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Note

Di-*O*-benzylidene derivatives of 1-deoxy-D-galactitol and 1-deoxy-L-mannitol

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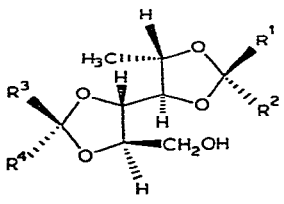
In connection with studies of the fragmentation of alditol acetates in electron-impact mass spectrometry, di-*O*-benzylidene derivatives of 1-deoxyhexitols were needed as intermediates in the synthesis of model substances. Di-*O*-benzylidene derivatives of 1-deoxy-D-galactitol[1] (L-fucitol), 1-deoxy-D-mannitol[2] (D-rhamnitol), and 1-deoxy-L-mannitol[3] have been described, although their structures have not been determined. We have now reinvestigated the di-*O*-benzylidene derivatives of 1-deoxy-D-galactitol and 1-deoxy-L-mannitol.

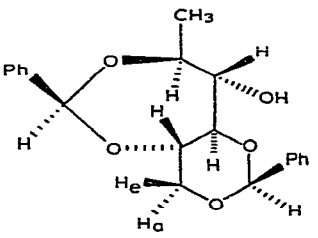
When 1-deoxy-D-galactitol was treated with benzaldehyde in 50% aqueous sulfuric acid, a mixture of di-*O*-benzylidene derivatives was obtained, as indicated by t.l.c. of the product. Methylation of the product, followed by acid hydrolysis, yielded comparable amounts of the 5- and 6-*O*-methyl derivatives of 1-deoxy-D-galactitol, which were identified by g.l.c.–m.s. of their alditol acetates[4]. One of the components (**1**) was obtained pure by chromatography on silica gel followed by crystallization. It had m.p. 124–125°, $[\alpha]_{578}$ 0° (chloroform), in reasonably good agreement with the published values[1], m.p. 115–116°, $[\alpha]_D$ +9° (acetone). Methylation analysis of **1** yielded 1-deoxy-6-*O*-methyl-D-galactitol. Partial hydrolysis with acid, followed by methylation analysis, yielded the 2,3,6- and 4,5,6-trimethyl ethers of 1-deoxy-D-galactitol. Thus, **1** is one of the four isomers of 2,3:4,5-di-*O*-benzylidene-1-deoxy-D-galactitol.

Two isomers of the analogous 1,6-di-*O*-benzoyl-2,3:4,5-di-*O*-benzylidene-galactitol are known[5]. In one of these, a *meso* form, the benzylidene protons are indistinguishable and give one signal in the n.m.r. spectrum. In the n.m.r. spectrum of the other isomer, a D,L form, they are separated by 0.04 p.p.m. In the n.m.r. spectrum of the 1-deoxy-D-galactitol derivative **1** (all spectra refer to solutions in deuteriochloroform), the signals from the benzylidene protons appeared at δ 5.90 and 5.99, respectively. This rather large difference may indicate that the substance is the 2,3(*R*):4,5(*R*) (**1a**) or the 2,3(*S*):4,5(*S*) (**1b**) isomer, in which the chemical environments of the two benzylidene protons should be significantly different. Attempts to distinguish these alternatives by n.m.r. studies of the monoacetate of **1**, using shift

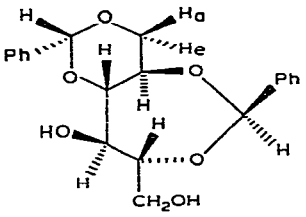
reagents and spin decoupling in order to identify the signals of the different protons, were not successful, as the signals for some protons were not sufficiently resolved.



1a $R^1 = R^3 = Ph$; $R^2 = R^4 = H$
1b $R^1 = R^3 = H$; $R^2 = R^4 = Ph$



2



3

No other pure component was isolated. The results indicate that the reaction product is a mixture of the 2,3:4,5- and 2,3:4,6-di-*O*-benzylidene derivatives. These are the expected equilibrium products according to the modified preference rules of Barker and Bourne[6] for the formation of cyclic acetals of alditols.

On treatment of 1-deoxy-L-mannitol with benzaldehyde in 50% aqueous sulfuric acid, component **2** crystallized from the reaction mixture. After recrystallization, it had m.p. 207–208°, $[\alpha]_{578}$ +61° (chloroform), in good agreement with published values[2,3]. The non-crystalline part of the reaction product, according to n.m.r., t.l.c., and methylation analysis, was a complex mixture and was not further investigated.

Methylation analysis of **2** yielded 1-deoxy-3-*O*-methyl-L-mannitol. Partial hydrolysis of fully methylated **2** with acid and methylation analysis of the product yielded 1-deoxy-2,3,5-tri-*O*-methyl-L-mannitol as the main tri-*O*-methyl derivative. These results indicate that **2** is a 2,5:4,6-di-*O*-benzylidene-1-deoxy-L-mannitol. In the n.m.r. spectrum of **2**, in deuteriochloroform, the benzylidene protons produce signals at δ 5.50 and 5.85, respectively. In 1,3(*R*):2,5:4,6(*R*)-tri-*O*-benzylidene-D-mannitol, the signals for the benzylidene protons in the 1,3-dioxane rings appeared[7] at δ 5.51 and 5.45 and that in the 1,3-dioxepane ring at δ 5.81. In the 1,3(*R*):2,5(*S*)-di-*O*-benzylidene-D-mannitol (**3**), the corresponding signals appear at δ 5.51 and 5.84, respectively[7].

In the n.m.r. spectrum of 1,3(*R*):2,5:4,6(*R*)-tri-*O*-benzylidene-D-mannitol, the signal for one of the two equatorial protons (H-1e or H-6e) in the 1,3-dioxane rings appears at the expected low field, δ 4.36 (q, *J* 4 and 9.5 Hz), but the other is shielded by the phenyl group linked to the dioxepane ring and appears at higher field. A corresponding, low-field signal, at δ 4.31, was also observed in the n.m.r. spectrum of **3**, which was therefore identified as the 1,3(*R*):2,5(*S*) derivative[7]. The absence of a signal in this region in the n.m.r. spectrum of **2** consequently suggests that **2** has the 2,5(*S*):4,6(*S*) configuration, as indicated in the formula.

According to the rules of Barker and Bourne[6], 2,5:4,6-di-*O*-benzylidene derivatives of 1-deoxy-D-mannitol would be the predicted equilibrium products. The

results, however, indicate that significant amounts of products having other structures are also present in the reaction mixture.

EXPERIMENTAL

General methods. — Optical rotations were measured at 22° with a Perkin–Elmer 141 polarimeter. N.m.r. spectra for solutions in deuteriochloroform (internal tetramethylsilane) were determined with a JEOL FX 100 spectrometer. T.l.c. and column chromatography were performed on silica gel. Ethyl acetate–light petroleum (1:2) was used as chromatographic solvent. G.l.c. was performed on a Perkin–Elmer 990 instrument, with a column (180 cm × 2 mm) of 3% of OV-225 on Gas Chrom Q (100/200 mesh), at 160°. For g.l.c.–m.s., a Varian MAT 311 instrument was used. The interpretations of the mass spectra were unambiguous and will not be discussed. Methylations were performed by the Hakomori[8] method.

*Benzylidenation of 1-deoxy-*D*-galactitol.* — A mixture of 1-deoxy-D-galactitol (1.2 g), 50% sulfuric acid (2.4 ml), and benzaldehyde (2 g), kept under nitrogen, was shaken for 24 h. The mixture was then poured into saturated, aqueous sodium hydrogen sulfite (20 ml), stirred for 2 h, and extracted with chloroform (2 × 20 ml). Concentration of the extracts gave a residue that showed two main spots (t.l.c.) at R_F 0.35 and 0.50 (major). Column chromatography yielded two fractions that corresponded to these spots. On methylation analysis, the faster product (680 mg) yielded comparable amounts of the 5- and 6-*O*-methyl derivatives of 1-deoxy-D-galactitol. The slower product (160 mg) crystallized and, after recrystallizations from ethanol, had m.p. 124–125°, $[\alpha]_{578}$ 0° (*c* 1.0, chloroform). N.m.r. data, *inter alia*: δ 1.45 (d, *J* 6 Hz, 3 H), 5.90 (s, 1 H), and 5.99 (s, 1 H).

Partial hydrolysis of the crystalline component with 50% aqueous acetic acid at 100° was monitored by t.l.c. Methylation analysis yielded the 2,3,6- and 4,5,6-tri-*O*-methyl derivatives of 1-deoxy-D-galactitol in addition to the ethers obtained from the unhydrolysed and fully hydrolysed product.

*Benzylidenation of 1-deoxy-*L*-mannitol.* — 1-Deoxy-L-mannitol (1.2 g) was benzylidenated by the foregoing procedure. A component crystallized from the reaction mixture, and was filtered off and washed successively with 5% aqueous sodium hydrogen carbonate, water, and ethyl ether. Crystallizations from ethanol yielded **2** (500 mg), m.p. 207–208°, $[\alpha]_{578}$ +61° (*c* 1.0 chloroform). N.m.r. data, *inter alia*: δ 1.46 (d, *J* 6 Hz, 3 H), 5.50 (s, 1 H), and 5.85 (s, 1 H).

Methylation analysis of the product revealed that partial hydrolysis of **2** was accompanied by acetal migration. In order to minimize this migration, **2** was methylated before the partial hydrolysis, which was performed in boiling 50% acetic acid–acetone (1:3). In the methylation analysis of this product, 1-deoxy-2,3,5-tri-*O*-methyl-L-mannitol was the main trimethyl ether.

The filtrate from the benzylidenation reaction was poured into aqueous sodium hydrogen sulfite and worked up as above. T.l.c. showed two main spots at R_F 0.5 (major) and 0.6. The minor component was identical to the crystalline derivative.

Methylation analysis of the main fraction yielded a mixture of monomethyl ethers, among which the 4-, 5-, and 6-*O*-methyl derivatives predominated.

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REFERENCES

1 M. L. WOLFROM, W. J. BURKE, AND E. A. METCALF, *J. Am. Chem. Soc.*, 69 (1947) 1667–1668.
2 C. A. LOBRY DE BRUYN AND W. ALBERDA VAN EKENSTEIN, *Rec. Trav. Chim.*, 18 (1899) 150–152.
3 E. VOTOČEK, F. VALENTIN, AND F. RAČ, *Collect. Czech. Chem. Commun.*, 2 (1930) 402–413.
4 H. BJÖRNDAL, B. LINDBERG, AND S. SVENSSON, *Carbohydr. Res.*, 5 (1967) 433–440.
5 N. BAGGETT, K. W. BUCK, A. B. FOSTER, M. H. RANDALL, AND J. M. WEBBER, *J. Chem. Soc.*, (1965) 3394–3400.
6 S. A. BARKER AND E. J. BOURNE, *Adv. Carbohydr. Chem.*, 7 (1952) 137–207.
7 D. J. BRECKNELL, R. M. CARMAN, AND J. J. KIBBY, *Aust. J. Chem.*, 29 (1976) 1749–1760.
8 S. HAKOMORI, *J. Biochem. (Tokyo)*, 55 (1964) 205–208.