subembodiment, a compound of Formula VII, VIII or IX, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently hydrogen or phosphate;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a second preferred subembodiment, a compound of Formula VII, VIII or IX, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are hydrogens;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula VII, VIII or IX, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

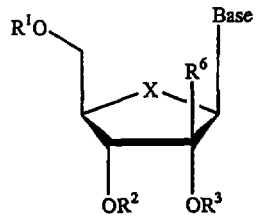
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently hydrogen or phosphate;

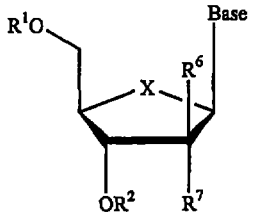
R^6 is alkyl; and

X is O.

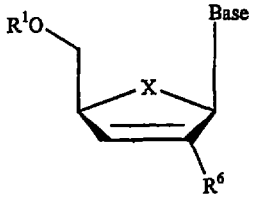
In a eighth principal embodiment, a compound of Formula X, XI or XII, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(X)



(XI)



(XII)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(loweralkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

In a first preferred subembodiment, a compound of Formula X, XI or XII, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently hydrogen or phosphate;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a second preferred subembodiment, a compound of Formula X, XI or XII, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are hydrogens;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula X, XI or XII, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

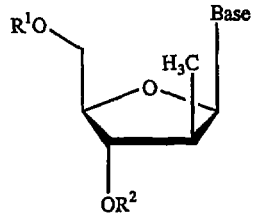
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H or phosphate;

R^6 is alkyl; and

X is O.

In even more preferred subembodiments, a compound of Formula XI, or its pharmaceutically acceptable salt or prodrug, is provided:



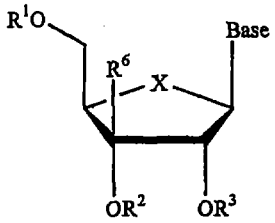
(XI)

wherein:

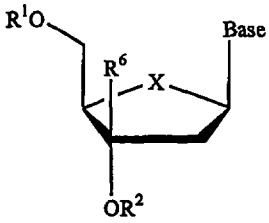
Base is a purine or pyrimidine base as defined herein; optionally substituted with an amine or cyclopropyl (e.g., 2-amino, 2,6-diamino or cyclopropyl guanosine); and

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 or R^2 is independently H or phosphate.

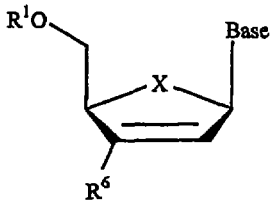
In a ninth principal embodiment a compound selected from Formula XIII, XIV or XV, or a pharmaceutically acceptable salt or prodrug thereof, is provided:



(XIII)



(XIV)



(XV)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl

and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 or R^3 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

In a first preferred subembodiment, a compound of Formula XIII, XIV or XV, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently hydrogen or phosphate;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a second preferred subembodiment, a compound of Formula XIII, XIV or XV, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are hydrogens;

R^6 is alkyl; and

X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula XIII, XIV or XV, or a pharmaceutically acceptable salt or prodrug thereof, is provided wherein:

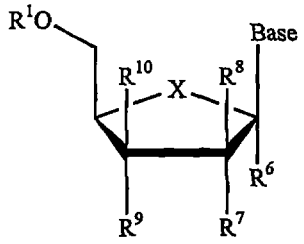
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently hydrogen or phosphate;

R^6 is alkyl; and

X is O.

In a tenth principal embodiment the invention provides a compound of Formula XVI, or a pharmaceutically acceptable salt or prodrug thereof:



(XVI)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a pi bond; and

X is O, S, SO_2 or CH_2.

In a first preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2, alkyl, alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O, S, SO_2 or CH_2.

In a second preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl, alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or

arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl, alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2, alkyl, alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (5) R^8 and R^{10} are H; and (6) X is O, S, SO_2 or CH_2.

In a fourth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl, alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2, alkyl, alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O.

In a fifth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a

cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^1; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O, S, SO_2 or CH_2.

In a sixth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^8 and R^{10} are H; and (6) X is O, S, SO_2, or CH_2.

In a seventh preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O.

In a eighth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or

pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are hydrogen; and (6) X is O, S, SO_2 or CH_2.

In a ninth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O.

In a tenth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a

cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^8 and R^{10} are hydrogen; and (6) X is O.

In an eleventh preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are hydrogen; and (6) X is O, S, SO_2 or CH_2.

In a twelfth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are hydrogen; and (6) X is O, S, SO_2, or CH_2.

In a thirteenth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2; (5) R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O.

In a fourteenth preferred subembodiment, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (5) R^8 and R^{10} are hydrogen; and (6) X is O.

In even more preferred subembodiments, a compound of Formula XVI, or its pharmaceutically acceptable salt or prodrug, is provided in which:

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is guanine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is cytosine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is thymine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is uracil; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is phosphate; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is ethyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is propyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is butyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

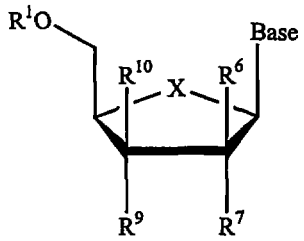
(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 is hydrogen and R^9 is hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is S;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is SO_2;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 and R^{10} are hydrogen; and (6) X is CH_2;

In a eleventh principal embodiment the invention provides a compound of Formula XVII, or a pharmaceutically acceptable salt or prodrug thereof:



(XVII)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 is H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a pi bond; and

X is O, S, SO_2 or CH_2.

In a first preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl

(including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)-amino; (5) R^{10} is H; and (6) X is O, S, SO_2, or CH_2.

In a second preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^{10} is H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a

cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)-amino; (5) R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O.

In a fourth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^{10} is H; and (6) X is O, S, SO_2 or CH_2.

In a fifth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7

and R^9 are independently OR^2; (5) R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O.

In a sixth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^{10} is H; and (6) X is O.

In a seventh preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^{10} is H; and (6) X is O.

In an eighth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4)

R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)-amino; (5) R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O, S, SO_2, or CH_2.

In a ninth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^{10} is H; and (6) X is O, S, SO_2, or CH_2.

In a tenth preferred subembodiment, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2; (5) R^{10} is H; and (6) X is O, S, SO_2, or CH_2.

In even more preferred subembodiments, a compound of Formula XVII, or its pharmaceutically acceptable salt or prodrug, is provided in which:

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is guanine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is cytosine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is thymine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is uracil; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is phosphate; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is ethyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is propyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

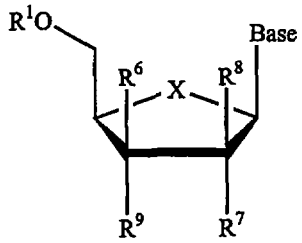
(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is butyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is S;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is SO_2; or

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^{10} is hydrogen; and (6) X is CH_2.

In an twelfth principal embodiment the invention provides a compound of Formula XVIII, or a pharmaceutically acceptable salt or prodrug thereof:



(XVIII)

wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower

alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, lower alkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a pi bond;

X is O, S, SO_2 or CH_2.

In a first preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (5) R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine; and (6) X is O, S, SO_2 or CH_2.

In a second preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6

is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di-(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O, S, SO_2 or CH_2.

In a third preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(lower-alkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^8 is H; and (6) X is O, S, SO_2 or CH_2.

In a fourth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or

di(loweralkyl)amino; (5) R^8 is H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O.

In a fifth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H; and (6) X is O, S, SO_2, or CH_2.

In a sixth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H, alkyl (including lower alkyl), chlorine, bromine, or iodine; and (6) X is O.

In a seventh preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl

(including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (4) R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; (5) R^8 is H; and (6) X is O.

In an eighth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, hydroxy, O-alkyl, O-alkenyl, chloro, bromo, fluoro, iodo, NO_2, amino, loweralkylamino or di(loweralkyl)amino; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H; and (6) X is O, S, SO_2 or CH_2.

In a ninth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H; and (6) X is O, S, SO_2, or CH_2.

In a tenth preferred subembodiment, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which: (1) Base is a purine or pyrimidine base as defined herein; (2) R^1 is independently H or phosphate; (3) R^6 is alkyl; (4) R^7 and R^9 are independently OR^2; (5) R^8 is H; and (6) X is O.

In even more preferred subembodiments, a compound of Formula XVIII, or its pharmaceutically acceptable salt or prodrug, is provided in which:

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is guanine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is cytosine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is thymine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is uracil; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is phosphate; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is ethyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is propyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is butyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is O;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is S;

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is SO_2; or

(1) Base is adenine; (2) R^1 is hydrogen; (3) R^6 is methyl; (4) R^7 and R^9 are hydroxyl; (5) R^8 is hydrogen; and (6) X is CH_2.

The β-D- and β-L-nucleosides of this invention belong to a class of anti-flavivirus or pestivirus agents that may inhibit flavivirus or pestivirus polymerase activity. Nucleosides can be screened for their ability to inhibit flavivirus or pestivirus polymerase activity *in vitro* according to screening methods set forth more particularly herein. One can readily determine the spectrum of activity by evaluating the compound in the assays described herein or with another confirmatory assay.

In one embodiment the efficacy of the anti-flavivirus or pestivirus compound is measured according to the concentration of compound necessary to reduce the plaque number of the virus *in vitro*, according to methods set forth more particularly herein, by 50% (i.e. the compound's EC_{50}). In preferred embodiments the compound exhibits an EC_{50} of less than 15 or 10 micromolar.

HCV is a member of the *Flaviviridae* family; however, now, HCV has been placed in a new monotypic genus, hepacivirus. Therefore, in one embodiment, the flavivirus or pestivirus is not HCV.

The active compound can be administered as any salt or prodrug that upon administration to the recipient is capable of providing directly or indirectly the parent compound, or that exhibits activity itself. Nonlimiting examples are the pharmaceutically acceptable salts (alternatively referred to as "physiologically acceptable salts"), and a compound, which has been alkylated or acylated at the 5'-position, or on the purine or pyrimidine base (a type of "pharmaceutically acceptable prodrug"). Further, the modifications can affect the biological activity of the compound, in some cases increasing the activity over the parent compound. This can easily be assessed by preparing the salt or prodrug and testing its antiviral activity according to the methods described herein, or other methods known to those skilled in the art.

II. Definitions

The term alkyl, as used herein, unless otherwise specified, refers to a saturated straight, branched, or cyclic, primary, secondary, or tertiary hydrocarbon of typically C_1 to C_{10}, and specifically includes methyl, trifluoromethyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, *t*-butyl, pentyl, cyclopentyl, isopentyl, neopentyl, hexyl, isohexyl, cyclohexyl, cyclohexylmethyl, 3-methylpentyl, 2,2-dimethylbutyl, and 2,3-dimethylbutyl. The term includes both substituted and unsubstituted alkyl groups. Moieties with which the alkyl group can be substituted are selected from the group consisting of hydroxyl, amino, alkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, sulfate, phosphonic acid, phosphate, or phosphonate, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, hereby incorporated by reference.

The term lower alkyl, as used herein, and unless otherwise specified, refers to a C_1 to C_4 saturated straight, branched, or if appropriate, a cyclic (for example, cyclopropyl) alkyl group, including both substituted and unsubstituted forms. Unless otherwise specifically stated in this application, when alkyl is a suitable moiety, lower alkyl is preferred. Similarly, when alkyl or lower alkyl is a suitable moiety, unsubstituted alkyl or lower alkyl is preferred.

The term alkylamino or arylamino refers to an amino group that has one or two alkyl or aryl substituents, respectively.

The term "protected" as used herein and unless otherwise defined refers to a group that is added to an oxygen, nitrogen, or phosphorus atom to prevent its further reaction or for other purposes. A wide variety of oxygen and nitrogen protecting groups are known to those skilled in the art of organic synthesis.

The term aryl, as used herein, and unless otherwise specified, refers to phenyl, biphenyl, or naphthyl, and preferably phenyl. The term includes both substituted and unsubstituted moieties. The aryl group can be substituted with one or more moieties selected from the group consisting of hydroxyl, amino, alkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, sulfate, phosphonic acid, phosphate, or phosphonate, either unprotected, or protected as necessary, as known to those skilled in the art, for example, as taught in Greene, *et al.*, Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

The term alkaryl or alkylaryl refers to an alkyl group with an aryl substituent. The term aralkyl or arylalkyl refers to an aryl group with an alkyl substituent.

The term halo, as used herein, includes chloro, bromo, iodo, and fluoro.

The term purine or pyrimidine base includes, but is not limited to, adenine, N^6-alkylpurines, N^6-acylpurines (wherein acyl is C(O)(alkyl, aryl, alkylaryl, or arylalkyl), N^6-benzylpurine, N^6-halopurine, N^6-vinylpurine, N^6-acetylenic purine, N^6-acyl purine, N^6-hydroxyalkyl purine, N^6-thioalkyl purine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, thymine, cytosine, 5-fluorocytosine, 5-methylcytosine, 6-azapyrimidine, including 6-azacytosine, 2- and/or 4-mercaptopyrmidine, uracil, 5-halouracil, including 5-fluorouracil, C^5-alkylpyrimidines, C^5-benzylpyrimidines, C^5-halopyrimidines, C^5-vinylpyrimidine, C^5-acetylenic pyrimidine, C^5-acyl pyrimidine, C^5-hydroxyalkyl purine, C^5-amidopyrimidine, C^5-cyanopyrimidine, C^5-nitropyrimidine, C^5-aminopyrimidine, N^2-alkylpurines, N^2-alkyl-6-thiopurines, 5-azacytidinyl, 5-azauracilyl, triazolopyridinyl, imidazolopyridinyl, pyrrolopyrimidinyl, and pyrazolo-pyrimidinyl. Purine bases include, but are not limited to, guanine, adenine, hypoxanthine, 2,6-diaminopurine, and 6-chloropurine. Functional oxygen and nitrogen groups on the base can be protected as necessary or desired. Suitable protecting groups are well known to those skilled in the art, and include trimethylsilyl, dimethylhexylsilyl, *t*-butyldimethylsilyl and *t*-butyldiphenylsilyl, trityl, alkyl groups, and acyl groups such as acetyl and propionyl, methanesulfonyl, and p-toluenesulfonyl. Alternatively, the purine or pyrimidine base can optionally substituted such that it forms a viable prodrug,

which can be cleaved in vivo. Examples of appropriate substituents include acyl moiety, an amine or cyclopropyl (e.g., 2-amino, 2,6-diamino or cyclopropyl guanosine).

The term acyl refers to a carboxylic acid ester in which the non-carbonyl moiety of the ester group is selected from straight, branched, or cyclic alkyl or lower alkyl, alkoxyalkyl including methoxymethyl, aralkyl including benzyl, aryloxyalkyl such as phenoxymethyl, aryl including phenyl optionally substituted with halogen, C_1 to C_4 alkyl or C_1 to C_4 alkoxy, sulfonate esters such as alkyl or aralkyl sulphonyl including methanesulfonyl, the mono, di or triphosphate ester, trityl or monomethoxytrityl, substituted benzyl, trialkylsilyl (e.g. dimethyl-t-butylsilyl) or diphenylmethylsilyl. Aryl groups in the esters optimally comprise a phenyl group. The term "lower acyl" refers to an acyl group in which the non-carbonyl moiety is lower alkyl.

As used herein, the term "substantially free of" or "substantially in the absence of" refers to a nucleoside composition that includes at least 85 or 90% by weight, preferably 95% to 98 % by weight, and even more preferably 99% to 100% by weight, of the designated enantiomer of that nucleoside. In a preferred embodiment, in the methods and compounds of this invention, the compounds are substantially free of enantiomers.

Similarly, the term "isolated" refers to a nucleoside composition that includes at least 85 or 90% by weight, preferably 95% to 98 % by weight, and even more preferably 99% to 100% by weight, of the nucleoside, the remainder comprising other chemical species or enantiomers.

The term "independently" is used herein to indicate that the variable, which is independently applied, varies independently from application to application. Thus, in a compound such as R"XYR", wherein R" is "independently carbon or nitrogen," both R" can be carbon, both R" can be nitrogen, or one R" can be carbon and the other R" nitrogen.

The term host, as used herein, refers to an unicellular or multicellular organism in which the virus can replicate, including cell lines and animals, and preferably a human. Alternatively, the host can be carrying a part of the flavivirus or pestivirus genome, whose replication or function can be altered by the compounds of the present invention. The term host specifically refers to infected cells, cells transfected with all or part of the flavivirus or pestivirus genome and animals, in particular, primates (including chimpanzees) and humans. In most animal applications of the present invention, the host is a human patient. Veterinary

applications, in certain indications, however, are clearly anticipated by the present invention (such as chimpanzees).

The term "pharmaceutically acceptable salt or prodrug" is used throughout the specification to describe any pharmaceutically acceptable form (such as an ester, phosphate ester, salt of an ester or a related group) of a nucleoside compound which, upon administration to a patient, provides the nucleoside compound. Pharmaceutically acceptable salts include those derived from pharmaceutically acceptable inorganic or organic bases and acids. Suitable salts include those derived from alkali metals such as potassium and sodium, alkaline earth metals such as calcium and magnesium, among numerous other acids well known in the pharmaceutical art. Pharmaceutically acceptable prodrugs refer to a compound that is metabolized, for example hydrolyzed or oxidized, in the host to form the compound of the present invention. Typical examples of prodrugs include compounds that have biologically labile protecting groups on a functional moiety of the active compound. Prodrugs include compounds that can be oxidized, reduced, aminated, deaminated, hydroxylated, dehydroxylated, hydrolyzed, dehydrolyzed, alkylated, dealkylated, acylated, deacylated, phosphorylated, dephosphorylated to produce the active compound. The compounds of this invention possess antiviral activity against flavivirus or pestivirus, or are metabolized to a compound that exhibits such activity.

III. Nucleotide Salt or Prodrug Formulations

In cases where compounds are sufficiently basic or acidic to form stable nontoxic acid or base salts, administration of the compound as a pharmaceutically acceptable salt may be appropriate. Examples of pharmaceutically acceptable salts are organic acid addition salts formed with acids, which form a physiological acceptable anion, for example, tosylate, methanesulfonate, acetate, citrate, malonate, tartarate, succinate, benzoate, ascorbate, α-ketoglutarate, and α-glycerophosphate. Suitable inorganic salts may also be formed, including, sulfate, nitrate, bicarbonate, and carbonate salts.

Pharmaceutically acceptable salts may be obtained using standard procedures well known in the art, for example by reacting a sufficiently basic compound such as an amine with a suitable acid affording a physiologically acceptable anion. Alkali metal (for example, sodium, potassium or lithium) or alkaline earth metal (for example calcium) salts of carboxylic acids can also be made.

Any of the nucleosides described herein can be administered as a nucleotide prodrug to increase the activity, bioavailability, stability or otherwise alter the properties of the nucleoside. A number of nucleotide prodrug ligands are known. In general, alkylation, acylation or other lipophilic modification of the mono, di or triphosphate of the nucleoside will increase the stability of the nucleotide. Examples of substituent groups that can replace one or more hydrogens on the phosphate moiety are alkyl, aryl, steroids, carbohydrates, including sugars, 1,2-diacylglycerol and alcohols. Many are described in R. Jones and N. Bischofberger, *Antiviral Research*, **27** (1995) 1-17. Any of these can be used in combination with the disclosed nucleosides to achieve a desired effect.

The active nucleoside can also be provided as a 5'-phosphoether lipid or a 5'-ether lipid, as disclosed in the following references, which are incorporated by reference herein: Kucera, L.S., N. Iyer, E. Leake, A. Raben, Modest E.K., D.L.W., and C. Piantadosi, "Novel membrane-interactive ether lipid analogs that inhibit infectious HIV-1 production and induce defective virus formation," *AIDS Res. Hum. Retro Viruses*, **1990**, *6*, 491-501; Piantadosi, C., J. Marasco C.J., S.L. Morris-Natschke, K.L. Meyer, F. Gumus, J.R. Surles, K.S. Ishaq, L.S. Kucera, N. Iyer, C.A. Wallen, S. Piantadosi, and E.J. Modest, "Synthesis and evaluation of novel ether lipid nucleoside conjugates for anti-HIV activity," *J. Med. Chem.*, **1991**, *34*, 1408-1414; Hosteller, K.Y., D.D. Richman, D.A. Carson, L.M. Stuhmiller, G.M. T. van Wijk, and H. van den Bosch, "Greatly enhanced inhibition of human immunodeficiency virus type 1 replication in CEM and HT4-6C cells by 3'-deoxythymidine diphosphate dimyristoylglycerol, a lipid prodrug of 3,-deoxythymidine," *Antimicrob. Agents Chemother.*, **1992**, *36*, 2025-2029; Hosetler, K.Y., L.M. Stuhmiller, H.B. Lenting, H. van den Bosch, and D.D. Richman, "Synthesis and antiretroviral activity of phospholipid analogs of azidothymidine and other antiviral nucleosides." *J. Biol. Chem.*, **1990**, *265*, 61127.

Nonlimiting examples of U.S. patents that disclose suitable lipophilic substituents that can be covalently incorporated into the nucleoside, preferably at the 5'-OH position of the nucleoside or lipophilic preparations, include U.S. Patent Nos. 5,149,794 (Sep. 22, 1992, Yatvin et al.); 5,194,654 (Mar. 16, 1993, Hostetler et al., 5,223,263 (June 29, 1993, Hostetler et al.); 5,256,641 (Oct. 26, 1993, Yatvin et al.); 5,411,947 (May 2, 1995, Hostetler et al.); 5,463,092 (Oct. 31, 1995, Hostetler et al.); 5,543,389 (Aug. 6, 1996, Yatvin et al.); 5,543,390 (Aug. 6, 1996, Yatvin et al.); 5,543,391 (Aug. 6, 1996, Yatvin et al.); and 5,554,728 (Sep. 10, 1996; Basava et al.), all of which are incorporated herein by reference. Foreign patent applications that disclose lipophilic substituents that can be attached to the nucleosides of the

present invention, or lipophilic preparations, include WO 89/02733, W0 90/00555, W0 91/16920, W0 91/18914, W0 93/00910, W0 94/26273, W0 96/15132, EP 0 350 287, EP 93917054.4, and W0 91/19721.

IV. Combination and Alternation Therapy

It has been recognized that drug-resistant variants of viruses can emerge after prolonged treatment with an antiviral agent. Drug resistance most typically occurs by mutation of a gene that encodes for an enzyme used in viral replication. The efficacy of a drug against flavivirus or pestivirus infection can be prolonged, augmented, or restored by administering the compound in combination or alternation with a second, and perhaps third, antiviral compound that induces a different mutation from that caused by the principle drug. Alternatively, the pharmacokinetics, biodistribution or other parameter of the drug can be altered by such combination or alternation therapy. In general, combination therapy is typically preferred over alternation therapy because it induces multiple simultaneous stresses on the virus.

Nonlimiting examples of antiviral agents that can be used in combination or alternation with the compounds disclosed herein include:

(1) an interferon and/or ribavirin (Battaglia, A.M. *et al.*, Ann. Pharmacother. 34:487-494, 2000); Berenguer, M. *et al.* Antivir. Ther. 3(Suppl. 3):125-136, 1998);

(2) Substrate-based NS3 protease inhibitors (Attwood *et al., Antiviral peptide derivatives*, PCT WO 98/22496, 1998; Attwood *et al., Antiviral Chemistry and Chemotherapy* 10.259-273, 1999; Attwood *et al., Preparation and use of amino acid derivatives as anti-viral agents,* German Patent Publication DE 19914474; Tung *et al. Inhibitors of serine proteases, particularly hepatitis C virus NS3 protease*, PCT WO 98/17679), including alphaketoamides and hydrazinoureas, and inhibitors that terminate in an electrophile such as a boronic acid or phosphonate. Llinas-Brunet et al, *Hepatitis C inhibitor peptide analogues,* PCT WO 99/07734.

(3) Non-substrate-based inhibitors such as 2,4,6-trihydroxy-3-nitro-benzamide derivatives(Sudo K. *et al., Biochemical and Biophysical Research Communications,* 238:643-647, 1997; Sudo K. *et al. Antiviral Chemistry and Chemotherapy* 9:186, 1998), including

RD3-4082 and RD3-4078, the former substituted on the amide with a 14 carbon chain and the latter processing a *para*-phenoxyphenyl group;

(4) Thiazolidine derivatives which show relevant inhibition in a reverse-phase HPLC assay with an NS3/4A fusion protein and NS5A/5B substrate (Sudo K. *et al., Antiviral Research* 32:9-18, 1996), especially compound RD-1-6250, possessing a fused cinnamoyl moiety substituted with a long alkyl chain, RD4 6205 and RD4 6193;

(5) Thiazolidines and benzanilides identified in Kakiuchi N. *et al. J. EBS Letters* 421:217-220; Takeshita N. *et al. Analytical Biochemistry* 247:242-246, 1997;

(6) A phenan-threnequinone possessing activity against protease in a SDS-PAGE and autoradiography assay isolated from the fermentation culture broth of *Streptomyces* sp., Sch 68631 (Chu M. *et al., Tetrahedron Letters* 37:7229-7232, 1996), and Sch 351633, isolated from the fungus *Penicillium griscofuluum,* which demonstrates activity in a scintillation proximity assay (Chu M. *et al., Bioorganic and Medicinal Chemistry Letters* 9:1949-1952);

(7) Selective NS3 inhibitors based on the macromolecule elgin c, isolated from leech (Qasim M.A. *et al., Biochemistry* 36:1598-1607, 1997);

(8) Helicase inhibitors (Diana G.D. *et al., Compounds, compositions and methods for treatment of hepatitis C,* U.S. Patent No. 5,633,358; Diana G.D. *et al., Piperidine derivatives, pharmaceutical compositions thereof and their use in the treatment of hepatitis C,* PCT WO 97/36554);

(9) Polymerase inhibitors such as nucleotide analogues, gliotoxin (Ferrari R. *et al. Journal of Virology* 73:1649-1654, 1999), and the natural product cerulenin (Lohmann V. *et al., Virology* 249:108-118, 1998);

(10) Antisense phosphorothioate oligodeoxynucleotides (S-ODN) complementary to sequence stretches in the 5' non-coding region (NCR) of the virus (Alt M. *et al., Hepatology* 22:707-717, 1995), or nucleotides 326-348 comprising the 3' end of the NCR and nucleotides 371-388 located in the core coding region of the IICV RNA (Alt M. *et al., Archives of Virology* 142:589-599, 1997; Galderisi U. *et al., Journal of Cellular Physiology* 181:251-257, 1999);

(11) Inhibitors of IRES-dependent translation (Ikeda N *et al., Agent for the prevention and treatment of hepatitis C,* Japanese Patent Publication JP-08268890; Kai Y. *et al. Prevention and treatment of viral diseases,* Japanese Patent Publication JP-10101591);

(12) Nuclease-resistant ribozymes. (Maccjak D.J. *et al.*, *Hepatology 30* abstract 995, 1999); and

(13) Other miscellaneous compounds including 1-amino-alkylcyclohexanes (U.S. Patent No. 6,034,134 to Gold *et al.*), alkyl lipids (U.S. Patent No. 5,922,757 to Chojkier *et al.*), vitamin E and other antioxidants (U.S. Patent No. 5,922,757 to Chojkier *et al.*), squalene, amantadine, bile acids (U.S. Patent No. 5,846,964 to Ozeki *et al.*), N-(phosphonoacetyl)-L-aspartic acid, (U.S. Patent No. 5,830,905 to Diana *et al.*), benzenedicarboxamides (U.S. Patent No. 5,633,388 to Diana *et al.*), polyadenylic acid derivatives (U.S. Patent No. 5,496,546 to Wang *et al.*), 2',3'-dideoxyinosine (U.S. Patent No. 5,026,687 to Yarchoan *et al.*), and benzimidazoles (U.S. Patent No. 5,891,874 to Colacino *et al.*).

V. Pharmaceutical Compositions

Host, including humans, infected with flavivirus or pestivirus, or a gene fragment thereof can be treated by administering to the patient an effective amount of the active compound or a pharmaceutically acceptable prodrug or salt thereof in the presence of a pharmaceutically acceptable carrier or diluent. The active materials can be administered by any appropriate route, for example, orally, parenterally, intravenously, intradermally, subcutaneously, or topically, in liquid or solid form.

A preferred dose of the compound for flavivirus or pestivirus infection will be in the range from about 1 to 50 mg/kg, preferably 1 to 20 mg/kg, of body weight per day, more generally 0.1 to about 100 mg per kilogram body weight of the recipient per day. The effective dosage range of the pharmaceutically acceptable salts and prodrugs can be calculated based on the weight of the parent nucleoside to be delivered. If the salt or prodrug exhibits activity in itself, the effective dosage can be estimated as above using the weight of the salt or prodrug, or by other means known to those skilled in the art.

The compound is conveniently administered in unit any suitable dosage form, including but not limited to one containing 7 to 3000 mg, preferably 70 to 1400 mg of active ingredient per unit dosage form. A oral dosage of 50-1000 mg is usually convenient.

Ideally the active ingredient should be administered to achieve peak plasma concentrations of the active compound of from about 0.2 to 70 μM, preferably about 1.0 to 10

μM. This may be achieved, for example, by the intravenous injection of a 0.1 to 5% solution of the active ingredient, optionally in saline, or administered as a bolus of the active ingredient.

The concentration of active compound in the drug composition will depend on absorption, inactivation, and excretion rates of the drug as well as other factors known to those of skill in the art. It is to be noted that dosage values will also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed composition. The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at varying intervals of time.

A preferred mode of administration of the active compound is oral. Oral compositions will generally include an inert diluent or an edible carrier. They may be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches or capsules. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition.

The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring. When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials which modify the physical form of the dosage unit, for example, coatings of sugar, shellac, or other enteric agents.

The compound can be administered as a component of an elixir, suspension, syrup, wafer, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings and flavors.

The compound or a pharmaceutically acceptable prodrug or salts thereof can also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action, such as antibiotics, antifungals, anti-inflammatories, or other antivirals, including other nucleoside compounds. Solutions or suspensions used for parenteral, intradermal, subcutaneous, or topical application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parental preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

If administered intravenously, preferred carriers are physiological saline or phosphate buffered saline (PBS).

In a preferred embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation.

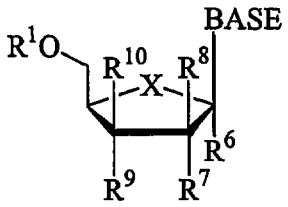
Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) are also preferred as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811 (which is incorporated herein by reference in its entirety). For example, liposome formulations may be prepared by dissolving appropriate lipid(s) (such as stearoyl phosphatidyl ethanolamine, stearoyl phosphatidyl choline, arachadoyl phosphatidyl choline, and cholesterol) in an inorganic solvent that is then evaporated, leaving behind a thin film of dried lipid on the surface of the container. An aqueous solution of the active compound or its monophosphate, diphosphate, and/or triphosphate derivatives is then introduced into the container. The container is then swirled by hand to free lipid material from the sides of the container and to disperse lipid aggregates, thereby forming the liposomal suspension.

VI. Processes for the Preparation of Active Compounds

The nucleosides of the present invention can be synthesized by any means known in the art. In particular, the synthesis of the present nucleosides can be achieved by either alkylating the appropriately modified sugar, followed by glycosylation or glycosylation followed by alkylation of the nucleoside. The following non-limiting embodiments illustrate some general methodology to obtain the nucleosides of the present invention.

A. General Synthesis of 1'-C-Branched Nucleosides

1'-C-Branched ribonucleosides of the following structure:



wherein BASE is a purine or pyrimidine base as defined herein;

R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10}can come together to form a pi bond;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate;

R^6 is an alkyl, halogeno-alkyl (i.e. CF_3), alkenyl, or alkynyl (i.e. allyl); and

X is O, S, SO_2 or CH_2

can be prepared by one of the following general methods.

1) Modification from the lactone

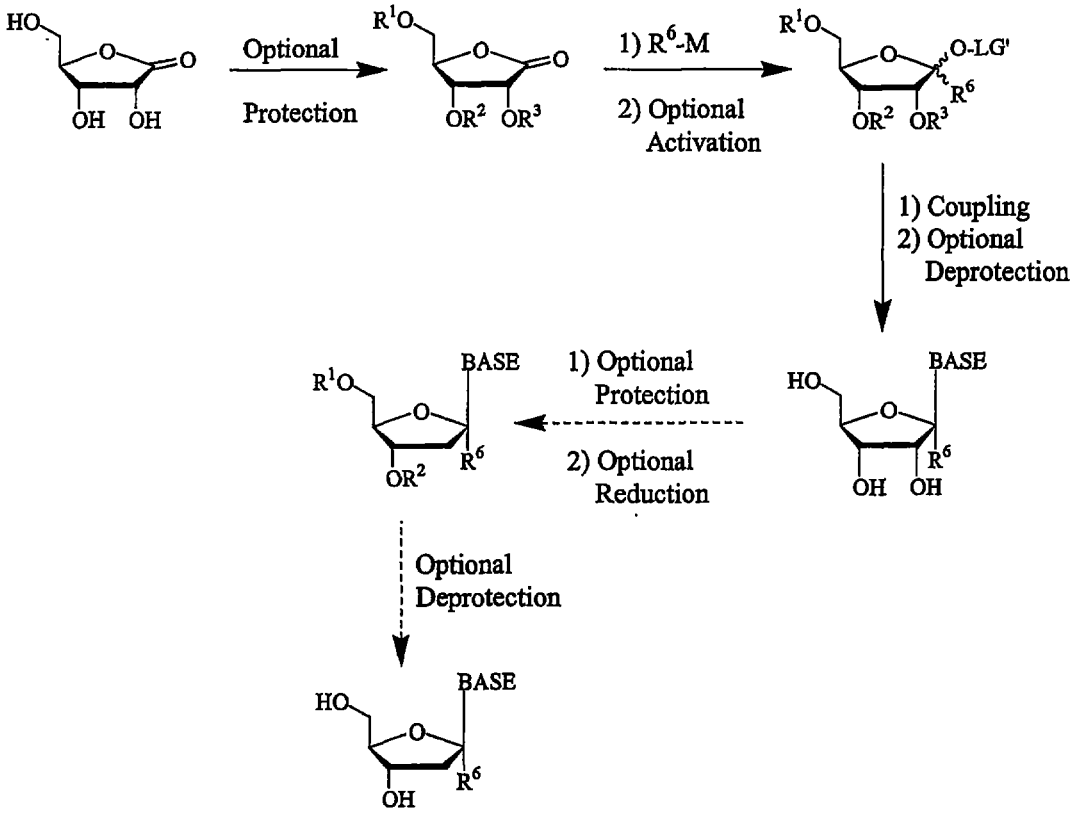
The key starting material for this process is an appropriately substituted lactone. The lactone can be purchased or can be prepared by any known means including standard epimerization, substitution and cyclization techniques. The lactone can be optionally protected with a suitable protecting group, preferably with an acyl or silyl group, by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991. The protected lactone can then be coupled with a suitable coupling agent, such as an organometallic carbon nucleophile, such as a Grignard reagent, an organolithium, lithium dialkylcopper or R^6-$SiMe_3$ in TBAF with the appropriate non-protic solvent at a suitable temperature, to give the 1'-alkylated sugar.

The optionally activated sugar can then be coupled to the BASE by methods well known to those skilled in the art, as taught by Townsend Chemistry of Nucleosides and Nucleotides, Plenum Press, 1994. For example, an acylated sugar can be coupled to a silylated base with a lewis acid, such as tin tetrachloride, titanium tetrachloride or trimethylsilyltriflate in the appropriate solvent at a suitable temperature.

Subsequently, the nucleoside can be deprotected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

In a particular embodiment, the 1'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 1**. Alternatively, deoxyribo-nucleoside is desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

Scheme 1



2. Alternative method for the preparation of 1'-C-branched nucleosides

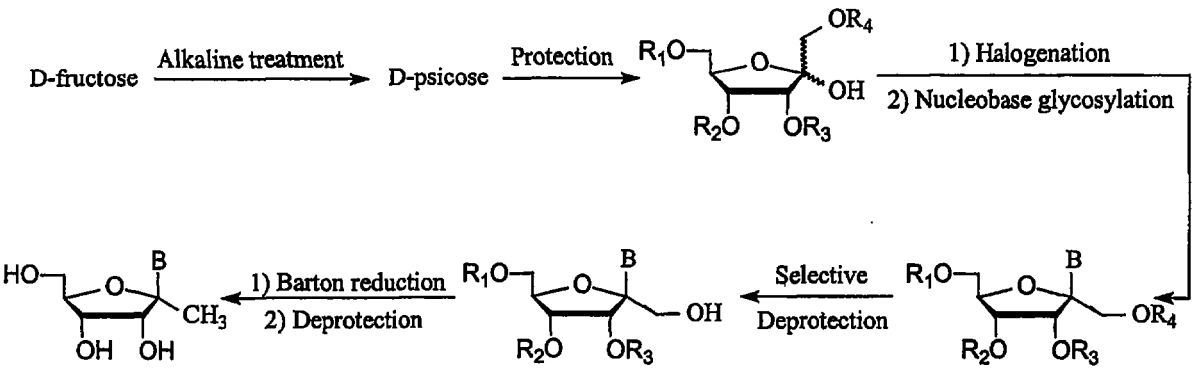
The key starting material for this process is an appropriately substituted hexose. The hexose can be purchased or can be prepared by any known means including standard epimerization (e.g. via alkaline treatment), substitution and coupling techniques. The hexose can be selectively protected to give the appropriate hexa-furanose, as taught by Townsend Chemistry of Nucleosides and Nucleotides, Plenum Press, 1994.

The 1'-hydroxyl can be optionally activated to a suitable leaving group such as an acyl group or a halogen via acylation or halogenation, respectively. The optionally activated sugar can then be coupled to the BASE by methods well known to those skilled in the art, as taught by Townsend Chemistry of Nucleosides and Nucleotides, Plenum Press, 1994. For example, an acylated sugar can be coupled to a silylated base with a lewis acid, such as tin tetrachloride, titanium tetrachloride or trimethylsilyltriflate in the appropriate solvent at a suitable temperature. Alternatively, a halo-sugar can be coupled to a silylated base with the presence of trimethylsilyltriflate.

The 1'-CH_2-OH, if protected, can be selectively deprotected by methods well known in the art. The resultant primary hydroxyl can be functionalized to yield various C-branched nucleosides. For example, the primary hydroxyl can be reduced to give the methyl, using a suitable reducing agent. Alternatively, the hydroxyl can be activated prior to reduction to facilitate the reaction; i.e. via the Barton reduction. In an alternate embodiment, the primary hydroxyl can be oxidized to the aldehyde, then coupled with a carbon nucleophile, such as a Grignard reagent, an organolithium, lithium dialkylcopper or R^6-$SiMe_3$ in TBAF with the appropriate non-protic solvent at a suitable temperature.

In a particular embodiment, the 1'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 2**. Alternatively, deoxyribo-nucleoside is desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

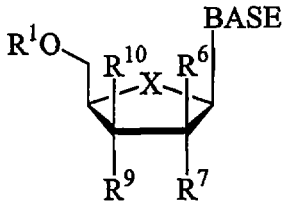
Scheme 2



In addition, the L-enantiomers corresponding to the compounds of the invention can be prepared following the same general methods (1 or 2), beginning with the corresponding L-sugar or nucleoside L-enantiomer as starting material.

B. General Synthesis of 2'-C-Branched Nucleosides

2'-C-Branched ribonucleosides of the following structure:



wherein BASE is a purine or pyrimidine base as defined herein;

R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a pi bond;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate;

R^6 is an alkyl, halogeno-alkyl (i.e. CF_3), alkenyl, or alkynyl (i.e. allyl); and

X is O, S, SO_2 or CH_2

can be prepared by one of the following general methods.

1. Glycosylation of the nucleobase with an appropriately modified sugar

The key starting material for this process is an appropriately substituted sugar with a 2'-OH and 2'-H, with the appropriate leaving group (LG), for example an acyl group or a

halogen. The sugar can be purchased or can be prepared by any known means including standard epimerization, substitution, oxidation and reduction techniques. The substituted sugar can then be oxidized with the appropriate oxidizing agent in a compatible solvent at a suitable temperature to yield the 2'-modified sugar. Possible oxidizing agents are Jones reagent (a mixture of chromic acid and sulfuric acid), Collins's reagent (dipyridine Cr(VI) oxide, Corey's reagent (pyridinium chlorochromate), pyridinium dichromate, acid dichromate, potassium permanganate, MnO_2, ruthenium tetroxide, phase transfer catalysts such as chromic acid or permanganate supported on a polymer, Cl_2-pyridine, H_2O_2-ammonium molybdate, $NaBrO_2$-CAN, NaOCl in HOAc, copper chromite, copper oxide, Raney nickel, palladium acetate, Meerwin-Pondorf-Verley reagent (aluminum *t*-butoxide with another ketone) and *N*-bromosuccinimide.

Then coupling of an organometallic carbon nucleophile, such as a Grignard reagent, an organolithium, lithium dialkylcopper or R^6-$SiMe_3$ in TBAF with the ketone with the appropriate non-protic solvent at a suitable temperature, yields the 2'-alkylated sugar. The alkylated sugar can be optionally protected with a suitable protecting group, preferably with an acyl or silyl group, by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

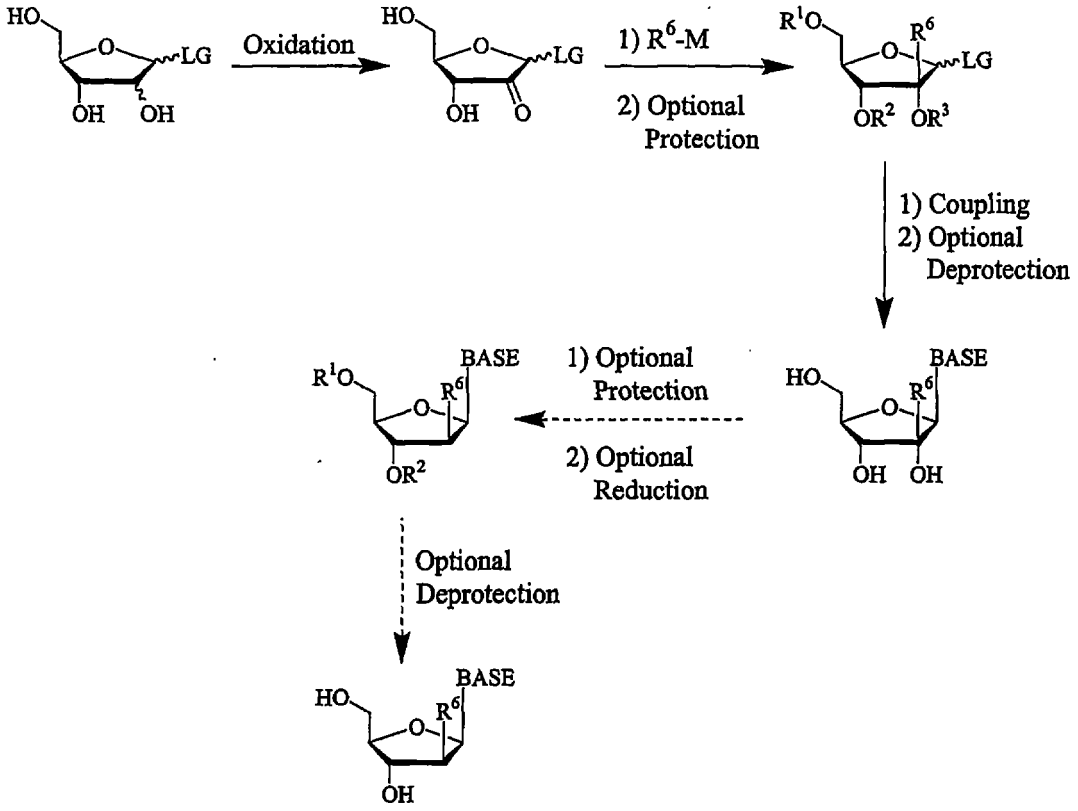
The optionally protected sugar can then be coupled to the BASE by methods well known to those skilled in the art, as taught by Townsend Chemistry of Nucleosides and Nucleotides, Plenum Press, 1994. For example, an acylated sugar can be coupled to a silylated base with a lewis acid, such as tin tetrachloride, titanium tetrachloride or trimethylsilyltriflate in the appropriate solvent at a suitable temperature. Alternatively, a halo-sugar can be coupled to a silylated base with the presence of trimethylsilyltriflate.

Subsequently, the nucleoside can be deprotected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

In a particular embodiment, the 2'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 3**. Alternatively, deoxyribo-nucleoside is desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-

OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

Scheme 3



2. Modification of a pre-formed nucleoside

The key starting material for this process is an appropriately substituted nucleoside with a 2'-OH and 2'-H. The nucleoside can be purchased or can be prepared by any known means including standard coupling techniques. The nucleoside can be optionally protected with suitable protecting groups, preferably with acyl or silyl groups, by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

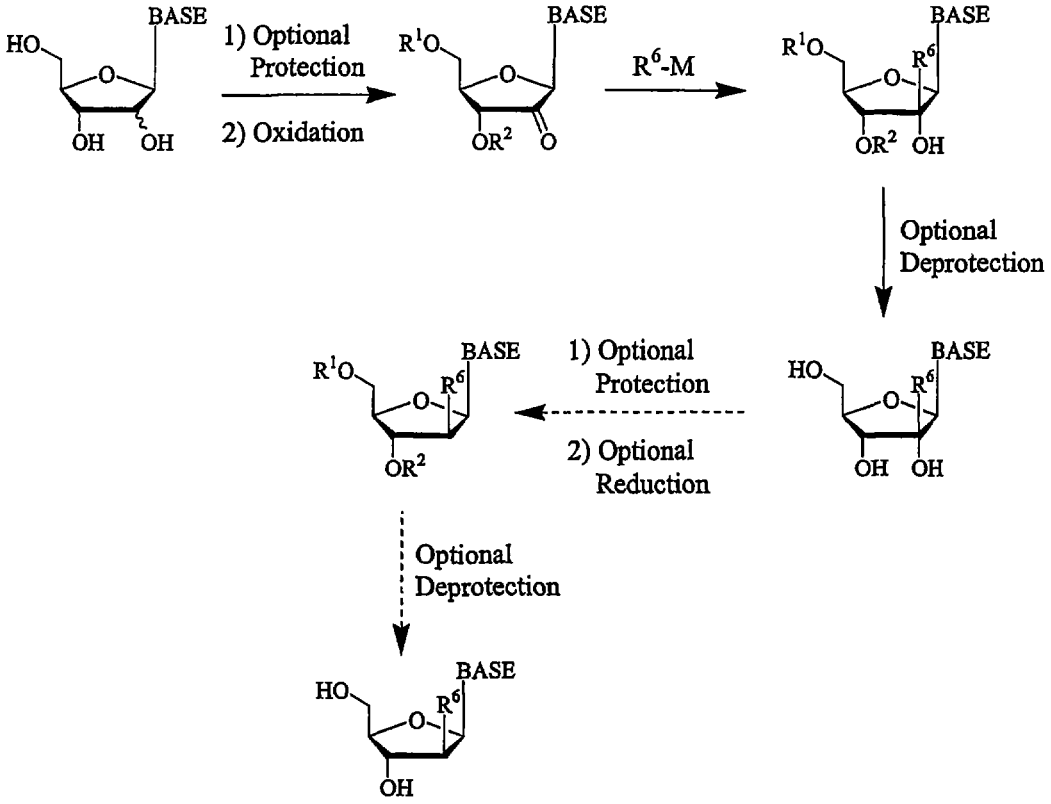
The appropriately protected nucleoside can then be oxidized with the appropriate oxidizing agent in a compatible solvent at a suitable temperature to yield the 2'-modified

sugar. Possible oxidizing agents are Jones reagent (a mixture of chromic acid and sulfuric acid), Collins's reagent (dipyridine Cr(VI) oxide, Corey's reagent (pyridinium chlorochromate), pyridinium dichromate, acid dichromate, potassium permanganate, MnO_2, ruthenium tetroxide, phase transfer catalysts such as chromic acid or permanganate supported on a polymer, Cl_2-pyridine, H_2O_2-ammonium molybdate, $NaBrO_2$-CAN, NaOCl in HOAc, copper chromite, copper oxide, Raney nickel, palladium acetate, Meerwin-Pondorf-Verley reagent (aluminum *t*-butoxide with another ketone) and *N*-bromosuccinimide.

Subsequently, the nucleoside can be deprotected by methods well known to those skilled in the art, as taught by GreeneGreene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

In a particular embodiment, the 2'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 4**. Alternatively, deoxyribo-nucleoside is desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

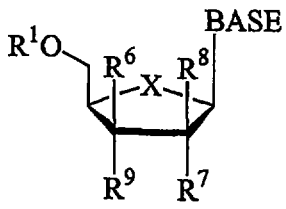
Scheme 4



In another embodiment of the invention, the L-enantiomers are desired. Therefore, the L-enantiomers can be corresponding to the compounds of the invention can be prepared following the same foregoing general methods, beginning with the corresponding L-sugar or nucleoside L-enantiomer as starting material.

C. General Synthesis of 3'-C-Branched Nucleosides

3'-C-Branched ribonucleosides of the following structure:



wherein BASE is a purine or pyrimidine base as defined herein;

R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a pi bond;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 is independently H or phosphate;

R^6 is an alkyl, halogeno-alkyl (i.e. CF_3), alkenyl, or alkynyl (i.e. allyl); and

X is O, S, SO_2 or CH_2

can be prepared by one of the following general methods.

1 Glycosylation of the nucleobase with an appropriately modified sugar

The key starting material for this process is an appropriately substituted sugar with a 3'-OH and 3'-H, with the appropriate leaving group (LG), for example an acyl group or a halogen. The sugar can be purchased or can be prepared by any known means including standard epimerization, substitution, oxidation and reduction techniques. The substituted sugar can then be oxidized with the appropriate oxidizing agent in a compatible solvent at a suitable temperature to yield the 3'-modified sugar. Possible oxidizing agents are Jones reagent (a mixture of chromic acid and sulfuric acid), Collins's reagent (dipyridine Cr(VI) oxide, Corey's reagent (pyridinium chlorochromate), pyridinium dichromate, acid dichromate, potassium permanganate, MnO_2, ruthenium tetroxide, phase transfer catalysts such as chromic acid or permanganate supported on a polymer, Cl_2-pyridine, H_2O_2-ammonium molybdate, $NaBrO_2$-CAN, NaOCl in HOAc, copper chromite, copper oxide, Raney nickel, palladium acetate, Meerwin-Pondorf-Verley reagent (aluminum *t*-butoxide with another ketone) and *N*-bromosuccinimide.

Then coupling of an organometallic carbon nucleophile, such as a Grignard reagent, an organolithium, lithium dialkylcopper or R^6-$SiMe_3$ in TBAF with the ketone with the appropriate non-protic solvent at a suitable temperature, yields the 3'-C-branched sugar. The 3'-C-branched sugar can be optionally protected with a suitable protecting group, preferably with an acyl or silyl group, by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

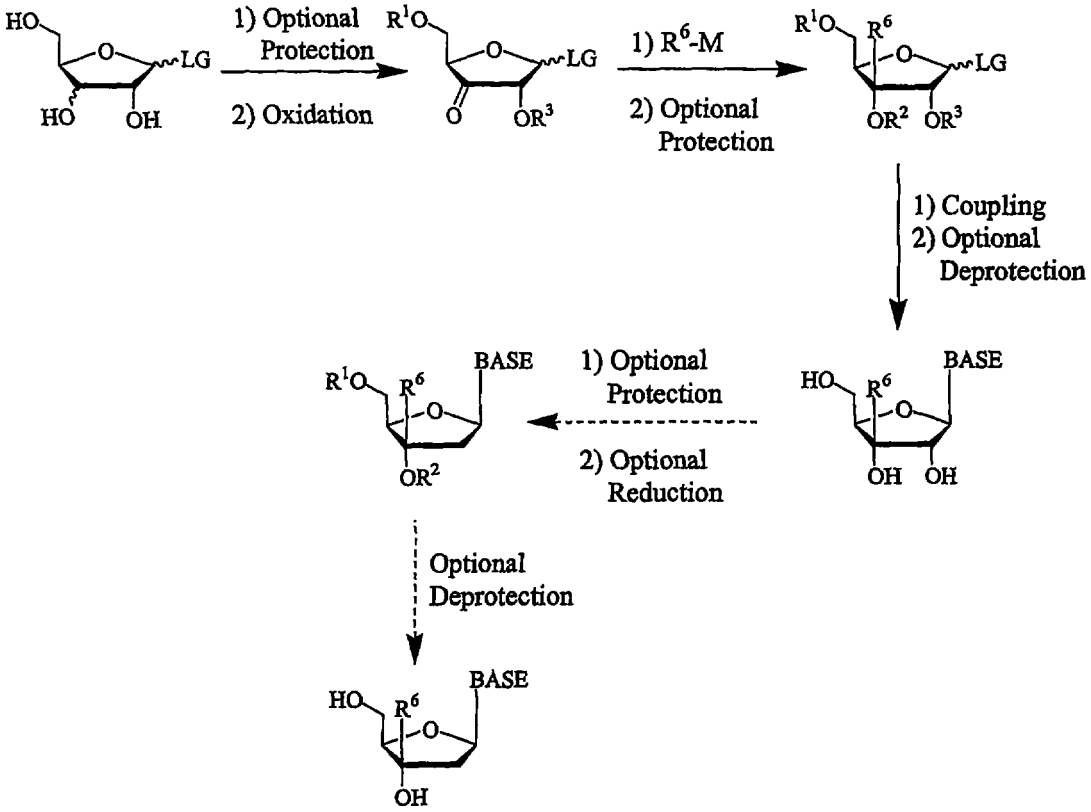
The optionally protected sugar can then be coupled to the BASE by methods well known to those skilled in the art, as taught by Townsend Chemistry of Nucleosides and Nucleotides, Plenum Press, 1994. For example, an acylated sugar can be coupled to a silylated base with a lewis acid, such as tin tetrachloride, titanium tetrachloride or trimethylsilyltriflate in the appropriate solvent at a suitable temperature. Alternatively, a halo-sugar can be coupled to a silylated base with the presence of trimethylsilyltriflate.

Subsequently, the nucleoside can be deprotected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

In a particular embodiment, the 3'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 5**. Alternatively, deoxyribo-nucleoside is

desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

Scheme 5



2. Modification of a pre-formed nucleoside

The key starting material for this process is an appropriately substituted nucleoside with a 3'-OH and 3'-H. The nucleoside can be purchased or can be prepared by any known means including standard coupling techniques. The nucleoside can be optionally protected with suitable protecting groups, preferably with acyl or silyl groups, by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

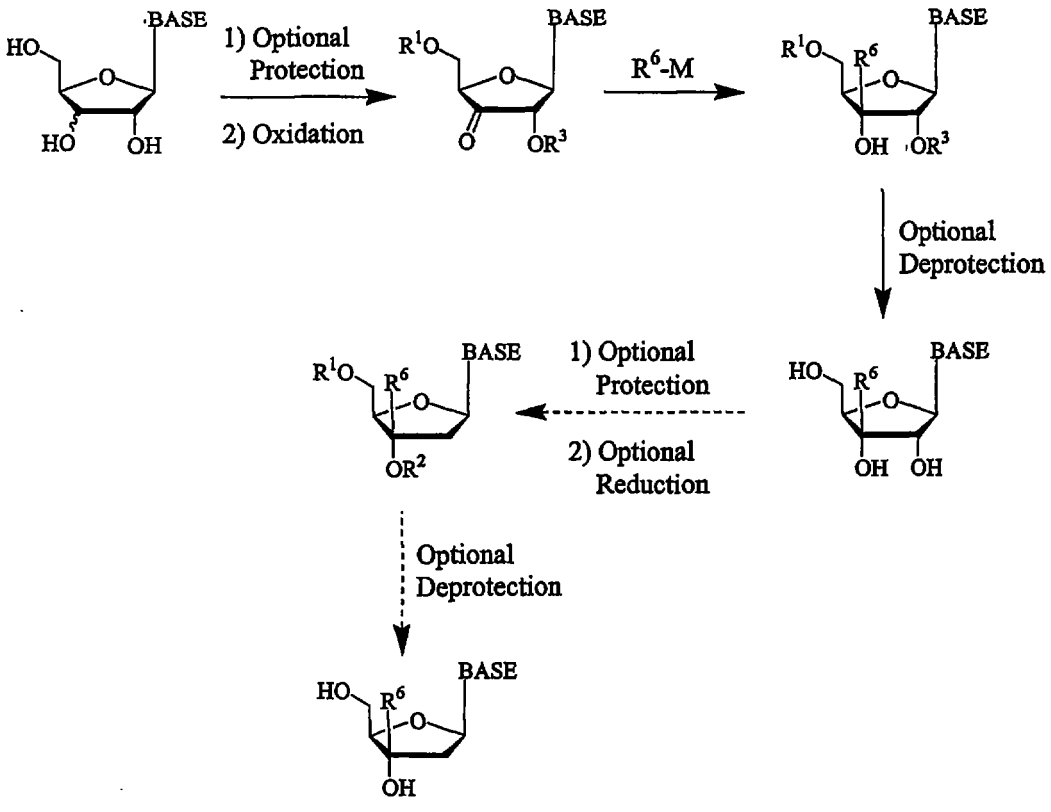
The appropriately protected nucleoside can then be oxidized with the appropriate oxidizing agent in a compatible solvent at a suitable temperature to yield the 2'-modified

sugar. Possible oxidizing agents are Jones reagent (a mixture of chromic acid and sulfuric acid), Collins's reagent (dipyridine Cr(VI) oxide, Corey's reagent (pyridinium chlorochromate), pyridinium dichromate, acid dichromate, potassium permanganate, MnO_2, ruthenium tetroxide, phase transfer catalysts such as chromic acid or permanganate supported on a polymer, Cl_2-pyridine, H_2O_2-ammonium molybdate, $NaBrO_2$-CAN, NaOCl in HOAc, copper chromite, copper oxide, Raney nickel, palladium acetate, Meerwin-Pondorf-Verley reagent (aluminum *t*-butoxide with another ketone) and *N*-bromosuccinimide.

Subsequently, the nucleoside can be deprotected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991.

In a particular embodiment, the 3'-C-branched ribonucleoside is desired. The synthesis of a ribonucleoside is shown in **Scheme 6**. Alternatively, deoxyribo-nucleoside is desired. To obtain these nucleosides, the formed ribonucleoside can optionally be protected by methods well known to those skilled in the art, as taught by Greene *et al.* Protective Groups in Organic Synthesis, John Wiley and Sons, Second Edition, 1991, and then the 2'-OH can be reduced with a suitable reducing agent. Optionally, the 2'-hydroxyl can be activated to facilitate reduction; i.e. via the Barton reduction.

Scheme 6



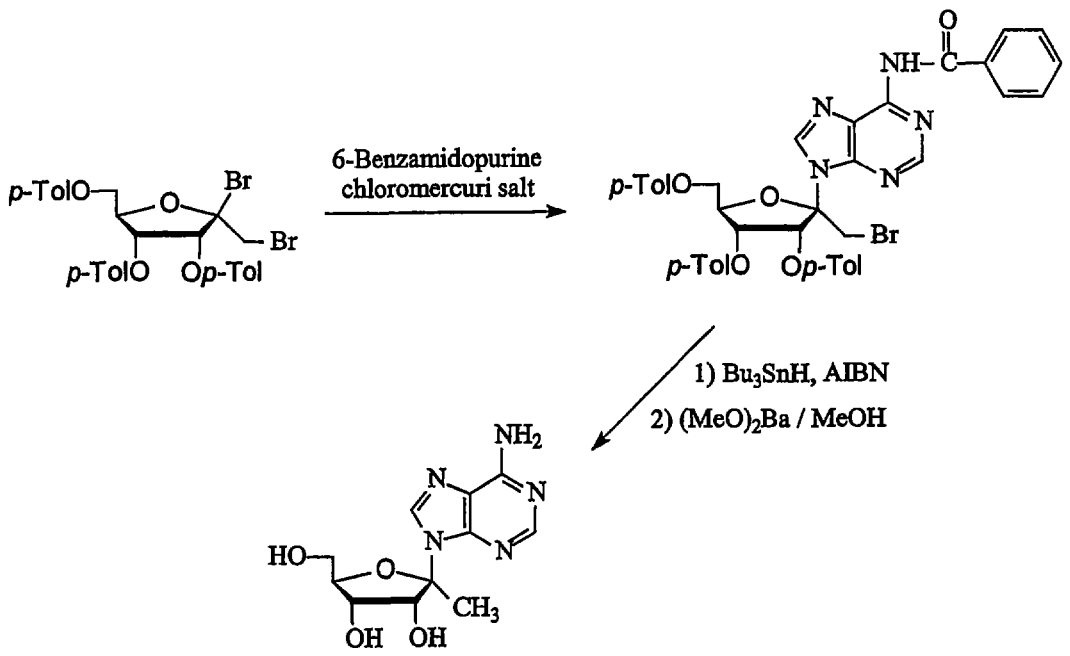
In another embodiment of the invention, the L-enantiomers are desired. Therefore, the L-enantiomers can be corresponding to the compounds of the invention can be prepared following the same foregoing general methods, beginning with the corresponding L-sugar or nucleoside L-enantiomer as starting material.

EXAMPLES

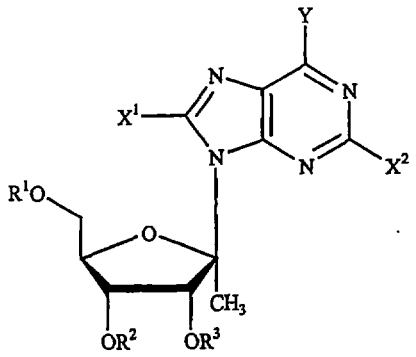
Example 1: Preparation of 1'-C-methylriboadenine via 6-amino-9-(1-deoxy-β-D-psicofuranosyl)purine

The title compound could also be prepared according to a published procedure (J. Farkas, and F. Sorm, "Nucleic acid components and their analogues. XCIV. Synthesis of 6-amino-9-(1-deoxy-β-D-psicofuranosyl)purine" *Collect. Czech. Chem. Commun.* **1967**, 32, 2663-2667; J. Farkas", *Collect. Czech. Chem. Commun.* **1966**, 31, 1535) (**Scheme 7**).

Scheme 7



In a similar manner, but using the appropriate sugar and pyrimidine or purine bases, the following nucleosides of Formula I are prepared.



(I)

wherein:

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	H	H
H	H	H	H	H	NH_2
H	H	H	H	H	NH-cyclopropyl
H	H	H	H	H	NH-methyl
H	H	H	H	H	NH-ethyl
H	H	H	H	H	NH-acetyl
H	H	H	H	H	OH
H	H	H	H	H	OMe
H	H	H	H	H	OEt
H	H	H	H	H	O-cyclopropyl
H	H	H	H	H	O-acetyl
H	H	H	H	H	SH
H	H	H	H	H	SMe
H	H	H	H	H	SEt
H	H	H	H	H	S-cyclopropyl
H	H	H	H	H	F
H	H	H	H	H	Cl
H	H	H	H	H	Br
H	H	H	H	H	I
monophosphate	H	H	H	H	NH_2
monophosphate	H	H	H	H	NH-acetyl
monophosphate	H	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	H	NH-methyl

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	H	H	H	H	NH-ethyl
monophosphate	H	H	H	H	OH
monophosphate	H	H	H	H	O-acetyl
monophosphate	H	H	H	H	OMe
monophosphate	H	H	H	H	OEt
monophosphate	H	H	H	H	O-cyclopropyl
monophosphate	H	H	H	H	SH
monophosphate	H	H	H	H	SMe
monophosphate	H	H	H	H	SEt
monophosphate	H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	H	F
monophosphate	H	H	H	H	Cl
monophosphate	H	H	H	H	Br
monophosphate	H	H	H	H	I
diphosphate	H	H	H	H	NH_2
diphosphate	H	H	H	H	NH-acetyl
diphosphate	H	H	H	H	NH-cyclopropyl
diphosphate	H	H	H	H	NH-methyl
diphosphate	H	H	H	H	NH-ethyl
diphosphate	H	H	H	H	OH
diphosphate	H	H	H	H	O-acetyl
diphosphate	H	H	H	H	OMe
diphosphate	H	H	H	H	OEt
diphosphate	H	H	H	H	O-cyclopropyl
diphosphate	H	H	H	H	SH
diphosphate	H	H	H	H	SMe
diphosphate	H	H	H	H	SEt
diphosphate	H	H	H	H	S-cyclopropyl
diphosphate	H	H	H	H	F
diphosphate	H	H	H	H	Cl
diphosphate	H	H	H	H	Br

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	H	I
triphosphate	H	H	H	H	NH_2
triphosphate	H	H	H	H	NH-acetyl
triphosphate	H	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	H	NH-methyl
triphosphate	H	H	H	H	NH-ethyl
triphosphate	H	H	H	H	OH
triphosphate	H	H	H	H	OMe
triphosphate	H	H	H	H	OEt
triphosphate	H	H	H	H	O-cyclopropyl
triphosphate	H	H	H	H	O-acetyl
triphosphate	H	H	H	H	SH
triphosphate	H	H	H	H	SMe
triphosphate	H	H	H	H	SEt
triphosphate	H	H	H	H	S-cyclopropyl
triphosphate	H	H	H	H	F
triphosphate	H	H	H	H	Cl
triphosphate	H	H	H	H	Br
triphosphate	H	H	H	H	I
monophosphate	monophosphate	monophosphate	H	H	NH_2
monophosphate	monophosphate	monophosphate	H	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	H	OH
monophosphate	monophosphate	monophosphate	H	H	F
monophosphate	monophosphate	monophosphate	H	H	Cl
diphosphate	diphosphate	diphosphate	H	H	NH_2
diphosphate	diphosphate	diphosphate	H	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	H	OH
diphosphate	diphosphate	diphosphate	H	H	F
diphosphate	diphosphate	diphosphate	H	H	Cl
triphosphate	triphosphate	triphosphate	H	H	NH_2
triphosphate	triphosphate	triphosphate	H	H	NH-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	triphosphate	triphosphate	H	H	OH
triphosphate	triphosphate	triphosphate	H	H	F
triphosphate	triphosphate	triphosphate	H	H	Cl
H	H	H	F	H	NH_2
H	H	H	F	H	NH-cyclopropyl
H	H	H	F	H	OH
H	H	H	F	H	F
H	H	H	F	H	Cl
H	H	H	Cl	H	NH_2
H	H	H	Cl	H	NH-cyclopropyl
H	H	H	Cl	H	OH
H	H	H	Cl	H	F
H	H	H	Cl	H	Cl
H	H	H	Br	H	NH_2
H	H	H	Br	H	NH-cyclopropyl
H	H	H	Br	H	OH
H	H	H	Br	H	F
H	H	H	Br	H	Cl
H	H	H	NH_2	H	NH_2
H	H	H	NH_2	H	NH-cyclopropyl
H	H	H	NH_2	H	OH
H	H	H	NH_2	H	F
H	H	H	NH_2	H	Cl
H	H	H	SH	H	NH_2
H	H	H	SH	H	NH-cyclopropyl
H	H	H	SH	H	OH
H	H	H	SH	H	F
H	H	H	SH	H	Cl
acetyl	H	H	H	H	NH_2
acetyl	H	H	H	H	NH-cyclopropyl
acetyl	H	H	H	H	OH

R^1	R^2	R^3	X^1	X^2	Y
acetyl	H	H	H	H	F
acetyl	H	H	H	H	Cl
acetyl	H	H	F	H	NH_2
acetyl	H	H	F	H	NH-cyclopropyl
acetyl	H	H	F	H	OH
acetyl	H	H	F	H	F
acetyl	H	H	F	H	Cl
H	acetyl	acetyl	H	H	NH_2
H	acetyl	acetyl	H	H	NH-cyclopropyl
H	acetyl	acetyl	H	H	OH
H	acetyl	acetyl	H	H	F
H	acetyl	acetyl	H	H	Cl
acetyl	acetyl	acetyl	H	H	NH_2
acetyl	acetyl	acetyl	H	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	H	OH
acetyl	acetyl	acetyl	H	H	F
acetyl	acetyl	acetyl	H	H	Cl
monophosphate	acetyl	acetyl	H	H	NH_2
monophosphate	acetyl	acetyl	H	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	H	OH
monophosphate	acetyl	acetyl	H	H	F
monophosphate	acetyl	acetyl	H	H	Cl
diphosphate	acetyl	acetyl	H	H	NH_2
diphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	H	OH
diphosphate	acetyl	acetyl	H	H	F
diphosphate	acetyl	acetyl	H	H	Cl
triphosphate	acetyl	acetyl	H	H	NH_2
triphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	H	OH
triphosphate	acetyl	acetyl	H	H	F

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	acetyl	acetyl	H	H	Cl
H	H	H	H	NH_2	H
H	H	H	H	NH_2	NH_2
H	H	H	H	NH_2	NH-cyclopropyl
H	H	H	H	NH_2	NH-methyl
H	H	H	H	NH_2	NH-ethyl
H	H	H	H	NH_2	NH-acetyl
H	H	H	H	NH_2	OH
H	H	H	H	NH_2	OMe
H	H	H	H	NH_2	OEt
H	H	H	H	NH_2	O-cyclopropyl
H	H	H	H	NH_2	O-acetyl
H	H	H	H	NH_2	SH
H	H	H	H	NH_2	SMe
H	H	H	H	NH_2	SEt
H	H	H	H	NH_2	S-cyclopropyl
H	H	H	H	NH_2	F
H	H	H	H	NH_2	Cl
H	H	H	H	NH_2	Br
H	H	H	H	NH_2	I
monophosphate	H	H	H	NH_2	NH_2
monophosphate	H	H	H	NH_2	NH-acetyl
monophosphate	H	H	H	NH_2	NH-cyclopropyl
monophosphate	H	H	H	NH_2	NH-methyl
monophosphate	H	H	H	NH_2	NH-ethyl
monophosphate	H	H	H	NH_2	OH
monophosphate	H	H	H	NH_2	O-acetyl
monophosphate	H	H	H	NH_2	OMe
monophosphate	H	H	H	NH_2	OEt
monophosphate	H	H	H	NH_2	O-cyclopropyl
monophosphate	H	H	H	NH_2	SH

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	H	H	H	NH_2	SMe
monophosphate	H	H	H	NH_2	SEt
monophosphate	H	H	H	NH_2	S-cyclopropyl
monophosphate	H	H	H	NH_2	F
monophosphate	H	H	H	NH_2	Cl
monophosphate	H	H	H	NH_2	Br
monophosphate	H	H	H	NH_2	I
diphosphate	H	H	H	NH_2	NH_2
diphosphate	H	H	H	NH_2	NH-acetyl
diphosphate	H	H	H	NH_2	NH-cyclopropyl
diphosphate	H	H	H	NH_2	NH-methyl
diphosphate	H	H	H	NH_2	NH-ethyl
diphosphate	H	H	H	NH_2	OH
diphosphate	H	H	H	NH_2	O-acetyl
diphosphate	H	H	H	NH_2	OMe
diphosphate	H	H	H	NH_2	OEt
diphosphate	H	H	H	NH_2	O-cyclopropyl
diphosphate	H	H	H	NH_2	SH
diphosphate	H	H	H	NH_2	SMe
diphosphate	H	H	H	NH_2	SEt
diphosphate	H	H	H	NH_2	S-cyclopropyl
diphosphate	H	H	H	NH_2	F
diphosphate	H	H	H	NH_2	Cl
diphosphate	H	H	H	NH_2	Br
diphosphate	H	H	H	NH_2	I
triphosphate	H	H	H	NH_2	NH_2
triphosphate	H	H	H	NH_2	NH-acetyl
triphosphate	H	H	H	NH_2	NH-cyclopropyl
triphosphate	H	H	H	NH_2	NH-methyl
triphosphate	H	H	H	NH_2	NH-ethyl
triphosphate	H	H	H	NH_2	OH

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	H	H	H	NH_2	OMe
triphosphate	H	H	H	NH_2	OEt
triphosphate	H	H	H	NH_2	O-cyclopropyl
triphosphate	H	H	H	NH_2	O-acetyl
triphosphate	H	H	H	NH_2	SH
triphosphate	H	H	H	NH_2	SMe
triphosphate	H	H	H	NH_2	SEt
triphosphate	H	H	H	NH_2	S-cyclopropyl
triphosphate	H	H	H	NH_2	F
triphosphate	H	H	H	NH_2	Cl
triphosphate	H	H	H	NH_2	Br
triphosphate	H	H	H	NH_2	I
monophosphate	monophosphate	monophosphate	H	NH_2	NH_2
monophosphate	monophosphate	monophosphate	H	NH_2	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2	OH
monophosphate	monophosphate	monophosphate	H	NH_2	F
monophosphate	monophosphate	monophosphate	H	NH_2	Cl
diphosphate	diphosphate	diphosphate	H	NH_2	NH_2
diphosphate	diphosphate	diphosphate	H	NH_2	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	NH_2	OH
diphosphate	diphosphate	diphosphate	H	NH_2	F
diphosphate	diphosphate	diphosphate	H	NH_2	Cl
triphosphate	triphosphate	triphosphate	H	NH_2	NH_2
triphosphate	triphosphate	triphosphate	H	NH_2	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	NH_2	OH
triphosphate	triphosphate	triphosphate	H	NH_2	F
triphosphate	triphosphate	triphosphate	H	NH_2	Cl
H	H	H	F	NH_2	NH_2
H	H	H	F	NH_2	NH-cyclopropyl
H	H	H	F	NH_2	OH
H	H	H	F	NH_2	F

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	F	NH_2	Cl
H	H	H	Cl	NH_2	NH_2
H	H	H	Cl	NH_2	NH-cyclopropyl
H	H	H	Cl	NH_2	OH
H	H	H	Cl	NH_2	F
H	H	H	Cl	NH_2	Cl
H	H	H	Br	NH_2	NH_2
H	H	H	Br	NH_2	NH-cyclopropyl
H	H	H	Br	NH_2	OH
H	H	H	Br	NH_2	F
H	H	H	Br	NH_2	Cl
H	H	H	NH_2	NH_2	NH_2
H	H	H	NH_2	NH_2	NH-cyclopropyl
H	H	H	NH_2	NH_2	OH
H	H	H	NH_2	NH_2	F
H	H	H	NH_2	NH_2	Cl
H	H	H	SH	NH_2	NH_2
H	H	H	SH	NH_2	NH-cyclopropyl
H	H	H	SH	NH_2	OH
H	H	H	SH	NH_2	F
H	H	H	SH	NH_2	Cl
acetyl	H	H	H	NH_2	NH_2
acetyl	H	H	H	NH_2	NH-cyclopropyl
acetyl	H	H	H	NH_2	OH
acetyl	H	H	H	NH_2	F
acetyl	H	H	H	NH_2	Cl
acetyl	H	H	F	NH_2	NH_2
acetyl	H	H	F	NH_2	NH-cyclopropyl
acetyl	H	H	F	NH_2	OH
acetyl	H	H	F	NH_2	F
acetyl	H	H	F	NH_2	Cl

R^1	R^2	R^3	X^1	X^2	Y
H	acetyl	acetyl	H	NH_2	NH_2
H	acetyl	acetyl	H	NH_2	NH-cyclopropyl
H	acetyl	acetyl	H	NH_2	OH
H	acetyl	acetyl	H	NH_2	F
H	acetyl	acetyl	H	NH_2	Cl
acetyl	acetyl	acetyl	H	NH_2	NH_2
acetyl	acetyl	acetyl	H	NH_2	NH-cyclopropyl
acetyl	acetyl	acetyl	H	NH_2	OH
acetyl	acetyl	acetyl	H	NH_2	F
acetyl	acetyl	acetyl	H	NH_2	Cl
monophosphate	acetyl	acetyl	H	NH_2	NH_2
monophosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	NH_2	OH
monophosphate	acetyl	acetyl	H	NH_2	F
monophosphate	acetyl	acetyl	H	NH_2	Cl
diphosphate	acetyl	acetyl	H	NH_2	NH_2
diphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	NH_2	OH
diphosphate	acetyl	acetyl	H	NH_2	F
diphosphate	acetyl	acetyl	H	NH_2	Cl
triphosphate	acetyl	acetyl	H	NH_2	NH_2
triphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	NH_2	OH
triphosphate	acetyl	acetyl	H	NH_2	F
triphosphate	acetyl	acetyl	H	NH_2	Cl
H	H	H	H	Cl	H
H	H	H	H	Cl	H
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	NH-methyl
H	H	H	H	Cl	NH-ethyl

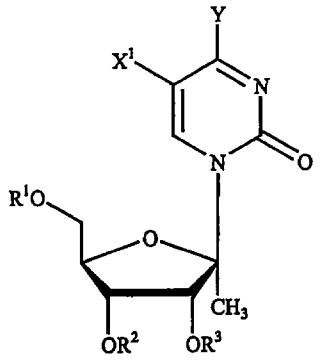
R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	Cl	NH-acetyl
H	H	H	H	Cl	OH
H	H	H	H	Cl	OMe
H	H	H	H	Cl	OEt
H	H	H	H	Cl	O-cyclopropyl
H	H	H	H	Cl	O-acetyl
H	H	H	H	Cl	SH
H	H	H	H	Cl	SMe
H	H	H	H	Cl	SEt
H	H	H	H	Cl	S-cyclopropyl
monophosphate	H	H	H	Cl	NH_2
monophosphate	H	H	H	Cl	NH-acetyl
monophosphate	H	H	H	Cl	NH-cyclopropyl
monophosphate	H	H	H	Cl	NH-methyl
monophosphate	H	H	H	Cl	NH-ethyl
monophosphate	H	H	H	Cl	OH
monophosphate	H	H	H	Cl	O-acetyl
monophosphate	H	H	H	Cl	OMe
monophosphate	H	H	H	Cl	OEt
monophosphate	H	H	H	Cl	O-cyclopropyl
monophosphate	H	H	H	Cl	SH
monophosphate	H	H	H	Cl	SMe
monophosphate	H	H	H	Cl	SEt
monophosphate	H	H	H	Cl	S-cyclopropyl
diphosphate	H	H	H	Cl	NH_2
diphosphate	H	H	H	Cl	NH-acetyl
diphosphate	H	H	H	Cl	NH-cyclopropyl
diphosphate	H	H	H	Cl	NH-methyl
diphosphate	H	H	H	Cl	NH-ethyl
diphosphate	H	H	H	Cl	OH
diphosphate	H	H	H	Cl	O-acetyl

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	Cl	OMe
diphosphate	H	H	H	Cl	OEt
diphosphate	H	H	H	Cl	O-cyclopropyl
diphosphate	H	H	H	Cl	SH
diphosphate	H	H	H	Cl	SMe
diphosphate	H	H	H	Cl	SEt
diphosphate	H	H	H	Cl	S-cyclopropyl
triphosphate	H	H	H	Cl	NH_2
triphosphate	H	H	H	Cl	NH-acetyl
triphosphate	H	H	H	Cl	NH-cyclopropyl
triphosphate	H	H	H	Cl	NH-methyl
triphosphate	H	H	H	Cl	NH-ethyl
triphosphate	H	H	H	Cl	OH
triphosphate	H	H	H	Cl	OMe
triphosphate	H	H	H	Cl	OEt
triphosphate	H	H	H	Cl	O-cyclopropyl
triphosphate	H	H	H	Cl	O-acetyl
triphosphate	H	H	H	Cl	SH
triphosphate	H	H	H	Cl	SMe
triphosphate	H	H	H	Cl	SEt
triphosphate	H	H	H	Cl	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	NH_2
monophosphate	monophosphate	monophosphate	H	Cl	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	OH
diphosphate	diphosphate	diphosphate	H	Cl	NH_2
diphosphate	diphosphate	diphosphate	H	Cl	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	Cl	OH
triphosphate	triphosphate	triphosphate	H	Cl	NH_2
triphosphate	triphosphate	triphosphate	H	Cl	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	Cl	OH
H	H	H	F	Cl	NH_2

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	F	Cl	NH-cyclopropyl
H	H	H	F	Cl	OH
H	H	H	Cl	Cl	NH_2
H	H	H	Cl	Cl	NH-cyclopropyl
H	H	H	Cl	Cl	OH
H	H	H	Br	Cl	NH_2
H	H	H	Br	Cl	NH-cyclopropyl
H	H	H	Br	Cl	OH
H	H	H	NH_2	Cl	NH_2
H	H	H	NH_2	Cl	NH-cyclopropyl
H	H	H	NH_2	Cl	OH
H	H	H	SH	Cl	NH_2
H	H	H	SH	Cl	NH-cyclopropyl
H	H	H	SH	Cl	OH
acetyl	H	H	H	Cl	NH_2
acetyl	H	H	H	Cl	NH-cyclopropyl
acetyl	H	H	H	Cl	OH
acetyl	H	H	F	Cl	NH_2
acetyl	H	H	F	Cl	NH-cyclopropyl
acetyl	H	H	F	Cl	OH
H	acetyl	acetyl	H	Cl	NH_2
H	acetyl	acetyl	H	Cl	NH-cyclopropyl
H	acetyl	acetyl	H	Cl	OH
acetyl	acetyl	acetyl	H	Cl	NH_2
acetyl	acetyl	acetyl	H	Cl	NH-cyclopropyl
acetyl	acetyl	acetyl	H	Cl	OH
monophosphate	acetyl	acetyl	H	Cl	NH_2
monophosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	Cl	OH
diphosphate	acetyl	acetyl	H	Cl	NH_2
diphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	acetyl	acetyl	H	Cl	OH
triphosphate	acetyl	acetyl	H	Cl	NH_2
triphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	Cl	OH
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	OH
H	H	H	H	Br	NH_2
H	H	H	H	Br	NH-cyclopropyl
H	H	H	H	Br	OH

Alternatively, the following nucleosides of Formula IV are prepared, using the appropriate sugar and pyrimidine or purine bases.



(IV)

wherein:

R^1	R^2	R^3	X^1	Y
H	H	H	H	H
H	H	H	H	NH_2
H	H	H	H	NH-cyclopropyl
H	H	H	H	NH-methyl
H	H	H	H	NH-ethyl
H	H	H	H	NH-acetyl
H	H	H	H	OH

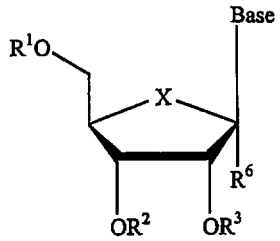
R^1	R^2	R^3	X^1	Y
H	H	H	H	OMe
H	H	H	H	OEt
H	H	H	H	O-cyclopropyl
H	H	H	H	O-acetyl
H	H	H	H	SH
H	H	H	H	SMe
H	H	H	H	SEt
H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	NH_2
monophosphate	H	H	H	NH-acetyl
monophosphate	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	NH-methyl
monophosphate	H	H	H	NH-ethyl
monophosphate	H	H	H	OH
monophosphate	H	H	H	O-acetyl
monophosphate	H	H	H	OMe
monophosphate	H	H	H	OEt
monophosphate	H	H	H	O-cyclopropyl
monophosphate	H	H	H	SH
monophosphate	H	H	H	SMe
monophosphate	H	H	H	SEt
monophosphate	H	H	H	S-cyclopropyl
diphosphate	H	H	H	NH_2
diphosphate	H	H	H	NH-acetyl
diphosphate	H	H	H	NH-cyclopropyl
diphosphate	H	H	H	NH-methyl
diphosphate	H	H	H	NH-ethyl
diphosphate	H	H	H	OH
diphosphate	H	H	H	O-acetyl
diphosphate	H	H	H	OMe
diphosphate	H	H	H	OEt

R^1	R^2	R^3	X^1	Y
diphosphate	H	H	H	O-cyclopropyl
diphosphate	H	H	H	SH
diphosphate	H	H	H	SMe
diphosphate	H	H	H	SEt
diphosphate	H	H	H	S-cyclopropyl
triphosphate	H	H	H	NH_2
triphosphate	H	H	H	NH-acetyl
triphosphate	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	NH-methyl
triphosphate	H	H	H	NH-ethyl
triphosphate	H	H	H	OH
triphosphate	H	H	H	OMe
triphosphate	H	H	H	OEt
triphosphate	H	H	H	O-cyclopropyl
triphosphate	H	H	H	O-acetyl
triphosphate	H	H	H	SH
triphosphate	H	H	H	SMe
triphosphate	H	H	H	SEt
triphosphate	H	H	H	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2
monophosphate	monophosphate	monophosphate	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	OH
diphosphate	diphosphate	diphosphate	H	NH_2
diphosphate	diphosphate	diphosphate	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	OH
triphosphate	triphosphate	triphosphate	H	NH_2
triphosphate	triphosphate	triphosphate	H	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	OH
H	H	H	F	NH_2
H	H	H	F	NH-cyclopropyl
H	H	H	F	OH

R^1	R^2	R^3	X^1	Y
H	H	H	Cl	NH_2
H	H	H	Cl	NH-cyclopropyl
H	H	H	Cl	OH
H	H	H	Br	NH_2
H	H	H	Br	NH-cyclopropyl
H	H	H	Br	OH
H	H	H	NH_2	NH_2
H	H	H	NH_2	NH-cyclopropyl
H	H	H	NH_2	OH
H	H	H	SH	NH_2
H	H	H	SH	NH-cyclopropyl
H	H	H	SH	OH
acetyl	H	H	H	NH_2
acetyl	H	H	H	NH-cyclopropyl
acetyl	H	H	H	OH
acetyl	H	H	F	NH_2
acetyl	H	H	F	NH-cyclopropyl
acetyl	H	H	F	OH
H	acetyl	acetyl	H	NH_2
H	acetyl	acetyl	H	NH-cyclopropyl
H	acetyl	acetyl	H	OH
acetyl	acetyl	acetyl	H	NH_2
acetyl	acetyl	acetyl	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	OH
monophosphate	acetyl	acetyl	H	NH_2
monophosphate	acetyl	acetyl	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	OH
diphosphate	acetyl	acetyl	H	NH_2
diphosphate	acetyl	acetyl	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	OH
triphosphate	acetyl	acetyl	H	NH_2

R^1	R^2	R^3	X^1	Y
triphosphate	acetyl	acetyl	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	OH

Alternatively, the following nucleosides of Formula VII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(VII)

wherein:

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	2,4-O-Diacetyluracil
H	H	H	CH_3	O	Hypoxanthine
H	H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	H	CH_3	O	Thymine
H	H	H	CH_3	O	Cytosine
H	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	Uracil
H	H	H	CH_3	O	5-Fluorouracil
H	H	H	CH_3	S	2,4-O-Diacetyluraci
H	H	H	CH_3	S	Hypoxanthine
H	H	H	CH_3	S	2,4-O-Diacetylthymine

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	S	Thymine
H	H	H	CH_3	S	Cytosine
H	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	S	Uracil
H	H	H	CH_3	S	5-Fluorouracil
monophosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	O	Hypoxanthine
monophosphate	H	H	CH_3	O	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	O	Thymine
monophosphate	H	H	CH_3	O	Cytosine
monophosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	O	Uracil
monophosphate	H	H	CH_3	O	5-Fluorouracil
monophosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	S	Hypoxanthine
monophosphate	H	H	CH_3	S	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	S	Thymine
monophosphate	H	H	CH_3	S	Cytosine
monophosphate	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	S	4-(N,N-diacetyl)cytosine

R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	S	Uracil
monophosphate	H	H	CH_3	S	5-Fluorouracil
diphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	O	Hypoxanthine
diphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
diphosphate	H	H	CH_3	O	Thymine
diphosphate	H	H	CH_3	O	Cytosine
diphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	H	CH_3	O	Uracil
diphosphate	H	H	CH_3	O	5-Fluorouracil
diphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	S	Hypoxanthine
diphosphate	H	H	CH_3	S	2,4-O-Diacetylthym
diphosphate	H	H	CH_3	S	Thymine
diphosphate	H	H	CH_3	S	Cytosine
triphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	O	Hypoxanthine
triphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	O	Thymine
triphosphate	H	H	CH_3	O	Cytosine
triphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine

R^1	R^2	R^3	R^6	X	Base
triphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	H	H	CH_3	O	Uracil
triphosphate	H	H	CH_3	O	5-Fluorouracil
triphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	S	Hypoxanthine
triphosphate	H	H	CH_3	S	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	S	Thymine
triphosphate	H	H	CH_3	S	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	O	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	monophosphate	monophosphate	CF_3	O	Thymine
monophosphate	monophosphate	monophosphate	CF_3	O	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	Uracil
monophosphate	monophosphate	monophosphate	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	S	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	monophosphate	CF_3	S	Thymine
monophosphate	monophosphate	monophosphate	CF_3	S	Cytosine

R^1	R^2	R^3	R^6	X	Base
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	Uracil
monophosphate	monophosphate	monophosphate	CF_3	S	5-Fluorouracil
acetyl	acetyl	acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
H	H	H	CH_3	O	6-O-acetyl guanine
H	H	H	CH_3	O	8-fluoroguanine
H	H	H	CH_3	O	guanine
H	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	O	2-fluoroadenine
H	H	H	CH_3	O	8-fluoroadenine
H	H	H	CH_3	O	2,8-difluoro-adenine
H	H	H	CH_3	O	adenine
H	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
H	H	H	CH_3	S	6-O-acetyl guanine
H	H	H	CH_3	S	8-fluoroguanine

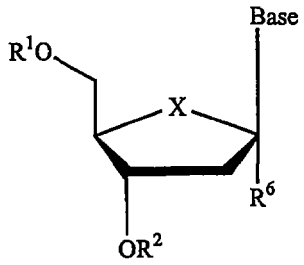
R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	S	guanine
H	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	S	2-fluoroadenine
H	H	H	CH_3	S	8-fluoroadenine
H	H	H	CH_3	S	2,8-difluoro-adenine
H	H	H	CH_3	S	adenine
monophosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	O	6-O-acetyl guanine
monophosphate	H	H	CH_3	O	8-fluoroguanine
monophosphate	H	H	CH_3	O	guanine
monophosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
monophosphate	H	H	CH_3	O	2-fluoroadenine
monophosphate	H	H	CH_3	O	8-fluoroadenine
monophosphate	H	H	CH_3	O	2,8-difluoro-adenine
monophosphate	H	H	CH_3	O	adenine
monophosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	S	6-O-acetyl guanine
monophosphate	H	H	CH_3	S	8-fluoroguanine
monophosphate	H	H	CH_3	S	guanine
monophosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
monophosphate	H	H	CH_3	S	2-fluoroadenine
monophosphate	H	H	CH_3	S	8-fluoroadenine

R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	S	2,8-difluoro-adenine
monophosphate	H	H	CH_3	S	adenine
diphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
diphosphate	H	H	CH_3	O	6-O-acetyl guanine
diphosphate	H	H	CH_3	O	8-fluoroguanine
diphosphate	H	H	CH_3	O	guanine
diphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	O	2-fluoroadenine
diphosphate	H	H	CH_3	O	8-fluoroadenine
diphosphate	H	H	CH_3	O	2,8-difluoro-adenine
diphosphate	H	H	CH_3	O	adenine
diphosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
diphosphate	H	H	CH_3	S	6-O-acetyl guanine
diphosphate	H	H	CH_3	S	8-fluoroguanine
diphosphate	H	H	CH_3	S	guanine
diphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	S	2-fluoroadenine
diphosphate	H	H	CH_3	S	8-fluoroadenine
diphosphate	H	H	CH_3	S	2,8-difluoro-adenine
diphosphate	H	H	CH_3	S	adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine

R^1	R^2	R^3	R^6	X	Base
triphosphate	H	H	CH_3	O	6-O-acetyl guanine
triphosphate	H	H	CH_3	O	8-fluoroguanine
triphosphate	H	H	CH_3	O	guanine
triphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	O	2-fluoroadenine
triphosphate	H	H	CH_3	O	8-fluoroadenine
triphosphate	H	H	CH_3	O	2,8-difluoro-adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	H	CH_3	S	6-O-acetyl guanine
triphosphate	H	H	CH_3	S	8-fluoroguanine
triphosphate	H	H	CH_3	S	guanine
triphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	S	2-fluoroadenine
triphosphate	H	H	CH_3	S	8-fluoroadenine
triphosphate	H	H	CH_3	S	2,8-difluoro-adenine
triphosphate	H	H	CH_3	S	adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	O	guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-fluoroadenine

R^1	R^2	R^3	R^6	X	Base
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	O	2,8-difluoro-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	S	guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	2,8-difluoro-adenine
monophosphate	monophosphate	monophosphate	CF_3	S	adenine
acetyl	acetyl	acetyl	CF_3	O	guanine
acetyl	acetyl	acetyl	CF_3	S	guanine
acetyl	acetyl	acetyl	2-bromo-vinyl	O	guanine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	guanine

Alternatively, the following nucleosides of Formula VIII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(VIII)

wherein

R^1	R^2	R^6	X	Base
H	H	CH_3	O	2,4-O-Diacetyluracil
H	H	CH_3	O	Hypoxanthine
H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	CH_3	O	Thymine
H	H	CH_3	O	Cytosine
H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	CH_3	O	Uracil
H	H	CH_3	O	5-Fluorouracil
H	H	CH_3	S	2,4-O-Diacetyluracil
H	H	CH_3	S	Hypoxanthine
H	H	CH_3	S	2,4-O-Diacetylthymine
H	H	CH_3	S	Thymine
H	H	CH_3	S	Cytosine
H	H	CH_3	S	4-(N-mono-acetyl)cytosine
H	H	CH_3	S	4-(N,N-diacetyl)cytosine
H	H	CH_3	S	Uracil
H	H	CH_3	S	5-Fluorouracil
monophosphate	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	CH_3	O	Hypoxanthine
monophosphate	H	CH_3	O	2,4-O-Diacetylthymine
monophosphate	H	CH_3	O	Thymine
monophosphate	H	CH_3	O	Cytosine

R^1	R^2	R^6	X	Base
monophosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	H	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	H	CH_3	O	Uracil
monophosphate	H	CH_3	O	5-Fluorouracil
monophosphate	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	CH_3	S	Hypoxanthine
monophosphate	H	CH_3	S	2,4-O-Diacetylthymine
monophosphate	H	CH_3	S	Thymine
monophosphate	H	CH_3	S	Cytosine
monophosphate	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	H	CH_3	S	Uracil
monophosphate	H	CH_3	S	5-Fluorouracil
diphosphate	H	CH_3	O	2,4-O-Diacetyluracil
diphosphate	H	CH_3	O	Hypoxanthine
diphosphate	H	CH_3	O	2,4-O-Diacetylthymine
diphosphate	H	CH_3	O	Thymine
diphosphate	H	CH_3	O	Cytosine
diphosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	CH_3	O	Uracil
diphosphate	H	CH_3	O	5-Fluorouracil
diphosphate	H	CH_3	S	2,4-O-Diacetyluracil
diphosphate	H	CH_3	S	Hypoxanthine
diphosphate	H	CH_3	S	2,4-O-Diacetylthymine
diphosphate	H	CH_3	S	Thymine
diphosphate	H	CH_3	S	Cytosine
diphosphate	H	CH_3	S	4-(N-mono-acetyl)cytosine
diphosphate	H	CH_3	S	4-(N,N-diacetyl)cytosine
diphosphate	H	CH_3	S	Uracil
diphosphate	H	CH_3	S	5-Fluorouracil

R^1	R^2	R^6	X	Base
triphosphate	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	CH_3	O	Hypoxanthine
triphosphate	H	CH_3	O	2,4-O-diacethylthymine
triphosphate	H	CH_3	O	Thymine
triphosphate	H	CH_3	O	Cytosine
triphosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	H	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	H	CH_3	O	Uracil
triphosphate	H	CH_3	O	5-Fluorouracil
triphosphate	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	CH_3	S	Hypoxanthine
triphosphate	H	CH_3	S	2,4-O-Diacetylthymine
triphosphate	H	CH_3	S	Thymine
triphosphate	H	CH_3	S	Cytosine
triphosphate	H	CH_3	S	4-(N-mono-acetyl)cytosine
triphosphate	H	CH_3	S	4-(N,N-diacetyl)cytosine
triphosphate	H	CH_3	S	Uracil
triphosphate	H	CH_3	S	5-Fluorouracil
monophosphate	monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	CF_3	O	Hypoxanthine
monophosphate	monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	monophosphate	CF_3	O	Thymine
monophosphate	monophosphate	CF_3	O	Cytosine
monophosphate	monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	CF_3	O	Uracil
monophosphate	monophosphate	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	CF_3	S	Hypoxanthine
monophosphate	monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	CF_3	S	Thymine

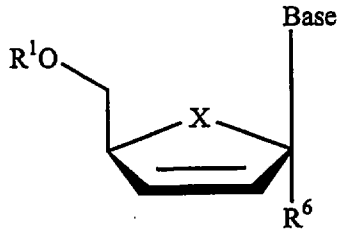
R^1	R^2	R^6	X	Base
monophosphate	monophosphate	CF_3	S	Cytosine
monophosphate	monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	CF_3	S	Uracil
monophosphate	monophosphate	CF_3	S	5-Fluorouracil
acetyl	acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine
H	H	CH_3	O	2-(N,N-diacetyl)-guanine
H	H	CH_3	O	6-O-acetyl guanine
H	H	CH_3	O	8-fluoroguanine
H	H	CH_3	O	guanine
H	H	CH_3	O	6-(N,N-diacetyl)-adenine
H	H	CH_3	O	2-fluoroadenine
H	H	CH_3	O	8-fluoroadenine
H	H	CH_3	O	2,8-difluoro-adenine
H	H	CH_3	O	adenine
H	H	CH_3	S	2-(N,N-diacetyl)-guanine
H	H	CH_3	S	6-O-acetyl guanine
H	H	CH_3	S	8-fluoroguanine
H	H	CH_3	S	guanine
H	H	CH_3	S	6-(N,N-diacetyl)-adenine
H	H	CH_3	S	2-fluoroadenine
H	H	CH_3	S	8-fluoroadenine
H	H	CH_3	S	2,8-difluoro-adenine
H	H	CH_3	S	adenine
monophosphate	H	CH_3	O	2-(N,N-diacetyl)-guanine
monophosphate	H	CH_3	O	6-O-acetyl guanine

R^1	R^2	R^6	X	Base
monophosphate	H	CH_3	O	8-fluoroguanine
monophosphate	H	CH_3	O	guanine
monophosphate	H	CH_3	O	6-(N,N-diacetyl)-adenine
monophosphate	H	CH_3	O	2-fluoroadenine
monophosphate	H	CH_3	O	8-fluoroadenine
monophosphate	H	CH_3	O	2,8-difluoro-adenine
monophosphate	H	CH_3	O	adenine
monophosphate	H	CH_3	S	2-(N,N-diacetyl)-guanine
monophosphate	H	CH_3	S	6-O-acetyl guanine
monophosphate	H	CH_3	S	8-fluoroguanine
monophosphate	H	CH_3	S	guanine
monophosphate	H	CH_3	S	6-(N,N-diacetyl)-adenine
monophosphate	H	CH_3	S	2-fluoroadenine
monophosphate	H	CH_3	S	8-fluoroadenine
monophosphate	H	CH_3	S	2,8-difluoro-adenine
monophosphate	H	CH_3	S	adenine
diphosphate	H	CH_3	O	2-(N,N-diacetyl)-guanine
diphosphate	H	CH_3	O	6-O-acetyl guanine
diphosphate	H	CH_3	O	8-fluoroguanine
diphosphate	H	CH_3	O	guanine
diphosphate	H	CH_3	O	6-(N,N-diacetyl)-adenine
diphosphate	H	CH_3	O	2-fluoroadenine
diphosphate	H	CH_3	O	8-fluoroadenine
diphosphate	H	CH_3	O	2,8-difluoro-adenine
diphosphate	H	CH_3	O	adenine
diphosphate	H	CH_3	S	2-(N,N-diacetyl)-guanine
diphosphate	H	CH_3	S	6-O-acetyl guanine
diphosphate	H	CH_3	S	8-fluoroguanine
diphosphate	H	CH_3	S	guanine
diphosphate	H	CH_3	S	6-(N,N-diacetyl)-adenine
diphosphate	H	CH_3	S	2-fluoroadenine

R^1	R^2	R^6	X	Base
diphosphate	H	CH_3	S	8-fluoroadenine
diphosphate	H	CH_3	S	2,8-difluoro-adenine
diphosphate	H	CH_3	S	adenine
triphosphate	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	CH_3	O	6-O-acetyl guanine
triphosphate	H	CH_3	O	8-fluoroguanine
triphosphate	H	CH_3	O	guanine
triphosphate	H	CH_3	O	6-(N,N-diacetyl)-adenine
triphosphate	H	CH_3	O	2-fluoroadenine
triphosphate	H	CH_3	O	8-fluoroadenine
triphosphate	H	CH_3	O	2,8-difluoro-adenine
triphosphate	H	CH_3	O	adenine
triphosphate	H	CH_3	S	2-(N,N-diacetyl)-guanine
triphosphate	H	CH_3	S	6-O-acetyl guanine
triphosphate	H	CH_3	S	8-fluoroguanine
triphosphate	H	CH_3	S	guanine
triphosphate	H	CH_3	S	6-(N,N-diacetyl)-adenine
triphosphate	H	CH_3	S	2-fluoroadenine
triphosphate	H	CH_3	S	8-fluoroadenine
triphosphate	H	CH_3	S	2,8-difluoro-adenine
triphosphate	H	CH_3	S	adenine
monophosphate	monophosphate	CF_3	O	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	CF_3	O	6-O-acetyl guanine
monophosphate	monophosphate	CF_3	O	8-fluoroguanine
monophosphate	monophosphate	CF_3	O	guanine
monophosphate	monophosphate	CF_3	O	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	CF_3	O	2-fluoroadenine
monophosphate	monophosphate	CF_3	O	8-fluoroadenine
monophosphate	monophosphate	CF_3	O	2,8-difluoro-adenine
monophosphate	monophosphate	CF_3	O	adenine
monophosphate	monophosphate	CF_3	S	2-(N,N-diacetyl)-guanine

R^1	R^2	R^6	X	Base
monophosphate	monophosphate	CF_3	S	6-O-acetyl guanine
monophosphate	monophosphate	CF_3	S	8-fluoroguanine
monophosphate	monophosphate	CF_3	S	guanine
monophosphate	monophosphate	CF_3	S	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	CF_3	S	2-fluoroadenine
monophosphate	monophosphate	CF_3	S	8-fluoroadenine
monophosphate	monophosphate	CF_3	S	2,8-difluoro-adenine
monophosphate	monophosphate	CF_3	S	adenine
acetyl	acetyl	CF_3	O	guanine
acetyl	acetyl	CF_3	S	guanine
acetyl	acetyl	2-bromo-vinyl	O	guanine
acetyl	acetyl	2-bromo-vinyl	S	guanine

Alternatively, the following nucleosides of Formula IX are prepared, using the appropriate sugar and pyrimidine or purine bases.



(IX)

wherein:

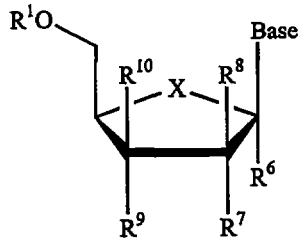
R^1	R^6	X	Base
H	CH_3	O	2,4-O-Diacetyluracil
H	CH_3	O	Hypoxanthine
H	CH_3	O	2,4-O-Diacetylthymine
H	CH_3	O	Thymine
H	CH_3	O	Cytosine

R^1	R^6	X	Base
H	CH_3	O	4-(N-mono-acetyl)cytosine
H	CH_3	O	4-(N,N-diacetyl)cytosine
H	CH_3	O	Uracil
H	CH_3	O	5-Fluorouracil
H	CH_3	S	2,4-O-Diacetyluracil
H	CH_3	S	Hypoxanthine
H	CH_3	S	2,4-O-Diacetylthymine
H	CH_3	S	Thymine
H	CH_3	S	Cytosine
H	CH_3	S	4-(N-mono-acetyl)cytosine
H	CH_3	S	4-(N,N-diacetyl)cytosine
H	CH_3	S	Uracil
H	CH_3	S	5-Fluorouracil
monophosphate	CH_3	O	2,4-O-Diacetyluracil
monophosphate	CH_3	O	Hypoxanthine
monophosphate	CH_3	O	2,4-O-Diacetylthymine
monophosphate	CH_3	O	Thymine
monophosphate	CH_3	O	Cytosine
monophosphate	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	CH_3	O	Uracil
monophosphate	CH_3	O	5-Fluorouracil
monophosphate	CH_3	S	2,4-O-Diacetyluracil
monophosphate	CH_3	S	Hypoxanthine
monophosphate	CH_3	S	2,4-O-Diacetylthymine
monophosphate	CH_3	S	Thymine
monophosphate	CH_3	S	Cytosine
monophosphate	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	S	4-(N,N-diacetyl)cytos
monophosphate	CH_3	S	Uracil
monophosphate	CH_3	S	5-Fluorouracil

R^1	R^6	X	Base
diphosphate	CH_3	O	2,4-O-Diacetyluracil
diphosphate	CH_3	O	Hypoxanthine
diphosphate	CH_3	O	2,4-O-Diacetylthymine
diphosphate	CH_3	O	Thymine
diphosphate	CH_3	O	Cytosine
diphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	CH_3	O	Uracil
diphosphate	CH_3	O	5-Fluorouracil
diphosphate	CH_3	S	2,4-O-Diacetyluracil
diphosphate	CH_3	S	Hypoxanthine
diphosphate	CH_3	S	2,4-O-Diacetylthymine
diphosphate	CH_3	S	Thymine
diphosphate	CH_3	S	Cytosine
triphosphate	CH_3	O	2,4-O-Diacetyluracil
triphosphate	CH_3	O	Hypoxanthine
triphosphate	CH_3	O	2,4-O-Diacetylthymine
triphosphate	CH_3	O	Thymine
triphosphate	CH_3	O	Cytosine
triphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	CH_3	O	Uracil
triphosphate	CH_3	O	5-Fluorouracil
triphosphate	CH_3	S	2,4-O-Diacetyluracil
triphosphate	CH_3	S	Hypoxanthine
triphospahate	CH_3	S	2,4-O-Diacetylthymine
triphospahate	CH_3	S	Thymine
triphospahate	CH_3	S	Cytosine
monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	CF_3	O	Hypoxanthine
monophosphate	CF_3	O	2,4-O-Diacetylthymine

R^1	R^6	X	Base
monophosphate	CF_3	O	Thymine
monophosphate	CF_3	O	Cytosine
monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	O	4-(N,N-diacetyl)cytos
monophosphate	CF_3	O	Uracil
monophosphate	CF_3	O	5-Fluorouracil
monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	CF_3	S	Hypoxanthine
monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	CF_3	S	Thymine
monophosphate	CF_3	S	Cytosine
monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	CF_3	S	Uracil
monophosphate	CF_3	S	5-Fluorouracil
acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine

Alternatively, the following nucleosides of Formula XVI are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XVI)

wherein:

R^1	R^6	R^7	R^8	X	Base	R^{10}	R^9
H	CH_3	H	H	O	2,4-O-Diacetyluracil	OH	Me
H	CH_3	H	H	O	Hypoxanthine	OH	Me

R^1	R^6	R^7	R^8	X	Base	R^{10}	R^9
H	CH_3	H	H	O	2,4-O-Diacetylthymine	OH	Me
H	CH_3	H	H	O	Thymine	OH	Me
H	CH_3	H	H	O	Cytosine	OH	Me
H	CH_3	H	H	O	4-(N-mono-acetyl)cytosine	OH	Me
H	CH_3	H	H	O	4-(N,N-diacetyl)cytosine	OH	Me
H	CH_3	H	H	O	Uracil	OH	Me
H	CH_3	H	H	O	5-Fluorouracil	OH	Me
H	CH_3	H	H	S	2,4-O-Diacetyluracil	OH	Me
H	CH_3	H	H	S	Hypoxanthine	OH	Me
H	CH_3	H	H	S	2,4-O-Diacetylthymine	OH	Me
H	CH_3	H	H	S	Thymine	OH	Me
H	CH_3	H	H	S	Cytosine	OH	Me
H	CH_3	H	H	S	4-(N-mono-acetyl)cytosine	OH	Me
H	CH_3	H	H	S	4-(N,N-diacetyl)cytosine	OH	Me
H	CH_3	H	H	S	Uracil	OH	Me
H	CH_3	H	H	S	5-Fluorouracil	OH	Me
monophosphate	CH_3	H	H	O	2,4-O-Diacetyluracil	OH	Me
monophosphate	CH_3	H	H	O	Hypoxanthine	OH	Me
monophosphate	CH_3	H	H	O	2,4-O-Diacetylthymine	OH	Me
monophosphate	CH_3	H	H	O	Thymine	OH	Me
monophosphate	CH_3	H	H	O	Cytosine	OH	Me
monophosphate	CH_3	H	H	O	4-(N-mono-acetyl)cytosine	OH	Me
monophosphate	CH_3	H	H	O	4-(N,N-diacetyl)cytosine	OH	Me
monophosphate	CH_3	H	H	O	Uracil	OH	Me
monophosphate	CH_3	H	H	O	5-Fluorouracil	OH	Me
monophosphate	CH_3	H	H	S	2,4-O-Diacetyluracil	OH	Me
monophosphate	CH_3	H	H	S	Hypoxanthine	OH	Me
monophosphate	CH_3	H	H	S	2,4-O-Diacetylthymine	OH	Me
monophosphate	CH_3	H	H	S	Thymine	OH	Me
monophosphate	CH_3	H	H	S	Cytosine	OH	Me
monophosphate	CH_3	H	H	S	4-(N-mono-acetyl)cytosine	OH	Me

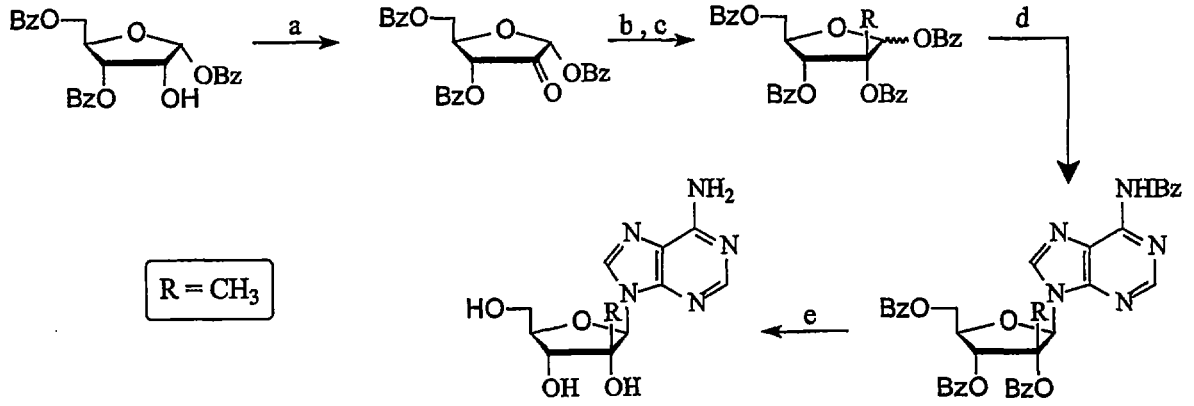
R^1	R^6	R^7	R^8	X	Base	R^{10}	R^9
monophosphate	CH_3	H	H	S	4-(N,N-diacetyl)cytosine	OH	Me
monophosphate	CH_3	H	H	S	Uracil	OH	Me
monophosphate	CH_3	H	H	S	5-Fluorouracil	OH	Me
diphosphate	CH_3	H	H	O	2,4-O-Diacetyluracil	OH	Me
diphosphate	CH_3	H	H	O	Hypoxanthine	OH	Me
diphosphate	CH_3	H	H	O	2,4-O-Diacetylthymine	OH	Me
diphosphate	CH_3	H	H	O	Thymine	OH	Me
diphosphate	CH_3	H	H	O	Cytosine	OH	Me
diphosphate	CH_3	H	H	O	4-(N-mono-acetyl)cytosine	OH	Me
diphosphate	CH_3	H	H	O	4-(N,N-diacetyl)cytosine	OH	Me
diphosphate	CH_3	H	H	O	Uracil	OH	Me
diphosphate	CH_3	H	H	O	5-Fluorouracil	OH	Me
diphosphate	CH_3	H	H	S	2,4-O-Diacetyluracil	OH	Me
diphosphate	CH_3	H	H	S	Hypoxanthine	OH	Me
diphosphate	CH_3	H	H	S	2,4-O-Diacetylthymine	OH	Me
diphosphate	CH_3	H	H	S	Thymine	OH	Me
diphosphate	CH_3	H	H	S	Cytosine	OH	Me
triphosphate	CH_3	H	H	O	2,4-O-Diacetyluracil	OH	Me
triphosphate	CH_3	H	H	O	Hypoxanthine	OH	Me
triphosphate	CH_3	H	H	O	2,4-O-Diacetylthymine	OH	Me
triphosphate	CH_3	H	H	O	Thymine	OH	Me
triphosphate	CH_3	H	H	O	Cytosine	OH	Me
triphosphate	CH_3	H	H	O	4-(N-mono-acetyl)cytosine	OH	Me
triphosphate	CH_3	H	H	O	4-(N,N-diacetyl)cytosine	OH	Me
triphosphate	CH_3	H	H	O	Uracil	OH	Me
triphosphate	CH_3	H	H	O	5-Fluorouracil	OH	Me
triphosphate	CH_3	H	H	S	2,4-O-Diacetyluracil	OH	Me
triphosphate	CH_3	H	H	S	Hypoxanthine	OH	Me
triphosphate	CH_3	H	H	S	2,4-O-Diacetylthymine	OH	Me
triphosphate	CH_3	H	H	S	Thymine	OH	Me
triphosphate	CH_3	H	H	S	Cytosine	OH	Me

R^1	R^6	R^7	R^8	X	Base	R^{10}	R^9
monophosphate	CF_3	H	H	O	2,4-O-Diacetyluracil	OH	Me
monophosphate	CF_3	H	H	O	Hypoxanthine	OH	Me
monophosphate	CF_3	H	H	O	2,4-O-Diacetylthymine	OH	Me
monophosphate	CF_3	H	H	O	Thymine	OH	Me
monophosphate	CF_3	H	H	O	Cytosine	OH	Me
monophosphate	CF_3	H	H	O	4-(N-mono-acetyl)cytosine	OH	Me
monophosphate	CF_3	H	H	O	4-(N,N-diacetyl)cytosine	OH	Me
monophosphate	CF_3	H	H	O	Uracil	OH	Me
monophosphate	CF_3	H	H	O	5-Fluorouracil	OH	Me
monophosphate	CF_3	H	H	S	2,4-O-Diacetyluracil	OH	Me
monophosphate	CF_3	H	H	S	Hypoxanthine	OH	Me
monophosphate	CF_3	H	H	S	2,4-O-Diacetylthymine	OH	Me
monophosphate	CF_3	H	H	S	Thymine	OH	Me
monophosphate	CF_3	H	H	S	Cytosine	OH	Me
monophosphate	CF_3	H	H	S	4-(N-mono-acetyl)cytosine	OH	Me
monophosphate	CF_3	H	H	S	4-(N,N-diacetyl)cytosine	OH	Me
monophosphate	CF_3	H	H	S	Uracil	OH	Me
monophosphate	CF_3	H	H	S	5-Fluorouracil	OH	Me
acetyl	CH_3	H	H	O	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	H	H	S	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	OH	H	O	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	OH	H	S	4-(N,N-diacetyl)cytosine	H	Br

Example 2: Preparation of 2'-C-methylriboadenine

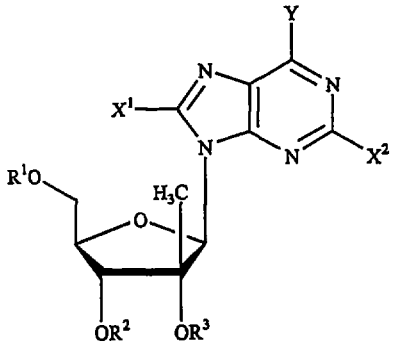
The title compound was prepared according to a published procedure (R.E. Harry-O'kuru, J.M. Smith, and M.S. Wolfe, "A short, flexible route toward 2'-C-branched ribonucleosides", *J.Org. Chem.* **1997**, 62, 1754-1759) **(Scheme 8)**.

Scheme 8



(a) Dess-Martin periodinane; (b) MeMgBr / $TiCl_4$; (c) BzCl, DMAP, Et_3N; (d) bis(trimethylsilyl)acetamide, N^6-benzoyl adenine, TMSOTf; (e) NH_3 / MeOH

In a similar manner, but using the appropriate sugar and pyrimidine or purine bases, the following nucleosides of Formula II are prepared.



(II)

wherein:

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	H	H
H	H	H	H	H	NH_2
H	H	H	H	H	NH-cyclopropyl
H	H	H	H	H	NH-methyl
H	H	H	H	H	NH-ethyl
H	H	H	H	H	NH-acetyl
H	H	H	H	H	OH
H	H	H	H	H	OMe
H	H	H	H	H	OEt

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	H	O-cyclopropyl
H	H	H	H	H	O-acetyl
H	H	H	H	H	SH
H	H	H	H	H	SMe
H	H	H	H	H	SEt
H	H	H	H	H	S-cyclopropyl
H	H	H	H	H	F
H	H	H	H	H	Cl
H	H	H	H	H	Br
H	H	H	H	H	I
monophosphate	H	H	H	H	NH_2
monophosphate	H	H	H	H	NH-acetyl
monophosphate	H	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	H	NH-methyl
monophosphate	H	H	H	H	NH-ethyl
monophosphate	H	H	H	H	OH
monophosphate	H	H	H	H	O-acetyl
monophosphate	H	H	H	H	OMe
monophosphate	H	H	H	H	OEt
monophosphate	H	H	H	H	O-cyclopropyl
monophosphate	H	H	H	H	SH
monophosphate	H	H	H	H	SMe
monophosphate	H	H	H	H	SEt
monophosphate	H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	H	F
monophosphate	H	H	H	H	Cl
monophosphate	H	H	H	H	Br
monophosphate	H	H	H	H	I
diphosphate	H	H	H	H	NH_2
diphosphate	H	H	H	H	NH-acetyl
diphosphate	H	H	H	H	NH-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	H	NH-methyl
diphosphate	H	H	H	H	NH-ethyl
diphosphate	H	H	H	H	OH
diphosphate	H	H	H	H	O-acetyl
diphosphate	H	H	H	H	OMe
diphosphate	H	H	H	H	OEt
diphosphate	H	H	H	H	O-cyclopropyl
diphosphate	H	H	H	H	SH
diphosphate	H	H	H	H	SMe
diphosphate	H	H	H	H	SEt
diphosphate	H	H	H	H	S-cyclopropyl
diphosphate	H	H	H	H	F
diphosphate	H	H	H	H	Cl
diphosphate	H	H	H	H	Br
diphosphate	H	H	H	H	I
triphosphate	H	H	H	H	NH_2
triphosphate	H	H	H	H	NH-acetyl
triphosphate	H	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	H	NH-methyl
triphosphate	H	H	H	H	NH-ethyl
triphosphate	H	H	H	H	OH
triphosphate	H	H	H	H	OMe
triphosphate	H	H	H	H	OEt
triphosphate	H	H	H	H	O-cyclopropyl
triphosphate	H	H	H	H	O-acetyl
triphosphate	H	H	H	H	SH
triphosphate	H	H	H	H	SMe
triphosphate	H	H	H	H	SEt
triphosphate	H	H	H	H	S-cyclopropyl
triphosphate	H	H	H	H	F
triphosphate	H	H	H	H	Cl

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	H	H	H	H	Br
triphosphate	H	H	H	H	I
monophosphate	monophosphate	monophosphate	H	H	NH_2
monophosphate	monophosphate	monophosphate	H	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	H	OH
monophosphate	monophosphate	monophosphate	H	H	F
monophosphate	monophosphate	monophosphate	H	H	Cl
diphosphate	diphosphate	diphosphate	H	H	NH_2
diphosphate	diphosphate	diphosphate	H	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	H	OH
diphosphate	diphosphate	diphosphate	H	H	F
diphosphate	diphosphate	diphosphate	H	H	Cl
triphosphate	triphosphate	triphosphate	H	H	NH_2
triphosphate	triphosphate	triphosphate	H	H	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	H	OH
triphosphate	triphosphate	triphosphate	H	H	F
triphosphate	triphosphate	triphosphate	H	H	Cl
H	H	H	F	H	NH_2
H	H	H	F	H	NH-cyclopropyl
H	H	H	F	H	OH
H	H	H	F	H	F
H	H	H	F	H	Cl
H	H	H	Cl	H	NH_2
H	H	H	Cl	H	NH-cyclopropyl
H	H	H	Cl	H	OH
H	H	H	Cl	H	F
H	H	H	Cl	H	Cl
H	H	H	Br	H	NH_2
H	H	H	Br	H	NH-cyclopropyl
H	H	H	Br	H	OH
H	H	H	Br	H	F

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	Br	H	Cl
H	H	H	NH_2	H	NH_2
H	H	H	NH_2	H	NH-cyclopropyl
H	H	H	NH_2	H	OH
H	H	H	NH_2	H	F
H	H	H	NH_2	H	Cl
H	H	H	SH	H	NH_2
H	H	H	SH	H	NH-cyclopropyl
H	H	H	SH	H	OH
H	H	H	SH	H	F
H	H	H	SH	H	Cl
acetyl	H	H	H	H	NH_2
acetyl	H	H	H	H	NH-cyclopropyl
acetyl	H	H	H	H	OH
acetyl	H	H	H	H	F
acetyl	H	H	H	H	Cl
acetyl	H	H	F	H	NH_2
acetyl	H	H	F	H	NH-cyclopropyl
acetyl	H	H	F	H	OH
acetyl	H	H	F	H	F
acetyl	H	H	F	H	Cl
H	acetyl	acetyl	H	H	NH_2
H	acetyl	acetyl	H	H	NH-cyclopropyl
H	acetyl	acetyl	H	H	OH
H	acetyl	acetyl	H	H	F
H	acetyl	acetyl	H	H	Cl
acetyl	acetyl	acetyl	H	H	NH_2
acetyl	acetyl	acetyl	H	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	H	OH
acetyl	acetyl	acetyl	H	H	F
acetyl	acetyl	acetyl	H	H	Cl

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	acetyl	acetyl	H	H	NH_2
monophosphate	acetyl	acetyl	H	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	H	OH
monophosphate	acetyl	acetyl	H	H	F
monophosphate	acetyl	acetyl	H	H	Cl
diphosphate	acetyl	acetyl	H	H	NH_2
diphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	H	OH
diphosphate	acetyl	acetyl	H	H	F
diphosphate	acetyl	acetyl	H	H	Cl
triphosphate	acetyl	acetyl	H	H	NH_2
triphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	H	OH
triphosphate	acetyl	acetyl	H	H	F
triphosphate	acetyl	acetyl	H	H	Cl
H	H	H	H	NH_2	H
H	H	H	H	NH_2	NH_2
H	H	H	H	NH_2	NH-cyclopropyl
H	H	H	H	NH_2	NH-methyl
H	H	H	H	NH_2	NH-ethyl
H	H	H	H	NH_2	NH-acetyl
H	H	H	H	NH_2	OH
H	H	H	H	NH_2	OMe
H	H	H	H	NH_2	OEt
H	H	H	H	NH_2	O-cyclopropyl
H	H	H	H	NH_2	O-acetyl
H	H	H	H	NH_2	SH
H	H	H	H	NH_2	SMe
H	H	H	H	NH_2	SEt
H	H	H	H	NH_2	S-cyclopropyl
H	H	H	H	NH_2	F

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	NH_2	Cl
H	H	H	H	NH_2	Br
H	H	H	H	NH_2	I
monophosphate	H	H	H	NH_2	NH_2
monophosphate	H	H	H	NH_2	NH-acetyl
monophosphate	H	H	H	NH_2	NH-cyclopropyl
monophosphate	H	H	H	NH_2	NH-methyl
monophosphate	H	H	H	NH_2	NH-ethyl
monophosphate	H	H	H	NH_2	OH
monophosphate	H	H	H	NH_2	O-acetyl
monophosphate	H	H	H	NH_2	OMe
monophosphate	H	H	H	NH_2	OEt
monophosphate	H	H	H	NH_2	O-cyclopropyl
monophosphate	H	H	H	NH_2	SH
monophosphate	H	H	H	NH_2	SMe
monophosphate	H	H	H	NH_2	SEt
monophosphate	H	H	H	NH_2	S-cyclopropyl
monophosphate	H	H	H	NH_2	F
monophosphate	H	H	H	NH_2	Cl
monophosphate	H	H	H	NH_2	Br
monophosphate	H	H	H	NH_2	I
diphosphate	H	H	H	NH_2	NH_2
diphosphate	H	H	H	NH_2	NH-acetyl
diphosphate	H	H	H	NH_2	NH-cyclopropyl
diphosphate	H	H	H	NH_2	NH-methyl
diphosphate	H	H	H	NH_2	NH-ethyl
diphosphate	H	H	H	NH_2	OH
diphosphate	H	H	H	NH_2	O-acetyl
diphosphate	H	H	H	NH_2	OMe
diphosphate	H	H	H	NH_2	OEt
diphosphate	H	H	H	NH_2	O-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	NH_2	SH
diphosphate	H	H	H	NH_2	SMe
diphosphate	H	H	H	NH_2	SEt
diphosphate	H	H	H	NH_2	S-cyclopropyl
diphosphate	H	H	H	NH_2	F
diphosphate	H	H	H	NH_2	Cl
diphosphate	H	H	H	NH_2	Br
diphosphate	H	H	H	NH_2	I
triphosphate	H	H	H	NH_2	NH_2
triphosphate	H	H	H	NH_2	NH-acetyl
triphosphate	H	H	H	NH_2	NH-cyclopropyl
triphosphate	H	H	H	NH_2	NH-methyl
triphosphate	H	H	H	NH_2	NH-ethyl
triphosphate	H	H	H	NH_2	OH
triphosphate	H	H	H	NH_2	OMe
triphosphate	H	H	H	NH_2	OEt
triphosphate	H	H	H	NH_2	O-cyclopropyl
triphosphate	H	H	H	NH_2	O-acetyl
triphosphate	H	H	H	NH_2	SH
triphosphate	H	H	H	NH_2	SMe
triphosphate	H	H	H	NH_2	SEt
triphosphate	H	H	H	NH_2	S-cyclopropyl
triphosphate	H	H	H	NH_2	F
triphosphate	H	H	H	NH_2	Cl
triphosphate	H	H	H	NH_2	Br
triphosphate	H	H	H	NH_2	I
monophosphate	monophosphate	monophosphate	H	NH_2	NH_2
monophosphate	monophosphate	monophosphate	H	NH_2	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2	OH
monophosphate	monophosphate	monophosphate	H	NH_2	F
monophosphate	monophosphate	monophosphate	H	NH_2	Cl

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	diphosphate	diphosphate	H	NH_2	NH_2
diphosphate	diphosphate	diphosphate	H	NH_2	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	NH_2	OH
diphosphate	diphosphate	diphosphate	H	NH_2	F
diphosphate	diphosphate	diphosphate	H	NH_2	Cl
triphosphate	triphosphate	triphosphate	H	NH_2	NH_2
triphosphate	triphosphate	triphosphate	H	NH_2	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	NH_2	OH
triphosphate	triphosphate	triphosphate	H	NH_2	F
triphosphate	triphosphate	triphosphate	H	NH_2	Cl
H	H	H	F	NH_2	NH_2
H	H	H	F	NH_2	NH-cyclopropyl
H	H	H	F	NH_2	OH
H	H	H	F	NH_2	F
H	H	H	F	NH_2	Cl
H	H	H	Cl	NH_2	NH_2
H	H	H	Cl	NH_2	NH-cyclopropyl
H	H	H	Cl	NH_2	OH
H	H	H	Cl	NH_2	F
H	H	H	Cl	NH_2	Cl
H	H	H	Br	NH_2	NH_2
H	H	H	Br	NH_2	NH-cyclopropyl
H	H	H	Br	NH_2	OH
H	H	H	Br	NH_2	F
H	H	H	Br	NH_2	Cl
H	H	H	NH_2	NH_2	NH_2
H	H	H	NH_2	NH_2	NH-cyclopropyl
H	H	H	NH_2	NH_2	OH
H	H	H	NH_2	NH_2	F
H	H	H	NH_2	NH_2	Cl
H	H	H	SH	NH_2	NH_2

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	SH	NH_2	NH-cyclopropyl
H	H	H	SH	NH_2	OH
H	H	H	SH	NH_2	F
H	H	H	SH	NH_2	Cl
acetyl	H	H	H	NH_2	NH_2
acetyl	H	H	H	NH_2	NH-cyclopropyl
acetyl	H	H	H	NH_2	OH
acetyl	H	H	H	NH_2	F
acetyl	H	H	H	NH_2	Cl
acetyl	H	H	F	NH_2	NH_2
acetyl	H	H	F	NH_2	NH-cyclopropyl
acetyl	H	H	F	NH_2	OH
acetyl	H	H	F	NH_2	F
acetyl	H	H	F	NH_2	Cl
H	acetyl	acetyl	H	NH_2	NH_2
H	acetyl	acetyl	H	NH_2	NH-cyclopropyl
H	acetyl	acetyl	H	NH_2	OH
H	acetyl	acetyl	H	NH_2	F
H	acetyl	acetyl	H	NH_2	Cl
acetyl	acetyl	acetyl	H	NH_2	NH_2
acetyl	acetyl	acetyl	H	NH_2	NH-cyclopropyl
acetyl	acetyl	acetyl	H	NH_2	OH
acetyl	acetyl	acetyl	H	NH_2	F
acetyl	acetyl	acetyl	H	NH_2	Cl
monophosphate	acetyl	acetyl	H	NH_2	NH_2
monophosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	NH_2	OH
monophosphate	acetyl	acetyl	H	NH_2	F
monophosphate	acetyl	acetyl	H	NH_2	Cl
diphosphate	acetyl	acetyl	H	NH_2	NH_2
diphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl

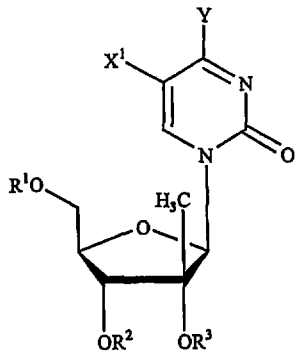
R^1	R^2	R^3	X^1	X^2	Y
diphosphate	acetyl	acetyl	H	NH_2	OH
diphosphate	acetyl	acetyl	H	NH_2	F
diphosphate	acetyl	acetyl	H	NH_2	Cl
triphosphate	acetyl	acetyl	H	NH_2	NH_2
triphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	NH_2	OH
triphosphate	acetyl	acetyl	H	NH_2	F
triphosphate	acetyl	acetyl	H	NH_2	Cl
H	H	H	H	Cl	H
H	H	H	H	Cl	H
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	NH-methyl
H	H	H	H	Cl	NH-ethyl
H	H	H	H	Cl	NH-acetyl
H	H	H	H	Cl	OH
H	H	H	H	Cl	OMe
H	H	H	H	Cl	OEt
H	H	H	H	Cl	O-cyclopropyl
H	H	H	H	Cl	O-acetyl
H	H	H	H	Cl	SH
H	H	H	H	Cl	SMe
H	H	H	H	Cl	SEt
H	H	H	H	Cl	S-cyclopropyl
monophosphate	H	H	H	Cl	NH_2
monophosphate	H	H	H	Cl	NH-acetyl
monophosphate	H	H	H	Cl	NH-cyclopropyl
monophosphate	H	H	H	Cl	NH-methyl
monophosphate	H	H	H	Cl	NH-ethyl
monophosphate	H	H	H	Cl	OH
monophosphate	H	H	H	Cl	O-acetyl

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	H	H	H	Cl	OMe
monophosphate	H	H	H	Cl	OEt
monophosphate	H	H	H	Cl	O-cyclopropyl
monophosphate	H	H	H	Cl	SH
monophosphate	H	H	H	Cl	SMe
monophosphate	H	H	H	Cl	SEt
monophosphate	H	H	H	Cl	S-cyclopropyl
diphosphate	H	H	H	Cl	NH_2
diphosphate	H	H	H	Cl	NH-acetyl
diphosphate	H	H	H	Cl	NH-cyclopropyl
diphosphate	H	H	H	Cl	NH-methyl
diphosphate	H	H	H	Cl	NH-ethyl
diphosphate	H	H	H	Cl	OH
diphosphate	H	H	H	Cl	O-acetyl
diphosphate	H	H	H	Cl	OMe
diphosphate	H	H	H	Cl	OEt
diphosphate	H	H	H	Cl	O-cyclopropyl
diphosphate	H	H	H	Cl	SH
diphosphate	H	H	H	Cl	SMe
diphosphate	H	H	H	Cl	SEt
diphosphate	H	H	H	Cl	S-cyclopropyl
triphosphate	H	H	H	Cl	NH_2
triphosphate	H	H	H	Cl	NH-acetyl
triphosphate	H	H	H	Cl	NH-cyclopropyl
triphosphate	H	H	H	Cl	NH-methyl
triphosphate	H	H	H	Cl	NH-ethyl
triphosphate	H	H	H	Cl	OH
triphosphate	H	H	H	Cl	OMe
triphosphate	H	H	H	Cl	OEt
triphosphate	H	H	H	Cl	O-cyclopropyl
triphosphate	H	H	H	Cl	O-acetyl

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	H	H	H	Cl	SH
triphosphate	H	H	H	Cl	SMe
triphosphate	H	H	H	Cl	SEt
triphosphate	H	H	H	Cl	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	NH_2
monophosphate	monophosphate	monophosphate	H	Cl	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	OH
diphosphate	diphosphate	diphosphate	H	Cl	NH_2
diphosphate	diphosphate	diphosphate	H	Cl	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	Cl	OH
triphosphate	triphosphate	triphosphate	H	Cl	NH_2
triphosphate	triphosphate	triphosphate	H	Cl	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	Cl	OH
H	H	H	F	Cl	NH_2
H	H	H	F	Cl	NH-cyclopropyl
H	H	H	F	Cl	OH
H	H	H	Cl	Cl	NH_2
H	H	H	Cl	Cl	NH-cyclopropyl
H	H	H	Cl	Cl	OH
H	H	H	Br	Cl	NH_2
H	H	H	Br	Cl	NH-cyclopropyl
H	H	H	Br	Cl	OH
H	H	H	NH_2	Cl	NH_2
H	H	H	NH_2	Cl	NH-cyclopropyl
H	H	H	NH_2	Cl	OH
H	H	H	SH	Cl	NH_2
H	H	H	SH	Cl	NH-cyclopropyl
H	H	H	SH	Cl	OH
acetyl	H	H	H	Cl	NH_2
acetyl	H	H	H	Cl	NH-cyclopropyl
acetyl	H	H	H	Cl	OH

R^1	R^2	R^3	X^1	X^2	Y
acetyl	H	H	F	Cl	NH_2
acetyl	H	H	F	Cl	NH-cyclopropyl
acetyl	H	H	F	Cl	OH
H	acetyl	acetyl	H	Cl	NH_2
H	acetyl	acetyl	H	Cl	NH-cyclopropyl
H	acetyl	acetyl	H	Cl	OH
acetyl	acetyl	acetyl	H	Cl	NH_2
acetyl	acetyl	acetyl	H	Cl	NH-cyclopropyl
acetyl	acetyl	acetyl	H	Cl	OH
monophosphate	acetyl	acetyl	H	Cl	NH_2
monophosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	Cl	OH
diphosphate	acetyl	acetyl	H	Cl	NH_2
diphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	Cl	OH
triphosphate	acetyl	acetyl	H	Cl	NH_2
triphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	Cl	OH
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	OH
H	H	H	H	Br	NH_2
H	H	H	H	Br	NH-cyclopropyl
H	H	H	H	Br	OH

Alternatively, the following nucleosides of Formula V are prepared, using the appropriate sugar and pyrimidine or purine bases.



(V)

wherein:

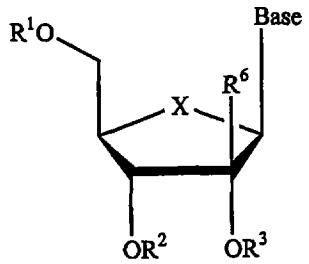
R^1	R^2	R^3	X^1	Y
H	H	H	H	H
H	H	H	H	NH_2
H	H	H	H	NH-cyclopropyl
H	H	H	H	NH-methyl
H	H	H	H	NH-ethyl
H	H	H	H	NH-acetyl
H	H	H	H	OH
H	H	H	H	OMe
H	H	H	H	OEt
H	H	H	H	O-cyclopropyl
H	H	H	H	O-acetyl
H	H	H	H	SH
H	H	H	H	SMe
H	H	H	H	SEt
H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	NH_2
monophosphate	H	H	H	NH-acetyl
monophosphate	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	NH-methyl
monophosphate	H	H	H	NH-ethyl
monophosphate	H	H	H	OH
monophosphate	H	H	H	O-acetyl

R^1	R^2	R^3	X^1	Y
monophosphate	H	H	H	OMe
monophosphate	H	H	H	OEt
monophosphate	H	H	H	O-cyclopropyl
monophosphate	H	H	H	SH
monophosphate	H	H	H	SMe
monophosphate	H	H	H	SEt
monophosphate	H	H	H	S-cyclopropyl
diphosphate	H	H	H	NH_2
diphosphate	H	H	H	NH-acetyl
diphosphate	H	H	H	NH-cyclopropyl
diphosphate	H	H	H	NH-methyl
diphosphate	H	H	H	NH-ethyl
diphosphate	H	H	H	OH
diphosphate	H	H	H	O-acetyl
diphosphate	H	H	H	OMe
diphosphate	H	H	H	OEt
diphosphate	H	H	H	O-cyclopropyl
diphosphate	H	H	H	SH
diphosphate	H	H	H	SMe
diphosphate	H	H	H	SEt
diphosphate	H	H	H	S-cyclopropyl
triphosphate	H	H	H	NH_2
triphosphate	H	H	H	NH-acetyl
triphosphate	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	NH-methyl
triphosphate	H	H	H	NH-ethyl
triphosphate	H	H	H	OH
triphosphate	H	H	H	OMe
triphosphate	H	H	H	OEt
triphosphate	H	H	H	O-cyclopropyl
triphosphate	H	H	H	O-acetyl

R^1	R^2	R^3	X^1	Y
triphosphate	H	H	H	SH
triphosphate	H	H	H	SMe
triphosphate	H	H	H	SEt
triphosphate	H	H	H	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2
monophosphate	monophosphate	monophosphate	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	OH
diphosphate	diphosphate	diphosphate	H	NH_2
diphosphate	diphosphate	diphosphate	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	OH
triphosphate	triphosphate	triphosphate	H	NH_2
triphosphate	triphosphate	triphosphate	H	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	OH
H	H	H	F	NH_2
H	H	H	F	NH-cyclopropyl
H	H	H	F	OH
H	H	H	Cl	NH_2
H	H	H	Cl	NH-cyclopropyl
H	H	H	Cl	OH
H	H	H	Br	NH_2
H	H	H	Br	NH-cyclopropyl
H	H	H	Br	OH
H	H	H	NH_2	NH_2
H	H	H	NH_2	NH-cyclopropyl
H	H	H	NH_2	OH
H	H	H	SH	NH_2
H	H	H	SH	NH-cyclopropyl
H	H	H	SH	OH
acetyl	H	H	H	NH_2
acetyl	H	H	H	NH-cyclopropyl
acetyl	H	H	H	OH

R^1	R^2	R^3	X^1	Y
acetyl	H	H	F	NH_2
acetyl	H	H	F	NH-cyclopropyl
acetyl	H	H	F	OH
H	acetyl	acetyl	H	NH_2
H	acetyl	acetyl	H	NH-cyclopropyl
H	acetyl	acetyl	H	OH
acetyl	acetyl	acetyl	H	NH_2
acetyl	acetyl	acetyl	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	OH
monophosphate	acetyl	acetyl	H	NH_2
monophosphate	acetyl	acetyl	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	OH
diphosphate	acetyl	acetyl	H	NH_2
diphosphate	acetyl	acetyl	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	OH
triphosphate	acetyl	acetyl	H	NH_2
triphosphate	acetyl	acetyl	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	OH

Alternatively, the following nucleosides of Formula X are prepared, using the appropriate sugar and pyrimidine or purine bases.



(X)

wherein:

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	2,4-O-Diacetyluracil

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	Hypoxanthine
H	H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	H	CH_3	O	Thymine
H	H	H	CH_3	O	Cytosine
H	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	Uracil
H	H	H	CH_3	O	5-Fluorouracil
H	H	H	CH_3	S	2,4-O-Diacetyluraci
H	H	H	CH_3	S	Hypoxanthine
H	H	H	CH_3	S	2,4-O-Diacetylthymine
H	H	H	CH_3	S	Thymine
H	H	H	CH_3	S	Cytosine
H	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	S	Uracil
H	H	H	CH_3	S	5-Fluorouracil
monophosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	O	Hypoxanthine
monophosphate	H	H	CH_3	O	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	O	Thymine
monophosphate	H	H	CH_3	O	Cytosine

R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	O	Uracil
monophosphate	H	H	CH_3	O	5-Fluorouracil
monophosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	S	Hypoxanthine
monophosphate	H	H	CH_3	S	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	S	Thymine
monophosphate	H	H	CH_3	S	Cytosine
monophosphate	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	S	Uracil
monophosphate	H	H	CH_3	S	5-Fluorouracil
diphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	O	Hypoxanthine
diphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
diphosphate	H	H	CH_3	O	Thymine
diphosphate	H	H	CH_3	O	Cytosine
diphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	H	CH_3	O	Uracil
diphosphate	H	H	CH_3	O	5-Fluorouracil

R^1	R^2	R^3	R^6	X	Base
diphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	S	Hypoxanthine
diphosphate	H	H	CH_3	S	2,4-O-Diacetylthym
diphosphate	H	H	CH_3	S	Thymine
diphosphate	H	H	CH_3	S	Cytosine
triphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	O	Hypoxanthine
triphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	O	Thymine
triphosphate	H	H	CH_3	O	Cytosine
triphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	H	H	CH_3	O	Uracil
triphosphate	H	H	CH_3	O	5-Fluorouracil
triphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	S	Hypoxanthine
triphosphate	H	H	CH_3	S	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	S	Thymine
triphosphate	H	H	CH_3	S	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	O	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetylthymine

R^1	R^2	R^3	R^6	X	Base
monophosphate	monophosphate	monophosphate	CF_3	O	Thymine
monophosphate	monophosphate	monophosphate	CF_3	O	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	Uracil
monophosphate	monophosphate	monophosphate	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	S	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	monophosphate	CF_3	S	Thymine
monophosphate	monophosphate	monophosphate	CF_3	S	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	Uracil
monophosphate	monophosphate	monophosphate	CF_3	S	5-Fluorouracil
acetyl	acetyl	acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	2-(N,N-diacetyl)-guanine

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	6-O-acetyl guanine
H	H	H	CH_3	O	8-fluoroguanine
H	H	H	CH_3	O	guanine
H	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	O	2-fluoroadenine
H	H	H	CH_3	O	8-fluoroadenine
H	H	H	CH_3	O	2,8-difluoro-adenine
H	H	H	CH_3	O	adenine
H	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
H	H	H	CH_3	S	6-O-acetyl guanine
H	H	H	CH_3	S	8-fluoroguanine
H	H	H	CH_3	S	guanine
H	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	S	2-fluoroadenine
H	H	H	CH_3	S	8-fluoroadenine
H	H	H	CH_3	S	2,8-difluoro-adenine
H	H	H	CH_3	S	adenine
monophosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	O	6-O-acetyl guanine
monophosphate	H	H	CH_3	O	8-fluoroguanine
monophosphate	H	H	CH_3	O	guanine
monophosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine

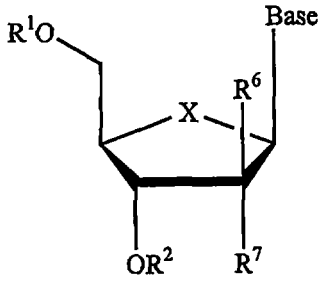
R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	O	2-fluoroadenine
monophosphate	H	H	CH_3	O	8-fluoroadenine
monophosphate	H	H	CH_3	O	2,8-difluoro-adenine
monophosphate	H	H	CH_3	O	adenine
monophosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	S	6-O-acetyl guanine
monophosphate	H	H	CH_3	S	8-fluoroguanine
monophosphate	H	H	CH_3	S	guanine
monophosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
monophosphate	H	H	CH_3	S	2-fluoroadenine
monophosphate	H	H	CH_3	S	8-fluoroadenine
monophosphate	H	H	CH_3	S	2,8-difluoro-adenine
monophosphate	H	H	CH_3	S	adenine
diphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
diphosphate	H	H	CH_3	O	6-O-acetyl guanine
diphosphate	H	H	CH_3	O	8-fluoroguanine
diphosphate	H	H	CH_3	O	guanine
diphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	O	2-fluoroadenine
diphosphate	H	H	CH_3	O	8-fluoroadenine
diphosphate	H	H	CH_3	O	2,8-difluoro-adenine
diphosphate	H	H	CH_3	O	adenine

R^1	R^2	R^3	R^6	X	Base
diphosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
diphosphate	H	H	CH_3	S	6-O-acetyl guanine
diphosphate	H	H	CH_3	S	8-fluoroguanine
diphosphate	H	H	CH_3	S	guanine
diphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	S	2-fluoroadenine
diphosphate	H	H	CH_3	S	8-fluoroadenine
diphosphate	H	H	CH_3	S	2,8-difluoro-adenine
diphosphate	H	H	CH_3	S	adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	H	CH_3	O	6-O-acetyl guanine
triphosphate	H	H	CH_3	O	8-fluoroguanine
triphosphate	H	H	CH_3	O	guanine
triphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	O	2-fluoroadenine
triphosphate	H	H	CH_3	O	8-fluoroadenine
triphosphate	H	H	CH_3	O	2,8-difluoro-adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	H	CH_3	S	6-O-acetyl guanine
triphosphate	H	H	CH_3	S	8-fluoroguanine
triphosphate	H	H	CH_3	S	guanine

R^1	R^2	R^3	R^6	X	Base
triphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	S	2-fluoroadenine
triphosphate	H	H	CH_3	S	8-fluoroadenine
triphosphate	H	H	CH_3	S	2,8-difluoro-adenine
triphosphate	H	H	CH_3	S	adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	O	guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	O	2,8-difluoro-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	S	guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	2,8-difluoro-adenine

R^1	R^2	R^3	R^6	X	Base
monophosphate	monophosphate	monophosphate	CF_3	S	adenine
acetyl	acetyl	acetyl	CF_3	O	guanine
acetyl	acetyl	acetyl	CF_3	S	guanine
acetyl	acetyl	acetyl	2-bromo-vinyl	O	guanine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	guanine

Alternatively, the following nucleosides of Formula XI are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XI)

wherein:

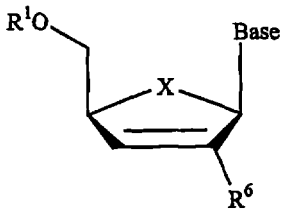
R^1	R^2	R^7	R^6	X	Base
H	H	H	CH_3	O	2,4-O-Diacetyluracil
H	H	H	CH_3	O	Hypoxanthine
H	H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	H	CH_3	O	Thymine
H	H	H	CH_3	O	Cytosine
H	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	Uracil
H	H	H	CH_3	O	5-Fluorouracil
H	H	H	CH_3	S	2,4-O-Diacetyluracil
H	H	H	CH_3	S	Hypoxanthine

R^1	R^2	R^7	R^6	X	Base
H	H	H	CH_3	S	2,4-O-Diacetylthymine
H	H	H	CH_3	S	Thymine
H	H	H	CH_3	S	Cytosine
H	H	H	CH_3	S	4-(N-mono-acetyl)cytosin
H	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	S	Uracil
H	H	H	CH_3	S	5-Fluorouracil
			CH_3		
monophosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	O	Hypoxanthine
monophosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
monophosphate	H	H	CH_3	O	Thymine
monophosphate	H	H	CH_3	O	Cytosine
monophosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	O	Uracil
monophosphate	H	H	CH_3	O	5-Fluorouracil
monophosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	S	Hypoxanthine
monophosphate	H	H	CH_3	S	2,4-O-Diacetylthymine
monophosphate	H	H	CH_3	S	Thymine
monophosphate	H	H	CH_3	S	Cytosine
monophosphate	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	S	Uracil
monophosphate	H	H	CH_3	S	5-Fluorouracil
diphosphate	H	H	CH_3	O	2,4-O-Diacetylurac
diphosphate	H	H	CH_3	O	Hypoxanthine
diphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine

R^1	R^2	R^7	R^6	X	Base
diphosphate	H	H	CH_3	O	Thymine
diphosphate	H	H	CH_3	O	Cytosine
diphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	H	CH_3	O	Uracil
diphosphate	H	H	CH_3	O	5-Fluorouracil
diphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	S	Hypoxanthine
diphosphate	H	H	CH_3	S	2,4-O-Diacetylthym
diphosphate	H	H	CH_3	S	Thymine
diphosphate	H	H	CH_3	S	Cytosine
triphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	O	Hypoxanthine
triphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	O	Thymine
triphosphate	H	H	CH_3	O	Cytosine
triphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytos
triphosphate	H	H	CH_3	O	Uracil
triphosphate	H	H	CH_3	O	5-Fluorouracil
triphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	S	Hypoxanthine
triphosphate	H	H	CH_3	S	2,4-O-Diacetylthym
triphosphate	H	H	CH_3	S	Thymine
triphosphate	H	H	CH_3	S	Cytosine
monophosphate	monophosphate	Br	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	Br	CF_3	O	Hypoxanthine
monophosphate	monophosphate	Br	CF_3	O	2,4-O-Diacetylthymine
monophosphate	monophosphate	Br	CF_3	O	Thymine

R^1	R^2	R^7	R^6	X	Base
monophosphate	monophosphate	Br	CF_3	O	Cytosine
monophosphate	monophosphate	Br	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	Br	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	Br	CF_3	O	Uracil
monophosphate	monophosphate	Br	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	Br	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	Br	CF_3	S	Hypoxanthine
monophosphate	monophosphate	Br	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	Br	CF_3	S	Thymine
monophosphate	monophosphate	Br	CF_3	S	Cytosine
monophosphate	monophosphate	Br	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	Br	CF_3	S	4-(N,N-diacetyl)cytos
monophosphate	monophosphate	Br	CF_3	S	Uracil
monophosphate	monophosphate	Br	CF_3	S	5-Fluorouracil
acetyl	acetyl	NO2	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	NO2	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	NO2	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	NO2	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine

Alternatively, the following nucleosides of Formula XII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XII)

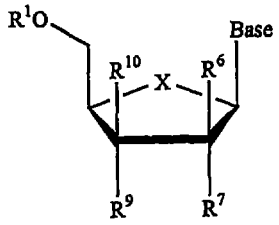
wherein:

R^1	R^6	X	Base
H	CH_3	O	2,4-O-Diacetyluracil
H	CH_3	O	Hypoxanthine
H	CH_3	O	2,4-O-Diacetylthymine
H	CH_3	O	Thymine
H	CH_3	O	Cytosine
H	CH_3	O	4-(N-mono-acetyl)cytosine
H	CH_3	O	4-(N,N-diacetyl)cytosine
H	CH_3	O	Uracil
H	CH_3	O	5-Fluorouracil
H	CH_3	S	2,4-O-Diacetyluracil
H	CH_3	S	Hypoxanthine
H	CH_3	S	2,4-O-Diacetylthymine
H	CH_3	S	Thymine
H	CH_3	S	Cytosine
H	CH_3	S	4-(N-mono-acetyl)cytosine
H	CH_3	S	4-(N,N-diacetyl)cytosine
H	CH_3	S	Uracil
H	CH_3	S	5-Fluorouracil
monophosphate	CH_3	O	2,4-O-Diacetyluracil
monophosphate	CH_3	O	Hypoxanthine
monophosphate	CH_3	O	2,4-O-Diacetylthymine
monophosphate	CH_3	O	Thymine
monophosphate	CH_3	O	Cytosine
monophosphate	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	CH_3	O	Uracil
monophosphate	CH_3	O	5-Fluorouracil
monophosphate	CH_3	S	2,4-O-Diacetyluracil
monophosphate	CH_3	S	Hypoxanthine
monophosphate	CH_3	S	2,4-O-Diacetylthymine
monophosphate	CH_3	S	Thymine

R^1	R^6	X	Base
monophosphate	CH_3	S	Cytosine
monophosphate	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	CH_3	S	Uracil
monophosphate	CH_3	S	5-Fluorouracil
diphosphate	CH_3	O	2,4-O-Diacetyluracil
diphosphate	CH_3	O	Hypoxanthine
diphosphate	CH_3	O	2,4-O-Diacetylthymine
diphosphate	CH_3	O	Thymine
diphosphate	CH_3	O	Cytosine
diphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	CH_3	O	Uracil
diphosphate	CH_3	O	5-Fluorouracil
diphosphate	CH_3	S	2,4-O-Diacetyluracil
diphosphate	CH_3	S	Hypoxanthine
diphosphate	CH_3	S	2,4-O-Diacetylthymine
diphosphate	CH_3	S	Thymine
diphosphate	CH_3	S	Cytosine
triphosphate	CH_3	O	2,4-O-Diacetyluracil
triphosphate	CH_3	O	Hypoxanthine
triphosphate	CH_3	O	2,4-O-Diacetylthymine
triphosphate	CH_3	O	Thymine
triphosphate	CH_3	O	Cytosine
triphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	CH_3	O	Uracil
triphosphate	CH_3	O	5-Fluorouracil
triphosphate	CH_3	S	2,4-O-Diacetyluracil
triphosphate	CH_3	S	Hypoxanthine
triphosphate	CH_3	S	2,4-O-Diacetylthymine

R^1	R^6	X	Base
triphosphate	CH_3	S	Thymine
triphosphate	CH_3	S	Cytosine
monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	CF_3	O	Hypoxanthine
monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	CF_3	O	Thymine
monophosphate	CF_3	O	Cytosine
monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	CF_3	O	Uracil
monophosphate	CF_3	O	5-Fluorouracil
monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	CF_3	S	Hypoxanthine
monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	CF_3	S	Thymine
monophosphate	CF_3	S	Cytosine
monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	CF_3	S	Uracil
monophosphate	CF_3	S	5-Fluorouracil
acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine

Alternatively, the following nucleosides of Formula XVII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XVII)

wherein:

R^1	R^6	R^7	X	Base	R^9	R^{10}
H	CH_3	H	O	2,4-O-Diacetyluracil	NHAc	Me
H	CH_3	H	O	Hypoxanthine	NH2	Me
H	CH_3	H	O	2,4-O-Diacetylthymine	NHAc	Me
H	CH_3	H	O	Thymine	NH2	Me
H	CH_3	H	O	Cytosine	NH2	Me
H	CH_3	H	O	4-(N-mono-acetyl)cytosine	NHAc	Me
H	CH_3	H	O	4-(N,N-diacetyl)cytosine	NHAc	Me
H	CH_3	H	O	Uracil	NH2	Me
H	CH_3	H	O	5-Fluorouracil	NH2	Me
H	CH_3	H	S	2,4-O-Diacetyluracil	NHAc	Me
H	CH_3	H	S	Hypoxanthine	NH2	Me
H	CH_3	H	S	2,4-O-Diacetylthymine	NHAc	Me
H	CH_3	H	S	Thymine	NH2	Me
H	CH_3	H	S	Cytosine	NH2	Me
H	CH_3	H	S	4-(N-mono-acetyl)cytosine	NHAc	Me
H	CH_3	H	S	4-(N,N-diacetyl)cytosine	NHAc	Me
H	CH_3	H	S	Uracil	NH2	Me
H	CH_3	H	S	5-Fluorouracil	NH2	Me
monophosphate	CH_3	H	O	2,4-O-Diacetyluracil	NHAc	Me
monophosphate	CH_3	H	O	Hypoxanthine	NH2	Me
monophosphate	CH_3	H	O	2,4-O-Diacetylthymine	NHAc	Me
monophosphate	CH_3	H	O	Thymine	NH2	Me
monophosphate	CH_3	H	O	Cytosine	NH2	Me
monophosphate	CH_3	H	O	4-(N-mono-acetyl)cytosine	NHAC	Me
monophosphate	CH_3	H	O	4-(N,N-diacetyl)cytosine	NHAc	Me
monophosphate	CH_3	H	O	Uracil	NH2	Me
monophosphate	CH_3	H	O	5-Fluorouracil	NH2	Me
monophosphate	CH_3	H	S	2,4-O-Diacetyluracil	NHAc	Me
monophosphate	CH_3	H	S	Hypoxanthine	NH2	Me
monophosphate	CH_3	H	S	2,4-O-Diacetylthymine	NHAc	Me

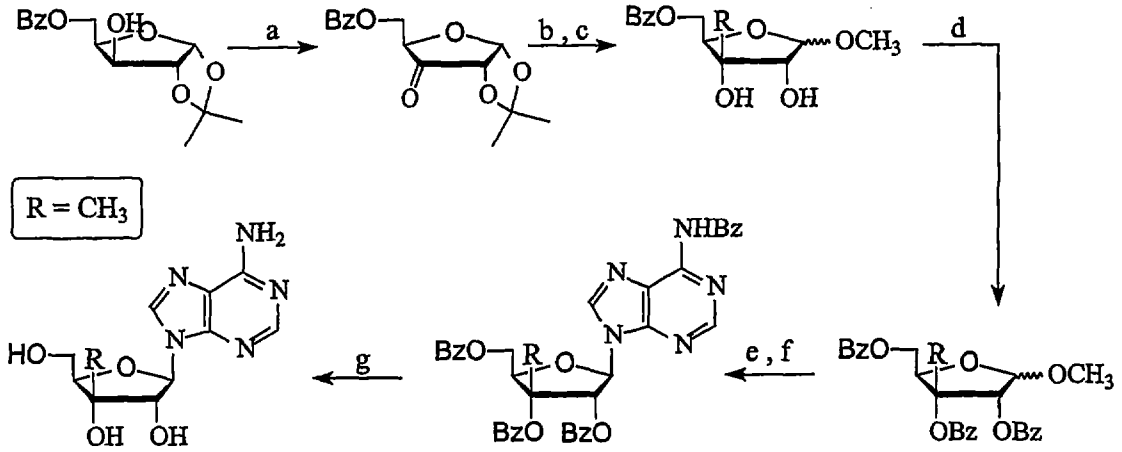
R^1	R^6	R^7	X	Base	R^9	R^{10}
monophosphate	CH_3	H	S	Thymine	NH2	Me
monophosphate	CH_3	H	S	Cytosine	NH2	Me
monophosphate	CH_3	H	S	4-(N-mono-acetyl)cytosine	NHAc	Me
monophosphate	CH_3	H	S	4-(N,N-diacetyl)cytosine	NHAc	Me
monophosphate	CH_3	H	S	Uracil	NH2	Me
monophosphate	CH_3	H	S	5-Fluorouracil	NH2	Me
diphosphate	CH_3	H	O	2,4-O-Diacetyluracil	NHAc	Me
diphosphate	CH_3	H	O	Hypoxanthine	NH2	Me
diphosphate	CH_3	H	O	2,4-O-Diacetylthymine	NH2	Me
diphosphate	CH_3	H	O	Thymine	NH2	Me
diphosphate	CH_3	H	O	Cytosine	NH2	Me
diphosphate	CH_3	H	O	4-(N-mono-acetyl)cytosine	NHAc	Me
diphosphate	CH_3	H	O	4-(N,N-diacetyl)cytos	NHAc	Me
diphosphate	CH_3	H	O	Uracil	NH2	Me
diphosphate	CH_3	H	O	5-Fluorouracil	NH2	Me
diphosphate	CH_3	H	S	2,4-O-Diacetyluracil	NH2	Me
diphosphate	CH_3	H	S	Hypoxanthine	NH2	Me
diphosphate	CH_3	H	S	2,4-O-Diacetylthymine	NHAc	Me
diphosphate	CH_3	H	S	Thymine	NH2	Me
diphosphate	CH_3	H	S	Cytosine	NH2	Me
triphosphate	CH_3	H	O	2,4-O-Diacetyluracil	NHAc	Me
triphosphate	CH_3	H	O	Hypoxanthine	NHAc	Me
triphosphate	CH_3	H	O	2,4-O-Diacetylthymine	NHAc	Me
triphosphate	CH_3	H	O	Thymine	NH2	Me
triphosphate	CH_3	H	O	Cytosine	NH2	Me
triphosphate	CH_3	H	O	4-(N-mono-acetyl)cytosine	NHAc	Me
triphosphate	CH_3	H	O	4-(N,N-diacetyl)cytosine	NH2	Me
triphosphate	CH_3	H	O	Uracil	NH2	Me
triphosphate	CH_3	H	O	5-Fluorouracil	NH2	Me
triphosphate	CH_3	H	S	2,4-O-Diacetyluracil	NH2	Me
triphosphate	CH_3	H	S	Hypoxanthine	NH2	Me

R^1	R^6	R^7	X	Base	R^9	R^{10}
triphosphate	CH_3	H	S	2,4-O-Diacetylthymine	NH2	Me
triphosphate	CH_3	H	S	Thymine	NH2	Me
triphosphate	CH_3	H	S	Cytosine	NH2	Me
monophosphate	CF_3	H	O	2,4-O-Diacetyluracil	NH2	Me
monophosphate	CF_3	H	O	Hypoxanthine	NH2	Me
monophosphate	CF_3	H	O	2,4-O-Diacetylthymine	NH2	Me
monophosphate	CF_3	H	O	Thymine	NH2	Me
monophosphate	CF_3	H	O	Cytosine	NH2	Me
monophosphate	CF_3	H	O	4-(N-mono-acetyl)cytosine	NH2	Me
monophosphate	CF_3	H	O	4-(N,N-diacetyl)cytosine	NH2	Me
monophosphate	CF_3	H	O	Uracil	NH2	Me
monophosphate	CF_3	H	O	5-Fluorouracil	NH2	Me
monophosphate	CF_3	H	S	2,4-O-Diacetyluracil	NH2	Me
monophosphate	CF_3	H	S	Hypoxanthine	NH2	Me
monophosphate	CF_3	H	S	2,4-O-Diacetylthymine	NH2	Me
monophosphate	CF_3	H	S	Thymine	NH2	Me
monophosphate	CF_3	H	S	Cytosine	NH2	Me
monophosphate	CF_3	H	S	4-(N-mono-acetyl)cytosine	NH2	Me
monophosphate	CF_3	H	S	4-(N,N-diacetyl)cytosine	NH2	Me
monophosphate	CF_3	H	S	Uracil	NH2	Me
monophosphate	CF_3	H	S	5-Fluorouracil	NH2	Me
acetyl	CH_3	H	O	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	H	S	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	OH	S	4-(N,N-diacetyl)cytosine	H	Br

Example 3: Preparation of 3'-C-methylriboadenine

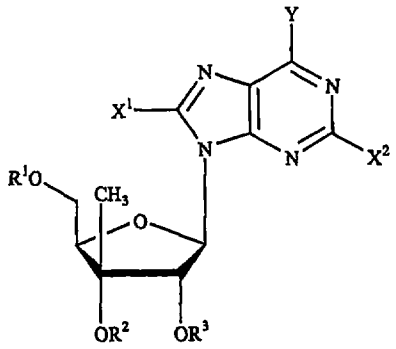
The title compound can be prepared according to a published procedure (R.F. Nutt, M.J. Dickinson, F.W. Holly, and E. Walton, "Branched-chain sugar nucleosides. III. 3'-C-methyladenine", *J.Org. Chem.* **1968**, 33, 1789-1795) (**Scheme 9**).

Scheme 9



(a) RuO_2 / $NaIO_4$; (b) MeMgI / $TiCl_4$; (c) HCl / MeOH / H_2O; (d) BzCl / pyridine; (e) AcBr, HBr / AcOH; (f) chloromercuri-6-benzamidopurine; (g) NH_3 / MeOH.

In a similar manner, but using the appropriate sugar and pyrimidine or purine bases, the following nucleosides of Formula III are prepared.



(III)

wherein:

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	H	H
H	H	H	H	H	NH_2
H	H	H	H	H	NH-cyclopropyl
H	H	H	H	H	NH-methyl
H	H	H	H	H	NH-ethyl
H	H	H	H	H	NH-acetyl
H	H	H	H	H	OH

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	H	OMe
H	H	H	H	H	OEt
H	H	H	H	H	O-cyclopropyl
H	H	H	H	H	O-acetyl
H	H	H	H	H	SH
H	H	H	H	H	SMe
H	H	H	H	H	SEt
H	H	H	H	H	S-cyclopropyl
H	H	H	H	H	F
H	H	H	H	H	Cl
H	H	H	H	H	Br
H	H	H	H	H	I
monophosphate	H	H	H	H	NH_2
monophosphate	H	H	H	H	NH-acetyl
monophosphate	H	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	H	NH-methyl
monophosphate	H	H	H	H	NH-ethyl
monophosphate	H	H	H	H	OH
monophosphate	H	H	H	H	O-acetyl
monophosphate	H	H	H	H	OMe
monophosphate	H	H	H	H	OEt
monophosphate	H	H	H	H	O-cyclopropyl
monophosphate	H	H	H	H	SH
monophosphate	H	H	H	H	SMe
monophosphate	H	H	H	H	SEt
monophosphate	H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	H	F
monophosphate	H	H	H	H	Cl
monophosphate	H	H	H	H	Br
monophosphate	H	H	H	H	I
diphosphate	H	H	H	H	NH_2

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	H	NH-acetyl
diphosphate	H	H	H	H	NH-cyclopropyl
diphosphate	H	H	H	H	NH-methyl
diphosphate	H	H	H	H	NH-ethyl
diphosphate	H	H	H	H	OH
diphosphate	H	H	H	H	O-acetyl
diphosphate	H	H	H	H	OMe
diphosphate	H	H	H	H	OEt
diphosphate	H	H	H	H	O-cyclopropyl
diphosphate	H	H	H	H	SH
diphosphate	H	H	H	H	SMe
diphosphate	H	H	H	H	SEt
diphosphate	H	H	H	H	S-cyclopropyl
diphosphate	H	H	H	H	F
diphosphate	H	H	H	H	Cl
diphosphate	H	H	H	H	Br
diphosphate	H	H	H	H	I
triphosphate	H	H	H	H	NH_2
triphosphate	H	H	H	H	NH-acetyl
triphosphate	H	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	H	NH-methyl
triphosphate	H	H	H	H	NH-ethyl
triphosphate	H	H	H	H	OH
triphosphate	H	H	H	H	OMe
triphosphate	H	H	H	H	OEt
triphosphate	H	H	H	H	O-cyclopropyl
triphosphate	H	H	H	H	O-acetyl
triphosphate	H	H	H	H	SH
triphosphate	H	H	H	H	SMe
triphosphate	H	H	H	H	SEt
triphosphate	H	H	H	H	S-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	H	H	H	H	F
triphosphate	H	H	H	H	Cl
triphosphate	H	H	H	H	Br
triphosphate	H	H	H	H	I
monophosphate	monophosphate	monophosphate	H	H	NH_2
monophosphate	monophosphate	monophosphate	H	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	H	OH
monophosphate	monophosphate	monophosphate	H	H	F
monophosphate	monophosphate	monophosphate	H	H	Cl
diphosphate	diphosphate	diphosphate	H	H	NH_2
diphosphate	diphosphate	diphosphate	H	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	H	OH
diphosphate	diphosphate	diphosphate	H	H	F
diphosphate	diphosphate	diphosphate	H	H	Cl
triphosphate	triphosphate	triphosphate	H	H	NH_2
triphosphate	triphosphate	triphosphate	H	H	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	H	OH
triphosphate	triphosphate	triphosphate	H	H	F
triphosphate	triphosphate	triphosphate	H	H	Cl
H	H	H	F	H	NH_2
H	H	H	F	H	NH-cyclopropyl
H	H	H	F	H	OH
H	H	H	F	H	F
H	H	H	F	H	Cl
H	H	H	Cl	H	NH_2
H	H	H	Cl	H	NH-cyclopropyl
H	H	H	Cl	H	OH
H	H	H	Cl	H	F
H	H	H	Cl	H	Cl
H	H	H	Br	H	NH_2
H	H	H	Br	H	NH-cyclopropyl

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	Br	H	OH
H	H	H	Br	H	F
H	H	H	Br	H	Cl
H	H	H	NH_2	H	NH_2
H	H	H	NH_2	H	NH-cyclopropyl
H	H	H	NH_2	H	OH
H	H	H	NH_2	H	F
H	H	H	NH_2	H	Cl
H	H	H	SH	H	NH_2
H	H	H	SH	H	NH-cyclopropyl
H	H	H	SH	H	OH
H	H	H	SH	H	F
H	H	H	SH	H	Cl
acetyl	H	H	H	H	NH_2
acetyl	H	H	H	H	NH-cyclopropyl
acetyl	H	H	H	H	OH
acetyl	H	H	H	H	F
acetyl	H	H	H	H	Cl
acetyl	H	H	F	H	NH_2
acetyl	H	H	F	H	NH-cyclopropyl
acetyl	H	H	F	H	OH
acetyl	H	H	F	H	F
acetyl	H	H	F	H	Cl
H	acetyl	acetyl	H	H	NH_2
H	acetyl	acetyl	H	H	NH-cyclopropyl
H	acetyl	acetyl	H	H	OH
H	acetyl	acetyl	H	H	F
H	acetyl	acetyl	H	H	Cl
acetyl	acetyl	acetyl	H	H	NH_2
acetyl	acetyl	acetyl	H	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	H	OH

R^1	R^2	R^3	X^1	X^2	Y
acetyl	acetyl	acetyl	H	H	F
acetyl	acetyl	acetyl	H	H	Cl
monophosphate	acetyl	acetyl	H	H	NH_2
monophosphate	acetyl	acetyl	H	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	H	OH
monophosphate	acetyl	acetyl	H	H	F
monophosphate	acetyl	acetyl	H	H	Cl
diphosphate	acetyl	acetyl	H	H	NH_2
diphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	H	OH
diphosphate	acetyl	acetyl	H	H	F
diphosphate	acetyl	acetyl	H	H	Cl
triphosphate	acetyl	acetyl	H	H	NH_2
triphosphate	acetyl	acetyl	H	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	H	OH
triphosphate	acetyl	acetyl	H	H	F
triphosphate	acetyl	acetyl	H	H	Cl
H	H	H	H	NH_2	H
H	H	H	H	NH_2	NH_2
H	H	H	H	NH_2	NH-cyclopropyl
H	H	H	H	NH_2	NH-methyl
H	H	H	H	NH_2	NH-ethyl
H	H	H	H	NH_2	NH-acetyl
H	H	H	H	NH_2	OH
H	H	H	H	NH_2	OMe
H	H	H	H	NH_2	OEt
H	H	H	H	NH_2	O-cyclopropyl
H	H	H	H	NH_2	O-acetyl
H	H	H	H	NH_2	SH
H	H	H	H	NH_2	SMe
H	H	H	H	NH_2	SEt

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	H	NH_2	S-cyclopropyl
H	H	H	H	NH_2	F
H	H	H	H	NH_2	Cl
H	H	H	H	NH_2	Br
H	H	H	H	NH_2	I
monophosphate	H	H	H	NH_2	NH_2
monophosphate	H	H	H	NH_2	NH-acetyl
monophosphate	H	H	H	NH_2	NH-cyclopropyl
monophosphate	H	H	H	NH_2	NH-methyl
monophosphate	H	H	H	NH_2	NH-ethyl
monophosphate	H	H	H	NH_2	OH
monophosphate	H	H	H	NH_2	O-acetyl
monophosphate	H	H	H	NH_2	OMe
monophosphate	H	H	H	NH_2	OEt
monophosphate	H	H	H	NH_2	O-cyclopropyl
monophosphate	H	H	H	NH_2	SH
monophosphate	H	H	H	NH_2	SMe
monophosphate	H	H	H	NH_2	SEt
monophosphate	H	H	H	NH_2	S-cyclopropyl
monophosphate	H	H	H	NH_2	F
monophosphate	H	H	H	NH_2	Cl
monophosphate	H	H	H	NH_2	Br
monophosphate	H	H	H	NH_2	I
diphosphate	H	H	H	NH_2	NH_2
diphosphate	H	H	H	NH_2	NH-acetyl
diphosphate	H	H	H	NH_2	NH-cyclopropyl
diphosphate	H	H	H	NH_2	NH-methyl
diphosphate	H	H	H	NH_2	NH-ethyl
diphosphate	H	H	H	NH_2	OH
diphosphate	H	H	H	NH_2	O-acetyl
diphosphate	H	H	H	NH_2	OMe

R^1	R^2	R^3	X^1	X^2	Y
diphosphate	H	H	H	NH_2	OEt
diphosphate	H	H	H	NH_2	O-cyclopropyl
diphosphate	H	H	H	NH_2	SH
diphosphate	H	H	H	NH_2	SMe
diphosphate	H	H	H	NH_2	SEt
diphosphate	H	H	H	NH_2	S-cyclopropyl
diphosphate	H	H	H	NH_2	F
diphosphate	H	H	H	NH_2	Cl
diphosphate	H	H	H	NH_2	Br
diphosphate	H	H	H	NH_2	I
triphosphate	H	H	H	NH_2	NH_2
triphosphate	H	H	H	NH_2	NH-acetyl
triphosphate	H	H	H	NH_2	NH-cyclopropyl
triphosphate	H	H	H	NH_2	NH-methyl
triphosphate	H	H	H	NH_2	NH-ethyl
triphosphate	H	H	H	NH_2	OH
triphosphate	H	H	H	NH_2	OMe
triphosphate	H	H	H	NH_2	OEt
triphosphate	H	H	H	NH_2	O-cyclopropyl
triphosphate	H	H	H	NH_2	O-acetyl
triphosphate	H	H	H	NH_2	SH
triphosphate	H	H	H	NH_2	SMe
triphosphate	H	H	H	NH_2	SEt
triphosphate	H	H	H	NH_2	S-cyclopropyl
triphosphate	H	H	H	NH_2	F
triphosphate	H	H	H	NH_2	Cl
triphosphate	H	H	H	NH_2	Br
triphosphate	H	H	H	NH_2	I
monophosphate	monophosphate	monophosphate	H	NH_2	NH_2
monophosphate	monophosphate	monophosphate	H	NH_2	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2	OH

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	monophosphate	monophosphate	H	NH_2	F
monophosphate	monophosphate	monophosphate	H	NH_2	Cl
diphosphate	diphosphate	diphosphate	H	NH_2	NH_2
diphosphate	diphosphate	diphosphate	H	NH_2	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	NH_2	OH
diphosphate	diphosphate	diphosphate	H	NH_2	F
diphosphate	diphosphate	diphosphate	H	NH_2	Cl
triphosphate	triphosphate	triphosphate	H	NH_2	NH_2
triphosphate	triphosphate	triphosphate	H	NH_2	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	NH_2	OH
triphosphate	triphosphate	triphosphate	H	NH_2	F
triphosphate	triphosphate	triphosphate	H	NH_2	Cl
H	H	H	F	NH_2	NH_2
H	H	H	F	NH_2	NH-cyclopropyl
H	H	H	F	NH_2	OH
H	H	H	F	NH_2	F
H	H	H	F	NH_2	Cl
H	H	H	Cl	NH_2	NH_2
H	H	H	Cl	NH_2	NH-cyclopropyl
H	H	H	Cl	NH_2	OH
H	H	H	Cl	NH_2	F
H	H	H	Cl	NH_2	Cl
H	H	H	Br	NH_2	NH_2
H	H	H	Br	NH_2	NH-cyclopropyl
H	H	H	Br	NH_2	OH
H	H	H	Br	NH_2	F
H	H	H	Br	NH_2	Cl
H	H	H	NH_2	NH_2	NH_2
H	H	H	NH_2	NH_2	NH-cyclopropyl
H	H	H	NH_2	NH_2	OH
H	H	H	NH_2	NH_2	F

R^1	R^2	R^3	X^1	X^2	Y
H	H	H	NH_2	NH_2	Cl
H	H	H	SH	NH_2	NH_2
H	H	H	SH	NH_2	NH-cyclopropyl
H	H	H	SH	NH_2	OH
H	H	H	SH	NH_2	F
H	H	H	SH	NH_2	Cl
acetyl	H	H	H	NH_2	NH_2
acetyl	H	H	H	NH_2	NH-cyclopropyl
acetyl	H	H	H	NH_2	OH
acetyl	H	H	H	NH_2	F
acetyl	H	H	H	NH_2	Cl
acetyl	H	H	F	NH_2	NH_2
acetyl	H	H	F	NH_2	NH-cyclopropyl
acetyl	H	H	F	NH_2	OH
acetyl	H	H	F	NH_2	F
acetyl	H	H	F	NH_2	Cl
H	acetyl	acetyl	H	NH_2	NH_2
H	acetyl	acetyl	H	NH_2	NH-cyclopropyl
H	acetyl	acetyl	H	NH_2	OH
H	acetyl	acetyl	H	NH_2	F
H	acetyl	acetyl	H	NH_2	Cl
acetyl	acetyl	acetyl	H	NH_2	NH_2
acetyl	acetyl	acetyl	H	NH_2	NH-cyclopropyl
acetyl	acetyl	acetyl	H	NH_2	OH
acetyl	acetyl	acetyl	H	NH_2	F
acetyl	acetyl	acetyl	H	NH_2	Cl
monophosphate	acetyl	acetyl	H	NH_2	NH_2
monophosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	NH_2	OH
monophosphate	acetyl	acetyl	H	NH_2	F
monophosphate	acetyl	acetyl	H	NH_2	Cl

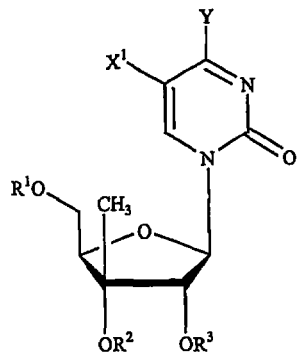
R^1	R^2	R^3	X^1	X^2	Y
diphosphate	acetyl	acetyl	H	NH_2	NH_2
diphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	NH_2	OH
diphosphate	acetyl	acetyl	H	NH_2	F
diphosphate	acetyl	acetyl	H	NH_2	Cl
triphosphate	acetyl	acetyl	H	NH_2	NH_2
triphosphate	acetyl	acetyl	H	NH_2	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	NH_2	OH
triphosphate	acetyl	acetyl	H	NH_2	F
triphosphate	acetyl	acetyl	H	NH_2	Cl
H	H	H	H	Cl	H
H	H	H	H	Cl	H
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	NH-methyl
H	H	H	H	Cl	NH-ethyl
H	H	H	H	Cl	NH-acetyl
H	H	H	H	Cl	OH
H	H	H	H	Cl	OMe
H	H	H	H	Cl	OEt
H	H	H	H	Cl	O-cyclopropyl
H	H	H	H	Cl	O-acetyl
H	H	H	H	Cl	SH
H	H	H	H	Cl	SMe
H	H	H	H	Cl	SEt
H	H	H	H	Cl	S-cyclopropyl
monophosphate	H	H	H	Cl	NH_2
monophosphate	H	H	H	Cl	NH-acetyl
monophosphate	H	H	H	Cl	NH-cyclopropyl
monophosphate	H	H	H	Cl	NH-methyl
monophosphate	H	H	H	Cl	NH-ethyl

R^1	R^2	R^3	X^1	X^2	Y
monophosphate	H	H	H	Cl	OH
monophosphate	H	H	H	Cl	O-acetyl
monophosphate	H	H	H	Cl	OMe
monophosphate	H	H	H	Cl	OEt
monophosphate	H	H	H	Cl	O-cyclopropyl
monophosphate	H	H	H	Cl	SH
monophosphate	H	H	H	Cl	SMe
monophosphate	H	H	H	Cl	SEt
monophosphate	H	H	H	Cl	S-cyclopropyl
diphosphate	H	H	H	Cl	NH_2
diphosphate	H	H	H	Cl	NH-acetyl
diphosphate	H	H	H	Cl	NH-cyclopropyl
diphosphate	H	H	H	Cl	NH-methyl
diphosphate	H	H	H	Cl	NH-ethyl
diphosphate	H	H	H	Cl	OH
diphosphate	H	H	H	Cl	O-acetyl
diphosphate	H	H	H	Cl	OMe
diphosphate	H	H	H	Cl	OEt
diphosphate	H	H	H	Cl	O-cyclopropyl
diphosphate	H	H	H	Cl	SH
diphosphate	H	H	H	Cl	SMe
diphosphate	H	H	H	Cl	SEt
diphosphate	H	H	H	Cl	S-cyclopropyl
triphosphate	H	H	H	Cl	NH_2
triphosphate	H	H	H	Cl	NH-acetyl
triphosphate	H	H	H	Cl	NH-cyclopropyl
triphosphate	H	H	H	Cl	NH-methyl
triphosphate	H	H	H	Cl	NH-ethyl
triphosphate	H	H	H	Cl	OH
triphosphate	H	H	H	Cl	OMe
triphosphate	H	H	H	Cl	OEt

R^1	R^2	R^3	X^1	X^2	Y
triphosphate	H	H	H	Cl	O-cyclopropyl
triphosphate	H	H	H	Cl	O-acetyl
triphosphate	H	H	H	Cl	SH
triphosphate	H	H	H	Cl	SMe
triphosphate	H	H	H	Cl	SEt
triphosphate	H	H	H	Cl	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	NH_2
monophosphate	monophosphate	monophosphate	H	Cl	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	Cl	OH
diphosphate	diphosphate	diphosphate	H	Cl	NH_2
diphosphate	diphosphate	diphosphate	H	Cl	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	Cl	OH
triphosphate	triphosphate	triphosphate	H	Cl	NH_2
triphosphate	triphosphate	triphosphate	H	Cl	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	Cl	OH
H	H	H	F	Cl	NH_2
H	H	H	F	Cl	NH-cyclopropyl
H	H	H	F	Cl	OH
H	H	H	Cl	Cl	NH_2
H	H	H	Cl	Cl	NH-cyclopropyl
H	H	H	Cl	Cl	OH
H	H	H	Br	Cl	NH_2
H	H	H	Br	Cl	NH-cyclopropyl
H	H	H	Br	Cl	OH
H	H	H	NH_2	Cl	NH_2
H	H	H	NH_2	Cl	NH-cyclopropyl
H	H	H	NH_2	Cl	OH
H	H	H	SH	Cl	NH_2
H	H	H	SH	Cl	NH-cyclopropyl
H	H	H	SH	Cl	OH
acetyl	H	H	H	Cl	NH_2

R^1	R^2	R^3	X^1	X^2	Y
acetyl	H	H	H	Cl	NH-cyclopropyl
acetyl	H	H	H	Cl	OH
acetyl	H	H	F	Cl	NH_2
acetyl	H	H	F	Cl	NH-cyclopropyl
acetyl	H	H	F	Cl	OH
H	acetyl	acetyl	H	Cl	NH_2
H	acetyl	acetyl	H	Cl	NH-cyclopropyl
H	acetyl	acetyl	H	Cl	OH
acetyl	acetyl	acetyl	H	Cl	NH_2
acetyl	acetyl	acetyl	H	Cl	NH-cyclopropyl
acetyl	acetyl	acetyl	H	Cl	OH
monophosphate	acetyl	acetyl	H	Cl	NH_2
monophosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	Cl	OH
diphosphate	acetyl	acetyl	H	Cl	NH_2
diphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	Cl	OH
triphosphate	acetyl	acetyl	H	Cl	NH_2
triphosphate	acetyl	acetyl	H	Cl	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	Cl	OH
H	H	H	H	Cl	NH_2
H	H	H	H	Cl	NH-cyclopropyl
H	H	H	H	Cl	OH
H	H	H	H	Br	NH_2
H	H	H	H	Br	NH-cyclopropyl
H	H	H	H	Br	OH

Alternatively, the following nucleosides of Formula VI are prepared, using the appropriate sugar and pyrimidine or purine bases.



(VI)

wherein:

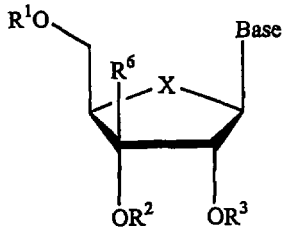
R^1	R^2	R^3	X^1	Y
H	H	H	H	H
H	H	H	H	NH_2
H	H	H	H	NH-cyclopropyl
H	H	H	H	NH-methyl
H	H	H	H	NH-ethyl
H	H	H	H	NH-acetyl
H	H	H	H	OH
H	H	H	H	OMe
H	H	H	H	OEt
H	H	H	H	O-cyclopropyl
H	H	H	H	O-acetyl
H	H	H	H	SH
H	H	H	H	SMe
H	H	H	H	SEt
H	H	H	H	S-cyclopropyl
monophosphate	H	H	H	NH_2
monophosphate	H	H	H	NH-acetyl
monophosphate	H	H	H	NH-cyclopropyl
monophosphate	H	H	H	NH-methyl
monophosphate	H	H	H	NH-ethyl
monophosphate	H	H	H	OH
monophosphate	H	H	H	O-acetyl

R^1	R^2	R^3	X^1	Y
monophosphate	H	H	H	OMe
monophosphate	H	H	H	OEt
monophosphate	H	H	H	O-cyclopropyl
monophosphate	H	H	H	SH
monophosphate	H	H	H	SMe
monophosphate	H	H	H	SEt
monophosphate	H	H	H	S-cyclopropyl
diphosphate	H	H	H	NH_2
diphosphate	H	H	H	NH-acetyl
diphosphate	H	H	H	NH-cyclopropyl
diphosphate	H	H	H	NH-methyl
diphosphate	H	H	H	NH-ethyl
diphosphate	H	H	H	OH
diphosphate	H	H	H	O-acetyl
diphosphate	H	H	H	OMe
diphosphate	H	H	H	OEt
diphosphate	H	H	H	O-cyclopropyl
diphosphate	H	H	H	SH
diphosphate	H	H	H	SMe
diphosphate	H	H	H	SEt
diphosphate	H	H	H	S-cyclopropyl
triphosphate	H	H	H	NH_2
triphosphate	H	H	H	NH-acetyl
triphosphate	H	H	H	NH-cyclopropyl
triphosphate	H	H	H	NH-methyl
triphosphate	H	H	H	NH-ethyl
triphosphate	H	H	H	OH
triphosphate	H	H	H	OMe
triphosphate	H	H	H	OEt
triphosphate	H	H	H	O-cyclopropyl
triphosphate	H	H	H	O-acetyl

R^1	R^2	R^3	X^1	Y
triphosphate	H	H	H	SH
triphosphate	H	H	H	SMe
triphosphate	H	H	H	SEt
triphosphate	H	H	H	S-cyclopropyl
monophosphate	monophosphate	monophosphate	H	NH_2
monophosphate	monophosphate	monophosphate	H	NH-cyclopropyl
monophosphate	monophosphate	monophosphate	H	OH
diphosphate	diphosphate	diphosphate	H	NH_2
diphosphate	diphosphate	diphosphate	H	NH-cyclopropyl
diphosphate	diphosphate	diphosphate	H	OH
triphosphate	triphosphate	triphosphate	H	NH_2
triphosphate	triphosphate	triphosphate	H	NH-cyclopropyl
triphosphate	triphosphate	triphosphate	H	OH
H	H	H	F	NH_2
H	H	H	F	NH-cyclopropyl
H	H	H	F	OH
H	H	H	Cl	NH_2
H	H	H	Cl	NH-cyclopropyl
H	H	H	Cl	OH
H	H	H	Br	NH_2
H	H	H	Br	NH-cyclopropyl
H	H	H	Br	OH
H	H	H	NH_2	NH_2
H	H	H	NH_2	NH-cyclopropyl
H	H	H	NH_2	OH
H	H	H	SH	NH_2
H	H	H	SH	NH-cyclopropyl
H	H	H	SH	OH
acetyl	H	H	H	NH_2
acetyl	H	H	H	NH-cyclopropyl
acetyl	H	H	H	OH

R^1	R^2	R^3	X^1	Y
acetyl	H	H	F	NH_2
acetyl	H	H	F	NH-cyclopropyl
acetyl	H	H	F	OH
H	acetyl	acetyl	H	NH_2
H	acetyl	acetyl	H	NH-cyclopropyl
H	acetyl	acetyl	H	OH
acetyl	acetyl	acetyl	H	NH_2
acetyl	acetyl	acetyl	H	NH-cyclopropyl
acetyl	acetyl	acetyl	H	OH
monophosphate	acetyl	acetyl	H	NH_2
monophosphate	acetyl	acetyl	H	NH-cyclopropyl
monophosphate	acetyl	acetyl	H	OH
diphosphate	acetyl	acetyl	H	NH_2
diphosphate	acetyl	acetyl	H	NH-cyclopropyl
diphosphate	acetyl	acetyl	H	OH
triphosphate	acetyl	acetyl	H	NH_2
triphosphate	acetyl	acetyl	H	NH-cyclopropyl
triphosphate	acetyl	acetyl	H	OH

Alternatively, the following nucleosides of Formula XIII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XIII)

wherein:

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	2,4-O-Diacetyluracil
H	H	H	CH_3	O	Hypoxanthine

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	H	CH_3	O	Thymine
H	H	H	CH_3	O	Cytosine
H	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	Uracil
H	H	H	CH_3	O	5-Fluorouracil
H	H	H	CH_3	S	2,4-O-Diacetyluraci
H	H	H	CH_3	S	Hypoxanthine
H	H	H	CH_3	S	2,4-O-Diacetylthymine
H	H	H	CH_3	S	Thymine
H	H	H	CH_3	S	Cytosine
H	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
H	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	S	Uracil
H	H	H	CH_3	S	5-Fluorouracil
monophosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	O	Hypoxanthine
monophosphate	H	H	CH_3	O	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	O	Thymine
monophosphate	H	H	CH_3	O	Cytosine
monophosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine

R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	O	Uracil
monophosphate	H	H	CH_3	O	5-Fluorouracil
monophosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	H	CH_3	S	Hypoxanthine
monophosphate	H	H	CH_3	S	2,4-O-Diacetylthym
monophosphate	H	H	CH_3	S	Thymine
monophosphate	H	H	CH_3	S	Cytosine
monophosphate	H	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	H	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	H	H	CH_3	S	Uracil
monophosphate	H	H	CH_3	S	5-Fluorouracil
diphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
diphosphate	H	H	CH_3	O	Hypoxanthine
diphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
diphosphate	H	H	CH_3	O	Thymine
diphosphate	H	H	CH_3	O	Cytosine
diphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	H	CH_3	O	Uracil
diphosphate	H	H	CH_3	O	5-Fluorouracil
diphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil

R^1	R^2	R^3	R^6	X	Base
diphosphate	H	H	CH_3	S	Hypoxanthine
diphosphate	H	H	CH_3	S	2,4-O-Diacetylthym
diphosphate	H	H	CH_3	S	Thymine
diphosphate	H	H	CH_3	S	Cytosine
triphosphate	H	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	O	Hypoxanthine
triphosphate	H	H	CH_3	O	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	O	Thymine
triphosphate	H	H	CH_3	O	Cytosine
triphosphate	H	H	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	H	H	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	H	H	CH_3	O	Uracil
triphosphate	H	H	CH_3	O	5-Fluorouracil
triphosphate	H	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	H	CH_3	S	Hypoxanthine
triphosphate	H	H	CH_3	S	2,4-O-Diacetylthymine
triphosphate	H	H	CH_3	S	Thymine
triphosphate	H	H	CH_3	S	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	O	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	monophosphate	monophosphate	CF_3	O	Thymine
monophosphate	monophosphate	monophosphate	CF_3	O	Cytosine

R^1	R^2	R^3	R^6	X	Base
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	O	Uracil
monophosphate	monophosphate	monophosphate	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	monophosphate	CF_3	S	Hypoxanthine
monophosphate	monophosphate	monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	monophosphate	CF_3	S	Thymine
monophosphate	monophosphate	monophosphate	CF_3	S	Cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	monophosphate	CF_3	S	Uracil
monophosphate	monophosphate	monophosphate	CF_3	S	5-Fluorouracil
acetyl	acetyl	acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine
H	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
H	H	H	CH_3	O	6-O-acetyl guanine
H	H	H	CH_3	O	8-fluoroguanine

R^1	R^2	R^3	R^6	X	Base
H	H	H	CH_3	O	guanine
H	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	O	2-fluoroadenine
H	H	H	CH_3	O	8-fluoroadenine
H	H	H	CH_3	O	2,8-difluoro-adenine
H	H	H	CH_3	O	adenine
H	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
H	H	H	CH_3	S	6-O-acetyl guanine
H	H	H	CH_3	S	8-fluoroguanine
H	H	H	CH_3	S	guanine
H	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
H	H	H	CH_3	S	2-fluoroadenine
H	H	H	CH_3	S	8-fluoroadenine
H	H	H	CH_3	S	2,8-difluoro-adenine
H	H	H	CH_3	S	adenine
monophosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	O	6-O-acetyl guanine
monophosphate	H	H	CH_3	O	8-fluoroguanine
monophosphate	H	H	CH_3	O	guanine
monophosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
monophosphate	H	H	CH_3	O	2-fluoroadenine
monophosphate	H	H	CH_3	O	8-fluoroadenine

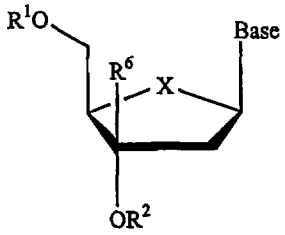
R^1	R^2	R^3	R^6	X	Base
monophosphate	H	H	CH_3	O	2,8-difluoro-adenine
monophosphate	H	H	CH_3	O	adenine
monophosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine
monophosphate	H	H	CH_3	S	6-O-acetyl guanine
monophosphate	H	H	CH_3	S	8-fluoroguanine
monophosphate	H	H	CH_3	S	guanine
monophosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
monophosphate	H	H	CH_3	S	2-fluoroadenine
monophosphate	H	H	CH_3	S	8-fluoroadenine
monophosphate	H	H	CH_3	S	2,8-difluoro-adenine
monophosphate	H	H	CH_3	S	adenine
diphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
diphosphate	H	H	CH_3	O	6-O-acetyl guanine
diphosphate	H	H	CH_3	O	8-fluoroguanine
diphosphate	H	H	CH_3	O	guanine
diphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	O	2-fluoroadenine
diphosphate	H	H	CH_3	O	8-fluoroadenine
diphosphate	H	H	CH_3	O	2,8-difluoro-adenine
diphosphate	H	H	CH_3	O	adenine
diphosphate	H	H	CH_3	S	2-(N,N-diacetyl)-guanine

R^1	R^2	R^3	R^6	X	Base
diphosphate	H	H	CH_3	S	6-O-acetyl guanine
diphosphate	H	H	CH_3	S	8-fluoroguanine
diphosphate	H	H	CH_3	S	guanine
diphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
diphosphate	H	H	CH_3	S	2-fluoroadenine
diphosphate	H	H	CH_3	S	8-fluoroadenine
diphosphate	H	H	CH_3	S	2,8-difluoro-adenine
diphosphate	H	H	CH_3	S	adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	H	CH_3	O	6-O-acetyl guanine
triphosphate	H	H	CH_3	O	8-fluoroguanine
triphosphate	H	H	CH_3	O	guanine
triphosphate	H	H	CH_3	O	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	O	2-fluoroadenine
triphosphate	H	H	CH_3	O	8-fluoroadenine
triphosphate	H	H	CH_3	O	2,8-difluoro-adenine
triphosphate	H	H	CH_3	O	2-(N,N-diacetyl)-guanine
triphosphate	H	H	CH_3	S	6-O-acetyl guanine
triphosphate	H	H	CH_3	S	8-fluoroguanine
triphosphate	H	H	CH_3	S	guanine
triphosphate	H	H	CH_3	S	6-(N,N-diacetyl)-adenine
triphosphate	H	H	CH_3	S	2-fluoroadenine

R^1	R^2	R^3	R^6	X	Base
triphosphate	H	H	CH_3	S	8-fluoroadenine
triphosphate	H	H	CH_3	S	2,8-difluoro-adenine
triphosphate	H	H	CH_3	S	adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	O	guanine
monophosphate	monophosphate	monophosphate	CF_3	O	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	2-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	O	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	O	2,8-difluoro-adenine
monophosphate	monophosphate	monophosphate	CF_3	O	adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-(N,N-diacetyl)-guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-O-acetyl guanine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroguanine
monophosphate	monophosphate	monophosphate	CF_3	S	guanine
monophosphate	monophosphate	monophosphate	CF_3	S	6-(N,N-diacetyl)-adenine
monophosphate	monophosphate	monophosphate	CF_3	S	2-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	8-fluoroadenine
monophosphate	monophosphate	monophosphate	CF_3	S	2,8-difluoro-adenine
monophosphate	monophosphate	monophosphate	CF_3	S	adenine
acetyl	acetyl	acetyl	CF_3	O	guanine
acetyl	acetyl	acetyl	CF_3	S	guanine

R^1	R^2	R^3	R^6	X	Base
acetyl	acetyl	acetyl	2-bromo-vinyl	O	guanine
acetyl	acetyl	acetyl	2-bromo-vinyl	S	guanine

Alternatively, the following nucleosides of Formula XIV are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XIV)

wherein:

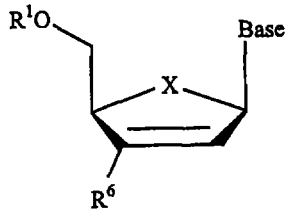
R^1	R^2	R^6	X	Base
H	H	CH_3	O	2,4-O-Diacetyluracil
H	H	CH_3	O	Hypoxanthine
H	H	CH_3	O	2,4-O-Diacetylthymine
H	H	CH_3	O	Thymine
H	H	CH_3	O	Cytosine
H	H	CH_3	O	4-(N-mono-acetyl)cytosine
H	H	CH_3	O	4-(N,N-diacetyl)cytosine
H	H	CH_3	O	Uracil
H	H	CH_3	O	5-Fluorouracil
H	H	CH_3	S	2,4-O-Diacetyluracil
H	H	CH_3	S	Hypoxanthine
H	H	CH_3	S	2,4-O-Diacetylthymine
H	H	CH_3	S	Thymine
H	H	CH_3	S	Cytosine
H	H	CH_3	S	4-(N-mono-acetyl)cytosin
H	H	CH_3	S	4-(N,N-diacetyl)cytosine

R^1	R^2	R^6	X	Base
H	H	CH_3	S	Uracil
H	H	CH_3	S	5-Fluorouracil
monophosphate	H	CH_3	O	2,4-O-Diacetyluracil
monophosphate	H	CH_3	O	Hypoxanthine
monophosphate	H	CH_3	O	2,4-O-Diacetylthym
monophosphate	H	CH_3	O	Thymine
monophosphate	H	CH_3	O	Cytosine
monophosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	H	CH_3	O	4-(N,N-diacetyl)cytos
monophosphate	H	CH_3	O	Uracil
monophosphate	H	CH_3	O	5-Fluorouracil
monophosphate	H	CH_3	S	2,4-O-Diacetyluracil
monophosphate	H	CH_3	S	Hypoxanthine
monophosphate	H	CH_3	S	2,4-O-Diacetylthym
monophosphate	H	CH_3	S	Thymine
monophosphate	H	CH_3	S	Cytosine
monophosphate	H	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	H	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	H	CH_3	S	Uracil
monophosphate	H	CH_3	S	5-Fluorouracil
diphosphate	H	CH_3	O	2,4-O-Diacetyluracil
diphosphate	H	CH_3	O	Hypoxanthine
diphosphate	H	CH_3	O	2,4-O-Diacetylthymine
diphosphate	H	CH_3	O	Thymine
diphosphate	H	CH_3	O	Cytosine
diphosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	H	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	H	CH_3	O	Uracil
diphosphate	H	CH_3	O	5-Fluorouracil
diphosphate	H	CH_3	S	2,4-O-Diacetyluracil
diphosphate	H	CH_3	S	Hypoxanthine

R^1	R^2	R^6	X	Base
diphosphate	H	CH_3	S	2,4-O-Diacetylthymine
diphosphate	H	CH_3	S	Thymine
diphosphate	H	CH_3	S	Cytosine
triphosphate	H	CH_3	O	2,4-O-Diacetyluracil
triphosphate	H	CH_3	O	Hypoxanthine
triphosphate	H	CH_3	O	2,4-O-Diacetylthymine
triphosphate	H	CH_3	O	Thymine
triphosphate	H	CH_3	O	Cytosine
triphosphate	H	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	H	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	H	CH_3	O	Uracil
triphosphate	H	CH_3	O	5-Fluorouracil
triphosphate	H	CH_3	S	2,4-O-Diacetyluracil
triphosphate	H	CH_3	S	Hypoxanthine
triphosphate	H	CH_3	S	2,4-O-Diacetylthymine
triphosphate	H	CH_3	S	Thymine
triphosphate	H	CH_3	S	Cytosine
monophosphate	monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	monophosphate	CF_3	O	Hypoxanthine
monophosphate	monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	monophosphate	CF_3	O	Thymine
monophosphate	monophosphate	CF_3	O	Cytosine
monophosphate	monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	CF_3	O	Uracil
monophosphate	monophosphate	CF_3	O	5-Fluorouracil
monophosphate	monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	monophosphate	CF_3	S	Hypoxanthine
monophosphate	monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	monophosphate	CF_3	S	Thymine
monophosphate	monophosphate	CF_3	S	Cytosine

R^1	R^2	R^6	X	Base
monophosphate	monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	monophosphate	CF_3	S	Uracil
monophosphate	monophosphate	CF_3	S	5-Fluorouracil
acetyl	acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine

Alternatively, the following nucleosides of Formula XV are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XV)

wherein:

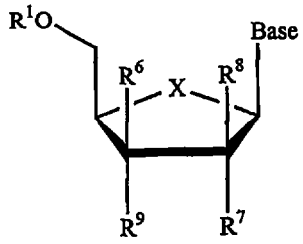
R^1	R^6	X	Base
H	CH_3	O	2,4-O-Diacetyluracil
H	CH_3	O	Hypoxanthine
H	CH_3	O	2,4-O-Diacetylthymine
H	CH_3	O	Thymine
H	CH_3	O	Cytosine
H	CH_3	O	4-(N-mono-acetyl)cytosine
H	CH_3	O	4-(N,N-diacetyl)cytosine
H	CH_3	O	Uracil
H	CH_3	O	5-Fluorouracil
H	CH_3	S	2,4-O-Diacetyluracil

R^1	R^6	X	Base
H	CH_3	S	Hypoxanthine
H	CH_3	S	2,4-O-Diacetylthymine
H	CH_3	S	Thymine
H	CH_3	S	Cytosine
H	CH_3	S	4-(N-mono-acetyl)cytosine
H	CH_3	S	4-(N,N-diacetyl)cytosine
H	CH_3	S	Uracil
H	CH_3	S	5-Fluorouracil
monophosphate	CH_3	O	2,4-O-Diacetyluracil
monophosphate	CH_3	O	Hypoxanthine
monophosphate	CH_3	O	2,4-O-Diacetylthymine
monophosphate	CH_3	O	Thymine
monophosphate	CH_3	O	Cytosine
monophosphate	CH_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	O	4-(N,N-diacetyl)cytosine
monophosphate	CH_3	O	Uracil
monophosphate	CH_3	O	5-Fluorouracil
monophosphate	CH_3	S	2,4-O-Diacetyluracil
monophosphate	CH_3	S	Hypoxanthine
monophosphate	CH_3	S	2,4-O-Diacetylthymine
monophosphate	CH_3	S	Thymine
monophosphate	CH_3	S	Cytosine
monophosphate	CH_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CH_3	S	4-(N,N-diacetyl)cytosine
monophosphate	CH_3	S	Uracil
monophosphate	CH_3	S	5-Fluorouracil
diphosphate	CH_3	O	2,4-O-Diacetyluracil
diphosphate	CH_3	O	Hypoxanthine
diphosphate	CH_3	O	2,4-O-Diacetylthymine
diphosphate	CH_3	O	Thymine
diphosphate	CH_3	O	Cytosine

R^1	R^6	X	Base
diphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
diphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
diphosphate	CH_3	O	Uracil
diphosphate	CH_3	O	5-Fluorouracil
diphosphate	CH_3	S	2,4-O-Diacetyluracil
diphosphate	CH_3	S	Hypoxanthine
diphosphate	CH_3	S	2,4-O-Diacetylthymine
diphosphate	CH_3	S	Thymine
diphosphate	CH_3	S	Cytosine
triphosphate	CH_3	O	2,4-O-Diacetyluracil
triphosphate	CH_3	O	Hypoxanthine
triphosphate	CH_3	O	2,4-O-Diacetylthymine
triphosphate	CH_3	O	Thymine
triphosphate	CH_3	O	Cytosine
triphosphate	CH_3	O	4-(N-mono-acetyl)cytosine
triphosphate	CH_3	O	4-(N,N-diacetyl)cytosine
triphosphate	CH_3	O	Uracil
triphosphate	CH_3	O	5-Fluorouracil
triphosphate	CH_3	S	2,4-O-Diacetyluracil
triphosphate	CH_3	S	Hypoxanthine
triphosphate	CH_3	S	2,4-O-Diacetylthymine
triphosphate	CH_3	S	Thymine
triphosphate	CH_3	S	Cytosine
monophosphate	CF_3	O	2,4-O-Diacetyluracil
monophosphate	CF_3	O	Hypoxanthine
monophosphate	CF_3	O	2,4-O-Diacetylthymine
monophosphate	CF_3	O	Thymine
monophosphate	CF_3	O	Cytosine
monophosphate	CF_3	O	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	O	4-(N,N-diacetyl)cytosine
monophosphate	CF_3	O	Uracil

R^1	R^6	X	Base
monophosphate	CF_3	O	5-Fluorouracil
monophosphate	CF_3	S	2,4-O-Diacetyluracil
monophosphate	CF_3	S	Hypoxanthine
monophosphate	CF_3	S	2,4-O-Diacetylthymine
monophosphate	CF_3	S	Thymine
monophosphate	CF_3	S	Cytosine
monophosphate	CF_3	S	4-(N-mono-acetyl)cytosine
monophosphate	CF_3	S	4-(N,N-diacetyl)cytosine
monophosphate	CF_3	S	Uracil
monophosphate	CF_3	S	5-Fluorouracil
acetyl	CF_3	O	4-(N,N-diacetyl)cytosine
acetyl	CF_3	S	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	O	4-(N,N-diacetyl)cytosine
acetyl	2-bromo-vinyl	S	4-(N,N-diacetyl)cytosine

Alternatively, the following nucleosides of Formula XVIII are prepared, using the appropriate sugar and pyrimidine or purine bases.



(XVIII)

wherein:

R^1	R^6	R^7	X	Base	R^8	R^9
H	CH_3	OH	O	2,4-O-Diacetyluracil	H	Me
H	CH_3	OH	O	Hypoxanthine	H	Me
H	CH_3	OH	O	2,4-O-Diacetylthymine	H	Me
H	CH_3	OH	O	Thymine	H	Me
H	CH_3	OH	O	Cytosine	H	Me

R^1	R^6	R^7	X	Base	R^8	R^9
H	CH_3	OH	O	4-(N-mono-acetyl)cytosine	H	Me
H	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Me
H	CH_3	OH	O	Uracil	H	Me
H	CH_3	OH	O	5-Fluorouracil	H	Me
H	CH_3	OH	S	2,4-O-Diacetyluracil	H	Me
H	CH_3	OH	S	Hypoxanthine	H	Me
H	CH_3	OH	S	2,4-O-Diacetylthymine	H	Me
H	CH_3	OH	S	Thymine	H	Me
H	CH_3	OH	S	Cytosine	H	Me
H	CH_3	OH	S	4-(N-mono-acetyl)cytosine	H	Me
H	CH_3	OH	S	4-(N,N-diacetyl)cytosine	H	Me
H	CH_3	OH	S	Uracil	H	Me
H	CH_3	OH	S	5-Fluorouracil	H	Me
monophosphate	CH_3	OH	O	2,4-O-Diacetyluracil	H	Me
monophosphate	CH_3	OH	O	Hypoxanthine	H	Me
monophosphate	CH_3	OH	O	2,4-O-Diacetylthymine	H	Me
monophosphate	CH_3	OH	O	Thymine	H	Me
monophosphate	CH_3	OH	O	Cytosine	H	Me
monophosphate	CH_3	OH	O	4-(N-mono-acetyl)cytosine	H	Me
monophosphate	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Me
monophosphate	CH_3	OH	O	Uracil	H	Me
monophosphate	CH_3	OH	O	5-Fluorouracil	H	Me
monophosphate	CH_3	OH	S	2,4-O-Diacetyluracil	H	Me
monophosphate	CH_3	OH	S	Hypoxanthine	H	Me
monophosphate	CH_3	OH	S	2,4-O-Diacetylthymine	H	Me
monophosphate	CH_3	OH	S	Thymine	H	Me
monophosphate	CH_3	OH	S	Cytosine	H	Me
monophosphate	CH_3	OH	S	4-(N-mono-acetyl)cytosine	H	Me
monophosphate	CH_3	OH	S	4-(N,N-diacetyl)cytosine	H	Me
monophosphate	CH_3	OH	S	Uracil	H	Me
monophosphate	CH_3	OH	S	5-Fluorouracil	H	Me

R^1	R^6	R^7	X	Base	R^8	R^9
diphosphate	CH_3	OH	O	2,4-O-Diacetyluracil	H	Me
diphosphate	CH_3	OH	O	Hypoxanthine	H	Me
diphosphate	CH_3	OH	O	2,4-O-Diacetylthymine	H	Me
diphosphate	CH_3	OH	O	Thymine	H	Me
diphosphate	CH_3	OH	O	Cytosine	H	Me
diphosphate	CH_3	OH	O	4-(N-mono-acetyl)cytosine	H	Me
diphosphate	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Me
diphosphate	CH_3	OH	O	Uracil	H	Me
diphosphate	CH_3	OH	O	5-Fluorouracil	H	Me
diphosphate	CH_3	OH	S	2,4-O-Diacetyluracil	H	Me
diphosphate	CH_3	OH	S	Hypoxanthine	H	Me
diphosphate	CH_3	OH	S	2,4-O-Diacetylthymine	H	Me
diphosphate	CH_3	OH	S	Thymine	H	Me
diphosphate	CH_3	OH	S	Cytosine	H	Me
triphosphate	CH_3	OH	O	2,4-O-Diacetyluracil	H	Me
triphosphate	CH_3	OH	O	Hypoxanthine	H	Me
triphosphate	CH_3	OH	O	2,4-O-Diacetylthymine	H	Me
triphosphate	CH_3	OH	O	Thymine	H	Me
triphosphate	CH_3	OH	O	Cytosine	H	Me
triphosphate	CH_3	OH	O	4-(N-mono-acetyl)cytosine	H	Me
triphosphate	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Me
triphosphate	CH_3	OH	O	Uracil	H	Me
triphosphate	CH_3	OH	O	5-Fluorouracil	H	Me
triphosphate	CH_3	OH	S	2,4-O-Diacetyluracil	H	Me
triphosphate	CH_3	OH	S	Hypoxanthine	H	Me
triphosphate	CH_3	OH	S	2,4-O-Diacetylthymine	H	Me
triphosphate	CH_3	OH	S	Thymine	H	Me
triphosphate	CH_3	OH	S	Cytosine	H	Me
monophosphate	CF_3	OH	O	2,4-O-Diacetyluracil	H	Me
monophosphate	CF_3	OH	O	Hypoxanthine	H	Me
monophosphate	CF_3	OH	O	2,4-O-Diacetylthymine	H	Me

R^1	R^6	R^7	X	Base	R^8	R^9
monophosphate	CF_3	OH	O	Thymine	H	Me
monophosphate	CF_3	OH	O	Cytosine	H	Me
monophosphate	CF_3	OH	O	4-(N-mono-acetyl)cytosine	H	Me
monophosphate	CF_3	OH	O	4-(N,N-diacetyl)cytosine	H	Me
monophosphate	CF_3	OH	O	Uracil	H	Me
monophosphate	CF_3	OH	O	5-Fluorouracil	H	Me
monophosphate	CF_3	OH	S	2,4-O-Diacetyluracil	H	Me
monophosphate	CF_3	OH	S	Hypoxanthine	H	Me
monophosphate	CF_3	OH	S	2,4-O-Diacetylthymine	H	Me
monophosphate	CF_3	OH	S	Thymine	H	Me
monophosphate	CF_3	OH	S	Cytosine	H	Me
monophosphate	CF_3	OH	S	4-(N-mono-acetyl)cytosine	H	Me
monophosphate	CF_3	OH	S	4-(N,N-diacetyl)cytosine	H	Me
monophosphate	CF_3	OH	S	Uracil	H	Me
monophosphate	CF_3	OH	S	5-Fluorouracil	H	Me
acetyl	CH_3	OH	O	4-(N,N-diacetyl)cytosine	H	Br
acetyl	CH_3	OH	S	4-(N,N-diacetyl)cytosine	H	Br

VII. Anti-Flavivirus or Pestivirus Activity

Compounds can exhibit anti-flavivirus or pestivirus activity by inhibiting flavivirus or pestivirus polymerase, by inhibiting other enzymes needed in the replication cycle, or by other pathways.

EXAMPLES

The test compounds were dissolved in DMSO at an initial concentration of 200 μM and then were serially diluted in culture medium.

Unless otherwise stated, baby hamster kidney (BHK-21) (ATCC CCL-10) and Bos Taurus (BT) (ATCC CRL 1390) cells were grown at 37°C in a humidified CO_2 (5%) atmosphere. BHK-21 cells were passaged in Eagle MEM additioned of 2 mM L-glutamine,

10% fetal bovine serum (FBS, Gibco) and Earle's BSS adjusted to contain 1.5 g/L sodium bicarbonate and 0.1 mM non-essential amino acids. BT cells were passaged in Dulbecco's modified Eagle's medium with 4 mM L-glutamine and 10% horse serum (HS, Gibco), adjusted to contain 1.5 g/L sodium bicarbonate, 4.5 g/L glucose and 1.0 mM sodium pyruvate. The vaccine strain 17D (YFV-17D) (Stamaril®, Pasteur Merieux) and Bovine Viral Diarrhea virus (BVDV) (ATCC VR-534) were used to infect BHK and BT cells, respectively, in 75 cm^2 bottles. After a 3 day incubation period at 37°C, extensive cytopathic effect was observed. Cultures were freeze-thawed three times, cell debris were removed by centrifugation and the supernatant was aliquoted and stored at -70°C. YFV-17D and BVDV were titrated in BHK-21 and BT cells, respectively, that were grown to confluency in 24-well plates.

Example 4: Phosphorylation Assay of Nucleoside to Active Triphosphate

To determine the cellular metabolism of the compounds, HepG2 cells were obtained from the American Type Culture Collection (Rockville, MD), and were grown in 225 cm^2 tissue culture flasks in minimal essential medium supplemented with non-essential amino acids, 1% penicillin-streptomycin. The medium was renewed every three days, and the cells were subcultured once a week. After detachment of the adherent monolayer with a 10 minute exposure to 30 mL of trypsin-EDTA and three consecutive washes with medium, confluent HepG2 cells were seeded at a density of 2.5 x 10^6 cells per well in a 6-well plate and exposed to 10 μM of [^{3}H] labeled active compound (500 dpm/pmol) for the specified time periods. The cells were maintained at 37°C under a 5% CO_2 atmosphere. At the selected time points, the cells were washed three times with ice-cold phosphate-buffered saline (PBS). Intracellular active compound and its respective metabolites were extracted by incubating the cell pellet overnight at –20°C with 60% methanol followed by extraction with an additional 20 μL of cold methanol for one hour in an ice bath. The extracts were then combined, dried under gentle filtered air flow and stored at –20°C until HPLC analysis. The preliminary results of the HPLC analysis are tabulated in **Table 1**.

Table 1

Time (h)	[pmol/million cells] β-D-2'-CH_3-riboA-TP	β-D-2'-CH_3-riboU-TP	β-D-2'-CH_3-riboC-TP	β-D-2'-CH_3-riboG-TP
2	33.1	0.40	2.24	ND
4	67.7	1.21	3.99	ND
8	147	1.57	9.76	2.85
24	427	6.39	34.9	0.91
30	456	7.18	36.2	3.22
48	288	9.42	56.4	6.26

Example 5: Bioavailability Assay in Cynomolgus Monkeys

Within 1 week prior to the study initiation, the cynomolgus monkey was surgically implanted with a chronic venous catheter and subcutaneous venous access port (VAP) to facilitate blood collection and underwent a physical examination including hematology and serum chemistry evaluations and the body weight was recorded. Each monkey (six total), received approximately 250 uCi of ^3H activity with each dose of active compound, namely β-D-2'-CH_3-riboG at a dose level of 10 mg/kg at a dose concentration of 5 mg/mL, either via an intravenous bolus (3 monkeys, IV), or via oral gavage (3 monkeys, PO). Each dosing syringe was weighed before dosing to gravimetrically determine the quantity of formulation administered. Urine samples were collected via pan catch at the designated intervals (approximately 18-0 hours pre-dose, 0-4, 4-8 and 8-12 hours post-dosage) and processed. Blood samples were collected as well (pre-dose, 0.25, 0.5, 1, 2, 3, 6, 8, 12 and 24 hours post-dosage) via the chronic venous catheter and VAP or from a peripheral vessel if the chronic venous catheter procedure should not be possible. The blood and urine samples were analyzed for the maximum concentration (C_{max}), time when the maximum concentration was achieved (T_{max}), area under the curve (AUC), half life of the dosage concentration ($T_{½}$), clearance (CL), steady state volume and distribution (V_{ss}) and bioavailability (F), which are tabulated in **Tables 2** and **3**, and graphically illustrated in **Figures 2** and **3**, respectively.

Table 2: Oral Bioavailability in Monkeys

	Dose (mg)	AUC (ng/mL x h)	Norm AUC (ng/mL x h/mg)	Mean Norm AUC (ng/mL x h/mg)	F (%)
IV Monkey 1	46.44	13614	293.2		
IV Monkey 2	24.53	6581	268.3		
IV Monkey 3	20.72	6079	293.4	284.9	
PO Monkey 1	29.04	758	26.1		
PO Monkey 2	30.93	898	29.0		
PO Monkey 3	30.04	1842	61.3	38.8	13.6

Table 3: Experimental Pharmacokinetics of β-D-2'-CH_3-riboG in Cynomolgus Monkeys

	IV	PO
Dose/Route (mg/kg)	10	10
C_{max} (ng/mL)	6945.6 ± 1886.0	217.7 ± 132.1
T_{max} (hr)	0.25 ± 0.00	2.00 ± 1.00
AUC (ng/mL x hr)	8758.0 ± 4212.9	1166.0 ± 589.6
$T_{½}$ (hr)	7.9 ± 5.4	10.3 ± 4.1
CL (L/hr/kg)	1.28 ± 0.48	
V_{ss} (L/kg)	2.09 ± 0.54	
F (%)	13.8	

Example 6: Bone Marrow Toxicity Assay

Human bone marrow cells were collected from normal healthy volunteers and the mononuclear population was separated by Ficoll-Hypaque gradient centrifugation as described previously by Sommadossi J-P, Carlisle R. "Toxicity of 3'-azido-3'-deoxythymidine and 9-(1,3-dihydroxy-2-propoxymethyl)guanine for normal human hematopoietic progenitor cells *in vitro*" Antimicrobial Agents and Chemotherapy 1987; 31:452-454; and Sommadossi J-P, Schinazi RF, Chu CK, Xie M-Y. "Comparison of cytotoxicity of the (-)- and (+)-enantiomer of 2',3'-dideoxy-3'-thiacytidine in normal human bone marrow progenitor cells" Biochemical Pharmacology 1992; 44:1921-1925. The culture assays for CFU-GM and BFU-E were performed using a bilayer soft agar or methylcellulose method. Drugs were diluted in tissue culture medium and filtered. After 14 to 18 days at 37°C in a humidified atmosphere of 5% CO_2 in air, colonies of greater than 50 cells were counted using an inverted microscope. The results in **Table 4** are presented as the percent inhibition of colony formation in the presence of drug compared to solvent control cultures.

Table 4: Human Bone Marrow Toxicity CFU-GM and BFU-E Clonogenic Assays

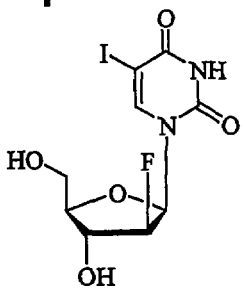
Treatment	IC_{50} in μM	
	CFU-GM	BFU-E
ribavirin	~ 5	~ 1
β-D-2'-CH_3-riboA	> 100	> 100
β-D-2'-CH_3-riboU	> 100	> 100
β-D-2'-CH_3-riboC	> 10	> 10
β-D-2'-CH_3-riboG	> 10	> 100

Example 7: Mitochondria Toxicity Assay

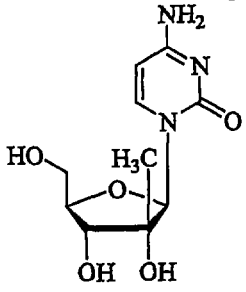
HepG2 cells were cultured in 12-well plates as described above and exposed to various concentrations of drugs as taught by Pan-Zhou X-R, Cui L, Zhou X-J, Sommadossi J-P, Darley-Usmer VM. "Differential effects of antiretroviral nucleoside analogs on mitochondrial function in HepG2 cells" Antimicrob Agents Chemother 2000; 44:496-503. Lactic acid levels in the culture medium after 4 day drug exposure was measured using a Boehringer lactic acid assay kit. Lactic acid levels were normalized by cell number as measured by hemocytometer count. The preliminary results from this assay are tabulated in **Table 5.**

Table 5: Mitochondrial Toxicity Study (L-lactic acid assay)

	Conc. (μM)	lactate (mg/10^6 cell)	% of Control
Control		2.18	
FIAU	10	3.73	170.4
β-D-2'-CH_3-riboC	1	2.52	115.3
	10	2.36	107.9
	50	2.26	103.4
	100	2.21	101.2



FIAU



β-D-2'-CH_3-riboC

Example 8: Cytotoxicity Assay

Cells were seeded at a rate of between 5 x 10^3 and 5 x 10^4/well into 96-well plates in growth medium overnight at 37°C in a humidified CO_2 (5%) atmosphere. New growth medium containing serial dilutions of the drugs was then added. After incubation for 4 days, cultures were fixed in 50% TCA and stained with sulforhodamineB. The optical density was read at 550 nm. The cytotoxic concentration was expressed as the concentration required to reduce the cell number by 50% (CC_{50}). The data is tabulated in **Table 6.**

Table 6: MDBK versus Human Hepatoma

Compound	CC_{50}, μM		
	MDBK	Huh7	HepG2
β-D-2'-CH_3-riboA	20	40	50-60
β-D-2'-CH_3-riboU	> 250	> 250	> 250
β-D-2'-CH_3-riboC	100	> 250	150
β-D-2'-CH_3-riboG	100	> 250	> 250
Ribavirin	5	25	150

Example 9: Cell Protection Assay (CPA)

The assay was performed essentially as described by Baginski, S. G.; Pevear, D. C.; Seipel, M.; Sun, S. C. C.; Benetatos, C. A.; Chunduru, S. K.; Rice, C. M. and M. S. Collett "Mechanism of action of a pestivirus antiviral compound" *PNAS USA* **2000**, 97(14), 7981-7986. MDBK cells (ATCC) were seeded onto 96-well culture plates (4,000 cells per well) 24 hours before use. After infection with BVDV (strain NADL, ATCC) at a multiplicity of infection (MOI) of 0.02 plaque forming units (PFU) per cell, serial dilutions of test compounds were added to both infected and uninfected cells in a final concentration of 0.5% DMSO in growth medium. Each dilution was tested in quadruplicate. Cell densities and virus inocula were adjusted to ensure continuous cell growth throughout the experiment and to achieve more than 90% virus-induced cell destruction in the untreated controls after four days post-infection. After four days, plates were fixed with 50% TCA and stained with sulforhodamine B. The optical density of the wells was read in a microplate reader at 550 nm. The 50% effective concentration (EC_{50}) values were defined as the compound concentration that achieved 50% reduction of cytopathic effect of the virus. The results are tabulated in **Table 7. Figures 4** and **5** provide a graphical illustration of the methodology used to arrive

at the 50% effective concentration (EC_{50}) values for β-D-2'-CH_3-riboG and ribavirin. **Figure 6** compares the results of the CPA for β-D-2'-CH_3-riboG, β-D-2'-CH_3-riboC, β-D-2'-CH_3-riboU, β-D-2'-CH_3-riboA and ribavirin

Table 7: Cell Protection Assay

	EC_{50}, μM	CC_{50}, μM
β-D-2'-CH_3-riboA	2	20
β-D-2'-CH_3-riboU	20	> 250
β-D-2'-CH_3-riboC	2	100
β-D-2'-CH_3-riboG	4	100
Ribavirin	> 3	5

Example 10: Plaque Reduction Assay

For each compound the effective concentration was determined in duplicate 24-well plates by plaque reduction assays. Cell monolayers were infected with 100 PFU/well of virus. Then, serial dilutions of test compounds in MEM supplemented with 2% inactivated serum and 0.75% of methyl cellulose were added to the monolayers. Cultures were further incubated at 37°C for 3 days, then fixed with 50% ethanol and 0.8% Crystal Violet, washed and air-dried. Then plaques were counted to determine the concentration to obtain 90% virus suppression and tabulated in **Table 8**. **Figure 7** is a graphical illustration of the results from the Plaque Reduction Assay. **Figure 8** is an image of BVDV plaque formation in the presence of increasing concentrations of β-D-2'-CH_3-riboU.

Table 8: Viral Suppression via Plaque Reduction Assay

	EC_{90}, μM
β-D-2'-CH_3-riboA	< 3
β-D-2'-CH_3-riboU	< 81
β-D-2'-CH_3-riboC	< 9
β-D-2'-CH_3-riboG	< 9

Example 11: Yield Reduction Assay

For each compound the concentration to obtain a 6-log reduction in viral load was determined in duplicate 24-well plates by yield reduction assays. The assay was performed

as described by Baginski, S. G.; Pevear, D. C.; Seipel, M.; Sun, S. C. C.; Benetatos, C. A.; Chunduru, S. K.; Rice, C. M. and M. S. Collett "Mechanism of action of a pestivirus antiviral compound" *PNAS USA* **2000**, 97(14), 7981-7986, with minor modifications. Briefly, MDBK cells were seeded onto 24-well plates (2 x 105 cells per well) 24 hours before infection with BVDV (NADL strain) at a multiplicity of infection (MOI) of 0.1 PFU per cell. Serial dilutions of test compounds were added to cells in a final concentration of 0.5% DMSO in growth medium. Each dilution was tested in triplicate. After three days, cell cultures (cell monolayers and supernatants) were lysed by three freeze-thaw cycles, and virus yield was quantified by plaque assay. Briefly, MDBK cells were seeded onto 6-well plates (5 x 105 cells per well) 24 h before use. Cells were inoculated with 0.2 mL of test lysates for 1 hour, washed and overlaid with 0.5% agarose in growth medium. After 3 days, cell monolayers were fixed with 3.5% formaldehyde and stained with 1% crystal violet (w/v in 50% ethanol) to visualize plaques. The plaques were counted to determine the concentration to obtain a 6-log reduction in viral load as tabulated in **Table 9**. **Figure 9** is a graphical illustration of the results from the Yield Reduction Assay. **Figure 8** is an image of BVDV yield reduction in the presence of increasing concentrations of β-D-2'-CH_3-riboC.

Table 9: Concentration to Obtain 6-log Reduction

	Conc. for 6-log Reduction (μM)
β-D-2'-CH_3-riboU	120
β-D-2'-CH_3-riboG	20
β-D-2'-CH_3-riboC	20
β-D-2'-CH_3-riboA	9

Example 12: Comparative Cytotoxicity

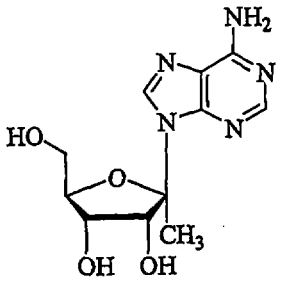
Table 10 summarizes the cytoxicity of two compounds of this invention, β-D-1'-CH_3-riboA and β-D-2'-CH_3-riboA, in comparison to RBV ("ribavirin"), in various cell systems.

Table 10: Comparative Cytotoxicity* (CC_{50})

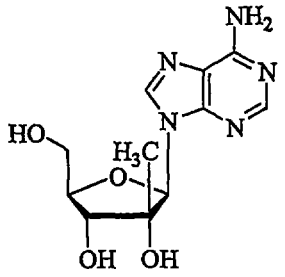
	BD	BHK	VERO	MT-4
β-D-1'-CH_3-riboA	>100	200	>100	18
β-D-2'-CH_3-riboA	75	22	22	6.6
RBV	ND	50	11	ND

* Compound concentration (μM) required to reduce the viability of cells by 50%.

The chemical structures for β-D-1'-CH_3-riboA and β-D-2'-CH_3-riboA are as follows:



β-D-1'-CH_3-riboA



β-D-2'-CH_3-riboA

Table 11 summarizes the antiviral activity of β-D-1'-CH_3-riboA and β-D-2'-CH_3-riboA against several viruses within the flavivirus and pestivirus genuses.

Table 11: Comparative Antiviral Activity* (EC_{50})

	BVDV	YFV	PICO	VSV	HIV-1
β-D-1'-CH3-riboA	10	7.0	51	>100	>18
β-D-2'-CH3-riboA	0.1	0.2	5.0	>100	>6.6
RBV	ND	30	>30	ND	ND

* Compound concentration (μM) required to reduce the plaque number by 50%. The following virus-cell system were used: BVDC-BT, YFV-BHK, PICO (Cosxackie B1 and Polio Sabin)/VSV – Vero.

Table 12 summarizes the antiviral activity and toxicity of β-D-2'-methyl-riboG, β-D-2'-methyl-riboC and β-D-2'-methyl-riboU, against a couple of viruses within the flavivirus and pestivirus genuses.

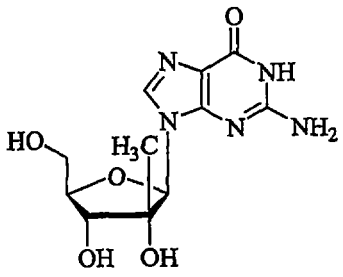
Table 12: Comparative Antiviral Activity* (EC_{50})

	BVDV		YFV	
	EC_{50}*	CC_{50}**	EC_{50}*	CC_{50}**
β-D-2'-CH_3-riboG	2	>100	1.2	20
β-D-2'-CH_3-riboC	3.7	>100	70	>100
β-D-2'-CH_3-riboU	20	>100	33	>100

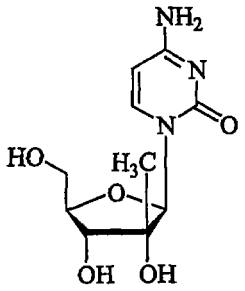
* Compound concentration (μM) required to reduce the plaque number by 50%. The following virus-cell system were used: BVDC-BT and YFV-BHK.

* Compound concentration (μM) required to reduce the viability of cells by 50%.

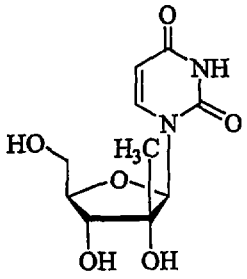
The chemical structures for β-D-2'-CH_3-riboG, β-D-2'-CH_3-riboC and β-D-2'-CH_3-riboU are as follows:



β-D-2'-CH_3-riboG



β-D-2'-CH_3-riboC



β-D-2'-CH_3-riboU

Table 13 summarizes the anti-viral activity of several compounds of this invention against BVDV in three different assays.

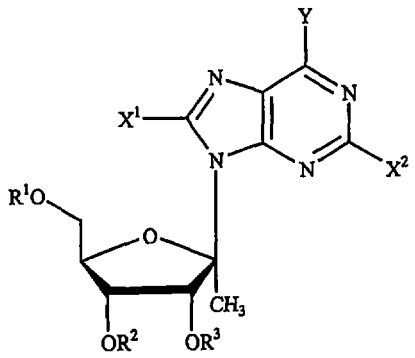
Table 13: for BVDV

Compound	Cell Protection (EC_{50}, μM)	Plaque Reduction (EC_{90}, μM)	Yield Reduction EC_{90}, μM	Yield Reduction 6 $\log_{10}$ reduction (μM)	Cytotoxicity Huh7 cells (EC_{50}, μM)
β-D-2'-CH_3-riboA	2	< 3	< 2	9	50
β-D-2'-CH_3-riboT	> 250	ND	ND	ND	> 250
β-D-2'-CH_3-riboU	20	< 81	24	120	> 250
β-D-2'-CH_3-riboC	2	< 9	< 4	20	> 250
β-D-2'-CH_3-riboG	4	< 9	3	20	> 250
β-D-2'-CH_3-riboI	45	ND	ND	ND	> 250
Ribavirin	> 3	> 200	> 20	toxic	20

This invention has been described with reference to its preferred embodiments. Variations and modifications of the invention, will be obvious to those skilled in the art from the foregoing detailed description of the invention.

We Claim:

1. A compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

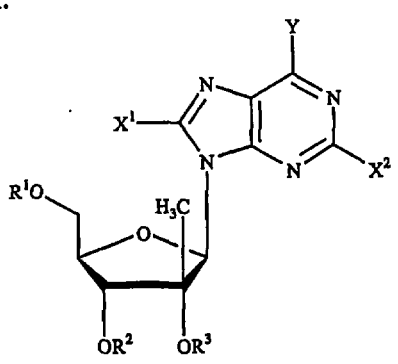
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

2. A compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, wherein:

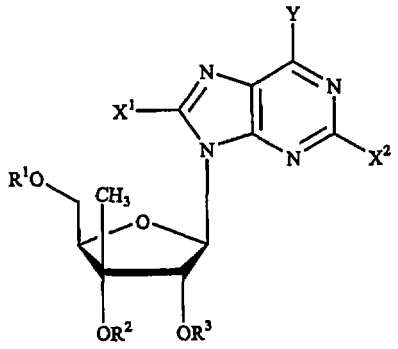
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

3. A compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is

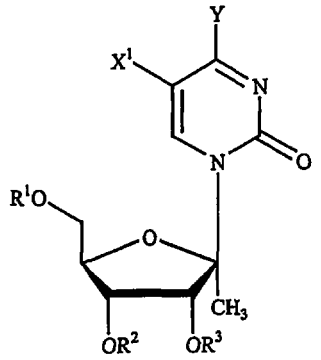
capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

4. A compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

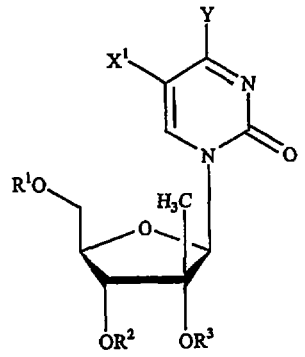
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

5. A compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, wherein:

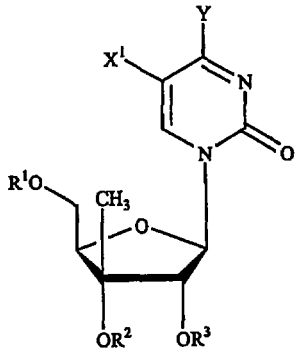
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

6. A compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, wherein:

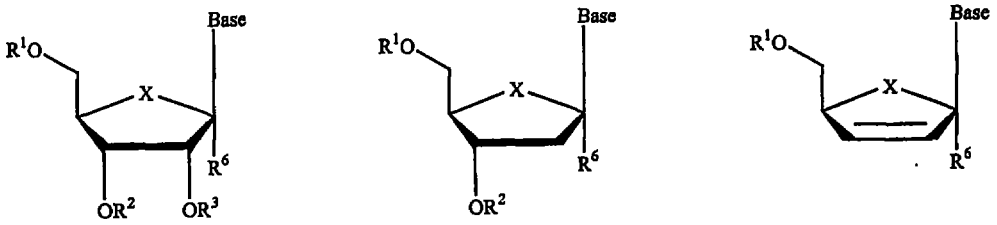
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

7. A compound selected from Formulas VII, VIII and IX:



(VII) (VIII) (IX)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

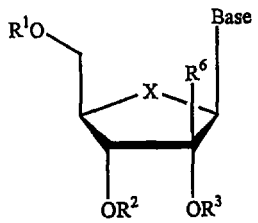
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is

capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

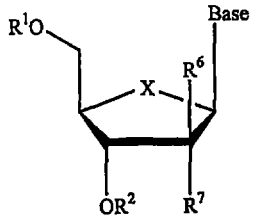
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

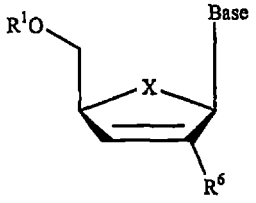
8. A compound of Formulas X, XI and XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

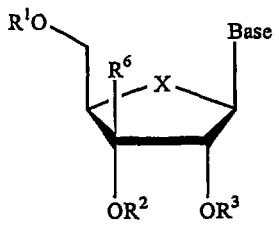
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

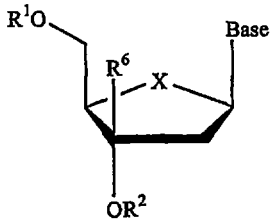
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

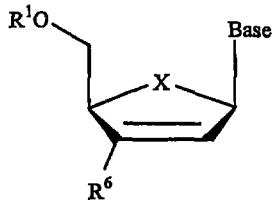
9. A compound selected from Formulas XIII, XIV and XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, wherein:

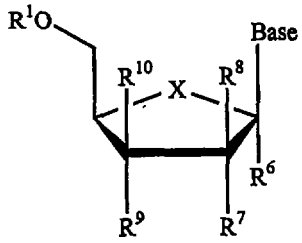
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

10. A compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

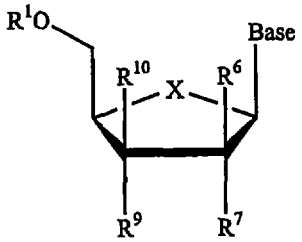
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

11. A compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl

(including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

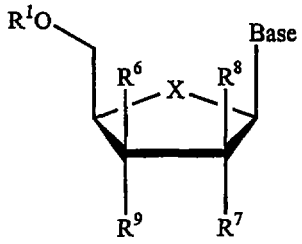
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

12. A compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or

other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

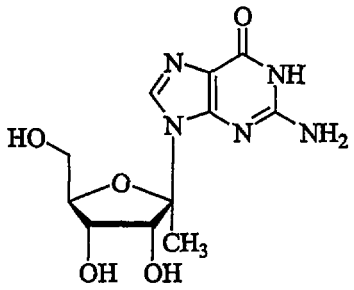
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

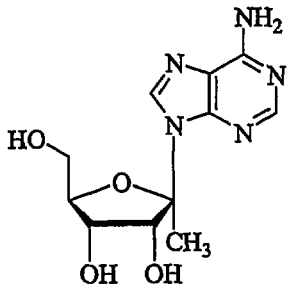
X is O, S, SO_2 or CH_2.

13. A compound of the structure:



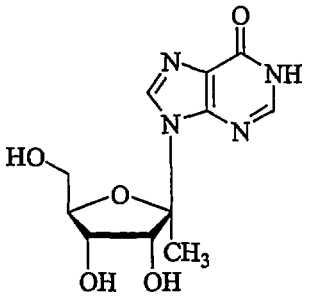
or a pharmaceutically acceptable salt thereof.

14. A compound of the structure:



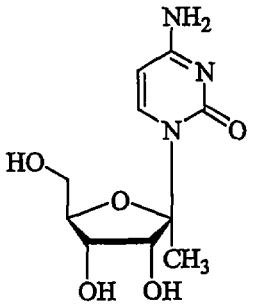
or a pharmaceutically acceptable salt thereof.

15. A compound of the structure:



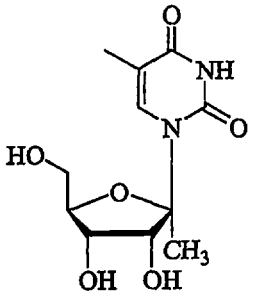
or a pharmaceutically acceptable salt thereof.

16. A compound of the structure:



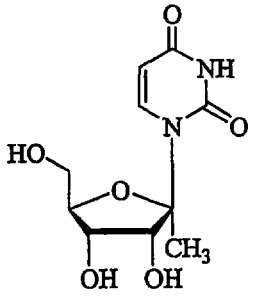
or a pharmaceutically acceptable salt thereof.

17. A compound of the structure:



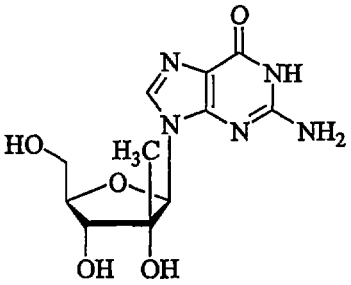
or a pharmaceutically acceptable salt thereof.

18. A compound of the structure:



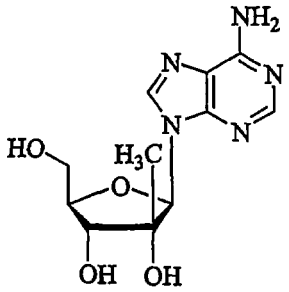
or a pharmaceutically acceptable salt thereof.

19. A compound of the structure:



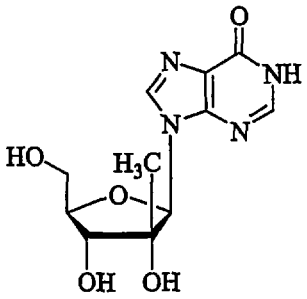
or a pharmaceutically acceptable salt thereof.

20. A compound of the structure:



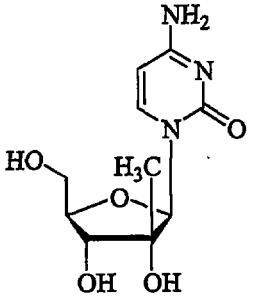
or a pharmaceutically acceptable salt thereof.

21. A compound of the structure:



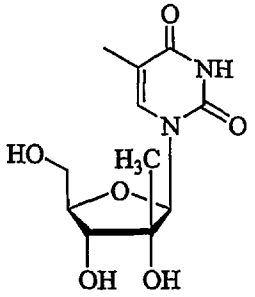
or a pharmaceutically acceptable salt thereof.

22. A compound of the structure:



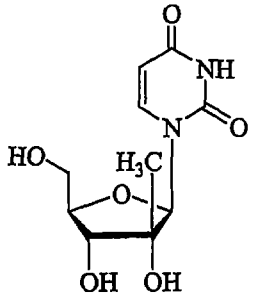
or a pharmaceutically acceptable salt thereof.

23. A compound of the structure:



or a pharmaceutically acceptable salt thereof.

24. A compound of the structure:



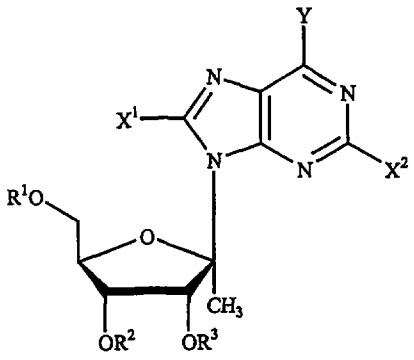
or a pharmaceutically acceptable salt thereof.

25. The compound as described in any of the preceding claims 1-24, wherein the said compound is in the form of a dosage unit.

26. The compound as described in claim 187, wherein the dosage unit contains 10 to 1500 mg of said compound.

27. The compound as described in claim 187 or 188, wherein said dosage unit is a tablet or capsule.

28. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

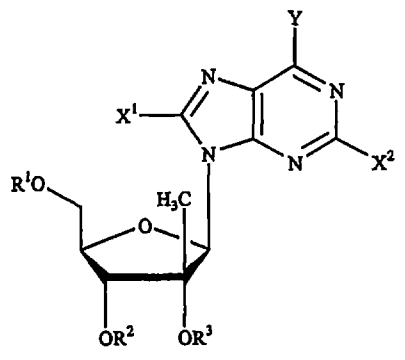
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

29. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

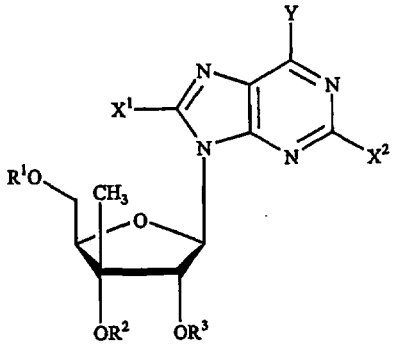
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

30. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with

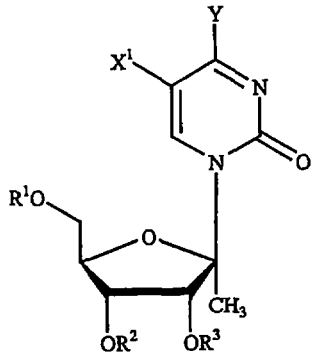
one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

31. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

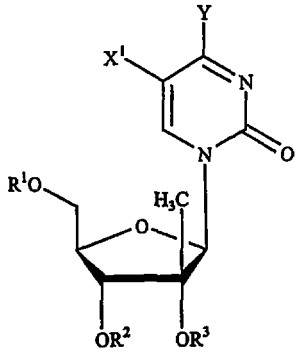
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

32. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

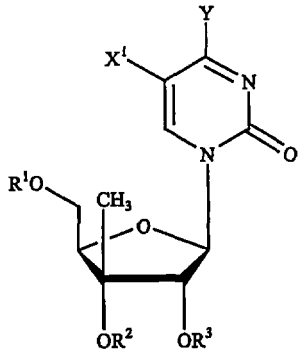
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

33. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

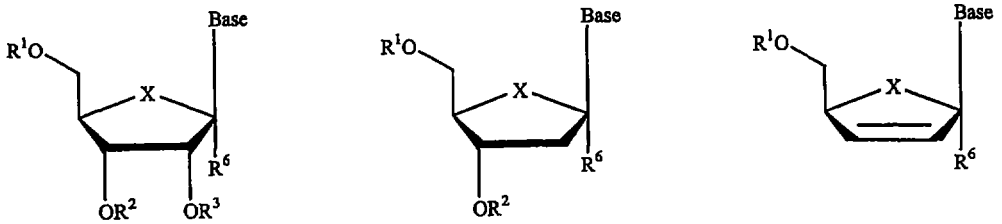
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

34. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formulas VII, VIII or IX:



(VII) (VIII) (IX)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

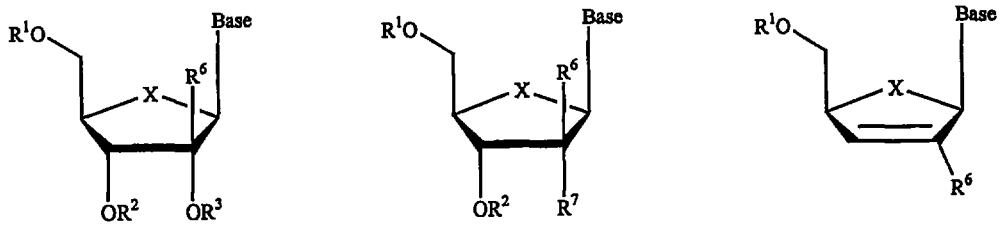
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

35. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula X, XI or XII:



(X) (XI) (XII)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

Base is a purine or pyrimidine base as defined herein;

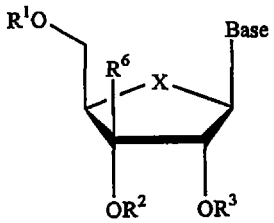
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

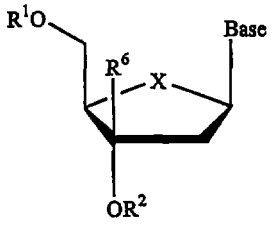
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

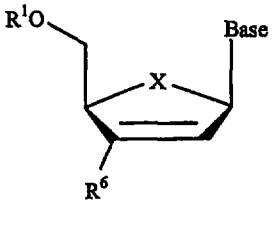
36. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XIII, XIV or XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

Base is a purine or pyrimidine base as defined herein;

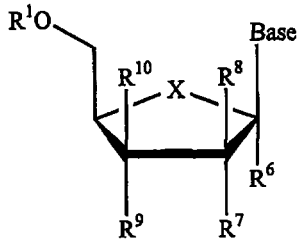
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl

(including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

37. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -

O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

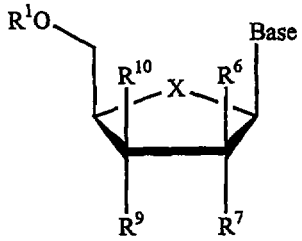
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$ or -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

38. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -

O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

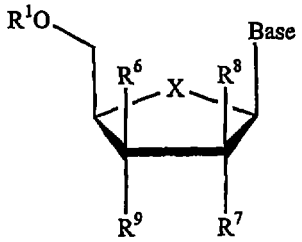
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

39. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

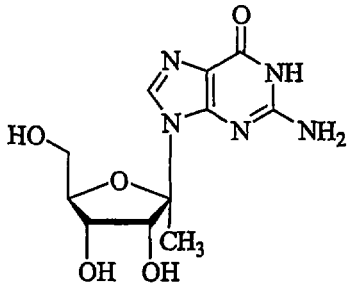
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

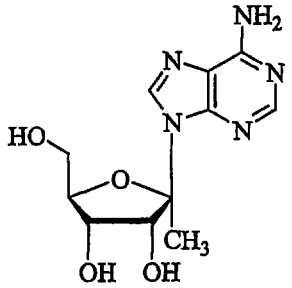
X is O, S, SO_2 or CH_2.

40. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



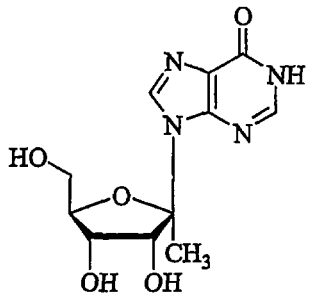
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

41. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



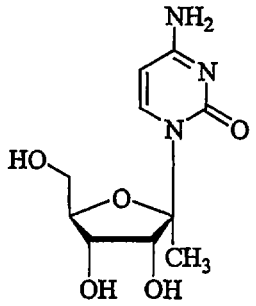
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

42. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



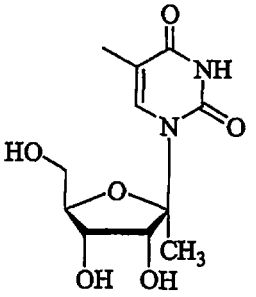
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

43. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



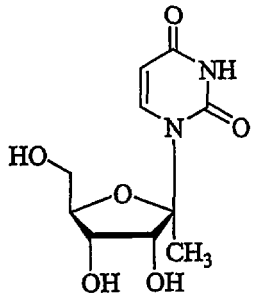
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

44. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



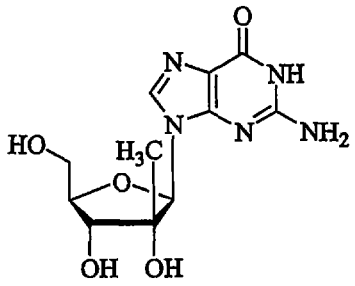
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

45. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



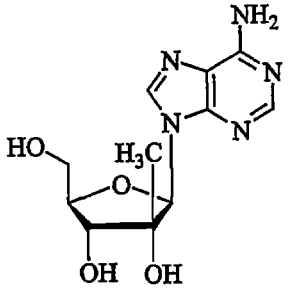
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

46. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



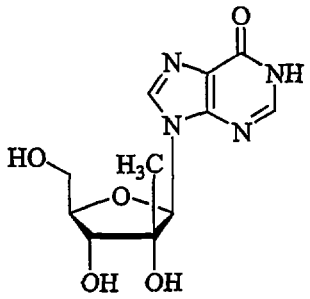
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

47. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



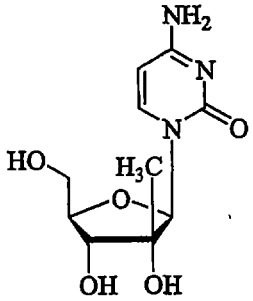
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

48. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



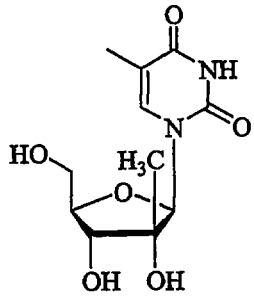
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

49. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



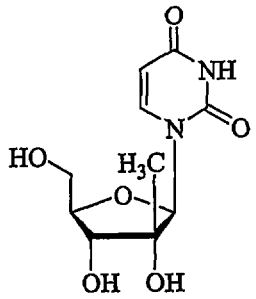
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

50. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



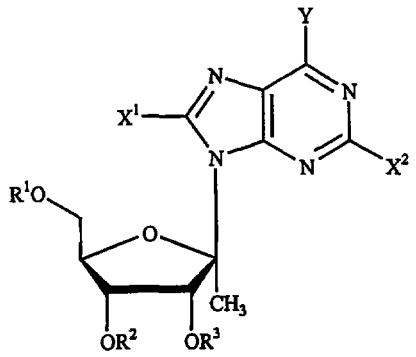
or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

51. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

52. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

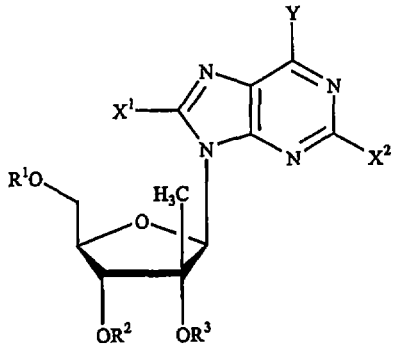
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

53. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

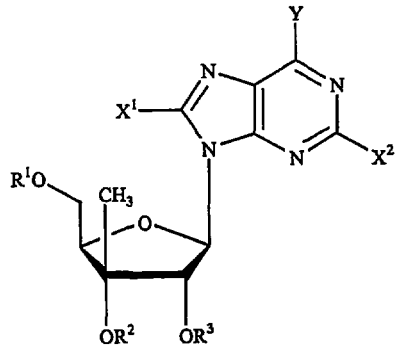
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

54. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

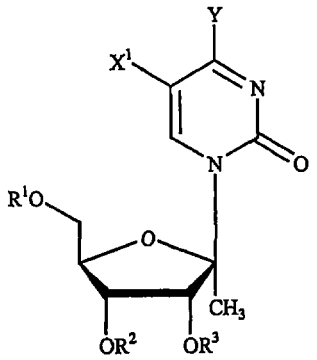
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

55. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

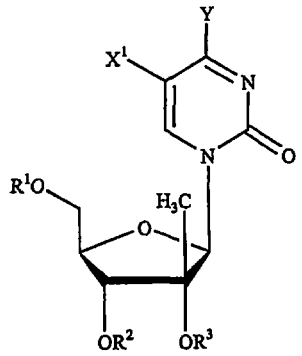
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

56. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

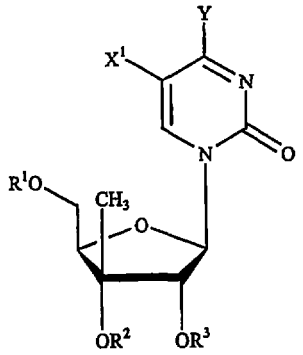
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

57. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

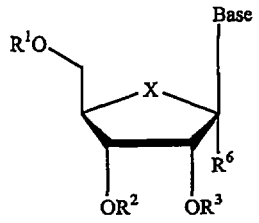
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

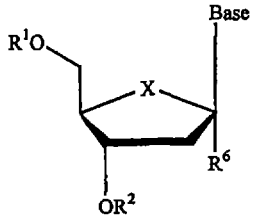
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

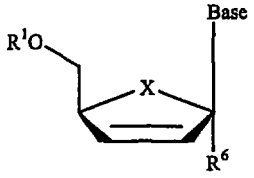
58. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula VII, VIII or IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

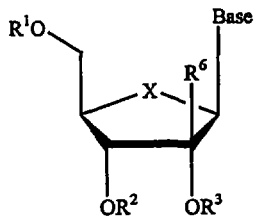
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

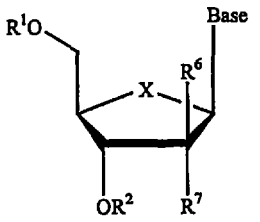
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

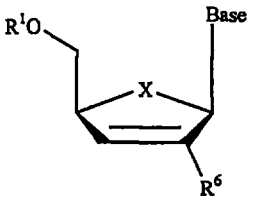
59. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula X, XI or XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

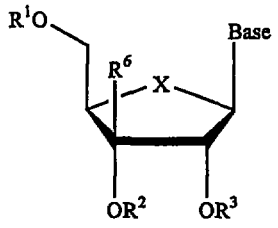
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

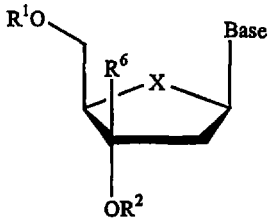
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

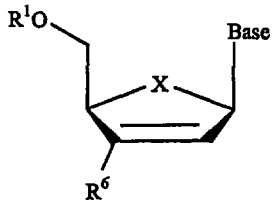
60. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XIII, XIV or XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

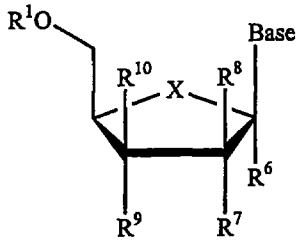
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl

(including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

61. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -

O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

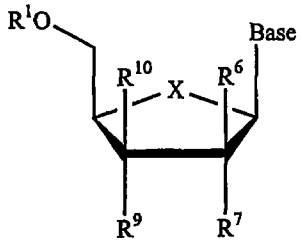
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2, or CH_2.

62. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -

O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

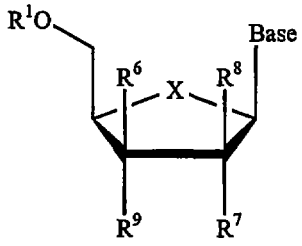
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

63. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

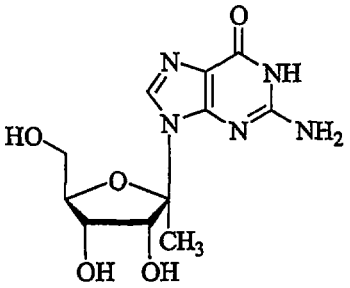
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino; ,

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

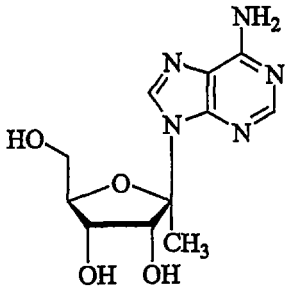
X is O, S, SO_2 or CH_2.

64. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



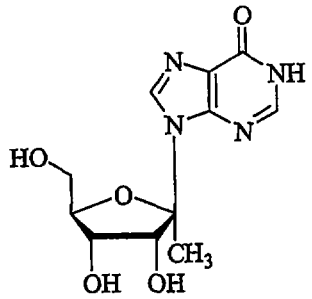
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

65. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



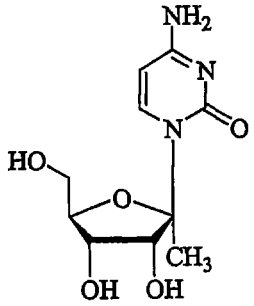
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

66. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



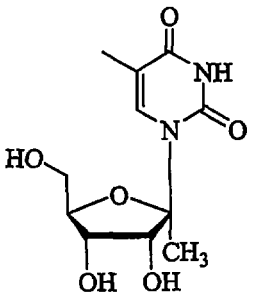
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

67. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



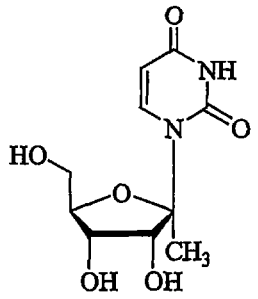
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

68. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



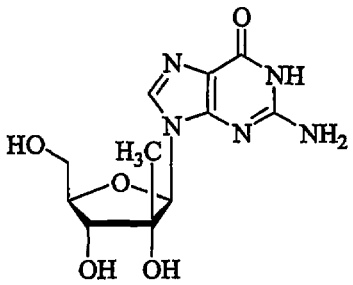
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

69. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



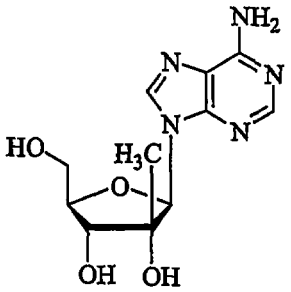
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

70. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



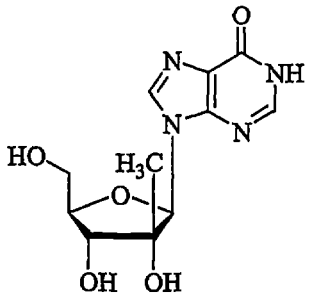
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

71. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



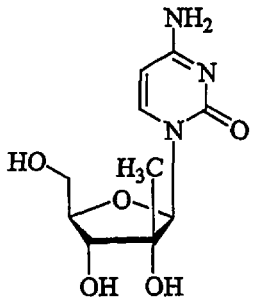
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

72. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



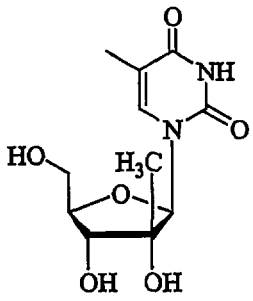
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

73. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



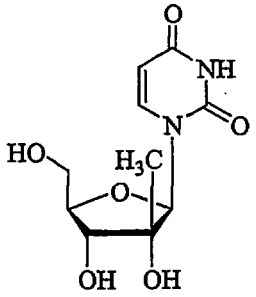
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

74. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

75. A pharmaceutical composition for the treatment or prophylaxis of a flavivirus or pestivirus in a host, comprising an effective amount of a compound of structure:



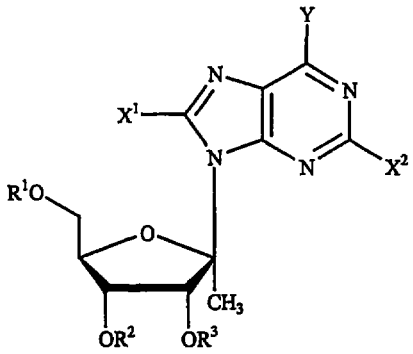
or a pharmaceutically acceptable salt thereof, in combination with one or more other antivirally effective agents.

76. The pharmaceutical composition as described in any of the preceding claims 28-75, wherein the said compound is in the form of a dosage unit.

77. The pharmaceutical composition as described in claim 76, wherein the dosage unit contains 10 to 1500 mg of said compound.

78. The pharmaceutical composition as described in claim 75 or 76, wherein said dosage unit is a tablet or capsule.

79. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower

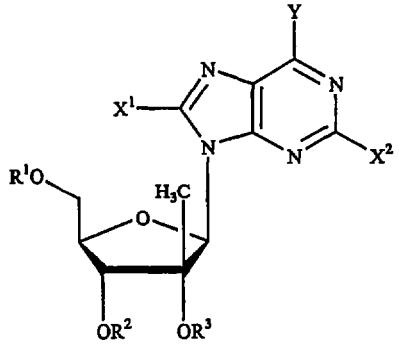
alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

80. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, wherein:

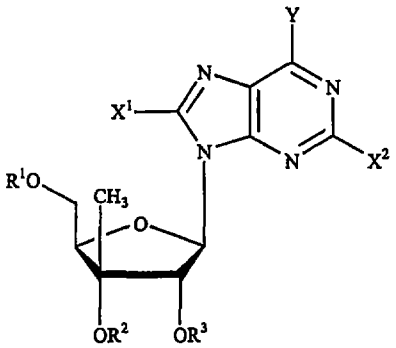
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

81. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, wherein:

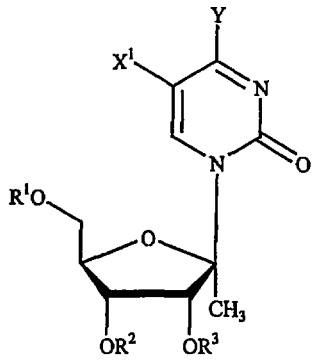
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

82. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

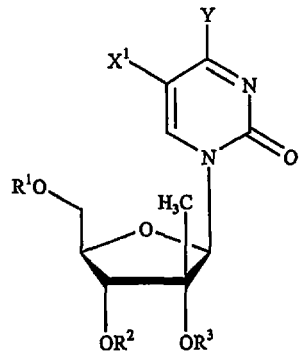
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

83. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, wherein:

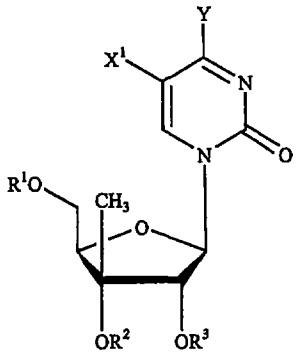
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

84. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, wherein:

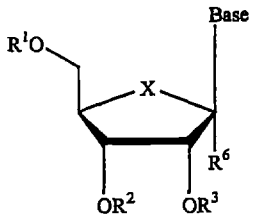
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

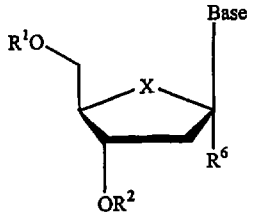
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

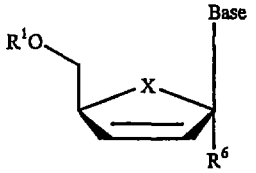
85. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VII, VIII or IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, wherein:

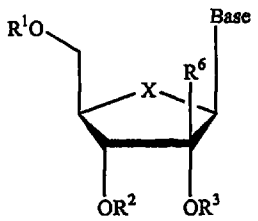
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

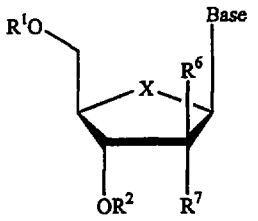
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

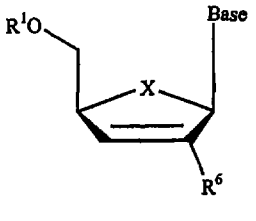
86. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula X, XI or XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

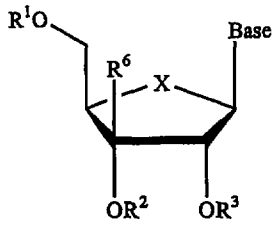
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

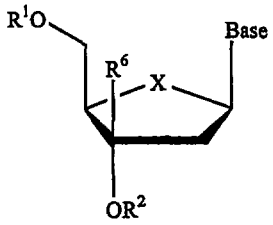
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

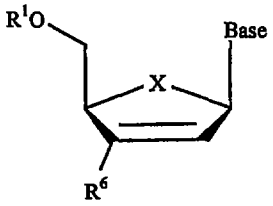
87. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XIII, XIV or XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

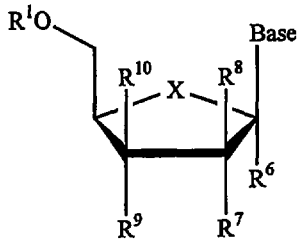
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with

one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

88. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

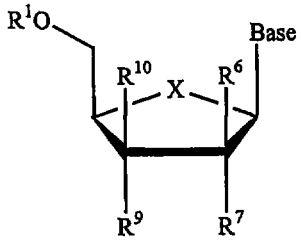
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

89. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

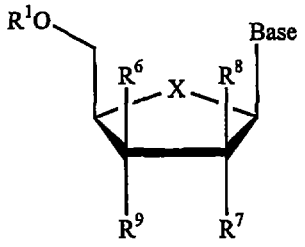
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

90. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, wherein:

Base is a purine or pyrimidine base as defined herein;

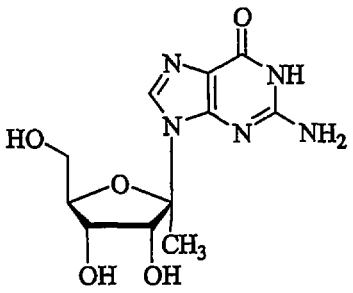
R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

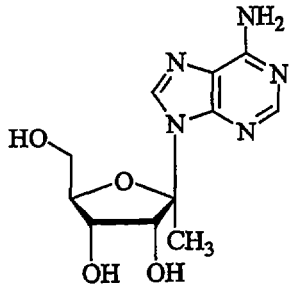
R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;
alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and
X is O, S, SO_2 or CH_2.

91. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



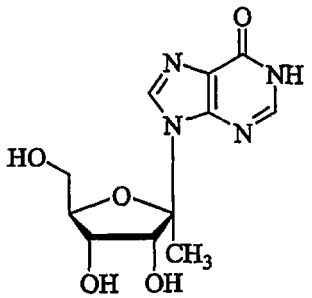
or a pharmaceutically acceptable salt thereof.

92. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



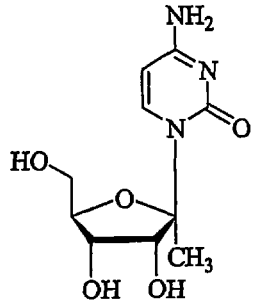
or a pharmaceutically acceptable salt thereof.

93. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



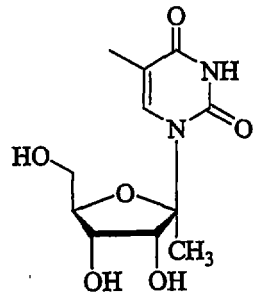
or a pharmaceutically acceptable salt thereof.

94. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



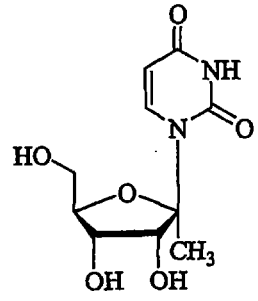
or a pharmaceutically acceptable salt thereof.

95. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



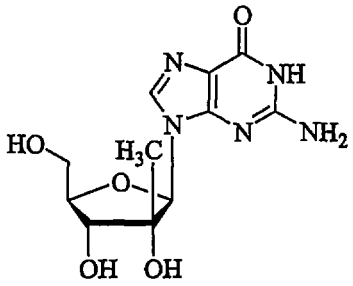
or a pharmaceutically acceptable salt thereof.

96. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



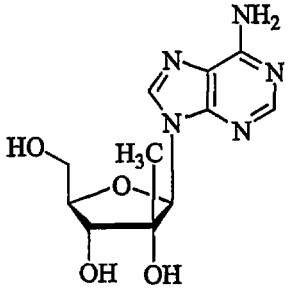
or a pharmaceutically acceptable salt thereof.

97. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



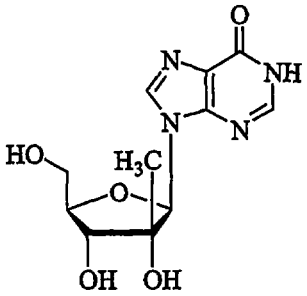
or a pharmaceutically acceptable salt thereof.

98. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



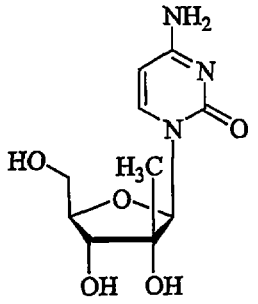
or a pharmaceutically acceptable salt thereof.

99. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



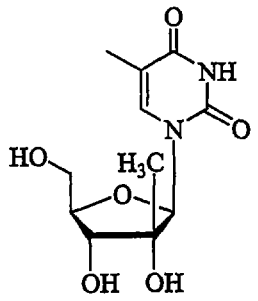
or a pharmaceutically acceptable salt thereof.

100. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



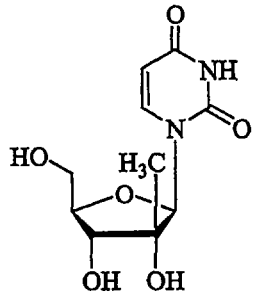
or a pharmaceutically acceptable salt thereof.

101. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



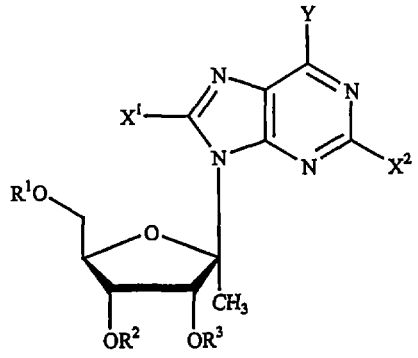
or a pharmaceutically acceptable salt thereof.

102. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt thereof.

103. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

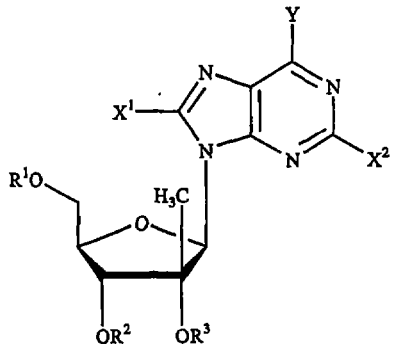
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

104. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

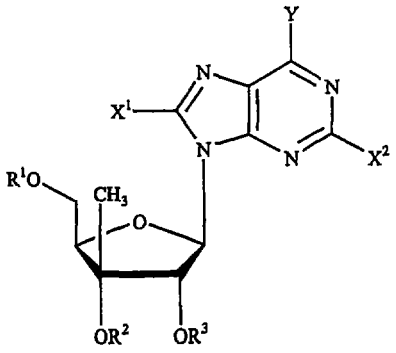
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

105. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

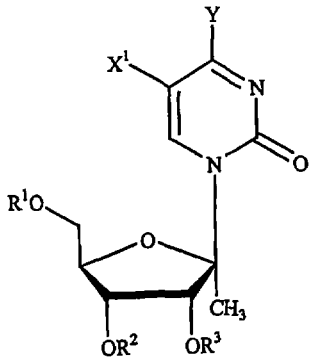
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

106. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

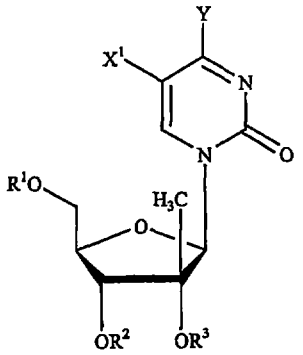
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

107. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

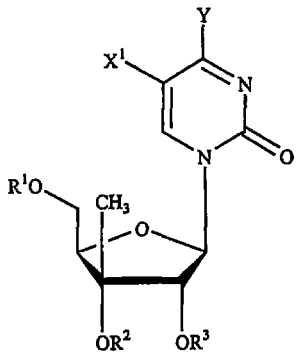
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

108. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

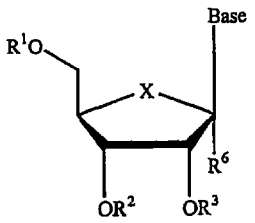
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

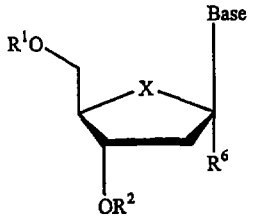
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

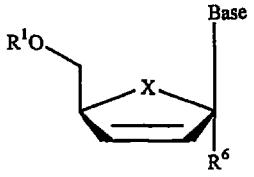
109. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula VII, VIII or IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

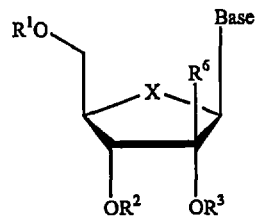
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

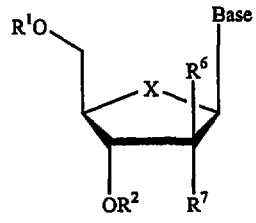
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

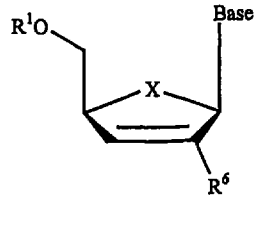
110. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula X, XI or XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

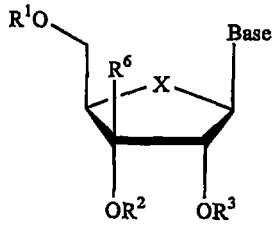
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

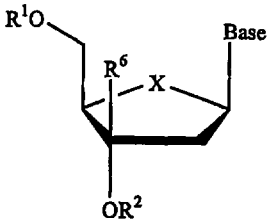
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

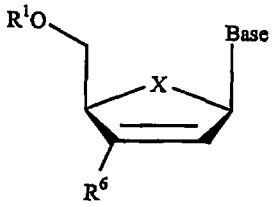
111. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XIII, XIV or XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

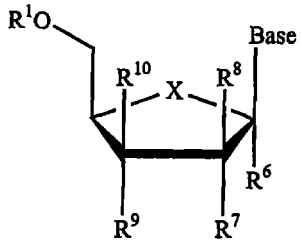
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl

(including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

112. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

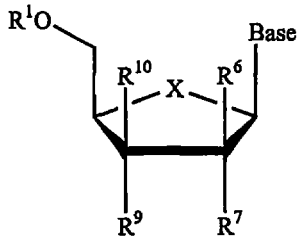
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

113. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

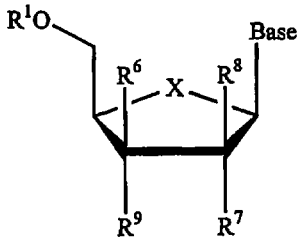
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

114. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an anti-virally effective amount of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more other antivirally effective agents, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -

O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

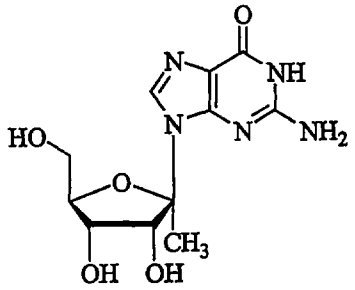
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

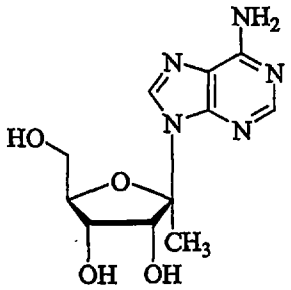
X is O, S, SO_2 or CH_2.

115. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



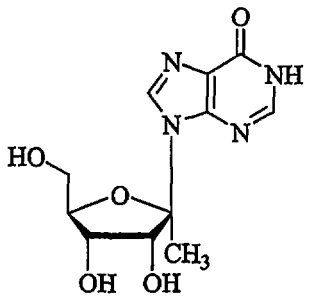
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

116. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



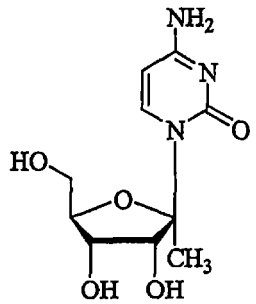
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

117. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



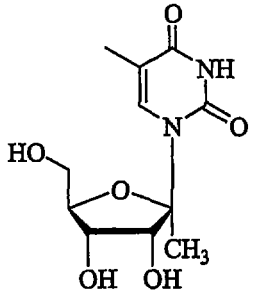
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

118. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



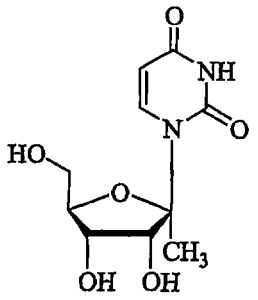
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

119. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



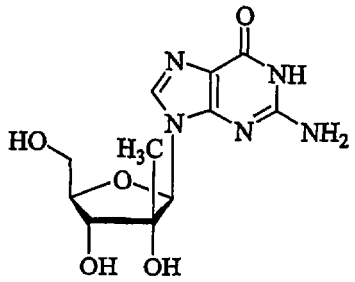
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

120. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



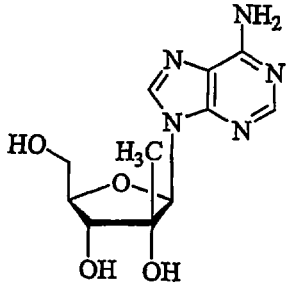
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

121. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



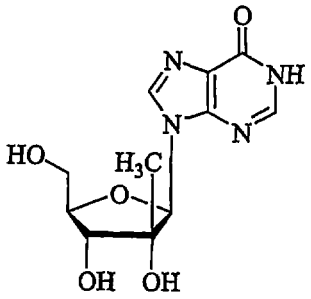
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

122. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



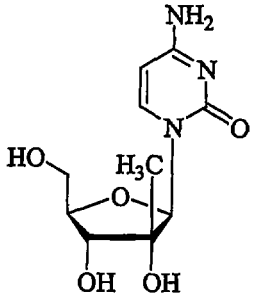
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

123. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



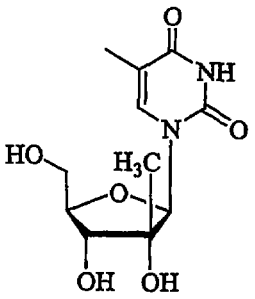
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

124. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



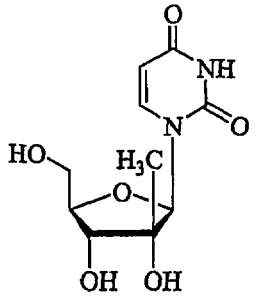
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

125. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

126. A method for the treatment or prophylaxis of a flavivirus or pestivirus infection in a host, comprising administering an antivirally effective amount of a compound of the structure:



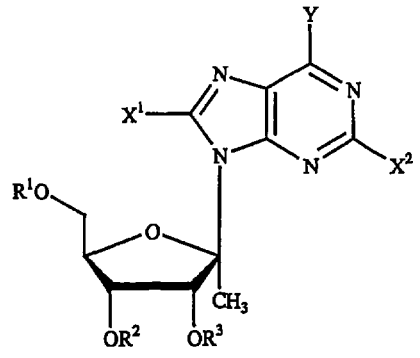
or a pharmaceutically acceptable salt thereof, in combination or alternation with one or more antivirally effective agents.

127. Method of treatment as described in any of the preceding claims 79-126, wherein the said compound is in the form of a dosage unit.

128. Method of treatment as described in claim 127, wherein the dosage unit contains 10 to 1500 mg of said compound.

129. Method of treatment as described in claim 127 or 128, wherein said dosage unit is a tablet or capsule.

130. A use of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower

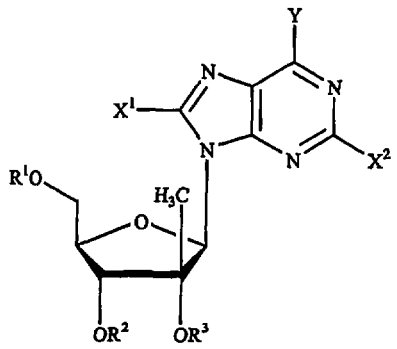
alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

131. A use of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

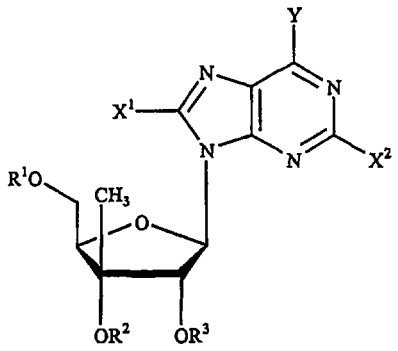
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

132. A use of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

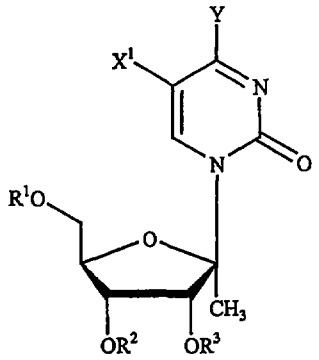
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

133. A use of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

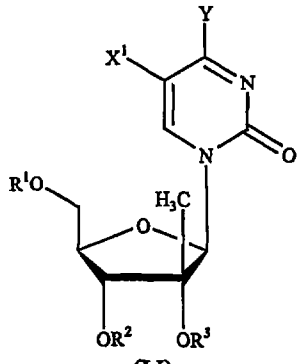
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

134. A use of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

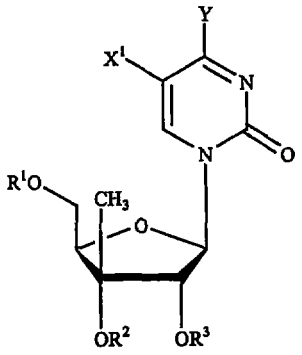
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

135. A use of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid,

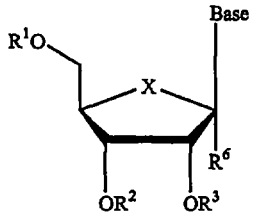
including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

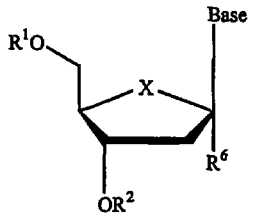
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

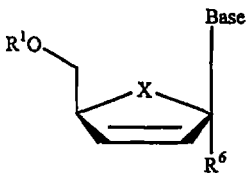
136. A use of a compound selected from Formulas VII, VIII and IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

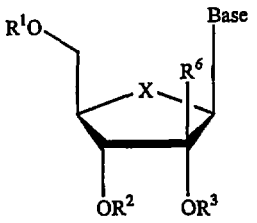
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

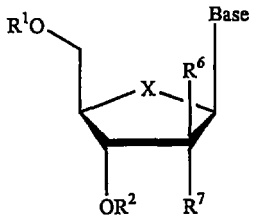
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

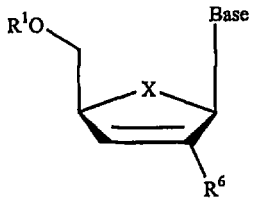
137. A use of a compound of Formulas X, XI and XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

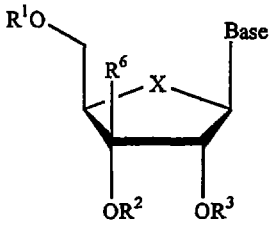
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

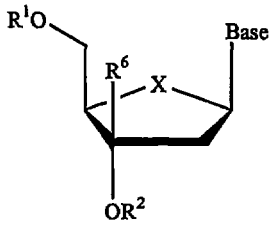
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

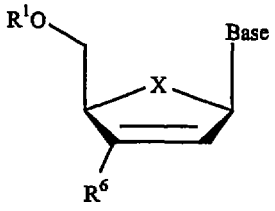
138. A use of a compound selected from Formulas XIII, XIV and XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

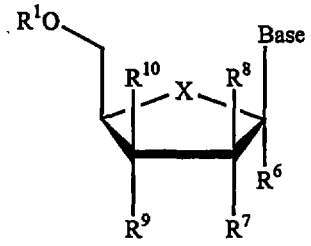
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

139. A use of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

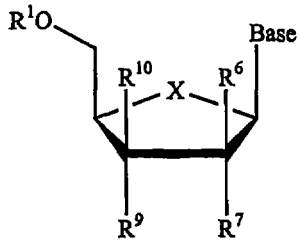
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

140. A use of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

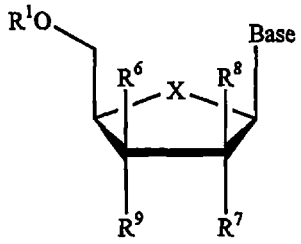
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

141. A use of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with

one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

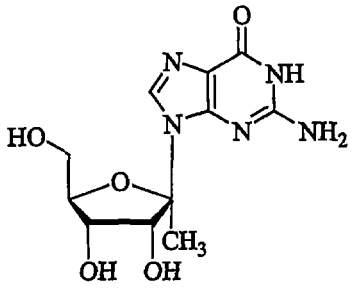
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

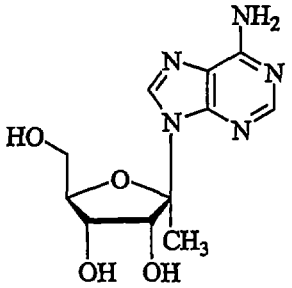
X is O, S, SO_2 or CH_2.

142. A use of a compound of the structure:



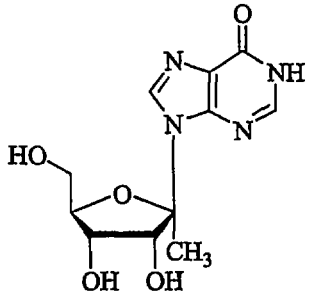
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

143. A use of a compound of the structure:



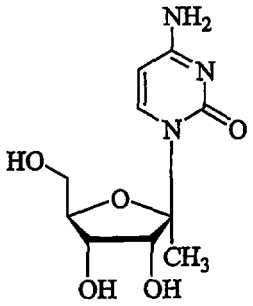
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

144. A use of a compound of the structure:



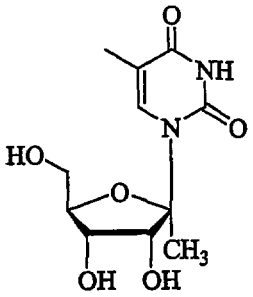
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

145. A use of a compound of the structure:



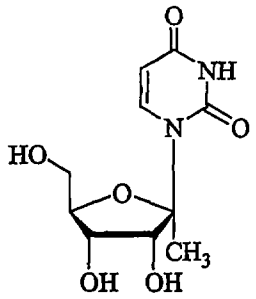
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

146. A use of a compound of the structure:



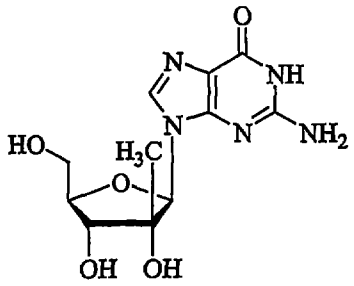
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

147. A use of a compound of the structure:



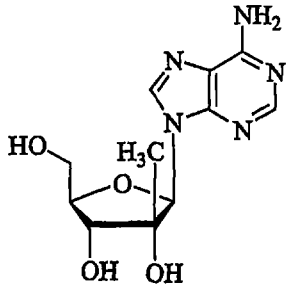
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

148. A use of a compound of the structure:



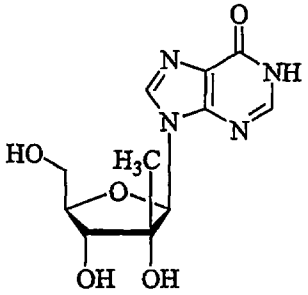
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

149. A use of a compound of the structure:



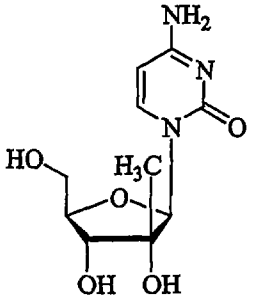
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

150. A use of a compound of the structure:



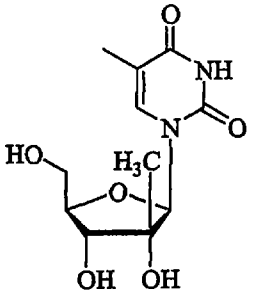
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

151. A use of a compound of the structure:



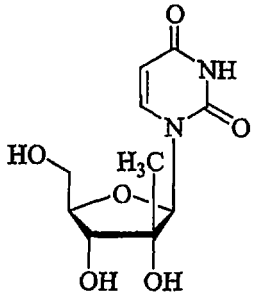
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

152. A use of a compound of the structure:



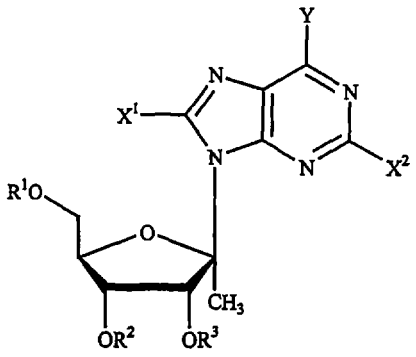
or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

153. A use of a compound of the structure:



or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

154. A use of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

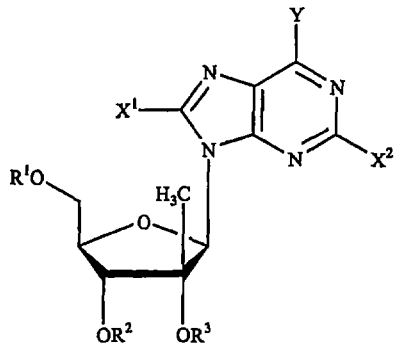
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

155. A use of a compound of Formula II:



(II)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

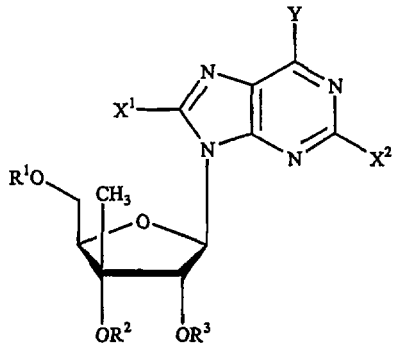
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are is independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

156. A use of a compound of Formula III:



(III)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

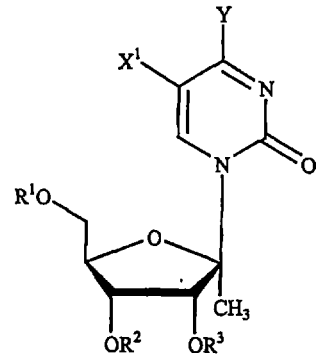
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 and X^2 are independently selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

157. A use of a compound of Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

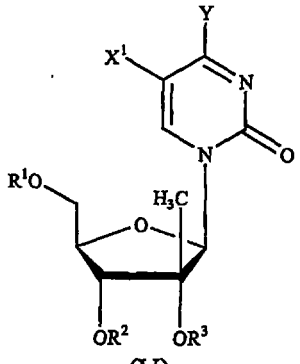
R^1, R^2 and R^3 are independently H, phosphate (including mono-, di- or triphosphate and a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

158. A use of a compound of Formula V:



(V)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

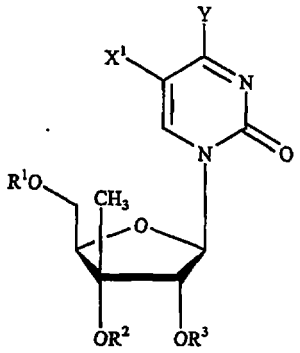
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

159. A use of a compound of Formula VI:



(VI)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid,

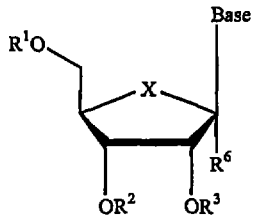
including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate; and

Y is hydrogen, bromo, chloro, fluoro, iodo, OR^4, NR^4R^5 or SR^4;

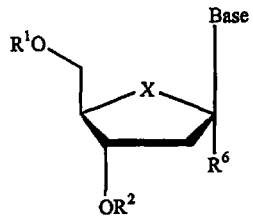
X^1 is selected from the group consisting of H, straight chained, branched or cyclic alkyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, chloro, bromo, fluoro, iodo, OR^4, NR^4NR^5 or SR^4; and

R^4 and R^5 are independently hydrogen, acyl (including lower acyl), or alkyl (including but not limited to methyl, ethyl, propyl and cyclopropyl).

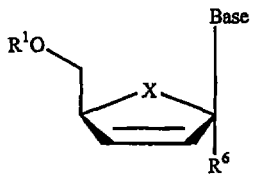
160. A use of a compound selected from Formulas VII, VIII and IX:



(VII)



(VIII)



(IX)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

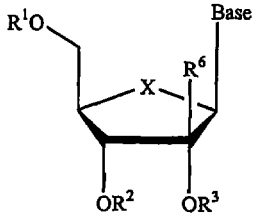
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

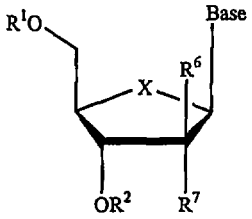
R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, 2-Br-ethyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), CF_3, chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2, or CH_2.

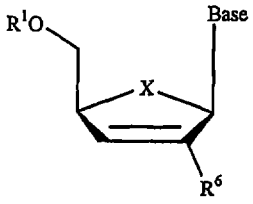
161. A use of a compound of Formulas X, XI and XII:



(X)



(XI)



(XII)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

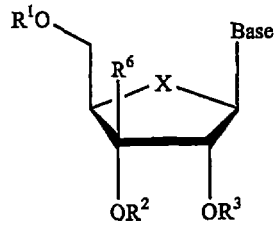
R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

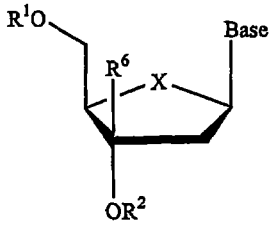
R^7 is hydrogen, OR^3, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

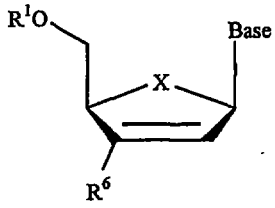
162. A use of a compound selected from Formulas XIII, XIV and XV:



(XIII)



(XIV)



(XV)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

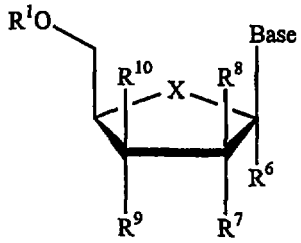
Base is a purine or pyrimidine base as defined herein;

R^1, R^2 and R^3 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1, R^2 and R^3 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$; and

X is O, S, SO_2 or CH_2.

163. A use of a compound of Formula XVI:



(XVI)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

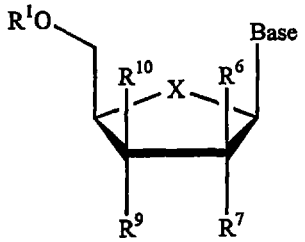
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^8 and R^{10} are independently H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, R^7 and R^{10}, R^8 and R^9, or R^8 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

164. A use of a compound of Formula XVII:



(XVII)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

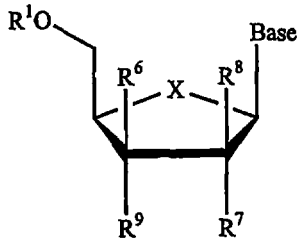
R^7 and R^9 are independently hydrogen, OR^2, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chlorine, bromine, iodine, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

R^{10} is H, alkyl (including lower alkyl), chlorine, bromine, or iodine;

alternatively, R^7 and R^9, or R^7 and R^{10} can come together to form a bond; and

X is O, S, SO_2 or CH_2.

165. A use of a compound of Formula XVIII:



(XVIII)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus, wherein:

Base is a purine or pyrimidine base as defined herein;

R^1 and R^2 are independently H; phosphate (including monophosphate, diphosphate, triphosphate, or a stabilized phosphate prodrug); acyl (including lower acyl); alkyl (including lower alkyl); sulfonate ester including alkyl or arylalkyl sulfonyl including methanesulfonyl and benzyl, wherein the phenyl group is optionally substituted with

one or more substituents as described in the definition of aryl given herein; a lipid, including a phospholipid; an amino acid; a carbohydrate; a peptide; a cholesterol; or other pharmaceutically acceptable leaving group which when administered *in vivo* is capable of providing a compound wherein R^1 and R^2 are independently H or phosphate;

R^6 is hydrogen, hydroxy, alkyl (including lower alkyl), azido, cyano, alkenyl, alkynyl, Br-vinyl, -C(O)O(alkyl), -C(O)O(lower alkyl), -O(acyl), -O(lower acyl), -O(alkyl), -O(lower alkyl), -O(alkenyl), chloro, bromo, fluoro, iodo, NO_2, NH_2, -NH(lower alkyl), -NH(acyl), -N(lower alkyl)$_2$, -N(acyl)$_2$;

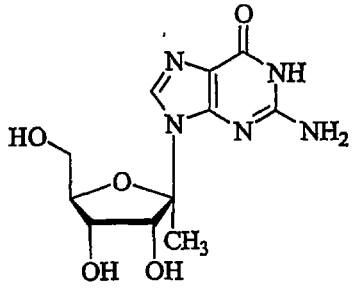
R^7 and R^9 are independently hydrogen, OR^2, alkyl (including lower alkyl), alkenyl, alkynyl, Br-vinyl, O-alkenyl, chlorine, bromine, iodine, NO_2, amino, loweralkylamino, or di(loweralkyl)amino;

R^8 is H, alkyl (including lower alkyl), chlorine, bromine or iodine;

alternatively, R^7 and R^9, or R^8 and R^9 can come together to form a bond; and

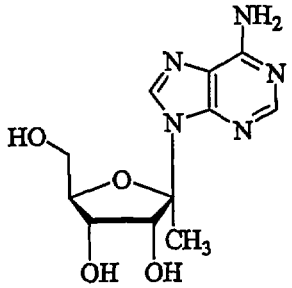
X is O, S, SO_2 or CH_2.

166. A use of a compound of the structure:



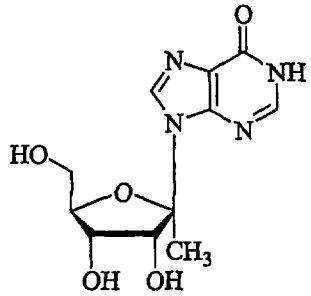
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

167. A use of a compound of the structure:



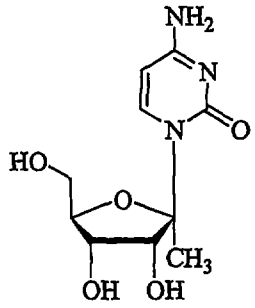
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

168. A use of a compound of the structure:



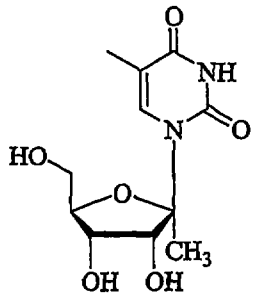
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

169. A use of a compound of the structure:



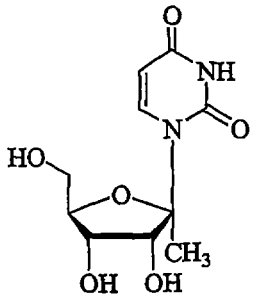
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

170. A use of a compound of the structure:



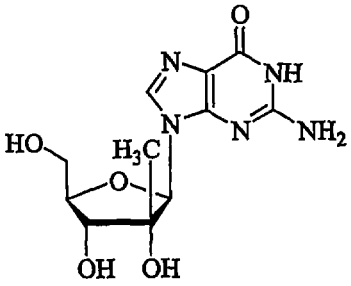
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

171. A use of a compound of the structure:



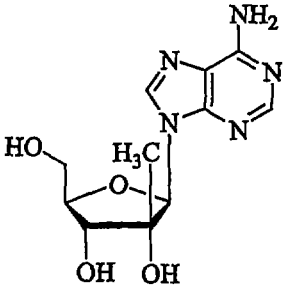
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

172. A use of a compound of the structure:



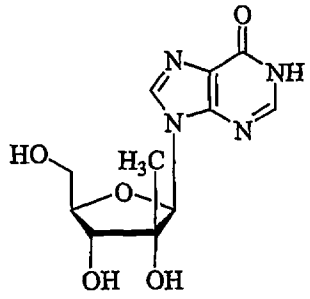
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

173. A use of a compound of the structure:



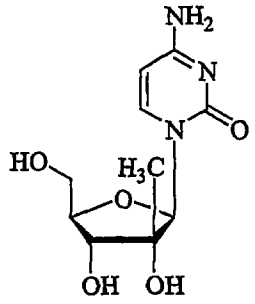
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

174. A use of a compound of the structure:



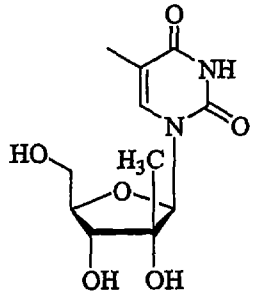
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

175. A use of a compound of the structure:



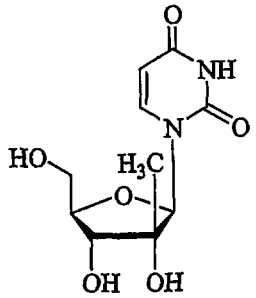
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

176. A use of a compound of the structure:



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

177. A use of a compound of the structure:



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of a host infected with the flavivirus or pestivirus.

178. Use of the compound as described in any of the preceding claims 130-177, wherein the said compound is in the form of a dosage unit.

179. Use of the compound of claim 101, wherein the dosage unit contains 178 to 1500 mg of said compound.

180. Use of the compound of claim 178 or 179, wherein said dosage unit is a tablet or capsule.