Inversion of Configuration in 2,6-Dideoxy Sugars. Triflate Displacement by Benzoate and Nitrite Anions

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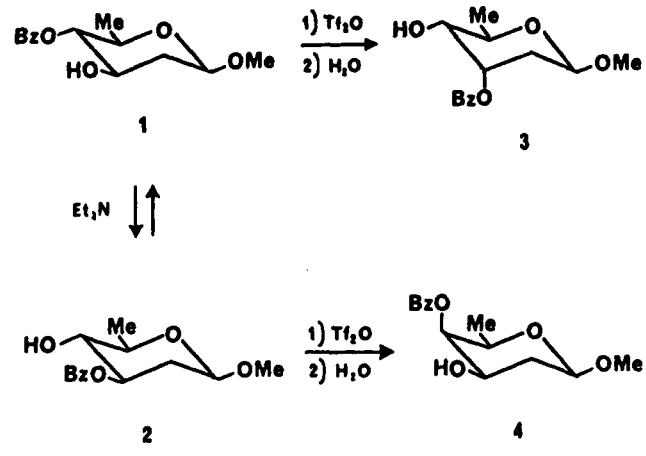
Interconversion among 2,6-dideoxy sugars at room temperature has been accomplished in high yield. The eight possible methyl 3- and 4-*O*-benzoyl-2,6-dideoxy-β-D-hexopyranosides 1–8 have been interconverted using their corresponding triflates as intermediates. Triflates derived from compounds 1, 2, 7, and 8 undergo internal displacement by the neighboring benzoyl group, inverting configuration at the triflyloxy-bearing carbon atom. Triflates of compounds 3–6 do not experience internal reaction; however, configuration was inverted in these compounds at room temperature by reaction with tetrabutylammonium nitrite. To illustrate the value of these reactions in oligosaccharide synthesis, configuration was inverted in three disaccharides composed of 2,6-dideoxy sugar residues.

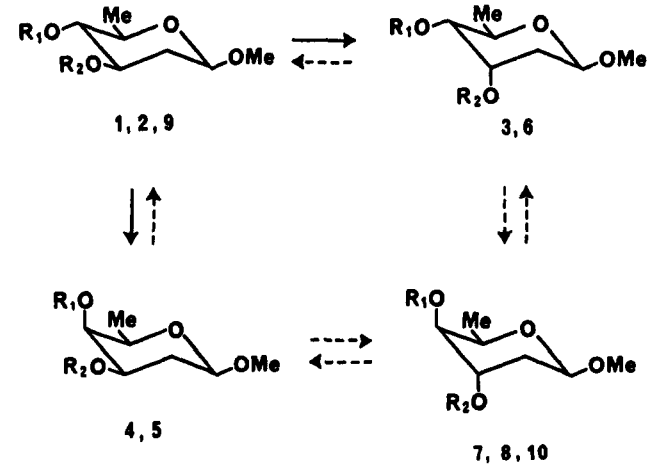
Several years ago, internal triflate displacement by a neighboring benzoyl group was shown to be a simple technique for converting methyl 2,6-dideoxy-β-D-*arabino*-hexopyranosides 1 and 2 into the corresponding *ribo* 3 and *lyxo* 4 isomers (Scheme I).[1] Since the conditions for these reactions were quite mild (room temperature, inert solvent) and the yields were high, this method appeared to be generally well-suited for inversion of configuration in carbohydrates and it was particularly attractive for sensitive compounds. It was desirable, therefore, to determine the extent to which this type of internal displacement could be relied upon for interconversions other than those shown in Scheme I.

The situation with respect to interconversion of benzoylated 2,6-dideoxy-β-D-hexopyranosides, exclusive of the present work, is summarized in Scheme II. There are eight reactions that relate these compounds by inversion of configuration at a single chiral center. The two transformations shown in Scheme I are known reactions,[1] and this fact is indicated in Scheme II by the solid arrows. The goal of the work described here, therefore, was to determine which of the remaining six reactions (arrows with broken lines) could be accomplished by internal triflate displacement. Also, for those triflates not capable of internal reaction, a second goal was to find effective bimolecular substitution reactions for configuration inversion.

Scheme I



Scheme II



1, 4, 6, 7 R_1 = Bz, R_2 = H

2, 3, 5, 8 R_1 = H, R_2 = Bz

9, 10 R_1 = R_2 = Bz

Results and Discussion

The first two compounds investigated were methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (11) and methyl 3-*O*-benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (12; Scheme III). Unlike triflates 1 and 2,[1] compounds 11 and 12 both were stable in a mixture of chloroform, 2,6-di-*tert*-butyl-4-methylpyridine, and water at room temperature; however, stirring 11 and tetrabutylammonium benzoate in toluene for 24 h gave the substitution product methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (9) in 90% yield. Compound 12, which was far less reactive than 11, required heating for 30 min under reflux in toluene to produce methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (10) in 73% yield (Scheme III). Bimolecular substitution, therefore, represented a workable method, particularly in ribo to arabino conversion, for simultaneous protection and inversion of configuration.

It seemed probable that situations would arise in which it would be desirable to invert configuration at a chiral center but not simultaneously introduce benzoyl protection. Also, since reaction of 12 with benzoate required heating, uncertainty existed about the ability of some oligosaccharides to survive such conditions. As a result of these concerns, another substitution process, one which

(1) (a) Binkley, R. W.; Sivik, M. R. *J. Org. Chem.* **1986**, *51*, 2619. (b) Binkley, R. W.; Sivik, M. R. *J. Carbohydr. Chem.* **1986**, *5*, 647.

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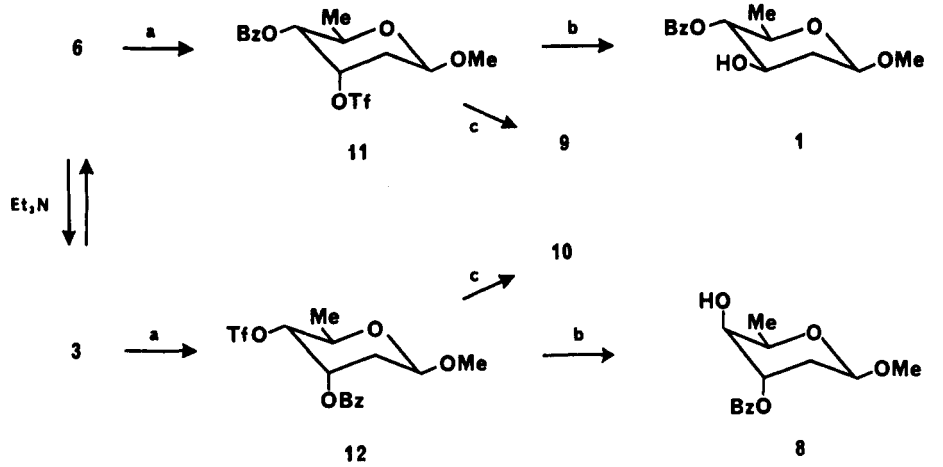
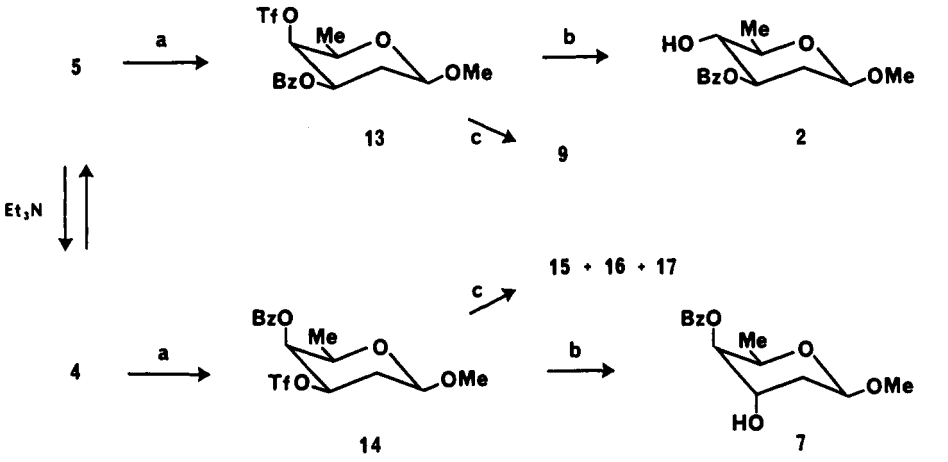
Scheme III[a]



[a] Key: (a) Tf_2O, C_5H_5N, CH_2Cl_2; (b) n-$Bu_4N^+NO_2^-$; (c) n-$Bu_4N^+BzO^-$.

Scheme IV[a]

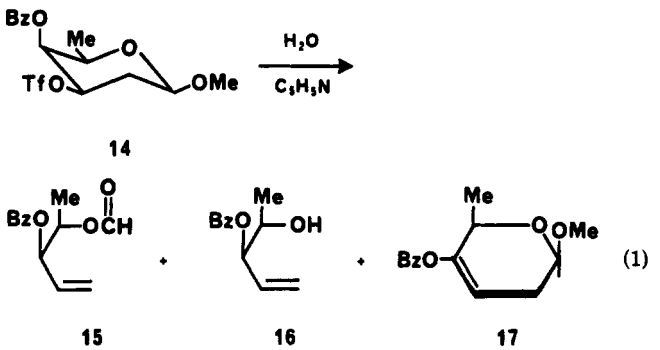


[a] Key: (a) Tf_2O, C_5H_5N, CH_2Cl_2; (b) n-$Bu_4N^+NO_2^-$; (c) n-$Bu_4N^+BzO^-$.

might complement the benzoate reaction and overcome its limitations, was considered. Several years ago, Dax and co-workers[2] reported that triflate displacement by nitrite ion produced alcohols with inverted configuration. This type of reaction, which appeared to be a promising second substitution process, in fact, did work exceptionally well. Reaction of the triflate **12** with tetrabutylammonium nitrite for 2 days at room temperature gave methyl 3-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (**8**) in 96% yield. The reaction with **11** was more rapid (6 h) and produced an 89% yield of methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (**1**; Scheme III).

Attention next turned to the triflates methyl 3-*O*-benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (**13**) and methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (**14**). It was expected that since these compounds both contained cis-related triflyloxy and benzoyloxy groups, they would exhibit reactivity similar to compounds **11** and **12**. One immediately observed similarity was the lack of internal triflate displacement under conditions that caused reaction of compounds **1** and **2**. A second similarity was that the 4-*O*-triflyl compound **13** reacted readily at room temperature with tetrabutylammonium benzoate and nitrite to yield, respectively, the C_4-inverted products **9** and **2** (Scheme IV). Differences did exist, however, in the reactivity of the triflate **14**.

Compound **14** previously had been found to experience ring-opening and elimination reactions upon heating in aqueous pyridine (eq 1);[3] consequently, it was important



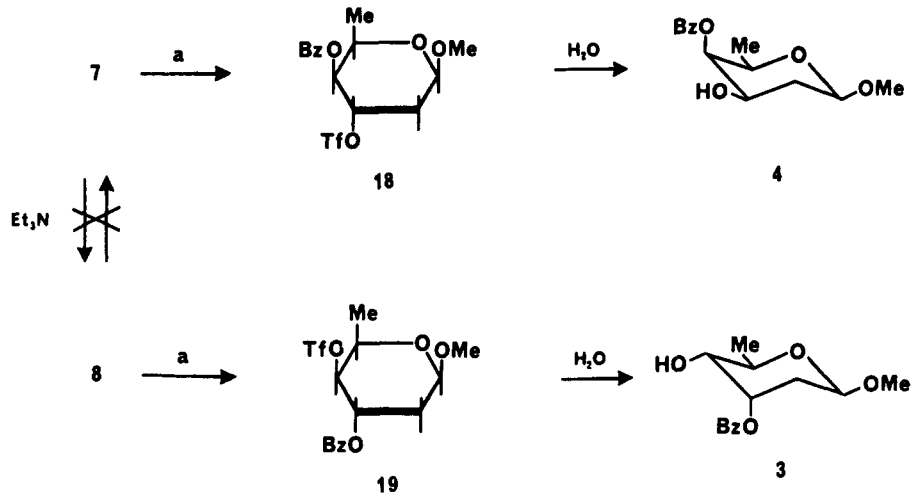
(1)

to determine whether a lyxo to xylo conversion was possible without activating the ring-opening or elimination processes. Reaction of **14** with tetrabutylammonium benzoate did not follow the desired course; rather, the previously observed products (**15–17**) were the only ones formed (Scheme IV). In contrast, treatment of **14** with tetrabutylammonium nitrite for 18 h at room temperature

(2) Rainer, A.; Dax, K.; Link, R. W.; Stutz, A. E. *Carbohydr. Res.* **1983**, *118*, C5.

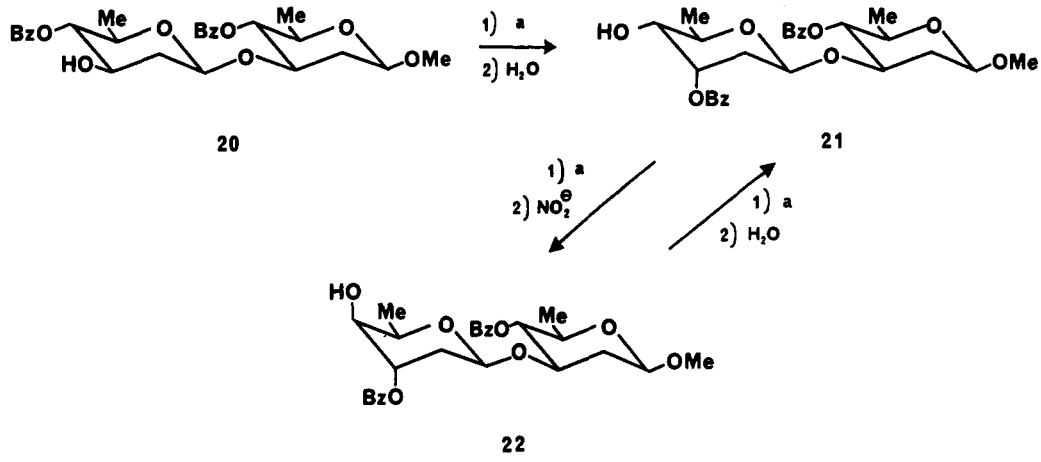
(3) (a) Binkley, R. W. *J. Carbohydr. Chem.* **1990**, *9*, 771. (b) Binkley, R. W. *J. Carbohydr. Chem.*, in press.

Scheme V[a]



[a] Key: (a) Tf_2O, C_5H_5N, CH_2Cl_2.

Scheme VI[a]



[a] Key: (a) Tf_2O, C_5H_5N, CH_2Cl_2.

provided an 88% yield of the substitution product methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexanopyranoside (7). (That this reaction took place so readily is an indication of the strength of the nitrite ion as a nucleophile.) When the reactions of 14 are compared with those of the triflates 11–13, it is clear that 11 and 13 exhibit the greater reactivity expected for compounds with axial leaving groups.[4]

The final two compounds to be studied were the triflates 18 and 19 derived from methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (7) and methyl 3-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (8), respectively. These compounds (18 and 19) each experienced internal triflate displacement at room temperature to give hexopyranosides 4 and 3, respectively (Scheme V). Compound 18, which began to decompose as soon as it was formed, was easily the most reactive of the triflates encountered in this study. If water was added to 18 immediately after formation, a 92% yield of 4 was realized. The triflate 19 required 4 days at room temperature in the presence of water to be converted into 3 (100% yield). The preferential formation of products with axial benzoyloxy groups was expected since transformations such as those shown in Scheme V (and Scheme I), where ortho acids are probable intermediates, are known to proceed in this fashion.[1,5,6]

The basic conclusion that can be drawn from study of the triflates of compounds 1–8 is that either by internal displacement involving a neighboring benzoyloxy group or by displacement with nitrite ion, configuration can be inverted at room temperature in every situation. These reactions provide considerable flexibility in interconversion among arabino, lyxo, ribo, and xylo residues in 2,6-dideoxyhexose systems.

Finally, since the primary purpose in developing these reactions was to be able to use them in altering the configuration in oligosaccharides under mild conditions, testing involving several disaccharides was undertaken (Scheme VI). First, methyl 4-*O*-benzoyl-3-*O*-(4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside (20) was converted to the corresponding triflate, which upon reaction with water for 12 h at room temperature gave the C'_3 inverted disaccharide, methyl 4-*O*-benzoyl-3-*O*-(3-*O*-benzoyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside (21). Reaction of 21 with triflic anhydride produced the corresponding triflate, which was displaced by nitrite ion to give, after 8 h at room temperature, methyl

(4) Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962; p 96.

(5) King, J. F.; Allbutt, A. D. *Can. J. Chem.* **1969**, *47*, 1445; **1970**, *48*, 1754.

(6) (a) Deslongchamps, P.; Atlani, P.; Frehel, D.; Malaval, A. *Can. J. Chem.* **1972**, *50*, 3405. (b) Deslongchamps, P.; Moreau, C.; Frehel, D.; Chenevert, R. *Can. J. Chem.* **1975**, *53*, 1204.

4-*O*-benzoyl-3-*O*-(3-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside (**22**). As a last conversion, compound **22** was transformed back into **21** by internal reaction (Scheme VI). Since these reactions occurred without difficulty and in the same fashion as those for the corresponding monosaccharides, it seems reasonable to expect that reactions observed for compounds **1–8** will follow similar pathways when applied to di- and trisaccharides.

Experimental Section

General Procedures. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were determined in $CDCl_3$. Column chromatography was conducted using a 2.5 × 15 cm column of 240–400 mesh silica gel with hexane–ethyl acetate (3:1) as the developer. TLC was done using silica gel plates developed with hexane–ethyl acetate (3:1), unless otherwise noted. Optical rotations were determined at 578 nm for solutions in ethyl acetate at 22 °C.

General Procedure for Synthesis of Triflates. To the sugar (4.0 mmol) and 1.5 mL of anhydrous pyridine in 20 mL of methylene chloride at −20 °C was added 1.6 mL (9.6 mmol) of triflic anhydride in 5 mL of methylene chloride. The cooling bath was then removed and the reaction mixture allowed to warm to room temperature over a period of 30 min. Saturated aqueous sodium bicarbonate solution (20 mL) was added to the rapidly stirred reaction mixture. The phases were separated, and the aqueous phase was extracted with 2 × 20 mL of methylene chloride. The solvent was distilled from the combined organic extracts and the residue extracted three times with boiling hexane (100 mL). The hexane was distilled from the combined hexane extracts to leave the triflate, which was generally colorless or pale yellow.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-β-D-*ribo*-hexopyranoside (6). Methyl 3-*O*-benzoyl-2,6-dideoxy-β-D-*ribo*-hexopyranoside[7] (**3**; 2.0 g, 8.8 mmol) was dissolved in 15 mL of triethylamine and heated under reflux for 24 h. ^{13}C NMR spectra run during the reaction indicated that equilibrium between compounds **3** and **6** had been reached. The solvent was distilled and the residue chromatographed in the standard fashion to give 0.80 g (3.5 mmol, 40%) of compound **6**, R_f 0.20; $[\alpha] = +27°$ ($c = 0.29$). Also isolated was 1.17 g (5.2 mmol, 59%) of compound **3**. Compound **6**: ^{1}H NMR δ 1.27 (H_6, $J_{5,6}$ = 6.3 Hz), 1.79 (H_{2a}, $J_{1,2a}$ = 9.3 Hz, $J_{2a,3}$ = 2.8 Hz), 2.13 (H_{2e}, $J_{1,2e}$ = 2.2 Hz, $J_{2e,3}$ = 4.0 Hz), 3.50 (OMe), 4.16 (H_5, $J_{4,5}$ = 9.3 Hz), 4.33 (H_3, $J_{3,4}$ = 2.1 Hz), 4.83 (H_4), 7.40–7.61, 8.00–8.07 (aromatic hydrogens); ^{13}C NMR δ 18.02 (C_6), 37.37 (C_2), 56.48 (OMe), 65.88 (C_3), 67.37 (C_5), 75.81 (C_4), 98.93 (C_1), 128.55, 129.63, 129.67, 133.44 (aromatic carbons), 165.60 (C=O). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.18; H, 6.69.

Reaction of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (11) with Tetrabutylammonium Benzoate. Compound **11**[3b] (1.00 g, 2.5 mmol) was dissolved in 10 mL of toluene containing 3.6 g (10.0 mmol) of tetrabutylammonium benzoate and water (4.0 mL). This mixture was heated under reflux and stirred rapidly for 4 h. The solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 0.83 g (2.25 mmol, 90%) of methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (**9**): $[\alpha] = -67°$ ($c = 11.2$), $R_f = 0.54$; ^{1}H NMR δ 1.34 (H_6, $J_{5,6}$ = 6.2 Hz), 1.88 (H_{2a}, $J_{1,2a} = J_{2a,3}$ = 9.7 Hz), 2.55 (H_{2e}, $J_{1,2e}$ = 2.0 Hz, $J_{2e,3}$ = 5.2 Hz, $J_{2a,2e}$ = 12.1 Hz), 3.55 (OMe), 3.72 (H_5, $J_{4,5}$ = 9.5 Hz), 4.62 (H_1), 5.22 (H_4, $J_{3,4}$ = 9.5 Hz), 5.37 (H_3), 7.30–7.52, 7.90, 8.01; ^{13}C NMR δ 17.71 (C_6), 36.63 (C_2), 56.73 (OMe), 70.33 (C_5), 71.49 (C_3), 74.63 (C_4), 100.34 (C_1), 128.35, 128.40, 129.57, 129.67, 129.71, 133.13, 133.21 (aromatic carbons), 165.76, 165.87 (C=O). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 67.96; H, 5.95.

Reaction of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (11) with Tetrabutylammonium Nitrite. Compound **11** (0.50 g, 1.25 mmol) was dissolved in 10 mL of toluene containing 1.0 g (3.5 mmol) of tetrabutylammonium nitrite. After the solution was stirred for 6 h, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 282 mg (1.11 mmol, 89%) of methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (**1**), identical in ^{1}H and ^{13}C NMR spectra with an authentic sample.[1b]

Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (12). The general procedure for triflate preparation gave **12** in quantitative yield as a colorless oil, which began to darken upon standing for several h at room temperature as a neat liquid. It was stable at −20 °C. Compound **12**: $[\alpha] = +8.7°$ ($c = 0.88$); $R_f = 0.50$ (5:1 hexane–ethyl acetate); ^{1}H NMR δ 1.46 (H_6, $J_{5,6}$ = 6.5 Hz), 2.02 (H_{2a}, $J_{1,2a}$ = 7.3 Hz, $J_{2a,2e}$ = 14.3 Hz, $J_{2a,3}$ = 3.3 Hz), 2.37 (H_{2e}, $J_{1,2e}$ = 2.6 Hz, $J_{2e,3}$ = 5.9 Hz), 3.49 (OMe), 4.29 (H_5, $J_{4,5}$ = 7.3 Hz), 4.81 (H_4, $J_{3,4}$ = 3.0 Hz), 5.79 (H_3), 7.45, −7.67, 8.03–8.09 (aromatic); ^{13}C NMR δ 18.23 (C_6), 34.71 (C_2), 56.42 (OMe), 67.05 (C_3), 69.11 (C_5), 85.76 (C_4), 118.43 (CF_3), 128.65, 129.30, 129.82, 133.67 (aromatic carbons), 165.14. Compound **12** was not sufficiently stable for elemental analysis.

Reaction of Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (12) with Tetrabutylammonium Benzoate. Compound **12** (1.00 g, 2.5 mmol) was dissolved in 10 mL of toluene containing 3.6 g (10.0 mmol) of tetrabutylammonium benzoate and water (4.0 mL). After the solution was heated under reflux for 30 min, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 414 mg (1.83 mmol, 73%) of methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (**10**); $[\alpha] = +40.6°$ ($c = 2.17$), $R_f = 0.15$ (10:1 hexane–ethyl acetate); ^{1}H NMR δ 1.33 (H_6, $J_{5,6}$ = 6.5 Hz), 2.07 (H_{2a}, $J_{1,2a}$ = 9.0 Hz, $J_{2a,3}$ = 3.2 Hz), 2.15 (H_{2e}, $J_{1,2e}$ = 2.9 Hz, $J_{2e,3}$ = 3.0 Hz), 3.58 (OMe), 4.27 (H_5, $J_{4,5}$ = 1.5 Hz), 4.81 (H_1), 5.09 (H_4, $J_{3,4}$ = 3.2 Hz), 5.46 (H_3), 7.42–7.67, 8.06–8.19 (aromatic hydrogens); ^{13}C NMR δ 16.63 (C_6), 32.04 (C_2), 56.56 (OMe), 68.74, 69.08, 69.31 (C_3–C_5), 99.54 (C_1), 128.48, 128.57, 129.73, 129.73, 130.03, 133.44, 133.45 (aromatic carbons), 164.74, 165.56 (C=O). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 67.86; H, 5.75.

Reaction of Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*ribo*-hexopyranoside (12) with Tetrabutylammonium Nitrite. Compound **12** (0.50 g, 1.25 mmol) was dissolved in 10 mL of toluene containing 1.15 g (4 mmol) of tetrabutylammonium nitrite. After the solution was stirred for 48 h at 23 °C, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 0.48 g (1.20 mmol, 96%) of methyl 3-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (**8**): $[\alpha] = -4.6°$ ($c = 0.52$); R_f = 0.31; mp 112–114 °C; ^{1}H NMR δ 1.35 (H_6, $J_{5,6}$ = 6.6 Hz), 2.01 (H_{2e}, $J_{1,2e}$ = 3.4 Hz, $J_{2e,3}$ = 3.1 Hz, $J_{2a,2e}$ = 14.3 Hz), 2.08 (H_{2a}, $J_{1,2a}$ = 8.6 Hz, $J_{2a,3}$ = 3.3 Hz), 3.53 (OMe), 3.55 (H_4, $J_{3,4}$ = 3.2 Hz, $J_{4,5}$ = 1.0 Hz), 4.06 (H_5), 5.37 (H_3), 7.44–7.59, 8.02–8.05 (aromatic hydrogens); ^{13}C NMR δ 16.40 (C_6), 31.01 (C_2), 56.37 (OMe), 67.67 (C_4), 69.82 (C_5), 71.63 (C_3), 99.90 (C_1), 128.52, 129.63, 129.87, 133.36 (aromatic carbons), 165.18 (C=O). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.35; H, 6.87.

Methyl 3-*O*-Benzoyl-2,6-dideoxy-β-D-*lyxo*-hexopyranoside (5). Methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*lyxo*-hexopyranoside[7] (**4**, 1.5 g, 6.6 mmol) was dissolved in 15 mL of triethylamine and heated under reflux for 18 h. ^{13}C NMR spectra run during the reaction indicated that equilibrium between compounds **4** and **5** had been reached. The solvent was distilled and the residue chromatographed in the standard fashion to give 0.75 g (3.3 mmol, 50%) of compound **5**, R_f 0.25; $[\alpha] = -5.9°$ ($c = 1.33$). Also isolated was 0.75 g (3.3 mmol, 50%) of compound **4**. Compound **5**: ^{1}H NMR δ 1.35 (H_6, $J_{5,6}$ = 6.5 Hz), 2.00 (H_{2a}, $J_{1,2a}$ = 9.5 Hz, $J_{2a,3}$ = 12.3 Hz), 2.10 (H_{2e}, $J_{1,2e}$ = 2.5 Hz, $J_{2e,3}$ = 5.0 Hz), 3.52 (OMe), 3.62 (H_5, $J_{4,5}$ = 0.8 Hz), 5.09 (H_3, $J_{3,4}$ = 2.9 Hz), 3.81 (H_4), 7.40–7.60, 8.03–8.10 (aromatic hydrocarbons); ^{13}C NMR δ 16.57 (C_6), 31.02 (C_2), 56.56 (OMe), 72.00 (C_3), 70.61 (C_5), 68.39 (C_4), 100.85 (C_1), 128.40, 129.63, 129.89, 133.22 (aromatic carbons), 165.85 (C=O). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.22; H, 6.64.

Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (13). The general procedure for triflate preparation gave **13** in quantitative yield as a colorless oil, which darkened upon standing at room temperature as a neat liquid. Compound **13**: $[\alpha] = -7.9°$ ($c = 0.76$); $R_f = 0.43$; ^{1}H NMR δ 1.41 (H_6, $J_{5,6}$ = 6.4 Hz), 2.02–2.18 (H_{2a}, H_{2e},

(7) Binkley, R. W. *J. Carbohydr. Chem.* **1990**, *9*, 771.

$J_{1,2a}$ = 8.8 Hz, $J_{2a,3}$ = 11.9 Hz, $J_{1,2e}$ = 2.9 Hz, $J_{2e,3}$ = 5.7 Hz), 3.55 (OMe), 3.86 (H_5, $J_{4,5}$ = <1 Hz), 5.05 (H_4, $J_{3,4}$ = 2.5 Hz), 5.32 (H_3), 7.42–7.62, 8.08–8.14 (aromatic); ^{13}C NMR δ 16.78 (C_6), 31.28 (C_2), 56.79 (OMe), 83.84 (C_3), 68.73 (C_5), 68.84 (C_4), 118.44 (CF_3), 128.52, 128.92, 130.07, 133.68 (aromatic carbons), 165.70. This compound was too unstable for satisfactory analysis.

Reaction of Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (13) with Tetrabutylammonium Benzoate. Compound 13 (1.00 g, 2.5 mmol) was dissolved in 10 mL of toluene containing 3.6 g (10.0 mmol) of tetrabutylammonium benzoate and water (4.0 mL). After the solution was heated under reflux for 30 min, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 789 mg (2.13 mmol, 85%) of methyl 3,4-di-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranoside (9), identical with that formed from reaction of 11 with tetrabutylammonium benzoate.

Reaction of Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (13) with Tetrabutylammonium Nitrite. Compound 13 (0.50 g, 1.25 mmol) was dissolved in 10 mL of toluene containing 1.15 g (4 mmol) of tetrabutylammonium nitrite. After the solution was stirred for 12 h at 23 °C, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 0.45 g (1.12 mmol, 90%) of compound 2, identical in NMR spectra with an authentic sample.[7]

Reaction of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (14) with Tetrabutylammonium Benzoate. Compound 14[3] (1.00 g, 2.5 mmol) was dissolved in 10 mL of toluene containing 3.6 g (10.0 mmol) of tetrabutylammonium benzoate and water (4.0 mL). This mixture was heated under reflux and stirred rapidly for 6 h. The solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 264 mg (1.13 mmol, 45%) of 15, 155 mg (0.75 mmol, 30%) of 16, and 57 mg (0.38 mmol, 9%) of 17. These compounds were identical in NMR spectra with those isolated from the heating of 14 in aqueous pyridine.[3]

Reaction of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*lyxo*-hexopyranoside (14) with Tetrabutylammonium Nitrite. Compound 14 (1.00 g, 2.25 mmol) was dissolved in 10 mL of toluene containing 3.6 g (10 mmol) of tetrabutylammonium nitrite. After the solution was stirred for 12 h at 23 °C, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 0.51 g (1.91 mmol, 85%) of methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranoside (7): [α] = −35.0° (*c* = 0.105), R_f = 0.27; ^1H NMR (C_6D_6) δ 1.30 (H_6, $J_{5,6}$ = 6.6 Hz), 2.04–2.17 (H_{2a}, H_{2e}, $J_{1,2e}$ = 3.1 Hz, $J_{2e,3}$ = 3.1 Hz, $J_{1,2a}$ = 8.7 Hz, $J_{2a,3}$ = 3.1 Hz), 3.53 (OMe), 5.06 (H_4, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 1.3 Hz), 4.35 (H_5), 4.19 (H_3), 7.11–7.24, 8.26–8.28 (aromatic hydrogens); ^{13}C NMR δ 16.59 (C_6), 34.24 (C_2), 56.61 (OMe), 72.02 (C_4), 67.83 (C_5), 66.89 (C_3), 99.25 (C_1), 128.48, 129.63, 129.94, 133.41 (aromatic carbons), 166.29 (C=O). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.20; H, 6.81.

Synthesis of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-[(trifluoromethyl)sulfonyl]-β-D-*xylo*-hexopyranoside (18) and Its Reaction with Water. Compound 7 (137 mg, 0.605 mmol) and 0.3 mL of pyridine were dissolved in 3 mL of dichloromethane and cooled to −20 °C. Triflic anhydride (282 mg, 1.0 mmol) in 1 mL of dichloromethane was added dropwise with stirring. The reaction mixture was removed from the cooling bath and allowed to warm to room temperature over a period of 30 min. TLC showed that the starting material had reacted and an unstable new compound had been formed. Water (0.3 mL) was added, and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was passed through a 1-cm layer of silica gel and the solvent evaporated from the solution to give 126 mg (0.56 mmol, 92%) of compound 4, identified by comparison of its NMR spectra with those of an authentic sample.[7]

Synthesis of Methyl 3-*O*-Benzoyl-2,6-dideoxy-4-*O*-[(trifluoromethyl)sulfonyl]-β-D-*xylo*-hexopyranoside (19) and Its Reaction with Water. Compound 8 (205 mg, 0.908 mmol) and 0.3 mL of pyridine were dissolved in 3 mL of dichloromethane and cooled to −20 °C. Triflic anhydride (423 mg, 1.5 mmol) in 1 mL of dichloromethane was added dropwise with stirring. The reaction mixture was removed from the cooling bath and allowed to warm to room temperature over a period of 30 min. TLC showed that the starting material had been consumed. Water (0.3 mL) was added, and the reaction mixture was stirred for 4 days at room temperature. The reaction mixture was passed through a 1-cm layer of silica gel and the solvent evaporated from the solution to give 204 mg (0.90 mmol, 100%) of compound 3, identified by comparison of its NMR spectra with those of an authentic sample.[1]

Methyl 4-*O*-Benzoyl-3-*O*-(3-*O*-benzoyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside (21). Methyl 4-*O*-benzoyl-3-*O*-(4-*O*-benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside[8] (20; 0.25 g, 0.50 mmol) was dissolved in 20 mL of dichloromethane. Pyridine (1 mL) was added, and the mixture was cooled to −20 °C. Triflic anhydride (0.28 g, 1.0 mmol) in 5 mL of dichloromethane was added dropwise to the stirred reaction mixture. After the solution had warmed to room temperature (1 h) and TLC indicated complete disappearance of starting material, 1.0 mL of water was added and the mixture stirred at room temperature for 24 h. The layers were separated, and the aqueous layer was extracted with 2 mL of dichloromethane. The solvent was distilled from the combined organic extracts and the residue chromatographed in the standard fashion to give 0.22 g (0.44 mmol, 88%) of compound 21: R_f = 0.15; [a] = −22° (*c* = 0.40); ^{13}C NMR δ 17.85 (C_6), 17.85 ($C_{6'}$), 36.68 (C_2), 36.24 ($C_{2'}$), 56.61 (OMe), 70.39 (C_5), 70.34 ($C_{5'}$), 71.78 ($C_{3'}$), 75.48 (C_4), 72.39 ($C_{4'}$), 74.16 (C_3), 94.93 ($C_{1'}$), 100.60 (C_1), 128.21, 128.55, 129.69, 129.88, 132.93, 133.44 (aromatic carbons), 165.89, 166.62 (C=O); ^1H NMR δ 1.23 (H_6, $J_{5,6}$ = 6.2 Hz), 1.09 ($H_{6'}$, $J_{5',6'}$ = 6.2 Hz), 1.77 ($H_{2a'}$, $J_{1',2a'}$ = 9.3 Hz, $J_{2a',3'}$ = 3.1 Hz), 1.77 (H_{2a}, $J_{1,2a}$ = 9.8 Hz, $J_{2a,3}$ = 12.1 Hz), 2.10 ($H_{2e'}$, $J_{1',2e'}$ = 2.1, $J_{2e',3'}$ = 3.5 Hz), 2.34 (H_{2e}, $J_{1,2e}$ = 1.8 Hz, $J_{2e,3}$ = 5.1 Hz), 3.31 ($H_{4'}$, $J_{3',4'}$ = 3.1 Hz, $J_{4',5'}$ = 9.5 Hz), 3.52 (OMe), 3.58 (H_5, $J_{4,5}$ = 9.3 Hz), 3.71 ($H_{5'}$, $J_{4',5'}$ = 9.5 Hz), 4.11 (H_3, $J_{3,4}$ = 9.3 Hz), 4.46 (H_1), 4.93 ($H_{1'}$), 4.92 (H_4), 5.42 ($H_{3'}$), 7.26–7.59, 7.99–8.08 (aromatic protons). Anal. Calcd for $C_{27}H_{32}O_9$: C, 64.79; H, 6.45. Found: C, 65.01; H, 6.44.

Methyl 4-*O*-Benzoyl-3-*O*-(3-*O*-benzoyl-2,6-dideoxy-β-D-*xylo*-hexopyranosyl)-2,6-dideoxy-β-D-*arabino*-hexopyranoside (22). Compound 21 (0.20 g, 0.40 mmol) was dissolved in 10 mL of toluene containing 0.30 g (1 mmol) of tetrabutylammonium nitrite. After the solution was stirred for 12 h at 23 °C, the solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 182 mg (0.36 mmol, 91%) of compound 22, [α] = −43° (*c* = 0.45), R_f = 0.15; ^{13}C NMR δ 17.86 (C_6), 16.10 ($C_{6'}$), 36.77 (C_2), 31.31 ($C_{2'}$), 56.62 (OMe), 70.33 (C_5), 69.53 ($C_{5'}$), 71.38 ($C_{3'}$), 75.62 (C_4), 67.45 ($C_{4'}$), 74.24 (C_3), 95.97 ($C_{1'}$), 100.59 (C_1), 128.35, 128.52, 129.59, 129.78, 130.11, 133.34, 133.11 (aromatic carbons), 165.01, 165.89 (C=O); ^1H NMR δ 1.31 (H_6, $J_{5,6}$ = 6.2 Hz), 1.01 ($H_{6'}$, $J_{5',6'}$ = 6.5 Hz), 1.79–1.95 ($H_{2a'}$, $H_{2e'}$, $J_{1',2a'}$ = 8.8 Hz, $J_{2a',3'}$ = 3.2 Hz, $J_{1',2e'}$ = 3.5 Hz, $J_{2e',3'}$ = 3.2 Hz), 1.76 (H_{2a}, $J_{1,2a}$ = 9.7 Hz, $J_{2a,3}$ = 11.9 Hz), 2.34 (H_{2e}, $J_{1,2e}$ = 1.9 Hz, $J_{2e,3}$ = 5.2 Hz), 3.36 ($H_{4'}$, $J_{3',4'}$ = 3.2 Hz), 3.52 (OMe), 3.61 (H_5, $J_{4,5}$ = 9.3 Hz), 3.87 ($H_{5'}$), 4.12 (H_3, $J_{3,4}$ = 9.3 Hz), 4.46 (H_1), 4.86 ($H_{1'}$), 4.92 (H_4), 5.23 ($H_{3'}$), 7.42–7.59, 7.97–8.08 (aromatic protons). Anal. Calcd for $C_{27}H_{32}O_9$: C, 64.79; H, 6.45. Found: C, 65.05; H, 6.40.

Conversion of 22 into 21. Compound 22 (0.20 g, 0.40 mmol) was dissolved in 20 mL of dichloromethane. One mL of pyridine was added and the mixture was cooled to −20 °C. Triflic anhydride (0.28 g, 1.0 mmol) in 5 mL of dichloromethane was added dropwise to the stirred reaction mixture. After the solution had warmed to room temperature (1 h) and TLC indicated complete disappearance of starting material, 1.0 mL of water was added and the mixture stirred at room temperature for 72 h. The layers were separated, and the aqueous layer was extracted with two mL of dichloromethane. The solvent was distilled from the combined organic extracts and the residue chromatographed in the standard fashion to give 0.20 g (0.40 mmol, 100%) of compound 21.

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