Tetrahedron, 1961, Vol. 15, pp. 26 to 34. Pergamon Press Ltd. Printed in Northern Ireland

NEW HETEROAROMATIC COMPOUNDS—XII[1]

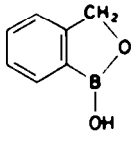
FURTHER EVIDENCE FOR THE AROMATICITY OF THE BORAZARENES

M. J. S. DEWAR and R. DIETZ
George Herbert Jones Laboratory, University of Chicago

(*Received* 18 *February* 1961)

Abstract—Snyder and his co-workers[2] have reported that the cyclic boric ester (I) is stable to hydrolysis and may be nitrated. These observations suggests that the stability of the heterocyclic boron compounds described in previous papers of this series might be due to their cyclic nature rather than to aromatic resonance. Their reactions with bases, and a comparison of the properties of 2:1-borazaronaphthalenes with those of their 3:4-dihydro derivatives seem to make this unlikely.

SNYDER[2] has reported that the internal ester (I) of *o*-hydroxymethyl phenylboronic acid is resistant to hydrolysis and may be nitrated; this suggests that part or even all of the stability of the heterocyclic boron compounds described in earlier papers of series might be due to their cyclic structures rather than to aromaticity of the boron-containing rings. Here we present additional evidence suggesting that this is not the case and that our compounds owe their stability to their aromatic structure. Part of this new evidence refers to the reactions of borazarene derivatives with bases and part to a comparison of the properties of derivatives of 2:1-borazaronaphthalene with those of the corresponding non-aromatic 3:4-dihydro derivatives.

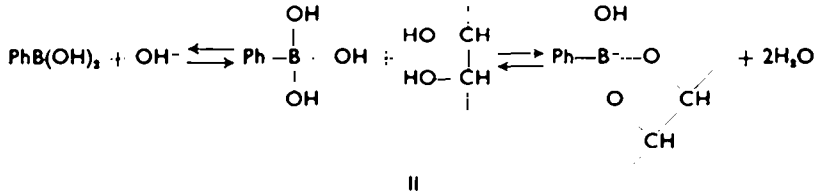


I

The acidity of a compound containing a hydroxy-substituted boron atom may arise in two ways. The acid may lose a proton to give a trigonal planar anion, or the boron atom may behave as a Lewis acid centre, and coordinate with a hydroxyl anion. The configuration about the boron atom would then be tetrahedral. The latter structure has been favored for the borate ion, on the basis of Raman spectroscopy[3] and for the phenyl boronate ion, because the acidity is diminished by *ortho*-substitution (F-strain)[4] and increased by the addition of polyols.[5] Lorand and Edwards[5] found that the formation constants of complexes between phenyl boronic acid and various polyols were larger than those of the corresponding boric acid–polyol complexes, and deduced that the phenyl boronate ion was tetrahedral. The

[1] Part XI: M. J. S. Dewar and V. P. Kubba *J. Amer. Chem. Soc.* In press.
[2] H. R. Snyder, A. J. Reedy and W. J. Lennarz *J. Amer. Chem. Soc.* **80**, 835 (1958); W. J. Lennarz and H. R. Snyder, *Ibid.* **82**, 2172 (1960).
[3] J. O. Edwards, G. C. Morrison, V. F. Ross and J. W. Schultz *J. Amer. Chem. Soc.* **77**, 266 (1955).
[4] D. H. McDaniel and H. C. Brown *J. Amer. Chem. Soc.* **77**, 3757 (1955).
[5] J. P. Lorand and J. O. Edwards *J. Org. Chem.* **24**, 769 (1959).

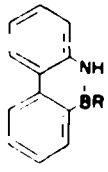
essential reaction was assumed to be of the following type:



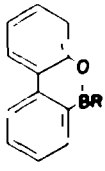
II

They found that the pH-depression tended to a maximum with increasing polyol concentration only in the case of mannitol and ascribed this behavior to the formation of neutral as well as anionic complexes.

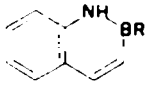
The acidity of derivatives of the heteroaromatic boron containing analogues of phenanthrene (III)[6] (IV)[7] and naphthalene (V)[8] described in previous papers in this series is of further interest since the participation of the boron atom in a cyclic conjugated system has been shown[6, 8] to modify its properties considerably and should allow ultra-violet spectroscopy to be used to follow the acid-base changes. We have



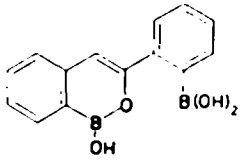
III
a, R = OH



IV
a R = OH



V
a R = OH
b R = Me
c R = Ph



VI

studied three heteroaromatic compounds from this viewpoint, 10-hydroxy-10,9-borazarophenanthrene (IIIa) 10-hydroxy-10,9-boroxarophenanthrene (IVa) and 2-hydroxy-2,1-borazaronaphthalene (Va). The isomerization product of 2,2′ tolandiboronic acid[9] which very probably[7] has the structure (VI) is also discussed and measurements were made on phenyl boronic acid and 2-biphenylboronic acid for comparison. Although Va exists[8] as bis(2,1-borazaro-2-naphthyl)ether in the solid state and IVa undergoes reversible dehydration, the formation of alkyl ethers[8,10] from IIIa, IVa and Va on crystallization from alcohols and the ease of their hydrolysis shows that all three exist as hydroxy-derivatives in solution in aqueous ethanol.

The acidities were compared as the pH-values of half-neutralized solutions of the acids in 1 : 1 aqueous ethanol. The point of half-neutralization was the calculated one since most of the acids were too weak to allow an accurate determination of the end-points in this solvent mixture. The effect of polyol was found by adding mannitol in concentrated aqueous solution at the half-neutralization point.

[6] M. J. S. Dewar, V. P. Kubba and R. Pettit *J. Chem. Soc.* 3073 (1958).
[7] M. J. S. Dewar and R. Dietz *J. Chem. Soc.* 1344 (1960).
[8] M. J. S. Dewar and R. Dietz *J. Chem. Soc.* 2728 (1959).
[9] R. L. Letsinger and J. R. Nazy *J. Amer. Chem. Soc.* **81**, 3013 (1959).
[10] M. J. S. Dewar, R. Dietz, V. P. Kubba and A. R. Lepley *J. Amer. Chem. Soc.* In press.

The pH-values of half-neutralized solutions of IIIa and Va did not differ significantly from those of the correspondingly diluted alkali and no increase in acidity was produced by added mannitol. Addition of alkali to an ethanol solution of Va produced a reversible spectral change (Fig. 1) but not in the direction of the corresponding 2-aminostyrene spectrum. No spectral change was produced when alkali was added to ethanolic solutions of 2-methyl and 2-phenyl-2,1-borazaronaphthalene (Vb,c). The reversible reaction of Va with alkali was therefore not one of co-ordination and the anion corresponding to Va must be planar. This reversal of the behavior

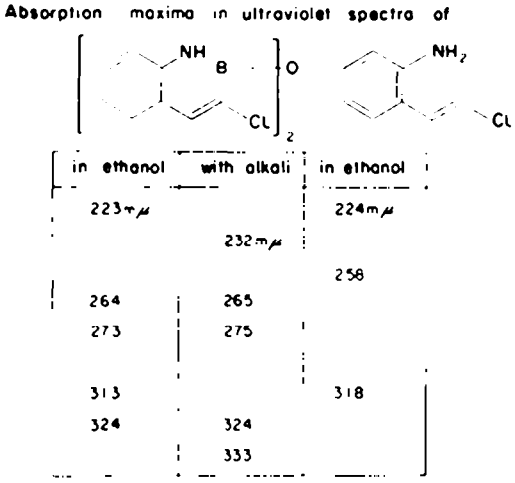


FIG. 1. Effect of added alkali on ultraviolet spectrum of a bis (2,1-borazaro-2-naphthyl)ether.

in acyclic boronic acids is compatible with the aromatic formulation of Va. The addition of a hydroxyl ion would remove the boron atom from conjugation and any aromatic stabilization energy would be lost. Similarly no change is produced in the spectra of any available 2,1-borazaronaphthalene by the addition of acid. The extreme weakness of the acids (IIIa and Va) may be explained likewise. Removal of a proton leaves a negative charge on the oxygen atom which reduces the extent of charge transfer from nitrogen to boron necessary for aromaticity. The annular boron atom in VI was reported[9] to show no acidity, even in the presence of mannitol, and this unexplained observation is clearly capable of similar rationalization.

The pH-values of half-neutralization of phenyl boronic acid, 2-biphenyl boronic and IVa were 11·0, 12·0 and 9·1 units. The difference between the first two was compatible with F-strain in the 2-biphenyl boronate ion, but the acidity of IVa was surprisingly high. It appears[11] to be one of the strongest boronic acids known and presents a most striking contrast to the behavior of the boron-nitrogen heterocycles discussed above, and particularly to that of VI. The acidities of IVa and the two acyclic boronic acids were increased by added mannitol. The resulting pH-depressions are shown (Fig. 2), and in each case tended towards a maximum.

The ultraviolet spectrum of 10-hydroxy-10,9-boroxarophenanthrene was measured with an excess of mannitol in neutral, acidic, and basic solution (Fig. 3). Under acidic conditions the spectrum was exactly like that in the absence of mannitol. No

[11] G. E. K. Branch, D. L. Yabroff and B. Bettman *J. Amer. Chem. Soc.* **56**, 937 (1934).

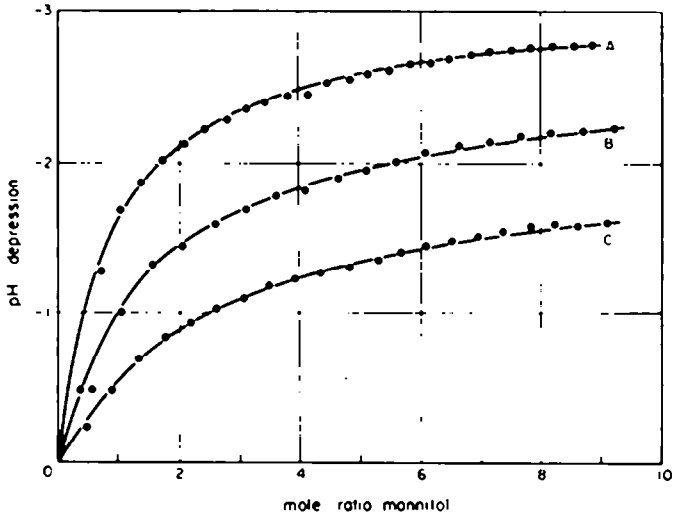


FIG. 2. Effect of mannitol added to half-neutralized solutions of A, phenylboronic acid; B, 2-biphenylboronic acid; C, 10-hydroxy-10,0-boroxarophenanthrene in 1:1 aqueous ethanol.

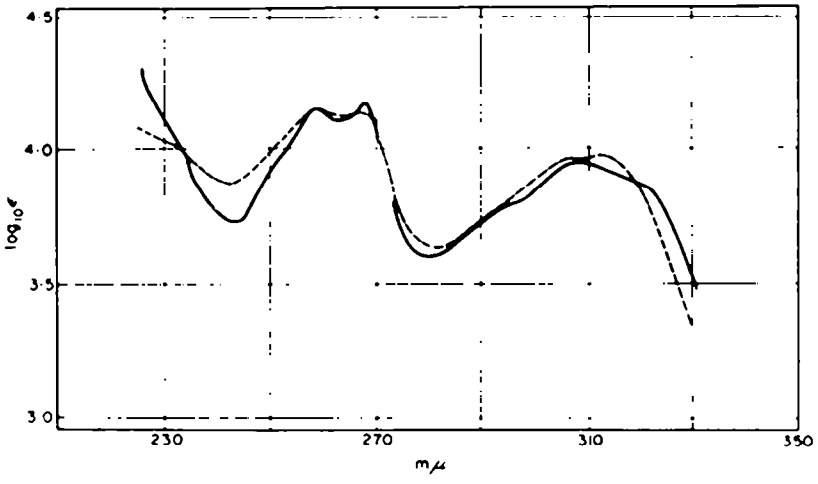


FIG. 3(a). Ultraviolet spectra of 10-hydroxy-10,9-boroxaropehnanthrene in 95 per cent ethanol with alkali (. . . . .) and with aqueous mannitol (– —).

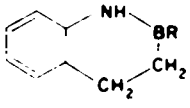
Absorption maxima in the ultraviolet spectrum of 10-hydroxy-10,9-boroxarophenanthrene in

Ethanol (mμ)	Ethanol with alkali (mμ)	Ethanol with mannitol (mμ)	Ethanol with acid and mannitol (mμ)
258			258
		259	
	260		
	267		
268			268
		269	
283			283
294			294
		309	
	310		

FIG. 3(b). Effect of added mannitol on ultraviolet spectra of 10-hydroxy-10,9-boroxarophenanthrene.

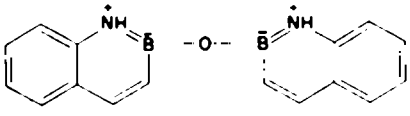
neutral complexes were formed. The neutral spectrum, however, resembled closely that of the anion; this was produced[7] reversibly by the addition of a little alkali to a solution of IVa, and reverted to the original spectrum with acid. The alkaline spectrum in presence of mannitol was very similar. Anionic complexes were therefore formed between IVa and mannitol. Their spectral similarity to the simple anion leaves little doubt that the ionic equilibria must resemble those of equation (II) and that the boron atom is tetrahedral and removed from conjugation in the anion. The only possible rationalization of the unusual acid strength of IVa and the total dissimilarity from VI is that the boroxarophenanthrene system is quite highly strained, as indeed is indicated by models, and that the strain is relieved when the boron atom adopts a tetrahedral configuration. The explanation given earlier[7] of the reduced aromaticity of the 10,9-boroxarophenanthrenes may well require modification and further work on the boroxaronaphthalenes is clearly necessary since the reported[9] lack of acidity of the annular boron atom in VI suggests that they resemble the 2,1-borazaronaphthalenes quite closely.

Further confirmation of the aromatic formulation of the latter compounds V has now been obtained. We hoped to reduce the non-benzenoid double bond to give derivatives of 3,4 dihydro-2,1-borazaronaphthalene (VI), and to demonstrate the unusual properties of IV were dependent on 3,4 unsaturation.

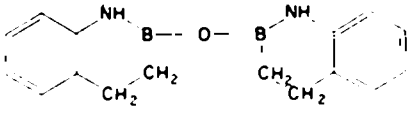


VII

Bis(2,1-borazaro-2-naphthyl) ether (VIII) proved to be fairly resistant to treatment which lead to the smooth reduction of most styrenes.[12] Recovery was 70 per cent when a 6-molar excess of sodium was added to a boiling solution of VII in ethanol. When n-butanol was used, bis(3,4-dihydro-2,1-borazaro-2-naphthyl)ether (IX) was formed in good yield. The structure of the product followed from elementary



VIII



IX

analysis; the identification in the infrared spectrum (Fig. 4) of peaks due to the stretching of aliphatic C—H-bonds (2915, 2882, 2825 cm $^{-1}$), absent in the spectrum of VIII, and of an N –H bond (3378 cm $^{-1}$); and the ultraviolet spectrum (Fig. 5) which resembled that of a 2-toluidine rather than that of VIII. An analogous reduction of 2-naphthol with sodium in amyl alcohol to give 2-hydroxy-1,2,3,4-tetrahydro naphthalene has long been known.[13]

When warmed in acetic anhydride (IX) gave a diacetyl derivative (X) as shown by elementary analysis and the absence of an NH stretching absorption in the I.R. spectrum (Fig. 4). After similar treatment VIII was recovered unchanged.

[12] K. N. Campbell and B. K. Campbell *Chem. Rev.* **31**, 85 (1942).
[13] E. Bamberger and W. Lodter *Ber.* **23**, 197 (1890).

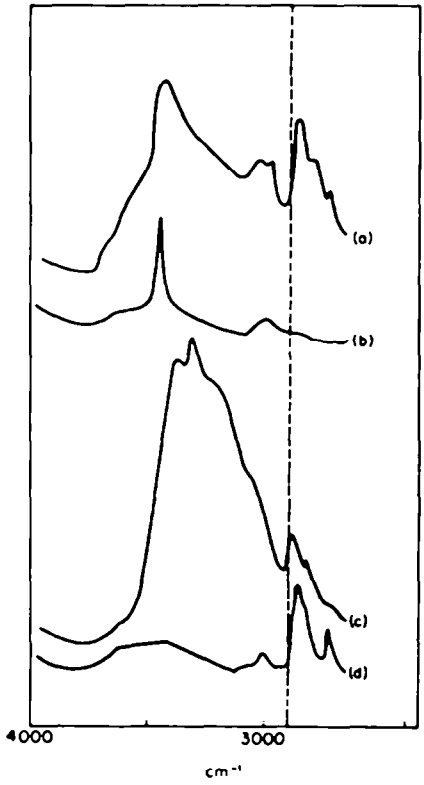


FIG. 4. Infrared spectra in hexachlorobutadiene mulls of (a) bis (3,4-dihydro-2,1-borazaro-2-naphthyl) ether; (b) bis (2,1-borazaro-2-naphthyl) ether; (c) 2-acetamidophenethyl boronic acid; (d) bis (1-acetyl-3,4-dihydro-2,1-borazaro-2-naphthyl) ether.
Absorption to the right of the broken line corresponds to saturated C—H stretching.

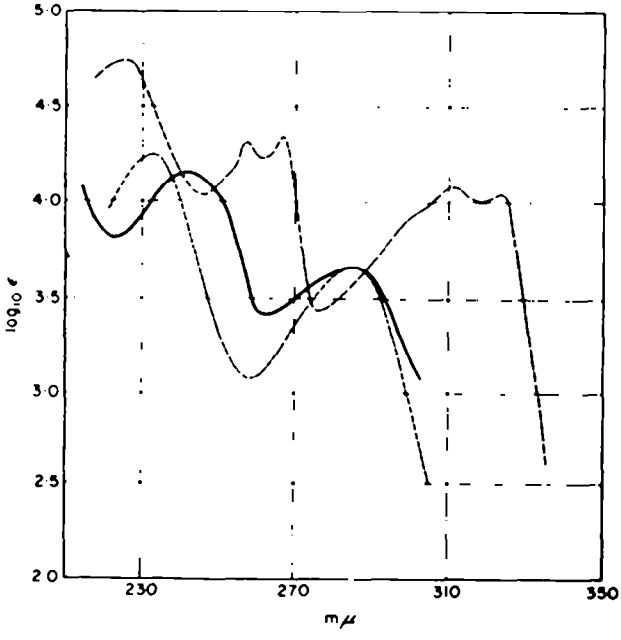
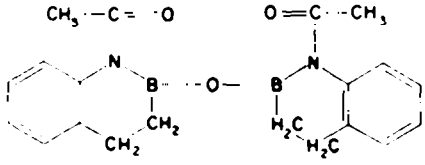


FIG. 5. Ultraviolet spectra of bis (3,4-dihydro-2,1-borazaro-2-naphthyl) ether in cyclohexane (– ——) of bis (2,1-borazaro-2-naphthyl) ether in cyclohexane (– – –) and of 2-toluidine in cyclo-octane with concentration doubled (. . . . . .).

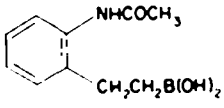
The unusual resistance to hydrolysis of the boron-nitrogen bond in the 2,1-borazaronaphthalenes was strongly indicative of their aromaticity. 2-Phenyl-2,1-borazaronaphthalene (Vc) was recovered unchanged after 3 hr boiling with concentrated hydrochloric acid and after 2 hr boiling with 40 per cent aqueous potassium hydroxide. Prolonged boiling of VIII in 10 per cent aqueous alkali[8] failed to produce an ultraviolet spectrum different from that of the anion, which was produced immediately and reversibly by the addition of a little alkali to an ethanolic solution.



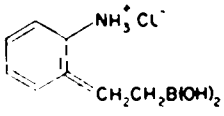
X

The stability of the boron–nitrogen bonds in IX and X was of a quite different order. Their melting points fell on storage in air, but returned to the original values after heating *in vacuo*. X dissolved in hot water and there crystallized a new compound, whose neutralization equivalent differed from that of X by the equivalent of 1·5 molecules of water. The infrared spectrum (Fig. 4) unlike that of X showed a broad N—H stretching absorption at 3336 cm $^{-1}$, and elementary analysis supported the formulation 2-acetamidophenethylboronic acid (XI). No sharp melting point could be obtained for XI, even in preheated baths, presumably because of slow cyclization to (X). On heating XI *in vacuo*, reconversion to (X) was quantitative.

2-Amino phenethyl boronic acid hydrochloride (XII) crystallized from solutions of IX in dilute hydrochloric acid. Cyclization of XII was apparently inhibited by the positive charge on the nitrogen atom, since a sharp melting point was observed and since no dehydration could be effected by heating *in vacuo*.

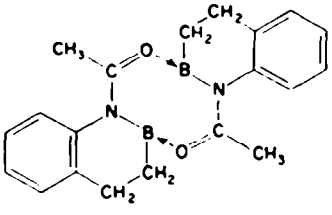


XI

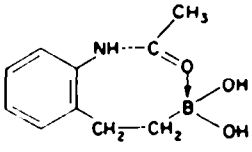


XII

One curious feature of X and XI was that their IR spectra showed no amide carbonyl absorption (1625–1700 cm^{-1}), although their preparation and interconversion leave their structures in no doubt. The only reasonable explanation seems to be that the carbonyl groups are internally chelated to boron (XIII and XIV), and that the weakened carbonyl absorption then appears at lower frequencies. The structures (XIII and XIV) are conformationally favorable and little strained.

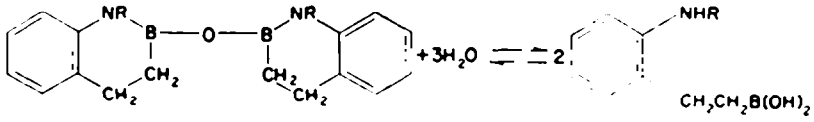


XIII



XIV

Reduction of the 3,4-double bond in the 2,1-borazaronaphthalenes resulted in a considerable modification in the properties of the system. The stability of the boron-nitrogen bond was reduced to an extent such that the reversible reaction (XV) took place, and acetylation of the amine function under normal conditions became possible,



XV

whereas we were unable to prepare an acetyl derivative of VIII. Both differences clearly reflected the aromaticity of the 2,1-borazaronaphthalenes.

EXPERIMENTAL

Acid strengths

Samples (ca. 25 mg) of the various acids were dissolved in a mixture of carbon dioxide-free water (25 ml) and ethanol (25 ml) at 15°. A slow stream of nitrogen was passed through the solution, and successive equal volumes of sodium hydroxide (0·05 N in CO_2-free water) and ethanol were added. The pH-value of the solution was measured after each pair of additions by means of a Pye Universal pH meter, with micro calomel and glass electrodes. The meter was standardized in a pH 5·6 aqueous buffer and the electrodes were stored in water and immersed in the solvent mixture for the minimum time consistent with accuracy. The difference in buffer readings before and after the titration never exceeded 0·02 pH units for the quoted values. Mannitol was added dropwise in 10 per cent aqueous solution. Duplicate determinations were carried out in all cases, the deviation never exceeding 0·05 pH units for the quoted values.

Neutralization equivalents were found by titration with standard alkali in the presence of mannitol. Bis(2,1-borazaro-2-naphthyl)ether was prepared from 2-amino styrene.[8] Analyses, including those for boron, were by Alfred Bernhardt, Mulheim, Germany.

Bis(3,4-dihydro-2,1-borazaro-2-naphthyl) ether

Freshly cut pieces of sodium (2·3 g; 0·1 g atoms) were added down the condenser to a vigorously stirred, boiling solution of bis(2,1-borazaro-2-naphthyl) ether (4·11 g, 0·015 mole) in n-butanol (300 ml). When the sodium had dissolved, water (500 ml) and hydrochloric acid were added until the aqueous layer was strongly acid. The butanol water azeotrope was removed at 100° and *c.* 30 mm before the red solution was cooled, made just alkaline with ammonia (sp.gr. 0·880) and extracted with ether (5 × 100 ml). The combined ethereal extracts were dried ($MgSo_4$) and evaporated to give a red oil which, when heated at 80° and 0·5 mm gave crude *bis (3,4-dihydro-2,1-borazaro-2-naphthyl)ether* as a pale yellow solid, m.p. 83–86° (3·8 g, 91%).

Crystallization under dry nitrogen from dry pentane removed the color and raised the melting point to 87·5–89°.

(Found: C, 69·6; H, 6·5; N, 10·0; B, 8·0%. Calc. for $C_{16}H_{16}N_2B_2O$ C, 69·6; H, 6·6; N, 10·2; B, 8·0%.

Bis(1-acetyl-3,4-dihydro-2,1-borazaro-2-naphthyl)ether.

The diacetyl derivatives was formed on warming bis(3,4-dihydro-2-1-borazaro-2-naphthyl)ether in acetic anhydride. Hydrolysis was avoided by removing the excess of reagent at 100° and 15 mm. Crystallization from chloroform–light petroleum (b.p. 60–80°) gave needles of the diacetyl derivative m.p. 280–282°.

(Found: C, 66·6; H, 6·2; N, 7·7; B, 6·4%. Neutralization equivalent 180.) Calc. for $C_{20}H_{22}N_2B_2O_3$ C, 66·7; H, 6·2; N, 7·8; B, 6·0%. Neutralization equivalent 181.

2-Acetamido phenethyl boronic acid

Crystallization of the above diacetyl derivative from water gave rectangular prisms of *2-acetamido phenethyl boronic acid*, which began to melt at 127°. No sharp melting point could be obtained, even in preheated baths.

(Found: C, 58·3; H, 6·8; N, 7·0; B, 5·5%. Neutralization equivalent 208. Calc. for $C_{10}H_{14}NO_3B$ C, 58·0; H, 6·8; N, 6·8; B, 5·2%. Neutralization equivalent 207.)

2-Amino phenethyl boronic acid hydrochloride

Crystallization of bis(3,4-dihydro-2,1-borazaro-2-naphthyl)ether from dilute hydrochloric acid (2 N) after treatment with charcoal gave long colorless needles of the *hydrochloride* m.p. 190–192°.

(Found: C, 47·3; H, 6·5; N, 7·0; Cl, 17·7; B, 5·7%. Calc. for $C_8H_{12}NClO_2BC$, 47·7; H, 6·5; N, 7·0; Cl, 17·6; B, 5·4%.)

Acknowledgements—The work described in this paper was carried out at Queen Mary College, University of London. We wish to thank the University of London for the award of the William Lincoln Shelley Research Studentship (to R. D.) the Kodak Co. for the gift of crude 2-aminophenethanol, and Dr. J. M. Davidson for a sample of 2-biphenyl boronic acid.