Figure 9 shows TGA data for Compound **5**.

Figure 10 shows in graphic form the data provided in Table 2.

Figure 11 shows in graphic form the data provided in Table 3.

Figure 12 shows in graphic form the data in Table 4.

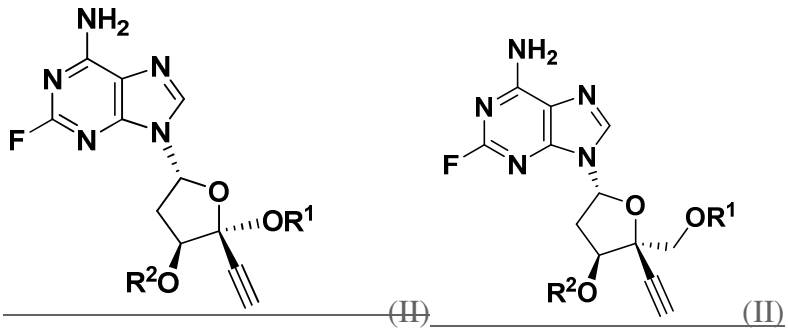
Figure 13 shows in graphic form data from Example 10.

Figure 14 shows XPRD data for Compound **2**.

Figure 15 shows XPRD data for Compound **6**.

DESCRIPTION OF PREFERRED EMBODIMENTS

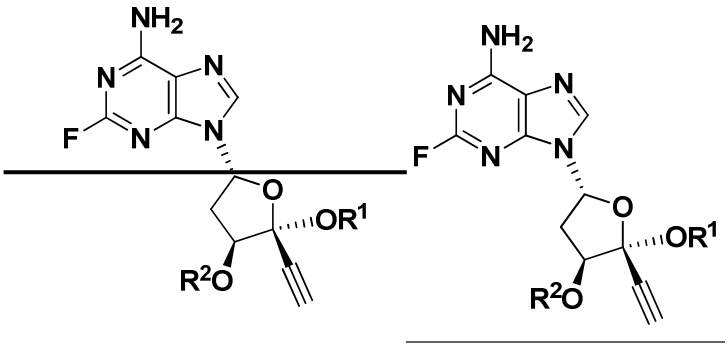
Extended *in vivo* viral suppression is achieved by diesters represented by Formula (II):



wherein R^1 and R^2 independently are -C(=O)R^3 and R^3 is a member of the group consisting of isopropyl, 3-pentyl, cyclopentyl and phenylmethyl. The foregoing diesters are prepared by reacting EFdA with the desired acid or acid anhydride and recovering the diester as a crystalline compound. The Examples below illustrate preparation of the preferred diesters.

WE CLAIM:

1. A compound of Formula (II):



(II)

wherein R^1 and R^2 independently are $-C(=O)R^3$ and R^3 is selected from the group consisting of isopropyl, 3-pentyl, cyclopentyl, phenyl, and phenylmethyl.

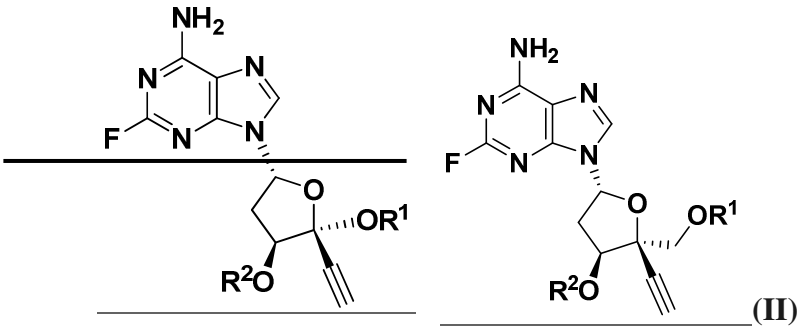
2. The compound of claim 1, which is crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-ethynyl-2-(isobutyryloxy)methyl) tetrahydrofuran-3-yl isobutyrate.

3. The compound of claim 1, which is crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-((2-ethylbutanoyl)oxy)methyl-2-ethynyltetrahydrofuran-3-yl 2-ethylbutanoate.

4. The compound of claim 1, which is crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-(((cyclopentanecarbonyl)oxy)methyl)-2-ethynyl-tetrahydrofuran-3-yl cyclopentanecarboxylate.

5. The compound of claim 1, which is crystaline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-ethynyl-2-((2-phenlacetoxy)methyl)tetrahydrofuran-3-yl 2-phenylacetate.

6. An aqueous parenteral suspension comprising a compound of Formula (II):



(II)

wherein R^1 and R^2 independently are $-C(=O)R^3$ and R^3 is selected from the group consisting of isopropyl, 3-pentyl (1-ethoxypropyl, cyclopentyl, and phenylmethyl;

a non-ionic surfactant;

a suspending agent; and water.

7. The aqueous parenteral suspension of claim 6, wherein said compound is present in an amount in the range of about 3 to 4.5 percent by weight of the suspension, said non-ionic surfactant is present in an amount in the range of about 0.1 to about 0.5 percent by weight of the suspension, and said suspending agent is present in an amount in the range of about 0.1 to about 0.5 weight percent by weight of the suspension.

8. The aqueous parenteral suspension of claim 6, wherein the non-ionic surfactant is polyoxyethylene (20) sorbitan monooleate.

9. The aqueous parenteral suspension of claim 6, wherein the suspending agent is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ~~hyroxypropyl~~ hydroxypropyl cellulose, and hydroxypropylmethyl cellulose.

10. The aqueous parenteral suspension of claim 6, wherein the compound is crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-ethynl-2((2-phenylacetoxy)methyl)-tetrahydrofuran-3-yl~~.~~ 2-phenylacetate.

11. The aqueous parenteral suspension of claim 6, wherein the compound is crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-((2-ethylbutanoyl)oxy)methyl-2-ethynyltetrahydrofuran-3-yl 2-ethylbutanoate.

12. Use of the compound of claims 1 to 5 ~~for~~in the preparation of a medicament~~A method~~ for prophylaxis of HIV infection in a patient, wherein the medicament is for *in vivo* suppression of human immunodeficiency virus in ~~a~~ the patient~~, which comprises parenterally administering to the patient an effective amount of the compound of claim 1 in an aqueous suspension~~.

~~13. The method of claim 12, wherein the administering is a three-month dosing regimen.~~

~~14. The method of claim 12, wherein said effective amount is a dose in the range of about 80 to about 800 mg.~~

~~15. The method of claim 12, wherein said effective amount is a dose in the range of about 200 to about 400 mg.~~

~~16~~13. The ~~method~~ use of claim 12, wherein the compound is crystalline (2R, 3S, 5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-ethynyl-2-((2-phenylacetoxy)methyl) tetrahydrofuran-3-yl 2-phenylacetate.

~~17~~14. The ~~method~~ use of claim 12, wherein the compound is crystalline (2R, 3S, 5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-((2-ethylbutanoyl)oxy)methyl-2-ethynyltetrahydrofuran-3-yl 2-ethylbutanoate.

15. The use of claim 12, wherein the medicament is an aqueous parenteral suspension comprising the compound; a non-ionic surfactant; a suspending agent; and water.

16. The use of claim 15, wherein said compound is present in an amount in the range of about 3 to 4.5 percent by weight of the suspension, said non-ionic surfactant is present in an amount in the range of about 0.1 to about 0.5 percent by weight of the suspension, and said suspending agent is present in an amount in the range of about 0.1 to about 0.5 weight percent by weight of the suspension.

17. The use of claim 15, wherein the non-ionic surfactant is polyoxyethylene (20) sorbitan monooleate,

18. The use of claim 15, wherein the suspending agent is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, hydroxypropyl cellulose, and hydroxypropylmethyl cellulose.

~~18~~19. Use of the compound of claims 1 to 5 for the preparation of a medicament~~A method~~ for prophylaxis of HIV infection in a human subject not infected with HIV~~ which comprises parenterally administering to the human subject an effective amount of the compound of claim 1 in an aqueous suspension in a semi-annual dosing regimen~~.

20. The use of claim 19, wherein the compound is crystalline (2R, 3S, 5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-ethynyl-2-((2-phenylacetoxy)methyl) tetrahydrofuran-3-yl 2-phenylacetate.

21. The use of claim 19, wherein the compound is crystalline (2R, 3S, 5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-((2-ethylbutanoyl)oxy)methyl-2-ethynyltetrahydrofuran-3-yl 2-ethylbutanoate.

22. The use of claim 19, wherein the ~~drug~~medicament is an aqueous parenteral suspension comprising the compound; a non-ionic surfactant; a suspending agent; and

water.

23. The use of claim 22, wherein said compound is present in an amount in the range of about 3 to 4.5 percent by weight of the suspension, said non-ionic surfactant is present in an amount in the range of about 0.1 to about 0.5 percent by weight of the suspension, and said suspending agent is present in an amount in the range of about 0.1 to about 0.5 weight percent by weight of the suspension.

24. The use of claim 22, wherein the non-ionic surfactant is polyoxyethylene (20) sorbitan monooleate,

25. The use of claim 22, wherein the suspending agent is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, ~~hyroxypropyl~~ hydroxypropyl cellulose, and hydroxypropylmethyl cellulose.

~~19. The method of claim 18, wherein said compound is administered in a unit dose amount in the range of about 80 to about 800 mg.~~

~~20. The method of claim 18, wherein said compound is administered in a dose volume in the range of about 0.5 to about 4 mL per dose.~~

~~21. The aqueous parenteral suspension of claim 6 or claim 7, wherein the non-ionic surfactant is polyoxyethylene (20) sorbitan monooleate.~~

~~22. The aqueous parenteral suspension of any one of claims 6, 7 or 21, wherein the suspending agent is selected from the group consisting of methyl cellulose, carboxymethyl cellulose, hyroxypropyl cellulose, and hydroxypropylmethyl cellulose.~~

~~23. The aqueous parenteral suspension of any one of claims 6, 7, 21 or 22, wherein the compound is crystalline (2R,3S,5R) 5-(6-amino-2-fluoro-9H-purin-9-yl) 2-~~

~~ethynl-2((2-phenylacetoxy)methyl)-tetrahydrofuran-3-yl. 2-phenylacetate or crystalline (2R,3S,5R)-5-(6-amino-2-fluoro-9H-purin-9-yl)-2-((2-ethylbutanoyl)oxy)methyl-2-ethynyltetrahydrofuran-3-yl 2-ethylbutanoate.~~

~~24. A method for *in vivo* suppression of human immunodeficiency virus (HIV) in a patient, which comprises parenterally administering to the patient an effective amount of the compound of any one of claims 1 to 5 in an aqueous suspension.~~

~~25. The method of claim 24, wherein the administering is a three-month dosing regimen.~~

~~26. A method for prophylaxis of HIV infection in a human subject not infected with HIV which comprises parenterally administering to the human subject an effective amount of the compound of any one of claim 1 to 5 in an aqueous suspension in a semi-annual dosing regimen.~~

~~27. The method of any one of claims 24 to 26, wherein said effective amount is a dose in the range of about 80 to about 800 mg.~~

~~28~~26. The ~~method~~ use of claim any one of claims ~~24~~ 12 to ~~27~~25, wherein said compound has~~is administered in~~ a dose volume in the range of about 0.5 to about 4 mL per dose.

~~29~~27. The ~~method~~ use of any one of claims 12 to 25~~24 to 28~~, wherein ~~administration of~~ the compound provides slow or controlled or sustained release of EFdA from the compound *in vivo*.

~~30~~28. The ~~method~~use of any one of claims 12 to 25 ~~24 to 29~~, wherein the type~~route~~ of ~~administration~~ the medicament ~~for compound~~ is selected from the group consisting of oral preparations, parenteral preparations, subcutaneous injections,

intravenous preparations, intramuscular preparations, intrastemal injections, infusions, and ~~release from an~~ implant.

~~31~~29. The ~~method~~ use of any one of claims 12 to 25~~24 to 30~~, wherein the compound is formulated as aqueous suspension, a solution, or encapsulated in particles for slow-release.

~~32. The method of any one of claims 24 to 31, wherein the viral infection is caused by HIV.~~

~~33. The method of any one of claims 24 to 31, wherein the viral infection is caused by HBV.~~

30~~34~~. The ~~method~~ use of any one of claims 12 to 25~~24 to 33~~, wherein the ~~drug~~medicament further comprises~~ing administering~~ an additional anti-HIV and/or anti-HBV agent.

~~35~~31. The ~~method~~ use of claim ~~34~~30, wherein the additional agent is selected from the group consisting of cabotegravir, dolutegravir, doravirine, elvitegravir, lersiverine, tenofovir disoproxil fumarate, tenofovir alafenamide fumarate, and lamivudine.

~~36~~32. Use of ~~a~~ the compound of any one of claims 1 to 11 for the preparation of a medicament for the treatment and prevention of a viral infection of HIV or HBV.