Organoboron Compounds. Part IX.[1] Diborinic Acids and their Derivatives

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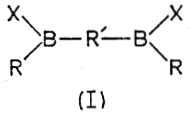
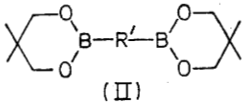
By treatment with Grignard reagents esters of the diboronic acids $(HO)_2B{\cdot}R'{\cdot}B(OH)_2$ are converted into the diborinic acids $RB(OH){\cdot}R'{\cdot}B(OH)R$, which are isolated in the form of their bis-2-aminoethyl esters. Acidification of the latter enables some of the free diborinic acids to be obtained. The hydrolysis, oxidation, and dehydration of the diborinic acids are described.

ALTHOUGH monoborinic acids, R_2BOH, and their derivatives have received considerable attention,[2] compounds of the type (I; X = OH, OR, *etc.*) containing two borinic groups have not so far been described. We have now prepared several such compounds by treating esters of suitable diboronic acids with the appropriate Grignard reagents. The manipulation of boronic esters derived from monohydric alcohols is complicated by their ready hydrolysis by moist air; accordingly we have examined the use of the bis-2,2-dimethyltrimethylene diboronates (II) which are readily prepared and are resistant to hydrolysis by atmospheric moisture.[1] The *p*-phenylenediboronate (II; R′ = *p*-C_6H_4) was treated under nitrogen with phenylmagnesium bromide (2·2 equiv.) at −70° and the resulting diborinic acid was isolated in the form of its crystalline bis-2-aminoethyl ester (Ia; X = O·CH_2·CH_2·NH_2) (48%). The related *BB*′-diaryldiborinates (Ib—f; X = O·CH_2·CH_2·NH_2) were prepared by similar reactions in yields of 21—72%. The corresponding *BB*′-dialkyl compounds (Ig and h; X = O·CH_2·CH_2·NH_2) could not be obtained in this way



(I)

a; R = Ph, R′ = *p*-C_6H_4
b; R = *p*-MeO·C_6H_4, R′ = *p*-C_6H_4
c; R = Ph, R′ = 2,5-SC_4H_2
d; R = Ph, R′ = $[CH_2]_4$
e; R = Ph, R′ = $[CH_2]_{10}$
f; R = Ph, R′ = *p*-C_6H_4·C_6H_4-*p*
g; R = Bu, R′ = *p*-C_6H_4
h; R = cyclo-C_6H_{11}, R′ = *p*-C_6H_4



(II)

and were instead prepared from tetrabutyl *p*-phenylenediboronate, which appears to be more reactive towards alkyl Grignard reagents than do the cyclic esters (II), presumably because of steric factors. Treatment of the thiophen-2,5-diyldiboronate (II; R′ = 2,5-SC_4H_2) with 2-thienylmagnesium bromide followed by 2-aminoethanol failed to give the diborinate (I; R = 2-SC_4H_3, R′ = 2,5-SC_4H_2, X = O·CH_2·CH_2·NH_2); the only product which could be isolated was 2-aminoethyl di-2-thienylborinate (25%). The formation of the latter, the structure of which follows from its alternative synthesis starting from 2-thienylmagnesium bromide and tributyl borate, suggests that the Grignard reaction follows its normal course but that the product undergoes some carbon–boron bond scission during the hydrolysis of the reaction mixture. Hydrolytic cleavage of the related compounds 2-thienylboronic acid,[3] di-2-thienylborinic acid,[4] and thiophen-2,5-diyldiboronic acid [1] is known to occur readily. The addition of 8-hydroxyquinoline to the acidified bis-2-aminoethyl diborinates (I; X = O·CH_2·CH_2·NH_2) or to the crude diborinic acids gave the diquinolin-8-yl diborinates [I; X = 8-(OC_9H_6N)] as highly insoluble yellow solids, which were purified with difficulty and are unaffected by hot dilute mineral acid.

We next examined the preparation of the free diborinic acids from the bis-2-aminoethyl diborinates (I; X = O·CH_2·CH_2·NH_2). Treatment of the diborinate (Ib; X = O·CH_2·CH_2·NH_2) in methanol with concentrated hydrochloric acid gave a mixture of the diborinic acid and its dimethyl ester (Ib; X = OMe). The latter was hydrolysed only slowly by moist air but more rapidly by water. It was best prepared by treating the bis-2-aminoethyl diborinate in methanol with glacial acetic acid and its structure follows from its proton n.m.r. spectrum [τ($CDCl_3$) 6·12 (6H, s) and 6·17 (6H, s) (*C*–OMe and *B*–OMe), 2·23, 2·38, 2·99, and 3·14 (8H, AA′XX′q terminal ring aromatic protons), 2·38 (4H, s, central ring aromatic protons)]. Attempted crystallisation of the crude diborinic acid from ethanol gave a product which showed similar i.r. absorption to that of the above ester and which is presumably the corresponding diethyl ester. This was more easily hydrolysed than was the dimethyl ester and when exposed to moist air was converted quickly and quantitatively into the pure diborinic acid (Ib; X = OH). Crystallisation from methanol of the crude diborinic acids obtained by the hydrolysis of the bis-2-aminoethyl diborinates (Ia and f; X = O·CH_2·CH_2·NH_2) again gave the corresponding dimethyl esters. The latter were readily hydrolysed, however, by moist nitrogen and gave the respective diborinic acids (Ia and f; X = OH). The reaction of the bis-2-aminoethyl diborinate (Ih; X = O·CH_2·CH_2·NH_2) with dilute hydrochloric acid and methanol gave the dicyclohexyldiborinic acid (Ih; X = OH) without difficulty but from similar hydrolyses of the esters (Ic and e; X = O·CH_2·CH_2·NH_2) the only product isolated was phenylboronic anhydride; this indicates

[1] Part VIII, I. G. C. Coutts, H. R. Goldschmid, and O. C. Musgrave, *J. Chem. Soc.* (*C*), 1970, 488.
[2] K. Torssell, *Progr. Boron Chem.*, 1964, **1**, 369; M. F. Lappert in 'The Chemistry of Boron and Its Compounds,' ed. E. L. Muetterties, Wiley, New York, 1967, p. 443.
[3] J. R. Johnson, M. G. Van Campen, and O. Grummit, *J. Amer. Chem. Soc.*, 1938, **60**, 111.
[4] H. J. Roth and B. Muller, *Naturwiss.*, 1963, **50**, 732.

that the diborinic acids which had been formed initially had undergone some carbon–boron bond scission.

In contrast to diphenylborinic acid [5] the fully benzenoid diborinic acids (Ia and f; X = OH) were unchanged after exposure to the air for 2 months. The dimethoxydiborinic acid (Ib; X = OH), like bis-*p*-methoxyphenylborinic acid, was also unaffected but the dicyclohexyl analogue (Ih; X = OH) was oxidised to *p*-phenylenediboronic acid under these conditions. Resistance to aerial oxidation thus appears to be associated with the more highly conjugated systems. The properties of the diphenyldiborinic acid (Ia; X = OH) differ from those of diphenylborinic acid in several other respects. The latter undergoes dehydration [6] at room temperature *in vacuo* but, in the form of its anhydride, is unaffected by steam-distillation.[7] The diborinic acid, on the other hand, undergoes dehydration only when heated at 175°/0·1 torr but is rapidly hydrolysed by boiling water to give benzene and phenylboronic acid, together with a little *p*-phenylenediboronic acid. Treatment of the diborinic acid with aqueous 2-aminoethanol in the presence of air results in the oxidation of the *p*-phenylene group with the formation of 2,5-bis-(2-hydroxyethylamino)-1,4-benzoquinone. This behaviour resembles that of *p*-phenylenediboronic acid,[1] which undergoes similar aerial oxidation in alkaline solution.

The dimethoxydiborinic acid (Ib; X = OH) forms a bis-4-dimethylaminopyridine adduct. The corresponding dimethyl diborinate (Ib; X = OMe) reacts with phosphorus pentachloride to give the expected *BB'*-dichloro-compound (Ib; X = Cl).

EXPERIMENTAL

The methods used for the analysis of the products and for their identification or characterisation were similar to those described in Part VIII.[1] With the 2-aminoethyl and the quinolin-8-yl mono- and di-borinates nitrogen was best determined by the Dumas method. Unless stated otherwise all operations involving Grignard reagents, and the borinic acids or their derivatives, were conducted under dry nitrogen.

Bis-2-aminoethyl Diborinates (I; X = O·CH_2·CH_2·NH_2). —*General procedure.* The Grignard reagent prepared from the appropriate alkyl or aryl bromide (0·22 mole), magnesium turnings (7·0 g., 0·29 mole) and dry ether (150 ml.) was added to a cooled, vigorously stirred suspension of the appropriate diboronate [1,8] (0·1 mole) in dry tetrahydrofuran (400 ml.) and dry ether (300 ml.) at such a rate that the temperature did not rise above −70°. The mixture was allowed to warm to room temperature overnight with stirring and was kept for 2 days. Ice-cold M-hydrochloric acid (300 ml.) was then added dropwise with stirring and the mixture was shaken with ether (3 × 500 ml.). The organic layers were combined, evaporated to *ca.* 300 ml. and added slowly to an ice-cold solution of 2-aminoethanol (40 ml.) in methanol (250 ml.) and water (200 ml.) through which nitrogen was passed. The mixture was kept at 0° until precipitation was complete and the resulting crystalline solid was collected, and washed successively with water and methanol. Purification of the solid was effected by (*a*) crystallisation from methanol–chloroform, or (*b*) dissolution in hot methanol containing acetic or hydrochloric acid followed by addition of hot aqueous 2-aminoethanol and subsequent crystallisation. The *bis-2-aminoethyl diborinates* prepared in this way are listed in Table 1.

TABLE 1

Bis-5-aminoethyl diborinates (I; X = O·CH_2·CH_2·NH_2)

Diborinate	Method *	Yield (%)	M.p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
BB'-Diphenyl-*p*-phenylene- (Ia)	*a*	48	271—271·5°	$C_{22}H_{26}B_2N_2O_2$	71·4	7·2	7·6	71·05	7·05	7·55
BB'-Bis-*p*-methoxyphenyl-*p*-phenylene- (Ib)	*a*	72	251—252	$C_{24}H_{30}B_2N_2O_4$ †	67·0	7·2	6·2	66·7	7·0	6·5
BB'-Diphenylthiophen-2,5-diyl- (Ic)	*a*	24	225—226	$C_{20}H_{24}B_2O_2N_2S$ ‡	63·1	6·4	7·5	63·5	6·4	7·4
BB'-Diphenyltetramethylene- (Id)	*a*	21	115—116	$C_{20}H_{30}B_2N_2O_2$	68·2	8·6	7·6	68·2	8·6	7·95
BB'-Diphenyldecamethylene- (Ie)	*a*	38	153—155	$C_{26}H_{42}B_2N_2O_2$	71·7	9·8	6·4	71·55	9·7	6·4
BB'-Diphenyl-4,4'-biphenylylene- (If)	*a*	25·5	224—225	$C_{28}H_{30}B_2N_2O_2$			6·6			6·25
BB'-Dibutyl-*p*-phenylene- (Ig)	*b*	13	170·5—171	$C_{18}H_{34}B_2N_2O_2$			8·3			8·45
BB'-Dicyclohexyl-*p*-phenylene- (Ih)	*b*	51	234—236	$C_{22}H_{38}B_2N_2O_2$			7·0			7·3

* The diborinates were prepared from the corresponding bis-2,2-dimethyltrimethylene diboronates (method *a*) or tetrabutyl diboronates (method *b*). † Found: MeO, 15·0. Required: 2MeO, 14·35%. ‡ Found: S, 8·8%. Required: S, 8·5%.

Attempted Preparation of Bis-2-aminoethyl BB'*-Di-2-thienylthiophen-2,5-diyldiborinate.*—A similar reaction between 2-thienylmagnesium bromide and bis-2,2-dimethyltrimethylene thiophen-2,5-diyldiboronate gave 2-aminoethyl di-2-thienylborinate (25%) (see later).

Diquinolin-8-yl Diborinates [I; X = 8-(OC_9H_6N)].—The addition of a saturated solution of 8-hydroxyquinoline in methanol to an acidified solution of a bis-2-aminoethyl diborinate in the same solvent, or to an ethereal solution of a crude diborinic acid, gave a precipitate of the corresponding *diquinolin-8-yl diborinate* which crystallised in yellow needles from chloroform–methanol or from chlorobenzene. The diborinates prepared in this way are listed in Table 2.

BB'*-Bis-*p*-methoxyphenyl-*p*-phenylenediborinic Acid* (Ib; X = OH).—A solution of bis-2-aminoethyl *BB'*-bis-*p*-methoxyphenyl-*p*-phenylenediborinate (5 g.) in hot methanol (50 ml.) was made just acid to litmus with concentrated hydrochloric acid and was then added to ice–water (20 ml.). The mixture of the diborinic acid and its dimethyl ester (see later) which was precipitated was collected and stirred with ice–water for 1 hr. to ensure complete hydrolysis. A chilled solution of the resulting diborinic acid in ethanol deposited colourless needles of the diethyl ester (m.p. 84—86°) which on exposure to moist air overnight gave the

[5] G. N. Chremos, H. Weidmann, and H. K. Zimmerman, *J. Org. Chem.*, 1961, **26**, 1683.
[6] E. W. Abel, S. H. Dandegaonker, W. Gerrard, and M. F. Lappert, *J. Chem. Soc.*, 1956, 4697.
[7] R. Neu, *Chem. Ber.*, 1954, **87**, 802.
[8] O. C. Musgrave, *Chem. and Ind.*, 1957, 1152.

diborinic acid as needles (2·5 g., 58%), m.p. 132—134° (Found: B, 6·3; MeO, 16·8. $C_{20}H_{20}B_2O_4$ requires B, 6·25; 2MeO, 17·95%). Mixed ethanolic solutions of the diborinic acid and 4-dimethylaminopyridine gave a precipitate of the *bis-4-dimethylaminopyridine adduct* which crystallised from ethanol–chloroform as prisms, m.p. 196—199° (Found: C, 68·8; H, 7·0; N, 9·4. $C_{20}H_{20}B_2O_4,2C_7H_{10}N_2$ requires C, 69·15; H, 6·85; N, 9·5%).

Dimethyl BB′-*Bis*-p-*methoxyphenyl*-p-*phenylenediborinate* (Ib; X = OMe).—Glacial acetic acid was added dropwise to a suspension of bis-2-aminoethyl *BB′*-bis-*p*-methoxyphenyl-*p*-phenylenediborinate (1 g.) in boiling methanol until all the ester had dissolved. The cooled solution deposited the *dimethyl diborinate* (0·56 g., 65%) which crystallised from chloroform–methanol in prisms, m.p. 155—157° (Found: C, 70·4; H, 6·4; B, 5·9; MeO, 29·0. $C_{22}H_{24}B_2O_4$ requires C, 70·65; H, 6·45; B, 5·8; 4MeO, 33·2%).

BB′-*Diphenyl*-p-*phenylene*- and BB′-*Diphenyl*-4,4′-*biphenylylene-diborinic Acid* (Ia and f; X = OH).—A suspension of bis-2-aminoethyl *BB′*-diphenyl-*p*-phenylenediborinate (6 g.) in methanol (35 ml.) was made just acid to litmus by the addition of concentrated hydrochloric acid and added to ice–water (450 ml.). Next day the solid which had separated was collected and crystallised from warm methanol. The resulting dimethyl ester, when exposed to a stream of moist nitrogen overnight, was converted into the *diborinic acid* (Ia; X = OH) (2·8 g., 60%), m.p. 105—107° (Found: B, 7·5. $C_{18}H_{16}B_2O_2$ requires B, 7·55%), which when dried at 175°/0·1 torr for 1 hr. gave the corresponding *anhydride* as a glass (Found: B, 8·25. $C_{18}H_{14}B_2O$ requires B, 8·05%).

Similar treatment of bis-2-aminoethyl *BB′*-diphenyl-4,4′-biphenylylenediborinate gave the corresponding *diborinic acid* (If; X = OH) (65%), m.p. 125—127° (Found: B, 6·15. $C_{24}H_{20}B_2O_2$ requires B, 6·0%).

BB′-*Dicyclohexyl*-p-*phenylenediborinic Acid* (Ih; X = OH).—A suspension of bis-2-aminoethyl *BB′*-dicyclohexyl-*p*-phenylenediborinate (3 g.) in methanol was made just acid to litmus with hydrochloric acid and added to ice. The resulting solid was washed with water and dried *in vacuo* over silica gel giving the *diborinic acid* (1·75 g., 75%) (Found: B, 7·3. $C_{18}H_{28}B_2O_2$ requires B, 7·25%). When exposed to air this became brown and after 4 weeks showed i.r. absorption identical with that of *p*-phenylenediboronic acid.

2-*Aminoethyl Di*-2-*thienylborinate*.—The Grignard reagent prepared from 2-bromothiophen (41 g.), magnesium (7 g.), and ether (60 ml.) was added with stirring to a cooled solution of tributyl borate (freshly distilled; 28 g.) in ether (150 ml.) at such a rate that the temperature did not rise above −70°. The mixture was allowed to warm to room temperature overnight, kept for 3 days, and made just acid to litmus with ice-cold M-hydrochloric acid. The organic layer was separated, the aqueous layer was extracted with ether, and the combined organic layers were evaporated to *ca.* 250 ml. The solution of the crude borinic acid was added to a mixture of 2-aminoethanol (20 ml.), methanol (50 ml.), and water (150 ml.) at 0° and the resulting precipitate was washed with water and dried. Crystallisation from methanol–chloroform gave 2-*aminoethyl di*-2-*thienylborinate* (20 g., 70·5%) as needles, m.p. 200—202° (Found: B, 4·6; N, 5·8; S, 27·0. $C_{10}H_{12}BNOS_2$ requires B, 4·55; N, 5·9; S, 27·05%).

BB′-*Dichloro*-BB′-*bis*-p-*methoxyphenyl*-p-*phenylenebisborane* (Ib; X = Cl).—A mixture of phosphorus pentachloride (5·15 g.), dimethyl *BB′*-bis-*p*-methoxyphenyl-*p*-phenylenediborinate (4·65 g.), and carbon tetrachloride (40 ml.) was boiled under reflux until gas evolution had ceased (15 min.) and filtered under dry nitrogen. Crystallisation of the residue from dry carbon tetrachloride gave the BB′-*dichlorobisborane* (1·28 g., 27%) as a nearly colourless solid which softened at >230° [Found: B, 5·6; Cl (by titration with alkali), 16·7. $C_{20}H_{18}B_2Cl_2O_2$ requires B, 5·65; Cl, 18·5%]. This on treatment with methanol evolved hydrogen chloride and regenerated the dimethyl diborinate (57%).

TABLE 2

Diquinolin-8-yl diborinates [I; X = 8-(OC_9H_6N)]

Diborinate	M.p. (decomp.)	Formula	Found (%) N	Required (%) N
BB′-Diphenyl-*p*-phenylene- (Ia)	>350°	$C_{36}H_{26}B_2N_2O_2$	4·9	5·2
BB′-Bis-*p*-methoxyphenyl-*p*-phenylene- (Ib)	281—283	$C_{38}H_{30}B_2N_2O_4$ *	4·8	4·65
BB′-Diphenylthiophen-2,5-diyl- (Ic)	289—293	$C_{34}H_{24}B_2N_2O_2S$	5·4	5·1
BB′-Diphenyltetramethylene- (Id)	263—264·5	$C_{34}H_{30}B_2N_2O_2$	5·3	5·4
BB′-Dibutyl-*p*-phenylene- (Ig)	251—253	$C_{32}H_{34}B_2N_2O_2$ †	6·0	5·6

* Found: MeO, 11·2. Required: 2MeO, 10·5%. † Found: C, 77·0; H, 7·1. Required: C, 76·85; H, 6·85%.

Hydrolytic Deboronation of BB′-*Diphenyl*-p-*phenylenediborinic Acid*.—(*a*) When the diborinic acid (2 g.) was boiled for 5 min. under nitrogen with water (60 ml.) in a 'heavy-entrainer' Dean and Stark apparatus, benzene (0·45 ml.) was obtained. The aqueous solution was cooled and *p*-phenylenediboronic acid (0·12 g.) crystallised as needles. Evaporation of the mother liquor under reduced pressure and crystallisation of the residue from carbon tetrachloride gave phenylboronic anhydride (0·95 g.), m.p. 223—224°.

(*b*) Aqueous 2-aminoethanol was added to a solution of the diborinic acid in methanol and the mixture was exposed to air for 2 days. Crystallisation of the resulting purple precipitate from water gave 2,5-bis-(2-hydroxyethylamino)-1,4-benzoquinone, m.p. 254—255° (decomp.), identical with an authentic specimen, m.p. 254—255° (decomp.) (lit.,[9] 262°).

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[9] S. Kanao and S. Inagawa, *J. Pharm. Soc. Japan*, 1938, **58**, 347.