*Carbohydrate Research*, 35 (1974) 247–250


## Note

# The reaction of methyl β-D-ribopyranoside with acetone*

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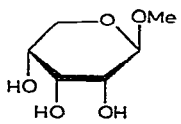
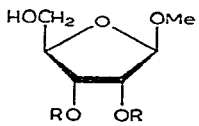
(Received October 25th, 1973; accepted for publication, November 7th, 1973)

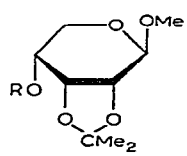
Levene and Stiller[1] suggested that when methyl β-D-ribopyranoside (**1**) is treated with acetone–sulphuric acid, acetal formation is accompanied by ring contraction and that methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (**2**) is formed in addition to pyranoside products. Two pyranoside products are likely, namely, the 2,3-acetal **3** and the 3,4-acetal **4**; one, isolated as its toluene-*p*-sulphonate derivative, was later shown[2] to be methyl 3,4-*O*-isopropylidene-2-*O*-toluene-*p*-sulphonyl-β-D-ribopyranoside (**5**). More recently, the enantiomer of **5** was synthesised[3] by an independent route, thereby providing further proof of the structure. Barker and coworkers[4] repeated the earlier work and, after methylating and hydrolysing the acetal products, identified 4-*O*-methyl-D-ribose in addition to the 2-*O*-methyl and 5-*O*-methyl derivatives, suggesting the presence of the 2,3-acetal **3** in the product mixture and confirming the earlier findings. However, in both of these preparations, the equilibrium mixture of methyl D-ribosides was used, and although it is mainly (66%) the β-pyranoside **1**, it is now known[5] to contain an appreciable amount (17%) of the β-furanoside **6**. The possibility existed then that this, rather than ring contraction, was the explanation of the formation of the furanoside acetal **2**. We have now reinvestigated this reaction with pure[6] methyl β-D-ribopyranoside (**1**).



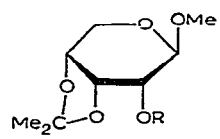

**1**




2 R,R = $CMe_2$
6 R = H




3 R = H
7 R = Ts




4 R = H
5 R = Ts

A control sample of the β-furanoside acetal **2** was obtained by treating crystalline methyl β-D-ribofuranoside (**6**) with acetone and sulphuric acid. T.l.c. monitoring of the reaction of the pyranoside **1** with acetone and sulphuric acid showed the reaction to be complete within minutes. Two products were formed, neither of which coincided on t.l.c. with the furanoside acetal **2**. All three compounds could be clearly distinguished by t.l.c. (relative $R_F$ values: **2**, 1.00, **3**, 0.91; **4**, 0.77). After a prolonged

*Dedicated to Dr. Horace S. Isbell, in honour of his 75th birthday.

reaction (24 h), there was still no indication of furanoside products and nor was there after using the Levene and Stiller conditions. Thus, it seems that the furanoside acetal **2** originally obtained arose from methyl β-D-ribofuranoside (**6**) already present in the starting material.

The two products from the pyranoside reaction were readily separated by chromatography on silica gel. The product eluted last from the column gave the known toluene-*p*-sulphonate **5** and was thus identified as the 3,4-acetal **4**. The product eluted first also gave a crystalline toluene-*p*-sulphonate, isomeric with **5**, which was shown to be methyl 2,3-*O*-isopropylidene-4-*O*-toluene-*p*-sulphonyl-β-D-ribopyranoside (**7**) as follows. It reacted only slowly with sodium benzoate in hot *N*,*N*-dimethylformamide. On treatment of the crude product (which still contained some sulphonate **7**) with sodium methoxide, the odour of methyl benzoate was detected, indicating the presence of a benzoate. The debenzoylated material was hydrolysed with acid, and paper chromatography demonstrated the presence of lyxose and ribose as the only reducing sugars in the hydrolysate. These results are in keeping with a benzoate displacement on the sulphonate **7** to give methyl 4-*O*-benzoyl-2,3-*O*-isopropylidene-α-L-lyxopyranoside, which on debenzoylation and hydrolysis gave L-lyxose; the ribose in the hydrolysate would have arisen from unchanged starting material. Confirmation of the structure came from a comparison of the p.m.r. spectra of the sulphonate **7** and the parent alcohol **3** (see Experimental for details). The H-4 signal for the sulphonate **7** was clearly discernible as a sextet at $\delta$ 4.9, but in the spectrum of the alcohol the H-4 signal was located upfield by ~0.9 p.p.m., where it was partially obscured by the H-2 signal. The positions of the signals of the other ring protons in the two compounds differed by less than 0.1 p.p.m. The p.m.r. spectra of the 3,4-acetal **4** and its sulphonate **5** were less well resolved, and only the H-1 and H-5,5′ signals could be identified.

## EXPERIMENTAL

*General methods.* — N.m.r. spectra were determined for solutions in deuteriochloroform, using tetramethylsilane as internal standard, at 90 or 60 MHz. Silica gel was used for t.l.c. (Gelman, I.T.L.C. Type SA) and column chromatography (Merck Kieselgel).

*Acetalation of methyl β-D-ribopyranoside* (**1**). — (*a*) The glycoside **1** (50 mg) was dissolved in acetone (5 ml) containing sulphuric acid (0.05 ml). Samples were taken after 5, 15, 45, and 120 min, and finally after 24 h, and neutralised with anhydrous sodium carbonate. T.l.c. showed the reaction to be complete within 15 min, with two spots corresponding to the acetals **3** and **4**. The 24-h samples gave the same result, and no furanoside acetal **6** could be detected.

(*b*) The glycoside **1** (20 mg) was shaken for 20 h in acetone (1 ml) containing sulphuric acid (0.002 ml) and anhydrous copper sulphate (4 mg). The reaction was neutralised with anhydrous sodium carbonate. T.l.c. then showed the presence of only the two acetals **3** and **4**.

(*c*) The glycoside **1** (0.83 g) was treated with acetone (20 ml) containing sulphuric acid (0.2 ml) for 20 min. The solution was neutralised with anhydrous sodium carbonate, filtered, and evaporated to a syrup. This was dissolved in ether and chromatographed on silica gel (40 g). Elution with ether gave the 2,3-acetal **3** (0.24 g, 23%) and then the 3,4-acetal **4** (0.47 g, 46%).

The 2,3-acetal **3** was bulb-distilled (100°/0.2 mmHg), after which it solidified and had m.p. 70–71°, $[\alpha]_D$ −77° (*c* 1.0, dichloromethane). N.m.r. data (90 MHz): δ4.58 (*d*, 1H, H-1, $J_{1,2}$ 3.6 Hz), 4.05 (*q*, 1H, H-2, $J_{2,3}$ 6.4 Hz), 4.40 (*q*, 1H, H-3, $J_{3,4}$ 4.0 Hz), ~4.0 (*m*, 1H, H-4), ~3.7 (*m*, 2H, H-5,5′), 3.46 (*s*, 3H, OMe), 2.49 (*s*, 1H, OH), 1.57 (*s*, 3H, CMe), and 1.39 (*s*, 3H, CMe) (Found: C, 52.4; H, 7.7. $C_9H_{16}O_5$ calc.: C, 52.9; H, 7.8%).

The 3,4-acetal **4** was also bulb-distilled (100°/0.2 mmHg) and had $[\alpha]_D$ −109° (*c* 1.2, dichloromethane). N.m.r. data (60 MHz): δ 4.48 (*d*, 1H, H-1, $J_{1,2}$ 5 Hz), 3.58 (*d*, 2H, H-5,5′), 3.36 (*s*, 3H, OMe), 3.00 (*s*, 1H, OH), 1.47 (*s*, 3H, CMe), and 1.32 (*s*, 3H, CMe) (Found: C, 52.7; H, 7.8%).

*Toluene-*p*-sulphonylation of the acetals* **3** *and* **4**. — The sulphonylations were carried out in the usual manner, using toluene-*p*-sulphonyl chloride and pyridine. They were left overnight at room temperature and finally heated to 60° for 2 h before being worked up.

The 2,3-acetal sulphonate **7** had m.p. 99–100° (from isopropyl ether–light petroleum), $[\alpha]_D$ −25° (*c*, 0.6, dichloromethane). N.m.r. data (90 MHz): δ 4.46 (*d*, 1H, H-1, $J_{1,2}$ 3.6 Hz), 3.99 (*q*, 1H, H-2, $J_{2,3}$ 6.4 Hz), 4.34 (*q*, 1H, H-3, $J_{3,4}$ 3.8 Hz), 4.89 (*o*, 1H, H-4, $J_{4,5}$ 6.4, $J_{4,5'}$ 7.6 Hz), ~3.7 (*m*, 2H, H-5,5′), 7.25 (*d*, 2H, ArH), 7.75 (*d*, 2H, ArH), 3.40 (*s*, 3H, OMe) 2.45 (*s*, 2H, ArMe), 1.51 (*s*, 3H, CMe), and 1.28 (*s*, 3H, CMe), (Found: C, 53.8; H, 6.4. $C_{16}H_{22}O_7S$ calc.: C, 53.6; H, 6.1%).

The 3,4-acetal sulphonate **5** had m.p. 145–146° (from isopropyl ether), $[\alpha]_D$ −110° (*c* 0.7, dichloromethane); lit.[2] m.p. 144–145°, $[\alpha]_D$ −113°. N.m.r. data (60 MHz): δ 4.50 (*d*, 1H, H-1, $J_{1,2}$ 4.5 Hz), 3.60 (*d*, 2H, H-5,5′), 7.25 (*d*, 2H, ArH), 7.75 (*d*, 2H, ArH), 3.10 (*s*, 3H, OMe), 2.43 (*s*, 3H, $ArCH_3$), 1.50 (*s*, 3H, CMe), and 1.30 (*s*, 3H, CMe).

*Benzoate displacement reaction on the* 2,3*-acetal sulphonate* **7**. — A solution of the sulphonate **7** (20 mg) in *N*,*N*-dimethylformamide (2 ml) containing sodium benzoate (50 mg) was kept at 140°. The reaction was monitored by t.l.c. After 72 h, starting material was still present, but there was also a product of slightly higher mobility which did not contain a sulphonic ester group (diphenylamine–u.v. test). The mixture was cooled and partitioned between water and dichloromethane, and the organic extract was dried and evaporated to a syrup. Last traces of *N*,*N*-dimethylformamide were removed by co-distillation with 1-butanol. The residue was dissolved in methanol (1 ml), a little sodium methoxide was added, and the solution was refluxed for 5 min; the odour of methyl benzoate was then observed. The solution was evaporated to dryness, and the residue was dissolved in M hydrochloric acid (0.5 ml) and heated to 80° for 30 min. Water (2 ml) was added, the solution was extracted with dichloromethane (2 ml), the aqueous layer was passed through a little

Dowex-1($AcO^-$) resin and evaporated to dryness, and the residue was taken up in a little methanol. Paper chromatography (Whatman No. 1 paper, 1-butanol saturated with water, downward displacement) of this solution revealed ribose and lyxose as the only reducing sugars.

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