A Practical Synthesis of Perdeuterated Deoxyribose and Deoxyribonucleosides[1]

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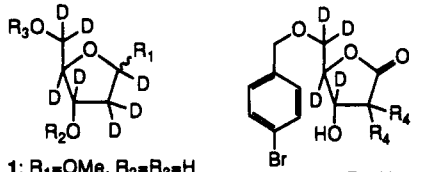
A stereoselective synthesis of perdeuterated deoxyribofuranoside (1) has been developed starting from known methyl 4-(2'-tetrahydropyranyloxy)-2-butynoate. The synthetic strategy involved the Sharpless asymmetric epoxidation of alcohol 7, followed by a tandem epoxide isomerization and opening with NaCN. The resulting lactone **4b** was then reduced via its TBDMS derivative with Dibal-D and subsequently converted to perdeuterated deoxyribofuranoside (1).

Recent advances in NMR spectroscopy have spurred the investigation of the three-dimensional structures of DNA oligomers and their interactions with both small and large molecules. Valuable information on conformation has been gleaned mainly by two-dimensional NMR correlated spectroscopy (COSY) and 2D nuclear Overhauser enhancement spectroscopy (NOESY). Even at higher field strength currently available, however, the complete spectral assignment is often hampered by extensive overlapping of signals. For the study of DNA of longer than 12–16 base pairs, for example, a remedy to this difficulty requires spectral editing such as three-dimensional NMR spectroscopy[2] or isotopic substitution.[3] Regiospecific incorporation of deuterium would facilitate the systematic spectral assignment by selective suppression of nonessential proton signals; the incorporation of the deuterated deoxyribose residues into remote sites of the DNA molecule would thus be useful in studying its adducts with carcinogens or drugs. The use of specifically deuterated nucleotides has also proved to be a powerful tool in the elucidation of the mechanisms of DNA damage by DNA cleaving drugs.[4]

Several research groups have recently reported the preparation of specifically deuterated deoxyribonucleosides for incorporation into synthetic DNA oligomers.[3-7] With a few notable exceptions employing enzymatic processes,[3a,b] a majority of the approaches have so far relied on chemical modification of readily available "chiral pool" starting materials; some have utilized nucleosides themselves[5] and others carbohydrates prior to coupling with heterocyclic bases.[6,7]

However, previously reported syntheses of deuterated deoxyribose often suffer from laborious multistep, though elegant, transformations. Furthermore, the stereospecific deuteration at the 4-position of deoxyribose has proved to be problematic.[5d,8] Thus, we felt that a general solution could be found in de novo asymmetric synthesis of deoxyribose. Herein we report a practical synthesis of perdeuterated deoxyribofuranosides **1** and **2** and the corresponding α-chloro derivative **3**, a key intermediate in nucleoside synthesis (vide infra), which is amenable to a large-scale preparation and also applicable to efficient syntheses of regioselectively deuterated deoxyriboses.



1: R_1=OMe, R_2=R_3=H
2: R_1=OMe, R_2=R_3=Tol
3: R_1=α-Cl, R_2=R_3=Tol

4a: R_4=H
4b: R_4=D

Results and Discussion

Recent remarkable progress in acyclic stereocontrol has brought forth a renaissance of interest in the stereoselective synthesis of carbohydrates. As a result, several syntheses

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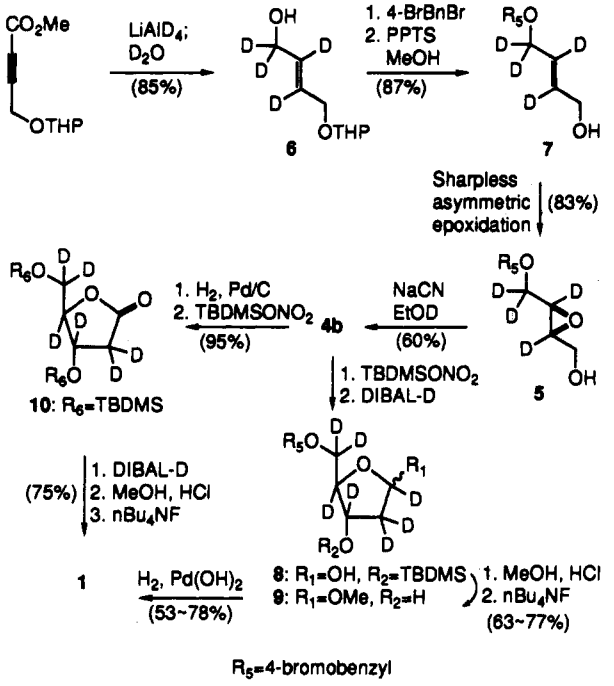
Scheme I



of deoxyribose have been reported.[9] Most approaches have relied upon the "chiral pool" source, i.e., 2,3-*O*-isopropylidene-D-glyceraldehyde, to establish absolute stereochemistry, and are not particularly suitable for the stereoselective synthesis of deuterated deoxyribose. It occurred to us that a more efficient synthetic method can be evolved by utilizing the Sharpless asymmetric epoxidation.[10]

In our synthetic planning we chose to go through the intermediacy of 3,4,5,5′-tetradeuterio-2-deoxyribonolactone (**4**). The deuteration at the 2,2′-position of the lactone should be readily accomplished by base-catalyzed H/D exchange. The lactone carbonyl can be reduced to the lactol using DIBAL[7] or disiamylborane,[9a,11] thus resulting in deuterium incorporation at the C-1 position. Lactone **4** would in turn be available in one-pot operation from epoxide **5** by Payne rearrangement and in situ nucleophilic ring opening with cyanide.[12]

As outlined in Scheme I, our starting material was found in known and readily available methyl 4-(2′-tetrahydropyranyloxy)-2-butynoate.[13] The $LiAlD_4$ reduction and quenching with D_2O yielded stereoselectively the *E*-allylic alcohol **6** in 80–85% yield,[14] resulting in an efficient incorporation of deuterium at the 3-, 4-, and 5,5′-positions of deoxyribose. The alcohol was then converted into the 4-bromobenzyl ether **7** by alkylation with 4-bromobenzyl bromide (NaH, THF) and subsequent deblocking of the THP group in 69% overall yield. The Sharpless asymmetric epoxidation of alcohol **7** afforded epoxide **5**, as a solid, in 83% yield and 87–93% ee, which could be recrystallized to optical purity. Our choice of 4-bromobenzyl protecting group was guided by a recent report that the epoxide of the corresponding *Z*-allyl alcohol was a crystalline solid which was recrystallized to enantiomerically pure form.[15]

Treatment of epoxide **5** with NaCN in refluxing EtOH–H_2O gave the crude acid,[16] which was lactonized (*p*-TsOH, toluene, reflux) without purification to provide deoxyribonolactone **4a** in ~60% overall yield. The use of EtOD–D_2O furnished directly the perdeuterated lactone **4b**. Formation of **4a,b** can be ascribed to the reversible Payne rearrangement of **5** and subsequent in situ selective nucleophilic attack by cyanide.

The hydroxyl group of lactone **4b** was then protected quantitatively by treatment with *tert*-butyldimethylsilyl nitrate.[17] The DIBAL-D[18] reduction was achieved most conveniently at −90 °C in THF to give lactol **8**. At −78 °C a small amount of overreduction was observed. Sequential treatment with methanolic HCl and *n*-Bu_4NF furnished uneventfully **9** in 63–77% overall yield from **4b**. Finally, the removal of the 4-bromobenzyl group was accomplished without H/D scrambling by dissolving metal reduction (Li, NH_3) or hydrogenolysis using either Pearlman's catalyst or Raney nickel W2 to produce perdeuterated deoxyribofuranoside **1** in 53–78% yield.

More conveniently, the initial debenzylation (H_2, 10% Pd/C) of **4b** followed by bissilylation of both hydroxyl groups gave lactone **10** in quantitative yield. Lactone **10** was converted uneventfully into **1** by employing the procedure of Harris (70% overall).[7] Diol **1** was then protected as bis(toluoyl) ester **2**, which was in turn converted into the chloro derivative **3** by the method of Hoffer.[19]

An alternate route to bis(toluoyl) ester **2** involving disiamylborane reduction[11] of lactone **11** was investigated. Lactone **11** was prepared in excellent yield by debenzylation (H_2, 10% Pd/C) of **4b**, followed by bistoluoylation. Subsequent treatment of lactone **11** with Sia_2BD gave the desired lactol **12** only in poor (23%) yield. In view of this disappointingly low yield, no further studies with Sia_2BD were undertaken.

The direct coupling reaction of a 2-deoxyribofuranosyl donor with the heterocyclic bases is known to often suffer

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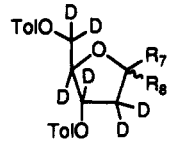

11: R_7=R_8=O
12: R_7=OH, R_8=D

from the formation of a mixture of anomers. Very recently, however, this difficulty has been circumvented efficiently by the use of Hoffer's α-chloro bis(toluoyl) sugar (cf. 3): Harris and co-workers have successfully converted the corresponding 1,2,2′-trideuterio-α-chloro derivative into 1′,2′,2″-trideuterio deoxythymidine, deoxycytidine, deoxyadenosine, and deoxyguanosine.[7] Thus, our work constitutes a formal synthesis of perdeuterated deoxyribonucleosides.

In summary, we have developed an efficient method for preparing perdeuterated and/or regioselectively deuterated deoxyriboses, which should be of utility in investigating the three-dimensional structures of DNA oligomers and their interactions with both small and large molecules. Our synthesis further underscores the usefulness of the Sharpless asymmetric epoxidation in natural product synthesis.

Experimental Section

General. All reactions were conducted under an atmosphere of dry nitrogen and in oven-dried glassware, and concentrations were performed under reduced pressure with a Büchi rotary evaporator. All solvents were purified before use. Ether, tetrahydrofuran, and toluene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from CaH_2. The normal processing of organic extracts consisted of washing the extract with brine, drying over Na_2SO_4 or $MgSO_4$, filtration, and concentration with a rotary evaporator.

NMR spectra were measured on commercially available spectrometers: ^1H at 300, 360, or 400, ^{13}C at 90 or 100, and ^2H at 61 MHz. For ^1H spectra tetramethylsilane was used as internal standard. ^{13}C NMR spectra were referenced with the δ 77.0 resonance of $CDCl_3$. ^2H NMR spectra were acquired in chloroform with $CDCl_3$ (7.26 ppm) as internal standard. Low and high resolution mass spectra were measured as fast atom bombardment (FAB) spectra with 3-nitrobenzyl alcohol as the matrix solvent. Optical rotations were measured at room temperature.

Melting points are uncorrected. Analytical thin layer chromatography (TLC) was performed by using Merck 60 F_{254} glass plates precoated with a 0.25-mm thickness of silica gel. Column chromatography was performed on kieselgel 60 (70–230 mesh) silica gel. Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (>95% by ^1H analysis) for use in subsequent reactions. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

(*E*)-4-(2-Tetrahydropyranyloxy)-2-buten-1-ol-*1,1,2,3-d*$_4$ (6). To a solution of methyl 4-(2-tetrahydropyranyloxy)-2-butynoate[13] (20 g, 81 mmol) in tetrahydrofuran (250 mL) at 0 °C was added lithium aluminum deuteride (5.5 g, 0.13 mol). The reaction mixture was stirred at room temperature for 9 h under a nitrogen atmosphere. The reaction was quenched at 0 °C with D_2O (6 mL), followed by the sequential addition of 3 N NaOH (6 mL) and H_2O (18 mL). The reaction mixture was then stirred at room temperature for an additional 30 min and filtered through Celite. The filter cake was thoroughly washed with EtOAc. The combined filtrate was then evaporated in vacuo to give 14.4 g (80%) of the crude alcohol 6 as a colorless oil. The crude product was used without further purification for the next step: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.48–1.88 (m, 7 H, O*H* included), 3.51 (m, 1 H), 3.86 (m, 1 H), 3.98 (d, *J* = 12.7 Hz, 1 H), 4.25 (d, *J* = 12.7 Hz, 1 H), 4.65 (m, 1 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 4.13 (br s, 2 D), 5.86 (br s, 1 D), 5.93 (br s, 1 D); ^{13}C NMR (100 MHz) δ 19.4, 25.4, 30.6, 62.2, 66.9, 98.0, 127.6 (t), 131.3 (t) (C-1 not shown); HRMS (M^+ + H) 177.1429 calcd for $C_9H_{13}D_4O_3$, found 177.1432.

(*E*)-4-[(*p*-Bromobenzyl)oxy]-2-buten-1-ol-*2,3,4,4-d*$_4$ (7). To a solution of alcohol 6 (14.36 g, 81 mmol) in 4:1 THF–DMF (250 mL) were added sequentially sodium hydride (5.06 g of a 50% suspension in oil, 0.1 mol) and *p*-bromobenzyl bromide (24.3 g, 97 mmol). The reaction mixture was stirred at room temperature for 8 h under a nitrogen atmosphere. The reaction was quenched with methanol and the solvent was removed in vacuo. The residue was diluted with water, and the aqueous layer was extracted three times with EtOAc. Normal workup gave the crude *p*-bromobenzylated product (35.4 g).

To a solution of the crude product in methanol was added PPTS (40 mg). The resulting mixture was stirred at room temperature for 9 h. After neutralization with solid $NaHCO_3$, the reaction mixture was concentrated and purified by column chromatography (5:2 Et_2O:hexane) to provide 32.16 g (87%) of allylic alcohol 7: ^1H NMR ($CDCl_3$, 300 MHz) δ 1.39 (t, *J* = 5.7 Hz, 1 H, OH), 4.15 (d, *J* = 5.7 Hz, 2 H), 4.45 (s, 2 H), 7.20 (d, *J* = 8.9 Hz, 2 H), 7.45 (d, *J* = 8.9 Hz, 2 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 3.98 (br s, 2 D), 5.92 (br s, 1 D), 6.02 (br s, 1 D); ^{13}C NMR (100 MHz) δ 62.9, 69.3 (weak m), 71.4, 121.5, 127.2 (t), 129.3, 131.5, 132.1 (t), 137.3; HRMS (M^+ – H) 259.0272 and 261.0251 calcd for $C_{11}H_8D_4O_2Br$, found 259.0262 & 261.0283.

(2*R*,3*R*)-3-[[(*p*-Bromobenzyl)oxy]dideuteriomethyl]oxiranemethanol-*2,3-d*$_2$ (5). To a cold (–23 °C), stirred suspension of powdered 4-Å molecular sieves (0.4 g) in CH_2Cl_2 (7 mL) under a nitrogen atmosphere were added sequentially titanium isopropoxide (0.19 g, 0.65 mmol), D-(–)-diisopropyl tartrate (0.10 mL, 0.89 mmol), and a 2.0 M solution of *tert*-butyl hydroperoxide in methylene chloride (3.2 mL, 6.4 mmol). After the resulting mixture was stirred at –23 °C for 30 min, a solution of allylic alcohol 7 (0.84 g, 3.26 mmol) in CH_2Cl_2 (3 mL) was added. The reaction mixture was then stored at –23 °C overnight. The reaction was quenched with water and allowed to warm to room temperature. A solution of 30% NaOH in brine (0.8 mL) was then added, and the resulting mixture was stirred vigorously for 30 min. The phases were separated and the aqueous layer was extracted three times with CH_2Cl_2. Normal workup and purification by column chromatography (1:2 hexane:EtOAc) gave 0.74 g (83%) of pure epoxide 5 as a colorless solid. Recrystallization with cold petroleum ether gave enantiomerically pure epoxide 5: mp 50–52 °C; $[\alpha]^{25}_D$ = +17° (*c* 1.5, $CHCl_3$)]; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.68 (br m, 1 H, O*H*), 3.67 (dd, *J* = 7.5 and 12.6 Hz, 1 H), 4.51 (dd, *J* = 5.5 and 12.6 Hz, 1 H), 4.47 (d, A of AB q, *J* = 11.0 Hz, 1 H), 4.54 (d, B of AB q, *J* = 11.0 Hz, 1 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.45 (d, *J* = 8.4 Hz, 2 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 3.01 (br s, 1 D), 3.20 (br s, 1 D), 3.46 (br s, 1 D), 3.74 (br s, 1 D); ^{13}C NMR (100 MHz) δ 53.6 (t), 55.1 (t), 61.0, 68.9 (weak m), 72.5, 121.6, 129.3, 131.5, 136.9; HRMS (M^+ – H) 275.0221 and 277.0200 calcd for $C_{11}H_8D_4O_3Br$, found 275.0213 and 277.0199. Anal. Calcd for $C_{11}H_8D_4O_3Br$: C, 47.67; Br, 28.83. Found: C, 47.91; Br, 28.62.

5-*O*-*p*-Bromobenzyl-2-deoxy-D-*erythro*-pentofuran-1-one-*2,2′,3,4,5,5′-d*$_6$ (4b). To a solution of epoxide 5 (0.7 g, 2.52 mmol) in 2:3 EtOD:D_2O (15 mL) was added sodium cyanide (372 mg, 7.58 mmol).[16] The reaction mixture was heated at reflux for 8 h. The ethanol was evaporated in vacuo and the aqueous residue extracted with ether. The aqueous layer was carefully acidified to pH 3–4 with concentrated hydrochloric acid at 0 °C in a hood. The aqueous phase was then saturated with NaCl and extracted six times with Et_2O. The ether extracts were dried (Na_2SO_4) and evaporated in vacuo to give the crude acid as a dark oil.

The crude acid was dissolved in toluene, and the solution was heated at reflux for 12 h with azeotropic removal of water using a Dean–Stark trap. The solvent was then removed in vacuo. The concentrate was purified by column chromatography (10:1 CH_2Cl_2:MeOH) to furnish 0.47 g (60% overall yield) of lactone 4b as a coloress solid: mp 63–65 °C; $[\alpha]^{25}_D$ = +2.9° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) 3615, 3400, 1753, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (br s, 1 H, O*H*), 4.43 (d, A of AB q, *J* = 10.8 Hz, 1 H), 4.51 (d, B of AB q, *J* = 10.8 Hz, 1 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 7.46 (d, *J* = 8.3 Hz, 2 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 2.39 (br s, 1 D), 2.86 (br s, 1 D), 3.62 (br s, 2 D), 4.46 (br s, 2 D); ^{13}C NMR (100 MHz) δ 37.9 (weak m), 68.5 (weak m), 69.2 (t), 72.8, 86.0 (t), 121.8, 129.4, 131.3, 136.3, 176.4; HRMS (M^+ + H) 307.0452 and

309.0432 calcd for $C_{12}H_8D_6O_4Br$, found 307.0399 and 309.0461. Anal. Calcd for $C_{12}H_8D_6O_4Br$: C, 46.92; Br, 26.01. Found: C, 47.04; Br, 25.88.

Methyl 5-*O*-*p*-Bromobenzyl-2-deoxy-α-(and β-)D-*erythro*-pentofuranoside-*1,2,2',3,4,5,5'*-d_7 (9). To a solution of *tert*-butyldimethylsilyl nitrate[17] (62 mg, 0.35 mmol) in THF (2 mL) containing pyridine (0.18 mL, 2.28 mmol) was added a solution of lactone **4b** (100 mg, 0.32 mmol) in THF (2 mL). The reaction mixture was stirred at room temperature for 8 h and then filtered through Celite. The filtrate was concentrated, diluted with Et_2O, washed twice with water, dried (Na_2SO_4), and evaporated in vacuo to give 136 mg (99%) of the crude silylated lactone as a white solid.

To a solution of the crude lactone thus obtained in CH_2Cl_2 at −90 °C was added dropwise a 1.4 M solution of diisobutylaluminum deuteride[18] in hexane–Et_2O (0.23 mL, 0.32 mmol). After being stirred for 2 h at −90 °C under a nitrogen atmosphere, the reaction mixture was quenched with MeOH and allowed to warm up to room temperature. The mixture was filtered, and the filtrate was washed with aqueous sodium potassium tartrate solution. The organic layer was dried (Na_2SO_4) and concentrated to give lactol **8** as a colorless oil (117 mg, 85%).

The crude lactol **8** was treated in 0.1 mL of 0.1% methanolic HCl for 40 min at room temperature. Powdered silver carbonate (25 mg) was added, and the reaction mixture was then filtered to remove the inorganic salts. The filtrate was concentrated to furnish the methyl furanoside with a partial loss of the silyl protecting group.

Finally, the residue was dissolved in THF (15 mL) and treated with 0.35 mL of a 1.0 M solution of tetra-*n*-butylammonium fluoride in THF at room temperature for 30 min. The solvent was evaporated in vacuo. The residue was diluted with brine and extracted three times with EtOAc. Normal workup and purification by column chromatography (1:2 Et_2O–CH_2Cl_2) gave 81 mg (91%) of **9** as a colorless oil: HRMS ($M^+ - D$) 321.0609 and 323.0588 calcd for $C_{13}H_{10}D_6O_4Br$, found 321.0603 and 323.0593.

For an analytical sample, the methyl furanoside **9** (a ~1:1 mixture of anomers) was separated. Data for the first fraction of R_f = 0.36 in 20:1 CH_2Cl_2–MeOH: $[\alpha]^{25}_D$ = +75° (*c* 1.48, $CHCl_3$); IR ($CHCl_3$) 3540, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.76 (s, 1 H, O*H*), 3.37 (s, 3 H), 4.48 (s, 2 H), 7.18 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 1.96 (br s, 1 D), 2.10 (br s, 1 D), 3.46 (br s, 1 D), 3.49 (br s, 1 D), 4.13 (br s, 1 D), 4.19 (br s, 1 D), 5.10 (br s, 1 D); ^{13}C NMR (100 MHz) δ 40.4 (weak m), 54.8, 69.8 (weak m), 72.5 (weak m), 72.8, 85.6 (weak m), 105.1 (t), 121.4, 129.3, 131.7, 137.0. Data for the second fraction of R_f = 0.32 in 20:1 CH_2Cl_2–MeOH: $[\alpha]^{25}_D$ = −59° (*c* 1.49, $CHCl_3$); IR ($CHCl_3$) 3540, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.77 (s, 1 H, O*H*), 3.31 (s, 3 H), 4.52 (s, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 7.47 (d, *J* = 8.3 Hz, 2 H); ^2H NMR ($CHCl_3$, 61 MHz) δ 2.03 (br s, 1 D), 2.18 (br s, 1 D), 3.48 (br s, 1 D), 3.54 (br s, 1 D), 4.00 (br s, 1 D), 4.36 (br s, 1 D), 5.05 (br s, 1 D); ^{13}C NMR (100 MHz) δ 40.5 (weak m), 54.9, 71.1 (weak m), 72.5 (weak m), 72.8, 83.2 (weak m), 104.7 (t), 121.5, 129.3, 131.7, 136.9.

3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pentofuran-1-one-*2,2',3,4,5,5'*-d_6 (10). To a solution of lactone **4b** (217 mg, 0.67 mmol) in EtOH (20 mL) was added 10% Pd/C (20 mg). The reaction mixture was stirred overnight under 1 atm of hydrogen and filtered through Celite. The filtrate was concentrated to give 87 mg (94%) of the corresponding diol as a 1:1 mixture of anomers. The diol was then treated with a solution of *tert*-butyldimethylsilyl nitrate[17] (270 mg, 1.4 mmol) in THF (8 mL) containing pyridine (0.7 mL, 9 mmol). The reaction mixture was stirred at room temperature for 8 h and then filtered through Celite. The filtrate was concentrated, diluted with Et_2O, washed twice with water, dried (Na_2SO_4), and evaporated in vacuo. The crude product was then purified by column chromatography to give 219 mg (95%) of the silylated lactone as a colorless oil: ^1H NMR ($CDCl_3$, 360 MHz) δ 0.07 (s, 3 H), 0.08 (s, 3 H), 0.10 (s, 6 H), 0.90 (s, 18 H).

More conveniently, the application of the identical reaction sequence on lactone **10** as described above provided furanoside **1** in 75% overall yield.

Methyl 2-Deoxy-α-(and β-)D-*erythro*-pentofuranoside-*1,2,2',3,4,5,5'*-d_7 (1). To a solution of 4-bromobenzyl ether **9** (120 mg, 0.37 mmol) in EtOH (15 mL) was added 20% $Pd(OH)_2$/C (16 mg). The reaction mixture was stirred under 1 atm of hydrogen for 12 h and filtered through Celite. The filtrate was concentrated to give 44 mg (78%) of **1** as a 1:1 mixture of anomers, which was used directly for the next step: ^1H NMR ($CDCl_3$, 300 MHz) δ 3.39 (s, 3 H), 3.38 (s, 3 H), 2.70 (br s, 1 H), 2.55 (br s, 1 H), 1.82 (br s, 1 H), 1.69 (br s, 1 H).

Methyl 3,5-Di-*O*-*p*-toluoyl-2-deoxy-α-(and β-)D-*erythro*-pentofuranoside-*1,2,2',3,4,5,5'*-d_7 (2). To a solution of diol **1** (40 mg, 0.26 mmol) in pyridine (2 mL) containing 4-(dimethylamino)pyridine (0.1 mg) was added *p*-toluoyl chloride (0.07 mL, 0.54 mmol). The reaction mixture was stirred at room temperature for 2.5 h and quenched with water. The mixture was extracted three times with Et_2O. Normal workup and purification of the resulting solid by chromatography on silica (10:2 hexane–EtOAc) gave 96 mg (95%) of **2** as a mixture of anomers (a colorless oil): IR ($CHCl_3$) 1745, 1625 cm^{-1}; HRMS ($M^+ + H$) 392.2091 calcd for $C_{22}H_{18}D_7O_6$, found 392.2065.

A small sample of anomers was separated for characterization purposes by SiO_2 column chromatography using 1:3 Et_2O–hexane as eluent. Data for the first fraction of R_f = 0.31 in 1:3 Et_2O–hexane: mp 65–67 °C; $[\alpha]^{25}_D$ = −47° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 360 MHz) δ 2.40 (s, 3 H), 2.41 (s, 3 H), 3.36 (s, 3 H), 7.21–7.23 (m, 4 H), 7.91 (d, *J* = 8.2 Hz, 2 H), 7.97 (d, *J* = 8.2 Hz, 2 H); ^2H NMR ($CHCl_3$, 76 MHz) δ 2.34 (br s, 1 D), 2.54 (br s, 1 D), 4.52 (br s, 3 D), 5.24 (br s, 1 D), 5.60 (br s, 1 D); ^{13}C NMR (100 MHz) δ 21.7 (2 C), 38.8 (weak m), 55.1, 64.5 (weak m), 75.5 (weak m), 81.5 (weak m), 105.1 (t), 126.9, 127.2, 129.0, 129.1, 129.7, 129.8, 143.7, 144.0, 166.1, 166.4. Data for the second fraction of R_f = 0.24 in 1:3 Et_2O–hexane: mp 66–68 °C; $[\alpha]^{25}_D$ = −144° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 360 MHz) δ 2.40 (s, 3 H), 2.41 (s, 3 H), 3.42 (s, 3 H), 7.21–7.23 (m, 4 H), 7.91 (d, *J* = 8.1 Hz, 2 H), 7.93 (d, *J* = 8.1 Hz, 2 H); ^2H NMR ($CHCl_3$, 76 MHz) δ 2.16 (br s, 1 D), 2.53 (br s, 1 D), 4.51 (br s, 3 D), 5.18 (br s, 1 D), 5.41 (br s, 1 D); ^{13}C NMR (100 MHz) δ 21.7 (2 C), 38.7 (weak m), 55.1, 64.5 (weak m), 74.4 (t), 80.8 (t), 105.0 (t), 127.0, 127.1, 129.1, 129.2, 129.7, 129.8, 143.8, 143.9, 166.3, 166.5.

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Supplementary Material Available: ^1H, ^2H, and ^{13}C NMR spectra (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.