

Note

A convenient method for the synthesis of 6-*O*-methyl-D-glucose

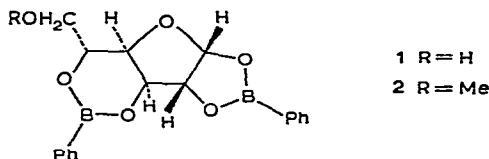
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Previously reported^{1,2} methods for the synthesis of 6-*O*-methyl-D-glucose from D-glucose involve several steps and/or overall yields of less than 20%. The intermediates used were such compounds as 1,2:3,5-di-*O*-alkylidene¹ or 1,2,3,4-tetra-*O*-acetyl derivatives of D-glucose². Although benzeneboronates of carbohydrates are readily obtainable, earlier attempts to use these compounds as intermediates in the synthesis of *O*-methyl derivatives were unsuccessful³⁻⁵. The report² that diazomethane, with boron trifluoride as catalyst, is an effective methylation reagent for partially acetylated carbohydrates prompted us to apply this reagent to benzeneboronates of carbohydrates.

We now report a simple method for the synthesis of 6-*O*-methyl-D-glucose, using α -D-glucofuranose 1,2:3,5-bis(benzeneboronate)^{4,6} (1) for the methylation step. The intermediate, 6-*O*-methyl- α -D-glucofuranose 1,2:3,5-bis(benzeneboronate) (2), was not isolated, since aqueous 1-butanol used in the chromatographic work-up of the reaction mixture effects complete hydrolysis of benzeneboronates⁷. Since α -D-glucofuranose 1,2:3,5-bis(benzeneboronate) can be obtained easily and in almost quantitative yield, the yield of the crystalline product represents a 40% conversion of D-glucose into 6-*O*-methyl-D-glucose. It is likely that the yield of the methylation step could be considerably increased by more efficient use of diazomethane.



The alkylation described here is complementary to the various esterifications^{6,8} of the primary hydroxyl group in compound **1**. Treatment of other benzeneboronates with diazomethane, in the presence of boron trifluoride, has provided access to partially methylated alditols, *viz.* 1- and 2-*O*-methylglycerol, 1-, 2-, and 3-*O*-methyl-*L-erythro*-butane-1,2,3-triol, 2- and 3-*O*-methyl-*ribo*-pentane-2,3,4-triol, and 2-*O*-methyl-*xylo*-pentane-2,3,4-triol. An account of this work will be the subject of another communication.

EXPERIMENTAL

α -D-Glucofuranose 1,2:3,5-bis(benzeneboronate) (1). — D-Glucose (1.00 g), benzeneboronic anhydride (1.15 g), and 2-methoxyethanol (30 ml) were heated on a steam bath for 1 h, after which time complete dissolution had occurred. Evaporation of the solvent under reduced pressure, followed by drying *in vacuo* over conc. sulphuric acid for 3 days yielded 1 (1.91 g), m.p. 160–161°. Recrystallisation from toluene raised the m.p. to 161–162°, lit.⁴ m.p. 166°.

6-O-Methyl- α -D-glucopyranose. — A solution of diazomethane (0.5 g) in dichloromethane (20 ml) was added to a cooled (*ca.* –5°) solution of 1 (1.20 g) and boron trifluoride etherate (0.04 ml) in dichloromethane (20 ml), until a yellow colour persisted for a short time (*ca.* 5–10 sec). After a further 30 min, the precipitated polymethylene was removed by filtration and the filtrate was evaporated under reduced pressure. The residue was fractionated on a cellulose column (3 cm × 30 cm), using 1-butanol saturated with water as eluant. Fractions which had R_G 1.92 (1-butanol-ethanol-water, 40:11:19) were combined and evaporated to dryness. The residue was twice recrystallised from ethanol to give 6-O-methyl- α -D-glucopyranose (0.27 g), m.p. and mixed m.p. 143–144°, $[\alpha]_D^{20} +95^\circ$ (5 min) → +61° (equil., *c* 1.0, water), M_G (borate) 0.88. These values are consistent with those reported^{1,9}.

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