Characterization of 1,2- and 1,3-Diols by Gas Chromatography–Mass Spectrometry of Cyclic Boronate Esters

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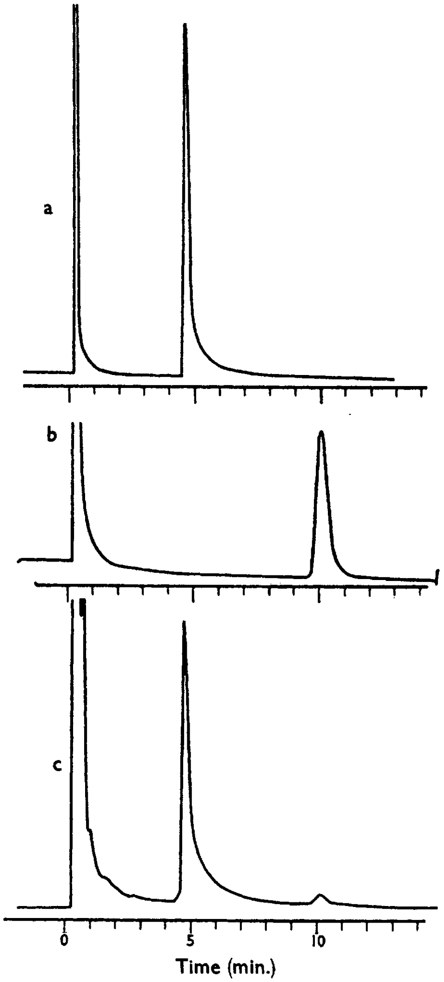


FIGURE 1. *Comparative gas chromatographic traces recorded at* 100° *using a* 6 *ft. column packed with* 1% *OV*-17 (*Supelco, Inc., Bellefonte, Pa.*) *coated on Gas-Chrom Q* (100—120 *mesh*: *Applied Science Laboratories, State College, Pa.*). *Nitrogen carrier gas,* 35 *ml./min.*; *flame ionization detector*; *recorder sensitivity* 1 × 10^{-9} *amp. full scale deflection*; *F*-11 *gas chromatograph* (*Perkin-Elmer Ltd., Beaconsfield, Bucks.*)

(*a*) *Styrene glycol* (1 *μg. in* 1 *μl. acetone*).

(*b*) *Styrene glycol n-butylboronate, prepared by adding* 1 *equiv. of n-butylboronic acid to the glycol solution as used for* (*a*) *and restoring the original volume*: 1 *μl. sample, equivalent to* 1 *μg. of glycol.*

(*c*) *Solution as used for* (*b*) *after addition of* 3 *equiv. of propane*-1,3-*diol and adjustment of volume*; 1 *μl. sample equivalent to* 1 *μg. of original glycol.*

THE wide occurrence of α- and β-diol groupings in organic natural products has led to a long-standing interest in their specific reactions, especially since by recent developments in gas-phase micro-analysis, the broader utility of functionalization can provide a means of structural elucidation—as, for example, in the study of diol acetonides derived from olefins.[1]

The ready formation of cyclic esters of boronic acids with suitably constituted diols is well known[2] and has been applied extensively in the carbohydrate field, especially by Ferrier and co-workers.[3] The derivatives do not appear to have been examined by gas chromatography. We are exploring their value in the characterization of oxygenated groupings (notably in terpenoids and steroids) by combined gas chromatography–mass spectrometry: initial results, for n-butylboronates and phenylboronates of diols, are reported here.

The cyclic esters were formed rapidly at room temperature[2,4,5] by mixing equimolar amounts of the boronic acid and diol in acetone solution. In most instances the resulting equilibrium[4] appeared to lie strongly towards ester formation. When samples were examined by gas chromatography, the only peaks observed were those ascribed to the cyclic boronates. The gas-chromatographic behaviour of the boronates was generally superior to that of the free diols (*cf.*, Figures 1a and b). Liberation of α-diols could in most cases be achieved in high yield *in situ* by adding 2—3 equiv. of propane-1,3-diol (Figure 1c). Certain "stable" esters, *e.g.*, those of indane-*cis*-1,2-diol,[1,5] remained unaffected by such addition: these also proved relatively stable to thin-layer chromatography, which led to hydrolysis of most of the esters. (Indane-*cis*-1,2-diol was particularly effective in liberating many other α-diols from their boronate esters).

Retention indices are cited in the Table, together with two features of the mass spectra, *viz.*, the most abundant ion ('base peak') and the relative intensity of the molecular ion, which was generally more prominent in the phenylboronates than in the n-butylboronates. Fragmentation patterns were usefully characteristic: for example the isomeric drimane derivatives (Nos. 2 and 3) gave markedly different spectra. Comparison of n-butyl- and phenyl-boronates indicated a degree of parallel behaviour and aided the assignment of probable

TABLE

	Diols	n-Butylboronates[a]				Phenylboronates[a]			
		(I)[b]	Molecular ion *m/e*	Molecular ion %	Base peak *m/e*	(I)[b]	Molecular ion *m/e*	Molecular ion %	Base peak *m/e*
1.	Cyclohexane-*cis*-1,2-diol[c]	1420	182	6	113	1820	202	58	160
2.	Drimane-7ξ,8ξ,11-triol 11-acetate[d] (isomer A)	2500	364	3	95	2980	384	34	95
3.	Drimane-7ξ,8ξ,11-triol 11-acetate[d] (isomer B)	2470	364	6	69	2940	384	19	309
4.	Indane-*cis*-1,2-diol[e]	1800	216	10	116	2250	236	100	236
5.	Styrene glycol[f]	1670	204	58	104	2100	224	94	223
6.	Glyceryl 1-myristate[g]	2650	368	1·5	98	3070	388	2	160
7.	5β-Pregnane-3α,17α,20α-triol	3260	402	8	81	(3740)[h]	422	12	105
8.	*o*-Hydroxymethylphenol (Saligenin)	1580	190	100	190	2010	210	94	209

[a] Mass spectra were recorded by Miss H. Humphrys and Miss J. Malcolm on an LKB 9000 instrument at 70 ev.

[b] Retention indices for 1% OV-17, determined with the assistance of Mr. K. Shepherd, using programmed-temperature gas chromatography.

[c] Phenylboronate, *cf.* ref. 9.

[d] Kindly supplied by Dr. K. H. Overton and Mr. J. Johnston. The compounds were *cis*-diols obtained by osmium tetroxide hydroxylation of drimenyl acetate.

[e] Phenylboronate, *cf.* ref. 1.

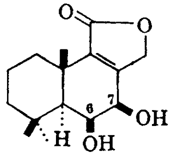
[f] Phenylboronate, *cf.* ref. 5.

[g] Possible isomerization to the 2-myristate derivative has not been excluded.

[h] Approximate value.

composition to the ions. Thus the phenylboronates of cyclohexane-*cis*-1,2-diol and of monomyristin gave a base peak at *m/e* 160, ascribable to a species $[C_6H_5BO_2C_3H_4]^{+\cdot}$: the corresponding n-butylboronates yielded analogous peaks (not here the most intense) at *m/e* 140. Such ions, containing boron, are frequently recognizable by virtue of the characteristic isotope distribution (${}^{10}B:{}^{11}B = 1:4{\cdot}2$).

A simple application of the phenylboronates has been made[6] to confirm the *cis*-diol system in the sesquiterpenoid (I). Formation of a cyclic ester was readily detected from a few μg. of diol by gas chromatography, and confirmed by combined gas chromatography–mass spectrometry (M^+, *m/e* 352, 65% of base peak). A related diol, epimeric at C-7, did not yield a cyclic ester.



(I)

The stability of many cyclic phenylboronates towards esterifying conditions has been demonstrated and exploited in the carbohydrate field.[7,8] For a number of boronate esters derived from diols possessing additional hydroxyl groups, we have found that trimethylsilyl ethers can be prepared without substantial hydrolysis of the cyclic ester groups. These and other "mixed" derivatives are of considerable value in the characterization of steroids in which the diol grouping comprises only one of a number of oxygenated substituents. We have found that cyclic boronate esters effectively stabilize corticosteroids for characterization by gas chromatography–mass spectrometry. This important application will be the subject of a further communication.

We thank the Medical Research Council for a grant.

(*Received, August 7th,* 1967; *Com.* 834.)

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