

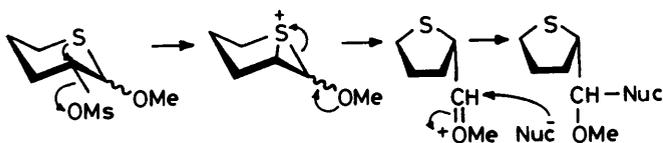
5-Thiopyranoses. Part 12.¹ Sulphur Participation in Displacement Reactions of Sulphonate Esters of 5-Thio-D-allose, 5-Thio-D-altrose, and 5-Thio-D-glucose Derivatives

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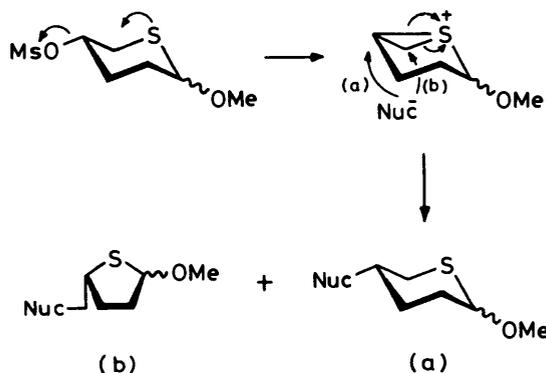
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Both sulphonate groups in methyl 2,3-anhydro-4,6-di-*O*-methylsulphonyl-5-thio- α -D-allopyranoside (**5**) readily undergo displacement reactions. The 4-sulphonate is the more reactive and is displaced with retention of configuration. Participation by the ring sulphur atom and formation of intermediate episulphonium ions is proposed in each displacement. There is evidence to suggest that ring expansion to give methyl 2,3-anhydro-4,5-di-*O*-methyl-6-thio- β -L-taloseptanoside (**19**) may occur in the reaction of (**5**) with methanol. Methyl 4,6-*O*-isopropylidene-2-*O*-methylsulphonyl-5-thio-3-*O*-*p*-tolylsulphonyl- α -D-glucopyranoside (**20**) is unreactive until the acetal group is removed, when ring contraction to give 2,5-dideoxy-2,5-epithio-3-*O*-*p*-tolylsulphonyl-D-mannose dimethyl acetal (**23**) occurs. Methyl 3,4-*O*-isopropylidene-2,6-di-*O*-methylsulphonyl-5-thio- α -D-altropyranoside (**30**) was too reactive to be isolated but appeared to react with methanol and chloride ions to give, *via* ring contraction, the 6-substituted 2,5-dideoxy-2,5-epithio-3,4-*O*-isopropylidene-D-allose dimethyl acetal derivatives (**32**) and (**36**), and, *via* ring contraction and ring expansion, 2,6-dideoxy-2,6-epithio-3,4-*O*-isopropylidene-5-*O*-methyl-L-talose dimethyl acetal (**35**).

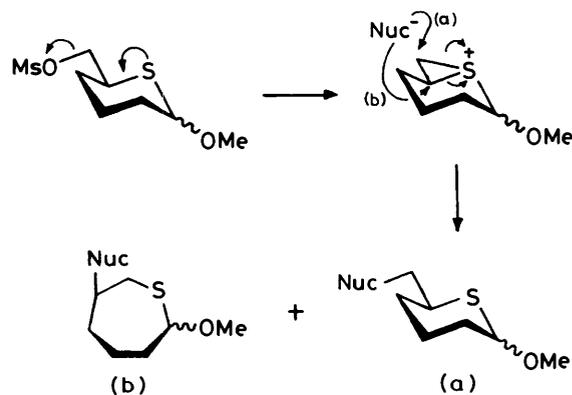
In an earlier paper² in this series it was shown that methyl 5-thiopentopyranoside 2- or 4-sulphonate esters readily underwent nucleophilic displacement reactions either with retention of configuration or with ring contraction. It was suggested² that these reactions proceeded *via* intermediate episulphonium ions formed by neighbouring group participation from the ring sulphur atom (Schemes 1 and 2). Sulphonate esters at C-3 did not show any unusual reactivity; apparently the cyclic sulphonium ions that would be formed by sulphur participation are too strained. We have now extended these studies to sulphonate esters of some methyl 5-thiohexopyranosides. A sulphonate at C-6 is also a β -ester with respect to the ring sulphur and displacement reactions might be expected to proceed as shown in Scheme 3 to give either pyranoside or septanoside products.



Scheme 1. Ms = MeS(O)₂⁻



Scheme 2.



Scheme 3.

The diol (**1**) was readily available from mild hydrolysis of methyl 2,3-anhydro-4,6-*O*-isopropylidene-5-thio- α -D-allopyranoside.³ Methylsulphonylation of the diol (**1**) gave a crystalline disulphonate (**5**), which decomposed within hours when kept at room temperature. This disulphonate not only offered the opportunity of examining the behaviour of a 6-sulphonate but also of comparing such a sulphonate with a 4-sulphonate in the same molecule. The behaviour of compound (**5**) with a variety of nucleophiles was examined.

When compound (**5**) was left overnight in cold methanol containing sodium benzoate a good yield of a crystalline monobenzoate monomethanesulphonate (**A**) was obtained. When this product was heated with methanolic sodium benzoate it afforded the same crystalline dibenzoate (**3**) as could be obtained by direct benzylation of the diol (**1**). Clearly the C-4 sulphonate in (**5**) had been substituted with retention of configuration *via* an episulphonium ion (*cf.* Scheme 2) but the sequence of displacement reactions and the involvement of an episulphonium ion, or not, in the substitution at C-6 had still to be determined. That reaction had taken place first at 4-C was

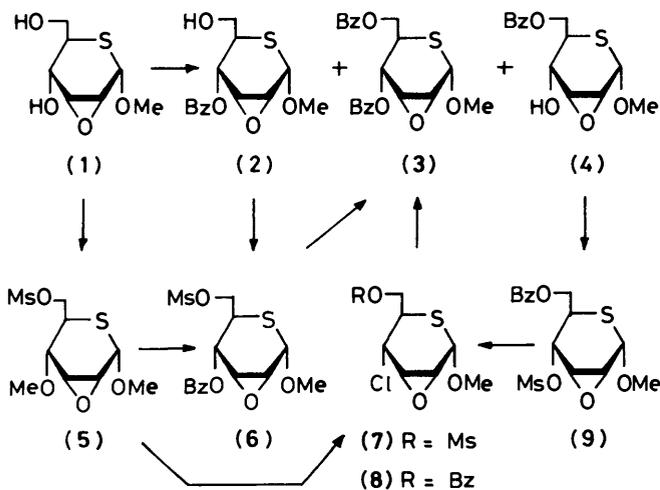
Table. ¹H N.m.r. data

Compd.	1-H	2-H	3-H	4-H	5-H	6-H _a	6-H _b	Other signals	J _{1,2}	J _{2,3}	J _{3,4}	J _{4,5}	J _{5,6_a}	J _{5,6_b}	J _{6_a,6_b}
(2) ^{a,b}	4.83	4.0←→3.0	5.63	4.0←→3.0				3.48 (OMe)	5.0		2.0	10.0			
(3) ^a	4.82	3.84	3.58	5.71	3.90	←4.52→		3.48 (OMe)	5.0	4.0	1.5	10.5	4.0		
(4) ^{a,b}	4.74	3.78	3.44	4.08	3.47	4.89	4.41	3.44 (OMe)	5.0	4.0	1.5	10.5	4.0	3.0	12.0
(5) ^a	4.77	3.85	3.62	5.20	3.69	4.51	4.33	3.43 (OMe); 3.15, 3.05 (2SO ₂ Me)	5.0	4.0	1.5	10.5	3.5	3.0	11.0
(6) ^a	4.84	3.82	3.57	5.60	3.80	4.44	4.36	3.48 (OMe); 2.97 (SO ₂ Me)	5.0	4.0	1.5	10.5	4.5	3.0	11.0
(7)	4.84	3.86	3.56	4.46	3.62	4.71	4.38	3.44 (OMe); 3.07 (SO ₂ Me)	4.5	3.5	1.5	9.5	3.5	2.0	10.0
(8) ^{a,c}	4.11	3.13	2.94	4.17	3.64	4.59	4.41	3.06 (OMe)	5.0	4.0	1.5	11.0	4.5	3.0	12.0
(9) ^a	4.76	3.84	ca. 3.5	4.20	4.6←→3.5			3.41 (OMe); 3.08 (SO ₂ Me)	5.0	4.0	1.5	11.0			
(11)	4.93	3.61	3.71	5.00	4.11	4.40	4.36	3.48 (OMe); 3.18, 3.09 (2SO ₂ Me)	3.0	4.0	1.5	10.0	3.5	2.5	11.5
(12) ^a	4.92	3.62	3.73	5.08	4.20	4.61	4.42	3.46 (OMe); 3.12 (SO ₂ Me)	3.0	4.0	1.5	9.5	2.0	5.0	12.0
(13) ^a	4.97	3.60	3.70	5.44	4.7←→4.2			3.49 (OMe)	3.0	4.0	1.5	9.0			
(14) ^{a,c}	4.41	2.98	3.10	3.67	4.08	←4.58→		3.17 (OMe); 2.95 (OH)	3.0	4.0	1.5	9.5	4.0		
(16)	4.77	3.79	3.14	3.83	3.53	4.63	4.31	3.53, 3.44 (2OMe); 3.05 (SO ₂ Me)	5.0	4.0	1.5	10.0	4.0	2.5	10.5
(20) ^{a,c}	4.81	5.07	5.32	3.64	3.05	3.49	3.40	3.01 (OMe); 2.82 (SO ₂ Me); 1.91 (ArMe); 1.02, 0.89 (CMe ₂)	3.0	9.5	9.0	9.5	5.5	10.0	10.5
(23) ^{a,b}	4.41	ca. 3.5	4.92	3.8←→3.2				3.37, 3.30 (2OMe); 2.44 (ArMe)	5.5	5.0	5.0				
(24) ^a	4.63	3.81	5.34	5.68	3.85	4.41	4.39	3.48, 3.35 (2OMe); 2.16 (ArMe)	6.0	6.0	6.0	6.5	7.5	6.0	
(26) ^{b,c}	4.67	3.62	3.4←→3.0					3.13 (2OMe)	8.5	2.0					
(27)	4.51	3.6←→3.0	→3.0	4.24	4.04			3.37, 3.47 (2OMe); 2.08 (COMe)	8.5				5.0	7.5	11.0

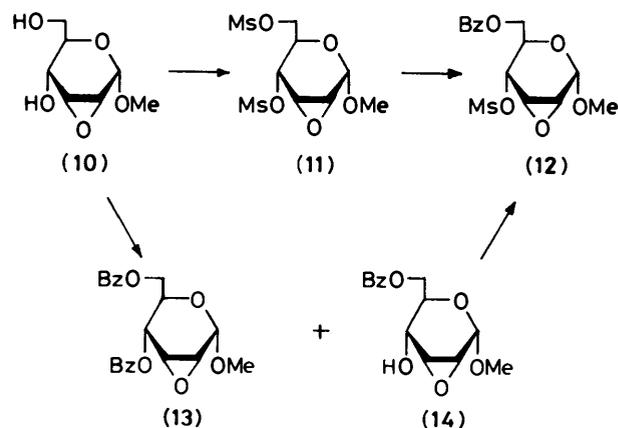
^a Also showed signals in aromatic region. ^b Also showed OH signal(s). ^c In hexadeuteriobenzene.

was shown by identification of the intermediate (A) as the 4-*O*-benzoate 6-*O*-methanesulphonate (6). Reaction of the diol (1) with a limited amount of benzoyl chloride gave a mixture, of the dibenzoate (3) and the two monobenzoates (2) and (4), which was readily separated by chromatography. The structures of the monobenzoates (2) and (4) followed from a comparison of their ¹H n.m.r. spectra with that of the dibenzoate (3) (see Table). Thus 4-H of compound (4) resonated at higher field than the corresponding hydrogens of compounds (2) and (3), thereby demonstrating the free hydroxy group at C-4 in (4). Methylsulphonylation of the monobenzoates (2) and (4) gave isomers (6) and (9), respectively, and compound (6) was found to be identical with (A). The sulphonate (9) reacted, as expected, with cold methanolic sodium benzoate to give, with retention of configuration, the dibenzoate (3) (Scheme 4).

The sulphonate ester at C-6 is clearly the less reactive in the disulphonate (5) but, as C-6 is achiral, it is difficult to decide whether it reacts *via* a simple S_N2 mechanism or *via* S-participation and an episulphonium ion. Evidence that it is the latter came from a study of the reaction of the known⁴ methyl 2,3-anhydro-4,6-di-*O*-methylsulphonyl- α -D-allopyranoside (11)



with sodium benzoate. No reaction occurred under the previous conditions, *i.e.* in hot or cold methanolic solution; however, when a refluxing solution of sodium benzoate in *N,N*-dimethylformamide (DMF) was used a crystalline product, shown to be the 6-*O*-benzoate (12), was obtained. Apparently the dimethyl compound (11) had reacted by a simple S_N2 displacement at the less hindered primary position. The much more vigorous conditions required to bring about this reaction are a strong indication that the sulphonate group in (6) underwent displacement *via* S-participation (*cf.* Scheme 5). The



structure of the benzoate-sulphonate (12) was deduced in similar manner to that of the thio compound (6). Partial benzylation of the diol (10) gave a syrupy dibenzoate (13) and a crystalline monobenzoate (14). Comparison of their ¹H n.m.r. spectra showed 4-H at δ 5.44 from the dibenzoate (13) compared with δ 3.67 from the monobenzoate (14), in keeping with the free hydroxy group being at C-4 in (14). Methylsulphonylation of the alcohol (14) gave the mixed disulphonate (12), identical with the product of the displacement reaction.

A possible explanation for the lower reactivity of the primary sulphonate ester in the disulphonate (5) can be seen from

conformational analysis. The coupling constants in the ^1H n.m.r. spectrum of compound (5), particularly $J_{4,5}$ (10.5 Hz), are in keeping with the 3H_5 conformation where the 4-sulphonate is quasiequatorial and suitably placed for S -participation. The similarity of $J_{5,6}$ and $J_{5,6}$ (3.5 and 3.0 Hz, respectively) suggests that the 6-sulphonate group is in a parallel 1,3-relationship (Figure 1a) with 4-H and, as such, inappropriately placed for S -participation. For this to occur the C-5—C-6 bond must rotate but then the 6-sulphonate comes into a parallel 1,3-relationship with the 4-sulphonate (Figure 1b), an energetically



(5) R = Ms

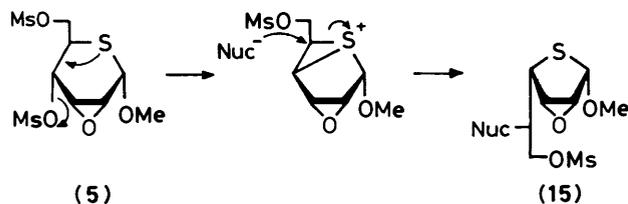
(6) R = Bz

Figure 1.

less favourable conformation. The same consideration applies to the benzoate methanesulphonate (6) ($J_{5,6}$, 4.5 Hz, and $J_{5,6}$, 3.0 Hz). It is interesting to note that in these and subsequent reactions of the *allo* compound (5) the epoxide is unaffected; apparently, geometric constraints do not allow participation by the ring sulphur in the opening of the oxirane ring.

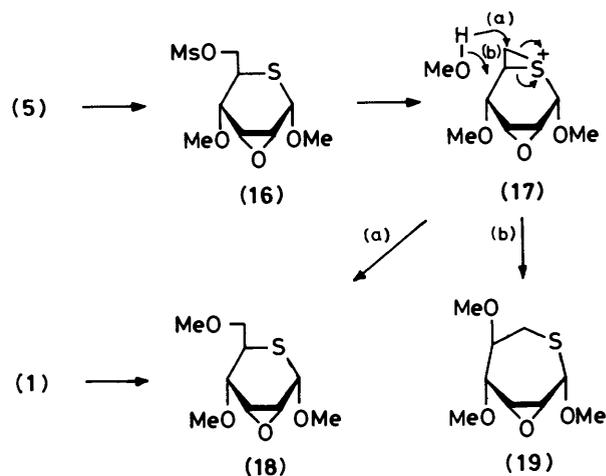
The disulphonate (5) reacted with a cold solution of benzyltriethylammonium chloride to give a single chlorine-containing crystalline product. The ^1H n.m.r. spectrum of this product showed a strong resemblance to that of the starting material (5) with the exception that the signal for 4-H was at higher field. The product still retained a methanesulphonate group and the structure (7) was assigned. As before the secondary sulphonate had proved more reactive and had undergone reaction *via* S -participation. The monobenzoate monosulphonate (9) similarly reacted to give the chloro compound (8). An attempt to convert (7) into (8), by heating (7) with a methanolic solution of sodium benzoate, failed, for the dibenzoate (3) was formed instead. Apparently S -participation allows the normally unreactive chlorine to undergo displacement.

In none of the foregoing reactions had products of ring contraction or ring expansion been observed. The former is probably not unexpected, for the resultant product, having undergone inversion at C-4 and C-5, would have the *L-manno* configuration (15) with an all-*cis* arrangement of the furanoside ring (Scheme 6). A similar explanation was offered² for the lack of lyxofuranoside products in related reactions of methyl 2,3-*O*-isopropylidene-4-*O*-methylsulphonyl-5-thio- β -D-ribofuranoside where only products with retained ribopyranoside



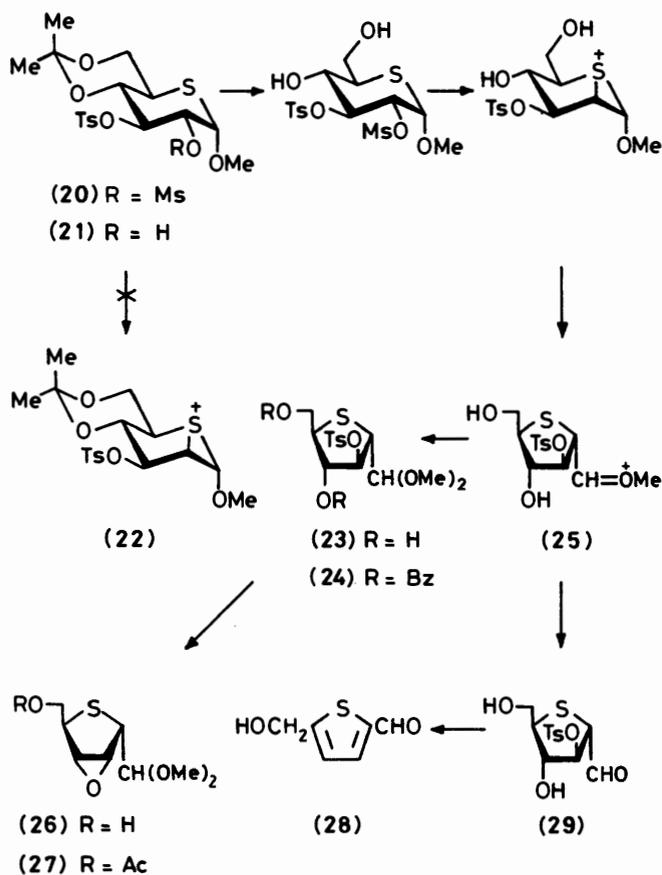
Scheme 6.

configuration were observed. A possible case of ring expansion was observed with methanol as the nucleophile. The disulphonate (5) reacted with cold methanol in the presence of barium carbonate to give a crystalline product containing two methoxy groups and a methanesulphonate group. Consideration of its ^1H n.m.r. spectrum and comparison of chemical shifts for 4-H as in the earlier cases led to the structure (16) being assigned. On being heated in methanol, compound (16) reacted further to give a syrupy major product and a crystalline minor product. The latter was shown to be the dimethyl ether (18) by independent synthesis by Purdie methylation of the diol (1). Mass spectra suggested that the syrupy product was isomeric with compound (18) and the ^1H n.m.r. spectrum, though incompletely resolved, showed the presence of three methoxy groups but differed from that of compound (18) in showing a high-field two-hydrogen multiplet. The *L*-taloseptanoside structure (19) is suggested for this product on the basis of the n.m.r. spectrum and the proposed mechanism of formation and reaction of the intermediate episulphonium ion (17) (Scheme 7). Methanol, being a good ionizing solvent but poor nucleophile, might be expected to favour an ' S_N1 -like' attack at the secondary C-5 rather than ' S_N2 -like' attack at the primary C-6 of the proposed intermediate (17).



Scheme 7.

The disulphonate (20) was readily obtained by methylsulphonylation of the known³ alcohol (21). When left in methanol containing barium carbonate compound (20) failed to react and could be recovered unchanged; higher temperatures led to decomposition. This lack of reactivity, despite the favourable juxtaposition of the methanesulphonate group and the ring sulphur atom, is probably due to the presence of the 4,6-acetal with its 1,3-dioxane ring. S -Participation would lead to a strained *trans*-fused bicyclic system in the resultant episulphonium ion (22). A similar situation was encountered² with methyl 3,4-*O*-isopropylidene-2-*O*-methylsulphonyl-5-thio- α -D-xylopyranoside which failed to react with nucleophiles; however, once the 3,4-acetal was removed, displacement reactions of the type shown in Scheme 1 proceeded readily. Accordingly, it was anticipated that, when compound (20) was left in methanol containing hydrogen chloride, the sequence of events shown in Scheme 8 would take place leading to the *D-manno* derivative (23). In the event a syrupy product was obtained in excellent yield, with spectral features and other properties in keeping with the structure (23). Thus the ^1H n.m.r. spectrum showed the presence of two methoxy groups, and a toluene-*p*-sulphonate group. The diol nature of compound (23)

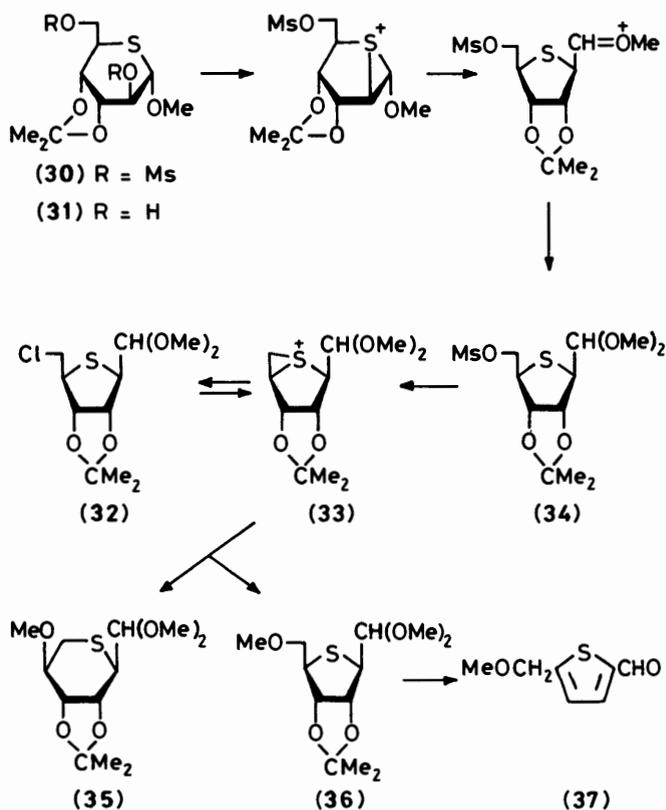
Scheme 8. $7s = p\text{-MeC}_6\text{H}_4\text{SO}_2^-$

was demonstrated by the formation of a crystalline dibenzoate (24). Though the ^1H n.m.r. spectrum of dibenzoate (24) was fully resolved the values of the coupling constants were of little value in confirming the stereochemistry of the product. Support for the *trans* arrangement of the sulphonate at C-3 and the hydroxy group at C-4 came from the ready loss of toluene-*p*-sulphonic acid on treatment with cold methanolic sodium methoxide and the formation of a syrupy product, tentatively identified as the epoxide (26), which showed a prominent peak at m/z 75 [$\text{CH}(\text{OMe})_2$] in its mass spectrum and gave a syrupy monoacetate (27).

Reaction of the disulphonate (20) with aqueous acetic acid containing potassium acetate gave a product with a remarkably simple ^1H n.m.r. spectrum and which was identified as the thiophene aldehyde (28). This presumably arose, as did (23), from the carboxonium ion (25), which reacted with water to give the aldehyde (29) which then aromatised to the thiophene (28) by loss of toluene-*p*-sulphonic acid and water. Interestingly the thiophene aldehyde (28) has been encountered⁵ previously as a product from the reaction of acids with 5-thio-D-fructofuranose derivatives.

The *allo* disulphonate (5) enabled a comparison of the reactivities of 4- and 6-sulphonate esters in the 5-thiohexopyranoside system to be made. It was hoped to make a similar comparison for 2- and 6-sulphonates by examining the reactions of the *altro* compound (30). The diol (31) was methylsulphonylated in the usual way with methanesulphonyl chloride in dichloromethane in the presence of triethylamine. The product (30) appeared to decompose during the work-up and could not be isolated. Accordingly, when the sulphonylation was judged complete, methanol and barium carbonate were added to the reaction mixture which was then stirred overnight at room

temperature. Work-up gave three products. The major product was a syrup whose mass spectrum indicated the molecular formula $\text{C}_{11}\text{H}_{19}\text{ClO}_4\text{S}$ and showed a prominent peak with m/z 75, suggesting a $\text{CH}(\text{OMe})_2$ fragment. The ^1H n.m.r. spectrum confirmed the presence of two methoxy groups as well as demonstrating an isopropylidene group and the absence of methanesulphonate groups. The mass spectra of the two minor products suggested that they were isomeric with molecular formula $\text{C}_{12}\text{H}_{22}\text{O}_5\text{S}$ and both contained a $\text{CH}(\text{OMe})_2$ fragment (prominent peak at m/z 75 in both cases). Their ^1H n.m.r. spectra indicated the presence of three methoxy groups and an isopropylidene group in both cases. The spectrum of one bore a fair resemblance to that of the major product whereas the spectrum of the other differed in showing signals for two coupled (J 13 Hz) hydrogens at higher field and suggesting a methylene group attached to sulphur. In the light of earlier reactions the structures (32), (36), and (35) are suggested for the major and two minor products, respectively, formed as shown in Scheme 4 where it has been assumed that the 2-sulphonate has undergone reaction first, to give the *allo* sulphonate (34). This then reacts, *via* the episulphonium ion (33), either with chloride ion or methanol to give the observed products (32), (35), and (36). The chloro compound (32) may well be a kinetic product in



Scheme 9.

this particular step for when it was warmed with methanol and barium carbonate the isomeric methoxy compounds (35) and (36) were obtained. The assumption that the 2-sulphonate reacts first requires that disulphonate (30) adopts the less favourable $^4\text{C}_1$ conformation with the equatorial 2-sulphonate group required for *S*-participation. Interestingly, a six-membered ring is retained in product (35) as a result of both ring contraction and ring expansion occurring. Further support for the structure of compound (36) came when, on treatment with

hot aqueous acetic acid, it yielded the methoxymethylthiophene aldehyde (37).

Experimental

M.p.s were measured on a Gallenkamp hot stage apparatus and are uncorrected. Optical rotations were measured in chloroform solution on a Bendix-NPL Type 143A polarimeter. N.m.r. spectra were recorded, unless otherwise stated, at 90 MHz (¹H) in deuteriochloroform solution with tetramethylsilane as an internal standard on a Bruker Spectrospin spectrometer. Silica gel was used for t.l.c. (Gelman, ITLC Type 5A) and column chromatography (Merck Kieselgel 7734). Organic extracts were dried with anhydrous magnesium sulphate, and evaporations were carried out under reduced pressure with bath temperature < 50 °C.

Methyl 2,3-Anhydro-5-thio- α -D-allopyranoside (1).—A solution of methyl 2,3-anhydro-4,6-O-isopropylidene-5-thio- α -D-allopyranoside³ (0.83 g) in 80% acetic acid (9 ml) was kept at 20 °C for 15 h. Solvents were removed, the residue was dissolved in ethyl acetate, and the solution was filtered through a little silica. Concentration of the eluate and cooling gave the diol (1) (0.62 g, 90%), m.p. 92–94 °C; [α]_D + 280° (c 0.7) (Found: C, 43.2; H, 6.2%; M⁺, 192.0456. C₇H₁₂O₄S requires C, 43.7; H, 6.3%; M, 192.0465); δ_{H} 4.77 (1 H, d, J_{1,2} 5 Hz, 1-H), 4.50–3.00 (6 H, m, 2-, 3-, 4-, and 5-H, and 6-H₂), and 3.47 (3 H, s, OMe).

Benzoylation of Methyl 2,3-Anhydro-5-thio- α -D-allopyranoside (1).—A solution of benzoyl chloride (0.07 ml) in dichloromethane (2 ml) was added slowly to an ice-cold stirred solution of the diol (1) (135 mg) in a mixture of dichloromethane (2 ml) and pyridine (1 ml). After the mixture had been kept for 16 h at 0 °C water (0.1 ml) was added to decompose any remaining benzoyl chloride and, after 10 min, the mixture was washed successively with dilute sulphuric acid and dilute aqueous potassium hydrogen carbonate and dried. Evaporation gave a syrup (210 mg) containing three components. Chromatography on silica (9 g) and elution with benzene–diethyl ether (9:1) gave first the dibenzoate (3) (65 mg, 23%), m.p. 158–160 °C (from ethanol); [α]_D + 296° (c 0.9) (Found: C, 62.8; H, 4.8%; M⁺, 400.1010. C₂₁H₂₀O₆S requires C, 63.0; H, 5.0%; M, 400.0980). Further elution with benzene–diethyl ether (7:3) gave the 4-benzoate (2) (29 mg, 14%), m.p. 112–114 °C (from di-isopropyl ether); [α]_D + 86° (c 0.9) [Found: C, 56.4; H, 5.4%; (M⁺ – OH), 279.0705. C₁₄H₁₆O₃S requires C, 56.7; H, 5.4%; (M⁺ – OH), 279.0691], and then the syrupy isomeric 6-benzoate (4) (110 mg, 53%), [α]_D + 131° (c 0.9) [Found: (M⁺ – OH), 279.0703].

Methyl 2,3-Anhydro-4,6-di-O-methylsulphonyl-5-thio- α -D-allopyranoside (5).—The diol (1) (150 mg) was dissolved in dry dichloromethane (3.5 ml) containing triethylamine (0.5 ml) and the solution was stirred and cooled to –10 °C. A cold solution of methanesulphonyl chloride (0.2 ml) in dichloromethane (3.5 ml) was added slowly to the above stirred solution. After about 10 min water was added and the mixture was separated. The organic extract was washed with ice-cold dilute aqueous potassium hydrogen carbonate, dried, and evaporated to give the disulphonate (5) (230 mg, 78%), m.p. 86–88 °C (decomp.) (from dichloromethane–diethyl ether); [α]_D + 160° (c 0.7) (Found: C, 30.8; H, 4.7. C₉H₁₆O₈S₂ requires C, 31.0; H, 4.7%). The compound decomposed within a few hours at room temperature.

Methyl 2,3-Anhydro-4-O-benzoyl-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (6).—The monobenzoate (2) (29 mg) was treated with methanesulphonyl chloride (0.02 ml), as described in the previous experiment, to give the sulphonate (6)

(35 mg, 95%), m.p. 127–129 °C (decomp.) (from dichloromethane–diethyl ether); [α]_D + 251° (c 1.1) (Found: C, 47.8; H, 4.75. C₁₅H₁₈O₇S₂ requires C, 48.1; H, 4.85%).

Methyl 2,3-Anhydro-6-O-benzoyl-4-O-methylsulphonyl-5-thio- α -D-allopyranoside (9).—Prepared as described above, from the monobenzoate (4) (104 mg), the sulphonate (9) (67 g, 51%) had m.p. 82–84 °C (decomp.) (from dichloromethane–diethyl ether); [α]_D + 192° (c 0.8) (Found: C, 47.7; H, 4.8%).

Benzoylation of Methyl 2,3-Anhydro- α -D-allopyranoside (10).—A solution of the diol (10)⁴ (270 mg) in pyridine (3 ml) containing benzoyl chloride (0.5 ml) was left overnight at 20 °C. Work-up in the usual way yielded a syrup (300 mg), which was chromatographed on silica (25 g). Elution with benzene–diethyl ether (2:1) gave first the syrupy dibenzoate (13) (220 mg, 37%), [α]_D + 199° (c 0.9) [Found: (M⁺ – OMe), 353.1032. C₂₁H₂₀O₇ requires (M⁺ – OMe), 353.1025], and then the monobenzoate (14) (48 mg, 11%), m.p. 140–142 °C (from di-isopropyl ether); [α]_D + 74° (c 0.6) (Found: C, 59.7; H, 5.7. C₁₄H₁₆O₆ requires C, 60.0; H, 5.75%).

Methyl 2,3-Anhydro-6-O-benzoyl-4-O-methylsulphonyl- α -D-allopyranoside (12).—The benzoate (14) (44 mg) was treated with methanesulphonyl chloride (0.02 ml) in dichloromethane (1.5 ml) containing triethylamine (0.1 ml) as described in earlier experiments, to give the sulphonate (12) (44 mg, 79%), m.p. 149–150 °C (from ethanol); [α]_D + 125° (c 1.2) (Found: C, 50.6; H, 5.1. C₁₅H₁₈O₈S requires C, 50.25; H, 5.0%).

Benzoate Displacement Reactions.—(a) *On Methyl 2,3-anhydro-4,6-di-O-methylsulphonyl-5-thio- α -D-allopyranoside (5).* A mixture of compound (5) (150 mg) and sodium benzoate (200 mg) in a mixture of methanol (5 ml) and dichloromethane (1 ml) was stirred for 25 h at 20 °C. The mixture was evaporated to dryness and the residue was partitioned between dichloromethane and water. The dried organic extract was passed through a little silica and evaporated to afford a crystalline residue (259 mg). Recrystallisation from dichloromethane–diethyl ether gave the 4-benzoate (6) (100 mg, 63%), m.p. and mixed m.p. 127–129 °C (decomp.).

(b) *On methyl 2,3-anhydro-4-O-benzoyl-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (6).* The sulphonate (6) (50 mg) was heated under reflux in a solution of sodium benzoate (80 mg) in methanol (5 ml) for 24 h. Evaporation of the mixture and work-up as in (a) above gave the dibenzoate (3) (45 mg, 84%), m.p. and mixed m.p. 158–160 °C (from ethanol).

(c) *On methyl 2,3-anhydro-6-O-benzoyl-4-O-methylsulphonyl-5-thio- α -D-allopyranoside (9).* A mixture of the sulphonate (9) (30 mg) and sodium benzoate (30 mg) in a mixture of methanol (3 ml) and dichloromethane (1 ml) was stirred overnight at 20 °C. Work-up as in (a) above gave the dibenzoate (3) (29 mg, 90%), m.p. and mixed m.p. 158–160 °C.

(d) *On methyl 2,3-anhydro-4,6-di-O-methylsulphonyl- α -D-allopyranoside (11).* A solution of the disulphonate (11)⁴ (50 mg) in DMF (2 ml) containing sodium benzoate (60 mg) was heated under reflux for 7 h. Work-up as in (a) above gave the benzoate (12) (50 mg, 93%), m.p. and mixed m.p. 149–150 °C.

(e) *On methyl 2,3-anhydro-4-chloro-4-deoxy-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (7).* A solution of the sulphonate (7) (see below) (180 mg) in methanol (10 ml) containing sodium benzoate (300 mg) was heated under reflux for 24 h. Work-up as in (a) above gave the dibenzoate (3) (50 mg, 20%), m.p. and mixed m.p. 158–160 °C.

Methyl 2,3-Anhydro-4-chloro-4-deoxy-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (7).—A solution of the disulphonate (5) (150 mg) in dichloromethane (5 ml) was added to a solution

of benzyltriethylammonium chloride (200 mg) in methanol (10 ml). The mixture was stirred for 2 h at 20 °C and then evaporated to dryness. The residue was partitioned between water and dichloromethane, and evaporation of the dried organic extract yielded a crystalline residue. Crystallisation from dichloromethane–diethyl ether gave the *chloro compound* (7) (112 mg, 90%), m.p. 130–131 °C; $[\alpha]_D + 218^\circ$ (*c* 1.3) (Found: C, 33.0; H, 4.8%; M^+ , 288.9875. $C_8H_{13}ClO_5S_2$ requires C, 33.3; H, 4.55%; *M*, 288.9893).

Methyl 2,3-Anhydro-6-O-benzoyl-4-chloro-4-deoxy-5-thio- α -D-allopyranoside (8).—A mixture of the sulphonate (9) (65 mg) and benzyltriethylammonium chloride (70 mg) in a mixture of methanol (3 ml) and dichloromethane (1 ml) was stirred overnight at 20 °C. Work-up as in the previous experiment gave the *chloro compound* (8) (45 mg, 82%), m.p. 126–127 °C (from di-isopropyl ether); $[\alpha]_D + 152^\circ$ (*c* 0.7) (Found: C, 53.9; H, 4.5. $C_{14}H_{15}ClO_4S$ requires C, 53.4; H, 4.8%).

Methyl 2,3-Anhydro-4-O-methyl-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (16).—A mixture of the disulphonate (5) (300 mg) and barium carbonate (350 mg) in a mixture of methanol (10 ml) and dichloromethane (2 ml) was stirred overnight at 20 °C. The mixture was filtered, and evaporated to dryness, and the residue was chromatographed on silica (4 g). Elution with benzene–diethyl ether (7:3) gave the *methyl ether* (16) (200 mg, 82%), m.p. 125–126 °C (from ethanol); $[\alpha]_D + 179^\circ$ (*c* 0.9) (Found: C, 37.95; H, 5.55%; M^+ , 284.0404. $C_9H_{16}O_6S_2$ requires C, 38.0; H, 5.7%; *M*, 284.0388).

Methyl 2,3-Anhydro-4,6-di-O-methyl-5-thio- α -D-allopyranoside (18).—A solution of the diol (1) (100 mg) in iodomethane (4 ml) was heated under reflux and freshly prepared dry silver oxide (300 mg) was added during 2 h in five equal portions. Heating was continued for a further 2 h. The mixture was filtered and evaporated to give a crystalline product. Recrystallisation from light petroleum (boiling range 60–80 °C) gave the *diether* (18) (100 mg, 87%), m.p. 97–99 °C; $[\alpha]_D + 304^\circ$ (*c* 1.4) (Found: C, 49.15; H, 7.35%; M^+ , 220.0768. $C_9H_{16}O_4S$ requires C, 49.1; H, 7.3%; *M*, 220.0769); δ_H 4.72 (1 H, d, $J_{1,2}$ 5 Hz, 1-H), 3.98–3.31 (6 H, m, 2-, 3-, 4-, and 5-H, and 6-H₂), 3.52 (3 H, s, OMe), 3.45 (3 H, s, OMe), and 3.38 (3 H, s, OMe).

Reaction of Methanol with Methyl 2,3-Anhydro-4-O-methyl-6-O-methylsulphonyl-5-thio- α -D-allopyranoside (16).—A stirred solution of the sulphonate (16) (240 mg) in methanol (8 ml) containing barium carbonate (300 mg) was heated under reflux for 2 h. The mixture was filtered and evaporated to give a syrup (200 mg), which was chromatographed on silica (10 g). Elution with benzene–diethyl ether (4:1) gave first a syrup, tentatively identified as *methyl 2,3-anhydro-4,5-di-O-methyl-6-thio- β -L-taloseptanoside* (19) (138 mg, 74%), $[\alpha]_D + 14^\circ$ (*c* 0.8) [Found: ($M^+ - OMe$), 189.0566. $C_9H_{16}O_4S$ requires ($M^+ - OMe$), 189.0585]; δ_H (C_6D_6) 4.38 (1 H, d, $J_{1,2}$ 6 Hz, 1-H), 3.25 (3 H, s, OMe), 3.24 (6 H, s, 2-OMe), 3.2–2.8 (4 H, m, 2-, 3-, 4-, and 5-H), and 2.11 (1 H, br, s, 6-H₂). Further elution gave the pyranoside (18) (25 mg, 13%), m.p. and mixed m.p. 97–99 °C.

Methyl 4,6-O-Isopropylidene-2-O-methylsulphonyl-5-thio-3-O-p-tolylsulphonyl- α -D-glucopyranoside (20).—The alcohol (21)³ (0.50 g) was methylsulphonylated, as in previous experiments, with methanesulphonyl chloride (0.29 ml) and triethylamine (1.2 ml) in dichloromethane (29 ml) to give the disulphonate (20) (0.55 g, 57%), m.p. 95–98 °C (from dichloromethane–diethyl ether); $[\alpha]_D + 143^\circ$ (*c* 1.0) (Found: C, 44.6; H, 5.4. $C_{18}H_{26}O_9S$ requires C, 44.8; H, 5.4%). The compound decomposed within a week at room temperature but could be kept for longer periods at –20 °C.

4,6-Di-O-benzoyl-2,5-dideoxy-2,5-epithio-3-O-p-tolylsulphonyl-D-mannose Dimethyl Acetal (24).—A solution of the disulphonate (20) (0.32 g) in methanol (6.5 ml) containing hydrogen chloride [from acetyl chloride (0.16 ml)] was left for 24 h at 20 °C. The reaction mixture was neutralised (PbCO₃), filtered, and evaporated to dryness. Trituration with ethyl acetate yielded a syrupy product (0.24 g, 96%), tentatively identified as the diol (23), $[\alpha]_D + 67^\circ$ (*c* 2.0). A portion (75 mg) of this product was benzoylated in the usual way with benzoyl chloride (0.4 ml) in pyridine (1 ml) to give the *dibenzoate* (24) (90 mg, 80%), m.p. 86–88 °C (from ethanol); $[\alpha]_D + 137^\circ$ (*c* 0.9) (Found: C, 59.65; H, 4.9. $C_{29}H_{30}O_9S_2$ requires C, 59.4; H, 5.15%).

6-O-Acetyl-3,4-anhydro-2,5-dideoxy-2,5-epithio-D-altrose Dimethyl Acetal (27).—A solution of the sulphonate (23) (80 mg) in methanol (3 ml) containing sodium methoxide [from sodium (30 mg)] was kept for 15 h at 20 °C and was then neutralised (CO₂) and evaporated to dryness. The residue was triturated with acetone to yield a syrupy product (35 mg, 80%) tentatively identified as the *epoxide* (26), $[\alpha]_D + 28^\circ$ (*c* 0.90) [Found: ($M^+ - OMe$), 175.0445. $C_8H_{14}O_4S$ requires $M^+ - OMe$, 175.0429]. The epoxide (26) (25 mg) was acetylated in the usual way with acetic anhydride (0.25 ml) in pyridine (0.6 ml) to give, after chromatography on silica and elution with benzene–diethyl ether (2:1), the syrupy *acetate* (27) (28 mg, 93%), $[\alpha]_D + 24^\circ$ (*c* 1.4) [Found: ($M^+ - OMe$), 217.0531. $C_{10}H_{16}O_5S$ requires ($M^+ - OMe$) 217.0535].

Action of Aqueous Acetic Acid on the Disulphonate (20).—The disulphonate (20) (200 mg) was stirred with 80% acetic acid (8 ml) containing potassium acetate (180 mg) for 45 min at 65 °C. The solvent was evaporated off and the residue was triturated with ethyl acetate to give a syrup (75 mg), which was dissolved in dichloromethane and passed through silica to give syrupy *5-hydroxymethylthiophene-2-carbaldehyde* (28) (50 mg, 85%) (Found: M^+ , 142.0101. $C_6H_6O_2S$ requires *M*, 142.0088); δ_H 9.80 (1 H, s, CHO), 7.67 (1 H, d, $J_{3,4}$ 4 Hz, 3-H), 7.07 (1 H, dt, J_{4,CH_2} 0.5 Hz, 4-H), 4.89 (2 H, br s, CH₂), and 2.19 (1 H, br s, OH). The *dinitrophenylhydrazone*, prepared in the usual way, had m.p. 147–149 °C (Found: C, 44.4; H, 3.3; N, 18.2. $C_{12}H_{10}N_2O_5S$ requires C, 44.7; H, 3.1; N, 17.4%).

Supposed Synthesis and Methanolysis of Methyl 3,4-O-Isopropylidene-2,6-di-O-methylsulphonyl-5-thio- α -D-altro-pyranoside (30).—An ice-cold solution of methanesulphonyl chloride (0.3 ml) in dry dichloromethane (6 ml) was added dropwise to a stirred solution of the diol (31)³ (300 mg) in dichloromethane (6 ml) containing triethylamine (0.8 ml) at –10 °C. After 20 min the solvent was removed and ice-cold methanol (15 ml) and barium carbonate (350 mg) were added. The mixture was stirred for 3 h at 0 °C and for a further 20 h at 20 °C. The mixture was filtered, the filtrate was evaporated to dryness, and the residue was partitioned between water and dichloromethane. Evaporation of the dried organic extract gave a syrup (206 mg), which was chromatographed on silica (15 g) and eluted with benzene–diethyl ether (4:1). First eluted was a syrup (130 mg, 36%) tentatively identified as *6-chloro-2,5,6-trideoxy-2,5-epithio-3,4-O-isopropylidene-D-allose dimethyl acetal* (32), $[\alpha]_D - 27^\circ$ (*c* 1.0) (Found: M^+ , 282.0689. $C_{11}H_{19}ClO_4S$ requires *M*, 282.0692); *m/z* 282 (M^+), 267 ($M - Me$), 251 ($M - OMe$), 247 ($M - Cl$), 207 [$M - CH(OMe)_2$], and 75 [base peak, CH(OMe)₂]. Eluted second was a syrup (42 mg, 12%) tentatively identified as *2,5-dideoxy-2,5-epithio-3,4-O-isopropylidene-6-O-methyl-D-allose dimethyl acetal* (36), $[\alpha]_D - 9^\circ$ (*c* 1.2) (Found: M^+ , 278.1196. $C_{12}H_{22}O_5S$ requires *M*, 278.1188); *m/z* 278 (M^+), 263 ($M - Me$), 247 ($M - OMe$), 203 [$M - CH(OMe)_2$], and 75 [base peak, CH(OMe)₂]. The last

fraction was also a syrup (20 mg, 6%) and was tentatively identified as 2,6-dideoxy-2,6-epithio-3,4-O-isopropylidene-5-O-methyl-L-talose dimethyl acetal (**35**), $[\alpha]_D - 8^\circ$ (*c* 0.6) (Found: M^+ , 278.1178); m/z 278 (M^+), 263 ($M - \text{Me}$), 247 ($M - \text{OMe}$), 203 [$M - \text{CH}(\text{OMe})_2$], and 75 [base peak, $\text{CH}(\text{OMe})_2$].

When the chloro compound (**32**) (180 mg) was heated under reflux with methanol (10 ml) and barium carbonate (350 mg) for 4 h, work-up as above yielded the methyl ethers (**36**) (80 mg, 44%) and (**35**) (50 mg, 28%).

Action of Aqueous Acetic Acid on the Methyl Ether (36).—The ether (**36**) (70 mg) was heated with 80% acetic acid (3 ml) at 85 °C for 3 h. The solvent was removed and the residue was chromatographed on silica and eluted with benzene-diethyl ether (2:1) to give syrupy 5-methoxymethylthiophene-2-carbaldehyde (**37**) (30 mg, 76%) (Found: M^+ , 156.0255. $\text{C}_7\text{H}_8\text{O}_2\text{S}$ requires M , 156.0245); δ_{H} 9.82 (1 H, s, CHO), 7.61 (1 H, d, $J_{3,4}$ 4 Hz, 3-H), 7.04 (1 H, dt, J_{4,CH_2} 0.5 Hz, 4-H), 4.62 (2 H, br s, CH_2), and 3.41 (3 H, s, OMe).

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