

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 occurred 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*₆ 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 heterocyclic 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 attributed 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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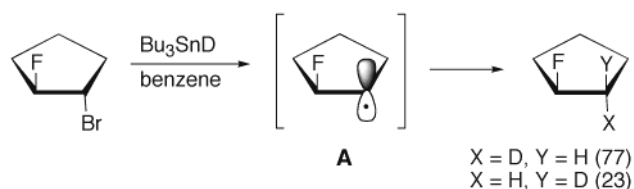
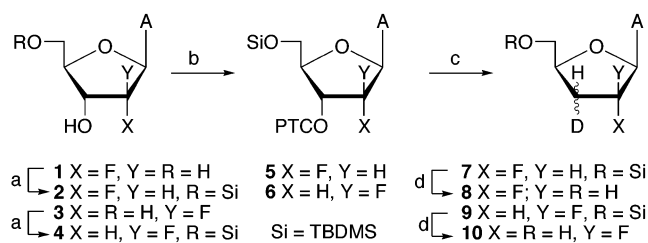


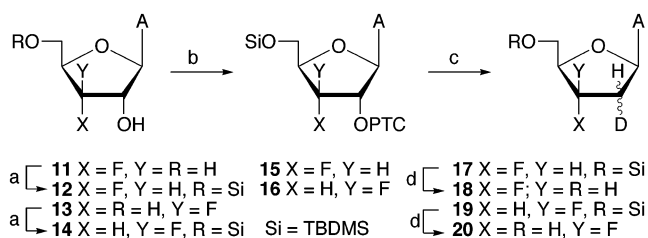
FIGURE 1. Structure of the pyramidalized β -fluorocyclopentyl radical intermediate (**A**) postulated to rationalize the anti stereoselectivity for deuterium transfer with tributyltin hydride.⁷

SCHEME 1^a



^a Key: (a) TBDMS-Cl/imidazole/DMF; (b) PTC-Cl/DMAP/MeCN; (c) $\text{Bu}_3\text{SnD/AIBN/toluene/85}^\circ\text{C}$; (d) $\text{NH}_4\text{F/MeOH}/\Delta$.

SCHEME 2^a



^a Key: (a) TBDMS-Cl/imidazole/DMF; (b) PTC-Cl/DMAP/MeCN; (c) $\text{Bu}_3\text{SnD/AIBN/toluene/85}^\circ\text{C}$; (d) $\text{NH}_4\text{F/MeOH}/\Delta$.

stabilized 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-workers¹² 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*

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' <i>R/S</i> , 64:36)	28
	8 (3' <i>R/S</i> , 64:36)	syn
6 , 2'-fluoro-arabino	9 (3' <i>R/S</i> , 93:7)	85
	10 (3' <i>R/S</i> , 92:8)	anti
15 , 3'-fluoro-ribo	17 (2' <i>R/S</i> , 15:85)	71
	18 (2' <i>R/S</i> , 14:86)	syn
16 , 3'-fluoro-xylo	19 (2' <i>R/S</i> , 7:93)	86
	20 (2' <i>R/S</i> , 7:93)	anti

^a Averages of duplicate experiments determined by ^1H NMR ($\text{H}2'/2''$ or $\text{H}3'/3''$) 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

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 ^1H NMR and were consistent with those determined with 5'-O-monomethoxytrityl derivatives¹³ (Table 1). Compounds **7**, **9**, **17**, and **19** were desilylated ($\text{NH}_4\text{F/MeOH}$)¹⁴ to give **8**,^{9,10} **10**,^{9,10} **18**,⁹ and **20**,⁹ respectively, with ^1H NMR data as reported except for simplification of multiplets and ~50% reduction in intensities of signals for $\text{H}3',3''$ (**8** and **10**) or $\text{H}2',2''$ (**18** and **20**). ^1H – ^1H and ^1H – ^{19}F coupling constants in spectra of **8**, **10**, **18**, and **20** were consistent with experimental^{9,10} and calculated¹⁵ values for other fluorodi-deoxynucleosides and had compatible magnitude reductions for coupling with ^2H . Epimeric ratios were determined more easily with some of the deprotected derivatives.

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** \rightarrow **7** (3'*R/S*, 64:36; syn F/D de 28) versus that for **6** \rightarrow **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'-fluoro-nucleosides (**15** \rightarrow **17** (syn F/D de 70) versus **16** \rightarrow **19** (anti F/D de 86)).¹⁶

Conclusions

It is clear that steric effects are decisive for determination of the stereoselectivity 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 $\text{NaB(OAc)}_3\text{H}$,^{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'.

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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

^1H (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 ($\text{EtOAc}/\text{NH}_4\text{Cl}/\text{H}_2\text{O}$). The organic layer was washed (brine), dried (Na_2SO_4), evaporated, and column chromatographed (5 → 10% $\text{MeOH}/\text{CHCl}_3$) to give **2** (59 mg, 70%): ^1H 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 (dd, $J = 16.0$, 53.0 Hz); MS m/z 384 (MH^+). Anal. Calcd for $\text{C}_{16}\text{H}_{26}\text{FN}_5\text{O}_3\text{Si}$ (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 ($\text{EtOAc}/\text{H}_2\text{O}$), and the organic layer was washed (0.1 M $\text{HCl}/\text{H}_2\text{O}$, $\text{NaHCO}_3/\text{H}_2\text{O}$, brine) and dried (Na_2SO_4). Volatiles were evaporated, and the residue was chromatographed (30% hexanes/ EtOAc → EtOAc) to give **5** (35 mg, 66%): ^1H 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 $\text{C}_{25}\text{H}_{30}\text{FN}_5\text{O}_4\text{SSi}$ (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%): ^1H 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 reported¹⁰ except for the following: ^1H 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 chromatographed (5 → 10% $\text{MeOH}/\text{CHCl}_3$) to give **8** (3'R/S, ~64:36; 6 mg, 60%) with data as reported^{9,10} except for the following: ^1H NMR ($\text{MeOH}-d_4$) 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 ($\text{MeOH}-d_4$) 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 reported¹⁰ except for the following: ^1H 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 ^1H 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: ^1H NMR ($\text{MeOH}-d_4$) 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 ($\text{MeOH}-d_4$) 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%): ^1H 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 $\text{C}_{16}\text{H}_{26}\text{FN}_5\text{O}_3\text{Si}$ (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%): ^1H 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 (ddd, $J = 3.3$, 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 $\text{C}_{16}\text{H}_{26}\text{FN}_5\text{O}_3\text{Si}$ (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%): ^1H 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 $\text{C}_{23}\text{H}_{30}\text{FN}_5\text{O}_4\text{SSi}$ (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%): ^1H 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 $\text{C}_{23}\text{H}_{30}\text{FN}_5\text{O}_4\text{SSi}$ (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 reported¹⁹ except for the following: ^1H 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 reported⁹ except for the following: ^1H NMR ($\text{MeOH}-d_4$) 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 ($\text{MeOH}-d_4$) 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%): ^1H 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 $\text{C}_{16}\text{H}_{25}\text{DFN}_5\text{O}_2\text{-Si}$ (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 reported⁹ except for the following: ^1H NMR ($\text{MeOH}-d_4$) 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 ($\text{MeOH}-d_4$) δ -194.91 (ddd, $J = 27.0$, 22.0, 54.0 Hz); MS m/z 255 (MH^+).

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