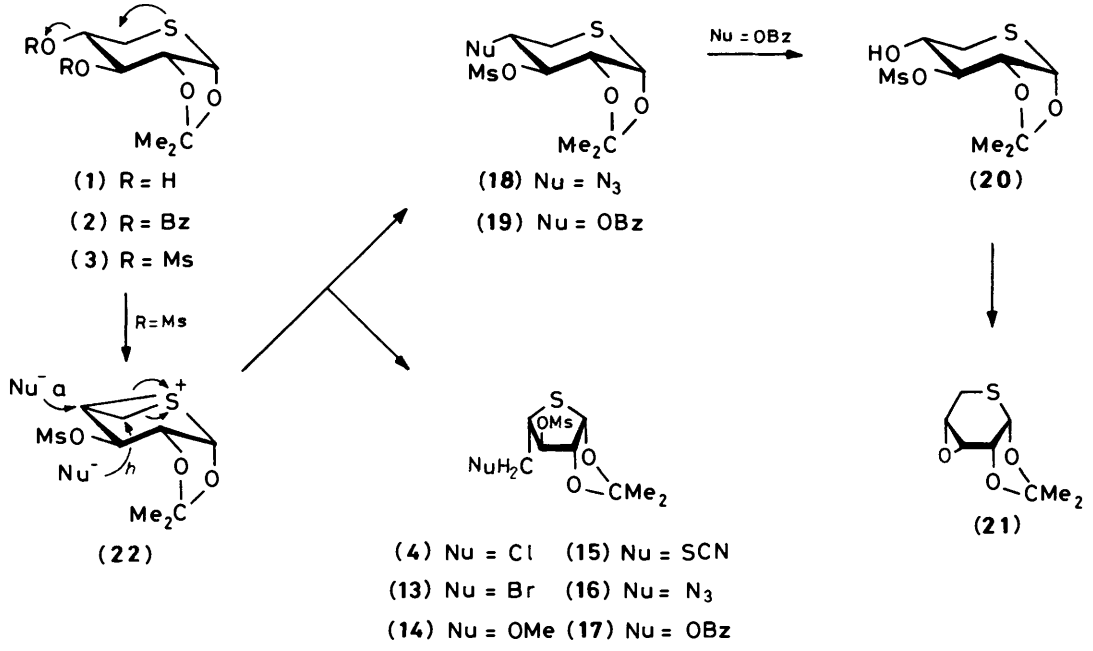
5-Thiopyranoses. Part 8.[1] Sulphur Participation in Displacement Reactions of Sulphonate Esters of 5-Thio-D-ribose and 5-Thio-D-xylose Derivatives

Neil A. Hughes* and Christopher J. Wood
School of Chemistry, The University, Newcastle upon Tyne NE1 7RU

The 4-methanesulphonate group of 1,2-*O*-isopropylidene-3,4-di-*O*-methylsulphonyl-5-thio-α-D-xylopyranose (**3**) is displaced by intramolecular attack by sulphur leading to a cyclic episulphonium ion (**22**) which then reacts with nucleophiles to give ring contracted 4-thio-β-L-arabinofuranose products (**4**) and (**13**)—(**17**) and, in some cases, products (**18**) and (**19**) with retained 5-thio-α-D-xylopyranose stereochemistry. Similar reactions with methyl 2,3(3,4)-*O*-isopropylidene-4(2)-*O*-methylsulphonyl-5-thio-D-ribopyranosides (**24**) and (**29**) also proceed *via* episulphonium ions (**25**) and (**30**) leading to products of retained stereochemistry such as methyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-5-thio-β-D-ribopyranoside (**26**) or of ring contraction *e.g.*, 2,5-dideoxy-2,5-epithio-3,4-*O*-isopropylidene-D-arabinose dimethyl acetal (**32**) respectively. The *trans*-acetal containing methyl 2,3-*O*-isopropylidene-4-*O*-methylsulphonyl-5-thio-α-D-xylopyranoside (**36**) fails to undergo reaction under the same conditions, presumably because of its inability to form the cyclic sulphonium ion (**37**).

The replacement of the ring oxygen atom of carbohydrates by sulphur results in a number of interesting changes in the properties of these compounds. Cyclic equilibria are affected,[2] new derivatives such as sulphoxides and sulphones are possible,[3] and chemical reactivities may be modified.[4] Sulphonate esters play an important role in carbohydrate chemistry and the presence of a nucleophilic sulphur atom elsewhere in the molecule could be expected to affect their reactions. Participation by sulphur is particularly effective when the sulphur is attached to the β-carbon with respect to the leaving group. This situation exists in the 2- and 4-*O*-sulphonates of 5-thiopyranoid derivatives and we now describe our results in the D-*ribo*- and D-*xylo* series.[5]



Although 1,2-*O*-isopropylidene-5-thio-α-D-xylopyranose (**1**) readily gave a crystalline dibenzoate (**2**),[6] attempted toluene-*p*-sulphonylation led only to extensive decomposition, but low temperature methanesulphonylation [7] in dichloromethane gave a crystalline dimethanesulphonate (**3**) which rapidly decomposed at room temperature. Although its ^{1}H n.m.r. spectrum could not be fully analysed it bore similarities with those of the diol (**1**) and the dibenzoate (**2**) (see Table 1) as expected for the structure (**3**). In methanol containing triethylamine hydrochloride the dimethanesulphonate (**3**) was smoothly converted into a chloro compound which was eventually shown to have the structure (**4**). The ^{1}H n.m.r. spectrum of compound (**4**), as well as showing the presence of a remaining methanesulphonate group at δ 3.14, suggested the presence of a 1,2-*O*-isopropylidenearabinofuranose system. The signal for 1-H appeared as a doublet (*J* 5 Hz), 2-H as a doublet of narrow triplets (*J* 5, 1, and 1 Hz) and 3-H as a narrow triplet (*J* 1 and 1 Hz). The second small coupling in the 2-H signal is probably due to long range coupling with 4-H (a W-configuration between these two hydrogens is possible in arabinofuranoses). Assignment of configuration in furanose systems from ^{1}H n.m.r. coupling constants is notoriously difficult because of the many conformations possible and at this stage the alternative *xylo* con-

Table 1. ^{1}H N.m.r. data for tetrahydrothiopyran derivatives

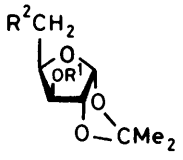
Compd.	1-H	2-H	3-H	4-H	5-H_e	5-H_a	Other signals	$J_{1,2}$	$J_{2,3}$	$J_{5,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5e,5a}$
(1)[a]	5.13	4.15	3.58	3.77	2.91	2.63	1.64, 1.47 (CMe_2); 3.67, 3.84 (OH)	5.0	7.0	10.0	4.0	9.5	13.0
(2)[a]	5.23	4.50	5.69	5.36	3.21	2.92	1.78, 1.48 (CMe_2)	5.0	8.0	10.0	4.0	9.5	13.0
(3)	5.10	4.30	4.8←→4.5		3.3←→2.8		3.18, 3.11 (SO_2Me); 1.59, 1.39 (CMe_2)	5.0	7.0				
(18)	5.17	4.24	4.56	3.78	2.72	2.99	3.23 (SO_2Me); 1.62, 1.43 (CMe_2)	4.5	8.0	10.0	4.0	11.0	14.0
(20)	5.09	4.24	4.51	3.86	2.69	2.91	3.19 (SO_2Me); 2.09 (OH); 1.61, 1.41 (CMe_2)	5.0	7.5	9.5	4.5	10.0	13.5
(24)	4.7←→4.4			5.50	3.1←→2.7		3.47 (OMe); 3.13 (SO_2 Me); 1.64, 1.41 (CMe_2)			1.0	6.0	10.0	
(26)[a]	4.7←→4.3			5.70	2.75	3.04	3.20 (OMe); 1.56; 1.34 (CMe_2)			1.5	5.5	10.0	11.0
(34)	4.80	4.2←→3.8			2.8←→2.5		3.53 (OMe); *ca.* 2.6 (OH); 1.47 (2) (CMe_2)	2.0					
(36)[b]	4.31	3.83	4.01	4.80	2.62	2.63	3.57 (OMe); 3.04 (SO_2 Me); 1.30, 1.26 (CMe_2)	2.0	9.0	9.0	6.5	9.0	
(38)	4.53	4.1←→3.6		4.90	2.60	2.75	3.50 (OMe); 3.0 (2) (OH); 2.10 (COMe)	2.0		8.0	6.0	8.0	14.0

[a] Ref. 6. [b] In deuteriobenzene.

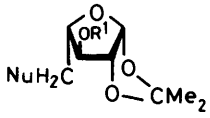
Table 2. ^{1}H N.m.r. data for tetrahydrothiophene derivatives

Compd.	1-H	2-H	3-H	4-H	5-H	5'-H	Other signals	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	Other couplings
(4)	6.04	4.99	5.56	4.2		3.6	3.14 (SO_2Me); 1.58, 1.33 (CMe_2)	5.0	1.0	1.0				1 ($J_{2,4}$)
(5)	5.98	4.82	5.13	4.40		3.74	3.12 (SO_2Me); 41.56, 1.34 (CMe_2)	4.0	0.5	1.5	7.0	7.0		
(6)	5.98	4.86	5.08	4.53	3.74	3.60	3.13 (SO_2Me); 1.53, 1.34 (CMe_2)	3.5	0	3.0	5.5	9.0	10.0	
(13)	6.00	4.92	5.52	3.9		3.3	3.05 (SO_2Me); 1.54 1.30 (CMe_2)	5.0	0	0				
(14)	5.85	4.85	5.30	3.7		3.3	3.00 (SO_2Me); 3.30 (OMe); 1.53, 1.30 (CMe_2)	5.0	1.0	1.0				
(15)	5.97	4.93	5.40	3.8	3.44	3.42	3.11 (SO_2Me); 1.54, 1.30 (CMe_2)	5.0	1.0	1.0	9.0	7.0		1 ($J_{2,4}$)
(16)	5.92	4.89	5.27		3.60		3.10 (SO_2Me); 1.55 1.30 (CMe_2)	5.0	1.0	1.0				
(17)	6.04	4.97	5.56	3.91	4.60	4.58	3.08 (SO_2Me); 1.62, 1.33 (CMe_2)	5.0	1.0	1.0	9.0	7.0		1 ($J_{2,4}$)
(32)[a]	4.92	3.29	4.43	4.25	2.61	2.31	3.26, 3.22 (OMe); 1.53, 1.14 (CMe_2)	8.5	4.0	5.5	0	4.0	12.5	

[a] In deuteriobenzene.



(6) R^1 = Ms, R^2 = Cl
(7) R^1 = H, R^2 = OH
(8) R^1 = Ms, R^2 = OMs
(9) R^1 = Ac, R^2 = Cl
(10) R^1 = H, R^2 = Cl



(5) R^1 = Ms, R^2 = Cl
(11) R^1 = H, R^2 = OTs
(12) R^1 = Ms, R^2 = OTs

figuration could not be ruled out. An attempt to resolve this uncertainty was made by synthesising the *arabino* and *xylo* oxygen analogues (**5**) and (**6**) and examining their ^{1}H n.m.r. spectra.

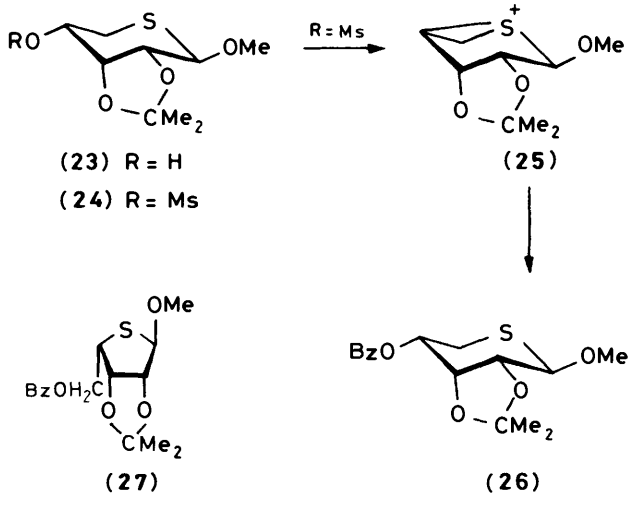
1,2-*O*-Isopropylidene-α-D-xylofuranose (**7**) was converted into its dimethanesulphonate (**8**) from which the primary sulphonate group was selectively displaced by chloride ions[8] to give the desired *xylo* compound (**6**). Alternatively compound (**7**) was treated with acetylsalicyloyl chloride[9] to give the chloro acetate (**9**) which on saponification gave the known[10] chloride (**10**), and mesylation of this then gave compound (**6**). 1,2-*O*-Isopropylidene-5-*O*-*p*-tolylsulphonyl-α-D-arabinofuranose (**11**) was first mesylated to give the disulphonate (**12**) which also underwent selective displacement of the primary toluene-*p*-sulphonate group to give the *arabino* compound (**5**). The values of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ for compounds (**5**) and (**6**) were 4, 0.5, and 1.5 Hz and 3.5, 0 and 3 Hz respectively. Comparison with these for the thio compound (**4**) (5, 1, and 1 Hz) clearly supported the *arabino* configuration for compound (**4**). However, in view of the small differences involved and the changes in geometry of a furanose ring when sulphur is substituted for oxygen, the structure (**4**) was finally confirmed by *X*-ray crystallography.[11]

The reaction of the dimethanesulphonate (**3**) with other nucleophiles was examined. Bromide, methoxide, thiocyanate, azide, and benzoate ions all reacted in a similar manner to

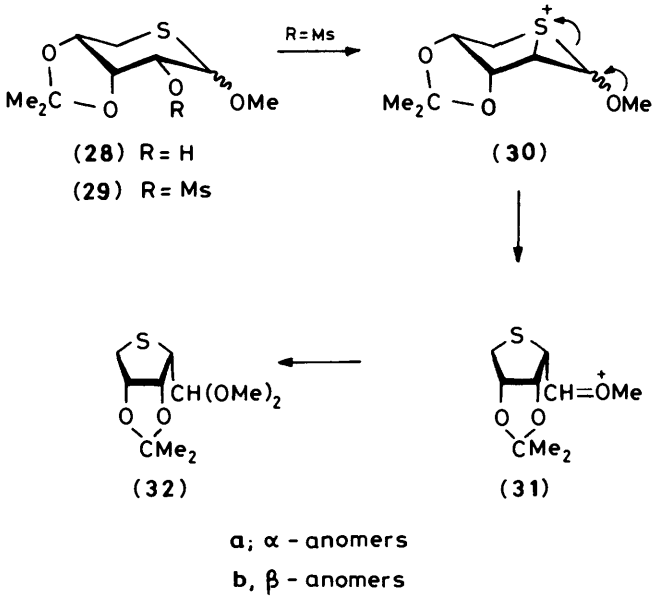
chloride ions giving rise to the 4-thio-β-L-arabinofuranose compounds (**13**), (**14**), (**15**), (**16**), and (**17**) whose structures followed from the close similarity of their ^{1}H n.m.r. spectra to that of compound (**4**) (see Table 2). Additional products were obtained in the azide and benzoate experiments. The former gave a second azide, isomeric with the major product, whose ^{1}H n.m.r. spectrum showed it to be the 4-azido-5-thioxylopyranose (**18**) with coupling constants almost identical to those of the dibenzoate (**2**). The second product from the benzoate experiment appeared to be the isomeric 4-*O*-benzoyl-1,2-*O*-isopropylidene-5-thio-α-D-xylopyranose (**19**) but it was more easily isolated as the corresponding alcohol (**20**) after debenzoylation with sodium methoxide. This reaction also gave a small amount of material, tentatively identified as 3,4-anhydro-1,2-*O*-isopropylidene-5-thio-α-D-ribopyranose (**21**), which had arisen from further reaction of the alcohol (**20**).

These reactions of the dimethanesulphonate (**3**), yielding products of ring contraction or displacement with retention of configuration, clearly proceed *via* the cyclic sulphonium ion (**22**). The dimethanesulphonate (**3**) almost certainly has the same $^4C_1$ conformation as is demonstrated by ^{1}H n.m.r. spectroscopy for the dibenzoate (**2**) ($J_{2,3}$ 8, $J_{3,4}$ 10, and $J_{4,5a}$ 10 Hz) and the sulphur is suitably positioned to intramolecularly displace the equatorial 4-methanesulphonate group. Attack then takes place preferentially at the primary position of the episulphonium ion (**22**) and is probably further influenced by the formation of a furanose ring bearing a *cis*-acetal, a particularly favourable system in carbohydrate chemistry.[12] A similar situation exists in the nitrous acid deamination of methyl 4-amino-4-deoxy-2,3-*O*-isopropylidene-α-D-lyxopyranoside which leads to methyl 2,3-*O*-isopropylidene-β-L-ribofuranoside.[13] It is interesting to note that the remaining methanesulphonate group in compounds (**4**) and (**13**)—(**17**) is unreactive even though it is on a β-carbon with respect to sulphur. Presumably this is because the tricyclic episulphonium ion which would result from intramolecular attack by sulphur is too strained to form readily.

It was expected that mesylation of methyl 2,3-*O*-isopropylidene-5-thio-β-D-ribopyranoside (**23**) would also lead to a reactive methanesulphonate (**24**) which, reacting *via* the episulphonium ion (**25**), would yield either 4-thio-L-lyxofuranoside or 5-thio-D-ribopyranoside products. Mesylation of compound (**23**) gave a reactive syrupy methanesulphonate (**24**) with the expected ^{1}H n.m.r. spectrum which clearly showed the $^4C_1$ conformation ($J_{4,5a}$ 10 Hz) with the equatorial methanesulphonate group. In contrast to the previous experiments treatment of this methanesulphonate with sodium benzoate in methanol gave only the known methyl 4-*O*-benzoyl-1,2-*O*-isopropylidene-5-thio-β-D-ribopyranoside (**26**) and none of the lyxofuranoside (**27**).

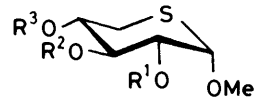


As both anomers of methyl 3,4-*O*-isopropylidene-5-thio-D-ribopyranoside (**28**) were available[6] it was of interest to convert them into the methanesulphonates (**29**) and examine their reactions. If, as expected, episulphonium ions (**30**) were formed, then a new course of reaction was possible in that they could be opened up by electron release from the methoxy group leading to the same ring contracted carboxonium ion (**31**). Both methanesulphonates (**29**) proved too reactive to permit any kind of characterisation and so were immediately allowed to react with methanol. Both gave the same final product, the dimethyl acetal (**32**), as expected from the reaction of the carboxonium ion (**31**) with methanol. The *cis*-relationship of 2-H and 3-H, and thus the D-*arabino* configuration, is clearly shown by the ^{1}H n.m.r. spectrum ($J_{2,3}$ 4 Hz).



In all the above cases a *cis*-acetal has been used to partially protect the thiopyranose ring. As has been shown,[4] these rings are capable of forming *trans*-acetals. Such an acetal should inhibit the formation of an episulphonium ion for it would lead to a highly strained structure with a *trans*-ring junction between two five membered rings. Methyl 5-thio-α-D-xylopyranoside (**33**)[14] reacted with 2,2-dimethoxypropane in the presence of an acid catalyst to give a mixture of 2,3- and 3,4-acetals (**34**) and (**35**) which could not be separated. Mesylation gave a mixture from which the 4-methanesulphonate (**36**) could be crystallised. Its structure followed from its ^{1}H n.m.r. spectrum in which 4-H appeared as the lowest field signal as a doublet of triplets (*J* 6.5, 9, and 9 Hz) which also demonstrated the $4C_1$ conformation. Although the crystalline sulphonate (**36**) decomposed on standing, this was evidently due to traces of acidic impurities for it remained unchanged when left in cold methanolic sodium methoxide. When heated in the same solution the only reaction it underwent was saponification leading to the parent alcohol (**34**). The methanesulphonate (**36**) could also be recovered unchanged after being heated with sodium benzoate in methanol. Clearly, even though the methanesulphonate group is equatorial, participation by sulphur is not occurring. That the inability to form the cyclic episulphonium ion (**37**) was inhibiting the reaction of the methanesulphonate (**36**) was shown by allowing it to react briefly with sodium acetate in hot aqueous acetic acid. The major product was methyl 4-*O*-acetyl-

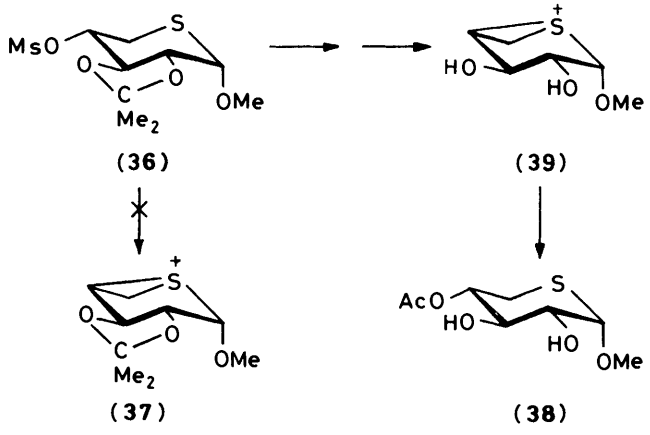
5-thio-α-D-xylopyranoside (**38**) together with a small amount of the xyloside (**33**). Apparently hydrolysis of the *trans*-acetal allows the cyclic episulphonium ion (**39**) to form which is then opened up by attack of acetate at C-4.



(**33**) $R^1 = R^2 = R^3 = H$

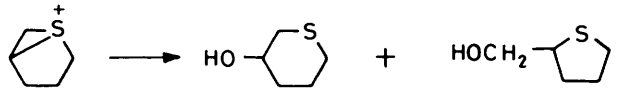
(**34**) $R^1 = R^2 = CMe_2$, $R^3 = H$

(**35**) $R^1 = H$, $R^2 = R^3 = CMe_2$



(**36**) (**39**) (**37**) (**38**)

The opening of the episulphonium ion (**39**) at C-4 contrasts with the C-5 opening of the related *xylo* ion (**22**) and, when considered alongside the *ribo* ion (**25**) where C-4 underwent attack, suggests that it is the overall stereochemistry of the episulphonium ion rather than primary-secondary considerations which determine the preferred route of reaction. The ions (**30**) are clearly special cases where the direction of opening is determined by electron release from the oxygen substituent. It is of interest that no products were obtained which contained an intact thiirane ring nor was a thiirane detected in the solvolysis of the unsubstituted episulphonium ion (**40**) which underwent opening mainly at the secondary position giving the tetrahydrothiopyran (**41**) (**82%**) and the tetrahydrothiofuran (**42**) (18%) as a minor product.[15]



(**40**) (**41**) (**42**)

The *trans*-acetal containing methanesulphonate (**36**) also failed to undergo displacement under more conventional S_N2 conditions. Thus it was recovered unchanged after being heated with sodium benzoate in *N,N*-dimethylformamide or hexamethylphosphoric triamide. This was unexpected, since a related oxygen compound, methyl 2,3-*O*-cyclohexylidene-4-*O*-*p*-tolylsulphonyl-α-D-xylopyranoside, reacts under these conditions to give methyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-β-L-arabinopyranoside.[16] A possible explanation for the lack of reactivity of the thio compound (**36**) is the 'hockey stick effect'[17] whereby the larger axial lone pair of the sulphur atom may repel the axial approach of a nucleophile to C-4.

Experimental

Melting points are uncorrected. Optical rotations were measured in chloroform solution. N.m.r. spectra were recorded at 90 MHz in deuteriochloroform solution with tetramethylsilane as an internal standard. Silica gel was used for t.l.c. (Gelman, ITLC Type SA) 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 < 40 °C (or < 10 °C for unstable sulphonate esters).

1,2-O-*Isopropylidene*-3,4-*di*-O-*methylsulphonyl*-5-*thio*-α-D-*xylopyranose* (**3**).—A solution of methanesulphonyl chloride (0.35 ml) in dichloromethane (5 ml) was added dropwise to a stirred solution of the diol (**1**)[6] (250 mg) and triethylamine (0.85 ml) in dichloromethane (5 ml) at 0 °C. After 10 min the mixture was washed with ice–water and the organic extract was dried and evaporated to a syrup (363 mg). This was dissolved in a small quantity of dichloromethane and crystallised by slow addition of either to give the *dimethanesulphonate* (**3**) (320 mg), m.p. 87—89 °C (decomp.); $[\alpha]_D$ +97° (*c*, 0.80). The compound decomposed within hours at room temperature and was too unstable to give a satisfactory microanalysis.

5-*Chloro*-5-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-4-*thio*-β-L-*arabinofuranose* (**4**).—The freshly prepared dimethanesulphonate (**3**) (250 mg) was added to a stirred solution of triethylamine hydrochloride (270 mg) in methanol (10 ml). The mixture was left overnight at room temperature and then evaporated to dryness. The residue was partitioned between dichloromethane and aqueous potassium hydrogen carbonate and the organic extract was dried and evaporated to a syrup (162 mg). Crystallisation from di-isopropyl ether gave the *chloro compound* (**4**) (90 mg), m.p. 103—104 °C, $[\alpha]_D$ +53° (*c*, 0.56) (Found: C, 35.4; H, 5.1. $C_9H_{15}ClO_5S_2$ requires C, 35.7; H, 5.0%).

5-*Chloro*-5-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-β-L-*arabinofuranose* (**5**).—A solution of methanesulphonyl chloride (2.8 ml) in dichloromethane (10 ml) was added slowly with stirring to an ice-cold solution of 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulphonyl-β-L-arabinofuranose (**11**)[18] (2.5 g) in dichloromethane (10 ml) containing triethylamine (3.0 ml). After 2 h at 0 °C the reaction was worked up as in the first experiment to give the disulphonate (**12**) (3.0 g) as a syrup. Anhydrous lithium chloride (1.6 g) was dissolved in hexamethylphosphoric triamide (8 ml) and toluene (30 ml) was added. The last traces of water were removed by distillation of toluene (20 ml). Further toluene (60 ml) was added and the solution was added to the syrupy disulphonate (**12**) and the mixture was heated under reflux overnight. After cooling, ether (50 ml) was added and the mixture was extracted repeatedly with water. The organic layer was dried and evaporated to dryness. Crystallisation of the residue from di-isopropyl ether gave the *chloro compound* (**5**) (0.9 g), m.p. 58—59 °C, $[\alpha]_D$ −4° (*c*, 0.50) (Found: C, 37.6; H, 5.3. $C_9H_{15}ClO_6S$ requires C, 37.7, H, 5.3%).

5-*Chloro*-5-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-α-D-*xylofuranose* (**6**).—(*a*) Using the same reagents, quantities and conditions as described in the previous experiment, 1,2-*O*-isopropylidene-α-D-xylofuranose (**7**) (1.4 g) was converted into the syrupy dimethanesulphonate (**8**) (2.5 g) which was then subjected to chloride displacement. The final product was chromatographed on silica and eluted with benzene–ether (9:1)

to give the desired *chloro compound* (**6**) (0.63 g), m.p. 68—69 °C (from di-*iso*propyl ether), $[\alpha]_D$ −77° (*c*, 1.00) (Found: C, 37.4; H, 5.4. $C_9H_{15}ClO_6S$ requires C, 37.7; H, 5.3%).

(*b*) A solution of the monoacetal (**7**) (340 mg) and acetylsalicyloyl chloride (400 mg) in anhydrous dioxane (5 ml) was left at room temperature for 48 h. Ether (20 ml) was added and the mixture was washed with dilute sodium carbonate, and the organic layer was dried and evaporated to give the crude 3-*O*-acetyl-5-chloro-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**9**) (250 mg). This was deacetylated with methanolic sodium methoxide to give the chloro alcohol (**10**) (190 mg), m.p. 93—94 °C (from di-isopropyl ether–light petroleum) (lit.,[10] 91—92 °C). This was mesylated in the usual way with methanesulphonyl chloride (0.17 ml) and triethylamine (0.4 ml) in dichloromethane (5 ml) to give the *title compound* (**5**) (210 mg), m.p. 68—69 °C.

5-*Bromo*-5-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-4-*thio*-β-L-*arabinofuranose* (**13**).—The dimethanesulphonate (**3**) (60 mg) was dissolved in dichloromethane (0.5 ml) and a solution of tetrabutylammonium bromide (260 mg) in methanol (4.5 ml) was added and the final solution was left overnight at room temperature. Work-up as in the related chloride experiment and crystallisation from ethyl acetate–ether gave the *bromo compound* (**13**) (40 mg), m.p. 110—111 °C, $[\alpha]_D$ +47° (*c*, 0.70) (Found: C, 31.2; H, 4.2. $C_9H_{15}BrO_5S_2$ requires C, 31.1; H, 4.35%).

1,2-O-*Isopropylidene*-3-O-*methylsulphonyl*-5-O-*methyl*-4-*thio*-β-L-*arabinofuranose* (**14**).—The dimethanesulphonate (**3**) (60 mg) was left in methanol (5 ml) containing sodium methoxide (50 mg) overnight at room temperature. Work-up as before and chromatography on silica gel gave the *methyl ether* (**14**) (44 mg) as a syrup, $[\alpha]_D$ +30° (*c*, 0.32) (Found: M^+, 298.0531. $C_{10}H_{18}O_6S_2$ requires *M*, 298.0545).

5-*Deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-4-*thio*-5-*thiocyanato*-β-L-*arabinofuranose* (**15**).—A solution of potassium thiocyanate (80 mg) and the methanesulphonate (**3**) (60 mg) in dichloromethane (0.05 ml) and methanol (4.5 ml) was left overnight at room temperature. The usual work-up yielded a syrup (60 mg) which was chromatographed on silica gel (3 g) when elution with benzene–ether (1:1) gave the *thiocyanate* (**15**) (44 mg) as a syrup, $[\alpha]_D$ +69° (*c*, 0.38), $\nu_{max.}$ 2 170 cm^{-1} (SCN) (Found: C, 36.8; H, 4.6; N, 4.45. $C_{10}H_{15}NO_5S_3$ requires C, 36.9; H, 4.65; N, 4.3%).

Reaction of the Dimethanesulphonate (**3**) *with Azide Ions.*—The dimethanesulphonate (**3**) (250 mg) was dissolved in dichloromethane (1 ml) and a solution of tetramethylammonium azide (320 mg) in methanol (20 ml) was added. After 15 h at room temperature the usual work-up gave a syrup (130 mg) which t.l.c. showed to contain two components. These were separated by preparative t.l.c. (multiple developments: benzene × 5). The faster running component was identified as 5-*azido*-5-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-4-*thio*-β-L-*arabinofuranose* (**16**) (73 mg), m.p. 65—66 °C (from ether–light petroleum), $[\alpha]_D$ +60° (*c*, 0.39), $\nu_{max.}$ 2 130 cm^{-1} (N_3) (Found: C, 35.0; H, 4.7; N, 13.6. $C_9H_{15}O_5N_3S_2$ requires C, 34.9; H, 4.9; N, 13.6%). The slower running component was shown to be the isomeric 4-*azido*-4-*deoxy*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-5-*thio*-α-D-*xylopyranose* (**18**) (48 mg), m.p. 85—86 °C (from di-isopropyl ether), $[\alpha]_D$ +200° (*c*, 0.35), $\nu_{max.}$ 2 130 cm^{-1} (N_3) (Found: C, 34.7; H, 4.8; N, 13.9%).

Reaction of the Dimethanesulphonate (**3**) *with Benzoate Ions.*—A solution of the dimethanesulphonate (**3**) (400 mg) and sodium benzoate (1.0 g) in methanol (20 ml) and dichloromethane (1 ml) was left overnight at room temperature. Work-up as before yielded a syrup (300 mg) containing two components which could not be separated chromatographically. An ethereal solution eventually gave crystals of one of the components which was identified as 5-O-*benzoyl*-1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-4-*thio*-β-L-*arabinofuranose* (**17**) (180 mg), m.p. 99—100 °C (decomp.) $[\alpha]_D$ +180° (*c*, 0.40); $\nu_{max.}$ 1 725 cm^{-1} (CO) (Found: C, 49.4; H, 5.3. $C_{16}H_{20}O_7S_2$ requires C, 49.5; H, 5.2%). The mother liquors were evaporated and the residue was dissolved in methanol (3.5 ml) containing sodium methoxide (30 mg). After 1 h at room temperature the solution was evaporated to dryness, the residue was partitioned between water and dichloromethane and the organic extract was dried and evaporated to a syrup (30 mg). Chromatography on silica (2 g) and elution with benzene–ether (3:1) yielded first a syrup (15 mg), tentatively identified as 3,4-anhydro-1,2-*O*-isopropylidene-5-thio-α-D-ribopyranose (**21**), *m/z* 188 (M^+), 173 (M^+ − Me), 170 ($M^+ - H_2O$), and then 1,2-O-*isopropylidene*-3-O-*methylsulphonyl*-5-*thio*-α-D-*xylopyranose* (**20**) (10 mg), m.p. 83—84 °C, $[\alpha]_D$ +264° (*c*, 0.52); $\nu_{max.}$ 3 500 cm^{-1} (OH) (Found: C, 38.2; H, 5.6. $C_9H_{16}O_6S_2$ requires C, 38.0; H, 5.7%).

Mesylation of Methyl 2,3-O-*Isopropylidene*-5-*thio*-β-D-*ribopyranoside* (**23**).—A solution of methanesulphonyl chloride (0.02 ml) in dichloromethane (1 ml) was added to a solution the acetal (**23**)[6] (30 mg) and triethylamine (0.05 ml) in dichloromethane (1 ml) at 0 °C. After 45 min the usual work-up gave the methanesulphonate (**24**) (45 mg) as an unstable syrup which was used without further purification.

Reaction of Sodium Benzoate with the Methanesulphonate (**24**).—The above compound (**24**) was dissolved in methanol (3 ml) containing sodium benzoate (125 mg). After 2 days at room temperature the solvent was removed and the residue partitioned between water and dichloromethane. The organic extract was dried and evaporated to a syrup (25 mg) which was shown by t.l.c. to contain two components. Chromatography on silica, eluting with benzene–ether (9:1), gave methyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-5-thio-β-D-ribopyranoside (**26**) (21 mg) whose ^1H n.m.r. spectrum was idenctical with that of authentic material.[6] The minor component (3 mg) was not identified.

2,5-*Dideoxy*-2,5-*epithio*-3,4-O-*isopropylidene*-D-*arabinose Dimethyl Acetal* (**32**).—(*a*) *From methyl* 3,4-O-*isopropylidene*-5-*thio*-α-D-*ribopyranoside* (**28a**). Methanesulphonyl chloride (0.04 ml) in dichloromethane (1 ml) was added to a solution of the acetal (**28a**)[6] (65 mg) and triethylamine (0.12 ml) in dichloromethane (1 ml) at 0 °C. After 2 h the solvent was removed and methanol (3 ml) and anhydrous sodium hydrogen carbonate (200 mg) were added to the residue and the mixture was stirred overnight at room temperature. The reaction mixture was evaporated to dryness and the residue was partitioned between water and dichloromethane. The organic layer was dried and evaporated to give a syrup (32 mg) which crystallised from light petroleum at −20 °C to give the *title compound* (**32**) (10 mg), m.p. 34—35 °C, $[\alpha]_D$ −45° (*c*, 0.40) (Found: C, 51.4; H, 7.6. $C_{10}H_{18}O_4S$ requires C, 51.3; H, 7.7%.)

(*b*) *From methyl* 3,4-O-*isopropylidene*-5-*thio*-β-D-*ribopyranoside* (**28b**). Treatment of the β-anomer (**28b**)[6] (30 mg) as described above for the α-anomer (**28a**) also gave the epithio compound (**32**) (10 mg), m.p. and mixed m.p. 34—35 °C.

Methyl 2,3-O-*Isopropylidene*-4-O-*methylsulphonyl*-5-*thio*-α-D-*xylopyranoside* (**36**).—Methyl 5-thio-α-D-xylopyranoside (**33**)[14] (360 mg) was added to a stirred solution of toluene-*p*-sulphonic acid (500 mg) in 2,2-dimethoxypropane (10 ml). Solution quickly occurred and after 5 min the reaction was

neutralised (Na_2CO_3), filtered and evaporated to a syrup. This was partitioned between dichloromethane and dilute potassium hydrogen carbonate, the organic extract was dried and evaporated to a syrup (529 mg) which was chromatographed on silica (3 g). Elution with benzene–ether (9:1) gave first a minor fast running component (15 mg) and then a mixture of the acetals (**34**) and (**35**) (410 mg). This mixture was mesylated in the usual way using methanesulphonyl chloride (0.25 ml) and triethylamine (0.65 ml) in dichloromethane (7 ml). The usual work-up gave a syrup (472 mg) which crystallised on addition of di-isopropyl ether to give the 4-*methanesulphonate* (**36**) (174 mg), m.p. 62—63 °C (decomp.), $[\alpha]_D$ +230° (*c*, 0.31). The compound decomposed too quickly to give a satisfactory microanalysis.

Reaction of the Methanesulphonate (**36**) *with Sodium Methoxide.*—A solution of the methanesulphonate (**36**) (40 mg) in methanol (2.5 ml) containing sodium methoxide (60 mg) was heated in a sealed tube at 100 °C for 1 h. The solution was then evaporated and the residue was partitioned between water and dichloromethane. The extract was dried and evaporated to a syrup (21 mg) which was purified by chromatography on silica (2 g), eluting with benzene–ether (9:1), to give *methyl* 2,3-O-*isopropylidene*-5-*thio*-α-D-*xylopyranoside* (**34**) (15 mg), m.p. 85—86 °C (from light petroleum), $[\alpha]_D$ +236° (*c*, 0.55) (Found: C, 48.8; H, 7.35. $C_9H_{16}O_4S$ requires C, 49.1; 7.3%).

Action of Sodium Acetate in Aqueous Acetic Acid on the Methanesulphonate (**36**).—A solution of compound (**36**) (44 mg) in 80% acetic acid (5 ml) containing sodium acetate (23 mg) was kept at 100 °C for 45 min. Solvents were removed and the residue was triturated with acetone–ether (1:1). Evaporation of the extract gave a mixture which was chromatographed on silica (2 g) eluting with ethyl acetate–ethanol (9:1). The major product eluted first and was identified as *methyl* 4-O-*acetyl*-5-*thio*-α-D-*xylopyranoside* (**38**) (22 mg), m.p. 110—111 °C (from ethyl acetate–ether), $[\alpha]_D$ +270° (*c*, 0.60); $\nu_{max.}$ 1 720 (CO) and 3 400 cm^{-1} (OH) (Found: C, 43.2; H, 6.25. $C_8H_{14}O_5S$ requires C, 43.1; H, 6.35%). Deacetylation of a sample of the acetate (**38**) gave material chromatographically indistinguishable from the minor product (2 mg) which eluted second from the above column and from methyl 5-thio-α-D-xylopyranoside (**33**).

Acknowledgements

We thank the S.E.R.C. for a grant (to C. J. W.), Dr. W. Clegg for the *X*-ray crystallographic determination, Dr. M. N. S. Hill and Mr. I. McKeag (for n.m.r. spectra) and Messrs P. Kelly and S. Addison (for mass spectra).

References

1 Part 7, N. A. Hughes and N. M. Munkombwe, *Carbohydr. Res.*, 1985, **136**, 411.
2 C. J. Clayton and N. A. Hughes, *Carbohydr. Res.*, 1967, **4**, 32.
3 C. J. Clayton, N. A. Hughes, and T. D. Inch, *Carbohydr. Res.*, 1975, **45**, 55.
4 W. Clegg, N. A. Hughes, and N. A. L. Al-Masoudi, *J. Chem. Soc., Chem. Commun.*, 1979, 320.
5 Preliminary communication: W. Clegg, N. A. Hughes, and C. J. Wood, *J. Chem. Soc., Chem. Commun.*, 1975, 300.
6 N. A. Hughes and C. J. Wood, *Carbohydr. Res.*, 1976, **49**, 225.
7 R. K. Crossland and K. L. Servis, *J. Org. Chem.*, 1970, **35**, 3195.
8 H. B. Sinclair, *Carbohydr. Res.*, 1970, **15**, 147.
9 A. A. Akhren, G. V. Zaitseva, and I. A. Mikhailopulo, *Carbohydr. Res.*, 1973, **30**, 223.
10 S. Akuja and T. Osawa, *Yakugaku Zasshi*, 1956, **76**, 1280.
11 W. Clegg, *Acta Crystallogr.*, 1975, **B31**, 2722.
12 J. A. Mills, *Adv. Carbohydr. Chem. Biochem.*, 1955, **10**, 1.
13 J. S. Brimacombe, J. Minshall, and L. C. N. Tucker, *Carbohydr. Res.*, 1974, **32**, C7.
14 R. L. Whistler and T. Van Es., *J. Org. Chem.*, 1963, **28**, 2303.
15 S. Ikegami, T. Asai, K. Tsuneoka, S. Matsumara, and S. Akaboshi, *Tetrahedron*, 1974, **30**, 2087.
16 F. H. Bissett, M. E. Evans, and F. W. Parrish, *Carbohydr. Res.*, 1967, **5**, 184.
17 N. S. Zefirov, V. S. Blagoveschensky, I. U. Kazimirchik, and N. S. Surova, *Tetrahedron*, 1971, **27**, 3111.
18 P. A. Levene and J. Compton, *J. Biol. Chem.*, 1936, **116**, 189.

Received 6th August 1985; *Paper* 5/1366