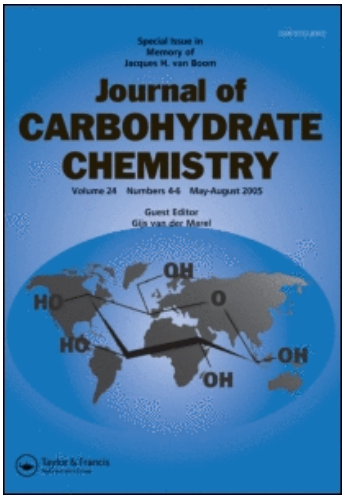

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Synthesis and Reactivity of Benzyl 2-O-Trifluoromethyl-Sulfonyl- and Benzyl 3-O-Trifluoromethylsulfonyl-β-D-Ribofuranoside - The first Evidence of Trifluoromethyl-Sulfonyl (Triflyl) Migration in Carbohydrates

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SYNTHESIS AND REACTIVITY OF BENZYL 2-O-TRIFLUOROMETHYL-SULFONYL- AND BENZYL 3-O-TRIFLUOROMETHYLSULFONYL-β-D-RIBOFURANOSIDE - THE FIRST EVIDENCE OF TRIFLUOROMETHYL-SULFONYL (TRIFLYL) MIGRATION IN CARBOHYDRATES

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ABSTRACT

Benzyl 2,5-di-O-(tert-butyldimethyl)silyl-3-O-triflyl-β-D-ribofuranoside (13) underwent triflyl migration upon O-desilylation with triethylammonium hydrogen fluoride in tetrahydrofuran affording benzyl 2-O-triflyl-β-D-ribo-furanoside (7) in ca. 5% yield, together with three other products, benzyl 3-O-triflyl-β-D-ribofuranoside (17), benzyl 2-O-(tert-butyldimethyl)silyl-3-O-triflyl-β-D-ribo-furanoside (18) and benzyl 3-deoxy-β-D-glycero-pento-furanos-2-uloside (16). In order to confirm the triflyl migration, a series of reactions were performed.

INTRODUCTION

The trifluoromethylsulfonate (triflate) group has been used increasingly in organic syntheses due to its excellent leaving ability and the low nucleophilicity of the anion generated.[1,2] During the course of our ongoing program to develop methods to

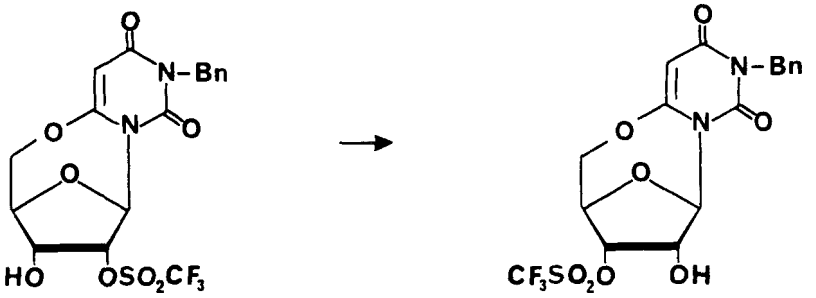


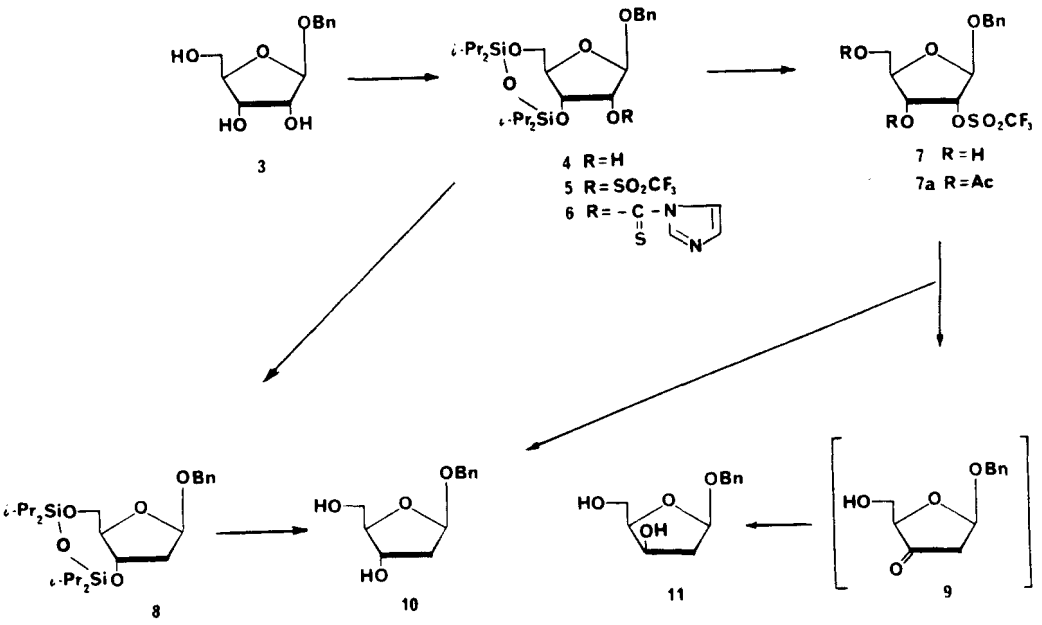
FIG. 1 Triflyl migration (1→2 interconversion) in solution of pyridine, Me_2SO or HMPA

introduce a substituent at the C-2' position of pyrimidine nucleosides in the "up" configuration by nucleophilic displacement reactions,[3-8] we discovered an intriguing triflyl migration reaction. In a previous paper,[6] we reported the quantitative conversion of 6,5'-anhydro-3-benzyl-1-(2-O-triflyl-β-D-ribofuranosyl)-barbituric acid (1, Figure 1) into the isomeric 3'-O-triflyl derivative 2.

In order to determine whether this isomerization is a special case occurring only in the conformationally unique 6,5'-anhydro-nucleoside system, or whether it is a more general reaction in a system containing vicinal cis-diol functions, we investigated the benzyl β-ribofuranoside system as a non-nucleoside model. We obtained evidence that triflyl migration did occur in the carbohydrate: the reaction as described below, however, took unexpectedly different course than did that with the nucleoside.

RESULTS AND DISCUSSION

Benzyl 2-O-triflyl-β-D-ribofuranoside (**7**, **Scheme 1**) was readily prepared from benzyl β-D-ribofuranoside[9] (**3**) in three steps by conversion into benzyl 3,5-O-(1,1,3,3-tetraisopropyldisiloxan-1,3-yl)-β-D-ribofuranoside (**4**) which was then triflylated to **5**. After O-desilylation benzyl 2-O-triflyl-β-D-ribofuranoside (**7**) was obtained. No 3,5 to 2,3 silyl migration was observed during triflylation of **4** into **5**, although such migration occurred quantitatively with 1,3-dimethylpseudouridine,[5,7] The structure of **5** was firmly established by its conversion into the 2-deoxy glycoside **10** via the O-desilylated derivative **7**, which was

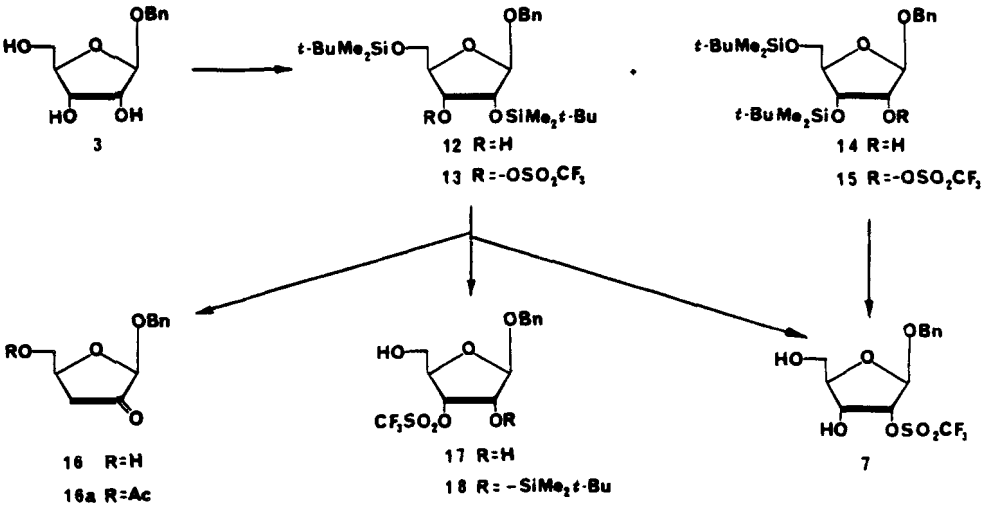


SCHEME 1

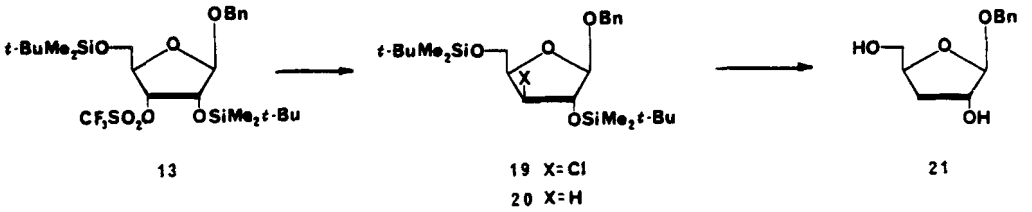
reduced with sodium borohydride. Treatment of **7** with sodium borohydride in acetonitrile[10] afforded a mixture of benzyl 2-deoxy-β-D-erythropentofuranoside (**10**) (5%) and benzyl 2-deoxy-β-D-threopentofuranoside (**11**) (49%). The major product **11** was apparently derived, via reduction, from the ketone intermediate **9**. When N,N-dimethylformamide (DMF) was used as the solvent **10** and **11** were obtained in 24 and 15% yield, respectively. Compound **10** was identical with the product obtained by reduction of the 2-(imidazolyl)thiocarbonyl derivative **6** with tri-n-butyltin hydride (n-Bu_3SnH) followed by O-desilylation of the product **8**.

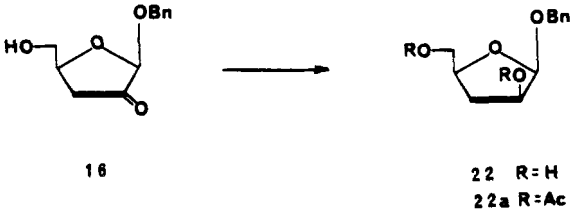
The synthesis of isomeric benzyl 3-O-triflyl-β-D-ribofuranoside **17** (**Scheme 2**) was not straightforward. Treatment of **3** with two equivalents of tert- butyl-dimethylsilyl chloride (BDMS-Cl) afforded a 1:1 mixture of the 2,5- and 3,5-di-O-silyl-D-ribosides (**12** and **14**, respectively) which were chromatographically separated. Compound **14** was readily converted into 2-triflate **7** by triflylation and desilylation. The 2,5-di-O-silylated riboside **12** was triflylated to **13** which was further converted into the 3-deoxy derivative **20** (**Scheme 3**) either by direct reduction with sodium borohydride or by way of the 3-chloro-D-xyloside **19** which was reduced with tri-n-butyltin hydride in the presence of 2,2'-azobis(methylpropionitrile) (AIBN).[11,12] Desilylation of **20** afforded benzyl 3-deoxy-β-D-erythropentofuranoside (**21**). Desilylation of **13** with fluoride gave a mixture of 3-triflate **17**, 2-triflate **7**, the monosilylated intermediate **18**, and the novel glycosuloside (**16**).

The product distribution upon desilylation of **13** is dependent upon the reaction conditions (see Table 1). Prolonged reaction



SCHEME 2





SCHEME 3

TABLE 1. Product distribution upon O-desilylation of 13

Reagent	Time hr	% of product 18	17	16	7
TEA/HF, THF	72	—	16	32	4
TEA/HF, THF	20	30	12	21	5
HF/CH_3CN	20	—	12	36	5
HF/CH_3CN	5	15	37	23	5

caused increased formation of ketone **16**. Shorter reaction time dramatically increased the ratio of 3-triflate **17**/ketone **16**. Deprotection, however, was not complete, and a significant amount of partially silylated glycoside **18** was isolated from the reaction mixture. For preparation of the 3-triflate **17**, the best yield (37%) was obtained when acidic conditions (HF/MeCN) were employed. Assignment of the 3-furanone structure for **16** is based on spectral analyses: a sharp singlet at δ 5.18 for the anomeric proton and a doublet, which integrated for two protons at δ 2.79 for H-3,3' in the ^1H NMR spectrum, and a strong band at 1780 cm^{-1} for C=O in the IR spectrum as well as and m/z at 223 ($M + H^+$) and 205 ($MH^+ - H_2O$) in the mass spectrum (chemical ionization), are consistent with the furanone structure **16**. Reduction of **16** afforded benzyl 3-deoxy-β-D-*threo*pentofuranoside (**22**) which was different from the 3-deoxy-*erythro*pentoside **21** obtained by desilylation of **20**.

One of the important features of the above O-de-silylation of 3-triflate **13** was the formation (albeit low yield, ca. 5%) of the 2-triflate **7**. The 2,5-di-O-silyl intermediate **12** was not contaminated with a detectable amount (<0.1%) of the 3,5-disilyl isomer **14** (analyzed by HPLC), and very little (<1%), if any, 2 to 3 silyl migration leading to **14** was observed during triflylation of **12** (analyzed by ^{1}H NMR). Therefore, the 2-triflate **7** must be derived from the 3-O-triflate **13** by a 3 to 2 triflyl migration. We have earlier observed a triflyl migration from the 2' to 3' positions in the 6,5'-anhydropyrimidine nucleoside system.[6] The triflyl migration in the reversed direction (3 to 2) in the ribofuranoside system is, therefore, unexpected.

In conclusion triflyl migration did occur, albeit to a small extent, in the ribofuranoside system. Triflyl migration, therefore, has to be taken into consideration when nucleophilic displacement of a triflate group in a vicinal cis-diol system is performed.[13]

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. TLC was performed on Uniplates purchased from Analtech Co., and column chromatography was carried out on Silica Gel G60 (70-230 mesh, ASTM, Merck). Elemental analyses were performed by M-H-W Laboratories and Galbraith Laboratories, Inc. ^{1}H NMR spectra were recorded on a JEOL FX90Q spectrometer using Me_4Si as the internal standard. Chemical shifts

are reported in ppm (δ), and signals are described as s(singlet), d (doublet), t (triplet), q (quartet), m (multiplet), brs (broad singlet), dd (double doublet), dm (double multiplet). Values given for coupling constants are first order. Mass spectral analyses (chemical ionization) were were performed in the Laboratory of Mass Spectrometric Biotechnology Resource, Rockefeller University.

Benzyl 3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-yl)-β-D-ribofuranoside (4). A mixture of benzyl β-D-ribofuranoside[9] (3) (2.4 g, 10 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.15 g, 10 mmol) in pyridine (50 mL) was stirred at room temperature for 20 h. The reaction was quenched by addition of EtOH (5 mL), and the mixture was diluted with EtOAc (100 mL), washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on a silica gel column using $CHCl_3$-EtOH (98:2 v/v) to give pure **4** (3.11 g, 64.6%) as a foam. ^1H NMR (Me_2SO-d_6) δ 7.30 (5H, s, Ph), 4.82 (1H, s, H-1), 4.49 (2H, ABq, CH_2Ph), 4.32 (1H, m, H-3), 3.89-3.84 (4H, m, H-3,4,5,5'), 1.00 (28H, brs, i-Pr). MS (m/z) 483 (MH^+), 465 ($MH^+ - H_2O$), 3.75 ($MH^+ - PhCH_2OH$).

Anal. Calcd for $C_{24}H_{42}O_6Si_2$: C, 59.71: H, 8.76: Si, 11.63. Found: C, 60.01: H, 8.97: Si, 11.24.

Benzyl 3,5-O-(1,1,3,3-Tetraisopropyldisiloxan-1,3-yl)-2-O-triflyl-β-D-ribofuranoside (5). To an ice cold solution of **4** (3.10 g, 6.43 mmol), DMAP (0.785 g) and Et_3N (1.79 mL) in CH_2Cl_2 (40 mL) was added dropwise TflCl (1.37 mL, 12.8 mmol). The mixture was stirred for 10 min at room temperature, and then EtOH (10 mL) was added. Removal of the solvents in vacuo and chromatography of the

residue on a silica gel column using $CHCl_3$ as the eluent furnished **5** (3.26 g, 83%) as a foam. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.32 (5H, brs, Ph), 5.33 (1H, s, H-1), 5.28 (1H, d, H-2, $J_{2,3}$ = 4.39 Hz), 4.61 (2H, ABq, C$\underline{H}_2$Ph), 4.63 (1H, m, H-3), 3.89 (3H, m, H-4,5,5'), 1.01-0.98 (28H, brs, $\underline{i}$-Pr). MS (m/z) 615 (MH^+), 507 (MH^+ - $PhCH_2OH$), 465 (MH^+ - TflOH).

Anal. Calcd for $C_{25}H_{41}F_3O_8SSi_2$: C, 48.86: H, 6.68: F, 9.28: S, 5.21. Found: C, 49.20: H, 7.00: F, 8.96: S, 5.05.

Benzyl 2-$\underline{O}$-(imidazol-1-yl)thiocarbonyl-3,5-$\underline{O}$-(1,1,3,3-tetraisopropyldisiloxan-1,3-yl)-β-$\underline{\underline{D}}$-ribofurano-side (6). A mixture of **5** (1.24 g, 2.56 mmol) and thiocarbonyldiimidazole (1.14 g, 6.37 mmol) in DMF (5 mL) was stirred at room temperature for 2 h. The mixture was partitioned between EtOAc (100 mL) and H_2O (25 mL). The organic layer was separated, washed (2 x 20 mL of H_2O), dried (Na_2SO_4), concentrated to dryness, and the residue was chromatographed (EtOAc-$\underline{n}$-hexane, 1:1) to give **6** (0.94 g, 62%) as a colorless foam. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 8.46 (1H, s, imidazole H-2), 7.49 (1H, t, imidazole H-5), 7.11 (1H, d, imidazole H-4), 7.33 (5H, brs, Ph), 5.90 (1H, d, H-2, $J_{2,3}$ = 4.39 Hz), 5.36 (1H, s, H-1), 4.71 (1H, m, H-3), 4.61 (2H, ABq, C$\underline{H}_2$Ph), 4.12-3.80 (3H, m, H-4,5,5'), 1.03-0.99 (21H, brs, $\underline{i}$-Pr), 0.79 (3H, s, $\underline{i}$-Pr). MS (m/z) 593 (MH^+), 485 (MH^+ - $PhCH_2OH$).

Anal Calcd for $C_{28}H_{44}N_2SSi_2$: C, 56.76: H, 7.43: N, 4.72. Found: C, 56.50: H, 7.29: N, 4.72.

Benzyl 2-$\underline{O}$-Triflyl-β-$\underline{\underline{D}}$-ribofuranoside (7). Compound **5** (3.20 g, 5.21 mmol) was dissolved in 1M Et_3NHF/THF (16 mL). After 7 h at

room temperature, the solution was concentrated in vacuo, and the residue was chromatographed on a silica gel column ($CHCl_3$-EtOH, 97:3 v/v). Compound **7** (1.27 g, 65.8%) was obtained as colorless crystals after recrystallization from CH_2Cl_2-petr. ether, mp 105-106 °C. ^1H NMR δ 7.34 (5H, s, Ph), 5.22 (1H, s, H-1), 5.04 (1H, d, H-2, $J_{2,3}$ = 4.39 Hz), 4.63 (2H, ABq, C<u>H</u>$_2$Ph), 4.34 (1H, dd after D_2O exchange, H-3, $J_{2,3}$ = 4.39, $J_{3,4}$ = 7.00 Hz), 3.85 (1H, m, H-4), 3.65 (1H, dd, H-5, $J_{4,5}$ = 3.08, $J_{5,5'}$ = 12.21 Hz). MS (m/z) 355 ($MH^+ - H_2O$).

Anal. Calcd for $C_{13}H_{15}F_3O_7S$: C, 41.94: H, 4.06: F, 15.30. Found: C, 42.31: H, 4.13: F, 15.29.

Upon acetylation of **7** with Ac_2O in pyridine, diacetate **7a** was obtained as a syrup. ^1H NMR δ 7.34 (5H, s, Ph), 5.44 (1H, s, H-1), 5.42 (1H, d, H-2, spacing 2.74 Hz), 4.66 (2H, ABq, C<u>H</u>$_2$Ph), 4.43-3.95 (4H, m, H-3,4,5,5'), 2.09 (3H, s, Ac), 1.96 (3H, s, Ac). MS (m/z) 457 (MH^+), 397 (MH^+ - AcOH), 349 (MH^+ - $PhCH_2OH$).

Anal. Calcd for $C_{17}H_{19}F_3O_9S$: C, 44.73: H, 4.19: F, 12.48: S, 7.02. Found: C, 44.61: H, 4.36: F, 12.19: S, 6.94.

Benzyl 2-Deoxy-3,5-<u>O</u>-(1,1,3,3-tetraisopropyldi-siloxan-1,3-yl)-β-<u>D</u>-<u>erythro</u>pentofuranoside (8). To a refluxing solution of **6** (592 mg, 1.0 mmol) in dry toluene (5 mL) was added a mixture of 2,2'-azobis(2-methylpropionitrile) (109 mg) and <u>n</u>-Bu_3SnH (703 mg, 2.41 mmol) in toluene (5 mL) was added dropwise over 15 min. The solvent was removed in vacuo, and the residue was twice chromatographed on a silica gel column (EtOAc-<u>n</u>-hexane, 1:1) to give pure **8** (368 mg, 79%) as a foam. ^1H NMR (Me_2SO-<u>d_6</u>) δ 7.30

(5H, brs, Ph), 5.14 (1H, d, H-1, $J_{1,2}$ = 4.39, $J_{1,2'}$ = 0 Hz), 4.63 (1H, m, H-3), 4.46 (2H, ABq, C$\underline{H}_2$Ph), 3.99-3.65 (3H, m, H-4,5,5'), 2.01-2.25 (2H, m, H-2,2'), 1.02-0.95 (24H, brs, $\underline{i}$-Pr). MS (m/z) 467 (MH^+), 359 (MH^+ - $PhCH_2OH$).

Anal Calcd. for $C_{24}H_{42}O_5Si_2$: C, 61.80: H, 9.01: Si, 12.01. Found: C, 61.83: H, 8.85: Si, 11.98.

Benzyl 2-Deoxy-β-$\underline{D}$-$\underline{erythro}$pentofuranoside (10). Compound **8** (233 mg, 0.5 mmol) was dissolved in 1M Et_3NHF in THF (1 mL), and the solution was left at room temperature overnight. The solvent was removed in vacuo, and the residue was chromatographed on a silica gel column ($CHCl_3$-EtOH, 95:5 v/v) to give **10** (139 mg, 62%) as an oil. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.31 (5H, brs, Ph), 5.20 (1H, dd, H-1, $J_{1,2}$ = 4.66, $J_{1,2'}$ = 2.74 Hz), 4.99 (1H, d, 3-OH), 4.64 (1H, t, 5-OH), 4.51 (2H, ABq, C$\underline{H}_2$Ph), 4.15 (1H, m, H-3), 3.70 (1H, m, H-4), 3.44 (2H, m, H-5,5'), 2.24 (1H, dt, H-2, $J_{1,2}$ = $J_{2,3}$ = 4.66, $J_{2,2'}$ = 13.72 Hz), 1.83 (1H, dt, H-2', $J_{1,2'}$ = $J_{2',3}$ = 2.3 Hz). MS (m/z) 223 (M - H).

Anal Calcd. for $C_{12}H_{16}O_4.H_2O$: C, 63.02: H, 7.29. Found: C, 63.28: H, 7.37. A small amount of H_2O was detected in the ^1H NMR spectrum of this sample.

Treatment of 7 with $NaBH_4$. To a solution of **7** (200 mg) in MeCN (10 mL) was added $NaBH_4$ (100 mg), and the mixture was stirred overnight at room temperature. The mixture was concentrated in vacuo, and the residue was partitioned between $CHCl_3$ (20 mL) and H_2O (1 mL). The aqueous layer was extracted with $CHCl_3$. The combined organic solutions were dried (Na_2SO_4), concentrated, and

the residue was chromatographed on a silica gel column using CH_2Cl_2-EtOH (98:2 v/v) as the eluent. **Benzyl β-D-threopentofuranoside (11)** (59 mg, 49%) was eluted from the column first, followed by **10** (6 mg, 5%). ^1H NMR for **11** (Me_2SO-d_6) δ 7.32 (5H, brs, Ph), 5.09 (1H, dd, H-1, $J_{1,2}$ = 5.76, $J_{1,2'}$ = 1.92 Hz), 4.55 (2H, ABq, CH_2Ph), 4.51 (1H, d, 3-OH), 4.40 (1H, t, 5-OH), 4.24 (1H, m, H-3), 3.96-3.52 (3H, m, H-4,5,5'), 2.24 (1H, dt, H-2, $J_{1,2}$ = 5.76, $J_{2,2'}$ = 13.72 Hz), 1.83 (1H, dt, H-2', $J_{1,2'}$ = 1.92, $J_{2,2'}$ = 13.72). MS (m/z) 223 (M - H).

Anal. Calcd for $C_{12}H_{16}O_4.1/4H_2O$: C, 63.02: H, 7.21. Found: C, 62.80: H, 7.37. A very small amount of H_2O was detected in the analytical sample by ^1H NMR.

When DMF was used instead of MeCN, **10** (29 mg, 24%) and **11** (18 mg, 15%) were obtained.

Benzyl 2,5-Di-O-(tert-butyldimethyl)silyl-β-D-ribofuranoside (12) and Benzyl 3,5-Di-O-(tert-butyldimethyl)silyl-β-D-ribofuranoside (14). A solution of tert-butyldimethylchlorosilane (0.33 g, 2.2 mmol), DBU (0.37 g, 2.4 mmol), and **3** (0.24 g, 1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 2 h. The mixture was washed successively with H_2O, 0.1 N HCl, H_2O, aqueous $NaHCO_3$, and dried ($MgSO_4$). After concentration of the solution, the residue was chromatographed on a silica gel column using $CHCl_3$ as the eluent. Compound **12**, which eluted from the column first, was obtained as a syrup (142 mg, 30%). ^1H NMR (Me_2SO-d_6) δ (5H, s, Ph), 4.78 (1H, s, H-1), 4.71 (1H, d, 3-OH), 4.55 (2H , ABq, CH_2Ph), 3.93-3.60 (5H, m, H-2,3,4,5,5'), 0.86 (18H, s, t-Bu), 0.06 (12H, s, Me).

Anal. Calcd for $C_{24}H_{44}O_5Si_2$: C, 61.49: H, 9.46: Si, 11.98. Found: C, 61.25: H, 9.14: Si, 12.14.

Following **12**, **14** (146 mg, 31% as a syrup) was eluted from the column. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.34 (5H, s, Ph), 4.96 (1H, d, 2-OH), 4.87 (1H, d, H-1, $J_{1,2}$ = 1.38 Hz), 4.58 (2H, ABq, C$\underline{H}_2$Ph), 4.16 (1H, m, H-3), 3.96-3.63 (4H, m, H-2,4,5,5'), 0.89 (18H, s, $\underline{t}$-Bu), 0.09 (12H, s, Me).

Anal. Calcd for $C_{24}H_{44}O_5Si_2$: C, 61.49: H, 9.46: Si, 11.98. Found: C, 61.18: H, 9.61: Si, 12.44.

Benzyl 2,5-Di-O-(tert-butyldimethyl)silyl-3-O-triflyl-β-D-ribofuranoside (13). A solution of **12** (1.65 g, 3.5 mmol), DMAP (0.43 g, 3.5 mmol) and Et_3N (0.71 g, 7 mmol) in CH_2Cl_2 (40 mL) was cooled to -10 °C while TflCl (1.19 g, 7 mmol) was added dropwise so that the temperature did not rise above -5 °C. After the addition, the mixture was stirred for 3 h at room temperature and then diluted with EtOH (5 mL). Concentration of the mixture in vacuo and chromatography of the residue ($CHCl_3$) furnished **13** (613 mg, 90%) as an oil. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.32 (5H, s, Ph), 5.26 (1H, brdd, H-3), 4.99 (1H, d, H-1, $J_{1,2}$ = 4.39 Hz), 4.66 (2H, ABq, C$\underline{H}_2$Ph), 4.45-4.25 (2H, m, H-2,4), 3.71 (2H, d, H-5,5'), 0.85 (18H, s, $\underline{t}$-Bu), 0.06 (12H, s, Me).

Anal. Calcd for $C_{25}H_{43}F_3O_7SSi_2$: C, 49.97: H, 7.21: F, 9.48: S, 5.33. Found: C, 49.92: H, 7.21: F, 9.46: S, 5.47.

In a similar manner, **14** (613 mg, 1.3 mmol) was converted into **benzyl 3,5-di-O-(tert-butyldimethyl)silyl-2-O-triflyl-β-D-ribofuranoside (15)** (661 mg, 84%) as an oil. ^1H NMR (Me_2SO-$\underline{d}_6$) δ

7.32 (5H, s, Ph), 5.23 (1H, d, H-2, $J_{2,3}$ = 8.23 Hz), 4.65 (2H, ABq, C$\underline{H}_2$Ph), 4.61 (1H, m, H-3), 3.91-3.72 (3H, m, H-4,5,5'), 0.86 (18H, s, $\underline{t}$-Bu), 0.12 (6H, s, Me). MS (m/e) 601 (MH^+).

Anal. Calcd for $C_{25}H_{43}F_3O_7SSi_2$: C, 49.97: H, 7.21: F, 9.48. Found: C, 49.76: H, 7.40: F, 9.84.

$\underline{O}$-Desilylation of 15. Compound **15** (200 mg, 0.33 mmol) was dissolved in 1M Et_3NHF/THF solution (2 mL), and the solution was kept overnight at room temperature. Only one major spot was detected on TLC ($CHCl_3$-EtOH, 19:1 v/v). Saturated $NaHCO_3$ solution (1 mL) was added, and then the mixture was extracted with $CHCl_3$ (5 mL x 6). The combined extracts were dried ($MgSO_4$), concentrated in vacuo, and the residue was chromatographed on a silica gel column ($CHCl_3$-EtOH, 98:2 v/v). Compound **7** (88 mg, 71%) was obtained after crystallization from CH_2Cl_2-petr. ether, mp 104-106 °C. The IR and ^1H NMR spectra of this sample were identical with those of **7** prepared earlier from **5**.

$\underline{O}$-Desilylation of 13. A. With Et_3NHF/THF. Compound **13** (1.136 g, 1.88mmol) was treated as above with 1M Et_3NHF/THF (10 mL) at room temperature for 20 h. Four product spots were detected on TLC. After neutralization of the reaction with aqueous $NaHCO_3$, the mixture was extracted with $CHCl_3$. The extracts were concentrated, and the residue was chromatographed ($CHCl_3$-EtOH, 98:2 v/v) to give the following products:

Benzyl 2-$\underline{O}$-($\underline{tert}$-butyldimethyl)silyl-3-$\underline{O}$-triflyl-β-$\underline{D}$-ribofuranoside (18), (216 mg, 30%) as a syrup. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.34 (5H, s, Ph), 5.30 (1H, brd, H-3), 4.96 (1H, d, H-1, $J_{1,2}$ =

4.12 Hz), 4.58 (2H, ABq, C<u>H</u>$_2$Ph), 4.49-4.15 (2H, m, H-2,4), 3.51 (2H, d, H-5,5'), 0.85 (9H, s, <u>t</u>-Bu), 0.08 (6H, s, Me). MS (m/z) 487 (MH^+), 379 (MH^+ - $PhCH_2OH$). This compound was too unstable for microanalysis.

Benzyl 3-deoxy-β-<u>D</u>-glycero<u></u>pentofuranos-3-uloside (16), (88 mg, 21%) as a liquid. ^{1}H NMR (C_5H_5N) δ 7.21 (5H, s, Ph), 5.18 (1H, s, H-1), 4.82 (2H, ABq, C<u>H</u>$_2$Ph), 4.73 (1H, m, H-4), 4.05 (2H, d, 4-C<u>H</u>$_2$OH, spacing 6.04 Hz), 2.79 (2H, d, H-3,3', spacing 7.14 Hz). MS (m/z) 223 (MH^+), 205 (MH^+ - H_2O).

Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.86: H, 6.31. Found: C, 65.09: H, 6.39.

This compound gave a mono-<u>O</u>-acetyl derivative **16a** as a liquid. ^{1}H NMR (Me_2SO-<u>d_6</u>) δ 7.33 (5H, s, Ph), 4.94 (1H, s, H-1), 4.61 (2H, ABq, C<u>H</u>$_2$Ph), 4.70-4.48 (1H, m, H-4), 4.24 (1H, dd, H-5, $J_{4,5}$ = 4.11, $J_{5,5'}$ = 11.66 Hz), 2.78 (1H, dd, H-3, $J_{3,4}$ = 7.68, $J_{3,3'}$ = 18.94 Hz), 2.47 (1H, dd, H-3', $J_{3',4}$ = 4.49, $J_{3',3}$ = 18.94 Hz), 1.98 (3H, s, Ac).

Benzyl 3-<u>O</u>-triflyl-β-<u>D</u>-ribofuranoside (17), (85 mg, 12.0%), mp 61-63 °C, after crystallization from Et_2O-petr. ether. ^{1}H NMR (C_5H_5N) δ 7.19 (5H, s, Ph), 5.68 (1H, t, H-3, $J_{2,3} = J_{3,4}$ = 4.06 Hz), 5.56 (1H, d, H-1, $J_{1,2}$ = 3.30 Hz), 4.83 (2H, ABq, C<u>H</u>$_2$Ph), 5.00-4.77 (2H, m, H-2,4), 4.12 (2H, d, H-5,5'). MS (m/z) 373 (MH^+), 355 (MH^+ - H_2O). This compound was too unstable for combustion analysis.

Benzyl 2-<u>O</u>-triflyl-β-<u>D</u>-ribofuranoside (7), (36 mg, 5.0%).

B. With MeCN/HF. Compound **13** (1.20 g, 2 mmol) was dissolved

in a mixture of MeCN (7 mL) and 48% aqueous HF (3 mL). After 5 h at room temperature, $CHCl_3$ (50 mL) and H_2O (5 mL) were added to the reaction mixture. The organic layer was washed successively with H_2O, aqueous $NaHCO_3$, H_2O, and dried ($MgSO_4$). After concentration of the solution, the residue was chromatograhed ($CHCl_3$-EtOH, 98:2 v/v) to furnish **18** (145 mg), **16** (102 mg), **17** (277 mg) and **7** (52 mg) in 15, 23, 37% and 5% yield, respectively.

Benzyl 3-Chloro-3-deoxy-2,5-di-O-(tert-butyldimethyl)silyl-β-D-xylofuranoside (19). A mixture of **13** (300 mg) and LiCl (300 mg) in HMPA (5 mL) was stirred for 2 h. The reaction was quenched by addition of EtOAc (20 mL) and H_2O (5 mL). The organic layer was washed with H_2O (5 x 5 mL), dried ($MgSO_4$), concentrated in vacuo, and the residue was chromatographed (CH_2Cl_2) to give **19** (90 mg, 37%) as a syrup. ^1H NMR (Me_2SO-d_6) δ 7.31 (5H, s, Ph), 4.87 (1H, brs, H-1), 4.59 (2H, ABq, CH_2Ph), 4.30 (3H, brs, H-2,3,4), 3.79 (2H, d, H-5,5'), 0.86 (9H, s, t-Bu), 0.84 (9H, s, t-Bu), 0.055 (12H, s, Me). MS (m/z) 487 (MH^+), 379 (MH^+ -$PhCH_2OH$).

Anal. Calcd for $C_{24}H_{43}ClO_4Si_2.1/2H_2O$: C, 58.65: H, 8.86: Cl, 7.23. Found: C, 58.52: H, 9.09: Cl, 6.92.

Benzyl 2,5-Di-O-(tert-butyldimethyl)silyl-3-deoxy-β-D-erythropentofuranoside (20). Method A. To a refluxing solution of **19** (85 mg, 0.17 mmol) in benzene (5 mL) was added a solution of n-Bu_3SnH (61.1 mg, 0.2 mmol) and a catalytic amount of AIBN in dry benzene (5 mL). The mixture was refluxed for 1 h, and then concentrated in vacuo. The residue was chromatographed on a silica gel column (CH_2Cl_2) to give **20** (77 mg, 97%) as a syrup. ^1H NMR

(Me_2SO-$\underline{d}_6$) δ 7.26 (5H, brs, Ph), 4.78 (1H, s, H-1), 4.50 (2H, ABq, C$\underline{H}_2$Ph), 4.19 (2H, m, H-2,4), 3.55 (2H, d, H-5,5'), 1.84-1.71 (2H, m, H-3,3'), 0.80-0.82 (18H, brs, $\underline{t}$-Bu), 0.03 (12H, s, Me). MS (m/z) 451 ($M - H^+$), 345 ($MH^+ - PhCH_2OH$), 287 ($MH^+ - PhCH_2OH -$ $\underline{t}$-Bu).

Anal. Calcd for $C_{24}H_{44}O_4Si_2$: C, 63.66: H, 9.79. Found: C, 63.51: H, 9.77.

Method B. To a solution of **13** (180 mg, 0.3 mmol) in dry MeCN (5 mL) was added $NaBH_4$ (34.2 mg, 0.9 mmol), and the mixture was stirred at room temperature for 5 days. After concentration of the mixture in vacuo, the residue was chromatographed (CH_2Cl_2-$\underline{n}$-hexane, 1:1) to give **20** (65 mg, 48%). The ^1H NMR spectrum of this sample was identical with that of an authentic sample.

Benzyl 3-Deoxy-β-$\underline{D}$-erythropentofuranoside (21). Compound **20** (250 mg) was dissolved in 1M Et_3NHF/THF (1 mL), and the solution was kept at room temperature for 20 h. After concentration of the solution in vacuo, the residue was chromatographed on a silica gel column using $CHCl_3$-EtOH (95:5 v/v) as the eluent to give **21** (86 mg, 69%) as a syrup. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.32 (5H, s, Ph), 5.03 (1H, d, 2-OH), 4.85 (1H, s, H-1), 4.66 (1H, t, 5-OH), 4.52 (2H, ABq, C$\underline{H}_2$Ph), 4.26 (1H, m, H-2), 4.05 (1H, m, H-4), 3.39 (2H, d, H-5,5'), 1.84-1.70 (2H, m, H-3,3'). MS (m/z) 225 (MH^+), 202 ($MH^+ - PhCH_2OH$).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.24: H, 7.19. Found: C, 64.30: H, 7.03.

Benzyl 3-Deoxy-β-$\underline{D}$-threopentofuranoside (22). To a cold solution (0 °C) of **16** (88 mg, 0.094 mmol) in EtOH (2 mL) was added

$NaBH_4$ (18 mg, 0.50 mmol), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with H_2O (5 mL), and extracted with $CHCl_3$ (3 x 5 mL). The combined extracts were concentrated and the residue was chromatographed ($CHCl_3$-EtOH, 98:2 v/v) to give **22** (27 mg, 30%) as an oil. ^1H NMR (Me_2SO-$\underline{d}_6$) δ 7.34 (5H, brs, Ph), 4.77 (1H, d, H-1, $J_{1,2}$ = 4.12 Hz), 4.30 (2H, ABq, $C\underline{H}_2Ph$), 4.17-3.83 (2H, m, H-2,4), 3.48 (1H, dd, H-5, $J_{4,5}$ = 6.04, $J_{5,5'}$ = 10.97 Hz), 3.31 (1H, dd, H-5', $J_{4,5'}$ = 5.76, $J_{5,5'}$ = 10.97 Hz), 2.10 (1H, octet, H-3, $J_{2,3}$ =7.69, $J_{3,4}$ = 7.26, $J_{3,3'}$ = 11.52 Hz), 1.56 (1H, apparent sextet, H-3', $J_{2,3'}$ = 9.25, $J_{3',4}$ = 10.84, $J_{3,3'}$ = 11.52 Hz). MS (m/z) 225 (MH^+), 117 (MH^+ - $PhCH_2OH$).

Treatment of **22** with Ac_2O in pyridine afforded **benzyl 2,5-di-O-acetyl-3-deoxy-β-D-threopentofuranoside (22a).** ^1H NHR (Me_2SO-$\underline{d}_6$) δ 7.30 (5H, brs, Ph), 5.13 (1H, d, H-1, $J_{1,2}$ = 4.39 Hz), 5.01-4.76 (1H, m, H-2), 4.55 (2H, ABq, $C\underline{H}_2Ph$), 4.18-4.11 (1H, m, H-4), 4.07 (2H, brs, H-5,5'), 2.40-1.73 (2H, m, H-3,3'), 2.02 (3H, s, Ac), 2.00 (3H, s, Ac). MS (m/z) 309 (MH^+), 201 (MH^+ - $PhCH_2OH$).

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