Thio-sugars. Part 9.[1] Derivatives of 3,6-Anhydro-5-thio-D-glucose

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Pyrolysis of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-(methylthio)thiocarbonyl-α-D-glucofuranose and of the β-L-*ido*-isomer gives low yields of the corresponding 5-(methylthio)carbonylthio-compounds; the main product is 2-(hydroxyacetyl)furan. The reaction of potassium thiobenzoate with 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose occurs approximately ten times more rapidly than that with the β-L-*ido*-isomer: the products are 3,6-anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene-5-thio-β-L-idofuranose and -α-D-glucofuranose, respectively. Basic, then acid-catalysed solvolysis of the latter product, in methanol, followed by acetylation, gives methyl 2-*O*-acetyl-5-*S*-acetyl-3,6-anhydro-α- and -β-D-glucofuranoside (no pyranoside is formed), but basic solvolysis, followed by hydrolysis with trifluoroacetic acid and acetylation, gives 2-*O*-acetyl-1,4:3,6-dianhydro-5-thio-α-D-glucopyranoside.

THE presence of a tetrahydrofuran ring in 3,6-anhydro-aldohexoses imposes an important constraint on the stability and even the co-existence of a furanose or a pyranose ring. Only 3,6-anhydroglucose and 3,6-anhydromannose can exist both as furanosides and as pyranosides; furthermore, contrary to the normal situation with simple glycosides, the furanoside is the thermodynamically more stable form. This is strikingly illustrated [2] by the extremely rapid acid-catalysed conversion of methyl 3,6-anhydro-α- and -β-D-glucopyranosides into the corresponding furanosides with retention of anomeric configuration, and similar transformations occur in the analogous 2-deoxyglucose and mannose derivatives.[3] However, it has been shown [4] that the 3,6-thioanhydroglucopyranoside (1) is not isomerised under these conditions, and this stability has been attributed to a reduction in the strain in the pyranoside ring, compared with that in the oxygen analogue, resulting from the greater length of the C–S bonds in the anhydro ring.

Recent investigations on thio-sugars have shown that the preferred cyclic form of a 4-thioaldose is furanose,[5] indicating that in this type of compound the formation of a hemithioacetal is dominant. This raises the question as to whether in a 3,6-anhydro-5-thioaldose a thiopyranose ring would be more favoured than the furanose, and a study has now been made to provide some evidence on this point. The essential requirement was a satisfactory synthesis of a 3,6-anhydro-glucose (or -mannose) derivative having a suitable thio-function at C-5.

The thermal rearrangement of a (methylthio)thiocarbonyloxy- to a (methylthio)carbonylthio-group proceeds with retention of configuration,[4] and we therefore began by converting 3,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose (2), by treatment with sodium hydroxide and carbon disulphide, followed by methylation with methyl iodide, into the 5-*O*-(methylthio)thiocarbonyl derivative (3). Pyrolysis of this compound, either by passage through a heated tube [6] at 500 °C, or by heating in boiling diphenyl ether,[7] gave only a 1—2% yield of the rearranged compound (4), isolated by t.l.c. The identity of this product was confirmed by analytical and spectroscopic evidence; in particular, it showed i.r. absorption at 1 650 cm^{-1} (S–CO–S), and the ^1H n.m.r. spectrum was very similar to that of the xanthate (3) with the exception that the signals for H-5 and the SMe protons were shifted upfield by 1.8 and 0.2 p.p.m., respectively. The major product from the pyrolysis was a crystalline sulphur-free compound which was identified as 2-(hydroxyacetyl)furan (25); this has previously been obtained by dehydration of glucose or sucrose,[8,9] and in the present circumstances could be derived from the xanthate (3) by a Chugaev elimination to give the unsaturated product (23), followed by the depicted rearrangement, with loss of acetone, to give the hydroxy-aldehyde (24) and thence the ketol (25).

It has been shown [4] that pyrolysis of the *gluco*-compound (13), in which the xanthate group at C-3 has the *exo*-configuration, gives a much better yield of rearranged product than is obtained from the *allo*-isomer (14), in which the *endo*-configuration imposes a constraint on the S_Ni reaction. The xanthate group in the 3,6-anhydro-compound (3) has the *endo*-configuration, and, though of no synthetical use for the project in hand, it was interesting to examine the behaviour of the *exo*-isomer (6), which was prepared from 3,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose (5). However, on pyrolysis the major product was again the furan derivative (25); a small amount of the rearranged product (7) was isolated (2.9%), and also the *S*-methyl

[1] Part 8, D. M. C. Hull, P. F. Orchard, and L. N. Owen, *J.C.S. Perkin I*, 1977, 1234.

[2] W. N. Haworth, L. N. Owen, and F. Smith, *J. Chem. Soc.*, 1941, 88.

[3] A. B. Foster, W. G. Overend, M. Stacey, and G. Vaughan, *J. Chem. Soc.*, 1954, 3367; A. B. Foster, W. G. Overend, and G. Vaughan, *ibid.*, p. 3625.

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[5] E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Amer. Chem. Soc.*, 1964, **86**, 5658; R. L. Whistler, W. E. Dick, T. R. Ingle, R. M. Rowell, and B. Urbas, *J. Org. Chem.*, 1964, **29**, 3723; J. P. H. Verheyden and J. G. Moffatt, *ibid.*, 1969, **34**, 2643; R. L. Whistler, U. G. Nayak, and A. W. Perkins, *ibid.*, 1970, **35**, 519; L. Vegh and E. Hardegger, *Helv. Chim. Acta*, 1973, **56**, 2020; B. Gross and F.-X. Oriez, *Carbohydrate Res.*, 1974, **36**, 385.

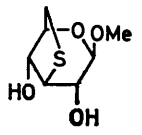
[6] M. Černý, J. Pacák, and V. Jina, *Monatsh.*, 1963, **94**, 632.

[7] E. J. Hedgley, W. G. Overend, and R. A. C. Rennie, *J. Chem. Soc.*, 1963, 4701.

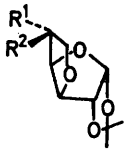
[8] R. E. Miller and S. M. Cantor, *J. Amer. Chem. Soc.*, 1952, **74**, 5236.

[9] K. Aso and H. Sugisawa, *Tohoku J. Agric. Res.*, 1954, **5**, 143; L. Telegdy-Kováts and A. Rajky, *Nahrung*, 1958, **2**, 893; C. J. Moye, *Austral. J. Chem.*, 1966, **19**, 2317; H. Sugisawa and K. Sudo, *Canad. Inst. Food Technol. J.*, 1969, **2**, 94.

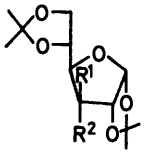
compound (8) (1.3%), presumably formed by the unusual extrusion reaction (17). Evidently the presence of a neighbouring methylene group [10] greatly facilitates *syn*-elimination in both the xanthates (3) and (6).



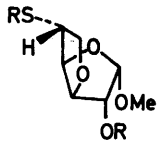
(1)



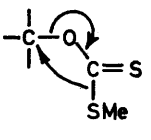
(2) R^1=OH, R^2= H
(3) R^1=O·CS·SMe, R^2=H
(4) R^1= S·CO·SMe, R^2= H
(5) R^1 = H, R^2 = OH
(6) R^1 =H, R^2= O·CS·SMe
(7) R^1 =H, R^2= S·CO·SMe
(8) R^1 = H, R^2 = SMe
(9) R^1 = H, R^2 = OTs
(10) R^1 = OTs, R^2 = H
(11) R^1 = SBz, R^2 = H
(12) R^1 = H, R^2 = SBz



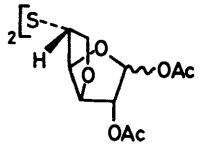
(13) R^1 =O·CS·SMe, R^2 = H
(14) R^1 = H, R^2 = O·CS·SMe



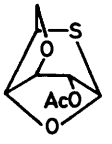
(15) R = Ac
(16) R = Bz



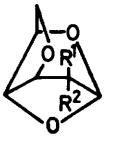
(17)



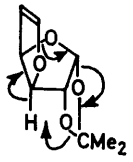
(18)



(19)



(20) R^1=H, R^2= OH
(21) R^1=OH, R^2=H
(22) R^1 = R^2 = H



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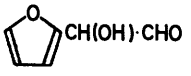
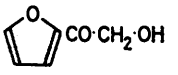


(24)



(25)

The yield of rearranged *gluco*-compound (4) was too small to make the pyrolytic route practicable, and a different approach was then adopted. 3,6-Anhydro-1,2-*O*-isopropylidene-β-L-idofuranose (5) was converted into the 5-*O*-tosyl derivative (9), in which the sulphonyloxy-group has the *exo*-configuration, and would therefore be expected to show some resistance towards S_N2 displacement.[11] Preliminary experiments showed that treatment with potassium thiobenzoate under forcing conditions (boiling dimethylformamide) led to extensive decomposition, but at lower temperatures the results were more promising. The reaction at 110 °C was followed quantitatively by ^{1}H n.m.r. spectroscopy, disappearance of the aryl-methyl resonance at τ 7.54 being monitored; for comparison, the same reaction was carried out under identical conditions on the *gluco*-isomer (10). The second-order rate constants for the *ido*- and the *gluco*-compound were 2.0×10^{-5} and 1.8×10^{-4} mol^{-1} s^{-1} l, respectively; thus the *endo*-tosyl compound reacts almost ten times as fast as the *exo*-isomer. On a preparative scale the *ido*-compound gave crystalline 3,6-anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene 5-thio-α-D-glucofuranose (11) in 27% yield, whilst the *gluco*-compound gave crystalline 3,6-anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene-5-thio-β-L-idofuranose (12) in 80% yield.

It was now necessary to remove both the isopropylidene group and the *S*-benzoyl group in the *gluco*-compound (11) to allow the possibility of the formation of a thiopyranose ring. Hydrolysis with aqueous acetic acid, followed by methoxide-catalysed solvolytic debenzoylation, gave a thiol (positive nitroprusside test). This did not necessarily rule out a thiopyranose structure, which in aqueous solution might have been in equilibrium with free thiol, but on acetylation a derivative was formed which from spectroscopic evidence contained an acetylthio-group and was evidently a furanose compound. When the thiobenzoate (11) was treated with sodium methoxide and then with hydrogen chloride in methanol it gave an oil which was separated by t.l.c. into two components, each of which was acetylated. The crystalline products were methyl 2-*O*-acetyl-5-*S*-acetyl-3,6-anhydro-5-thio-α-D-glucofuranoside (15) and the β-anomer, in each of which the presence of the *S*-acetyl group was evident from the i.r. and ^{1}H n.m.r. spectra; there was no evidence for the formation of any thiopyranoside. A similar result was obtained when the original oily mixture of methyl glucosides was benzoylated and then subjected to t.l.c.; two products were obtained, which were identified as methyl 3,6-anhydro-2-*O*-benzoyl-5-*S*-benzoyl-5-thio-α-D-glucofuranoside (16) and the β-anomer. The influence of the 3,6-bridge is therefore still sufficient to require a furanose structure for the sugar ring.

Reaction of the thiobenzoate (11) with sodium methoxide and then with aqueous sulphuric acid gave a foam, which on acetylation furnished only an inseparable mixture of the α- and the β-anomer of 5,5′-dithiobis-(1,2-di-*O*-acetyl-3,6-anhydro-5-deoxy-D-glucofuranose) (18) in the ratio *ca.* 5 : 1. When, however, aqueous trifluoroacetic acid was used instead of sulphuric acid,[12] subsequent acetylation, and purification by t.l.c., gave not only the mixed acetyl derivatives (18) but also a 42% yield of another product, identified by analysis and spectroscopy as 2-*O*-acetyl-1,4:3,6-dianhydro-5-thio-α-D-glucopyranose (19), which can also be considered as a 1,5:3,6-dianhydro-5-thio-β-D-glucofuranose. Thus the

[10] D. Horton and H. S. Prihar, *Carbohydrate Res.*, 1967, **4**, 115.
[11] *Cf.* L. D. Hall and P. R. Steiner, *Canad. J. Chem.*, 1970, **48**, 451.
[12] J. E. Christensen and L. Goodman, *Carbohydrate Res.*, 1968, **7**, 570.

thiopyranose ring can indeed be formed in the presence of the 3,6-anhydro-bridge, but apparently only when the furanose ring is itself retained and contributing to the stability of the system. The tricyclic compound (19) is a thio-derivative of 1,4:3,6-dianhydro-α-D-glucopyranose (20) (1,5:3,6-dianhydro-β-D-glucofuranose), which is obtained [13] by pyrolysis of amylose or 3,6-anhydroglucose; the *manno*-epimer (21) [13] and the 2-deoxy-compound (22) (incorrectly named as an α-furanose) [14] are also known. In the ^{1}H n.m.r. spectrum of the thio-compound (19), coupling constants which were measurable (see Table) were in close agreement with those reported [13,14] for the oxygen analogues; evidently the conformations of all four tricyclic compounds, which must adopt the $B_{1,4}$ form, are very similar.

EXPERIMENTAL

I.r. spectra and optical rotations (Perkin-Elmer 141 polarimeter) were recorded with solutions in chloroform, unless otherwise specified. ^{1}H N.m.r. spectra were recorded by a Varian T60 instrument for solutions in deuteriochloroform containing tetramethylsilane; proton assignments were based on analogy with published data on 3,6-anhydro-sugars.[11,13-15] Chemical shifts and coupling constants are recorded in the Table, except for 2-(hydroxyacetyl)furan and for compounds where few assignments were possible (parameters are included in the descriptions of these compounds). Mass spectra were obtained with a Vacuum Generators VG-7070 instrument.

Kieselgel$_{254}$ (Merck) was used for t.l.c., plates being developed with dichloromethane, unless otherwise specified. Extracts were dried over magnesium sulphate and concentrated under reduced pressure below 50 °C. Petroleum refers to the solvent of b.p. 40—60 °C.

3,6-*Anhydro*-1,2-O-*isopropylidene*-5-O-(*methylthio*)*thiocarbonyl*-α-D-*glucofuranose* (3).—A mixture of 3,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose [16] (6.0 g), dimethyl sulphoxide (10 ml), carbon disulphide (6 ml), and aqueous 5M-sodium hydroxide was vigorously stirred for 30 min. Methyl iodide (8.5 g) was then added, and the stirring was continued for a further 30 min. Dilution with water and extraction with chloroform gave the *methyl xanthate* (6.7 g), m.p. 67—68° (from methanol), $[\alpha]_D^{24}$ +56° (*c* 1.2), $\nu_{max.}$ 1 380 cm^{-1} (C=S) (Found: C, 45.2; H, 5.5; S, 22.1. $C_{11}H_{16}O_5S_2$ requires C, 45.2; H, 5.5; S, 21.9%).

Pyrolysis. The central section (300 mm) of an inclined (20°) 10 × 500 mm Pyrex tube was electrically heated to *ca*. 500 °C. The lower end was connected to a cooled receiver and the upper to a small dropping funnel. Under reduced pressure (water pump) the xanthate (3) (1.1 g), melted by local heating, was slowly introduced from the funnel. When no more material was being collected in the receiver the apparatus was allowed to cool and the contents of the tube were rinsed into the receiver with dichloromethane. Removal of solvent gave an orange oil (218 mg), which was separated by t.l.c. into (i) 2-(hydroxyacetyl)-furan (52 mg), m.p. 84—85° (sublimed), $\nu_{max.}$ 3 350 and 1 660 cm^{-1}; $\lambda_{max.}$ (EtOH) 271 (13 400) and 222 nm (ε 2 000); *m/e* 126 (M^+) and 95 ($M - CH_2OH$); τ 2.23 (1 H, d, $J_{4,5}$ 2 Hz, H-5), 2.59 (1 H, d, $J_{3,4}$ 4 Hz, H-3), 3.32 (1 H, q, $J_{3,4}$ 4, $J_{4,5}$ 2 Hz, H-4), 5.15 (2 H, s, CH_2), and 6.40br (1 H, s, OH) (Found: C, 57.4; H, 5.0. Calc. for $C_6H_6O_3$: C, 57.1; H, 4.8%) [lit.,[8,17] m.p. 83—84.5°, $\lambda_{max.}$ (H_2O) 275 (14 000) and 225 nm (ε 2 790)]; (ii) 3,6-*anhydro*-1,2-O-*isopropylidene*-5-S-(*methylthio*)*carbonyl*-5-*thio*-α-D-*glucofuranose* (4) (21 mg), m.p. 91—92° (from methanol), $[\alpha]_D^{20}$ +25° (*c* 0.15), $\nu_{max.}$ 1 650 cm^{-1} (S·CO) (Found: C, 45.4; H, 5.3; S, 22.5. $C_{11}H_{16}O_5S_2$ requires C, 45.2; H, 5.5; S, 21.9%); and (iii) starting material (49 mg), identified spectroscopically.

^{1}H N.m.r. parameters (τ values; *J* in Hz) [a]

Compound	H-1	H-2	H-3	H-4	H-5)	H-6a	H-6b	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
(3)	3.98 (d)	5.37 (t)		4.88 (t)	4.18 (m)	5.80 (q)	6.10 (q)	4	0	4	4	7	7	9
(4)	4.03 (d)	5.32 (t)		5.00 (t) [c]				4	0	4	4			
(6)	3.96 (d)	5.19 (d)		4.93br (d)	3.96 (d)	5.60 (q)	5.87 (q) [d]	3.5	0	3.5	0	4	2	11
(7)	3.96 (d)	5.29 (t)		5.04 (d)	5.45—5.8 (m)		6.04 (q) [e]	4	0	4	0		5	13
(11)	4.02 (d)	5.34 (d)		4.97br (t)	5.5—6.0 (m)		6.33 (q)	4					10	14
(12)	4.01 (d)	5.33 (m)		5.09 (d)	5.5—6.1 (m)		6.12 (q)	4					5	12
(19)	4.32 (s)	5.05 (s)		4.53 (t) [f]				0	0	5	5			

[a] Resonances of aromatic and isopropylidene protons are omitted. [b] Also τ 7.34 (3 H, s, SMe). [c] Also τ 5.5—6.4 (3 H, m) and 7.51 (3 H, s, SMe). [d] Also τ 7.27 (3 H, s, SMe). [e] Also τ 7.43 (3 H, s, SMe). [f] Also τ 5.6—6.1 (4 H, m) and 7.83 (3 H, s, OAc).

3,6-*Anhydro*-1,2-O-*isopropylidene*-5-O-(*methylthio*)*thiocarbonyl*-β-L-*idofuranose* (6).—Under the conditions used for the corresponding glucose derivative, 3,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose [18] (2.5 g) gave the *methyl xanthate* (2.6 g), m.p. 74—75° (from methanol), $[\alpha]_D^{25}$ +68° (*c* 1.3), $\nu_{max.}$ 1 380 cm^{-1} (Found: C, 45.2; H, 5.3; S, 21.9. $C_{11}H_{16}O_5S_2$ requires C, 45.2; H, 5.5; S, 21.9%).

Pyrolysis. The xanthate (6) (2.4 g) was pyrolysed in the heated tube as described for the glucose analogue. The product was separated by t.l.c. into four fractions: (i) 2-(hydroxyacetyl)furan (345 mg), spectroscopically identical with that previously described; (ii) 3,6-*anhydro*-1,2-O-*isopropylidene*-5-S-*methyl*-5-*thio*-β-L-*idofuranose* (8) (25 mg), an oil, τ 3.79 (1 H, d, H-1, $J_{1,2}$ 4 Hz), 4.5—5.4 (6 H, m), 7.74 (3 H, s, SMe), and 8.47 and 8.61 (6 H, 2s, CMe_2) (Found: C, 51.4; H, 6.6. $C_{10}H_{16}O_4S$ requires C, 51.7; H, 6.9%); (iii) 3,6-*anhydro*-1,2-O-*isopropylidene*-5-S-(*methylthio*)*carbonyl*-5-*thio*-β-L-*idofuranose* (7) (71 mg), an oil, $[\alpha]_D^{20}$ +1.4° (*c* 1.7), $\nu_{max.}$ (film) 1 650 cm^{-1} (Found: C, 45.3; H, 5.3; S,

[13] G. R. Bedford and D. Gardiner, *Chem. Comm.*, 1965, 287.
[14] J. S. Brimacombe, I. Da'Aboul, L. C. N. Tucker, N. Calvert, and R. J. Ferrier, *Carbohydrate Res.*, 1973, **27**, 254.
[15] R. J. Abrahams, L. D. Hall, L. Hough, and K. A. McLauchlan, *J. Chem. Soc.*, 1962, 3699; G. Birch, C. K. Lee, and A. C. Richardson, *Carbohydrate Res.*, 1971, **19**, 119.
[16] B. A. Lewis, F. Smith, and A. M. Stephen, *Methods Carbohydrate Chem.*, 1963, **2**, 183.
[17] *Cf.* F. Kipnis, H. Soloway, and J. Ornfelt, *J. Amer. Chem. Soc.*, 1948, **70**, 142; Y. L. Pascal, *Ann. Chim.* (*France*), 1968, xiv, **3**, 245.
[18] J. G. Buchanan and J. Conn, *J. Chem. Soc.*, 1965, 201.

22.2. $C_{11}H_{16}O_5S_2$ requires C, 45.2; H, 5.5; S, 21.9%); and (iv) starting material (102 mg).

3,6-*Anhydro*-1,2-O-*isopropylidene*-5-O-*tosyl*-β-L-*idofuranose* (9).—Toluene-*p*-sulphonyl chloride (12.0 g) was added to a stirred and cooled solution of 3,6-anhydro-1,2-*O*-isopropylidene-β-L-idofuranose (10.0 g) in pyridine (30 ml). The mixture was left at ambient temperature for 20 h and worked up in the usual way to give the 5-O-*tosyl derivative* (16.3 g), m.p. 92—93.5° (from aqueous ethanol), $[\alpha]_D^{24}$ +17° (*c* 1.0), $\nu_{max.}$ 1 365 cm^{-1} (OTs), τ 2.34 (4 H, ABq, aromatic), 4.13 (1 H, d, $J_{1,2}$ 3 Hz, H-1), 5.00br (1 H, s), 5.15—5.45 (3 H, m), 6.00 (2 H, d), 7.54 (3 H, s, ArMe), and 8.55 and 8.68 (6 H, 2s, CMe_2) (Found: C, 54.0; H, 5.85; S, 9.0. $C_{16}H_{20}O_7S$ requires C, 53.9; H, 5.7; S, 9.0%).

Rates of Reaction of 3,6-*Anhydro*-1,2-O-*isopropylidene*-5-O-*tosyl*-β-L-*idofuranose and* -α-D-*glucofuranose with Potassium Thiobenzoate*.—A solution of each tosyl compound (1.0 g) and potassium thiobenzoate (5.0 g) in dry dimethylformamide (10 ml) was maintained at 110 °C (oil-bath) with exclusion of moisture. At intervals, small samples were removed, diluted with water, and extracted with chloroform. The washed and dried extracts were evaporated, and the residue was examined by ^1H n.m.r. spectroscopy. The amount of unchanged substrate (*a*) was calculated from the relative proton integrals of the aryl methyl and the *gem*-dimethyl signals:

t/min	0	30	60	90	120	180	240	300
a (%) (*ido*)	100		84		64	52	40	32
a (%) (*gluco*)	100	30	6	2				

Pseudo-first-order rate constants were calculated from the straight-line plots of log *a* against *t*, and converted into the second-order constants: 2.0×10^{-5} (*ido*) and 1.8×10^{-4} $l\ mol^{-1}\ s^{-1}$ (*gluco*).

3,6-*Anhydro*-5-S-*benzoyl*-1,2-O-*isopropylidene*-5-*thio*-α-D-*glucofuranose* (11).—A solution of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-tosyl-β-L-idofuranose (6.0 g) and potassium thiobenzoate (30 g) in dry dimethylformamide (30 ml) was heated at 110 °C for 12 h in a closed flask. The mixture was then concentrated, diluted with water, and extracted with dichloromethane to give an oil which after three purifications by t.l.c. furnished the *thiobenzoate* (1.55 g), m.p. 85° [from petroleum (b.p. 60—80 °C)], $[\alpha]_D^{20}$ +35° (*c* 1.3), $\nu_{max.}$ 1 660 cm^{-1} (SBz) (Found: C, 59.8; H, 5.8; S, 9.9. $C_{16}H_{18}O_5S$ requires C, 59.6; H, 5.6; S, 9.95%).

3,6-*Anhydro*-5-S-*benzoyl*-1,2-O-*isopropylidene*-5-*thio*-β-L-*idofuranose* (12).—A solution of 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-tosyl-α-D-glucofuranose [16] (203 mg) and potassium thiobenzoate (1.0 g) in dry dimethylformamide (2 ml) was heated at 110 °C for 2 h and worked up as described in the preceding paragraph. One purification of the product by t.l.c. gave the *thiobenzoate* (158 mg), m.p. 74° (from petroleum), $[\alpha]_D^{22}$ +33.5° (*c* 0.9), $\nu_{max.}$ 1 660 cm^{-1} (Found: C, 59.9; H, 5.7; S, 9.9%).

Hydrolysis of 3,6-*Anhydro*-5-S-*benzoyl*-1,2-O-*isopropylidene*-5-*thio*-α-D-*glucofuranose*.—A solution of the thiobenzoate (11) (0.45 g) in acetic acid (6.5 ml) and water (3.5 ml) was heated on a steam-bath for 2 h, then evaporated to a syrup, which was purified by t.l.c. (ether) to give an amorphous solid, m.p. 110—115° (from dichloromethane–petroleum), $\nu_{max.}$ 3 400 (OH) and 1 660 cm^{-1} (SBz). This was dissolved in a solution prepared from sodium (10 mg) and methanol (10 ml) and kept under nitrogen for 20 min (t.l.c. then showed no starting material). Neutralisation with a trace of acetic acid, followed by evaporation, gave a syrup, which gave a strong positive reaction with alkaline sodium nitroprusside. Acetylation (acetic anhydride–pyridine), and purification of the product by t.l.c. gave a solid, m.p. 126—146°, $\nu_{max.}$ 1 740 (OAc) and 1 690 cm^{-1} (SAc), τ 3.43 (1 H, d, $J_{1,2}$ 5 Hz, H-1), 4.7—6.5 (6 H, m), 7.60 (3 H, s, SAc), 7.87 (6 H, s, 2 OAc), which was essentially 1,2-di-*O*-acetyl-5-*S*-acetyl-3,6-anhydro-5-thio-D-glucofuranose, but which could not be completely purified (Found: C, 49.1; H, 5.1; S, 10.2. Calc. for $C_{12}H_{16}O_7S$: C, 47.4; H, 5.3; S, 10.5%).

Methyl 2-O-*Acetyl*-5-S-*acetyl*-3,6-*anhydro*-5-*thio*-D-*glucofuranosides*.—A solution prepared from sodium (0.1 g) and dry methanol (8 ml) was added to a solution of 3,6-anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene-5-thio-α-D-glucofuranose (0.53 g) in dichloromethane (8 ml). The mixture was stirred under nitrogen and the reaction was monitored by t.l.c. until debenzoylation was complete (30 min). After 1 h, 10% hydrogen chloride in methanol (4 ml) was added, and again the reaction was monitored by t.l.c. (ether). After 19 h, the solution was neutralised with sodium hydrogen carbonate, filtered, diluted with water, and extracted with dichloromethane to give a syrup (0.18 g) which was a mixture of anomers (n.m.r.). Repeated t.l.c. gave (i) the β-form (102 mg), $[\alpha]_D^{26}$ −7.4° (*c* 1.2), $\nu_{max.}$ (film) 2 575 cm^{-1} (SH), τ 5.02 (1 H, s, H-1), and 6.48 (3 H, s, OMe); and (ii) the α-form (43 mg), $[\alpha]_D^{26}$ +178° (*c* 1.1), $\nu_{max.}$ 2 575 cm^{-1}, τ 5.00 (1 H, d, $J_{1,2}$ 4 Hz, H-1) and 6.48 (3 H, s, OMe), of methyl 3,6-anhydro-5-thio-D-glucofuranoside.

Acetylation (acetic anhydride–pyridine) gave, respectively, *methyl* 2-O-*acetyl*-5-S-*acetyl*-3,6-*anhydro*-5-*thio*-β-D-*glucofuranoside* (85 mg), m.p. 82° [from petroleum (b.p. 60—80 °C)], $[\alpha]_D^{26}$ +81° (*c* 0.9), $\nu_{max.}$ (paraffin mull) 1 740 (OAc) and 1 700 cm^{-1} (SAc), τ 4.91 (1 H, s, H-1), 6.59 (3 H, s, OMe), 7.63 (3 H, s, SAc), and 7.94 (3 H, s, OAc); and the α-*anomer* (15) (58 mg), m.p. 95—97° (sublimed), $[\alpha]_D^{20}$ +209° (*c* 2.3), $\nu_{max.}$ (paraffin mull) 1 740 and 1 700 cm^{-1}, τ 4.81 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 6.61 (3 H, s, OMe), 7.61 (3 H, s, SAc), and 7.88 (3 H, s, OAc) (Found: C, 47.8; H, 5.7; S, 12.1. $C_{11}H_{16}O_6S$ requires C, 47.8; H, 5.8; S, 11.6%).

Methyl 3,6-*Anhydro*-2-O-*benzoyl*-5-S-*benzoyl*-5-*thio*-D-*glucofuranosides*.—Sodium (20 mg) was added to a solution of 3,6-anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene-5-thio-α-D-glucofuranose (100 mg) in methanol (2 ml) and dichloromethane (0.5 ml). After the solution had been kept for 1 h under nitrogen, 10% hydrogen chloride in methanol (0.5 ml) was added, and, after a further 24 h under nitrogen, the solution was neutralised and worked up as described in the preceding section. The crude anomeric mixture was benzoylated (benzoyl chloride–pyridine) and the product separated by t.l.c. into (i) *methyl* 3,6-*anhydro*-2-O-*benzoyl*-5-S-*benzoyl*-5-*thio*-β-D-*glucofuranoside* (23 mg), a syrup, $[\alpha]_D^{28}$ +56° (*c* 0.1), $\nu_{max.}$ (film) 1 720 (OBz) and 1 660 cm^{-1} (SBz), τ 1.8—2.7 (10 H, m, aromatic), 4.57 (1 H, s, H-1), and 6.46 (3 H, s, OMe) (Found: C, 63.2; H, 5.2. $C_{21}H_{20}O_6S$ requires C, 63.0; H, 5.0%); and (ii) the α-*anomer* (16) (31 mg), m.p. 151° (from dichloromethane–petroleum), $[\alpha]_D^{20}$ +158° (*c* 0.3), $\nu_{max.}$ (paraffin mull) 1 720 and 1 660 cm^{-1}, τ 1.8—2.7 (10 H, m, aromatic), 4.57 (1 H, d, $J_{1,2}$ 4 Hz, H-1), and 6.59 (3 H, s, OMe) (Found: C, 62.7; H, 5.2; S, 8.2. $C_{21}H_{20}O_6S$ requires C, 63.0; H, 5.0; S, 8.0%).

Hydrolysis of 3,6-*Anhydro*-1,2-O-*isopropylidene*-5-*thio*-α-D-*glucofuranose*.—(*a*) 3,6-Anhydro-5-*S*-benzoyl-1,2-*O*-isopropylidene-5-thio-α-D-glucofuranose (1.0 g) was dissolved

in methanol (10 ml) and dichloromethane (2 ml). Sodium (0.1 g) was added, and the solution was kept under nitrogen for 15 min, then neutralised with carbon dioxide, and evaporated. The crude thiol, $\nu_{max.}$ (paraffin mull) 2 560 cm^{-1} (SH), was dissolved in a mixture of dioxan (20 ml) and 2% sulphuric acid (20 ml), and the solution was kept under nitrogen for 120 h, when t.l.c. showed reaction to be complete. After neutralisation with sodium hydrogen carbonate, and filtration, the solution was evaporated to a foam (0.67 g), which was acetylated (acetic anhydride–pyridine) to give *5,5′-dithiobis-(1,2-di-O-acetyl-3,6-anhydro-5-deoxy-D-glucofuranose)* (18) (0.20 g), m.p. 160—179° (from dichloromethane–petroleum), $\nu_{max.}$ 1 730 cm^{-1} (OAc), τ 3.50 (d, $J_{1,2}$ 4 Hz, H-1) and 3.80 (s, H-1) ($\alpha : \beta$ *ca.* 5 : 1) (Found: C, 44.9; H, 5.15; S, 12.2. $C_{20}H_{26}O_{12}S_2$ requires C, 44.7; H, 5.1; S, 12.6%).

(*b*) Similar debenzoylation of the same *S*-benzoyl compound (495 mg) gave the crude thiol, which was dissolved in trifluoroacetic acid (9 ml) and water (1 ml). After 10 min under nitrogen, the solution was evaporated to a syrup, which was acetylated (acetic anhydride–pyridine). The product was separated by t.l.c. into (i) the disulphide (18) (230 mg), which was further characterised by deacetylation (sodium methoxide in methanol) and benzoylation (benzoyl chloride–pyridine) to give *5,5′-dithiobis-(3,6-anhydro-1,2-di-O-benzoyl-5-deoxy-D-glucofuranose)* (148 mg), a syrup, $[\alpha]_D^{20}$ −95° (*c* 0.3), $\nu_{max.}$ (film) 1 720 cm^{-1} (OBz) (Found: C, 62.6; H, 4.75; S, 8.5. $C_{40}H_{34}O_{12}S_2$ requires C, 62.3; H, 4.45; S, 8.3%); and (ii) *2-O-acetyl-1,4:3,6-di-anhydro-5-thio-α-D-glucopyranose* (19) (114 mg), m.p. 109—110° (from methanol), $[\alpha]_D^{26}$ +78° (*c* 0.6), $\nu_{max.}$ 1 745 cm^{-1} (OAc), *m/e* 202 (M^+) and 159 (M − Ac) (Found: C, 47.5; H, 5.1; S, 15.2. $C_8H_{10}O_4S$ requires C, 47.5; H, 5.0; S, 15.8%).

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