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Synthesis of derivatives of 5-thio-L-idose*,†

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ABSTRACT

1,2-*O*:5,6-*S*,*O*-Di-isopropylidene-5-thio-β-L-idofuranose (**6**) was synthesised from 1,2-*O*-isopropylidene-3,5,6-tri-*O*-methanesulphonyl-α-D-glucofuranose (**1**). Hydrolysis of **6** yielded 5-thio-L-idose (**11**) and 1,6-anhydro-5-thio-β-L-idopyranose (**13**), characterised as the respective acetates **12** and **14**. Methanolysis of **6** gave methyl 5-thio-α- (**8**) and -β-L-idopyranoside (**7**), but methanolysis of the 3-methanesulphonate (**5**) of **6** gave methyl 3,6-anhydro-5-thio-α-L-talopyranoside (**16**). Both **7** and **8** adopted the unusual $^4C_1$ conformation in solution and gave the 2,3:4,6-di-*O*-isopropylidene acetals **19** and **18**, respectively. The β anomer **19** was less stable towards acid than the α anomer **18**. Methyl 2,3- (**22**) and 3,4-*O*-isopropylidene-5-thio-β-L-idopyranoside (**23**), characterised as the respective diacetates **20** and **21**, were also obtained from **7**.

INTRODUCTION

Some aspects of the chemistry of 5-thio-L-idose (**11**) were described by Adley and Owen in one of the first papers on "sulphur-in-the-ring" sugars[2]. The conformational features of idopyranoid derivatives have been the subject of much comment and investigation[3–5]. The replacement of oxygen by sulphur in the pyranoid ring has marked effects on the conformational equilibria[6,7] and, therefore, it was of interest to synthesise pyranoid derivatives of **11** and to study these equilibria. We now report on 5-thio-L-idose, its methyl glycosides, and the isopropylidene derivatives of these compounds.

DISCUSSION

Most syntheses of 5-thiohexoses have involved 5,6-epithio derivatives[8]. The present route to 5-thio-L-idose (**11**) and its derivatives is closely related to that of Adley and Owen[2], but takes advantage of the readily available[9] trimesylate **1** and contains features employed in the syntheses[10] of 5-thio-D-glucose and 5-thio-D-allose.

Selective displacement of the primary sulphonate group in **1** with potassium thiobenzoate (the thioacetate was less effective) gave the 6-thiobenzoate **2**. On treatment with sodium methoxide, **2** underwent debenzoylation and cyclisation to give the thiirane derivative **3**. Opening of the thiirane ring in **3** with refluxing acetic acid–acetic anhydride

* Dedicated to Professor Grant Buchanan on the occasion of his 65th birthday.
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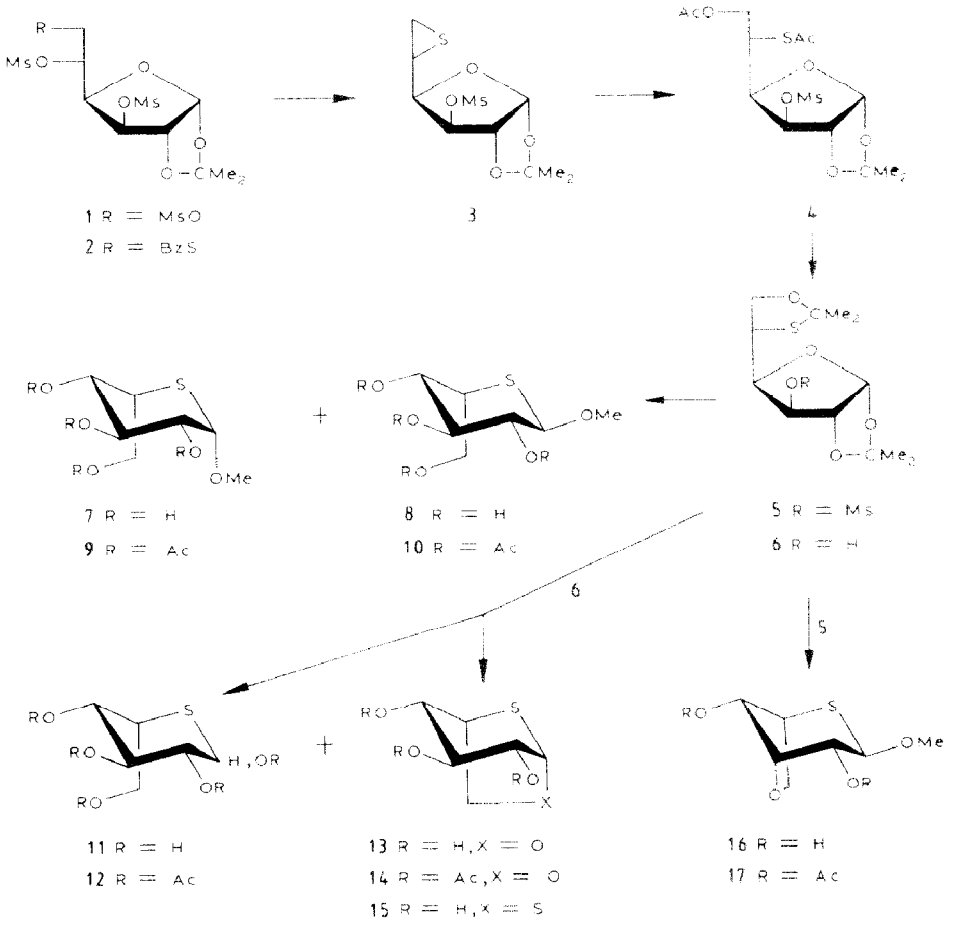

that contained sodium acetate afforded the diacetate **4**. When **4** was dissolved in methanol and 2,2-dimethoxypropane which contained toluene-*p*-sulphonic acid, the diacetal **5** was formed in good yield. Cleavage of the sulphonate group in **5** with sodium methoxide then gave 1,2-*O*:5,6-*S*,*O*-di-isopropylidene-5-thio-*β*-L-idofuranose (**6**). Each of the intermediates, with the exception of **5**, was crystalline and the overall yield of **6** from **1** was 23%.

On heating **6** with methanolic hydrochloric acid and fractionation of the products on an anion-exchange resin[11], methyl 5-thio-*β*-L-idopyranoside (**7**) was obtained with MeO-1 and HO-2 *cis*, followed by the minor product, the α anomer **8**. Neither **7** nor **8** was obtained crystalline and their structures were confirmed by the ^{1}H-n.m.r. data (Table I) which indicated mainly the $^4C_1$ conformations (**7** $J_{1,2}$ 3.5, $J_{2,3}$ 9.5, $J_{3,4}$ 9.5, $J_{4,5}$ 1.0 Hz; **8** $J_{1,2}$ 7.5, $J_{2,3}$ 8.5, $J_{3,4}$ 8.0 Hz). The slightly lower values of $J_{2,3}$ and $J_{3,4}$ for **8** suggested a small proportion of another conformation. Earlier studies of D-idopyranose and D-idopyranoside derivatives suggested[4,5] the $^4C_1$ conformation to be preferred, although some contribution from the $^1C_4$ conformation might be expected in certain circum-

stances. However, Auge and David[3] indicated that the $^4C_1$ conformation should be more preponderant than predicted previously and that the other conformer was more likely to be S_2^0 than $^1C_4$. For L-*ido* derivatives, these conformations become $^1C_4$, S_0^2, and $^4C_1$, respectively. Thus, the replacement of oxygen by sulphur resulted in a marked change, with the $^4C_1$ conformation being favoured.

In the major *β* anomer **7**, CH_2OH and MeO-1 are *syn*-diaxial and, as pointed out earlier[7], this situation is less adverse in a 5-thiopyranoside than in a normal pyranoside because of the greater length of the C–S bond. Moreover, the alternative $^1C_4$ conformation in **7** and **8** would be destabilised by the "hockey-stick" effect[12] *i.e.*, the *syn*-diaxial interaction of a *β*-oxygen with the axial lone pair of the sulphur. A similar situation was reported for a "nitrogen-in-the-ring" sugar, 5-benzyloxycarbonylamino-5,6-dideoxy-3-*O*-methanesulphonyl-*β*-L-idopyranose, which also exists in the $^4C_1$ form in solution. The anomers **7** and **8** gave the tetra-acetates **9** and **10**, respectively, but only the former was crystalline.

Hydrolysis of **6** with hot aqueous acetic acid gave a syrupy mixture in which 5-thio-L-idose (**11**) appeared to be the major component (six major ^{13}C signals with chemical shifts typical of a 5-thiohexose; Table II). Comparison of the chemical shift data with those of **7** and **8** suggested that the major product was the *β* anomer **11***β*. The syrup was acetylated to yield, after chromatography, two crystalline products. Although the major product appeared to be homogeneous in t.l.c., its ^1H-n.m.r. spectrum indicated a 3:1 mixture of two penta-acetates. Repeated crystallisation or chromatography failed to separate the isomers, but the major component appeared to be (^1H-n.m.r. data) 1,2,3,4,6-penta-*O*-acetyl-5-thio-*β*-L-idopyranose (**12***β*), which also adopted the $^4C_1$ conformation ($J_{1,2}$ 3.2, $J_{2,3}$ 9.8, $J_{3,4}$ 9.8, $J_{1,5}$ 1.0 Hz). The minor component was identified tentatively as the *α* anomer **12***α* on the basis of the $J_{1,2}$ value of 7.3 Hz and consideration of the n.m.r. spectra of **9** and **10**. Adley and Owen[2] also found 5-thio-L-idose (**11**) to be a syrup, acetylation of which gave two crystalline penta-acetates in the ratio 12:1. However, no ^1H-n.m.r. data were given and, as the nature of the product now reported became clear only with the availability of high-field ^1H-n.m.r. spectra, it is possible that the products described by Adley and Owen were mixtures with different proportions of **12***α* and **12***β* (see Experimental for a comparison of the properties).

The minor crystalline product isolated after acetylation of the mixture of products obtained on hydrolysis of **6** with acid was shown by its ^1H-n.m.r. spectrum to be 2,3,4-tri-*O*-acetyl-1,6-anhydro-5-thio-*β*-L-idopyranose (**14**). The spectrum contained only three signals for OAc and H-2,3,4 were axial ($J_{2,3}$ 8.1 and $J_{3,4}$ 8.5 Hz). The $J_{1,5}$ value of 1.5 Hz indicated a planar W arrangement for H-1,5 in equatorial positions of a $^4C_1$ conformation. The isolation of **14** indicated that the anhydrothio sugar **13** was present in the original hydrolysate. L-Idose is exceptional among the hexoses in that it readily undergoes conversion into 1,6-anhydro-*β*-L-idopyranose[14], but the formation of **13** was unexpected in view of the increased separation of C-1 and C-5 in the necessary $^4C_1$ conformation. The corresponding 1,6-epithio compound **15** has been reported[15], but C-1 and C-6 are more easily linked because of the larger sulphur atom.

The acid-catalysed methanolysis of the diacetal mesylate **5** gave a complex

TABLE I

^{1}H-N.m.r. data

Compound	*Chemical shift (p.p.m.)*							*Other signals*	*Coupling constants (Hz)*							*Other couplings*
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	
2[a]	5.98	4.98	5.12	4.50	5.18	4.30	4.20	3.27,3.20 (OMs); 1.52,1.35 (CMe_2)	3.5	<0.5	2.5	8.0	4.0	5.5	15.0	
3	5.99	4.77	5.02	3.79	3.07	2.53	2.29	3.13 (OMs); 1.48,1.32 (CMe_2)	4.0	<0.5	3.0	8.0	5.0	6.5	1.5	
4	5.94	4.83	5.08	4.40	4.15	4.35	4.21	3.19 (OMs); 2.38 (SAc); 2.09 (OAc); 1.51,1.33 (CMe_2)	3.6	<0.5	2.7	8.4	5.2	5.9	11.4	
5	5.94	4.79	5.04	4.30	3.84	4.21	4.12	3.16 (OMs); 1.69,1.62,1.51,1.32 (CMe_2)	4.0	<0.5	2.5	9.0	4.0	5.5	10.0	
6	5.94	4.50	4.78	4.11	3.98	4.43	4.05	3.76 (OH); 1.72,1.62,1.50,1.32 (CMe_2)	3.7	<0.5	2.2	6.4	1.9	5.5	10.1	3.0 ($J_{3,OH}$)
7[b]	4.57	3.83	3.73	4.03	3.06	4.04	3.80	3.43 (OMe)	3.5	9.5	9.5	5.0	5.0	9.0	11.0	1.0 ($J_{1,3}$)
8[b]	4.67	3.69	3.60	4.00	3.19	3.90	3.77	3.50 (OMe)	7.5	8.5	8.0	4.7	4.7	8.0	12.0	
9	4.65	5.15	5.64	5.29	3.39	4.51	4.46	3.49 (OMe); 2.07,2.06,2.06,2.04 (OAc)	2.4	10.3	10.4	5.6	6.5	7.1	11.7	
10	4.74	5.3	⟷	5.1	3.47	4.45	4.22	3.44 (OMe); 2.14,2.07,2.07,2.04 (OAc)	7.3				7.0	5.4	11.6	
12β	6.10	5.21	5.57	5.37	3.48	4.61	4.46	2.15,2.08,2.08,2.04,1.99 (OAc)	3.2	9.8	9.8	5.2	8.0	6.0	11.4	0.5 ($J_{1,3}$)
14	5.47	4.94	5.33	5.20	3.77	4.47	3.91	2.07,2.07,2.02 (OAc)	0.5	8.1	8.5	3.3	<0.5	3.3	9.3	1.5 ($J_{1,3}$)
17	4.78	4.91	4.16	5.19	3.28	4.20	4.06	3.42 (OMe); 2.08,2.04 (OAc)	8.5	<0.5	<0.5	1.0	<0.5	4.0	9.0	
18	4.83	3.86	3.97	4.27	3.71	4.00	3.60	3.41 (OMe); 1.47,1.45,1.45,1.42 (CMe_2)	6.6	10.7	6.3	5.0	6.5	7.3	12.0	

19	4.80	3.85	4.63	4.33	3.36	4.06	3.75	3.48 (OMe); 1.59,1.48,1.46,1.44 (CMe_2)	2.6	9.3	10.4	6.0	12.0	5.4	11.8
20	4.69	3.92	4.02	5.09	3.36	4.34	4.27	3.48 (OMe); 2.11,2.02 (OAc); 1.39,1.38 (CMe_2)	2.4	9.2	10.6	5.7	5.6	7.6	11.4
21	4.80	5.06	4.19	4.11	3.42	4.59	4.31	3.40 (OMe); 2.16,2.09 (OAc); 1.45,1.42 (CMe_2)	3.3	9.4	9.4	4.6	5.8	8.4	11.4

[a] Also showed signals in the aromatic region. [b] In D_2O.

TABLE II

^{13}C-N.m.r. data

Compound	*Chemical shift (p.p.m.)*										
	C-1	*C-2,C-3,C-4*	*C-5*	*C-6*	*OMe*	O_2CMe_2[a]	O_2CMe_2[b]	O_2CMe_2[a]	O_2CMe_2[b]	*OCO*Me	*OCO*Me
7[c]	87.1	77.6,76.6,72.4	49.1	63.7	58.6						
8[c]	85.5	77.5,75.1,75.0	46.6	62.2	60.3						
11[c]	78.0	76.3,76.0,72.6	48.5	63.7							
18	86.1	79.9,78.2,70.9	37.6	60.0	56.1	100.2	111.8	27.1,22.2	26.9,25.5		
19	83.5	79.3,75.1,72.0	38.3	60.7	57.2	98.4	109.6	29.8,24.9	27.1,26.3		
20	84.0	78.5,76.0,70.6	42.4	63.0	56.5		109.3		26.8,26.4	170.4,170.4	21.0,20.8
21	83.9	79.9,74.7,70.2	41.9	64.9	57.2		109.3		26.9,26.5	170.5,170.1	21.0,20.8

[a] 1,3-Dioxane. [b] 1,3-Dioxolane. [c] In D_2O.

mixture of products from which methyl 3,6-anhydro-5-thio-α-L-talopyranoside (**16**) was isolated and further characterised as the diacetate **17**. The ^{1}H-n.m.r. spectrum of **17** showed only one large J value ($J_{1,2}$ 8.5 Hz), apart from the geminal coupling, and the resonances of H-2 and H-4 were at lower field than that for H-3. Methyl 3,6-anhydro-hexopyranosides are obtained normally under alkaline conditions and on treatment with acid are converted into furanosides or acylic acetals[16]. The present result is unusual and is another example of the strong tendency of 5-thio sugars to adopt a pyranose form.

Following earlier work[17] with methyl 5-thio-D-glucopyranosides, it was expected that treatment of the pyranosides **7** and **8** with 2,2-dimethoxypropane and acetone in the presence of an acid catalyst would lead to the 2,3:4,6-diacetals **19** and **18**, respectively. In fact, the diacetal **18** was obtained and was crystalline, but **7** gave three products (t.l.c.) that were reconverted readily into **7**. Acetylation of the mixture and then chromatography yielded the diacetal **19** and the isomeric monoacetal diacetates **20** and **21**. The structures of **18**–**21** were deduced from their ^{1}H- and ^{13}C-n.m.r. spectra. Thus, **18** and **19** gave signals for two CMe_2 groups, whereas **20** and **21** each displayed signals for a CMe_2 and two OAc groups. Compounds **18**–**21** gave ^{13}C signals for CMe_2 groups that were characteristic of a *trans*-fused dioxolane system, and **18** and **19** also gave signals associated with a dioxane system[18]. Some of the chemical shifts were slightly outside the expected ranges, *e.g.*, for the dioxane system in **18** at 100.2 p.p.m. for CMe_2 (expected 97.1–99.9 p.p.m.) and 22.15 and 27.1 p.p.m. for CMe_2 (expected 18.2–19.3 and 28.6–29.7 p.p.m., respectively). Comparison of the ^{1}H-n.m.r. spectra of **20** and **21** with those of the diacetal **19** and the tetra-acetate **9** enabled the CMe_2 groups in **20** and **21** to be assigned to the 2,3 and 3,4 positions, respectively. Thus, the H-6 signals were in the same region, which confirmed the lack of a 4,6-acetal, and the signals for H-4 in **20** and H-2 in **21** were downfield of the related signals in **19** and in the same region as the corresponding signals in **9**. Hence, **22** and **23** were identified as products of the isopropylidenation of the β-glycoside **7**.

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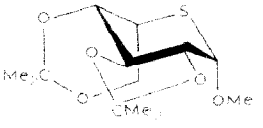

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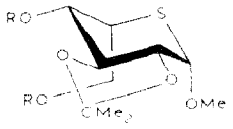

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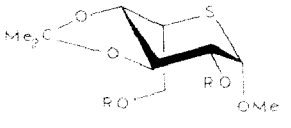

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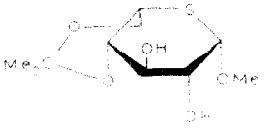
23 R = H



24

The instability of the β-idoside acetals **19**–**21** compared to that of the α-idoside diacetal **18** was reflected in the rates of hydrolysis. For a solution of the β anomer **19** in aq. 80% acetic acid at room temperature, t.l.c. after 1 min revealed the glycoside **7**, the monoacetals **22** and **23**, and a product tentatively identified as the 4,6-acetal **24**. The formation of the 3,4-acetal **23** indicated that acetal migration had occurred. Hydrolysis to **7** was complete in 20 min. In contrast, the α anomer **18** required 18 h for complete reaction and no monoacetals were detected during the hydrolysis. The relative instability of the β anomer **19** may be due to the fact that, with the molecule locked in the $^4C_1$ conformation by the 2,3-acetal, there is steric strain that is due to the interaction of MeO-1 and the CMe_2 groups.

Both **18** and **19** are unusual in that they are *cis*-fused 4,6-diacetals in which C-6 is axial. A similar situation exists in methyl 4,6-*O*-benzylidene-α-D-idopyranoside 2,3-carbonate[4], but this compound was obtained from the 2,3-carbonate which is locked in the $^1C_4$ conformation. In contrast, the $^4C_1$ conformation in **7** and **8** is favoured. Treatment of either **7** or **8** with acidified acetone gave poor yields of complex mixtures. Under these conditions, methyl 5-thio-α-D-glucopyranoside gave the 4,6-acetal in good yield[17]. The lack of reactivity of **7** and **8** must be associated with the axial orientation of the hydroxymethyl group, which may also be the reason why some of the ^{13}C resonances for the CMe_2 groups of **18**–**20** had chemical shifts that were outside the expected ranges.

It was not surprising that 5-thio-L-idose (**11**) did not react with acidified acetone. When 2,2-dimethoxypropane was added, **11** was converted into a complex mixture from which the furanoid 1,2:5,6-diacetal **6** was isolated. Under similar conditions, 5-thio-D-glucose gave the pyranoid 2,3:4,6-diacetal[17].

EXPERIMENTAL

General methods. — Melting points are uncorrected. N.m.r. spectra were recorded at 90 or 300 MHz (^1H) and 22.63 or 75.47 MHz (^{13}C) for solutions in $CDCl_3$ unless otherwise stated. T.l.c. was performed on silica gel SA (Gelman) and column chromatography on Kieselgel (Merck, 7734). The Zerolit-FF (HO^-) resin had a mesh size of 100–200 and a DVB content of 2–3%.

6-S-Benzoyl-1,2-O-isopropylidene-3,5-di-O-methanesulphonyl-6-thio-α-D-glucofuranose (**2**). — A mixture of 1,2-*O*-isopropylidene-3,5,6-tri-*O*-methanesulphonyl-α-D-glucofuranose[9] (**1**, 9.0 g) and potassium thiobenzoate (4.5 g) in dry acetone (180 mL) was heated under reflux for 3 h, then cooled, filtered, and concentrated to dryness. The residue was partitioned between water and dichloromethane, the organic phase was dried and concentrated, and the residue was recrystallised from ethanol to give **2** (8.4 g, 85%), m.p. 140–142°, $[\alpha]_D$ +35° (*c* 0.9, chloroform) (Found: C, 43.5; H, 4.8. $C_{18}H_{24}O_{10}S$ calc.: C, 43.5; H, 4.9%).

5,6-Dideoxy-5,6-epithio-1,2-O-isopropylidene-3-O-methanesulphonyl-β-L-idofuranose (**3**). — Sodium methoxide [from sodium (0.8 g)] in methanol (16 mL) was added slowly to a stirred solution of **2** (8.2 g) in dichloromethane (82 mL). After 15 min, the mixture was poured into water (100 mL), the organic layer was separated, dried, and

concentrated, and the residue was crystallised from ethanol to give **3** (4.2 g, 86%), m.p. 120–121°, $[\alpha]_D$ +17° (*c* 1.1, chloroform) (Found: C, 40.3; H, 5.3. $C_{10}H_{16}O_6S$ calc.: C, 40.5; H, 5.4%).

6-O-Acetyl-5-S-acetyl-1,2-O-isopropylidene-3-O-methanesulphonyl-5-thio-β-L-idofuranose (**4**). — A mixture of **3** (5.0 g), acetic anhydride (28 mL), acetic acid (6 mL), and sodium acetate (4.0 g) was heated under reflux for 24 h, then cooled, ice (5 g) was added and, after a further 30 min, the mixture was partitioned between water and dichloromethane. The organic layer was washed with dilute aqueous potassium hydrogen carbonate, dried, and concentrated. Crystallisation of the residue from ethanol gave **4** (2.6 g, 66%), m.p. 111–113°, $[\alpha]_D$ −13° (*c* 1.4, chloroform) (Found: C, 42.3; H, 5.5. $C_{14}H_{22}O_9S_2$ calc.: C, 42.2; H, 5.6%).

1,2-O:5,6-S,O-Di-isopropylidene-5-thio-β-L-idofuranose (**6**). — A solution of **4** (5.5 g) and toluene-*p*-sulphonic acid (0.9 g) in 2,2-dimethoxypropane (22 mL) and methanol (67 mL) was left at room temperature for 15 h, then neutralised (Na_2CO_3), and concentrated to dryness. The residue was partitioned between dichloromethane and water, and the organic phase was dried and concentrated to dryness. Column chromatography (1:1 ether–light petroleum) of the residue gave the mesylate **5** (4.3 g, 89%), isolated as a syrup, $[\alpha]_D$ +18.5° (*c* 0.6, chloroform).

A solution of **5** in methanol (50 mL) that contained sodium methoxide [from sodium (1.5 g)] was heated under reflux for 5 h. Water (50 mL) was added, the methanol was evaporated, and the remaining aqueous solution was extracted with dichloromethane. The extract was dried and concentrated to give **6** (1.8 g, 48%), m.p. 102–104° (from ether–light petroleum), $[\alpha]_D$ +40° (*c* 1.2, chloroform) (Found: C, 52.2; H, 7.3. $C_{12}H_{20}O_5S$ calc.: C, 52.2; H, 7.3%).

Methyl 5-thio-α- (**8**) *and -β-L-idopyranoside* (**7**). — A solution of **6** (0.40 g) in methanol (9 mL) and conc. hydrochloric acid (1 mL) was heated under reflux for 20 min, then neutralised ($PbCO_3$), filtered, and concentrated. The syrupy residue (0.36 g) was eluted from a column of Zeolit-FF (HO^-) resin with water to give, first, **7** (0.19 g, 62%), isolated as a syrup, $[\alpha]_D$ +130° (*c* 1.0, methanol). Mass spectrum: *m/z* 210.0560 (calc. for M^+ 210.0562).

The tetra-acetate (**9**) of **7**, prepared in the usual way, had m.p. 91–92° (from ethanol), $[\alpha]_D$ +74° (*c* 1.0, chloroform) (Found: C, 47.4; H, 5.6. $C_{15}H_{22}O_9S$ calc.: C, 47.6; H, 5.9%).

Eluted second was **8** (0.04 g, 13%), isolated as a syrup, $[\alpha]_D$ −124° (*c* 1.0, methanol). Mass spectrum: *m/z* 210.0569.

The syrupy tetra-acetate (**10**) of **8** had $[\alpha]_D$ −90° (*c* 1.0, chloroform).

Action of aqueous acetic acid on **6**. — A solution of **6** (0.20 g) in aq. 80% acetic acid (2 mL) was heated at 90° for 90 min, then concentrated to dryness to yield crude syrupy 5-thio-L-idose (**11**, 0.18 g). Acetylation of **11** with acetic anhydride (2 mL) and pyridine (3 mL) for 19 h at 20° gave a product (0.20 g), column chromatography (1:1 ether–light petroleum) of which gave, first, 2,3,4-tri-*O*-acetyl-1,5-anhydro-5-thio-β-L-idopyranose (**14**; 0.02 g, 9%), m.p. 120–122° (from ethanol), $[\alpha]_D$ +111° (*c* 0.8, chloroform) (Found: C, 47.55; H, 5.3. $C_{12}H_{16}O_7S$ calc.: C, 47.4; H, 5.3%).

Eluted second was 1,2,3,4,6-penta-*O*-acetyl-5-thio-α,β-L-idopyranose (**12**; 0.13 g, 44%), m.p. 94–100° (from ethanol), $[\alpha]_D$ +51° (*c* 0.8, chloroform); lit.[2] m.p. 90–92°, $[\alpha]_D$ +41°, and m.p. 103–104°, $[\alpha]_D$ +76° (Found: C, 47.1; H, 5.4. $C_{16}H_{22}O_{10}S$ calc.: C, 47.3; H, 5.5%).

Methyl 3,6-anhydro-5-thio-α-L-talopyranoside (**16**). — A solution of **5** (0.25 g) in methanol (5 mL) that contained conc. hydrochloric acid (0.5 mL) was heated under reflux for 3 h, then neutralised ($PbCO_3$), filtered, and concentrated. A solution of the residue in ethyl acetate–methanol was passed through a short column of silica gel and then concentrated to give **16** (22 mg, 16%), m.p. 148–150° (from ethyl acetate or chloroform), $[\alpha]_D$ −88° (*c* 0.4, methanol) (Found: C, 43.7; H, 6.3. $C_7H_{12}O_4S$ calc.: C, 43.7; H, 6.3%).

The diacetate (**17**) of **16** had m.p. 111–112° (from di-isopropyl ether), $[\alpha]_D$ −84° (*c* 1.1, chloroform) (Found: C, 47.7; H, 5.8. $C_{11}H_{16}O_6S$ calc.: C, 47.8; H, 5.8%).

Methyl 2,3:4,6-di-O-isopropylidene-5-thio-α-L-idopyranoside (**18**). — A mixture of **8** (80 mg) and toluene-*p*-sulphonic acid (60 mg) in acetone (5 mL) and 2,2-dimethoxypropane (1 mL) was stirred at 20° for 45 min, then neutralised (Na_2CO_3), and concentrated, the residue was partitioned between dichloromethane and water, and the organic layer was dried and concentrated. Column chromatography (1:2 ether–light petroleum) of the residue yielded **18** (93 mg, 84%), m.p. 96–97° (from light petroleum), $[\alpha]_D$ −171° (*c* 0.8, chloroform) (Found: C, 53.6; H, 7.6. $C_{13}H_{22}O_5S$ calc.: C, 53.8; H, 7.6%).

Acetalation of methyl 5-thio-β-L-idopyranoside (**7**). — The β-glycoside **7** (100 mg) was treated with acetone and 2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid as described above. The product was acetylated with acetic anhydride (1 mL) and pyridine (1 mL). After 15 h, the solvents were evaporated and the residue was subjected to column chromatography. Elution with 1:4 ether–light petroleum gave methyl 2,3:4,6-di-*O*-isopropylidene-5-thio-β-L-idopyranoside (**19**; 23 mg, 17%), m.p. 112–114° (from light petroleum), $[\alpha]_D$ +73° (*c* 0.8, chloroform) (Found: C, 53.0; H, 7.2. $C_{13}H_{22}O_5S$ calc.: C, 53.8; H, 7.6%).

Elution with 1:2 ether–light petroleum then gave syrupy methyl 2,6-di-*O*-acetyl-3,4-*O*-isopropylidene-5-thio-β-L-idopyranoside (**21**; 24 mg, 15%), $[\alpha]_D$ +81° (*c* 1.0, chloroform). Mass spectrum: *m/z* 334.1077 ($C_{14}H_{22}O_7S$ calc. *m/z* 334.1086 for M^+).

Eluted next was methyl 4,6-di-*O*-acetyl-2,3-*O*-isopropylidene-5-thio-β-L-idopyranoside (**20**; 27 mg, 17%), isolated as a syrup, $[\alpha]_D$ +117° (*c* 1.5, chloroform). Mass spectrum: *m/z* 334.1082.

Eluted last was the tetra-acetate **9** (20 mg, 11%), m.p. 91–92° (see above).

Acetalation of 5-thio-L-idose (**11**). — A crude sample of **11** [obtained from the diacetal **6** (0.50 g)] was stirred with acetone, 2,2-dimethoxypropane, and toluene-*p*-sulphonic acid as described above. Column chromatography (ether) of the product yielded **6** (0.22 g, 44%) as the major product with m.p. and mixture m.p. 102–104°.

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