Tetrahedron. Vol. 24, pp 1973 to 1980 Pergamon Press 1968 Printed in Great Britain

DERIVATIVES OF 5-DEOXY-5-THIO-D-XYLOSE

B. NESTADT and T. VAN ES[1]

Departments of Chemistry and Physiological Chemistry, University of the Witwatersrand,
Johannesburg, South Africa

(*Received in the UK* 23 *July* 1967; *accepted for publication* 22 *August* 1967)

Abstract—The synthesis of derivatives of 5-deoxy-5-thio-D-xylose is described. D-Threo-3,4-dihydroxy-3,4,5-tetrahydrothiophene-2-dimethylacetal (IVa) was isolated from the products of methanolysis of 1,2-O-isopropylidene-5-deoxy-5-thio-α-D-xylofuranoside (Ia).

IT HAS been shown that methanolysis of 1,2-O-isopropylidene-5-deoxy-5-seleno-α-D-xylofuranose gave rise to two isomeric di-methoxy compounds, $C_7H_{14}O_4Se$.[2] It was decided to investigate the nature of the products formed on methanolysis of other 1,2-O-isopropylidene sugars. It was found that methanolysis of 1,2-O-isopropylidene-α-D-glucofuranose or 1,2-O-isopropylidene-α-D-xylofuranose gave the methyl glycosides as the only product. Methanolysis of 1,2-O-isopropylidene-5-deoxy-5-thio-α-D-xylofuranose[3] (Ia), however, gave methyl α-D-xylothiopyranoside (IIa) as the main product but in addition small amounts of the β glycoside (IIb), *bis-(methyl 5-deoxy-*D*-xylofuranoside)-5,5'-disulphide* (IIIa), methyl *5-deoxy-5-thio-*D*-xylofuranoside* (IIIb) and two crystalline compounds were isolated. One of the crystalline compounds, $C_9H_{16}O_4S$ contained an isopropylidene and a methoxyl group. Acid hydrolysis of this compound gave acetone and a thiol initially and D-thiaxylose after more prolonged hydrolysis. These data suggest that the compound is methyl 3,5-O,S-*isopropylidene-5-deoxy-5-thio-*D*-xylofuranoside* (IIIc). This structure was confirmed by synthesis as follows. 1,2-O-Isopropylidene-5-deoxy-5-thio-D-xylofuranoside (Ia) was oxidized to *bis-(1,2-O-isopropylidene-5-deoxy-*D*-xylofuranoside)5,5'-disulphide* (Ib), methanolysis of this compound gave bis-(methyl-5-deoxy-D-xylofuranoside)-5,5'-disulphide (IIIa), which was reduced with sodium in ammonia to methyl-5-thio-D-xylofuranoside (IIIb). Brief treatment of this mercaptan with acidic acetone gave a compound identical with that obtained above. In addition a second crystalline compound was isolated. Elemental analysis and spectral evidence indicate that this compound is 1,2,3,5-*di-isopropylidene-5-deoxy-5-thio-*D-xylofuranoside (Ic). This compound was also formed when 1,2-O-isopropylidene-5-deoxy-5-thio-D-xylofuranoside (Ia) was treated with acidic acetone. As an initial product this reaction gave *isopropyl-di(5-thio-5-deoxy-1,2-O-isopropylidene-α-*D*-xylofuranose)-ketal* (Id).

The second crystalline compound isolated from the methanolysis of 1,2-O-isopropylidene-5-deoxy-5-thio-D-xylofuranose (Ia) had a molecular formula, $C_7H_{14}O_4S$ (IVa), and contained two OMe groups. Periodate oxidation indicated the presence of two adjacent OH groups. The compound IVa gave a positive test with periodate–Schiff's reagent which is characteristic for compounds which give rise to malondialdehyde derivatives,[4] e.g. 2-O-methylpyranosides.

The mass spectrum of the diacetate of IVa is very similar to those obtained for the diacetates of the selenium compounds,[2] $C_7H_{14}O_4Se$. The most noticeable feature in the spectrum is the very intense peak at *m/e* 75. It was initially thought that the compound was a mono-methyl methyl-5-deoxy-5-thio-D-xyloside and hence a number of these compounds were synthesized for comparison.

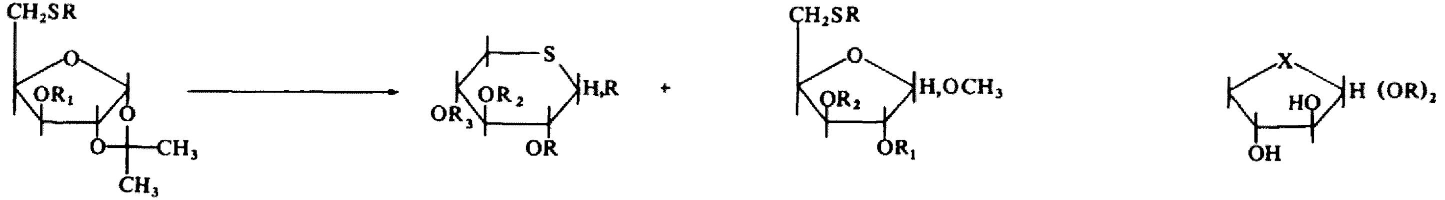
*Methyl-5-deoxy-5-thiomethyl-*D*-xylofuranoside* (IIId) was prepared as follows: 1,2-O-Isopropylidene-5-deoxy-5-thio-D-xylofuranose (Ia) was treated with one equivalent of sodium methoxide in methanol containing an excess of methyl iodide. Two products were formed, namely 1,2-O-*isopropylidene-5-deoxy-5-thiomethyl-*D-*xylofuranoside* (Ie) and *dimethyl-5-(1,2-O-isopropylidene-5-deoxy-*D*-xylofuranose)-sulphonium iodide* (If). The latter compound was also formed when 1,2-O-isopropylidene-5-deoxy-5-thiobenzyl-D-xylofuranose (Ig) was refluxed with methyl iodide. Methanolysis of the 5-thiomethyl compound gave the desired methyl 5-deoxy-5-thiomethyl-D-xylofuranoside (IIId) as a syrup. The mass spectrum of the diacetate of IIId showed a marked similarity to that of 1,2,3-tri-O-acetyl-5-O-methyl-D-xylofuranose.[5]

*Methyl-3-O-methyl-*D*-xylothiopyranoside* (IIc) was prepared by methylation of bis-(1,2-O-isopropylidene-5-deoxy-D-xylofuranose)5,5'-disulphide (Ib) with dimethyl sulphate. The resulting crystalline *bis-(1,2-O-isopropylidene-3-O-methyl-5-deoxy-*D*-xylofuranose)5,5'-disulphide* (Ih) was reduced to the mercaptan which on methanolysis gave the desired compound in crystalline form. The mass spectrum of the diacetate of IIc showed a molecular ion peak at *m/e* 278, also *m/e* 218, 158, 127 (successive loss of MeCOOH and OMe); 246 (loss of HOMe); 247, 187, 145 (loss of OMe, MeCOOH and $CH_2{=}C{=}O$). Also B (*m/e* 170, 128), B' (*m/e* 142, 100), and C (*m/e* 129, 115, 87 and 71) fragmentation was shown although to a smaller extent than in the corresponding D-xylose derivative.[5] Peaks at *m/e* 74, 75 and 116 were also observed as in the corresponding D-xylose derivative.

A number of synthetic sequences were explored for the synthesis of *methyl-2-O-methyl-*D*-xylothiopyranoside* (IId). Attempted benzylation of bis-(1,2-O-isopropylidene-5-deoxy-D-xylofuranose)5,5' disulphide (Ib) i.p.o. potassium hydroxide gave 1,2-O-isopropylidene-5-deoxy-5-thiobenzyl-D-xylofuranose (Ig). The use of pyridine or calcium carbonate instead of potassium hydroxide gave the unchanged starting material. 1,2-O-Isopropylidene-5-deoxy-5-thiobenzyl-D-xylofuranose (Ig) was benzylated and the syrupy product methanolysed to give an anomeric mixture of *methyl 3-O-benzyl-5-deoxy-5-thiobenzyl-*D*-xylofuranosides* (IIIe). Methylation gave *methyl 2-O-methyl-3-O-benzyl-5-deoxy 5-thiobenzyl-*D*-xylofuranoside* (IIIf). Reduction of this compound with sodium in ammonia was incomplete due to the low solubility of the compound in the reaction medium. A small amount of the desired methyl 2-O-methyl-D-xylothiopyranoside (IId) could be detected in the complex mixture formed from methanolysis of the above reduction product.

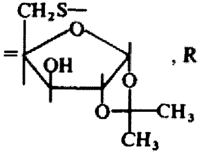
1,3,4-Tri-O-acetyl-D-*xylothiopyranose* (IIe) was prepared from 1-bromo-2,3,4-tri-O-acetyl-D-xylothiopyranose (IIf). Methylation of this compound with methyl iodide under a variety of conditions was unsuccessful. .

Methyl 3,5-O,S-isopropylidene-5-deoxy-5-thio-D-xylofuranoside (IIIc) was dissolved in ammonia and treated with sodium and methyl iodide. The resultant compound, $C_{11}H_{22}O_4S$, contained no free OH group. Based on Owen's findings,[6] the structure methyl 2-O-methyl 3-O-*isopropyl-5-deoxy-5-thiomethyl-*D*-xylofuran*oside (IIIg) was assigned to this product. Mass spectral evidence was in agreement with this structure because a molecular ion peak (*m/e* 250) and a peak at *m/e* 189 which represents the loss of the exocyclic —CH_2SCH_3, a feature characteristic of

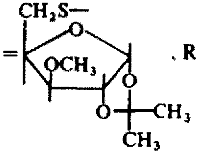


I   II   III   IV

Ia: $R = R_1 = H$

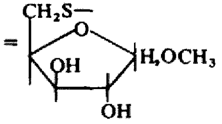
Ib: $R =$  , $R_1 = H$

Ic: $R + R_1 = C(CH_3)_2$
Id: $R_1 = H, R = \frac{1}{2}C(CH_3)_2$
Ie: $R = CH_3, R_1 = H$
If: $R = (CH_3)_2I, R_1 = H$
Ig: $R = CH_2C_6H_5, R_1 = H$

Ih: $R =$  , $R_1 = CH_3$

Ii: $R = R_1 = CH_2C_6H_5$

IIa: $R = OCH_3\alpha, R_1 = R_2 = R_3 = H$
IIb: $R = OCH_3\beta, R_1 = R_2 = R_3 = H$
IIc: $R = OCH_3, R_1 = R_3 = H, R_2 = CH_3$
IId: $R = OCH_3, R_1 = CH_3, R_2 = R_3 = H$
IIe: $R = R_2 = R_3 = R_4 = OAC, R_1 = H$
IIf: $R = Br, R_1 = R_2 = R_3 = OAC$

IIIa: $R =$  , $R_1 = R_2 = H$

IIIb: $R = R_1 = R_2 = H$
IIIc: $R + R_2 = C(CH_3)_2, R_1 = H$
IIId: $R = CH_3, R_1 = R_2 = H$
IIIe: $R = R_2 = CH_2C_6H_5, R_1 = H$
IIIf: $R = R_2 = CH_2C_6H_5, R_1 = CH_3$
IIIg: $R = R_1 = CH_3, R_2 = CH(CH_3)_2$
IIIh: $R + R_2 = C(CH_3)_2, R_1 = CH_3$

IVa: $X = S, R = CH_3$
IVb: $X = O, R = CH_3$
IVc: $X = O, R = CH_2C_6H_5$

furanose derivatives.[5] Methylation of methyl-3,5-O,S-isopropylidene-5-deoxy-5-thio-D-xylofuranoside (IIIc) with dimethyl sulphate gave *methyl-3,5-O,S-isopropylidene-2-O-methyl-5-deoxy-5-thio-D-xylofuranoside* (IIIh). Methanolysis of this compound gave a complex mixture from which methyl 2-O-methyl-α-D-xylothiopyranoside (IId) was isolated by preparative TLC. This compound was also isolated from the reaction mixture formed by brief treatment of methyl-α-D-xylothiopyranoside (IIa) with methyl iodide and silver oxide. The compound gave a positive test with periodate–Schiff's reagent.[4] The mass spectrum of the diacetate of this 2-O-methyl glycoside showed the expected molecular ion peak at *m/e* 278. Also characteristic for xylothiopyranosides the OMe group at C_1 was not lost as the first step but rather the loss of acetic acid took place, resulting in a series of peaks 218, 186 (loss of MeOH), 155 (loss of MeO). The B_1 peak[5] at *m/e* 170 was very intense but the related B_2 and B_3 *m/e* 128 and 86 were very weak. Below *m/e* 100 the spectrum was very similar to that of methyl-2-O-methyl-D-xylopyranoside.[5]

Spectral and chemical evidence showed that none of the mono methyl methyl-D-thioxylosides were identical with the unknown compound, $C_7H_{14}O_4S$. This compound (IVa) was also isolated in small amounts from the reaction mixture formed by treatment of methyl α-D-xylothiopyranoside (IIa) with methanol containing hydrogen chloride. Hydrolysis of IVa gave an aldehyde. The mass spectrum of the diacetate of IVa showed a base peak at *m/e* 75, also a molecular ion peak at *m/e* 278 and *m/e* 84 ascribed to the thiophene cation. The intense peak at *m/e* 75 is characteristic of a dimethyl acetal.[7] The IR spectrum of the compound also showed peaks characteristic for acetals.[8]

It is therefore proposed that the compound $C_7H_{14}O_4S$ is a C_2 anomer of *D-threo-3,4-dihydroxy-2,3,4,5-tetrahydrothiophene 2-dimethyl acetal* (IVa). The presence of the other anomer in the methanolysis mixture was suggested by a positive test with periodate–Schiff's reagent.[4] It is suggested that the positive periodate–Schiff's test is due to the malondialdehyde derivative, $OHCCH_2S\ CH(CHO)_2$ which would be formed on periodate oxidation in acidic solution of D-threo-3,4-dihydroxy-2,3,4,5-tetrahydrothiophene-2-dimethylacetal (IVa). *D-Threo-3,4-dihydroxy-2,3,4,5-tetrahydrofuran-2-dimethylacetal* (IVb) was prepared for comparison. Tosylation of D-xylose dibenzylmercaptal gave D-threo-3,4-dihydroxy-2,3,4,5-tetrahydrofuran-2-dibenzylmercaptal[9] (IVc). Treatment of the diacetate of IVc with mercuric chloride in methanol, followed by de-acetylation of the product gave the desired compound. The compound gave a positive test with periodate–Schiff's reagent.[4] The mass spectrum of the diacetate was similar in essential features to that observed for the suspected *D-threo-3,4-di-*O-acetyl-2,3,4,5-*tetrahydrothiophene-2-dimethylacetal*. The NMR spectrum was similar to those reported for the selenium compounds, $C_7H_{14}O_4Se$.[2]

EXPERIMENTAL

TLC was conducted on Merck Kieselgel-G 15% MeOH in benzene as irrigant. Detection was by spraying the plate with a solution of 10% H_2SO_4 in EtOH and then heating the plate.

M.ps were determined in an electrically heated copper block and are uncorrected.

IR spectra were measured with a Perkin–Elmer, Model 137 IR Spectrophotometer. NMR spectra were measured on a Varian A-60 Spectrophotometer. Chemical shifts are given in τ units at 60 Mc/s downfield from TMS as internal standard. Mass spectra were determined on an A.E.I. MS9 mass spectrometer.

All evaporations are done under vacuum below 50°.

Methanolysis of 1,2-O-*isopropylidene-5-deoxy-5-thio-α-D-xylofuranose* (Ia). The mercaptan[3] (9·0 g) and MeOH containing 2 % HCl (200 ml) were allowed to stand at room temp for 2 days. The soln was neutralized by passage through a column of Amberlite IR 45 (OH^-). The eluate was evaporated and the syrup taken up in a small amount of hot EtOAc. The soln was seeded and cooled to give methyl-α-D-xylothiopyranoside (7·0 g). The mother liquor was evaporated to give a syrup (1·5 g) which was examined by TLC. The components of the mixture were identified by TLC comparison with the pure compounds. R_f, 0·20 (compd IIIa); 0·24 (compd IIb); 0·31; 0·34 (compd IIIb); 0·35; 0·38, 0·45, 0·66.

The syrup (5·0 g) was applied to a column of silicagel (370 g) and was eluted with 15 % MeOH in benzene. Two crystalline compounds (R_f 0·31 and 0·45) were isolated. The faster moving component (500 mg) was recrystallized from hexane, m.p. 87–89° $[\alpha]_D^{20}$ −168 (*c*, 2 Chf). (Found: C, 49·2; H, 7·1; OMe, 14·5. $C_9H_{16}O_4S$ requires: C, 49·2; H, 7·3; OMe, 14·1 %); ν_{max}^{KBr}, 3220 (OH), 2860 (OMe), 1040, 1070, 1110, 1150, 1180 (isopropylidene), 930, 794 (furanose).

The slower moving component (31 mg) was recrystallized from EtOAc–hexane, m.p. 86–87° $[\alpha]_D^{20}$ +116° (*c*, 0·6 in Chf). (Found: C, 43·3; H, 7·2; OMe, 30·3; Mol. wt. 194, mass spectrometry,. $C_7H_{14}O_4S$ requires: C, 43·3; H, 7·2; OMe, 31·9 %; Mol. wt. 194); ν_{max}^{KBr} 3320 (OH), 2835 (OMe), 1190, 1133, 1088, 1052 (dimethylacetal). NMR (D_2O), 5·47 (probably part of a doublet, remainder obscured under the water peak); 5·62–6·07 (complex; 2 protons); 6·55 (single; 6 protons; 2 OMe); 6·98–7·4 (complex; 2 protons); 7·86 (doublet; 1 proton; *J*, 1·2 c/s). The diacetate of this compound showed *m/e* 278 (M, 0·1 %), 247 (M—OMe, 0·07 %), 218 (M—MeCOOH, 0·08 %), 187 (M—OMe—MeCOOH, 8·7 %), 186 (M—MeOH—MeCOOH, 5·1 %). 145 (187—CH_2CO, 6·6 %), 144 (186—CH_2CO, 11·7 %), 84 (thiophene cation, 10·4 %), 75 ($\overset{\oplus}{C}H(OMe)_2$, 100 %).

Periodate oxidation of the compound was carried out using the method of Aspinall and Ferrier.[10] The uptake of periodate was followed spectrophotometrically at 223 mμ. The following results were obtained (given time in hr. periodate consumed in molar proportions) ½. 0·73; 1½, 1·0; 5, 1·2; 7, 1·55; 33. 1·6. The slow uptake of periodate beyond one molar proportion is ascribed to oxidation of the sulphur in the compound.

Bis-(1,2-O-*isopropylidene-5-deoxy-α-D-xylofuranose*)5,5′-*disulphide* (Ib). Compound Ia (5·0 g) was dissolved in water (10 ml) containing a drop of ammonia (SG. 0·88). H_2O_2 (100 vol) was added dropwise until a positive iodide–starch test was observed. The solid (4·5 g, 90 %) m.p. 184° was filtered off and crystallized from water; $[\alpha]_D^{25}$ −77 (*c*, 1·5 in Chf). (Found: C, 46·6; H, 6·4. $(C_8H_{13}O_4S)_2$ requires: C, 46·8; H, 6·3 %.) The above compound (1·0 g) was refluxed for 2 hr with Ac_2O (10 ml) containing anhyd NaOAc (1·0 g). The mixture was poured into water and the solid which separated, crystallized from dil EtOH to give the acetate, m.p. 118–120 $[\alpha]_D^{25}$ −72 (*c*, 0·40 in Chf). (Found: C, 48·7; H, 6·0. $(C_{10}H_{15}O_5S)_2$ requires: C, 48·6; H, 6·1 %.)

Bis-(*methyl-5-deoxy-D-xylofuranoside*)5,5′-*disulphide* (IIIa). The above Ib (3·0 g) was methanolysed as described previously to give a syrup (2·54 g). TLC showed the presence of two major components of R_f 0·19 and 0·32. The slower-moving component (1·68 g) was the expected glycoside $[\alpha]_D^{24}$ +48 (*c*, 1·1 in Chf). (Found: C, 40·6; H, 6·4. $(C_6H_{11}O_4S)_2$ requires: C, 40·2; H, 6·2 %). The mass spectrum of the tetra-O-acetyl derivative of the glycoside gave the expected molecular ion peak *m/e* 526 (13 %). Other significant peaks were *m/e* 525 (62 %), 495 (M-31, 10 %), 264 (15 %), 231 (67 %), 217 (loss of exocyclic portion of the molecule, 4 %), 171 (37 %), 160 (25 %), 139 (50 %), 129 (100 %), 115 (79 %), 111 (33 %), 97 (25 %), 87 (17 %), 85 (19 %), 69 (14 %), 43 (> 100 %).

The faster component (0·53 g) gave $[\alpha]_D^{21}$ +23·6 (*c*, 0·48 in Chf). (Found: C, 44·5; H, 7·04; OMe, 19·3. $C_{12}H_{22}O_6S_2$ requires: C, 44·2; H, 6·7; OMe, 19·0 %). The IR spectra of these two compounds were very similar except in 1300–1500 region. The relative intensity of the bands at 3350 (OH) and 2850 (OMe) for the two compounds were reversed. The faster component was not investigated further.

Methyl-5-deoxy-5-mercapto-D-xylofuranoside (IIIb). Compound IIIa (1·0 g) was dissolved in liquid ammonia (50 ml) and the soln treated with Na until the blue colour persisted for 5 min. Excess NH_4Cl was added and the ammonia allowed to evaporate. The residue was repeatedly extracted with Chf. The extracts were washed with water, dried and evaporated to give a syrup (0·99 g) which gave a strong positive reaction with alkaline nitroprusside.

Methyl-3,5-O-S-*isopropylidene-5-deoxy-5-thio-D-xylofuranoside* (IIIc). The above IIIb was immediately treated with a soln of HCl (0·5 g) in acetone (50 ml). The reaction was monitored by TLC and after 10 min the solution was neutralized with IR 45 (OH^-). The soln was evaporated to a syrup (1·58 g). TLC revealed the presence of 3 components R_f 0·46, 0·59, 0·82. The mixture was separated on a column of silicagel to give IIIc (0·56 g) with identical m.p. and IR spectrum to the compound isolated from the methanolysis mixture. The compound (R_f, 0·82) crystallized (0·46 g), it was recrystallized from dil alcohol, m.p. 68–70° $[\alpha]_D^{30}$ −29·4 (*c*, 0·35 in Chf). (Found: C, 54·1; H, 7·5. $C_{11}H_{18}O_4S$ requires: C, 53·7; H, 7·3 %.)

IR in KBr showed absence of OH absorption and ν_{max} 1020, 1080, 1100, 1140, 1170, (isopropylidene).

*Isopropyl-di-(5-thio-5-deoxy-*1,2-O-*isopropylidene-α-*D-*xylofuranose)ketal* (Id). Compound Ia (1·0 g) was stirred at room temp with acetone (20 ml) and conc H_2SO_4 (0·1 ml). After 10 min a solid began to separate. After 1 hr the solid was filtered off and crystallized from EtOAc (0·60 g), m.p. 145; $[\alpha]_D^{21}$ −41 (*c*, 1·0 in Chf). (Found: C. 50·1; H. 6·9. $C_{19}H_{32}O_8S_2$ requires: C, 50·4; H, 7·1 %); ν_{max}^{KBr} 3350 (OH), 1030, 1060, 1100, 1130, 1160 (isopropylidene). When the reaction was allowed to proceed for longer than 1 hr, the above crystalline compound redissolved and TLC showed the presence of 1,2,3,5-di-isopropylidene-5-deoxy-5-thio-D-xylofuranose.

1,2-O-*Isopropylidene-5-deoxy-5-thiomethyl-α-*D-*xylofuranose* (Ie). Compound Ia (2·0 g), MeOH containing Na (0·22 g) and MeI (0·72 ml) were refluxed for 1 hr. The soln was evaporated and the residue was extracted with boiling hexane, on cooling needles separated (0·85 g). m.p. 90–91°, $[\alpha]_D^{27}$ −61·8° (*c*, 0·94 in Chf). (Found: C. 49·3; H. 7·2. $C_9H_{16}O_4S$ requires: C. 49·1; H, 7·3 %); ν_{max}^{KBr} 3300 (OH), 1325 (SCH_3), 1040, 1060, 1120. 1160 (isopropylidene).

The hexane-insoluble portion was crystallized from EtOH (1·5 g), to give If; m.p. 150–151°. (Found: C, 33·8; H, 5·4. $C_{10}H_{19}IO_4S$ requires: C, 33·1; H, 5·3 %); ν_{max}^{KBr} 3300 (OH), 1325 (SMe), 1040, 1070, 1080, 1115, 1160 (isopropylidene). The same compound was formed when Ig[3] was refluxed with MeI.

*Methyl-5-deoxy-5-thiomethyl-*D-*xylofuranoside* (IIId). Compound Ie (200 mg) was allowed to stand for two days at room temp with MeOH containing 2 % HCl (15 ml). The soln was neutralized and concentrated to a syrup (180 mg). The desired compound was isolated as a syrup by chromatography on silicagel using 15 % MeOH in benzene $[\alpha]_D^{27}$ −36 (*c*, 0·6 in Chf). Elemental analysis were erratic probably as a result of the hydroscopic nature of the compound. However, mass spectrometry gave the expected mol. wt. (194). ν_{max}^{Chf} 3350 (OH), 2860 (Me). The mass spectrum of the diacetate showed a molecular ion peak *m/e* 278 (10 %), also *m/e* 247 (10), 246 (10), 218 (40), 217 (23), 187 (5, 175 (5), 158 (84), 145 (40), 127 (135), 116 (74), 115 (190), 103 (68), 87 (45), 75 (48), 74 (100), 73 (25), 71 (64), 61 (45), 45 (65), 43 (480).

Bis-(1,2-O-*isopropylidene-*3-O-*methyl-5-deoxy-* D-*xylofuranose*)5,5′-*disulphide* (Ih). Compound Ib (1·0 g), THF (35 ml) and powdered KOH (5·0 g) were stirred and Me_2SO_4 (5·0 ml) was added over 1 hr. The reaction mixture was stirred overnight and water added to dissolve the solids. The reaction mixture was kept at 60° for ½ hr in order to hydrolyse excess Me_2SO_4, then adjusted to pH 9 and extracted with Chf. The extracts were washed with water, dried (Na_2SO_4) and evaporated to a syrup (1·2 g). TLC showed a major component R_f 0·95 and minor components R_f 0·50 and 0·38. The syrup was chromatographed on silicagel using 5 % MeOH in benzene as solvent. The desired compound (600 mg) was obtained as a crystalline material, recrystallization from EtOAc–hexane, m.p. 80–81°, $[\alpha]_D^{26}$ −222·5 (*c*, 0·94 in Chf). (Found: C, 49·6; H, 7·0. $(C_9H_{15}O_4S)_2$ requires: C, 49·3; H, 6·9 %); $^{KBr}_{max}$, 2850 (OMe), 1020, 1080, 1090, 1130, 1160 (isopropylidene) no OH absorption was observed.

*Methyl-*3-O-*methyl-*D-*xylothiopyranoside* (IIc). The above Ih (245 mg) was reduced with ammonia and Na as previously described to give a syrup (200 mg) which gave a strong positive test with sodium nitroprusside. This thiol, 1,2-O-isopropylidene-3-O-methyl-5-deoxy-5-mercapto-D-xylofuranose, was immediately treated with 2 % methanolic HCl (15 ml) and allowed to stand for 1 week, when all thiol activity had disappeared. The reaction mixture was neutralised with IR 45 (OH^-) and the soln evaporated to give a syrup (190 mg). TLC showed a major component R_f 0·27 and minor components R_f 0·14 and 0·51. Column chromatography on silicagel gave the desired compound (117 mg), m.p. 58–61°. The product was sublimed at 0·6 mm Hg, m.p. 62·5–63·5; $[\alpha]_D^{27}$ + 1·9 (*c*. 0·39 in Chf). (Found: C. 43·4; H. 7·7; mol. wt. 194, mass spectrometry. $C_7H_{14}O_4S$ requires: C, 43·3; H, 7·2 %; mol. wt. 194); ν_{max}^{KBr} 3400 (OH), 2800 (OMe), 895 (pyranose ring). Mass spectrometry of the diacetate, 278 (M, 11 %), 246 (6), 218 (11), 187 (3), 170 (5), 158 (95), 145 (19), 132 (34), 127 (141), 116 (34), 103 (47), 101 (35), 99 (35), 86 (26), 75 (43), 74 (100), 71 (73), 59 (22), 49 (54), 45 (44), 43 (317).

1,2-O-*Isopropylidene-*3-O-*benzyl-5-deoxy-5-thiobenzyl-*D-*xylofuranose* (Ii). Compound Ig (2·0 g), redistilled benzyl chloride (4·3 g) and powdered KOH (0·8 g) were heated with stirring for 3·5 hr on a water bath. The excess benzyl chloride was removed under high vacuum and the residue treated with water and Chf. The Chf was dried and evaporated to give a syrup (3·2 g). TLC showed this material to be pure apart from a trace of the starting material; $[\alpha]_D^{23}$ −77 (*c*, 0·62 in Chf). (Found: C. 68·2; H. 7·0. $C_{22}H_{26}O_4S$ requires: C. 68·4; H. 6·7 %.)

*Methyl-*3-O-*benzyl-5-deoxy-5-thiobenzyl-*D-*xylofuranose* (IIIe). The above Ii (1·0 g) and 2 % methanolic HCl were allowed to stand at room temp for 24 hr. The usual isolation procedure yielded a syrup (0·81 g). TLC showed this to consist of two major components R_f 0·57 and 0·66. The components were separated on a column of silicagel by using 3 % MeOH in benzene; Component (R_f 0·66), $[\alpha]_D^{23}$ +29·8 (*c*, 0·41 in Chf). (Found: C. 66·6; H. 7·0. $C_{20}H_{29}O_4S$ required: C, 66·7; H, 6·7 %) was assigned α-configuration.

Component (R_f 0·57). $[\alpha]_D^{23}$ −36·4 (*c.* 0·49 in Chf). (Found: C, 66·6; H, 7·0. $C_{20}H_{24}O_4S$ requires: C, 66·7; H, 6·7%) was assigned β-configuration.

Methyl-2-O-methyl-3-O-benzyl-5-deoxy-5-thiobenzyl-D-xylofuranose (IIIf). The above IIIe (171 mg), dry THF (15 ml) and powdered KOH (2·0 g) were stirred and Me_2SO_4 (2·0 ml) was added dropwise over 1 hr. The soln was stirred overnight at room temp. Water was added to dissolve the solid and the soln heated for 2 hr at 60° in order to hydrolyze the excess Me_2SO_4. The solution was adjusted to pH 9 and extracted with Chf. The extracts were washed with water, dried over Na_2SO_4 and evaporated to give a syrup (163 mg). TLC showed this to be homogeneous, R_f 0·86, $[\alpha]_D^{30}$ −72·5 (*c*, 0·28 in Chf). (Found: C, 67·2; H, 6·7. $C_{21}H_{26}O_4S$ requires: C, 67·4; H, 6·9%.)

By the same procedure the α-anomer (107 mg) gave a homogeneous syrup (108 mg), R_f 0·78, $[\alpha]_D^{30}$ +55·5 (*c.* 0·35 in Chf). (Found: C, 67·2, H, 7·1. $C_{21}H_{26}O_4S$ requires: C, 67·4; H, 6·9%); IR (in Chf) showed the absence of OH absorption in both components, the spectra were very similar except in the 800–1000 cm^{-1} region; the β anomer, ν_{max} 960, 875 and α anomer, ν_{max} 995, 920 and 890.

Methyl-2-O-methyl-D-xylothiopyranoside (IId). A mixture of the above IIIf (158 mg) was reduced in liquid ammonia (the material did not appear to dissolve) as described previously. The syrup was methanolysed with 2% methanolic HCl for 2 days. TLC of product showed R_f 0·11, 0·23, 0·36, 0·33, 0·45, 0·65 and 0·85. The component, R_f 0·23, was shown to be the desired compound by TLC comparison with a genuine sample (see later), also it gave a positive test with periodate—Schiff's reagent.[4]

1,3,4-*Tri-O-acetyl-D-xylothiopyranose* (IIe). This compound was prepared by the method described by Helferich,[11] yield 2·2 g (from 9·0 g D-thiaxylose), m.p. 156–160°, $[\alpha]_D^{20}$ +3·1 −2·2 (*c*, 2 in acetone: H_2O 1:1) in 12 days. (Found: C, 45·2; H, 5·5. $C_{11}H_{16}O_7S$ requires: C, 45·2; H, 5·5%.)

Methylations of methyl-3,5-O-S-isopropylidene-5-deoxy-5-thio-D-xylofuranoside (IIIc); *Methyl-2-O-5-S-dimethyl-3-O-isopropyl-5-deoxy-5-thio-D-xylofuranoside* (IIIg). Compound IIIe (300 mg) was dissolved in liquid ammonia and Na was added until the blue colour persisted. Excess MeI (5·0 ml) was added and the ammonia allowed to evaporate overnight in a stream of dry N_2. The residue was treated with water and Chf, the Chf layer was dried over Na_2SO_4 and evaporated to yield a syrup (321 mg). TLC showed major component R_f 0·91 and minor components 0·76, 0·64 and 0·42 (starting material). The crude syrup was applied to a column of silicagel and eluted with 5% MeOH in benzene. The compound (R_f 0·91) (300 mg) was isolated as a syrup; $[\alpha]_D^{23}$ −89 (*c.* 3·1 in Chf). (Found: C, 52·5; H, 8·9. $C_{11}H_{22}O_4S$ requires: C, 52·8; H, 8·8%.) Mass spectrum of this compound showed a molecular ion peak *m/e* 250 (7%) also *m/e* 218 (41), 189 (7), 145 (21), 129 (38), 119 (26), 103 (31), 101 (20), 91 (13), 89 (32), 87 (100), 61 (43), 57 (14), 45 (17), 43 (38), 41 (35).

The compound was unchanged on methanolysis. The reduction was repeated on a small scale but instead of MeI, excess NH_4Cl was added. The ammonia was allowed to evaporate and the residue showed a strong positive test for a thiol with sodium nitroprusside.

Methyl-2-O-methyl-3,5-O-S-isopropylidene-5-deoxy-5-thio-D-xylofuranoside (IIIh). Compound IIIc (200 mg), THF (20 ml) and powdered KOH (1·0 g) were stirred and Me_2SO_4 (1·0 g) slowly added over 1 hr. Stirring was continued for 24 hr. Water was added to dissolve the solids and the soln heated at 60° for 2 hr. The soln was adjusted to pH 9 and extracted with Chf. The extracts were washed with water, dried over Na_2SO_4 and evaporated to a syrup. Silicagel column chromatography of the syrup gave the desired compound (200 mg); $[\alpha]_D^{23}$ −20·6 (*c.* 0·86 Chf). (Found: C, 51·0; H, 7·3. $C_{10}H_{18}O_4S$ requires: C, 51·3, H, 7·7%.) IR showed the absence of OH absorption and ν_{max}^{Chf} 1040, 1120, 1190 (isopropylidene group).

Methyl-2-O-methyl-D-xylothiopyranoside (IId). The impure IIIh (100 mg), was methanolysed at room temp using 2% methanolic HCl. The reaction was monitored by TLC, the best reaction time was 18 days. TLC gave R_f 0·11, 0·23, 0·26, 0·32, 0·35, 0·44, 0·57, 0·63, 0·76. When the Hardy–Buchanan test[4] was applied, a yellow spot at R_f 0·23 was obtained. Some of the components were isolated by preparative TLC, namely methyl α-D-xylothiopyranoside (5 mg), a syrup (25 mg) R_f 0·23 which was identified by mass spectral and IR comparison (see below) as IId and another syrup (15 mg), whose acetate showed a molecular ion peak *m/e* 250 and appeared to be trimethoxy monoacetate of a thiapyranoside. The mass spectrum of the acetate of the 2-O-methyl compound showed a molecular ion peak at *m/e* 278 (3%), further *m/e* 218 (15), 185 (7), 186 (49), 184 (18), 171 (7), 170 (100), 169 (43), 155 (48), 145 (10), 144 (12), 143 (26), 142 (20), 129 (12), 127 (44), 117 (16), 116 (36), 106 (22), 103 (20), 101 (19), 100 (24), 98 (23), 88 (40), 85 (22), 75 (63), 74 (50), 43 (269).

Mono methylation of methyl-α-D-xylothiopyranoside (IIa). Methyl-α-D-xylothiopyranoside (0·5 g), THF (6 ml), MeI (6 ml) and Ag_2O (1·2 g) were stirred for 1 hr at room temp. The soln was filtered and the filtrate evaporated to give a syrup (0·70 g). TLC showed R_f 0·24 (starting material) 0·34, 0·59. The syrup was chromatographed to give 100 mg of a solid which was recrystallized from EtOAc–hexane, m.p. 33–35°; $[\alpha]_D^{21}$ +214 (*c.* 0·1 Chf). (Found: C, 43·3; H, 7·2; Mol. wt. 194, mass spectrometry. $C_7H_{14}O_4S$ requires:

C, 43·3; H, 7·2%; Mol. wt. 194), NMR (D_2O) 5·18 (doublet; one proton; J 2·0 c/s; anomeric proton); 6·58 (singlet; six protons, 2 Me). The compound gave a positive test with the Hardy–Buchanan reagent;[4] ν_{max}^{KBr} 3350, 3450 (OH), 2800 (Me), 890 (α-pyranose). The mass spectrum of the acetate of this compound was identical with that obtained above.

D-*Threo*-3,4-*dihydroxy*-2,3,4,5-*tetrahydrofuran*-2-*dimethylacetal* (IVb). Compound IVe[9] (0·60 g), pyridine (5 ml) and Ac_2O (5 ml) were allowed to stand at room temp overnight. The soln was diluted with water, neutralized with $NaHCO_3$ (solid) and extracted with Chf. The extracts were washed successively with cold dilute acid, $NaHCO_3$ aq and water, dried over Na_2SO_4. The extracts were evaporated to give a syrup (0·73 g). TLC revealed one spot R_f (5% MeOH in benzene), 0·78. The syrup crystallized from pet. ether (40–60°), m.p. 62, $[\alpha]_D^{20}$ +114 (c, 2·0 in Chf). (Found: C, 62·0; H, 6·0. $C_{23}H_{26}O_5S_2$ requires: C, 61·9; H, 5·8%.)

The above compound (0·70 g), dry MeOH (12 ml) and $CdCO_3$ (1·3 g) were warmed to 60° and a soln of $HgCl_2$ (3·2 g) in MeOH (6 ml) was added. The mixture was refluxed with stirring for 4 hr. The mixture was filtered and the residue washed thoroughly with MeOH. The filtrate was evaporated and the residue extracted with Chf and water. The Chf layer was washed with water until free of chloride, dried and evaporated to a syrup (0·40 g). TLC (5% MeOH–benzene) showed one spot R_f 0·60. The syrup was chromatographed on silicagel, $[\alpha]^{D}_{20}$ −17 (c, 1·0 in Chf). (Found: C, 50·2; H, 6·9. $C_{11}H_{18}O_7$ requires: C, 50·4; H, 6·9%); ν_{max}^{Chf} 2830 (OMe), 1730 (CO acetate). Mass spectrometry showed m/e 262 (M, 0·01%), 231 (M—OMe, 2·9), 202 (M—MeCOOH, 0·02), 171 (M—OMe—MeCOOH, 3·5), 129 (2), 128 (38), 75 ($\overset{\oplus}{CH}(OCH_3)_2$, 100), 68 (furan cation, 2), NMR ($CDCl_3$), 4·65 (double doublet; 1 proton), 4·82–5·00 (complex; 1 proton), 5·54 doublet; 1 proton: J 8·4 c/s; $CH(OMe)_2$), 5·6–6·4 (complex; 3 protons), 6·57 and 6·62 (singlets; 3 protons each; OMe), 7·89 and 7·92 (singlets; six protons; 2 OAc). The above D-threo-3,4-di-O-acetyl-2,3,4,5-tetrahydrofuran-2-dimethyl acetal (200 mg) was allowed to stand overnight with MeOH (5 ml) containing NaOMe (10 mg Na). The soln was neutralized with IR 120 and evaporated to a syrup (140 mg). TLC showed one spot R_f 0·29. When the plate was sprayed with 1% sodium periodate and exposed to SO_2 after 8 min and then sprayed with Schiff's reagent,[4] a yellow spot, R_f 0·29, was observed after 25 min; $[\alpha]_D^{20}$ +13·5 (c, 1·0 in Chf). (Found: C, 46·6; H, 8·1. $C_7H_{14}O_5$ requires: C, 47·2; H, 7·9%); ν_{max}^{film} 3380 (OH), 2830 (OMe), 1190, 1140 (dimethyl acetal).

Acknowledgements—One of us (B.N.) wishes to thank the South African Council for Scientific and Industrial Research for a bursary. The authors wish to thank Dr. S. Eggers and Dr. D. Pachler of the South African Council for Scientific and Industrial Research (Pretoria) for determining the NMR and mass spectra.

REFERENCES

[1] To whom all correspondence should be addressed.

[2] T. van Es and R. L. Whistler, *Tetrahedron* **23**, 2849 (1967).

[3] R. L. Whistler and D. L. Ingles, *J. Org. Chem.* **27**, 3896 (1962).

[4] F. E. Hardy and J. G. Buchanan, *J. Chem. Soc.* 5881 (1963).

[5] D. C. De Jongh and K. Biemann, *J. Am. Chem. Soc.* **85**, 2289 (1963).

[6] L. N. Owen, *J. Chem. Soc.* 416 (1966).

[7] R. A. Friedel and A. G. Sharkey, *Analyt. Chem.* **28**, 940 (1956).

[8] E. D. Bergman and S. Pinchas, *Rec. Trav. Chim.* **71**, 161 (1952).

[9] H. Zinner, H. Brandhoff, H. Schmandke, H. Kristen and R. Haun, *Chem. Ber.* **92**, 3151 (1959).

[10] G. O. Aspinall and R. J. Ferrier, *Chem. & Ind.* 1216 (1957).

[11] B. Helferich and W. Ost, *Chem. Ber.* **95**, 2616 (1962).