Synthesis of Per-*O*-alkylated 5-Thio-D-glucono-1,5-lactones and Transannular Participation of the Ring Sulphur Atom of 5-Thio-D-glucose Derivatives on Solvolysis under Acidic Conditions

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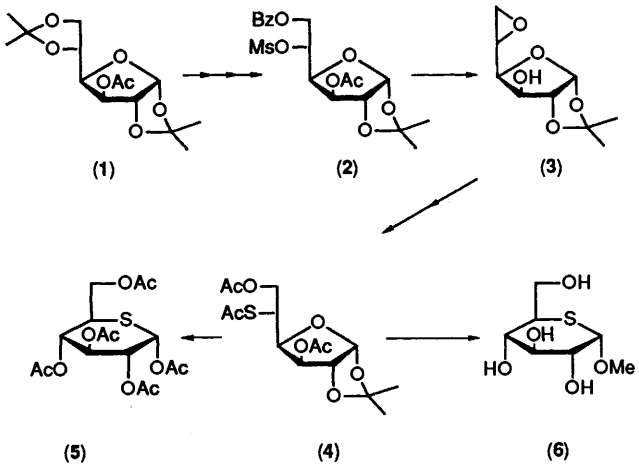
Per-*O*-alkylated 5-thio-D-glucono-1,5-lactones (**33**)–(**35**) were synthesized *via* acetolysis or hydrolysis of the corresponding methyl glycosides (**21**)–(**23**). Transannular participation of the sulphur atom on acid methanolysis of 3,6-di-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-α-D-glucofuranose and on acetolysis of the glycosides (**21**)–(**23**) was confirmed. These reactions gave unexpected 4-substituted derivatives (**14**), (**28**) and (**29**). Furthermore, similar participation on C-2 and C-6 was suggested from the formation of 2,5-dideoxy-2,5-epithio-4,6-di-*O*-methyl-D-mannose dimethyl acetal.

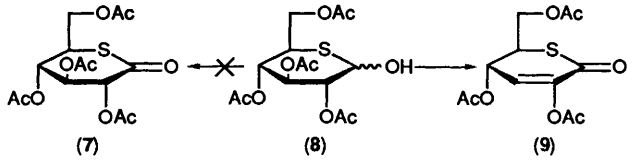
5-Thio-D-glucose (**10**)[1] has some interesting biological activities, such as an inhibitory effect against D-glucose transport across membranes and against enzymes capable of metabolizing carbohydrates.[2] 5-Thiosugars also have some interesting chemical properties. For example, Hughes and co-workers[3,4] have recently observed a case of sulphur participation in the displacement reaction of 2-, 4-, and 6-sulphonates of 5-thioaldopyranosides. In the course of synthesis of suitably protected 5-thio-D-gluconolactones as synthetic intermediates for the synthesis of orthothomycin analogues,[5] we observed[6] similar sulphur participation in the acid methanolysis and acetolysis of 5-thio-D-glucose derivates (**4**)–(**6**), (**10**), (**21**), (**22**), and (**36**). The methanolysis gave the 4-*O*-methyl glycoside (**14**) and the 4,6-di-*O*-methylated dimethyl acetal (**19**), and episulphonium ions (**13**), (**16**), and (**18**) were proposed as reaction intermediates. Although acetolysis of the methyl per-*O*-alkylated glycosides (**21**) and (**22**) in the presence of sulphuric acid gave the 1,4-diacetates (**28**) and (**29**), acetolysis in the presence of trifluoroacetic acid (TFA) gave the desired 1-acetates (**26**) and (**27**). We now report in detail the previously communicated transannular participation[6] and the synthesis of per-*O*-alkylated 5-thio-D-glucono-1,5-lactones (**33**)–(**35**).

5-Thio-D-glucose derivatives were prepared (Scheme 1) by modification of the method of Whistler and co-workers.[1,7] One of Whistler's methods[1] includes 1,2-*O*-isopropylidene-α-D-glucofuranose as an intermediate and has a drawback in the low selectivity of tosylation at the 5-hydroxy group of the corresponding 6-benzoate. To avoid tosylation at the 3-hydroxy group, those workers used the 3-*O*-benzyl derivative as an intermediate and obtained a higher total yield in this alternative method,[7] but the deprotection of the 3-*O*-benzyl group was somewhat cumbersome. Thus, we chose 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**)[8] as starting material, since the synthetic route from this compound might be free from a tedious deprotection step. The diacetal (**1**) was hydrolysed selectively at the 5,6-*O*-isopropylidene group with 90% aq. acetic acid and the product was benzoylated selectively at the primary hydroxy group; this was followed by methanesulphonylation to give the 6-*O*-benzoyl-5-*O*-methylsulphonyl derivative (**2**) in 76% yield from compound (**1**). Treatment of diester (**2**) with sodium methoxide gave the 5,6-epoxide (**3**)[9] in 66% yield. Treatment of epoxide (**3**) with thiourea, followed by acetolysis, gave the 5-thiofuranose (**4**)[1] in 68% yield from epoxide (**3**). The total yield of compound (**4**) from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was 32% in 7 steps, which is higher than that previously reported,[1] and the number of steps for the preparation of 5-thio-D-glucose is less than that in the other method.[7] The 5-thiofuranose (**4**) is the common synthetic intermediate for both the penta-acetate (**5**)[1] and the methyl glycoside (**6**),[1] whose preparations are described later in relation to the observed transannular participation of the sulphur atom.



Scheme 1. Bz = Benzoyl, Ms = methylsulphonyl.

Our attempt to prepare the tetra-*O*-acetyl-D-gluconolactone (**7**) was not successful. Treatment of the penta-acetate (**5**) with hydrazinium acetate gave the tetra-acetate (**8**) in 87% yield. Oxidation of compound (**8**) with dimethyl sulphoxide (DMSO) and acetic anhydride, however, resulted in the formation of the enolactone (**9**) in 71% yield (Scheme 2). A similar β-elimination



Scheme 2.

has been reported in the oxidation of the corresponding ring-oxygen analogue.[10] In both cases, the 3-*O*-acetyl group would be a good leaving group for β-elimination. Based on calculated

Table. Methanolysis of 5-thio-D-glucose derivatives.

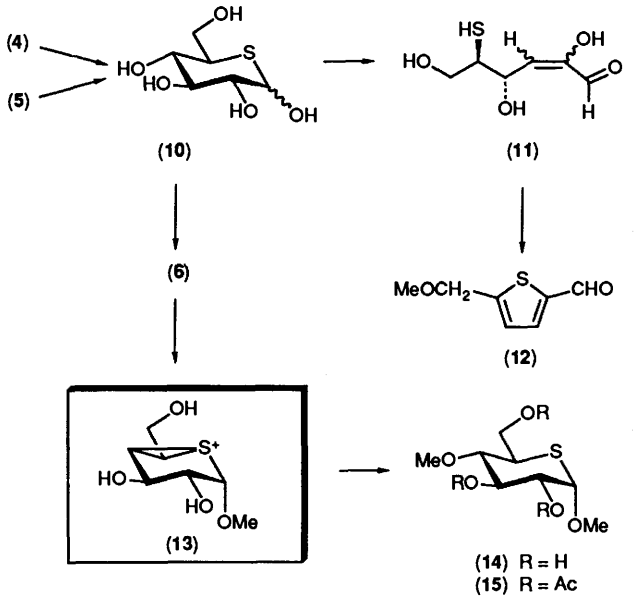
Entries		Starting materials (mmol; mM)[a]	Acidic medium[b]	Conditions		Products (%)			
				Temp.[c]	Time (h)	(6)	(14)	(19)	(12)
1	(4)	(0.28, 17)	A	room	24	34			
2	(4)	(0.28, 17)	A	room	50	33	7		
3	(4)	(0.32, 30)	B	room	168	60			
4	(4)	(0.58, 135)	B	reflux	0.5	42			
5	(4)	(1.38, 162)	B	reflux	1	62	5		
6	(4)	(1.40, 164)	B	reflux	1.5	62	10		
7	(4)	(1.37, 161)	B	reflux	5	31	27		
8	(4)	(0.55, 130)	B	reflux	9	16	23		trace
9	(4)	(1.38, 162)	B	reflux	13	13	26		9
10	(4)	(1.39, 163)	B	reflux	27	trace	18		24
11	(5)	(7.55, 142)	B	reflux	0.6	49	1		
12	(5)	(7.45, 146)	B	reflux	7	27	23		
13	(5)	(5.78, 143)	B	reflux	34	3	16		27
14	(10)	(0.53, 53)	A	reflux	12		27	14	
15	(6)	(0.57, 29)	A	reflux	20		14	18	
16	(10)	(0.66, 125)	B	reflux	12	11	24		16
17	(10)	(1.23, 144)	B	reflux	36		23		15
18	(6)	(0.26, 14)	B	reflux	20	trace	40		

[a] Amount (mmol) and conc. (mM). [b] A: 3% HCl–MeOH, B: 2.8% HCl–MeOH (4.4% water). [c] Reflux at a bath temperature of 70 °C.

angles,[11] a flattened $^{S}H_5$ conformation seems the most reasonable for compound (**9**), in contrast to the $^{5}H_O$ conformation of the oxygen analogue.[12]

On the other hand, per-*O*-benzylated D-gluconolactone has been prepared from the corresponding methyl glucoside in 2 steps.[10] Thus the glycoside (**6**) was prepared from the 5-thiofuranose (**4**), where some unexpected compounds, (**12**), (**14**), and (**19**), were formed as by-products (Schemes 3 and 4). Methanolysis of the 5-thiofuranose (**4**) was carried out in anhydrous 3% methanolic hydrogen chloride or in methanol containing conc. hydrogen chloride (2.8% HCl, 4.4% water), and best results were obtained under the aqueous conditions used at room temperature for a long reaction time or at reflux temperature for 1–1.5 h to give the glycoside (**6**) in 60–62% yield (Table, entries 3, 5, and 6). In the latter two cases, an unexpected second product, *i.e.*, the 4-*O*-methyl glycoside (**14**), was isolated. Structure (**14**) was confirmed by ^{1}H NMR data ($J_{3,4}$ 8.5, $J_{4,5}$ 11.0 Hz) of the triacetate (**15**), indicating the retention of configuration at C-4. In order to clarify the mechanism of formation of the 4-*O*-methyl glycoside (**14**), the time-dependence of product distribution in this reaction was examined (entries 4–10). The yield of the glycoside (**6**) reached a maximum value of 62% after 1–1.5 h as described above and then decreased gradually to trace amounts during 27 h. After 5 h the amount of compound (**14**) reached a maximum (*ca.* 30%), which was maintained for a further 10 h. The third product, the thiophene (**12**), was first formed after *ca.* 10 h. Methanolysis of the penta-acetate (**5**) under the same conditions gave the same products, and a similar time-dependence of the product distribution was observed (entries 11–13). The similarity of the results between these two compounds supports the presence of the same reaction intermediate, *i.e.* 5-thio-D-glucose (**10**). It was also supported by the result of the methanolysis of compound (**10**) (entries 16 and 17). The fact that the increase in yield of 4-*O*-methyl glycoside (**14**) correlates with the decrease in that of the glycoside (**6**) indicates conversion of tetraol (**6**) into the methyl ether (**14**) (Scheme 3). Compound (**6**) was methanolysed to give compound (**14**) after 20 h in 40% yield (entry 18).

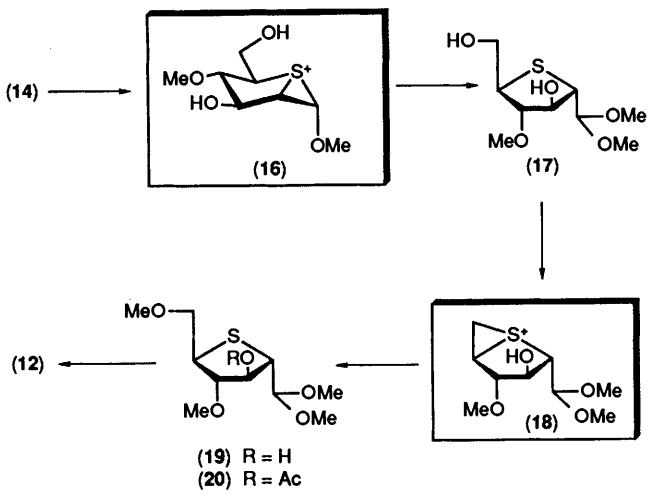
Recently, a similar substitution reaction at C-4 of 5-thiohexopyranosides with retention of configuration was observed by Al-Masoudi and Hughes[4] and they suggested that transannular participation of the ring sulphur atom generates a



Scheme 3.

bicyclic episulphonium ion as intermediate. In our cases also, the bicyclic episulphonium ion (**13**) is the most appropriate intermediate. In addition, this sulphur participation seems likely to occur under anhydrous conditions, considering the formation of the 4-*O*-methyl glycoside (**14**) even at room temperature (entry 2). Under anhydrous conditions, further sulphur participation at C-2 and C-6 was also suggested from the formation of the dimethyl acetal (**19**) which was obtained in 14 and 18% yield by the methanolysis of 5-thio-D-glucose (**10**) and of the glycoside (**6**) at reflux temperature for 12 h and 20 h, respectively (entries 14 and 15). The chemical shifts of C-2 and C-5 (δ_C 50.7 and 47.2) in the ^{13}C NMR spectrum of compound (**19**) indicate the formation of a 2,5-epithio ring. The coupling constants of the ring protons of compound (**19**) ($J_{2,3} = J_{3,4} = J_{4,5}$ = 6.3 Hz) not only coincide with those expected for a $^1T_2$ conformation but also closely resemble the reported values of 4,6-di-*O*-benzoyl-2,5-dideoxy-2,5-epithio-3-*O*-*p*-tolylsulphonyl-

D-mannose dimethyl acetal ($J_{2,3} = J_{3,4} = 6.0$, $J_{4,5}$ 6.5 Hz).[4] These facts, together with the mechanism of formation as shown in Scheme 4, supported the D-*manno* configuration of compound (**19**). The ring contraction and unusual methanolysis of the 6-hydroxy group were rationalized by the episulphonium intermediates (**16**) and (**18**). Rapid formation of compound (**18**) is supported by the fast solvolysis rate of 2-(*p*-nitrobenzoyloxymethyl)tetrahydrothiophene.[13] Anchimeric assistance due to similar participation of the sulphur atom has been suggested[4] to occur in the substitution reaction of 2-*O*-methylsulphonyl-5-thio-α-D-aldopyranoside derivatives in methanol in the presence of barium carbonate or hydrogen chloride. We can deduce that the thiophene (**12**) is formed by β- and successive δ-elimination reaction of the corresponding aldehyde of the dimethyl acetal (**19**). Methanolysis of this acetal (**19**) at reflux temperature for 15 h under aqueous conditions gave compound (**12**) in 27% yield. However, methanolysis, under aqueous conditions of the glycoside (**6**), 5-thio-D-glucose (**10**), and the 4-*O*-methyl glycoside (**14**) did not give the acetal (**19**) at all, and furthermore both compounds (**6**) and (**14**) did not give the thiophene (**12**) either. Therefore, it is appropriate to say that sulphur participation at C-2 as well as at C-4 is less effective under aqueous than under anhydrous conditions. Thus an alternative pathway for the formation of the thiophene (**12**) from the 5-thio-D-glucose (**10**) *via* the acyclic intermediate as (**11**) is plausible (Scheme 3). This pathway bears some analogy to that of the acid-catalysed formation of 2-furaldehyde from aldose *via* the corresponding 3-deoxyhexulose.[14]

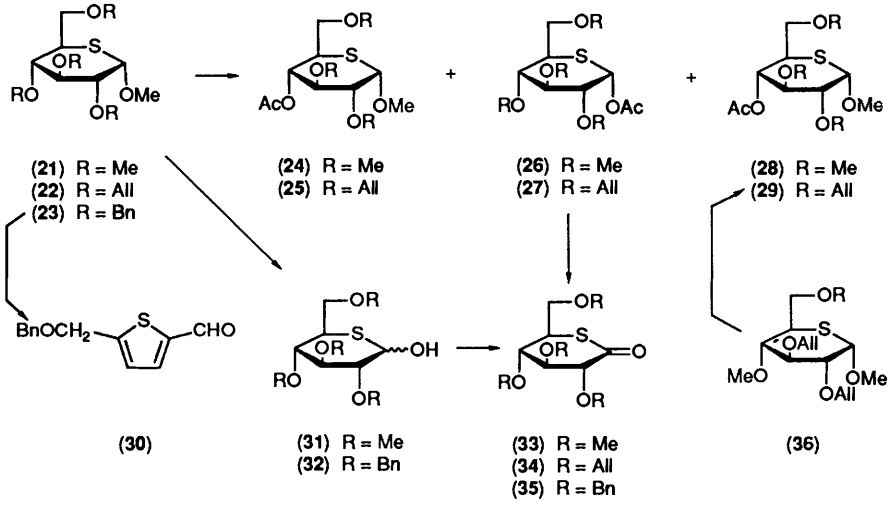


Scheme 4.

The three kinds of 2,3,4,6-tetra-*O*-alkyl, *i.e.*, methyl (**21**), allyl (**22**), and benzyl (**23**), derivatives of the glycoside (**6**) were prepared with the corresponding alkyl halide and sodium hydride in dimethylformamide (DMF) in 75, 83, and 83% yield, respectively. The per-*O*-methyl glycoside (**21**) was also obtained from the 4-*O*-methyl glycoside (**14**) in 71% yield. Allylation of compound (**14**) gave tri-*O*-allyl derivative (**36**) in 80% yield. These per-*O*-alkylated glycosides were then acetolysed. Unexpectedly, acetolysis of compound (**21**) in the presence of sulphuric acid gave the 1,4-diacetate (**28**) in 93% yield. This can be explained by similar anchimeric assistance of the ring-sulphur atom as described above for the formation of compound (**14**). Acetolysis of the tri-*O*-allyl derivative (**36**) gave the 1,4-diacetate (**29**) in 72% yield. On the other hand, acetolysis of the per-*O*-allyl glycoside (**22**) gave the 1-monoacetate (**27**) in 62% yield and a small amount of a mixture of two other products (Scheme 5). One of them is the 1,4-diacetate (**29**), whose structure was identified by ^{1}H NMR spectroscopy, and the other was deduced to be the 4-monoacetate (**25**) by ^{1}H and ^{13}C NMR spectroscopy. The different behaviour of the 4-*O*-allyl substituent toward acetolysis in comparison with that of the 4-*O*-methyl one can be explained by competitive inhibition of protonation for the oxygen atom at C-4 by protonation of the π-bond. Acetolysis of the per-*O*-benzyl derivative (**23**) gave three unidentified products and none of desired acetate.

Transannular participation of the sulphur atom observed in the above mentioned methanolysis and acetolysis may be rationalized by fundamental principles. For instance, Morita and Oae found that solvolysis rates of β-substituted thiacycloalkanes were greatly dependent on the ring size of the substrate.[15] One reason for this dependence can be ascribed to the degree of overlap between the 2p orbital of the β-carbenium ion and the lone pair of sulphur atom. On the other hand, evidence for the 3p-like lone-pair orbital on sulphur has been obtained from photoelectron spectroscopy[16] and a diffraction study[17] of the sulphur compound. Thus, in the sterically fixed 5-thioglucopyranoside ring, enough overlap for participation could be attained by a large 3p orbital on the sulphur atom being perpendicular to the C-5–S–C-1 plane. This large overlap is thought to be the most important origin of the transannular participation.

Another method of acetolysis was then examined. Acetolysis of the per-*O*-methyl glycoside (**21**) with TFA gave the



Scheme 5. All = Allyl, Bn = benzyl.

1-monoacetate (**26**) and the 4-monoacetate (**24**) in 48 and 8% yield, respectively. Acetolysis of the per-*O*-allyl derivative (**22**) with TFA gave only the 1-acetate (**27**) in 80% yield (Scheme 5). Thus, the occurrence of the transannular participation could be suppressed by using a weak acid. This can be explained by the higher ability of sulphur to participate with the α-carbenium ion than with the β-carbenium ion, as expected from the late formation of the 4-*O*-methyl glycoside (**14**) in the above mentioned methanolysis mechanism.

Hydrolysis of the per-*O*-methyl glycoside (**21**) with 76% aq. acetic acid containing sulphuric acid gave the tetra-*O*-methyl derivative (**31**) and the 1-acetate (**26**) in 45 and 7% yield, respectively. Hydrolysis of the per-*O*-benzyl derivative (**23**) with 69% aq. acetic acid containing sulphuric acid gave the tetra-*O*-benzyl derivative (**32**) in 38% yield. With 95% aq. acetic acid containing sulphuric acid, however, another thiophene derivative, compound (**30**), was obtained in 59% yield, with none of desired product. The mechanism of the formation of compound (**30**) is thought to be same as that of the thiophene derivative (**12**) in the methanolysis of 5-thio-D-glucose derivatives.

Oxidation of both the tetra-*O*-methyl derivative (**31**) and the tetra-*O*-benzyl derivative (**32**) with DMSO gave the tetra-*O*-methyl- (**33**) and the tetra-*O*-benzyl-5-thio-D-gluconolactone (**35**) in 70 and 77% yield, respectively. Deacetylation of the tetra-*O*-allyl 1-acetate (**27**), followed by oxidation with DMSO, gave the tetra-*O*-allyl-5-thio-D-gluconolactone (**34**). These per-*O*-alkylated 5-thiogluconolactone derivatives may provide synthetic intermediates for the synthesis of orthothomycin analogues by orthoesterification with diols.

Experimental

M.p.s were measured on a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were measured on a JASCO DIP-4 polarimeter. ^{1}H NMR spectra were recorded, unless otherwise stated, in deuteriochloroform solution with tetramethylsilane as internal standard on a JEOL JNM-PS100 spectrometer (100 MHz), or on a Bruker AM-500 spectrometer (500 MHz). ^{13}C NMR spectra were recorded on a JEOL JNM-FX90Q spectrometer. Column chromatography was performed on silica gel (Merck Kieselgel 7734) with the solvent system specified. Organic extracts were dried with anhydrous magnesium sulphate, and evaporations were conducted under reduced pressure with bath temperature below 40 °C. Distillation of a product was performed with a Buchi GKR-50 Kugelrohr apparatus.

3-O-*Acetyl*-6-O-*benzoyl*-1,2-O-*isopropylidene*-5-O-*methylsulphonyl*-α-D-*glucofuranose* (**2**).—A mixture of compound (**1**)[8] (10 g), acetic acid (150 ml), and water (20 ml) was shaken for 24 h at room temperature and was then evaporated. The residue was further co-evaporated several times with toluene to give a white solid. To a stirred solution of this solid in pyridine (15 ml)–dichloromethane (60 ml) at between −30 and −20 °C was slowly added a solution of benzoyl chloride (4.9 ml) in dichloromethane (40 ml) during 1 h, followed by methanesulphonyl chloride (14 ml). The reaction mixture was gradually warmed to room temperature and the mixture was stirred overnight, washed several times with aq. sodium hydrogen carbonate, and evaporated to give a white solid. The product was washed with ethanol and separated by filtration to give the *sulphonate* (**2**) (10 g, 68%) as a powder, m.p. 112–114 °C; $[\alpha]_D^{20}$ −6.6° (*c* 1.18, $CHCl_3$) (Found: C, 51.4; H, 5.1; S, 7.25. $C_{19}H_{24}O_{10}S$ requires C, 51.35; H, 5.4; S, 7.2%); δ_H 8.2–8.0 and 7.6–7.3 (5 H, m, ArH), 5.91 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 5.31 (1 H, d, $J_{3,4}$ 3.0 Hz, 3-H), 5.14 (1 H, ddd, $J_{4,5}$ 8.8, $J_{5,6a}$ 2.0, $J_{5,6b}$ 6.0 Hz, 5-H), 4.94 (1 H, dd, $J_{6a,6b}$ 13.0 Hz, 6-H^a), 4.54 (1 H, d, 2-H), 4.52 (1 H, dd, 4-H), 4.45 (1 H, dd, 6-H^b), 3.04 (3 H, s, SO_2Me), 2.16 (3 H, s, Ac), and 1.52 and 1.23 (each 3 H, s, CMe_2). An additional crop of the sulphonate (**2**) (1.3 g, 9%) was obtained from the mother liquor by column chromatography on silica gel (hexane–ethyl acetate, 3:1).

5,6-*Anhydro*-1,2-O-*isopropylidene*-β-L-*idofuranose* (**3**).—A solution of the sulphonate (**2**) (170 mg) in 0.05M-sodium methoxide–methanol (5 ml) was kept at room temperature for 9 h. After being cooled to 0 °C, the reaction mixture was neutralized with gaseous carbon dioxide and evaporated. The residue was dissolved in chloroform and washed with water. The organic layer was evaporated and chromatographed on a column of silica gel (hexane–ethyl acetate, 1:1) to give compound (**3**) (30 mg, 66%) as a solid, m.p. 75–76 °C (lit.,[9] 73–75 °C); $[\alpha]_D^{28}$ −24.6° (*c* 1.09, $CHCl_3$) {lit.,[9] $[\alpha]_D^{12}$ −25.2° (*c* 2.304, $CHCl_3$)}; δ_H 5.92 (1 H, d, $J_{1,2}$ 3.4 Hz, 1-H), 4.54 (1 H, d, 2-H), 4.34 (1 H, d, $J_{3,4}$ 3.0 Hz, 3-H), 4.17 (1 H, dd, $J_{4,5}$ 3.4 Hz, 4-H), 3.32 (1 H, q, $J_{5,6a} = J_{5,6b}$ = 3.4 Hz, 5-H), 2.83 (2 H, d, 6-H_2), and 1.47 and 1.30 (each 3 H, s, CMe_2).

3,6-*Di*-O-*acetyl*-5-S-*acetyl*-1,2-O-*isopropylidene*-5-*thio*-α-D-*glucofuranose* (**4**).—A mixture of the epoxide (**3**) (0.50 g) and thiourea (0.19 g) in methanol (13 ml) was kept at room temperature for 5 days and was then evaporated. Dichloromethane was added to the residue, insoluble solid was removed by filtration through Celite, and the filtrate was evaporated. A mixture of the residue and potassium acetate (0.40 g) in acetic acid (0.9 ml)–acetic anhydride (4.5 ml) was refluxed at 140 °C for 19 h. After the mixture had cooled, ice-cold water was added and the mixture was stirred for 1 h before being extracted with chloroform, and the extract was evaporated. The residue was dissolved in ethanol, decolourized with activated charcoal, evaporated after removal of the charcoal, and recrystallized from ethanol to give the crystalline thioacetate (**4**) (0.51 g). The mother liquor was evaporated and the residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 4:1) to give a further crop of compound (**4**) (0.10 g; total yield 68%), m.p. 152–154 °C (lit.,[1] 149 °C); $[\alpha]_D^{20}$ +7.6° (*c* 1.09, $CHCl_3$) [lit.,[1] $[\alpha]_D^{20}$ +7.4° (*c* 1.8, $CHCl_3$)}; δ_H 5.92 (1 H, d, $J_{1,2}$ 3.8 Hz, 1-H), 5.30 (1 H, d, $J_{3,4}$ 2.6 Hz, 3-H), 4.46–4.37 (4 H, m, 2- and 4-H, and 6-H_2), 4.13 (1 H, ddd, 5-H), 2.21 (3 H, s, SAc), 2.07 (6 H, s, OAc), and 1.51 and 1.31 (each 3 H, s, CMe_2).

2,3,4,6-*Tetra*-O-*acetyl*-5-*thio*-D-*glucopyranose* (**8**).—A mixture of the penta-acetate (**5**)[1] (61 mg) and hydrazinium acetate (16 mg) in DMF (1.2 ml) was stirred for 20 min at 50 °C. The reaction mixture was diluted with ethyl acetate and washed twice with aq. sodium chloride and evaporated. The residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 1:1) to give *compound* (**8**) (47 mg, 86%) as a solid, $[\alpha]_D^{20}$ +133.9° (*c* 1.60, $CHCl_3$) (Found: C, 46.4; H, 5.6. $C_{14}H_{20}O_9S$ requires C, 46.15; H, 5.5%); δ_H 5.62–5.04 (4 H, m, 1-, 2-, 3-, and 4-H), 4.34 (1 H, dd, $J_{5,6a}$ 5.0, $J_{6a,6b}$ 12.0 Hz, 6-H^a), 4.05 (1 H, dd, $J_{5,6b}$ 3.0 Hz, 6-H^b), 3.68 (1 H, ddd, $J_{4,5}$ 10.8 Hz, 5-H), 3.32 (1 H, br s, OH), 2.06 (6 H, s, Ac), and 2.04 and 2.00 (each 3 H, s, Ac).

2,4,6-*Tri*-O-*acetyl*-3-*deoxy*-5-*thio*-D-erythro-*hex*-2-*eno*-1,5-*lactone* (**9**).—A solution of compound (**8**) (0.94 g) in DMSO (7.5 ml) containing acetic anhydride (6.3 ml) was kept at room temperature for 38 h. The reaction mixture was diluted with water and extracted with diethyl ether. The extract was washed several times with water and evaporated. The residue was chromatographed on a column of silica gel (benzene–ethyl acetate, 6:1) to give the syrupy *enolactone* (**9**) (0.55 g, 71%), $[\alpha]_D^{20}$ +180.6° (*c* 1.40, $CHCl_3$) (Found: C, 47.65; H, 4.6; S, 10.4. $C_{12}H_{14}O_7S$ requires C, 47.7; H, 4.7; S, 10.6%); δ_H 6.37 (1 H, d,

$J_{3,4}$ 4.6 Hz, 3-H), 5.77 (1 H, dd, $J_{4,5}$ 7.0 Hz, 4-H), 4.48 (1 H, dd, $J_{5,6a}$ 5.4, $J_{6a,6b}$ 12.0 Hz, 6-H^a), 4.23 (1 H, $J_{5,6b}$ 6.8 Hz, 6-H^b), 3.95 (1 H, dt, 5-H), and 2.21, 2.13, and 2.09 (each 3 H, s, Ac); δ_C 189.2 (C-1), 170.1, 169.7, and 168.1 (C=O), 143.9 (C-2), 128.6 (C-3), 65.8 and 62.5 (C-4 and -6), 45.7 (C-5), and 20.6, 20.5, and 20.1 (*Me*CO).

General Methods for Methanolysis of 5-Thio-D-glucose Derivatives.—The amount of substrates and products, and reaction conditions are given in the Table. The reaction mixture was processed as follows. The reaction mixture (after cooling if necessary) was neutralized with lead carbonate and insoluble solid was removed by filtration through Celite. After evaporation of the filtrate, the residue was partitioned between water and chloroform. The aqueous layer was evaporated and the residue was fractionated on a column of Dowex 1 (HO^-) with water to give compound (**14**) as an amorphous solid in an early fraction, and compound (**6**) as a crystalline solid in a later fraction. The organic layer was evaporated and the residue was chromatographed on a column of silica gel [hexane–ethyl acetate, 2:1 (medium A) or 4:1 (medium B)] to give compound (**19**) as a syrup (medium A) or compound (**12**) as a syrup (medium B).

Methyl 5-thio-α-D-glucopyranoside (**6**) had m.p. 127–128 °C (lit.,[18] 126 °C); $\delta_H(D_2O)$ 5.03 (1 H, d, $J_{1,2}$ 3.0 Hz, 1-H), 4.50 (1 H, d, $J_{5,6a}$ 4.8 Hz, 6-H^a), 4.24–3.97 (3 H, m, 2-, 3-, and 4-H), 4.02 (1 H, d, $J_{5,6b}$ 6.5 Hz, 6-H^b), 3.86 (3 H, s, OMe), and 3.46 (1 H, ddd, $J_{4,5}$ 8.8 Hz, 5-H).

Compound (**6**) was acetylated with acetic anhydride–pyridine in the usual manner to give crystalline methyl 2,3,4,6-tetra-*O*-acetyl-5-thio-α-D-glycopyranoside, m.p. 97–98 °C (lit.,[18] 98–99 °C); $[\alpha]_D^{22}$ +217.8° (*c* 1.09, $CHCl_3$) [lit.,[18] $[\alpha]_D^{25}$ +224.8° (*c* 1.8, $CHCl_3$)]; δ_C 170.4, 170.0, 169.5, and 169.4 (C=O), 81.2 (C-1), 74.8, 72.3, and 70.9 (C-2, -3, and -4), 61.3 (C-6), 56.5 (OMe), 38.3 (C-5), and 20.7 and 20.5 (*Me*CO); and ^{1}H NMR spectral data were in good accord with those reported.[19]

Methyl 4-O-*methyl*-5-*thio*-α-D-*glucopyranoside* (**14**) had m.p. 101–103 °C; $[\alpha]_D^{20}$ +287.2° (*c* 1.22, MeOH) (Found: C, 42.4; H, 6.8; S, 14.1. $C_8H_{16}O_5S$ requires C, 42.8; H, 7.2; S, 14.3%); $\delta_H(D_2O)$ 5.05 (1 H, d, $J_{1,2}$ 2.8 Hz, 1-H), 4.40–3.78 (5 H, m, 2-, 3-, and 4-H, and 6-H_2), 4.00 and 3.87 (each 3 H, s, OMe), and 3.50 (1 H, ddd, $J_{4,5}$ 8.0, $J_{5,6a}$ 3.5, $J_{5,6b}$ 5.0 Hz, 5-H).

Compound (**14**) was acetylated with acetic anhydride–pyridine in the usual manner to give the *triacetate* (**15**) as a syrup, $[\alpha]_D^{20}$ +220.0° (*c* 1.85, $CHCl_3$) (Found: C, 47.9; H, 6.3; S, 9.1. $C_{14}H_{22}O_8S$ requires C, 48.0; H, 6.3; S, 9.15%); δ_H 5.42 (1 H, dd, $J_{2,3}$ 9.8, $J_{3,4}$ 8.5 Hz, 3-H), 5.09 (1 H, dd, $J_{1,2}$ 2.8 Hz, 2-H), 4.56 (1 H, d, 1-H), 4.36 (2 H, d, $J_{5,6a} = J_{5,6b}$ = 3.5 Hz, 6-H_2), 3.54 (1 H, dd, $J_{3,4}$ 8.5, $J_{4,5}$ 11.0 Hz, 4-H), 3.44 and 3.41 (each 3 H, s, OMe), 3.23 (1 H, dt, 5-H), and 2.10, 2.08, and 2.05 (each 3 H, s, Ac); δ_C 170.4, 170.1, and 169.4 (C=O), 81.9 (C-4), 81.2 (C-1), 75.0 (C-2), 72.4 (C-3), 61.9 (C-6), 60.1 and 56.4 (OMe), 39.4 (C-5), and 20.8 and 20.6 (*Me*CO).

2,5-*Dideoxy*-2,5-*epithio*-4,6-*di*-O-*methyl*-D-*mannose dimethyl acetal* (**19**) had $[\alpha]_D^{20}$ +88.3° (*c* 1.05, $CHCl_3$) (Found: C, 47.6; H, 7.4; S, 12.45. $C_{10}H_{20}O_5S$ requires C, 47.6; H, 8.0; S, 12.7%); δ_H(500 MHz) 4.42 (1 H, d, $J_{1,2}$ 8.2 Hz, 1-H), 4.12 (1 H, dt, $J_{2,3} = J_{3,4}$ = 6.3, $J_{3,OH}$ 4.0 Hz, 3-H), 3.62 (1 H, t, $J_{4,5}$ 6.3 Hz, 4-H), 3.61 (1 H, dd, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 10.0 Hz, 6-H^a), 3.51 (1 H, dd, $J_{5,6b}$ 6.1 Hz, 6-H^b), 3.50, 3.42, 3.40, and 3.37 (each 3 H, s, OMe), 3.40 (1 H, ddd, 5-H), and 3.39 (1 H, dd, 2-H); δ_C 107.3 (C-1), 89.2 (C-4), 78.7 (C-3), 74.8 (C-6), 59.2, 58.5, 54.4, and 53.6 (OMe), and 50.7 and 47.2 (C-2 and -5).

Acetylation of compound (**19**) with acetic anhydride–pyridine in the usual manner to give 3-O-*acetyl*-2,5-*dideoxy*-2,5-*epithio*-4,6-*di*-O-*methyl*-D-*mannose dimethyl acetal* (**20**) as a syrup, $[\alpha]_D^{20}$ +91.3° (*c* 1.40, $CHCl_3$) (Found: C, 48.6; H, 7.4; S, 11.2. $C_{12}H_{22}O_6S$ requires C, 49.0; H, 7.5; S, 10.9%); δ_H(500 MHz) 5.46 (1 H, t, $J_{2,3} = J_{3,4}$ = 4.2 Hz, 3-H), 4.46 (1 H, d, $J_{1,2}$ 8.2 Hz, 1-H), 3.87 (1 H, t, $J_{4,5}$ 4.2 Hz, 4-H), 3.57 (1 H, dd, $J_{5,6a}$ 7.4, $J_{6a,6b}$ 9.3 Hz, 6-H^a), 3.49 (1 H, dd, 2-H), 3.49 (1 H, ddd, $J_{5,6b}$ 6.2 Hz, 5-H), 3.43 (1 H, dd, 6-H^b), 3.42, 3.38, 3.36, and 3.35 (each 3 H, s, OMe), and 2.08 (3 H, s, Ac); δ_C 169.6 (C=O), 105.8 (C-1), 87.3 (C-4), 78.8 (C-3), 74.4 (C-6), 58.8, 57.8, 54.5, and 53.8 (OMe), 51.3 and 48.5 (C-2 and -5), and 21.0 (*Me*CO).

^{1}H And ^{13}C NMR spectra of the thiophene derivative (**12**) were in good accord with those reported;[20] δ_H 9.78 (1 H, s, CHO), 7.60 (1 H, d, $J_{3,4}$ 3.6 Hz, 4-H), 7.04 (1 H, d, 3-H), 4.62 and 4.64 (each 1 H, s, CH_2), and 3.43 (3 H, s, OMe); δ_C 182.7 (C=O), 152.1 (C-2), 143.4 (C-5), 136.2 (C-3), 126.5 (C-4), 69.4 (C-6), and 58.4 (OMe).

Methyl 2,3,4,6-*Tetra*-O-*methyl*-5-*thio*-α-D-*glucopyranoside* (**21**).—(a) *From compound* (**6**). A solution of compound (**6**) (2.2 g) in DMF (20 ml) was slowly added to a stirred suspension of 55% sodium hydride (4 g) in DMF (5 ml). After several hours, a solution of methyl iodide (3.3 ml) in DMF (10 ml) was slowly added to the reaction mixture at 0 °C and the mixture was stirred at room temperature overnight. After careful addition of ice-cold water, the reaction mixture was extracted with diethyl ether. The extract was washed with water and evaporated, and the residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 4:1) to give compound (**21**) (2.1 g, 75%) as a syrup.

(b) *From compound* (**14**). Treatment of compound (**14**) with 55% sodium hydride (0.2 g) and methyl iodide (0.17 ml) as described above for the methylation of compound (**6**) gave the penta-*O*-methyl compound (**21**) (126 mg, 71%).

Further purification of compound (**21**) was performed by distillation (Kugelrohr). The *per*-O-*methyl glycoside* (**21**) had $[\alpha]_D^{20}$ +267.2° (*c* 1.22, $CHCl_3$) (Found: C, 49.4; H, 8.45; S, 12.1. $C_{11}H_{22}O_5S$ requires C, 49.6; H, 8.3; S, 12.0%); δ_H 4.55 (1 H, d, $J_{1,2}$ 1.5 Hz, 1-H), 3.80 (1 H, dd, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 9.5 Hz, 6-H^a), 3.7–3.2 (4 H, m, 2-, 3-, and 4-H, and 6-H^b), 3.61, 3.57, 3.51, 3.45, and 3.38 (each 3 H, s, OMe), and 2.99 (1 H, ddd, $J_{4,5}$ 9.0, $J_{5,6b}$ 1.2 Hz, 5-H); δ_C 86.2, 84.9, and 83.8 (C-2, -3, and -4), 81.1 (C-1), 70.5 (C-6), 61.1, 60.7, 58.8, 58.3, and 56.2 (OMe), and 40.7 (C-5).

Methyl 2,3,4,6-*Tetra*-O-*allyl*-5-*thio*-α-D-*glucopyranoside* (**22**).—Treatment of compound (**6**) (3.45 g) with 55% sodium hydride (8 g) and allyl bromide (8.7 ml) as described for the methylation of this substrate, and purification of the product on silica gel (hexane–ethyl acetate, 9:1), gave the *alkyl derivative* (**22**) (5.05 g, 83%) as a syrup, $[\alpha]_D^{25}$ +181.5° (*c* 1.05, $CHCl_3$) (Found: C, 61.3; H, 7.8; S, 8.7. $C_{19}H_{30}O_5S$ requires C, 61.6; H, 8.2; S, 8.65%); δ_H 6.20–5.70 (4 H, m, C*H*=CH_2), 5.4–5.0 (8 H, m, CH=CH_2), 4.49–3.46 (14 H, m, 1-, 2-, 3-, and 4-H, 6-H_2, and CH_2O), 3.44 (3 H, s, OMe), and 3.09 (1 H, m, 5-H); δ_C 135.6, 135.1, and 134.5 (*C*H=CH_2), 117.4, 117.1, 116.5, and 116.2 (CH=*C*H_2), 83.9, 82.9, 82.3, and 81.9 (C-1, -2, -3, and -4), 74.8, 74.4, 72.4, and 72.2 (CH_2O), 67.9 (C-6), 56.4 (OMe), and 40.9 (C-5).

Methyl 2,3,4,6-*Tetra*-O-*benzyl*-5-*thio*-α-D-*glucopyranoside* (**23**).—Treatment of compound (**6**) (0.78 g) with 55% sodium hydride (1.3 g) and benzyl chloride (3.0 ml) as described above for the methylation, and purification of the product on silica gel (hexane–ethyl acetate, 8:1), gave the *benzyl derivative* (**23**) (1.75 g, 83%) as a syrup, $[\alpha]_D^{18}$ +82.4° (*c* 1.14, $CHCl_3$) (Found: C, 73.5; H, 6.6; S, 5.7. $C_{35}H_{38}O_5S$ requires C, 73.65; H, 6.7; S, 5.6%); δ_H 7.3–7.1 (20 H, m, ArH), 5.0–4.3 (9 H, m, 1-H and CH_2Ph), 4.0–3.4 (5 H, m, 2-, 3-, and 4-H, and 6-H_2), 3.40 (3 H, s, OMe), and 3.18 (1 H, m, 5-H); δ_C 139.0, 138.5, 128.4, 128.1, 128.0, and 127.7 (Ar), 84.4, 83.4, and 82.1 (C-2, -3, -4), 73.2 (*C*H_2Ph), 67.9 (C-6), 56.5 (OMe), and 41.1 (C-5).

Methyl 2,3,6-*Tri*-O-*allyl*-4-O-*methyl*-5-*thio*-α-D-*glucopyranoside* (**36**).—Treatment of compound (**14**) (75 mg) with 55% sodium hydride (80 mg) and allyl chloride (0.12 ml) as described for the allylation of compound (**6**), and purification of the product on silica gel (hexane–ethyl acetate, 9:1), gave the *title compound* (**36**), (92 mg, 80%) as a syrup, $[\alpha]_D^{20}$ +152.3° (*c* 1.27, $CHCl_3$) (Found: C, 59.3; H, 8.1; S, 9.35. $C_{17}H_{28}O_5S$ requires C, 59.3; H, 8.2; S, 9.3%); δ_H 6.2–5.7 (3 H, m, C*H*=CH_2), 5.4–5.0 (6 H, m, CH=CH_2), 4.48 (1 H, d, $J_{1,2}$ 2.0 Hz, 1-H), 4.5–3.3 (11 H, m, 2-, 3-, and 4-H, 6-H_2, and CH_2O), 3.60 and 3.46 (each 3 H, s, OMe), and 3.00 (1 H, m, 5-H); δ_C 135.6, 135.1, and 134.5 (*C*H=CH_2), 117.3, 117.0, and 116.1 (CH=*C*H_2), 83.9, 82.9, and 82.2 (C-1, -2, -3, and -4), 74.7, 72.3, 72.2, and 68.0 (C-6 and CH_2O), 61.1 and 56.4 (OMe), and 41.0 (C-5).

Acetolysis of the Per-O-*methyl Glycoside* (**21**).—(a) *In the presence of sulphuric acid.* A solution of compound (**21**) (185 mg) in acetic anhydride (3 ml)–acetic acid (12 ml) containing sulphuric acid (5×10^{-4} v/v) was kept at room temperature for 24 h. After addition of ice-cold water, the reaction mixture was extracted with chloroform. The extract was washed successively with aq. sodium hydrogen carbonate and water, and evaporated. The residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 3:1) to give 1,4-di-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-glucopyranose (**28**) (209 mg, 93%) as a syrup. Further purification was performed by treatment with 1×10^{-2} M-sodium methoxide in methanol, chromatography on a column of silica gel (hexane–ethyl acetate, 1:2), acetylation with acetic anhydride–pyridine, and chromatography on a column of silica gel (hexane–ethyl acetate, 2:1).

The *diacetate* (**28**) had $[\alpha]_D^{18}$ +242.9° (*c* 1.36, $CHCl_3$) (Found: C, 48.4; H, 6.7; S, 10.0. $C_{13}H_{22}O_7S$ requires C, 48.4; H, 6.9; S, 9.95%); δ_H(500 MHz) 6.16 (1 H, d, $J_{1,2}$ 3.2 Hz, 1-H), 5.12 (1 H, dd, $J_{3,4}$ 9.4, $J_{4,5}$ 10.5 Hz, 4-H), 3.53 (1 H, dd, $J_{2,3}$ 9.4 Hz, 2-H), 3.52, 3.45, and 3.31 (each 3 H, s, OMe), 3.44–3.38 (3 H, m, 5-H, and 6-H_2), 3.40 (1 H, t, 3-H), and 2.15 and 2.12 (each 3 H, s, Ac); δ_C 169.5 and 169.0 (C=O), 84.5 and 81.5 (C-2 and -3), 74.2 (C-4), 71.0 (C-6), 69.9 (C-1), 60.9, 59.0, and 58.2 (OMe), and 20.9 and 20.7 (*Me*CO).

(b) *In the presence of TFA.* A solution of compound (**21**) (500 mg) in a mixture of acetic anhydride (5 ml), acetic acid (17.5 ml), and TFA (2.5 ml) was heated at 65 °C for 3 h. After addition of ice-cold water, the reaction mixture was extracted with chloroform. The extract was washed successively with aq. sodium hydrogen carbonate and water, and evaporated. The residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 4:1) to give a crude mixture (377 mg), treatment of which with 5×10^{-3}M-sodium methoxide in the usual manner of deacetylation, and chromatography on silica gel (gradient elution with hexane–acetone, 6:1 ⟶ 5:2), gave three fractions. In the first fraction, substrate (**21**) was recovered (43 mg, 9%). Products in the second and third fractions were acetylated with acetic anhydride–pyridine in the usual manner to give methyl 4-*O*-acetyl-2,3,6-tri-*O*-methyl-5-thio-α-D-glucopyranoside (**24**) (42 mg, 8%) as a syrup and 1-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose (**26**) (267 mg, 48%) as a syrup, respectively.

The 4-*acetate* (**24**) had $[\alpha]_D^{24}$ +229.2° (*c* 0.85, $CHCl_3$) (Found: C, 48.9; H, 7.6; S, 10.9. $C_{12}H_{22}O_6S$ requires C, 49.0; H, 7.5; S, 10.9%); δ_H 5.09 (1 H, t, *J* 8.0 Hz, 4-H), 4.59 (1 H, d, $J_{1,2}$ 2.0 Hz, 1-H), 3.68–3.08 (5 H, m, 2-, 3-, and 5-H, and 6-H_2), 3.53 (6 H, s, OMe), 3.49 and 3.33 (each 3 H, s, OMe), and 2.12 (3 H, s, Ac); δ_C 169.7 (C=O), 85.8 and 81.9 (C-2 and -3), 81.1 (C-1), 74.8 (C-4), 71.1 (C-6), 61.1, 59.0, 58.6, and 56.5 (OMe) 39.5 (C-5), and 20.7 (*Me*CO).

The 1-acetate (**26**) had $[\alpha]_D^{20}$ +305.3° (*c* 1.03, $CHCl_3$) (Found: C, 48.7; H, 7.6; S, 10.8%); δ_H 6.06 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), 3.72 (1 H, dd, $J_{5,6a}$ 4.8, $J_{6a,6b}$ 9.8 Hz, 6-H^a), 3.62–3.02 (5 H, m, 2-, 3-, 4-, and 5-H, and 6-H^b), 3.77 (6 H, s, OMe), 3.40 and 3.32 (each 3 H, s, OMe), and 2.08 (3 H, s, Ac); δ_C 169.2 (C=O), 85.0, 84.7, and 83.3 (C-2, -3, and -4), 70.2 (C-1 and -6), 61.3, 61.0, 59.0, and 58.2 (OMe), 42.3 (C-5), and 21.0 (*Me*CO).

Hydrolysis of the Per-O-*methyl Glycoside* (**21**).—A solution of compound (**21**) (148 mg) in a mixture of acetic acid (25 ml), water (5.6 ml), and 1M-sulphuric acid (2.1 ml) was heated at 90 °C for 2 h. After addition of ice-cold, aq. sodium hydrogen carbonate, the reaction mixture was extracted with chloroform. The extract was washed successively with aq. sodium hydrogen carbonate and water, and evaporated. The residue was chromatographed on a column of silica gel (gradient elution with hexane–ethyl acetate, 3:1 ⟶ 1:1) to give the 1-acetate (**26**) (12 mg, 7%) in an early fraction, and 2,3,4,6-tetra-*O*-methyl-5-thio-α-D-glucopyranose (**31**) (63 mg, 45%) was a syrup in a later fraction. ^{1}H NMR spectral data of compound (**26**) were in accord with those reported above. The *tetramethyl ether* (**31**) had $[\alpha]_D^{28}$ +148.8° (*c* 1.53, $CHCl_3$) (Found: C, 47.5; H, 7.7; S, 12.6. $C_{10}H_{20}O_5S$ requires C, 47.6; H, 8.0; S, 12.7%); δ_H 4.98 (1 H, s, 1-H), 3.74 (1 H, dd, $J_{5,a}$ 3.8, $J_{6a,6b}$ 10.0 Hz, 6-H^a), 3.65–3.00 (5 H, m, 2-, 3-, 4-, and 5-H, and 6-H^b), 3.59, 3.55, 3.49, and 3.34 (each 3 H, s, OMe), and 2.89 (1 H, br s, OH). No signals corresponding to the β-anomer were observed. Acetylation of compound (**31**) with acetic anhydride–pyridine in the usual manner gave the 1-acetate (**26**).

Acetolysis of the Tri-O-allyl Ether (**36**).—Treatment of compound (**36**) (92 mg) with acetic anhydride (3 ml)–acetic acid (12 ml) containing sulphuric acid (5×10^{-4} v/v) as described above for the acetolysis of compound (**21**) (a), and chromatography on a column of silica gel (hexane–ethyl acetate, 6:1), gave 1,4-*di*-O-*acetyl*-2,3,6-*tri*-O-*allyl*-5-*thio*-α-D-*glucopyranose* (**29**) (77 mg, 72%) as a syrup, $[\alpha]_D^{18}$ +146.0° (*c* 1.29, $CHCl_3$) (Found: C, 56.95; H, 7.1; S, 8.0. $C_{19}H_{28}O_7S$ requires C, 57.0; H, 7.05; S, 8.0%); δ_H 6.08 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), 6.1–5.6 (3 H, m, C*H*=CH_2), 5.4–5.0 (7 H, m, 4-H and CH=CH_2), 4.4–3.3 (11 H, m, 2-, 3-, and 5-H, 6-H_2, and CH_2O), and 2.14 and 2.07 (each 3 H, s, Ac); δ_C 169.6 and 169.2 (C=O), 135.0, 134.4, and 134.1 (*C*H=CH_2), 117.6 (× 2) and 116.2 (CH=*C*H_2), 82.2 and 79.9 (C-2, -3), 74.7, 74.4, 72.4, 71.7, 70.8, and 68.6 (C-1, -4, and -6, and CH_2O), and 41.2 (C-5).

Acetolysis of the Tetra-O-*allyl Ether* (**22**).—(a) *In the presence of sulphuric acid.* Treatment of compound (**22**) (260 mg) with acetic anhydride (3.4 ml)–acetic acid (13.8 ml) containing sulphuric acid (5×10^{-4} v/v), as described for the acetolysis of compound (**21**) (a), and chromatography on silica gel (gradient elution with hexane–ethyl acetate, from 9:1 ⟶ 5:1) gave 1-O-acetyl-2,3,4,6-tetra-O-allyl-5-thio-α-D-glucopyranose (**27**) (173 mg, 62%) as a syrup in an early fraction, and a crude mixture (43 mg) of two products in a later fraction. One product in the mixture was assigned to be the 1,4-diacetate (**29**) from its ^{13}C and ^{1}H NMR spectral data on comparison with the authentic sample obtained above. The remaining signals in the ^{13}C and ^{1}H NMR spectra of the mixture indicated the presence of methyl 4-O-acetyl-2,3,6-tri-O-allyl-5-thio-α-D-glycopyranoside (**25**), δ_H 3.48 (s, OMe) and 2.05 (s, Ac); assignment of other signals was impossible; δ_C 169.7 (C=O), 135.1, 134.8, and 134.3 (*C*H=CH_2), 117.3 and 116.1 (CH=*C*H_2), 83.7, 82.2, and 80.1 (C-1, -2, and -3), 75.0, 72.4, 71.7, 70.8, and 68.7 (C-4, -6, and CH_2O), 56.6 (OMe), 39.7 (C-5), and 20.9 (*Me*CO).

(b) *In the presence of TFA.* Treatment of compound (**22**) (524 mg) with acetic anhydride (10 ml), acetic acid (35 ml), and TFA (5 ml) as described above for the acetolysis of compound (**21**) (b), and chromatography on a column of silica gel (hexane–ethyl acetate, 9:1), gave the 1-*acetate* (**27**) (450 mg, 80%), $[\alpha]_D^{20}$

+175.5° (*c* 1.47, $CHCl_3$) (Found: C, 60.2; H, 7.7; S, 7.6. $C_{20}H_{30}O_6S$ requires C, 60.3; H, 7.6; S, 8.05%); δ_H 6.04 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), 6.2–5.6 (4 H, m, C*H*=CH_2), 5.4–5.0 (8 H, m, CH=CH_2), 4.5–3.1 (14 H, 2-, 3-, 4-, and 5-H, 6-H_2, and CH_2O), and 2.10 (3 H, s, Ac); δ_C 169.3 (C=O), 135.4, 134.9, 134.6, and 134.3 (*C*H=CH_2), 117.3 (× 2), 116.7, and 116.2 (CH=*C*H_2), 82.8, 82.5, and 81.3 (C-2, -3, and -4), 74.9, 74.6, 72.2, 71.7, and 71.2 (C-1 and CH_2O), 67.6 (C-6), 42.5 (C-5), and 21.1 (*Me*CO).

*Hydrolysis of the Tetra-*O*-benzyl Glycoside* (**23**).—(a) *Under the conditions of higher water content.* Treatment of compound (**23**) (118 mg) with acetic acid (12.5 ml), water (5 ml), and 1M-sulphuric acid (0.63 ml) for 4 h as described for the hydrolysis of the per-*O*-methyl glycoside (**21**), and chromatography on a column of silica gel (hexane–ethyl acetate, 3:1), gave 2,3,4,6-*tetra*-O-*benzyl*-5-*thio*-D-*glucopyranose* (**32**) (53 mg, 50%), as a syrup, $[\alpha]_D^{25}$ +54.7° (*c* 1.76, $CHCl_3$) (Found: C, 73.8; H, 6.7; S, 5.2. $C_{34}H_{36}O_5S$ requires C, 73.35; H, 6.5; S, 5.75%); δ_C 138.8, 138.3, 137.8, 128.5, 128.3, 128.0, 127.9, 127.8, 127.7, and 127.5 (Ar), 84.4, 82.9, and 81.9 (C-2, -3, and -4), 76.2 (C-1), 73.2, 73.0, 71.6, and 67.8 (C-6 and CH_2Ph), and 41.3 (C-5).

Acetylation of compound (**32**) with acetic anhydride–pyridine in the usual manner gave 1-O-*acetyl*-2,3,4,6-*tetra*-O-*benzyl*-5-*thio*-α-D-*glucopyranose* as a syrup, $[\alpha]_D^{28}$ +133.4° (*c* 1.54, $CHCl_3$) (Found: C, 72.6; H, 6.3; S, 5.3. $C_{36}H_{38}O_6S$ requires C, 72.2; H, 6.4; S, 5.4%); δ_C 169.4 (C=O), 138.8, 138.2, 137.6, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, and 127.5 (Ar), 83.2, 83.1, and 81.5 (C-2, -3, and -4), 75.8, 73.3, 72.6, 70.8, and 67.5 (C-1, -6, and CH_2Ph), 42.6 (C-5), and 21.1 (*Me*CO).

(b) *Under the conditions of low water content.* Treatment of compound (**23**) (61 mg) with acetic acid (6.5 ml) and 1M-sulphuric acid (0.32 ml) for 1 h as described for the hydrolysis of compound (**21**), and chromatography on a column of silica gel (hexane–ethyl acetate, 6:1), gave 5-(benzyloxymethyl)-thiophene-2-carboxaldehyde (**30**) (14.5 mg, 59%) as a syrup, δ_H 9.83 (1 H, s, CHO), 7.63 (1 H, d, $J_{3,4}$ 4.0 Hz, 4-H), 7.33 (5 H, m, Ph), 7.04 (1 H, d, 3-H), and 4.71 and 4.57 (each 2 H, s, CH_2OCH_2Ph).

2,3,4,6-*Tetra*-O-*methyl*-5-*thio*-D-*glucono*-1,5-*lactone* (**33**).—A solution of compound (**31**) (42.5 mg) in DMSO (2 ml)–acetic anhydride (1.6 ml) was kept at room temperature for 42 h. After addition of ice-cold water, the reaction mixture was extracted with diethyl ether. The extract was washed with water and evaporated. The residue was chromatographed on a column of silica gel (hexane–ethyl acetate, 4:1) to give the *title compound* (**33**) (30 mg, 70%) as a syrup, $[\alpha]_D^{30}$ +213.1° (*c* 1.21, $CHCl_3$) (Found: C, 48.0; H, 7.3. $C_{10}H_{18}O_5S$ requires C, 48.0; H, 7.25%); δ_C 199.2 (C-1), 86.3, 84.4, and 81.4 (C-2, -3, and -4), 71.5 (C-6), 44.3 (C-5), and 59.1, 58.8, 58.5, and 58.3 (OMe).

2,3,4,6-*Tetra*-O-*allyl*-5-*thio*-D-*glucono*-1,5-*lactone* (**34**).—A mixture of compound (**27**) (173 mg), sodium hydrogen carbonate (0.2 g), and methanol (20 ml) was stirred at room temperature for 2 days and was then evaporated. The residue was partitioned between water and chloroform, and the organic phase was evaporated. Treatment of the residue with DMSO (10 ml) and acetic anhydride (8.5 ml) as described above for the preparation of compound (**33**), and chromatography on a column of silica gel (hexane–ethyl acetate, 11:1), gave the *title compound* (**34**) (127 mg, 55%) as a syrup, $[\alpha]_D^{20}$ +136.5° (*c* 1.58, $CHCl_3$) (Found: C, 60.7; H, 7.5; S, 9.05. $C_{18}H_{26}O_5S$ requires C, 61.0; H, 7.4; S, 9.05%); δ_C 199.3 (C-1), 134.3 (× 2), 134.1, and 133.6 (*C*H=CH_2), 118.2, 117.5 (× 3) (CH=*C*H_2), 84.3, 82.8, and 79.8 (C-2, -3, and -4), 72.3 (CH_2O), 68.9 (C-6), and 44.6 (C-5).

2,3,4,6-*Tetra*-O-*benzyl*-5-*thio*-D-*glucono*-1,5-*lactone* (**35**).—Treatment of compound (**32**) (74 mg) with DMSO (3 ml) and acetic anhydride (2.4 ml) as described for the preparation of compound (**33**), and chromatography on a column of silica gel (hexane–ethyl acetate, 10:1), gave the *title compound* (**35**) (57 mg, 77%) as a syrup, $[\alpha]_D^{28}$ +120.6° (*c* 0.99, $CHCl_3$) (Found: C, 73.1; H, 6.2; S, 5.9. $C_{34}H_{34}O_5S$ requires C, 73.6; H, 6.2; S, 5.8%); δ_C 198.2 (C-1), 136.6, 136.5, 136.4, 135.8, 127.3, 127.2, 126.9, 126.8, and 126.6 (Ar), 82.9, 81.6, and 78.9 (C-2, -3, and -4), 72.1 and 71.9 (CH_2Ph), 67.7 (C-6), and 43.7 (C-5).

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