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INTERACTION BETWEEN ACETONE AND SOME CARBOHYDRATE BENZENEBORONATES: SELECTIVE ACETONOLYSIS OF 2-PHENYL-1,3,2-DIOXABOROLANES

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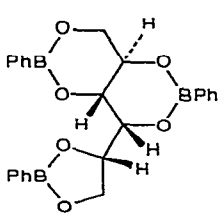
ABSTRACT

Treatment of D-glucitol 1,3:2,4:5,6-tris(benzeneboronate), D-mannitol 1,2:3,4:5,6-tris(benzeneboronate), and α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) with acidified acetone, followed by chromatography using lyotropic solvents, gives 5,6-*O*-isopropylidene-D-glucitol, 1,2-*O*-isopropylidene-D-mannitol, and 1,2-*O*-isopropylidene-α-D-glucofuranose, respectively, in yields of 43–78%.

INTRODUCTION

Cyclic alkane- and arene-boronates have received attention[1,2] as intermediates in the synthesis of carbohydrate derivatives, because they are readily obtainable in nearly quantitative yield and are easily hydrolysed. The utility in synthesis would be extended if graded hydrolysis or alcoholysis of bis- or tris-boronates could be achieved. With a few exceptions, such as the methanolysis of the nine-membered ring in galactitol 1,6:2,3:4,5-tris(ethylboronate)[3] and the six-membered ring in xylitol 1,3:4,5-bis(ethylboronate)[4], the products are usually the result of complete hydrolysis[5] or alcoholysis. The difference in stability of 1,3,2-dioxaborolanes and 1,3,2-dioxaborinanes is probably too small to allow selective hydrolysis. We have therefore sought the selective replacement of a benzeneboronate group (PhB<) so that the product is more stable to hydrolysis, and we now describe the selective acetonolysis of the benzeneboronates of D-glucitol (**1**), D-mannitol (**2**), D-glucose (**3**), and D-mannose.



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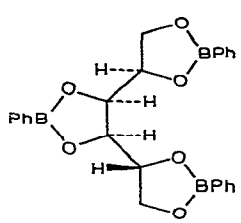

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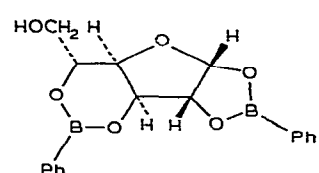

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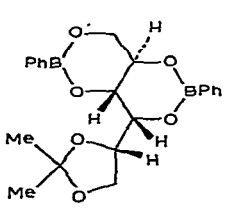
RESULTS AND DISCUSSION

It has been suggested[1] that a 6–60-fold excess of water causes complete hydrolysis of cyclic benzeneboronates. If the amount of water in admixture with acetone were kept below these levels, selective hydrolysis might occur and the liberated diols might be isopropylidenated. Alternatively, with the conjugate acid of acetone, selective acetonolysis might occur.

Treatment of D-glucitol 1,3:2,4:5,6-tris(benzeneboronate) (**1**) with dry acetone containing a small proportion of conc. sulphuric acid gave a single carbohydrate product in large yield. The electron-impact mass spectrum of the product mixture, obtained after removal of the sulphuric acid and acetone, contained peaks for **1** and benzeneboronic acid anhydride [$(PhBO)_3$] superposed on a series of peaks corresponding to an *O*-isopropylidene-D-glucitol bis(benzeneboronate) (*m/z* 394.1766, $C_{21}H_{24}B_2O_6$) and its expected fragments. An ion of greater abundance, $\%\Sigma_{40}$ 0.3, than the M^+ ion had *m/z* 395, $[M + 1]^+$. Such ions are frequently[6] encountered in the e.i.-mass spectra of cyclic acetals and ketals. An abundant ion with *m/z* 379.1516 ($C_{20}H_{21}B_2O_6$) indicated the loss of a methyl radical, a typical[6] fragmentation of *O*-isopropylidene compounds. The most abundant ion had *m/z* 101.0599 ($C_5H_9O_2$), which could only have arisen from a terminal 2,2-dimethyl-1,3-dioxolane moiety. These indicate that **1** had been converted into 5,6-*O*-isopropylidene-D-glucitol 1,3:2,4-bis(benzeneboronate) (**4**). Unfortunately, such compounds cannot be readily isolated from the reaction mixture.



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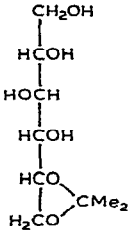

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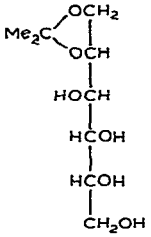

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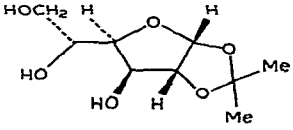

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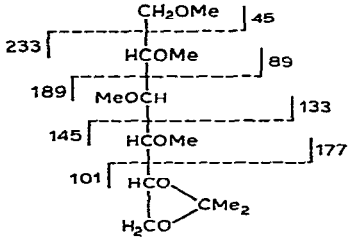

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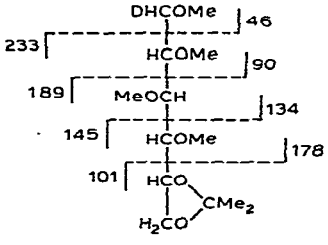

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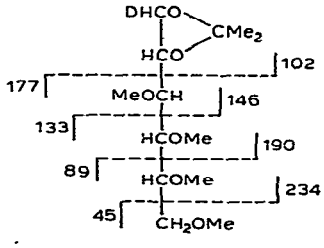

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Chromatography of the reaction mixture gave 5,6-*O*-isopropylidene-D-glucitol (**5**) (see Table I). The migration rate of **5** in molybdate electrophoresis showed[7] that it contained four adjacent hydroxyl-groups. The primary mass-spectral fragments obtained from the tetra-*O*-methyl derivative (**7**) of **5** and from the corresponding product (**8**) obtained from D-glucitol-*1*-d_1 tris(benzeneboronate) confirmed the 5,6-location of the *O*-isopropylidene group. For purposes of comparison, the primary fragments of 1,2-*O*-isopropylidene-3,4,5,6-tetra-*O*-methyl-D-glucitol-*1*-d_1 are shown in **9**.

TABLE I

ANALYSIS OF ACETONOLYSIS PRODUCTS

Benzeneboronate	*Product of acetonolysis and partial hydrolysis*		*Product of acetonolysis, partial hydrolysis, and acetylation*		
	R_{Glc}	Ms^a	T^b	$[M - 15]^+$ (% Σ_{40})	*Yield (%)*
D-Glucitol 1,3:2,4:5,6-tris-	2.41	0.93	2.67	2.5	43
D-Mannitol 1,2:3,4:5,6-tris-	3.40	0.93	2.15	3.8	78
α-D-Glucofuranose 1,2:3,5-bis-	2.61	—	1.90	6.6	63
D-Mannose bis-	2.78	—	2.03	—	trace
			2.16	10.0	50[c]
			2.24	—	trace

[a]Paper-electrophoretic migration-rate, relative to that of D-glucitol in molybdate[7]. [b]G.l.c. retention time, relative to that of 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-glucitol. [c]Estimated.

D-Mannitol forms the 1,2:3,4:5,6-tris(benzeneboronate)[8-10] (**2**) in almost quantitative yield[9]. Acetonolysis of **2** and partial hydrolysis of the resulting product gave 1,2-*O*-isopropylidene-D-mannitol (**6**, 78%). Acetonation[11] of D-mannitol in the presence of boric acid and partial hydrolysis of the resulting borate gave 15% of 1,2-*O*-isopropylidene-D-mannitol.

Acetonolysis of α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) at room temperature gave only a small yield of an *O*-isopropylidene derivative. This could be increased (Table I) by boiling the reaction mixture. The mass spectrum of the product of acetonolysis, partial hydrolysis, and acetylation was also indistinguishable from that of 3,5,6-tri-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose. The product of acetonolysis and partial hydrolysis was therefore 1,2-*O*-isopropylidene-α-D-glucofuranose (**10**).

E.i.-mass spectrometry of a crude D-mannose bis(benzeneboronate) preparation has shown[12] that it is a mixture of furanoid and pyranoid isomers, and acetonolysis, followed by chromatography and acetylation, gave, in high yield, a mixture of products which was not amenable to g.l.c. However, e.i.-mass spectrometry of the major component gave ions that could arise from molecular ions of tri-*O*-acetyl-*O*-isopropylidene-D-mannose through loss of $[Me]^{\cdot}$ from the isopropylidene group, $[AcO]^{\cdot}$ from C-1, $[CH_2OAc]^{\cdot}$ from a pyranoid form, and $[CH(OAc)CH_2OAc]^{\cdot}$ from a furanoid form, respectively. It is therefore likely that a 2,3-benzeneboronate had been replaced by a 2,3-*O*-isopropylidene group.

Although the concentration of water in the acidified acetone was not determined, we believe that it arises mainly from the conc. sulphuric acid and that the proportions of boronates and water were nearly equimolar. It has yet to be demonstrated whether water is at all essential for the reaction to occur. The fact that benzeneboronic anhydride rather than benzeneboronic acid was detected in the reaction mixture cannot be taken as evidence that PhBO [and thence $(PhBO)_3$] is a reaction product. Benezeneboronic acid dehydrates readily to give $(PhBO)_3$. The results of mechanistic studies will be reported elsewhere, but the results described here show that, in the four benzeneboronates studied, a 2-phenyl-1,3,2-dioxaborolane group can be selectively acetonolysed to give an *O*-isopropylidene derivative.

EXPERIMENTAL

General methods. — P.c. was performed with 1-butanol–ethanol–water (40:11:19), with detection by silver nitrate in acetone–ethanolic sodium hydroxide. For paper electrophoresis, 2% aqueous sodium molybdate dihydrate (adjusted to pH 5 with conc. H_2SO_4) was used.

Acetone (AnalaR grade) was dried over molecular sieve, type 4A.

T.l.c. was performed on silica gel (Camlab, Polygram Sil G) with butanone saturated with water. Benzeneboronic acid was detected with iodine vapour, and other compounds by charring with H_2SO_4.

G.l.c. was performed on a Pye 104 dual-column gas-chromatograph, fitted with glass columns (2 m × 4 mm i.d.) packed with 3% of OV225 on Gas Chrom Q; nitrogen was used as the carrier gas at ~40 ml/min. Retention times and peak areas were measured by a Hewlett Packard 3370B/71B integrator.

G.l.c.–m.s. was performed with a Perkin–Elmer F11 gas-chromatograph [fitted with a glass column (1.8 m × 44 mm i.d.) packed with 3% of OV225 on Gas Chrom Q and using helium as the carrier gas at 14 ml/min] linked *via* a Watson–Biemann separator to a Hitachi RMS-4 mass spectrometer operating at 80 eV and 50μA trap-current.

M.s. was performed with an A.E.I. MS-902 spectrometer operating at 70 eV and a trap current of 100μA. The low-resolution spectra and the precise masses were obtained by directly inserting the sample into the ion source maintained at 110°.

Acetonolysis of tris(benzeneboronates) of D-*glucitol and* D-*mannitol.* — Separate solutions of samples (0.06 g) of the tris(benzeneboronates) of D-glucitol and D-mannitol in dry acetone (20 ml) were acidified with conc. sulphuric acid (0.05 ml), left at room temperature for 14 h, and then neutralised with conc. ammonia, filtered, and concentrated under reduced pressure. P.c. and paper electrophoresis of the resulting syrups revealed, in addition to the hexitols and benzeneboronic acid, the components shown in Table I.

The yields of *O*-isopropylidene-D-glucitol and *O*-isopropylidene-D-mannitol were determined by chromatography on Whatman No. 3MM paper, elution of the carbohydrate components with water, acetylation, and quantitative g.l.c. The retention

times of the tetra-*O*-acetyl-*O*-isopropylidenehexitols are shown in Table I. Their yields (Table I) were calculated from the ratio of the peak areas corresponding to the tetra-*O*-acetyl-*O*-isopropylidenehexitol and the hexa-*O*-acetylhexitol.

Acetonolysis of bis(benzeneboronates) of D-*glucose and* D-*mannose.* — Separate solutions of α-D-glucofuranose 1,2:3,5-bis(benzeneboronate)[9] (0.1 g) and D-mannose bis(benzeneboronate)[12] (0.1 g) in dry acetone (10 ml) were acidified with conc. sulphuric acid (0.1 ml) and boiled under reflux for 15 h. Each solution was then processed and analysed as described above. The results are shown in Table I.

Methylation and g.l.c.–m.s. of O-isopropylidene derivatives. — D-Glucitol 1,3:2,4:5,6-tris(benzeneboronate), D-glucitol-*l*-d_1 1,3:2,4:5,6-tris(benzeneboronate), and D-mannitol 1,2:3,4:5,6-tris(benzeneboronate) (each, 0.03 g) were separately acetonolysed as described above. The reaction mixtures were fractionated on Whatman No. 3MM paper, but only the products having the R_{Glc} values shown in Table I were eluted from the chromatograms and conventionally methylated by shaking with *N*,*N*-dimethylformamide (0.5 ml), silver oxide (0.5 g), and methyl iodide (0.5 ml) for 24 h. Each product was analysed by g.l.c.–m.s. and found to contain a single component.

*1,2-O-Isopropylidene-*D-*mannitol*[11] (**6**). — A solution of D-mannitol 1,2:3,4:5,6-tris(benzeneboronate) (1 g) in dry acetone (30 ml) was acidified with conc. sulphuric acid (0.15 ml), left at room temperature for 2 days, and then neutralised (conc. ammonia), filtered, and concentrated to dryness under reduced pressure. A solution of the residue and propane-1,3-diol (0.6 g) in dry acetone (20 ml) was stored at room temperature for 3 h and then concentrated under reduced pressure; the 2-phenyl-1,3-dioxaborinane was distilled at 90°/1 mmHg. T.l.c. of the residue revealed a trace of benzeneboronic acid. The above procedure was repeated with more propane-1,3-diol (0.3 g), affording a residue free from benzeneboronic acid. The residue was extracted with boiling acetone (30 ml). Traces of D-mannitol were removed by elution of the extracted material from a column (1.5 × 85 cm) of Dowex-1 X8 (HO^-) resin (200–400 mesh) with water. Evaporation of fractions (10 ml) 15–19, with recrystallisation of the product from acetone, furnished **6** (0.22 g), m.p. and mixture m.p. 167–168°.

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