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Note

Diastereoisomers of methyl 4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside

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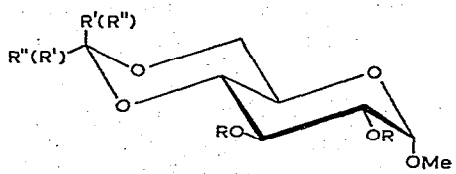
The acetal-exchange reaction, reported by Evans *et al.*[1], for preparing monoacetals from pinacolone, acetophenone, and benzophenone has been used for the synthesis of methyl 4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside, a model compound for the lignin–carbohydrate complex.

Treatment of methyl α-D-glucopyranoside with 2,2-dimethoxy-1-phenylpropane and *p*-toluenesulphonic acid in *N*,*N*-dimethylformamide at room temperature gave mainly (88%) methyl 4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside. T.l.c. of the product revealed the diastereoisomers **1** and **2**. The slower-moving isomer (**1**) was isolated by crystallisation, and the syrupy, faster-moving isomer **2** by chromatography on silica gel. Methylation of **1** or **2**, followed by hydrolysis, gave known methyl 2,3-di-*O*-methyl-α-D-glucopyranoside. Treatment of **1** with acetic anhydride–pyridine at room temperature gave the crystalline 2,3-diacetate (**1b**). The diacetate (**2b**) of **2** was non-crystalline.



1	R=H,	R'=Me,	R"=PhCH$_2$
2	R=H,	R'=PhCH$_2$,	R"=Me
1a	R=Me,	R'=Me,	R"=PhCH$_2$
2a	R=Me,	R'=PhCH$_2$,	R"=Me
1b	R=Ac,	R'=Me,	R"=PhCH$_2$
2b	R=Ac,	R'=PhCH$_2$,	R"=Me

In the n.m.r. spectra of **1**, **2**, **1a**, and **2a**, the respective signals (see Experimental) for Ph, H-1,2,3,4,5,6,6′, and MeO-1 were similarly located. Differences were found only for the substituents attached to the new asymmetric carbon atom. Thus, for **1**,

the signals for PhCH_2 and Me were singlets at δ 2.90 and 1.38, respectively. However, for **2**, the signal for PhCH_2 appeared as 1-proton doublets at δ 3.05 and 3.25, and that for Me was a singlet at δ 1.17. Similar results were observed for the diacetates **1b** and **2b**.

The acid-catalysed reaction of aldehydes (other than formaldehyde) with carbohydrates usually affords one isomer if a 1,3-dioxane ring is formed, but diastereoisomers may be obtained if a 1,3-dioxolane ring is formed[2]. For non-symmetrical ketones, two isomers are to be expected[2]. Evans *et al.*[1] presented some evidence for the existence of such isomers, and we have found that the diastereoisomers **1** and **2** are formed in the ratio 1:0.7 in the reaction of 2,2-dimethoxy-1-phenylpropane with methyl α-D-glucopyranoside.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter. N.m.r. spectra (80 MHz) were obtained with a TESLA BS-487 Spectrometer, for solutions in chloroform-*d*. *N*,*N*-Dimethylformamide was purified and dried as described by Bunge[3]. Trimethyl orthoformate[4] had b.p. 101–103°/760 mmHg. *p*-Toluenesulphonic acid was used as the monohydrate.

T.l.c. was performed on silica gel Merck PF_{254} with *A* ether–chloroform (2:1); *B* chloroform–light petroleum (b.p. 50–80°) (1:1); *C* ether–cyclohexane (5:1). Detection was performed by charring with 5% sulphuric acid in ethanol at ~150°. Column chromatography was performed on columns (120 × 2.5 cm) of Merck silica gel (0.063–0.1 mm mesh).

2,2-Dimethoxy-1-phenylpropane. — A solution of benzyl methyl ketone (12 g) and trimethyl orthoformate in dry methanol (60 ml) containing Dowex-50W x8(H^+) resin (1 g) was protected from moisture and boiled under reflux for 8 h. The solution was filtered on to a little Dowex-1(HO^-) resin and evaporated. The product, which was distilled from Dowex-1(HO^-) resin at 95–96°/15 mmHg, had no i.r. absorption for C=O.

Anal. Calc. for $C_{11}H_{16}O_2$: C, 73.29; H, 8.94. Found: C, 73.32; H, 8.88.

Reaction of methyl α-D-glucopyranoside with 2,2-dimethoxy-1-phenylpropane. — *p*-Toluenesulphonic acid (0.1 g) was added to a stirred solution of methyl α-D-glucopyranoside (7.8 g) and 2,2-dimethoxy-1-phenylpropane (8 g) in *N*,*N*-dimethylformamide (60 g). After 24 h, the solution was neutralised with Dowex-1(HO^-) resin, filtered, and concentrated under diminished pressure. A solution of the residue in chloroform (250 ml) was stored overnight at 0°. Unreacted glucoside crystallised and was removed. The filtrate was concentrated, and the syrupy residue was crystallised from ether–cyclohexane (1:1, 200 ml). Methyl 4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside (**1**) so obtained was thrice recrystallised from chloroform–cyclohexane (1:5) to give material (52%) which had m.p. 139.5–140°, $[\alpha]_D^{25}$ +72° (*c* 1, chloroform); ν_{max}^{KBr} 1490, 1600 (Ph), 3320 cm^{-1} (OH). N.m.r. data: δ 7.20 (*s*, Ph), 4.68 (*d*, H-1),

3.30–4.00 (*m*, H-2,3,4,5,6,6'), 3.38 (*s*, MeO-1), 2.90 (*s*, PhCH_2), 2.55 (*s*, OH), 1.38 (*s*, Me).

Anal. Calc. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.11. Found: C, 61.90; H, 7.13.

The mother liquors were combined and concentrated, and the syrupy residue was eluted from silica gel with solvent *C*. Combination and concentration of the appropriate fractions gave syrupy methyl 4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside (**2**, 36%), $[\alpha]_D^{25}$ +81° (*c* 1, chloroform); ν_{max}^{liquid} 1490, 1600 (Ph), 3320 cm^{-1} (OH). N.m.r. data: δ 7.18 (*s*, Ph), 4.68 (*d*, H-1), 3.30–4.00 (*m*, H-2,3,4,5,6,6'), 3.38 (*s*, MeO-1), 3.05 and 3.25 (1-proton *d*, PhCH_2), 2.45 (*s*, OH), 1.17 (*s*, Me).

Anal. Found: C, 61.90; H, 7.13.

Methylation of **1** *and* **2**. — Treatment of **1** with methyl iodide and silver oxide in *N*,*N*-dimethylformamide[1] yielded methyl 4,6-*O*-(1-benzylethylidene)-2,3-di-*O*-methyl-α-D-glucopyranoside (**1a**, 91%), m.p. 69–71°, $[\alpha]_D^{25}$ +76° (*c* 1, chloroform). N.m.r. data: δ 7.20 (*s*, Ph), 4.68 (*d*, H-1), 3.30–4.00 (*m*, H-2,3,4,5,6,6'), 3.38 (*s*, MeO-1), 3.48 and 3.52 (2 *s*, MeO-2 and MeO-3), 2.90 (*s*, PhCH_2), 1.38 (*s*, Me).

Anal. Calc. for $C_{18}H_{26}O_6$: C, 63.89; H, 7.72. Found: C, 63.81; H, 7.70.

Similarly, methyl 4,6-*O*-(1-benzylethylidene)-2,3-di-*O*-methyl-α-D-glucopyranoside (**2a**) was obtained from **2** as a syrup, $[\alpha]_D^{25}$ +82° (*c* 1, chloroform). N.m.r. data: δ 7.18 (*s*, Ph), 4.68 (*d*, H-1), 3.30–4.00 (*m*, H-2,3,4,5,6,6'), 3.38 (*s*, MeO-1), 3.48 and 3.52 (2 *s*, MeO-2 and MeO-3), 2.92 and 3.40 (1-proton *d*, PhCH_2) 1.17 (*s*, Me).

Anal. Found: C, 63.91; H, 7.74.

Acetylation of **1** *and* **2**. — Conventional esterification of **1** with acetic anhydride–pyridine, with recrystallisation of the product from ethyl acetate–light petroleum (1:1), gave methyl 2,3-di-*O*-acetyl-4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside (**1b**, 96%), m.p. 111–112°, $[\alpha]_D^{25}$ +93° (*c* 1, chloroform). N.m.r. data: δ 7.20 (*s*, Ph), 4.7–5.0 (*m*, H-1,2), 5.45 (*t*, H-3), 3.30–4.00 (*m*, H-4,5,6,6'), 3.38 (*s*, MeO-1), 2.85 (*s*, PhCH_2), 2.05 and 1.98 (2 *s*, AcO-2 and AcO-3), 1.38 (*s*, Me).

Anal. Calc. for: $C_{20}H_{26}O_8$: C, 60.90; H, 6.64. Found: C, 60.93; H, 6.60.

Similarly, methyl 2,3-di-*O*-acetyl-4,6-*O*-(1-benzylethylidene)-α-D-glucopyranoside (**2b**, 92%) was obtained as a syrup after column chromatography (solvent *B*), and had $[\alpha]_D^{25}$ +98° (*c* 1, chloroform); ν_{max}^{KBr} 1750 cm^{-1} (OAc), no absorption attributable to OH. N.m.r. data: δ 7.18 (*s*, Ph), 4.70–5.00 (*m*, H-1,2), 5.45 (*t*, H-3), 3.30–4.00 *m*, H-4,5,6,6'), 3.38 (*s*, MeO-1), 2.80 and 3.45 (1-proton *d*, PhCH_2), 2.05 (*s*, AcO-2 and AcO-3) 1.17 (*s*, Me).

Anal. Found: C, 60.98; H, 6.61.

Hydrolysis of methylated acetals **1a** *and* **2a**. — A sample (0.7 g) of **1a** or **2a** was hydrolysed in 75% acetic acid (20 ml) for 8 h at 40°; no starting material was then detectable by t.l.c. (solvent *A*). After evaporation of the solvent and chromatography of the residue, benzyl methyl ketone and methyl 2,3-di-*O*-methyl-α-D-glucopyranoside, m.p. and mixture m.p. 84–85°, were obtained.

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