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# SYNTHESIS OF 5-THIO-D-ARABINOSE AND 5-THIO-D-LYXOSE AND THEIR METHYL GLYCOPYRANOSIDES*

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ABSTRACT

1,2-*O*-Isopropylidene-5-*O*-toluene-*p*-sulphonyl-β-D-arabinofuranose has been converted into 5-thio-D-arabinose *via* 3-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-β-D-arabinofuranose. 5-Thio-D-lyxose was similarly obtained from methyl 2,3-*O*-isopropylidene-5-*O*-methanesulphonyl(or toluene-*p*-sulphonyl)-α-D-lyxofuranoside *via* methyl 5-*S*-acetyl(or benzoyl)-1,2-*O*-isopropylidene-5-thio-α-D-lyxofuranoside. The corresponding methyl thiopyranosides were obtained by methanolysis of the free sugars or the above thioester intermediates. All of the 5-thio-D-pentopyranoses and their methyl 5-thio-D-pentopyranosides are now known, and some of their properties are summarised.

## INTRODUCTION

5-Thio-D-xylose[2] was the first sulphur-in-ring pentose to be synthesised and was quickly followed by 5-thio-D-ribose[3]. Both of these syntheses involved a displacement by a sulphur nucleophile on an appropriate pentofuranose 5-sulphonate. A similar approach to 5-thio-L-arabinose seemed to be impracticable, because of the difficulty in preventing oxidation of an intermediate thiol to a disulphide[4]. An alternative route to this thio sugar utilised an intramolecular displacement in 5-*O*-toluene-*p*-sulphonyl-L-arabinose dibenzyl dithioacetal, leading to the benzyl 1,5-dithio-α- and -β-L-arabinopyranosides, although no attempt was made to convert these products into 5-thio-L-arabinose[5]. No synthesis of 5-thio-D- or -L-lyxose has yet been reported, although derivatives of 5-amino-5-deoxy-D-lyxose are known[6]. We now report effective syntheses of 5-thio-D-arabinose and 5-thio-D-lyxose, and the corresponding methyl 5-thiopyranosides.

*5-Thiopyranoses, Part VI. For Part V, see ref. 1.
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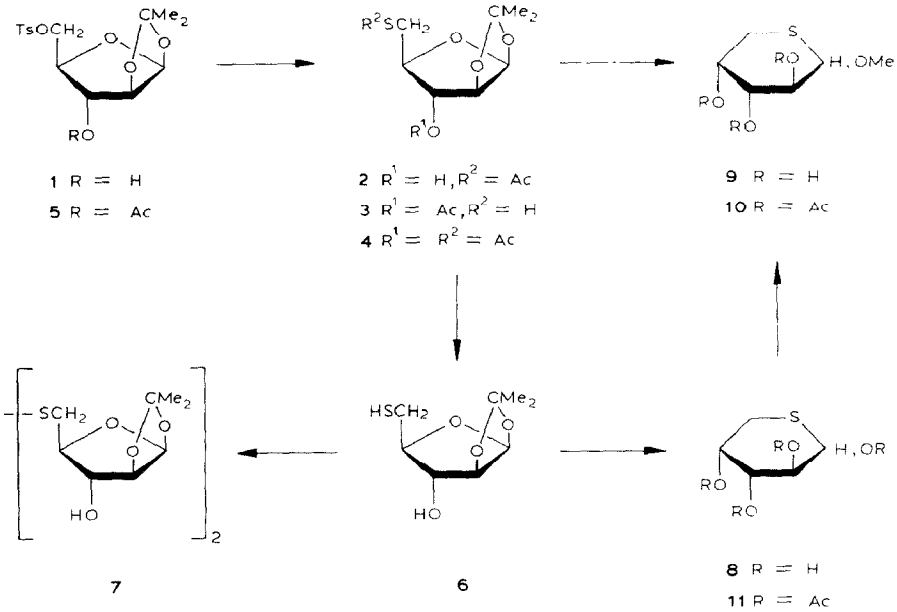
## DISCUSSION

The earlier exploratory work of Whistler and Rowell[4] was re-examined. Their route started from 1,2-*O*-isopropylidene-5-*O*-toluene-*p*-sulphonyl-β-L-arabinofuranose, which underwent displacement with sodium phenylmethanethiolate to give the corresponding 5-benzylthio derivative. Cleavage of the benzyl group then gave the corresponding 5-thiol, which could be converted into a crystalline 3,5-*O*,*S*-diacetyl derivative. However, on methanolysis, this derivative underwent simultaneous oxidation to disulphides and the yields of the expected methyl 5-thio-L-arabinopyranosides were low.

The present work was carried out in the D series. The enantiomer (**1**) of the above arabinofuranose derivative reacted readily with potassium thioacetate in hot *N*,*N*-dimethylformamide to give the thioacetate **2**. However, there was a tendency for the product to be contaminated with the isomeric acetate **3**, particularly if reaction times were prolonged. Similar behaviour has been observed in the *xylo* series[2]. Acetylation of **2** gave the *O*,*S*-diacetyl derivative **4**, enantiomeric with the product described by Whistler and Rowell[4], but better yields of **4** were obtained if the sulphonate **1** was first converted into the acetate **5** which then underwent the displacement reaction cleanly.




Deacetylation of **4** furnished the thiol **6**, which was readily oxidised in air to the disulphide **7**, but, with the exclusion of air, **6** could be hydrolysed by dilute sulphuric acid to give crystalline 5-thio-D-arabinose (**8**). The thio sugar **8** reacted only slowly with sodium nitroprusside, and its $^1$H-n.m.r. spectrum showed it to be

TABLE I

$^1$H-N.M R. DATA FOR *arabino* COMPOUNDS

| *Compound* | *Chemical shifts (p.p.m.)* | | | | | | | *Coupling constants (Hz)* | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *H-1* | *H-2* | *H-3* | *H-4* | *H-5* | *H-5'* | *Other signals* | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5}$ | $J_{4,5'}$ | $J_{5,5'}$ | *Other couplings* |
| **2**[a] | 5.89 | 4.54 | 4.17 | 4.04 | 3.29 | 3.22 | 2.38 (SAc); 2.61 (OH); 1.54, 1.32 ($CMe_2$) | 4.0 | 0.5 | 2.0 | 7.0 | 8.0 | 13.5 | 4.5 ($J_{3,OH}$) |
| **4**[a] | 5.91 | 4.58 | 5.08 | 4.14 | 3.36 | 3.26 | 2.37 (SAc); 2.10 (OAc); 1.59, 1.32 ($CMe_2$) | 4.0 | 0.5 | 1.0 | 6.5 | 8.0 | 17.5 | |
| **5**[a,d] | 5.86 | 4.52 | 4.98 | 4.23 | ⟷ | 4.17 | 2.43 (ArMe); 2.07 (OAc); 1.34, 1.26 ($CMe_2$) | 4.0 | 0.5 | 0.5 | | | | |
| **6**[b] | 5.81 | 4.44 | 4.19 | 3.93 | 2.81 | 2.69 | 2.20 (OH); 1.56 (SH); 1.50, 1.30 ($CMe_2$) | 4.0 | 0.5 | 2.0 | 6.5 | 8.0 | 13.5 | 7.5 ($J_{5,SH}$) 9.5 ($J_{5,SH}$) |
| **7**[a] | 5.95 | 4.57 | 4.41 | 4.30 | 3.07 | 3.05 | 2.47 (OH); 1.53, 1.32 ($CMe_2$) | 4.0 | 0.5 | 1.5 | 8.0 | 6.5 | | |
| **8**[c] | 4.96 | 3.98 | 3.78 | 4.28 | 3.19 | 2.58 | | 3.0 | 9.5 | 2.5 | 4.5 | 2.5 | 14.5 | 1.5 ($J_{1,5'}$) |
| **9α**[c] | 4.42 | 3.97 | 3.60 | 4.17 | 2.79 | 2.73 | 3.49 (OMe) | 7.0 | 7.0 | 3.0 | 5.5 | 3.5 | 14.0 | |
| **9β**[c] | 4.56 | 4.02 | 3.73 | 4.26 | 3.02 | 2.50 | 3.43 (OMe) | 3.0 | 10.0 | 3.0 | 1.5 | 4.0 | 14.5 | 1.5 ($J_{1,5'}$) |
| **10α**[a] | 4.34 | 5.33 | 5.02 | 5.37 | 3.10 | 2.52 | 3.42 (OMe); 2.09 (2), 2.12 (OAc) | 4.5 | 6.0 | 3.0 | 9.5 | 3.0 | 13.5 | 1.0 ($J_{3,5}$) |
| **10β**[b] | 5.80 | ⟷ | 5.20 | 4.68 | 3.14 | 2.68 | 3.46 (OMe); 2.03, 2.10, 2.19 (OAc) | | | | 1.5 | 4.0 | 14.0 | |
| **11α**[a] | 5.67 | 5.29 | 5.09 | 5.36 | 3.18 | 2.58 | 2.13(2), 2.11, 2.09 (OAc) | 4.5 | 5.5 | 2.5 | 9.5 | 3.0 | 13.0 | |
| **11β**[a] | 6.11 | 5.50 | 5.29 | 5.52 | 3.29 | 2.75 | 2.18, 2.17, 2.03, 2.01 (OAc) | 3.0 | 10.5 | 3.0 | 1.5 | 4.0 | 14.5 | 1.5 ($J_{1,5'}$) |

[a]In $CDCl_3$. [b]In $CCl_4$. [c]In $D_2O$. [d]Also showed signals in aromatic region.

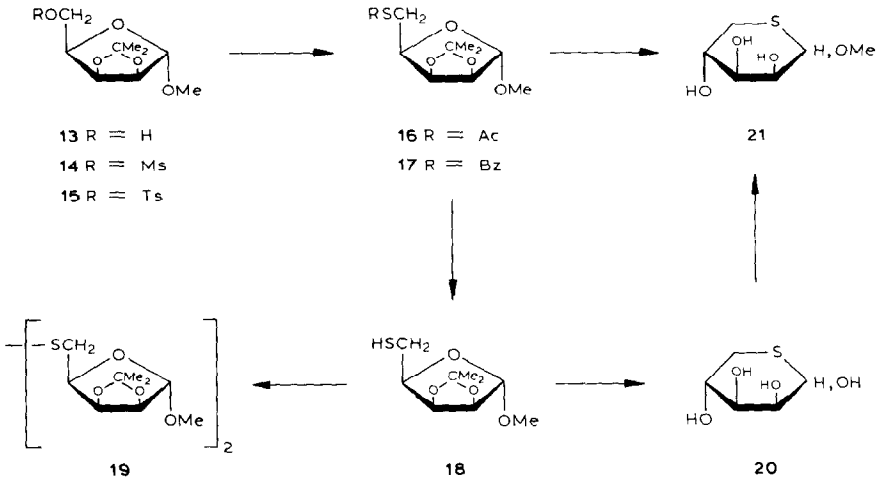
the β-pyranose form in the $^1C_4$ conformation ($J_{1,2}$ 3.0, $J_{2,3}$ 9.5 Hz). The optical rotation of a solution did not change significantly during several weeks, suggesting that little or no mutarotation had occurred. This and the β-anomeric configuration were confirmed by comparison of the $^{13}$C-n.m.r. spectrum of the solution with those of the related methyl 5-thio-α- and -β-D-arabinopyranosides (**9**).

When either the free sugar **8** or the precursor **4** was treated in an inert atmosphere with boiling methanolic hydrogen chloride, two products were obtained, neither of which was a thiol, and which were readily separated by chromatography on a basic ion-exchange resin[7]. The major product, eluted first, had a large, negative optical rotation and was assumed to be methyl 5-thio-β-D-arabinopyranoside (**9β**). This was followed by the minor product, the α anomer **9α**. The order of elution confirmed the anomeric assignments, glycosides with a 1,2-*cis* arrangement generally being eluted before those with 1,2-*trans* stereochemistry[7]. The coupling constants in the $^1$H-n.m.r. spectrum of **9β** were very similar to those of the free sugar (**8β**) (see Table I), indicating the $^1C_4$ conformation for **9β**. By contrast, the coupling constants ($J_{1,2} = J_{2,3} = 7$ Hz) of **9α** suggest an equilibrium between the $^1C_4$ and $^4C_1$ conformations for this compound. In the latter conformation, the methoxyl group is able to adopt an axial position. The change is even more pronounced for the related triacetate **10α**, where the $^4C_1$ conformation appears to be the dominant form ($J_{3,5e}$ 1, $J_{4,5e}$ 9.5 Hz).

The free sugar **8** gave a crystalline tetra-acetate and a small amount of a syrupy isomer. From their i.r. spectra, neither contained an *S*-acetyl group. $^1$H-N.m.r. spectroscopy showed the crystalline isomer to be the β anomer **11β** in the $^1C_4$ conformation, and the syrupy isomer was presumed to be the α anomer **11α** in the $^4C_1$ conformation from the close resemblance of its coupling constants with those of the α-triacetate **10α**. The β-tetra-acetate **11β** was also produced by acetolysis of the glycoside **9β**, but acetolysis of the diacetate **4** led to a mixture in which **11β** was only the minor component. The major component appeared to be a furanose tetra-acetate, since it showed i.r. absorptions at 1745 (OAc) and 1690 cm$^{-1}$ (SAc), and its $^1$H-n.m.r. spectrum contained prominent singlets at δ 2.33 (SAc), 2.22, 2.09, and 2.07 (3 OAc). Other workers[8] observed that acetolysis of 5-thiofuranoses does not lead exclusively to 5-thiopyranose acetates. Deacetylation of the mixture afforded the free sugar **8**. When a mixture of the benzyl 2,3,4-tri-*O*-acetyl-1,5-dithio-α- and -β-L-arabinosides, obtained in the earlier work[5], was acetolysed, it gave a good yield of crystalline 1,2,3,4-tetra-*O*-acetyl-5-thio-β-L-arabinopyranose (**12**), enantiomeric with **11β**, thus relating the two synthetic routes.

Methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside (**13**) gave a crystalline methanesulphonate **14** as well as the known[9] toluene-*p*-sulphonate **15**. The latter reacted readily with either potassium thioacetate or thiobenzoate in hot *N*,*N*-dimethylformamide to give the corresponding thioesters **16** or **17**. The thiobenzoate **17** was also obtained from **14**, but the reaction of this sulphonate with potassium thioacetate was considerably slower. Both **16** and **17** were deacylated to give the

thiol **18** which, by contrast with the *arabino*-thiol **6**, was much more stable to atmospheric oxidation but could be converted into the disulphide **19** by oxidation with iodine. Steric hindrance from the adjacent isopropylidene group probably accounts for the stabilty of the thiol **18**. Acid hydrolysis of **18** afforded crystalline 5-thio-D-lyxose (**20**), whose slow reaction with sodium nitroprusside and $^1$H-n.m.r. data ($J_{3,4} = J_{4,5a} = 9.0$ Hz) suggested a pyranoid ring in the $^4C_1$ conformation and whose optical rotation ($[\alpha]_D$ +24°) suggested the $\alpha$ configuration. The optical rotation of a stored solution did not change appreciably, suggesting that no significant mutarotation occurred. This conclusion and the $\alpha$ configuration were confirmed by the $^{13}$C-n.m.r. spectrum of the solution and its comparison with those of the related methyl 5-thio-$\alpha$- and -$\beta$-D-lyxopyranosides (**21**).




The glycosides **21** were obtained from **20** or the thioacetate **16** by methanolysis and were separated by chromatography on a basic ion-exchange resin. The minor product, the $\beta$-glycoside **21$\beta$**, was eluted before the major product, the $\alpha$-glycoside **21$\alpha$**, in keeping with the considerations mentioned earlier. The coupling constants in the $^1$H-n.m.r. spectrum of **21$\alpha$** were remarkably similar to those of the free sugar **20** (see Table II), indicating the $^4C_1$ conformation for this glycoside; the somewhat smaller value of $J_{3,4}$ (6.0 Hz) in the spectrum of the $\beta$ anomer suggests a contribution from the $^1C_4$ form, presumably because of the preference of MeO-1 for an axial orientation. As with the *arabino* compound, no furanoside products were detected in these methanolyses. Only the $\beta$-pyranoside **21$\beta$** gave a crystalline triacetate; **21$\alpha$** and the free sugar yielded only syrupy products.

With the syntheses reported here, all of the 5-thiopentoses and their methyl pyranosides are now known in the D series and it is appropriate to summarise their properties. Table III includes the $^{13}$C-n.m.r. data for the compounds in the *ribo*

TABLE II

$^1$H-N.M.R. DATA FOR *lyxo* COMPOUNDS

| Compound | Chemical shifts (p.p.m.) | | | | | | | Coupling constants (Hz) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *H-1* | *H-2* | *H-3* | *H-4* | *H-5* | *H-5'* | *Other signals* | $J_{1,2}$ | $J_{2,3}$ | $J_{3,4}$ | $J_{4,5}$ | $J_{4,5'}$ | $J_{5,5'}$ | *Other couplings* |
| **14**[a] | 4.91 | 4.57 | 4.73 | 4.22 | 4.57 | 4.50 | 3.34 (OMe); 3.08 (OMe); 1.46, 1.31 ($CMe_2$) | 0.5 | 6.0 | 3.0 | 5.0 | 6.0 | 10.5 | |
| **16**[a] | 4.86 | 4.53 | 4.66 | 3.99 | ←3.22→ | | 3.33 (OMe), 2.37 (SAc); 1.47, 1.31 ($CMe_2$) | 0.5 | 6.0 | 3.5 | 7.0 | 7.0 | | |
| **17**[a,d] | 4.91 | 4.58 | 4.73 | 4.12 | ←3.43→ | | 3.33 (OMe); 1.53, 1.38 ($CMe_2$) | 0.5 | 6.0 | 3.5 | 6.5 | 7.5 | | |
| **18**[b] | 4.70 | 4.43 | 4.62 | 3.91 | ←2.67→ | | 3.27 (OMe); 1.44 (SH); 1.40, 1.28 ($CMe_2$) | 0.5 | 6.0 | 3.0 | 7.0 | 7.0 | | 8.5 ($J_{5,SH}$) 8.5 ($J_{5',SH}$) |
| **19**[b] | 4.89 | 4.58 | 4.74 | 4.27 | 3.08 | 3.04 | 1.45, 1.32 ($CMe_2$) | 0.5 | 6.0 | 3.5 | 6.5 | 7.0 | 13.6 | |
| **20**[c] | 4.84 | 4.12 | 3.66 | 3.90 | 2.80 | 2.67 | | 4.0 | 3.0 | 9.0 | 9.5 | 5.0 | 13.0 | |
| **21α**[c] | 4.52 | 4.19 | 3.56 | 3.91 | 2.62 | 2.54 | 3.44 (OMe) | 4.0 | 3.0 | 9.5 | 9.0 | 5.5 | 13.0 | 1.0 ($J_{1,5'}$) |
| **21β**[c] | 4.62 | 4.18 | 3.68 | 4.08 | 3.00 | 2.42 | 3.47 (OMe) | 2.5 | 3.0 | 6.0 | 3.0 | 6.0 | 14.5 | |

[a]In $CDCl_3$. [b]In $CCl_4$. [c]In $D_2O$. [d]Also showed signals in aromatic region

TABLE III

$^{13}$C-N.M.R DATA FOR 5-THIO-D-PENTOSES AND METHYL 5-THIO-D-PENTOPYRANOSIDES

| *Compound* | *Chemical shifts (in p.p.m.)* | | | | | |
|---|---|---|---|---|---|---|
| | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *OMe* |
| *Sugars* | | | | | | |
| *β-arabino* (**8**) | 74.9[a] | 72.4[a] | 70.9[a] | 70.7[a] | 29.9 | |
| *α-lyxo* (**20**) | 76.9[a] | 74.3[a] | 72.8[a] | 69.9[a] | 29.0 | |
| *α-ribo* | 76.3[a] | 76.1[a] | 73.9[a] | 72.8[a] | 25.0 | |
| *β-ribo* | 76.7[a] | 75.2[a] | 73.5[a] | 72.4[a] | 30.8 | |
| *α-xylo*[b] | 75.8 | 78.0 | 76.2 | 75.8 | 29.6 | |
| *Glycosides* | | | | | | |
| *α-arabino* (**9α**) | 85.6 | 74.6[a] | 73.8[a] | 69.0[a] | 29.0 | 58.6 |
| *β-arabino* (**9β**) | 85.4 | 72.2[a] | 71.2[a] | 70.6[a] | 29.8 | 57.4 |
| *α-lyxo* (**21α**) | 87.1 | 73.5[a] | 73.2[a] | 69.9[a] | 28.6 | 57.0 |
| *β-lyxo* (**21β**) | 85.0 | 74.1[a] | 70.6[a] | 70.6[a] | 26.5 | 58.3 |
| *α-ribo*[c] | 89.8 | 71.6 | 72.6 | 74.4 | 22.8 | 57.4 |
| *β-ribo*[c] | 85.2 | 70.4 | 70.4 | 73.6 | 29.2 | 58.2 |
| *α-xylo*[c] | 84.6 | 76.3 | 75.2 | 74.2 | 27.9 | 57.2 |
| *β-xylo*[c] | 85.4 | 77.5 | 77.4 | 73.7 | 30.2 | 59.4 |

[a]Assignments may be interchanged. [b]Assignments from ref. 13. [c]Measured and assigned by S. D. Gero and G. Lukacs on material supplied by N. A. Hughes.

TABLE IV

$R_F$ VALUES[a] FOR 5-THIO-D-PENTOSES AND METHYL 5-THIO-D-PENTOPYRANOSIDES

| *Compound* | arabino | lyxo | ribo | xylo |
|---|---|---|---|---|
| Sugar | (**8**) 0.22 | (**20**) 0.26 | 0.35 | 0.27 |
| α-Glycoside | (**9α**) 0.51 | (**21α**) 0.61 | 0.59 | 0.58 |
| β-Glycoside | (**9β**) 0.51 | (**21β**) 0.54 | 0.68 | 0.53 |

[a]See Experimental.

TABLE V

EQUILIBRIUM PROPORTIONS OF α AND β ANOMERS OF METHYL 5-THIO-D-PENTOPYRANOSIDES AND THEIR OXYGEN ANALOGUES

| *Configuration* | *Thiopyranosides* | | *Pyranosides*[a] | | |
|---|---|---|---|---|---|
| | α | β | %[b] | α | β |
| *arabino* (**9**) | 8 | 92 | 71.7 | 34 | 66 |
| *lyxo* (**21**) | 91 | 9 | 98.6 | 90 | 10 |
| *ribo*[c] | 35 | 65 | 77.4 | 15 | 85 |
| *xylo*[d] | 93 | 7 | 94.9 | 69 | 31 |

[a]From ref. 11. [b]Pyranosides as percentage of total glycosides[11]. [c]Ref. 3. [d]See Experimental.

and *xylo* series as well as those for the *arabino* and *lyxo* compounds described in this paper. All of the thio derivatives are characterised by upfield shifts of the signals for C-1 (15–20 p.p.m.) and C-5 (30–40 p.p.m.), and other authors[10] have already commented on these differences in related 5-thiohexose derivatives. Likewise, Table IV gives the $R_F$ values for this family of compounds.

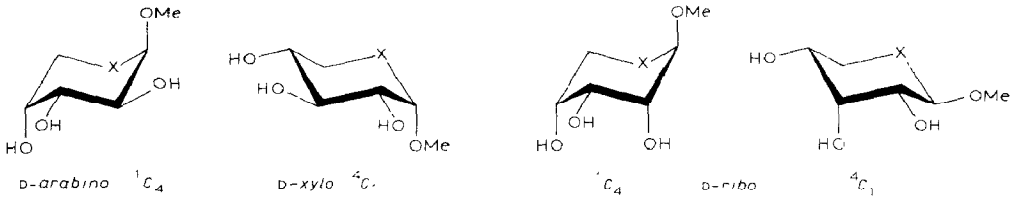
All of the thiopentoses show the expected preference for the thiopyranose ring in consequence of the greater nucleophilicity of sulphur over oxygen. All crystallise as pyranoses: β-D-*arabino*, α-D-*lyxo*, α- or β-D-*ribo*[3], and α-D-*xylo*[2]; only in the *ribo* case have both anomers been crystallised. All give only pyranosides on methanolysis, even 5-thio-D-arabinose (**8**) and 5-thio-D-ribose whose oxygen analogues give significant proportions of furanosides[11].

Of note is a comparison of the αβ-ratios for the thioglycosides with those of the oxygen analogues[11] (the comparison for free sugars is similar), and these are shown in Table V. The results can be divided into three classes. First, in the *arabino* and *xylo* series, the major pyranoside form becomes the preponderant thiopyranoside form, that is, the energy differences between α and β forms appear to have increased in the thiopyranosides. Second, the reverse trend is seen in the *ribo* series, where the preference for the β form is reduced for the sulphur analogue. Lastly, replacement of oxygen by sulphur has little effect in the *lyxo* series, where the α-glycosides are preponderant for both forms.

A possible explanation for the differences in the first two classes comes from the work of Lambert[12] who has shown that the thiopyranoid ring is more puckered than the pyranoid ring. Consequently, the distance between adjacent axial and equatorial groups is increased, leading to less strain, whereas the separation between adjacent equatorial groups is reduced, with an increase in strain.

The favoured glycosides in the first class (β-*arabino* and α-*lyxo*) are also the more conformationally stable, being $^1C_4$ and $^4C_1$, respectively (Scheme 1). In each of these compounds, MeO-1 is axial and HO-2 is equatorial, so that increased separation of these groups would reduce the steric strain. Essentially the same explanation was given by Lambert and Wharry[13] for the large propotion of α-pyranose form in solutions of 5-thio-D-xylose.

The situation with the *ribo* series is more complex, because the preferred conformations of the favoured β-glycosides are not the same. Thus, methyl β-D-ribopyranoside is a mixture of $^1C_4$ and $^4C_1$ forms, whereas the sulphur analogue is entirely $^4C_1$, as are both α forms[14]. The difference in the β forms arises from the



"hockey-stick effect", *i.e.*, the increased repulsive force between the axial lone-pair of electrons on the sulphur atom (as compared to oxygen) and a 1,3-related heteroatom substituent[15]. This interaction undoubtedly destabilises the $^1C_4$ form of the thioribopyranosides, where two such effects would be felt (axial hydroxyl groups at C-2 and C-4). In the $^4C_1$ conformation, the relationships between MeO-1 and HO-2 in the methyl 5-thio-α- and -β-D-ribopyranosides are axial–equatorial and equatorial–equatorial, respectively. Thus, there is a relief of strain in the α anomer and an increase in the β anomer, the nett effect being that the energy difference between the two anomers is reduced.

It should be noted that the "hockey-stick effect" is unlikely to affect the other thiopentopyranosides. In the *arabino* and *lyxo* series, there must always be one such effect whichever conformation is considered. In the *xylo* series, this applies only in the $^1C_4$ conformation, which is already the less-favoured conformation.

## EXPERIMENTAL

*General methods.* — Melting points are uncorrected. N.m.r. spectra were recorded at 90 ($^1$H) and 22.63 MHz ($^{13}$C) for solutions in deuteriochloroform or carbon tetrachloride (internal $Me_4Si$) or in deuterium oxide [internal $Me_3Si(CH_2)_3SO_3Na$]. Silica gel was used for t.l.c. (Gelman, ITLC type SA) and column chromatography (Merck Kieselgel 7734). The Zerolit FF anion-exchanger had mesh size 100–200 and a DVB content of 2–3%. $R_F$ values refer to chromatography on Whatman No. 1 paper in 1-butanol–water (86:14). Thiols and disulphides were detected with sodium nitroprusside[3]; otherwise, silver nitrate[16] (p.c.) and sulphuric acid (t.l.c.) were used.

*3-O-Acetyl-1,2-O-isopropylidene-5-O-toluene-p-sulphonyl-β-D-arabinofuranose* (**5**) — The tosylate[17] **1** (5.81 g) was treated overnight at room temperature with pyridine (20 mL) and acetic anhydride (10 mL). Work-up in the usual way and recrystallisation from ether–light petroleum gave **5** (6.55 g), m.p. 59–61°, $[\alpha]_D$ +27° (*c* 1.3, chloroform) (Found: C, 52.8; H, 5.7. $C_{17}H_{22}O_8S$ calc.: C, 52.8; H, 5.7%).

*5-S-Acetyl-1,2-O-isopropylidene-5-thio-β-D-arabinofuranose* (**2**). — A solution of **1** (0.36 g) in *N,N*-dimethylformamide (4 mL) containing potassium thioacetate (0.16 g) was heated at 100° for 2 h. The mixture was cooled, ether (10 mL) was added, and the precipitated salts were filtered off (Hyflo). The filtrate was evaporated to a syrup which was chromatographed on silica gel (20 g) with ether–light petroleum (1:1) to give **2** (0.16 g), m.p. 87–89° (from ether–light petroleum), $[\alpha]_D$ +51° (*c*0.3, chloroform) (Found: C, 48.4; H, 6.3. $C_{10}H_{16}O_5S$ calc.: C, 48.4; H, 6.5%).

*3-O-Acetyl-5-S-acetyl-1,2-O-isopropylidene-5-thio-β-D-arabinofuranose* (**4**). — *(a) From* **5**. The tosylate **5** (2.85 g) was heated with potassium thioacetate (1.14 g) in *N,N*-dimethylformamide (28 mL) for 1 h at 100°. Work-up, as in the previous experiment, gave **4** (2.05 g), m.p. 84–85° (from ethanol), $[\alpha]_D$ +13° (*c* 1.4,

chloroform) (Found: C, 50.1; H, 6.3. $C_{12}H_{18}O_6S$ calc.: C, 49.6; H, 6.2%); lit.[4] for the L form, m.p. 85° $[\alpha]_D$ −13.67°.

*(b) From* **2**. The thioacetate **2** (0.25 g) was treated overnight at room temperature with pyridine (2 mL) and acetic anhydride (1 mL). Work-up in the usual way gave **4** (0.29 g), m.p. 84–85°.

*Deacylation of* **4**. — Sodium (0.07 g) was added to a solution of **4** (0.22 g) in methanol (5 mL) under nitrogen. After 5 min at room temperature, acetic acid (2 mL) was added, and the mixture was diluted with water and extracted with dichloromethane. The extract was dried ($MgSO_4$), filtered, and evaporated to a syrup which was quickly chromatographed on silica gel (6 g) with benzene–ether (1:1). The early fractions contained the syrupy thiol **6** (0.10 g), $[\alpha]_D$ +4° (*c* 1.1, chloroform) [Found: mol.wt. (M − 15), 191.0400. $C_7H_{11}O_4S$ calc.: mol.wt. (M − 15), 191.0378].

The later fractions contained the disulphide **7** (57 mg), m.p. 160–163° (from ether), $[\alpha]_D$ +12° (*c* 0.9, chloroform) (Found: C, 46.35; H, 6.1. $C_{16}H_{26}O_8S_2$ calc.: C, 46.8; H, 6.4%); lit.[4] for the L form, m.p. 160°, $[\alpha]_D$ −23.53°.

*5-Thio-β-*D*-arabinopyranose* (**8**). — *(a) From the thiol* **6**. A solution of **6** (0.10 g) in 0.05M sulphuric acid, under nitrogen, was boiled under reflux for 15 min, cooled, and passed through Zerolit FF ($AcO^-$) resin. The eluate was evaporated to dryness and the residue crystallised from ethanol to give **8** (67 mg), m.p. 172–175°, $[\alpha]_D$ −250° (*c* 0.6, water) (Found: C, 36.1; H, 5.7. $C_5H_{10}O_4S$ calc.: C, 36.1; H, 6.0%).

*(b) From* **4**. A solution of **4** (0.29 g) in acetic anhydride (2.0 mL) and acetic acid (2.0 mL) containing conc. sulphuric acid (0.1 mL) was left at 0–5° for 2 days. A solution of sodium acetate (0.70 g) in water (5 mL) was added and, after 30 min, the solvents were removed. The residue was partitioned between water and dichloromethane, and the extract was dried ($MgSO_4$), filtered, and evaporated to give a syrup which was passed through a little silica gel with ether–light petroleum (1:1). The resulting mixture (0.22 g) of acetates was dissolved in methanol (4 mL) containing sodium methoxide [from sodium (10 mg)]. After 5 min, the mixture was neutralised ($CO_2$) and evaporated to dryness. The residue was extracted with hot ethanol to give **8** (80 mg), m.p. 173–175°.

*Methyl 5-thio-α- and -β-*D*-arabinopyranosides* (**9**). — *(a) From* **4**. A solution of **4** (0.30 g) in methanol (2.7 mL) and conc. hydrochloric acid (0.3 mL) was boiled under reflux for 1 h, cooled, neutralised ($PbCO_3$), filtered (Hyflo), and evaporated to dryness. The residue was chromatographed on a column (57 × 2 cm) of Zerolit FF ($HO^-$) resin with water. The β anomer **9β** (0.11 g) was eluted first; when crystallised from ethanol, it had m.p. 185–186°, $[\alpha]_D$ −452° (*c* 0.6, methanol) (Found: C, 40.0; H, 6.7. $C_6H_{12}O_4S$ calc.: C, 40.0; H, 6.7%). This was followed by the α anomer **9α** (10 mg), m.p. 122–124° (from ethyl acetate), $[\alpha]_D$ +149° (*c* 0.9, methanol) (Found: C, 39.9; H, 6.9%).

*(b) From* **8**. A solution of the thio sugar **8** (70 mg) in methanol (2.7 mL) was boiled under reflux for 1 h and worked-up as described in *(a)* to give **9β** (32 mg), m.p. 184–186°, and **9α** (4 mg), m.p. 122–124°.

*Methyl 2,3,4-tri-O-acetyl-5-thio-α- and -β-D-arabinopyranosides* (**10**). — Each glycoside **9** (60 mg) was treated with pyridine (1 mL) and acetic anhydride (0.6 mL) overnight at room temperature and then worked-up in the usual way.

The α-triacetate **10α** (0.10 g) had m.p. 118–119° (from ethanol), $[\alpha]_D$ −322° (*c* 1.1, chloroform) (Found: C, 47.1; H, 6.1. $C_{12}H_{18}O_7$ calc.: C, 47.2; H, 5.9%).

The β-triacetate **10β** (0.10 g) had m.p. 66–68° (from ether–light petroleum), $[\alpha]_D$ +85° (*c* 1, chloroform) (Found: C, 47.2, H, 5.9%).

*Acetylation of 5-thio-β-D-arabinopyranose* (**8**). — A solution of **8** (0.33 g) in pyridine (5 mL) and acetic anhydride (3 mL) was kept for 2 days at room temperature. Work-up in the usual way and crystallisation from ethanol gave the β-tetraacetate **11β** (0.50 g), m.p. 118–120°, $[\alpha]_D$ −308° (*c* 1.4, chloroform) (Found: C, 46.7; H, 5.6. $C_{13}H_{18}O_8S$ calc.: C, 46.7; H, 5.4%). The mother liquors from the above crystallisation contained material (0.17 g) which was chromatographed on silica gel (20 g) in ether. Early fractions contained mixtures, but later ones gave the α anomer **11α** as a syrup (95 mg), $[\alpha]_D$ +26° (*c* 1.1, chloroform).

*1,2,3,4-Tetra-O-acetyl-5-thio-β-L-arabinopyranose* (**12**). — A mixture of benzyl 2,3,4-tri-*O*-acetyl-5-thio-α- and -β-L-arabinopyranosides[5] (0.21 g) was dissolved in ice-cold acetic anhydride (5 mL), and conc. sulphuric acid (0.25 mL) was added. After 1 h at room temperature, the mixture was poured into aqueous potassium hydrogencarbonate and, after a further 30 min, was extracted with dichloromethane. The extract was dried ($MgSO_4$), filtered, and evaporated to give a residue which was chromatographed on silica gel (4 g). Elution with ether–light petroleum (4:1) and then with ether gave **12** (89 mg), m.p. 116–118° (from ethanol), $[\alpha]_D$ +295° (*c* 1, chloroform) (Found: C, 46.7; H, 5.2. $C_{13}H_{18}O_8S$ calc.: C, 46.7; H, 5.4%). The $^1$H-n.m.r. spectrum of **12** was identical with that of the D-form **11β**.

*Methyl 2,3-O-isopropylidene-5-O-methanesulphonyl-α-D-lyxofuranoside* (**14**). — A cold solution of methanesulphonyl chloride (3.5 mL) in dry dichloromethane (20 mL) was slowly added to a cooled (ice-bath) stirred solution of methyl 2,3-*O*-isopropylidene-α-D-lyxofuranoside[9] (**13**, 7.00 g) in dry dichloromethane (10 mL) containing triethylamine (5 mL). After a further 1 h at 0°, work-up in the usual way gave **14** (9.64 g), m.p. 99–101° (from ethanol), $[\alpha]_D$ +58° (*c* 0.93, chloroform) (Found: C, 42.7; H, 6.1. $C_{10}H_{18}O_7S$ calc.: C, 42.5; H, 6.4%).

*Methyl 5-S-acetyl-2,3-O-isopropylidene-5-thio-α-D-lyxofuranoside* (**16**). — *(a) From* **15**. A mixture of the tosylate[9] **15** (7.72 g) and potassium thioacetate (5.70 g) in *N,N*-dimethylformamide (80 mL) was heated at 100° for 4 h and then the solvent was removed under reduced pressure. The residue was partitioned between ether and water, and the organic extract was dried ($MgSO_4$), filtered, and passed through a short column of silica gel to give **16** (5.28 g), m.p. 40–43° (from aqueous methanol), $[\alpha]_D$ +65° (*c* 1.2, chloroform) (Found: C, 50.7; H, 7.0. $C_{11}H_{18}O_5S$ calc.: C, 50.4; H, 6.9%).

*(b) From* **14**. A solution of the mesylate **14** (68 mg) in *N,N*-dimethylformamide (2 mL) containing potassium thioacetate (55 mg) was heated at 100°

for 5 h. More potassium thioacetate (55 mg) was added and heating was continued for a further 5 h. Work-up as in (*a*) gave **16** (50 mg), m.p. 40–43°.

*Methyl 5-S-benzoyl-2,3-O-isopropylidene-5-thio-α-*D*-lyxofuranoside* (**17**). — *(a) From* **14**. A mixture of the mesylate **14** (3.00 g), potassium thiobenzoate (6.00 g), and *N,N*-dimethylformamide (45 mL) was heated at 100° for 6 h. Work-up as in the previous experiments gave **17** (3.30 g), m.p. 46–48° (from aqueous methanol), $[\alpha]_D$ +46° (*c* 1.1, chloroform) (Found: C, 58.8; H, 6.1. $C_{16}H_{20}O_5S$ calc.: C, 59.2; H, 6.2%).

*(b) From* **15**. Similar treatment of the tosylate **15** (0.70 g) gave **17** (0.63 g), m.p. 46–48°.

*Deacylation of* **16** *and* **17**. — *(a) 5-Thiobenzoate* **17**. Sodium (0.10 g) was added to a solution of **17** (0.58 g) in methanol (5 mL). After 1.5 h at room temperature, acetic acid (2 mL) was added, solvents were removed, and the residue was partitioned between water and dichloromethane. The organic extract was dried ($MgSO_4$), filtered, and evaporated to give a residue (0.54 g) which was chromatographed on silica gel (11.0 g). Elution with benzene–ether (99:1) gave the syrupy thiol **18** (0.32 g), $[\alpha]_D$ +60° (*c* 1.4, chloroform) (Found: mol.wt., 220.0768. $C_9H_{16}O_4S$ calc.: mol.wt., 220.0769). Elution with benzene–ether (4:1) then gave the disulphide **19** (24 mg), m.p. 59–61° (from aqueous methanol), $[\alpha]_D$ +30° (*c* 1, chloroform) (Found: C, 49.8; H, 6.8. $C_{18}H_{30}O_3S_2$ calc.: C, 49.3; H, 6.8%).

*(b) 5-Thioacetate* **16**. Deacetylation of **16** (0.26 g) in methanol (3 mL) to which sodium (23 mg) had been added was complete in 5 min. Acidification with acetic acid (1 mL) and work-up as in (*a*) gave only **18** (0.22 g). Longer reaction times led to increasing amounts of disulphide **19**.

*5-Thio-α-*D*-lyxopyranose* **20**. — The thiol **18** (0.73 g) was treated with boiling 0.05M sulphuric acid (25 mL) for 1 h. The solution was cooled, passed through Zerolit FF ($AcO^-$) resin, and evaporated. The residue was crystallised from ethanol to give **20** (0.20 g), m.p. 170–174°, $[\alpha]_D$ +24° (*c* 0.65, water) (Found: C, 36.0, H, 6.0. $C_5H_{10}O_4S$ calc.: C, 36.1; H, 6.0%).

*Methyl 5-thio-α- and -β-*D*-lyxopyranosides* (**21**). — *(a) From the thioacetate* **16**. A solution of **16** (1.0 g) in methanol (9 mL) containing conc. hydrochloric acid (1 mL) was boiled under reflux for 1 h. Work-up, as described for the corresponding arabinosides **9** with chromatography on Zerolit FF ($HO^-$) resin, gave, first, the β anomer **21β** (41 mg), m.p. 152–154° (from ethyl acetate), $[\alpha]_D$ −295° (*c* 0.5, methanol) (Found: C, 39.4; H, 6.5. $C_6H_{12}O_4S$ calc.: C, 40.0; H, 6.7%), and then the α anomer **21α** (0.44 g), m.p. 154–155° (from 2-propanol), $[\alpha]_D$ +213° (*c* 0.9, methanol) (Found: C, 39.9; H, 6.8%).

*(b) From* **20**. Similar treatment of the free sugar **20** (0.10 g) gave **21β** (6 mg), m.p. 153–154°, and **21α** (53 mg), m.p. 154–155°.

Only **21β** gave a crystalline triacetate. Methyl 2,3,4-tri-*O*-acetyl-5-thio-β-D-lyxopyranoside, prepared in the usual way, had m.p. 107–109° (from ether–light petroleum), $[\alpha]_D$ −225° (*c* 1.1, chloroform) (Found: C, 47.1; H, 5.9. $C_{12}H_{18}O_7S$ calc.: C, 47.2; H, 5.9%).

*Methanolysis of 5-thio-*D*-xylose.* — A solution of 5-thio-D-xylose[2] (1.30 g) in methanol (40 mL) containing conc. hydrochloric acid (1.2 mL) was boiled under reflux for 1.5 h, neutralised ($PbCO_3$), filtered, and evaporated. The residue was chromatographed on a column (20 × 2.6 cm) of Zerolit FF ($OH^-$) resin with water to give, first, methyl 5-thio-α-D-xylopyranoside (0.54 g), m.p. 112–114° (from ethyl acetate): lit.[18] m.p. 113°. Later fractions contained methyl 5-thio-β-D-xylopyranoside (30 mg), m.p. 159–161° (from ethanol): lit.[19] m.p. 162°.

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