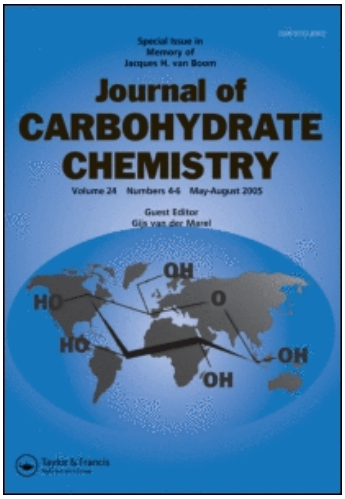

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A NEW RING-OPENING REACTION OF SUGAR TRIFLATES[1]

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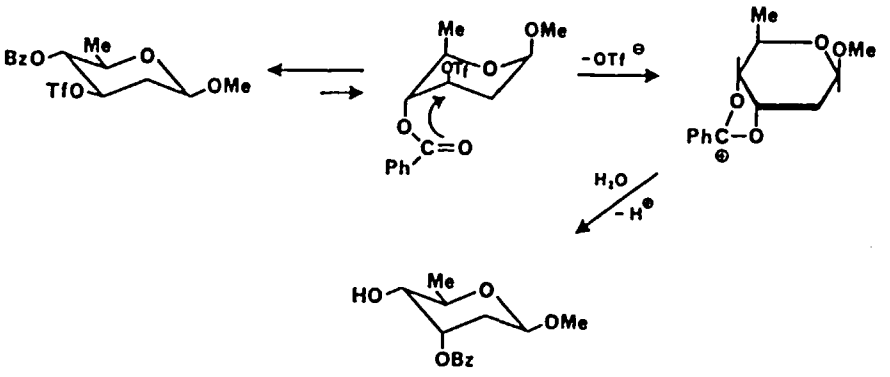
ABSTRACT

Heating methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-β-D-*lyxo*-hexopyranoside (1) at 100 °C in aqueous pyridine opens the pyranoid ring to form 3-*O*-benzoyl-2-*O*-formoyl-4-penten-2,3-diol (2) as the primary product. [Under the reaction conditions 2 is partially hydrolyzed to 3-*O*-benzoyl-4-penten-2,3-diol (3).] Mechanistic study of this reaction indicates that the carbocation 6 and the hemiacetal 7 are both intermediates in the reaction process. The importance of stereochemistry at C_1 and C_3 (the two chiral centers involved in the ring-opening reaction) was demonstrated by studying two additional triflates, methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-β-D-*ribo*-hexopyranoside (11) and methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-α-D-*lyxo*-hexopyranoside (14). Compound 11 experienced no ring-opening but rather exclusive triflate displacement by pyridine. For 14 the major process was E2 elimination to give methyl 4-*O*-benzoyl-2,3,6-trideoxy-α-D-*glycero*-hex-3-enopyranoside (15), while ring-opening was only a minor reaction pathway.

INTRODUCTION

Carbohydrate triflates occupy an important role in synthetic carbohydrate chemistry because they undergo substitution reactions readily with a wide variety of nucleophiles.[2,3] Even though competing elimination and ring-contraction processes are known to accompany triflate departure from some compounds,[4] the vast majority of triflate reactions with nucleophiles produce good yields of substitution products.

The exceptionally high reactivity of triflates, however, does create opportunities for reactions which are not normally associated with sulfonate esters. Some unusual triflate reactions, such as triflyl[5] and alkoxy[6] group migrations, are interesting for the information that they



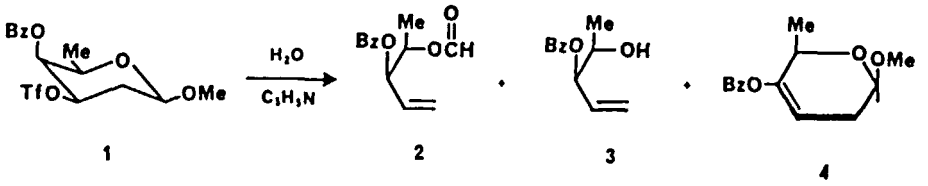
Scheme I

convey about this exceptional functional group, while other reactions have the additional feature of being synthetically useful. An example of the latter type of process is the internal displacement of the triflyloxy group by a neighboring (*trans*-related) benzoyloxy group (Scheme I). This displacement occurs under extremely mild conditions and represents a convenient method for inversion of configuration at a hydroxyl-bearing, chiral center.[7]

One question raised by the existence of the reaction described in Scheme I concerned the type of process which would take place when internal displacement was made difficult by a *cis* relationship between neighboring triflyloxy and benzoyloxy groups. In an effort to understand what would transpire in such a situation, investigation of several triflates was undertaken. The results from this study, including the discovery of a new triflate reaction, are described in this paper.

RESULTS AND DISCUSSION

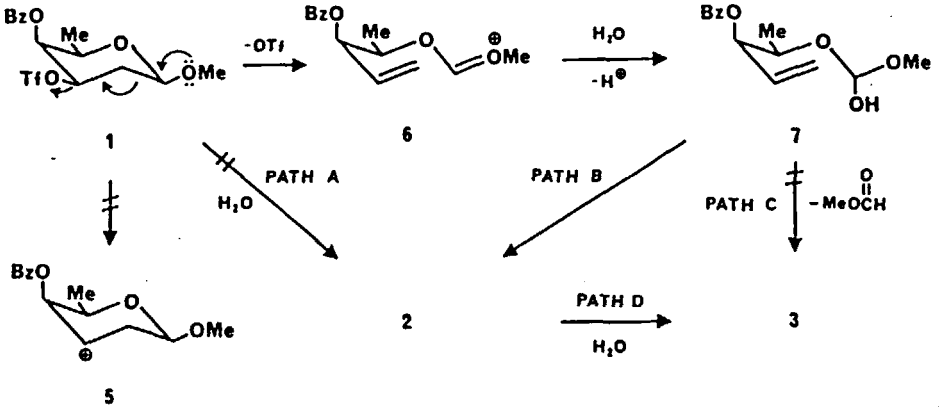
When methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-β-D-*lyxo*-hexopyranoside (1) was allowed to stand at room temperature in aqueous pyridine (conditions under which the reaction shown in Scheme I took place), no reaction occurred. When 1 was heated for 45 min at 100 °C in this solvent, two esters (2 and 3) of 4-penten-2,3-diol were formed in 47% and 40% yields, respectively; in addition, a small amount (9%) of methyl 4-*O*-benzoyl-2,3,6-trideoxy-β-D-*glycero*-hex-3-enopyranoside (4) was produced (eq 1). The structures of the major products (2 and 3) sug-



1 2 3 4

gested that a reaction was occurring in which there was simultaneous loss of the triflyloxy group and opening of the pyranoid ring (Scheme II). (Although triflate departure before ring opening was an *a priori* possibility, such a reaction was rendered unlikely by the absence of products arising from capture of the cyclic cation 5.[8])

The formation of compounds 2 and 3 did raise several questions. One of these concerned whether water was participating in the process during ring opening (Scheme II, path A) or simply was reacting with the cation 6 after its formation (path B). A method for choosing between these possibilities depended upon producing a stable compound analogous to the proposed intermediate 7. Fortunately, when methanol replaced water in the reaction of 1, a stable orthoester (8) did form. If formation of 8 were occurring in a concerted fashion, reaction of 1 with an alcohol other than methanol should produce a single orthoester while a pair of diastereomers would be expected from the intermediacy of 6. When reaction was con-



1 6 7 2 3 5

Scheme II

ducted using CD_3OD in place of water, a mixture of the diastereomeric orthoesters 9 and 10 was produced. This result supported the stepwise pathway B.

(eq.2)

R=H 8 R = R′ = H

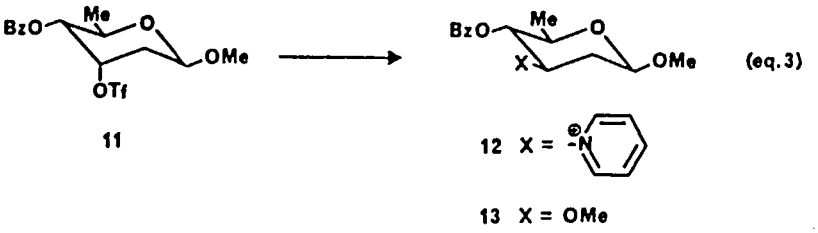
R=D 9 R = H, R′ = D

10 R = D, R′ = H

Another uncertainty about the mechanism of this reaction was related to the formation of the benzoate ester 3. Compound 3 could be produced either directly from 7 (Scheme II, path C) or by hydrolysis of 2 (path D). Since 7 also is a probable intermediate in hydrolysis of 8 and since orthoesters are easily hydrolyzed, it was possible to generate 7 and observe its reaction under conditions which did not permit the hydrolysis of 2. Under these conditions (moist silica gel and room temperature) only compound 2 was formed; therefore, 2 was concluded to be the sole primary product from reaction of the triflate 1 in the presence of water. (Consistent with this conclusion was the observation that, when 2 was heated in aqueous pyridine, 3 was produced.)

Other issues related to the reaction of 1 concerned the importance of the stereochemistry at C-1 and C-3 (the two chiral centers involved in the ring-opening process) to the course of the reaction. Inversion of configuration at C-3 in 1 would change the trans-antiparallel arrangement of the C_3-O and C_1-C_2 bonds and, thus, might prevent ring opening. This inversion of configuration did, in fact, alter the course of the reaction. When the C-3 inverted[9] methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-β-D-*ribo*-hexopyranoside (11) was heated at 100 °C in aqueous pyridine, only the substitution product 12 was formed (62% yield). Likewise, when 11 was heated in methanol, only methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-methyl-β-D-*arabino*-hexopyranoside (13) was produced (eq 3). Proper orbital alignment appears to be essential to the ring-opening reaction.

In contrast to stereochemical change at C-3, inversion of configuration at C-1 still permitted ring opening to take place but its importance

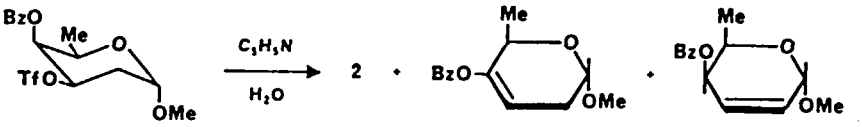


11

12 X =

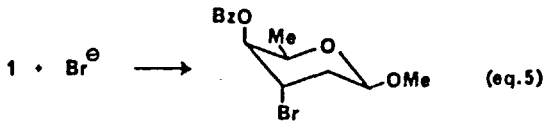
13 X = OMe

was dramatically reduced (4% yield of 2). The major product (53%) from heating methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-triflyl-α-D-*lyxo*-hexopyranoside (14) in aqueous pyridine was methyl 4-*O*-benzoyl-2,3,6-trideoxy-α-D-*glycero*-hex-3-enopyranoside (15). Also, accompanying 15 was a smaller amount (15%) of a second elimination product (16). It is reasonable to expect that ring opening would occur more easily from the β-anomer 1 than from the α-anomer 14 since during ring opening both compounds presumably are proceeding through the cationic intermediate 6 and the more stable (anomeric effect) α-anomer would be expected to require a greater amount of energy to reach the transition state for this reaction. The greater energy requirement for ring-opening in the α-anomer appears to be sufficient to allow simple elimination to become the favored process for 14.



14 15 16

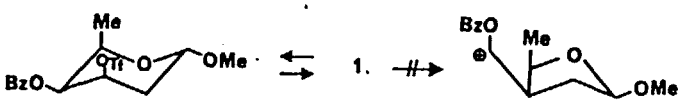
The fundamental question raised by the reaction of the triflate 1 is why does ring-opening compete so effectively with the more typical reactions of substitution, elimination, or even ring-contraction. Since the reactivity of 1 is determined by its structure and by the reaction conditions, understanding what is taking place depends upon analysis of the molecular structure of 1 and its potential for reaction with the various reagents present. Thus, substitution does not take place when 1 reacts with aqueous pyridine because an effective nucleophile is absent. (When reaction is conducted in the presence of tetrabutylammonium bromide,



(eq.5)

17

simple displacement to give the bromodeoxy sugar 17 is the only reaction observed.) E2 elimination from compound 1 requires the molecule to assume an unfavorable conformation (18) and, therefore, should have a reduced probability due to the low population of this conformation. Finally, the lack of ring contraction is an indication of the relative ease in forming cation 19 as opposed to 6. Formation of 19 requires the development of positive charge on a carbon atom bearing an electron withdrawing benzoyl group; consequently, formation of the more stable 6 should be favored.



18 19

A finally observation is that a ring-opening reaction of the type observed for 1 can be viewed as an example of a Grob fragmentation.[10] This type of process has not been observed previously for carbohydrate triflates but is known to occur in other carbohydrate systems.[11] The discovery of reactions of the type described here suggests that the chemistry of triflates, particularly when effective nucleophiles are absent, merits continued study.

EXPERIMENTAL

General Procedures. Column chromatography was conducted using a 2.5 x 15 cm column of 240-400 mesh silica gel (Baker) developed with 1:10 ethyl acetate - hexane. TLC was done using Whatmann silica gel 60A plates developed with 1:10 ethyl acetate - hexane. NMR spectra were determined a Brucker AC300F spectrometer with deuterochloroform as the solvent. Chemical shifts are relative to tetramethylsilane (δ = 0.0). Optical rotations were determined at 578 nm for solutions in ethyl acetate at 22 °C using a Perkin-Elmer model 241 spectrometer.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-trifluoromethylsulfonyl-β-D-*lyxo*-hexopyranoside (1). Methyl 4-*O*-benzoyl-2,6-dideoxy-β-D-*lyxo*-

hexopyranoside[7f] (0.60 g, 2.6 mmol) was dissolved in 15 mL of dichloromethane which contained 1.18 g (15 mmol) of pyridine. This solution was stirred and cooled to -20 °C and a solution of 1.5 g (5.3 mmol) of triflic anhydride was added in a dropwise manner. As soon as the addition was complete, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature over a period of one h. The solvent then was removed under reduced pressure and the residue chromatographed in the standard fashion to give 1.00 g (2.5 mmol, 96%) of 1, mp = 101–102 °C, [α] = +28° (c = 0.40); R_f = 0.17. ^{1}H NMR: δ 1.08 (H_6, $J_{5,6}$ = 6.4 Hz), 2.10 (H_{2e}, $J_{1,2e}$ = 2.1 Hz, $J_{2e,2a}$ = 12.2 Hz, $J_{2e,3}$ = 5.1 Hz), 2.31 (H_{2a}, $J_{1,2a}$ = 9.4 Hz, $J_{2a,3}$ = 12.0 Hz), 2.94 (H_5, $J_{4,5}$ = 0.8 Hz), 3.31 (OMe), 3.84 (H_1), 4.89 (H_3, $J_{3,4}$ = 3.3 Hz), 5.51 (H_4), 6.96–7.17, 8.11–8.21 (aromatic protons). ^{13}C NMR: δ 16.37 (C_6), 33.54 (C_2), 56.10 (OMe), 68.87 (C_5), 69.05 (C_4), 83.48 (C_3), 99.83 (C_1), 118.99 (CF_3, $J_{C,F}$ = 317 Hz), 128.71, 130.12, 133.42 (aromatic carbons), 165.67 (C=O). Compound 1 was stable at - 15 °C but began to decompose in several h at room temperature. It could be kept for days at room temperature in dichloromethane solution containing a tertiary amine.

Reaction of Triflate 1 in Aqueous Pyridine. Compound 1 (0.60 g, 1.5 mmol) was dissolved in 10 mL of pyridine and 1.0 mL of water. This mixture was heated at 100 °C for 45 min. The solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 164 mg (0.7 mmol, 47%) of 3-benzoyl-2-formoyl-4-penten-2,3-diol (2), [α] = +92° (c = 0.29); R_f = 0.22 (1:10, ethyl acetate - hexane), and 123 mg (0.6 mmol, 40%) of 3-benzoyl-4-penten-2,3-diol (3), [α] = +77° (c = 0.24), R_f = 0.18 (1:4, ethyl acetate - hexane), and 34 mg (0.23 mmol, 9%) of methyl 4-*O*-benzoyl-2,3,6-trideoxy-β-D-*glycero*-hex-3-enopyranoside (4), [α] = -146° (c = 0.076). Compound 2: ^{1}H NMR: δ 1.33 (H_1, $J_{1,2}$ = 6.5 Hz), 5.35 (H_2, $J_{1,2}$ = 6.3 Hz, $J_{2,3}$ = 6.5 Hz), 5.36 (H_{5C}, $J_{3,5C}$ = 1.2 Hz, $J_{4,5C}$ = 10.5 Hz), 5.47 (H_{5T}, $J_{3,5T}$ = 10 Hz, $J_{4,5T}$ = 17.1 Hz), 5.57 (H_3, $J_{3,4}$ = 6.5 Hz), 5.87 (H_4), 7.40–7.59, 8.05–8.08 (aromatic protons); ^{13}C NMR: δ 16.33 (C_1), 70.22 (C_2), 76.00 (C_3), 119.88 (C_5), 132.12 (C_4), 128.49, 129.82, 133.24 (aromatic carbons), 160.25 (HC=O), 165.40 (ArC=O). Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found C, 66.88; H, 5.89. Compound 3: ^{1}H NMR: δ 1.27 (H_1, $J_{1,2}$ = 6.4 Hz), 4.01 (H_2, $J_{2,3}$ = 6.2 Hz), 5.34 (H_{5C}, $J_{3,5C}$ = 1.2 Hz, $J_{4,5C}$ = 10.6 Hz), 5.39 (H_3, $J_{3,4}$ = 6.2 Hz, 5.44 (H_{5T}, $J_{3,5T}$ = 1.3 Hz, $J_{4,5T}$ = 17.2 Hz), 5.93 (H_4), 7.41–7.63, 8.05–8.10 (aromatic protons); ^{13}C NMR: δ 18.80 (C_1), 68.98 (C_2), 79.16 (C_3), 119.14 (C_5), 133.06 (C_4), 128.46, 129.68, 130.04, 133.20 (aromatic carbons), 165.81 (C=O). Anal. calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found C, 69.98; H, 6.89. Compound 4: ^{1}H NMR: δ 1.36 (H_6, $J_{5,6}$ = 6.7 Hz), 2.38–2.44 (H_2, $H_{2'}$), 3.54 (OMe), 4.65 (H_5, $J_{2,5}$ = 1.7 Hz, $J_{2',5}$ = 3.3 Hz), 4.78 (H_1, $J_{1,2}$

= 6.2 Hz, $J_{1,2'}$ = 5.0 Hz), 5.52 (H_3, $J_{2,3}$ = 1.6 Hz, $J_{2',3}$ = 4.1 Hz), 7.42-7.66, 8.03-8.11 (aromatic protons); ^{13}C NMR: δ 18.14 (C_6), 30.52 (C_2), 56.38 (OMe), 69.39 (C_5), 99.61 (C_1), 110.08 (C_3), 148.90 (C_4), 128.60, 130.02, 133.62 (aromatic carbons), 164.60 (C=O). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50. Found: 67.99; H, 6.62.

Reaction of 1 with Methanol. Compound 1 (0.44 g, 1.1 mmol) was dissolved in 5 mL of methanol containing 0.62 g (3.0 mmol) of 2,6-di-*tert*-butyl-4-methylpyridine and heated at 100 °C in a sealed tube for 15 min. The solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 265 mg (0.95 mmol, 86%) of 3-benzoyl-2-(dimethoxymethyl)-4-penten-2,3-diol (8), R_f = 0.53 (3:1 hexane - ethyl acetate); ^1H NMR: δ 1.27 (H_1, $J_{1,2}$ = 6.4 Hz), 3.28, 3.33 (OMe), 4.07 (H_2, $J_{2,3}$ = 6.7 Hz, 5.20 [C<u>H</u>(OMe)$_2$], 5.32 (H_{5c}, $J_{3,5c}$ = 1.2 Hz, $J_{4,5c}$ = 10.6 Hz), 5.42 (H_{5t}, $J_{3,5t}$ = 1.3 Hz, $J_{4,5t}$ = 17.3 Hz), 5.58 (H_3, $J_{3,4}$ = 6.5 Hz), 5.96 (H_4), 7.38-7.61, 8.04-8.13 (aromatic protons); ^{13}C NMR: δ 16.51 (C_1), 50.97, 51.53 (OMe), 71.43 (C_2), 76.79 (C_3), 113.74 [<u>C</u>H(OMe)$_2$], 118.54 (C_5), 132.72 (C_4), 128.42, 129.67, 133.06 (aromatic carbons), 165.44 (C=O). Compound 8 decomposed slowly on silica gel to produce compound 2. Although there was no 2 present in the crude reaction mixture (NMR), after chromatography samples of 8 always contained a small amount of 2, even though these compounds have very different R_f values.

Reaction of 1 with Methanol-d_4. The reaction and the product isolation were conducted in a manner identical to that for reaction 1 with methanol except that CD_3OD replaced methanol. The ^1H NMR spectrum of the inseparable mixture of products (9 and 10) exhibited methoxy resonances at 3.33 and 3.28 δ. The 3.28 resonance was approximately twice as intense as that at 3.33. The ^{13}C NMR spectrum also exhibited methoxy resonances of unequal intensity at 51.54 and 50.97 δ. The spectra of these compounds was otherwise identical to that of compound 8.

Reaction of 1 with Tetrabutylammonium Bromide. Compound 1 (0.30 g, 0.75 mmol) was dissolved in 10 mL of toluene containing 1.0 g (3.1 mmol) of tetrabutylammonium bromide. After standing at room temperature for 1 h, the reaction mixture was extracted twice with water. The aqueous extracts were discarded and the organic solvent was evaporated under reduced pressure to give 236 mg (0.72 mmol, 96%) of methyl 4-*O*-benzoyl-3-bromo-2,3,6-trideoxy-β-D-*xylo*-hexopyranoside (17), [α] = +30° (c = 0.29), R_f = 0,20 (1:10, ethyl acetate - hexane); ^1H NMR: δ 1.30 (H_6, $J_{5,6}$ = 6.5 Hz), 2.16 (H_{2e}, $J_{1,2e}$ = 2.3 Hz, $J_{2e,3}$ = 2.4 Hz, $J_{2e,2a}$ = 14.4 Hz), 2.26 (H_{2a}, $J_{1,2a}$ = 8.7 Hz, $J_{2a,3}$ = 3.8 Hz), 4.49 (H_3, $J_{3,4}$ = 3.4 Hz), 4.50 (H_5), 4.86 (H_1), 5.06 (H_4, $J_{4,5}$ = 1.2

Hz), 6.96-7.16, 8.08. 8.11 (aromatic hydrogens); ^{13}C NMR: δ 16.84 (C_6), 34.62 (C_2), 46.09 (C_3), 56.65 (OMe), 67.59 (C_5), 71.18 (C_4), 99.33 (C_1), 128.53, 129.29, 129.97, 133.55 (aromatic carbons), 165.62 (C=O). Anal. Calcd for $C_{14}H_{17}BrO_6$: C, 51.06; H, 5.21. Found C, 50.86; H, 5.23.

Synthesis of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-trifluoromethylsulfonyl-*β*-D-*ribo*-hexopyranoside (11). Methyl 4-*O*-benzoyl-2,6-dideoxy-*β*-D-*ribo*-hexopyranoside[7e] (0.72 g, 3.1 mmol) was dissolved in 15 mL of dichloromethane which contained 1.42 g (18 mmol) of pyridine. This solution was stirred and cooled to -20 °C and a solution of 1.8 g (6.4 mmol) of triflic anhydride was added in a dropwise manner. As soon as the addition was complete, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature over a period of one h. Saturated aqueous sodium bicarbonate (10 mL) was added and the reaction mixture was stirred for 15 min. The layers were separated and the aqueous layer was extracted with dichloromethane (2 x 15 mL). The organic layers were combined and the solvent removed under reduced pressure. The residue was extracted with two 50 mL portions of hexane. The hexane extracts were combined and the solvent distilled to give 1.2 g (3.0 mmol, 97%) of 11, R_f = 0.60 (3:1 hexane - ethyl acetate). (Compound 11 decomposed upon standing at room temperature for several hours.) ^1H NMR: δ 1.26 (H_6, $J_{5,6}$ = 6.2 Hz), 2.10 (H_{2a}, $J_{1,2a}$ = 9.4 Hz, $J_{2a,3}$ = 2.7 Hz), 2.38 (H_{2e}, $J_{1,2e}$ = 2.0 Hz, $J_{2e,3}$ = 2.5), 3.37 (OMe), 4.27 (H_5, $J_{4,5}$ = 9.7 Hz), 4.80 (H_1), 4.91 (H_4, $J_{3,4}$ = 2.7 Hz), 5.49 (H_3), 7.42, 7.45, 7.48, 7.56, 7.58, 8.07, 8.09 (aromatic); ^{13}C NMR: δ 17.35 (C_6), 34.49 (C_2), 55.34 (OMe), 61.08 (C_5), 71.71 (C_4), 82.64 (C_3), 96.24 (C_1), 118.55 (CF_3), 129.00, 128.66, 129.98, 133.78 (aromatic carbons), 165.51 (C=O).

Reaction of 11 with Pyridine. Compound 11 (200 mg, 0.50 mmol) was dissolved in 2 mL of pyridine and heated at 100 °C in an NMR tube for 15 min. The solvent was distilled under reduced pressure and the residue chromatographed (20:1 ethyl acetate - methanol) to give 149 mg (0.31 mmol, 62%) of 12, $[\alpha]$ = -160° (c = 0.082). ^1H NMR: δ 1.32 (H_6, $J_{5,6}$ = 6.2 Hz), 2.32 (H_{2a}, $J_{1,2a}$ = 8.8 Hz, $J_{2a,3}$ = 12.6 Hz), 2.79 (H_{2e}, $J_{1,2e}$ = 1.8 Hz, $J_{2e,3}$ = 4.8 Hz), 3.52 (OMe), 4.07 (H_5, $J_{4,5}$ = 9.0 Hz), 4.90 (H_1), 5.19 (H_4, $J_{3,4}$ = 10.1 Hz), 5.67 (H_3), 7.38, 7.40, 7.54, 7.57, 7.59, 7.86, 7.88 (aromatic protons); ^{13}C NMR: δ 17.71 (C_6), 37.16 (C_2), 56.93 (OMe), 70.34, 70.66, 74.84 (C_3, C_4, C_5), 99.91 (C_1), 128.61, 129.72, 34.23 (aromatic carbons), 165.61 (C=O).

Reaction of 11 with Methanol. Compound 11 (136 mg, 0.60 mmol) and 205 mg (1.0 mmol) of 2,6-di-*t*-butyl-4-methylpyridine were dissolved in 4 mL of methanol and heated in a sealed tube at 100 °C for 15 min. The sol-

vent was evaporated under reduced pressure and the residue was chromatographed in the standard fashion to give 126 mg (0.45 mmol, 74%) of methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-methyl-β-D-*arabino*-hexopyranoside (13), $[\alpha] = -177°$ (c = 0.19), $R_f = 0.53$ (3:1 hexane - ethyl acetate) . ^1H NMR: δ 1.27 (H_6, $J_{5,6}$ = 6.1 Hz), 1.66 (H_{2a}, $J_{1,2a}$ = 9.5 Hz, $J_{2a,3}$ = 12.3 Hz), 2.39 (H_{2e}, $J_{1,2e}$ = 1.7 Hz, $J_{2e,3}$ = 4.9 Hz), 3.32 (OMe), 3.51 (C_3, $J_{3,4}$ = 9.4 Hz), 3.52 (OMe), 3.55 (H_5, $J_{4,5}$ = 9.4 Hz), 4.46 (H_1), 4.94 (H_4), 7.43, 7.46, 7.48, 7.56, 7.58, 8.05, 8.07 (aromatic protons); ^{13}C NMR: δ 17.70 (C_6), 36.02 (H_2), 56.58 (OMe), 56.88 (OMe), 70.32 (C_5), 76.28 (C_4), 78.17 (C_3), 100.78 (C_1), 128.42, 129.74, 133.10 (aromatic carbons), 165.78 (C=O). Anal Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.12; H, 7.22.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-trifluoromethylsulfonyl-α-D-*lyxo*-hexopyranoside (14). Methyl 4-*O*-benzoyl-2,6-dideoxy-α-D-*lyxo*-hexopyranoside[7c] (120 mg, 0.53 mmol) was dissolved in 5 mL of dichloromethane which contained 0.32 g (4 mmol) of pyridine. This solution was stirred and cooled to -20 °C and a solution of 0.45 g (1.6 mmol) of triflic anhydride was added in a dropwise manner. As soon as the addition was complete, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature over a period of one h. The solvent then was removed under reduced pressure and the residue chromatographed in the standard fashion to give 211 mg (0.53 mmol, 100%) of 14, $[\alpha] = +59°$ (c = 0.70); $R_f = 0.17$. ^1H NMR: δ 1.23 (H_6, $J_{5,6}$ = 6.5 Hz), 2.20 (H_{2e}, $J_{1,2e} < 1$ Hz, $J_{2e,2a}$ = 12.3 Hz, $J_{2e,3}$ = 5.2 Hz), 2.43 (H_{2a}, $J_{1,2a}$ = 3.6 Hz, $J_{2a,3}$ = 12.3 Hz), 4.41 (H_5, $J_{4,5} < 1$ Hz), 3.37 (OMe), 4.98 (H_1), 5.43 (H_3, $J_{3,4}$ = 3.4 Hz), 5.59 (H_4), 7.43-7.67, 8.09-8.13 (aromatic protons). ^{13}C NMR: δ 16.56 (C_6), 31.74 (C_2), 55.14 (OMe), 65.21 (C_5), 70.09 (C_4), 81.98 (C_3), 98.24 (C_1), 118.49 (CF_3, $J_{C,F}$ = 319 Hz), 128.60, 129.21, 130.01, 133.58 (aromatic carbons), 165.64 (C=O). Compound 14 began to decompose when kept as a neat liquid overnight. It could be kept for days at room temperature in dichloromethane solution containing a tertiary amine.

Reaction of Triflate 14 in Aqueous Pyridine. Compound 14 (200 mg, 0.50 mmol) was dissolved in 10 mL of pyridine and 1.0 mL of water. This mixture was heated at 100 °C for 25 min. The solvent was removed under reduced pressure and the residue chromatographed in the standard fashion to give 59 mg (0.16 mmol) of unreacted 14, 2.3 mg (0.01 mmol, 4%) of 3-benzoyl-2-formoyl-4-penten-2,3-diol (2), 66 mg (0.27 mmol, 53%) of methyl 4-*O*-benzoyl-2,3,6-trideoxy-α-D-*glycero*-hex-3-enopyranoside (15), $R_f = 0.32$, and 19 mg (0.07 mmol, 15%) of methyl 4-*O*-benzoyl-2,3,6-trideoxy-α-D-*threo*-hex-2-enopyranoside (16). Compound 15: ^1H NMR: δ 1.32

(H_6, $J_{5,6}$ = 6.7 Hz), 2.30 (H_2, $J_{1,2}$ = 1.2 Hz, $J_{2,3}$ = 5.3 Hz, $J_{2a,5}$ =2.9 Hz), 2.65 ($H_{2'}$, $J_{1,2'}$ = 4.5 Hz, $J_{2',3}$ = $J_{2',5}$ = 2.9 Hz), 3.49 (OMe), 4.59 (H_5), 4.88 (H_1), 5.55 (H_3), 7.41-7.63, 8.03-8.11 (aromatic protons); ^{13}C NMR: δ 17.36 (C_6), 30.05 (C_2), 55.26 (OMe), 63.37 (C_5), 96.54 (C_1), 108.47 (C_3), 147.89 (C_4), 128.55, 130.00, 133.50 (aromatic carbons), 164.50 (C=O). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50. Found: 68.13; H, 6.63. Compound **16**: ^1H NMR: δ 1.32 (H_6, $J_{5,6}$ = 6.7 Hz), 3.48 (OMe), 4.33 (H_5, $J_{4,5}$ = 2.5 Hz), 4.98 (H_1, $J_{1,2}$ = 2.9 Hz), 5.15 (H_4, $J_{3,4}$ = 5.2 Hz), 6.06 (H_2, $J_{2,3}$ = 10.1 Hz), 6.21 (H_3); ^{13}C NMR: δ 16.23 (C_6), 55.66 (OMe), 64.88 (C_4), 65.51 (C_5), 95.31 (C_1), 126.05 (C_3), 133.15 (C_2), 128.55, 129.99, 133.49 (aromatic carbons), 164.48 (C=O). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50. Found: 67.41; H, 6.64.

REFERENCES AND FOOTNOTES

1. A portion of this work has appeared in preliminary form, R. W. Binkley, *J. Carbohydr. Chem.*, **9**, 771 (1990).

2. For a review of the reactions of carbohydrate triflates see: R. W. Binkley and M. G. Ambrose, *J. Carbohydr. Chem.*, **3**, 1 (1984).

3. Some recent references to substitution reactions involving carbohydrate triflates (and the nucleophile used) are: (a) A. G. M. Barrett and S. A. Lebold, *J. Org. Chem.*, 55, 3853 (1990) (iodide); (b) Fatima, F. Zaman, M. S. Shekhani, A. Malik, and W. Voelter, *Liebigs Ann. Chem.*, 389 (1990) (-CH_2CN); (c) G. W. J. Fleet, N. G. Ramsden, and D. R. Witty, *Tetrahedron*, 45, 319 (1989) (azide); (d) G. Tarara and D. Hoppe, *Synthesis*, 89 (1989) (acetate); (e) R. W. Binkley, M. G. Ambrose, and D. G. Hehemann, *J. Carbohydr. Chem.*, 6, 203 (1987) (halides); (f) H. J. G. Broxterman, J. J. Neefjes, G. A. van der Marel, H. L. Ploegh, and J. H. van Boom, *J. Carbohydr. Chem.*, 7, 593 (1988) (benzyl amine); (g) M. S. Shekhani and W. Voelter, *Chemiker-Zeitung*, 113, 1 (1989) (hydrogen sulfate); (h) M. Blanc-Muesser and H. Driguez, *J. Chem. Soc. Perkin Trans. I*, 3345 (1988) (thioacetate).

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8. The other alternative, heterolytic C_1-C_2 bond cleavage prior to triflate departure, was not deemed to be a realistic possibility. If such a reaction could occur, C_1-C_2 fragmentation reactions would be common rather than rare for pyranosides.

9. To compare the effect of stereochemical change at C-3 in 1 it was necessary to change stereochemistry at C-4 also since, otherwise, an internal displacement analogous to that shown in Scheme I would be expected.

10. C. A. Grob and P. W. Schiess, *Angew. Chem., Int. Ed. Engl.*, 6, 1 (1967).

11. The Grob fragmentation has been observed previously in carbohydrate systems. See W. W. Zajac, Jr., P. Dampawan, and D. Ditrow, *J. Org. Chem.*, 51, 2617 (1986) and references cited therein.