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BENZENEBORONATES OF ACYCLIC TRIOLS

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ABSTRACT

Structures have been assigned to the benzeneboronates of glycerol, DL-butane-1,2,4-triol, L-*erythro*-butane-1,2,3-triol, and L-*arabino*-, *ribo*-, and *xylo*-pentane-2,3,4-triols All, except the benzeneboronate of *xylo*-pentane-2,3,4-triol, are mixtures of isomers The abundance of the isomers has been related to conformational effects

INTRODUCTION

Thermodynamic and mechanistic aspects of the formation and hydrolysis of benzeneboronates of 1,2- and 1,3-diols have been investigated in several laboratories[1–4] We now report on the structures of the benzeneboronates formed from acyclic triols

It has already been reported[1,5] that the benzeneboronate of glycerol has structure **1** (Fig 1) The assignment was based, *inter alia*, on the amount of periodate reduced (~1 mol) by the *O*-phenylcarbamoylglycerol obtained after treatment of the recrystallised glycerol benzeneboronate with phenyl isocyanate, followed by hydrolysis of the benzeneboronate ring These experiments have been repeated, with only small modifications, and have shown that, in aqueous *N*,*N*-dimethylformamide, the *O*-phenylcarbamoylglycerol reduced 0 84 mol of periodate with concomitant formation of 0 83 mol of formaldehyde These results essentially confirm the earlier conclusions However, although the melting points of the benzeneboronate and its phenylcarbamoyl derivative had indicated a reasonable degree of purity, it seemed likely that the discrepancy between the above values and unity was due to the benzeneboronate being a mixture of compounds **1** and **2** Results obtained with benzeneboronates of other triols were similarly suspect Mass spectrometry had also indicated that some of these substances might be mixtures of isomeric modifications[6] It thus seemed necessary to determine the composition of mixtures of products, qualitatively as well as quantitatively

RESULTS AND DISCUSSION

The triols used for the preparation of benzeneboronates are shown in Table I,

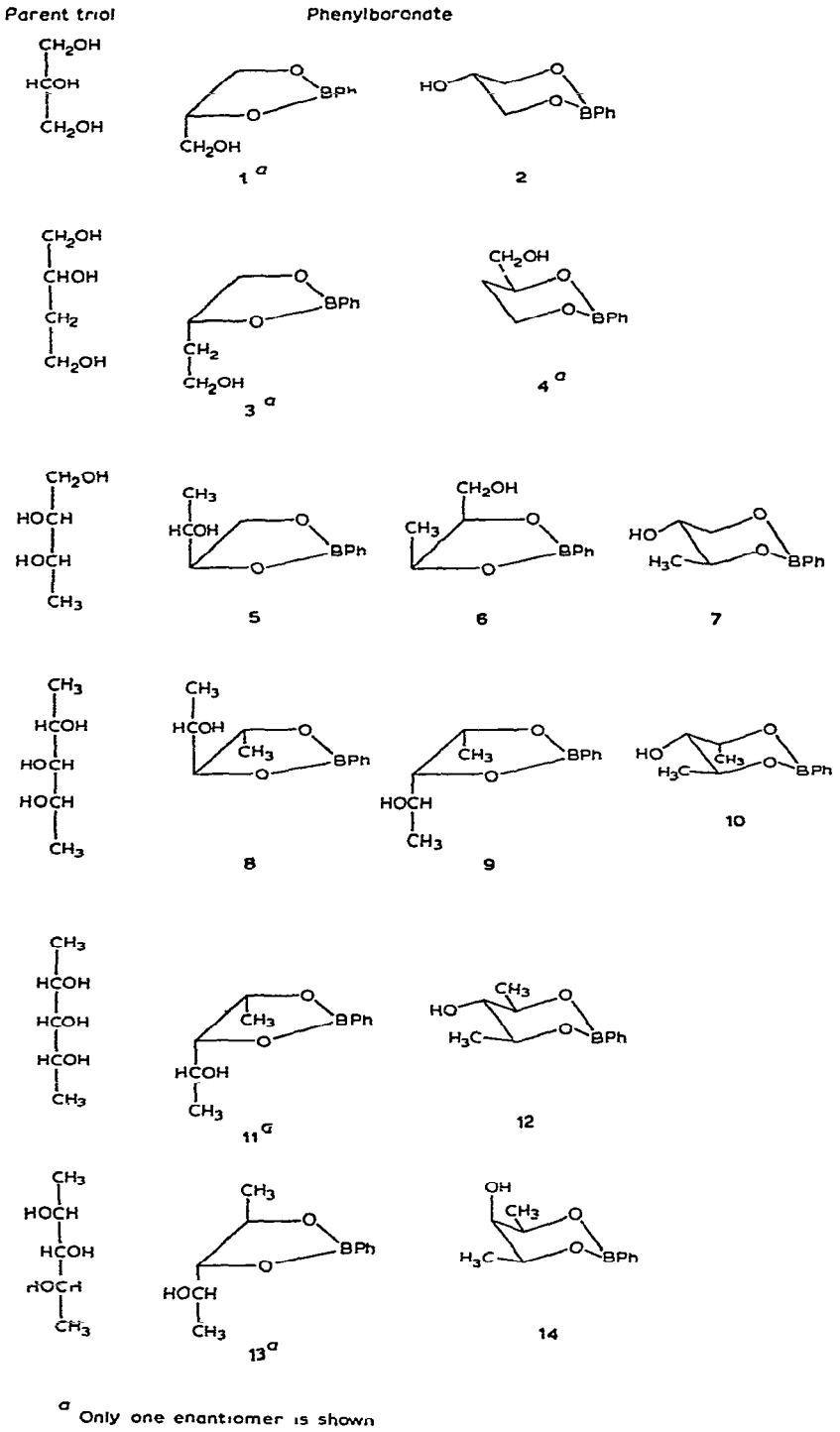
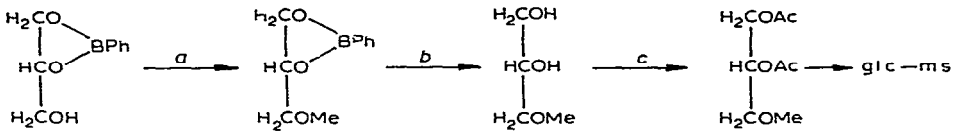


Fig. 1 Possible structures of benzeneboronates of triols

together with the properties of the benzeneboronate preparations obtained by reaction between the triols and 0 33 mol of benzeneboronic anhydride Crystalline materials were obtained from glycerol and L-*erythro*-butane-1,2,3-triol The other triols produced viscous liquids, approximately one half of which could be distilled The discrepancies in the boron analyses of the products from *ribo*- and *xylo*-pentane-2,3,4-triol are probably due to incomplete reaction, the distillates and the involatile residues containing, respectively, unreacted triol and benzeneboronic anhydride The mass spectra of these involatile residues contained peaks corresponding to the molecular ion of benzeneboronic anhydride, *i e*, $C_{18}H_{15}B_3O_3^{+\cdot}$ (*m/e* 312) The mass spectrum of the involatile residue obtained from *xylo*-pentane-2,3,4-triol also contained a peak corresponding to an ion with mass number (*m/e* 421) greater than that of the molecular ion of a monomeric benzeneboronate, *i e*, $C_{11}H_{15}BO_3^{+\cdot}$ (*m/e* 206) For the other products, the ions of highest mass number corresponded to the molecular ion of a monomeric benzeneboronate Essentially no further differences between each pair of distillate and involatile residue were revealed by the subsequent analysis (see below) We thus conclude that the involatile residues are polymeric modifications of the monomeric distillate

The method of analysis of the benzeneboronates involved the following chemical transformations, outlined for a benzeneboronate of glycerol (scheme 1) (*a*) methylation of the unsubstituted hydroxyl group, using diazomethane in the presence of boron trifluoride [it is unlikely that this reagent effects rearrangement of benzeneboronate rings, as α-D-glucofuranose 1,2 3,5-bis(benzeneboronate)[7] gives 6-*O*-methyl-α-D-glucofuranose 1,2 3,5-bis(benzeneboronate) as the sole product[8a] and in almost quantitative yield[8b]]; (*b*) hydrolysis of the boronate ring, and (*c*) acetylation of the hydroxyl groups generated in step (*b*) The reaction mixture thus obtained was analysed by g l c –m s



Scheme 1.

The primary fragmentation modes under electron impact of *O*-acetyl-*O*-methyl-alditols are now well-established[9,10]. We have shown that the primary fragments (resulting from the fission of one bond and occurring with abundance >10% of base peak) from di-*O*-acetyl derivatives of authentic[11] 1-*O*-methyl-DL-glycerol (**16**) and 2-*O*-methylglycerol (**17**) have *m/e* 45 and 117, respectively (Fig 2). Thus, the mass numbers of primary fragments can also be used in the assignment of structures to compounds encountered in the present investigation (Fig 2) Benzeneboronates which failed to become methylated in step (*a*) of scheme 1 will, by the above procedure,

TABLE I

PROPERTIES AND ANALYSIS OF BENZENEBORONATES OF TRIOLS (FOR DETAILS SEE TEXT)

Parent triol	*Boronate fraction*	*M p (degrees)*	*B.p*	*Analysis*			*G l.c –m s. of products from methylation, hydrolysis, and acetylation*					*Order of abundance of boronate*
				Molecular ion (and m/e)	*B (%)*		T[a]	*Mole fraction*	*Primary fragment* (m/e)	*Identity*	*Parent boronate*	
					Found	*Calc.*						
Glycerol	Recryst (benzene–hexane)	76–78		$C_9H_{11}BO_3$ (178 0801)	6 10	6 10	0.31 0 38 1.00	0 61 0 38 0 01	45 117 145	**16** **17** **15**	**1** **2**	**1<2**
	Crude reaction product						0 31 0 38	0 31 0 69	45 117	**16** **17**	**1** **2**	**2>1**
DL-Butane-1,2,4-triol[1]	Distillate		100–103° 0 05 mmHg	$C_{10}H_{13}BO_3$ (192 0960)	5.55	5 62	0 29 0 32 0 96	0 07 0 88 0 05	45,131 45 159	**19** **20** **18**	**3** **4**	**4>3**
	Involatile residue			$C_{10}H_{13}BO_3$ (192.0956)	5 72	5 62	0 29 0.32 0 96	0 06 0 89 0 05	45,131 45 159	**19** **20** **18**	**3** **4**	**4>3**

L-*erythro*-Butane-1,2,3-triol	Recryst. (hexane)	75–76		$C_{10}H_{13}BO_3$ (192 0954)	5 60	5 62	0 31 0 35 0 37 0 80	0.08 0 26 0.51 0 15	45 59 117,131 87,145	**24** **22** **23** **21**	**6** **5** **7**	See text
L-*arabino*-Pentane-2,3,4-triol[16]	Distillate		90–94° 0 2 mmHg	$C_{11}H_{15}BO_3$ (206 1114)	5 25	5 24	0 32 0 71	96 4	59 87,159	**26** **25**	8 and 9[b]	8>9[b]
	Involatile residue			$C_{11}H_{15}BO_3$ (206 1117)	5 33	5.24	0.32 0 71	95 5	59 87,159	**26** **25**	8 and 9[b]	8>9[b]
ribo-Pentane-2,3,4-triol	Distillate		116–120° 1 0 mmHg	$C_{11}H_{15}BO_3$ (206 1117)	4 85	5 24	0 29 0 31 0 65	24 72 4	59 131 87,159	**26** **27** **25**	**11** **12**	**12>11**
	Involatile residue			$C_{11}H_{15}BO_3$ (206.1110)	6 36	5 24	0 29 0 31 0 65	21 71 8	59 131 87,159	**26** **27** **25**	**11** **12**	**12>11**
xylo-Pentane-2,3,4-triol	Distillate		82–84° 0 1 mmHg	$C_{11}H_{15}BO_3$ (206 1115)	4 88	5 24	0 40	100	59	**26**	**13**	**13** only
	Involatile residue			$C_{11}H_{15}BO_3$ (206 1118)	6 47	5 24	0 40	100	59	**26**	**13**	**13** only

[a]Retention volume relative to that of tri-*O*-acetylglycerol [b]Assigned by using deuterium-labelled triol (see text)

be obtained as tri-*O*-acetyl derivatives. These can also be characterised from their primary fragments The results of the g l c–m.s analysis are shown in Table I

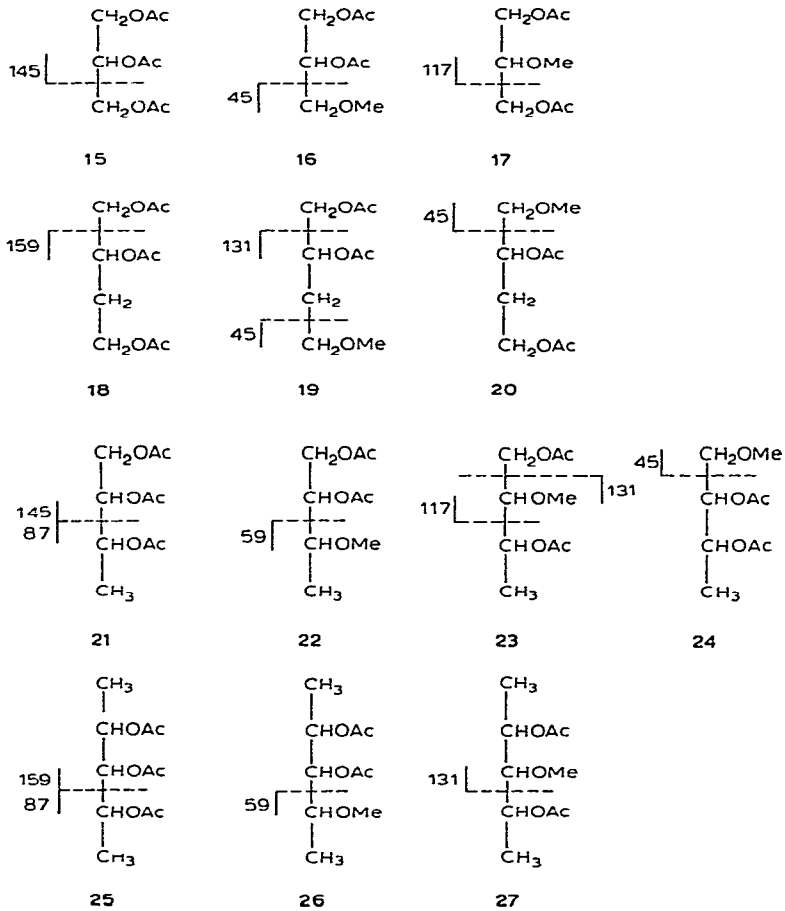


Fig 2 Primary fragmentation modes of tri-*O*-acetyltriols and di-*O*-acetyl-*O*-methyltriols (stereochemistry at asymmetric carbon atoms is not shown)

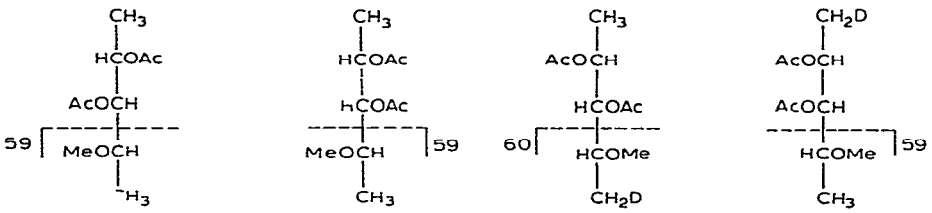
It is unlikely that any significant amount of the di-*O*-acetyl-*O*-methyl derivatives arises from unreacted triol, which some benzeneboronates might contain The pentane-2,3,4-triols would otherwise be expected to give mixtures of all possible isomers It is likely that unreacted triols are converted into tri-*O*-methyl derivatives which, because of their small retention volume, could not be detected

Since steps (*b*) and (*c*) of Scheme 1 are known[12–14] to proceed quantitatively, the amounts of the tri-*O*-acetyl derivatives obtained indicate the extent of the methylation reaction [step (*a*)] Table I shows that, with the exception of the benzeneboronate of L-*erythro*-butane-1,2,3-triol, this is >90% Although it was not always possible to

determine accurately the ratio of the products (if more than one) from the reaction between triols and benzeneboronic anhydride, the order of their abundance could, nevertheless, be ascertained

The results of the periodate oxidation of the *O*-phenylcarbamoylglycerol might suggest that the recrystallised glycerol benzeneboronate contains the 1,3- (**2**) and the DL-1,2-benzeneboronate (**1**) in the ratio 0 2 1 However, the results of the analysis according to Scheme 1 show that the recrystallised and the crude glycerol benzeneboronate contain the isomers **2** and **1** in the ratio 0.6 1 and 2 2 1, respectively It is apparent that the recrystallisation of glycerol benzeneboronate, as well as the isolation of the *O*-phenylcarbamoylglycerol benzeneboronate, had effected a partial fractionation of isomers These results show that the material to which a structure (**1**) has already been assigned[1 5] is not the major product, which is, in fact, glycerol 1,3-benzeneboronate (**2**).

On the evidence presented so far, the 2,3-diacetoxy-4-methoxypentane (**26**) obtained from the benzeneboronate of L-*arabino*-(or L-*lyxo*-)pentane-2,3,4-triol could have the L-*arabino* (**28**) or/and the L-*lyxo* configuration (**29**) This ambiguity was removed by using the benzeneboronate of D-*lyxo*-pentane-2,3,4-triol-*1*-d_1 The mass spectrum of the product, obtained by Scheme 1, contained peaks corresponding to primary fragments with *m/e* 60 (from **30**) and 59 (from **31**) with relative abundance of 5 7 1. The benzeneboronate obtained from L-*arabino*-(or L-*lyxo*-)pentane-2,3,4-triol is thus a 5 7 1 mixture of L-*arabino*-(**8**) and L-*lyxo*-pentane-2,3,4-triol 2,3-benzeneboronate (**9**)



28 29 30 31

The results obtained with the recrystallised benzeneboronate of L-*erythro*-butane-1,2,3-triol are reported merely to show that, in spite of its reasonably sharp melting-point, it is a mixture of all the three possible isomers (**5**, **6**, and **7**) Insufficient material was available for a more-accurate determination of the relative abundance of the isomers **5**–**7**.

Table I shows that, of the six triols investigated, only one, *xylo*-pentane-2,3,4-triol, forms a single benzeneboronate The other benzeneboronate preparations proved to be mixtures of structural isomers From their order of abundance, the following general observations are made The 6-membered-ring isomer is the major product if the non-hydrogen substituents on the 6-membered ring are equato-

rially disposed [*cf.* benzeneboronates of glycerol (**2**), DL-butane-1,2,4-triol (**4**), and *ribo*-pentane-2,3,4-triol (**12**)] When the 6-membered-ring isomer would possess such substituents axially disposed (*cf.* **10** and **14**), the 5-membered-ring isomers are the exclusive products [*cf* benzeneboronates of L-*arabino*-pentane-2,3,4-triol (**8** and **9**) and *xylo*-pentane-2,3,4-triol (**13**)] As anticipated, a 5-membered-ring isomer (**8**) with 1,2-*trans*-disposed carbon substituents is formed more readily than the isomer (**9**) possessing these substituents in a *cis* relationship

As yet, it is not clear whether the formation of bis-benzeneboronates follows the above pattern Although structures have been assigned[15] to some of the compounds formed from polyhydroxy compounds, studies analogous to those described here have not yet been carried out

EXPERIMENTAL

G l c –mass spectrometry — A Perkin–Elmer F11 gas-chromatograph containing a glass column (2 m × 1 mm) packed with 10% P P E on Chromosorb W (100–120 mesh) was used The carrier gas, helium, was removed from the effluent by passage through a Biemann separator The effluent was then passed into a Hitachi RMS-4 mass spectrometer operating at 80 eV and 50 μamp target current

Synthesis of triols — The structures of the synthesised triols and the purity of all triols were verified by periodate oxidation and g l c , respectively

L-erythro-*Butane-1,2,3-triol* — D-Erythrose (7 0 g), conc hydrochloric acid (10 5 ml), and ethanethiol (10 5 ml) were shaken for 3 h Water (100 ml) was added, and the mixture was neutralised with sodium carbonate and extracted with dichloromethane (2 × 100 ml) The extracts were combined, dried, and evaporated to yield D-erythrose diethyl dithioacetal as a syrup (10 2 g)

Treatment of this syrup (10 2 g) in refluxing ethanol (400 ml) with Raney nickel (180 ml) for 2 h, followed by removal of the nickel (decantation) and distillation, gave the title triol (2 1 g), b p 125–128°/1 mmHg, $[\alpha]_D^{22}$ +17 3° (*c* 2 5, water)

ribo-*Pentane-2,3,4-triol* — A mixture of 2,3,4-tri-*O*-benzoyl-1,5-di-*O*-toluene-*p*-sulphonylribitol[17] (50 0 g), lithium aluminium hydride (9 0 g), and dry tetrahydrofuran (800 ml) was refluxed and stirred for 4 h Excess hydride was destroyed with aqueous sodium hydroxide (10 ml, 15%), and insoluble material was removed and extracted with boiling methanol (1 litre). The extract was evaporated, the residue was dissolved in water (100 ml), and the solution was treated with Amberlite IR-120(H^+) resin The tetrahydrofuran solution was evaporated, and the residue was dissolved in water (100 ml) and extracted with toluene (100 ml) The aqueous solution was treated with Amberlite IR-120(H^+) resin, combined with that similarly treated above, treated with Amberlite IR-45(OH^-) resin until neutral, and distilled to give the title triol (3.5 g), b.p 146–150°/1 mmHg

xylo-*Pentane-2,3,4-triol* — 2,3,4-Tri-*O*-benzoyl-1,5-di-*O*-toluene-*p*-sulphonylxylitol[17] (50 g) was treated, as for the corresponding ribitol derivative above, to give

the title triol (2 8 g), b p 88–92°/0 5 mmHg The tri-*O*-acetyl derivative[17] had m p 122–124°

D-lyxo-*Pentane-2,3,4-triol*-1-d_1 — 5-Deoxy-D-arabinose-*5*-d_1 diethyl dithioacetal (1 55 g), m p 108–109°, was obtained from 5-*O*-toluene-*p*-sulphonyl-D-arabinose diethyl dithioacetal[18] (6 g) by the method of Zinner *et al* [19], using lithium aluminium deuteride Treatment with Raney nickel (15 ml) in 80% ethanol (150 ml) for 5 min, followed by extraction of the nickel with ethanol and distillation of the combined ethanolic solutions, yielded the title triol (0 50 g), b p 75–80°/0 1 mmHg

Preparation of benzeneboronates of triols — Triol (0 5–2 g) and benzeneboronic anhydride [$(PhBO)_3$, 0 33 molecular proportion] were heated in boiling benzene or toluene for 5–14 h The crude reaction product obtained by evaporation of solvent was, if solid, recrystallised (for glycerol and L-*erythro*-butane-1,2,3-triol), or distilled In the latter case, only approximately half of the product could be distilled, the involatile residue being extremely viscous The properties of the products are shown in Table I

*Preparation of di-*O*-acetyl-*O*-methyltriols* — The benzeneboronate of a triol (~0 02 g) was dissolved in a solution of boron trifluoride etherate in dichloromethane (0 16%, 1 ml) and cooled to −5° Diazomethane in dichloromethane (5 ml, prepared by the method of DeBoer and Backer[20]) was added, and after 3 min a further portion of 5 ml was added, causing a yellow colour to persist for ~10 sec After 30 min at −5°, the solvent was evaporated and the residue was hydrolysed with warm water (2 ml) at 80° The benzeneboronic acid thus produced was converted into bromobenzene, boric acid, and hydrobromic acid by addition of bromine water[13] (3%, 0 6 ml) After standing for 15 min at 20°, the solution was evaporated and co-distilled with methanol (4 × 2 ml) The residue was acetylated by using acetic anhydride (4 ml) and pyridine (4 ml) After 10 min at 90°, the solution was evaporated and the residue was analysed by combined g l c –m s Peak areas were determined by weighing cut-outs from the gas–liquid chromatograms The results are listed in Table I

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