695. *Phenylboronates of Acyclic Polyhydroxy-compounds*

By E. J. BOURNE, E. M. LEES, and H. WEIGEL

The preparation of phenylboronates of several acyclic polyhydroxy-compounds (and of D-glucose) is described. The derivatives of glycerol and galactitol have been shown to be the 1,2- and 1,3-4,6-diphenylboronate, respectively. Conformational aspects are discussed.

PHENYLBORONIC ACID reacts [1–5] with certain cyclic and acyclic diols and polyols to give cyclic phenylboronates. With the exception of phenylboronates of some glycosides,[4] detailed structures have not been assigned to the derivatives of polyols. Previously [6] we reported the effect of the presence of phenylboronic acid on the chromatographic behaviour of polyols. We now report the preparation of phenylboronates of some acyclic polyols (and D-glucose) and the structural analysis of the derivatives of galactitol and glycerol.

The properties of the phenylboronates are shown in Table 2. In the determination of the boron content of these compounds use was made of the absorption peak at 219 mμ of solutions of phenylboronic acid in aqueous methanol. Polymeric structures can be discarded on the basis of molecular-weight determinations made on the phenylboronates of glycerol, D-mannitol, and D-glucose.

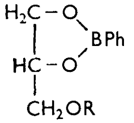
Glycerol Phenylboronate.—The two possible structures of a glycerol phenylboronate are (Ia) and (IIa). As in the case of galactitol bisphenylboronate (see below) it was not possible to effect satisfactory toluene-*p*-sulphonylation or methylation of the unsubstituted

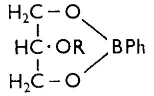
---

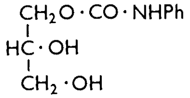
[1] H. G. Kuivila, A. H. Keough, and E. J. Soboczenski, *J. Org. Chem.*, 1954, **19**, 780.
[2] M. L. Wolfrom and J. Solms, *J. Org. Chem.*, 1956, **21**, 815.
[3] J. M. Sugihara and C. M. Bowman, *J. Amer. Chem. Soc.*, 1958, **80**, 2443.
[4] R. J. Ferrier, *J.*, 1961, 2325; R. J. Ferrier, D. Prasad, A. Rudowski, and I. Sangster, *J.*, 1964, 3330.
[5] A. Finch and J. C. Lockhart, *J.*, 1962, 3723.
[6] E. J. Bourne, E. M. Lees, and H. Weigel, *J. Chromatog.*, 1963, **11**, 253.

hydroxyl group. However, treatment with phenyl isocyanate gave an *O*-phenylcarbamoylglycerol phenylboronate (Ib or IIb). Its hydrolysis and the separation of the products (III or IV and phenylboronic acid) was effected by paper chromatography,[6] but the *O*-phenylcarbamoylglycerol, an oil, could not be distilled without decomposition.

In order to establish the structure of the *O*-phenylcarbamoylglycerol (III or IV) the mixture of *O*-phenylcarbamoylglycerol and phenylboronic acid, obtained by addition of water to a solution of the *O*-phenylcarbamoylglycerol phenylboronate (Ib or IIb) in dioxan, was treated directly with sodium periodate. The effect of the presence of phenylboronic acid was ascertained by periodate oxidation of glycerol phenylboronate, and phenylboronic anhydride $(PhBO)_3$. Under the same conditions *O*-phenylcarbamoylglycerol phenylboronate, glycerol phenylboronate, and phenylboronic anhydride consumed, respectively, 1·81, 2·82, and 2·40 mol. of periodate. Thus, the *O*-phenylcarbamoylglycerol consumed 1·0 mol. of periodate and in addition it produced 1·1 mol. of formaldehyde. These results are compatible with structure (III) and show that the glycerol phenylboronate was in fact the 1,2-phenylboronate (Ia). They also confirm the structure postulated by Bowie and Musgrave [7] on the grounds of relative rates of hydrolysis of cyclic phenylboronates with 5- and 6-membered heterocyclic rings.

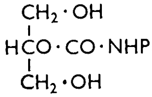

(Ia: R = H)
(Ib: R = CO·NHPh)


(IIa: R = H)
(IIb: R = CO·NHPh)



$$\begin{array}{l}CH_2O\cdot CO\cdot NHPh\\ \quad|\\ HC\cdot OH\\ \quad|\\ CH_2\cdot OH\end{array}$$

(III)



$$\begin{array}{l}CH_2\cdot OH\\ \quad|\\ HCO\cdot CO\cdot NHPh\\ \quad|\\ CH_2\cdot OH\end{array}$$

(IV)

Galactitol Bisphenylboronate.—By heating solutions containing varying molar proportions of galactitol and phenylboronic acid in anhydrous or aqueous acetone, Sugihara and Bowman obtained in each case a galactitol trisphenylboronate.[3] However, our method (method 1) always gave a bisphenylboronate, even when phenylboronic anhydride and galactitol were used in the molar ratio of 1 : 1.

As in the case of glycerol 1,2-phenylboronate, the galactitol bisphenylboronate could not be satisfactorily toluene-*p*-sulphonylated or methylated.

Benzoylation of galactitol bisphenylboronate, followed by treatment with an acetolysing mixture,[8] gave the known 1,3,4,6-tetra-*O*-acetyl-2,5-di-*O*-benzoylgalactitol. Treatment of galactitol bisphenylboronate with phenyl isocyanate gave a bis-*O*-phenylcarbamoylgalactitol bisphenylboronate which, on hydrolysis in aqueous dioxan, yielded a bis-*O*-phenylcarbamoylgalactitol. This compound proved to be not very suitable for studies with sodium periodate or lead tetra-acetate, because of its low solubility in water and its ready hydrolysis in glacial acetic acid.

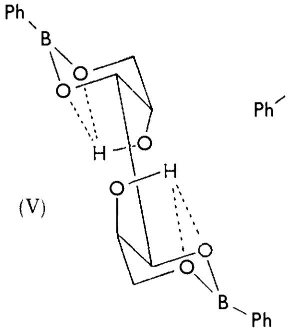
For the above reason, and in view of the low yields of 1,3,4,6-tetra-*O*-acetyl-2,5-di-*O*-benzoylgalactitol and bis-*O*-phenylcarbamoylgalactitol bisphenylboronate, an alternative approach to elucidate the structure of the galactitol bisphenylboronate was the preparation of a bis-*O*-phenylcarbamoylgalactitol by an unambiguous route. Thus, 1,3-4,6-di-*O*-benzylidenegalactitol was converted into 1,3-4,6-di-*O*-benzylidene-2,5-bis-*O*-phenylcarbamoylgalactitol which, on hydrolysis, gave 2,5-bis-*O*-phenylcarbamoylgalactitol. This was identical with the bis-*O*-phenylcarbamoylgalactitol obtained from galactitol bisphenylboronate. The latter was thus galactitol 1,3-4,6-bisphenylboronate.

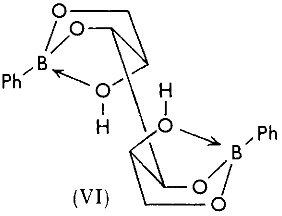
General Observations.—The above results show that reactions of acyclic polyols with phenylboronic anhydride yield both 5- and 6-membered ring systems. The galactitol 1,3-4,6-bisphenylboronate might have the conformation [(V); for clarity the $C_{(3)}$–$C_{(4)}$ bond is enlarged and C-bond H atoms are omitted] with intramolecular hydrogen bonding

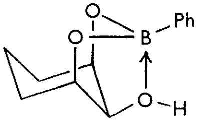
---

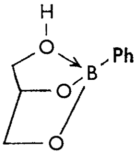
[7] R. A. Bowie and O. C. Musgrave, *J.*, 1963, 3945.
[8] W. T. Haskins, R. M. Hann, and C. S. Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 132.

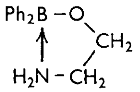
between the unsubstituted hydroxyl groups and the ring oxygen atoms. In this case, absorption at *ca.* 3580 cm.$^{-1}$ would be expected.[9,10] However, it exhibited only one sharp absorption band at 3636 cm.$^{-1}$, characteristic of a free hydroxyl group.[9] The complete absence of intramolecular hydrogen bonding suggests that the oxygen atoms on $C_{(2)}$ and $C_{(5)}$ co-ordinate with the corresponding boron atoms (VI). (The co-ordinating electron pair of the oxygen is not directly involved in the O–H bonding. Thus, the influence of this type of co-ordination on the O–H stretching frequency should be small.) This is supported by the fact that phenylboronic acid markedly affects the chromatographic mobility of only those six-membered cyclic polyhydroxy-compounds which possess a *cis-cis*-1,2,3-triol group.[6,11] Structure (VII) has been suggested as that being formed during the chromatographic process. It is evident that the hetero-ring systems in (VI) and (VII) are identical.

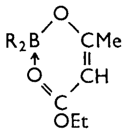

(V)


(VI)


(VII)


(VIII)


(IX)


(X)

The glycerol 1,2-phenylboronate exhibited absorption bands at 3630 and 3597 cm.$^{-1}$, the ratio of intensities being *ca.* 1 : 2. The appreciable amount of intramolecular hydrogen bonding (3597 cm.$^{-1}$) probably arises in the same way as that in cyclohexane-1,2-diols, since the oxygen atom of the hydroxymethyl group and that on $C_{(2)}$ can be brought into the same spatial disposition as those in cyclohexane-1,2-diols. The smaller amount of free hydroxyl absorption (3630 cm.$^{-1}$) may be due to (*a*) the ring strain inherent in forming a hydrogen bond from the extra-annular hydroxymethyl group and/or (*b*) co-ordination of the oxygen atom of the hydroxymethyl group with the boron atom, resulting in non-planarity of the phenylboronate ring (VIII).

Boron is strongly electrophilic by virtue of its tendency to fill the vacant orbital and complete the octet. Consequently, the properties of many boron compounds have been explained by postulating internal co-ordination of an electron-donating atom with boron, *e.g.*, 2-aminoethyl diphenylborinate (IX)[12] and 2-ethoxycarbonyl-1-methylvinyl di-*n*-butyl- and diphenyl-borinate (X, R = *n*-butyl or phenyl).[13] Such co-ordination would render the unsubstituted hydroxyl groups in galactitol 1,3-4,6-bisphenylboronate and glycerol 1,2-phenylboronate less reactive towards the reagents used (*i.e.*, methyl iodide, benzoyl chloride, toluene-*p*-sulphonyl chloride) than in the case of hydrogen bond formation. The failure or low yields of the reactions are thus compatible with structures (VI) and (VIII).

EXPERIMENTAL

Boron Analysis.—The plot of absorption at 219 mμ against concentration of solutions of phenylboronic acid (0·01—0·1mM) in 50% aqueous methanol gave a straight line. The

---

[9] L. P. Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.

[10] J. S. Brimacombe, A. B. Foster, M. Stacey, and D. H. Whiffen, *Tetrahedron*, 1958, **4**, 351.

[11] R. J. Ferrier, W. O. Overend, G. A. Rafferty, H. M. Hall, and N. R. Williams, *Proc. Chem. Soc.*, 1963, 133.

[12] R. L. Letsinger and I. Skoog, *J. Amer. Chem. Soc.*, 1955, **77**, 2491.

[13] W. Gerrad, M. F. Lappert, and R. Shafferman, *J.*, 1958, 3648.

graph was used to determine the quantity of boron (in the form of PhB<) in solutions of phenylboronates in 50% aqueous methanol.

Molecular Weights.—These were determined according to the method of Finch and Gardner[14] using benzene as solvent.

Preparation of Phenylboronates of Polyols.—The quantities used, the yields obtained, and properties of the phenylboronates are shown in Tables 1 and 2.

TABLE 1

Preparation of phenylboronates

		Phenylboronic anhydride		Polyol		
Parent polyol	Method	Weight (g.)	Solvent (ml.)	Weight (g.)	Solvent (ml.)	Yield (g.)
Glycerol	1	2·3	10[a]	22	10[b]	2·5
Erythritol	1	1·7	15[a]	1·0	15[b]	2·0
D-Arabinitol	1	0·69	5[a]	0·50	5[b]	0·90
Galactitol	1	5·0	25[a]	4·4	150[b]	7·0
D-Glucitol	1	8·6	25[a]	5·0	25[b]	13·0
2,4-*O*-benzylidene-	2	0·12		0·15	25[c]	0·24
1,3-2,4-di-*O*-ethylidene-	2	0·09		0·20	25[c]	0·27
D-Mannitol	1	8·6	25[a]	5·0	25[b]	13·0
1,6-di-*O*-benzoyl-	2	0·06		0·10	25[c]	0·13
D-Glucose	1	5·8	20[a]	5·0	20[a]	7·0

[a] Methanol. [b] Water. [c] Acetone.

TABLE 2

Properties of phenylboronates

			M		C (%)		H (%)		B (%)	
Parent polyol	M. p.	Formula	Found	Reqd.	Found	Reqd.	Found	Reqd.	Found	Reqd.
Glycerol	74·5—76·5° *	$C_9H_{11}BO_3$	178	178·0	60·0	60·7	6·1	6·2	6·0	6·1
Erythritol	88	$C_{16}H_{16}B_2O_4$							7·4	7·4
D-Arabinitol	114—116	$C_{17}H_{18}B_2O_5$							6·7	6·7
Galactitol	125—130	$C_{18}H_{20}B_2O_6$			59·9	61·1	6·0	5·7	6·3	6·1
D-Glucitol	189	$C_{24}H_{23}B_3O_6$			62·8	65·5	4·8	5·3	7·4	7·4
2,4-*O*-benzylidene-	199 *	$C_{25}H_{24}B_2O_6$			67·5	67·9	5·0	5·5		
1,3-2,4-di-*O*-ethylidene-	88 *	$C_{16}H_{21}BO_6$			59·6	60·0	6·1	6·6	3·3	3·4
D-Mannitol	137 *	$C_{24}H_{23}B_3O_6$	440	439·9	62·9	65·5	4·9	5·3	7·4	7·4
1,6-di-*O*-benzoyl-	150 *	$C_{32}H_{28}B_2O_8$			67·9	68·4	4·9	5·0		
D-Glucose	166	$C_{18}H_{18}B_2O_6$	325—365	352·0	61·2	61·4	5·3	5·2	6·1	6·2

* Recrystallised from dry hexane.

The m. p. of the known phenylboronates, *i.e.*, of glycerol,[7] D-glucitol,[3] and D-mannitol,[3] agree with those reported in the literature.

Method 1. Phenylboronic anhydride in methanol was added to the polyol in water. After *ca.* 1 hr. the solid product was filtered off, washed with hot water and cold methanol, and dried.

Method 2. Phenylboronic anhydride and the polyol in acetone were refluxed for *ca.* 1 hr. The solvent was distilled off and the residue was recrystallised from dry hexane.

Paper Chromatography.—The solvent was butan-1-ol–ethanol–water (40 : 11 : 19). Under the conditions used the phenylboronates hydrolysed[2,6] to give the polyols, detectable with silver nitrate in acetone–alcoholic sodium hydroxide,[15] and phenylboronic acid, detectable under ultraviolet light.

Infrared Spectra.—These were measured in 4 cm. layers in CCl_4 solution on the Unicam S.P. 100 spectrometer using a 3000 l.p.i. grating. Concentration of compounds was <0·005M.

*Attempted Toluene-*p*-sulphonylation of Galactitol Bisphenylboronate.*—Toluene-*p*-sulphonyl chloride (1·6 g.) was added to a solution of galactitol bisphenylboronate (1 g.) in dry pyridine (25 ml.) and kept at room temperature for 48 hr. Paper chromatography revealed components with R_F 0·18 (major, identical with galactitol), 0·37 (trace), and 0·55 (trace).

---

[14] A. Finch and P. J. Gardner, *J. Inorg. Nuclear Chem.*, 1963, **25**, 927.

[15] W. E. Trevelyan, D. P. Procter, and J. S. Harrison, *Nature*, 1950, **166**, 444.

Benzoylation of Galactitol Bisphenylboronate.—Benzoyl chloride (0·66 ml.) was added to an ice-cooled solution of galactitol bisphenylboronate (1 g.) in dry pyridine (15 ml.), and the mixture kept overnight at room temperature. Pyridine was removed by distillation under reduced pressure. The syrupy residue was treated overnight with a mixture of acetic anhydride, glacial acetic acid, and concentrated sulphuric acid (35 : 15 : 1, vol./vol./vol.; 15 ml.) and then poured on ice. The solid was recrystallised from absolute ethanol to give 1,3,4,6-tetra-*O*-acetyl-2,5-di-*O*-benzoylgalactitol [8] (150 mg.), m. p. 156° (Found: C, 59·6; H, 5·7%. Calc. for $C_{28}H_{30}O_{12}$: C, 60·2; H, 5·4%). The infrared spectrum revealed the presence of carbonyl groups and the absence of hydroxyl groups.

2,5-*Bis*-O-*phenylcarbamoyl-galactitol* 1,3-4,6-*Bisphenylboronate.*—Phenyl isocyanate (3·5 ml.) was added to a suspension of galactitol bisphenylboronate (5 g.) in dry benzene (50 ml.). Heating gave a solution which was refluxed for 18 hr. The solid material obtained on cooling was recrystallised from benzene to give 2,5-*bis*-O-*phenylcarbamoylgalactitol* 1,3-4,6-*bisphenylboronate* (1 g.), m. p. 223—224° (Found: C, 64·7; H, 5·3; N, 4·8%. $C_{32}H_{30}B_2N_2O_8$ requires C, 64·9; H, 5·1; N, 4·7%).

2,5-*Bis*-O-*phenylcarbamoylgalactitol from* 2,5-*Bis*-O-*phenylcarbamoylgalactitol* 1,3-4,6-*Bisphenylboronate.*—Water (25 ml.) was added to a solution of 2,5-bis-*O*-phenylcarbamoylgalactitol 1,3-4,6-bisphenylboronate (0·5 g.) in dioxan (5 ml.). The *bis*-O-*phenylcarbamate* produced (0·27 g.) had m. p. 257° (Found: C, 57·8; H, 5·6; N, 6·6%. $C_{20}H_{22}N_2O_8$ requires C, 57·4; H, 5·3; N, 6·7%).

1,3-4,6-*Di*-O-*benzylidene*-2,5-*bis*-O-*phenylcarbamoylgalactitol.*—Phenyl isocyanate (3 ml.) was added to a solution of 1,3-4,6-di-*O*-benzylidenegalactitol [8] (5 g.) in dimethylformamide (50 ml.). Heating to 60° for 30 min. produced crystalline 1,3-4,6-*di*-O-*benzylidene*-2,5-*bis*-O-*phenylcarbamoylgalactitol* (5·5 g.), m. p. 343° (Found: C, 68·2; H, 5·3; N, 4·8%. $C_{34}H_{32}N_2O_8$ requires C, 68·4; H, 5·4; N, 4·7%).

2,5-*Bis*-O-*phenylcarbamoylgalactitol from* 1,3-4,6-*Di*-O-*benzylidene*-2,5-*bis*-O-*phenylcarbamoylgalactitol.*—A suspension of 1,3-4,6-di-*O*-benzylidene-2,5-bis-*O*-phenylcarbamoylgalactitol (5 g.) in dioxan (25 ml.) and water (250 ml.) was refluxed in the presence of Amberlite IR-120(H^+). After filtration the resin was washed with dioxan (50 ml.). 2,5-Bis-*O*-phenylcarbamoylgalactitol (0·48 g.) was deposited by addition of water (250 ml.) to the filtrate. It had m. p. 257°. Admixture with the material obtained from 2,5-bis-*O*-phenylcarbamoylgalactitol 1,3-4,6-bisphenylboronate caused no depression in m. p.

Attempted Toluene-p-*sulphonylation of Glycerol Phenylboronate.*—The procedure was that used for galactitol bisphenylboronate. Chromatography of the reaction mixture revealed glycerol as the only polyol component.

1-O-*Phenylcarbamoylglycerol* 2,3-*Phenylboronate.*—Phenyl isocyanate (3 ml.) was added to a solution of glycerol phenylboronate (5 g.) in dry benzene (100 ml.), and the whole refluxed for 6 hr. The residue obtained after evaporation was recrystallised from benzene–light petroleum (b. p. 60—80°) to give 1-O-*phenylcarbamoylglycerol phenylboronate* (5 g.), m. p. 117° (Found: C, 64·5; H, 5·3; N, 4·9%. $C_{16}H_{16}BNO_4$ requires C, 64·7; H, 5·4; N, 4·7%).

Periodate Oxidations.—Phenylboronic anhydride $(PhBO)_3$ (24·7 mg.), glycerol 1,2-phenylboronate (44·7 mg.), and 1-*O*-phenylcarbamoylglycerol 2,3-phenylboronate (52·3 mg.) were separately dissolved in dioxan (25 ml.). Water (65 ml.) and 0·1N-sodium periodate (10 ml.) were added to each solution. After 28 hr. the periodate consumptions (mol.) were as follows: phenylboronic anhydride, 2·40; glycerol 1,2-phenylboronate, 2·82; 1-*O*-phenylcarbamoylglycerol 2,3-phenylboronate, 1·81. 1-*O*-Phenylcarbamoylglycerol 2,3-phenylboronate produced 1·10 mol. formaldehyde, estimated by the chromotropic acid method [16] and identified as its dimedone derivative. Under the same conditions ethyl *N*-phenylcarbamate did not consume periodate.[17]

The authors are indebted to the D.S.I.R. for financial assistance, and Dr. D. Steele for collaboration in infrared analysis.

Chemistry Department, Royal Holloway College, University of London,
Englefield Green, Surrey.
[*Received, November* 12*th*, 1964.]

---

[16] W. E. A. Mitchell and E. Percival, *J.*, 1954, 1423.

[17] N. Sufi and H. Weigel, unpublished results.