

**749.** *Organoboron Compounds. Part V.\* The Hydrolysis of Cyclic Phenylboronates.*

By R. A. BOWIE and O. C. MUSGRAVE.

The ease of hydrolysis of cyclic phenylboronates is shown to be governed by the size, and by the degree of substitution, of the heterocyclic ring. A stereochemical explanation is proposed.

SIMPLE alkyl esters of phenylboronic acid are hydrolysed readily by water or moist air,<sup>5</sup> but esters formed from aliphatic diols show marked differences in behaviour towards water. Some are hydrolysed rapidly while others are so stable that they can be prepared in aqueous solution.<sup>6</sup> In order to learn more about the factors controlling ease of hydrolysis we have prepared the phenylboronates of a wide variety of 1,2-, 1,3-, and 1,4-diols. These esters, the properties of which are recorded in Table 1, are monomeric and therefore contain respectively 5-, 6-, and 7-membered rings. Esters containing 8- or 9-membered rings could not be obtained because pentane-1,5-diol<sup>7</sup> and hexane-1,6-diol gave involatile phenylboronates which are presumably polymeric. The hydrolysis of the cyclic esters was investigated by measuring their increases in weight on exposure to air saturated with water vapour (Table 2). All the esters which showed marked increases deposited phenylboronic acid, so confirming the view that hydrolysis had occurred. The 1,2-, 1,3-, and

\* The papers in refs. 1—4 are regarded as earlier Parts of this series.

<sup>1</sup> Musgrave and Park, *Chem. and Ind.*, 1955, 1552.

<sup>2</sup> Musgrave, *J.*, 1956, 4305.

<sup>3</sup> Musgrave, *Chem. and Ind.*, 1957, 1152.

<sup>4</sup> Cowie, Jackson, and Musgrave, *Chem. and Ind.*, 1959, 1248.

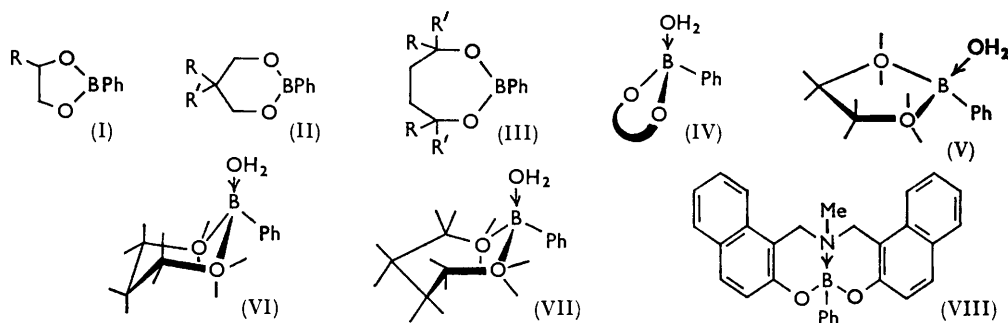
<sup>5</sup> See, e.g., Torssell, *Acta Chem. Scand.*, 1954, **8**, 1779.

<sup>6</sup> Kuivila, Keough, and Soboczenski, *J. Org. Chem.*, 1954, **19**, 780.

<sup>7</sup> Sugihara and Bowman, *J. Amer. Chem. Soc.*, 1958, **80**, 2443.

1,4-diols regenerated are hygroscopic but fortunately the members of each group absorb water at a similar rate and an estimate of the relative ease of hydrolysis of the parent esters can be made.

The reactivities of the esters appear to depend on (a) the size of the heterocyclic ring, and (b) the number of alkyl substituents which this ring carries. The rate of hydrolysis of 5-membered-ring esters falls as the hydrogen atoms attached to the ring are replaced by alkyl or aryl groups. Ethylene phenylboronate (I; R = H) is hydrolysed rapidly, similar esters containing one or two methyl substituents take up water less readily, and those with three or four methyl substituents are completely unaffected.



The alkyl substituents in esters (I; R = MeO·CH<sub>2</sub> or HO·[CH<sub>2</sub>]<sub>2</sub> or HO·[CH<sub>2</sub>]<sub>4</sub>) have effects comparable with that of the methyl group in the propylene ester (I; R = Me), and as the glycerol ester resembles its ether (I; R = MeO·CH<sub>2</sub>) in its rate of hydrolysis it appears to have the 5-membered-ring structure (I; R = HO·CH<sub>2</sub>) rather than the alternative 6-membered-ring arrangement (II; R = HO, R' = H). Hydrolysis of the ester (I; R = Ph), which has only one substituent group, is very slow; the benzpinacol ester is completely unaffected by water.

The 6-membered-ring phenylboronates are much more resistant to hydrolysis than are the corresponding 5-membered-ring compounds. The phenylboronate (II; R = R' = H) is the only one which takes up water at an appreciable rate. In contrast, the 7-membered-ring phenylboronates are all hydrolysed rapidly. Alkyl substitution, as in (III; R = H, R' = Me, or R = R' = Me) lowers the rate of water-uptake but fails to stabilise the esters.

These results can be explained by extending the arguments<sup>8</sup> used in accounting for the reactivities of certain boric esters of diols. Many of the reactions of phenylboronic acid and of its derivatives involve the initial formation of a tetraco-ordinated boron atom,<sup>9</sup> and the hydrolysis of the phenylboronates by water presumably follows a similar course (cf. the hydrolysis of trialkyl borates<sup>10</sup>), giving first the complex (IV) which then undergoes ring scission. The rates of hydrolysis of trialkyl borates<sup>11</sup> have been related to the steric requirements for the initial co-ordination of water, and the rates of water-uptake of the phenylboronates presumably depend on the ease of formation of the complex (IV), *i.e.*, on the tendency of the boron atom to become tetrahedral. The 5-membered-ring phenylboronates possess considerable ring-strain (the bond angles OBO and BOC in trimethyl borate<sup>12</sup> are 120° and 113° ± 3°, respectively) which can be relieved by co-ordination as in

<sup>8</sup> Dale, J., 1961, 922; Hubert, Hargitay, and Dale, J., 1961, 931.

<sup>9</sup> Lorand and Edwards, *J. Org. Chem.*, 1959, **24**, 769; Kuivila and Wiles, *J. Amer. Chem. Soc.*, 1955, **77**, 4830 and previous papers.

<sup>10</sup> Scattergood, Miller, and Gammon, *J. Amer. Chem. Soc.*, 1945, **67**, 2150.

<sup>11</sup> Steinberg and Hunter, *Ind. Eng. Chem.*, 1957, **49**, 174.

<sup>12</sup> Bauer and Beach, *J. Amer. Chem. Soc.*, 1941, **63**, 1394.

(V) when both the boron and the ring-oxygen atoms become tetrahedral. This leads to an increase in the number of bond interactions but those between the C-H bonds and the oxygen electron-pairs<sup>13</sup> are not sufficiently strong to prevent the addition of water to ethylene phenylboronate. Substitution by methyl groups<sup>14</sup> results in stronger interactions which oppose the tendency for boron to become tetrahedral, and with three or four methyl substituents the co-ordination of water is prevented. This steric opposition is assisted by the inductive effects of the methyl groups which promote the oxygen-boron dative  $\pi$ -bonding. In phenylethylene phenylboronate the two phenyl groups interact unfavourably if the co-ordination of water with the boron atom is attempted.

The 6-membered-ring phenylboronates are free from ring-strain and the co-ordination of water to give the complex (VI) is impeded by the resulting axial interactions. Even the simplest member of this group, trimethylene phenylboronate, therefore takes up water slowly and the small steric and inductive effects resulting from the methyl group in the ester from butane-1,3-diol are sufficient to inhibit the reaction completely. In the esters (II; R, R' = alkyl) the axial alkyl group would interact with the axial electron-pairs of the oxygen atoms if the boron atom were to become tetrahedral. The substituent groups may be part of a 6- or a 4-membered ring (II; R + R' = CH<sub>2</sub>·O·CH<sub>2</sub>·O·CH<sub>2</sub> or CH<sub>2</sub>·O·CH<sub>2</sub>). The ester from *o*-hydroxymethylphenol is stable because the co-ordination of water would lead to pseudo-axial interaction with a C-H bond of the methylene group.

Water reacts with the 7-membered-ring phenylboronates to give the arrangement (VII) in which the ring is much more flexible than in the corresponding 6-membered-ring compounds. The bond interactions are weaker and there is little obstruction to hydrolysis. Alkyl substituents reduce the ease of co-ordination somewhat, possibly by their inductive effects.

The insensitivity of some of the above esters towards water was further demonstrated by their formation on mixing of aqueous solutions of phenylboronic acid and the diol. The phenylboronates of 2,2,4-trimethylpentane-1,3-diol, 2-hydroxymethyl-2-methylpropane-1,3-diol, phenylethane-1,2-diol, 2-methylpentane-2,4-diol, butane-1,3-diol, and 2,2-dimethylpropane-1,3-diol were readily obtained but glycerol and propane-1,3-diol failed to react. The pinacol ester has previously been obtained in this way.<sup>6</sup>

The stability towards water shown by pentaerythritol bisphenylboronate<sup>6</sup> and by various diol esters of aliphatic boronic acids<sup>15</sup> and of aliphatic and aromatic diboronic acids<sup>16</sup> can be explained by the above arguments.

The phenylboronates obtained from esters of tartaric acid and from *cis*-cyclohexane-1,2-diol<sup>6</sup> are unstable in the presence of water and clearly resemble the *meso*-butane-2,3-diol ester in this respect. The co-ordination of water with the phenylboronate of *cis*-indane-1,2-diol, which also contains a 5-membered heterocyclic ring, would lead to a strong interaction between an oxygen electron-pair and a C-H bond of the methylene group. This ester is consequently unaffected by water.<sup>6</sup>

The phenylboronate of *NN*-di-(2-hydroxy-1-naphthylmethyl)methylamine would be expected to be hydrolysed readily if it contained a 10-membered ring. Its stability towards water indicates that it contains a transannular N→B bond (VIII) similar to that in diethanolamine phenylboronate.<sup>1</sup>

#### EXPERIMENTAL

*Preparation of the Phenylboronates.*—The diols and triols (0.025 mole) were separately heated with phenylboronic anhydride (0.025 mole) in boiling toluene until the evolution of

<sup>13</sup> Brown, Brewster, and Shechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.

<sup>14</sup> Cf. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, 1962, p. 125.

<sup>15</sup> Darling, U.S.P. 2,710,252/1955.

<sup>16</sup> Bamford and Fordham, S.C.I. Monograph No. 13, Society of Chemical Industry, London, 1961, p. 320.

water was complete, after which the solvent was removed at 60°/15 mm. The liquid esters were purified by distillation, and the solid ones by crystallisation from light petroleum (b. p. 80—90°) or toluene. The esters (see Table 1) were obtained in yields of 80—95% and were

TABLE I.  
Diol and triol phenylboronates.

Diol or triol used	Formula of ester	B. p./mm.	M. p. (evac. capillary)	B (%)		M	
				Reqd.	Found	Reqd.	Found
Ethylene glycol	C <sub>8</sub> H <sub>9</sub> BO <sub>2</sub> <sup>a</sup>	47—48°/0.15	—	7.3	7.25	147.95	148
Propane-1,2-diol	C <sub>9</sub> H <sub>11</sub> BO <sub>2</sub> <sup>b</sup>	50—52°/0.15	—	6.7	6.6	162.0	170
meso-Butane-2,3-diol	C <sub>10</sub> H <sub>13</sub> BO <sub>2</sub> <sup>c</sup>	68—71°/0.2	—	6.15	6.1	176.0	170
2-Methylbutane-2,3-diol	C <sub>11</sub> H <sub>16</sub> BO <sub>2</sub>	65—70°/0.2	—	5.7	5.65	190.1	200
Pinacol	C <sub>12</sub> H <sub>17</sub> BO <sub>2</sub> <sup>d</sup>	60°/0.4	28—30°	5.3	5.3	204.05	201
3-Methoxypropane-1,2-diol	C <sub>10</sub> H <sub>13</sub> BO <sub>3</sub>	99—100°/0.9	—	5.65	5.6	192.0	192
Glycerol	C <sub>9</sub> H <sub>11</sub> BO <sub>3</sub>	—	75.5—76.5°	6.1	6.1	178.0	180
Butane-1,2,4-triol	C <sub>10</sub> H <sub>13</sub> BO <sub>3</sub>	110—112°/0.2	—	5.65	5.4	192.0	203
Hexane-1,2,6-triol	C <sub>12</sub> H <sub>17</sub> BO <sub>3</sub>	180°/0.15	—	4.9	4.85	220.05	230
Phenylethane-1,2-diol	C <sub>14</sub> H <sub>13</sub> BO <sub>2</sub>	118—120°/0.4	—	4.85	4.85	224.05	226
Benzpinacol	C <sub>32</sub> H <sub>25</sub> BO <sub>2</sub> <sup>e</sup>	110—112°/0.05	172—175°	—	—	452.35	415
Propane-1,3-diol	C <sub>9</sub> H <sub>11</sub> BO <sub>2</sub>	80—82°/0.2	26—28°	6.7	6.6	162.0	170
Butane-1,3-diol	C <sub>10</sub> H <sub>13</sub> BO <sub>2</sub> <sup>f</sup>	73—75°/0.2	19.5—20.5°	6.15	6.1	176.0	180
Pentane-2,4-diol*	C <sub>11</sub> H <sub>15</sub> BO <sub>2</sub>	70—72°/0.2	—	5.7	5.65	190.1	188
2-Methylpentane-2,4-diol	C <sub>12</sub> H <sub>17</sub> BO <sub>2</sub>	74—76°/0.2	20—21°	5.3	5.25	204.05	202
2,4-Dimethylpentane-2,4-diol	C <sub>13</sub> H <sub>19</sub> BO <sub>2</sub>	74—77°/0.2	55—56°	4.95	4.95	218.1	220
2,2-Dimethylbutane-1,3-diol	C <sub>12</sub> H <sub>17</sub> BO <sub>2</sub>	78—80°/0.3	27—29°	5.3	5.25	204.05	202
2-Ethylhexane-1,3-diol*	C <sub>14</sub> H <sub>21</sub> BO <sub>2</sub>	100—104°/0.2	—	4.65	4.6	232.15	240
2,2-Dimethylpropane-1,3-diol	C <sub>11</sub> H <sub>15</sub> BO <sub>2</sub>	—	65—65.5°	5.7	5.8	190.1	189
2,2-Diethylpropane-1,3-diol	C <sub>13</sub> H <sub>19</sub> BO <sub>2</sub>	124°/0.15	25—26°	4.95	5.05	218.1	220
Pentaerythritol monoformal	C <sub>12</sub> H <sub>15</sub> BO <sub>4</sub>	—	112—113°	4.6	4.7	234.05	232
3,3-Bishydroxymethyl-oxetan <sup>g</sup>	C <sub>11</sub> H <sub>13</sub> BO <sub>3</sub>	—	105—106°	5.3	5.25	204.05	220
2-Hydroxymethyl-2-methylpropane-1,3-diol	C <sub>11</sub> H <sub>15</sub> BO <sub>3</sub>	—	105—106°	5.25	5.25	206.05	204
2,2,4-Trimethylpentane-1,3-diol	C <sub>14</sub> H <sub>21</sub> BO <sub>2</sub>	100—102°/0.3	—	4.65	4.55	232.15	240
o-Hydroxymethylphenol	C <sub>13</sub> H <sub>11</sub> BO <sub>2</sub>	116—119°/0.25	42°	5.15	5.1	210.05	214
Butane-1,4-diol	C <sub>10</sub> H <sub>13</sub> BO <sub>2</sub> <sup>h</sup>	78°/0.1	69—71°	6.15	6.1	176.0	172
(±)-Hexane-2,5-diol	C <sub>12</sub> H <sub>17</sub> BO <sub>2</sub>	88—90°/0.3	37—38°	5.3	5.3	204.05	210
2,5-Dimethylhexane-2,5-diol	C <sub>14</sub> H <sub>21</sub> BO <sub>2</sub>	80—84°/0.2	54—55°	4.65	4.65	232.15	252
NN-Di-(2-hydroxy-1-naphthylmethyl)methylamine <sup>i</sup>	C <sub>29</sub> H <sub>24</sub> BNO <sub>2</sub> <sup>j</sup>	—	332—332.5°	—	—	429.3	445

\* Stereochemical configurations unknown.

<sup>a</sup> Pailer and Fenzl (*Monatsh.*, 1961, **92**, 1294) give b. p. 93—95°/10 mm. <sup>b</sup> Ref. *a* gives b. p. 103—107°/10 mm. <sup>c</sup> Lit.,<sup>7</sup> b. p. 75—77°/1 mm. <sup>d</sup> Lit.,<sup>8</sup> b. p. 128—130°/20 mm., m. p. 29—30°. <sup>e</sup> Found: C, 84.7; H, 5.6. C<sub>32</sub>H<sub>25</sub>BO<sub>2</sub> requires C, 84.95; H, 5.55%. <sup>f</sup> Lit.,<sup>7</sup> b. p. 85—86°/1 mm. <sup>g</sup> Issidorides and Matar, *J. Amer. Chem. Soc.*, 1955, **77**, 6382. <sup>h</sup> Lit.,<sup>7</sup> b. p. 90—95°/1 mm. <sup>i</sup> Burke, Kolbezen, and Stephens, *J. Amer. Chem. Soc.*, 1952, **74**, 3601. <sup>j</sup> Purified by repeated sublimation at 230—280°/10<sup>-3</sup> mm. [Found: N (Kjeldahl), 3.2. C<sub>29</sub>H<sub>24</sub>BNO<sub>2</sub> requires N, 3.25%].

handled in a dry nitrogen atmosphere. Boron was determined by photometric titration in aqueous ethanol with 0.1N-sodium hydroxide in the presence of a large excess of mannitol, with Thymol Blue-Cresol Red indicator. Molecular weights were determined ebullioscopically in benzene solution.

*Water Uptake.*—Approximate values of the uptake in moist air are given in Table 2.

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TABLE 2.  
Uptake of water by cyclic phenylboronates.\*

Phenylboronate obtained from	Water uptake (moles per mole of ester) at 18°		
	4 Days	16 Days	32 Days
Ethylene glycol .....	0.9	2.5	5.6
Propane-1,2-diol .....	0.5	1.2	1.9
<i>meso</i> -Butane-2,3-diol .....	0.3	0.8	1.2
3-Methoxypropane-1,2-diol .....	0.7	1.9	3.2
Glycerol .....	0.1	1.5	3.3
Butane-1,2,4-triol .....	1.7	3.9	5.9
Hexane-1,2,6-triol .....	1.2	2.6	3.9
Phenylethane-1,2-diol .....	0.0	0.0	0.1
Propane-1,3-diol .....	0.2	0.4	0.5
Butane-1,4-diol .....	3.1	8.0	13.0
(±)-Hexane-2,5-diol .....	3.3	6.2	8.7
2,5-Dimethylhexane-2,5-diol .....	1.2	2.2	2.4

\* The other esters listed in Table 1 were unaffected by exposure to moist air.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,  
OLD ABERDEEN.

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