Note

Ring-opening of methyl 2,3-anhydro-D-ribofuranosides

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The reaction of methyl 2,3-anhydro-D-ribofuranosides with benzylthiolate ions was investigated as a possible route to 2-thio derivatives of D-arabinose. Such compounds should be capable of forming a five-membered, sulfur-containing ring of the 2,5-anhydro-type[1] via a 5-sulfonic ester.

It had been found[2] that ring-opening of methyl 2,3-anhydro-α-D-lyxofuranoside with benzylthiolate ion gave methyl 3-*S*-benzyl-3-thio-α-D-arabinofuranoside exclusively. However, the corresponding β-anomer gave a 6:4 mixture of methyl 2-*S*-benzyl-2-thio-β-D-lyxofuranoside and methyl 3-*S*-benzyl-3-thio-β-D-xylofuranoside.

Methyl 2,3-anhydro-β-D-ribofuranoside, when treated with benzylthiolate ion gave mainly one compound, identified by desulfurization as methyl 3-*S*-benzyl-3-thio-β-D-xylofuranoside (**1**). Even after introduction of the bulky triphenylmethyl ether group at C-5, ring opening with benzylthiolate ion still occurred only at C-3.

Methyl 2,3-anhydro-α-D-ribofuranoside with benzylthiolate ion gave a mixture of the 3-*S*-benzyl-3-thio-D-*xylo* and 2-*S*-benzyl-2-thio-D-*arabino* isomers (**2** and **3**, respectively), in the approximate ratio 3:7. These two compounds have nearly identical R_F values by t.l.c. with a variety of solvents. The mixed isomers were separated from other impurities by chromatography, and they gave a satisfactory analysis. However, attempted separation of the two isomers by chromatography under a variety of conditions was unsuccessful. The proportion of isomers was determined by n.m.r. spectroscopy; two distinct absorptions, at τ 5.24 and 5.15, respectively, were observed for H-1 in the two isomers. An attempt to open the oxirane ring in methyl 5-*O*-trityl-2,3-anhydro-α-D-ribofuranoside with α-toluenethiol gave unchanged starting material, even after prolonged times of reaction.

These results are in agreement with those found on oxirane ring-opening in methyl 2,3-anhydro-D-ribofuranosides with bromide ions[3], where the β-anomer gave the 3-bromo derivative exclusively but the α-anomer gave a mixture of 2- and 3-bromo derivatives in 2:1 ratio.

EXPERIMENTAL

General methods. — T.l.c. was performed on Kieselgel G (Merck) with methanol in benzene as irrigant. Melting points were determined on an electrically heated

Kofler block. I.r. spectra were measured with a Perkin–Elmer Model 137 spectrophotometer. N.m.r. spectra were measured with a Varian HA-100 instrument and chemical shifts are expressed as τ units with Me_4Si as internal standard. Evaporations were performed under vacuum below 50°.

*Methyl 3-S-benzyl-3-thio-β-*D*-xylofuranoside* (**1**). — Methyl 2,3-anhydro-β-D-ribofuranoside (1.46 g, 10 mmoles), α-toluenethiol (1.86 g, 15 mmoles), sodium methoxide [from 0.345 g (15 mmoles) of sodium], and methanol (40 ml) were refluxed overnight. The solution was neutralized with acetic acid and evaporated. The residue was extracted with chloroform and the extracts were evaporated. A methanolic solution of the resulting syrup was passed through a column of Amberlite IR-45 (OH^-) resin to remove excess α-toluenethiol. The column was washed thoroughly with methanol and the eluate was evaporated to a syrup (2.7 g) T.l.c. (10% methanol in benzene) showed some unchanged starting material (R_F 0.48), an intense spot (R_F 0.39), and a minor component (R_F 0.36). The syrup was separated on a column of silica gel (200 g) by using 10% methanol in benzene. The desired compound (1.34 g) was obtained as a syrup, $[\alpha]_D^{25}$ $-78°$ (*c* 2.16, chloroform); n.m.r. ($CDCl_3+D_2O$): τ 2.62 (5-proton singlet, Ph), 5.23 (1-proton doublet, $J_{1,2}$ 2.5 Hz, H-1), 5.78–6.0 (2 protons, complex, probably H-2 and H-4), 6.23 (2-proton singlet, benzylic CH_2), 6.39 (2-proton doublet, *J* 4.0 Hz, H-5), 6.64 (3-proton singlet, OCH_3), 6.75–7.04 (1-proton multiplet, H-3).

Anal. Calc. for $C_{13}H_{18}O_4S$: C, 57.8; H, 6.7. Found: C, 57.4; H, 6.8.

The di-*p*-nitrobenzoate of **1** had m.p. 109° (from ethyl acetate–hexane), $[\alpha]_D^{25}$ $-35°$ (*c* 1.0, chloroform).

Anal. Calc. for $C_{27}H_{24}N_2O_{10}S$: C, 57.0; H, 4.2; N, 4.9. Found: C, 57.0; H, 4.3; N, 5.1.

The diacetate of **1** was a syrup, $[\alpha]_D^{25}$ $-43°$ (*c* 1.0, chloroform).

Anal. Calc. for $C_{17}H_{22}O_6S$: C, 57.6; H, 6.2. Found: C, 57.5; H, 6.3.

*Methyl 2,5-di-O-acetyl-3-deoxy-β-*D-threo-*pentofuranoside.* — The diacetate of **1** (0.50 g), Raney nickel (5.0 g), and ethanol (30 ml) were refluxed overnight with stirring. The mixture was filtered and the residue washed repeatedly with hot ethanol. The filtrate was evaporated to a syrup (0.34 g) that by t.l.c. (5% methanol in benzene) showed the title compound (R_F 0.69) and a weak spot having R_F 0.24 (deacetylated title compound). The product was resolved on a column of silica gel (70 g) by using 5% methanol in benzene: yield 0.30 g, $[\alpha]_D^{25}$ $-85.2°$ (*c* 0.51, chloroform); ν_{max}^{film} no OH absorption, 1735 cm^{-1} (acetate carbonyl); n.m.r. ($CDCl_3$): τ 4.91 (1-proton triplet, *J* 3.0 Hz, H-2), 5.13 (1-proton singlet, H-1), 6.76 (3-proton singlet, OCH_3), 7.93 (6-proton singlet, $OCOCH_3$).

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.7; H, 6.9. Found: C, 51.6; H, 6.9.

Its n.m.r. spectrum showed a singlet for H-1 as also found for methyl 3-deoxy-5-*O*-triphenylmethyl-β-D-*threo*-pentafuranoside[4].

*Methyl 3-S-benzyl-3-thio-α-*D*-xylofuranoside* (**2**) *and methyl 2-S-benzyl-2-thio-α-*D*-arabinofuranoside* (**3**). — Methyl 2,3-anhydro-α-D-ribofuranoside (1.46 g, 10 mmoles) was treated with benzylthiolate ion as described for the β-anomer. T.l.c.

(10% methanol in benzene) showed the presence of traces of starting material (R_F 0.38) and a mixture of **2** and **3** (R_F 0.28). The mixture of isomers (2.0 g) was isolated by column chromatography on silica gel (200 g) with 10% methanol in benzene; $[\alpha]_D^{25}$ +38.7° (*c* 4.94, chloroform); ν_{max}^{film} 3230 cm^{-1} (OH); n.m.r. ($CDCl_3$ with D_2O added): τ 2.70 (5-proton singlet, Ph), 5.15 (doublet, *J* 4.5 Hz) and 5.24 (doublet, *J* 2.5 Hz, ratio 3:7), 6.21 (2-proton singlet, benzylic CH_2), 6.73 (3-proton singlet, OCH_3).

Anal. Calc. for $C_{13}H_{18}O_4S$: C, 57.8; H, 6.7. Found: C, 57.8; H, 6.7.

The mixed diacetates of **2** and **3** were obtained as a syrup, $[\alpha]_D^{25}$ +107° (*c* 2.2, chloroform).

Anal. Calc. for $C_{17}H_{22}O_6S$: C, 57.6; H, 6.2. Found: C, 57.5; H, 6.3.

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