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The synthesis of 2,3-dideoxy-2-fluoro-3-*C*-methylpentose-containing nucleosides via [3,3]-sigmatropic rearrangements

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ABSTRACT

[3,3]-Sigmatropic rearrangement of in situ-formed [O,O]-silyl ketene acetals of butenyl fluoroacetates was used as the key step in the synthesis of racemic 2,3-dideoxy-2-fluoro-3-*C*-methylpentofuranoses. The product pentofuranoses were transformed further into pyrimidine and purine nucleosides. The conformations of the synthetic carbohydrates were confirmed by single-crystal X-ray diffraction studies and indicated that previous structural assignments made by NMR were in error.

INTRODUCTION

Nucleoside analogues, bearing a substituent at C-2′ other than hydrogen or hydroxyl have been proposed to selectively eliminate a virus or a neoplast without affecting a normal cell's metabolism. The 3′-alkyl branched nucleosides **2–5**, analogues of cordycepin (3′-deoxyadenosine, **1**), a nucleoside antibiotic produced by *Cordyceps militars* and *Aspergillus nodulans* fungi[1–5], have been reported to exhibit antiviral activity. While the 3′-alkyl nucleoside inhibits RNA synthesis as well as DNA and protein biosynthesis, the activity of these compounds may be attributed to improved transport of the nucleosides across cell membranes because of lipophilicity of the alkyl substituent. Other factors which also might be important are decreased rates of inactivation by adenosine deaminase and enhanced kinase phosphorylation of nucleoside to the nucleotide. It is proposed[6] that enzymatic degradation may be further suppressed by substitution of the hydroxyl group by fluorine at C-2′. To test this hypothesis, a new approach to the preparation of 3-alkyl-2,3-dideoxy-2-fluoro-sugar-containing nucleosides was developed to facilitate preparation of fluorinated analogues of cordycepin.

The effects of fluorine on the activity of carbohydrates and nucleosides are well known[7]. Illustrative of the advantageous effects of fluorination reported in the

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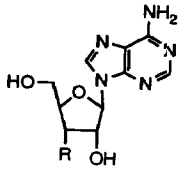


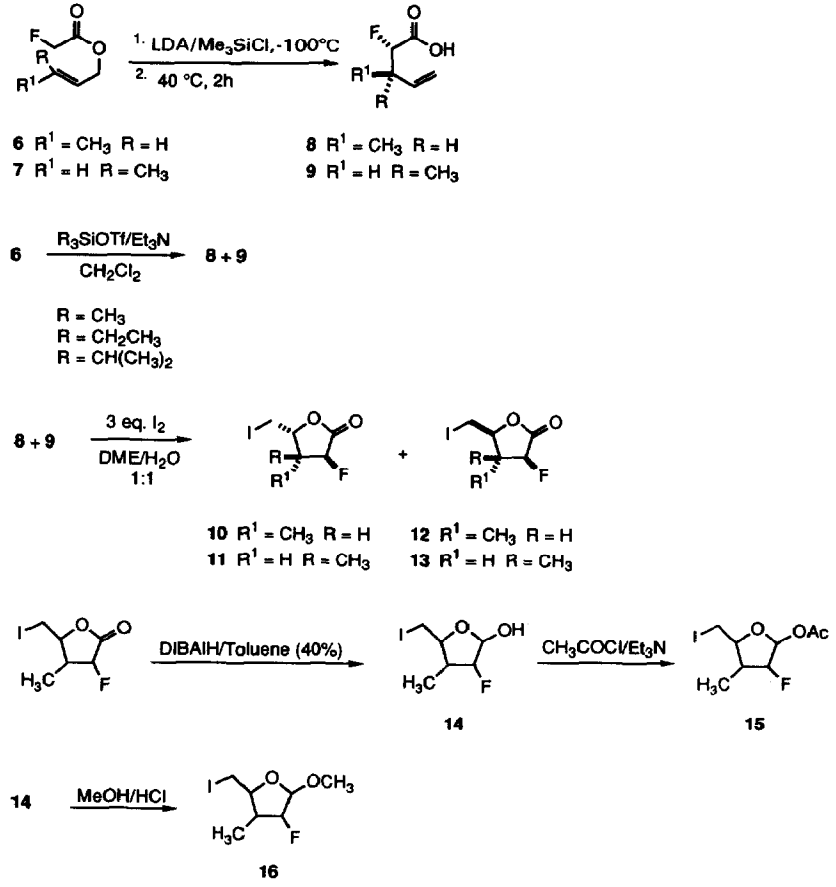
1 R = H
2 R = CH_3
3 R = CH_2CH_3
4 R = $(CH_2)_3CH_3$
5 R = $(CH_2)_5CH_3$

literature[8,9], (*S*)-2′-fluorodaunorubicin has significant therapeutic advantages over daunorubicin[10,11]. 2-Fluoro sugars in particular are typically prepared by direct fluorination[12], displacement of suitable leaving groups with fluoride ion[13], or by using diethylaminosulfur trifluoride (DAST)[14]. Ring-opening reactions of aziridines[10,15] and epoxides[16] may also be employed. Fluorinated sugars have also been prepared from fluorinated building blocks, principally by the Reformatsky reaction of bromofluoroacetates[17] or by the directed aldol reaction of fluoroacetates[18].

RESULTS AND DISCUSSION

Herein we report the preparation of 2-deoxy-2-fluoro carbohydrates from fluorinated building blocks by the Ireland ester-enolate Claisen rearrangement. The Claisen rearrangement, previously employed in a variety of natural-product syntheses[19], is sensitive to α-substituents[20], such as fluorine[21]. The Ireland ester-enolate Claisen rearrangement was previously employed with butenyl α-fluoroacetates[22] to form 2-fluoro-3-methyl-4-pentenoic acids, **8** and **9** (Scheme 1) but the previous structural assignments of these materials made by NMR have been found to be in error.

In earlier work, it was shown that (*E*)-2-butenyl fluoroacetate **6**, prepared in 87% yield by addition of fluoroacetyl chloride to a dichloromethane solution of (*E*)-2-butenol, can be deprotonated using 1 equiv of LDA at −100°C. The ester-enolate Claisen rearrangement of (*E*)-2-butenyl fluoroacetate, **6**, resulted in 16% yield of the 3-methyl-2-fluoro-4-pentenoic acids, **8** and **9**, with a modest diastereoselectivity of 4:1. The yield improved to 62% when 3 equiv of LDA was employed; however the reaction was no longer diastereoselective. Apparently epimerization of fluorinated carbon of the product 2-fluoro-3-methyl-4-pentenoic acid (**8**) occurs in the presence of excess LDA. Also, undesired side-reactions resulting from single-electron transfer reactions occur[23]. The result of these limitations is that a practical yield of rearranged product **8** is difficult to realize when the scale of the reaction is increased. For [3,3]-sigmatropic rearrangements to be useful for preparing the crucial fluorinated building block, the reaction



Scheme 1.

conditions had to be significantly improved. Treatment of the (*E*)-2-butenyl fluoroacetate with triethylamine and trimethylsilyl trifluoromethanesulfonate in dichloromethane formed the rearranged acid in reproducibly acceptable yields, and with very good diastereoselectivity[24]. The rearrangement of (*E*)-2-butenyl fluoroacetate (**6**) while heating under reflux overnight in dichloromethane, proceeded in quantitative yield to form **8** and **9** in a ratio of 3:1. The selectivity improved to 5.8:1 when the reaction was performed[25] at room temperature but the yield was 85%. When 1.6 equiv of triisopropylsilyl trifluoromethanesulfonate was used in the presence of 5 equiv of triethylamine, the rearrangement of the ester proceeded at room temperature in quantitative yield with a **8**:**9** ratio of 15:1. The rearrangement of the (*Z*)-2-butenyl fluoroacetate (**7**) under the same conditions proceeded also in quantitative yield but with an **8**:**9** ratio of 1:8.

We have also shown earlier that iodolactonization of a 4:1 mixture of **8** and **9**, under thermodynamic conditions with 3 equiv of iodine in 1:1 dimethoxyethane

(DME)–water[22], yielded a white solid in 56% yield with a **11** and **13** to **10** and **12** ratio of 11:1. The product iodolactones were surprisingly volatile, increasing the difficulty of isolation. Lactonization with iodine in acetonitrile proceeded in higher yield (85%) but the stereoselectivity of the process was degraded somewhat.

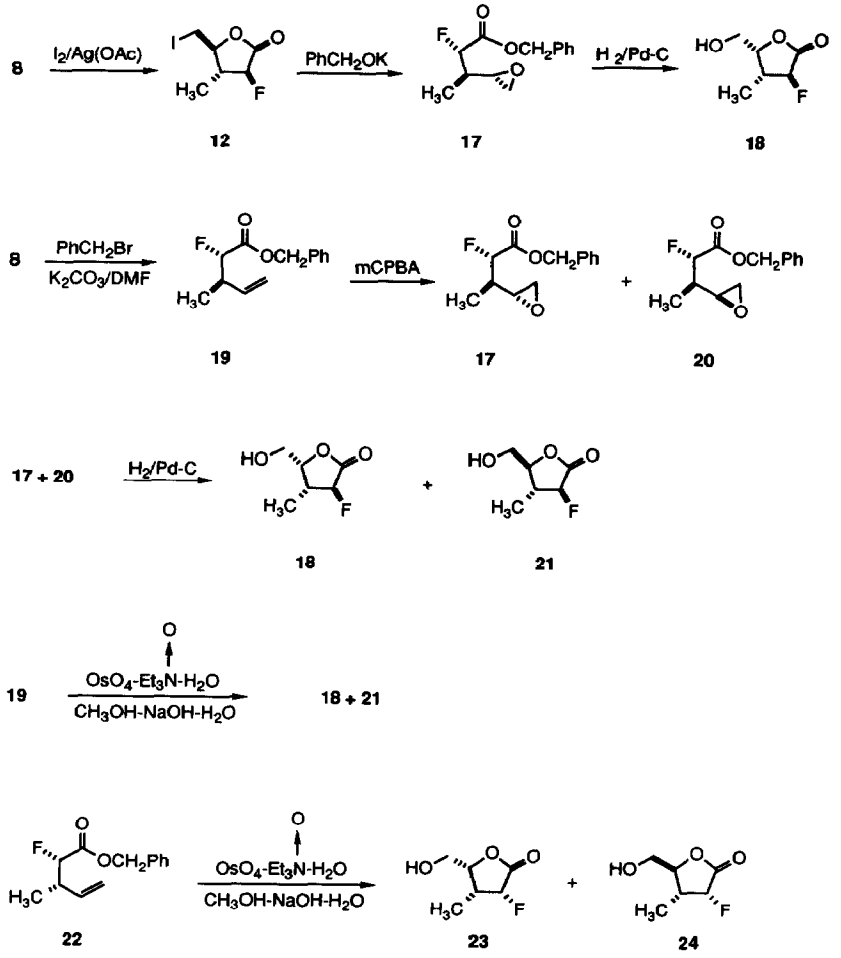
Diisobutylaluminum hydride reduction of the iodolactones, **10–13**, effected in dry toluene at −78°C for 2.5 h, gave an amber oil in 59% yield. The desired lactols, **14**, were purified by chromatography.

Prior to attempting displacement of the iodide, we protected the anomeric hydroxyl group. Acetylation of **14** with 1.1 equiv of acetyl chloride in dichloromethane in the presence of 2.2 equiv triethylamine resulted in a quantitative yield of the acetates **15** which were characterized by GLC–MS (*m/z* 301.95). Methylation of **14** with methanol in the presence of Amberlite IR-120 HCP in methanol as solvent resulted[23] in a low yield of **16**. However, quantitative methyl glycoside formation was possible by stirring the lactols **14** in methanolic HCl for 30 min at 0°C, followed by stirring overnight at room temperature.

Nucleophilic displacement of the iodide of 5-iodofuranoses[23,26] was problematic. Displacement with silver acetate in refluxing acetic acid did not occur[26]. Displacement reactions with silver trifluoroacetate in DMF failed with both **16** and **15**[23]. Only products of elimination were isolated, there was no evidence for incorporation of the trifluoroacetoxy group. Treatment of **11** with silver nitrate in acetone and deionized water[27] also yielded none of the desired alcohol.

The iodolactonization of the *anti*-enriched 2-fluoro-3-methyl-4-pentenoic acid (**8**) with iodine in the presence of silver acetate yielded very cleanly, after heating under reflux for 16 h, the iodo-arabinono-1,4-lactone **12** in 78% yield (Scheme 2). Conversion of the iodolactone **12** into the desired hydroxy-xylono-1,4-lactone **18** was possible using the method of Still and co-workers[28]. The potassium alkoxide of benzyl alcohol was prepared at 5°C and the iodolactone **12** was immediately added. The epoxide **17**, which when hydrogenolytically deprotected in the presence of palladium on carbon in 1,4-dioxane spontaneously lactonized to the 5-hydroxy-xylono-1,4-lactone, **18**. Quantitative epoxidation of benzyl ester, **19**, with *m*-chloroperoxybenzoic acid in chloroform formed the epoxides **20** and **17** in a 1:1.2 ratio. Hydrogenolysis of the mixture of **20** and **17** over palladium on carbon in 1,4-dioxane yielded the arabinono- and xylono-1,4-lactones, **21** and **18** in 41 and 17% yields, respectively, after separation by chromatography. The preparation of the arabinono-1,4-lactone may be improved by *syn* hydroxylation of the alkene **19**, with osmium tetraoxide[29]. Cleavage of the osmylate ester was effected with triethylamine-*N*-oxide–water. Saponification of the benzyl ester with methanolic sodium hydroxide followed by lactonization afforded the arabino- and the xylono-1,4-lactones, **21** and **18**, in 63 and 14% yields, respectively.

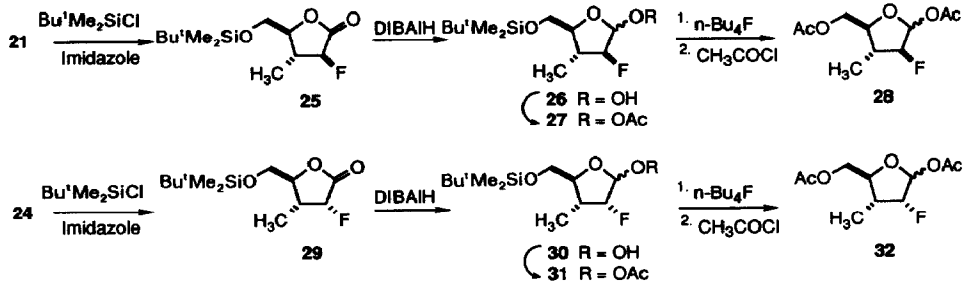
In the same manner, the benzyl ester of *syn*-2-fluoro-3-methyl-4-pentenoic acid, **22**, was prepared in quantitative yield. *syn*-Hydroxylation of **22** followed by saponification and lactonization formed the ribono- and lyxono-1,4-lactones, **24** and **23**, in 33 and 8% yields, respectively.



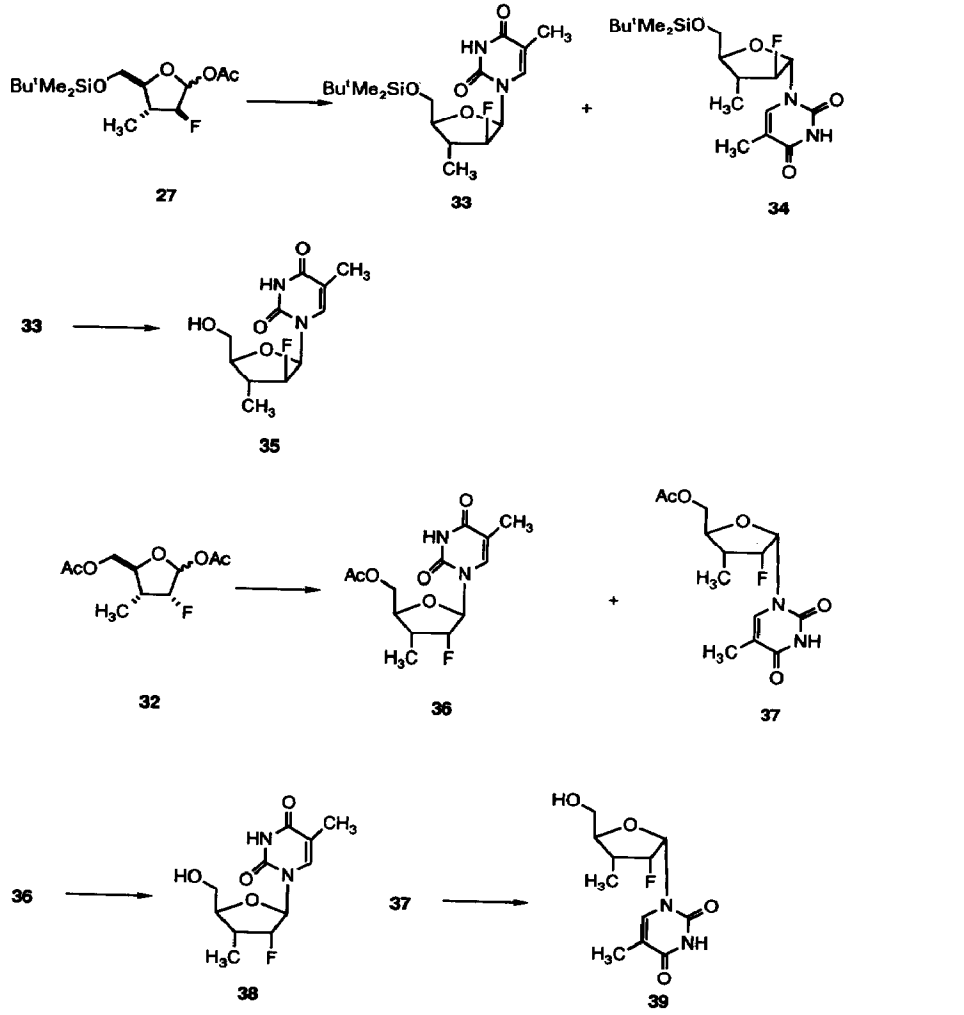
Scheme 2.

Silylation of lactone **21** with *tert*-butyldimethylchlorosilane in the presence of imidazole in DMF afforded the protected lactone **25** in 92% yield (Scheme 3).

Diisobutylaluminum hydride reduction of the lactone in ether for 1 h at −78°C followed by acetylation produced the anomeric acetate **27** in 89% overall yield. Desilylation with tetra-*n*-butylammonium fluoride followed by acetylation with acetyl chloride in the presence of triethylamine, afforded the 1,5-di-*O*-acetylarabinose analogue [28] in 76% yield. Silylation of the C-5 hydroxyl of ribonolactone **24** with *tert*-butylchlorodimethylsilane in the presence of imidazole in DMF afforded the protected lactone **29** in 85% yield. Diisobutylaluminum hydride reduction of the lactone in ether for 1 h at −78°C, followed by acetylation gave the anomeric acetate **31** in 84% overall yield. On desilylation and acetylation, the 1,5-di-*O*-acetylribose analogue **32** was obtained in 76% yield.



Scheme 3.



Scheme 4.

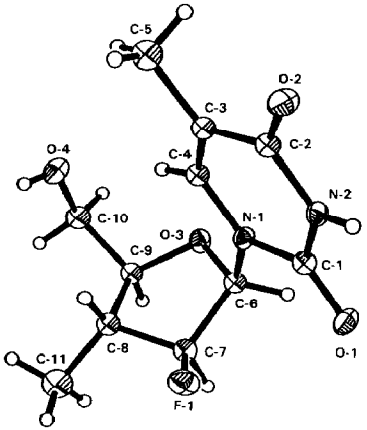


Fig. 1. ORTEP plot from a single-crystal X-ray diffraction study of compound **35**.

Glycosylation of the 1-*O*-acetyl-5-*O*-silylarabinose **27** with 2,4-bis(trimethylsilyl)-thymine in the presence of potassium iodide in acetonitrile and dibenzo-18-crown-6 afforded the thymidine nucleosides, **33** and **34**, in 89% yield with an $\alpha:\beta$ ratio of 5:1 (Scheme 4).

On separation of the anomers by column chromatography, the β anomer was desilylated to yield crystalline 5′-hydroxythymidine analogue **35**. The relative stereochemistry of the β anomer of **35** was confirmed by single-crystal X-ray diffraction studies (Fig. 1). The yield of glycosylation was low when trimethylsilyl triflate was employed; desilylation of the starting material was a competing side-reaction. Under the same conditions, glycosylation of the 5-*O*-acetylribo-furanose **31** afforded the α anomer **36** and β anomer **37** in 28 and 55% yields, respectively. Both compounds were deprotected and structurally characterized by single-crystal X-ray diffraction as well. (Figs. 2 and 3)

Glycosylation of 1-*O*-acetyl-5-*O*-*tert*-butyldimethylsilylarabinofuranose (**27**) with 6,9-bis(trimethylsilyl)adenine in the presence of potassium iodide in acetonitrile and dibenzo-18-crown-6 proceeded in very low yield. However, glycosylation of the 1,5-di-*O*-acetylarabinofuranose (**28**) with 6-chloro-9-trimethylsilylpurine with trimethylsilyl triflate afforded the 9-(α-furanosyl)purine **40**, 9-(β-furanosyl)purine **43**, 7-(α-furanosyl)purine **41**, and 7-(β-furanosyl)purine **42**, in 17, 31, 17, and 11% yields, respectively. Ratios were determined by ^{1}H and ^{13}C NMR spectroscopy (Scheme 5).

Following improvement of methods used for formation of the reactive *O*-silyl ketene acetal intermediate, Claisen rearrangement yields 2-fluoro-3-methyl-4-pentenoic acids, useful in the preparation of 2′-fluoro-3′-methylpurine and pyrimidine nucleosides. Confirmation of the structural assignments by single-crystal X-ray structure determination of the structural assignments previously made by NMR[22] clearly indicated that those previous assignments were in error. Application of our methods for the remote induction of asymmetry via fluoroacetamide via

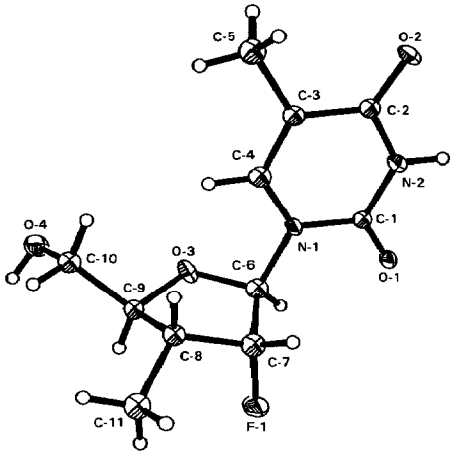


Fig. 2. ORTEP plot of compound **38**.

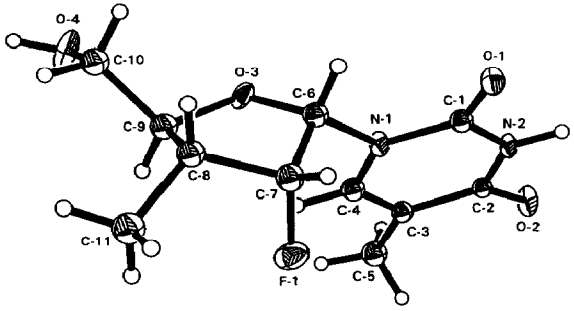
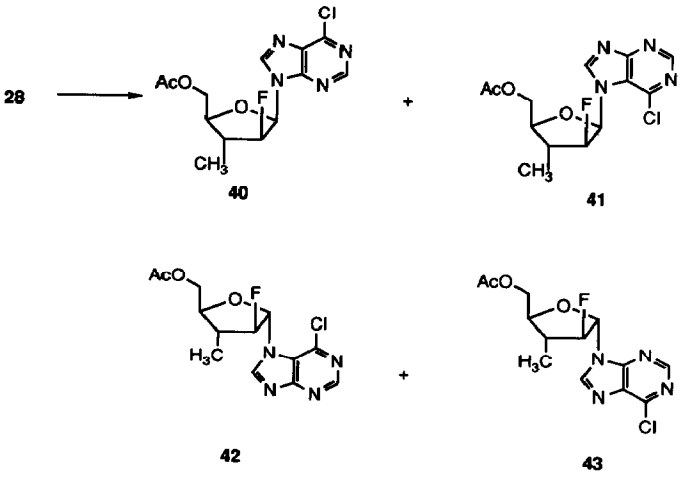


Fig. 3. ORTEP plot of compound **39**.



Scheme 5.

fluoroacetamide acetal Claisen rearrangement[30], would enable the asymmetric synthesis of the desired nucleosides via the optically active fluoropentenoic acids.

EXPERIMENTAL

General methods.—^1H, ^{13}C, and ^{19}F NMR spectra were recorded with a Varian XL-300 NMR spectrometer at 299.9, 75.4, and 282.2 MHz, respective.y Chemical shifts (δ) of all spectra are reported in ppm. Chemical shifts of ^1H and ^{13}C NMR spectra in $CDCl_3$ are reported relative to Me_4Si (0.00 ppm) as the internal standard. The chemical shifts of ^{19}F NMR spectra of samples in $CDCl_3$ are reported relative to $CFCl_3$ (0.00 ppm) as the internal standard. Coupling constants are reported as J values in Hz. The abbreviations used are s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet).

Gas chromatography–mass spectra (GC–MS) were recorded with a Hewlett–Packard electron-impact mass spectrometer EIMS 5970 with an ionization energy of 70 eV. The instruments were operated in series with a Hewlett–Packard 5890 Series II gas chromatograph equipped with a 12 m × 0.53 mm HP-1 capillary column, and flame-ionization detector manifold.

Thin-layer chromatography on plates precoated with silica gel 60 F_{254} of 0.2-mm thickness (Merck) was used to monitor reactions. Column chromatography was performed using Merck Silica gel 60 (230–400 mesh), Davisil Silica Gel 62 (60-200 mesh), or Florisil (60–100 mesh). Melting points were determined on a Mel-Temp apparatus. Solutions were evaporated under diminished pressure.

Caution: Fluoroacetyl chloride is a fatal poison affecting the central nervous system and may cause epileptic convulsions and ventricular fibrillation. It was handled with extreme care in an efficient fume hood while wearing gloves, a respirator, and a standard laboratory safety garment. All α-fluoroacetates were likewise assumed to be extremely poisonous.

Solvents were freshly distilled prior to use. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl. *N,N*-dimethylformamide (DMF) was dried by heating under reflux over BaO and was distilled at 25 torr. Toluene was dried by distillation from sodium. Diisopropylamine, CH_2Cl_2, MeCN, Me_3SiCl, MeOH, and hexane were distilled from CaH_2. Acetone was dried by first heating under reflux over, and then distilling from, anhyd K_2CO_3. Acetyl chloride was distilled carefully at 52°C. Lithium diisopropylamide (LDA) was prepared by dropwise addition of a 1.5 M solution of MeLi in Et_2O (Aldrich) to a THF solution of dry diisopropylamine under Ar below 0°C. The mixture was stirred for 10 min at 0°C.

Elemental combustion microanalyses were performed by either Desert Analytics, Tucson, AZ or by M-H-W Laboratories, Phoenix, AZ.

A Nicolet R3m/V diffractometer was used for single-crystal X-ray diffraction. Lorenz and polarization corrections were applied to the data. All the nonhydrogen

atoms were located by direct methods. The hydrogen atoms were included at their idealized positions.

2-Fluoro-3-methyl-4-pentenoic acid[25] (**8**).—(*E*)-2-Butenyl fluoroacetate (6.45 g, 48.8 mmol) was added to a solution of 45 mL of CH_2Cl_2 and 33.6 mL of Et_3N (240 mmol) under Ar. The mixture was cooled below −60°C and triisopropylsilyl trifluoromethanesulfonate (21 mL, 78.1 mmol) was added to the mixture dropwise. The mixture was allowed to warm to room temperature gradually, stirred for 3 days, and then the mixture was concentrated. Ether (~ 100 mL) and a 1.3 M aq NaOH (150 mL) were added to the residue. The aqueous phase was separated and was then acidified with concd HCl. Ethyl acetate was added to the solution and the organic phase separated, washed twice with water, dried over $MgSO_4$ and concentrated in vacuo to yield **8** and **9** (6.4 g, 99%) (15:1, **8** to **9**); ^{1}H NMR ($CDCl_3$): δ 5.83 (ddd, 1H, $J_{H3,H4}$ 7, $J_{H4,H5,cis}$ 10. $J_{H4,H5,trans}$ 17 Hz. C*H*=CH$_2$), 5.17 (d, 1 H, $J_{H4,H5,trans}$ 17 Hz, CH=CH–*H*,*trans*), 5.13 (d, 1 H, $J_{H4,H5,cis}$ 10 Hz, CH=CH–*H*,*cis*), 4.87 (dd, 1 H, $J_{H2,F}$ 49, $J_{H2,H3}$ 4 Hz. C*H*F), 2.79 [dddq, 1 H, $J_{H2,H3}$ 4, $J_{H3,CH3}$ 7, $J_{H3,F}$ 28, $J_{H3,H4}$ 7 Hz, C*H*(CH$_3$)], 1.11 [d, 3 H, $J_{H3,CH3}$ 7 Hz, CH(C*H*$_3$)]; ^{13}C NMR ($CDCl_3$): δ 174.48 (d, $J_{C1,F}$ 25 Hz, C=O), 137.29 (d, $J_{C4,F}$ 3 Hz, *C*H=CH$_2$). 116.68 (CH=*C*H$_2$), 91.15 (d, $J_{C2,F}$ 189 Hz, *C*HF), 40.14 (d, $J_{C3,F}$ 19 Hz, *C*HCH$_3$), 13.44 (d, $J_{C,F}$ 4 Hz, CH*C*H$_3$); ^{19}F NMR ($CDCl_3$): δ −200.51 (dd, $J_{H2,F}$ 49, $J_{H3,F}$ 28 Hz).

2-Fluoro-5-iodo-3-C-methyl-2,3,5-trideoxy-pentofuranoses (**14**).—To a flame-dried, three-necked, round-bottom flask under Ar, containing 0.17 g (0.66 mmol) of **10–13** in 7.1 mL of toluene and cooled to −78°C, was added 0.54 mL (0.82 mmol) of a solution of 0.15 mL of neat diisobutylaluminum hydride (DIBAl-H, Aldrich) in 0.39 mL of dry toluene. After stirring at −78°C for 2.5 h the reaction was quenched with 0.03 mL (0.7 mmol) of $MeOH_2$ warmed to room temperature and treated with satd NH_4Cl until a precipitate formed. The mixture was centrifuged and the supernatant was decanted. The solid precipitate was washed with anhyd Et_2O. After centrifugation, the supernatants were combined and concentrated. Column chromatography of the residue over silica gel using CH_2Cl_2 as eluent yielded **14** (0.10 g, 59%) as an amber oil; ^{1}H NMR ($CDCl_3$): δ 5.65 (d, 1 H, $J_{H1,F}$ 11 Hz, C*H*OH, *β-arabino*), 5.61 (d, 1 H, $J_{H1,F}$ 10 Hz, C*H*OH, *α-arabino*), 5.53 (d, 1 H, $J_{H1,F}$ 11 Hz, C*H*OH, *α-ribo*), 4.88 (dd, 1 H, $J_{H2,H3}$ 3, $J_{H2,F}$ 52 Hz, C*H*F, *α-ribo*), 4.85 (dd, 1 H, $J_{H2,H3}$ 3, $J_{H2,F}$ 53 Hz, C*H*F, *α-arabino*), 4.77 (dd, 1 H, $J_{H2,H3}$ 2, Hz, $J_{H2,F}$ 53 Hz, C*H*F, *β-arabino*), 4.61 (dd, 1 H, $J_{H4,F}$ 4, $J_{H4,H5}$ 8, $J_{H4,H5'}$ 10 Hz, C*H*O,*α-ribo*), 4.01 (dd, 1 H, $J_{H4,H5}$ 6, $J_{H4,H5'}$ 12 Hz, C*H*O), 3.89 (d, 1 H, $J_{H4,H5}$ 4, $J_{H4,H5'}$ 9 Hz, C*H*O), 3.50 (dd, 1 H, $J_{H4,H5}$ 4, $J_{H5,H5,gem}$ 11 Hz, CHI-*H*), 3.27–3.40 (m, 2H, C*H*$_2$I), 3.19 (dd, 1 H, $J_{H4,H5} = J_{H5,H5,gem}$ 10 Hz, CHI-*H*, *α-ribo*), 2.76 (ddq, 1 H, $J_{H2,H3}$ 3, Hz, $J_{H3,F}$ 31, Hz, $J_{H3,CH3}$ 8 Hz, C*H*CH$_3$, *α-ribo*), 2.10–2.45 (m, 1 H, C*H*CH$_3$, *α* + *β-arabino*), 1.31 (d, 3 H, J_{H3,CH_3} 7 Hz, 3H, CHC*H*$_3$, *α-arabino*), 1.21 (d, 3 H, J_{H3,CH_3} 7 Hz, CHC*H*$_3$, *β-arabino*), 1.18 (d, 3 H, J_{H3,CH_3} 8 Hz, CHC*H*$_3$, *α-ribo*); ^{13}C NMR ($CDCl_3$): δ 101.89 (d, $J_{C2,F}$ 180 Hz, *C*HF, *α-arabino*), 101.20 (d, $J_{C1,F}$ 36 Hz, *C*HOH, *α-arabino*), 99.72 (d, $J_{C1,F}$; 33 Hz, *C*HOH, *α-ribo*), 99.03 (d, $J_{C1,F}$ 34 Hz, *C*HOH, *β-arabino*), 98.20 (d, $J_{C2,F}$ 181

Hz, *C*HF, *α-ribo*), 97.76 (d, $J_{C2,F}$ 181 Hz, *C*HF, *β-arabino*), 85.07 (*C*HO, *α-arabino*), 83.75 (*C*HO, *α-ribo*), 81.71 (*C*HO, *β-arabino*), 45.02 (d, $J_{C3,F}$ 20 Hz, $CHCH_3$, *α-arabino*), 41.21 (d, $J_{C3,F}$ 19 Hz, $CHCH_3$, *α-ribo*), 37.68 (d, $J_{C3,F}$ 20 Hz, $CHCH_3$, *β-arabino*), 15.99 (d, $J_{C,F}$ 8 Hz, CH_3, *α-arabino*), 9.51 (d, $J_{C,F}$ 12 Hz, CH_3, *β-arabino*), 9.44 (CH_2I, *α-ribo*), 8.7 (CH_2I, *β-arabino*), 7.59 (CH_2I, *α-arabino*), 7.36 (d, $J_{C,F}$ 8 Hz, CH_3, *α-ribo*); ^{19}F NMR ($CDCl_3$): δ −179.19 (dddd, $J_{H1,F}$ 11, $J_{H2,F}$ 54, $J_{H3,F}$ 31, $J_{H4,F}$ 4 Hz, *α-ribo*), −198.73 (ddd, $J_{H1,F}$ 11, $J_{H2,F}$ 52, $J_{H3,F}$ 38 Hz, *α-arabino*), −202.81 (ddd, $J_{H1,F}$ 11, $J_{H2,F}$ 54, $J_{H3,F}$ 34 Hz, *β-arabino*), −207.29 (dd, $J_{H2,F}$ 52, $J_{H3,F}$ 21 Hz, *β-ribo*).

1-O-Acetyl-2-fluoro-5-iodo-3-C-methyl-2,3,5-trideoxy-pentofuranoses (**15**).—To a solution of 0.07 g (0.3 mmol) of **14** and 0.08 mL (0.6 mmol) of Et_3N in 11.7 mL of CH_2Cl_3 was added 0.02 mL (0.3 mmol) of AcCl. After stirring for 30 min at room temperature, the mixture was concentrated by evaporation. Chromatography of the residue over silica gel using CH_2Cl_2 as eluent yielded the anomeric acetate **15** (0.08 g, 100%); GC–MS: *m/z* 301.95 (parent peak); IR (neat): 2976 (m), 2939 (m), 2885 (w), 1748 (s C=O), 1460 (m), 1418 (m), 1375 (s), 1228 (s), 1172 (m), 1124 (s), 1010 9s), 787 (m), 710 (w) cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.34 (d, 1 H, $J_{H1,F}$ 10 Hz, C*H*OAc, *α-arabino*), 6.30 (d, 1 H, $J_{H1,F}$ 9 Hz, C*H*OAc, *α-ribo*), 6.26 (d, 1 H, $J_{H1,F}$ 5 Hz, C*H*OAc, *β-ribo*), 6.21 (d, 1 H, $J_{H1,F}$ 10 Hz, C*H*OAc, *β-arabino*), 4.86 (dd, 1 H, $J_{H2,H3}$ 4, $J_{H2,F}$ 52 Hz, C*H*F, *α-ribo*), 4.82 (dd, 1 H, $J_{H2,H3}$ 3, $J_{H2,F}$ 52 Hz, C*H*F, *β-arabino*), 4.75 (dd, 1 H, $J_{H2,H3}$ 2, $J_{H2,F}$ 51 Hz. C*H*F, *α-arabino*), 4.57 (ddd, $J_{H3,H4}$ 6, $J_{H4,H5} = J_{H4,H5} = 8$ Hz, –C*H*O–, *α-ribo*), 4.00 (ddd, 1 H, $J_{H3,H4}$ 1, $J_{H4,H5}$ 5, $J_{H4,H5}$ 8Hz, C*H*O, *α-arabino*), 3.72–3.80 (m, 1 H, C*H*O, *β-arabino*, *β-ribo*), 3.17–3.48 (m, 2 H, CH_2I), 2.56–2.73 (m, 1 H, $CHCH_3$), 2.25–2.42 (m, 1 H, $CHCH_3$), 2.11 [s, 3 H, C(O)CH_3, *β-arabino*, *β-ribo*], 2.06 (s, 3 H, C(O)CH_3, *α-ribo*), 2.04 (s, 3 H, C(O)CH_3, *α-arabino*), 1.27 [s, 3 H, C(O) CH_3, *β-ribo*], 1.26 (d, 3 H, J_{H3,CH_3} Hz, CHCH_3, *α-ribo*), 1.17 (d, 3 H, J_{H3,CH_3} 7 Hz, CHCH_3, *α-arabino*), 1.13 (d, 3 H, J_{H3,CH_3} 7 $J_{C,F}$ 1 Hz, CHCH_3, *α-ribo*). ^{13}C NMR ($CDCl_3$): δ 169.17 (*C*=O), 101.04 (d, $J_{C2,F}$ 181 Hz, *C*HF, *α-arabino*), 100.35 (d, $J_{C1,F}$ 38 Hz, *C*HOAc, *α-ribo*), 98.13 (d, $J_{C1,F}$ 34 Hz, *C*HOAc, *α-arabino*), 96.96 (d, $J_{C2,F}$ 185 Hz, *C*HF, *α-ribo*), 86.92 (*C*HO, *α-arabino*), 83.51 (*C*HO, *β-arabino*), 83.39 (*C*HO, *β-ribo*), 82.87 (*C*HO, *α-ribo*), 44.55 (d, $J_{C3,F}$ 22 Hz, $CHCH_3$, *α-arabino*), 41.49 (d, $J_{C3,F}$ 19 Hz, $CHCH_3$, *β-arabino*), 41.42 (d, $J_{C3,F}$ 21 Hz, $CHCH_3$, *β-ribo*), 37.83 (d, J_{C3F} 18 Hz, $CHCH_3$, *α-ribo*), 21.14 [C(O)*C*H_3, *β-arabino*, *β-ribo*], 21.03 [C(O)*C*H_3, *α-ribo*], 20.99 [C(O)*C*H_3, *α-arabino*], 16.34 (d, $J_{C,F}$ 8 Hz, CH*C*H_3, *α-arabino*), 9.50 (d, $J_{C,F}$ 9 Hz, CH*C*H_3), 8.47 (CH_2I), 7.45 (d, $J_{C,F}$ 10 Hz, CH*C*H_3, *α-ribo*), 6.80 (CH_2I, *α-ribo*), 4.71 (CH_2I, *α-arabino*); ^{19}F NMR ($CDCl_3$): δ −178.13 (ddd, $J_{H1,F}$ 11, $J_{H2,F}$ 51, $J_{H3,F}$ 31 Hz, *α-ribo*), −198.94 (ddd, $J_{H1,F}$ 8, $J_{H2,F}$ 52, $J_{H3,F}$ 33 Hz, *α-arabino*), −202.74 (dd, $J_{H2,F}$ 52, $J_{H3,F}$ 20 Hz, *β-ribo*), −203.24 (ddd, $J_{H1,F}$ 11, $J_{H2,F}$ 52, $J_{H3,F}$ 35 Hz, *β-arabino*).

Methyl 2-fluoro-5-iodo-3-C-methyl-2,3,5-trideoxy-pentofuranosides (**16**).—Dry HCl was bubbled through a solution of **14**, (0.08 g, 0.3 mol) in 10 mL of anhyd MeOH (cooled in an ice bath) until saturated. After stirring overnight, the mixture

was concentrated by evaporation. Chromatography of residue over silica gel using CH_2Cl_2 as eluent yielded **16** as a pink oil (0.08 g, 100%); GC–MS: *m/z* 274.10 (parent peak); IR (neat): 2968 (m), 2933 (m), 2834 (m) 1460 (m), 1416 (w), 1389 (m), 1366 (w), 1312 (w), 1248 (w), 1195 (m), 1106 (s), 1079 (m), 1052 (s), 1012 (m), 965 (m), 937 (m), 786 (m), 734 (m), 708 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.14 (d, 1 H, $J_{H1,F}$ 11 Hz, C*H*OMe, *α-ribo*), 5.09 (d, 1 H, $J_{H1,F}$ 11 Hz, C*H*OMe, *α-arabino*), 5.03 (d, 1 H, $J_{H1,F}$ 11 Hz, C*H*OMe, *β-arabino*), 4.84 (dd, 1 H, $J_{H2,H3}$ 4, $J_{H2,F}$ 53 Hz, C*H*F, *α-arabino*), 4.82 (dd, 1 H, $J_{H2,H3}$ 4, $J_{H2,F}$ 52 Hz, C*H*F, *β-arabino*), 4.71 (dd, 1 H, $J_{H2,H3}$ 2, $J_{H2,F}$ 52 Hz, C*H*F, *α-ribo*), 4.48 (ddd, 1 H, $J_{H4,F}$ 5, $J_{H4,H5}$ $J_{H4,H5'}$ 9 Hz, C*H*O, *α-ribo*), 3.92 (dd, 1 H, $H_{H4,H5}$ 9, $J_{H4,H5'}$ 12 Hz, C*H*O, *β-arabino*), 3.85 (dd, 1 H, $J_{H4,H5}$ 6, *J* H4,H5′ 11 Hz, C*H*O, *α-arabino*), 3.44 (s, 3 H, OCH_3, *β-arabino*), 3.43 (d, $J_{H4,H5}$ 9 Hz, CHI-*H*, *β-arabino*), 3.43 (s, 3 H, OCH_3, *α-ribo*), 3.42 (d, 1 H, $J_{H4,H5'}$ 12 Hz, CHI-*H*, *β-arabino*), 3.41 (s, 3 H, OCH_3, *α-arabino*), 3.37 (d, 1 H, $J_{H4,H5}$ 9 Hz, CHI-*H*, *α-ribo*), 3.35 (d, 1 H, $J_{H4,H5'}$ 9 Hz, CHI-*H*, *α-ribo*), 3.27 (d, 1 H, $J_{H4,H5}$ 6 Hz, CHI-*H*, *α-arabino*), 3.24 (d, 1 H, $J_{H4,H5'}$ 11 Hz, CHI-*H*, *α-arabino*), 2.66 (ddq, 1 H, $J_{H2,H3}$ 4, $J_{H3,F}$ 34, J_{H3,CH_3} 7 Hz, C*H*CH_3, *α-ribo*), 2.13–2.35 (m, 1 H, C*H*CH_3, *β-arabino*, *α-arabino*), 1.26 (d, 3 H, J_{H3,CH_3} 7 Hz, CH_3, *α-ribo*), 1.22 (dd, 3 H, J_{H3,CH_3} 7, $J_{CH_3,F}$ 1 Hz, CH_3, *β-arabino*), 1.17 (dd, 3 H, J_{H3,CH_3} 7, $J_{CH_3,F}$ 1 Hz, CH_3, *α-arabino*); ^{13}C NMR ($CDCl_3$): δ 107.34 (d, $J_{C1,F}$ 36 Hz, *C*HOMe, *α-ribo*), 106.12 (d, $J_{C1,F}$ 33 Hz, *C*HOMe, *β-arabino*), 105.34 (d, $J_{C1,F}$ 32 Hz, *C*HOMe, *α-arabino*), 101.79 (d, $J_{C2,F}$ 178 Hz, *C*HF, *α-arabino*), 97.77 (d, $J_{C2,F}$ 180 Hz, *C*HF, *β-arabino*), 97.40 (d, $J_{C2,F}$ 182 Hz, *C*HF, *α-ribo*), 84.64 (*C*HO, *α-arabino*), 83.97 (*C*HO, *α-ribo*), 81.22 (*C*HO, *β-arabino*), 55.02 (O*C*H_3, *α-ribo*), 54.85 (O*C*H_3, *β-arabino*), 54.75 (O*C*H_3, *α-arabino*), 45.17 (d, $J_{C3,F}$ 20 Hz, *C*H*C*H_3, *α-arabino*), 41.70 (d, $J_{C3,F}$ 21 Hz, *C*H*C*H_3, *α-ribo*), 38.01 (d, $J_{C3,F}$ 17 Hz, *C*H*C*H_3, *β-arabino*), 16.04 (CH*C*H_3, *α-arabino*), 10.14 (d, $J_{C,F}$ 11 Hz, *C*H_3, *β-arabino*), 9.15 (*C*H_2I, *α-ribo*), 7.44 (*C*H_2I, *β-arabino*), 7.40 (d, $J_{C,F}$ 7 Hz, *C*H_3, *α-ribo*), 6.11 (*C*H_2I, *α-arabino*); ^{19}F NMR ($CDCl_3$): δ −179.57 (ddd, $J_{H1,F}$ 11, $J_{H2,F}$ 52, $J_{H3,F}$ 31 Hz, *α-ribo*), −200.01 (dddd, $J_{H1,F}$ 11, $J_{H2,F}$ 53, $J_{H3,F}$ 34, $J_{CH_3,F}$ 1 Hz, *α-arabino*), −203.57 (dddd, $J_{H1,F}$ 11, $J_{H2,F}$ 52, $J_{H3,F}$ 34, $J_{CH_3,F}$ 1 Hz, *β-arabino*).

2,3-Dideoxy-2-fluoro-3-C-methyl-xylono-1,4-lactone (**18**) *via epoxide* **17**.—A 1 M solution of potassium *tert*-butoxide in THF (2.5 mL) was added to a solution of benzyl alcohol (0.36 mL, 3.19 mmol) in THF under Ar with stirring. To the solution was added a solution of 2-fluoro-5-iodo-3-*C*-methyl-2,3,5-trideoxy-arabinono-1,4-lactone (0.58 g, 2.25 mmol) in THF (4 mL) at 0°C. The solution was stirred for 30 min. Ether (20 mL) and water (20 mL) were added to the solution, and the organic layer was separated, washed with brine, dried with anhyd $MgSO_4$, and evaporated. To the residue were added 1,4-dioxane (7 mL) and 10% Pd–C (0.05 g). The flask which contained the mixture was evacuated and then H_2 was introduced into the flask. The mixture was vigorously stirred for 3 h and was then filtered to remove the catalyst. The filtrate was evaporated and the residue was purified by chromatography (25 : 1 CH_2Cl_2–acetone) to give **18** (0.20 g, 60%); ^1H

NMR ($CDCl_3$): δ 5.13 (dd, 1 H, $J_{2,F}$ 53.4, $J_{2,3}$ 10.0 Hz, H-2), 4.48 (dm, 1 H, $J_{3,4}$ 8.2 Hz, H-4), 3.90 (dt, 1 H, $J_{4,5} = J_{3,5} = 2.4$, $J_{5,5'}$ 12.7 Hz, H-5), 3.72 (dd, 1 H, $J_{4,5'}$ 1.4, $J_{5,5'}$ 12.7 Hz, H-5'), 2.7–2.9 (m, 1 H, H-3), 2.35–2.65 (br, 1 H, –OH), 1.28 (d, 3 H, *J* 7.7 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 90.3 (d, *J* 190.3 Hz, C-2), 80.2 (d, *J* 8.0 Hz, C-4), 60.4 (s, C-5), 39.6 (d, *J* 19.2 Hz, C-3), 11.6 (s, Ch_3). ^{19}F NMR ($CDCl_3$): δ −194.5 (dd, *J* 26.0, $J_{2,F}$ 53.0 Hz). Anal. Calcd for $C_6H_9FO_3$: C, 48.65; H, 6.08. Found: C, 48.61; H, 6.02.

Benzyl syn-*2-fluoro-3-methyl-4-pentenoate* (**22**).—To a mixture of *syn*-2-fluoro-3-methyl-4-pentenoic acid **9** (0.80 g, 6.06 mmol) and K_2CO_3 (1.10 g, 8.09 mmol) in DMF was added ~ benzyl bromide (1.1 mL, 9.25 mmol) at room temperature, and the mixture was stirred vigorously for 16 h. Ether (30 mL) and water (30 mL) were added to the mixture. The organic layer was separated, washed with water twice, dried with $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel using 1:35 EtOAc–hexane as eluent to give pure **22** (1.31 g, 98%); ^1H NMR ($CDCl_3$): δ 7.3–7.5 (s, 5 H, Ar), 5.75 (ddd, 1 H, $J_{3,4}$ 7.1, $J_{4,5}$ 9.8, $J_{4,5'}$ 18.0 Hz, H-4), 5.20 (s, 2 H, CH_2), 5.04 (d, 1 H, $J_{4,5}$ 9.8 Hz, H-5), 5.30 (d, 1 H, $J_{4,5'}$ 18.0 Hz, H-5'), 2.65–2.9 (m, 1 H, H-3), 1.14 (d, 3 H, J_{3,CH_3} 7.8 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 168.7 (d, *J* 24.1 Hz, C-1), 160.7 (s, ph), 136.2 (d, *J* 3.7 Hz, C-4), 128.6–128.5 (ph), 117.1 (s, C-5), 91.9 (d, *J* 189.5 Hz, C-2), 66.9 (s, CH_2Ph), 40.8 (d, *J* 20.2 Hz, C-3), 15.8 (d, *J* 2.3 Hz, C(3)-CH_3); ^{19}F NMR ($CDCl_3$): δ −200.5 (dd, $J_{2,F}$ 49.0, $J_{3,F}$ 27.7 Hz); *Anal.* Calcd. for $C_{13}H_{15}FO_2$: C, 70.27; H, 6.76. Found: C, 70.24; H, 6.86.

Benzyl anti-*2-fluoro-3-methyl-4-pentenoate* (**19**).—The experimental procedure was as for the formation of compound **22**, and gave **19** in quantitative yield; ^1H NMR ($CDCl_3$): δ 7.45–7.24 (m, 5 H, Ph), 5.79 (ddd, 1 H, $J_{3,4}$ 7.3, $J_{4,5}$ 10.2, $J_{4,5'}$ 16.8 Hz, H-4), 5.20 (s, 2 H, OCH_2), 5.17 (d, 1 H, *J* 16.3 Hz, H-5'), 5.10 (d, 1 H, *J* 10.2 Hz, H-5), 4.84 (dd, 1 H, *J* 4.0 *J* 48.9 Hz, H-2), 2.63–2.90 (m, 1 H, H-3'), 1.05 (d, 3 H, *J* 7.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 168.8 (d, *J* 24.0 Hz, C=O), 160.8 (s, Ph), 137.5 (d, *J* 2.3 Hz, C-4), 128.3–128.8 (m, Ph), 116.5 (s, C-5), 91.6 (d, *J* 189.4 Hz, C-2), 67.0 (s, OCH_2), 40.5 (d, *J* 21.6 Hz, C-3), 13.7 (d, *J* 5.0 Hz, CH_3); ^{19}F NMR ($CDCl_3$): δ −199.5(dd, $J_{2,F}$ 48.9, $J_{3,F}$ 29.5 Hz). Anal. Calcd for $C_{13}H_{15}FO_2$: C, 70.27; H, 6.76. Found: C, 70.34; H, 6.79.

2,3-Dideoxy-2-fluoro-3-C-methyl-arabinono- and -xylono-1,4-lactones (**18** *and* **21**).—Osmium tetraoxide (4 wt.% solution in toluene, 2.0 mL) was added to the solution of benzyl *anti*-2-fluoro-3-methyl-4-pentenoate (1.43 g, 6.44 mmol) in acetone (25 mL) at room temperature, and the solution was stirred in the dark for 5 min. Trimethylamine *N*-oxide dihydrate (2.0 g, 18.0 mmol) was added and then water (6 mL), and the solution was stirred in the dark for 16 h at room temperature. Sodium sulfite (1.1 g) was added and then the solution was evaporated. Potassium hydroxide (0.50 g, 8.93 mmol) in 10:1 MeOH–H_2O (11 mL) was added to the mixture and the solution was stirred for 30 min. Concentrated HCl (1.0 mL) was added to the solution, which was then evaporated to dryness. Acetonitrile (25 mL) was added to the residue and the solution was refluxed for 3

h. After cooling, CH_2Cl_2 (50 mL) and water (50 mL) were added. The organic layer was separated, dried with anhyd $MgSO_4$ and evaporated. The residue was purified with column chromatography on silica gel using 30:1 CH_2Cl_2–acetone as eluent to give **18** and **21** (0.13 g, 13.6%).

Spectral data for **21**. ^{1}H NMR ($CDCl_3$): δ 4.84 (dd, 2 H, $J_{2,F}$ 52.0, $J_{2,3}$ 10.2 Hz, H-2), 4.05 (ddd, 1 H, $J_{4,5}$ 2.4, $J_{4,5'}$ 4.6, $J_{3,4}$ 9.8 Hz, H-4), 3.92 (dt, 1 H, $J_{4,5}$ 2.4, $J_{3,5}$ 2.4, $J_{5,5'}$ 13.2 Hz, H-5), 3.64 (dd, 1 H, $J_{4,5'}$ 4.6, $J_{5,5'}$ 13.2 Hz, H-5′) ~3.0 (br, 1 H, OH), 2.6–2.8 (m, 1 H, H-3), 1.23 (d, 3 H, J_{3,CH_3} 7.0 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 171.2 (d, J 22.5 Hz, C-1), 91.7 (d, J 197.8 Hz, C-2), 82.2 (d, J 7.6 Hz, C-4), 60.8 (s, C-5), 37.4 (d, J 19.4 Hz, C-3), 13.5 (s, CH_3); ^{19}F NMR ($CDCl_3$): δ −200.23 (dd, $J_{2,F}$ 52.0, $J_{3,F}$ 21.9 Hz). Anal. Calcd for $C_6H_9FO_3$: C, 48.65; H, 6.08. Found: C, 48.49; H, 5.95.

Spectral data for **18**. Compound **18** prepared in this way gave spectral data and elemental analysis identical to those already described.

2,3-Dideoxy-2-fluoro-3-methyl-arabinono- and -xylono-1,4-lactones (**18** *and* **21**) *via the epoxides* **17** *and* **20**.—3-Chloroperoxybenzoic acid (50–60%, 2.5 g) was added to a solution of benzyl *anti*-2-fluoro-3-methyl-4-pentenoate (1.50 g, 6.76 mmol) in $CHCl_3$ (20 mL) and the mixture was refluxed for 2 h. After cooling, the mixture was filtered to remove 3-chlorobenzoic acid, the filtrate was washed with satd Na_2SO_3 and water, dried with anhyd $MgSO_4$ and evaporated to give the crude epoxides. A small amount was purified by column chromatography on silica gel (10:1 *n*-hexane–EtOAc) for analysis. To the crude epoxides were added 1,4-dioxane (15 mL) and 10% Pd–C (0.10 g). The flask which contained the mixture was evacuated and H_2 was introduced. The mixture was vigorously stirred for 3 h at room temperature and was then filtered to remove the catalyst. The filtrate was evaporated and the residue was purified by chromatography (25:1 CH_2Cl_2–acetone) to give **18** (0.41 g, 41%) and **21** (0.17 g, 17.0%).

Spectral data. Compounds **18** and **21** prepared in this way gave spectral data and elemental analyses identical to those already described.

2,3-Dideoxy-2-fluoro-3-methyl-ribono- and -lyxono-1,4-lactones (**24** *and* **23**).—Trimethylamine oxide dihydrate (7.0 g, 63.1 mmol) was added to a solution of **22** (5.3 g, 23.9 mmol) in acetone (60 mL) and water (10 mL). Osmium tetraoxide (4 wt% solution in toluene, 5 mL) was added to the solution in the dark at room temperature with stirring. The solution was stirred overnight. Sodium sulfite (4.0 g) was added and the solution was then evaporated to dryness. Acetonitrile (50 mL) was added and the solution was refluxed for 4 h. After cooling, CH_2Cl_2 (200 mL) and water (100 mL) were added, and the organic layer was separated, washed with water, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by chromatography (30:1 CH_2Cl_2–acetone) to give **24** (1.15 g, 32.5%) and **23** (0.40 g, 11.3%).

Spectral data for **23**. ^{1}H NMR ($CDCl_3$): δ 5.24 (dd, 1 H, $J_{2,3}$ 7.0, $J_{2,F}$ 51.0 Hz, H-2), 4.58 (m, 1 H, H-4), 3.89 (dd, 1 H, $J_{4,5}$ 7.2, $J_{5,5'}$ 12.1 Hz, H-5), 3.80 (dd, 1 H, J_4,5′ 3.7, $J_{5,5'}$ 12.1 Hz, H-5′), 1.06 (dd, 3 H, J_{3,CH_3} 7.0, J_{F,CH_3} 2.3 Hz, C(3)-CH_3):

^{13}C NMR ($CDCl_3$): δ 171.8 (d, *J* 22.2 Hz, C-1), 87.8 (d, *J* 198.5 Hz, C-2), 79.8 (d, *J* 5.6 Hz, C-4), 61.3 (s, C-5), 35.8 (d, *J* 18.3 Hz, C-3) Hz, 6.2 (d, *J* 9.2 Hz, C(3)-CH_3); ^{19}F NMR ($CDCl_3$): δ −208.5 (dd, $J_{2,F}$ 51.0, $J_{3,F}$ 11.0 Hz). Anal. Calcd for $C_6H_9FO_3$: C, 48.65; H, 6.08. Found: C, 48.49; H, 5.95.

Spectral data for **24**. ^1H NMR ($CDCl_3$): δ 5.25 (dd, 1 H, $J_{2,3}$ 6.6, $J_{2,F}$ 52.5 Hz, H-2), 4.32 (m, 1 H, H-4), 3.98 (dd, 1 H, $J_{4,5}$ 2.4, $J_{5,5'}$ 12.7 Hz, H-5), 3.70 (dd, H-1, $J_{4,5'}$ 3.0, *J* 5,5′ 12.7 Hz, H-5′), 2.6–2.85 (m, 1 H, H-3), 1.20 (dd, 3 H, J_{3,CH_3} 6.6, J_{F,CH_3} 2.4 Hz, C(3)-CH_3); ^{13}C NMR ($CDCl_3$): δ 172.5 (d, *J* 20.8 Hz, C-1), 87.6 (d, *J* 191.2 Hz, C-2), 85.8 (s, C-4), 61.8 (s, C-5), 35.5 (d, *J* 19.3 Hz, C-3), 10.7 (d, *J* 10.9 Hz, C(3)-CH_3); ^{19}F NMR ($CDCl_3$): δ −207.7 (dd, $J_{3,F}$ 20.4, $J_{2,F}$ 51.6 Hz). Anal. Calcd. for $C_6H_9FO_3$: C, 48.65; H, 6.08. Found: C, 48.61; H, 6.02.

*5-O-(*tert*-Butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-methyl)-arabinono-1,4-lactone* (**25**).—To a solution of **21** (0.11 g, 0.74 mmol) in DMF (3 mL) was added imidazole (0.08 g, 1.17 mmol) and *t*-butylchlorodimethylsilane (0.15 g, 1.00 mmol) at room temperature. The solution was stirred overnight at room temperature. Ethyl acetate (10 mL) and water (10 mL) were added, and the organic layer was separated, washed with water, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by column chromatography (6:1 *n*-hexane–EtOAc) to give **25** (0.18 g 92.4%); ^1H NMR ($CDCl_3$): δ 4.86 (dd, 1 H, $J_{2,3}$ 9.9, $J_{2,F}$ 52.0 Hz, H-2), 4.05 (dt, 1 H, $J_{4,5} = J_{4,5'}$ 3.7, $J_{3,4}$ 9.2 Hz, H-4), 3.94 (ddd, 1 H, $J_{3,5}$ 1.4, $J_{4,5}$ 3.7, $J_{5,5'}$ 12.3 Hz, H-5), 3.78 (dd, 1 H, $J_{4,5'}$ 3.7, $J_{5,5'}$ 12.3 Hz, H-5′), 1.29 [d, 3 H, J_{3,CH_3} 7.0 Hz, C-(3)-CH_3], 0.90 (s, 9 H, *t*-Bu), 0.09 [s, 6 H, $Si(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ 213.3 (d, *J* 4.6 Hz, C-1), 91.8 (d, *J* 196.6 Hz, C-2), 81.8 (d, *J* 9.5 Hz, C-4), 61.5 (s, C-5), 37.6 (d, *J* 19.4 Hz, C-3), 25.7 [s, $(CH_3)_3C$], 18.4 [s, $(CH_3)_3C$], 13.8 [s, C-(3)-CH_3]. ^{19}F NMR ($CDCl_3$): δ −199.7 (dd, $J_{3,F}$ 21.0, $J_{2,F}$ 52.2 Hz). Anal. Calcd for $C_{12}H_{23}Fo_3Si$: C, 54.96; H, 8.78 Found: C, 54.80; H, 8.73.

*5-*tert*-Butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-C-methyl-arabinofuranose* (**26**).—Diisobutylaluminum hydride (0.70 mL, 3.93 mmol) was added to a solution of **25** (0.98 g, 3.74 mmol) in Et_2O (20 mL) under an inert atmosphere at −78°C. The reaction was stirred for 1.5 h at −78°C and then quenched with MeOH (0.5 mL). The mixture was allowed to warm to room temperature and satd NH_4Cl (3 mL) and CH_2Cl_2 were added. The mixture was filtered and the filtrate was washed with water, dried with anhyd $MgSO_4$, and evaporated to give **26** (0.95 g, 96.2%). This product was used for the next reaction without further purification.

Spectral data for **26α**. ^1H NMR ($CDCl_3$): δ 6.26 (d, 1 H, $J_{1,2}$ 4.5, $J_{1,F}$ 0, H-1), 4.65 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 9.1, $J_{2,F}$ 53.4 Hz, H-2), 3.65–3.8 (m, 3 H, H-4, H-5, H-5′), 2.35–2.5 (m, 1 H, H-3), 2.09 (s, 3 H, Ac), 1.21 [d, 3 H, J_{3,CH_3} 7.0 Hz, C(3)-CH_3], 0.91 (s, 9 H, *t*-Bu), 0.07 [s, 6 H, $Si(CH_3)_2$]; ^{13}C NMR ($CDCl_3$); δ 169.8 (s, O-C-CH_3), 95.1 (d, *J* 199.7 Hz, C-2), 93.0 (d, *J* 18.5 Hz, C-1), 84.3 (d, *J* 8.7 Hz, C-4), 64.9 (s, C-5), 37.0 (d, *J* 17.6 Hz, C-3), 25.8 [s, $C(CH_3)_3$], 21.2 [s, $OCCH_3$], 18.3 [s, $C(CH_3)_3$], 14.4 [s, C-(s)-CH_3]. ^{19}F NMR ($CDCl_3$): δ −204.9 dd, $J_{3,F}$ 18.5, $J_{2,F}$ 53.4 Hz).

Spectral data for **26β**. ^1H NMR ($CDCl_3$): δ 6.27 (d, 1 H, $J_{1,2}$ 0, $J_{1,F}$ 10.7 Hz,

H-1), 4.72 (dd, 1 H, $J_{2,3}$ 2.0, $J_{2,F}$ 52.7 Hz, H-2), 3.91 (1 H, H-4), 3.78 (dd, 1 H, $J_{4,5}$ 4.2, $J_{5,5'}$ 10.8 Hz, H-5), 3.68 (dd, 1 H, $J_{4,5'}$ 6.0, $J_{5,5'}$ 10.8 Hz, H-5'), 2.2–2.5 (m, 1 H, H-3), 2.08 (s, 3 H, Ac), 1.23 [d, 3 H, J_{3,CH_3} 7.3 Hz, C(3)-CH_3], 0.90 (s, 9H, *t*-Bu), 0.07 [s, 6 H, $Si(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 169.3 (s, $OCCH_3$), 101.6 (d, J 182.9 Hz, C-2), 100.3 (d, J 35.1 Hz, C-1), 87.4 (s, C-4), 64.1 (s, C-5), 40.9 (d, J 21.6 Hz, C-3), 25.8 [s, $C(CH_3)_3$], 21.0 (s, $OCCH_3$), 18.2 [s, $C(CH_3)_3$], 15.7 [d, J 7.0 Hz, C(3)-CH_3]. ^{19}F NMR ($CDCl_3$): δ −179.7 (ddd, $J_{1,F} \sim 10$, $J_{2,F}$ 51.6, $J_{3,F}$ 31.7 Hz).

*1-O-Acetyl-5-O-*tert*-butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-C-methylarabino-furanose* (**27**).— Acetyl chloride (0.30 mL, 4.20 mmol) was added to a solution of **26** (0.95 g, 3.60 mmol) and Et_3N (0.70 mL, 5.03 mmol) in CH_2Cl_2 (7 mL) at 0°C with stirring. The mixture was stirred for 2 h at room temperature, and was then washed with water twice, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel using 5:1 *n*-hexane–EtOAc as eluant to give pure **27** (1.02 g, 92.6%); ^1H NMR ($CDCl_3$): δ 6.16 (d, 1 H, $J_{1,2}$ 0, $J_{1,F}$ 10.0 Hz, H-1), 4.75 (dd, 1 H, $J_{1,2}$ 0, $J_{2,3}$ 4.1, $J_{2,F}$ 52.3 Hz, H-2), 3.89 (dt, 1 H, $J_{4,5} = J_{4,5'} = 4.5$, $J_{3,4}$ 9.2 Hz, H-4), 3.72 (dd, 1 H, $J_{4,5}$ 4.6, $J_{5,5'}$ 11.3 Hz, H-5), 3.65 (dd, 1 H, $J_{4,5'}$ 4.5, $J_{5,5'}$ 11.3 Hz, H-5'), 1.98 (s, 3 H, Ac), 1.10 [d, 3 H, J_{3,CH_3} 6.8 Hz, C(3)-CH_3], 0.85 [s, 9 H, S:$C(CH_3)_3$], 0.01 [s, 6H, $Si(CH_3)$]; ^{13}C NMR ($CDCl_3$): δ 169.2 (s, O=*C*=OCH_3), 98.7 (d, J 31.0 Hz, C-1), 97.2 (d, J 182.4 Hz, C-2), 86.1 (s, C-4), 63.7 (s, C-6), 36.5 (d, J 19.0 Hz, C-3), 25.8 [s, S:$C(CH_3)_3$], 21.0 (s, O-C-CH_3), 18.3 [s, $SiC(CH_3)_3$], 9.0 [d, J 7.7 Hz, C(3)-CH_3)]; ^{19}F NMR ($CDCl_3$): (main:minor 4.6:1) δ −203.9 (ddd, $J_{1,F}$ 8.5, $J_{2,F}$ 51.6, $J_{3,F}$ 37.3 Hz, main), −211.0 (ddd, $J_{1,F}$ 11.0, $J_{2,F}$ 52.0, $J_{3,F}$ 22.0 Hz, minor). Anal. Calcd for $C_{14}H_{27}FO_4Si$: C, 54.90; H, 8.82. Found: C, 55.06; H, 8.64.

*1-(5-*tert*-Butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-C-methyl-β- and α-arabino-furanosyl)thymine* (**33** *and* **34**).—Compound **27** (0.40 g, 1.31 mmol) in toluene (7 mL) was added at room temperature to a 3-necked flask containing dibenzo-18-crown-6 (0.09 g, 0.25 mmol) and KI (0.26 g, 1.57 mmol) under Ar. To the solution was added 2,4-bis(trimethylsilyl)thymine in MeCN (7 mL), which was prepared from thymine (0.24 g, 1.90 mmol), hexamethyldisilazane, and a catalytic amount of $(NH_4)_2SO_4$. The mixture was refluxed for 4 h with vigorous stirring. After cooling, CH_2Cl_2 (30 mL) and water (30 mL) were added. The organic layer was separated, washed with water, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by chromatography (12:1 CH_2Cl_2–acetone) to recover the starting material (0.23 g) and to give **33**, α anomer (0.14 g, 28.8%) mp 132–134°C and **34**, β anomer (0.04 g, 8.2%) mp 131–33°C.

Spectral data for **33**. ^1H NMR ($CDCl_3$): δ 9.9–9.6 (br, 1 H, NH), 7.42 (s, 1 H, H-6), 6.12 (dd, 1 H, $J_{1',2'}$ 4.0, $J_{1',F}$ 16.4 Hz, H-1'), 4.86 (dt, 1 H, $J_{1',2'} = J_{2',3'} = 4.0$, $J_{2',F}$ 54.3 Hz, H-2'), 3.87 (dd, 1 H, $J_{4',5'a}$ 4.2, $J_{5',5'b}$ 11.2 Hz, H-5'a), 3.78 (dd, 1 H, $J_{4',5'b}$ 4.2, $J_{5'a,5'b}$ 11.2 Hz, H-5'b), 3.67 (dt, 1 H, $J_{4',5'a} = J_{4',5'b} = 4.2$, $J_{3',4'}$ 6.7 Hz, H-4'), 2.4–2.6 (m, 1 H, H-3'), 1.92 (s, 3 H, Ac), 1.19 [d, 3 H, J_{3',CH_3} 7.4 Hz, C-3(3')-CH_3], 0.93 (s, 9 H, *t*-Bu), 0.11 [s, 6-H, $Si(CH_3)_2$]; ^{13}C NMR ($CDCl_3$): δ 163.9 (s, C-4), 150.5 (s, C-2), 136.6 (d, J 4.1 Hz, C-6), 109.9 (s, C-5), 96.6 (d, J 192.0

Hz, C-2'), 84.0 (d, J 4.3 Hz, C'-4), 83.6 (d, J 16.3 Hz, C-1'), 62.9 (s, C-6'), 39.8 (d, J 21.2 Hz, C-3'), 25.8 [s, C(CH_3)$_3$], 18.3 [s, C(CH_3)$_3$], 15.3 [d, J 4.7 Hz, C(3')-CH_3], 12.4 [s, C(4)-CH_3], −5.4 (s, Si-CH_3), −5.5 (s, Si-CH_3); ^{19}F NMR ($CDCl_3$): δ −188.8 (ddd, $J_{1',F}$ 16.4, $J_{2',F}$ 54.3, $J_{3',F}$ 26.0 Hz). Anal. Calcd for $C_{17}H_{29}FN_2O_4Si$: C, 54.84; H, 7.80; N, 7.53. Found: C, 54.74; H, 8.00; N, 7.46.

1-(2,3-Dideoxy-2-fluoro-3-C-methyl-α-arabinofuranosyl)thymine (**35**).—A 1 M solution of tetrabutylammonium fluoride in THF (0.30 mL) was added to a solution of compound **33** (0.07 g, 0.12 mmol) at room temperature with stirring. The solution was stirred for 2 h and then CH_2Cl_2 (25 mL) and water (5 mL) were added. The organic layer was separated, washed with brine, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by chromatography (10:1 CH_2CH_2–EtOH) to give **35** (0.05 g, quantitative yield), mp 156–157°C; ^{1}H NMR (acetone): δ 7.82 (t, 1 H, J 1.7 Hz, H-6), 6.15 (dd, 1 H, $J_{1',2'}$ 5.0, $J_{1',F}$ 11.3 Hz, H-1'), 5.02 (dt, 1 H, $J_{1',2'} = J_{2',3'} = 5.0$, $J_{2',F}$ 54.8 Hz, H-2'), 3.7–3.9 (m, 1 H, H-4', H-5'a, H-5'b), 1.82 [d, 3 H, J 1.7 Hz, C-(5)-CH_3], 1.21 [d, 3 H, J_{3',CH_3} 6.7 Hz, C(3')-CH_3]; ^{13}C NMR (acetone): 175.6 (s, C-4), 151.2 (s, C-2), 137.6 (d, J 4.1 Hz, C-6), 109.6 (s, C-5), 97.9 (d, J 191.4 Hz, C-2'), 84.5 (d, J 6.6 Hz, C-4'), 83.5 (d, J 17.3 Hz, C-1'), 61.6 (s, C-5'), 39.3 (d, 1J 20.2 Hz, C-3'), 14.3 [d, J 2.9 Hz, C(3')-CH_3], 12.5 [s, C(5)-CH_3]; ^{19}F NMR (acetone): δ −191.8 (ddd, $J_{1',F}$ 11.3, $J_{2',F}$ 54.8, $J_{3',F}$ 27.0 Hz). Anal. Calcd for $C_{11}H_{15}FN_2O_4$: C, 51.16; H, 5.81; N, 10.85; Found: C, 51.34; H, 6.00; N, 10.66.

Crystal data for **35**. $C_{11}H_{15}FN_2O_4$, monoclinic, space group $P2_1/c$, $a = 5.682(2)$ Å, $b = 13.134(6)$ Å, $c = 16.127(7)$ Å, $V = 1203.5$ Å^3. $D_c = 1.425$ g cm^{-3}, $\mu = 1.1$, $Z = 4$, λ (Mo$K\alpha$) = 0.71073 Å (graphite monochromator), $T = 298$ K. A Nicolet R3m/V diffractometer was used to collect 3042 reflections ($3° < 2\theta < 55°$) on a colorless crystal, $0.20 \times 0.25 \times 0.60$ mm^3. Of these, 2782 were unique and 1484 observed ($F_o > 6\sigma F_o$). Lorentz and polarization corrections were applied to the data. All of the nonhydrogen atoms were located by direct methods. $R = 0.0565$, $R_w = 0.0569$, GOF = 2.0220.

1,5-Di-O-acetyl-2,3-dideoxy-2-fluoro-3-C-methyl-arabinofuranose (**28**).—To a solution of **27** (0.50 g, 1.63 mmol) in THF (5 mL) was added a 1 M solution of tetrabutylammonium fluoride in THF (2.0 mL) at room temperature with stirring. The stirring was continued for 30 min, and then CH_2Cl_2 (25 mL) was added. The organic layer was separated, washed with brine, dried with anhyd $MgSO_4$, and evaporated. To the residue were added CH_2Cl_2 (5 mL) and Et_3N (0.45 mL, 3.23 mmol). Acetyl chloride (0.25 mL, 2.10 mmol) was added at 0°C with stirring. The stirring was continued for 2 h at room temperature. Dichloromethane (25 mL) and water (10 mL) were added. The organic layer was separated, washed with brine, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by column chromatography (4:1 n-hexane–acetone) to give **28** (0.30 g, 78.5%); ^{1}H NMR ($CDCl_3$): δ 6.27 (d, 1 H, $J_{1,2}$ 0, $J_{1,F}$ 10.8 Hz, H-1), 4.70 (dd, 1 H, $J_{1,2}$ 0, $J_{2,3}$ 2.4, $J_{2,F}$ 52.0 Hz, H-2), 4.0–4.25 (m, 3 H, H-4, H-5, H-5'), 2.1–2.3 (m, H-3), 2.04, 2.03 (6 H, Ac), 1.20 [d, 3 H, J_{3,CH_3} 7.2 Hz, C(3)-CH_3]; ^{13}C NMR ($CDCl_3$): δ 170.6 (s,

-OCO-CH_3), 169.0 (s, -O*C*O-CH_3), 100.9 (d, *J* 181.8 Hz, C-2), 100.0 (d, *J* 37.4 Hz, C-1), 84.5 (s, C-4), 64.4 (s, C-5), 40.9 (d, *J* 21.5 Hz, C-3), 20.8 (s, OCO-*C*H_3), 20.6 (s, -OCO-*C*H_3), 15.2 [d, *J* 7.0 Hz, C(3)-CH_3]; ^{19}F NMR ($CDCl_3$): δ −179.8 (ddd, $J_{1,F}$ 10.7, $J_{2,F}$ 51.7, $J_{3,F}$ 32.6 Hz), −205.0 (dd, $J_{1,F}$ 0, $J_{2,F}$ 57.0, $J_{3,F}$ 18.6 Hz). Anal. Calcd for $C_{10}H_{15}FO_5$: C, 51.28; H, 6.41. Found: C, 51.45; H, 6.62.

*5-*O*-tert-Butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-*C*-methyl-ribofuranose* (**30**).—Diisobutylaluminum hydride (0.75 mL, 4.21 mmol) was added to a solution of *5-O-tert*-butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-methyl-ribono-1,4-lactone (**29**; 1.03 g, 3.93 mmol) in Et_2O (20 mL) at −78°C with stirring. The solution was stirred for 1 h at −78°C. Workup was as for the formation of *5-O-tert*-butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-*C*-methyl-arabinose to yield **30** (1.01 g, 97.3%).

*1-*O*-Acetyl-5-*O*-tert-butyldimethylsilyl-2,3-dideoxy-2-fluoro-3-*C*-methyl-ribofuranose* (**31**).—The experimental procedure was as for the formation of compound **27** with a yield of 83.7%; ^{1}H NMR ($CDCl_3$): δ 6.16 (d, 1 H, $J_{1,2}$ 0, $J_{1,F}$ 10.0 Hz, H-1), 4.75 (dd, 1 H, $J_{1,2}$ 0, $J_{2,3}$ 4.1, $J_{2,F}$ 52.3 Hz, H-2), 3.89 (dt, 1 H, $J_{4,5} = J_{4,5'} = 4.5$, $J_{3,4}$ 9.2 Hz, H-4), 3.72 (dd, 1 H, $J_{4,5}$ 4.6, $J_{5,5'}$ 11.3 Hz, H-5), 3.65 (dd, 1 H, $J_{4,5'}$ 4.5, $J_{5,5'}$ 11.3 Hz, H-5′), 1.98 (s, 3 H, Ac), 1.10 [d, 3 H, J_{3CH_3} 6.8 Hz, C(3)-CH_3], 0.85 [s, 9 H, S:C(C*H*$_3$)$_3$], 0.01 [s, 6 H, Si(C*H*$_3$)$_2$]; ^{13}C NMR ($CDCl_3$): δ 169.2 (s, O=*C*=OCH$_3$), 98.7 (d, *J* 31.0 Hz, C-1), 97.2 (d, *J* 182.4 Hz, C-2), 86.1 (s, C-4), 63.7 (s, C-6), 36.5 (d, *J* 19.0 Hz, C-3), 25.8 [s, SiC(*C*H$_3$)$_3$], 21.0 (s, O-C-*C*H$_3$), 18.3 [s, Si*C*(CH$_3$)$_3$], 9.0 [d, *J* 7.7 Hz, C(3)-*C*H$_3$)]; ^{19}F NMR ($CDCl_3$): (main : minor 4.6 : 1) δ −203.9 (dd, $J_{1,F}$ 8.5, $J_{2,F}$ 51.6, $J_{3,F}$ 37.3 Hz, main), −211.0 (ddd, $J_{1,F}$ 11.0, $J_{2,F}$ 52.0, $J_{3,F}$ 22.0 Hz, minor) Anal. Calcd for $C_{14}H_{27}FO_4Si$: C, 54.90; H, 8.82. Found: C, 55.20; H, 8.65.

*1,5-Di-*O*-acetyl-2,3-dideoxy-2-fluoro-3-*C*-methyl-ribofuranose* (**32**).—The experimental procedure was as for the formation of compound **28**; ^{1}H NMR ($CDCl_3$): δ 6.20 (d, 1 H, $J_{1,2}$ 0, Hz, $J_{1,F}$ 9.8 Hz, H-1), 4.76 (dd, 1 H, $J_{1,2}$ 0, Hz, $J_{2,3}$ 3.3, Hz, $J_{2,F}$ 51.7 Hz, H-2).

*1-(5-*O*-Acetyl-2,3-dideoxy-2-fluoro-3-*C*-methyl-β- and -α-ribofuranosyl)thymines* (**36** *and* **37**).—To a solution of compound **32** (0.50 g, 2.14 mmol) in MeCN (5 mL) was added 2,4-bis(trimethylsilyl)thymine in MeCN (10 mL), which was prepared from thymine (0.80 g, 6.35 mmol), hexamethyldisilazane, and a catalytic amount of $(NH_4)_2SO_4$ at room temperature with stirring. To the solution was added trimethylsilyl trifluoromethanesulfonate (2.0 mL, 10.4 mmol) at room temperature with stirring. The solution was stirred overnight, and then CH_2Cl_2 (40 mL) and satd $NaHCO_3$ (40 mL) were added. The organic layer was separated, washed with water, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by column chromatography (3 : 2 *n*-hexane–EtOAc) to give **37** (0.35 g, 55.1%) mp 166–168°C and **36** (0.18 g, 27.6%) mp 158–160°C.

^{1}H NMR ($CDCl_3$): δ 9.63 [s, 1 H, N(3)-H], 7.23 (s, 1 H, H-6), 6.20 (d, $J_{1',2'}$ 0, $J_{1',F}$ 22.0 Hz, H-1′), 5.06 (d, 1 H, $J_{1',2'} = J_{2',3'} = 0$, $J_{2,F}$ 53.7 Hz, H-2′), 4.42 (d, 1 H, $J_{4',5'a} < 1.0$, $J_{5'a,5'b}$ 12.2 Hz, H-5′a), 4.27 (dm, 1 H, $J_{3',4'} \sim 10.5$, H-4′), 4.14 (dd, 1 H, $J_{4',5'b}$ 4.9, $J_{5'a,5'b}$ 12.2 Hz, H-5′b), 2.3–2.5 (dm, 1 + H, H-3′), 2.13 (s, 3 H, Ac), 1.95

[s, 3 H, C(5)-CH_3], 1.20 [d, 3 H, J_{3',CH_3} 6.8 Hz, C(3')-CH_3]; ^{13}C NMR ($CDCl_3$): δ 1.70.6 (s, OCO-CH_3), 164.1 (s, C-4), 150.6 (s, C-2), 136.1 (d, *J* 5.0 Hz, C-6), 109.9 (s, C-5), 93.5 (d, *J* 190.1 Hz, C-2'), 86.0 (d, *J* 15.0 Hz, C-1'), 82.2 (s, C-4'), 63.5 (s, C-5'), 39.0 (d, *J* 18.9 Hz, C-3'), 20.6 (s, OCO-CH_3), 12.3 [s, C(5)-CH_3], 9.0 [d, *J* 7.1 Hz, C(3')-CH_3]; ^{19}F NMR ($CDCl_3$): δ −210.6 (ddd, $J_{1',F}$ 21.0, $J_{2',F}$ 52.6, $J_{3',F}$ 33.9 Hz). Anal. Calcd for $C_{13}H_{17}FN_2O_5$: C, 52.00; H, 5.67; N, 9.33. Found: C, 52.24; H, 5.89; N, 9.38.

1-(2,3-Dideoxy-2-fluoro-3-methyl-β-ribofuranosyl)thymine (**38**).—The experimental procedure was as for the formation of **39** (*vide infra*) and gave a quantitative yield of **38**, mp 205–208°C; ^{1}H NMR (CD_3OD): δ 8.07 [br, s, 1 H, N(3)-H], 5.93 (d, 1 H, $J_{1',2'}$ 0, $J_{1',F}$ 17.6 Hz, H-1'), 5.99 (dd, 1 H, $J_{1',2'}$ 0, $J_{2',3'}$ 4.0, $J_{2',F}$ 52.7 Hz, H-2'), 4.03 (dd, 1 H, $J_{4',5'a} \sim 2.0$, $J_{5'a,5'b}$ 12.6 Hz, H-5a), 3.92 (dm, 1 H, $J_{3',4'} \sim 9.5$ Hz, H-4'), 3.72 (dd, 1 H, $J_{4',5'b}$ 2.7, $J_{5'a,5'b}$ 12.6 Hz, H-5'b), 2.3–2.5 (m, 1 H, H-3'), 1.85 [s, 3 H, C(5)-CH_3], 1.10 [d, 3 H, J_{3',CH_3} 6.8 Hz, C(3')-CH_3]; ^{13}C NMR (CD_3OD): δ 166.5 (s, C-4), 152.0 (s, C-2), 137.9 (s, C-6), 110.7 (s, C-5), 99.9 (d, *J* 182.9 Hz, C-2'), 90.6 (d, *J* 37.4 Hz, C-1'), 87.6 (s, C-4'), 60.5 (s, C-5'), 36.2 (d, *J* 20.3 Hz, C-3'), 12.5 [s, C(5)-CH_3], 8.3 [d, *J* 7.7 Hz, C(3')-CH_3]; ^{19}F NMR (CD_3OD): δ −195.7 (ddd, $J_{1',F}$ 14.8, $J_{2',F}$ 50.5, $J_{3',F}$ 34.7 Hz). Anal. Calcd for $C_{11}H_{15}FN_2O_4$: C, 51.16; H, 5.81; N, 10.85. Found: C, 51.34; H, 6.04; N, 10.85.

Crystal data for **38**. $C_{11}H_{15}FN_2O_4$, monoclinic, space group $P2_1/c$, $a = 4.822(2)$ Å, $b = 13.225(7)$ Å, $c = 18.655(8)$ Å, $V = 1186(1)$ Å^3, $D_c = 1.446$ g cm^{-3}, $\mu = 1.1$, $Z = 4$, λ(MoKα) = 0.71073 Å (graphite monochromator), $T = 298$ K. A Nicolet R3m/V diffractometer was used to collect 1724 reflections ($3° < 2\theta < 45°$) on a colorless crystal, $0.15 \times 0.15 \times 0.40$ mm^3. Of these, 1558 were unique and 894 observed ($F_o > 6\sigma F_o$). Lorentz and polarization corrections were applied to the data. All the nonhydrogen atoms were located by direct methods. $R = 0.0543$, $R_w = 0.0549$, GOF = 1.737.

1-(2,3-Dideoxy-2-fluoro-3-methyl-α-ribofuranosyl)thymine (**39**).—An aqueous solution (0.5 mL) of NaOH (0.02 g, 0.50 mmol) was added to a solution of **37** in MeOH (5 mL) at room temperature with stirring. The solution was stirred for 30 min and then acetic acid (0.15 mL) was added. The solution was evaporated and the residue was purified by column chromatography (30 : 1 CH_2Cl_2–EtOH) to give **39** (0.16 g, 99.2%), mp 187–188°C; ^{1}H NMR ($CDCl_3$): δ 9.7 (broad, 1 H, N(3)-H], 7.24 [s, C(6)-H], 6.19 (dd, 1 H, $J_{1',2'}$ 2.0, $J_{1',F}$ 22.7 Hz, H-1'), 5.04 (dt, 1 H, $J_{1',2'} = J_{2',3'} = 2.0$, $J_{2',F}$ 54.1 Hz, H-2'), 4.14 (dm, 1 H, $J_{3',4'} \sim 9.6$ Hz, H-4'), 3.97 (dd, 1 H, $J'_{,5'a}$ 1.6, $J_{5'a,5'b}$ 12.5 Hz, H-5'a), 3.63 (dd, 1 H, $J_{4',5'b}$ 3.6, $J_{5'a,5'b}$ 12.5 Hz, H-5'b), 2.45–2.70 (dm, 1 H, H-3'), 1.9 [s, 3 H, C(5)-CH_3], 1.16 [d, 3 H, J_{3',CH_3} 6.1 Hz, C(3')-CH_3]; ^{13}C NMR ($CDCl_3$): δ 164.3 (s, C-4), 150.6 (s, C-2), 136.6 (d, *J* 2.8 Hz, C-6), 110.0 (s, C-5), 94.2 (d, *J* 190.4 Hz, C-2'), 86.1 (d, *J* 15.0 Hz, C-1') Hz, 85.5 (s, C-4'), 61.4 (s, C-5'), 37.6 (d, *J* 18.8 Hz, C-3'), 12.4 [s, C(5)-CH_3], 9.0 [d, *J* 6.7 Hz, C(3')-CH_3]; ^{19}F NMR ($CDCl_3$): δ −209.8 (ddd, $J_{1',F}$ 21.3, $J_{2',F}$ 55.0, $J_{3',F}$ 32.8 Hz). Anal. Calcd for $C_{11}H_{15}FN_2O_4$: C, 51.16; H, 5.81; N, 10.85. Found: C, 51.17; H, 5.81; N, 10.68.

Crystal data for **39**. $C_{11}H_{15}FN_2O_4$, monoclinic, space group $P2_1/c$, $a = 9.249(3)$ Å, $b = 13.863(5)$ Å, $c = 9.735(3)$ Å, $V = 1181.1(7)$ Å^3, $D_c = 1.452$ g cm^{-3}, $\mu = 1.1$, $Z = 4$, λ (Mo$K\alpha$) = 0.71073 Å (graphite monochromator), $T = 298$ K. Nicolet R3m/V diffractometer was used to collect 1763 reflections ($3° < 2\theta < 45°$). Of these, 1554 were unique and 673 observed ($F_o > 6\sigma F_o$). Lorentz and polarization corrections were applied to the data. All the nonhydrogen atoms were located by direct methods. $R = 0.0697$, $R_w = 0.0668$, GOF = 1.89.

9-(5-O-Acetyl-2,3-dideoxy-2-fluoro-3-methyl-β- or -α-arabinofuranosyl)-6-chloropurine (**40** *and* **43**) *and 7-(5-O-acetyl-2,3-dideoxy-2-fluoro-3-methyl-β- or -α-arabinofuranosyl)-6-chloropurine* (**41** *and* **42**).—To a solution of compound **28** (0.25 g, 1.07 mmol) in MeCN (5 mL) was added trimethylsilylated 6-chloropurine in MeCN (7 mL), which was prepared from 6-chloropurine (0.30 g, 1.94 mmol), hexamethyldisilazane, and a catalytic amount of $(NH_4)_2SO_4$ under Ar at room temperature. Trimethylsilyl trifluoromethanesulfonate (0.80 mL, 4.14 mmol) was added with stirring at 0°C. The stirring was continued for 2 days and CH_2Cl_2 (25 mL) was added. The solution was washed with brine, dried with anhyd $MgSO_4$, and evaporated. The residue was purified by column chromatography (3:1 *n*-hexane–EtOAc) to give **43** (0.06 g, 17%), **40** (0.11 g, 31.3%), **42** (0.06 g, 17%), and **41** (0.04 g, 11.3%).

Spectral data for **40**. ^{1}H NMR ($CDCl_3$): δ 8.70 (s, 1 H, H-2), 8.39 (d, 1 H, $J_{8,F}$ 2.6 Hz, H-8), 6.46 (dd, 1 H, $J_{1'2'}$ 3.9, $J_{1',F}$ 15.4 Hz, H-1'), 4.96 (dt, 1 H, $J_{1',2'}$ 3.9, $J_{2',F}$ 53.3 Hz, H-2'), 4.37 (dd, 1 H, $J_{4',5'a}$ 6.0, $J_{5'a,5'b}$ 12.2 Hz, H-5'a), 4.32 (d, 1 H, $J_{4',5'b}$ 3.2, $J_{5'a,5'b}$ 12.2 Hz, H-5'b), 3.99 (dt, 1 H, $J_{4',5'a}$ $J_{3',4'}$ 6.0, $J_{4',5'b}$ 3.2 Hz, H-5'b), 2.53–2.75 (m, 1 H, H-3'), 2.09 (s, 3 H, Ac), 1.28 [d, 3 H, J_{3',CH_3} 6.5 Hz, C(3')-CH_3]; ^{13}C NMR ($CDCl_3$): δ 170.5 (s, O*C*O-CH_3), 152.0 (s, C-2), 151.3 (s), 149.9 (s), 144.5 (s), 144.3 9d, *J* 5.3 Hz, C-8), 95.9 (d, *J* 194.5 Hz, C-2'), 83.4 (d, *J* 16.3 Hz, C-1'), 82.2 (d, *J* 5.0 Hz, C-4'), 63.9 (s, C-5'), 40.2 (d, *J* 20.3 Hz, C-3'), 20.7 (s, OCO-*C*H_3), 15.2 [d, *J* 7.6 Hz, C93')-*C*H_3]; ^{19}F NMR ($CDCl_3$): δ −188.0 (ddd, $J_{1',F}$ 15.6, $J_{2',F}$ 57.0, $J_{3',F}$ 23.8 Hz). Anal. Calcd for $C_{13}H_{14}ClFN_4O_3$: C, 47.49; H, 4.26; N, 17.05. Found: C, 48.33; H, 4.91; N, 14.89.

Spectral data for **41**. ^{1}H NMR ($CDCl_3$): δ 8.85 (s, 1 H, H-2), 8.71 (d, 1 H, $J = 1.7$ Hz, H-8), 6.74 (dd, 1 H, $J_{1',2'}$ 4.8, $J_{1',F}$ 10.2 Hz, H-1'), 5.02 (dt, 1 H, $J_{1',2'} = J_{2',3'} = 4.8$, $J_{1',F}$ 53.4 Hz, H-2'), 4.42 (dd, 1 H, $J_{4',5'a}$ 5.0, $J_{5'a,5'b}$ 12.9 Hz, H-5'a), 4.35 (ddd, 1 H, $J_{4',5'b} \sim 2.0$, $J_{5'a,5'b}$ 12.9, $J_{5'b,F} \sim 1.6$ Hz, H-5'b), 4.03 (ddd, 1 H, $J_{4',5'a}$ 5.0, $J_{4',5'b} \sim 2.0$, $J_{3',4'}$ 10.3 Hz, H-4'), 2.4–2.6 (m, 1 H, H-3'), 2.14 (s, 3 H, Ac), 1.25 [d, J_{3',CH_3} 6.7 Hz, C(3')-CH_3]. ^{13}C NMR ($CDCl_3$): δ 170.4 (s, O*C*O*C*H_3), 163.1 (s), 152.5 (s), C-2), 149.8 (s), 147.2 (d, *J* 4.0 Hz, C-8), 142.4 (s), 96.3 (d, *J* 197.6 Hz, C-2'), 85.3 (d, *J* 17.1 Hz, C-1'), 82.1 (d, *J* 5.1 Hz, C-4'), 63.0 (s, C-5'), 38.7 (d, *J* 20.3 Hz, C-3'), 20.7 (s, OCO-*C*H_3), 14.2 [d, *J* 3.9 Hz, C(3')-CH_3]; ^{19}F NMR ($CDCl_3$): δ −192.0 (ddd, $J_{1',F}$ 8.8, $J_{2',F}$ 53.8, $J_{3',F}$ 22.5 Hz). Anal. Calcd for $C_{13}H_{19}ClFN_4O_3$: C, 47.49; H, 4.26; N, 17.05. Found: C, 48.24; H, 4.92; N, 15.84.

Spectral data for **42**. ^{1}H NMR ($CDCl_3$): δ 8.89 (s, 1 H, H-2), 8.46 (s, 1 H, H-8); 6.65 (dd, 1 H, $J_{1',2'}$ 2.9, $J_{1',F}$ 12.5 Hz, H-1'), 5.10 (ddd, 1 H, $J_{1',2'}$ 2.9, $J_{2',3'}$ 4.5, $J_{2',F}$

51.7 Hz, H-2′), 4.43 (dt, 1 H, $J_{3',4'} \sim 10.8$, $J_{4',5'}$ 4.9 Hz, H-4′), 4.30 (d, 2 H, $J_{4',5'}$ 4.9 Hz, H-5′), 2.5–2.7 (m, 1 H, H-3′), 2.12 (s, 3 H, Ac), 1.14 [d, 3 H, J_{3',CH_3} 7.3 Hz, C(3)-CH_3]; ^{13}C NMR ($CDCl_3$): δ 170.6 (s, $OCOCH_3$), 162.7 (s), 152.9 (s, C-2), 149.9 (s), 147.2, 145.7 (s, C-8), 101.5 (d, *J* 191.4 Hz, C-2′), 91.2 (d, *J* 35.9 Hz, C-1′), 85.4 (d, *J* 4.4 Hz, C-4′), 64.4 (s, C-5′), 40.8 (d, *J* 20.1 Hz, C-3′), 20.7 (s, $OCOCH_3$), 15.5 [d, *J* 3.4 Hz, C(3′)-CH_3]; ^{19}F NMR ($CDCl_3$): δ −181.6 (ddd, $J_{1',F}$ 12.2, $J_{2',F}$ 51.9, $J_{3',F}$ 30.2 Hz). Anal. Calcd for $C_{13}H_{14}ClFN_4O_3$: C, 47.49; H, 4.26; N, 17.05. Found: C, 48.09; H, 4.77; N, 15.95.

Spectral data for **43**. ^{1}H NMR ($CDCl_3$): δ 8.67 (s, 1 H, H-2), 8.20 (s, 1 H, H-8), 6.12 (dd, 1 H $J_{1',2'}$ 3.5, $J_{1',F}$ 15.5 Hz, H-1′), 5.69 (ddd, 1 H, $J_{1',2'}$ 3.5, $J_{2',3'}$ 6.8, $J_{2',F}$ 54.1 Hz, H-2′), 4.48 (ddd, 1 H, $J_{3',4'}$ 9.5, $J_{4',5'a}$ 3.0, $J_{4',5'b}$ 5.6 Hz, H-4′), 4.27 (dd, 1 H, $J_{4',5'a}$ 3.0, $J_{5'a,5'b}$ 12.5 Hz, H-5′a), 4.13 (dd, 1 H, $J_{4',5'b}$ 5.6, $J_{5'a,5'b}$ 12.5 Hz, H-5′b), 2.4–2.6 (m, 1 H, H-3′), 2.02 (s, 3 H, Ac), 1.26 [d, 3 H, J_{3',CH_3} 6.8 Hz, C(3′)-CH_3]; ^{13}C NMR ($CDCl_3$): δ 170.5 (s, $OCOCH_3$), 151.9 (s, C-2), 151.4 (s), 150.9 (s), 144.6 (s, C-8), 132.5 (s), 99.9 (d, *J* 189.5 Hz, C-2′), 89.4 (d, *J* 35.4 Hz, C-1′), 84.2 (d, *J* 7.5 Hz, C-4′), 63.5 (s, C-5′), 41.6 (d, *J* 19.9 Hz, C-3′), 20.6 (s, -OCO-CH_3), 13.0 [s, C(3′)-CH_3]; ^{19}F NMR ($CDCl_3$): δ −188.1 (ddd, $J_{1',F}$ 14.6, $J_{2',F}$ 55.6, $J_{3',F}$ 23.0 Hz). Anal. Calcd for $C_{13}H_{14}ClFN_4O_3$: C, 47.49; H, 4.26; N, 17.05. Found: C, 48.12, H, 4.57; N, 16.00.

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SUPPLEMENTARY MATERIAL AVAILABLE

ORTEP drawings for **35, 38**, and **39** as well as listings of isotropic and anisotropic thermal parameters, bond distances and bond angles, 40 pages are deposited*.

REFERENCES

1 R.J. Suhadolnik, *Nucleoside Antibiotics*, Wiley-Interscience, New York, NY, 1970, pp 50–76.
2 S. Frederiksen and H. Klenow, in A.C. Sartorelli and D.G. Johns, (Eds.), *Antineoplastic and Immunosuppressive Agents II*, Springer-Verlag, New York, NY, 1975, pp 657–664.
3 S. Frederiksen and A.H. Rasmussen, *Cancer Res.*, 27 (1967) 385–391.
4 (a) E. Walton, F.W. Holly, G.E. Boxer, R.F. Nutt, and S.R. Jenkins, *J. Med. Chem.*, 8 (1965) 659–663. (b) S.R. Jenkins, F.W. Holly, and E. Walton, *J. Org. Chem.*, 30 (1965) 2851–2852. (c) M.J.

* Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre. The coordinates may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Dickinson, F.W. Holly, E. Walton, and J. Zimmerman, *J. Med. Chem.*, 10 (1967) 1165–1166. (d) E. Walton, F.W. Holly, G.E. Boxer, and R.F. Nutt, *J. Org. Chem.*, 31 (1966) 1163–1169. (e) H.T. Shigeura, G.E. Boxer, M.L. Meloni, and S.D. Sampson, *Biochemistry*, 5 (1966) 994–1004.

5 A. Resowsky, H. Lazarus, and A. Yamashita, *J. Med. Chem.*, 19 (1976) 1265–1270.

6 (a) F.S. Philips, A. Feinber, T.-C. Chou, P.M. Vidal, T.-L. Su, K.A. Watanabe, and J.J. Fox, *Cancer Res.*, 43 (1983) 3618. (b) V.E. Marquez, C.K.-H. Tseng, J.A. Kelley, H. Mitsuya, S. Broder, J.S. Roth, and J.S. Driscoll, *Biochem. Pharm.*, 36 (1987) 2718.

7 (a) J.T. Welch, *Tetrahedron*, 43 (1987) 323–3197. (b) J.T. Welch and S. Eswarakrishnan, *Fluorine in Bioorganic Chemistry*, Wiley, New York, NY, 1991, Chap. 8.

8 J.J. Fox, C. Lopez, and K.A. Watanabe, in F.G. de las Heras and S. Vega, (Eds.), *Medicinal Chemistry Advances*, Pergamon, Oxford, 1981, pp 27–40.

9 J.J. Fox, K.A. Watanabe, T.C. Chou, R.F. Schinazi, K.F. Soike, I. Fourel, G. Hantz, and C. Trepo, in N.F. Taylor, (Ed.), *Fluorinated Carbohydrates*, American Chemical Society, Washington, DC, 1988, Chap. 10.

10 S. Castillon, A. Dessinges, R. Faghih, G. Lukacs, A. Olesker, and T.T. Thang, *J. Org. Chem.*, 50 (1985) 4913–4917.

11 H.H. Baer and L. Siemsen, *Can. J. Chem.*, 66 (1988) 187–190.

12 (a) J.G. Shelling, D. Dolphin, P. Wirz, R.E. Cobbledick, and F.W.B. Einstein, *Carbohydr. Res.*, 132 (1984) 241–259. (b) C.-Y. Shiue, C.D. Arnett, and A.P. Wolf, *Eur. J. Nucl. Med.*, 9 (1984) 77–80. (c) M. Diksic and D. Jolly, *J. Carbohydr. Chem.*, 4 (1985) 265–271. (d) M. Diksic and D. Jolly, *Carbohydr. Res.*, 153 (1986) 17–24. (e) G.T. Bida, N. Satyamurthy, and J.R. Barrio, *J. Nucl. Med.*, 25 (1984) 1327–1334. (f) M.J. Adam, B.D. Pate, J.-R. Nesser, and L.D. Hall, *Carbohydr. Res.*, 124 (1983) 215–124. (g) M. Diksic and D. Jolly, *Int. J. Appl. Radiat. Isot.*, 34 (1983) 893–896. (h) C.-Y. Shiue, P.A. Salvadori, A.P. Wolf, J.S. Fowler, and R.R. MacGregor, *Nucl. Med. Biol. Adv., Proc. 3rd World Congr.*, 2 (1982) (Pub. 1983) 2125–2129. (i) C.-Y. Shiue, P.A. Salvadori, A.P. Wolf, J.S. Fowler, and R.R. MacGregor, *J. Nucl. Med.*, 23 (1982) 899–903. (j) C.J.S. Van Rijn, J.D.M. Herscheid, G.W.M. Visser, and A. Hoekstra, *Int. J. Appl. Radiat. Isot.*, 36 (1985) 111–115. (k) M.J. Adam, *J. Chem. Soc., Chem. Commun.*, (1982) 730–731. (l) W. Korytnyk and S. Valentekovic-Horvat, *Tetrahedron Lett.*, 21 (1980) 1493–1496. (m) S. Sood, G. Firnau, and E.S. Garnett, *Int. J. Appl. Radiat. Isot.*, 34 (1983) 743–745.

13 (a) L.H. Brito Baptistella, A.J. Marsaioli, P.M. Imamura, S. Castillon, A. Olesker, and G. Lukacs, *Carbohydr. Res.*, 152 (1986) 310–315. (b) T. Ogawa and Y. Takahashi, *J. Carbohydr. Chem.*, 2 (1983) 461–467. (c) A. Olesker, A. Dessinges, T.T. Thang, and G. Lukacs, *C.R. Seances. Acad. Sci. Ser.*, 2 (1982) 575–577. (d) T. Haradahira, M. Maeda, Y. Kai, and M. Kojima, *J. Chem. Soc., Chem. Commun.*, (1985) 364–365. (e) S. Levy, E. Livni, D. Elmaleh, and W. Curatolo, *J. Chem. Soc., Chem. Commun.*, (1982) 972–973. (f) T. Haradahira, M. Maeda, Y. Kai, H. Omae, and M. Kojima, *Chem. Pharm. Bull.*, 33 (1985) 165–172. (g) T. Tewson, *J. Org. Chem.*, 48 (1983) 3507–3510. (h) C.H. Tann, P.R. Brodfuehrer, S.P. Brundidge, S., Sapino, Jr., and H.G. Howell, *J. Org. Chem.*, 50 (1985) 3644–3547. (i) U. Reichman, K.A. Watanabe, and J.J. Fox, *Carbohydr. Res.*, 42 (1975) 233–240.

14 (a) D.G. Drueckhammer and C.H. Wong, *J. Org. Chem.*, 50 (1985) 5912–5913. (b) C.Y. Shiue and A.P. Wolf, *J. Fluorine Chem.*, 31 (1986) 255–263. (c) K. Biggadike, A.D. Borthwick, A.M. Exall, B.E. Kirk, and R.A. Ward, *J. Chem. Soc., Chem. Commun.*, (1988) 898–900.

15 (a) L. Helena, L.H.B. Baptistella, A.J. Marsaioli, J.D. de Souza Filho, G.G. de Oliviera, A.B. de Oliviera, A. Dessinges, S. Castillon, A. Olesker, T.T. Thang, and G. Lukacs, *Carbohydr. Res.*, 140 (1985) 51–59. (b) T.W. Flechtner and H. Pohlid, *J. Carbohydr. Chem.*, 3 (1984) 107–116. (c) M.K. Gurjar, V.J. Patil, J.S. Yadav, and A.V. Rama Rao, *Carbohydr. Res.*, 135 (1984) 174–177. (d) D. Picq and D. Anker, *J. Carbohydr. Chem.*, 4 (1985) 113–123.

16 (a) W.A. Szarek, G.W. Hay, and M.M. Perlmutter, *J. Chem. Soc., Chem. Commun.*, (1982) 1253–1254. (b) W.A. Szarek, G.W. Hay, B. Doboszewski, and M.M. Perlmutter, *Carbohydr. Res.*, 155 (1986) 107–118. (c) K. Ok, Y. Takagi, T. Tsuchiya, S. Umezawa, and H. Umezawa, *Carbohydr. Res.*, 169 (1987) 69–81.

17 L.W. Hertel, J.S. Kroin, J.W. Misner, and J.M. Tustin, *J. Org. Chem.*, 53 (1988) 2406–2409.

18 S. Eswarakrishnan, Ph.D. Thesis, State University of New York at Albany, 1986.

19 (a) R.E. Ireland, R.H. Mueller, and A.K. Willard, *J. Am. Chem. Soc.*, 98 (1976) 2868–2877. (b) R.E. Ireland, L. Courtney, and B. Fitzsimmons, *J. Org. Chem.*, 48 (1983) 5186–5198e. (c) G.R. Martinez,

P.A. Grieco, E. Williams, K. Kanai, and C.V. Srinivasan, *J. Am. Chem. Soc.*, 104 (1982) 1436–1438. (d) R.E. Ireland, J.P. Daub, G.S. Mandel, and N.S. Mandel, *J. Org. Chem.*, 48 (1983) 1312–1325. (e) S. Danishefsky, R.L. Funk, and J.F. Kerwin, *J. Am. Chem. Soc.*, 102 (1980) 6889–6891. (f) P.A. Bartlett, D.J. Tanzella, and J.F. Barstow, *J. Org. Chem.*, 47 (1982) 3941–3945. (g) P.A. Bartlett and J.F. Barstow, *J. Org. Chem.*, 47 (1982) 3933–3941.

20 (a) S.E. Denmark and M.A. Harmata, *J. Am. Chem. Soc.*, 104 (1982) 4972–4974. (b) S.E. Denmark and M.A. Harmata, *J. Org. Chem.*, 48 (1983) 3369–3370. (c) S.E. Denmark, J.E. Marlin, and R.L. Dorow, *Abstr. Papers*, 191st National Meeting of the American Chemical Society, New York City, NY American Chemical Society, Washington, DC, 1986, ORGN 273. (d) T. Sato, H. Tsunekawa, H. Hohama, and T. Fujisawa, *Chem. Lett.*, (1986) 1553–1556. (e) S.D. Burke, G.J. Pacofsky, and A.D. Piscopio, *Tetrahedron Lett.*, 27 (1986) 3345–3348. (f) S.D. Burke, F.J. Schoenen, and C.W. Murtiashaw, *Tetrahedron Lett.*, 27 (1986) 449–452. (g) S.D. Burke, D.M. Armistead, F.J. Schoenen, and J.M. Fevig, *Tetrahedron Lett.*, 42 (1986) 2787–2810. (h) J. Kallmerten and M.D. Wittman, *Tetrahedron Lett.*, 27 (1986) 2443–2446. (i) J. Kallmerten and T.J. Gould, *J. Org. Chem.*, 51 (1986) 1152–1155. (j) R.E. Ireland and M.D. Varney, *J. Am. Chem. Soc.*, 106 (1984) 3368–3670. (k) D.P. Curran and Y.-G. Suh, *J. Am. Chem. Soc.*, 106 (1984) 5002–5004. (l) T. Fujisawa, K. Tajima, M. Ito, and T. Sata, *Chem. Lett.*, (1984) 1169–1172. (m) B.K. Carpenter and C.J. Burrows, *Tetrahedron Lett.*, 103 (1981) 6983–6984. (n) S.D. Burke, D.M. Armistead, and F.J. Schoenen, *J. Org. Chem.*, 49 (1984) 4320–4322. (o) J. Kallmerten and T.J. Guold, *Tetrahedron Lett.*, 24 (1983) 5177–5180, (p) S.D. Burke, W.F. Gobare, and G.J. Pacofsky, *J. Org. Chem.*, 48 (1983) 5221–5228. (q) C.J. Burrows and B.K. Carpenter, *J. Am. Chem. Soc.*, 101 (1981) 6984–6986.

21 (a) W.R. Dolbier, Jr., A.C. Alty, and O. Phanstiehl IV, *J. Am. Chem. Soc.*, 109 (1987) 3046–3050. (b) W.R. Dolbier, Jr., K.S. Medinger, A. Greensberg, and J.F. Liebman, *Tetrahedron* 32 (1982) 2415–2420. (c) J.F.M. Oth and R. Merenyi, *Tetrahedron Lett.* (1968) 3941–3946. (d) B. DeCorte, N. DeKimpe, and J.T. Welch, *J. Org. Chem.*, 55 (1990) 4981–4983. (e) J.T. Welch and J.S. Samartino, *J. Org. Chem.*, 50 (1985) 3663–3665. (f) B. Metcalfe, E. Jarvi, and J.P. Burkhart, *Tetrahedron Lett.*, 26 (1985) 2861–2864. (g) J.T. Welch and S. Eswarakrishnan, *J. Org. Chem.*, 50 (1985) 5909–5910.

22 J.T. Welch, J.S. Plummer, and T.-S. Chou, *J. Org. Chem.*, 56 (1991) 353–359.

23 J.S. Plummer, Ph.D. Thesis, State University of New York at Albany, 1988.

24 (a) T. Yokozawa, T. Nakai, and N. Ishikawa, *Tetrahedron Lett.*, 25 (1984) 3991–3994. (b) T. Yokozawa, T. Nakai, and N. Ishikawa, *Tetrahedron Lett.*, 25 (1984) 3987–3990.

25 K. Araki and J.T. Welch, *Tetrahedron Lett.*, 34 (1993) 2251–2254.

26 D.J. Tanzella, Ph.D. Thesis, University of California, Berkley, 1980.

27 H.H. Wasserman, P.S. Mariano, and P.M. Keehn, *J. Org. Chem.*, 36 (1971) 1765–1769.

28 D.B. Collum, J.H. McDonald, III, and W.C. Still, *J. Am. Chem. Soc.*, 102 (1980) 2118–2120.

29 (a) J.K. Cha, W.J. Christ, and Y. Kishi, *Tetrahedron Lett.*, 24 (1983) 3943–3946. (b) J.K. Cha, W.J. Christ, and Y. Kishi, *Tetrahedron Lett.*, 24 (1983) 3947–3950. (c) G. Stork and M. Kahn, *Tetrahedron Lett.*, 24 (1983) 3951–3954. (d) M. Schröder, *Chem. Rev.*, 80 (1980) 187–213. (e) R. Criegee, *Justus Liebigs Ann. Chem.*, 522 (1936) 75–96.

30 T. Yamazaki, J.T. Welch, J.S. Plummer, and R. Gimi, *Tetrahedron Lett.*, 32 (1991) 4267–4270.