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INTERACTION OF BENZENEBORONIC ANHYDRIDE WITH ACYCLIC VICINAL PENTAOLS: METHYLATION ANALYSIS AND E.I.-MASS SPECTROMETRY OF THE PRODUCTS

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ABSTRACT

The bis(benzeneboronates) obtained by the interaction of benzeneboronic anhydride with D-arabinitol, ribitol, xylitol, 1-deoxy-D-glucitol, 1-deoxy-L-gulitol, 1-deoxy-L-mannitol, and 1-deoxy-D-talitol are mixtures and contain isomeric 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo[4.4.0]decanes, 4,4′-bi-2-phenyl-1,3,2-dioxaborolanes, and 2-phenyl-4-(2-phenyl-1,3,2-dioxaborolan-4-yl)-1,3,2-dioxaborinanes.

INTRODUCTION

The products of the reaction between benzeneboronic anhydride [$(PhBO)_3$] and vicinal triols and tetraols are mainly mixtures of structural isomers. Thus, the preparations obtained from vicinal triols[1] are mixtures of 2-phenyl-1,3,2-dioxaborolanes and 2-phenyl-1,3,2-dioxaborinanes, whereas those from vicinal tetraols[2] are mixtures of 4,4′-bi-2-phenyl-1,3,2-dioxaborolanes and 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo[4.4.0]decanes. In several cases, the compositions of such mixtures have been related to conformational effects within the products. We now report on the benzeneboronates of seven acyclic (vicinal) pentaols, namely, D-arabinitol, ribitol, xylitol, 1-deoxy-D-glucitol, 1-deoxy-L-gulitol, 1-deoxy-L-mannitol, and 1-deoxy-D-talitol. The methods used were methylation analysis and electron-impact(e.i.)-mass spectrometry.

RESULTS AND DISCUSSION

Crystalline preparations of bis(benzeneboronates) of D-arabinitol, ribitol, and xylitol have been reported[3,4], but it is doubtful whether these are the sole products of the reaction between the pentaols and benzeneboronic anhydride. Oxidation by periodate[4] of the *O*-phenylcarbamoylpentaols, obtained after treatment of the recrystallised bis(benzeneboronates) with phenyl isocyanate, followed by hydrolysis of the boronate ring, has already indicated that these materials are likely to be mixtures

TABLE I

SIGNIFICANT IONS PRODUCED FROM BENZENEBORONATES OF PENTAOLS

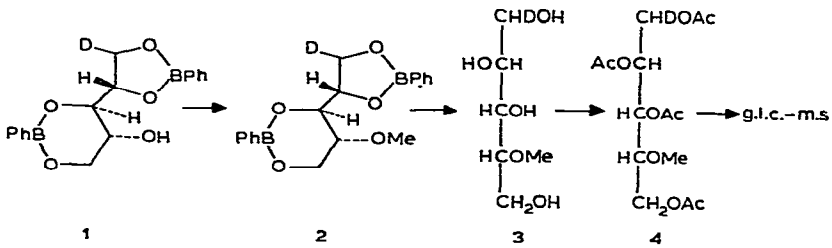
Parent pentaol	*Abundances of ions (% Σ_{30})*									
	m/z *31*	m/z *147*	m/z *159*	m/z *160*	m/z *161*	m/z *173*	m/z *174*	m/z *177*	$[M-31]^+$	M^{+a}
D-Arabinitol (**18**)	2.6	8.2	2.2	0.1	—	—	—	0.7	0.2	2.2 (324.1328)
Ribitol (**22**)	2.0	14.0	8.8	6.0	—	—	—	0.8	0.5	1.4 (324.1354)
Xylitol (**26**)	2.8	17.0	8.8	5.3	—	—	—	4.9	0.2	3.7 (324.1328)
1-Deoxy-D-glucitol (**30**)	4.0	3.2	3.2	—	2.8	0.8	0.6	—	0.7	2.0 (338)
1-Deoxy-L-gulitol (**34**)	3.0	1.2	0.8	2.3	6.9	0.2	0.7	—	—	0.2 (338)
1-Deoxy-L-mannitol (**41**)	0.6	6.1	8.2	—	1.4	1.4	0.7	0.2	—	1.1 (338.1498)
1-Deoxy-D-talitol (**45**)	2.0	5.5	8.1	3.8	5.5	1.2	0.6	1.8	0.4	2.0 (338.1504)

[a]The *m/z* value is given in parentheses.

of structural isomers. Unfortunately, g.l.c. proved to be unsatisfactory for fractionation of the bis(benzeneboronate) preparations. We have therefore performed the analysis on the crude bis(benzeneboronates).

The largest ions in the low-resolution mass spectrum of each benzeneboronate preparation had *m/z* corresponding to the expected molecular ion, M^{+}. Precise mass measurements confirmed these assignments and that the preparations were indeed bis(benzeneboronates) (Table I).

The bis(benzeneboronates) were subjected to methylation analysis, illustrated in Scheme 1 for a bis(benzeneboronate) of D-arabinitol-*1*-d_1 and used in the analysis of benzeneboronates of acyclic triols[1]; there is a formal analogy with linkage analysis of polysaccharides[5]. Methylation was effected with diazomethane–boron trifluoride, and was followed by hydrolysis, acetylation of the resulting *O*-methylpentaol, and g.l.c.–m.s.



Scheme 1. Methylation analysis of bis(benzeneboronates) of pentaols.

It could be argued[6,7] that benzeneboronates possessing a suitably orientated hydroxyl group should be regarded as tautomers, that they could isomerise (*e.g.*, **5**→**7**) *via* ionic intermediates (*e.g.*, **6**), and that methylation could involve a change of structure. However, treatment[8] of α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) with diazomethane–boron trifluoride gives 6-*O*-methyl-α-D-glucofuranose 1,2:3,5-bis(benzeneboronate) as the sole product and in almost quantitative yield[1]. In order to ascertain whether the structures of benzeneboronates of acyclic polyols remain

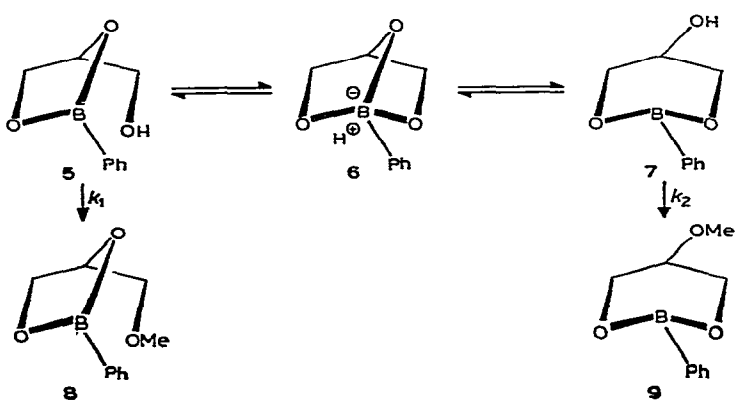


TABLE II

METHYLATION ANALYSIS OF BIS(BENZENEBORONATES) OF PENTAOLS

Parent pentaol	*G.l.c.–m.s. of products from methylation, hydrolysis, and acetylation*				
	T[a]	*Mole fraction*	*Primary fragments*[b] (m/z)	*Identity*	*Parent boronate*
D-Arabinitol (18)	1.20	0.52	45	11[c]	19,20
	1.70	0.48	117,261	10[c]	21
Ribitol (22)	0.92	0.86	45	11	23,24
	1.23	0.14	117,261	10	25
Xylitol (26)	1.25	0.95	45,289	11	27,28
	1.58	0.05	117,261	10	29
1-Deoxy-D-glucitol (30)	1.57	0.79	45	17	31,32
	2.08	0.21	117,275	16	33
1-Deoxy-L-gulitol (34)	1.21	0.74	45	17	35,36
	1.48	0.19	59	14	37,38
	1.60	0.02	117,275	16	39
	1.80	0.05	131,261	15	40
1-Deoxy-L-mannitol (41)	1.19	0.79	45	17	42,43
	1.80	0.21	117,275	16	44
1-Deoxy-D-talitol (45)	0.86	0.42	45	17	46,47
	1.06	0.40	59	14	48,49
	1.91	0.18	131,261	15	50

[a]Retention time relative to that of 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-glucitol. [b]See Fig. 1. [c]Assigned by using deuterium-labelled pentaol.

unchanged during methylation, we have reinvestigated the methylation analysis of the two benzeneboronates of glycerol[1].

If the rates of isomerisation **5**⇄**7** were comparable to, or faster than, those (k_1 and k_2) of the methylation reactions, the results of the methylation analysis would reflect the relative values of k_1 and k_2 and the resulting data would be of little value in structure determination. However, if isomerisation were the rate-determining process, whether $k_1 = k_2$ or $k_1 \neq k_2$, the more abundant ether (**8** or **9**) would correspond to the more abundant benzeneboronate (**5** or **7**). Methylation analysis of the crude and recrystallised benzeneboronate preparations of glycerol revealed[1] **9** and **8** to be the respective, more abundant products of methylation. Thus, if isomerisation occurs at all, the rate-determining processes are the isomerisation reactions **5**⇄**7**, and methylation analysis is a valid method for structure determination of benzeneboronates possessing a hydroxyl group*.

*Note added in proof. The boron in such structures as **5** and **7**, *i.e.*, possessing a hydroxyl group suitably orientated for the formation of ionic intermediates (*e.g.*, **6**), would be expected to play the same role as that in the BF_3 of the methylating reagent (diazomethane–boron trifluoride), and methylation should be achieved by reaction with diazomethane alone. Since this report was submitted, the two benzeneboronates of glycerol were separately treated with diazomethane, but no products could be detected. Therefore, **6** is not formed and the criticism[7] of our earlier work has no experimental basis. We thank Dr. R. A. Hancock for helpful discussions.

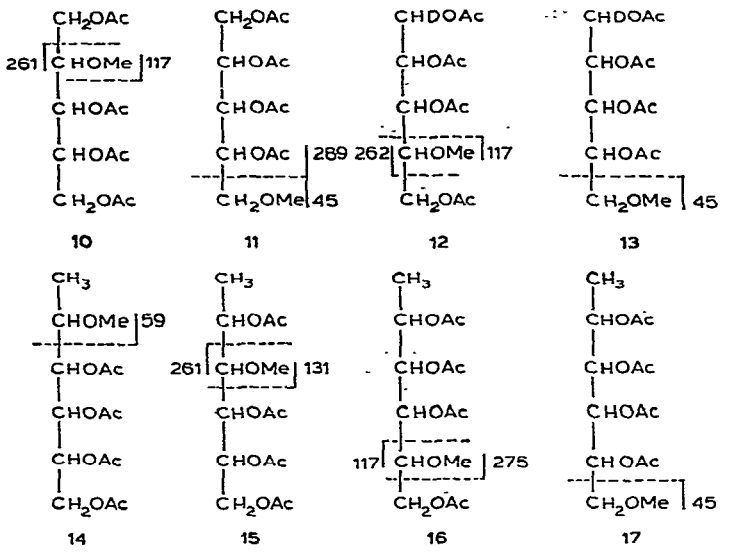


Fig. 1. Primary fragmentation modes of tetra-*O*-acetyl-*O*-methylpentaols (stereochemistry at asymmetric carbon atoms is not shown).

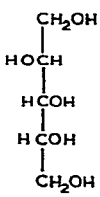
Chromatography showed that methylation was essentially complete, and the results of the methylation analysis revealed that each bis(benzeneboronate) preparation in Table II was a mixture of structural isomers. The possible structures are shown in Fig. 2; it is unlikely that isomers are formed which possess the 1,3,2-dioxaborepane ring[9]. The method does not, of course, distinguish between 4,4'-bi-2-phenyl-1,3,2-dioxaborolanes (*e.g.*, **20**) and 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo-[4.4.0]decanes (*e.g.*, **19**; see below), but each preparation was shown to contain a 2-phenyl-4-(2-phenyl-1,3,2-dioxaborolan-4-yl)-1,3,2-dioxaborinane (*e.g.*, **21**), with mole fractions ranging from 0.02 (**39**) to 0.48 (**21**).

From the data in Table II, the 1,3,4,5-tetraacetoxy-2-methoxypentane (**10**) and 1,2,3,4-tetraacetoxy-5-methoxypentane (**11**) could have the D-*arabino* and/or the L-*lyxo* configuration. This ambiguity was removed by using D-arabinitol-*1*-d_1; mass spectrometry of the product obtained according to Scheme 1, and having *T* 1.20, then showed that the ratio of the ions with *m/z* 45 and 46 remained unchanged (*cf.* **13**). On the other hand, the product with *T* 1.70 gave a mass spectrum with peaks corresponding to *m/z* 117 and 262, but not 261 (*cf.* **12**). Consequently, the components with *T* 1.20 and 1.70 were 1,2,3,4-tetra-*O*-acetyl-5-*O*-methyl- and 1,2,3,5-tetra-*O*-acetyl-4-*O*-methyl-D-arabinitol, respectively, originating from the bis(benzeneboronates) shown in Fig. 2.

E.i.-mass spectrometry

E.i.-m.s. of the crude benzeneboronate preparations confirmed that each contained a component possessing a primary hydroxyl group, evidenced by the

Parent pentaol



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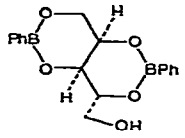
Benzeneboronate



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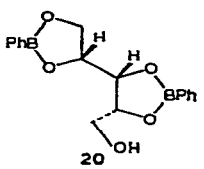

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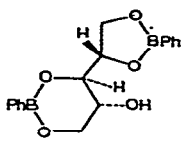

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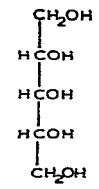

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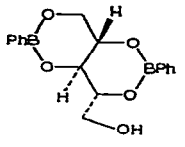

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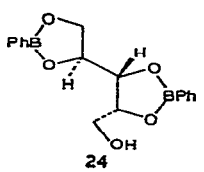

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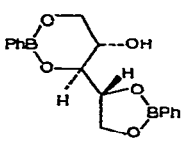

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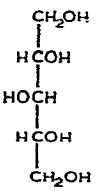

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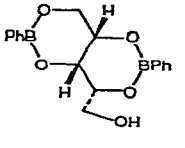

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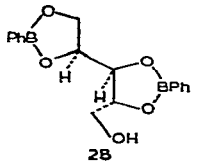

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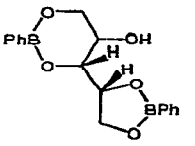

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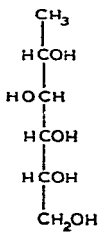

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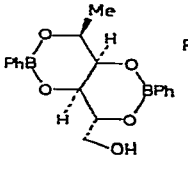

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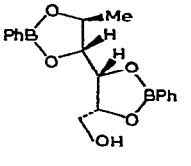

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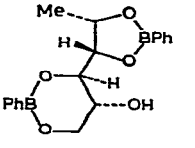

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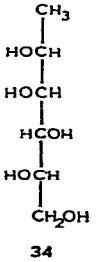

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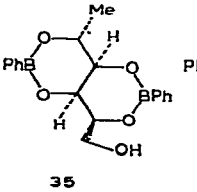

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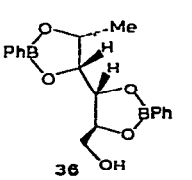

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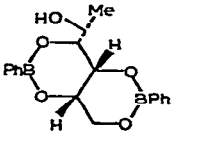

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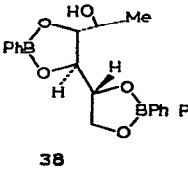

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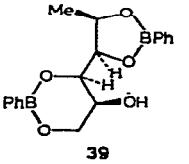

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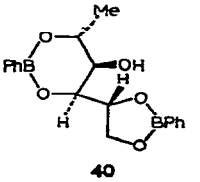

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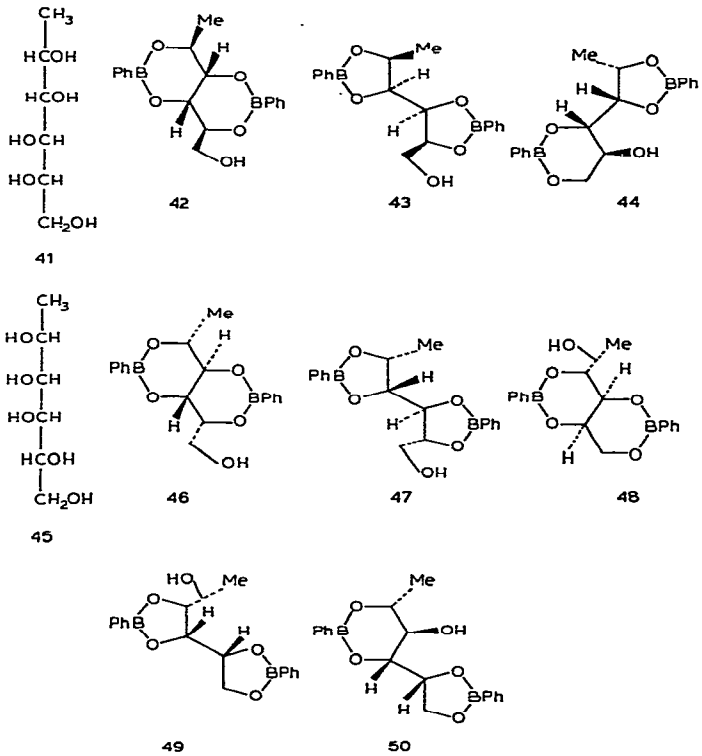
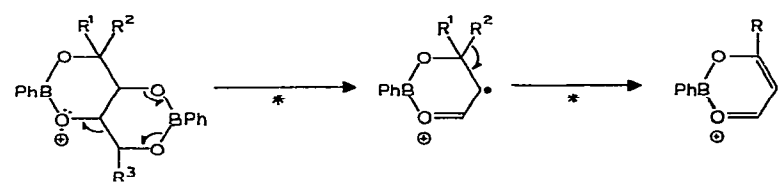


Fig. 2. Structures of bis(benzeneboronates) of pentaols.

formation of an $[M - 31]^+$ ion and/or the ion with m/z 31 corresponding to $[CH_3O]^+$.

It has been shown[2] that the isomeric 4,4'-bi-2-phenyl-1,3,2-dioxaborolanes and 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo[4.4.0]decanes can be distinguished by their e.i.-induced fragmentation, giving rise to D- (Scheme 2) and B-ions (Scheme 3), respectively. Table I shows that the benzeneboronate preparations of the

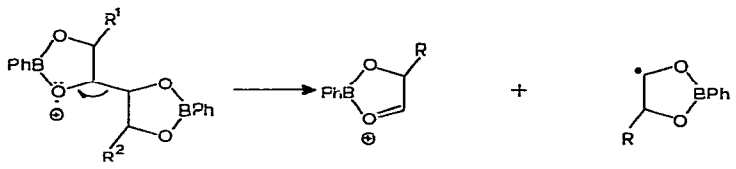


51a $R^1=R^2=H, R^3=CH_2OH$; m/z 324 52a $R^1=R^2=H$; m/z 160 53a R=H; m/z 159

51b $R^1=H, R^2=Me, R^3=CH_2OH$; m/z 338 52b $R^1=H, R^2=Me$; m/z 174 53b R=Me; m/z 173

51c $R^1=R^2=H, R^3=CH(OH)CH_3$; m/z 338

Scheme 2. Fragmentation of molecular ions of 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo[4.4.0] decanes, giving D-ions: *, transition evidenced by metastable ion.



54a $R^1=H, R^2=CH_2OH$; *m/z* 324 55a R=H; *m/z* 147 56a R= H

54b $R^1=Me, R^2=CH_2OH$; *m/z* 338 55b R=Me; *m/z* 161 56b R= Me

54c $R^1=H, R^2=CH(OH)CH_3$; *m/z* 338 55c $R=CH_2OH$; *m/z* 177 56c $R=CH_2OH$

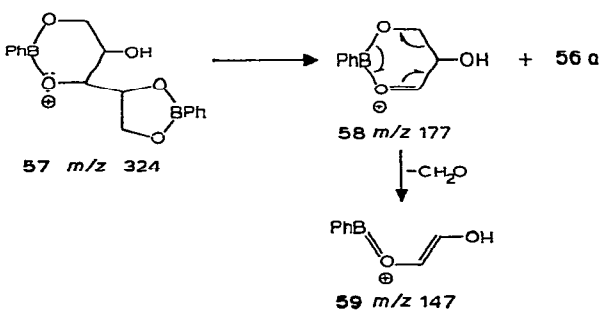
56d $R=CH(OH)CH_3$

Scheme 3. Fragmentation of molecular ions of 4,4′-bi-2-phenyl-1,3,2-dioxaborolanes, giving B-ions.

seven pentaols each gave D-ions (*m/z* 159, 160, 173, and/or 174). Therefore they contain the corresponding derivatives shown in Fig. 2, namely, **19**, **23**, **27**, **31**, **35**, **37**, **42**, **46**, and **48**.

Unfortunately, the isomeric 4,4′-bi-2-phenyl-1,3,2-dioxaborolanes and 2-phenyl-4-(2-phenyl-1,3,2-dioxaborolan-4-yl)-1,3,2-dioxaborinanes, *e.g.*, **20** and **21**, respectively, cannot be distinguished by their primary fragments. Both would be expected to give ions with *m/z* 147 (**55a**) and 177 (**55c** or **58**). However, of the possible structures (*cf.* methylation analysis) of the bis(benzeneboronates) of 1-deoxy-D-talitol, only the 5-methyl-5′-hydroxymethyl-4,4′-bi-2-phenyl-1,3,2-dioxaborolane **47** could give ions with *m/z* 61 and 177 (*cf.* Table I). 1-Deoxy-D-talitol therefore gives at least four benzeneboronates, namely **46**, **47**, **48**, and **50**.

The ion with *m/z* 177 in the mass spectrum of the benzeneboronate preparation of xylitol could be either the ion **55c** (from **28**) or **58** (from **29**). As the boronate **29** represents only 5% of the product (cf. Table II), it is unlikely that an ion of such abundance (% Σ_{30} 4.9) arises from **29** and it more likely originates from the boronate **28**. For the same reason, the fragments with *m/z* 147 (**55a**; see also below) from the boronate preparations of D-arabinitol, ribitol, and xylitol are likely to be formed from compounds **20**, **24**, and **28**, respectively.



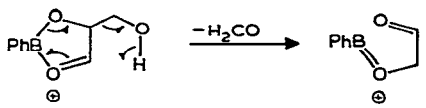
57 *m/z* 324 **58** *m/z* 177 **59** *m/z* 147

Scheme 4.

The boronate preparations of 1-deoxy-D-glucitol and 1-deoxy-D-mannitol each gave an ion with *m/z* 147 ($C_8H_8BO_2^+$). Such ions cannot be primary fragments

from the possible structures **31**, **32**, and **33**, or **42**, **43**, and **44**. However, they could arise from the primary ions **58** and **55c** by loss of CH_2O (as shown in Schemes 4 and 5, respectively) and, indeed, these transitions are evidenced by metastable ions.

A distinction between these two routes cannot be made, but, in view of the foregoing conclusions, it is likely that all of the pentaols examined gave the boronates shown in Fig. 2 and that, therefore, a significant portion of the ions with *m/z* 147 are formed as designated by **58**→**59** and **55c**→**60**.



55 c *m/z* 177 60 *m/z* 147

Scheme 5.

The methods used here do not allow a quantitative assessment of the relative proportions of the 4,4′-bi-2-phenyl-1,3,2-dioxaborolanes and 2,7-diphenyl-1,3,6,8-tetraoxa-2,7-diborabicyclo[4.4.0]decanes. On the other hand, the 2-phenyl-4-(2-phenyl-1,3,2-dioxaborolan-4-yl)-1,3,2-dioxaborinane derivatives possessing in each chair conformation of the 6-membered ring an axial hydroxyl and/or methyl group (**29**, **39**, and **40**) are only minor products (*cf.* Table II).

EXPERIMENTAL

Benzeneboronates of pentaols. — A mixture of pentaol (~0.5 g), benzeneboronic anhydride [$(PhBO)_3$, 0.66 mol., except for ribitol where 6 mol. was used], and dry 2-methoxyethanol (10 ml) was heated at ~100° for 1 h. Evaporation of the solvent under reduced pressure yielded either a white, crystalline residue, or a viscous syrup from which water was removed by repeated dissolution in toluene and evaporation of the solvent.

Tetra-O-acetyl-O-methylpentaols. — To a solution of each pentaol bis(benzeneboronate) (~0.10 g) in 0.1% boron trifluoride etherate in 1,2-dimethoxyethane (5 ml) at −10° was added diazomethane in dichloromethane (5 ml; prepared by the method of de Boer and Backer[10]); after 3 min, a further portion (5 ml) was added, causing a yellow colour to persist for ~0.5 h. P.c. (1-butanol–ethanol–water, 40:11:19) of the reaction mixture revealed either traces of pentaol or its absence.

Polymethylene was removed, the filtrate was concentrated under reduced pressure to a small volume, and fractionated on Whatman 3MM paper with 1-butanol–ethanol–water (40:11:19). Each *O*-methylpentaol was eluted with water from the appropriate area of the chromatogram. Concentration of the eluate under reduced pressure left a thin syrup that was treated with acetic anhydride (1 ml) and pyridine (1 ml) at 90° for 10 min. The solvent was evaporated and the residue (dissolved in chloroform) was subjected to g.l.c. and g.l.c.–m.s.

G.l.c. was performed on a Pye 104 dual-column gas-chromatograph containing glass columns (2.7 m × 4 mm i.d.) packed with 3% of OV225 on Gas Chrom Q (100–120 mesh), and using nitrogen at ~40 ml/min. Retention times (T) and peak areas were measured with a Hewlett Packard 3370B/71B integrator.

G.l.c.–m.s. was performed on a Perkin–Elmer F11 gas chromatograph [containing a glass column (3.7 m × 4 mm i.d.) packed as described above, and using helium at ~14 ml/min and a Watson–Bieman separator] connected to a Hitachi RMS-4 mass spectrometer operating at 80 eV.

M.s. was performed on an A.E.I. MS-902 spectrometer operating at 70 eV with a trap current of 100 μA. Low-resolution spectra, precise masses, and metastable-ion data were obtained by the direct-insertion procedure with the ion source maintained at 110 or 160° [1-deoxy-L-gulitol bis(benzeneboronate) preparation].

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