Action of Base on the Di-*O*-methanesulfonyl Esters of Methyl α-D-Glucopyranoside: Displacement Order and End Products

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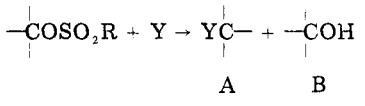
Action of base on the six methyl di-*O*-methanesulfonyl-α-D-glucopyranosides gave a series of methyl anhydro-*O*-methanesulfonyl-α-D-hexosides, which were further transformed by base into either methyl anhydro-α-D-hexosides or methyl dianhydro-α-D-hexosides. An order of preference $C_4 > C_6 > C_2$ for the vicinal S_N2 sulfonyloxy group displacements is discussed. An order of end product preference is suggested among four reactions that methyl anhydro-*O*-methanesulfonyl-α-D-hexosides commonly undergo with base. This latter preference order accounts for the observed products in the multistepped, second sulfonyloxy group removal. The unreported methyl 2,4- and 3,6-di-*O*-methanesulfonyl-α-D-glucopyranosides (as their di-*O*-benzoyl products) were prepared for this study.

Use of the sulfonate esters of carbohydrates[1] for derivational and synthetic purposes has been widespread. Not only are the starting sulfonyl chlorides, usually methanesulfonyl (mesyl) and *p*-toluenesulfonyl (tosyl), readily available, but also the reaction proves easy to carry out and most carbohydrate sulfonates are crystalline, thus making purification relatively simple. In addition, sulfonate esters undergo a ready reaction with nucleophilic reagents (Y). Generally, product A (Scheme I) predominates, particularly when the sulfonate ester is derived from a primary alcohol. Until the introduction of dipolar aprotic solvents[1,2] the attempted displacement of secondary carbohydrate sulfonates usually resulted in product B being isolated. Many examples are now reported of secondary sulfonate displacements. The scope and many factors that influence the sulfonate displacements are well discussed.[1]

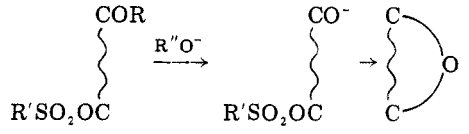
With partially substituted carbohydrate sulfonates, many times isolated by acetylating or benzoylating the unsulfonated hydroxyl groups, treatment with base results in a sulfonyloxy displacement taking a different route in that the nucleophilic attacking group is a carbohydrate alkoxide. An internal ether, an anhydro sugar, results[3] as shown in Scheme II. Since the S_N2 displacement of the sulfonyloxy group involves a rear-side attack of the alkoxide, the antiperiplanar orientation of the leaving sulfonyloxy group and the entering alkoxide restricts the number of alkoxide sites that can participate when the alkoxide is located on a pyranosyl or furanosyl ring.

In addition to the steric requirement for a rear-side displacement of the sulfonyloxy group, a ring-size preference is experimentally observed. Methyl 6-*O*-tosyl-α-D-mannopyranoside on treatment with base yields methyl 3,6-anhydro-α-D-mannopyranoside,[4] not a 2,6-anhydro mannoside, yet both anhydro mannosides are possible. And it is not that 2,6-anhydro glycosides cannot be prepared, because methyl 2,6-anhydro-α-D-altropyranoside[5] and methyl 2,6-anhydro-3,4-di-*O*-methyl-α-D-mannopyranoside[6] have been prepared by sulfonyloxy displacement. In the displacement of a C_6-sulfonyloxy group by a ring hydroxyl, the mannoside and altroside examples point out that in the pyranosyl ring the chair conformation predominantly controls the end product (mannoside), but if reaction is made impossible in the chair conformation, the boat conformation will enter.

Scheme I

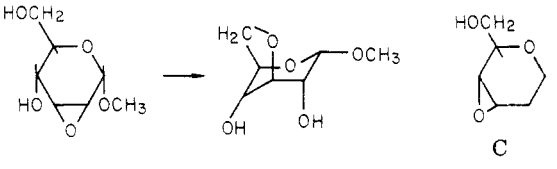


Scheme II

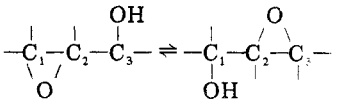


R = H, Ac, Bz; R′ = CH_3, *p*-$CH_3C_6H_4$; R″ = H, CH_3

Scheme III



Scheme IV



In a pyranose ring, when the steric alignment of a sulfonyloxy and hydroxyl group on adjacent carbons is trans-diaxially disposed, an easy displacement occurs to form an epoxide. Displacement, for example, of a 2-*O*-sulfonyloxy group in methyl glycosides is practically impossible.[1] Yet, methyl 3,4,6-tri-*O*-acetyl-2-*O*-tosyl-β-D-glucopyranoside[7] and methyl 6-deoxy-2-*O*-tosyl-α-D-glucopyranoside[8] form the corresponding 2,3-anhydro mannosides.

When the stereochemical arrangement is such that the 6-hydroxymethyl is trans to a 2,3-anhydro group in py-

(1) 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).

(2) E. J. Reist, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, 80, 5775 (1958); E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, 24, 1618 (1959).

(3) S. Peat, *Adv. Carbohydr. Chem.*, 2, 38 (1946); N. R. Williams, *Adv. Carbohydr. Chem. Biochem.*, 25, 109 (1970).

(4) F. Valentin, *Collect. Czech. Chem. Commun.*, 6, 354 (1934).

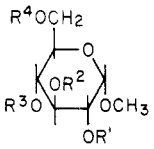
(5) D. A. Rosenfeld, N. K. Richtmyer, and C. S. Hudson, *J. Am. Chem. Soc.*, 70, 2201 (1948).

(6) E. D. M. Eades, D. H. Ball, and L. Long, Jr., *J. Org. Chem.*, 30, 3949 (1965).

(7) W. N. Haworth, E. L. Hurst, and L. Panizzon, *J. Chem. Soc.*, 154 (1934).

(8) J. Jarý, K. Čapek, and J. Kovár, *Collect. Czech. Chem. Commun.*, 29, 930 (1964).

Table I. Starting Methyl Di-O-mesyl-α-D-glucopyranosides



compd no.	R¹	R²	R³	R⁴	ref
1	Ms[a]	Ms	H	H	11
2	Ms	Bz	Ms	Bz	*b*
3	Ms	H	H	Ms	11
4	Bz	Ms	Ms	Bz	12
5	Bz	Ms	Bz	Ms	*b*
6	Bz	Bz	Ms	Ms	13

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

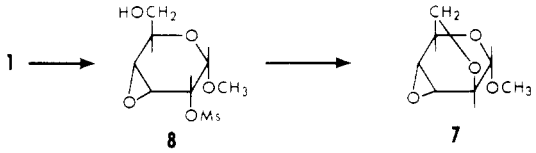
ranosyl and furanosyl rings, an isomerization occurs. Methyl 2,3-anhydro-α-D-allopyranoside[9] on treatment with alkali gave methyl 3,6-anhydro-α-D-glucopyranoside (Scheme III), whereas a related 1,5:3,4-dianhydro-2-deoxy-D-*ribo*-hexitol (C) when similarly treated does not yield a 3,6-anhydride.[9] Studies, notably by Buchanan,[10] have determined that under basic conditions an epoxide which contains a vicinal hydroxyl group trans may undergo a transformation wherein the stereochemical configuration of the C_2 (Scheme IV) is inverted through an epoxide migration.

The reactions of methyl di-O-sulfonyloxyglycopyranosides with base are recorded.[3] Most of these reactions are carried out on the 4,6-O-benzylidene derivatives which not only block two hydroxyls from participating in reactions but also severely restrict the conformational forms. Few examples were found wherein the pyranosyl ring was unblocked and unrestricted. Since so few examples were found, a systematic study on the reactions of the six methyl di-O-mesyl-α-D-glucopyranosides with base was carried out and is reported below.

Results

Four of the six possible di-O-mesyl derivatives (2,3; 2,6; 3,4; 4,6) (see Table I) were recorded either as the free mesylate or as the related di-O-benzoate. The two unreported derivatives, the 2,4- and 3,6-di-O-mesylates, were synthesized. When methyl 3-O-benzoyl-2,4,6-tri-O-mesyl-α-D-glucopyranoside[11] was allowed to react with lithium benzoate in dimethylformamide at 70–80 °C, a conventional workup provided crystalline **2**, mp 176–177 °C (Table I). Methyl 2-O-benzoyl-3-O-mesyl-α-D-glucopyranoside[14] was allowed to react successively with 1 molar equiv of mesyl chloride and benzoyl chloride in pyridine. Workup of the reaction produced a chromatographically homogenous form whose ^1H NMR spectra agreed with compound **5**.

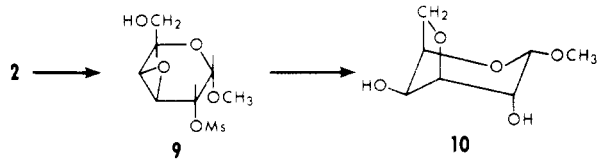
2,3-Di-O-mesyl Reaction. When 1 was treated in ethanol solution with excess sodium hydroxide, an examination of the mixture with TLC revealed three spots, two of which overlapped R_f ~0.3–0.4 and one R_f 0.7. Further study revealed that the faster of the two overlapping spots was unchanged 1 and that on heating to reflux only the R_f 0.7 spot remained. A practical method for separating this mixture was finally worked out (see Experimental Section); the R_f 0.7 compound was a crystalline solid, mp 78–80 °C, agreeing with a molecular formula $C_7H_{10}O_4$ (**7**), and the R_f ~0.35 compound, isolated as its acetate, was a syrup agreeing with a formula $C_{10}H_{16}O_8S$ (**8**). Compound 8 on heating with dilute alkali was transformed to **7**.



8 **7**

From the ^1H NMR spectrum (see Table II) of **8** it was easily seen that a 3,4-anhydro group was present, since the H_3 and H_4 (δ 3.14 and 2.99) were located upfield straddling the CH_3O (δ 3.08) group. From the combination of the analysis, ^1H NMR spectra, and structure of the starting material, compound **8** was assigned the structure methyl 6-O-acetyl-3,4-anhydro-2-O-mesyl-α-D-allopyranoside. Compound **7** by ^1H NMR spectroscopy shows no exchangeable protons, and the H_3 and H_4 (δ 3.08 and 2.66) are upfield above the CH_3O (δ 3.22), indicating a 3,4-anhydro group. The analysis, ^1H NMR spectrum, and method of preparation establish the structure of **7** as methyl 2,6:3,4-dianhydro-α-D-altropyranoside.

2,4-Di-O-mesyl Reaction. Compound **2** slowly dissolved when stirred in an ethanolic sodium hydroxide solution to produce a single spot by TLC. After neutralization and extraction, a crystalline material, mp 87–88 °C, was isolated. Chemical analysis fitted a $C_8H_{14}O_7S$, a methyl anhydro-O-mesylhexoside. The ^1H NMR spectrum of this compound, as well as its corresponding monobenzoate derivative, shows an H_3 and H_4 chemical shift (upfield) near the CH_3O peak, thus establishing this product as methyl 3,4-anhydro-2-O-mesyl-α-D-galactopyranoside (**9**). On further treatment in boiling 0.1 N NaOH solution, **9** was converted to methyl 3,6-anhydro-α-D-galactopyranoside (**10**).



9 **10**

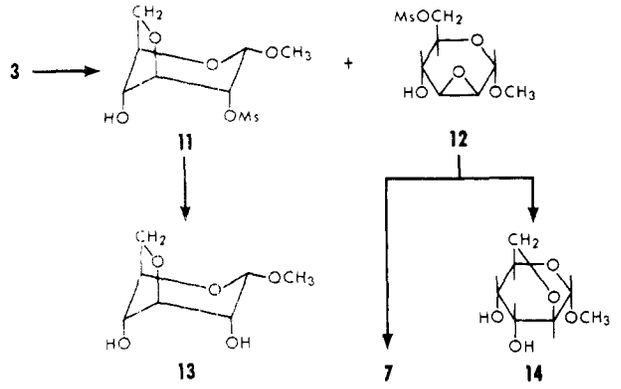
2,6-Di-O-mesyl Reaction. Reaction of **3** with ethanolic sodium hydroxide is reported[15] to yield methyl 3,6-anhydro-2-O-mesyl-α-D-glucopyranoside (**11**). Repetition of this reaction does yield **11**, but examination of the mother liquors by TLC revealed four other spots. If the reaction was carried out at 0–5 °C, **3** produced **11** when examined by TLC (R_f 0.27) plus another spot R_f 0.45. After neutralization, concentration, and trituration with acetone, the reaction product was crystallized from ethanol, giving **11**. The ethanolic mother liquor after concentration was chromatographed, which separated the R_f 0.45 as a syrup from **11**. ^1H NMR spectroscopy revealed a methoxy, mesylate, and exchangeable proton, but conversion of the syrup to its monoacetate, also a syrup, clearly pointed out by ^1H NMR spectroscopy that the syrup was a 2,3-anhydro

(9) A. B. Foster, M. Stacey, and S. V. Vardheim, *Acta Chem. Scand.*, **12**, 1819 (1958).
(10) J. G. Buchanan, *J. Chem. Soc.*, 2511 (1958); J. G. Buchanan and R. Fletcher, *ibid.*, 6316 (1965); J. G. Buchanan and R. Fletcher, *J. Chem. Soc. C*, 1926 (1966).
(11) H. B. Sinclair, *Carbohydr. Res.*, **50**, 247 (1976).
(12) T. Suami and T. Shoji, *Bull. Chem. Soc. Jpn.*, **43**, 2948 (1970); N. L. Holder and B. Fraser-Reid, *Can. J. Chem.*, **51**, 3357 (1973); J. S. Brimacombe, I. Da'aboul, and L. C. N. Tucker, *J. Chem. Soc., Perkin Trans. 1*, 979 (1975).
(13) J. Hill, L. Hough, and A. C. Richardson, *Carbohydr. Res.*, **8**, 7 (1968).
(14) R. W. Jeanloz and D. A. Jeanloz, *J. Am. Chem. Soc.*, **80**, 5692 (1958).
(15) R. C. Chalk, D. H. Ball, and L. Long, Jr., *J. Org. Chem.*, **31**, 1509 (1966); M. L. Wolfram, Y. Hung, P. Chakravarty, G. U. Yuen, and D. Horton, *ibid.*, **31**, 2227 (1966).

Table II. ^{1}H NMR Parameters

	chemical shift (δ value)									*J* values, Hz				
compd no.	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
2	5.02 d	4.75 dd	5.85 dd	4.97 m	4.07 4.33 m	4.55 m 4.67 m	3.47	2.82 2.85						$CDCl_3$
5	4.99 d	5.21 dd	5.69 dd	5.47 dd	3.86–4.18		2.88	2.28 2.08		4.0	9.0	9.0		benzene-d_6
7	4.80 dd	3.83 dd	3.08 m	2.66 m	~3.5	~3.7	3.22			3.0	4.0		$J_{1,3}$ = 3.0	benzene-d_6
8 (6-Ac)	4.70 d	4.80 dd	3.14 m	2.99 m	3.9–4.3		3.08	2.47	Ac = 1.72	4.0	3.0	5.0		benzene-d_6
8 (6-Bz)	4.70 d	4.82 dd	~3.1 m	~2.98 m	4.1–4.4		3.05	2.38		5.0	3.0			benzene-d_6
9	4.50 d	4.76 d	~3.4	~3.5	4.02	3.58–3.73	3.22	~3.4	OH = 3.88	4.0				acetonitrile-d_3
9 (6-Bz)	~4.6	~4.6	3.14 d	2.75 dd	3.98–4.10	4.22–4.56	3.01	2.27						benzene-d_6
12 (4-Ac)	3.76 s	3.20	3.06	4.87 d	3.80–4.05	4.16–4.24	3.45	3.00	Ac = 2.11		3.5		$J_{4,5}$ = 3.0	$CDCl_3$
15	5.00 d	3.68 dd	3.64 dd	5.40 dd	4.08–4.24	4.04–3.83	3.37	3.42		3.0	4.0	2.0	$J_{4,5}$ = 9.0	pyridine-d_5
16	4.80 d	2.92–3.04		4.57	4.1–4.4		3.21			2.0				benzene-d_6
17	5.16 d	3.59 dd	5.86 dd		4.18–4.46		2.98		Ac = 1.68	6.0	9.0	6.0		benzene-d_6
18	4.84 d	3.93 dd	5.33 dd	4.95 dd	3.92–4.16	2.68–3.04	3.14		Ac = 1.66 1.68	4.0	8.0	5.0	$J_{4,5}$ = 4.0	benzene-d_6
19	4.82 d	3.45	3.37	3.48–3.67		4.14–4.45	3.34	2.99		3.0				acetonitrile-d_3
19 (4-Bz)	4.94 d	3.57 dd	3.67 dd	5.29 m	4.16–4.43		3.46	2.96		3.0	4.0	2.0		$CDCl_3$
20	4.60 d	3.64	(3.23	3.11)	4.12–4.50		3.39	3.04		4.0				acetonitrile-d_3

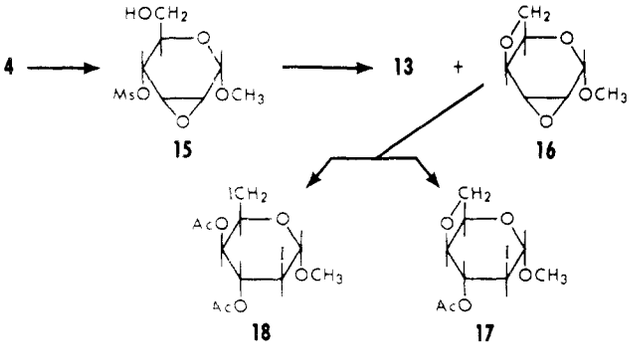
hexoside. This syrup's H_2–H_3 chemical shifts (δ 3.20, 3.06) are upfield and show no coupling to the C_1 or C_4 proton.[16] The structure was assigned methyl 2,3-anhydro-6-*O*-mesyl-α-D-mannopyranoside (**12**).



On heating **11** in ethanolic 0.1 N NaOH, an examination of the reaction mixture by TLC revealed that **11** was converted to a single, slower migrating product. Workup of the reaction yielded a crystalline product, mp 106–108 °C, which was converted to a crystalline di-*O*-acetate, mp 132–134 °C. These products compared in every physical constant with known methyl 3,6-anhydro-α-D-glucopyranoside (**13**) or its di-*O*-acetate.

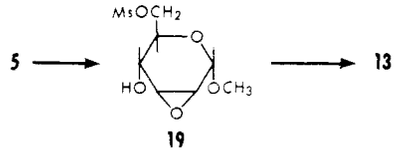
When **12** was heated under reflux in 0.1 N NaOH, TLC indicated **12** was transferred into two slower moving spots. Chromatography of the reaction mixture separated the two slower moving products. The faster of these two products crystallized, and the physical value of this crystalline product agreed in every way with compound **7**. The slower moving product was crystallized and analyzed for $C_7H_{12}O_5$, a methyl anhydrohexoside. Since the ^1H NMR did not show any protons that could be assigned as being attached to an epoxide ring, the structure was presumed to be methyl 2,6-anhydro-α-D-altropyranoside (**14**) and was confirmed by comparison with an authentic sample.

3,4-Di-*O*-mesyl Reaction. Dissolution occurred when **4** was stirred in ethanolic sodium hydroxide, and TLC revealed a single spot. Workup yielded a crystalline product, mp 138–140 °C, whose analysis fitted $C_8H_{14}O_7S$, a methyl anhydromesylhexoside. The ^1H NMR spectrum readily established a 2,3-anhydro structure, since the H_2–H_3 chemical shift was upfield. Consequently, the structure was assigned as methyl 2,3-anhydro-4-*O*-mesyl-α-D-allopyranoside (**15**).



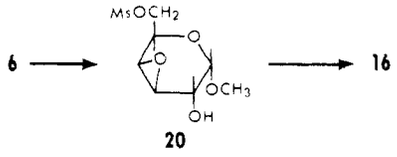
Heating **15** under reflux in 0.1 N NaOH TLC revealed two spots, one much faster than the starting compound and one slower. The mixture was easily separated by chromatography. The slower moving spot was readily identified as compound **13**. The faster moving spot proved to be a crystalline solid, mp 58–60 °C, and analyzed for $C_7H_{10}O_4$. The ^1H NMR spectrum indicated a 2,3-anhydro since the H_2–H_3 protons were located upfield near the CH_3O singlet; also, no exchangeable protons were present. A structure was assigned as methyl 2,3:4,6-dianhydro-α-D-gulopyranoside (**16**). When **16** was heated with a mixture of sodium iodide and acetic acid in acetone and this reaction mixture was acetylated, chromatography separated the mixture into two compounds, which after crystallization analyzed for a methyl *O*-acetylanhydrodeoxyiodohexoside and a methyl di-*O*-acetyldideoxydiiodohexoside. The ^1H NMR spectrum of the monoiodohexoside shows a coupling constant of $J_{1,2}$ = 6.0, $J_{2,3}$ = 9.0, and $J_{3,4}$ = 6.0 Hz, and thus supports the structure as a methyl 3-*O*-acetyl-4,6-anhydro-2-deoxy-2-iodo-α-D-idopyranoside (**17**) in a skew-like conformation. And, the spectrum of the diiodohexoside shows a coupling constant of $J_{1,2}$ = 4.0, $J_{2,3}$ = 8.0, $J_{3,4}$ = 5.0, and $J_{4,5}$ = 4.0 Hz, supporting the assigned structure of methyl 3,4-di-*O*-acetyl-2,6-dideoxy-2,6-diiodo-α-D-idopyranoside (**18**) in a skewed conformation.

3,6-Di-*O*-mesyl Reaction. A suspension of compound **5** dissolved on stirring in ethanolic sodium hydroxide, and after about 4 h TLC revealed a single spot. Neutralization and workup of the reaction resulted in a crystalline product, mp 81–83 °C. Chemical analysis fitted a methyl anhydro-*O*-mesylhexoside, and ^1H NMR spectroscopy of this product and its corresponding monobenzoate established the structure as methyl 2,3-anhydro-6-*O*-mesyl-α-D-allopyranoside (**19**). Treatment of **19** with 0.1 N NaOH converted it to a single product whose structure was readily identified as methyl 3,6-anhydro-α-D-glucopyranoside (**13**).



4,6-Di-*O*-mesyl Reaction. A suspension of compound **6** was stirred in ethanolic sodium hydroxide; by the time the mixture was homogenous, TLC revealed two widely separated spots. After neutralization and extraction a syrup was obtained, which was chromatographically separated. Further work established that the slowly migrating compound was converted with dilute alkali into the faster moving spot and that no experimental procedure was found wherein only the slower moving spot was exclusively formed.

The slower moving spot was isolated as a crystalline solid, mp 114–115 °C, whose analysis fitted a methyl anhydro-*O*-mesylhexoside and whose ^1H NMR spectrum clearly established its structure as methyl 3,4-anhydro-6-*O*-mesyl-α-D-galactopyranoside (**20**). The faster moving spot proved to be the dianhydro compound **16** that was isolated from the 3,4-di-*O*-mesyl reaction.



Discussion

The products isolated from the complete desulfonylation of the six di-*O*-mesyl esters of methyl α-D-glucopyranoside by alkali can be explained by established reactions. However, it is an unusual example where the reaction pathway does not involve a combination of displacement,

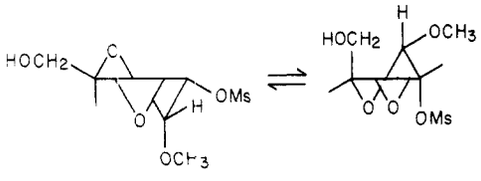
(16) D. H. Buss, L. Hough, L. D. Hall, and J. F. Manville, *Tetrahedron*, 21, 69 (1965); F. Sweet and R. K. Brown, *Can. J. Chem.*, 46, 1481 (1968).

isomerization, or migration, as depicted in Scheme I–IV, to account for the products, though some unexpected reactivities and preferences have to be called on to explain the isolated products.

The ^1H NMR spectrum proved to be a most useful tool for establishing in the epoxides whether the location was the 2,3 or 3,4 structure. Since the epoxide protons appear[16] upfield from their usual location and, in the examples here, near or overlapping the glycosidic methoxyl singlet, the decoupling of the downfield H_1 doublet in all examples but one readily identified if a 2,3- or 3,4-epoxide was present. In that one example, compound **12**, H_1 and H_4 protons were not coupled to the adjacent H_2 or H_3 protons, but this behavior of the H_1 and H_4 protons has been noted[16] earlier where the 2,3-epoxide and glycosidic oxygen are trans.

The conversion by base of the 2,3-di-*O*-mesylate **1** into the 3,4-anhydroalloside **8** was expected, even though unreported, on the basis of previous information.[3] The subsequent conversion to **8** into the 2,6:3,4-dianhydroaltroside **7** was unexpected, particularly in view of the inertness of C_2 sulfonates on pyranoside ring to displacement.[1]

An examination of molecular models appears to offer an explanation for this unusually facile displacement. As a consequence of the 3,4-epoxide, the C_2–C_3–C_4–C_5 reside in a plane and will result in the two half-chair conformations as shown. In the conformer, in which the C_5-



hydroxylmethyl and C_2-OMs are quasi-axial, two features can be noted. First, the C_6-hydroxyl group is situated in excellent position for a rear-side displacement, and second, no 1,3-diaxial interactions are present that will interfere with the entering nucleophile. This latter effect, sometimes referred to as the β-trans-axial effect,[1] has been noted; for example, methyl 2,3,6-tri-*O*-benzoyl-4-*O*-mesyl-α-D-mannopyranoside is resistant to the action of sodium benzoate in dimethylformamide.[17]

In the 2,4-*O*-mesyl reaction, base treatment could result in a 2,3-epoxide, 3,4-epoxide, or a mixture of both, but only the 3,4-anhydrogalactoside **9** was found, which agrees with the reported reference in nucleophilic displacement of C_4 vs. C_2 sulfonates.[1] The subsequent treatment of galactoside **9** with base points outs the strong inhibitory effect, mentioned above, that a β-trans-axial group exhibits on nucleophilic displacement. On comparing compound **8** with **9**, the only difference is the cisoid or transoid relationship of the 3,4-epoxide with the C_2-OMs group. With no β-trans-axial group, C_2 displacement occurs, whereas with a β-trans-axial group, a completely different product was isolated. This difference can be explained by, first, hydrolysis of the mesyl ester, second, isomerization of the 3,4-anhydrogalactoside to 2,3-anhydroguloside; and third, isomerization of 2,3-anhydroguloside to 3,6-anhydrogalactoside. These last two isomerizations have been reported.[10]

Reaction of the 2,6-*O*-mesylate with base provided an interesting contrast on the relative reactivity of the C_6- and C_2-sulfonate toward displacement. The C_6-displacement product, **11**, predominates over the C_2-displacement product **12**. The further action of base on **11** results in a hydrolysis to methyl 3,6-anhydro-α-D-glucopyranoside (**13**). But further action of base on **12** resulted in two products; one was assigned the dianhydroaltroside (**7**) structure and the second was assigned a 2,6-anhydroaltroside (**14**) structure. Compound **7** was explained as arising by a 2,3-anhydromannoside to 3,4-anhydroaltroside isomerization and subsequent displacement of the C_6-OMs group with the C_2-OH. Compound **14** was produced by ring opening of the 2,3-epoxide, according to the Fürst–Plattner rule,[3] to yield a methyl 6-*O*-mesyl-α-D-altroside that was transformed by displacement to the 2,6-anhydroaltroside.

The displacement of one sulfonate group in the 3,4-di-*O*-mesyl reaction produced the expected 2,3-anhydroalloside (**15**). Compound **15**, on treatment with base, produced a major and minor product. The major one was readily identified as methyl 3,6-anhydro-α-D-glucopyranoside (**13**), which was obviously derived by 2,3- → 3,6-anhydride isomerization and mesylate hydrolysis, but it could not be determined if the hydrolysis occurred before or following the isomerization. Since the minor product was determined as a methyl dianhydrohexoside, it was considered most likely that the C_6-OH had displaced the C_4-OMs, forming a 4,6-anhydro structure. To further support this structure, the ^1H NMR spectrum pointed out that the H_2 and H_3 protons were upfield near the OCH_3 singlet or that the 2,3-anhydro group was still present. Reaction of the dianhydro hexoside with sodium iodide and acetic acid, followed by acetylation, produced a separable mixture of a monoiodoanhydro and diiodohexoside, whose structures were assigned as both idosides on the basis of the observed ^1H NMR spectra. Compound **17**, the monoiodo compound, exhibited coupling of $J_{1,2}$ = 6.0, $J_{2,3}$ = 9.0, and $J_{3,4}$ = 6.0 Hz; these large couplings indicate an all-transoid arrangement of the H_1–H_2–H_3–H_4, an idoside in a boat or skew conformation. An examination of models pointed out that although there is a β-trans-axial group to the epoxide, the combination of the 2,3- and 4,6-anhydro rings restricts the conformation mobility and holds the 4,6-anhydro rings at such an angle that steric approach of the nucleophile I^- at the C_2 would appear probable. The examination also pointed out that, in the methyl 4,6-anhydro-2-deoxy-2-iodoidopyranoside, the conformer where the H_1, H_2, and H_3 are equatorial-like (approximately a 60° dihedral angle), the iodine and the 4,6-anhydro ring cannot be readily accommodated because of steric hindrance, whereas a conformer(s) where the H_1, H_2, and H_3 show a 140–180° dihedral angle relieves this severe iodoanhydro steric hindrance as well as the 1,3-diaxial interaction of the C_1-OCH_3 and C_3-OAc group. In a formal sense, the opening of the 2,3-epoxide follows the established[3] Fürst–Plattner rules leading to a preponderance of a trans-diaxial product; it is here that various steric effects result in a subsequent conformational change, with a trans-diequatorial conformer being formed. The diiodohexoside, **18**, because of the proton coupling, $J_{1,2}$ = 4.0, $J_{2,3}$ = 8.0, $J_{3,4}$ = 5.0, and $J_{4,5}$ = 4.0 Hz, was also assigned a skewed idoside structure.

Although 3,6-di-*O*-mesyl **5** could give either a 2,3- or 3,4-anhydrohexoside, its reaction with base yielded only the methyl 2,3-anhydro-6-*O*-mesylallopyranoside (**19**). Further treatment of **19** with base produced methyl 3,6-anhydro-α-D-glucopyranoside (**13**), which can be easily explained as a mesylate hydrolysis, and the 2,3- → 3,6-anhydro isomerization.

Although other workers[18] have reported the conversion

(17) A. C. Richardson and J. M. Williams, *Chem. Commun.*, 104 (1965).

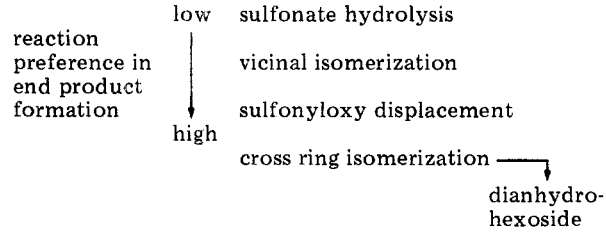
(18) J. Yoshimura, K. Sato, H. Hashimoto, and K. Shimizu, *Bull. Chem. Soc. Jpn.*, **50**, 3305 (1977). G. Siewert and O. Westphal, *Justus Liebigs Ann. Chem.*, **720**, 171 (1969).

of benzyl 2,3-di-*O*-benzoyl-4,6-di-*O*-mesyl(and -tosyl)-α-D-glucopyranoside to a 3,4-anhydro-6-*O*-mesyl(tosyl)-galactoside, the authors did not report its facile conversion into the 2,3:4,6-dianhydro guloside. Obviously, the reaction conditions, namely sodium methoxide in chloroform at 0–5 °C vs. ethanolic sodium hydroxide at room temperature to reflux temperature (~75 °C), must account for the reaction being carried further. Although the displacement of either the C_4-OMs or the C_6-OMs group by the C_3OH group was possible, only the C_4 displacement was observed. The facile conversion of the 3,4-anhydro-6-*O*-mesyl-galactoside to the 2,3:4,6-dianhydroguloside can be explained by a 3,4-anhydrogalactoside isomerizing to a 2,3-anhydroguloside and the subsequent C_6-OMs displacement by the C_4-OH group.

Except for the 2,6-di-*O*-mesylglucoside, the first product on alkaline didesulfonylation was a monosulfonyl epoxide, and even in the 2,6-isomer about 15% yield of the 2,3-anhydromannoside was isolated. This behavior in the 2,6-isomer was not unexpected in view of the well-reported inertness of C_2-sulfonates to nucleophilic displacements.[1] A conclusion was reached that the proximity of the alkoxide and the antiperiplanar alignment of the vicinal alkoxide and sulfonyloxy group in the 1C(D) conformer of glucopyranoside dominated the first displacement. For example, the order of preference in nucleophilic displacement of the glucopyranoside sulfonates is observed as $C_6 > C_4 \gg C_2$,[1] whereas by comparing compounds **2**, **3**, and **6** displacements the observed order for the vicinal displacement of a sulfonyloxy group is $C_4 > C_6 > C_2$.

The only example of an order of preference of hydroxyl reactivity was the 3,6-di-*O*-mesylglucoside **5**. The 2-OH displaced the 3-OMs group, not the 4-OH; this observation agrees with the report[19] that the monosodium derivative of methyl α-D-glucopyranoside on methylation gives the 2-*O*-methyl ether.

Removal of the sulfonyloxy group in the anhydro-*O*-mesylhexosides, though leading to relatively simple products, could only be accounted for by an array of reaction pathways. A practical set of preferences was formulated to account for the products. The reactions were (a) hydrolysis, (b) internal sulfonyloxy displacement by a ring alkoxide, (c) cross ring isomerization of the type shown in Scheme III, and (d) vicinal isomerization of the type shown in Scheme IV. It should be recalled that the steric requirements for the sulfonyloxy displacement and both isomerizations are presumed to be present; of course, if these requirements are not present then this particular preference will be bypassed. Two additional points need comment. First, the β-trans-axial effect will override a preference; second, if a sulfonyloxy group is removed by internal displacement producing a dianhydro hexoside, further reaction is stopped, since this displacement is effectively irreversible. Using the information above, a preference sequence was drawn that will account for the observed products in the desulfonylation of the anhydro-*O*-mesylhexosides.



(19) M. L. Wolfram and M. A. El-Taraboulsi, *J. Am. Chem. Soc.*, **75**, 5350 (1953).

Experimental[20] Section

General Methods. TLC was performed on precoated plates of silica gel F-254 of 0.25-mm layers with the specified solvents. The plates were air-equilibrated. Spots were rendered visible by spraying with 5% ethanolic sulfuric acid and heating until charring occurred. Column chromatography was performed on Silica Woelm TSC by dissolving the sample in a small amount of a low-boiling solvent, adding Silica Woelm TSC to obtain a free-flowing powder, placing this powder on the dry column, and developing the column with solvent. ^{1}H NMR spectra were obtained with a Varian HA-100 spectrometer. Chemical shifts were compared against internal tetramethylsilane and reported as δ values. Mass spectra were obtained with a Nuclide 90G double-focusing spectrometer. Melting points are uncorrected. Analytical samples were dried at 10–20 torr in the presence of sulfuric acid and sodium hydroxide for 24–48 h. Solutions were evaporated in vacuo.

Methyl 2,3-Di-*O*-mesyl-α-D-glucopyranoside (1). This compound was prepared by the method of Sinclair.[11]

Methyl 2,6-Di-*O*-mesyl-α-D-glucopyranoside (3). This compound was prepared by the method of Mitra et al.[21] with the modification reported by Sinclair.[11]

Methyl 2,6-Di-*O*-benzoyl-3,4-di-*O*-mesyl-α-D-glucopyranoside (4). The procedure of Holder and Fraser-Reid[12] was followed in preparing this compound. It was obtained as a chromatographically homogenous form.

Methyl 2,3-Di-*O*-benzoyl-4,6-di-*O*-mesyl-α-D-glucopyranoside (6). This compound was prepared by the procedure of Hill et al.[13]

Methyl 3,6-Di-*O*-benzoyl-2,4-di-*O*-mesyl-α-D-glucopyranoside (2). A mixture of methyl 3-*O*-benzoyl-2,4,6-tri-*O*-mesyl-α-D-glucopyranoside[11] (10.0 g), lithium benzoate (10.0 g), and *N*,*N*-dimethylformamide (150 mL) was heated to 75 ± 2 °C for 18 h and cooled to room temperature, and the solution was poured into ice water (1 L). The solid that separated was filtered and dried in air: weight 10.2 g; mp 172–177 °C. Recrystallization from an ethyl acetate (100 mL)–ethanol (500 mL) mixture yielded an analytical sample: weight 8.5 g (81%); mp 176–177 °C.

Anal. Calcd for $C_{23}H_{26}O_{12}S_2$: C, 49.45; H, 4.69; S, 11.48. Found: C, 49.58; H, 5.02; S 11.51.

Methyl 2,4-Di-*O*-benzoyl-3,6-di-*O*-mesyl-α-D-glucopyranoside (5). Methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-mesyl-α-D-glucopyranoside[22] (15.0 g) was suspended in a mixture of dioxane (350 mL), water (150 mL), and 2.2 N H_2SO_4 (10 mL), and the reaction was heated to reflux, maintained for 2 h, and cooled to room temperature. After a solution of sodium hydrogen carbonate (2.0 g in 50 mL of water) was added and the mixture was vigorously stirred for 15 min, the reaction mixture was evaporated to a syrup. This syrup was partitioned between water (50 mL) and ethyl acetate (50 mL). The aqueous phase was extracted with an additional four 50-mL portions of ethyl acetate. The combined ethyl acetate extracts were dried and evaporated to a syrup, which was dissolved by warming a mixture of ethyl acetate (100 mL)–toluene (100 mL)–pyridine (3 mL). On cooling, the methyl 2-*O*-benzoyl-3-*O*-mesyl-α-D-glucopyranoside·pyridine complex[14] crystallized slowly: weight 12.3 g, mp ~120–130 °C. This pyridine complex (5 g) was dissolved in pyridine (60 mL) and cooled to −20 °C, and mesyl chloride (0.95 mL) was added with stirring. The reaction was allowed to proceed at −10 °C for 6 h and the mixture was stored for 16 h at 5 °C, whereupon benzoyl chloride (1.50 mL) was added and the mixture was allowed to stand 5 days at 5 °C. When the mixture was poured into ice water (600 mL), a thick syrup separated. After decanting of the aqueous phase, the syrup was dissolved in ethanol and the ethanol was evaporated, leaving a syrup in which a major spot (R_f 0.29) and a minor spot (R_f 0.44) were revealed by TLC in toluene–ethyl acetate 10:1 v/v). Dry column chromatography (4 × 47 cm), using toluene–ethyl acetate 1300:130 mL, 700:100 mL collected in 10-mL fractions, separated the major and minor spots. The fractions

(20) 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.

(21) A. K. Mitra, D. H. Ball, and L. Long, Jr., *J. Org. Chem.*, **27**, 160 (1962).

(22) R. W. Jeanloz and D. A. Jeanloz, *J. Am. Chem. Soc.*, **79**, 2579 (1957).

containing the major spot were combined and evaporated to a syrup, which when dissolved in methylene chloride and evaporated was converted to a white solid: chromatographically homogenous; weight 5.7 g.

General Procedure for the Reaction of the Methyl Di-*O*-mesyl-α-D-glucopyranosides or Methyl Anhydro-*O*-mesyl-α-D-hexosides with Base. The appropriate compound was covered with either ethanolic sodium hydroxide or sodium hydroxide. The mixture was stirred (S) at room temperature, warmed (W) on a steam bath until homogenous and then stored at room temperature, or heated (R) to reflux and maintained for the specified time. The reaction mixture was cooled to room temperature, neutralized by passing in carbon dioxide, diluted with four to five volumes of water, and continuously extracted with ethyl acetate for 16–18 h. After drying, the extract was evaporated. If a solid resulted, it was usually recrystallized. But, if a syrup resulted or TLC indicated the solid was a mixture, dry column chromatography was carried out with the specified solvents. The fractions, which were monitored by TLC, were pooled accordingly and evaporated.

Each compound will be listed as follows: grams of starting compound; milliliters of ethanol; milliliters of NaOH; heating, if any, S, W, R; time of base action (h); if ethyl acetate extract was recrystallized (X) or if dry column chromatography (DCC) was used, with column dimensions.

Any major variations from the above directions will be individually noted.

Reaction of 1 with base: 3.0, 30, 20, S, 120, DCC 3 × 43 cm, developed with toluene–ethyl acetate 300:600 mL, ethyl acetate 800 mL.

The fractions containing the faster moving spot, R_f 0.42, in toluene–ethyl acetate 1:2 v/v, crystallized on evaporation, mp 75–80 °C. Recrystallization from ethanol (or ether) gave an analytical sample of **7**, mp 78–80 °C.

Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 52.99; H, 6.41.

The fractions containing the slower moving spot, R_f 0.29, were acetylated (acetic anhydride–pyridine 10:10 mL, 48 h) and evaporated to a syrup. The syrup was distilled at 1–2 torr and a bath temperature ~250 °C to yield **8** as a thick oil.

Anal. Calcd for $C_{10}H_{16}O_8S$: C, 40.53; H, 5.44. Found: C, 40.19; H, 5.35.

Reaction of 8 with base (this rection was also carried out with unacetylated syrupy **8**): 0.5, 20, 15, R, 2, DCC 1.5 × 30 cm, toluene–ethyl acetate 1:2 v/v; compound **7**, mp 79–80 °C, resulted.

Reaction of 2 with base: 4.0, 20, 30, W, 1, X. Two crystallizations from ethanol gave fine needles of **9**, mp 84–87 °C. The two mother liquors were retained, combined, and after evaporation placed on a dry column chromatography (1.5 × 33 cm) and developed with ethyl acetate. The first and second fractions were discarded. The remaining fractions (monitored by TLC) were pooled and evaporated to yield **9**, mp 87–90 °C.

The two crystalline fractions were combined and recrystallized from ethanol (10 mL) and diluted with ether (20 mL). Long, glistening needles of **9** slowly deposited: weight 1.10 g; mp 89–90 °C.

Anal. Calcd for $C_8H_{14}O_7S$: C, 37.79; H, 5.55. Found: C, 37.56; H, 5.50.

Methyl 3,4-Anhydro-6-*O*-benzoyl-2-*O*-mesyl-α-D-galactopyranoside (9-Bz). Compound **9** (112.8 mg) was dissolved in pyridine (2 mL) and cooled to 5 °C; benzoyl chloride (0.15 mL) was added and the reaction mixture was stored 16 h at 5 °C. The mixture was poured into ice water (50 mL), and the aqueous solution was extracted with five 10-mL portions of chloroform. After being dried and evaporated, the chloroform extracts yielded an oil. The oil was placed on a dry column chromatograph (1.7 × 9 cm) and developed with toluene–ethyl acetate 1:1 v/v. The appropriate fractions were combined and evaporated to an oil, which on chilling turned crystalline, mp 73–76 °C. Recrystallization from ethanol (0.5 mL) yielded an analytical sample of 9-Bz, mp 76.5–77.8 °C.

Anal. Calcd for $C_{15}H_{18}O_8S$: C, 50.27; H, 5.06. Found: C, 50.37; H, 5.00.

Reaction of 9 with base: 1.4, 0, 100 (0.1 N), R, 3, DCC 1.5 × 17 cm, ethyl acetate. In addition to unaltered **9**, a second compound, R_f 0.30 (ethyl acetate), was isolated, mp 136–138 °C. A melting point of this product with known methyl 3,6-anhydro-α-D-galactopyranoside was undepressed.

Reaction of 3 with base: 6.0, 50, 35, S at 5 °C, 168, X. Two crystallizations from ethanol gave 1.60 g, mp 117–118 °C, of **11** (a melting point of this product with known methyl 3,6-anhydro-2-*O*-mesyl-α-D-glucopyranoside was undepressed). Mother liquors from the two crystallizations were combined, diluted to 250 mL with water, placed in a continuous extractor, and extracted with ethyl acetate for 18 h. Concentration of the extract gave 2.50 g of semi-solid product, which was placed on a dry column chromatograph (3.8 × 47 cm) and developed with toluene–ethyl acetate 250:250 mL, 200:300 mL, and 150:350 mL, and ethyl acetate 600 mL. The appropriate fractions corresponding to the R_f 0.46 and 0.28 spots were pooled and concentrated. The R_f 0.28 pooling gave an additional amount of **11**: 1.12 g; mp 116–118 °C. The R_f 0.46 pooling gave a syrup, 0.44 g, which could not be rendered crystalline. (From five similar reaction sequences the weight ratio of R_f 0.28/0.46 varied from 4 to 6:1.) Acetylation of the above syrup with an acetic anhydride–pyridine mixture, followed by concentration and dry column chromatography (toluene–ethyl acetate 1:1 v/v), produced a thick syrup that could not be crystallized nor could an acceptable analytical sample by obtained; but the ^1H NMR left no doubt that the syrup was methyl 4-*O*-acetyl-2,3-anhydro-6-*O*-mesyl-α-D-mannopyranoside (12-4Ac), and thus that the original syrup was compound **12**.

Reaction of 11 with base: 1.3, 0, 100 (0.1 N), R, 12, X. Evaporation deposited crystalline **13**, mp 108–109 °C. A melting point of this product with known methyl 3,6-anhydro-α-D-glucopyranoside was undepressed.

Reaction of 12 with base: 0.440, 0, 35 (0.1 N), R, 3, DCC 1.5 × 36 cm, toluene–ethyl acetate 67:134 mL, ethyl acetate–methanol 200:6 mL. Two compounds were separated, R_f 0.35 and 0.15 (toluene–ethyl acetate 1:2 v/v). The R_f 0.35 fractions yielded on evaporation crystalline **7**: mp 78–80 °C; 113 mg.

The R_f 0.15 fractions slowly crystallized: mp 85–92 °C; 60 mg. Recrystallization from ethanol (0.5 mL) gave an analytical sample of **14**, mp 95–96 °C.

Anal. Calcd for $C_7H_{12}O_5$: C, 47.72; H, 6.86. Found: C, 47.70; H, 6.85.

A melting point of this product with known methyl 2,6-anhydro-α-D-altropyranoside[5] was undepressed.

Reaction of 4 with base: 26.2, 160, 160, W, 3, X. Recrystallization from ethyl acetate gave an analytical sample of **15**, mp 138–139 °C.

Anal. Calcd for $C_8H_{14}O_7S$: C, 37.79; H, 5.55. Found: C, 37.65; H, 5.66. A mass spectrum shows a strong (m/e $-OCH_3$) peak 223.

Reaction of 15 with base: 3.7, 0, 300 (0.1 N), R, 5, DCC 3 × 47 cm toluene–ethyl acetate 200:200, 130:270, ethyl acetate 400, ethyl acetate–methanol 390:10, 350:50. The appropriate fractions corresponding to R_f 0.50 and 0.16 (toluene–ethyl acetate 1:2 v/v) spots were pooled and evaporated.

The R_f 0.50 concentrate crystallized and was recrystallized from ether to yield **16**, mp 58–59 °C.

Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 52.82; H, 6.39. A mass spectrum shows a molecular ion m/e 158.

The R_f 0.16 concentrate crystallized. Recrystallization from ethyl acetate gave **13**, mp 106–108 °C.

Methyl 3-*O*-Acetyl-4,6-anhydro-2-deoxy-2-iodo-α-D-idopyranoside (17) and Methyl 3,4-Di-*O*-acetyl-2,6-dideoxy-2,6-diiodo-α-D-idopyranoside (18). Compound **16** (1.0 g) was dissolved in a mixture containing sodium iodide (10 g), acetic anhydride (5 mL), sodium acetate (1 g), acetic acid (5 mL), and acetone (100 mL), and heated to reflux and maintained for 18 h. Evaporation of the acetone left a semi-solid that was transferred to a separator funnel with water (100 mL) and methylene chloride (20 mL). The aqueous layer was extracted with an additional four 20-mL portions of methylene chloride. The combined methylene chloride extracts were washed with 100 mL each of water (containing a trace of sodium thiosulfate), 5% sodium bicarbonate, and water, and then dried. Evaporation of the methylene chloride layer left a yellow syrup, which was acetylated with acetic anhydride (5 mL)–pyridine (5 mL). TLC (toluene–ethyl acetate 10:1 v/v) on the acetylated mixture revealed two major spots, R_f 0.58 and 0.32, and several minor to trace spots. After evaporation of the acetylating mixture a syrup remained, which was placed

on a dry column chromatograph (1.5 × 36 cm) and developed as follows: toluene–ethyl acetate 200:10 mL, 100:10 mL. The appropriate fraction containing the R_f 0.58 and R_f 0.32 spots were pooled and evaporated. (Handling of these iodo compounds beyond this point must be carried out in very dimly lighted rooms, otherwise decomposition becomes pronounced.)

The pooled concentrated R_f 0.58 fractions left a syrup, which was dissolved in ethanol by warming. On cooling, needles of **18** separated, mp 101–103 °C.

Anal. Calcd for $C_{11}H_{16}I_2O_6$: C, 26.52; H, 3.24; I, 50.96. Found: C, 26.71; H, 3.39; I, 50.87.

The pooled concentrated R_f 0.32 fractions left a syrup which was dissolved in ethanol by warming. On cooling, platelets of **17** separated, mp 84–85 °C.

Anal. Calcd for $C_9H_{13}IO_5$: C, 32.92; H, 3.99; I, 38.68. Found: C, 33.12; H, 3.98; I, 38.26.

Reaction of 5 with base: 2.02, 50, 17, W, 4, X. Evaporation of the extract gave a crystalline solid, mp 71–78 °C. Recrystallization gave an analytical sample of **19**, mp 81–83 °C. Mass spectrum shows a strong (m/e $-OCH_3$) peak 223.

Anal. Calcd for $C_8H_{14}O_7S$: C, 37.79; H, 5.55. Found: C, 37.60; H, 5.65.

Methyl 2,3-Anhydro-4-*O*-benzoyl-6-*O*-mesyl-α-D-allopyranoside (19-Bz). Compound **19** (128 mg) was dissolved in pyridine (2 mL) and cooled to −20 °C, benzoyl chloride (0.1 mL) was added and the reaction mixture was stored for 18 h at −20 °C and 24 h at 5 °C. On the addition of water (3 mL), a solid separated and was removed by filtration. Recrystallization from ethanol (5 mL) gave the benzoate ester **19-Bz**, mp 157–158 °C. Mass spectrum shows a strong (m/e − OCH_3) peak 327.

Reaction of 19 with base: 0.141, 0, 25 (0.04 N), R, 18, DCC 1.5 × 17 cm ethyl acetate. Evaporation gave crystalline **13**, mp 106–108 °C.

Reaction of 6 with base: 4.2, 100, 40, W, 4-18, X or DCC. The ratio of **16**/**20** will depend on the length of heating and time of reaction. For example, 1 h of refluxing will yield only the dianhydrohexoside **16**. If the reaction is neutralized too quickly, small quantities of methyl 4,6-di-*O*-mesyl-α-D-glucopyranoside can be detected. A 4-h room-temperature reaction on evaporation gave a tacky solid, which was crystallized from ethanol (7 mL)–ether (7 mL) to give 1.23 g of product, mp 98–104 °C. A subsequent crystallization gave 1.12 g, mp 100–104 °C. TLC on this product (toluene–ethyl acetate 1:2 v/v) revealed a major spot R_f 0.38 (**20**) and minor spot R_f 0.14 (methyl 4,6-di-*O*-mesyl-α-D-glucopyranoside). Applying 218 mg to a dry column chromatograph (1.5 × 17 cm) and developing with toluene–ethyl acetate 1:2 v/v eluted the R_f 0.38 spot. Evaporation of the pooled fractions gave a syrup, which on standing crystallized: 155 mg, mp 114–115 °C.

Anal. Calcd for $C_8H_{14}O_7S$: C, 37.79; H, 5.55. Found: C, 37.61; H, 5.60.

Developing the column with ethyl acetate–methanol 15:1 v/v eluted 56 mg of R_f 0.14 spot.

Reaction of 20 with base: 0.20, 0, 25 (0.1 N), R, 5, DCC 1.5 × 15 cm, toluene–ethyl acetate 1:2 v/v. Evaporation gave crystalline **16**, mp 57–59 °C.

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Registry No. **1**, 22860-24-8; **2**, 70941-12-7; **3**, 14257-63-7; **4**, 29781-02-0; **5**, 70941-13-8; **6**, 22435-33-2; **7**, 70941-14-9; **8**, 70941-15-0; **8** (6-Ac), 70941-16-1; **8** (6-Bz), 70941-17-2; **9**, 70941-18-3; **9** (6-Bz), 70941-19-4; **11**, 10226-98-9; **12**, 70941-20-7; **12** (4-Ac), 70941-21-8; **13**, 13407-60-8; **14**, 29411-58-3; **15**, 70941-22-9; **16**, 70941-23-0; **17**, 70941-24-1; **18**, 70941-25-2; **19**, 70941-26-3; **19** (4-Bz), 70941-27-4; **20**, 70941-28-5; methyl 3-*O*-benzoyl-2,4,6-tri-*O*-mesyl-α-D-glucopyranoside, 61252-79-7; methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-mesyl-α-D-glucopyranoside, 28538-15-0; methyl 2-*O*-benzoyl-3-*O*-mesyl-α-D-glucopyranoside·pyridine, 70941-30-9; methyl 3,6-anhydro-α-D-galactopyranoside, 5540-31-8; methyl 4,6-di-*O*-mesyl-α-D-glucopyranoside, 70941-31-0.

Synthesis of Seven- and Eight-Carbon Sugar Derivatives from 2,3:5,6-Di-*O*-isopropylidene-D-gulono-1,4-lactone and Preparation of a New Anhydro Sugar[1]

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2,3:5,6-Di-*O*-isopropylidene-D-gulono-1,4-lactone (**1**) was condensed with ethyl bromoacetate in the presence of zinc to give the expected Reformatsky product, ethyl 2-deoxy-4,5:7,8-di-*O*-isopropylidene-α-D-*gulo*-3-octulofuranosonate (**2**). Treatment of **2** with methanol and an acid ion-exchange resin afforded the completely blocked methyl α-glycoside **3**, the methyl 4,5-*O*-isopropylidene α-glycoside **4**, and a 3,8-anhydro sugar **5**. Proof of the structure of **5** was based upon NMR spectroscopy and periodate oxidation. The main product, **4**, was converted to the 7,8-di-*O*-benzoate **6** and 7,8-di-*O*-methanesulfonate **7**. Sodium iodide elimination of the latter yielded the 7,8-olefinic glycoside **8**. Glycoside **4** was reduced with calcium borohydride to give methyl 2-deoxy-4,5-*O*-isopropylidene-α-D-*gulo*-3-octulofuranoside (**9**). Treatment of **4** with sodium metaperiodate gave the 7-aldehydo derivative **10** which was reduced with Raney nickel to give the seven-carbon sugar. Tosylation of the primary hydroxyl group gave the 7-*O*-tosylate **12**.

Decoyinine and psicofuranine are nucleoside antibiotics[2] differing from each other only in the unsaturation of the former at the terminal position (Chart I). Psicofuranine is closely related to adenosine except for a hydroxymethyl group that occupies the position on the anomeric carbon atom normally occupied by the hydrogen atom. The biochemical role of the hydroxymethyl group has not been elucidated. At the very minimum it can be presumed that it provides an additional site for hydrogen bonding to an enzyme. As part of a program of synthesis of decoyinine analogues and in order to explore the biological effect of a change in structure at the anomeric carbon atom, a route was sought to replace the hydroxymethyl group with a

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(2) R. J. Suhadolnik, "Nucleoside Antibiotics", Wiley-Interscience, New York, 1970.

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