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The β-Fluorine Effect. Electronic Versus Steric Effects in Radical Deoxygenations of Fluorine-Containing Pentofuranose Nucleosides

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Stereoselective pyramidalization of free radicals by a vicinal fluorine substituent, the β-fluorine effect, was invoked to rationalize a 77:23 anti/syn ratio of 2-deuterio-1-fluorocyclopentanes obtained by radical reduction of *trans*-2-fluoro-1-bromocyclopentane with tributyltin deuteride (Dolbier, W. R., Jr.; Bartberger, M. D. *J. Org. Chem.* **1995**, *60*, 4984−4985). We have evaluated analogous reductions of the four possible stereoisomers of some adenine 2′(3′)-fluoro-3′(2′)-*O*-phenoxythiocarbonyl nucleoside derivatives. In all cases, the steric effect of adenine on the β face directs deuterium transfer from the stannane to C2′(C3′) on the α face of the furanose ring. However, the β-fluorine effect enhances ratios of deuterium transfer anti to the vicinal fluorine substituent.

Introduction

Stereoselectivity in free radical reactions is an area of considerable interest.[1,2] We have shown that radical deoxygenation of 2′-*O*-phenoxythiocarbonyl (PTC) esters of 3′,5′-bis-*O*-silyl-protected adenosine (or its arabino epimer) with tributyltin deuteride gave 2′(*R*/*S*)-deuterio-2′-deoxy derivatives (∼88:12). This indicated that deuterium transfer from the bulky tributylstannane to a C2′ radical occurrred with pronounced stereoselectivity at the less hindered α-face (ribo).[3] Ishido and co-workers found even greater stereoselectivity (as high as 99:1) for triethylborane-initiated stannane-[4a] or tris(trimethylsilyl)-silane-mediated[4b] deuterium transfers with 2′-*O*-PTC esters or 2′-bromo-2′-deoxynucleosides at low temperatures. Marquez and co-workers reported that radical-mediated deoxygenations of nucleoside xanthate esters with dilauroyl peroxide/(2-propanol-d_8 or diglyme-d_{14}) also showed preference for the α-face of nucleoside derivatives.[5] They noted that abstraction of deuterium from solvent was enhanced by a β-fluorine substituent, and especially when fluorine and the xanthate ester group were trans.[5] Reduction of (3′,5′-bis-*O*-silyl-2′-keto or 2′,5′-bis-*O*-silyl-3′-keto)nucleosides with sodium borohydride[6a] or sodium triacetoxyborohydride[6b,c] also gave products from predominant attack at the α-face. The above results demonstrate that steric effects (i.e., preferential delivery of hydrogen or hydride anti to the heterocylic base in nucleosides) play a major role in the stereochemical outcome of such reactions.

Dolbier and Bartberger observed anti selectivity (77:23) with tributyltin hydride-mediated reduction of β-fluorocyclopentyl radicals (**A**, Figure 1).[7] Other steric effects on the selectivity of deuterium transfer were precluded in that unsubstituted ring system. Effects of a vicinal fluoro substituent on the diastereoselectivity of deuterium transfer were attributted to anti versus syn pyramidalization of radicals in the transition state.[7] A β-oxygen effect on radical deoxygenation of thionocarbonate esters was examined and found to be indirect rather than stereoelectronic.[8]

We now report competition between steric and β-fluorine effects, including the impact of fluorine regio- and stereochemistry, on radical deoxygenations of 2′(3′)-*O*-phenoxythiocarbonyl (PTC) esters of fluoropentofuranosyl-adenine nucleosides. One product, the glycosyl-

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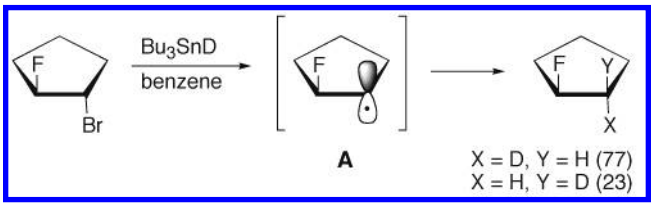
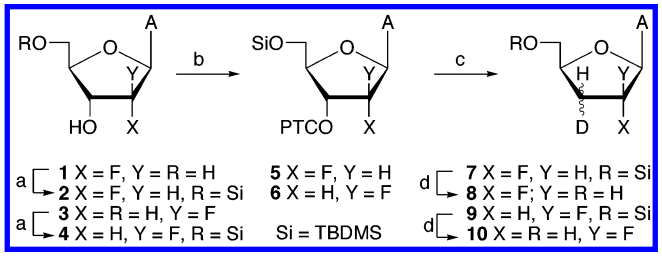


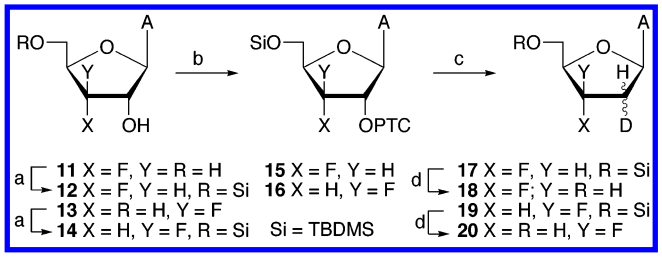
FIGURE 1. Structure of the pyramidalized β-fluorocyclopentyl radical intermediate (**A**) postulated to rationalize the anti stereoselectivity for deuterium transfer with tributyltin hydride.[7]

SCHEME 1[a]



[a] Key: (a) TBDMS−Cl/imidazole/DMF; (b) PTC−Cl/DMAP/MeCN; (c) Bu_3SnD/AIBN/toluene/85 °C; (d) NH_4F/MeOH/Δ.

SCHEME 2[a]



[a] Key: (a) TBDMS−Cl/imidazole/DMF; (b) PTC−Cl/DMAP/MeCN; (c) Bu_3SnD/AIBN/toluene/85 °C; (d) NH_4F/MeOH/Δ.

stablized 9-(2,3-dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)adenine, is an inhibitor of HIV.[9−11]

Results and Discussion

The methodology of Pankiewicz and co-workers[12] was employed to prepare 2′-deoxy-2′-fluoroadenosine (**1**) and its arabino epimer **3** (Scheme 1), and 3′-deoxy-3′-fluoroadenosine (**11**) and its xylo epimer **13** (Scheme 2). Silylation (O5′) of fluoro nucleosides **1**, **3**, **11**, and **13** (TBDMS−Cl) gave **2**, **4**, **12**, and **14**, which were treated with PTC−Cl to give 5′-*O*-TBDMS-2′-deoxy-2′-fluoro-3′-*O*-PTC-adenosine (**5**) and its arabino epimer **6**, and 5′-*O*-TBDMS-3′-deoxy-3′-fluoro-2′-*O*-PTC-adenosine (**15**) and its xylo epimer **16**, respectively.

Treatment of **5** with tributyltin deuteride gave 5′-*O*-TBDMS-2′,3′-dideoxy-3′(*R*/*S*)-deuterio-2′-fluoroadenosine (**7**), and **6** gave the 3′(*R*/*S*)-deuterio-2′-fluoro-*threo* epimers **9**; **15** gave 5′-*O*-TBDMS-2′,3′-dideoxy-2′(*R*/*S*)-deuterio-3′-fluoroadenosine (**17**), and **16** gave the 2′(*R*/*S*)-deuterio-3′-fluoro-*threo* epimers **19**. Ratios of deuterium epimers were determined by ^{1}H NMR and were consistent with those determined with 5′-*O*-monomethoxytrityl derivatives[13] (Table 1). Compounds **7**, **9**, **17**, and **19** were desilylated (NH_4F/MeOH)[14] to give **8**,[9,10] **10**,[9,10] **18**,[9] and **20**,[9] respectively, with ^{1}H NMR data as reported except for simplification of multiplets and ∼50% reduction in intensities of signals for H3′,3″ (**8** and **10**) or H2′,2″ (**18** and **20**). ^{1}H−^{1}H and ^{1}H−^{19}F coupling constants in spectra of **8**, **10**, **18**, and **20** were consistent with experimental[9,10] and calculated[15] values for other fluorodideoxynucleosides and had compatible magnitude reductions for coupling with ^{2}H. Epimeric ratios were determined more easily with some of the deprotected derivatives.

TABLE 1. Ratios of Deuterium Substitution with Radical Deoxygenation of 2′(3′)-*O*-PTC Derivatives of Fluoropentofuranosyladenine Nucleosides[a,b]

2′(3′)-*O*-PTC-3′(2′)-fluoro substrate	ratio of 2′/2″(3′/3″)-deuterio epimers	F/D diastereotopic excess (de)
5, 2′-fluoro-ribo	**7** (3′*R*/*S*, 64:36)	28
	8 (3′*R*/*S*, 64:36)	syn
6, 2′-fluoro-arabino	**9** (3′*R*/*S*, 93:7)	85
	10 (3′*R*/*S*, 92:8)	anti
15, 3′-fluoro-ribo	**17** (2′*R*/*S*, 15:85)	71
	18 (2′*R*/*S*, 14:86)	syn
16, 3′-fluoro-xylo	**19** (2′*R*/*S*, 7:93)	86
	20 (2′*R*/*S*, 7:93)	anti

[a] Averages of duplicate experiments determined by ^{1}H NMR (H2′/2" or H3′/3") analysis. [b] Radical reduction of 5′-*O*-monomethoxytrityl analogues of **15** and **16** gave the same ratios of deuterio epimers [3′-F-ribo (2′*R*/*S*, 15:85) and 3′-F-xylo (2′*R*/*S*, 8:92)].[13]

The data in Table 1 indicate that stereoselectivity for deuterium abstraction by a pentofuranosyl radical with a β-fluoro substituent is dominated by the steric influence of the heterocyclic base. In all cases, the major product has deuterium on the α face (trans to the base on the β face) independent of the position or orientation of the fluorine atom. However, comparison of the data for conversion of **5** → **7** (3′*R*/*S*, 64:36; syn F/D de 28) versus that for **6** → **9** (3′*R*/*S*, 93:7; anti F/D de 86) shows that the orientation of the β-fluorine relative to the radical center can have a significant effect on deuterium transfer stereochemistry. A less pronounced but parallel trend was observed for deuterium abstraction with 3′-fluoronucleosides (**15** → **17** (syn F/D de 70) versus **16** → **19** (anti F/D de 86)).[16]

Conclusions

It is clear that steric effects are decisive for determination of the stereoslectivity of transfer of deuterium

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(16) The greater α stereoselectivity for radical reduction of **15** compared to that of **5** probably results from the larger steric effect of the heterocyclic base at C2′ relative to C3′. Reductions of ketonucleosides with $NaBH_4$,[6a] or especially with $NaB(OAc)_3H$,[6b,c] are known to give products from predominant attack by the hydride reagent at the less hindered α face of the sugar ring. Such reductions proceed with significantly greater stereoselectivity at C2′ than at C3′.

from tributyltin hydride to fluoropentofuranosyl radicals generated from these adenine nucleoside derivatives. In all cases, deuterium abstraction occurs at the less hindered α face of the sugar ring trans to the heterocyclic base. However, this α face stereoselectivity is enhanced by the anti effect of a vicinal fluorine substituent with an arabino or xylo orientation (on the β face of the ring). A smaller anti effect is still apparent with a vicinal fluorine on the α face (ribo orientations). Complex stereoelectronic/steric interactions might be involved with these furanose rings that have electronegative (F, O, N) substituents.

Experimental Section

^{1}H (Me_4Si) (400 MHz) and ^{19}F (CCl_3F) (376.4 MHz) NMR spectra were determined with solutions in $CDCl_3$ unless otherwise noted. Mass spectra (MS) were obtained by atmospheric pressure chemical ionization (APCI) techniques. Reagent-grade chemicals were used, and solvents were dried by reflux over and distillation from CaH_2 under an argon atmosphere. Merck kieselgel 60-F_{254} was used for TLC, and Merck kieselgel 60 (230−400 mesh) was used for column chromatography.

5′-*O*-(*tert*-Butyldimethylsilyl)-2′-deoxy-2′-fluoroadenosine (2). Procedure A. TBDMS−Cl (63 mg, 0.44 mmol) and imidazole (43 mg, 0.66 mmol) were added to **1**[12a] (59 mg, 0.22 mmol) in dried DMF (3 mL) at ambient temperature, and the solution was stirred overnight. H_2O (1.0 mL) was added; volatiles were evaporated, and the residue was partitioned (EtOAc//NH_4Cl/H_2O). The organic layer was washed (brine), dried (Na_2SO_4), evaporated, and column chromatographed (5 → 10% MeOH/$CHCl_3$) to give **2** (59 mg, 70%): ^{1}H NMR δ 0.14 (s, 6H), 0.93 (s, 9H), 3.93 (dd, J = 2.5, 11.7 Hz, 1H), 4.09 (dd, J = 2.4, 11.7 Hz, 1H), 4.19−4.25 (m, 1H), 4.72 (ddd, J = 4.4, 6.5, 17.5 Hz, 1H), 5.45 (ddd, J = 2.2, 4.2, 52.9 Hz, 1H), 6.02 (dd, J = 2.2, 15.0 Hz, 1H), 6.28 (br s, 2H), 8.23 (s, 1H), 8.38 (s, 1H); ^{19}F NMR δ −204.33 (dt, J = 16.0, 53.0 Hz); MS m/z 384 (MH^+). Anal. Calcd for $C_{16}H_{26}FN_5O_3Si$ (383.5): C, 50.11; H, 6.83; N, 18.26. Found: C, 50.33; H, 6.99; N, 18.01.

9-[5-*O*-(*tert*-Butyldimethylsilyl)-2-deoxy-2-fluoro-β-D-arabinofuranosyl]adenine (4). Treatment of **3**[10,12a] (40 mg, 0.15 mmol) using procedure A gave **4**[10] (36.5 mg, 64%): ^{19}F NMR δ −198.02 (dt, J = 17.0, 51.0 Hz).

5′-*O*-(*tert*-Butyldimethylsilyl)-2′-deoxy-2′-fluoro-3′-*O*-(phenoxythiocarbonyl)adenosine (5). Procedure B. PTC−Cl (21.5 μL, 27 mg, 0.15 mmol) was added dropwise to a stirred solution of **2** (39 mg, 0.1 mmol) and DMAP (55 mg, 0.45 mmol) in MeCN (3 mL). Stirring was continued for 5 h, and volatiles were evaporated. The residue was partitioned (EtOAc/H_2O), and the organic layer was washed (0.1 M HCl/H_2O, $NaHCO_3$/H_2O, brine) and dried (Na_2SO_4). Volatiles were evaporated, and the residue was chromatographed (30% hexanes/EtOAc → EtOAc) to give **5** (35 mg, 66%): ^{1}H NMR δ 0.15 (s, 6H), 0.95 (s, 9H), 3.98 (dd, J = 2.0, 11.8 Hz, 1H), 4.11 (dd, J = 1.8, 11.7 Hz, 1H), 4.59−4.63 (m, 1H), 5.77 ("dt", J = 3.9, 51.7 Hz, 1H), 5.90 (br s, 2H), 6.04 ("dt", J = 5.6, 13.1 Hz, 1H), 6.47 (dd, J = 3.2, 15.0 Hz, 1H), 7.15 (d, J = 8.5 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 8.20 (s, 1H), 8.39 (s, 1H); ^{19}F NMR δ −205.26 (dt, J = 14.0, 51.0 Hz); MS m/z 520 (MH^+). Anal. Calcd for $C_{23}H_{30}FN_5O_4SSi$ (519.7): C, 53.16; H, 5.82; N, 13.48. Found: C, 52.88; H, 5.61; N, 13.77.

9-[5-*O*-(*tert*-Butyldimethylsilyl)-2-deoxy-2-fluoro-3-*O*-(phenoxythiocarbonyl)-β-D-arabinofuranosyl]adenine (6). Treatment of **4** (36 mg, 0.094 mmol) using procedure B gave **6**[10] (28 mg, 57%): ^{1}H NMR δ 0.15 (s, 6H), 0.96 (s, 9H), 3.95 (dd, J = 4.7, 11.0 Hz, 1H), 4.02 (dd, J = 4.8, 10.7 Hz, 1H), 4.39−4.44 (m, 1H), 5.57 (dd, J = 2.8, 49.6 Hz, 1H), 6.01 (dd, J = 2.6, 15.6 Hz, 1H), 5.73 (br s, 2H), 6.59 (dd, J = 2.6, 22.0 Hz, 1H), 7.16 (d, J = 7.6 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 8.16 (s, 1H), 8.40 (s, 1H); ^{19}F NMR δ −199.19 (dt, J = 18.0, 51.0 Hz).

5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′-dideoxy-3′(*R*/*S*)-deuterio-2′-fluoroadenosine (7). Procedure C. A solution of **5** (17 mg, 0.32 mmol), AIBN (1.2 mg, 0.007 mmol), and Bu_3SnD (17.4 μL, 18 mg, 0.064 mmol) in toluene (1 mL) was deoxygenated (Ar) for 30 min and then heated for 3 h at 85 °C. Volatiles were evaporated, and the residue was chromatographed (EtOAc) to give **7** (3′*R*/*S*, ∼64:36; 8.5 mg, 67%) with data as reported[10] except for the following: ^{1}H NMR δ 2.23 (dd, J = 5.1, 19.3 Hz, 0.36H), 2.49 (ddd, J = 4.0, 10.7, 42.3 Hz, 0.64H), 4.60 (dt, J = 2.6, 10.6 Hz, 1H), 5.42 (dd, J = 3.7, 51.5 Hz, 1H), 6.33 (d, J = 16.5 Hz, 1H); ^{19}F NMR δ −181.04 (ddd, J = 16.5, 42.0, 51.5 Hz); MS m/z 369 (MH^+).

2′,3′-Dideoxy-3′(*R*/*S*)-deuterio-2′-fluoroadenosine (8). Procedure D. NH_4F (100 mg, 2.7 mmol) was added to a stirred solution of **7** (3′*R*/*S*, ∼64:36; 15 mg, 0.04 mmol) in MeOH (2 mL), and stirring was continued for 26 h at reflux. Volatiles were evaporated, and the residue was chromatograhed (5 → 10% MeOH/$CHCl_3$) to give **8** (3′*R*/*S*, ∼64:36; 6 mg, 60%) with data as reported[9,10] except for the following: ^{1}H NMR (MeOH-d_4) δ 2.30 (dd, J = 5.4, 19.5 Hz, 0.36H), 2.53 (ddd, J = 4.3, 9.7, 38.2 Hz, 0.64H), 4.53−4.57 (m, 1H), 5.52 (dd, J = 4.2, 52.0 Hz, 1H), 6.30 (d, J = 16.8 Hz, 1H); ^{19}F NMR (MeOH-d_4) δ −182.62 (ddd, J = 16.0, 38.0, 52.0 Hz); MS m/z 255 (MH^+).

9-[5-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-3(*R*/*S*)-deuterio-2-fluoro-β-D-*threo*-pentofuranosyl]adenine (9). Treatment of **6** (10 mg, 0.02 mmol) using procedure C gave **9** (3′*R*/*S*, ∼93:7; 6.5 mg, 90%) with data as reported[10] except for the following: ^{1}H NMR δ 2.46 (dd, J = 3.4, 26.8 Hz, 0.93H), 2.58 (br d, J = 30.0 Hz, 0.07H), 4.30 ("q", J = 5.1 Hz, 1H), 5.30 (dt, J = 2.6, 53.6 Hz, 1H), 6.34 (dd, J = 3.2, 18.1 Hz, 1H); ^{19}F NMR δ −188.04 (dt, J = 23.0, 53.0 Hz); MS m/z 369 (MH^+). Our ^{1}H NMR spectrum of **9** is in agreement with that of 9-[5-*O*-benzoyl-2,3-dideoxy-3(*R*/*S*)-deuterio-2-fluoro-β-D-*threo*-pentofuranosyl]-6-methoxypurine (3′*R*/*S*, ∼89:11) obtained by deoxygenation of the 3′-xanthate with lauroyl peroxide/2-propanol-d_8.[5]

9-[2,3-Dideoxy-3(*R*/*S*)-deuterio-2-fluoro-β-D-*threo*-pentofuranosyl]adenine (10). Treatment of **9** (3′*R*/*S*, ∼93:7; 12.5 mg, 0.035 mmol) using procedure D gave **10** (3′*R*/*S*, ∼92:8; 5 mg, 60%) with data as reported[9,10] except for the following: ^{1}H NMR (MeOH-d_4) δ 2.30 ("dt", J = 4.2, 27.2 Hz, 0.92H), 2.55 ("dt", J = 6.8, 31.0 Hz, 0.08H), 4.27 ("q", J = 5.2 Hz, 1H), 5.29 (dt, J = 2.7, 54.1 Hz, 1H), 6.26 (dd, J = 3.5, 16.8 Hz, 1H); ^{19}F NMR (MeOH-d_4) δ −182.62 (ddd, J = 17.0, 27.0, 54.0 Hz); MS m/z 255 (MH^+).

5′-*O*-(*tert*-Butyldimethylsilyl)-3′-deoxy-3′-fluoroadenosine (12). Treatment of **11**[17] (80 mg, 0.3 mmol) using procedure A gave **12** (76 mg, 67%): ^{1}H NMR δ −0.02 (s, 3H), 0.04 (s, 3H), 0.79 (s, 9H), 3.83−3.87 (m, 2H), 4.58 (dt, J = 2.8, 26.4 Hz, 1H), 4.74 (ddd, J = 4.5, 7.0, 24.7 Hz, 1H), 5.19 (dd, J = 4.4, 54.5 Hz, 1H), 5.86 (br s, 2H), 6.02 (d, J = 7.2 Hz, 1H), 8.08 (s, 1H), 8.33 (s, 1H); ^{19}F NMR δ −199.45 (dt, J = 26.0, 54.0 Hz); MS m/z 384 (MH^+). Anal. Calcd for $C_{16}H_{26}FN_5O_3Si$ (383.5): C, 50.11; H, 6.83; N, 18.26. Found: C, 49.89; H, 6.99; N, 18.03.

9-[5-*O*-(*tert*-Butyldimethylsilyl)-3-deoxy-3-fluoro-β-D-xylofuranosyl]adenine (14). Treatment of **13**[18] (45 mg, 0.17 mmol) using procedure A gave **14** (44.5 mg, 69%): ^{1}H NMR δ 0.11 (s, 6H), 0.91 (s, 9H), 4.03 (dd, J = 6.1, 10.2 Hz, 1H), 4.08 (dd, J = 6.4, 10.5 Hz, 1H), 4.56 (dtd, J = 3.3, 5.9, 26.8 Hz, 1H), 4.66 (dt, J = 1.7, 15.4 Hz, 1H), 5.16 (ddd, J = 2.0, 2.9, 51.2 Hz, 1H), 5.93 (br s, 2H), 6.01 (d, J = 1.5 Hz, 1H), 7.99 (s, 1H), 8.31 (s, 1H); ^{19}F NMR δ −203.72 (ddd, J = 16.0, 26.0, 50.0 Hz); MS m/z 384 (MH^+). Anal. Calcd for $C_{16}H_{26}FN_5O_3Si$ (383.5): C, 50.11; H, 6.83; N, 18.26. Found: C, 50.01; H, 6.72; N, 18.08.

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5′-*O*-(*tert*-Butyldimethylsilyl)-3′-deoxy-3′-fluoro-2′-*O*-(phenoxythiocarbonyl)adenosine (15). Treatment of **12** (24 mg, 0.062 mmol) using procedure B gave **15** (24 mg, 74%): ^{1}H NMR δ 0.16 (s, 6H), 0.96 (s, 9H), 3.93 (dd, J = 2.5, 11.5 Hz, 1H), 4.01 (dd, J = 1.6, 11.4 Hz, 1H), 4.59 (dt, J = 1.7, 25.8 Hz, 1H), 5.61 (dd, J 4.3, 54.1 Hz, 1H), 5.98 (br s, 2H), 6.28 (ddd, J = 4.3, 7.6, 20.7 Hz, 1H), 6.60 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 7.6 Hz, 2H), 7.3 (t, J = 7.3 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 8.20 (s, 1H), 8.42 (s, 1H); ^{19}F NMR δ −199.24 (ddd, J = 21.0, 26.0, 54.0 Hz); MS m/z 520 (MH^+). Anal. Calcd for $C_{23}H_{30}FN_5O_4SSi$ (519.7): C, 53.16; H, 5.82; N, 13.48. Found: C, 53.35; H, 5.95; N, 13.09.

9-[5-*O*-(*tert*-Butyldimethylsilyl)-3-deoxy-3-fluoro-2-*O*-(phenoxythiocarbonyl)-β-D-xylofuranosyl]adenine (16). Treatment of **14** (44 mg, 0.12 mmol) using procedure B gave **16** (30 mg, 50%): ^{1}H NMR δ 0.14 (s, 6H), 0.95 (s, 9H), 3.99−4.09 (m, 2H), 4.49 (dtd, J = 3.0, 7.5, 28.5 Hz, 1H), 5.39 (dd, J = 2.6, 49.8 Hz, 1H), 5.73 (br s, 2H), 6.09 (d, J = 13.3 Hz, 1H), 6.50 (s, 1H), 7.15 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.8 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 8.09 (s, 1H), 8.40 (s, 1H); ^{19}F NMR δ −199.19 (dt, J = 18.0, 51.0 Hz); MS m/z 520 (MH^+). Anal. Calcd for $C_{23}H_{30}FN_5O_4SSi$ (519.7): C, 53.16; H, 5.82; N, 13.48. Found: C, 53.44; H, 6.09; N, 13.21.

5′-*O*-(*tert*-Butyldimethylsilyl)-2′,3′dideoxy-2′(*R*/*S*)-deuterio-3′-fluoroadenosine (17). Treatment of **15** (17.5 mg, 0.034 mmol) using procedure C gave **17** (2′*R*/*S*, ∼15:85; 6.5 mg, 54%) with data as reported[19] except for the following: ^{1}H NMR δ 2.73 (ddd, J = 8.7, 4.8, 39.1 Hz, 0.85H), 2.82 (dd, J = 4.2, 18.8 Hz, 0.15H), 4.44 (dt, J = 3.3, 26.4 Hz, 1H), 5.36 (dd, J = 4.6, 53.5 Hz, 1H), 6.55 (d, J = 8.9 Hz, 1H); ^{19}F NMR δ −176.95 (ddd, J = 26.6, 37.7, 52.7 Hz); MS m/z 369 (MH^+).

2′,3′-Dideoxy-2′(*R*/*S*)-deuterio-3′-fluoroadenosine (18). Treatment of **17** (2′*R*/*S*, ∼15:85; 5 mg, 0.014 mmol) using procedure D gave **18** (2′*R*/*S*, ∼14:86; 2.8 mg, 81%) with data as reported[9] except for the following: ^{1}H NMR (MeOH-d_4) δ 2.66 (dd, J = 5.4, 20.6 Hz, 0.14H), 2.94 (ddd, J = 4.3, 9.3, 40.8 Hz, 0.86H), 4.38 (dt, J = 2.7, 27.3 Hz, 1H), 5.40 (dd, J = 4.6, 53.6 Hz, 1H), 6.43 (d, J = 9.4 Hz, 1H); ^{19}F NMR (MeOH-d_4) δ −173.44 (ddd, J = 28.0, 41.0, 53.0 Hz); MS m/z 255 (MH^+).

9-[5-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-2(*R*/*S*)-deuterio-3-fluoro-β-D-*threo*-pentofuranosyl]adenine (19). Treatment of **16** (8.6 mg, 0.017 mmol) using procedure C gave **19** (2′*R*/*S*, ∼7:93; 3 mg, 65%): ^{1}H NMR δ 0.11 (s, 6H), 0.93 (s, 9H), 2.72 (d, J = 15.4 Hz, 0.93H), 2.85 (br d, J = 44.0 Hz, 0.07H), 3.99 (dd, J = 5.9, 10.2 Hz, 1H), 4.04 (dd, J = 7.1, 10.1 Hz, 1H), 4.20 (dddd, J = 2.5, 6.0, 7.2, 28.6 Hz, 1H), 5.36 (dd, J = 2.0, 53.4 Hz, 1H), 5.79 (br s, 2H), 6.56 (s, 1H), 8.13 (s, 1H), 8.34 (s, 1H); ^{19}F NMR δ −193.82 (ddd, J = 22.0, 27.0, 54.0 Hz); MS m/z 369 (MH^+). Anal. Calcd for $C_{16}H_{25}DFN_5O_2Si$ (368.5): C, 52.15; H, 6.84; N, 19.00. Found: C, 52.07; H, 6.99; N, 18.71.

9-[2,3-Dideoxy-2(*R*/*S*)-deuterio-3-fluoro-β-D-*threo*-pentofuranosyl]adenine (20). Treatment of **19** (2′*R*/*S*, ∼7:93; 4 mg, 0.011 mmol) using procedure D gave **20** (2′*R*/*S*, ∼7:93; 2.7 mg, 98%) with data as reported[9] except for the following: ^{1}H NMR (MeOH-d_4) δ 2.75 (dd, J = 1.4, 21.3 Hz, 0.93H), 2.96 (dd, J = 7.1, 45.9 Hz, 0.07H), 4.26 (dtd, J = 2.7, 6.4, 29.2 Hz, 1H), 5.42 (dd, J = 2.6, 54.1 Hz, 1H), 6.59 (d, J = 1.4 Hz, 1H); ^{19}F NMR (MeOH-d_4) δ −194.91 (ddd, J = 27.0, 22.0, 54.0 Hz); MS m/z 255 (MH^+).

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