Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 1589–1598

TETRAHEDRON: *ASYMMETRY*

# Synthesis of unsaturated fluoride containing D- and L-pyranosyl nucleosides

Kyeong Lee, Wen Zhou, Laura-Lee C. Kelley, Cory Momany and Chung K. Chu*

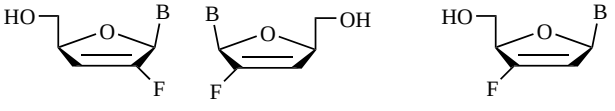
*Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, The University of Georgia, Athens, GA 30602, USA*

Received 28 January 2002; accepted 19 July 2002

**Abstract**—A series of fluorinated pyranosyl nucleosides in D- and L-configurations, **16**, **19**–**20**, **25**, **28**–**29**, have been synthesized. Starting from 1,2-*O*-isopropylidene-D-glyceraldehyde, homologated templates (3*S*)-**6** and (3*R*)-**6** were prepared by vinylation of fluoroenal **3**, which were transformed to give allylic alcohols, **8** and **21**, in three steps, respectively. The key intermediate triols **9** and **22** were obtained by *O*-benzoyl group migration from the primary hydroxyl group to the neighboring secondary hydroxyl group. Under basic conditions, ring closure reaction of **9** and **22** afforded unsaturated pyranosyl derivatives **10** and **23**, respectively, while under acidic conditions unsaturated furanosyl compounds **12** were formed. *N*-Glycosylation of the pyranosyl acetates with silylated bases under Vorbrüggen conditions then gave the protected nucleosides, which were converted to the free nucleosides. However, condensation of the unsaturated furanosyl intermediate **12** did not provide the desired nucleosides. Structural and stereochemical assignments of the synthesized compounds were based on the NOESY spectra of **16a** and **16b**, as well as the X-ray crystal structure of **19a**. 

## 1. Introduction

2′,3′-Dideoxy-(d2N) and 2′,3′-didehydro-2′,3′-dideoxy-nucleosides (d4N) have been a rich source of antiviral agents.[1–4] As part of our antiviral drug discovery program, we have recently reported the synthesis of L-2′-fluoro-2′,3′-unsaturated nucleosides (L-2′-F-d4Ns) and found that several compounds of this series displayed moderate to potent antiviral activities, including anti-HIV-1 (human immunodeficiency virus type 1) and anti-hepatitis B virus (HBV) activities in human peripheral blood mononuclear (PBM) cells and 2.2.15 cells, respectively (Fig. 1).[5–7] Among these, the adenine and hypoxanthine derivatives with D-configurations exhibited interesting anti-HIV-1 activity and showed favorable cross-resistance profiles with respect to the 3TC (2′,3′-dideoxy-3′-thiacytidine or lamivudine) resistant viral isolates.[7] Furthermore, the cytosine and 5-fluorocytosine derivatives from the L-series displayed potent anti-HBV activity.[8]




D-β-2'-F-d4N (B = pyrimidines, and purines)

L-β-2'-F-d4N

D-β-3'-F-d4N (B = T, C, and A)

**Figure 1.** Fluorinated 2′,3′-unsaturated nucleosides.

In view of these interesting biological results, it was of interest to introduce a fluoro atom at the 3′ position of 2′,3′-didehydro-2′,3′-dideoxy nucleosides and to study the structure–activity relationships (SAR) of this class of compounds. So far, three 3′-fluoride containing d4Ns, including cytosine, thymine and adenine derivatives with D-configuration, have been synthesized and reported to be active against HIV-1 (Fig. 1).[8,9] Herein, we wish to report the synthetic approaches of 3′-fluoride-containing pyranosyl nucleosides in D- and L-configurations.

## 2. Results and discussion

1,2-*O*-Isopropylidene-D-glyceraldehyde **1** was reacted with diethyl α-fluorophosphonoacetate to give a mixture of fluoroesters in a 9:1 ratio in favor of the (*E*)-isomer (Scheme 1).[5,6] Treatment of **2** with 1 M DIBAL-H/hexanes gave α,β-unsaturated aldehydes **3**

* Corresponding author. Tel.: (706) 542-5379; fax: (706) 542-5381; e-mail: dchu@rx.uga.edu

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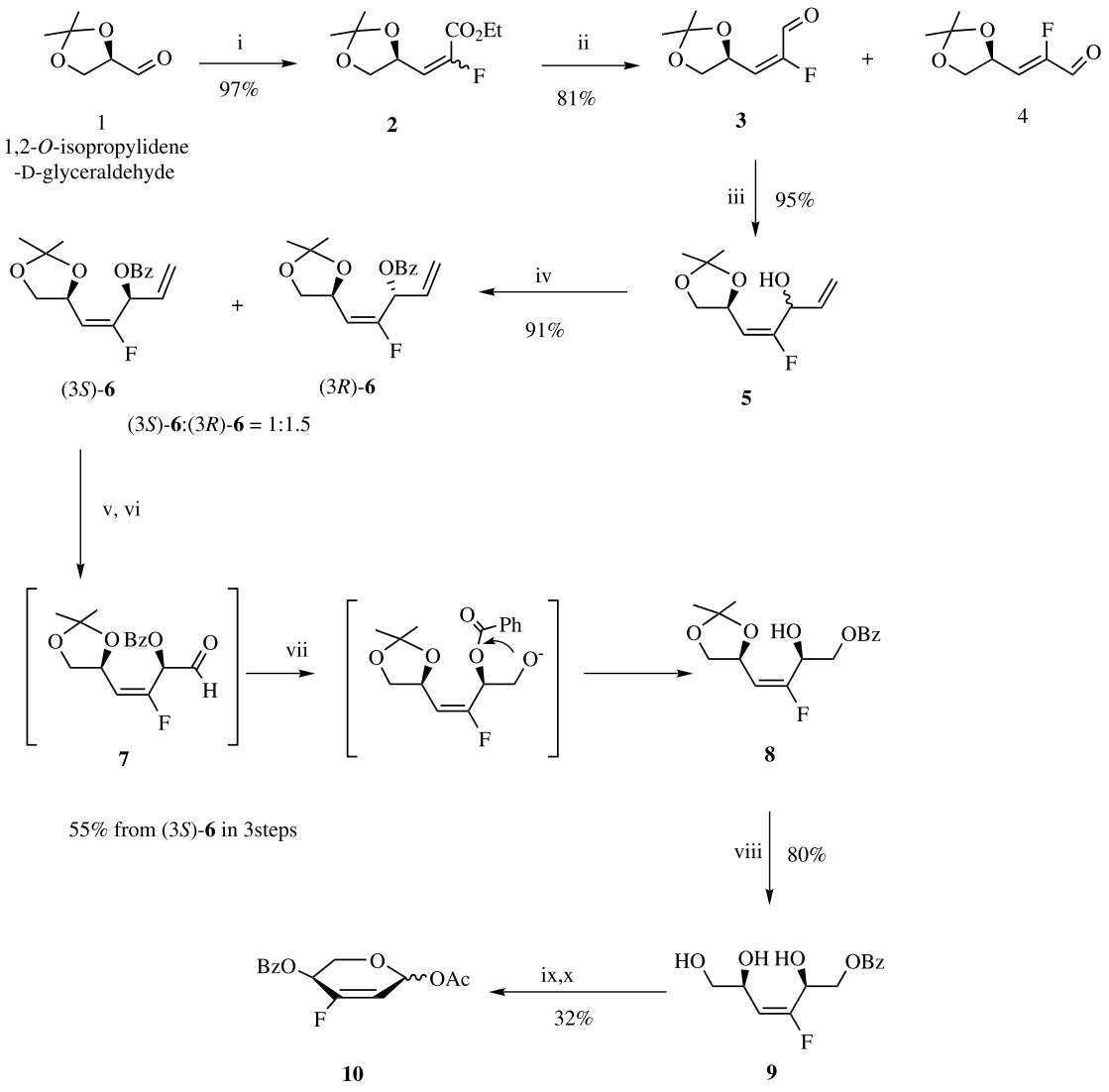
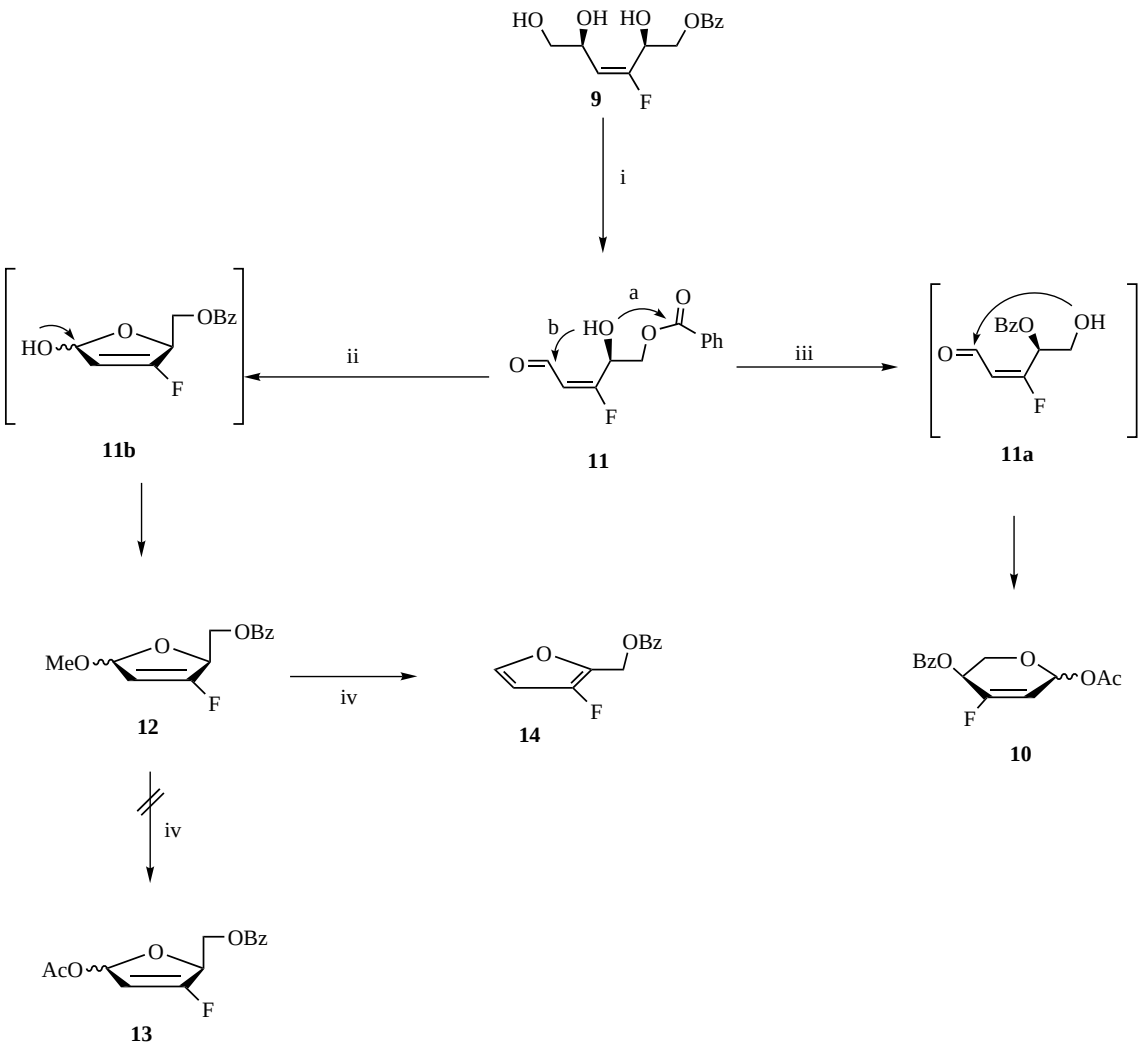
PII: S0957-4166(02)00438-X




**Scheme 1.** *Reagents and conditions*: (i) $(EtO)_2P(O)CHFCO_2Et$, NaHMDS, THF, −78°C; (ii) DIBAL-H in hexanes, ether, −78°C; (iii) vinylmagnesium bromide, THF, −78°C; (iv) BzCl, pyr., $CH_2Cl_2$, 0°C; (v) cat. $OsO_4$, NMO, acetone, water; (vi) $NaIO_4$, EtOH, $H_2O$; (vii) $NaBH_4$, 0°C; (viii) conc. HCl, EtOH; (ix) $NaIO_4$, aq. EtOH; (x) $Ac_2O$, pyr.

and **4** in good yield and the resulting (*E*)- and (*Z*)-isomers were separated by flash silica gel column chromatography (12.5% EtOAc/hexanes). Reaction of compound **3** with vinylmagnesium bromide in THF at −78°C, followed by benzoyl protection of the resulting alcohols gave (3*S*)-**6** and (3*R*)-**6** in a ratio of 1:1.5, which were separated by chromatography over silica gel (6.5% EtOAc/hexanes). The homologated template **8** was successfully obtained from the diene (3*S*)-**6** in three steps, including oxidative cleavage of vinyl group, followed by reduction in 54% yield. First, (3*S*)-**6** was treated with a catalytic amount of osmium tetroxide and a stoichiometric amount of the secondary oxidant 4-methylmorpholine *N*-oxide (NMO) in aqueous acetone to generate a vicinal diol.[10,11] *cis*-Hydroxylation occurred selectively from the less hindered face of the double bond. The diol was then immediately treated with sodium periodate, followed by usual work-up to give an aldehyde,[7] which underwent reduction and benzoyl group migration in the presence of sodium borohydride to provide the secondary allylic alcohol **8**. A doublet signal for the secondary hydroxyl group in **8** was detected by proton NMR.

With **8** in hand, it was expected that deprotection of the acetonide group followed by oxidative cyclization and subsequent acetylation would give to the necessary sugar moiety **13** (Scheme 2). However, under the reaction conditions, the intermediate **11** isomerized to **11a** by *O*-acyl group migration, which leads to the thermodynamically more stable six-membered ring intermediates **10** (path a), rather than the five-membered ring intermediate **12** (path b) as illustrated in Scheme 2.[12] This unexpected result was later confirmed at the final stage by NMR spectrum, as well as by X-ray crystallography (Fig. 3). Due to the unique structure of vinyl fluoride-containing pyranose **10**, it was of interest to synthesize 3′-fluorinated pyranosyl L-nucleoside series. Treatment of the triol **9** with sodium periodate led to an equilibrium mixture, and subsequent treatment with

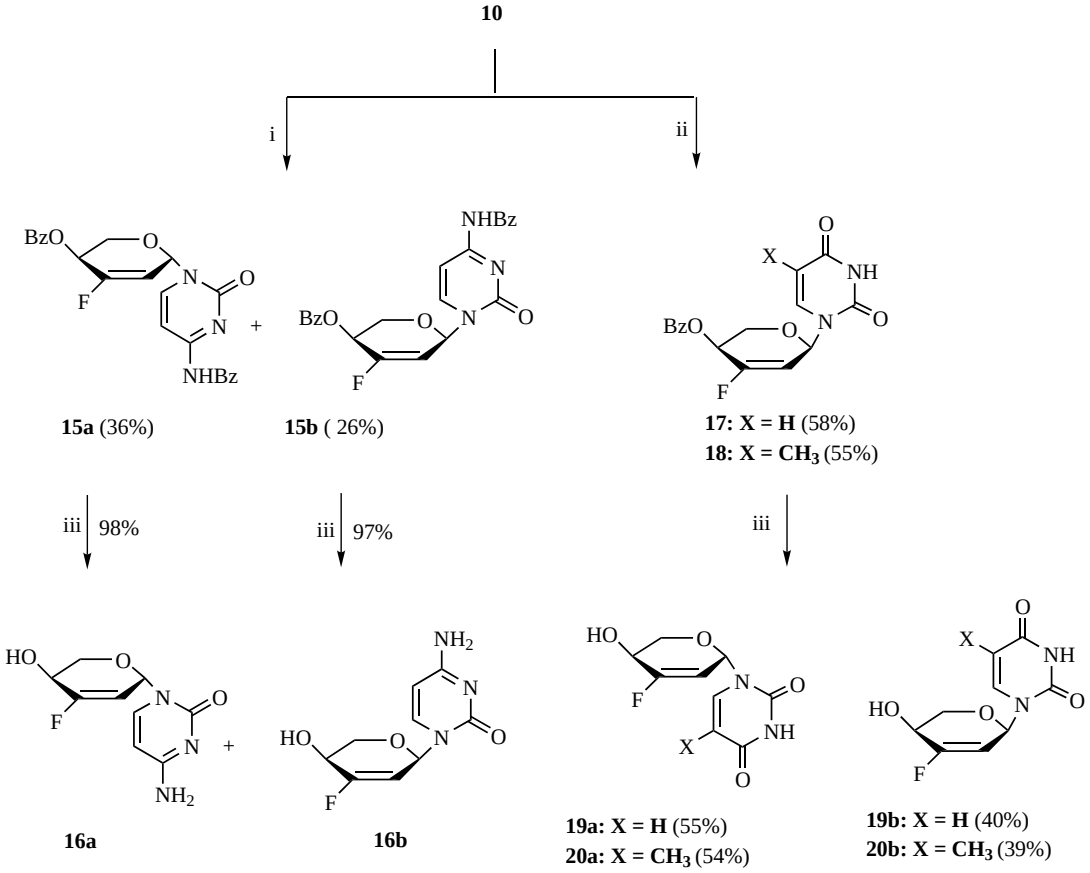



**Scheme 2.** *Reagents and conditions*: (i) $NaIO_4$, EtOH, $H_2O$; (ii) PPTS, MeOH, reflux; (iii) $Ac_2O$, Pyr, rt; (iv) conc. $H_2SO_4$, $AcOH/Ac_2O$.

pyridine and acetic anhydride gave **10** as a major product (30–32% from **9** in two steps) (Scheme 1). The use of lead acetate as an oxidant gave similar yields.

We then considered the cyclization of **11** under acidic conditions. As shown in Scheme 2, the triol **9** was oxidized with sodium periodate, followed by treatment with pyridinium *p*-toluene sulfonate in refluxing methanol to afford the desired five-membered ring intermediate **12** (path b). However, the conversion of **12** to furanosyl acetate **13** failed under various acidic conditions. Instead, these reactions resulted in the formation of 2-benzyloxymethyl-3-fluorofuran derivative **14**. Furthermore, coupling of **12** with various bases under the Vorbrüggen conditions only yielded 2-benzyloxymethyl-3-flurofuran **14** instead of furanosyl nucleosides, even at very low temperature (−30 to −40°C).[13] It is conceivable that, because the H-4′ proton of **12** is an allylic proton and is relatively acidic, the 3′-fluorine substituent may destabilize the C-1′ cation to give the thermodynamically more stable product **14**.

As shown in Scheme 3, coupling of the acetate **10** with bis-(trimethylsilyl)-$N^4$-benzoylcytosine under Vorbrüggen conditions gave an anomeric mixture of the protected nucleosides **15a** ((6*S*)-isomer) and **15b** ((6*R*)-isomer) in a ratio of 1.4:1 which was separated on silica gel (50% EtOAc/hexanes). Ammonolysis of each isomer produced the D-cytidine analogues **16a** and **16b**. The protected thymine or uracil congeners **17** and **18** were prepared by condensation of **10** with trimethylsilylthymine or uracil in the presence of TMSOTf as Lewis acid (54.7–57.7%). After debenzoylation using saturated methanolic ammonia and chromatographic separation (6.25% EtOAc/hexanes), the free nucleoside analogues **19**–**20** were obtained in good yields. Analogously, intermediate **21** was also prepared from (3*R*)-**6** and used for *N*-glycosylations with various silylated heterocycles to produce the corresponding L-analogues, **25**, **28** and **29** (Scheme 4). All of the spectral properties of the L-nucleosides were in agreement with those of their corresponding D-counterparts.




**Scheme 3.** *Reagents and conditions*: (i) silylated $N^4$-Bz-cytosine, TMSOTf, DCE; (ii) silylated uracil or thymine, TMSOTf, DCE (iii) $NH_3$/MeOH.

The structural and stereochemical assignments for the final nucleosides were based on the NMR spectrum and confirmed by X-ray crystallographic analysis (Fig. 3). Based on the respective $^1$H NMR spectrum of the free nucleosides, which showed a doublet signal for the hydroxyl group instead of a triplet signal in DMSO-$d_6$, it was assigned as a secondary hydroxyl group rather than a primary hydroxyl group in the pyranose sugar moiety **10**. Assignments of the anomeric configurations of the final nucleosides were based on 2D NOESY experiments on **16a** and **16b** (Fig. 2). A correlation between H-4′ and H-1′ was observed for **16b**, whereas no such cross peak existed in **16a**. Instead, a correlation between the 4′-OH and Hb-5′ protons was observed in **16a**. These assignments as well as the D- and L-configurations were finally confirmed by X ray crystallographic analysis of **19a** (Fig. 3).[14]

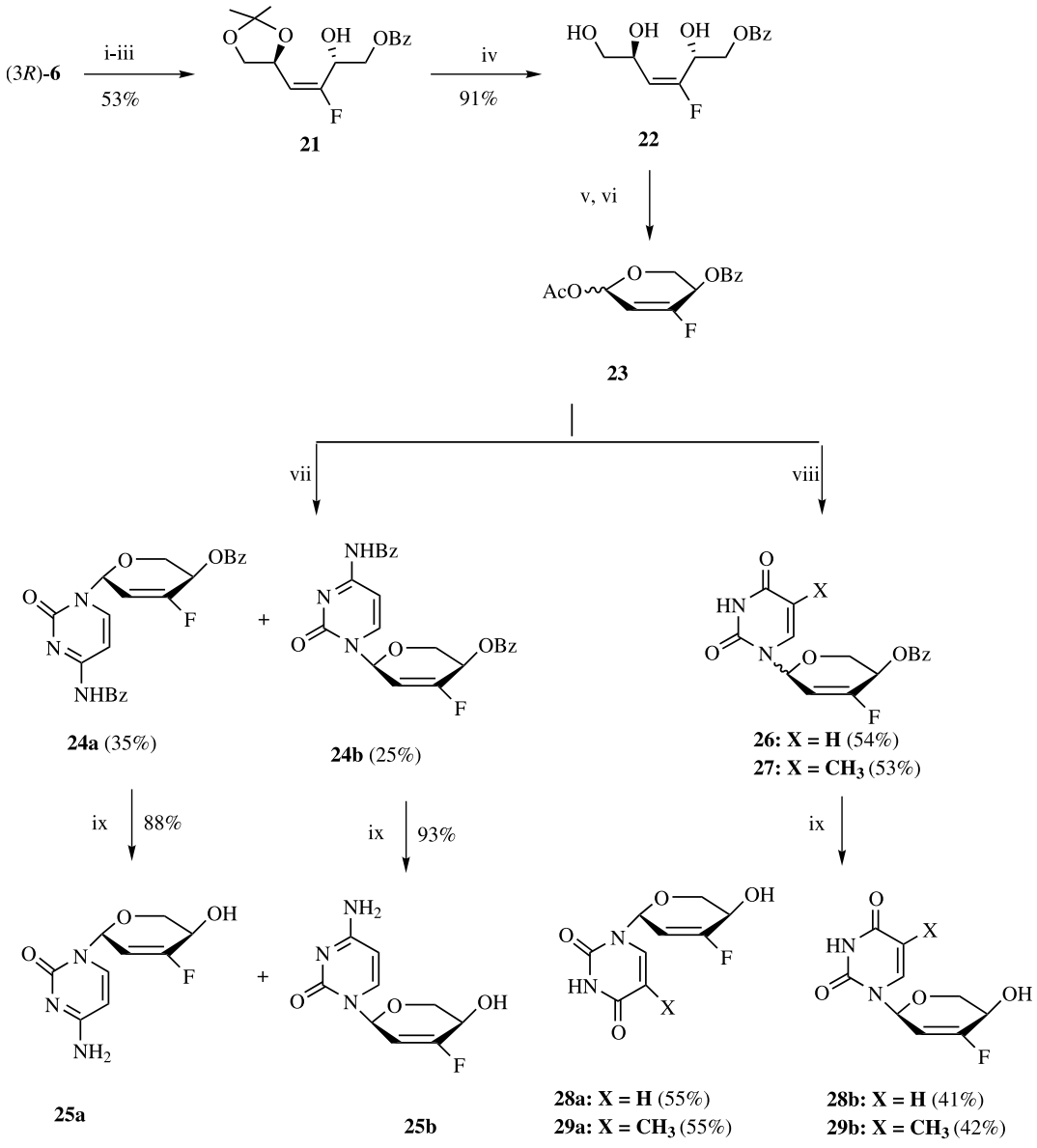
In summary, novel D- and L-series of 3′-fluoro substituted pyranosyl nucleosides were synthesized by utilizing the homologated alcohols **8** and **21** as chiral templates. The homologated alcohols were prepared via 1,2-addition of vinyl group to fluoroenal intermediate **3** starting from 1,2-*O*-isopropylidene-D-glyceraldehyde. The synthesized nucleosides were evaluated against HIV-1 in human peripheral blood mononuclear cells. However, no significant antiviral activity was detected.

## 3. Experimental

Melting points were determined on a Mel-temp II laboratory device and are uncorrected. NMR spectra were recorded on a Bruker AMX400 MHz spectrometers with tetramethylsilane as the internal reference; chemical shifts ($\delta$) are reported in parts per million (ppm), and the signals are described as s (singlet), d (doublet), t (triplet), q (quartet), br s (broad singlet), dm (doublet of multiplet) and m (multiplet). UV spectra were obtained on a Beckman DU 650 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. All reactions were monitored using thin-layer chromatography on Analtech, 200 mm silica gel GF plates.

### 3.1. (*E*)/(*Z*)-Ethyl-3-[(*S*)-2,2-dimethyl-(1,3)-dioxolan-4-yl]-2-fluoroacrylate, 2

A solution of triethyl 2-fluorophosphonoacetate (39.2 g, 162 mmol) in THF (70 mL) was cooled to −78°C and sodium bis(trimethylsilyl)amide (1.0 M solution in THF, 162 mL, 162 mmol) was added dropwise. The mixture was kept for 30 min at −78°C, then a solution of D-(*R*)-glyceraldehyde acetonide[15] (19.14 g, 147 mmol) in THF (70 mL) was added. After being stirred for 1 h at −78°C, the reaction mixture was treated with aqueous $NH_4Cl$ and extracted with ether. The ether




**Scheme 4.** *Reagents and conditions*: (i) cat. $OsO_4$, NMO, acetone, water; (ii) $NaIO_4$, EtOH, $H_2O$; (iii) $NaBH_4$, 0°C; (iv) conc. HCl, EtOH; (v) $NaIO_4$, aq. EtOH; (vi) $Ac_2O$, pyr.; (vii) silylated $N^4$-Bz-cytosine, TMSOTf, DCE; (viii) silylated uracil or thymine; (ix) $NH_3$/MeOH.

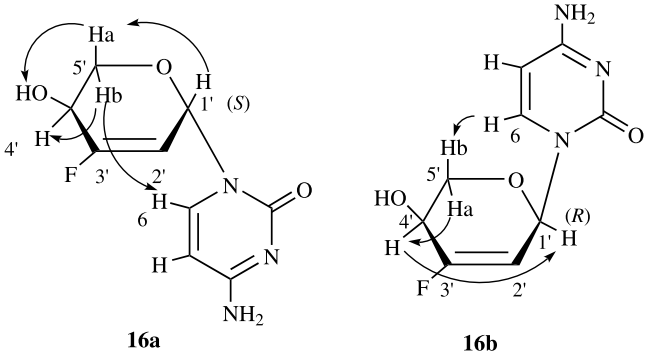



**Figure 2.** NOE correlations from NOESY spectra of **16a** and **16b**.

phase was washed with saturated NaCl, dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel to give a (*E*) and (*Z*) mixture **2** (9:1 by $^1H$ NMR) as yellowish oil (34.6 g, 97.9%): $^1H$ NMR ($CDCl_3$) $\delta$ 1.34, 1.36 (2 t, $J=8$ Hz, 3H), 1.40, 1.45 (2s, 6H), 3.69 (m, 1H), 4.28 (m, 3H), 5.02 (m, 1H), 5.40 (m, 1H), 6.02 (dd, $J=8$, 20 Hz, 1H), 6.18 (dd, $J=8$, 32 Hz, 1H).

### 3.2. (*E*)-3-[(*S*)-2,2-Dimethyl-(1,3)-dioxolan-4-yl]-2-fluoro-propenal, 3

A solution of **2** (22.58 g, 103.48 mmol) in ether (100 mL) was cooled to −78°C and DIBAL-H (1.0 M solution in hexanes, 140 mL, 140 mmol) was added drop-

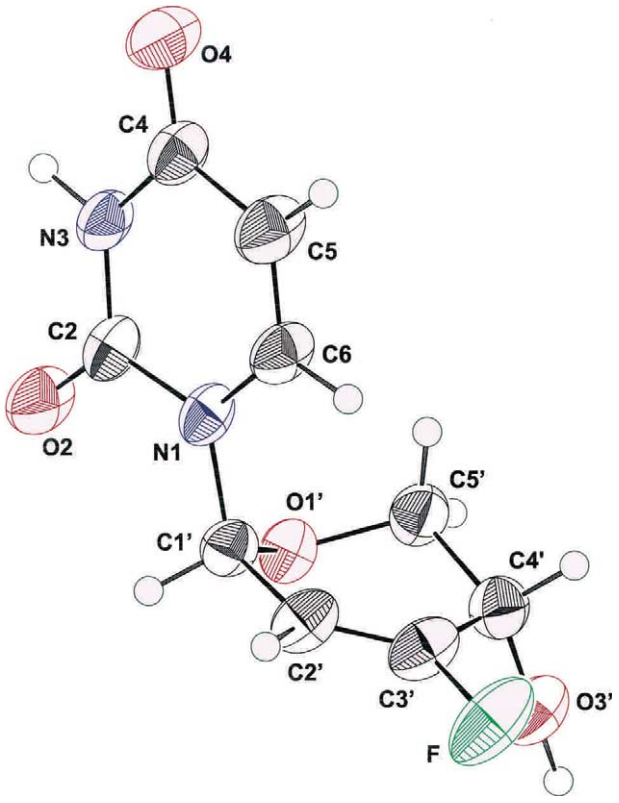



**Figure 3.** ORTEP drawing of the X-ray crystallographic structure (+)-1-[(1*S*,4*S*)-3-fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]uracil **19a**.

wise under nitrogen. The mixture was stirred for 1.5 h at −78°C, and the cold mixture was treated with dilute nitric acid, washed with water. The combined organic layer was dried ($Na_2SO_4$), filtered, and concentrated to dryness. The residue was chromatographed on silica gel to isolate **3** as yellowish oil (14.5 g, 81%): $^1$H NMR ($CDCl_3$) $\delta$ 1.419, 1.461 (2s, 6H), 3.71 (dd, $J$=8.4, 6.4 Hz, 1H), 4.29 (dd, $J$=8.4, 6.8 Hz, 1H), 5.25 (ps dd, $J$=14.4, 6.8 Hz, 1H), 6.11 (dd, $J$=17.4, 8 Hz, 1H), 8.96 (d, $J$=11.6 Hz, 1H).

### 3.3. (*E*)-1-[(*S*)-2,2-Dimethyl-(1,3)-dioxolan-4-yl]-2-fluoropenta-1,4-diene-3-ol, 5

Vinyl magnesium bromide (1 M in THF) was dissolved in THF (45 mL) under nitrogen, the mixture was then cooled to −78°C and treated with a solution of the enal **3** (13.01 g, 74.0 mmol) in THF. The resulting mixture was stirred for 1 h at −78°C. The cold mixture was treated with dilute nitric acid, washed with water, and dried ($Na_2SO_4$). Evaporation of the solvent and purification on silica gel (20% EtOAc/hexanes) gave a diastereomeric mixture **5** as pale yellowish oil (14.28 g, 95.4%), which was used as such for the next step: $^1$H NMR ($CDCl_3$) $\delta$ 1.395, 1.427 (2 s, 6H), 4.13 (m, 2H), 4.83 (m, 1H), 5.02 (m, 1H), 5.23–5.47 (m, 3H), 5.98 (m, 1H). Anal. calcd for $C_{10}H_{15}FO_3 \cdot 0.1H_2O$: C, 58.87; H, 7.51. Found: C, 58.93; H, 7.43%.

### 3.4. (+)-(*E*)-(4*S*)-4-[(3*S*)-*O*-Benzoyl-2-fluoro-1,4-dienyl]-2,2-dimethyl-(1,3)-dioxolane, (3*S*)-6 and its (−)-(3*R*)-isomer, (3*R*)-6

To a solution of alcohols **5** (18.81 g, 93.01 mmol) in $CH_2Cl_2$ (200 mL) was added pyridine (22.5 mL, 279 mmol) and benzoyl chloride (13.5 mL, 116.27 mmol) at 0°C, and the resulting mixture was stirred for 1 h at 0°C. After completion of the reaction, ice was added to the reaction mixture and stirred for 30 min at rt. The resulting mixture was concentrated under vacuo, washed with dilute HCl, satd $NaHCO_3$ and brine. The combined organic layer was dried and concentrated to dryness, which was purified by column chromatography (6.5% EtOAc/hexanes) to give (3*S*)-**6** (10.43 g) and (3*R*)-**6** (15.64 g) as yellowish oils in 91.49% yield [(3*S*)-**6**:(3*R*)-**6** = 1:1.5].

(3*S*)-**6**: $[\alpha]_D^{27}$ +9.0 (*c* 0.7, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.427, 1.407 (2s, 6H), 3.61, 4.09 (m, 2H), 4.94 (m, 1H), 4.34–5.53 (m, 3H), 6.03 (m, 1H), 6.24–6.32 (m, 1H), 7.44–8.09 (m, 5H). Anal. calcd for $C_{17}H_{19}FO_3 \cdot 0.7H_2O$: C, 67.40; H, 6.79. Found: C, 67.09; H, 6.32%.

(3*R*)-**6**: $[\alpha]_D^{27}$ −17.61 (*c* 0.6, $CHCl_3$); $^1$H NMR ($CDCl_3$) $\delta$ 1.408, 1.432 (2s, 6H), 3.61 (dd, $J$=8.4, 6.8 Hz, 1H), 4.23 (dd, $J$=8.4, 6 Hz, 1H), 5.02 (m, 1H), 5.41 (m, 2H, H-5a, 1H), 5.60 (m, 1H), 6.06 (m, 1H), 6.27–6.36 (m, 1H), 7.44–8.18 (m, 5H). Anal. calcd for $C_{17}H_{19}FO_3$: C, 66.65; H, 6.25. Found: C, 66.82, H, 6.40%.

### 3.5. (−)-(*E*)-(4*S*)-4-[(*S*)-2,2-Dimethyl-(1,3)-dioxolan-4-yl]-1-*O*-benzoyl-3-fluorobut-3-en-2-ol, 8

To a solution of compound (3*S*)-**6** (8.94 g, 29.18 mmol) in acetone (340 mL) at room temperature was added a stock osmylation solution (295 mL of solution consisting of 4-methylmorpholine *N*-oxide (77.5 g) and osmium tetroxide (1.9 g) in water (567 mL)). The resulting mixture was stirred at room temperature for 1 h. The reaction mixture was then concentrated to the half of its original volume, the resulting solution was dissolved in EtOAc, and washed with satd sodium bisulfite solution and brine. The organic phase was dried, filtered, and concentrated to give crude diol, which was used without further purification.

To a solution of the diol in ethanol (170 mL) was added sodium periodate (6.99 g, 32.69 mmol) in water (130 mL) portionwise. The resulting solution was stirred at room temperature for 45 min. After the completion of the reaction as shown by TLC analysis, the mixture was cooled to 4°C and was treated with sodium borohydride (4.42 g, 116.74 mmol). The reaction mixture was stirred for 30 min, and then neutralized with glacial acetic acid to pH 7. Removal of ethanol and standard work-up gave an oil, which was purified on silica gel (ethyl acetate/hexanes 1:3) to yield benzoyl group-migrated alcohol **8** [4.97 g, 54.9% from (3*S*)-**6**]: $[\alpha]_D^{27}$ −7.3 (*c* 0.19, $CHCl_3$); $^1$H NMR (DMSO-$d_6$) $\delta$ 1.276, 1.310 (2 s, 6H), 3.39 (ps t, $J$=7.6 Hz, 1H), 3.85 (dd, $J$=7.6, 6.4 Hz, 1H), 4.94 (m, 2H), 4.84 (m, 2H), 5.29 (dd, $J$=20.4, 9.2 Hz, 1H), 5.97 (d, $J$=5.2 Hz, $D_2O$ exchangeable, 1H), 7.53–7.97 (m, 5H). Anal. calcd for $C_{16}H_{19}FO_5$: C, 61.93; H, 6.17. Found: C, 61.82; H, 6.28%.

### 3.6. (−)-(*E*)-(2*S*,5*S*)-6-*O*-Benzoyl-4-fluorohex-3-ene-1,2,5-triol, 9

A solution of **8** (3.806 g, 12.265 mmol) in ethanol was treated with diluted hydrochloric acid in ethanol (3.1 mL conc. HCl/50 mL EtOH) at 0°C and the resulting solution was stirred at room temperature for 3 h. After concentration and coevaporation, the resulting residue was purified on silica gel (4% $MeOH/CH_2Cl_2$) to give triol **9** (2.65 g, 80%): $[\alpha]_D^{25}$ −6.6 (*c* 1.45, MeOH); $^1H$ NMR (DMSO-$d_6$) $\delta$ 4.23 (m, 4H), 4.68 (t, $J=2$ Hz, $D_2O$ exchangeable, 1H), 4.80 (m, 1H), 4.95 (d, $J=4.8$ Hz, $D_2O$ exchangeable, 1H), 5.17 (dd, $J=22$, 8.8 Hz, 1H), 5.77 (t, $J=4.4$ Hz, $D_2O$ exchangeable, 1H), 7.51–8.00 (m, 5H). Anal. calcd for $C_{13}H_{15}FO_5 \cdot 0.5H_2O$: C, 55.91; H, 5.77. Found: C, 55.78; H, 5.75%.

### 3.7. (4*S*)-4-*O*-Benzoyl-3-fluoro-1-*O*-acetyl-2,5-dihydro-2*H*-pyrane, 10

A suspension of sodium periodate (1.21 g, 4.74 mmol) in water (10 mL) was added dropwise to the solution of triol **9** (1.22 g, 5.68 mmol) in ethanol (50 mL) at 0°C, and the resulting solution was stirred for 1 h at room temperature. The reaction mixture was filtered and the filtrate was concentrated. The residue was then extracted with EtOAc, and the combined organic layer was dried, filtered (anhydrous $MgSO_4$), and concentrated to give crude intermediate, which was used as such for the next step.

Acetic anhydride (1.78 mL, 18.96 mmol) was added to a solution of lactols **11** in pyridine (25 mL) at 0°C and the resulting mixture was stirred for 4 h at rt. The reaction mixture was concentrated in vacuo and purified by silica gel column chromatography (8% EtOAc/hexanes) to give acetates **10** (426 mg, 32.1% from **9**) as yellowish oil: $^1H$ NMR ($CDCl_3$) $\delta$ 2.12, 2.15 (s, 3H), 4.15, 4.34 (m, 2H), 5.54, 5.62 (m, 1H), 5.70, 5.82 (m, 1H), 6.43, 6.57 (m, 1H), 7.44, 8.09 (m, 5H). Anal. calcd for $C_{14}H_{13}FO_5$: C, 60.00; H, 4.68. Found: C, 60.72; H, 5.01%.

### 3.8. 1-Methoxy-4-benzoxymethyl-3-fluoro-2-buten-4-olide, 13

To a solution of lactols **11** in dry methanol was added PPTS. The resulting mixture was stirred and heated under reflux for 1 h. After removal of solvent, the residue was purified by silica gel column chromatography (5% EtOAc/hexanes) to give anomeric mixture **13** as a colorless solid (70% from **9**). $^1H$ NMR ($CDCl_3$) $\delta$ 3.36, 3.42 (s, 3H), 4.39, 4.64 (m, 2H), 4.83, 5.07 (m, 1H), 5.33 (s, 1H), 5.65, 5.77 (m, 1H), 7.43 (m, 2H), 7.55 (m, 1H), 8.03, 8.10 (d, 2H). Anal. calcd for $C_{13}H_{13}FO_4$: C, 61.90; H, 5.19. Found: C, 62.04, H, 5.27%.

### 3.9. 2-Benzoxymethyl-3-fluorofuran, 14

To a solution of **13** (400 mg) acetic acid (4 mL), acetic anhydride (1 mL) was added dropwise conc. Sulphuric acid (0.1 mL) at 4°C. The reaction mixture was stirred for 5 min and then neutralized by addition of $NaHCO_3$. After standard work up, the residue was purified by silica gel column chromatography (5% EtOAc/hexanes) to give a colorless oil of **14**. $^1H$ NMR ($CDCl_3$) $\delta$ 5.06 (s, 2H), 6.31 (d, $J=9.5$ Hz, 1H)), 7.24 (m, 1H), 7.45 (m, 2H), 7.56 (m, 1H), 8.08 (d, 2H). MS (FAB): 220 ($M^+$).

### 3.10. (−)-(*E*)-(4*R*)-4-[(*S*)-2,2-Dimethyl-(1,3)-dioxolan-4-yl]-1-*O*-benzoyl-3-fluoro-but-3-en 2-ol, 21

The titled compound (4.50 g) was prepared from (3*R*)-**6** (8.33 g, 27.19 mmol) by similar method for the preparation of **8** in 53.3% yield (three steps): $[\alpha]_D^{27}$ −9.1 (*c* 0.68, $CHCl_3$); $^1H$ NMR (DMSO-$d_6$) $\delta$ 1.329, 1.369 (2 s, 6H), 3.39 (ps t, $J=8$ Hz, 1H), 3.85 (dd, $J=8$, 6.4 Hz, 1H), 4.31 (m, 2H′), 4.84 (m, 2H), 5.29 (dd, $J=20.8$, 9.2 Hz, 1H), 5.97 (d, $J=5.2$ Hz, $D_2O$ exchangeable, 1H), 7.52–7.98 (m, 5H). Anal. calcd for $C_{16}H_{19}FO_5 \cdot 0.2H_2O$: C, 61.22; H, 6.23. Found: C, 61.16, H, 6.28%.

### 3.11. (−)-(*E*)-(2*S*,5*R*)-6-*O*-Benzoyl-4-fluoro-hex-3-ene-1,2,5-triol, 22

The titled compound (3.12 g) was prepared from **21** (3.957 g, 12.751 mmol) by similar method for the preparation of **9** in 90.5%: $[\alpha]_D^{25}$ −4.3 (*c* 1.23, MeOH); $^1H$ NMR (DMSO-$d_6$) $\delta$ 4.30 (m, 4H), 4.70 (m, $D_2O$ exchangeable, 1H), 4.83 (m, 1H), 4.90 (m, $D_2O$ exchangeable, 1H), 5.22 (dd, $J=22.4$, 8.8 Hz, 1H), 8.00 (m, $D_2O$ exchangeable, 1H), 7.51–8.00 (m, 5H). Anal. calcd for $C_{13}H_{15}FO_5 \cdot 0.5H_2O$: C, 55.91; H, 5.77. Found: C, 55.71; H, 5.84%.

### 3.12. (3*R*)-3-*O*-Benzoyl-4-fluoro-6-acetoxy-3, 6-dihydro-2*H*-pyrane, 23

The title compound (465 mg) was prepared from **22** (1.51 g, 5.59 mmol) by similar method for the preparation of **10** in 29.7% yield (two steps): $^1H$ NMR ($CDCl_3$) $\delta$ 2.11, 2.15 (s, 3H), 4.15, 4.34 (m, 2H), 5.54, 5.62 (m, 1H), 5.70, 5.82 (m, 1H), 6.43, 6.57 (m, 1H), 7.43–8.09 (m, 5H). Calcd for $C_{14}H_{13}FO_5$: C, 60.00; H, 4.68. Found: C, 60.50; H, 4.90%.

### 3.13. General procedure for condensation of 10 or 23 with heterocycles

A mixture of $N^4$-benzoylcytosine (270 mg, 1.26 mmol), hexamethyldisilazane (15 mL) and ammonium sulfate (20 mg) was heated under reflux for 4 h under nitrogen. The clear solution obtained was concentrated to dryness in vacuo. A solution of the sugar portion **10** (286 mg, 0.836 mmol) in anhydrous DCE (15 mL) and TMSOTf (0.32 mL, 1.68 mL) was added to the silylated base at 0°C. The resulting mixture was stirred for 6 h under nitrogen, poured into ice-cold satd $NaHCO_3$ solution (10 mL) and stirred for 15 min. The resulting mixture was washed, dried ($Na_2SO_4$) and concentrated in vacuo. The anomeric mixture was separated by silica gel column chromatography (50% EtOAc/hexanes) to afford **15a** (131 mg, 36.2%) and **15b** (92.8 mg, 25.5%) as solids.

### 3.14. 1-[(1*S*,4S)-3-Fluoro 4-*O*-Benzoyl-5-dihydro-2,3-enpyranosyl]-$N^4$-benzoylcytosine, 15a and its (1*R*)-isomer, 15b

**15a**: UV (MeOH) $\lambda_{max}$ 302.0 nm; $^1$H NMR ($CDCl_3$) $\delta$ 4.06–4.27 (m, 2H′), 5.73 (dd, $J=12.4$, 2.8 Hz, 1H), 5.81 (m, 1H), 6.84 (dd, $J=2.4$, 5 Hz, 1H), 7.44–8.09 (m, 7H). Anal. calcd for $C_{23}H_{18}FN_3O_5$: C, 63.45; H, 4.17; N, 9.65. Found: C, 63.42; H, 4.16; N, 9.55. **15b**: UV (MeOH) $\lambda_{max}$ 302.5 nm; $^1$H NMR ($CDCl_3$) $\delta$ 4.03–4.33 (m, 2H), 5.56 (d, $J=9.6$ Hz, 1H), 5.65 (dd, $J=1.6$, 12 Hz, 1H), 6.68 (d, $J=8$ Hz, 1H), 7.39–8.04 (m, 7H). Anal. calcd for $C_{23}H_{18}FN_3O_5$: C, 63.45; H, 4.17; N, 9.65. Found: C, 63.29; H, 4.25; N, 9.50%.

### 3.15. 1-[(4*S*)-3-Fluoro 4-*O*-Benzoyl-5-dihydro-2,3-enpyranosyl]uracil, 17

Silylated uracil, which was prepared from thymine (194 mg, 1.73 mmol) and HMDS (10 mL), was treated with **10** (323 mg, 1.15 mmol) and TMSOTf (0.33 mL, 1.73 mmol) in dry DCE at rt for 12 h under nitrogen. After work-up similar to that of **15**, purification by silica gel column chromatography (3% MeOH/$CHCl_3$) gave an inseparable anomeric mixture **17** (221 mg, 57.7%): UV (MeOH) $\lambda_{max}$ 257.0 nm; $^1$H NMR ($CDCl_3$) $\delta$ 3.96–4.26 (m, 2H), 5.50–5.81 (m, 2H), 5.22 (m, 1H), 6.60, 6.61 (m, 1H), 7.36–8.02 (m, 6H), 9.30, 9.33 (s, 1H). Anal. calcd for $C_{16}H_{13}FN_2O_5 \cdot 0.1C_4H_{10}O$: C, 57.99; H, 4.15; N, 8.25. Found: C, 57.99; H, 4.48; N, 7.85%.

### 3.16. 1-[(4*S*)-3-Fluoro 4-*O*-benzoyl-5-dihydro-2,3-enpyranosyl]thymine, 18

Silylated thymine, which was prepared from thymine (119 mg, 0.95 mmol) and HMDS (10 mL), was treated with **10** (177 mg, 0.63 mmol) and TMSOTf (0.18 mL, 0.95 mmol) in dry DCE at rt for 8 h under nitrogen. After work-up similar to that of **15**, purification by silica gel column chromatography (3% MeOH/$CHCl_3$) gave an inseparable anomeric mixture **18** (120 mg, 55%): UV (MeOH) $\lambda_{max}$ 263.0 nm; $^1$H NMR ($CDCl_3$) $\delta$ 1.96, 1.98 (s, 3H), 4.28, 4.06 (m, 2H), 5.17, 5.36 (m, 1H), 5.55, 5.80 (m, 1H), 6.57, 6.64 (m, 1H), 7.15, 7.23 (s, 1H), 7.44–8.11 (m, 5H), 8.23, 8.25 (s, 1H). Anal. calcd for $C_{17}H_{15}FN_2O_5 \cdot 0.2H_2O$: C, 58.35; H, 4.44; N, 8.01. Found: C, 58.06; H, 4.50; N, 7.35%.

### 3.17. 1-[(1*R*,4*R*)-3-Fluoro 4-*O*-Benzoyl-5-dihydro-2,3-enpyranosyl]$N^4$-benzoylcytosine, 24a and its (1*S*)-isomer, 24b

Silylated $N^4$-benzoylcytosine [prepared from 239 mg (1.11 mmol) of $N^4$-benzoylcytosine and 10 mL of HMDS], a solution of **23** (253 mg, 0.74 mmol) in dry methylene chloride (10 mL), and TMSOTf (0.21 mL, 1.11 mmol) were reacted for overnight at rt under nitrogen. After work-up similar to that of **15**, isolation by preparative TLC (50% EtOAc/hexanes) afforded **24a** (118 mg, 35.4%) and **24b** (85 mg, 25.4%) as white solids.

**24a**: UV (MeOH) $\lambda_{max}$ 302.5 nm; $^1$H NMR ($CDCl_3$) $\delta$ 4.06–4.27 (m, 2H, H), 5.73 (dd, $J=12.4$, 2.4 Hz, 1H), 5.81 (m, 1H), 6.84 (dd, $J=2.4$, 5 Hz, 1H), 7.44–8.09 (m, 7H). Anal. calcd for $C_{23}H_{18}FN_3O_5 \cdot 0.3H_2O$: C, 62.67; H, 4.25; N, 9.53. Found: C, 62.54; H, 4.15; N, 9.57%.

**24b**: UV (MeOH) $\lambda_{max}$ 302.5 nm; $^1$H NMR ($CDCl_3$) $\delta$ 4.03–4.32 (m, 2H), 5.56 (d, $J=9.6$ Hz, 1H), 5.65 (dd, $J=1.6$, 12 Hz, 1H), 6.68 (d, $J=8$ Hz, 1H), 7.39–8.04 (m, 7H). Anal. calcd for $C_{23}H_{18}FN_3O_5 \cdot 0.2H_2O$: C, 62.93; H, 4.22; N, 9.57. Found: C, 62.63; H, 4.15; N, 9.52%.

### 3.18. 1-[(4*R*)-3-Fluoro 4-*O*-Benzoyl-5-dihydro-2,3-enpyranosyl]uracil, 26

Silylated uracil, which was prepared from uracil (152 mg, 1.36 mmol) and HMDS (10 mL), was treated with **23** (152 mg, 0.90 mmol) and TMSOTf (0.26 mL, 1.36 mmol) in dry methylene chloride (12 mL). The mixture was stirred overnight at rt under nitrogen. After work-up similar to that of **15**, purification by preparative TLC (50% EtOAc/hexanes) gave an inseparable anomeric mixture **26** (161.8 mg, 54.1%): UV (MeOH) $\lambda_{max}$ 257.0 nm; $^1$H NMR ($CDCl_3$) $\delta$ 3.95–4.26 (m, 2H), 5.50–5.81 (m, 2H), 5.22 (m, 1H), 6.59, 6.61 (m, 1H) 7.36–8.04 (m, 6H), 9.30, 9.32 (s, 1H). Anal. calcd for $C_{16}H_{13}FN_2O_5$: C, 57.83; H, 3.94; N, 8.43. Found: C, 57.90; H, 4.48; N, 8.07%.

### 3.19. 1-[(4*R*)-3-Fluoro 4-*O*-Benzoyl-5-dihydro-2,3-enpyranosyl]thymine, 27

Silylated thymine, which was prepared from thymine (181.6 mg, 1.44 mmol) and HMDS (10 mL), was treated with **23** (270 mg, 0.96 mmol) and TMSOTf (0.28 mL, 1.44 mmol) in dry DCE (15 mL). The mixture was stirred at rt overnight under nitrogen. After work-up similar to that of **15**, purification by silica gel column chromatography (50% EtOAc/hexanes) gave an inseparable anomeric mixture **27** (175.5 mg, 52.8%): UV (MeOH) $\lambda_{max}$ 263.0 nm; $^1$H NMR ($CDCl_3$) $\delta$ 1.96, 1.97 (s, 3H), 4.30, 4.06 (m, 2H), 5.17, 5.36 (m, 1H), 5.55, 5.80 (m, 1H), 6.57, 6.64 (m, 1H), 7.15, 7.23 (s, 1H), 7.44, 8.11 (m, 5H), 8.24, 8.25 (s, 1H). Anal. calcd for $C_{17}H_{15}FN_2O_5 \cdot 0.2H_2O$: C, 58.35; H, 4.44; N, 8.01. Found: C, 57.99; H, 4.46; N, 7.78%.

### 3.20. (+)-1-[(1*S*,4*S*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]cytosine, 16a

Compound **15a** (85.2 mg, 0.2 mmol) was treated with saturated methanolic ammonia (30 mL) and the resulting solution was stirred at rt for 24 h. The reaction mixture was then concentrated under reduced pressure and the residue was purified by silica gel column chromatography (12.5% MeOH/$CH_2Cl_2$) and subsequent recrystallization from hexanes–MeOH–$CH_2Cl_2$ to give **16a** (43.6 mg, 98%) as a crystalline solid: mp 177–180°C; UV ($H_2O$) $\lambda_{max}$ 266.0 nm; $[\alpha]_D^{27}$ +19.5 (*c* 0.29, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.57–3.91 (m, 2H), 4.11 (m, 1H), 5.50 (m, 1H), 5.66 (d, $J=7.3$ Hz), 5.77 (d, $J=6.4$ Hz, $D_2O$ exchangeable, 1H), 6.44 (m, 1H), 7.21,

7.25 (2s, $D_2O$ exchangeable, 2H), 7.53 (d, $J=7.2$ Hz, 1H, H-6). Anal. calcd for $C_9H_{10}FN_3O_3\cdot 0.6H_2O\cdot 0.1C_3H_6O$: C, 45.81; H, 4.88; N, 17.23. Found: C, 46.20; H, 4.69; N, 17.17%.

### 3.21. (+)-1-[(1*R*,4*S*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]cytosine, 16b

Compound **16b** was prepared from **15b** on a 0.15 mmol scale by the method described for compound **14a**. Silica gel column chromatography (12.5% MeOH/$CH_2Cl_2$) and subsequent recrystallization from hexanes–MeOH–$CH_2Cl_2$ gave **16b** (33.2 mg, 97.4%) as a crystalline solid: mp 168–170°C; UV ($H_2O$) $\lambda_{max}$ 266.0 nm; $[\alpha]_D^{25}$ +10.6 (*c* 0.68, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.83 (m, 2H), 4.12 (m, 1H), 5.48 (m, 1H), 5.77 (m, $D_2O$ exchangeable, 2H), 6.38 (m, 1H), 7.26, 7.31 (2s, $D_2O$ exchangeable, 2H), 7.54 (d, $J=7.2$ Hz, 1H). Anal. calcd for $C_9H_{10}FN_3O_3\cdot 0.6H_2O\cdot 0.1C_3H_6O$: C, 45.81; H, 4.88; N, 17.23. Found: C, 45.77; H, 4.62; N, 17.23%.

### 3.22. (+)-1-[(1*S*,4*S*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]uracil, 19a and its (+)-(1*R*,4*S*)-isomer, 19b

A anomeric mixture **17** (155 mg, 0.47 mmol) was treated with saturated methanolic ammonia (50 mL) and the resulting solution was stirred at rt for 10 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by preparative TLC (5% MeOH/$CH_2Cl_2$) to separate **19a** (59.2 mg, 55.2%) and **19b** (43 mg, 40.1%), which were recrystallized from MeOH–$CH_2Cl_2$, respectively.

**19a**: mp 185–188°C; UV (MeOH) $\lambda_{max}$ 257.0 nm; $[\alpha]_D^{24}$ +17.9 (*c* 0.41, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.79–3.92 (m, 2H), 4.09 (m, 1H), 5.58 (dd, $J=1.67$, 11.3 Hz, 1H), 5.71 (d, $J=8$ Hz, $D_2O$ exchangeable, 1H), 5.82 (d, $J=7.4$ Hz, 1H), 6.35 (m, 1H), 7.64 (d, $J=8.0$ Hz, 1H), 11.43 (s, 1H). Anal. calcd for $C_9H_9FN_2O_4$: C, 47.37; H, 3.98; N, 12.28. Found: C, 47.36; H, 4.07; N, 12.27.

**19b**: mp 182–184°C; UV (MeOH) $\lambda_{max}$ 257.0 nm; $[\alpha]_D^{25}$ +34.8 (*c* 0.26, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.63–3.92 (m, 2H), 4.16 (m, 1H), 5.52 (d, $J=2.8$ Hz), 5.56 (m, 1H), 5.81 (d, $J=6.6$ Hz, 1H), 6.32 (d, $J=7.2$ Hz, 1H), 7.60 (d, $J=8.0$ Hz, 1H), 11.44 (s, 1H). Anal. calcd for $C_9H_9FN_2O_4$: C, 47.37; H, 3.98; N, 12.28. Found: C, 47.43; H, 4.11; N, 12.23%.

### 3.23. (+)-1-[(1*S*,4*S*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]thymine, 20a and its (+)-(1*R*,4*S*)-isomer, 20b

Compounds **20a** and **20b** were prepared from **16** on a 0.42 mmol scale by the method described for compounds **19a** and **19b**. Preparative TLC (5% MeOH/$CH_2Cl_2$) followed by trituations with ether gave **20a** (54.4 mg, 53.5%) and **20b** (39.4 mg, 38.7%) as white solids.

**20a**: mp 175–176°C; UV (MeOH) $\lambda_{max}$ 263.0 nm; $[\alpha]_D^{25}$ +37.05 (*c* 0.21, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 1.87 (s, 3H), 3.83–4.18 (m, 3H), 5.28 (m, 1H), 6.38 (d, $J=7$ Hz, 1H), 7.24 (s, 1H), 8.21 (s, 1H). Anal. calcd for $C_{10}H_{11}FN_2O_4\cdot 0.1C_4H_{10}O$: C, 50.04; H, 4.85; N, 11.22. Found: C, 50.12; H, 4.85; N, 11.37%.

**20b**: mp 184–185°C; UV (MeOH) $\lambda_{max}$ 262.0 nm; $[\alpha]_D^{25}$ +16.88 (*c* 0.23, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 1.79 (s, 3H), 3.85 (m, 2H), 4.04 (m, 1H), 5.55 (m, 1H), 5.79 (d, $J=7.8$ Hz, 1H), 6.31 (d, $J=7.2$ Hz, 1H), 7.42 (s, 1H), 11.41 (s, 1H). Anal. calcd for $C_{10}H_{11}FN_2O_4\cdot 0.1CH_4O$: C, 48.98; H, 4.98; N, 10.98. Found: C, 48.95; H, 4.81; N, 10.74%.

### 3.24. (−)-1-[(1*R*,4*R*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]cytosine, 25a

Compound **25a** was prepared from **24a** on a 0.22 mmol scale by the method described for compound **16a**. Silica gel column chromatography (12.5% MeOH/$CH_2Cl_2$) gave **25a** (45 mg, 88.4%) as a white solid: mp 176–178°C; UV ($H_2O$) $\lambda_{max}$ 266.0 nm; $[\alpha]_D^{26}$ −22.4 (*c* 0.25, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.57–3.93 (m, 2H), 4.11 (m, 1H), 5.50 (dd, $J=2.8$, 14.8 Hz, 1H), 5.66 (d, $J=7.3$ Hz, 1H), 5.77 (d, $J=6.4$ Hz, $D_2O$ exchangeable, 1H), 6.44 (m, 1H), 7.21, 7.25 (2s, $D_2O$ exchangeable, 2H), 7.53 (d, $J=7.2$ Hz, 1H). Anal. calcd for $C_9H_{10}FN_3O_3$: C, 47.58; H, 4.44; N, 18.50. Found: C, 47.50; H, 4.38; N, 18.25%.

### 3.25. (−)-1-[(1*S*,4*R*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]cytosine, 25b

Compound **25b** was prepared from **24b** on a 0.18 mmol scale by the method described for compound **16a**. Silica gel column chromatography (12.5% MeOH/$CH_2Cl_2$) gave **25b** (37.8 mg, 92.5%) as a white solid: mp 167–169°C; UV ($H_2O$) $\lambda_{max}$ 266.0 nm; $[\alpha]_D^{25}$ −11.25 (*c* 0.27, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.83 (m, 2H), 4.12 (m, 1H), 5.48 (m, 1H), 5.77 (m, 2H, $D_2O$ exchangeable, 1H), 6.38 (m, 1H), 7.26, 7.31 (2s, $D_2O$ exchangeable, 2H), 7.54 (d, $J=7.2$ Hz, 1H). Anal. calcd for $C_9H_{10}FN_3O_3\cdot 0.4CH_2Cl_2$: C,43.23; H, 4.17; N, 16.09. Found: C, 43.33; H, 4.30; N, 16.31%.

### 3.26. (−)-1-[(1*R*,4*R*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]uracil, 28a and its (−)-(1*S*,4*R*)-isomer, 28b

Compounds **28a** and **28b** were prepared from **24** on a 0.39 mmol scale by the method described for compounds **19a** and **19b**. Preparative TLC (5% MeOH/$CH_2Cl_2$) followed by crystallization from MeOH–$CH_2Cl_2$ gave **28a** (48.4 mg, 54.7%) and **28b** (36.5 mg, 41%) as white solids.

**28a**: mp 186–188°C; UV (MeOH) $\lambda_{max}$ 257.0 nm; $[\alpha]_D^{25}$ −17.76 (*c* 0.32, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.79–3.92 (m, 2H), 4.08 (m, 1H), 5.58 (dd, $J=1.6$, 12 Hz, 1H), 5.71 (d, $J=8$ Hz, 1H), 5.82 (d, $J=7.8$ Hz, 1H), 6.35 (m, 1H), 7.64 (d, $J=7.8$ Hz, 1H), 11.43 (s, 1H). Anal. calcd for $C_9H_9FN_2O_4$: C, 47.37; H, 3.98; N, 12.28. Found: C, 47.59; H, 4.09; N, 12.37%.

**28b**: mp 180–182°C; UV (MeOH) $\lambda_{max}$ 257.0 nm; $[\alpha]_D^{25}$ −36.36 (*c* 0.18, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 3.63–

3.92 (m, 2H), 4.16 (m, 1H), 5.52 (d, $J=3.2$ Hz, 1H), 5.56 (m, 1H), 5.81 (d, $J=6.6$ Hz, 1H), 6.32 (d, $J=7.2$ Hz, 1H), 7.60 (d, $J=8.0$ Hz, 1H), 11.44 (s, 1H). Anal. calcd for $C_9H_9FN_2O_4$: C, 47.37; H, 3.98; N, 12.28. Found: C, 47.08; H, 4.01; N, 12.04%.

### 3.27. (−)-1-[(1*R*,4*R*)-3-Fluoro-4-hydroxy-5-dihydro-2,3-enpyranosyl]thymine, 29a and its (−)-(1*S*,4*R*)-isomer, 29b

Compounds **29a** and **29b** were prepared from **27** on a 0.35 mmol scale by the method described for compounds **19a** and **19b**. Preparative TLC (5% MeOH/$CH_2Cl_2$) followed by trituations with ether gave **29a** (46.7 mg, 55.1%) and **29b** (35.9 mg, 42.3%) as white solids.

**29a**: mp 177–179°C; UV (MeOH) $\lambda_{max}$ 262.0 nm; $[\alpha]_D^{25}$ −37.61 (*c* 0.44, MeOH); $^1$H NMR (DMSO-$d_6$) $\delta$ 1.87 (s, 3H), 3.83–4.18 (m, 3H), 5.28 (m, 1H), 6.38 (d, $J=7.2$ Hz, 1H), 7.24 (s, 1H). Anal. calcd for $C_{10}H_{11}FN_2O_4\cdot 0.1C_3H_6O$: C, 49.88; H, 4.74; N, 11.30. Found: C, 50.01; H, 4.80; N, 11.30%.

**29b**: mp 185–187°C; UV (MeOH) $\lambda_{max}$ 262.0 nm; $[\alpha]_D^{25}$ −16.3 (*c* 0.22, MeOH); $^1$H NMR (DMSO-$d_6$) d 1.80 (s, 3H), 3.85 (m, 2H), 4.04 (m, 1H), 5.54 (m, 1H), 5.79 (d, $J=7.8$ Hz, 1H), 6.31 (m, 1H), 7.42 (s, 1H), 11.41 (s, 1H). Anal. calcd for $C_{10}H_{11}FN_2O_4\cdot 0.2C_4H_{10}O$: C, 50.47; H, 5.10; N, 10.90. Found: C, 50.97; H, 5.15; N, 10.46%.

## Acknowledgements

This research was supported by the US Public Research grants (AI 32351). We thank Dr. Raymond F. Schinazi of Emory University School of Medicine/VA Medical Center for anti-HIV evaluation.

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