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Note

Interaction between methanol and D-glucose bis(benzeneboronate): synthesis of methyl D-glucofuranosides

JUNE BRIGGS, IAN R. MCKINLEY, AND HELMUT WEIGEL

The Bourne Laboratory, Royal Holloway College (University of London), Egham, Surrey TW20 OEX (Great Britain)

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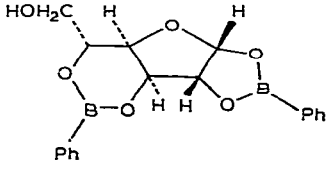
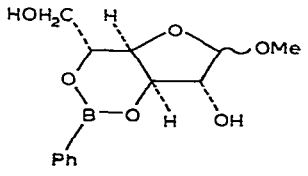
Furanosides are the kinetically controlled products of the acid-catalysed alcoholysis of monosaccharides and ring-expand to the thermodynamically more stable pyranosides[1–3]. If conditions are optimised, furanosides may be obtained in good yields. The relative proportions of furanosides and pyranosides, as well as α and β isomers, produced by the Fischer glycosidation[4] of suitable monosaccharides, such as D-allose, may be changed[5] by the presence of alkaline-earth metal ions with which they form complexes. Frequently, the synthesis of furanosides is accomplished in several stages[6] and may involve the alcoholysis of such compounds as 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-carbonate. Acid-catalysed acetonolysis[7] of 2-phenyl-1,3,2-dioxaborolanes replaces the benzeneboronate group (PhB<) and gives 2,2-dimethyl-1,3-dioxolanes, leading to improved syntheses of isopropylidene derivatives of some carbohydrates. We now report on the acid-catalysed alcoholysis of α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) (**1**).



1



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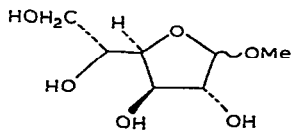

3

When **1** was treated with acidified methanol at room temperature for 72 h or 10 days, p.c. revealed almost quantitative conversion into methyl D-glucofuranosides (**3**) (the benzeneboronate group of the intermediate being hydrolysed during the chromatography). Only traces of methyl D-glucopyranosides were detected. G.l.c.[8] of the acetylated methanolysis product revealed, in addition to traces of methyl 2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranoside, methyl 2,3,5,6-tetra-*O*-acetyl-α- and -β-D-glucofuranosides in the ratio 1:10. The last two components gave identical e.i.-mass spectra, which were characteristic of methyl 2,3,5,6-tetra-*O*-acetylhexofurano-

sides[9]. The αβ-ratio for the methyl D-glucofuranosides formed[10] in 0.1M methanolic methanesulphonic acid was 1:1.7.

It is considered unlikely that methanolysis of **1** gave D-glucose which, under the conditions of the Fischer method[4], was then converted into **3**. In 2M methanolic methanesulphonic acid, the ring expansion of methyl D-glucofuranosides follows[10] the first-order rate law ($k_0^{25°}$ 7.5 × 10^{-6} sec^{-1}). Therefore, under the conditions used here (~0.1M H_2SO_4), methyl D-glucofuranosides should have been converted largely into pyranosides. However, only traces of methyl D-glucopyranosides were detected.

Furthermore, the c.i.-mass spectrum of a methanolysis mixture from which sulphuric acid had been removed with barium carbonate exhibited three peaks between *m/z* 180–300, corresponding to ions with *m/z* 281, 249, and 231, with relative abundances of 1, 10, and 2, respectively. These peaks can be assigned to the $[M+1]^+$ ion (*m/z* 281) of methyl α,β-D-glucofuranoside 3,5-benzeneboronate (**2**), from which methanol (*m/z* 249) as well as water (*m/z* 231) is eliminated.

Thus, the acid-catalysed methanolysis of **1** gives methyl α,β-D-glucofuranoside 3,5-benzeneboronate (**2**) and reflects the stability of some benzeneboronates in alcoholic media[11]. Ring expansion is prevented by the 3,5-benzeneboronate group.

Although the yield of isolated methyl D-glucofuranosides (**3**) was not optimised, the methanolysis of **1** affords, in a single operation, methyl β-D-glucofuranoside in 90% yield.

EXPERIMENTAL

Methanolysis of α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) (**1**). — To a solution of **1**[12] (3.5 g) in dry methanol (100 ml) was added conc. sulphuric acid (0.5 ml). The mixture was stored at room temperature for 72 h, and p.c. (1-butanol–ethanol–water, 40:11:19) then revealed components with R_{Glc} 1.58 (trace), 2.0 (major carbohydrate component), and 3.78 (benzeneboronic acid). The mixture was treated overnight with methanol-washed Amberlite IR-45(HO^-) resin (25 ml), filtered, and concentrated. A portion (0.21 g) of the syrupy residue (2.25 g) was fractionated on Whatman No. 17 paper (above solvent system), and the product (0.13 g) corresponding to the methyl D-glucosides was eluted with water. A portion (~15 mg), when oxidised with 0.03M $NaIO_4$, gave 0.90 mol of formaldehyde as determined by the chromotropic acid method[13].

Another portion (~10 mg) was treated with acetic anhydride–pyridine, and the product analysed by g.l.c.[7]. Components with retention times (relative to that of methyl 2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranoside) of 0.50 and 0.60 had peak areas in the ratio 1:10.

The acetylated methyl D-glucosides were analysed by g.l.c.–m.s.[7].

The c.i.-mass spectrum was obtained with a VG Micromass 12F mass spectrometer, and with 2-methylpropane at a pressure[14] in the ion source of 0.1 torr.

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