Thio-sugars. Part 8.[1] Methyl 2,3-Anhydro-5-thio-α-D-ribopyranoside and Methyl 3,4-Anhydro-5-thio-α-D-ribopyranoside

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Selective reaction of the primary sulphonate group in 1,2-*O*-isopropylidene-3,5-di-*O*-tosyl-α-D-xylofuranose with potassium thiobenzoate gives 5-*S*-benzoyl-1,2-*O*-isopropylidene-3-*O*-tosyl-5-thio-α-D-xylofuranose, which is converted by hydrogen chloride in methanol into methyl 3-*O*-tosyl-5-thio-α-D-xylopyranoside, from which the title epoxides are obtained by treatment with base. The constitutions of these epoxides are deduced from the ^{1}H n.m.r. spectra of their acetates. Reaction of the 4-*O*-methyl derivative of the 2,3-epoxide with sodium *O*-methyl dithiocarbonate gives methyl 2,3-dideoxy-4-*O*-methyl-2,3-thiocarbonyldithio-5-thio-α-D-arabinopyranoside, and similar treatment of the 2-*O*-methyl ether of the 3,4-epoxide gives methyl 3,4-dideoxy-2-*O*-methyl-3,4-thiocarbonyldithio-5-thio-α-D-xylopyranoside; the configurations of these cyclic trithiocarbonates are established from their ^{1}H n.m.r. spectra.

Methyl 5-*S*-benzoyl-3-*O*-tosyl-5-thio-α-D-xylofuranoside is converted by base into methyl 3,5-dideoxy-3,5-epithio-α-D-xylofuranoside; the β-anomer behaves similarly and also gives 5,5′-*S*-methylenebis(methyl 2,3-anhydro-5-thio-β-D-ribofuranoside) by competitive interaction of the intermediate 5-thiol with the dichloromethane solvent.

ANHYDRO-SUGARS of the oxiran type are versatile intermediates in carbohydrate chemistry, but no such compounds have been described which are derivatives of thio-sugars having sulphur in place of oxygen in the sugar ring; the title compounds represent the first examples of this new class.

In confirmation of the expectation that the *exo*-sulphonate group at C-3 in 1,2-*O*-isopropylidene-3,5-di-*O*-tosyl-α-D-xylofuranose (1) would be fairly resistant towards S_N2 displacement,[2] an almost quantitative yield of the 5-thiobenzoate (2) was obtained by reaction with potassium thiobenzoate in dimethylformamide for 2 h at 120 °C. Reaction of the same ditosyl compound with potassium thiocyanate in the same solvent proceeded much more slowly, and after 28 h some starting material was still present and only a low yield of the 5-thiocyanate (3) was obtained. On the other hand, substitution of both sulphonyloxy-groups occurred on reaction with potassium thioacetate for only 9 h, the 3,5-bisthioacetate (5) being obtained.

To form the thiopyranose ring system from the thiobenzoate (2) it is only necessary to generate the free thiol group at C-5 and to remove the isopropylidene function, preferably under conditions which would result in the formation of a methyl glycoside; both the possible sequential routes were investigated. Debenzoylation with sodium methoxide in methanol gave the 5-thiol (4), which was easily oxidised to a disulphide, and to avoid the losses involved in isolation of the thiol the debenzoylation was monitored by t.l.c.; when this reaction was complete the methanolic solution was acidified with hydrogen chloride and heated, to afford, in 52% overall yield, a crystalline glycoside. The optical rotation ($[\alpha]_D$ +211°) and the ^{1}H n.m.r. spectrum ($J_{1,2}$ 2; $J_{2,3}$ and $J_{3,4}$ 9 Hz) showed that this was methyl 3-*O*-tosyl-5-thio-α-D-xylopyranoside (9) with the expected $^4C_1$ conformation in solution. The alternative procedure was to treat the 5-thiobenzoate (2) with hydrogen chloride in methanol; the reaction was monitored by t.l.c. and by ^{1}H n.m.r., which demonstrated a rapid loss of the isopropylidene function and formation of an anomeric mixture of xylofuranosides, followed by slow debenzoylation and rearrangement to thiopyranoside.

Reaction of methyl 3-*O*-tosyl-5-thio-α-D-xylopyranoside (9) with sodium methoxide gave a mixture of methyl 2,3-anhydro-5-thio-α-D-ribopyranoside (10) and the 3,4-anhydro-isomer (13) in about equal proportions, which were separated, with some difficulty, by t.l.c. Their ^{1}H n.m.r. spectra did not provide sufficient evidence to permit individual constitutional allocations, but this became possible when the ^{1}H n.m.r. spectra of the *O*-acetyl derivatives (11) and (14) were examined. The spectra of the original epoxides both included a broad unresolved signal at τ *ca.* 5.8, but in the spectrum of each acetate this signal was shifted downfield and was now a sharply resolved quartet, the other signals being virtually unchanged; this identified the C*H*·OAc signal, and to recognise the particular acetate (14) it was only necessary to establish, by decoupling, in which of the two derivatives that proton was coupled to the anomeric proton. This proved to be the acetate of the faster running (t.l.c.) epoxide, which therefore is the 3,4-anhydro-compound (13).

The half chair conformation $^5H_5$ (16) of the acetate (11) should be more stable than the ^5H_S (17), in which there is a quasiaxial acetoxy-group, interaction between lone pairs on sulphur and oxiran oxygen, and an unfavourable anomeric effect associated with the equatorial methoxy-group. This expectation is supported by several features of the ^{1}H n.m.r. spectrum. The chemical shift of the anomeric proton (τ 5.24) lies in the region characteristic[3] of an equatorial disposition, and this signal, in addition to the coupling to H-2 ($J_{1,2}$ 4 Hz) showed a small long-range coupling ($J_{1,3}$ *ca.* 1 Hz) consistent with

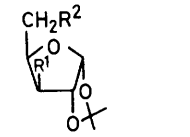
[1] Part 7, M. V. Jesudason and L. N. Owen, *J.C.S. Perkin I*, 1974, 2024.

[2] *Cf.* M. L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, 1962, **27**, 4505; J. M. Heap and L. N. Owen, *J. Chem. Soc.* (*C*), 1970, 712.

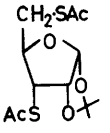
[3] J. G. Buchanan, R. Fletcher, K. Parry, and W. A. Thomas, *J. Chem. Soc.* (*B*), 1969, 377.

the almost planar W arrangement [3,4] of H-1, C-1, C-2, C-3, and H-3; furthermore the couplings $J_{4,5a}$ (12 Hz) and $J_{4,5e}$ (5 Hz) confirm that H-4 is quasiaxial.

Similar consideration of the non-bonded interactions in the two half-chair conformations (18) and (19) of the acetate (14) leads to the conclusion that the $^{S}H_{1}$ conformation (18) should be the more stable. Evidence from the ^{1}H of these reacted with potassium thiocyanate in boiling ethanol to give a mixture, from which a major component was isolated in each case; neither could be completely purified, but analytical and spectral data indicated that they were essentially the 2,3- and the 3,4-epithio-compounds (21) and (22). The mass spectrum of the former showed a peak at $M - 1$, whereas that of the latter



(1) $R^1 = R^2 = OTs$
(2) $R^1 = OTs$, $R^2 = SBz$
(3) $R^1 = OTs$, $R^2 = SCN$
(4) $R^1 = OTs$, $R^2 = SH$



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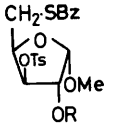

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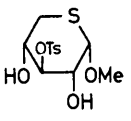
(8) R = Bz



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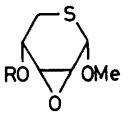

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(11) R = Ac
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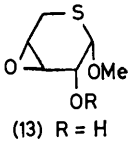

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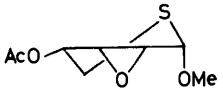

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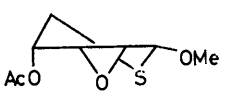

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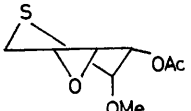

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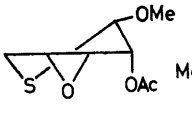

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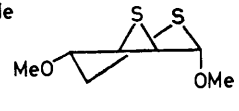

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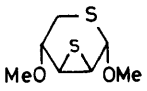

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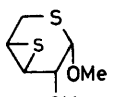

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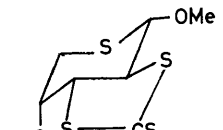

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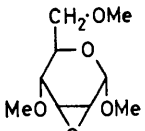

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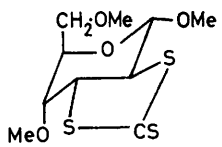

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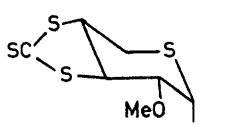

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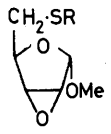

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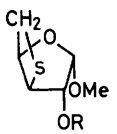
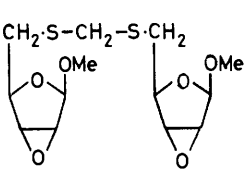
(28) R = Bz



(29) R = H
(30) R = Ac



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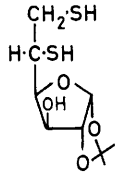

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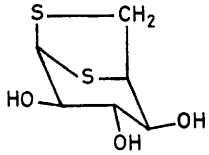

(33)

n.m.r. spectrum of this derivative is less substantial than that provided by the 4-*O*-acetyl isomer, the only significant feature being the chemical shift of the anomeric proton (τ 5.42) which again is consistent with an equatorial disposition for H-1.

The reactions of sugar oxirans with thiocyanates to give thiirans,[5] and with dithiocarbonates to give trithiocarbonates,[1] were described earlier, and it was pointed out that the mechanisms of these reactions are such that a neighbouring hydroxy-group in a *cis*-relationship to the epoxide ring can participate at an intermediate stage and give rise to a product in which the episulphide or trithiocarbonate ring occupies a 'migrated' position. This complication could evidently arise with the epoxides (10) and (13), which were therefore converted by Purdie methylation into the methyl ethers (12) and (15). Each episulphide showed the presence of the molecular ion itself; other prominent peaks ($M - 31$, $M - 33$, $M - 65$) were common to both.

When the methylated 2,3-epoxide (12) was treated with sodium *O*-methyl dithiocarbonate in methanol, a single yellow crystalline trithiocarbonate was isolated in 46% yield after t.l.c. A second yellow product, presumably the alternative *trans*-2,3-isomer, was visible as a separate band, but it was present only in trace amount. The conversion of an epoxide into a trithiocarbonate proceeds through an episulphide of inverted configuration,[1] which in this instance would be the D-*lyxo*-compound (21); further attack on this by dithiocarbonate at C-2 would give a 2,3-trithiocarbonate with the D-*xylo*-configuration, whereas attack at C-3 would result in a D-*arabino*-configuration. The ^{1}H n.m.r. spectrum was

[4] L. D. Hall and J. F. Manville, *Carbohydrate Res.*, 1968, **8**, 295.

[5] M. V. Jesudason and L. N. Owen, *J.C.S. Perkin I*, 1974, 2019.

analysed in detail by conventional decoupling techniques, and the magnitude of $J_{1,2}$ (9.5 Hz) indicated a diaxial disposition for H-1 and H-2, whilst the small values for $J_{3,4}$ (2.4), $J_{4,5a}$ (3.6), and $J_{4,5e}$ (2.0 Hz) proved that there is no diaxial relationship between H-4 and any neighbouring proton. These features are incompatible with the necessary $^4C_1$ conformation of a *xylo*-configuration but are completely in accord with the $^1C_4$ conformation (23) of methyl 2,3-dideoxy-4-*O*-methyl-2,3-thiocarbonyldithio-5-thio-α-D-arabinopyranoside. Attack had therefore occurred essentially specifically at C-3 in the intermediate episulphide (21), suggesting that it reacts in the $^SH_5$ conformation (20). Stereochemically, the result of the reaction on the epoxide (12) is similar to that in which methyl 2,3-anhydro-4,6-di-*O*-methyl-α-D-allopyranoside (24) was converted into the *altro*-trithiocarbonate (25).[1]

When the methylated 3,4-epoxide (15) was similarly treated, it likewise gave one solid trithiocarbonate (33% yield) with an indication, by t.l.c., of only a trace of another yellow product. The intermediate 3,4-L-*arabino*-episulphide (22) could in principle give a 3,4-trithiocarbonate having either the L-*lyxo*- or the D-*xylo*-configuration, by attack at C-3 or C-4, respectively. The only distinguishing stereochemical feature which should be evident in the ^{1}H n.m.r. spectrum of the trithiocarbonate is the relation between H-2 and H-3, being equatorial–axial for the *lyxo*-configuration (conformation $^1C_4$) and diaxial for the *xylo*-configuration (conformation $^4C_1$). The normal spectrum could not be satisfactorily analysed because of the overlapping signals from H-1, H-3, and H-4, but by the use of a lanthanide shift reagent the H-1 signal was moved downfield and that of H-3 was revealed as a triplet with $J_{2,3}$ and $J_{3,4}$ both 11 Hz. Consequently, H-2, H-3, and H-4 are all axially oriented and the trithiocarbonate is identified as methyl 3,4-dideoxy-2-*O*-methyl-3,4-thiocarbonyldithio-5-thio-α-D-xylopyranoside (26).

A different and unfruitful route to the methyl ether of the 3,4-epoxide had been investigated before this compound was eventually obtained by the method described above. The 5-thiobenzoate (2), on treatment at ambient temperature with hydrogen chloride in methanol, gave a mixture of methyl 5-*S*-benzoyl-3-*O*-tosyl-5-thio-α-D-xylofuranoside (6) and the β-anomer, which were separated by t.l.c. Attempts to methylate the α-anomer with methyl iodide and barium oxide,[6] or with methyl iodide and silver oxide in dimethylformamide [7] gave a product which appeared from the ^{1}H n.m.r. spectrum to be mainly the 2,3-epoxide (28) (absence of tolyl methyl, only one methoxy-group, correct ratio of aromatic to non-aromatic protons), but by the normal Purdie procedure the 2-*O*-methyl derivative (7) was obtained, together with some of the epoxide (28) and the 2-benzoate (8). The ester (8), which was identical with a sample prepared by benzoylation of the α-xyloside (6), must arise by intermolecular acylation by the thiobenzoate function; the 6-thiol, which presumably was formed in an equivalent amount, was not detected and was possibly discarded with the silver salts. Debenzoylation of the 2-*O*-methyl compound (7) gave the 5-thiol, but attempts to rearrange this to a thiopyranoside, by treatment with acidic methanol, did not give a recognisable product. Debenzoylation of the unmethylated compound (6), with sodium methoxide in methanol–dichloromethane, gave a high yield of the known [8] methyl 3,5-dideoxy-3,5-epithio-α-D-xylofuranoside (29), the identity of which was supported by conversion into the crystalline acetate (30); the ^{1}H n.m.r. spectra of these thietans were in excellent agreement with those reported.[8] The configuration at C-3 in the sulphonate (6) is such that the episulphide cannot be formed by direct displacement, and the reaction must proceed through the 2,3-*ribo*-epoxide (27) which is then attacked intramolecularly at C-3 by the thiol group.

When the β-anomer of the thiobenzoate (6) was debenzoylated under the same conditions, the β-isomer [8] of the 3,5-episulphide (29) was obtained together with a substance identified as the methylenedithio-compound (31) by microanalysis, mass spectrum, and ^{1}H n.m.r. spectrum [which included a sharp singlet at τ 6.16 ($S{\cdot}CH_2{\cdot}S$)]. This must have been formed from the β-anomer of the thiol (27) by competitive attack of the thiol anion on the dichloromethane co-solvent, which suggests that the intramolecular attack on the epoxide, leading to the 3,5-episulphide, is sterically less favourable with the β-compound than it is with the α-form (27).

Although 1,6-epithio-derivatives of aldohexofuranose,[9,10] aldohexopyranose,[11] and aldohexothiofuranose sugars [10] are known, no such derivative of a thiopyranose sugar has yet been described. An earlier attempt to make such a compound, by acidic hydrolysis of 1,2-*O*-isopropylidene-5,6-dithio-L-idofuranose (32), gave no identifiable product,[12] but repetition of this experiment under milder conditions has now afforded 1,6-dideoxy-1,6-epithio-5-thio-β-L-idopyranose (33), the dithio-analogue of the well known 1,6-anhydro-β-D-idopyranose.[13]

EXPERIMENTAL

I.r. spectra were recorded with solutions in chloroform (unless otherwise specified) and ^{1}H n.m.r. spectra with solutions in deuteriochloroform (Varian A60, T60, or HA100 instrument); proton assignments confirmed by decoupling are indicated by asterisks. Mass spectra were recorded with a Perkin-Elmer 270 instrument at 70 eV. Optical rotations were measured, for solutions in chloroform (unless otherwise specified), with a Perkin-Elmer 141 polarimeter. Kieselgel GF254 (Merck) was used for t.l.c., and silica M.F.C.

[6] *Cf.* R. Kuhn, H. H. Baer, and A. Seeliger, *Annalen*, 1958, **611**, 236.
[7] R. Kuhn, H. Trischmann, and I. Löw, *Angew. Chem.*, 1955, **67**, 32.
[8] L. Goodman, *J. Amer. Chem. Soc.*, 1964, **86**, 4167.
[9] R. L. Whistler and B. Urbas, *J. Org. Chem.*, 1965, **30**, 2721.
[10] J. M. Cox and L. N. Owen, *J. Chem. Soc.* (*C*), 1967, 1122.
[11] M. Akagi, S. Tejima, and M. Haga, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 58; R. L. Whistler and P. A. Seib, *Carbohydrate Res.*, 1966, **2**, 93.
[12] T. J. Adley and L. N. Owen, *J. Chem. Soc.* (*C*), 1966, 1287.
[13] E. Sorkin and T. Reichstein, *Helv. Chim. Acta*, 1945, **28**, 1.

(Hopkin and Williams) for column chromatography. Extracts were dried over magnesium sulphate, and solvents were removed under reduced pressure below 50 °C. Petroleum refers to the solvent of b.p. 40—60 °C.

5-S-*Benzoyl*-1,2-O-*isopropylidene*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranose* (2).—A solution of 1,2-*O*-isopropylidene-3,5-di-*O*-tosyl-α-D-xylofuranose (35 g) [14] and potassium thiobenzoate (26.5 g) in dry dimethylformamide (45 ml) was stirred in nitrogen for 1 h at 80 °C. The mixture was then cooled, diluted with water, and extracted with chloroform to give a red oil which crystallised on trituration with ethanol. The *thiobenzoate* (2) (32.2 g) had m.p. 93—94° (from ethanol), $[\alpha]_D^{21}$ −87° (*c* 1.3), $\nu_{max.}$ 1 660 (SBz) and 1 370 cm^{-1} (OTs) (Found: C, 56.7; H, 5.5; S, 13.8. $C_{22}H_{24}O_7S_2$ requires C, 56.9; H, 5.2; S, 13.8%).

5-*Deoxy*-1,2-O-*isopropylidene*-5-*thiocyanato*-3-O-*tosyl*-α-D-*xylofuranose* (3).—Treatment of the same ditosyl compound (2.0 g) with potassium thiocyanate (1.0 g) in dimethylformamide (10 ml) for 28 h at 120 °C, followed by dilution with water and extraction with chloroform, gave an oil, which was purified by column chromatography (ether–petroleum, 4 : 1) to give the *thiocyanate* (3) (0.2 g), $[\alpha]_D^{20}$ −30° (*c* 1.0), $\nu_{max.}$ 2 180 cm^{-1} (SCN) (Found: C, 50.0; H, 5.0; N, 3.4; S, 16.6. $C_{16}H_{19}NO_6S_2$ requires C, 49.9; H, 5.0; N, 3.6; S, 16.6%).

3,5-*Di*-S-*acetyl*-1,2-O-*isopropylidene*-3,5-*dithio*-α-D-*ribofuranose* (5).—The same ditosyl compound (1.7 g) and potassium thioacetate (5.0 g) were heated together in dimethylformamide (10 ml) for 9 h at 120 °C under nitrogen, and the product worked up in the same way to give the *bisthioacetate* (0.85 g), m.p. 110° (from ethanol), $[\alpha]_D^{25}$ +64° (*c* 0.6), $\nu_{max.}$ 1 685 cm^{-1} (SAc) (Found: C, 46.9; H, 5.9; S, 20.7. $C_{12}H_{18}O_5S_2$ requires C, 47.0; H, 5.9; S, 20.9%).

1,2-O-*Isopropylidene*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranose* (4).—0.25M-Sodium methoxide in methanol (10 ml) was added to a solution of 5-*S*-benzoyl-1,2-*O*-isopropylidene-3-*O*-tosyl-5-thio-α-D-xylofuranose (0.8 g) in dioxan (5 ml). After 20 min the solution was neutralised with carbon dioxide and evaporated to dryness. The residue was dissolved in water, acidified at 0 °C with hydrochloric acid, and extracted with chloroform to give an oil. Column chromatography (ether) furnished a solid, which on crystallisation from ethanol gave the *thiol* (0.6 g), m.p. 78—79°, $[\alpha]_D^{20}$ −54° (*c* 2.2), $\nu_{max.}$ 2 590 cm^{-1} (SH) (Found: C, 50.0; H, 5.6; S, 17.7; thiol S, 9.0%; M^+, 360. $C_{15}H_{20}O_6S_2$ requires C, 50.0; H, 5.6; S, 17.8; thiol S, 8.9%; *M*, 360).

Oxidation of a solution of this thiol, in methanol, with aqueous potassium tri-iodide, gave 5,5′-*dithiobis*-(5-*deoxy*-1,2-O-*isopropylidene*-3-O-*tosyl*-α-D-*xylofuranose*), m.p. 174—175° (from ethanol), $[\alpha]_D^{20}$ −102° (*c* 2.0) (Found: C, 50.1; H, 5.4; S, 17.6%; M^+, 718. $C_{30}H_{38}O_{12}S_4$ requires C, 50.1; H, 5.3; S, 17.8%; *M*, 718).

Methyl 3-O-*Tosyl*-5-*thio*-α-D-*xylopyranoside* (9).—(i) A solution prepared from sodium (1.2 g) in dry methanol (100 ml) was added to a solution of 5-*S*-benzoyl-1,2-*O*-isopropylidene-3-*O*-tosyl-5-thio-α-D-xylofuranose (20 g) in chloroform (100 ml). Preliminary small-scale experiments, in which samples were removed and rapidly evaporated in a stream of nitrogen, and the residues examined in paraffin mull by i.r. spectroscopy, had established that the absorption at 1 660 cm^{-1} (SBz) disappeared after *ca.* 15 min, and was replaced by the carbonyl band of methyl benzoate at 1 720 cm^{-1}. Therefore, after 15 min, 4M-hydrogen chloride in methanol (30 ml) was added, and the solution was boiled under reflux for 3 h. It was then neutralised with sodium hydrogen carbonate, filtered, and evaporated. The residue was partitioned between chloroform and water, and the dried organic layer was concentrated to give a pasty solid. Recrystallisation from ethanol–petroleum gave crystals (7.6 g) of the *thioxyloside* (9), m.p. 130—132° (decomp.), $[\alpha]_D^{19}$ +211° (*c* 2.0), $\nu_{max.}$ 3 520 (OH) and 1 350 cm^{-1} (OTs), τ 2.45 (4 H, ABq, aromatic), 5.38 (1 H, t, H-3,* $J_{2,3}$ and $J_{3,4}$ 9 Hz), 5.60 (1 H, d, H-1,* $J_{1,2}$ 3 Hz), 6.2 (2 H, m, H-2,* $J_{1,2}$ 3, $J_{2,3}$ 9 Hz, overlapping m, H-4*), 6.62 (3 H, s, OMe), 6.88 (1 H, d, OH, *J* 4 Hz), 7.2—7.5 (3 H, m, H-5, H-5′, and OH), and 7.62 (3 H, s, ArMe) (Found: C, 46.85; H, 5.4; S, 19.1. $C_{13}H_{18}O_6S_2$ requires C, 46.7; H, 5.4; S, 19.2%).

(ii) A 10% solution of hydrogen chloride in dry methanol (100 ml) was added to a solution of 5-*S*-benzoyl-1,2-*O*-isopropylidene-3-*O*-tosyl-5-thio-α-D-xylofuranose (10 g) in dichloromethane (20 ml) and the mixture was boiled under reflux for 24 h, then neutralised with sodium hydrogen carbonate, filtered, and evaporated to dryness. Extraction of the residue with dichloromethane gave the thioxyloside (4.2 g), identical (m.p. and spectra) with that described in the previous paragraph.

Methyl 2,3- *and* 3,4-*Anhydro*-5-*thio*-α-D-*ribopyranosides* (10) *and* (13).—A solution prepared from sodium (1.0 g) and dry methanol (25 ml) was added to methyl 3-*O*-tosyl-5-thio-α-D-xylopyranoside (5.0 g) dissolved in dry dichloromethane (25 ml). A white precipitate was immediately formed, and after 20 min the mixture was diluted with water (50 ml) and dichloromethane (50 ml); the aqueous layer was separated and extracted with dichloromethane (3 × 50 ml), and the combined organic solutions were dried and evaporated to an oil. Several fractional separations by t.l.c. (dichloromethane) gave (i) *methyl* 2,3-*anhydro*-5-*thio*-α-D-*ribopyranoside* (1.0 g, 41%), a syrup, $[\alpha]_D^{22}$ +307° (*c* 3.0), $\nu_{max.}$ (film) 3 400 (OH) and 3010 cm^{-1} (epoxide C–H), τ 5.30 (1 H, q, H-1, $J_{1,2}$ 5, $J_{1,3}$ 1 Hz), 5.8br (1 H, q, H-4, $J_{4,5a}$ 11, $J_{4,5e}$ 5 Hz), 6.20 (1 H, t, H-2, $J_{1,2}$ and $J_{2,3}$ 5 Hz), 6.53 (3 H, s, OMe), 6.4—6.7 (2 H, m), 7.05 (1 H, q, H-5a, $J_{5a,5e}$ 11.5, $J_{4,5a}$ 11 Hz), and 7.65 (1 H, q, H-5e, $J_{5a,5e}$ 11.5, $J_{4,5e}$ 5 Hz) (Found: C, 44.3; H, 6.2; S, 19.6%; M^+, 162. $C_6H_{10}O_3S$ requires C, 44.4; H, 6.2; S, 19.8%; *M*, 162); and (ii) *methyl* 3,4-*anhydro*-5-*thio*-α-D-*ribopyranoside* (0.76 g, 31%), m.p. 52—53°, $[\alpha]_D^{19}$ +268° (*c* 1.2), $\nu_{max.}$ (film) 3 400 (OH) and 3 010 cm^{-1} (epoxide C–H), τ 5.62 (1 H, d, H-1,* $J_{1,2}$ 5 Hz), 5.8—6.05 (1 H, m, H-2*), 6.38 (1 H, septet, H-4, $J_{3,4}$ 4, $J_{4,5a}$ 1, $J_{4,5e}$ 6 Hz), 6.62 (3 H, s, OMe), 6.77 (1 H, q, H-3, $J_{2,3}$ 3, $J_{3,4}$ 4 Hz), 6.99 (1 H, q, H-5a, $J_{4,5a}$ 1, $J_{5a,5e}$ 14 Hz), and 7.36 (1 H, q, H-5e, $J_{4,5e}$ 6, $J_{5a,5e}$ 14 Hz) (Found: C, 44.2; H, 6.05; S, 19.3%; M^+, 162).

Methyl 4-O-*Acetyl*-2,3-*anhydro*-5-*thio*-α-D-*ribopyranoside* (11).—Acetylation of the 2,3-epoxide (52 mg) with acetic anhydride (54 mg) in pyridine (1 ml) gave the acetate (64 mg), an oil (which subsequently crystallised; m.p. 43—52°), $[\alpha]_D^{22}$ +290° (*c* 1.2), $\nu_{max.}$ (film) 1 730 cm^{-1} (OAc), τ 4.70 (1 H, q of d, H-4, $J_{3,4}$ 1, $J_{4,5a}$ 12, and $J_{4,5e}$ 6 Hz), 5.24 (1 H, q, H-1, $J_{1,2}$ 4, $J_{1,3}$ 1 Hz), 6.20 (1 H, t, H-2, $J_{1,2}$ and $J_{2,3}$ 4 Hz), 6.50 (3 H, s, OMe), 6.5 (1 H, obscured, H-3), 6.90 (1 H, q, H-5a, $J_{4,5a}$ 12, $J_{5a,5e}$ 13 Hz), 7.62 (1 H, q, H-5e, $J_{4,5e}$ 5, $J_{5a,5e}$ 13 Hz), and 7.86 (3 H, s, OAc) (Found: C, 46.9; H, 5.95; S, 15.5. $C_8H_{12}O_4S$ requires C, 47.05; H, 5.9; S, 15.7%).

Methyl 2-O-*Acetyl*-3,4-*anhydro*-5-*thio*-α-D-*ribopyranoside* (14).—Similarly, the 3,4-epoxide (50 mg) gave the *acetate* (63 mg), an oil, $[\alpha]_D^{22}$ +238° (*c* 1.4), $\nu_{max.}$ 1 730 cm^{-1} (OAc)

[14] P. Karrer and A. Boettcher, *Helv. Chim. Acta*, 1953, **36**, 837.

(film), τ 4.71 (1 H, q, H-2,* $J_{1,2}$ 2.2, $J_{2,3}$ 1.2 Hz), 5.42 (1 H, d, H-1,* $J_{1,2}$ 2.2 Hz), 6.36 (1 H, septet, H-4, $J_{3,4}$ 5, $J_{4,5a}$ 1.5, $J_{4,5e}$ 6 Hz), 6.65 (3 H, s, OMe), 6.75—6.9 (1 H, m, H-3), 6.91 (1 H, q, H-5a, $J_{4,5a}$ 1.5, $J_{5a,5e}$ 15 Hz), 7.32 (1 H, q, H-5e, $J_{4,5e}$ 6, $J_{5a,5e}$ 15 Hz), and 7.86 (3 H, s, OAc) (Found: C, 47.0; H, 5.9; S, 15.3. $C_8H_{12}O_4S$ requires C, 47.05; H, 5.9; S, 15.7%).

Methyl 2,3-*Anhydro*-4-O-*methyl*-5-*thio*-α-D-*ribopyranoside* (12).—Silver oxide (2.5 g; freshly prepared and dried) was added to a solution of methyl 2,3-anhydro-5-thio-α-D-ribopyranoside (0.78 g) in methyl iodide (25 ml). The suspension was vigorously stirred and heated under reflux for 24 h; t.l.c. then showed reaction to be complete. The silver salts were removed and washed with dichloromethane, the washings were added to the methyl iodide solution, and the solvents were evaporated off to leave the *methyl ether* as an oil (0.84 g), $[\alpha]_D^{18}$ +270° (*c* 2.3), τ 5.20 (1 H, q, H-1, $J_{1,2}$ 4, $J_{1,3}$ 1 Hz), 6.20 (1 H, t, H-2, $J_{1,2}$ and $J_{2,3}$ 4 Hz), *ca.* 6.2 (1 H, obscured, H-4), 6.42 (3 H, s, OMe), 6.48 (3 H, s, OMe), *ca.* 6.4 (1 H, obscured H-3), 6.99 (1 H, q, H-5a, $J_{4,5a}$ 10, $J_{5a,5e}$ 13 Hz), and 7.64 (1 H, q, H-5e, $J_{4,5e}$ 4, $J_{5a,5e}$ 13 Hz) (Found: C, 47.5; H, 6.85; S, 17.8. $C_7H_{12}O_3S$ requires C, 47.7; H, 6.9; S, 18.2%).

Methyl 3,4-*Anhydro*-2-O-*methyl*-5-*thio*-α-D-*ribopyranoside* (15).—Methyl 3,4-anhydro-5-thio-α-D-ribopyranoside (0.70 g) was methylated under the same conditions and gave the *methyl ether* (0.75 g), m.p. 74—76° (from di-isopropyl ether), $[\alpha]_D^{18}$ +133° (*c* 0.3), τ 5.35 (1 H, d, H-1, $J_{1,2}$ 4 Hz), 6.08 (1 H, q, H-2, $J_{1,2}$ 4, $J_{2,3}$ 2 Hz), 6.43 (3 H, s, OMe), 6.50 (3 H, s, OMe), and 6.2—7.6 (4 H, m) (Found: C, 47.6; H, 6.8; S, 17.6. $C_7H_{12}O_3S$ requires C, 47.7; H, 6.9; S, 18.2%).

Methyl 2,3-*Dideoxy*-2,3-*epithio*-4-O-*methyl*-5-*thio*-α-D-*lyxopyranoside* (21).—Methyl 2,3-anhydro-4-*O*-methyl-5-thio-α-D-ribopyranoside (0.25 g) and potassium thiocyanate (0.50 g) were dissolved in ethanol (10 ml) and water (2 ml). The solution was boiled under reflux for 17 h, and was then diluted with water and extracted with dichloromethane to give a red syrup, whch was subjected to three successive treatments by t.l.c. (the first in dichloromethane, the last two in ether) to yield the slightly impure episulphide (82 mg) as a pale yellow oil, $[\alpha]_D^{25}$ −175° (*c* 1.5), τ 4.98 (1 H, d, H-1, $J_{1,2}$ 3 Hz), 5.4—6.9 (5 H, m), 6.73 (3 H, s, OMe), and 6.76 (3 H, s, OMe) (Found: C, 43.4; H, 6.4; S, 31.1. Calc. for $C_7H_{12}O_2S_2$: C, 43.7; H, 6.3; S, 33.35%).

Methyl 3,4-*Dideoxy*-3,4-*epithio*-2-O-*methyl*-5-*thio*-β-L-*arabinopyranoside* (22).—Similar treatment of methyl 3,4-anhydro-2-*O*-methyl-5-thio-α-D-ribopyranoside (95 mg) with potassium thiocyanate (200 mg) in ethanol (10 ml) and water (2 ml) gave the episulphide (74 mg) as an oil (which could not be completely purified), $[\alpha]_D^{28}$ +371° (*c* 0.4), τ 5.35 (1 H, d, H-1, $J_{1,2}$ 3 Hz), 6.0—7.4 (5 H, m), 6.42 (3 H, s, OMe), and 6.51 (3 H, s, OMe) (Found: C, 44.8; H, 6.4; S, 31.6%; M^+, 192. Calc. for $C_7H_{12}O_2S_2$: C, 43.7; H, 6.3; S, 33.35%; *M*, 192).

Methyl 2,3-*Dideoxy*-4-O-*methyl*-2,3-*thiocarbonyldithio*-5-*thio*-α-D-*arabinopyranoside* (23).—Carbon disulphide (2 ml) was added slowly to a cooled solution prepared from sodium (144 mg) and methanol (10 ml), followed by methyl 2,3-anhydro-4-*O*-methyl-5-thio-α-D-ribopyranoside (124 mg). The mixture was boiled under reflux for 24 h, then cooled, diluted with water, and extracted with dichloromethane to give an orange syrup which by t.l.c. (dichloromethane) furnished the *trithiocarbonate* (88 mg), m.p. 134—135° (from ether), $[\alpha]_D^{20}$ +16° (*c* 0.9), $\nu_{max.}$ (paraffin mull) 1 200, 1 130, 1 110, 1 060, and 880 cm^{-1}, τ 4.89 (1 H, q, H-2*, $J_{1,2}$ 9.5, $J_{2,3}$ 12.5 Hz), 5.19 (1 H, d, H-1*, $J_{1,2}$ 9.5 Hz), 5.62 (1 H, q, H-3*, $J_{2,3}$ 12.5, $J_{3,4}$ 2.4 Hz), 6.16 (1 H, quint, H-4*, $J_{3,4}$ 2.4, $J_{4,5e}$ 2.0, $J_{4,5a}$ 3.6 Hz), 6.51 (3 H, s, OMe), 6.56 (3 H, s, OMe), 6.85 (1 H, q, H-5a*, $J_{4,5a}$ 3.6, $J_{5a,5e}$ 15.0 Hz), and 7.10 (1 H, q, H-5e*, $J_{4,5e}$ 2.0, $J_{5a,5e}$ 15.0 Hz) (Found: C, 35.5; H, 4.6; S, 48.0. $C_8H_{12}O_2S_4$ requires C, 35.8; H, 4.5; S, 47.8%).

Methyl 3,4-*Dideoxy*-2-O-*methyl*-3,4-*thiocarbonyldithio*-5-*thio*-α-D-*xylopyranoside* (26).—Similar treatment of methyl 3,4-anhydro-2-*O*-methyl-5-thio-α-D-ribopyranoside (117 mg) with a reagent prepared from sodium (145 mg), methanol (10 ml), and carbon disulphide (2 ml), for 55 h under reflux, gave a brown oil which was purified by t.l.c. to give the *trithiocarbonate* (60 mg), m.p. 101—102° (from petroleum), $[\alpha]_D^{20}$ +386° (*c* 0.94), $\nu_{max.}$ (paraffin mull) 1 110, 1 080, 1 055, and 890 cm^{-1}, τ 5.24 (1 H, t, H-3, $J_{2,3}$ and $J_{3,4}$ 11 Hz), 5.33 (1 H, d, H-1, $J_{1,2}$ 2 Hz), 5.41 (1 H, sext, H-4, $J_{3,4}$ 11, $J_{4\,5a}$ 11, $J_{4,5e}$ 3 Hz), 6.11 (1 H, q, H-2, $J_{1,2}$ 2, $J_{2,3}$ 11 Hz), 6.52 (3 H, s, OMe), 6.64 (3 H, s, OMe), 6.95 (1 H, q, H-5a, $J_{4,5a}$ 11, $J_{5a,5e}$ 13 Hz), and 7.42 (1 H, q, H-5e, $J_{4,5e}$ 3, $J_{5a,5e}$ 13 Hz) [measurements assisted by use of Eu(fod)$_3$] (Found: C, 35.7; H, 4.4; S, 47.3. $C_8H_{12}O_2S_4$ requires C, 35.8; H, 4.5; S, 47.8%).

Methyl 5-S-*Benzoyl*-3-O-*tosyl*-5-*thio*-α- *and* -β-D-*xylofuranosides*.— 5-*S*-Benzoyl-1,2-*O*-isopropylidene-3-*O*-tosyl-5-thio-α-D-xylofuranoside (2.24 g) was stirred with methanolic 4M-hydrogen chloride (20 ml), and sufficient dichloromethane to dissolve the solid was added. The solution was stirred for 2 h (t.l.c. then showed the absence of starting material), and then neutralised with solid sodium hydrogen carbonate, filtered, and evaporated. The residual oil was separated by t.l.c. (dichloromethane) into two components: (i) (slower running) *methyl* 5-S-*benzoyl*-3-O-*tosyl*-5-*thio*-β-D-*xylofuranoside* (0.44 g), m.p. 97—99° (from ether–petroleum), $[\alpha]_D^{22}$ −60° (*c* 1.0), $\nu_{max.}$ 3 450 (OH), 1 660 (SBz), and 1 370 cm^{-1} (OTs), τ 1.95—2.75 (9 H, m, aromatic), 5.05—5.25 (2 H, m), 5.35—5.75 (2 H, m), 6.60 (3 H, s, OMe), 6.70 (2 H, d, H-5, $J_{4,5}$ 7 Hz), 6.85 (1 H, s, OH), and 7.58 (3 H, s, ArMe) (Found: C, 54.9; H, 5.1; S, 14.6. $C_{20}H_{22}O_7S_2$ requires C, 54.8; H, 5.1; S, 14.6%); and (ii) *methyl* 5-S-*benzoyl*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranoside* (0.26 g), m.p. 68—70° (from ether–petroleum), $[\alpha]_D^{22}$ +62° (*c* 1.7), $\nu_{max.}$ 3 470 (OH), 1 660 (SBz), and 1 365 cm^{-1} (OTs), τ 2.0—2.75 (9 H, m, aromatic), 4.98 (1 H, d, H-1, $J_{1,2}$ 4 Hz), 5.15 (1 H, q, H-3, $J_{2,3}$ 5, $J_{3,4}$ 3 Hz), 5.4—5.8 (2 H, m), 6.53 (3 H, s, OMe), 6.70 (2 H, d, H-5, $J_{4,5}$ 7 Hz), 7.08 (1 H, s, OH), and 7.50 (3 H, s, ArMe) (Found: C, 54.8; H, 5.0; S, 14.4%).

Benzoylation (benzoyl chloride–pyridine) of the α-anomer gave *methyl* 2-O-*benzoyl*-5-S-*benzoyl*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranoside*, m.p. 105° (from dichloromethane–petroleum), $[\alpha]_D^{25}$ +148° (*c* 0.7), $\nu_{max.}$ 1 725 (OBz), 1 665 (SBz), and 1 375 cm^{-1} (OTs), τ 1.8—2.95 (14 H, aromatic), 4.45—4.85 (3 H, m), 5.40 (1 H, q), 6.4—6.8 (2 H, m), 6.65 (3 H, s, OMe), and 7.75 (3 H, s, ArMe) (Found: C, 59.5; H, 4.9; S, 11.5. $C_{27}H_{26}O_8S_2$ requires C, 59.8; H, 4.8; S, 11.8%).

Methylation of 5-S-*Benzoyl*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranoside*.—(*a*) Barium oxide (0.36 g) was added to a solution of the xyloside (0.21 g) in methyl iodide (5 ml) and the suspension was vigorously stirred and boiled under reflux for 13 h. The barium salts were then filtered off and washed with dichloromethane, and the filtrate and washings were evaporated to an oil, which was mainly methyl 2,3-anhydro-5-*S*-benzoyl-5-thio-α-D-ribofuranoside (28), $\nu_{max.}$ (film) 1 660 cm^{-1} (SBz), τ 1.8—2.75 (5 H, m, aromatic), 4.76 (1 H, m), 5.45 (1 H, m), 6.28 (2 H, m), 6.49 (3 H, s, OMe), and 6.4—6.85 (2 H, m).

(*b*) Methyl iodide (0.6 g) was added in three portions, during 1 h, to a vigorously stirred suspension of silver oxide (0.57 g) in a solution of the xyloside (0.50 g) in dimethylformamide (5 ml). After being stirred for 24 h the mixture was filtered, and the filtrate and washings were diluted with water and extracted with dichloromethane to give an oil. By t.l.c. a main component was isolated; the ^{1}H n.m.r. spectrum indicated that it was mainly the epoxide obtained in the previous experiment.

(*c*) The xyloside (218 mg), silver oxide (350 mg), and methyl iodide (5 ml) were heated together under reflux for 9 h with vigorous stirring. The mixture was then filtered, the silver salts were washed with dichloromethane, and the filtrate and washings were evaporated. The residual oil was separated by t.l.c. into three components: (i) the 2,3-anhydro-compound (22 mg), identical (n.m.r. spectrum) with that obtained by procedure (*a*); (ii) *methyl* 5-S-*benzoyl*-2-O-*methyl*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranoside* (68 mg), a syrup, $[\alpha]_D^{25}$ +70° (*c* 0.7), $\nu_{max.}$ (film) 1 660 (SBz) and 1 375 cm^{-1} (OTs), τ 1.9—2.75 (9 H, m, aromatic), 4.8—5.15 (2 H, m, including d, H-1, $J_{1,2}$ 5 Hz), 5.58 (1 H, q), 6.05 (1 H, t), 6.55 (3 H, s, OMe), 6.70 (3 H, s, OMe), 6.5—6.7 (2 H, m), and 7.55 (3 H, s, ArMe) (Found: C, 55.75; H, 5.4; S, 13.6. $C_{21}H_{24}O_7S_2$ requires C, 55.7; H, 5.35; S, 14.2%); and (iii) methyl 2-*O*-benzoyl-5-*S*-benzoyl-3-*O*-tosyl-5-thio-α-D-xylofuranoside (62 mg), m.p. and mixed m.p. 105—106°.

Debenzoylation of Methyl 5-S-*Benzoyl*-2-O-*methyl*-3-O-*tosyl*-5-*thio*-α-D-*xylofuranoside*.—The thiobenzoate (0.30 g) was dissolved in methanol (5 ml) and sodium (0.10 g) was added. After 30 min the solution was diluted with water and extracted with dichloromethane to give an oil, which by t.l.c. was separated into (i) methyl benzoate and (ii) methyl 2-*O*-methyl-3-*O*-tosyl-5-thio-α-D-xylofuranoside (0.14 g), a pale yellow syrup, $\nu_{max.}$ (film) 2 600 (SH) and 1 380 cm^{-1} (OTs), τ 2.33 (4 H, ABq, aromatic), 4.8—5.1 (2 H, m, including d, H-1, $J_{1,2}$ 5 Hz), 5.60 (1 H, q, H-4), 6.05 (1 H, t, H-2, $J_{1,2}$ and $J_{2,3}$ 5 Hz), 6.53 (3 H, s, OMe), 6.70 (3 H, s, OMe), 7.20 (2 H, q, H-5, $J_{4,5}$ 6, $J_{5,SH}$ 9 Hz), 7.50 (3 H, s, ArMe), and 8.40 (1 H, t, SH, $J_{5,SH}$ 9 Hz).

A solution of the thiol (115 mg) in methanolic M-hydrogen chloride (10 ml) was boiled under reflux in nitrogen for 22 h. The product was a complex mixture (t.l.c.) from which no pure material could be isolated.

Methyl 3,5-*Dideoxy*-3,5-*epithio*-α-D-*xylofuranoside* (29).—A solution prepared from sodium (0.10 g) in dry methanol (2 ml) was added to a solution of methyl 5-*S*-benzoyl-3-*O*-tosyl-5-thio-α-D-xylofuranoside (2.0 g) in dry dichloromethane (2 ml) under nitrogen. After 5 min the mixture was diluted with water and extracted with dichloromethane to give an oil, which on purification by t.l.c. afforded the episulphide (0.64 g, 86%), $[\alpha]_D^{26}$ +211° (*c* 2.1) (lit.,[8] $[\alpha]_D^{24}$ +222°).

Acetylation (acetic anhydride–pyridine) gave the 2-acetate, m.p. 65—66°, $[\alpha]_D^{26}$ +254° (*c* 2.6) (Found: C, 46.8; H, 5.8; S, 15.6. Calc. for $C_8H_{12}O_4S$: C, 47.0; H, 5.9; S, 15.7%) (lit.,[8] m.p. 64.5—65.5°, $[\alpha]_D^{24}$ +256°).

The ^{1}H n.m.r. spectra of these products agreed with the recorded data.[8]

Methyl 3,5-*Dideoxy*-3,5-*epithio*-β-D-*xylofuranoside*.—A solution prepared from sodium (0.2 g) in dry methanol (5 ml) was added to a solution of methyl 5-*S*-benzoyl-3-*O*-tosyl-5-thio-β-D-xylofuranoside (1.0 g) in dry dichloromethane (5 ml). After 2 h the mixture was worked up as described for the α-anomer, and gave (i) the episulphide (91 mg, 25%), m.p. 48—50°, $[\alpha]_D^{26}$ −56° (*c* 2.9) (lit.,[8] m.p. 47—50°, $[\alpha]_D^{25}$ −73°); and (ii) 5,5′-S-*methylenebis*(*methyl* 2,3-*anhydro*-5-*thio*-β-D-*ribofuranoside*) (31) (129 mg, 34%), m.p. 115—116° (from ether), $[\alpha]_D^{25}$ −239° (*c* 0.6), $\nu_{max.}$ 3 050 cm^{-1} (epoxide C–H), τ 5.00 (1 H, s, H-1), 5.70 (1 H, t, H-4, $J_{3,4}$ 0, $J_{4,5a}$ and $J_{4,5b}$ 8 Hz), 6.1—6.4 (2 H, m), 6.16 (1 H, s, $\frac{1}{2}$S·CH_2·S), 6.55 (3 H, s, OMe), 7.03 (1 H, q, H-5, $J_{4,5}$ 8, $J_{5,5'}$ 13 Hz), 7.35 (1 H, q, H′-5, $J_{4,5'}$ 8, $J_{5a,5'}$ 13 Hz) (integrals based on the half molecule) (Found: C, 46.9; H, 5.85; S, 19.1%; M^+, 336. $C_{13}H_{20}O_6S_2$ requires C, 46.4; H, 6.0; S, 19.1%; *M*, 336).

Acetylation of the episulphide [fraction (i)] gave the 2-acetate, an oil, $[\alpha]_D^{26}$ −28° (*c* 0.5) (Found: C, 46.9; H, 5.8; S, 16.1. Calc. for $C_8H_{12}O_4S$: C, 47.0; H, 5.9; S, 15.7%) (lit.,[8] oil, $[\alpha]_D^{24}$ −36°). The ^{1}H n.m.r. spectra of the acetate, and of its precursor, were in agreement with reported data.[8]

1,6-*Dideoxy*-1,6-*epithio*-5-*thio*-β-L-*idopyranose* (33).—A solution of 1,2-*O*-isopropylidene-5,6-dithio-β-L-idofuranose [12] (1.2 g) in acetic acid (35 ml) and water (15 ml) was boiled under reflux for 40 h in nitrogen and then evaporated to an oil, which was taken up in hot methanol, treated with charcoal, and recovered; it then crystallised. Recrystallisation from ethanol, followed by sublimation at 150 °C (10^{-5} mmHg), gave the *epithio-compound* (0.20 g), m.p. 194—197°, $[\alpha]_D^{26}$ +174° (*c* 1.1 in water) (Found: C, 37.2; H, 5.2; S, 32.7%; M^+, 194. $C_6H_{10}O_3S_2$ requires C, 37.1; H, 5.2; S, 33.0%; *M*, 194).

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