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Synthesis of 2′,3′-dideoxy-3′-fluoro-L-ribonucleosides as potential antiviral agents from D-sorbitol

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Abstract

2′,3′-Dideoxy-3′-fluoro-L-ribonucleosides were synthesized as potential antiviral agents. The key intermediate, methyl 5-*O*-benzoyl-2,3-dideoxy-3-fluoro-L-ribofuranoside, which was prepared from D-sorbitol, was condensed with pyrimidine and purine bases to obtain the respective nucleosides. Among them, the cytosine analogue 2′,3′-dideoxy-3′-fluoro-α-L-cytidine showed a moderate anti-HBV activity.

Keywords: D-Sorbitol; 2′,3′-Dideoxy-3′-fluoro-L-ribonucleosides; 3′-Deoxy-3′-fluoro-D-thymidine (FLT)

1. Introduction

Recently, a number of nucleosides with the unnatural L-configuration have been reported as potent chemotherapeutic agents against human immunodeficiency virus (HIV), hepatitis B virus (HBV), and cancer. These include β-L-1-(2-hydroxymethyl-1,3-oxathiolan-4-yl)-5-cytosine (3TC) [1], β-L-1-(2-hydroxymethyl-1,3-oxathiolan-4-yl)-5-fluorocytosine (FTC) [2], β-L-2′,3′-dideoxypentofuranosyl-5-fluorocytosine (L-FddC) [3], 2′,3′-didehydro-2′,3′-dideoxy-β-L-fluorocytidine (β-L-Fd4C) [4], L-1-(2-hydroxymethyl-1,3-dioxolan-4-yl)-cytosine [L-OddC] [5] and 2′-fluoro-5-methyl-β-L-arabinofuranosyluracil (L-FMAU) [6]. It is intriguing that these L-nucleosides have potent biological activity, while some of them show lower toxicity profiles in comparison with their D-counterparts. For example, L-FMAU showed greater potency against HBV and lower toxicity than D-FMAU [6].

2′,3′-Dideoxy-3′-fluoro-D-ribonucleosides [7,8] have been known to have potent antiviral activities. Among them, 3′-deoxy-3′-fluoro-D-thymidine (FLT) has been reported to be as potent as that of AZT against HIV [9]. However, the use of FLT as an antiviral agent has been limited due to its severe hematopoietic toxicities [10]. Thus, we have synthesized the L-counterparts of the 3′-fluorinated-D-nucleosides as potential antiviral agents. Herein we report the synthesis of 2′,3′-dideoxy-3′-fluoro-L-ribonucleosides and their antiviral activities.

2. Results and discussion

In order to synthesize the 2′,3′-dideoxy-3′-fluoro-L-ribonucleosides, we adopted a

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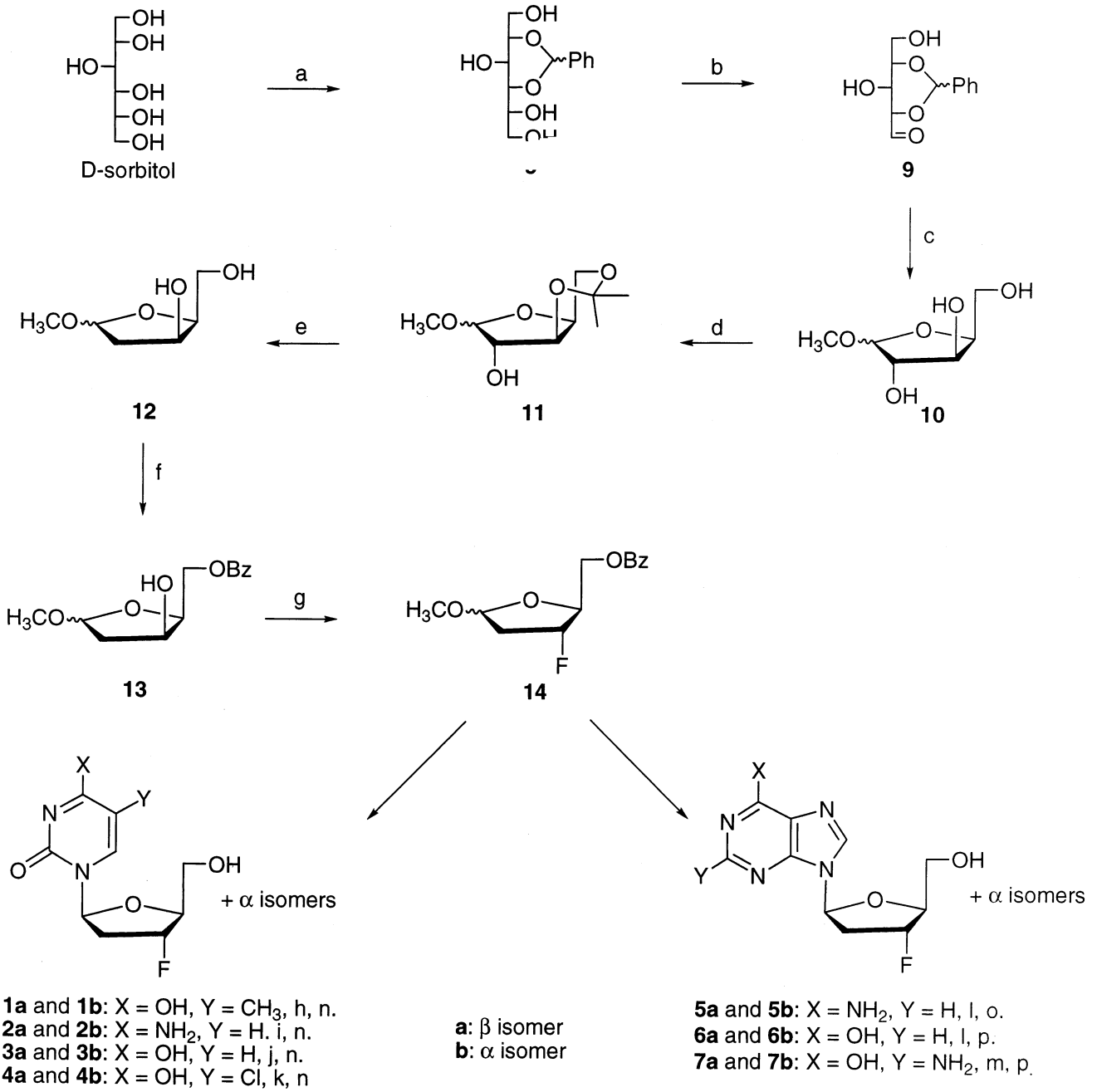
method used in the synthesis of AZT and FLT from D-xylose, reported by Fleet et al. and Gurjar et al. [11]. However, we utilized D-sorbitol as the starting material instead of expensive L-xylose. D-Sorbitol was converted into benzylidene-L-xylose **9** by selective protection, following oxidative cleavage via intermediate **8** by the known procedure [12]. Intermediate **9** was then readily converted into methyl L-xylofuranoside **10** by using 5% hydrochloric acid in methanol without significant contamination of pyranoside in 62% yield from D-sorbitol, which was pure enough to use for the next reaction without purification. However, in the original procedure [12], intermediate **9** was hydrolysed to free L-xylose which, according to our experiences, is not easy to purify. The selective protection of **10** with acetone and TsOH gave intermediate **11** with a free 2-hydroxy group in 82% yield. The D-counterpart of this intermediate has frequently been used for the synthesis of 3′-substituted-D-nucleosides such as AZT or FLT [11,13]. Thus we successfully utilized inexpensive D-sorbitol for the preparation of the desired L-xylose derivative, which, otherwise, should be prepared from expensive L-xylose. Therefore, this new procedure may provide a great potential in its utilization for the synthesis of 2′- and/or 3′-modified L-nucleosides. Intermediate **11** was converted into **12** by a Barton-type deoxygenation, followed by an acidic hydrolysis in one pot in 61% yield [11]. Intermediate **12** was selectively protected with BzCl and pyridine in dichloromethane at -10 °C to give **13** in 73% yield, which was fluorinated with TBAF via a triflate intermediate to afford the key intermediate **14** in 46% yield. The condensation of **14** with silylated pyrimidine or purine bases, followed by deprotection and base modification, if necessary, gave 2′,3′-dideoxy-3′-fluoro-L-ribonucleosides in 26–65% overall yields from **14** using Vorbrüggen conditions (Scheme 1). The anomeric separation of thymidine (**1a** and **1b**), cytidine (**2a** and **2b**), and uridine (**3a** and **3b**) analogues was conducted at the deprotected stages by silica gel chromatography, whereas 5-chlorouridine analogues **4a** and **4b** were readily separated at the protected stage. For the preparation of adenosine analogues **5a** and **5b**, 6-chloropurine was condensed with **14**, and the resulting 6-chloropurine nucleoside intermediate was converted into the adenosine analogue by treatment with methanol saturated with NH_3 in a steel bomb at 90 °C and was separated to give the β anomer **5a** and α anomer **5b** by silica gel column chromatography. Inosine derivatives **6a** and **6b** were also obtained from the 6-chloropurine nucleoside intermediates by treatment with 2-mercaptoethanol and $NaOCH_3$ under refluxing conditions and subsequent separation using silica gel column chromatography. Guanosine analogues **7a** and **7b** were prepared by the condensation of **14** with silylated 2-amino-6-chloropurine at room temperature, which gave virtually one regioisomer with a λ_{max} at 320 nm. The intermediate was refluxed in CH_3CN without catalyst for 17 h to give an N^9-regioisomer with a λ_{max} at 309 nm. The isomer was converted by treatment with 2-mercaptoethanol and $NaOCH_3$ under refluxing conditions, followed by silica gel column chromatography to give guanosine analogues **7a** and **7b** (Fig. 1).

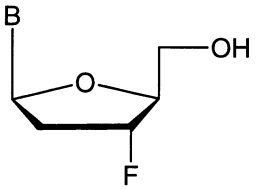
The stereochemical assignment of the final nucleosides were made on the basis of 1D and 2D NMR spectroscopy. The anomers with higher field resonance for H-4′ were assigned as the β isomers, and the ones with lower chemical shifts were assigned as the α isomers based on the deshielding effect of the heterocycle on the α isomers (Table 1). This assignment was further confirmed by NOESY spectra of the representative nucleoside intermediates **1a** and **1b** (Fig. 2). Other characteristics of the ^1H NMR spectra of the β isomers include: the splitting pattern of H-1′ of all β isomers of this series shows a double doublet with relatively large $J_{1',2'}$ and $J_{1',2''}$ values, whereas most α isomers show a single doublet or double doublet with smaller $J_{1',2'}$ and $J_{1',2''}$ values (Table 1), which is consistent with those of the reported D-analogues [11a,b,14].

The synthesized L-ribonucleosides were evaluated against HIV and HBV. Among them, the cytosine analogue **2a** showed moderate anti-HBV activity (10 μM in 2.2.15 cell line) with no cytotoxicity up to 100 μM (Table 2). Interestingly, the 2′,3′-dideoxy-3′-fluoro-L-ribonucleosides were devoid of HIV activity in vitro, in contrast to the D-enan-

tiomers, in particular FLT. In addition, the structure–activity relationship study indicates that the 3′-fluoro function in the β-L-configuration seems to have a profound effect on antiviral activity. For example, the synthesized compound, 2′,3′-dideoxy-3′-fluoro-L-cytidine (**2a**) was much less effective against HIV-1 and HBV in vitro than 2′,3′-dideoxy-L-cytidine [3b]. The low or lack of antiviral activity of the synthesized L-nucleosides may be due to their low effectiveness as substrates for the activating enzymes, the cellular nucleoside or nucleotide kinases, since the triphosphates of many inactive nucleosides have been found to



Scheme 1. Reagents: (a) PhCHO, HCl, H_2O. (b) $NaIO_4$, H_2O, −7 °C. (c) 5% HCl–MeOH. (d) TsOH, $CuSO_4$, acetone. (e) [i] NaH, THF. [ii] CS_2. [iii] MeI. [iv] Bu_3SnH, xylene, reflux. [v] TsOH, MeOH. (f) BzCl, Py, CH_2Cl_2, −10 °C. (g) [i] Tf_2O, Py, CH_2Cl_2. [ii] TBAF, THF. (h) Silylated thymine, Me_3SiOTf, CH_3CN. (i) Silylated N^4-benzoylcytosine, Me_3SiOTf, CH_3CN. (j) Silylated uracil, Me_3SiOTf, CH_3CN. (k) Silylated 5-chlorouracil, Me_3SiOTf, CH_3CN. (l) Silylated 6-chloropurine, Me_3SiOTf, CH_3CN. (m) [i] Silylated 2-amino-6-chloropurine, Me_3SiOTf, CH_3CN. [ii] reflux, CH_3CN. (n) NH_3–MeOH, 90 °C. (p) $HOCH_2CH_2SH$, $NaOCH_3$, MeOH, reflux.



1a (B = thymine)
2a (B = cytosine)
3a (B = uracil)
4a (B = 5-Cl-uracil)
5a (B = adenine)
6a (B = hypoxanthine)
7a (B = guanine)

Fig. 1. 2′,3′-Dideoxy-3′-L-fluororibonucleosides.

Table 1
Some selected ^{1}H NMR data for the new L-nucleosides

Compound #	H-1′ $J_{1',2'}$ and $J_{1',2''}$ (Hz)	H-4′ δ (ppm)
1a	5.55, 9.07	4.23
b	7.21	4.66
2a	5.63, 8.77	4.32
b	7.18	4.78
3a	5.62, 8.00	4.16
b	6.81	4.57
4a	5.60, 8.87	4.27
b	m [a]	4.69
5a	5.61, 9.39	4.16
b	1.31, 7.29	4.66
6a	6.24, 8.90	4.41
b	m [a]	4.63
7a	5.77, 9.41	4.34
b	2.21, 6.67	4.57

[a] Multiplet.

be potent inhibitors of the target enzymes such as HIV reverse transcriptase or HBV DNA polymerase [15].

3. Experimental

Melting points (mp) were determined on a Mel-Temp II apparatus and are uncorrected. NMR spectra were recorded on a Bruker 400 AMX spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) in the indicated solvents. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Mass spectra were recorded on a Micromass Autospec high-resolution mass spectrometer in fast-atom bombardment (FAB) mode. UV spectra were obtained on a Beckman DU 650 spectrophotometer. Elemental analyses were performed by Atlantic Microlab, Inc., and all the elemental analyses are within 0.4% of the theoretical values.

Methyl α/β-L-xylofuranoside (**10**).—To a solution of D-sorbitol (100 g, 0.55 mol) in water (70 mL), benzylaldehyde (60 mL) and concd HCl (13 mL) were added at 0 °C. The resulting mixture was stirred for 6 h at room temperature (rt), during which a product precipitated. After dilution with water (50 mL), the precipitate was filtered and the filter cake was washed with water (250 mL) and EtOAc (250 mL). The filter cake was suspended in water (1200 mL) containing Na_2CO_3 (8 g) and heated at 100 °C for 3 h to remove residual benzaldehyde. After filtration while hot, the filtrate was kept at 0 °C for 3 h and the crystalline solid thus generated (compound **8**, 100 g, 67%) was collected by filtration. Compound **8** (100 g, 0.37 mol) was suspended in water (400 mL) and cooled to −7 °C. To the

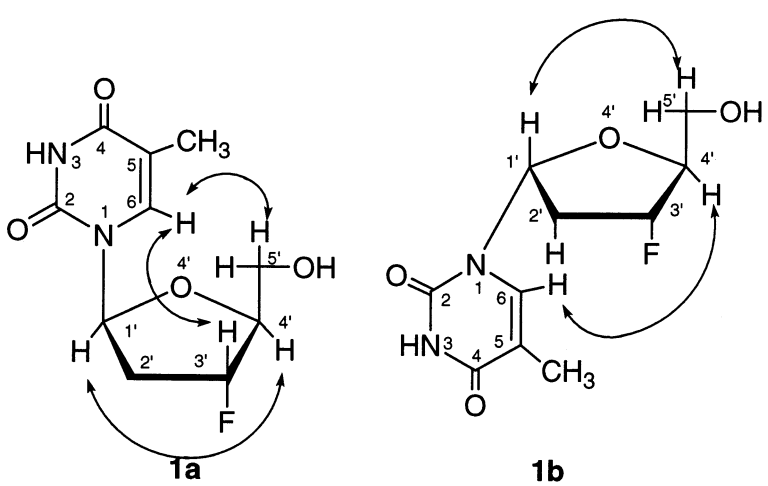
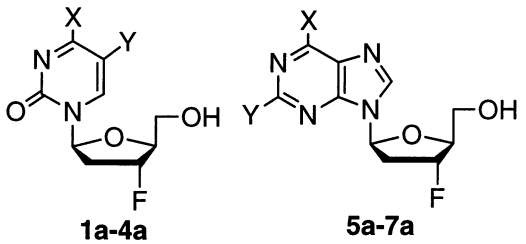


Fig. 2. NOE correlations from NOESY spectra of intermediates **1a** and **1b**.

Table 2
Antiviral activities and cytotoxicities of 2′,3′-dideoxy-3′-L-fluororibonucleosides



1a-4a **5a-7a**

No	X	Y	Antiviral activities EC_{50} (μM)		Cytotoxicities IC_{50} (μM)		
			HBV (2.2.15)	HIV (PBM)	Vero	PBM	CEM
1a	OH	CH_3	>10	>100	>100	>100	>100
2a	NH_2	H	10.0	>100	>100	>100	>100
3a	OH	H	>10	>100	>100	>100	>100
4a	OH	Cl	>10	>100	>100	>100	>100
5a	NH_2	H	>10	>100	>100	>100	>100
6a	OH	H	>10	>100	>100	>100	>100
7a	OH	NH_2	>10	>51.3	>100	>100	>100

suspension of compound **8**, $NaIO_4$ (111 g, 0.52 mol) in water (400 mL) was added over 30 min with vigorous stirring at −7 °C. The reaction mixture was neutralized with solid Na_2CO_3, treated with absolute EtOH (1000 mL), and stirred for 10 min. After removal of the generated solids by filtration, the filtrate was evaporated to one-third volume, and the solid generated during the evaporation was removed by filtration. The filtrate was concentrated to a solid residue, which was dissolved in absolute EtOH (500 mL) and the insoluble solid was again removed by filtration. The filtrate was evaporated to give crude compound **9** as a white solid (82 g, 93%) [12]. Compound **9** was dissolved in 0.5% HCl in MeOH (2 L). The resulting solution was stirred at rt for 20 h and neutralized with solid Na_2CO_3 (40 g). After concentration, the residue was obtained was dissolved in water (700 mL) and washed with ether (2 × 250 mL). The aqueous layer was evaporated to a residue, which was dissolved in CH_2Cl_2 (200 mL), and insoluble salt was removed by filtration. The filtrate was dried over Na_2SO_4, filtered, and concentrated to a syrup as an anomeric mixture of **10** (56 g, 62% from D-sorbitol), which was used for next reaction without further purification. A small amount of compound **10** was purified by silica gel column chromatography (10:1 $CHCl_3$–MeOH) for characterization: ^1H NMR (DMSO-d_6 + D_2O): δ 4.71 and 4.70 (d, s, 1 H, $J_{1,2}$ 4.09 Hz, H-1, α and β isomer), 4.02–3.93 (m, 2 H, H-2, H-3, α and β isomer), 3.86 and 3.78 (2 m, 1 H, H-4, α and β isomer), 3.61–3.33 (m, 2 H, H-5, α and β isomer), 3.30 and 3.21 (2 s, 3 H, CH_3O-1, α and β isomer); FABMS m/z 165 $(M+H)^+$. Anal. Calcd for $C_6H_{12}O_5 \cdot 0.1\ CHCl_3$: C, 41.61; H, 6.93. Found: C, 41.23; H, 6.88.

Methyl 3,5-di-O-isopropylidene-α-L-xylofuranoside (**11a**) *and methyl 3,5-di-O-isopropylidene-β-L-xylofuranoside* (**11b**).—Compound **11** was prepared as a syrup in 82% yield (α/β = 1.5:1 determined by NMR spectroscopy) from compound **10** by the method described by Baker et al. [13]. For characterization, a small amount of compound **11** was separated by silica gel column chromatography (10:1–5:1 hexanes–EtOAc) to the less polar compound **11a** and the more polar **11b** as syrup: Compound **11a** (α isomer): $[\alpha]_D^{25}$ −18.5° (*c* 3.0, H_2O; lit. $[\alpha]_D^{24}$ +17.6° for D-enantiomer at *c* 2.0 in H_2O); ^1H NMR ($CDCl_3$): δ 5.14 (d, 1 H, $J_{1,2}$ 4.06 Hz, H-1),

4.20–3.89 (m, 5 H, H-2, H-3, H-4, H-5), 3.55 (s, 3 H, CH_3O-1), 1.41 (s, 3 H, CH_3–), 1.35 (s, 3 H, CH_3–); FABMS *m/z* 205 $(M+H)^+$. Compound **11b** (β isomer): $[\alpha]_D^{25}$ +68.5° (*c* 3.0, H_2O; lit. $[\alpha]_D^{24}$ −64.2° for D-enantiomer at *c* 2.0 in H_2O); ^1H NMR ($CDCl_3$): δ 4.87 (s, 1 H, H-1), 4.24 (m, 1 H, H-4), 4.16–4.14 (m, 2 H, H-2, H-3), 3.98 (dd, 1 H, $J_{4,5}$ 4.70, $J_{5,5'}$ 12.07 Hz, H-5), 3.82 (dd, 1 H, $J_{4,5'}$ 5.10, $J_{5,5'}$ 12.07 Hz, H-5), 3.45 (s, 3 H, CH_3O-1), 1.40 (s, 3 H, CH_3–), 1.39 (s, 3 H, CH_3–); FABMS *m/z* 205 $(M+H)^+$.

Methyl 2-deoxy-α/β-L-xylofuranoside (**12**). —Compound **12** was prepared as a syrup from compound **11** by the method described by Fleet et al. [11a,b] in 61% yield: ^1H NMR ($CDCl_3$): δ 5.17 and 5.04 (dd, $J_{1,2}$ 2.78, $J_{1,2'}$ 5.18 Hz, and d, $J_{1,2}$ 4.69 Hz, 1 H, H-1, α and β isomer), 4.55 and 4.39 (2m, 1 H, H-4, α and β isomer), 4.14–4.01 (m, 3 H, H-3, H-5, α and β isomer), 3.40 and 3.39 (2s, 3 H, CH_3O-1, α and β isomer), 2.28–2.08 (m, 2 H, H-2, α and β isomer); FABMS *m/z* 149 $(M+H)^+$.

Methyl 5-O-benzoyl-2-deoxy-α/β-L-xylofuranoside (**13**).—To a solution of compound **12** (8.0 g, 53.96 mmol) and pyridine (9 mL) in CH_2Cl_2 (300 mL), BzCl (6.3 mL, 53.96 mmol) in CH_2Cl_2 (300 mL) was added over 2 h at −10 °C, and the resulting mixture was stirred for an additional hour at −10 °C. The reaction was quenched with water (50 mL), washed with 0.2 N HCl (70 mL), satd aq $NaHCO_3$ (70 mL), and brine (100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated to a residue, which was purified by silica gel column chromatography ($CHCl_3$) to give an anomeric mixture of **13** as a syrup (10 g, 73%). ^1H NMR ($CDCl_3$): δ 8.11–7.35 (m, 5 H, Ar, α and β isomer), 5.20 and 5.08 (dd, $J_{1,2}$ 3.57, $J_{1,2'}$ 5.61 Hz, and d, $J_{1,2}$ 4.23 Hz, 1 H, H-1, α and β isomer), 4.80–4.75 and 4.70–4.51 (2 m, 1 H, H-5, α and β isomer), 4.47–4.34 (m, 2 H, H-3, H-4, α and β isomer), 3.41 and 3.39 (2 s, 3 H, CH_3O-1, α and β isomer), 2.28–2.08 (m, 2 H, α and β isomer); FABMS *m/z* 253 $(M+H)^+$. Anal. Calcd for $C_6H_{12}O_4 \cdot 0.2\ H_2O$: C, 61.02; H, 6.46. Found: C, 60.97; H, 6.53.

Methyl 5-O-benzoyl-2,3-dideoxy-3-fluoro-α/β-L-ribofuranoside (**14**) *[11].*—To a solution of compound **13** (5.0 g, 19.82 mmol) and pyridine (6 mL) in CH_2Cl_2 (100 mL), triflic anhydride (10 g, 35.44 mmol) was added over 5 min, and the resulting mixture was stirred for 30 min at −50 °C. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed consecutively with cold 2 N HCl (50 mL), satd aq $NaHCO_3$ (70 mL), and brine (100 mL). After drying over Na_2SO_4, filtration, and concentration, the residue was dissolved in THF (70 mL) containing TBAF (1 M in THF, 28 mL). The resulting mixture was stirred for 18 h at rt and concentrated to a residue, which was purified by silica gel column chromatography (10:1 hexanes–EtOAc) to give an anomeric mixture of **14** (2.3 g, 46%) as a syrup. For the α isomer: ^1H NMR ($CDCl_3$): δ 8.00 (d, 2 H, Ar), 7.60–7.44 (m, 3 H, Ar), 5.17 (dd, 1 H, $J_{2,3}$ 5.32, $J_{3,F}$ 56.17 Hz, H-3), 5.18 (d, 1 H, $J_{1,2}$ 3.56 Hz, H-1), 4.61 (d, 1 H, $J_{4,F}$ 23.63 Hz, H-4), 4.44 (d, 2 H, $J_{5,5'}$ 4.11 Hz, H-5), 3.43 (s, 3 H, CH_3O-1), 2.26–2.20 (m, 2 H, H-2); FABMS *m/z* 255 $(M+H)^+$. Anal. Calcd for $C_{13}H_{15}FO_4$: C, 61.41; H, 5.95. Found: C, 61.49; H, 5.94.

3′-Deoxy-3′-fluoro-β-L-thymidine (**1a**) *and 3′-deoxy-3′-fluoro-α-L-thymidine* (**1b**).—A mixture of thymine (726 mg, 5.75 mmol), $(NH_4)_2SO_4$ (60 mg), and HMDS (25 mL) was refluxed at 140 °C for 20 h. After removal of the solvent under reduced pressure, the resulting syrup was dissolved in anhyd CH_3CN (25 mL). To the solution of the silylated base in CH_3CN, compound **14** (585 mg, 2.30 mmol), followed by Me_3SiOTf (0.5 mL, 2.59 mmol), was added at rt. The resulting reaction mixture was stirred for 20 h, neutralized with satd aq $NaHCO_3$, diluted with EtOAc (100 mL), washed with water (30 mL), and dried over Na_2SO_4. The filtration, followed by concentration, gave a solid residue, which was dissolved in MeOH satd with NH_3 (30 mL), stirred at rt for 20 h, and concentrated. The resulting residue was separated by silica gel column chromatography (5:1–1:1 hexanes–EtOAc) to give compound **1a** (210 mg, 37%) and compound **1b** (158 mg, 28%) as white solids. Compound **1a**: mp 180–181 °C; $[\alpha]_D^{25}$ −2.51° (*c* 0.51, MeOH; lit. $[\alpha]_D^{20}$ 0.80° in MeOH for the D-enantiomer [11b]), −5.79° (*c* 0.39, H_2O); UV (H_2O) λ_{max} 265.5 nm (ε 12,120, pH 7),

266.0 nm (ε 10,020, pH 11), 265.5 nm (ε 11,390, pH 2); ^{1}H NMR (CD_3OD): δ 7.82 (s, 1 H, H-6), 6.30 (dd, 1 H, $J_{1,2'}$ 5.55, $J_{1,2''}$ 9.07 Hz, H-1′), 5.26 (dd, 1 H, $J_{2',3'}$ 4.65, $J_{3',F}$ 53.94 Hz, H-3′), 4.23 (d, 1 H, $J_{4',F}$ 27.52 Hz, H-4′), 3.77 (s, 2 H, H-5′), 2.50 (m, 1 H, H-2′), 2.35 (m, 1 H, H-2″), 1.88 (s, 3 H, CH_3-5); ^{13}C NMR (CD_3OD): δ 166.4, 152.4, 137.9, 111.9, 95.9 (d, *J* 175.4 Hz), 86.9 (d, *J* 23.7 Hz), 86.3, 62.7 (d, *J* 11.0 Hz), 39.1 (d, *J* 20.6 Hz), 12.5; FABMS *m/z* 245 $(M+H)^+$; Anal. Calcd for $C_{10}H_{13}FN_2O_4$: C, 49.18; H, 5.37; N, 11.47. Found: C, 49.18; H, 5.29; N, 11.40. Compound **1b**: mp 164–165 °C; $[\alpha]_D^{25}$ −2.17° (*c* 0.28, H_2O); UV (H_2O) λ_{max} 267.5 nm (ε 12,200, pH 7), 268.0 nm (ε 10,300, pH 11), 268.0 nm (ε 11,400, pH 2); ^{1}H NMR (CD_3OD): δ 7.48 (s, 1 H, H-6), 6.30 (d, 1 H, $J_{1',2'}$ 7.52 Hz, H-1′), 5.28 (dd, 1 H, $J_{2',3'}$ 5.23, $J_{3',F}$ 54.21 Hz, H-3′), 4.66 (dd, 1 H, $J_{4',5'}$ 4.05, $J_{4',F}$ 24.62 Hz, H-4′), 3.64 (m, 2 H, H-5′), 2.75 (m, 1 H, H-2′), 2.37 (m, 1 H, H-2″), 1.88 (s, 3 H, CH_3-5); ^{13}C NMR (CD_3OD): δ 166.0, 152.3, 137.5, 111.0, 95.7 (d, *J* 174.2 Hz), 89.3 (d, *J* 22.6 Hz), 88.2, 62.9 (d, *J* 11.3 Hz), 40.4 (d, *J* 20.1 Hz), 12.5; FABMS *m/z* 245 $(M+H)^+$; Anal. Calcd for $C_{10}H_{13}FN_2O_4$: C, 49.18; H, 5.37; N, 11.47. Found: C, 49.01; H, 5.36; N, 11.37.

*2′,3′-Dideoxy-3′-fluoro-β-*L*-cytidine* (**2a**) *and 2′,3′-dideoxy-3′-fluoro-α-*L*-cytidine* (**2b**). —The silylated cytosine was prepared from N^4-benzoylcytosine (778 mg, 3.62 mmol), as previously described, and dissolved in anhyd CH_3CN (20 mL). To the solution of the silylated base in CH_3CN, compound **14** (591 mg, 2.32 mmol), followed by Me_3SiOTf (0.5 mL, 2.59 mmol), was added at rt and the resulting mixture was stirred for 12 h and neutralized with satd aq $NaHCO_3$. After the same work-up previously described for compound **1**, the obtained residue was dissolved in MeOH satd with NH_3 (30 mL), stirred at rt for 20 h, and concentrated to a residue, which was separated by silica gel column chromatography (10:1–5:1 $CHCl_3$–MeOH) to give compound **2a** (190 mg, 36%) and compound **2b** (120 mg, 23%) as white solids. Compound **2a**: mp 190–192 °C; $[\alpha]_D^{25}$ −44.7° (*c* 0.30, H_2O); UV (H_2O) λ_{max} 269.5 nm (ε 12,050, pH 7), 270.0 nm (ε 12,370, pH 11), 278.0 nm (ε 18,080, pH 2); ^{1}H NMR (CD_3OD): δ 7.74 (d, 1 H, $J_{5,6}$ 7.58 Hz, H-6), 6.22 (dd, 1 H, $J_{1',2'}$ 5.63, J_1 8.77 Hz, H-1′), 5.86 (d, 1 H, $J_{5,6}$ 7.51 Hz, H-5), 5.22 (dd, 1 H, $J_{2',3'}$ 4.65, $J_{3',F}$ 53.21 Hz, H-3′), 4.32 (dt, 1 H, $J_{4',5'}$ 4.19, $J_{4',F}$ 27.21 Hz, H-4′), 3.70 (d, 2 H, $J_{5',5''}$ 4.25 Hz, H-5′), 2.61 (m, 1 H, H-2′), 2.21 (m, 1 H, H-2″); ^{13}C NMR (CD_3OD): δ 168.9, 158.4, 144.3, 111.5, 98.3 (d, *J* 173.7 Hz), 88.5, 88.2 (d, *J* 22.6 Hz), 64.3 (d, *J* 11.2 Hz), 41.2 (d, *J* 20.7 Hz); FABMS *m/z* 230 $(M+H)^+$; Anal. Calcd for $C_9H_{12}FN_3O_3$: C, 47.16; H, 5.28; N, 18.33. Found: C, 46.95; H, 5.20; N, 18.22. Compound **2b**: mp 186–188 °C; $[\alpha]_D^{25}$ +13.5° (*c* 0.27, MeOH); UV (H_2O) λ_{max} 270.5 nm (ε 12,010, pH 7), 271.0 nm (ε 12,360, pH 11), 277.0 nm (ε 18,000, pH 2); ^{1}H NMR (CD_3OD): δ 7.70 (d, 1 H, $J_{5,6}$ 7.57 Hz, H-6), 6.17 (d, 1 H, $J_{1',2'}$ 7.18 Hz, H-1′), 5.96 (d, 1 H, $J_{5,6}$ 7.51 Hz, H-5), 5.25 (dd, 1 H, $J_{2',3'}$ 7.18, $J_{3',F}$ 53.03 Hz, H-3′), 4.78 (partially obscured by the solvent peak, H-4′), 3.64 (m, 2 H, H-5′), 2.65 (m, 1 H, H-2′), 2.42 (dd, 1 H, $J_{2',2''}$ 15.93, $J_{2'',F}$ 23.49 Hz, H-2″); ^{13}C NMR (CD_3OD): δ 168.3, 158.3, 144.3, 111.0, 98.1 (d, *J* 172.8 Hz), 90.0, 89.9 (d, *J* 23.5 Hz), 64.5 (d, *J* 11.2 Hz), 42.1 (d, *J* 20.1 Hz); FABMS *m/z* 230 $(M+H)^+$; Anal. Calcd for $C_9H_{12}FN_3O_3$: C, 47.16; H, 5.28; N, 18.33. Found: C, 46.98; H, 5.25; N, 18.29.

*β-2′,3′-Dideoxy-3′-fluoro-*L*-uridine* (**3a**) *and α-2′,3′-dideoxy-3′-fluoro-*L*-uridine* (**3b**).—The silylated uracil was prepared from uracil (410 mg, 3.60 mmol), as previously described, and dissolved in anhyd CH_3CN (20 mL). To the solution of the silylated base in CH_3CN, compound **14** (582 mg, 2.29 mmol), followed by Me_3SiOTf (0.5 mL, 2.59 mmol), was added at rt and the resulting reaction mixture was stirred for 12 h and neutralized with satd $NaHCO_3$. After the same work-up previously described for compound **1**, the obtained residue was dissolved in MeOH satd with NH_3 (30 mL), stirred at rt for 20 h, and concentrated to a residue, which was separated by silica gel column chromatography (20:1 $CHCl_3$–MeOH) to give compound **3a** (120 mg, 23%) and compound **3b** (100 mg, 19%) as white solids. Compound **3a**: mp 190–192 °C; $[\alpha]_D^{25}$ −24.8° (*c* 0.36, H_2O); UV (H_2O) λ_{max}

260.5 nm (ε 11,950, pH 7), 260.5 nm (ε 8,560, pH 11), 260.5 nm (ε 12,940, pH 2); ^{1}H NMR (DMSO-d_6): δ 11.36 (s, 1 H, H-3), 7.74 (d, 1 H, $J_{5,6}$ 8.11 Hz, H-6), 6.18 (dd, 1 H, $J_{1',2'}$ 5.62, $J_{1',2''}$ 8.00 Hz, H-1′), 5.67 (d, 1 H, $J_{5,6}$ 8.09 Hz, H-5), 5.26 (dd, 1 H, $J_{2',3'}$ 4.32, $J_{3',F}$ 53.91 Hz, H-3′), 5.20 (t, 1 H, $J_{5',HO-5'}$ 5.09 Hz, HO-5′), 4.16 (dm, 1 H, $J_{4',F}$ 27.56 Hz, H-4′), 3.58 (dq, 2 H, $J_{4',5'}$ 3.46, $J_{4',5''}$ 4.40 Hz, $J_{5',5''}$ 11.90 Hz, H-5′), 2.44 (m, 1 H, H-2′), 2.25 (m, 1 H, H-2″); ^{13}C NMR (DMSO-d_6): δ 166.4, 153.9, 143.7, 105.7, 98.2 (d, *J* 173.0 Hz), 88.4 (d, *J* 22.6 Hz), 88.5, 64.5 (d, *J* 11.0 Hz), 40.7 (d, *J* 20.4 Hz); FABMS *m*/*z* 231 $(M+H)^+$; Anal. Calcd for $C_9H_{11}FN_2O_4$: C, 46.96; H, 4.82; N, 12.17. Found: C, 47.03; H, 4.88; N, 12.11. Compound **3b**: mp 184–186 °C; $[\alpha]_D^{25}$ +3.71° (*c* 0.40, H_2O); UV (H_2O) λ_{max} 262.5 nm (ε 12,010, pH 7), 262.5 nm (ε 12,360, pH 11), 262.0 nm (ε 12,930, pH 2); ^{1}H NMR (DMSO-d_6): δ 11.32 (s, 1 H, H-3), 7.45 (d, 1 H, $J_{5,6}$ 8.11 Hz, H-6), 6.14 (d, 1 H, $J_{1',2'}$ 6.81 Hz, H-1′), 5.64 (d, 1 H, $J_{5,6}$ 8.11 Hz, H-5), 5.30 (dd, 1 H, $J_{2',3'}$ 4.89, $J_{3',F}$ 54.16 Hz, H-3′), 5.08 (s, 1 H, HO-5′), 4.57 (dt, 1 H, $J_{4',5'}$ 4.47, $J_{4',F}$ 24.48 Hz, H-4′), 3.49 (dd, 1 H, $J_{4',5'}$ 3.56, $J_{5',5''}$ 11.73 Hz, H-5′), 3.40 (dd, 1 H, $J_{4',5''}$ 5.17, $J_{5',5''}$ 11.70 Hz, H-5″), 2.70 (dm, 1 H, $J_{2',F}$ 42.47 Hz, H-2′), 2.25 (dd, 1 H, $J_{2',2''}$ 15.79, $J_{2'',F}$ 24.39 Hz, H-2″); ^{13}C NMR (DMSO-d_6): δ 166.1, 153.7, 143.4, 105.6, 97.9 (d, *J* 172.6 Hz), 89.6 (d, *J* 22.2 Hz), 87.6, 64.3 (d, *J* 10.9 Hz), 40.8 (d, *J* 20.2 Hz); FABMS *m*/*z* 231 $(M+H)^+$; Anal. Calcd for $C_9H_{11}FN_2O_4$: C, 46.96; H, 4.82; N, 12.17. Found: C, 46.66; H, 4.87; N, 11.93.

*5-Chloro-2′,3′-dideoxy-3′-fluoro-β-*L*-uridine* (**4a**) *and 5-chloro-2′,3′-dideoxy-3′-fluoro-α-*L*-uridine* (**4b**).—The silylated 5-chlorouracil was prepared from 5-chlorouracil (691 mg, 4.72 mmol), as previously described, and dissolved in anhyd CH_3CN (30 mL). To the solution of the silylated base in CH_3CN, compound **14** (600 mg, 2.36 mmol), followed by Me_3SiOTf (0.5 mL, 2.59 mmol), was added at rt, and the resulting mixture was stirred for 10 h and neutralized with satd aq $NaHCO_3$. After the same work-up previously described for compound **1**, the obtained residue was separated by silica gel chromatography (1:1 cyclohexane–EtOAc) to give β and α isomers. The separated anomers were dissolved in MeOH satd with NH_3 (30 mL), and stirred at rt for 20 h. After concentration, the residues were purified by silica gel column chromatography (20:1 $CHCl_3$–MeOH) to give compound **4a** (100 mg, 16%) and compound **4b** (101 mg, 16%) as white solids. Compound **4a**: mp 186–188 °C; $[\alpha]_D^{25}$ −20.0° (*c* 0.23, H_2O); UV (H_2O) λ_{max} 275.0 nm (ε 8,810, pH 7), 273.5 nm (ε 6,230, pH 11), 275.5 nm (ε 8,910, pH 2); ^{1}H NMR (CD_3OD): δ 8.35 (s, 1 H, H-6), 6.29 (dd, 1 H, $J_{1',2'}$ 5.60, $J_{1',2''}$ 8.87 Hz, H-1′), 5.26 (dd, 1 H, $J_{2',3'}$ 4.77, $J_{3',F}$ 53.78 Hz, H-3′), 4.27 (dm, 1 H, $J_{4',F}$ 27.23 Hz, H-4′), 3.75 (d, 2 H, $J_{4',5'}$ 3.46 Hz, H-5′), 2.56 (m, 1 H, H-2′), 2.28 (dm, 1 H, $J_{2'',F}$ 39.36 Hz, H-2″); ^{13}C NMR (CD_3OD): δ 162.5, 150.1, 139.2, 111.0, 93.5 (d, *J* 174.1 Hz), 87.3 (d, *J* 24.8 Hz), 86.9, 62.5 (d, *J* 11.5 Hz), 40.7 (d, *J* 20.5 Hz); FABMS *m*/*z* 265 $(M+H)^+$; Anal. Calcd for $C_9H_{10}ClFN_2O_4$: C, 40.85; H, 3.81; N, 10.59. Found: C, 40.65; H, 3.79; N, 10.51. Compound **4b**: mp 174–178 °C; $[\alpha]_D^{25}$ +14.9° (*c* 0.38, H_2O); λ_{max} 275.0 nm (ε 8,700, pH 7), 274.0 nm (ε 6,080, pH 11), 275.5 nm (ε 8,610, pH 2); ^{1}H NMR (CD_3OD): δ 8.32 (s, 1 H, H-6), 6.24 (m, 1 H, H-1′), 5.29 (dd, 1 H, $J_{2',3'}$ 5.35, $J_{3',F}$ 54.05 Hz, H-3′), 4.69 (dm, 1 H, $J_{4',F}$ 27.23 Hz, H-4′), 3.88 (d, 2 H, $J_{4',5'}$ 3.40 Hz, H-5′), 2.61 (m, 1 H, H-2′), 2.27 (m, 1 H, H-2″); ^{13}C NMR (CD_3OD): δ 163.2, 150.7, 140.0, 111.3, 93.6 (d, *J* 173.0 Hz), 88.2 (d, *J* 25.7 Hz), 87.7, 63.2 (d, *J* 11.0 Hz), 41.2 (d, *J* 20.9); FABMS *m*/*z* 265 $(M+H)^+$; Anal. Calcd for $C_9H_{10}ClFN_2O_4$: C, 40.85; H, 3.81; N, 10.59. Found: C, 40.74; H, 3.77; N, 10.60.

*2′,3′-Dideoxy-3′-fluoro-β-*L*-adenosine* (**5a**) *and 2′,3′-dideoxy-3′-fluoro-α-*L*-adenosine* (**5b**).—The silylated 6-chloropurine was prepared from 6-chloropurine (608 mg, 3.94 mmol), as previously described, and dissolved in anhyd CH_3CN (20 mL). To the solution of the silylated base in CH_3CN, compound **14** (500 mg, 1.97 mmol), followed by Me_3SiOTf (0.46 mL, 2.38 mmol), was added at rt, and the resulting reaction mixture was stirred for 12 h and neutralized with satd aq $NaHCO_3$. After the same work-up previously described for compound **1**, the thus obtained residue was dissolved in MeOH satd with NH_3 (30 mL) and heated at 90 °C in a steel bomb for

18 h. After concentration, the resulting residue was separated by silica gel column chromatography (30:1 $CHCl_3$–MeOH) to give compound **5a** (80 mg, 16%) and compound **5b** (75 mg, 15%) as white solids. Compound **5a**: mp 196–198 °C; $[\alpha]_D^{25}$ +32.3° (*c* 0.47, H_2O); UV (H_2O) λ_{max} 259.0 nm (ε 16,370, pH 7), 259.0 nm (ε 16,180, pH 11), 257.0 nm (ε 15,930, pH 2); ^{1}H NMR (CD_3OD): δ 8.29 (s, 1 H, H-8), 8.16 (s, 1 H, H-2), 6.44 (dd, 1 H, $J_{1',2'}$ 5.61, $J_{1',2''}$ 9.39 Hz, H-1′), 5.41 (dd, 1 H, $J_{2',3'}$ 4.47, $J_{3',F}$ 53.56 Hz, H-3′), 4.16 (dt, 1 H, $J_{4',5'}$ 2.87, $J_{4',F}$ 27.39 Hz, H-4′), 3.82 (m, 2 H, H-5′), 2.95 (m, 1 H, H-2′), 2.69 (m, 1 H, H-2′); ^{13}C NMR (CD_3OD): δ 157.6, 153.5, 149.9, 141.7, 120.9, 96.4 (d, *J* 174.1 Hz), 87.9 (d, *J* 23.3 Hz), 87.4, 63.3 (d, *J* 11.2 Hz), 39.4 (d, *J* 20.9); FABMS *m*/*z* 254 $(M+H)^+$; Anal. Calcd for $C_{10}H_{12}FN_5O_2$: C, 47.43; H, 4.78; N, 27.66. Found: C, 47.35; H, 4.78; N, 27.57. Compound **5b**: mp 192–194 °C; $[\alpha]_D^{25}$ −63.9° (*c* 0.63, H_2O); UV (H_2O) λ_{max} 259.0 nm (ε 16,290, pH 7), 259.5 nm (ε 15,740, pH 11), 257.5 nm (ε 15,690, pH 2); ^{1}H NMR (CD_3OD): δ 8.21 (s, 1 H, H-8), 8.20 (s, 1 H, H-2), 6.54 (dd, 1 H, $J_{1',2'}$ 1.31, $J_{1',2''}$ 7.29 Hz, H-1′), 5.38 (dd, 1 H, $J_{2',3'}$ 5.27, $J_{3',F}$ 54.73 Hz, H-3′), 4.66 (dt, 1 H, $J_{4',5'}$ 3.72, $J_{4',F}$ 25.42 Hz, H-4′), 3.68 (m, 2 H, H-5′), 2.99–2.72 (m, 2 H, H-2′); ^{13}C NMR (CD_3OD): δ 157.5, 153.5, 150.1, 141.2, 120.1, 96.0 (d, *J* 175.4 Hz), 89.11 (d, *J* 23.0 Hz), 86.7, 62.7 (d, *J* 11.0 Hz), 40.3 (d, *J* 20.4 Hz); FABMS *m*/*z* 254 $(M+H)^+$; Anal. Calcd for $C_{10}H_{12}FN_5O_2$: C, 47.43; H, 4.78; N, 27.66. Found: C, 47.33; H, 4.84; N, 27.52.

*2′,3′-Dideoxy-3′-fluoro-β-*L*-inosine* (**6a**) *and 2′,3′-dideoxy-3′-fluoro-α-*L*-inosine* (**6b**).—The silylated 6-chloropurine was prepared from 6-chloropurine (608 mg, 3.93 mmol), as previously described, and dissolved in anhyd CH_3CN (20 mL). To the solution of the silylated base in CH_3CN, compound **14** (500 mg, 1.97 mmol), followed by Me_3SiOTf (0.46 mL, 2.38 mmol), was added at rt, and the resulting reaction mixture was stirred for 12 h and neutralized with satd aq $NaHCO_3$. After the same work-up previously described for compound **1**, the residue thus obtained was dissolved in MeOH (60 mL) to which 1 N NaOMe (3.3 mL) and 2-mercaptoethanol (0.3 mL) were added. The resulting mixture was refluxed for 6 h, neutralized with 0.1 N HCl, and filtered. The filtrate was concentrated to a residue, which was separated by silica gel column chromatography (10:1 $CHCl_3$–MeOH) to give compound **6a** (70 mg, 14%) and compound **6b** (70 mg, 14%) as white solids. Compound **6a**: mp 208–212 °C; $[\alpha]_D^{25}$ +34.0° (*c* 2.0, H_2O); UV (H_2O) λ_{max} 248.5 nm (ε 13,400, pH 7), 253.5 nm (ε 14,000, pH 11), 249.0 nm (ε 14,150, pH 2); ^{1}H NMR (D_2O): δ 8.21 (s, 1 H, H-8), 8.11 (s, 1 H, H-2), 6.43 (dd, 1 H, $J_{1',2'}$ 6.24, $J_{1',2''}$ 8.90 Hz, H-1′), 5.38 (dd, 1 H, $J_{2',3'}$ 4.91, $J_{3',F}$ 53.95 Hz, H-3′), 4.41 (dt, 1 H, $J_{4',5'}$ 4.03, $J_{4',F}$ 26.95 Hz, H-4′), 3.72 (m, 2 H, H-5′), 2.90–2.73 (m, 2 H, H-2′); ^{13}C NMR ($D_2O + CD_3OD$): δ 158.5, 148.5, 146.2, 140.4, 124.5, 95.3 (d, *J* 175.3), 86.1 (d, *J* 23.8), 85.3, 61.4 (d, *J* 11.1 Hz), 37.8 (d, *J* 21.3 Hz); FABMS *m*/*z* 255 $(M+H)^+$; Anal. Calcd for $C_{10}H_{11}FN_4O_3$: C, 47.25; H, 4.36; N, 22.04. Found: C, 47.15; H, 4.39; N, 21.90. Compound **6b**: mp 206–208 °C; $[\alpha]_D^{25}$ −98.1° (*c* 2.0, H_2O); UV (H_2O) λ_{max} 248.0 nm (ε 13,790, pH 7), 253.0 nm (ε 15,140, pH 11), 248.5 nm (ε 13,390, pH 2); ^{1}H NMR (D_2O): δ 8.18 (s, 1 H, H-8), 8.10 (s, 1 H, H-2), 6.40 (m, 1 H, H-1′), 5.34 (dm, 1 H, $J_{3',F}$ 53.67 Hz, H-3′), 4.63 (dt, 1 H, $J_{4',5'}$ 4.11, $J_{4',F}$ 26.19 Hz, H-4′), 3.63 (d, 2 H, $J_{4',5'}$ 4.28 Hz, H-5′), 2.93–2.70 (m, 2 H, H-2′); ^{13}C NMR ($D_2O + CD_3OD$): δ 158.8, 148.5, 146.1, 139.9, 124.3, 94.7 (d, *J* 174.3 Hz), 87.6 (d, *J* 23.5 Hz), 85.6, 61.1 (d, *J* 11.3 Hz), 38.6 (d, *J* 20.5 Hz); FABMS *m*/*z* 255 $(M+H)^+$; Anal. Calcd for $C_{10}H_{11}FN_4O_3 \cdot 0.3$ MeOH: C, 46.89; H, 4.36; N, 21.24. Found: C, 46.58; H, 4.58; N, 21.39.

*2′,3′-Dideoxy-3′-fluoro-β-*L*-guanosine* (**7a**) *and 2′,3′-dideoxy-3′-fluoro-α-*L*-guanosine* (**7b**).—The silylated 2-amino-6-chloropurine was prepared from 2-amino-6-chloropurine (700 mg, 4.13 mmol), as previously described, and dissolved in anhyd CH_3CN (20 mL). To the solution of the silylated base in CH_3CN, compound **14** (500 mg, 1.97 mmol), followed by Me_3SiOTf (0.5 mL, 2.59 mmol), was added at rt, and the resulting mixture was stirred at rt for 10 h and neutralized with satd aq $NaHCO_3$. After the same work-up previously described for compound **1**, the obtained residue was purified by silica gel column chromatography (40:1 $CHCl_3$–MeOH) to give a regioisomer as an anomeric mixture with λ_{max}

320 nm (700 mg, 91%) as a sole product. The purified residue was dissolved in CH_3CN (200 mL), refluxed for 18 h, and purified by silica gel column chromatography (40:1 $CHCl_3$–MeOH) to give the desired N^9-nucleoside, the 2-amino-6-chloropurine derivative with λ_{max} 309 nm (330 mg, 47%), which was dissolved in MeOH (60 mL) and treated with 1 N NaOMe (2.6 mL) and mercaptoethanol (0.2 mL). The resulting mixture was refluxed for 17 h, neutralized with 0.1 N HCl, and filtered. After concentration, the residue was separated by silica gel column chromatography (10:1–5:1 $CHCl_3$–MeOH) to give compound **7a** (70 mg, 13%) and compound **7b** (70 mg, 13%) as white solids. Compound **7a**: mp 220–222 °C; $[\alpha]_D^{25}$ + 50.5° (*c* 0.2, H_2O); UV (H_2O) λ_{max} 251.5 nm (ε 11,050, pH 7), 265.0 nm (ε 7,840, pH 11), 254.0 nm (ε 9,870, pH 2); ^1H NMR (D_2O): δ 7.87 (s, 1 H, H-8), 6.24 (dd, 1 H, $J_{1',2'}$ 5.77, $J_{1',2''}$ 9.41 Hz, H-1′), 5.34 (dd, 1 H, $J_{2',3'}$ 4.45, $J_{3',F}$ 53.00 Hz, H-3′), 4.34 (dt, 1 H, $J_{4',5'}$ 3.20, $J_{4',F}$ 26.65 Hz, H-4′), 3.70 (m, 2 H, H-5′), 2.85–2.60 (m, 2 H, H-2′); ^{13}C NMR (D_2O + CD_3OD): δ 152.5, 151.4, 145.1, 138.1, 118.5, 95.4 (d, *J* 174.9 Hz), 85.7 (d, *J* 23.5 Hz), 84.6, 61.4 (d, *J* 11.2 Hz), 37.2 (d, *J* 20.0 Hz); FABMS *m*/*z* 270 $(M + H)^+$; Anal. Calcd for $C_{10}H_{12}FN_5O_3 \cdot 0.65$ MeOH: C, 44.10; H, 5.07; N, 24.15. Found: C, 43.85; H, 4.68; N, 23.95. Compound **7b**: mp 198–202 °C; $[\alpha]_D^{25}$ − 83.5°(*c* 0.2, H_2O); UV (H_2O) λ_{max} 252.0 nm (ε 10,520, pH 7), 267.0 nm (ε 7,970, pH 11) 253.5 nm (ε 9,730, pH 2); ^1H NMR (D_2O): δ 7.85 (s, 1 H, H-8), 6.28 (dd, 1 H, $J_{1',2'}$ 2.21, $J_{2',3'}$ 6.67 Hz, H-1′), 5.32 (dd, 1 H, $J_{2',3'}$ 4.51, $J_{3',F}$ 55.38 Hz, H-3′), 4.57 (dt, 1 H, $J_{4',5'}$4.15, $J_{4',F}$ 25.50 Hz, H-4′), 3.61 (d, 2 H, $J_{4',5'}$ 4.23 Hz, H-5′), 2.87–2.67 (m, 2 H, H-2′); ^{13}C NMR (D_2O + CD_3OD): δ 153.0, 151.5, 141.9, 137.6, 117.4, 94.7 (d, *J* 173.7 Hz), 87.2 (d, *J* 23.4 Hz), 84.6, 61.1 (d, *J* 11.1 Hz), 38.2 (d, *J* 20.0 Hz); FABMS *m*/*z* 270 $(M + H)^+$; Anal. Calcd for $C_{10}H_{12}FN_5O_3 \cdot 0.5$ MeOH: C, 44.22; H, 4.95; N, 24.55. Found: C, 44.02; H, 4.62; N, 24.68.

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