Note

Derivatives of 1-deoxy-6-thio-D-fructose

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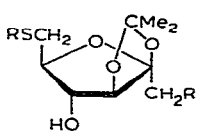
Feather and Whistler[1] reported that both the hydrolysis and methanolysis of 1-deoxy-2,3-*O*-isopropylidene-6-thio-D-fructose (**1**) gave a similar mixture of components and that, under acidic conditions, **1** was readily dehydrated to methyl 2-thienyl ketone.

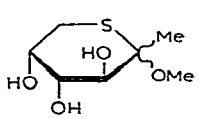
It was of interest to establish the nature of the compounds formed from **1** on methanolysis, because these compounds may be intermediates in the dehydration sequence that finally leads to methyl 2-thienyl ketone.

6-*S*-Benzyl-2,3-*O*-isopropylidene-6-thio-1-*O*-*p*-tolylsulfonyl-D-fructofuranose[1] was reduced with lithium aluminum hydride to give 6-*S*-benzyl-1-deoxy-2,3-*O*-isopropylidene-6-thio-D-fructofuranose (**2**). In addition, a small proportion of 2,3-*O*-isopropylidene-6-*S*-benzyl-6-thio-D-fructofuranose (**3**) was formed. Reduction of **2** with sodium in ammonia gave **1**.

Partial hydrolysis or methanolysis of **1** gave a mixture that contained two major components, whereas continued hydrolysis or methanolysis gave methyl 2-thienyl ketone. The methanolysis mixture was neutralized after an appropriate reaction time (as judged by t.l.c. analysis). Two main intermediates were isolated by chromatography. The mass spectrum of one of these, a crystalline solid having no free thiol group, showed a molecular ion at *m/e* 194. These data, and n.m.r. data, indicate that this product is a methyl 1-deoxy-6-thio-D-fructopyranoside (**4**). The second compound, a syrup, showed a molecular ion at *m/e* 162, no thiol activity and a carbonyl absorption at 1635 cm^{-1}. These and n.m.r. data are in agreement with a probable structure **5**. This compound was readily dehydrated in acidic solution to



1 R = R′ = H
2 R = $PhCH_2$; R′ = H
3 R = $PhCH_2$; R′ = OH



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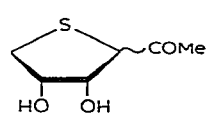

5

methyl 2-thienyl ketone. Compound **5** may arise by a nucleophilic attack of the ring sulfur atom on C-2 under the acidic conditions.

The conversion of **5** into a thiophene derivative is not without precedent, since it is known that anhydrides such as 2,5-anhydroaldoses are readily converted into 2-furaldehyde derivatives under mild conditions[2]. 2,5-Anhydrides have been suggested in the past[3,4], as intermediates in dehydrations to 2-furaldehyde derivatives, but have been generally discounted in recent years after more extensive studies of the mechanism of dehydration reactions[5]. However, the findings presented here indicate that, at least in the formation of thiophene derivatives from thio sugars, such compounds may constitute important intermediates.

EXPERIMENTAL

General — T.l.c. was performed on Kieselgel G (Merck). Melting points were determined on a Fisher–Johns apparatus. I.r. spectra were measured with a Perkin–Elmer Model 700 spectrophotometer. N.m.r. spectra were recorded with a Varian A-60 spectrophotometer. Chemical shifts are given in τ units with Me_4Si as the internal standard. Mass spectra were determined with a Hitachi Perkin–Elmer RMU 7 mass spectrometer. Evaporations were conducted under diminished pressure below 50°.

6-S-Benzyl-1-deoxy-2,3-O-isopropylidene-6-thio-D-fructose (**2**). — 6-*S*-Benzyl-2,3-*O*-isopropylidene-6-thio-1-*O*-*p*-tolylsulfonyl-D-fructose (20 g) was reduced as described previously[1]. A syrup (10.0 g) was isolated. T.l.c. (5% methanol–benzene) showed two main components, R_F 0.74 and 0.26. The mixture was separated by column chromatography on silica gel (400 g) with 5% methanol–benzene to give **2** (7.4 g), m.p. 97–98° (ethyl acetate–hexane) and 6-*S*-benzyl-2,3-*O*-isopropylidene-6-thio-D-fructose (**3**, 2.25 g), m.p. 95–96° (ethyl acetate–hexane).

1-Deoxy-2,3-O-isopropylidene-6-thio-D-fructofuranose (**1**). — Compound **2** was reduced with sodium in ammonia as previously described to give **1**, m.p. 75–77°.

Methyl 1-deoxy-6-thio-D-fructopyranoside (**4**) *and 3,6-anhydro-1-deoxy-6-thio-D-arabino(or D-xylo)-hexulose* (**5**). — Compound **1** (1.0 g), methanol containing 2% hydrogen chloride (25 ml) was kept for 2.25 h at room temperature. The reaction mixture was neutralized by passage through a column of Dowex 1-X8 (OH^-). The column was washed thoroughly with methanol and the effluent was evaporated to a syrup (0.72 g). T.l.c. (15% methanol–ethyl acetate) showed components having R_F 0.94, 0.85, and 0.62. The mixture was resolved on a column of silica gel (100 g) with 10% methanol–benzene to give the component having R_F 0.85 (**4**), yield 100 mg; m.p. 155–161° (ethyl acetate), $[\alpha]_D^{25}$ −196° (*c* 0.68, methanol); N.m.r. (D_2O): τ 5.86 (1 proton, complex), 6.32 (2-proton doublet, *J* 2.4 Hz), 6.79 (3-proton singlet, OCH_3), 7.27 (1-proton doublet, *J* 2.4 Hz), 7.58 (1 proton, complex), 8.63 (3-proton singlet, CH_3); mass spectrum: *m/e* 194 (5.8) (M^+), 176 (0.8), 162 (24.8), 144 (5.3), 118 (7.9), 117 (100.0), 102 (9.0), 101 (13.2), 99 (17.6), 91 (55.0), 90 (31.8), 88 (26.7), 87 (20.0), 86 (55.1), 85 (11.9), 75 (21.0), 74 (12.5), 73 (37.0), 61 (19.8), 60 (35.3), 59 (59.6), 58 (23.3), 57 (30.7), 55 (13.7), 47 (13.9), 46 (21.0), 45 (62.5).

Anal. Calc. for $C_7H_{14}O_4S$: C, 43.3; H, 7.2. Found: C, 43.2; H, 7.1.

The triacetate of **4** was a syrup, $[\alpha]_D^{25}$ −168° (*c* 0.7, chloroform).

Anal. Calc. for $C_{13}H_{20}O_7S$: C, 48.7; H, 6.3; mol. wt., 320. Found: C, 48.5; H, 6.2; mol. wt., 320 (mass spectrum).

The component having R_F 0.94 (**5**) was a syrup, yield 570 mg, $[\alpha]_D^{25}$ −69° (*c* 3.8, methanol); n.m.r. (D_2O): τ 5.43 (1-proton doublet, *J* 5.0 Hz, H-2), 6.34–6.50 (2 protons, complex), 7.03–7.17 (2-protons, complex), 8.46 (3-proton singlet, $COCH_3$); ν_{max}^{film} 3370 (OH), 1635 cm^{-1} (ketone); mass spectrum: *m/e* 162 (14.9) (M^+), 144 (10.3), 134 (3.5), 126 (5.1), 119 (1.9), 116 (4.8), 115 (6.1), 112 (4.2), 111 (10.3), 110 (4.8), 103 (5.1), 102 (20.2), 101 (21.2), 100 (5.8), 99 (4.5), 98 (4.5), 97 (4.2), 90 (6.1), 89 (11.9), 88 (8.0), 87 (32.4), 86 (36.6), 85 (25.4), 84 (8.6), 77 (19.3), 76 (27.3), 74 (50.1), 73 (74.1), 72 (4.8), 71 (9.0), 70 (4.5), 69 (31.1), 68 (24.4), 67 (4.2), 63 (4.2), 61 (33.4), 60 (16.4), 59 (23.1), 58 (18.6), 57 (100), 56 (13.2), 55 (29.2), 53 (9.3), 47 (2.0), 46 (11.2), 45 (54.4).

Anal. Calc. for $C_6H_{10}O_3S$: C, 44.4; H, 6.2. Found: C, 44.6; H, 6.1.

The diacetate of **5** had m.p. 98–99° (sublimation), $[\alpha]_D^{25}$ −62° (*c* 2.84, chloroform); $\nu_{max}^{CHCl_3}$ 1735 (acetate), 1635 cm^{-1} (ketone); n.m.r. ($CDCl_3$): τ 5.00 (1-proton doublet, *J* 2.4 Hz), 5.20 (1-proton doublet, 5.0 Hz), 5.31 (1-proton doublet, *J* 2.4 Hz), 6.75–6.97 (2 protons, complex), 7.87, 7.92 (6-proton singlets, OAc), 8.23 (3-proton singlet, $COCH_3$).

Anal. Calc. for $C_{10}H_{14}O_5S$: C, 48.8; H, 5.7; Mol. wt. 246. Found: C, 48.7; H, 5.6; mol. wt. (mass spectrum) 246.

REFERENCES

1 M. S. Feather and R. L. Whistler, *J. Org. Chem.*, 28 (1963) 1567.
2 M. Cifonelli, J. A. Cifonelli, R. Montgomery, and F. Smith, *J. Amer. Chem. Soc.*, 77 (1955) 121.
3 J. U. Nef, *Ann.*, 376 (1910) 1.
4 W. N. Haworth and W. G. M. Jones, *J. Chem. Soc.*, (1944) 667.
5 E. F. L. J. Anet, *Advan. Carbohyd. Chem.*, 19 (1964) 181.