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SYNTHESIS OF 5-THIO-D-ALTROSE AND SOME OF ITS DERIVATIVES*

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ABSTRACT

Acid-catalysed methanolysis of 6-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose gave the methyl 5-thio-3-*O*-toluene-*p*-sulphonyl-α- and -β-D-glucopyranosides (**5**). Treatment of **5** with acidified 2,2-dimethoxypropane and then sodium methoxide gave the methyl 2,3-anhydro-4,6-*O*-isopropylidene-5-thio-α- and -β-D-allopyranosides. Epoxide opening with aqueous sodium hydroxide then gave mixtures of methyl 4,6-*O*-isopropylidene-5-thio-α- or -β-D-altropyranosides (**9**) and the corresponding *gluco* compounds **10**. Mild, acid hydrolysis converted **9** into the methyl 5-thio-α- and -β-D-altropyranosides and more vigorous hydrolysis gave 5-thio-D-altrose. Methyl 3,4-*O*-isopropylidene-5-thio-α-D-altropyranoside was obtained when the 4,6-acetal **9a** was left in acidified acetone. The methyl 2,3:4,6-di-*O*-isopropylidene-5-thio-α- and -β-D-glucopyranosides were quickly produced by the action of acidified 2,2-dimethoxypropane on the 4,6-acetals **10**. Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-altropyranoside (**17a**) was shown to exist mainly in the $^4C_1$ conformation, but the β anomer **17b** and 1,2,3,4,6-penta-*O*-acetyl-5-thio-β-D-altropyranose both adopt mainly the $^1C_4$ conformation.

INTRODUCTION

The most commonly used synthetic routes[2,3] from D-glucose to D-altrose involve conversion of the former into a 4,6-acetal of a 2,3-anhydro-D-hexopyranoside with a fixed $^4C_1$ conformation. Attack of the epoxide by hydroxide ions then results mainly in diaxial opening, leading to D-altrose derivatives. In seeking to adapt this approach to a synthesis of 5-thio-D-altrose (**1**), the 5-thio-D-glucose derivative **2**[4], which we had already used in a synthesis of 5-thio-D-allose[1], seemed a promising starting-material. We now report in full[5] on the synthesis of **1**.

*5-Thio-pyranoses, Part 10. For Part 9, see ref. 1.
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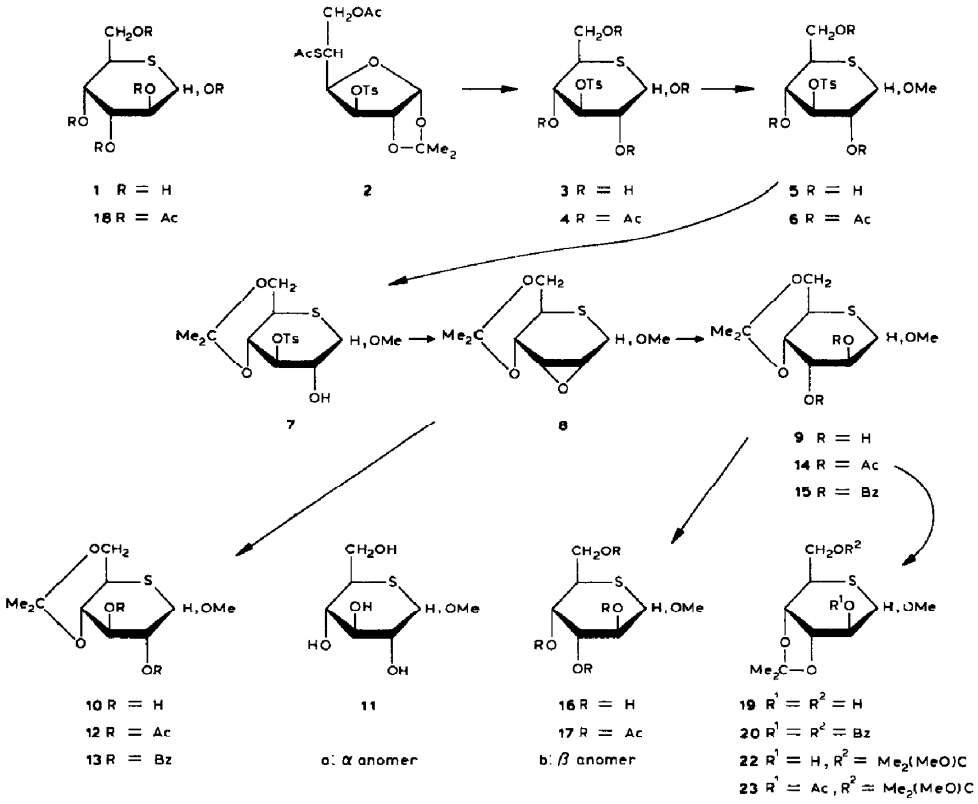


DISCUSSION

Earlier methanolyses[6,7] of 5-*S*-acyl-1,2-*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-xylofuranoses had led to excellent yields of methyl 5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-xylopyranoside. When the 5-thio-D-glucose derivative **2** was subjected to the same reaction conditions, the initial product was 5-thio-3-*O*-toluene-*p*-sulphonyl-D-glucose (**3**), characterised as the α-tetra-acetate **4a**. On prolonged reaction, **2** was converted into the methyl glycosides **5**; the major product, the α-anomer **5a**, was obtained crystalline as was its triacetate **6a**. Behaviour of this kind in the methanolysis of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was observed by Collins[8], who showed that D-glucose was the initial product which was then converted into glucofuranosides and finally into glucopyranosides.

On treatment with 2,2-dimethoxypropane, **5a** gave the highly crystalline 4,6-acetal **7a** and similar treatment of the material in the mother liquors from the crystallisation of **5a** gave the β anomer **7b**. The anomeric configurations, the sulphonate-substituted C-3, and the $^4C_1$ conformation for these compounds were clearly demonstrated by their ^{1}H-n.m.r. spectra (see Table I). Reaction with cold sodium methoxide converted **7a** and **7b** into the corresponding *allo*-epoxides **8**.

TABLE I

^{1}H-N.M.R. DATA FOR *gluco* AND *allo* 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'*		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
4a[a,d]	6.14	5.5 ⟵		→ 5.0	3.50	4.40	4.07	2.42 (ArMe); 2.19, 2.04 1.97, 1.78 (OAc)	2.5				5.0	3.0	12.0
5a[a,d]	4.53	4.82	4.1 ⟷	3.6	3.15	4.1 ⟷	3.6	3.28 (OMe); 2.44 (ArMe)	3.0	9.0	9.0	10.0	5.0	10.0	
6a[a,d]	4.62	5.5 ⟵		→ 5.1	3.3	4.36	4.01	3.41 (OMe); 2.40 (ArMe); 2.02, 1.90, 1.80 (OAc)	1.5				4.5	3.5	12.0
7a[a,d]	4.60	3.93	4.69	3.81	3.00	3.76	3.63	3.44 (OMe); 2.44 (ArMe); 1.21, 0.97 (CMe_2)	3.0	9.0	9.0	10.5	6.5	10.0	11.5
7b[a,d,e]	4.44	3.94	4.54	3.84	2.72	3.86	3.67	3.56 (OMe); 2.43 (ArMe); 1.26, 1.13 (CMe_2)	9.0	9.0	9.0	10.5	5.5	10.5	11.0
8a[b,e]	4.37	3.21	2.97	3.98	3.7 ⟵		→ 3.3	3.14 (OMe); 1.43, 1.22 (CMe_2)	4.5	4.0	1.0	9.5			
8b[a]	5.08	3.50	3.24	4.39	3.27		3.70	3.44 (OMe); 1.53, 1.44 (CMe_2)	2.0	4.5	1.0	9.5	7.5	7.5	
10a[c]	4.45	3.9 ⟵					→ 3.1	3.44 (OMe); 1.49, 1.37 (CMe_2)	1.0						
10b[a]	4.42	4.1 ⟵					→ 3.3	3.55 (OMe); 1.51, 1.44 (CMe_2)	9.0						
12[b]	4.21	5.60	5.21	3.88	2.53	3.62	3.43	3.10 (OMe); 1.77, 1.74 (OAc) 1.38, 1.13 (CMe_2)	9.0	9.0	9.0	10.0	5.0	11.0	11.0
13a[c,d]	4.82	5.32	5.73	4.12	3.31	3.80	3.72	3.43 (OMe); 1.42, 1.30 (CMe_2)	3.0	10.0	9.5	9.5	3.0	10.0	11.0
21a[b]	4.37	4.2 ⟵					→ 3.0	3.00 (OMe); 1.40, 1.35(2) 1.20 (CMe_2)	1.5						
21b[b,e]	4.48	4.11	3.36	3.98	2.76	3.73	3.62	3.21 (OMe); 1.42, 1.34(2) 1.17 (CMe_2)	9.0	8.5	9.0	9.5	5.0	10.5	11.0

[a]In $CDCl_3$. [b]In C_6D_6. [c]In CCl_4. [d]Also showed signals in the aromatic region. [e]At 220 MHz.

TABLE II

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

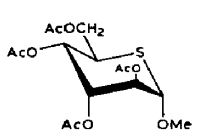
Compound	*Chemical shift (p.p.m.)*							*Other signals*	*Coupling constant (Hz)*							*Other couplings*
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	
9a[a]	4.49	4.29	4.0↔3.7	4.25	4.0	⟷	3.7	3.48 (OMe); 1.39, 1.31 (CMe_2)	3.0	4.0	2.5	10.5				
9b[a]	5.03	4.22	4.00	4.13	3.24	3.80	3.79	3.51 (OMe); 1.50, 1.41 (CMe_2)	2.0	4.0	3.0	10.0	7.5	9.0	11.0	
14a[b]	4.31	2.10	4.82	4.12	3.8	⟷	3.4	3.38 (OMe); 2.14, 2.06 (OAc) 1.51, 1.32 (CMe_2)	3.0	3.5	3.0	9.5				
14b[a]	4.81	5.31	5.27	4.27	3.24	3.80	3.78	3.43 (OMe); 2.14, 2.10 (OAc) 1.49, 1.34 (CMe_2)	2.0	5.0	2.5	10.5	7.0	9.0		
15a[b]	4.50	5.53	5.32	4.50	3.9	⟷	3.6	3.39 (OMe); 1.53, 1.27 (CMe_2)	2.5	3.5	3.5					
15b[a]	5.05	5.73	5.68	4.48	3.49	3.92	3.90	3.45 (OMe); 1.51, 1.28 (CMe_2)	2.0	5.0	3.0	10.0	7.0	9.0		
17a[b,d]	4.39	5.13	5.06	5.34	3.58	4.43	4.00	3.44 (OMe); 2.17, 2.07, 2.06, 2.01 (OAc)	3.0	4.0	3.0	10.0	5.0	3.5	12.0	
17b[b,d]	4.60	5.29	5.36	5.51	3.02	4.36	4.29	3.44 (OMe); 2.14, 2.08, 2.03, 1.97 (OAc)	2.5	10.5	2.5	3.5	6.5	9.5	11.5	1.5 ($J_{1,5}$)
18b[a]	6.16	5.51	5.40	5.66	3.21	←4.47→		2.18(2), 2.12, 2.03, 2.01 (OAc)	2.5	10.5	2.0	3.5	8.0	8.0		1.0 ($J_{1,5}$)
19[a]	4.52	3.96	4.11	4.40	3.31	3.88	3.80	3.43 (OMe); 1.49, 1.37 (CMe_2)	6.5	8.0	6.5	10.0	4.5	5.0		
20[c,d]	4.51	5.95	4.21	4.40	3.54	4.60	4.51	3.04 (OMe); 1.44, 1.15 (CMe_2)	6.0	8.0	6.5	9.5	4.5	5.5	12.0	
22[a]	4.46	3.91	4.07	4.39	3.35	3.68	3.65	3.40, 3.21 (OMe); 1.44, 1.33(3) (CMe_2)	6.0	8.0	6.0	10.0	4.0	4.0	10.0	
23[b]	4.44	5.22	4.4	4.0	3.28	←3.61→		3.22, 3.16 (OMe); 1.38, 1.30(2), 1.27 (CMe_2)	7.0	9.0	7.0	9.5	4.0	4.0		

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

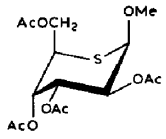
The expected $^{S}H_5$ conformations for the epoxides **8** were confirmed by the ^{1}H-n.m.r. spectra ($J_{4,5}$ 9.5 Hz), which differed significantly only in their $J_{1,2}$ values (4.5 and 2.0 Hz for **8a** and **8b**, respectively).

On being heated with aqueous sodium hydroxide, the epoxides **8** gave mixtures of the *altro* and *gluco* derivatives **9** and **10**. The *gluco* compounds **10** were readily identified since mild acid hydrolysis removed the 4,6-*O*-isopropylidene groups to give the known[9] methyl 5-thio-D-glucopyranosides (**11**). The identity of the *altro* compounds **9** followed from their ^{1}H-n.m.r. spectra (see Table II) which showed values for $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ of 4.0, 3.0, and 10.0 Hz, respectively, for both anomers. The *gluco* compounds **10** were further characterised as the diacetate **12b** and dibenzoate **13a**, and the *altro* compounds **9** as the diacetates **14** and dibenzoates **15**. The proportions of *altro* and *gluco* products formed in these epoxide openings differed significantly from those obtained with similar oxygen analogues. In the epoxide opening of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside with sodium hydroxide[10] or sodium methoxide[11], *gluco* compounds accounted for <10% of the product. Rather more *gluco* compound was obtained in the reaction of the β anomer with sodium methoxide[12], when *altro* and *gluco* products were obtained in the ratio 86:14. The reactions of the thio-epoxides gave increased amounts of *gluco* products. Thus, the α-epoxide **8a** gave the *altro* and *gluco* compounds **9a** and **10a** in the ratio 85:15, while the β-epoxide **8b** afforded **9b** and **10b** in almost equal amounts (51:49). A possible explanation for this change is that axial attack by a nucleophile at C-2 is discouraged by the *syn*-axial interaction with the axial lone-pair orbital of the ring sulphur atom. This explanation was offered for similar results of epoxide opening in methyl 2,3(3,4)-anhydro-5-thio-α-D-ribopyranosides[7], and for the failure[13] of methyl 2,3-*O*-isopropylidene-4-*O*-methanesulphonyl-5-thio-α-D-xylopyranoside to undergo displacement reactions at C-4.

Mild acid hydrolysis of the *altro* acetals **9** led to the methyl 5-thio-α- and -β-D-altropyranosides (**16**), both of which gave crystalline tetra-acetates **17** whose ^{1}H-n.m.r. spectra showed that they existed mainly in different chair conformations. Thus, the α anomer **17a** showed coupling constants ($J_{2,3}$ 4.0, $J_{3,4}$ 3.0, and $J_{4,5}$ 10.0 Hz) very similar to those of the earlier *altro* derivatives which adopt the $^4C_1$ conformation. The contrasting values for the β anomer **17b** ($J_{2,3}$ 10.5, $J_{3,4}$ 2.5, $J_{4,5}$ 3.5 Hz) suggest that it exists mainly in the $^1C_4$ conformation which is further supported by the existence of long-range coupling between H-1 and H-5 ($J_{1,5}$ ~1.5 Hz) arising from the W-arrangement of these two hydrogens. Thus, both anomers adopt conformations in which the anomeric methoxyl group has the preferred axial configuration. A *syn*-diaxial arrangement of the hydroxymethyl group and MeO-1 in a conventional pyranoside is considered most unlikely[14]; however, such an arrangement in a 5-thiopyranoside is probably less adverse because of the increased separation of the groups as a consequence of carbon–sulphur bonds being longer than carbon–oxygen bonds. The "hockey-stick effect"[15], the *syn*-diaxial interaction of a β-oxygen with an axial lone-pair of the sulphur, is presumably similar in either the



17a ($^4C_1$)



17b ($^1C_4$)

$^4C_1$ or the $^1C_4$ *altro* conformation (involving AcO-2 and AcO-4, respectively) and so has no effect on the conformational preference.

Hydrolysis of the α-glycoside **16** or the acetal **9** with hot, dilute mineral acid gave crystalline 5-thio-D-altrose (**1**), which reacted only slowly with sodium nitroprusside (indicative of a pyranose form lacking a free thiol group) and mutarotated from $-68°$ to $-48°$ (suggesting the β anomer). This is also the crystalline form of D-altrose[16]. Acetylation of **1** gave a syrupy penta-acetate **18b**, whose ^{1}H-n.m.r. coupling constants were very similar to those of the tetra-acetate **17b**, confirming the β-pyranose form and also the $^1C_4$ conformation. On treatment with acidic methanol, **1** gave the glycosides **16a** and **16b** in the ratio 1:4, thus following the same trend as other 5-thiohexoses where the preferred glycoside has 1,2-*cis* stereochemistry[1,9]. The ^{13}C-n.m.r. spectra for the glycosides **16** are listed in Table III. The spectrum of the free sugar **1** showed twelve lines when mutarotation was complete, those of the β form still being the larger ($\alpha\beta$-ratio 2:3). As with 5-thio-D-allose and 5-thio-D-glucose and their glycosides[1], the biggest difference between anomeric pairs is shown by the signals for C-5, that of the α anomer being at higher field.

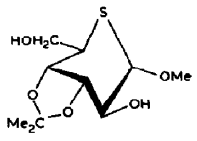
When methyl 4,6-*O*-isopropylidene-α-D-altropyranoside was treated with acidified acetone, it isomerised into the 3,4-acetal[3]. The thio compound **9** behaved similarly, giving methyl 3,4-*O*-isopropylidene-5-thio-α-D-altropyranoside (**19**), which was further characterised as its dibenzoate **20**. The coupling constants in the ^{1}H-n.m.r. spectra of these compounds were very similar and a large $J_{4,5}$ value (10.0 Hz) suggested the $^4C_1$ conformation. However, the larger values of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ agree closely with those reported[17] (6.0, 8.8, and 6.6 Hz) for methyl 2-deoxy-2-iodo-3,4-*O*-isopropylidene-α-D-altropyranoside for which the $^0S_2$ conformation has been proposed[17].

TABLE III

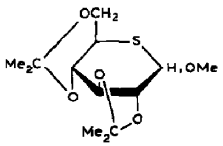
^{13}C-N.M.R. DATA[a]

Compound	*Chemical shift (in p.p.m.)*				
	C-1	*C-2, C-3, C-4*	*C-5*	*C-6*	*OMe*
1a	75.4	74.0, 73.3, 70.0	44.9	62.8	
1b	75.1	72.2, 71.6, 69.1	48.8	64.7	
16a	86.0	73.4, 72.8, 69.6	42.8	62.6	58.0
16b	86.2	71.7, 71.6, 68.3	49.8	64.7	57.3

[a]Measured at 22.63 MHz for solutions in D_2O.



19 ($^5S_2$)



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Treatment of either methyl 4,6-*O*-isopropylidene-5-thio-α- or -β-D-glucopyranoside (**10**) with 2,2-dimethoxypropane, acetone, and an acid catalyst gave the 2,3:4,6-diacetals **21**, both in crystalline form. The ready formation of *trans*-acetals in 5-thiopyranose systems has been observed previously[18]. The ^{1}H-n.m.r. spectrum of the β anomer **21b** confirmed the $^4C_1$ conformation as the major species in solution, with large values for $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ (9.0, 9.0, 9.5, and 9.5 Hz, respectively), but the spectrum of the α anomer **21a** could not be an analysed owing to the coincidence of signals from H-2,3,4,5,6,6'. However, the ^{13}C-n.m.r. spectrum clearly demonstrated the presence of 1,3-dioxane and 1,3-dioxolane rings[19].

The separation of the *altro* and *gluco* products **9** and **10** from the opening of the epoxides **8** required careful chromatography. Advantage was taken of the previous reaction to simplify this separation. Brief treatment of the product mixture with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid converted the *gluco* products **10** into the diacetals **21**, but left the *altro* compounds **9** unchanged and thus easily separated from the diacetals **21**. Prolonged exposure of **9** to the reagent led to the 6-(1-methoxy-1-methylethyl) ether **22**, characterised as its crystalline acetate **23** whose ^{1}H-n.m.r. spectrum showed the expected downfield shift for the H-2 signal. Evidently, migration of the isopropylidene group had occurred and the primary hydroxyl group thus exposed had undergone transacetalation with the 2,2-dimethoxypropane. Reactions of this type with this reagent and isolated alcohols, preferably primary, have been observed[20].

EXPERIMENTAL

General methods. — See Part 6[21].

*1,2,4,6-Tetra-*O*-acetyl-5-thio-3-*O*-toluene-*p*-sulphonyl-α-*D*-glucopyranoside* (**4**). — A solution of 6-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose (**2**, 0.47 g) in methanol (10 mL) containing conc. hydrochloric acid (0.5 mL) and water (0.5 mL) was boiled under reflux for 45 min, cooled, neutralised ($PbCO_3$), filtered, and evaporated to dryness. The residue was partitioned between water and dichloromethane, and the aqueous phase was evaporated (bath temperature, 40°) to leave the tosylate **3** as a syrup (0.27 g). This was dissolved in pyridine (3 mL) and acetic anhydride (1.5 mL), and left overnight at room temperature. Work-up in the usual way, with column chromatography (silica gel, 4:1 benzene–ether) of the product, gave **4a** (70 mg), m.p. 121–123° (from di-isopropyl ether), $[\alpha]_D$ +150° (*c* 0.9, chloroform) (Found: C, 48.4; H, 4.9. $C_{21}H_{26}O_{11}S_2$ calc.: C, 48.6; H, 5.05%).

*Methyl 5-thio-3-*O*-toluene-*p*-sulphonyl-α-*D*-glucopyranoside* (**5a**). — A solution of the diacetate **2** (9.5 g) in methanol (160 mL) and conc. hydrochloric acid (8 mL) was boiled under reflux for 6 h. The mixture was neutralised ($PbCO_3$), filtered, and evaporated to dryness. A solution of the residue in ethyl acetate was then passed through a little silica gel, concentrated, and cooled to give **5a** (4.8 g), m.p. 141–142° (dec.), $[\alpha]_D$ +188° (*c* 0.8, methanol) (Found: C, 45.8; H, 5.5. $C_{14}H_{20}O_7S_2$ calc.: C, 46.1; H, 5.5%). Evaporation of the mother liquors gave a syrup (2.1 g) containing approximately equal quantities of the anomers (**5**).

The triacetate **6a**, prepared from **5a** in the usual way, had m.p. 144–146°, $[\alpha]_D$ +144° (*c* 0.9, dichloromethane) (Found: C, 49.1; H, 5.3. $C_{20}H_{26}O_{10}S_2$ calc.: C, 48.95; H, 5.35%).

*Methyl 4,6-*O*-isopropylidene-5-thio-3-*O*-toluene-*p*-sulphonyl-α- and -β-*D*-glucopyranosides* (**7**). — (*a*) *α Anomer* **7a**. The glycoside **5a** (4.8 g) was stirred with acetone (4.8 mL) and 2,2-dimethoxypropane (24 mL) containing toluene-*p*-sulphonic acid (0.40 g) until all the material had dissolved. After a further 10 min, the solution was neutralised with anhydrous sodium carbonate, filtered, and evaporated. The residue was partitioned between water and dichloromethane, and the organic layer was dried and evaporated. Recrystallisation of the residue from acetone–di-isopropyl ether gave **7a** (4.9 g), m.p. 154–155°, $[\alpha]_D$ +159° (*c* 0.5, dichloromethane) (Found: C, 50.1; H, 5.8. $C_{17}H_{24}O_7S_2$ calc.: C, 50.5; H, 6.0%).

(*b*) *β Anomer* **7b**. The syrup (0.48 g, containing the mixture of anomers **5**) obtained in the earlier experiment was dissolved in acetone (4.5 mL) and 2,2-dimethoxypropane (2.5 mL) containing toluene-*p*-sulphonic acid (40 mg). After 20 min at room temperature, the mixture was worked-up as for the α anomer. Two recrystallisations of the product from acetone–di-isopropyl ether gave **7b** (40 mg), m.p. 138° (dec.), $[\alpha]_D$ −42° (*c* 0.55, dichloromethane) (Found: C, 50.6; H, 5.9%).

*Methyl 2,3-anhydro-4,6-*O*-isopropylidene-5-thio-α- and -β-*D*-allopyranosides* (**8**). — (*a*) *α Anomer* **8a**. A solution of the tosylate **7a** (4.4 g) in methanol (90 mL) containing sodium methoxide (2.5 g) was left overnight at room temperature, neutralised (CO_2), and evaporated to dryness. The residue was partitioned between water and dichloromethane, and the organic layer was dried and passed through silica gel (2 g). Evaporation then gave **8a** (2.5 g), which crystallised after several months; m.p. 60–63° (from di-isopropyl ether), $[\alpha]_D$ +281° (*c* 0.7, chloroform) (Found: C, 51.45; H, 6.8. $C_{10}H_{14}O_4S$ calc.: C, 51.7; H, 6.9%).

(*b*) *β Anomer* **8b**. The syrup (1.25 g) containing the mixture of anomers **5** was treated with acetone (12 mL) and 2,2-dimethoxypropane (6 mL) containing toluene-*p*-sulphonic acid (0.1 g) as described in the earlier experiment. The crude product (1.35 g) was left in methanol (55 mL) containing sodium methoxide (2.0 g) overnight at room temperature. Work-up, as in (*a*), gave a syrup (0.75 g) which was chromatographed on silica gel (40 g). Elution with benzene–ether (9:1) gave, first, **8b** (0.25 g), m.p. 72–74° (from light petroleum), $[\alpha]_D$ −74° (*c* 1, chloroform) (Found: C, 51.85; H, 7.0%). Further elution gave **8a** (0.25 g), m.p. and mixture m.p. 60–63°.

Action of aqueous sodium hydroxide on methyl 2,3-anhydro-5-thio-α- and -β-

D-*allopyranosides* (**8**). — (*a*) *α Anomer* **8a**. The epoxide **8a** (3.7 g) was stirred vigorously with a boiling solution of sodium hydroxide (4.0 g) in water (100 mL) for 3 h. The cooled solution was neutralised (CO_2) and then extracted continuously with ethyl acetate. Evaporation of the extract gave a mixture (3.6 g) which was chromatographed on silica gel (100 g) with ethyl acetate. First eluted, after a small quantity of impurity, was methyl 4,6-*O*-isopropylidene-5-thio-α-D-altropyranoside (**9a**) (2.2 g), which crystallised after long standing; m.p. 115–117° (from ether–di-isopropyl ether), $[\alpha]_D$ +202° (*c* 0.6, chloroform) (Found: C, 48.3; H, 7.3. $C_{10}H_{18}O_5S$ calc.: C, 48.0; H, 7.3%). This was followed by the syrupy *gluco* isomer **10a** (0.40 g), $[\alpha]_D$ +290° (*c* 0.6, chloroform) (Found: mol. wt. 250.0875. $C_{10}H_{18}O_5S$ calc.: mol. wt. 250.0881). The dibenzoate **13a**, prepared in the usual way, had m.p. 121–123° (from aqueous ethanol), $[\alpha]_D$ +231° (*c* 0.9, chloroform) (Found: C, 63.3; H, 5.8. $C_{24}H_{26}O_7S$ calc.: C, 62.85; H, 5.7%).

(*b*) *β Anomer* **8b**. A mixture of **8b** (0.61 g), sodium hydroxide (0.6 g), and water (17 mL) was stirred vigorously under reflux for 9 h. Work-up as described above gave a mixture (0.54 g) which was chromatographed on silica gel (30 g) with ether. First eluted was methyl 4,6-*O*-isopropylidene-5-thio-β-D-altropyranoside (**9b**, 0.23 g), m.p. 137–138° (from di-isopropyl ether), $[\alpha]_D$ −9° (*c* 1, chloroform) (Found: C, 47.7; H, 7.2). Later fractions contained the *gluco* isomer **10b** (0.22 g), m.p. 137–139° (from di-isopropyl ether), $[\alpha]_D$ −74° (*c* 0.55, chloroform) (Found: C, 47.8; H, 7.1.). The diacetate **11b**, prepared in the usual way, had m.p. 126–128° (from di-isopropyl ether), $[\alpha]_D$ −56° (*c* 0.7, chloroform) (Found: C, 50.6; H, 6.6. $C_{13}H_{19}O_7S$ calc.: C, 50.3; H, 6.6%).

*Methyl 2,3-di-*O*-acetyl-4,5-*O*-isopropylidene-5-thio-α- and -β-*D*-altropyranosides* (**14**). — These compounds were prepared in the usual way with acetic anhydride and pyridine. The α anomer **14a** had m.p. 84–85° (from light petroleum), $[\alpha]_D$ +163° (*c* 0.6, chloroform) (Found: C, 50.3; H, 6.6. $C_{14}H_{22}O_7S$ calc.: C, 50.6; H, 6.9%).

The β anomer **14b** was a syrup, $[\alpha]_D$ −83° (*c* 0.6, chloroform) [Found: mol. wt. (M − Me) 319.0843. $C_{14}H_{22}O_7S$ calc.: mol. wt. (M − Me) 319.0851].

*Methyl 2,3-di-*O*-benzoyl-4,6-*O*-isopropylidene-5-thio-α- and -β-*D*-altropyranosides* (**15**). — These compounds were prepared by using benzoyl chloride in pyridine in the usual way. The α anomer **15a** had m.p. 143–144° (from ethanol), $[\alpha]_D$ +41° (*c* 0.7, chloroform) (Found: C, 62.9; H, 5.85. $C_{24}H_{26}O_7S$ calc.: C, 62.85; H, 5.7%).

The β anomer **15b** had m.p. 135–136° (from ethanol), $[\alpha]_D$ −127° (*c* 0.8, chloroform) (Found: C, 62.95; H, 5.7%).

*Treatment of methyl 4,6-*O*-isopropylidene-5-thio-*D*-gluco- and -*D*-altropyranosides* (**9**) *and* (**10**) *with aqueous acetic acid.* — A solution of each acetal (0.10 g) in 80% acetic acid (2 mL) was left overnight at room temperature and then evaporated to give the following products (each ~85 mg).

Methyl 5-thio-α-D-glucopyranoside (**11a**), recrystallised from ethyl acetate, had m.p. and mixture m.p. 125–127°.

Methyl 5-thio-β-D-glucopyranoside (**11b**) was a syrup identified as the tetra-

acetate, which crystallised from di-isopropyl ether and had m.p. and mixture m.p. 84–86°.

Methyl 5-thio-α-D-altropyranoside (**16a**) was a syrup, $[\alpha]_D$ +151° (*c* 1, methanol) (Found: mol. wt. 210.0567. $C_7H_{14}O_5S$ calc.: mol. wt. 210.0562); the tetra-acetate **17a**, prepared in the usual way, had m.p. 92–93° (from di-isopropyl ether), $[\alpha]_D$ +122° (*c* 1.35, chloroform) (Found: C, 47.6; H, 5.8. $C_{15}H_{22}O_9S$ calc.: C, 47.6; H, 5.9%).

Methyl 5-thio-β-D-altropyranoside (**16b**) had m.p. 143–145° (from ethyl acetate), $[\alpha]_D$ −130° (*c* 1, methanol) (Found: C, 40.0; H, 6.7. $C_7H_{14}O_5S$ calc.: C, 40.0; H, 6.7%). The tetra-acetate **17b** had m.p. 125–127° (from di-isopropyl ether), $[\alpha]_D$ −152° (*c* 0.6, chloroform) (Found: C, 48.0; H, 5.9%).

*5-Thio-*D*-altrose* (**1**). — A solution of the α-glycoside **16a** (1.6 g) in 0.05M sulphuric acid was kept at 75° for 6 h. The cooled solution was neutralised ($BaCO_3$), filtered, and evaporated. The syrupy residue was triturated with hot ethanol, which on concentration and cooling yielded **1** (0.75 g), m.p. 177–178°, $[\alpha]_D$ −68→ −48° (final) (*c* 0.9, water) (Found: C, 37.05; H, 6.2. $C_6H_{12}O_5S$ calc.: C, 36.7; H, 6.2%).

Similar treatment of the acetal **9** also afforded **1**.

*1,2,3,4,6-Penta-*O*-acetyl-5-thio-β-*D*-altropyranose* (**18b**). — The sugar **1** (0.10 g) was left in pyridine (2.0 mL) and acetic anhydride (1.2 mL) for 2 days at room temperature. The solvents were removed, and the residue was chromatographed on silica gel (4 g). Elution with benzene–ether (4:1) gave **18b** (0.19 g), $[\alpha]_D$ −122° (*c* 1, chloroform) [Found: mol. wt. (M − OAc) 347.0845. $C_{16}H_{22}O_{10}S$ calc.: mol. wt. (M − OAc) 347.0801].

Methanolysis of **1**. — A solution of **1** (0.10 g) in methanol (5.0 mL) containing hydrogen chloride (0.10 g) was left for 1 day at room temperature, then neutralised ($PbCO_3$), filtered, and evaporated to leave a syrup (0.12 g). This was chromatographed on a column (20 × 2.0 cm) of Zerolit FF (HO^-) resin with water. First eluted was an unidentified material (5 mg), and then the β-altroside **16b** (49 mg) which, crystallised from ethyl acetate, had m.p. and mixture m.p. 143–145°. Eluted last was the syrupy α-altroside **16a** (12 mg).

*Methyl 3,4-*O*-isopropylidene-5-thio-α-*D*-altropyranoside* (**19**). — The 4,6-acetal **9** (0.14 g) was left in acetone (15 mL) containing toluene-*p*-sulphonic acid (75 mg) overnight at room temperature. The acid was then neutralised (Na_2CO_3), and the mixture worked-up in the usual way to give a syrup (0.15 g). This was chromatographed on silica gel (10 g), and elution with ethyl acetate gave, first, an unidentified material (17 mg) and then **19** (0.13 g), m.p. 63–65° (from ether), $[\alpha]_D$ +152° (*c* 0.8, chloroform) (Found: C, 48.15; H, 7.25. $C_{10}H_{18}O_5S$ calc.: C, 48.0; H, 7.3%). The dibenzoate **20**, prepared in the usual way, had m.p. 101–102°, $[\alpha]_D$ +54° (*c* 0.6, chloroform) (Found: C, 63.15; H, 5.5. $C_{24}H_{26}O_7S$ calc.: C, 62.9; H, 5.7%).

*Methyl 2,3:4,6-di-*O*-isopropylidene-5-thio-α- and -β-*D*-glucopyranosides* (**21**). — (*a*) *α Anomer*. The mono-acetal **10a** (0.10 g) was dissolved in acetone (8 mL) and 2,2-dimethoxypropane (4 mL) containing toluene-*p*-sulphonic acid (40 mg). After 30 min at room temperature, the acid was neutralised and the mixture

worked-up in the usual way to give **21a** (74 mg), m.p. 133–135° (from light petroleum), $[\alpha]_D$ +251° (*c* 1.6, chloroform) (Found: C, 53.8; H, 7.8. $C_{13}H_{22}O_5S$ calc.: C, 53.8; H, 7.6%).

(*b*) *β Anomer.* The mono-acetal **10b** (0.11 g) was treated as in (*a*) to give a product (69 mg) which was chromatographed on silica gel (4 g) with benzene–ether (19:1) to give **21b** (63 mg), m.p. 144–145° (from di-isopropyl ether), $[\alpha]_D$ −64° (*c* 0.6, chloroform) (Found: C, 54.0; H, 7.7%).

*Methyl 3,4-O-isopropylidene-6-O-(1-methoxy-1-methylethyl)-5-thio-α-*D*-altropyranoside* (**22**). — A solution of **9a** (0.15 g) in acetone (4 mL) and 2,2-dimethoxypropane (4 mL) containing toluene-*p*-sulphonic acid (40 mg) was left overnight at room temperature. Neutralisation with sodium carbonate and work-up with dichloromethane gave a syrup (0.20 g). Chromatography on silica gel (10 g) with ether gave **22** (0.16 g), $[\alpha]_D$ +274° (*c* 1.1, chloroform) [Found: mol. wt. (M − Me) 307.1250. $C_{14}H_{26}O_6S$ calc.: mol. wt. (M − Me) 307.1215].

The acetate **23**, prepared in the usual way, had m.p. 79–82° (from light petroleum), $[\alpha]_D$ +122° (*c* 1, chloroform) (Found: C, 53.1; H, 7.7. $C_{16}H_{28}O_7S$ calc.: C, 52.75; H, 7.7%).

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