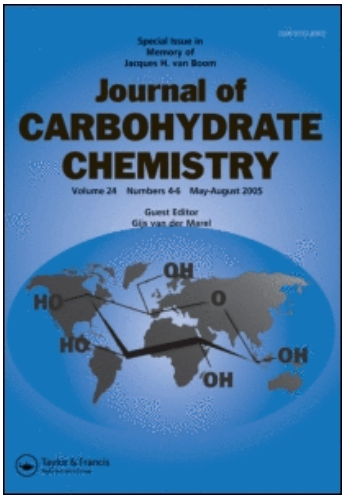

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Reactions of a New Type of Intermediate Formed by Triflate Rearrangement

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REACTIONS OF A NEW TYPE OF INTERMEDIATE FORMED BY TRIFLATE REARRANGEMENT[1]

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ABSTRACT

Treatment of methyl 4-O-benzoyl-2,6-dideoxy-ß-D-arabino-hexopyranoside (6) with triflic anhydride in the presence of 2,6-di-t-butyl-4-methylpyridine (7) produces methyl 4-O-benzoyl-2,6-dideoxy-3-O-(trifluoromethylsulfonyl)-ß-D-arabino-hexopyranoside (8), a compound which rearranges to a new and highly unstable triflate (10) upon standing at room temperature. Bromide ion reacts with 10 to give methyl 4-O-benzoyl-3-bromo-2,3,6-trideoxy-ß-D-arabino-hexopyranoside (11), a product of displacement at C-3. A similar reaction takes place with nitrate ion to give methyl 4-O-benzoyl-2,6-dideoxy-3-O-nitro-ß-D-arabino-hexopyranoside (15). Reaction of 10 with water and with tributyltin hydride results in capture of the cation 12, formed by ionization of 10, to give methyl 3-O-benzoyl-2,6-dideoxy-ß-D-ribo-hexopyranoside (14) and methyl 3,4-O-benzylidene-2,6-dideoxy-ß-D-ribo-hexopyranoside (16), respectively. The cation 12 also reacts with methanol to afford the orthobenzoates 17 and 18.

INTRODUCTION

Trifluoromethanesulfonate (triflate) displacement from carbohydrates has added a new dimension to the chemistry of these compounds.[2] Triflate displacement allows many substitution reactions to take place under

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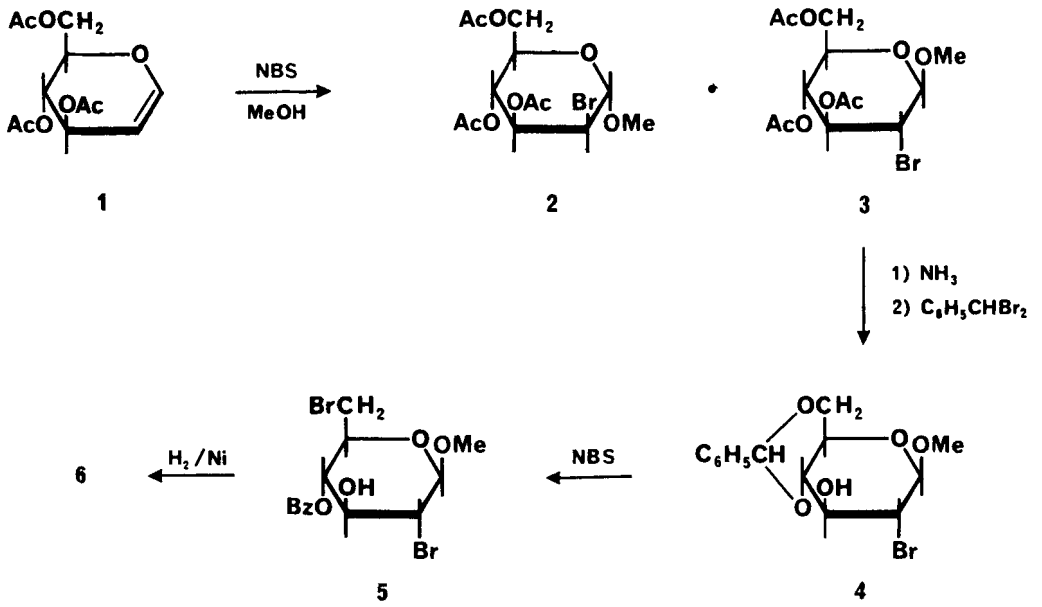
much milder conditions than otherwise would be possible. In some instances displacement of the triflyloxy group actually permits reactions to occur which could not take place using other leaving groups.[2] It is in this latter category that the reactions described in this paper belong; that is, they are made possible by the high reactivity of the triflyloxy group.

RESULTS AND DISCUSSION

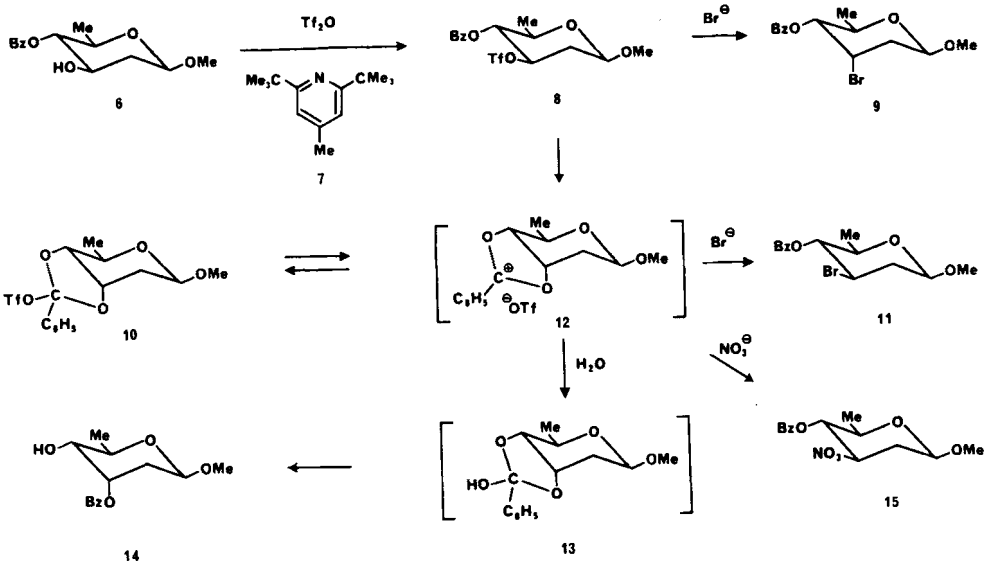
Methyl 4-O-benzoyl-2,6-dideoxy-ß-D-arabino-hexopyranoside (6), a compound needed for synthesis of analogs of the antitumor agent mithramycin, was obtained using the set of reactions shown in Scheme 1. Addition of triflic anhydride to a dichloromethane

Scheme 1



solution of 6 and of 2,6-di-t-butyl-4-methylpyridine (7) at room temperature quantitatively produced the expected triflate 8 (Scheme 2). Reaction of 8 with tetrabutylammonium bromide produced 4-O-benzoyl-3-bromo-2,3,6-trideoxy-ß-D-ribo-hexopyranoside (9), the normal S_N2 substitution product. If, however, the reaction mixture containing the triflate was allowed to stand at room temperature without bromide addition, the triflate 8 rearranged completely to a new compound in four hours. The new compound was stable in solution in

Scheme 2



the presence of the hindered base 7 for a short period of time but after eight hours showed evidence of decomposition (purple color began to develop) and after twenty-four hours had become a black, insoluble material. Even though this new compound was unstable, it was possible to obtain its ^{1}H and ^{13}C NMR spectra. These spectra had several revealing features. In the ^{13}C NMR spectrum there was no resonance for a carbonyl carbon and those for C-3 and C-4 were unusually far downfield (δ 87.57 and 85.92). In the ^{1}H NMR spectrum resonances for H-3 and H-4 also were quite far downfield (δ 6.35 and 5.88, respectively) and the coupling constants for H-3 indicated that the C-3 configuration was not the same as in the triflate 8. These NMR spectra indicated that the unstable rearrangement product was compound 10. Confirmation of this structure was made by chemical reaction. First, reaction of 10 with tetrabutylammonium bromide occurred with inversion of configuration at C-3 to give methyl 4-O-benzoyl-3-bromo-2,3,6-trideoxy-ß-D-arabino-hexo-pyranoside (11), a product of double inversion at C-3. Second, water was added to a solution of 10 in anticipation that reaction would occur with the cation 12 to produce the orthoacid 13. Compound 13 would be expected to be unstable and experience ring opening[3] to form methyl 3-O-benzoyl-2,6-dideoxy-ß-D-ribo-hexo-

pyranoside (14), the product isolated from this reaction. Thus, the reactions of the triflate 10 with bromide ion and water (outlined in Scheme 2) confirmed the structure for this compound (10) suggested by the NMR spectra.

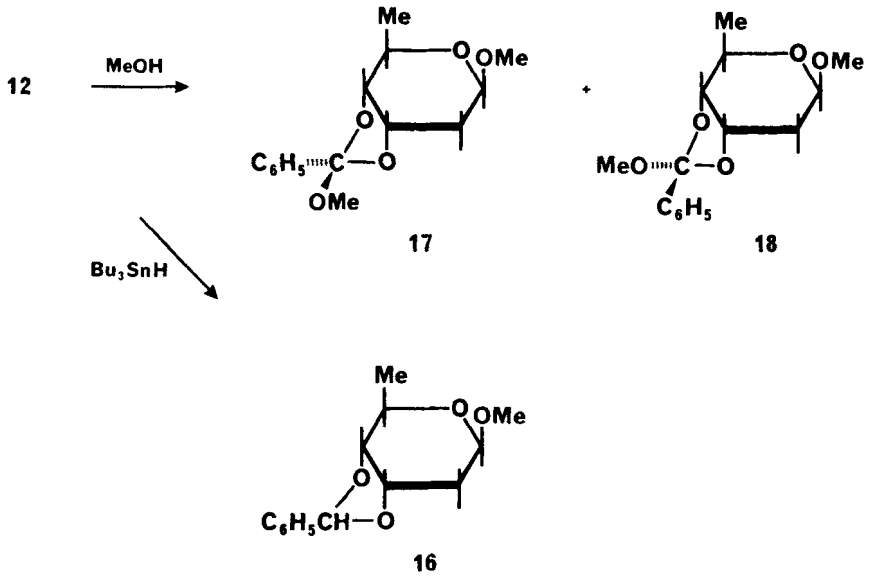
Reaction of the triflate 10 with other nucleophiles provided additional examples of the two basic types of displacement experienced by this compound. Nitrate ion, like bromide, caused substitution at C-3 while the less reactive nucleophiles methanol and tributyltin hydride, like water, gave products resulting from substitution at the carbon bearing the triflyloxy group. The behavior of 10 in the presence of these nucleophiles suggested that 10 was in equilibrium with the benzoxonium ion 12 (Scheme 2) and that 12 actually was the reactive intermediate in the observed substitution reactions.

A nucleophile should react with the carbocationic center in 12 much more readily than it reacts at C-3 or C-4. If reaction at the cationic center leads to a stable product, no C-3 or C-4 substitution should be observed; thus, when tributyltin hydride is added to a solution of 12, a stable benzylidene acetal (16) is formed. Likewise, when methanol reacts with 12, orthoester formation results (Scheme 3). In those cases where nitrate and bromide ions are the

nucleophiles, reaction also occurs preferentially at the carbocationic center but such reaction is reversible. Eventual nucleophilic attack at C-3 (a sterically more accessible carbon than C-4) is irreversible and leads to the substitution products 11 and 15, respectively.

Benzoxonium ions such as 12 have been generated in other ways. Neighboring group participation of an benzoyl group during ionization of a glycosyl halide is a common method for forming this type of ion. Benzoxonium ions also have been produced by hydride abstraction using the triphenylmethyl cation (Scheme

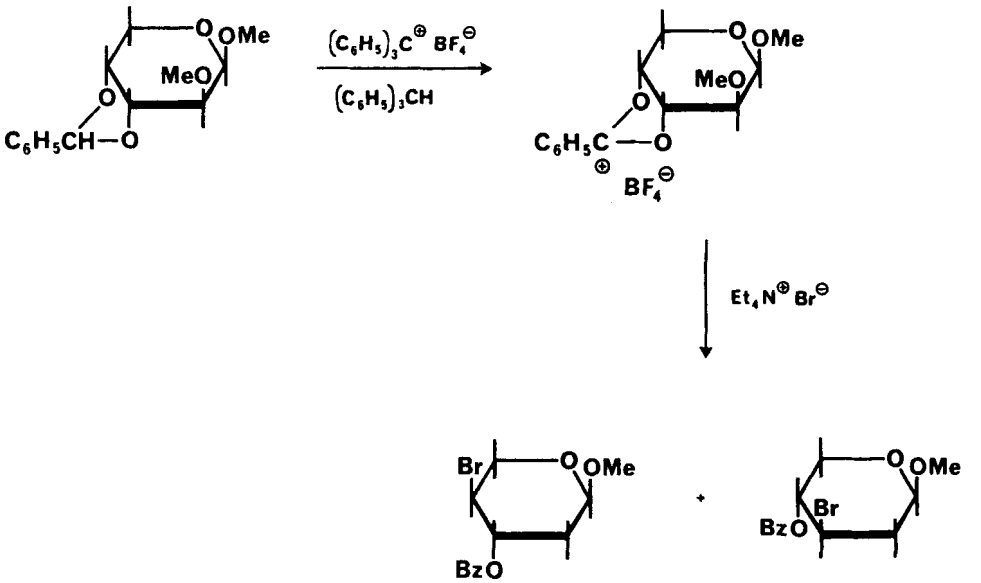
Scheme 3



4).[4] Cations generated in this way are formed in the absence of effective nucleophiles; thus, the conditions for their formation are comparable to those under which 12 is produced. When nucleophiles are added to benzoxonium ions produced by hydride abstraction, reactions take place which are similar to those observed for 12 (Scheme 4).[4]

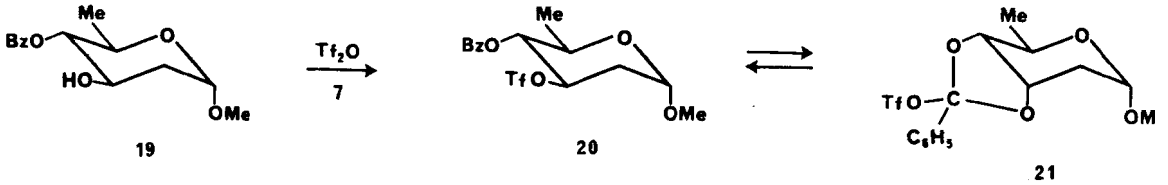
Inspection of molecular models for 10 and its α-anomer (21) indicated that 21 should be more sterically hindered than 10 due to the configuration at the anomeric carbon. Also, the parallel dipoles

Scheme 4



established by the carbon-oxygen bonds at C-1 and C-3 in compound 21 could be a destablizing factor. These destabilizing influences could cause the rearrangement of the triflate 20 to be more difficult than that observed for the triflate 8. To determine if these factors would effect formation of 21, methyl 4-O-benzoyl-2,6-dideoxy-α-D-arabino-hexopyranoside (19) was converted to the corresponding triflate 20 (Scheme 5). The ^{1}H NMR spectrum of the reaction mixture after three hours showed that a rearrangement similar to that observed for 8 was occurring. Subsequent spectral observations revealed that the rate of rearrangement appeared to be decreasing and, in fact, appeared to stop after eight hours. This behavior was consistent with a pseudo equilibrium between triflates 20 and 21. (It was not a true equilibrium because gradual decomposition of this mixture was taking place.) An equilibrium between 20 and 21, when compared with the apparently complete rearrangement of 10 into 12, was

Scheme 5



consistent with the stereoelectronic destablization of the triflate 21 indicated by the molecular models.

In conclusion, it is worth noting that the triflates 12 and 21 are the most reactive carbohydrate triflates upon which direct observation has yet been made. The existence of these compounds suggests that anomeric triflates, proposed intermediates in some glycosidation reactions,[5] may be stable compounds in solution. Stable anomeric triflates could be useful intermediates in glycoside synthesis.

EXPERIMENTAL

General Information. ^{1}H and ^{13}C NMR spectra were obtained using a Varian FT-80A spectrometer with $CDCl_3$ as the solvent and Me_4Si (δ = 0.00) as the internal standard.

Synthesis of Methyl 3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-α-D-mannopyranoside (2) and Methyl 3,4,6-Tri-O-acetyl-2-bromo-2-deoxy-β-D-glucopyranoside (3). The general procedure followed was a modification of that described by Monneret and Choay.[6] 3,4,6-Tri-O-acetyl-1,5-anhydro-2-deoxy-D-arabino-hex-1-enitol (1) (40.09 g, 0.1473 mol) and N-bromosuccinimide (27.52 g, 0.1546 mol) were combined with 500 mL of methanol. The flask was stoppered, immediately placed in an ice bath, and stirred until solution was complete. The reaction

mixture then was placed in the refrigerator at 4 °C for 14 h. The crystalline material (12.5 g) which formed was removed by filtration and washed twice with 20 mL portions of methanol. The filtrate and the washings were combined and the solvent was evaporated under reduced pressure to leave a residue which was stirred with 300 mL of ethyl ether. The precipitate (succinimide) which formed immediately was removed by filtration and washed twice with 20 mL portions of ethyl ether. The ethyl ether was removed under reduced pressure and the residue extracted repeatedly with boiling hexane (4 x 500 mL) until no more hexane soluble material remained. The hexane insoluble material consisted of additional succinimide and was discarded. The solvent was distilled from the hexane soluble material and this material was dissolved in 50 mL of methanol and placed in the freezer at - 5 °C overnight. The crystalline material which formed was collected, washed, and combined with the 12.5 g of crystals already obtained. The entire amount was recrystallized from methanol to give 16.4 g (0.0427 mol, 29%) of 3,4,6-tri-O-acetyl-2-bromo-2-deoxy-ß-D-glucopyranoside (3), mp 136.5-138 °C (lit.[6] 136-137 °C). The ^{1}H NMR spectrum was identical to that reported in reference 6. ^{13}C NMR: δ 20.55, 20.67

(CH$_3$C=O), 49.35 (C-2), 57.54 (OCH$_3$), 61.87 (C-6), 69.26 (C-5), 71.92, 74.69 (C-3, C-4), 103.29 (C-1), 169.42, 169.72, 170.53 (C=O).

After removal of the crystalline ß-anomer (3), evaporation of the methanol gave 41.9 g (0.109 mol, 74%) of the clear syrupy methyl 3,4,6-tri-O-acetyl-2-bromo-2-deoxy-α-D-mannopyranoside (2), identified by comparsion with the reported ^{1}H NMR spectrum[6] and by the ^{13}C NMR spectrum: δ 20.55 (CH$_3$C=O), 49.21 (C-2), 55.45 (OMe), 62.23 (C-6), 66.09, 68.87, 69.10 (C-3, C-4, C-5), 100.80 (C-1), 169.37, 169.84, 170.55 (C=O).

Synthesis of Methyl 4,6-O-Benzylidene-2-bromo-2-deoxy-ß-D-glucopyranoside (4). Compound 3 (14.62 g, 0.0382 mol) was stirred with a mixture of 50 mL of concentrated ammonia and 300 mL of methanol for 24 h. The solvent was evaporated under reduced pressure and 250 mL of chloroform was added. The reaction mixture was heated to boiling and the solvent was distilled at atmospheric pressure until the distillate was no longer cloudy. The remaining chloroform was removed under reduced pressure. Anhydrous pyridine (200 mL) was added and the solution heated under reflux. To this boiling solution was added 6.2 mL (10.0 g, 0.040 mol) of α,α-dibromotoluene and the heating was continued for 90 min. The solution was then allowed to cool to room

temperature and was then added to 500 mL of a rapidly stirred 5% sodium bicarbonate solution. The entire reaction mixture, including some solid material which had formed, was added to the sodium bicarbonate solution. After stirring for 1 h, the solid material suspended in the aqueous solution was collected by filtration and washed twice with 10 mL portions of methanol. This material was recrystallized from ethyl acetate to give 8.6 g (0.0249 mol, 65%) of methyl 4,6-O-benzylidene-2-bromo-2-deoxy-ß-D-glucopyranoside (4), mp 202-203 °C (lit.[7] 208-209 °C). ^{13}C NMR: δ 54.29 ($O\underline{C}H_3$), 57.74 (C-2), 66.40 (C-5), 68.51 (C-6), 74.51 (C-3), 81.16 (C-4), 102.03 ($\underline{C}HC_6H_5$), 103.85 (C-1), 126.32, 128.41, 129.39 (aromatic).

Synthesis of Methyl 4-O-Benzoyl-2,6-dibromo-2,6-dideoxy-ß-D-glucopyranoside (5). Compound 4 (10.29 g, 0.0298 mol), 5.83 g (0.0328 mol) of N-bromosuccinimide, and 11.8 g (0.060 mol) of barium carbonate were combined with 400 mL of benzene and the stirred reaction mixture was heated to reflux, maintained there for 30 min, and then allowed to cool to room temperature while the stirring was continued. The mixture was then filtered and the solids washed with 100 mL of benzene. The filtrate and washing were combined and the solvent distilled under reduced

pressure. The residue was chromatographed on a 2.5 x 15 cm column packed with 230-400 mesh silica gel. The column was eluted with 600 mL of 3:1 hexane-ethyl acetate; 20 mL fractions were collected. Fractions 5-19 were combined and the solvent distilled under reduced pressure to give 11.31 g (0.02654 mol, 89%) of methyl 4-O-benzoyl-2,6-dibromo-2,6-dideoxy-ß-D-glucopyranoside (5), mp 149-150 °C. ^{1}H NMR: δ 2.69 (s, OH), 3.62 (s, OCH_3), 3.38-4.13 (m, H-2, H-3, H-5, H-6, H-6'), 4.54 (d, H-1, $J_{1,2}$ = 8.3 Hz), 5.09 (dd, H-4, $J_{3,4} = J_{4,5}$ = 9.0 Hz), 7.44-7.64 and 7.96-8.09 (m, aromatic); ^{13}C NMR: δ 30.98 (C-6), 54.14 (C-2), 57.39 (OCH_3), 73.67, 74.01, 75.51 (C-3, C-4, C-5), 103.00 (C-1), 128.32, 128.61, 129.93, and 133.79 (aromatic), 165.89 (C=O). Anal. Calcd for $C_{14}H_{16}Br_2O_5$: C, 39.75; H, 3.90. Found: C, 40.04, H, 4.01.

Synthesis of Methyl 4-O-Benzoyl-2,6-dideoxy-ß-D-arabino-hexopyranoside (6). Raney nickel (54 mL of a 50% slurry in water) was stirred successively for five minutes with 100 mL of methanol (twice) and 100 mL of ethyl acetate (twice). To this catalyst in 300 mL of ethyl acetate was added compound 5 (11.31 g, 0.02667 mol) and triethylamine (15 mL). This mixture was stirred vigorously while the flask was purged slowly with hydrogen at atmospheric pressure. After 20 h, the

reaction mixture was filtered and the solid material (Raney nickel and triethylammonium bromide) was removed by filtration and washed twice with 100 mL portions of ethyl acetate. The solvent was evaporated from the solution and the combined washings to leave a clear liquid. This material was stirred with 50 mL of ethyl ether. The insoluble material (triethylammonium bromide) was removed by filtration, washed twice with 50 mL portions of ethyl ether, and discarded. The solvent was removed from the filtrate and combined washings under reduced pressure to afford 6.88 g (0.0258 mol, 97%) of methyl 4-O-benzoyl-2,6-dideoxy-β-D-arabino-hexopyranoside (6), mp 54-57 °C. ^{1}H NMR: δ 1.30 (d, 3H, H-6, $J_{5,6}$ = 6.2 Hz), 1.73 (ddd, H-2a, $J_{1,2a}$ = 9.5 Hz, $J_{2a,2e}$ = 12.7 Hz, $J_{2a,3}$ = 11.7 Hz), 2.34 (ddd, H-2e, $J_{1,2e}$ = 2.1 Hz, $J_{2e,3}$ = 5.2 Hz), 3.51 (s, OCH_3), 3.48-4.05 (m, H-3, H-5), 4.46 (dd, H-1), 4.74 (dd, H-4, $J_{3,4}$ = $J_{4,5}$ = 9.1 Hz), 7.43-7.55 and 7.98-8.10 (m, aromatic); ^{13}C NMR: δ 17.80 (C-6), 39.36 (C-2), 56.42 (OMe), 69.84, 69.99 (C-3, C-5), 79.04 (C-4), 100.59 (C-1), 128.43, 129.03, 129.78, 133.32 (aromatic), 166.85 (C=O).

Synthesis and Rearrangement of Methyl 4-O-Benzoyl-2,6-dideoxy-3-O-(trifluoromethylsulfonyl)-β-D-arabino-hexopyranoside (8).

Methyl 4-O-benzoyl-2,6-dideoxy-β-D-arabino-

hexopyranoside (6) (3.88 g, 14.6 mmol) and 6.6 g (31 mmol) of 2,6-di-t-butyl-4-methylpyridine (7) were dissolved in 70 mL of anhydrous CH_2Cl_2. To this stirred, cooled solution (ice bath) was added 2.57 mL (4.32 g, 15.2 mmol) of triflic anhydride in 35 mL of CH_2Cl_2. A precipitate began to form after a few minutes. After 1 h, the ice bath was removed and the solution allowed to warm to room temperature. Tlc and NMR analysis showed that the starting material had disappeared and methyl 4-O-benzoyl-2,6-dideoxy-3-O-(trifluoromethylsulfonyl)-ß-D-arabino-hexopyranoside (8) had formed. Although compound 8 was not stable for an extended time period, it existed long enough in solution to be identified by its NMR spectra. ^{1}H NMR: δ 1.30 (H-6, d, $J_{5,6}$ = 6.3 Hz), 1.88-2.07 (m, H-2a, 2.55 (ddd, H-2e, $J_{2,2}$ =12.6 Hz, $J_{2e,1}$ = 2.0 Hz, $J_{2e,3}$ = 4.8 Hz), 3.51 (s, OCH_3), 3.80 (dq, H-5, $J_{4,5}$ = 9.0 Hz), 4.52 (dd, H-1, $J_{1,2a}$ =9.5 Hz), 5.01-5.21 (H-3, H-4), 7.43-7.54 and 7.99-8.10 (aromatic); ^{13}C NMR: δ 17.59 (C-6), 37.70 (C-2), 56.87 (OCH_3), 69.96 (C-5), 73.53 (C-4), 84.44 (C-3), 99.53 (C-1), 128.55, 129.67, 129.87, 133.67 (aromatic). Resonances from the base 7 were also present. The triflate 8 began to rearrange to a new and unstable compound at room temperature. After 8 h, the rearrangement was complete. This new

material was identified as compound 10 by its NMR spectra. ^{1}H NMR: δ 1.28 (d, H-6, $J_{5,6}$ = 7.1 Hz), 2.29-2.61 (m, H-2a), 2.93 (ddd, H-2e, $J_{2a,2e}$ = 16.9 Hz, $J_{2e,3}$ = 4.3 Hz, $J_{2e,1}$ = 4.6 Hz), 3.40 (s, 3H, OCH_3), 4.33 (dq, H-5, $J_{4,5}$ = 8.6 Hz), 4.86 (dd, H-1, $J_{1,2a}$ = 5.2 Hz), 5.88 (dd, H-4, $J_{3,4}$ = 4.3 Hz), 6.35 (ddd, H-3, $J_{2,3a}$ = 4.3 Hz), 7.44-8.32 (m, aromatic); ^{13}C NMR: δ 18.64 (C-6), 37.00 (C-2), 55.57 (OCH_3), 68.42 (C-5), 85.92, 87.57 (C-3, C-4), 96.06 (C-1), 129.89 ($PhCO_3$), 130.21, 134.00, 141.17 (aromatic). Resonances from the base 7 also were present. Compound 10 decomposed slowly in solution at room temperature. After 24 h, 10 had become an insoluble black material.

Synthesis of Methyl 4-O-Benzoyl-3-bromo-2,3,6-trideoxy-ß-D-ribo-hexopyranoside (9). To a solution of 0.51 g (2.5 mmol) of di-t-butyl-4-methylpyridine (7) and 0.59 g (2.1 mmol) of triflic anhydride in 5 mL of $CDCl_3$ was added 0.52 g (2.0 mmol) of methyl 4-O-benzoyl-2,6-dideoxy-ß-D-arabino-hexopyranoside (6) at room temperature. After 15 min the triflate 8 had formed. To this solution then was added 0.81 g (2,5 mmol) of tetrabutylammonium bromide. After 1 h the solvent was evaporated under reduced pressure and the reaction mixture was chromatographed on a 2.5 x 15 cm column of 230-400 mesh silica gel. The column was

first eluted with hexane (100 mL) to remove the base 7 and then with 250 mL of 8% ethyl acetate in hexane to give 0.60 g (1.8 mmol, 93%) of methyl 4-O-benzoyl-3-bromo-2,3,6-trideoxy-ß-D-ribo-hexopyranoside (9), a liquid. ^{1}H NMR: δ 1.33 (d, H-6, $J_{5,6}$ = 6.2 Hz), 1.85-2.60 (m, H-2a, H-2e), 3.51 (s, OCH_3), 4.21 (dq, H-5, $J_{4,5}$ = 8.6 Hz), 4.67 (dd, H-4, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ = 8.7 Hz), 4.80-4.89 (m, H-3), 4.92 (dd, H-1, $J_{1,2a}$ =3.5 Hz, $J_{1,2e}$ = 7.7 Hz), 7.42-7.54 and 8.00-8.12 (aromatic); ^{13}C NMR: δ 17.69 (C-6), 38.85 (C-2), 50.16 (C-3), 56.51 (OCH_3), 69.07 (C-5), 73.25 (C-4), 99.08 (C-1), 128.52, 129.53, 129.85, 133.46 (aromatic), 165.50 (C=O). Anal. Calcd. for $C_{14}H_{17}BrO_4$: C, 51.08; H, 5.21. Found: C, 51.22, H, 5.20.

Synthesis of Methyl 4-O-Benzoyl-3-bromo-2,3,6-trideoxy-ß-D-arabino-hexopyranoside (11). The triflate 8 was synthesized from 6 (0.55 g, 2.1 mmol) in the manner described above (for preparation of 9) and then allowed to stand for 4 h while it rearranged to compound 10. Tetrabutylammonium bromide (0.82 g, 2.51 mmol) was added to the reaction mixture and, after 1 h, the solvent was distilled under reduced pressure. The reaction mixture was chromatographed as described for compound 9 to give 0.51 g (1.6 mmol, 74%) of methyl 4-O-benzoyl-3-bromo-2,3,6-trideoxy-ß-D-arabino-hexo-

pyranoside (11), mp 119 °C. ^{1}H NMR: δ 1.29 (d, H-6, $J_{5,6}$ = 6.3 Hz), 2.20 (ddd, H-2a, $J_{2a,2e}$ = 12.9 Hz, $J_{2a,1}$ = $J_{2a,3}$ = 9.3 Hz), 2.61 (ddd, H-2e, $J_{2e,1}$ = 2.1 Hz, $J_{2e,3}$ = 5.1 Hz), 3.51 (s, OCH_3), 3.59 (dq, H-5, $J_{4,5}$=9.6 Hz), 4.16 (ddd, H-3, $J_{3,4}$ = 9.6 Hz), 4.44 (dd, H-1), 5.10 (dd, H-4), 7.43-7.55 and 8.00-8.12 (aromatic); ^{13}C NMR: δ 18.11 (C-6), 41.93 (C-2), 46.58 (C-3), 56.64 (OCH_3), 72.29 (C-5), 77.06 (C-4), 101.13(C-1), 128.48, 129.84, 133.36 (aromatic), 166.00 (C=O). Anal. Calcd. for $C_{14}H_{17}BrO_4$: C, 51.08; H, 5.21. Found C, 51.31; H, 5.37.

Synthesis of Methyl 3-O-Benzoyl-2,6-dideoxy-β-D-ribo-hexopyranoside (14). Compound 6 (3.878 g, 14.6 mmol) and 6.60 g (31.2 mmol) of 2,6-di-t-butyl-4-methylpyridine (7) were dissolved in 100 mL of dry methylene chloride. This solution was cooled to 0 °C and maintained there while 2.57 mL (4.32 g, 15.3 mmol) of triflic anhydride in 10 mL of methylene chloride was slowly added. Once the addition was complete, the reaction mixture was allowed to warm to room temperature over a period of two h. Tlc analysis (on silica gel plates using 1:3 ethyl acetate-hexane) showed that the starting material had been consumed and a new material had formed. Water 1.0 mL (0.055 mol) was added and the reaction mixture was stirred at room

temperature for twelve h. The reaction mixture was then poured into 200 mL of a stirred solution of aqueous sodium bicarbonate. The organic and aqueous layers were separated and the aqueous layer washed with two 100 mL portions of methylene chloride. The solvent was removed from the combined organic extracts and the residue was chromatographed on a 2.5 x 15 cm column of silica gel using 1:4 ethyl acetate-hexane; 20 mL fractions were collected. Fractions 2 and 3 contained 2,6-di-t-butyl-4-methylpyridine (7). Fractions 9-17 contained 3.42 g of a liquid which crystallized on standing. This material was recrystallized from hexane to give 3.01 g (0.0113 mol, 77%) of methyl 3-O-benzoyl-2,6-dideoxy-ß-D-ribo-hexopyranoside (14), mp 97-98 °C. ^{1}H NMR: δ 1.35 (d, H-6, $J_{5,6}$ = 6.2 Hz), 1.82 (ddd, H-2a, $J_{1,2a}$ = 9.3 Hz, $J_{2a,2e}$ = 14.4 Hz, $J_{2a,3}$ = 2.9 Hz), 2.10 (ddd, H-2e, $J_{1,2e}$ = 2.2 Hz, $J_{2e,3}$ = 3.0 Hz), 3.45 (H-4), 3.86 (dq, H-5, $J_{4,5}$ = 9.1 Hz), 4.65 (dd, H-1), 5.49 (ddd, H-3, $J_{3,4}$ = 2.7 Hz); ^{13}C NMR: δ 18.23 (C-6), 35.83 (C-2), 56.25 (OMe), 70.65, 71.59, 72.25 (C-3, C-4, C-5), 99.09 (C-1), 128.50, 129.00, 130.16, 133.25 (aromatic), 166.33 (C=O). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.01 H, 6.90.

Synthesis of Methyl 4-O-Benzoyl-2,6-dideoxy-3-O-nitro-ß-D-arabino-hexopyranoside (15). The triflate 10 (2.1 mmol) was synthesized as described above

(preparation of compound 11) and reacted with 0.76 g (2.1 mmol) of tetrabutylammonium nitrate for 1 h at room temperature. Solvent removal and chromatography as described in the preparation of compound 11, afforded 0.46 g (1.5 mmol, 70%) of 4-O-benzoyl-2,6-dideoxy-3-O-nitro-ß-D-arabino-hexopryanoside (15), mp 132-134 °C, ^{1}H NMR: δ 1.32 (d, H-6, $J_{5,6}$ = 6.2 Hz), 1.65-2.03 (m, H-2a), 2.51 (ddd, H-2e, $J_{2a,2e}$ = 11.7 Hz, $J_{2e,1}$ = 2.0 Hz, $J_{2e,3}$ = 5.0 Hz), 3.53 (s, OCH_3), 3.69 (dq, H-5, $J_{4,5}$ = 9.4 Hz), 4.58 (dd, H-1, $J_{1,2a}$ = 2.0 Hz), 5.03 (dd, H-4, $J_{3,4}$ = 9.4 Hz), 5.33 (ddd, H-3), 7.43-7.55 and 7.94-8.06 (m, aromatic); ^{13}C NMR: δ 17.69 (C-6), 35.49 (C-2), 56.78 (OCH_3), 70.44 (C-5), 72.75 (C-3), 79.46 (C-4), 99.97 (C-1), 128.59, 129.10, 129.79, 133.60 (aromatic), 165.32 (C=O).

Synthesis of Methyl 3,4-O-Benzylidene-2,6-dideoxy-ß-D-ribo-hexopyranoside (16). The triflate 10 (2.1 mmol) was synthesized as described above (preparation of compound 11) and reacted with 0.61 g (2.1 mmol) of tributyltin hydride to give 0.45 g (1.7 mmol, 82%) of methyl 3,4-O-benzylidene-2,6-dideoxy-ß-D-ribo-hexopyranoside (16).[8] The isolation procedure was the same as that used for compound 11. ^{1}H NMR: δ 1.32 (d, H-6, $J_{5,6}$ = 6.0 Hz), 1.99 (ddd, H-2a, $J_{2,2}$ = 14.7 Hz, $J_{1,2a}$ = 8.2 Hz, $J_{2a,3}$ = 5.1 Hz), 2.38 (ddd, H-2e, $J_{1,2e}$ = 2.9 Hz, $J_{2e,3}$ = 3.0 Hz), 3.45 (s, OCH_3), 3.55 (dq, H-5,

$J_{4,5}$ = 8.9 Hz, $J_{5,6}$ = 6.0 Hz), 3.82 (dd, H-4, $J_{3,4}$ = 5.1 Hz), 4.43 (ddd, H-3), 4.66 (dd, H-1), 5.85 (s, CHAr), 7.37-7.44 (m, aromatic). ^{13}C NMR: δ 18.21 (C-6), 32.62 (C-2), 55.93 (OCH_3), 71.40 (C-5), 75.07, 76.25 (C-3, C-4), 99.02 (C-1), 103.64 (CHAr), 126.23, 128.19, 129.09 (aromatic).

Synthesis of Methyl 2,6-dideoxy-β-D-ribo-hexopyranoside 3,4-(methyl orthobenzoates) (17 and 18). The triflate 10 (2.1 mmol) was synthesized as described above (preparation of compound 11) and reacted with 1 mL of methanol to give 0.55 g (2.0 mmol, 95%) of a mixture of the orthoesters 17 and 18. These compounds could not be separated by chromatography because they experienced reaction on the chromatography column to form compound 14. It was possible to determine the ^{13}C NMR spectrum of each by examination of the spectrum for the mixture. ^{13}C NMR: δ (major isomer) 18.50 (C-6), 32.55 (C-2), 50.97 ($ArCOCH_3$), 56.10 (OCH_3), 70.45 (C-5), 73.57, 77.64 (C-3, C-4), 99.14 (C-1), 126.12, 128.21, 129.03 (aromatic); (minor isomer) 18.76 (C-6), 32.73 (C-2), 50.97 ($ArCOCH_3$), 56.10 (OCH_3), 70.45 (C-5), 73.33, 77.11 (C-3, C-4), 99.14 (C-1), 126.12, 128.21, 129.03 (aromatic). These spectra, when combined with the reaction of this mixture to give compound 14, allowed identification of these compounds as the orthoesters 17 and 18.

Reaction of Methyl 4-O-Benzoyl-2,6-dideoxy-α-D-arabino-hexopyranoside (19) with Triflic Anhydride. To a solution of 0.51 g (2.5 mmol) of di-t-butyl-4-methylpyridine (7) and 0.59 g (2.1 mmol) of triflic anhydride in 5 mL of $CDCl_3$ was added 0.52 g (2.0 mmol) of methyl 4-O-benzoyl-2,6-dideoxy-α-D-arabino-hexopyranoside (19)[9] at room temperature. After 15 min methyl 4-O-benzoyl-2,6-dideoxy-3-(trifluoromethylsulfonyl)-α-D-arabino-hexopyranoside (20) had formed. Compound 20 was not a stable material but it was possible to obtain NMR spectra. ^1H NMR: δ 1.30 (d, H-6, $J_{5,6}$ = 6.7 Hz), 2.03-2.17 (m, H-2a), 2.42-2.63 (m, H-2e), 3.36 (OCH_3), 3.98 (dq, H-5, $J_{4,5}$ = 9.2 Hz), 4.86 (dd, H-1, $J_{1,2e} = J_{1,2a}$ = 3.2 Hz), 5.14 (dd, H-4, $J_{3,4}$ = 9.2 Hz), 5.35 (ddd, H-3, $J_{2a,3}$ = 9.2 Hz, $J_{2e,3}$ = 5.2 Hz), 6.90-7.53, 8.01-8.13 (aromatic). ^{13}C NMR: δ 17.60 (C-6), 36.70 (C-2), 54.98 (OCH_3), 66.24 (C-5), 73.89 (C-4), 84.09 (C-3), 97.62 (C-1), 128.54, 129.94, 133.62 (aromatic). Resonances for compound 7 also were present. After 8 h compound 20 had partially rearranged 21 (21:20 = 3:1). The mixture of these two stayed in this ratio as polymerization took place. It was possible to obtain partial NMR data for compound 21 even though compounds 20 and 7 also were present in solution. ^1H NMR δ 2.49-2.64 (m, H-2a, H-2e), 3.22 (OCH_3), 4.33 (dq, H-5, $J_{5,6}$ = 6.3, $J_{4,5}$ = 5.6 Hz), 4.88

(dd, H-1, $J_{1,2a} = J_{1,2e} = 3.2$ Hz), 5.84 (dd, H-4, $J_{3,4} = 8.7$ Hz), 6.34 (ddd, H-3, $J_{2a,3} = J_{2e,3} = 4.4$ Hz), 7.44-7.78, 8.00-8.31 (aromatic). ^{13}C NMR: δ 19.32 (C-1), 36.62 (C-2), 55.39 (OCH_3), 63.69 (C-5), 84.36 (C-4), 86.40 (C-3), 95.38 (C-1), 130.21, 133.66, 141.21 (aromatic).

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