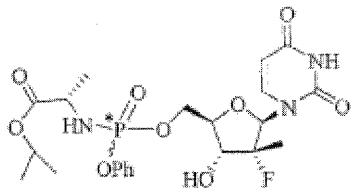
Nucleotides and Nucleic Acids, 2001, 20, 1091-1098; Lee, W.A., et al., *Antimicrobial Agents and Chemotherapy,* 2005, 49, 1898); US 2006/0241064; and WO 2007/095269.

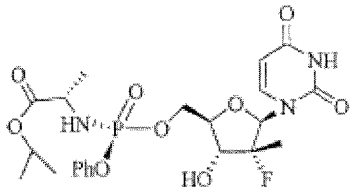
Also limiting the utility of nucleosides as viable therapeutic agents is their sometimes poor physicochemical and pharmacokinetic properties. These poor properties can limit the intestinal absorption of an agent and limit uptake into the target tissue or cell. To improve on their properties prodrugs of nucleosides have been employed. It has been demonstrated that preparation of nucleoside phosphoramidates improves the systemic absorption of a nucleoside and furthermore, the phosphoramidate moiety of these "pronucleotides" is masked with neutral lipophilic groups to obtain a suitable partition coefficient to optimize uptake and transport into the cell dramatically enhancing the intracellular concentration of the nucleoside monophosphate analog relative to administering the parent nucleoside alone. Enzyme-mediated hydrolysis of the phosphate ester moiety produces a nucleoside monophosphate wherein the rate limiting initial phosphorylation is unnecessary. To this end, U.S. Patent Application 12/053,015, which corresponds to WO 2008/121634 and US 2010/0016251, discloses a number of phosphoramidate nucleoside prodrugs, many of which show activity in an HCV assay. Several compounds disclosed in US 2010/0016251 were tested as a potential clinical candidate for approval by the FDA.

Summary ~~of the Invention~~

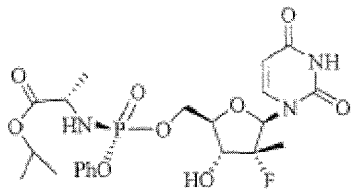
Disclosed herein is a compound represented by formula 4 and its respective phosphorus-based diastereomers represented by formulas S_p-4 and R_p-4.



4

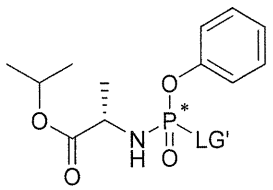


S_P-4



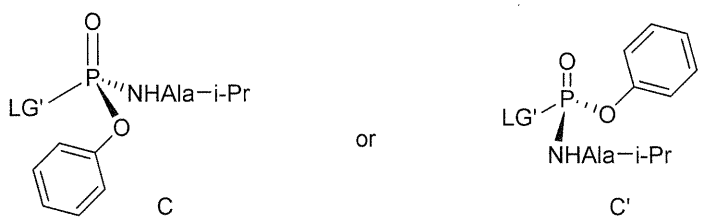
R_P-4

In one aspect of the present disclosure, there is provided a compound represented by the structure:



wherein LG' is tosylate, camphorsulfonate, an aryloxide, or an aryloxide substituted with at least one electron withdrawing group.

In another aspect of the present disclosure, there is provided a compound represented by the structure:



C C'

wherein LG' is a leaving group.

Brief Description of the Drawings

Figure 1. High resolution XRD diffractogram of 4.

Figure 2. High resolution XRD diffractogram of R_p-4.

Figure 3. High resolution XRD diffractogram of S_p-4 (Form 1).

Figure 4. High resolution XRD diffractogram of S_p-4 (Form 1).

Figure 5. High resolution XRD diffractogram of S_p-4- CH_2Cl_2 (Form 2).

Figure 6. High resolution XRD diffractogram of S_p-4-$CHCl_3$ (Form 3).

Figure 7. High resolution XRD diffractogram of S_p-4 (Form 4).

Figure 8. High resolution XRD diffractogram of S_p-4 (Form 5).

Figure 9. High resolution XRD diffractogram of S_p-4 (amorphous).

Figure 10. X-Ray Crystal Structure for S_p-4 (Form 1)

Figure 11. X-Ray Crystal (Isotropic) Structure for S_p-4•CH_2Cl_2 (Form 2)

Figure 12. X-Ray Crystal (Anisotropic) Structure for S_p-4•CH_2Cl_2 (Form 2)

Figure 13. X-Ray Crystal Structure for S_p-4•$CHCl_3$ (Form 3)

Figure 14. FT-IR spectrum of 4.

Figure 15. FT-IR spectrum of R_p-4.

Figure 16. FT-IR spectrum of *S*p-4

Figure 17. TGA and DSC analysis of 4.

Figure 18. TGA and DSC analysis of R_P-4.

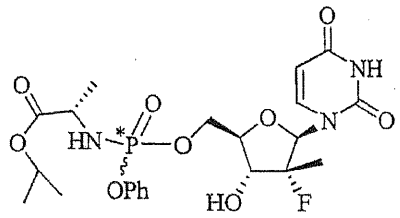
Figure 19. TGA and DSC analysis of S_P-4.

Figure 20A. X-Ray Crystal Structure for 8 (S_p-isomer) (molecule no. 1 of the asymmetric unit).

Figure 20B. X-Ray Crystal Structure for 8 (S_p-isomer) (molecule no. 2 of the asymmetric unit).

Claims

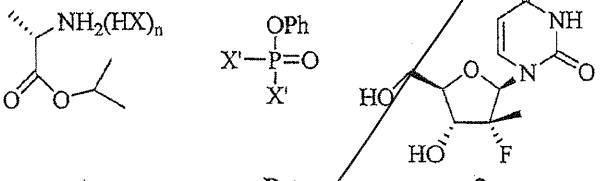
1. A process for preparing compound represented by formula 4:



4

wherein P* represents a chiral phosphorus atom, which comprises:

a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising **4**;



A **B** **3**

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen

b) reacting the first mixture with a protecting compound to obtain a second mixture comprising **4**; and

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain **4**.

2. The process as claimed in claim 1, wherein for A, X is chloride and n is 1.

3. The process as claimed in claim 2, wherein A is substantially anhydrous.

4. The process as claimed in claim 3, wherein the base is N-methylimidazole.

5. The process as claimed in claim 4, wherein the mole ratio of A-to-B-to-3 is about 1.6-to-1.3-to-1.

6. The process as claimed in claim 1, wherein the protecting compound is t-butyl-dimethyl-silyl-chloride.

7. A composition obtained by the process as claimed in any one of claims 1-6, wherein the composition comprises **4** in an amount that is at least about 95% by weight of the composition.

8. The composition of claim 7, wherein the composition comprises **4** in an amount that is at least about 97% by weight of the composition.

9. The composition of claim 7, wherein the composition comprises **4** in an amount that is at least about 99% by weight of the composition.

10. The composition of claim 7, wherein the composition comprises **4** in an amount that is at least about 99.9% by weight of the composition.

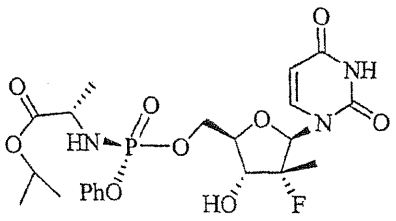
11. A process for determining the chemical purity of the compound **4** prepared by the processes of any one of claims 1-6 or the composition of any one of claims 7-10, which comprises:

analyzing by HPLC the compound or the composition comprising the compound.

12. A process for determining the crystallinity of the compound **4** prepared by the processes of any one of claims 1-6 or the composition of any one of claims 7-10, which comprises:

analyzing by XRPD, X-ray crystallography, or optical microscopy the compound or the composition comprising the compound.

13. A compound represented by the formula R_P-4



R_P-4

14. The compound of claim 13, wherein the compound is a solvate, a hydrate, or anhydrous.

15. The compound of claim 14, wherein the compound is a hydrate and the hydrate comprises about 0.1 to about 5 mol H_2O.

16. The compound of claim 13, wherein the compound is amorphous, crystal-like, crystalline, or a combination thereof.

17. The compound of claim 16, wherein the compound is crystalline.

18. A composition for the treatment and/or prophylaxis of hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus, comprising a pharmaceutically acceptable medium and the compound of any one of claims 13-17.

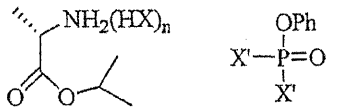
19. A method for treating a host infected with hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus comprising administering an effective amount of the compound of any one of claims 13-17.

20. A method for treating a host infected with hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus comprising administering an effective amount of the compound of any one of claims 13-17 in combination with at least one anti-viral agent.

21. A use of the compound of any one of claims 13-17 the compound represented by formula I in the manufacture of a medicament for the treatment of any condition that results from an infection by hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus.

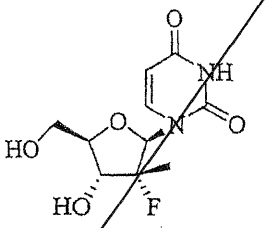
22. A process for preparing the compound of claim 13, which comprises:

a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising R_P-4;



A

B



3

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen

b) reacting the first mixture with a protecting compound to obtain a second mixture comprising R_P-4; and

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain purified R_P-4.

23. The process as claimed in claim 22, wherein for A, X is chloride and n is 1.

24. The process as claimed in claim 23, wherein A is substantially anhydrous.

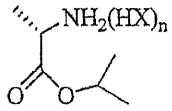
25. The process as claimed in claim 24, wherein the base is N-methylimidazole.

26. The process as claimed in claim 25, wherein the mole ratio of A-to-B-to-3 is about 1.6-to-1.3-to-1.

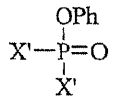
27. The process as claimed in claim 22, wherein the protecting compound is t-butyl-dimethyl-silyl-chloride.

28. A process for preparing the compound as claimed in claim 17, which comprises:

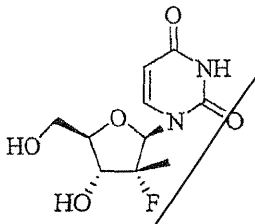
a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising R_P-4



A



B



3

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen;

b) reacting the first mixture with a protecting compound to obtain a second mixture;

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain a third mixture;

d) dissolving or suspending the second mixture or the third mixture in a solvent;

e) optionally followed by seeding with crystalline R_P-4; and

f) adding sufficient anti-solvent to obtain crystalline R_P-4.

29. A composition obtained by the process as claimed in any one of claims 22-28, wherein the composition comprises R_P-4 in an amount that is at least about 95% by weight of the composition.

30. The composition of claim 29, wherein the composition comprises R_P-4 in an amount that is at least about 97% by weight of the composition.

31. The composition of claim 29, wherein the composition comprises R_P-4 in an amount that is at least about 99% by weight of the composition.

32. The composition of claim 29, wherein the composition comprises R_P-4 in an amount that is at least about 99.9% by weight of the composition.

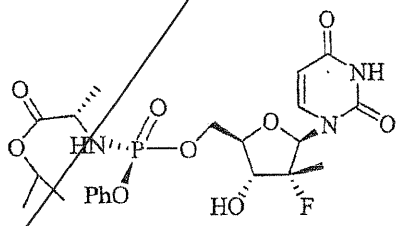
33. A process for determining the chemical purity of the compound of any one of claims 13-17 or the composition as claimed in any one of claims 18 and 29-32, which comprises:

analyzing by HPLC the compound or the composition comprising the compound.

34. A process for determining the crystallinity of the compound of any one of claims 13-17 or the composition as claimed in any one of claims 18 and 29-32, which comprises:

analyzing by XRPD, X-ray crystallography or optical microscopy the compound or the composition comprising the compound.

35. A compound represented by the formula S_P-4



S_P-4

36. The compound of claim 35, wherein the compound is a solvate, a hydrate, or anhydrous.

37. The compound of claim 36, wherein the compound is a hydrate and the hydrate comprises about 0.1 to about 5 mol H_2O.

38. The compound of claim 35, wherein the compound is amorphous, crystal-like, crystalline, or combination thereof.

39. The compound of claim 38, wherein the compound is crystalline.

40. A composition for the treatment and/or prophylaxis of hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus, comprising a pharmaceutically acceptable medium and the compound of any one of claims 35-39.

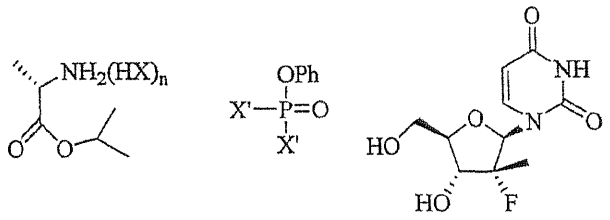
41. A method for treating a host infected with hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus comprising administering an effective amount of the compound of any one of claims 35-39.

42. A method for treating a host infected with hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus comprising administering an effective amount of the compound of any one of claims 35-39 in combination with at least one anti-viral agent.

43. A use of the compound of any one of claims 35-39 the compound represented by formula I in the manufacture of a medicament for the treatment of any condition that results from an infection by hepatitis C virus, West Nile virus, yellow fever virus, dengue virus, rhinovirus, polio virus, hepatitis A virus, bovine viral diarrhea virus or Japanese encephalitis virus.

44. A process for preparing the compound claim 35, which comprises:

a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising S_P-4;



A **B** **3**

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen

b) reacting the first mixture with a protecting compound to obtain a second mixture comprising S_P-**4**; and

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain purified S_P-**4**.

45. The process as claimed in claim 44, wherein for A, X is chloride and n is 1.

46. The process as claimed in claim 45, wherein A is substantially anhydrous.

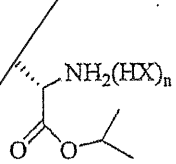
47. The process as claimed in claim 46, wherein the base is N-methylimidazole.

48. The process as claimed in claim 47, wherein the mole ratio of A-to-B-to-**3** is about 1.6-to-1.3-to-1.

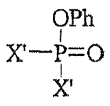
49. The process as claimed in claim 44, wherein the protecting compound is t-butyl-dimethyl-silyl-chloride.

50. A process for preparing the compound as claimed in claim 39, which comprises:

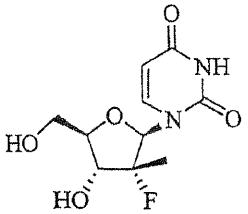
a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising S_P-**4**



A



B



3

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen;

b) reacting the first mixture with a protecting compound to obtain a second mixture;

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain purified S_P-4;

d) dissolving or suspending the second mixture or the purified S_P-4 in a solvent followed by seeding with crystalline S_P-4 at about room temperature;

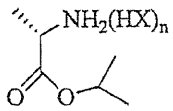
f) collecting a first solid the majority of which comprises S_P-4;

g) dissolving or suspending the first solid in a solvent at its reflux temperature; and

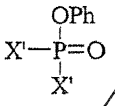
h) cooling or adding an anti-solvent to obtain a second solid.

51. A process for preparing the compound as claimed in claim 39, which comprises:

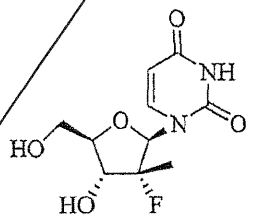
a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising S_P-4



A



B



3

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen;

b) reacting the first mixture with a protecting compound to obtain a second mixture;

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain purified S_P-4;

d) dissolving or suspending the second mixture or the purified S_P-4 in a first solvent followed by adding an anti-solvent so as to obtain a first composition in which the residual solvent/anti-solvent is removed by decanting to obtain a residue;

e) treating the residue with a solution containing the first solvent and anti-solvent to yield a second composition whereby upon reducing the pressure affords a first solid;

f) dissolving or suspending the first solid using a second solvent so as to obtain a third composition;

g) adding seed crystals of S_P-4 to the third composition;

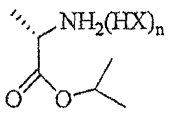
h) collecting a second solid;

i) dissolving or suspending the second solid in a third solvent, optionally heated to the reflux temperature of the third solvent to obtain a fourth composition, and , if necessary, and

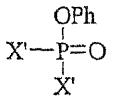
j) cooling the fourth composition to obtain a third solid comprising S_P-4 which is collected by filtration.

52. A process for preparing the compound as claimed in claim 39, which comprises:

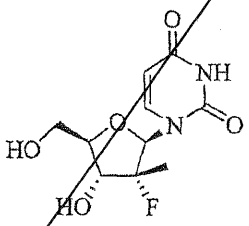
a) reacting an isopropyl-alanate, **A**, a di-X'-phenylphosphate, **B**, 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a base to obtain a first mixture comprising S_P-4



A



B



3

wherein X is a conjugate base of an acid, n is 0 or 1, and X' is a halogen;

b) reacting the first mixture with a protecting compound to obtain a second mixture;

c) optionally subjecting the second mixture to crystallization, chromatography, or extraction in order to obtain a third mixture;

d) adding silica gel to the second mixture or the third mixture followed by solvent evaporation to afford a dry slurry;

e) stirring the dry slurry in a first solvent/anti-solvent combination to obtain a first wet slurry;

f) decanting the first solvent/anti-solvent combination from the first wet slurry to obtain a second wet slurry and a first composition;

g) adding to the second wet slurry a second solvent/anti-solvent combination followed by stirring;

h) decanting the second solvent/anti-solvent combination from the second wet slurry to obtain a third wet slurry and a second composition

i) optionally repeating steps g)–h) on the third wet slurry or additional wet slurries;

j) evaporating the solvent from the second composition, and optionally any additional composition obtained from optional step i) to obtain a first solid;

k) dissolving or suspending the first solid in a solution containing a third solvent and optionally a fourth solvent to obtain a third composition;

l) optionally adding seed crystals of S_P-4 to the third composition;

m) obtaining from the third composition a second solid comprising S_P-4; and

n) optionally recrsytallizing the second solid using a third solvent to obtain a third solid comprising S_P-4.

53. A composition obtained by the process as claimed in any one of claims 44-52, wherein the composition comprises S_P-4 in an amount that is at least about 95% by weight of the composition.

54. The composition of claim 53, wherein the composition comprises S_P-4 in an amount that is at least about 97% by weight of the composition.

55. The composition of claim 53, wherein the composition comprises S_P-4 in an amount that is at least about 99% by weight of the composition.

56. The composition of claim 53, wherein the composition comprises S_P-4 in an amount that is at least about 99.9% by weight of the composition.

57. A process for determining the chemical purity of the compound of any one of claims 35-39 or the composition of any one of claims 40 and 53-56, which comprises:

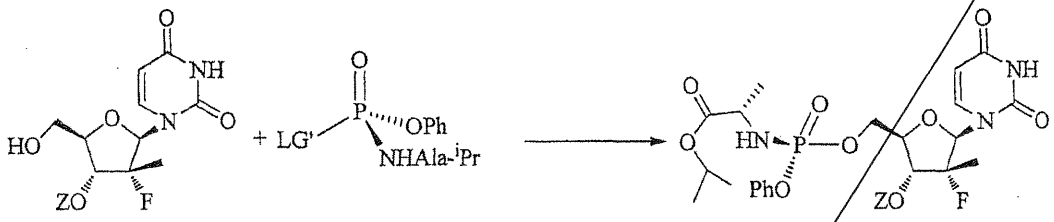
analyzing by HPLC the compound or the composition comprising the compound.

58. A process for determining the crystallinity of the compound of any one of claims 35-39 or the composition of any one of claims 40 and 53-56, which comprises:

analyzing by XRPD, X-ray crystallography, or optical microscopy the compound or the composition comprising the compound.

59. A process for preparing the compound of claim 13, which comprises:

a) reacting an isopropyl-alanyl-phosphoramidate, **C'**, with 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a basic reagent to obtain protected or unprotected R_P-**4**



3 **C'**

wherein Z is a protecting group or hydrogen and LG' is a leaving group.

60. The process of claim 59, which further comprises optionally deprotecting protected R_P-**4** and subjecting R_P-**4** to chromatography, extraction, or crystallization in order to obtain purified R_P-**4**.

61. The process of claim 59 which further comprises

1) reacting (LG')P(O)$(LG)_2$, wherein LG, independent of LG', is a leaving group, with

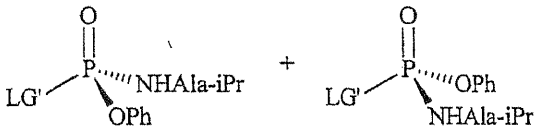
(i) isopropyl-alanate and a first base to obtain (LG')P(O)(LG)(Ala-^{i}Pr) followed by reacting (LG')P(O)(LG)(Ala-^{i}Pr) with phenol and a second base to obtain a mixture comprising **C** and **C'**,

(ii) phenol and a first base to obtain (LG')P(O)(LG)(OPh) followed by reacting (LG')P(O)(LG)(OPh) with isopropyl-alanate and a second base to obtain a mixture comprising **C** and **C'**, or

(iii) combining isopropyl-alanate, phenol, and at least one base to obtain a mixture comprising **C** and **C'**; or

2) reacting (PhO)P(O)$(LG)_2$, wherein LG', independent of LG, is a leaving group, with

(i) isopropyl-alanate and a first base to obtain (PhO)P(O)(LG)(Ala-^{i}Pr) followed by reacting (PhO)P(O)(LG)(Ala-^{i}Pr) with a leaving group precursor and a second base to obtain a mixture comprising **C** and **C'**,



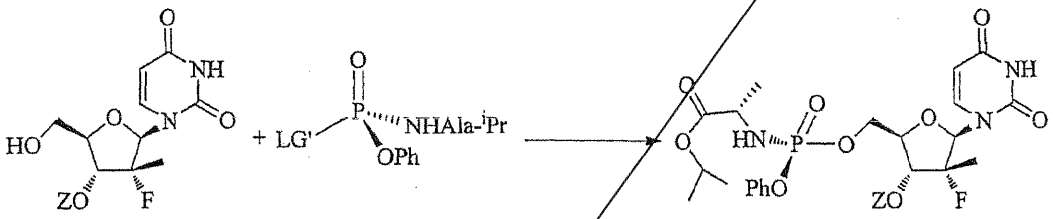
C C'

and

subjecting the mixture to extraction, chromatography, or crystallization to obtain **C'**.

62. A process for preparing the compound of claim 35, which comprises:

a) reacting an isopropyl-alanyl-phosphoramidate, **C**, with 2'-deoxy-2'-fluoro-2'-C-methyluridine, **3**, and a basic reagent to obtain protected or unprotected S_P-**4**



3 C

wherein Z is a protecting group or hydrogen and LG' is a leaving group.

63. The process of claim 62, which further comprises optionally deprotecting protected R_P-**4** and subjecting the obtained S_P-**4** to chromatography, extraction, or crystallization in order to obtain purified S_P-**4**.

64. The process of claim 62 which further comprises

1) reacting (LG')P(O)$(LG)_2$, wherein LG, independent of LG', is a leaving group, with

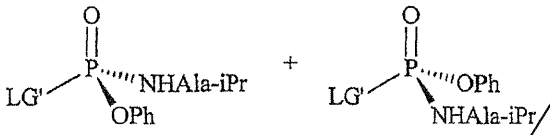
(i) isopropyl-alanate and a first base to obtain (LG')P(O)(LG)(Ala-^{i}Pr) followed by reacting (LG')P(O)(LG)(Ala-^{i}Pr) with phenol and a second base to obtain a mixture comprising **C** and **C'**,

(ii) phenol and a first base to obtain (LG')P(O)(LG)(OPh) followed by reacting (LG')P(O)(LG)(OPh) with isopropyl-alanate and a second base to obtain a mixture comprising **C** and **C'**, or

(iii) combining isopropyl-alanate, phenol, and at least one base to obtain a mixture comprising **C** and **C'**; or

2) reacting $(PhO)P(O)(LG)_2$, wherein LG', independent of LG, is a leaving group, with

(i) isopropyl-alanate and a first base to obtain (PhO)P(O)(LG)(Ala-^{i}Pr) followed by reacting (PhO)P(O)(LG)(Ala-^{i}Pr) with a leaving group precursor and a second base to obtain a mixture comprising **C** and **C'**,



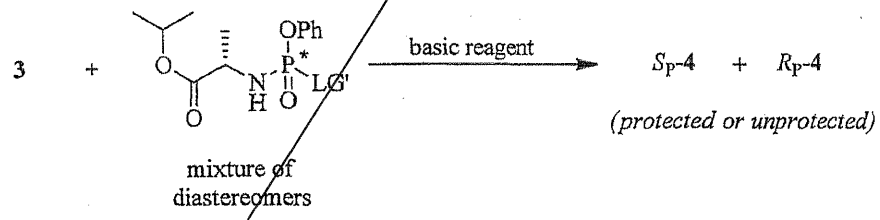
C C'

and

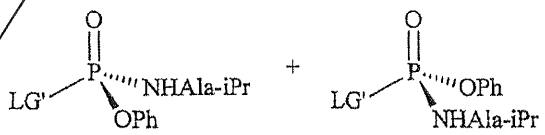
subjecting the mixture to extraction, chromatography, or crystallization to obtain **C**.

65. A process for preparing the compound of claim 35, which comprises:

a) reacting an isopropyl-alanyl-phosphoramidate with 3'-O-protected or unprotected **3**, and a basic reagent to obtain a composition comprising protected or unprotected S_P-4



wherein the isopropyl-alanyl-phosphoramidate is comprised of a mixture of diastereomers represented by the following structures:



C C'

wherein the ratio of **C**:**C'** is about 1:1.

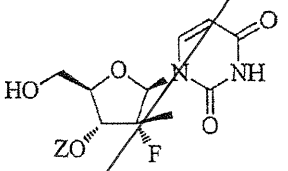
66. The process of claim 65, wherein the basic reagent is t-butylmagnesium chloride and the ratio of **C**:**C'** is greater than or equal to about 1:1.

67. The process of claim 65, wherein the basic reagent is t-butylmagnesium chloride and the ratio of **C:C'**; is greater than about 1:1.

68. The process of claim 65, wherein the basic reagent is t-butylmagnesium chloride and the ratio of **C:C'** is at least about 1.5:1, about 2.3:1, about 4:1, about 5.7:1, about 9:1, about 19:1, about 32.3:1, about 49:1, or about 99:1.

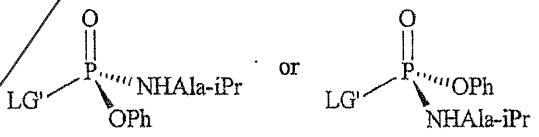
69. The process of claim 65, wherein the LG' is p-nitrophenoxide, the basic reagent is t-butylmagnesium chloride, and the ratio of **C:C'** is at least about 1.5:1, about 2.3:1, about 4:1, about 5.7:1, about 9:1, about 19:1, about 32.3:1, about 49:1, or about 99:1.

70. A compound selected from among **3a**, **3b**, **3c**, and **3d**



3a: Z = -C(O)$CH_2CH_2C(O)CH_3$
3b: Z = -C(O)OCH_2Ph
3c: Z = -Si(Me)$_2{}^t$Bu
3d: Z = -Si(^{i}Pr)$_2$OSi(^{i}Pr)$_2$OH

71. A compound represented by the following structures



C C'

where LG' is a leaving group.

72. The compound of claim 71, wherein LG' is tosylate, camphorsulfonate, an aryloxide, or an aryloxide substituted with at least one electron withdrawing group.

73. The compound of claim 71, wherein LG' is p-nitrophenoxide, p-chlorophenoxide, o-chlorophenoxide, 2,4-dinitrophenoxide, or pentafluorophenoxide.

74. The compound of claim 71, wherein LG' is p-nitrophenoxide.

75. The compound of claim 74 in crystalline form.

76. A process for preparing **C** or **C'** of claim 71, which comprises:

1) reacting $(LG')P(O)(LG)_2$, with

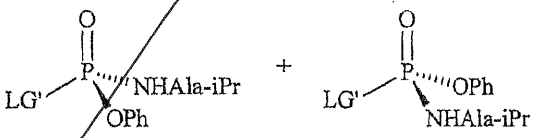
(i) isopropyl-alanate and a first base to obtain $(LG')P(O)(LG)(Ala\text{-}^{i}Pr)$ followed by reacting $(LG')P(O)(LG)(Ala\text{-}^{i}Pr)$ with phenol and a second base to obtain a mixture comprising **C** and **C'**,

(ii) phenol and a first base to obtain $(LG')P(O)(LG)(OPh)$ followed by reacting $(LG')P(O)(LG)(OPh)$ with isopropyl-alanate and a second base to obtain a mixture comprising **C** and **C'**, or

(iii) combining isopropyl-alanate, phenol, and at least one base to obtain a mixture comprising **C** and **C'**; or

2) reacting $(PhO)P(O)(LG)_2$, wherein LG', independent of LG, is a leaving group, with

(i) isopropyl-alanate and a first base to obtain $(PhO)P(O)(LG)(Ala\text{-}^{i}Pr)$ followed by reacting $(PhO)P(O)(LG)(Ala\text{-}^{i}Pr)$ with a leaving group precursor and a second base to obtain a mixture comprising **C** and **C'**,



C C'

and

subjecting the mixture to extraction, chromatography, or crystallization to obtain **C or C'**.

77. The process of claim 76, which comprises subjecting the mixture to crystallization, said process further comprises:

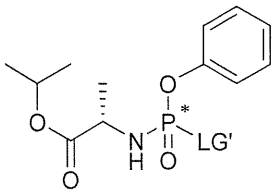
3) dissolving or suspending the mixture in a solvent and

4) adding seed crystals of C or C'.

78. A compound of claim 13 or of claim 35, wherein said compound is isotopically labeled.

Claims

1. A compound represented by the structure:



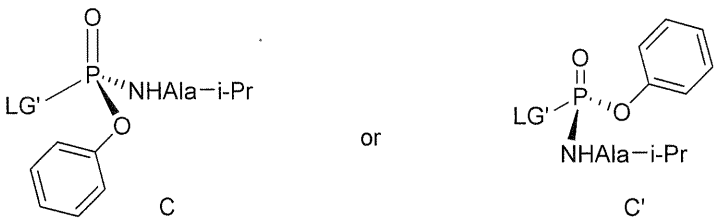
wherein LG' is tosylate, camphorsulfonate, an aryloxide, or an aryloxide substituted with at least one electron withdrawing group.

2. The compound according to claim 1, wherein LG' is p-nitrophenoxide, p-chlorophenoxide, o-chlorophenoxide, 2,4-dinitrophenoxide, or pentafluorophenoxide.

3. The compound according to claim 2, wherein LG' is p-nitrophenoxide.

4. The compound according to claim 2, wherein LG' is pentafluorophenoxide.

5. A compound represented by the structure:

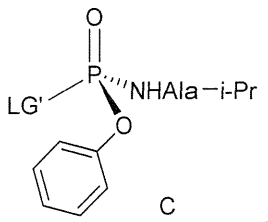


wherein LG' is a leaving group.

6. The compound according to claim 5, wherein LG' is tosylate, camphorsulfonate, an aryloxide, or an aryloxide substituted with at least one electron withdrawing group.

7. The compound according to claim 5, wherein LG' is p-nitrophenoxide, p-chlorophenoxide, o-chlorophenoxide, 2,4-dinitrophenoxide, or pentafluorophenoxide.

8. The compound according to claim 5, wherein the compound is represented by the structure:



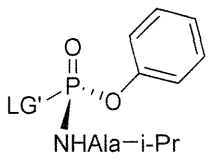
C .

9. The compound according to claim 8, wherein LG' is p-nitrophenoxide, p-chlorophenoxide, o-chlorophenoxide, 2,4-dinitrophenoxide, or pentafluorophenoxide.

10. The compound according to claim 9, wherein LG' is p-nitrophenoxide.

11. The compound according to claim 9, wherein LG' is pentafluorophenoxide.

12. The compound according to claim 5, wherein the compound is represented by the structure:



C' .

13. The compound according to claim 12, wherein LG' is p-nitrophenoxide, p-chlorophenoxide, o-chlorophenoxide, 2,4-dinitrophenoxide, or pentafluorophenoxide.

14. The compound according to claim 13, wherein LG' is p-nitrophenoxide.

15. The compound according to claim 13, wherein LG' is pentafluorophenoxide.