filtered with suction. The damp solid cake was dissolved in chloroform, and the solution was processed in the usual manner, giving 0.845 g of pure (TLC) **4** as a beige solid (see Table I).

(*R*)-(-)-Methyl 2-Methyl-2-[(methylsulfonyl)oxy]-4-(2,4,5-trimethyl-3,6-dioxo-1,4-cyclohexadien-1-yl)butanoate (20). To a stirred solution of 0.746 g (2.66 mmol) of benzoquinone **11b** in 18 mL of dichloromethane, cooled in an ice-bath, was added 2.43 mL (1.77 g, 17.5 mmol) of triethylamine followed by 1.35 mL (2.01 g, 17.5 mmol) of methanesulfonyl chloride. The mixture was kept at 0 °C for 64 h and then treated with water. The dichloromethane solution was processed in the usual manner to give 1.45 g of an oily product which was chromatographed on 75 g of silica gel. Elution with 9:1 toluene–ethyl acetate afforded 0.69 g (72.5%) of methanesulfonate **20** as a yellow solid. Recrystallization of a sample from hexane–ethyl acetate provided yellow crystals: mp 112–114 °C; $[\alpha]^{25}_D$ -5.24° (*c* 1.05, $CHCl_3$); UV_{max} 260 nm (ε 19 600), 267 (20 000), 343 (275); IR 1750 (ester C=O), 1642 (quinone), 1352, 1178 cm^{-1} (SO_2); NMR ($CDCl_3$) δ 3.73 (s, 3, CO_2CH_3), 3.18 (s, 3, SO_2CH_3), 2.10 (m, 2, CH_2), 2.03, 1.99 (2 s, CH_3C=), 1.84 (s, 3, CH_3).

Anal. Calcd for $C_{16}H_{22}O_7S$: C, 53.62; H, 6.19; S, 8.95. Found: C, 53.59; H, 6.14; S, 8.61.

Mesylate **20** could also be purified by recrystallization from methanol.

Methyl (*S*)-(-)-3,4-Dihydro-6-hydroxy-2,5,7,8-tetramethyl-2*H*-1-benzopyran-2-carboxylate (22). (a) Reduction of 20 with Sodium Dithionite. A slurry of 0.358 g (1 mmol) of quinone methanesulfonate **20** in 5 mL of methanol was stirred rapidly at room temperature while a solution of 0.261 g (1.5 mmol) of sodium dithionite in 3 mL of 1 N aqueous sodium hydroxide was added dropwise over a 5-min period. The resulting mixture was stirred at room temperature for 20 min and then refluxed for 5 min. After the mixture cooled, 20 mL of water was added, and the colorless slurry was filtered with suction. The solid was washed with water then dried under high vacuum, giving 0.246 g (93.2%) of chromanol ester **22** as a colorless solid: mp 132.5–135 °C; $[\alpha]^{25}_D$ -60.62° (*c* 3.09, CH_3OH). This material was homogeneous on TLC analysis.

(b) Catalytic Hydrogenation of 20. A mixture of 1 g (2.79 mmol) of quinone methanesulfonate **20**, 0.2 g of 5% palladium on charcoal, and 125 mL of methanol was stirred in an atmosphere of hydrogen until gas uptake ceased. The catalyst was filtered with suction on a pad of Celite, and the filtrate (containing **21**) was immediately treated with 8.3 mL (11.16 mmol) of 1.34 M methanolic sodium methoxide. After being stirred for 1 h at room temperature, the solution was acidified with 3 N aqueous hydrochloric acid and poured into saturated brine. Workup with ether in the usual manner gave 0.638 g of a tan solid which was chromatographed on 25 g of silica gel. Elution with 19:1 and 9:1 toluene–ethyl acetate furnished 0.491 g (66.7%) of ester **22** as a colorless solid, $[\alpha]^{25}_D$ -59.93° (*c* 3.01, CH_3OH).

(c) Reduction of 20 with Sodium Borohydride. To a solution of 0.5 g (1.4 mmol) of quinone mesylate **20** in 30 mL of methanol, at room temperature, was added a solution of 20.2 mg (0.53 mmol) of sodium borohydride in 10 mL of methanol, dropwise, with stirring. After the mixture was stirred at room temperature for 50 min, 5.77 mL (7.73 mmol) of 1.34 M methanolic sodium methoxide was added, and stirring was continued for 2 h at room temperature. The resulting solution was acidified with 1 N aqueous hydrochloric acid, poured into saturated brine, and worked up with ether in the usual manner. The crude, crystalline product (0.34 g) was chromatographed on 20 g of silica gel. Elution with 19:1 and 9:1 toluene–ethyl acetate gave 0.311 g (84.1%) of ester **22** as a colorless solid: mp 131–134 °C; $[\alpha]^{25}_D$ -60.46° (*c* 3.88, CH_3OH).

Acknowledgment. We express our gratitude to the personnel of our Physical Chemistry Department for carrying out many of the spectral, microanalytical, and polarimetric determinations required in this work. We are grateful to Dr. J. W. Scott, who furnished generous samples of various intermediates and valuable information. The support and encouragement provided by Dr. G. Saucy are also greatly appreciated.

Registry No. **1**, 10191-41-0; **4**, 53101-49-8; **5**, 7559-04-8; **6**, 14745-36-9; **7**, 18920-63-3; **10b**, 70897-16-4; **10c**, 53730-40-8; **10d**, 77286-97-6; **11a**, 77257-11-5; **11b**, 70874-20-3; **11c**, 77257-12-6; **11d**, 77257-13-7; **12a**, 77286-98-7; **12b**, 77286-99-8; **12c**, 77257-14-8; **12d**, 77257-15-9; **20**, 70874-21-4; **21**, 77270-00-9; **22**, 70897-17-5; **23**, 69371-85-3; **24**, 69427-83-4.

Products from the Base Treatment of the Tri-*O*- and Tetra-*O*-methanesulfonyl Esters of Methyl α-D-Glucopyranoside

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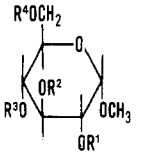
Treatment of the four tri-*O*-methanesulfonyl and tetra-*O*-methanesulfonyl esters of methyl α-D-glucopyranoside gave as initial products methyl anhydro-*O*-methanesulfonyl- and anhydro-di-*O*-methanesulfonyl-α-D-hexosides. Further base treatment transformed these initial products into a variety of anhydro-, anhydro-*O*-methanesulfonyl-, and dianhydrohexosides and one olefinic hexoside, depending on the initial product. An order of preference, $C_4 > C_6 > C_2$, for the internal sulfonyloxy group displacement was found. The end product preferences noted in Scheme I accounted for the observed products.

Reaction of carbohydrate sulfonates with various nucleophilic reagents is well recorded.[2] The many factors that influence the sulfonate displacements are discussed. If the carbohydrate sulfonate is partially substituted (or the free hydroxyl groups are esterified with carboxyl groups), the treatment with base results in the displacement taking a different route. An internal ether, an anhydro sugar, is formed, and, if the stereochemical arrangement is suitable, either a cross-ring isomerization of the methyl 2,3-anhydro-α-D-allopyranoside to methyl 3,6-anhydro-α-D-glucopyranoside type or a vicinal isomerization of the methyl 3,4-anhydro-α-D-altropyranoside to methyl 2,3-anhydro-α-D-mannopyranoside type can further occur. Base hydrolysis of sulfonates will occur only if the above reactions or isomerizations cannot occur; the hydrolysis is difficult. These alkaline displacements and

(1) The mention of firm names or trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.

(2) R. S. Tipson, *Adv. Carbohydr. Chem.*, 8, 107 (1953); D. H. Ball and F. W. Parrish, *ibid.*, 23, 233 (1968); D. H. Ball and F. W. Parrish, *Adv. Carbohydr. Chem. Biochem.*, 24, 139 (1969).

Table I. Starting Methyl Mesyl-α-D-glucopyranosides



compd	R^1	R^2	R^3	R^4	ref
1	Bz[a]	Ms	Ms	Ms	*b*
2	Ms	Bz	Ms	Ms	5
3	Ms	Ms	H	Ms	5
4	Ms	Ms	Ms	Bz	*b*
5	Ms	Ms	Ms	Ms	6

[a] Bz = benzoyl, Ms = methanesulfonyl. [b] This study.

isomerizations are summarized and discussed by Williams.[3]

Most reports[2,3] on the base reactions of carbohydrate sulfonates have involved monosubstituted sulfonates or acetal- (or ketal) blocked sulfonates. Although much information was gathered from these studies, the fact that these positional and conformational restrictions could give atypical results was tacitly recognized. Recently a study of the action of base on the six di-*O*-mesyl esters of methyl α-D-glucopyanoside was reported.[4] The results were unusual in that the internal displacement of the first sulfonate to yield a methyl anhydro-*O*-mesyl-α-D-hexoside showed a $C_4 > C_6 > C_2$ displacement preference, not the usual $C_6 > C_4 \gg C_2$ preference[2] shown with external nucleophiles.

Displacement of the various methyl anhydro-*O*-mesyl-α-D-hexosides was also unusual in that the main products were two different methyl dianhydro-α-D-hexosides and two different methyl anhydro-α-D-hexosides. A reaction preference was proposed as shown in Scheme I[4] to account for the observed products.

Since the study of the reaction of the six methyl di-*O*-mesyl-α-D-glucopyranosides with base produced unusual results and since no report was found in a similar study of the tri-*O*- and tetra-*O*-mesyl esters, a systematic study of these compounds with base is reported below.

Results

Three (2,3,6-, 2,4,6-, and 2,3,4,6-) of the five mesyl esters were recorded either as the free ester or its related *O*-benzoate (see Table I). Methyl 2-*O*-benzoyl-3,4,6-tri-*O*-mesyl-α-D-glucopyranoside (1) was synthesized by permesylation of methyl 2-*O*-benzoyl-3-*O*-mesyl-α-D-glucopyranoside–pyridine complex.[4] When **5** was reacted with lithium benzoate in dimethylformamide at 80 °C, crystalline **4**, the 2,3,4-tri-*O*-mesyl ester (mp 117–120 °C), was obtained.

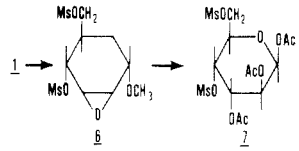
3,4,6-Tri-*O*-mesyl Reaction. When **1** was stirred in a dioxane–sodium hydroxide mixture, TLC revealed the progressive disappearance of **1** (R_f 0.79) and the progressive appearance of a single spot of R_f 0.55. After neutralization and dilution, a solid slowly separated from solution. Elemental analysis established that the solid was a methyl anhydro-di-*O*-mesylhexoside, and ^{1}H NMR spectroscopy (Table II) established that the solid was methyl 2,3-anhydro-4,6-di-*O*-mesyl-α-D-allopyranoside (**6**).

Acetolysis of **6** gave a tri-*O*-acetyl derivative whose structure was assigned as 1,2,3-tri-*O*-acetyl-4,6-di-*O*-mesyl-β-D-altropyranoside (**7**) because of the small coupling

Table II. ^{1}H NMR Parameters

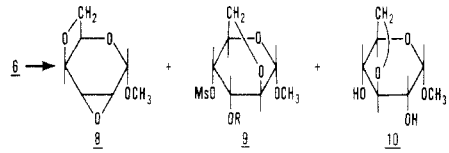
	chemical shift, δ									*J* value, Hz					
compd	H_1	H_2	H_3	H_4	H_5	$H_{6,6'}$	OCH_3	CH_3SO_2	other	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	other	solvent
1	5.10 d	~5.2 m	~5.3 m	4.86 dd	4.10 m	4.5 m	3.40	2.96, 3.07, 3.21		3	8	9		$CDCl_3$
3 (R^4 = Ac)	4.97 d	4.57 dd	5.05–5.15		~3.9	4.02, 4.16	3.27	2.74, 2.78, 2.80	2.02 (Ac)	4	9		4 ($J_{5,6}$)	$CDCl_3$ + benzene-d_6
4 (R^4 = H)	4.07 d	4.70 dd	4.03 dd	4.84 dd	3.7–3.9		3.44	3.24, 3.25, 3.26	4.1 (OH)	4	9	9		acetone-d_6
4 (R^4 = Bz)	4.88 d	4.26 dd	5.16 dd	4.83 dd	3.7 m	4.40 dd, 4.79 dd	2.92	2.45, 2.68, 2.74		4	9	9		benzene-d_6
6	4.93 d		3.5–3.7	5.02	4.14	4.4	3.46	3.04, 3.14		2	4	1		$CDCl_3$
7	5.98 d	~5	4.4	~5	4.4–4.5			3.06, 3.08	2.10, 2.16 (Ac)	~1	~1	~1		$CDCl_3$
9 (R = Bz)	5.00 d		4.2–4.3	5.4	~4.3	~3.8	3.24	3.02		~1				$CDCl_3$
11	4.83 d	4.55 d			4.2–4.5		3.43	3.10, 3.20		6				acetone-d_6
13	4.88 s		3.4–3.6	4.65 d	~3.9	~4.3	3.43	3.02, 3.10					9 ($J_{4,5}$)	$CDCl_3$
18	4.98 d	5.12 dd			~4.3	~4.5	3.52	3.16, 3.22		6	~1			$CDCl_3$
19 (R = Ac)	4.94 s		5.97 d	4.49 dd	4.20 dd	4.35 d	3.52	3.06, 3.16	2.09 (Ac)			3	9 ($J_{4,5}$), 4 ($J_{5,6}$)	$CDCl_3$

(3) N. R. Williams, *Adv. Carbohydr. Chem. Biochem.*, **25**, 109 (1970).
(4) H. B. Sinclair, *J. Org. Chem.*, **44**, 3361 (1979).
(5) H. B. Sinclair, *Carbohydr. Res.*, **50**, 247 (1976).
(6) B. Helferich and A. Gnüchtel, *Ber. Dtsch. Chem. Ges.*, **72**, 712 (1938).

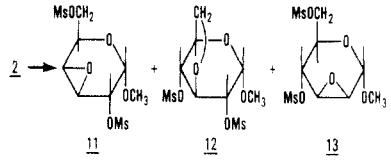


values (~1 Hz) of the ring protons.

Further reaction of **6** with base was slow. TLC revealed the progressive disappearance of **6** and appearance of three spots: R_f's 0.14, 0.24, 0.55. Neutralization, extraction, and chromatography separated the mixture into the respective spots as well as unaltered **6**. The R_f 0.55 spot was readily identified as **8**[4] and the R_f 0.14 spot as **10**.[4] The R_f 0.24 spot, a syrup, was converted with benzoyl chloride–pyridine to a crystalline benzoate ester whose mass spectra showed strong peaks at 327 and 236, corresponding to m/e – OCH_3 and m/e – C_6H_5COOH, and ^1H NMR spectra showed small J values in the ring protons. The structure was assigned as methyl 2,6-anhydro-3-*O*-benzoyl-4-*O*-mesyl-α-D-altropyranoside (**9**, R = Bz).

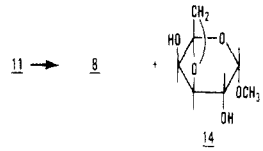


2,4,6-Tri-*O*-mesyl Reaction. Reaction of **2** with sodium hydroxide in ethanol–dioxane revealed by TLC two major spots (R_f 0.43, 0.32) and a minor spot (R_f 0.50). After neutralization and extraction, the remaining syrup was separated by chromatography into the respective spots. The R_f 0.32 spot was readily identified as **12**.[7] Through

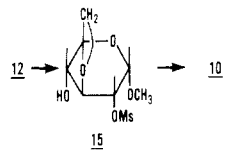


a combination of analysis and ^1H NMR, the crystalline R_f 0.43 spot was assigned the structure methyl 3,4-anhydro-2,6-di-*O*-mesyl-α-D-galactopyranoside (**11**). Although a satisfactory analysis could not be obtained, the ^1H NMR left no doubt that the syrupy minor spot (R_f 0.50) was compound **13**.

Heating **11** in dilute sodium hydroxide gave on workup and chromatography compounds **8** and **14**, readily identified from known samples.[4]



Heating **12** in dilute sodium hydroxide gave on workup and chromatography compounds **15** and **10**. No evidence could be found for the presence of methyl 3,6-anhydro-4-*O*-mesyl-α-D-glucopyranoside, which agrees with the instability reported for the related 4-*O*-*p*-toluenesulfonyl derivative.[7b]

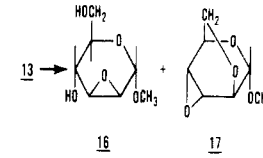


(7) (a) R. C. Chalk, D. H. Ball, and L. Long, Jr., *J. Org. Chem.*, 31, 1509 (1966); (b) M. L. Wolfram, Y. Hung, P. Chakravarty, G. U. Yuen, and D. Horton, *ibid.*, 31, 2227 (1966).

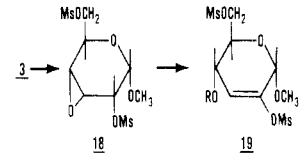
Scheme I

reaction preference in end product formation	low → high	sulfonate hydrolysis vicinal isomerization sulfonyloxy displacement cross-ring isomerization → dianhydro formation

Heating **13** in dilute sodium hydroxide gave on workup and chromatography **16** and **17**, readily identified from known samples.[4,8]

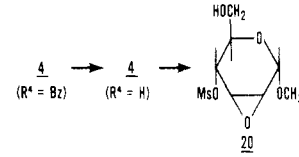


2,3,6-Tri-*O*-mesyl Reaction. When **3** was allowed to react with sodium hydroxide, TLC revealed three overlapping spots (R_f ~0.40). After neutralization, extraction, and evaporation, the syrup was acetylated. The acetylated mixture revealed three spots on TLC: R_f 0.62, 0.55, 0.37. By chromatography the mixture was separated into a compound (R_f 0.62) that by elemental analysis agreed with $C_{11}H_{18}O_{10}S_2$ and by ^1H NMR showed two mesyl groups, one acetyl group, one methoxyl group, and one olefinic proton. ^1H NMR further showed that the H_1 was a singlet, that the olefinic proton was H_3, and that there was no H_2 proton. The structure was assigned as methyl 4-*O*-acetyl-3-deoxy-2,6-di-*O*-mesyl-α-D-*arabino*-hex-2-enopyranoside (**19**). The compound with R_f 0.37, whose analysis agreed with $C_9H_{16}O_9S_2$ and ^1H NMR spectrum showed a 3,4-anhydro group, two mesyl groups, and one methoxyl group, was assigned the structure methyl 3,4-anhydro-2,6-di-*O*-mesyl-α-D-allopyranoside (**18**).



When **18** was allowed to react with base, **19** was isolated. If the solution was heated, complete destruction of **18** and **19** was noted—a reddish brown solution resulted.

2,3,4-Tri-*O*-mesyl Reaction. Ethanolic sodium hydroxide converted **4** (R^4 = Bz) into a mixture that TLC separated into two compounds (R_f 0.39, 0.28). After workup, these compounds were readily separated by chromatography. The R_f 0.39 spot was readily established as methyl 2,3,4-tri-*O*-mesyl-α-D-glucopyranoside (**4**, R^4 = H). The R_f 0.28 spot was also established as methyl 2,3-anhydro-4-*O*-mesyl-α-D-allopyranoside (**20**) by comparison with an authentic sample.[4]



2,3,4,6-Tetra-*O*-mesyl Reaction. After a mixture of **5** in dioxane–sodium hydroxide was heated, neutralized, and extracted, the extract revealed two compounds by TLC (**5** → **6**). Chromatography readily separated this

(8) J. G. Buchanan and J. C. P. Schwarz, *J. Chem. Soc.*, 4770 (1962).

mixture into starting 5 and 6.

Discussion

Although a standardized procedure[4] was used for working up the reaction mixtures of the six di-*O*-mesyl esters of methyl α-D-glucopyranoside with base, the products from the tri-*O*- and tetra-*O*-mesyl esters varied so markedly in solubility that a standardized workup was not developed. Also, the conditions needed to result in reaction with the tri-*O*- and tetra-*O*-mesyl series were usually more aggressive than those with the di-*O*-mesyl esters; as a result, more trace products were noted by TLC, and the reaction mixtures were commonly tan to dark brown in color. ^{1}H NMR readily established the presence of a 2,3-, 3,4-, or 3,6-anhydro structure.

With base, 1 was readily converted to methyl 2,3-anhydro-4,6-di-*O*-mesyl-α-D-allopyranoside (6), a known compound.[9] Acetolysis of 6 gave a tri-*O*-acetyl-di-*O*-mesylhexoside. Because the anhydro ring opening was expected to follow the Fürst–Plattner rule of diaxial opening,[3] the acetolysis product 7 was predicted to possess an altrose stereochemistry; the ^{1}H NMR agreed with this assignment. Reaction of 6 with base produced three compounds which were separated by chromatography. The two minor products were identified as methyl 2,3:4,6-dianhydro-α-D-gulopyranoside (8) and methyl 3,6-anhydro-α-D-glucopyranoside (10) by comparison with known compounds.[4] The major product, a syrup, was converted by benzoyl chloride–pyridine to a crystalline methyl anhydro-*O*-benzoyl-*O*-mesyl-α-D-hexoside. The structure was assigned from analysis and ^{1}H NMR and mass spectroscopy as 9.

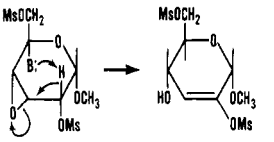
Hydrolysis of 6 to give either methyl 2,3-anhydro-6-*O*-mesyl-α-D-allopyranoside or methyl 2,3-anhydro-4-*O*-mesyl-α-D-allopyranoside and their subsequent transformations by base to 8 and 10, respectively, are reported.[4] Diaxial opening of the 2,3-anhydro group in 6 to give an altroside and its subsequent 2-OH displacement of the 6-*O*-mesyl group to give a 2,6-anhydro altroside would explain compound 9. A similar sequence was reported[4] to account for the minor product, methyl 2,6-anhydro-α-D-altropyranoside, by the action of base on methyl 2,3-anhydro-6-*O*-mesyl-α-D-allopyranoside. The epoxide ring opening predominated over the mesyl hydrolyses.

From the di-*O*-mesyl study[4] the conclusion was reached that, in methyl α-D-glucopyranoside, the internal displacement of the mesyl group exhibited a $C_4 > C_6 > C_2$ preference. Reaction of 2 with base provided an excellent demonstration of this preference, since all three displacements are possible. Three compounds, a major, a minor, and a trace compound, were isolated and identified as 11–13, respectively. On further treatment with base, 11 yielded 8 and 14, which were previously identified.[4] Compound 12 on treatment with base was converted to 15, which was converted[4] to 10. No evidence could be found that methyl 3,6-anhydro-4-*O*-mesyl-α-D-glucopyranoside was produced as an intermediate to 10. On treatment with base, 13 gave 16 and 17.[4]

The two products isolated from base treatment of 11 are explained by hydrolysis of either the 2-*O*-mesyl or the 6-*O*-mesyl group and previously reported[4] reaction sequences. Conversion of 12 → 15 → 10 is a sequential base hydrolysis. Conversion of 13 to 16 involved hydrolysis of the 6-*O*-mesyl group, and because the product, methyl 2,3-anhydro-4-*O*-mesyl-α-D-mannopyranoside, is not sterically aligned for a cross-ring or vicinal isomerization, the 4-*O*-mesyl group is removed by hydrolysis to yield 16. Although 16 can undergo a vicinal isomerization, Buchanan and Schwarz[8] report the manno–altro equilibrium to favor the manno isomer by >90%. Conversion of 13 to 17 involved hydrolysis of the 4-*O*-mesyl group and reported isomerizations.[4]

Treatment of 3 with base revealed by TLC three overlapping spots. A practical method of separation involved acetylation and chromatography. The three compounds were identified as 18, acetylated 3 (3, R^3 = Ac), and the unusual olefinic sugar 19 (R = Ac). Compound 18 was identified from ^{1}H NMR and elemental analysis. Compound 19 (R = Ac) proved unusual when first examined by ^{1}H NMR. No H_2 was found, H_3 was downfield (δ 5.97), and H^1 was a singlet. When the analysis and mass and ^{1}H NMR spectral information was put together, the only consistent structure was 19 (R = Ac). When 18 was treated with base, only 19 (R = Ac) was isolated after workup.

Apparently the conjunction of three structural features resulted in this: (i) a glycosidic group attached next to H_1, (ii) a proton (H_2) in an axial (or psuedoaxial) position and activated by a mesyl group, and (iii) an epoxide group vicinal to the proton (H_2) and in a trans relationship to the proton. In a sense, this reaction is a trans-diaxial elimination.



Further treatment of 19 with base required aggressive conditions and invariably resulted in intractable material. Hydrolysis of the enol mesylate would yield a 2-oxo-3-deoxyhexose, a class of sugars that is well reported[10] to be most susceptible to multiple elimination reactions under conditions far less aggressive than those needed for mesylate hydrolysis.

Reaction of 4 with base revealed the stability of the mesyl group to hydrolysis. Compound 4 (R^4 = H) was isolated, and it was further transformed by base to 20,[4] whose reaction with base is reported.[4]

Reaction of 5 with base produced 6. Among the various mesyl esters, apparently the 2-*O*-mesyl is hydrolyzed first, which would result in 1 (R = H); the intermediate, 1 (as reported above), was converted to 6.

This study reconfirms that the internal displacement of mesyl group in methyl α-D-glucopyranoside to yield an anhydrohexoside does follow a $C_4 > C_6 > C_2$ preference.[4] The results offer no reason for altering Scheme I, originally proposed[4] for the di-*O*-mesyl series, to account for the observed products in the tri-*O*- and tetra-*O*-mesyl series.

Experimental Section

TLC was performed on precoated plates of 0.25-mm layers of silica gel F-254 with the specified solvents. The plates were rendered visible by spraying with 5% ethanolic sulfuric acid and heating until charring occurred. The plates were air equilibrated. Dry-column chromatography was performed on Woelm TSC silica by dissolving the sample in a small amount of low-boiling solvent, adding Woelm TSC silica to obtain a free-flowing powder, placing the powder on the dry column, and developing the column with solvent. Each fraction was monitored by TLC, and the appropriate fractions were pooled. When sodium hydroxide solutions were neutralized to pH ~8, dry ice was added in small pieces. ^{1}H NMR spectra were obtained with a Varian XL-100 spectrometer. Chemical shifts were compared against internal tetramethylsilane and reported as δ values. Mass spectra were obtained with a Du Pont 491 spectrometer. Analytical samples were dried for 24–48 h at 10–20 torr in the presence of sulfuric

(9) S. Dimitriyevich and N. F. Taylor, *Carbohydr. Res.*, 11, 531 (1969).
(10) I. Lundt and C. Pederson, *Carbohydr. Res.*, 35, 187 (1974); F. W. Lichtenhaler, K. Strobel, and G. Reidel, *ibid.*, 49, 57 (1976).

acid and sodium hydroxide pellets. Solutions were evaporated in vacuo.

Methyl 3-O-Benzoyl-2,4,6-tri-O-mesyl-α-D-glucopyranoside (2). This compound was prepared by the method of Sinclair.[5]

Methyl 2,3,4,6-Tetra-O-mesyl-α-D-glucopyranoside (5). The procedure of Helferich and Gnüchtel[6] was followed in preparing this compound.

Methyl 2,3,6-Tri-O-mesyl-α-D-glucopyranoside (3). This compound was prepared by the method of Sinclair[4] with the following modification. Pouring the mixture into an ice–water slush gave a syrup. Instead of extracting this syrup, it was seeded after the ice melted and gently stirred. Over a 4–6-h period of syrup converted to a crystalline solid, which after air-drying to constant weight melted at 140–143 °C. Although the solid contained a trace of compound **5**, it was suitable for further work.

Methyl 2-O-Benzoyl-3,4,6-tri-O-mesyl-α-D-glucopyranoside (1). Methyl 2-*O*-benzoyl-3-*O*-mesyl-α-D-glucopyranoside–pyridine complex[4] (10.0 g) was dissolved in pyridine (150 mL), the mixture was cooled to −20 °C, and mesyl chloride (5.0 mL) was added with stirring. The reaction was allowed to proceed at −10 °C for 6 h and then at 5 °C for 4 days. Water (5 mL) was added, and the mixture was evaporated to a tacky semisolid material, which was transferred to a separatory funnel with water (250 mL) and ethyl acetate (50 mL). The organic layer was separated, and the aqueous layer was extracted with four 50-mL portions of ethyl acetate. The combined organic extracts were washed with water (250 mL), dried, and evaporated to a tacky solid, which TLC (toluene–ethyl acetate, 2:1 v/v) revealed as compound **1** (R_f 0.40) with a trace of starting compound (R_f 0.10) and a trace of unknown substance (R_f 0.58). Dry-column chromatography (4.0 × 35 cm) readily separated this mixture when developed with toluene–ethyl acetate (600/300 and 150/100 mL). Evaporation gave an amorphous, chromatographically homogeneous solid.

Methyl 6-O-Benzoyl-2,3,4-tri-O-mesyl-α-D-glucopyranoside (4). A mixture of compound **5** (7.84 g), lithium benzoate (8.0 g), and *N,N*-dimethylformamide (130 mL) was heated to 80 ± 1 °C with gentle stirring for 18–20 h. After cooling to room temperature, the mixture was poured into an ice–water slush. The solid that separated by filtration was washed with ice–water (~100 mL) and dried in air to constant weight: 8.21 g; mp 60–100 °C. Recrystallization from a mixture of acetone (20 mL) and methanol (200 mL) gave an analytical samples: 6.37 g (77.4%); mp 117–120 °C.

Anal. Calcd for $C_{17}H_{24}O_{13}S_3$: C, 38.34; H, 4.54. Found: C, 38.30; H, 4.43.

Reaction of 1 and Derived Products. A mixture **1** (2.0 g), dioxane (30 mL), and 0.5 N NaOH (30 mL) was stirred until homogeneous (~10 min) and allowed to stand at room temperature for 1–1.25 h, whereupon the mixture was diluted with water (140 mL) and the solution was neutralized. Slowly a white solid separated; after storage overnight at 5 °C, the solid was separated by filtration and washed with ice–water (50 mL). The solid was pure **6**: 1.077 g (86.2%); mp 134–135 °C (lit.[9] mp 138 °C).

Anal. Calcd for $C_9H_{16}O_9S_2$: C, 32.52; H, 4.85. Found: C, 32.27; H, 4.92.

To an ice-cold mixture of acetic anhydride (10 mL) containing concentrated sulfuric acid (1 mL) was added **6** (0.68 g) with stirring. After ~5 min the mixture, which was homogenous, was stored at 5 °C for 18–20 h, poured into ice–water (100 mL) containing sodium acetate (2 g), and stirred at room temperature for ~2 h. After storage overnight at 5 °C, the solid was separated by filtration, washed with ice–water (20 mL) and dried in air: 0.57 g; mp 128–132 °C dec. A sample (95.8 mg) was placed on a dry column (1.5 × 17 cm) and developed with toluene–ethyl acetate (100 mL/100 mL). Evaporation gave a solid which on recrystallization from acetone (1 mL)–water (5 mL) gave an analytical sample of **7**: 75.5 mg; mp 147.5–148.5 °C.

Anal. Calcd for $C_{14}H_{22}O_{13}S_2$: C, 36.36; H, 4.79. Found: C, 36.58; H, 4.70.

A mixture of **6** (500 mg), dioxane (12 mL), and 0.5 N sodium hydroxide (15 mL) was heated to 40 ± 1 °C for 12 days. TLC (toluene–ethyl acetate, 1:2 v/v) revealed the progressive disappearance of **6** (R_f 0.42) and progressive appearance of three other spots at R_f 0.14, 0.24, and 0.55. The dark brown reaction mixture was neutralized, evaporated to a small volume (~5 mL), diluted with water (~75 mL), and continuously extracted with ethyl acetate for 18–20 h. Evaporation of the extract left a syrup (130 mg), which was placed on a dry column (1.5 × 36 cm) and developed with toluene–ethyl acetate (200 mL/200 mL) and ethyl acetate (200 mL). The appropriate fractions were pooled and evaporated. Progressive elution from the column gave the following: R_f 0.55 spot, crystallized weight 5.3 mg, mp 57–59 °C, methyl 2,3:4,6-dianhydro-α-D-gulopyranoside[5] (**8**); R_f 0.42 spot, 20.1 mg, unchanged starting material (**6**); R_f 0.24 spot, syrup, 62.7 (see later); R_f 0.14 spot, 9.9 mg, mp 108–109 °C, methyl 3,6-anhydro-α-D-glucopyranoside[5] (**10**). The above syrup (62.7 mg) was dissolved in pyridine (1 mL), and benzoyl chloride (0.05 mL) was added. After this mixture was allowed to stand at room temperature for 20 h, water (6 mL) was added dropwise with good stirring.

A crystalline solid separated, which was separated by filtration after chilling the solution. After being dried, the methyl 2,6-anhydro-3-*O*-benzoyl-4-*O*-mesyl-α-D-altropyranoside (**9**, R = Bz; 73.1 mg) melted at 156–157 °C. A mass spectrum showed strong peaks at 327 and 236, corresponding to m/e − OCH_3 and m/e − $C_6H_5CO_2H$.

Reaction of 2 and Derived Products. A mixture of **2** (1.0 g), dioxane (10 mL), ethanol (15 mL), and 1 N sodium hydroxide (10 mL) was stirred at room temperature; the solution was homogenous in about 4 h. After 5 h, TLC (toluene–ethyl acetate, 1:1 v/v) revealed three spots: R_f 0.50, 0.43, and 0.32. After 20 h, the mixture was diluted with water (100 mL), neutralized, and placed in a continuous extractor for ~18 h with ethyl acetate. Evaporation of the extract left a syrup, which was placed on a dry column (1.5 × 39 cm); the column then was developed with toluene–ethyl acetate (250 mL/250 mL). Progressive elution from the column gave the following: R_f 0.50 spot, syrup, 4 mg, methyl 2,3-anhydro-4,6-di-*O*-mesyl-α-D-mannopyranoside (**13**); R_f 0.43 spot, crystalline, 419.0 mg, mp 79–82 °C, methyl 3,4-anhydro-2,6-di-*O*-mesyl-α-D-galactopyranoside (**11**); R_f 0.32 spot, crystalline, 98.5 mg, mp 158–159 °C, methyl 3,6-anhydro-2,4-di-*O*-mesyl-α-D-glucopyranoside (**12**). Recrystallization of **11** (215 mg) by dissolution in warm chloroform (1 mL) and addition of warm ethanol (10 mL) gave an analytical sample of **11**, mp 80–81 °C.

Anal. Calcd for $C_9H_{16}O_9S_2$: C, 32.52; H, 4.85. Found: C, 32.80; H, 5.00.

Compound **11** (216 mg) was heated to reflux in 0.1 N sodium hydroxide (25 mL), maintained at reflux for 3 h, and cooled, and the dark brown solution was neutralized. TLC (ethyl acetate) revealed two spots: R_f 0.73, 0.22. The reaction mixture was placed in a continuous exractor overnight with ethyl acetate. Evaporation of the extract left a yellow syrup, which was placed on a dry column (1.5 × 15 cm) and developed with toluene–ethyl acetate (75 mL/75 mL) and ethyl acetate–methanol (100 mL/10 mL). Progressive elution gave the following: R_f 0.73 spot, crystalline, 27.9 mg, mp 56–58 °C, methyl 2,3:4,6-dianhydro-α-D-allopyranoside[5] (**8**); R_f 0.22 spot, crystalline, 13.1 mg, mp 136–138 °C, methyl 3,6-anhydro-α-D-galactopyranoside (**14**).

Compound **12** (1.0 g) was heated under reflux in 0.1 N sodium hydroxide (100 mL) for 7.5 h and cooled, and the dark brown solution was neutralized. TLC (ethyl acetate) revealed three spots: R_f 0.67, 0.45, 0.29. Continuous extraction for 18–20 h gave on evaporation of the extract a yellow syrup, which deposited some crystalline material: 135 mg; mp 149–152 °C (slightly impure starting **12**). Separation of the syrupy portion gave 465 mg of material, which was placed on a dry column (1.5 × 38 cm) and developed with ethyl acetate. Progressive elution from the column gave the following: R_f 0.67 spot, crystalline, 45.2 mg, mp 158–159 °C, methyl 3,6-anhydro-2,4-di-*O*-mesyl-α-D-glucopyranoside (**12**); R_f 0.45 spot, crystalline, 120.4 mg, mp 116–119 °C, methyl 3,6-anhydro-2-*O*-mesyl-α-D-glucopyranoside (**15**); R_f 0.29 spot, crystalline, 244.0 mg, mp 106–108 °C, methyl 3,6-anhydro-α-D-glucopyranoside (**10**).

Syrupy **13** (0.84 g) was heated under reflux in 0.1 N sodium hydroxide (100 mL) for 2 h and cooled, and the brown solution was neutralized. TLC (toluene–ethyl acetate, 1:1 v/v) revealed two spots: R_f 0.30, 0.12. Continuous extraction of the reaction mixture overnight gave on evaporation a yellow syrup, which was placed on a dry column (1.5 × 36 cm) and developed with toluene–ethyl acetate (100 mL/100 mL, 28 mL/42 mL) and ethyl

acetate–methanol (100 mL/5 mL, 100 mL/15 mL). Progressive elution from the column gave the following: R_f 0.30 spot, crystalline, 191.0 mg, mp 78–80 °C, methyl 2,6:3,4-dianhydro-α-D-altropyranoside[5] (17); R_f 0.12 spot, crystalline, 113.3 mg, mp 81–82 °C, methyl 2,3-anhydro-α-D-mannopyranoside (16).

Reaction of 3 and Derived Products. A mixture of 3 (2.18 g), dioxane (40 mL), water (10 mL), and 1 N sodium hydroxide (15 mL) was stirred until homogenous (~15 min) and allowed to stand for 5 days. TLC (toluene–ethyl acetate, 1:2 v/v) revealed two areas (three overlapping compounds): R_f 0.41, 0.37. The mixture was neutralized, evaporated to ~15 mL, and transferred to a separatory funnel with water (~100 mL) and dichloromethane (~10 mL). After separation of the organic layer, the aqueous layer was extracted with ten 10-mL portions of dichloromethane. The combined organic extracts were dried and evaporated to a syrup (1.7 g). This syrup was dissolved in dioxane (25 mL), and pyridine (2 mL) and acetic anhydride (1 mL) were added. After the mixture was allowed to stand overnight, TLC (toluene–ethyl acetate, 1:2 v/v) revealed three spots: *Rf* 0.64, 0.55, 0.37. Excess acetic anhydride was destroyed with water (1 mL) by allowing the mixture to stand ~20 h. Evaporation left a syrup that was placed on a dry column chromatograph (3.8 × 47 cm) and developed with toluene–ethyl acetate (600 mL/300 mL, 500 mL/500 mL, 300 mL/600 mL). Progressive elution from the column gave the following. R_f 0.64 spot: crystalline, 240 mg, mp 99–100 °C, methyl 4-*O*-acetyl-3-deoxy-2,6-di-*O*-mesyl-α-D-*arabino*-hex-2-enopyranoside (19). Anal. Calcd for $C_{11}H_{18}O_{10}S_2$: C, 35.29, H, 4.84. Found: C, 35.00; H, 4.84. A mass spectrum showed peaks at 343 and 332, corresponding to m/e – OCH_3 and m/e – $CH_2{=}C{=}O$. R_f 0.55 spot: amorphous solid, 670 mg, methyl 4-*O*-acetyl-2,3,6-tri-*O*-mesyl-α-D-glucopyranoside (3, R^3 = Ac), containing some (~10%) compound 5 (an impurity in the starting material). R_f 0.37 spot: crystalline, 740 mg, mp 130–131 °C, methyl 3,4-anhydro-2,6-di-*O*-mesyl-α-D-allopyranoside (18). Anal. Calcd for $C_9H_{16}O_9S_2$: C, 32.52; H, 4.85. Found: C, 32.8; H, 4.9. A mass spectrum showed a peak at 301, corresponding to m/e – OCH_3.

A mixture of 18 (164 mg), dioxane (3 mL), water (1.5 mL), and 1 N sodium hydroxide (1 mL) was allowed to stand 5 days, and the brown solution was neutralized. When this solution was diluted with water (5 mL), crystalline material separated from the solution; it was removed by filtration. This crystalline material was slightly impure starting compound 18: mp 128–131 °C; 38.2 mg. The filtrate was extracted with three 10-mL portions of dichloromethane. After drying, the extracts were evaporated to a syrup, which was dissolved in dichloromethane (5 mL), and pyridine (1 mL) and acetic anhydride (0.5 mL) were added. After the mixture had been allowed to stand overnight, methanol (1 mL) was added to destroy excess anhydride. Three days later, the mixture was evaporated to a syrup. The evaporation was repeated two times with toluene (5 mL) to remove pyridine. The syrup was placed on a dry column (1.5 × 16 cm) and developed with toluene–ethyl acetate (50 mL/25 mL, 50 mL/50 mL, 50 mL/100 mL). Progressive elution from the column gave the following: 19, crystalline, 5.3 mg, mp 98–99 °C; 18, crystalline, 35.2 mg, mp 130–131 °C.

Reaction of 4 and Derived Products. A mixture of 4 (4.6 g), ethanol (200 mL), and 1 N sodium hydroxide (40 mL) was stirred until the solution was homogenous (~3 h) and then allowed to stand overnight. TLC (toluene–ethyl acetate, 1:2 v/v) showed two spots: R_f 0.39, 0.28. After neutralization and evaporation the mixture, a semisolid was covered with water (125 mL) and ethyl acetate (50 mL) and transferred to a separatory funnel. An additional four 50-mL portions of ethyl acetate were used to extract the aqueous portion. The combined extracts were dried and evaporated to an amorphous solid. Dry column chromatography (3.5 × 43 cm) and development with toluene–ethyl acetate (300 mL/600 mL, 200 mL/700 mL) and ethyl acetate–methanol (450 mL/50 mL) gave two spots progressively. R_f 0.39 spot: solid, recrystallized from acetone–ethanol (1:1 v/v, ~0.2 g/mL), 1.75 g, mp 137–139 °C, methyl 2,3,4-tri-*O*-mesyl-α-D-glucopyranoside (4, R^4 = H). Anal. Calcd for $C_{10}H_{20}O_{12}S_3$: C, 28.03; H, 4.70; S, 22.45. Found: C, 28.12; H, 4.67; S, 22.27. R_f 0.28 spot: solid, recrystallized from acetone (3 mL), 2.82 mg, mp 140–141 °C, methyl 2,3-anhydro-4-*O*-mesyl-α-D-allopyranoside[5] (20).

Reaction of 5 and Derived Products. A mixture of 5 (1.0 g), dioxane (30 mL), and 0.2 N sodium hydroxide (30 mL) was heated to 50 ± 1 °C for 7.5 h, cooled, and neutralized. After evaporation of the dark brown mixture to a small volume, it was covered with water (100 mL) and extracted with ten 10-mL portions of dichloromethane. TLC (toluene–ethyl acetate, 1:2 v/v) revealed three spots: R_f 0.55, 0.43, 0.31. Evaporation of the combined extracts, followed by dry-column chromatography (2.6 × 46 cm) with development by toluene–ethyl acetate (300 mL/300 mL, 150 mL/300 mL) gave the following: R_f 0.55 spot, solid, recrystallized from ethanol–acetone, 317 mg, mp 145–146 °C, unaltered 5; R_f 0.43 spot, solid, recrystallized from ethanol–acetone, 113 mg, mp 133–135 °C, 6; R_f 0.31 spot, syrup, 40 mg. Although this latter spot appeared homogenous, on reaction with benzoyl chloride in pyridine at least four different spots were revealed by TLC, and it was not investigated further.

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Registry No. 1, 76947-05-2; 2, 61252-79-7; 3 (R^3 = Ac; R^1, R^2, R^3 = Ms), 76947-06-3; 3 (R^3 = H; R^1, R^2, R^3 = Ms), 61252-77-5; 4 (R^4 = H; R^1, R^2, R^3 = Ms), 76947-07-4; 4 (R^4 = Bz; R^1, R^2, R^3 = Ms), 76947-08-5; 5, 6160-89-0; 6, 26922-78-1; 7, 76947-09-6; 8, 70941-23-0; 9 (R = Bz), 76947-10-9; 10, 76947-11-0; 11, 76947-12-1; 12, 76947-13-2; 13, 76947-14-3; 14, 5540-31-8; 15, 10226-98-9; 16, 23262-47-7; 17, 70941-14-9; 18, 76947-15-4; 19 (R = Ac), 76947-16-5; 20, 70941-22-9; methyl 2-*O*-benzoyl-3-*O*-mesyl-α-D-glucopyranoside–pyridine complex, 70941-30-9.

Acylation of Dibasic Compounds Containing Amino Amidine and Aminoguanidine Functions

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The site of acylation in difunctional compounds containing an amine and either an amidine or guanidine can be determined from the ultraviolet absorption spectrum of the acylated product. If the amidine or guanidine has been acylated, the product possesses a chromophore that is pH dependent, whereas if an amide was formed, the chromophore is independent of pH.

There exists a modest class of compounds (1–8, Chart I) whose characteristic functional groups are combinations of amides, amidines, and guanidines.[1-6] These amido amidines and guanidines possess a remarkable spectrum

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