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SYNTHESIS OF 5-THIO-D-ALLOSE AND THE METHYL 5-THIO-α- AND -β-D-ALLOPYRANOSIDES*

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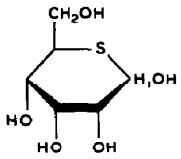
ABSTRACT

5,6-Anhydro-1,2-*O*-isopropylidene-3-*O*-methanesulphonyl-α-D-idofuranose was converted, *via* the related *gluco*-5,6-episulphide, into 6-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-3-*O*-methanesulphonyl-5-thio-α-D-glucofuranose (**9**). Replacement of the acetyl groups of **9**, or the related 3-toluene-*p*-sulphonate, by an isopropylidene group and saponification of the sulphonate group gave 1,2-*O*:5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-glucofuranose (**2**). Epimerisation at C-3 of **2** by an oxidation–reduction sequence gave 1,2-*O*:5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-allofuranose (**20**) which was hydrolysed to 5-thio-D-allose (**1**). Methyl 5-thio-α- and -β-D-allopyranoside were obtained from **1** or by methanolysis of **20**. Similar hydrolysis or methanolysis of **2** gave 5-thio-D-glucose or methyl 5-thio-α- and -β-D-glucopyranoside, respectively, thus providing a convenient variation on earlier synthetic routes to these compounds. ^{13}C-N.m.r. data are given for several of these 5-thio-*allo* and -*gluco* derivatives.

INTRODUCTION

Two of the first 5-thiohexopyranoses to be synthesised were 5-thio-L-idose[2] and 5-thio-D-glucose[3]. More recently, 5-thio-D-galactose[4] has been obtained and our own first approaches to this series have been concerned with 5-thio-D-allose (**1**) and 5-thio-D-altrose[5]. We now report in full on **1**.



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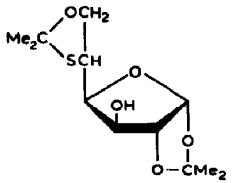

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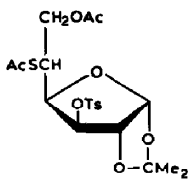

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*5-Thiopyranoses. Part 9, For Part 8, see ref. 1.
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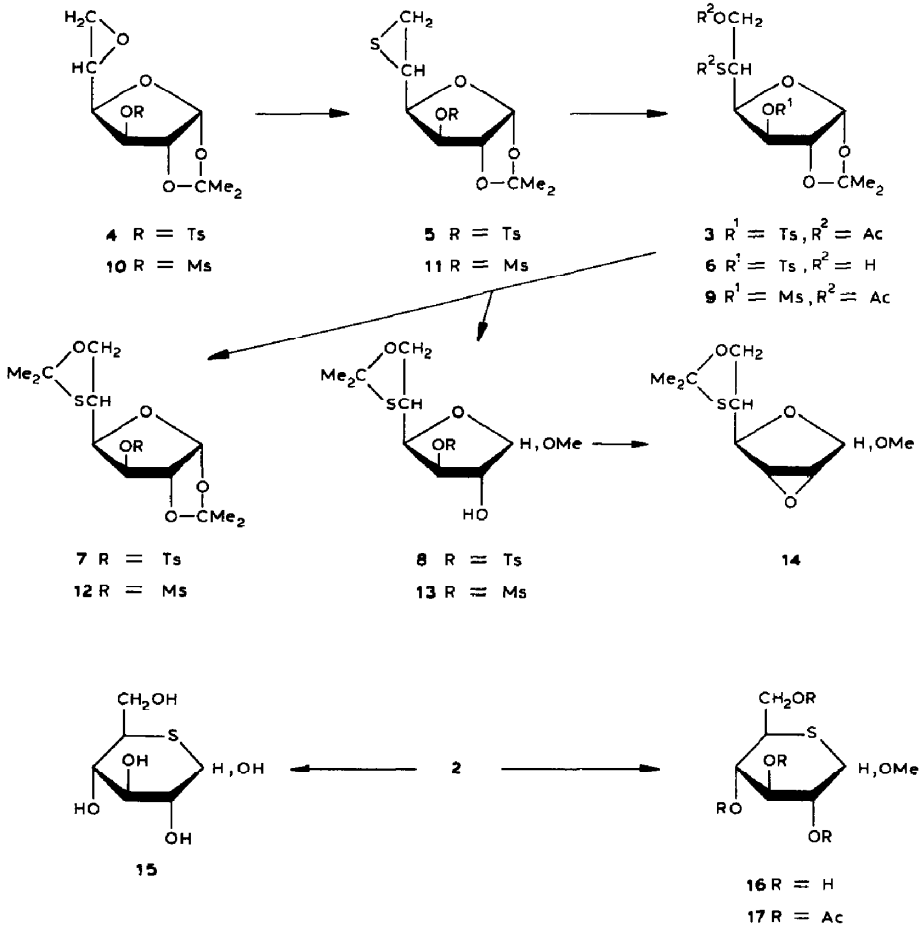
DISCUSSION

The most frequently used synthesis[6] of D-allose is by epimerisation at C-3 of D-glucose by means of an oxidation–reduction sequence on 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and an obvious route to 5-thio-D-allose (**1**) is by application of this sequence to the 5-thio analogue **2**. A convenient starting-material appeared to be the 5-thioglucose derivative **3** which had been obtained[7] from the *ido*-epoxide **4** *via* the *gluco*-episulphide **5**.

Treatment of **3** with sodium methoxide gave only the episulphide **5** and none of the thiol **6**. This reaction of vicinal acetate thioacetates has been observed[8] before and results from initial cleavage of the thioacetate, with the resulting thiolate causing displacement of the adjacent acetate group. Reduction of **3** with lithium aluminium hydride did not proceed cleanly and further suggested that alkaline reagents were best avoided. The replacement of the acetyl groups of **3** by an isopropylidene group was best achieved in a one-pot reaction involving methanol, 2,2-dimethoxypropane, and an acid catalyst. Presumably, transesterification with

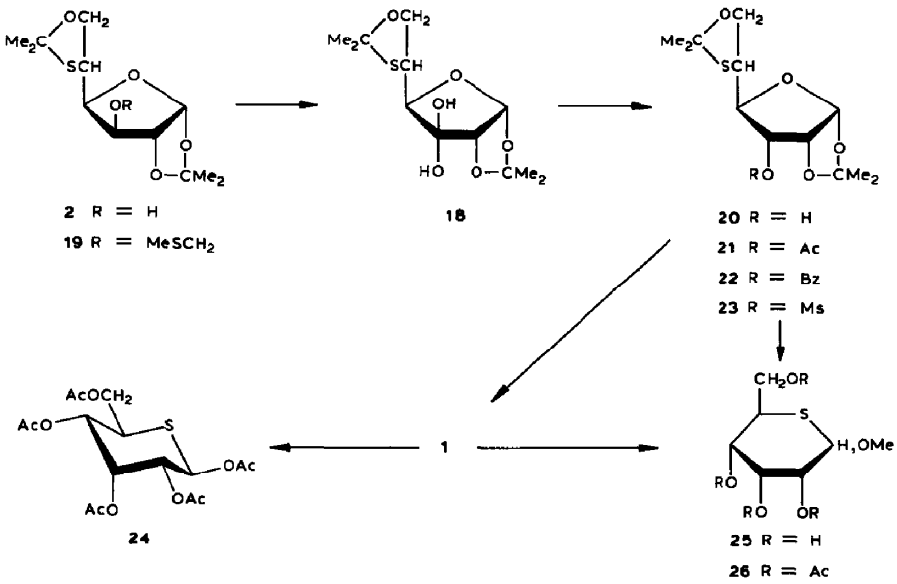


methanol occurred first, leading to the thiol-alcohol **6**, which was then converted into the acetal **7** by the 2,2-dimethoxypropane. Two by-products were detected, which appeared to be the methyl furanosides **8** formed by the competing methanolysis of the 1,2-*O*-isopropylidene groups of **3**, **6**, or **7**. Saponification of the sulphonate group in **7** by sodium methoxide proceeded smoothly to give the desired diacetal **2**.

Later, it was found that the mesylate **9** was a more convenient starting-material than the tosylate **7**, since the epoxide **10** was more easily prepared[9] than the corresponding tosylate **4**, and the episulphide **11** and the diacetal **12** were more easily crystallised than the related tosylates **5** and **7**. As with **3**, the deacetylation–acetalation of **9** was accompanied by methanolysis of the 1,2-*O*-isopropylidene group, leading to the furanosides **13**. These products were not separated but treated with sodium methoxide to give the *allo*-epoxides **14**, which were also obtained from the corresponding tosylates **8**. The sulphonate group of **12** was readily cleaved to give the diacetal **2**.

Confirmation of the structure of **2** came from its hydrolysis to 5-thio-D-glucose[3] (**15**). Methanolysis of **2** gave the known methyl 5-thio-α- and -β-D-gluco-pyranosides (**16**) in the same proportions (αβ-ratio 4:1) as found when prepared[10] from the free sugar **15**. In the earlier preparation, they were isolated as their tetra-acetates **17** but, in our hands, they could be isolated as the glycosides **16** by chromatography on a basic ion-exchange resin[11]. The α anomer **16a** was eluted first, as expected from its 1,2-*cis* stereochemistry[11]. All of the intermediates in this route from D-glucose to **15** and **16**, *via* the epoxide **10** and the diacetal **2**, are highly crystalline and thus it offers a convenient variation on earlier syntheses.

Oxidation of the diacetal **2** was best achieved with acetic anhydride–methyl



sulphoxide[12] and the resulting ketone was isolated as the crystalline hydrate **18**. Unfortunately, the methylthiomethyl ether **19** was a major by-product. Reduction of **18** with sodium borohydride appeared to proceed stereospecifically, giving only the *allo*-diacetal **20**.

The acetate **21**, benzoate **22**, and mesylate **23** were crystalline and their ^{1}H-n.m.r. spectra (Table I) demonstrated the *allo* configuration ($J_{2,3}$ 5.0 Hz). Indeed, the *J* values for H-1,2,3,4 of the acetate **21** were almost identical to those of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[13], the respective $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ values being 4.0, 5.0, and 9.0 Hz, and 3.7, 4.7, and 8.0 Hz.

Hydrolysis of the diacetal **20** in hot aqueous acetic acid gave crystalline 5-thio-D-allose (**1**) which reacted only slowly with sodium nitroprusside, indicating a pyranose form lacking a free thiol group. The $[\alpha]_D$ value of **1** increased from +75 to +119° (water), suggesting the β-pyranose form, and this was confirmed by acetylation which gave a single penta-acetate, the ^{1}H-n.m.r. spectrum of which was consistent with 1,2,3,4,6-penta-*O*-acetyl-5-thio-β-D-allopyranose (**24**) in the $^4C_1$ form ($J_{1,2}$ 9.5, $J_{4,5}$ 10.5 Hz). The ^{1}H-n.m.r. spectrum of **1** was too complex for analysis and the ^{13}C-n.m.r. spectrum showed 10 lines (see later), probably as a consequence of mutarotation. D-Allose also crystallises in the β-pyranose form[14].

When 5-thio-D-allose (**1**) was treated with cold methanolic hydrogen chloride for 1 day, or briefly with the boiling reagent, it was converted into the methyl α,β-pyranosides **25**. The same mixture could be obtained by similar treatment of the diacetal **20**. Chromatography of the α,β-mixture **25** on a basic ion-exchange resin gave, first, a syrupy (+)-glycoside and then a crystalline (−)-glycoside in the ratio 2:3. The order of elution and optical rotations suggested that these products were the α (**25a**) and β anomer (**25b**), respectively, and this conclusion was confirmed by their conversion into the related tetra-acetates **26**, the ^{1}H-n.m.r. spectra (Table II) of which were fully resolved. Thus, **26a** had $J_{1,2}$ 3.5 and $J_{4,5}$ 11.0 Hz, whereas **26b** had $J_{1,2}$ 8.5 and $J_{4,5}$ 9.0 Hz, which clearly demonstrated the anomeric configurations and the $^4C_1$ conformations. The slightly smaller values of $J_{4,5}$ for **26b** suggested a small contribution from the $^1C_4$ form, perhaps as a result of the anomeric effect. A similar situation is seen in the spectra of methyl 2,3,4,6-tetra-*O*-acetyl-5-thio-D-glucopyranosides (**17**), $J_{4,5}$ being smaller (9.5 Hz) for the β anomer **17b** (*cf.* 11.0 Hz for the α anomer **17a**). The same effect has been found in methyl 2,3,4-tri-*O*-acetyl-5-thio-α- and -β-D-ribopyranoside and has been discussed at length[15].

The ^{13}C-n.m.r. spectra of the allosides **25** are recorded in Table III. The signals for the sulphur-substituted C-5 appear at highest field and also distinguish the two anomers. The α anomer **25a** has MeO-1 *syn*-diaxial to H-5, which increases[16] the shielding of C-5, the signal of which had the lower chemical shift. The signals for C-1, C-6, and OMe were also readily identified but, apart from the values for C-5, the chemical shift differences between the anomers are only slight. No attempt was made to assign the signals for C-2,3,4 unambiguously, but comparison with the spectra[17] of methyl α- and β-D-allopyranoside suggested that the main

TABLE I

^{1}H-N.M.R. DATA FOR FURANOSE COMPOUNDS

Compound	*Chemical shift (p.p.m.)*							*Other signals*	*Coupling constant (Hz)*						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
2[a]	5.83	4.42			3.5–4.4			2.69 (OH); 1.66, 1.60, 1.47, 1.29 (2 CMe_2)	3.5	0					
7[b,d]	5.93	4.82	4.87	4.22	3.52	4.38	4.05	2.47 (ArMe); 1.59, 1.52, 1.49, 1.30 (2 CMe_2)	4.0	0	3.0	10.5	2.5	4.5	10.0
9[b]	5.93	4.85	5.06	4.41	4.04	4.37	4.32	3.04 (SO_2Me); 2.33 (SCOMe); 2.02 (OCOMe); 1.47, 1.29 (CMe_2)	3.5	0	2.5	11.0	3.0	4.5	11.5
11[a]	5.92	4.72	4.86	3.55	3.00	2.64	2.40	3.10 (SO_2Me); 1.44, 1.30 (CMe_2)	3.5	0	3.0	8.5	6.0	5.0	1.0
12[b]	5.95	4.82	4.95	4.31	3.66	4.40	4.14	3.10 (SO_2Me); 1.68, 1.60, 1.51, 1.31 (2 CMe_2)	4.0	0	3.0	10.0	2.0	5.0	10.0
14a[c]	4.81	3.18	3.38	4.17	2.98	4.20	3.77	3.33 (OMe); 1.48, 1.42 (CMe_2)	1.0	2.5	0	9.0	2.5	5.0	10.0
14b[b]	4.97	3.69[e]	3.64[e]	4.02	3.40	4.44	4.09	3.37 (OMe); 1.61, 1.70 (CMe_2)	0	2.5	0	11.0	2.5	5.0	9.5
19[a]	5.73	4.43			3.6–4.4			4.60 (OCH_2S); 2.17 (SMe); 1.63, 1.54, 1.44, 1.25 (2 CMe_2)	4.0	0					
20[a]	5.61	4.46			3.6–4.2			2.34 (OH); 1.62, 1.58, 1.52, 1.31 (2 CMe_2)	4.0	4.5					
21[c]	5.45	4.51	4.89	4.29	3.57	4.02	3.81	1.74 (COMe); 1.53, 1.42, 1.37, 1.04 (2 CMe_2)	4.0	5.0	9.0	6.0	3.5	5.5	10.0
22[c,d]	5.47	4.67	5.03	4.49	3.61	4.13	3.88	1.54, 1.44, 1.40, 1.07 (2 CMe_2)	4.0	5.0	8.5	6.5	3.5	5.5	10.0
23[c]	5.12	4.14	4.49	4.08	3.49	3.81	3.65	2.39 (SO_2Me); 1.53, 1.37 (2), 1.00 (2 CMe_2)	4.0	5.0	9.0	6.0	4.0	6.5	10.5

[a]In CCl_4. [b]In $CDCl_3$. [c]In C_6D_6. [d]Also showed signals in aromatic region. [e]Assignment uncertain.

TABLE II

^{1}H-N.M.R. DATA FOR PYRANOSE COMPOUNDS

Compound	*Chemical shift (p.p.m.)*							*Other signals*	*Coupling constant (Hz)*						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
17a[a,d]	4.60	5.00	5.28	5.13	3.33	4.41	3.88	3.46 (OMe); 2.03 (2), 1.97, 1.94 (4 COMe)	3.0	10.0	9.0	11.0	5.0	3.0	12.0
17b[c,d]	4.19	5.56	5.22	5.45	2.70	4.29	4.00	3.46 (OMe); 2.01, 1.97 (2), 1.94 (4 COMe)	8.0	8.0	10.0	9.5	5.5	4.0	12.0
24[b]	6.11	5.29	5.58	5.20	3.66	4.24	4.22	2.16, 2.09, 2.08, 2.02, 2.01 (5 COMe)	9.5	2.5	2.5	10.5	5.0	4.0	11.5
26a[b]	4.62	5.20	5.60	5.26	3.62	4.40	4.16	3.44 (OMe); 2.14, 2.08, 2.07, 2.00 (4 COMe)	3.5	3.0	3.0	11.0	4.5	3.0	12.0
26b[b]	4.79	5.26	5.54	5.21	3.48	←4.26→		3.48 (OMe); 2.14, 2.08, 2.04, 2.01 (4 COMe)	8.5	3.0	2.5	9.0	5.0	5.0	

[a]In CCl_4. [b]In $CDCl_3$. [c]In C_6D_6. [d]Measured at 220 MHz.

TABLE III

^{13}C-N.M.R. DATA[a]

Compound	*Chemical shifts (p.p.m.)*										
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*OMe*	O_2CMe_2	$OSCMe_2$	O_2CMe_2	$OSCMe_2$
allo *series*											
1a	76.0[b]	74.1[b]	72.3[b]	72.3[b]	39.9	61.4					
1b	76.3[b]	75.8[b]	73.2[b]	72.2[b]	45.3	62.1					
25a	85.4	75.3[b]	72.6[b]	72.3[b]	39.1	61.5	57.8				
25b	84.2	74.9[b]	72.8[b]	71.8[b]	45.7	62.7	59.0				
20	103.5	80.7	73.9	79.4	52.5	71.7		112.9	94.9	26.6, 26.5	30.9(2)
28[c]	103.9	79.8	72.5	78.9	75.6	65.8		112.8, 109.8		26.5(2), 26.2, 25.0	
gluco *series*											
15[d]	75.4	77.6	75.9	45.4	62.6						
16a	84.7	76.3[b]	75.5[b]	74.8[b]	44.1	61.5	57.4				
16b	86.7	79.4[b]	79.4[b]	76.0[b]	48.1	63.3	61.1				
2	105.3	85.2	75.2	82.6	48.0	72.4		111.7	92.6	26.8, 26.2	31.5, 30.7
27[c]	105.1	85.1	74.7	81.2	72.9	67.5		111.4, 109.2		26.5(2), 25.9, 25.0	

[a]Measured at 22.63 MHz in $CDCl_3$. [b]Assignments may be interchanged. [c]Ref. 21. [d]Ref. 17.

effect of replacing oxygen by sulphur at C-5 was on the α-carbons, C-1 and C-5, the signals of which were shifted upfield by 15–16 and 28–29 p.p.m., respectively. Surprisingly, C-6 was not obviously affected, but it is possible that the signal of the other β-carbon, C-4, may be shifted downfield.

The ^{13}C-n.m.r. spectrum of 5-thio-D-allose showed 10 lines as a result of mutarotation (Table III) and an attempt was made to assign them to the α (**1a**) and β form (**1b**) by consideration of the differences in intensity and by comparison with the values for the allosides **25a** and **25b**. When mutarotation was complete, the intensities of the signals suggested an αβ-ratio of ~1:1. This finding contrasts with that for D-allose which, at equilibrium, consists[18] of the β-pyranose (77.5%), α-pyranose (14%), and furanose (8.5%) forms. A similar situation has been found with 5-thio-D-arabinose[19], 5-thio-D-xylose[20], and 5-thio-D-glucose[21]. The explanation offered by Lambert and Wharry[20,21] is that puckering of the pyranose ring by the sulphur atom accentuates the vicinal equatorial–equatorial interactions and diminishes the vicinal axial–equatorial interactions. The α anomer of each of the above sugars having a common stereochemistry at C-2 would reflect this effect.

The ^{13}C-n.m.r. spectrum of 5-thio-D-glucose (**15**) showed six major lines[21] (listed in Table III together with those of the glucosides **16**). The C-5 signals of **16** are also found at highest field and again show the biggest difference between the two anomers, the signal of C-5 of the α anomer **16a** having the lower chemical shift. 5-Thio-D-glucose (**15**) exists[21] mainly in the α-pyranose form and its ^{13}C-n.m.r. spectrum closely resembles that of the α-glucoside **16a**.

Recently, Buchanan and co-workers have shown[22] that the chemical shifts of the signals of the acetal and methyl carbons of cyclic isopropylidene acetals are diagnostic of the ring systems involved. Diacetals **2** and **20** contain one 1,3-oxathiolane ring and one 1,3-dioxolane ring. The ^{13}C-n.m.r. spectra[17] of these compounds and also those of the well-known 1,2:5,6-di-*O*-isopropylidene-α-D-gluco- (**27**) and -allo-furanose (**28**) are also listed in Table III. The effect of substituting sulphur for oxygen at C-5 is greatest on C-5, the signal of which is shifted upfield by 23–25 p.p.m. The signal of the 5,6-acetal carbon atom is also shifted upfield by 15–17 p.p.m., whereas those of the methyl groups are shifted downfield by ~6 p.p.m. A similar downfield shift is observed for the signal of C-6 in contrast to the allosides **25** where the signal for C-6 is unaffected. The signal of the remaining β-carbon with respect to sulphur, C-4, shows only a slight downfield shift (~1 p.p.m.).

EXPERIMENTAL

General methods. — See Part 6[19].

*1,2-O:5,6-S,O-Di-isopropylidene-5-thio-3-O-toluene-*p*-sulphonyl-α-D-gluco-furanose* (**7**). — A solution of 6-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose[7] (**3**, 0.47 g) in methanol (6 mL) and 2,2-dimethoxypropane (2 mL) containing toluene-*p*-sulphonic acid (0.10 g) was left

overnight at room temperature, then neutralised with anhydrous sodium carbonate, filtered, and concentrated to dryness. The residue was partitioned between dichloromethane and dilute aqueous potassium hydrogencarbonate. The organic solution was dried and concentrated. Column chromatography (benzene–ether, 9:1) of the syrupy residue gave, first, **7** (0.22 g, 55%), m.p. 92–93° (from aqueous methanol), $[\alpha]_D$ −102° (*c* 0.9, dichloromethane) (Found: C, 53.1; H, 6.0. $C_{19}H_{26}O_7S_2$ calc.: C, 53.0; H, 6.1%).

Eluted second was a syrupy product identified tentatively as methyl 5,6-*S*,*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-glucofuranoside (**8a**; 12 mg, 3%), $[\alpha]_D$ −14° (*c* 0.6, dichloromethane). ^{1}H-N.m.r. data ($CDCl_3$): *inter alia* δ 5.08 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1), 3.58 (s, 3 H, OMe), 2.56 (s, 3 H, Ar*Me*), 1.60 and 1.53 (2 s, 6 H, CMe_2). Eluted later was a syrupy product identified tentatively as the β-furanoside **8b** (30 mg, 7%), $[\alpha]_D$ −134° (*c* 0.5, dichloromethane). ^{1}H-N.m.r. data ($CDCl_3$): *inter alia* δ 4.84 (s, 1 H, H-1), 3.40 (s, 3 H, OMe), 2.54 (s, 3 H, Ar*Me*), 1.60 and 1.55 (2 s, 6 H, CMe_2).

*5,6-Dideoxy-5,6-epithio-1,2-*O*-isopropylidene-3-*O*-methanesulphonyl-α-*D*-glucofuranose* (**11**). — A solution of 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-methanesulphonyl-β-L-idofuranose[9] (**10**, 3.2 g) and thiourea (1.7 g) in methanol (50 mL) was left at room temperature overnight and then concentrated. The residue was partitioned between water and ether–dichloromethane (4:1). The organic solution was dried and concentrated, and the residue was crystallised from ethanol to give **11** (3.2 g, 95%), m.p. 93–96°, $[\alpha]_D$ −98° (*c* 0.9, dichloromethane) (Found: C, 40.3; H, 5.4. $C_{10}H_{16}O_6S_2$ calc.: C, 40.5; H, 5.4%).

*6-*O*-Acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-3-*O*-methanesulphonyl-5-thio-α-*D*-glucofuranose* (**9**). — A mixture of **11** (3.2 g), anhydrous sodium acetate (4.0 g), acetic anhydride (44 mL), and acetic acid (8 mL) was boiled under reflux for 15 h, then cooled, added to ice–water (300 mL), and stirred for 2 h. The precipitate was collected and dried, and a solution in dichloromethane (10 mL) was passed through silica gel (5 g) to remove coloured impurities. The eluate was concentrated and the residue was crystallised from ethanol to give **9** (2.8 g, 65%), m.p. 157–159°, $[\alpha]_D$ −11° (*c* 0.9, dichloromethane) (Found: C, 42.6; H, 5.3. $C_{14}H_{22}O_9S_2$ calc.: C, 42.2; H, 5.6%).

*1,2-*O*:5,6-*S*,*O*-Di-isopropylidene-3-*O*-methanesulphonyl-5-thio-α-*D*-glucofuranose* (**12**). — To a solution of **9** (2.5 g) in methanol (2.8 mL) and 2,2-dimethoxypropane (10 mL) at 20° was added a solution of toluene-*p*-sulphonic acid (0.50 g) in methanol (12 mL). The mixture was left overnight at room temperature, then neutralised with anhydrous sodium carbonate, filtered, and concentrated to dryness. The residue was partitioned between dilute aqueous potassium hydrogencarbonate and dichloromethane. The organic solution was dried and concentrated, and the residue was crystallised from ethanol to yield **12** (1.2 g, 54%), m.p. 147–149°, $[\alpha]_D$ −109° (*c* 0.7, chloroform) (Found: C, 43.7; H, 6.2. $C_{13}H_{22}O_7S_2$ calc.: C, 44.0; H, 6.3%).

*Methyl 2,3-anhydro-5,6-*S*,*O*-isopropylidene-5-thio-α- and -β-*D*-allofuranos-*

ides (**14**). — Concentration of the mother liquors of the previous experiment yielded material (0.50 g) containing the methyl 5,6-*S,O*-isopropylidene-3-*O*-methanesulphonyl-5-thio-D-glucofuranosides (**13**). A solution of this residue in methanol (20 mL) containing sodium methoxide (0.25 g) was stored for 5 min at room temperature, neutralised (CO_2), and concentrated to dryness. The residue was partitioned between water and dichloromethane, and the organic solution was dried and concentrated. Column chromatography (benzene–ether, 9:1) of the syrupy residue gave, first, the β anomer **14b** (0.11 g, 31%), m.p. 57–58° (from di-isopropyl ether), $[\alpha]_D$ −59° (*c* 0.55, chloroform) (Found: C, 51.6; H, 7.0. $C_{10}H_{16}O_4S$ calc.: C, 51.7; H, 6.9%). Eluted second was the α anomer **14a** (0.07 g, 20%), m.p. 67–70° (from di-isopropyl ether), $[\alpha]_D$ +15° (*c* 1, chloroform) (Found: C, 51.8; H, 6.9%).

Similar treatment of the methyl 5,6-*S,O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-5-thio-α- (**8a**) and -β-D-glucofuranoside (**8b**) (15 mg each) gave material that was chromatographically and spectroscopically indistinguishable from **14a** and **14b**, respectively.

1,2-O:5,6-S,O-Di-isopropylidene-5-thio-α-D-glucofuranose (**2**). — (*a*) *From* **12**. A solution of the mesylate **12** (0.72 g) in methanol (45 mL) containing sodium methoxide (4.0 g) was boiled under reflux for 4 h, then neutralised (CO_2), and concentrated to dryness. The residue was partitioned between water and dichloromethane, the organic solution was dried and concentrated, and the residue was crystallised from light petroleum to give **2** (0.45 g, 80%), m.p. 58–60°, $[\alpha]_D$ −85° (*c* 0.6, chloroform) (Found: C, 51.85; H, 7.0. $C_{12}H_{20}O_5S$ calc.: C, 52.1; H, 7.3%).

(*b*) *From* **7**. Treatment of the tosylate **7** (1.0 g) as in (*a*) gave **2** (0.42 g, 65%), m.p. and mixture m.p. 58–60°.

5-Thio-D-glucose (**15**). — A solution of the diacetal **2** (0.70 g) in acetic acid (14 mL) and water (7 mL) was kept at 95° for 90 min and then concentrated to give **15** (0.50 g, 100%) as a syrup which, on seeding, crystallised from ethanol; m.p. and mixture m.p. (with authentic material) 135–138°.

Reactions of 1,2-O-:5,6-S,O-di-isopropylidene-5-thio-α-D-glucofuranose (**2**). — (*a*) *Methanolysis*. A solution of **2** (0.30 g) in methanol (9 mL) and conc. hydrochloric acid (0.5 mL) was boiled under reflux for 30 min, neutralised ($PbCO_3$), filtered, and concentrated. The syrupy residue (0.26 g) crystallised from ethyl acetate to give methyl 5-thio-α-D-glucopyranoside (**16a**; 0.11 g, 48%), m.p. 123–125°, $[\alpha]_D$ +337° (*c* 0.7, methanol); lit.[10], m.p. 124–125°, $[\alpha]_D$ +326.5° (methanol).

The mother liquors were concentrated, and the residue was eluted from a column (20 × 1.3 cm) of Zeolit-FF (HO^-) resin with water. Early fractions contained **16a** (45 mg, 19%) and later fractions contained syrupy methyl 5-thio-β-D-glucopyranoside (**16b**; 30 mg, 13%), $[\alpha]_D$ −64° (*c* 1.4, methanol); lit.[10], $[\alpha]_D$ −51.4° (methanol).

Acetylation of the β anomer gave the tetra-acetate **17b**, m.p. 90–92° (from di-isopropyl ether), $[\alpha]_D$ −28° (*c* 1.1, chloroform); lit.[10], m.p. 92–93°, $[\alpha]_D$ −26.9° (chloroform).

(*b*) *Oxidation*. A solution of **2** (2.2 g) in methyl sulphoxide (16 mL) and acetic anhydride (11 mL) was left at 20° for 2 days and then concentrated, and a solution of the residue in ether was extracted (3 ×) with aqueous 40% sodium hydrogensulphite. The pH of the extract was adjusted to 8 with sodium hydrogencarbonate and the solution was extracted continuously with ethyl acetate to give the ketone as a syrup (0.95 g, 44%) which crystallised as 1,2-*O*:5,6-*S*,*O*-di-isopropylidene-5-thio-α-D-*ribo*-hexofuranos-3-ulose hydrate (**18**) on storage in the atmosphere. Recrystallisation from di-isopropyl ether gave material having m.p. 110–111°, $[\alpha]_D$ −23° (*c* 0.7, chloroform) (Found: C, 49.3; H, 6.9. $C_{12}H_{20}O_6S$ calc.: C, 49.3; H, 6.9%).

Concentration of the dried ether layer and column chromatography (benzene–ether, 9:1) of the residue gave syrupy 1,2-*O*:5,6-*S*,*O*-di-isopropylidene-3-*O*-methylthiomethyl-5-thio-α-D-allofuranose (**19**; 1.1 g, 41%), $[\alpha]_D$ −150° (*c* 1.3, dichloromethane) (Found: *m/z* 336.1093 (M^+). $C_{14}H_{24}O_5S_2$ calc.: *m/z* 336.1065].

1,2-O:5,6-S,O-Di-isopropylidene-5-thio-α-D-allofuranose (**20**). — Sodium borohydride (0.10 g) was added in portions during 1 h to a solution of **18** (0.36 g) in ethanol (3 mL) and water (3 mL). The solvents were then removed and the residue was partitioned between dichloromethane and aqueous potassium hydrogencarbonate. The organic solution was dried and concentrated, and the residue was crystallised from light petroleum to yield **20** (0.32 g, 88%), m.p. 67–69°, $[\alpha]_D$ −37° (*c* 0.6, chloroform) (Found: C, 52.2; H, 7.2. $C_{12}H_{20}O_5S$ calc.: C, 52.1; H, 7.3%).

The 3-acetate **21**, prepared in the usual way, had m.p. 64–65° (from light petroleum), $[\alpha]_D$ +27° (*c* 0.9, dichloromethane) (Found: C, 53.2; H, 7.1. $C_{14}H_{22}O_6S$ calc.: C, 52.8; H, 7.0%).

The 3-benzoate **22**, prepared in the usual way, had m.p. 101–102° (from ethanol), $[\alpha]_D$ +34° (*c* 0.9, chloroform) (Found: C, 60.2; H, 6.3. $C_{19}H_{24}O_6S$ calc.: C, 60.0; H, 6.4%).

The 3-methanesulphonate **23**, prepared using mesyl chloride and triethylamine in dichloromethane, had m.p. 150° (dec.), $[\alpha]_D$ +16° (*c* 0.9, chloroform) (Found: C, 43.7; H, 6.2. $C_{13}H_{22}O_7S_2$ calc.: C, 44.05; H, 6.3%).

5-Thio-D-allose (**1**). — A solution of **20** (1.0 g) in 50% aqueous acetic acid (20 mL) was kept at 90° for 2 h. The solvents were removed and the residue was crystallised from ethanol to give **1** (0.60 g, 85%), m.p. 170–174°, $[\alpha]_D$ +75→+115° (equil.; *c* 1, water) (Found: C, 36.8; H, 6.1. $C_6H_{12}O_5S$ calc.: C, 36.7; H, 6.2%).

1,2,3,4,6-Penta-O-acetyl-5-thio-β-D-allopyranose (**24**). — The sugar **1** (0.50 g) was treated for 2 days at room temperature with acetic anhydride (6 mL) in pyridine (8 mL). The solvents were removed and column chromatography (benzene–ether, 4:1) of the residue gave syrupy **24** (0.92 g, 89%), $[\alpha]_D$ −10° (*c* 1.1, chloroform) [Found: *m/z* 347.0768 (M^+ − OAc). $C_{16}H_{22}O_{10}S$ − OAc calc.: *m/z* 347.0800].

Methyl 5-thio-α- and -β-D-allopyranosides (**25**). — The sugar **1** (0.76 g) was treated with methanol (20 mL) containing hydrogen chloride (0.20 g) for 1 day at

room temperature. The mixture was then neutralised ($PbCO_3$), filtered, and concentrated to a syrup (0.73 g) which was eluted from a column (51 × 2.4 cm) of Zeolit FF (HO^-) resin with water. Eluted first was the syrupy α anomer **25a** (0.37 g, 45%), $[\alpha]_D$ +289° (*c* 0.5, methanol) [Found: *m/z* 210.0571 (M^+). $C_7H_{14}O_5S$ calc.: *m/z* 210.0562].

Further elution gave the β anomer **25b** (0.14 g, 17%), m.p. 123–125° (from ethyl acetate), $[\alpha]_D$ −98° (*c* 0.6, methanol) (Found: C, 40.2; H, 6.75. $C_7H_{14}O_5S$ calc.: C, 40.0; H, 6.7%).

A similar α,β-mixture **25** was obtained by treatment of **20** with methanol–hydrochloric acid as described above for **2**.

*Methyl 2,3,4,6-tetra-O-acetyl-5-thio-α- and -β-*D*-allopyranosides* (**26**). — Each glycoside **25** (50 mg) was treated with acetic anhydride (0.5 mL) and pyridine (1 mL) at room temperature for 1 day and the mixture was worked-up in the usual way.

The α-tetra-acetate **26a** (90 mg, 100%) was a syrup, $[\alpha]_D$ +183° (*c* 1.2, chloroform) [Found: *m/z* 319.0823 (M^+ − OAc). $C_{15}H_{22}O_9S$ − OAc calc.: *m/z* 319.0851].

The β-tetra-acetate **26b** (80 mg, 87%) had m.p. 118–120° (from di-isopropyl ether), $[\alpha]_D$ −42° (*c* 0.7, chloroform) (Found: C, 47.4; H, 5.9. $C_{15}H_{22}O_9S$ calc.: C, 47.6; H, 5.9%).

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