The Preparation of Esters of Alkyl- and Aryl-boronic Acids.

By P. B. Brindley, W. Gerrard, and M. F. Lappert.

[Reprint Order No. 6303.]

Di-*n*-butyl boronate was prepared from *n*-butylmagnesium bromide (1 mol.), or, in better yield, from *n*-butyl-lithium (1 mol.) and tri-*n*-butyl borate. The *n*-octyl reagents and tri-*n*-butyl borate gave *n*-butyl di-*n*-octylboronite as principal product. Owing to the greater ease of hydrolysis of arylboronates, the same method was not practicable for the preparation of esters of phenylboronic acid, but these were obtained in excellent yields by esterification of the acid or anhydride by an azeotropic method, not suitable for the *tert.*-butyl ester. This was obtained by action of phenylboron dichloride on *tert.*-butyl alcohol and pyridine.

During investigation of the chemistry of boron esters, a number of esters of alkyl- and aryl-boronic acids, $R'\cdot B(OR)_2$, were required, and owing to the sparsity of information, their preparation had to be examined in detail. By the controlled oxidation of spontaneously inflammable triethylboron, $BEt_3 + O_2 \longrightarrow Et\cdot B(OEt)_2$, Frankland and Duppa (*Proc. Roy. Soc.*, 1859, **10**, 568; *J.*, 1862, **15**, 363) prepared diethyl ethylboronate; but Meerwein and Sönke (*J. prakt. Chem.*, 1936, **147**, 251) stated that it is difficult to obtain the ester free from concurrently formed ethyl diethylboronite and triethyl borate. Johnson and Van Campen (*J. Amer. Chem. Soc.*, 1938, **60**, 121) quantitatively converted tri-*n*-butylboron into the boronate by means of absolutely dry air. Wiberg and Krüerke recently (*Z. Naturforsch.*, 1953, **8**b, 608, 609, 610) obtained dimethyl methylboronate by the reaction $Si(OMe)_4 + Me\cdot BBr_2 \longrightarrow Me\cdot B(OMe)_2 + Si(OMe)_2Br_2$. Khotinsky and Melamed (*Ber.*, 1909, **42**, 3090) obtained certain alkyl esters of phenyl- or *m*-tolyl-boronic acids in unstated yields as intermediates in the preparation of the acids from the arylmagnesium bromide and the borate at 0°. Michaelis and Becker (*Ber.*, 1882, **15**, 180) prepared diethyl phenylboronate by the interaction of ethanol and phenylboron dichloride (prepared from boron trichloride and diphenylmercury). From α-naphthylboron dichloride and sodium methoxide, the corresponding boronate was prepared by Michaelis (*Annalen*, 1901, **315**, 19).

n-Butylmagnesium bromide and tri-*n*-butyl borate gave di-*n*-butyl *n*-butylboronate in 42% yield [see (1)], the boronate being freed from metal alkoxide and unchanged borate (which has a similar b. p.) by taking advantage of the greater ease of hydrolysis of the latter. Yields were better (60%) when alkyl-lithium was used in place of the Grignard reagent [see (2)] and a suitable apparatus was designed for this procedure. By either method, tri-*n*-butyl borate and the *n*-octyl reagent afforded mainly *n*-butyl di-*n*-octylboronite, $R_2B\cdot OBu^n$.

$$\text{(1)} \qquad R'MgHal + B(OR)_3 \longrightarrow R'B(OR)_2 + MgHal\cdot OR$$

$$\text{(2)} \qquad R'Li + B(OR)_3 \longrightarrow R'B(OR)_2 + LiOR$$

Neither method was satisfactory for the direct preparation of esters of phenylboronic acid, because the essential treatment with water to decompose the metal alkoxide also largely hydrolysed the boronate.

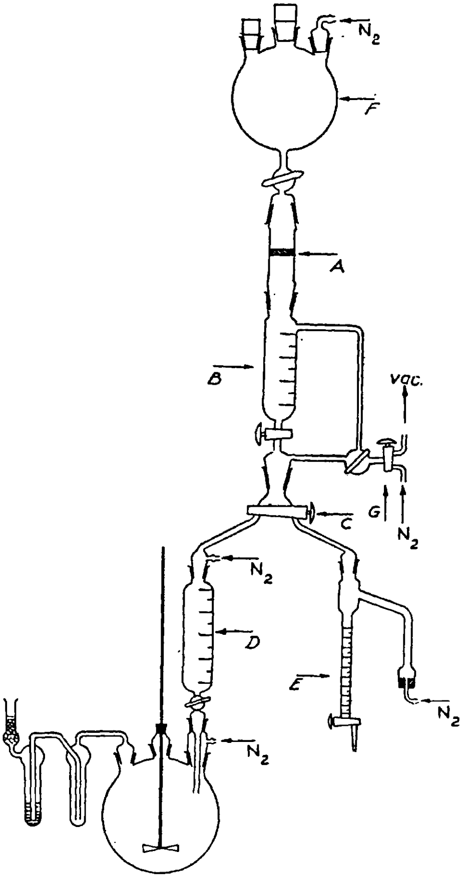
In the procedure now described, the phenylboronic acid was deliberately obtained (60%) [see (3)] (Bean and Johnson, *J. Amer. Chem. Soc.*, 1932, **54**, 4415), and then either esterified directly (see also Toyssell, *Acta Chem. Scand.*, 1954, **8**, 1779, a paper that appeared since completion of the present manuscript) or first dehydrated, by heating, to the anhydride which was then similarly esterified. The latter procedure very considerably reduced the reaction time. Esterification was by an azeotropic method which led to yields of 80—96% (see Table). Yields of acid were poorer (36%) when phenyl-lithium was used. The procedure was not successful with the *tert.*-butyl ester; but by an alternative scheme (4), which appears to be of general applicability, the ester was obtained in 69% yield.

$$\begin{tikzcd}
\text{(3)} \quad B(OBu^n)_3 + PhMgBr \arrow[r, "+H_2O"] & Ph{\cdot}B(OH)_2 \arrow[rr, "2ROH"] \arrow[dr, "-H_2O"] & & Ph{\cdot}B(OR)_2 \\
 & & Ph{\cdot}BO \arrow[ur, "+2ROH"'] &
\end{tikzcd}$$

$$\begin{tikzcd}
\text{(4)} \quad Ph{\cdot}B(OH)_2 \arrow[r] & Ph{\cdot}B(OEt)_2 \arrow[r, "BCl_3"] & Ph{\cdot}BCl_2 \arrow[r, "2ROH + 2C_5H_5N"] & Ph{\cdot}B(OR)_2 + 2C_5H_5N,HCl
\end{tikzcd}$$

Experimental

Addition of n-*Butyl-lithium* (1 *Mol.*) *to Tri*-n-*butyl Borate* (1 *Mol.*).—This order of addition gave the better result, and it was advantageous to remove unchanged lithium from the alkyl-lithium solution before use, and to avoid contact with the atmosphere. Therefore the apparatus shown in the diagram was designed. *n*-Butyl-lithium in ether was prepared in the flask *F*, by the method of Gilman, Beel, Brannen, Bullock, Dunn, and Miles (*J. Amer. Chem. Soc.*, 1949, **71**, 1499) from lithium wire and *n*-butyl bromide at −10° in an atmosphere of nitrogen. For this operation, flask *F* was detached from the main apparatus and supported at bench level. By slight reduction of pressure in *B*, the solution was transferred *via* the coarse sintered-glass filter (*A*) to the reservoir (*B*) and thence by means of a two-way tap (*C*) into a dropping-funnel (*D*) or into a sampling burette (*E*), which permitted the concentration of the *n*-butyl-lithium solution to be determined by Gilman and Haubein's procedure (*ibid.*, 1944, **66**, 1515). Free running through the sintered plate was ensured by periodically reversing the direction of the nitrogen flow through *B* by means of tap *G*. The *n*-butyl-lithium (30·2 g., 1 mol.) in ether was added dropwise to tri-*n*-butyl borate (108 g., 1 mol.) in ether at −60°. After treatment with water, the dried ethereal solution afforded the boronate (56·2 g., 60%), b. p. 108·5°/13 mm., n_D^{20} 1·4169, d_4^{20} 0·8300 (Found: C, 67·5; H, 12·7; B, 4·9. Calc. for $C_{12}H_{27}O_2B$: C, 67·4; H, 12·6; B, 5·1%).



Addition of n-*Butylmagnesium Bromide to Tri*-n-*butyl Borate.*—The Grignard reagent (1 mol.) in ether was added dropwise (1 hr.) with vigorous stirring to the borate (13·9 g., 1 mol.) in ether (100 c.c.) at −70°, whereupon the mixture was poured into ice–water and carefully neutralised with dilute hydrochloric acid. The ethereal layer was washed with water and dried ($MgSO_4$), and the boronate (5·30 g., 42%), b. p. 105°/10 mm., n_D^{20} 1·4180, was obtained. Delay in dealing with the primary reaction mixture resulted in lower yields.

Attempted Preparation of Di-n-*butyl* n-*Octylboronate.*—*n*-Octyl-lithium (42·4 g., 1 mol.) in ether (725 c.c.) was added (1·2 hr.) dropwise with vigorous stirring to tri-*n*-butyl borate (85 g., 1·04 mol.) in ether (600 c.c.) at −60°. After being washed with dilute hydrochloric acid, and dried, the ethereal solution afforded n-*butyl di*-n-*octylboronite* (60·0 g.), b. p. 80—88°/0·001 mm., n_D^{20} 1·4309—1·4315, which after two redistillations yielded the pure ester, b. p. 84°/0·005 mm., n_D^{20} 1·4312, d_4^{20} 0·8036 (Found : C, 77·7; H, 14·2; B, 3·4. $C_{20}H_{43}OB$ requires C, 77·4; H, 14·0; B, 3·5%).

n-Octylmagnesium bromide (58 g., 1 mol.) in ether was added (2 hr.) dropwise with stirring to tri-*n*-butyl borate (62 g., 1 mol.) in ether at −60°. The mixture was set aside for 18 hr., whereupon the ethereal solution after being washed and dried gave *n*-butyl di-*n*-octylboronite (33 g.), b. p. 80°/0·005 mm., n_D^{20} 1·4288, d_4^{20} 0·824 (Found : B, 3·5%), and *di*-n-*octyl* n-*octylboronate* (10 g.), b. p. 125—132°/0·005 mm., n_D^{20} 1·4409, d_4^{20} 0·842 (Found : C, 75·6; H, 13·2; B, 4·0. $C_{24}H_{51}O_2B$ requires C, 75·4; H, 13·4; B, 2·8%).

Attempted Preparation of Phenylboronates.—Phenyl-lithium (40·8 g., 1 mol.) in ether was added (1·6 hr.) dropwise with stirring to tri-*n*-butyl borate (110 g., 1 mol.) in ether at −60°. After rapid washing, volatile matter was removed from the ethereal portion at 18°/0·1 mm. Phenylboronic acid (12·5 g.), m. p. 206—208° (Found : B, 8·4. Calc. for $C_6H_7O_2B$: B, 8·9%), separated and was filtered off. The filtrate after a number of distillations gave *di*-n-*butyl phenylboronate* (10%), b. p. 97°/0·2 mm., n_D^{17} 1·4800 (Found : B, 4·6. $C_{14}H_{23}O_2B$ requires B, 4·6%). The overall conversion of borate into boronate or boronic acid was 36%.

To the borate (72·3 g., 1 mol.) in ether at −70° was added (3·3 hr.) with stirring phenylmagnesium bromide (57 g., 1 mol.) in ether. After being washed and dried the ethereal solution afforded crude di-*n*-butyl phenylboronate (18·6 g., 25%), which on redistillation had b. p. 70—72°/0·02 mm., n_D^{21} 1·4828 (Found : B, 4·4%), and a solid residue, which after recrystallisation from hot water gave pure phenylboronic acid (12·8 g., 33·4%), m. p. 209—212°. Total conversion into boronic acid or ester, 58·4%.

Esterification of Phenylboronic Acid.—The results are shown in the Table. Phenylboronic acid or anhydride (50 g., 1 mol.) was heated with the appropriate alcohol (3·5 mols.) in a flask fitted with an efficient fractionating column (Snyder–Schriner type, 30 cm.) provided with a heating-jacket and a total-reflux partial take-off head. This type of column gave an efficient separation of alcohol–water azeotrope and excess of alcohol, but as the hold-up was considerable, the column was removed before the final distillation of the ester and a nitrogen-bubbler was used.

					Found (%)			Calc. (%)		
R in Ph·B(OR)$_2$	Yield (pure) (%)	B. p./mm.	d_4^{20}	n_D^{20}	C	H	B	C	H	B
Et	73	50°/0·4	0·9540	1·4785	67·3	8·3	6·1	67·5	8·5	6·1
Bu^n	83	94°/0·3	0·9245	1·4751	71·8	9·7	4·7	71·8	9·9	4·6
Bu^i	96	55°/0·2	0·9163	1·4711	71·95	9·98	4·55	71·8	9·9	4·6
Bu^s *	93	49°/0·2	0·9073	1·4658	71·9	10·1	4·6	71·8	9·9	4·6
CHMe·C_6H_{13}^{n} * †	92	119°/0·01	0·8847	1·4666	76·9	11·5	3·0	76·26	11·35	3·1
CMe$_3$·CH$_2$ * †	80	74°/0·2	0·9003	1·4678	73·8	10·7	4·0	73·3	10·4	4·1
CCl$_3$·CH$_2$ * †	96	118°/0·01	—	1·5333 ‡	§	—	2·7	§	—	2·8

* New compounds. † In these experiments Ph·BO was used. ‡ Supercooled. § Found : Cl, 54·5. Required : Cl, 55·3%.

In the preparation of diethyl phenylboronate, the acid (1 mol.), ethanol (6 mol.), and benzene (8 mol.) were heated (24 hr.) to maintain slow distillation of, successively, the ternary azeotrope (b. p. 65°), the binary (C_6H_6–EtOH) azeotrope (b. p. 68°), and finally excess of benzene, before distillation of the ester.

Preparation of Di-tert.-*butyl Phenylboronate.*—To *tert.*-butyl alcohol (6·05 g., 2 mol.) and pyridine (7·1 g., 2 mol.) in chloroform (100 c.c.) at −70° was added dropwise (0·4 hr.) with shaking phenylboron dichloride (7·05 g., 1 mol.) in chloroform (20 c.c.). After 36 hr. at 20°, the solvent was removed (20°/15 mm.—20°/1 mm.). *n*-Pentane was added, and pyridinium chloride (7·2 g , 70%) (Found : Cl, 29·6; C_5H_5N, 66·6. Calc. for C_5H_6NCl : Cl, 30·7; C_5H_5N, 68·5%) was filtered off. The filtrate gave the crude ester (8·3 g., 80%) which on redistillation afforded *di*-tert.-*butyl phenylboronate* (69%), b. p. 42°/0·01 mm., n_D^{20} 1·4635, d_4^{20} 0·9053 (Found : B, 4·59. $C_{14}H_{23}O_2B$ requires B, 4·62%). Phenylboron dichloride was prepared by the interaction of diethyl phenylboronate and boron trichloride.

THE NORTHERN POLYTECHNIC,
HOLLOWAY ROAD, LONDON, N.7.

[*Received, April 6th,* 1955.]