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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, NORTHWESTERN UNIVERSITY]

Organoboron Compounds. XIII. Boronic Acids with Neighboring Unsaturated Groups[1]

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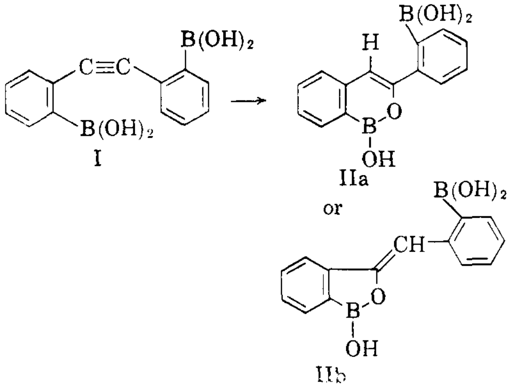
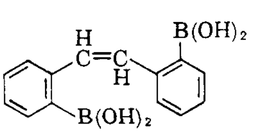
2,2′ Stilbenediboronic acid, 2-vinylbenzeneboronic acid, and 2-tolanboronic acid are described. None of these compounds isomerizes under conditions which convert 2,2′-tolandiboronic acid to a heterocyclic compound (II).

2,2′-Tolandiboronic acid (I) readily isomerizes in an alkaline medium or in solutions containing potassium acid tartrate to give a heterocyclic compound, which has been formulated as either IIa or IIb.[4]

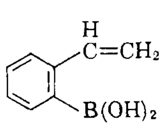


I IIa IIb

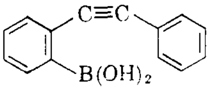
In order to gain further information concerning the reactions of boronic acid groups with neighboring unsaturated linkages, we prepared 2,2′-stilbenediboronic acid (III), 2-vinylbenzeneboronic acid (IV), and 2-tolanboronic acid (V) and subjected them to conditions which would effect the transformation of I to II. Particular attention was directed to 2-tolanboronic acid, for should this compound yield a product analogous to II, it would be possible by oxidative degradation to determine whether the hetero-ring was five- or six-membered.



III



IV



V

Neither the stilbenediboronic acid nor the vinylbenzeneboronic acid yielded isolable rearrangement products under the conditions examined. In each case the major portion of the boronic acid was recovered unchanged, as shown by the infrared spectrum. The vinyl group in 2-vinylbenzeneboronic acid possessed normal reactivity with respect to polymerization. Like 4-vinylbenzeneboronic acid[5] compound IV yielded when warmed with azobisisobutyronitrile a brittle polymer, which was insoluble in ether or benzene but soluble in alkaline solutions.

More surprising, no isomerization was observed with 2-tolanboronic acid.[6] This fact shows that both boronic acid groups in 2,2′-tolandiboronic acid must play a role in the isomerization and suggests that the reaction may involve concerted donation of a proton by one boronic acid group and a hydroxide ion by the other (which is complexed with hydroxide or tartrate ion) to the two carbon atoms joined by the triple bond. Models indicate that a

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(1) For the previous paper in this series see R. L. Letsinger and S. B. Hamilton, *J. Org. Chem.*, **25**, 592 (1960).

(2) National Science Foundation Undergraduate Summer Research Participant.

(3) National Science Foundation Predoctoral Fellow.

(4) R. L. Letsinger and J. R. Nazy, *J. Am. Chem. Soc.*, **81**, 3013 (1959). Product II is unusual in that, though formally a boronate ester, it resists hydrolysis in acidic, neutral and weakly alkaline media and titrates as a monoboronic acid. The recently demonstrated stability of the six-membered heterocyclic B-O-C system in 9,10-boroxarophenanthrene [M. J. S. Dewar and R. Dietz, *J. Chem. Soc.*, 1344 (1960)] increases the plausibility of structure IIa.

(5) R. L. Letsinger and S. B. Hamilton, *J. Am. Chem. Soc.*, 81, 3009 (1959).

(6) A small amount of 2-bromo-2′-tolanboronic acid was isolated from one of the reactions used in the preparation of 2,2′-tolandiboronic acid (see Ref. 4). The structure, deduced from the mode of formation and analyses of the compound and its dihydrobenzoboradiazole derivative (ref. 4), is strongly supported by the ultraviolet spectrum ($\lambda_{\max}^{C_2H_5OH}$ 287,306; shoulders at 272,297 mμ), which is almost superposable upon the spectrum of 2,2′-tolandiboronic acid Like 2-tolanboronic acid, this compound did not isomerize when warmed in an alkaline, aqueous-alcoholic solution.

concerted process of this type would not be excluded on geometrical grounds in the case of the *trans*-2,2′-stilbenediboronic acid.[7] It is therefore apparent that reaction of a boronic acid group with a neighboring alkene group is less favored than reaction with a neighboring alkyne group.

2,2′-Stilbenediboronic acid and 2-tolanboronic acid were prepared from the corresponding bromo compounds in the manner by which 2,2′-tolandiboronic acid was made from 2,2′-dibromotolan. This involved metal-halogen interchange with butyllithium, boronation with *n*-butyl borate, and hydrolysis. 2-Vinylbenzeneboronic acid was obtained both by reaction of 2-vinylphenylmagnesium chloride with *n*-butyl borate and by dehydrobromination of 2-(1-bromoethyl)benzeneboronic anhydride with quinoline. The latter reaction gave much the better yield. By contrast, it may be noted that both boronation of 4-vinylphenylmagnesium chloride[5,8] and dehydrobromination of 4-(1-bromoethyl)benzeneboronic anhydride[9] afforded satisfactory yields of 4-vinylbenzeneboronic acid.

The structures of the boronic acids are based on the synthetic paths, analyses, formation of derivatives (with *o*-phenylenediamine or by oxidation with hydrogen peroxide), and spectral data. The marked similarity in the infrared and ultraviolet spectra of 2,2′-tolandiboronic acid and 2-tolanboronic acid is particularly significant. Neither I nor V absorbed appreciably in the 10–11 μ region, indicating the absence of *trans*-stilbenes. Their infrared spectra differed primarily in that 2-tolanboronic acid showed a strong band at 14.6 μ, indicative of a compound with an unsubstituted phenyl group. In the ultraviolet both compounds exhibited maxima and shoulders in the 270–310 mμ region of the type expected for tolan compounds.

EXPERIMENTAL

All organometallic reactions were carried out with efficient stirring in a nitrogen atmosphere. Butyllithium was prepared from butyl bromide.[10] Unless otherwise specified, the boronic acid was isolated from the reaction of *n*-butyl borate with the organolithium compound by adding dilute hydrochloric acid to the reaction mixture. The ether layer was combined with an ether extract of the aqueous layer and extracted several times with dilute sodium hydroxide solution. On acidification of the alkaline solution the boronic acid precipitated. It was collected either by filtration or ether extraction and recrystallized from alcohol-water solutions. Dihydrobenzoboradiazole derivatives were prepared by heating the boronic acids with *o*-phenylenediamine in toluene as previously described.[11] Melting points were taken on a Fisher-Johns block. Infrared spectra were taken with a Baird spectrometer with the sample in potassium bromide unless otherwise specified. Ultraviolet spectra were obtained with a Cary recording spectrophotometer. Carbon, hydrogen, and nitrogen analyses were made by Miss H. Beck; boron analyses were obtained by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

2,2′-Stilbenediboronic acid (III) (J. N.). A solution containing 8.35 g. (0.0247 mole) of *trans*-2,2′-dibromostilbene[4] in 35 ml. of ether was added to 65 ml. of 0.759*M* butyllithium (0.049 mole) in ether at ice temperature and the mixture was stirred for 30 min.

A 25-ml. aliquot of the reaction mixture was pipetted into a Dry Ice-ether slurry. Subsequent acidification and isolation of the carboxylic acid yielded 1.37 g. (83%) of crude 2,2′-stilbenedicarboxylic acid; m.p. 241–247°. After recrystallization from ethanol a sample melted at 260–262° (lit.,[12] m.p. 263–265°); λ_{max} 5.90 μ. The structure of the acid was further verified by preparation of the dimethyl ester by heating the acid in methanol with a catalytic amount of sulfuric acid; m.p. 100–101.5° (lit.,[12] m.p. 101–102°); λ_{max} 5.80 μ. The formation of the known dicarboxylic acid on carbonation demonstrated that 2,2′-lithiostilbene had been produced in good yield.

The major portion (75 ml.) of the dilithiostilbene solution was cooled to −75° and treated with a solution of *n*-butyl borate (9.75 g., 0.0423 mole) in ether. A rise in temperature to −55° was noted. The mixture was cooled to −75°, stirred for an hour, allowed to warm to 0° and hydrolyzed with dilute hydrochloric acid. Conventional work-up yielded 4.34 g. (87%) of 2,2′-stilbenediboronic acid, m.p. 198–205°. After recrystallization it melted at 205–210°; $\lambda_{max}^{ethanol}$ 302 mμ (log ε 3.35), 238 mμ (log ε 2.94). A strong band at 3.0 μ and the absence of a bond between 14 and 15[13] μ indicated that the compound was an acid rather than an anhydride. The neutralization equivalent of the diboronic acid (titration in presence of mannitol) was 133; that calculated for $C_{14}H_{14}B_2O_4$, 134.0. A dihydrobenzoboradiazole derivative[11] was prepared and found to melt at 270–274°.

Anal. Calcd. for $C_{26}H_{22}B_2N_4$: N, 13.60. Found: N, 13.35.

2-Ethylbenzeneboronic anhydride (T.S.). 2-Ethylphenylmagnesium bromide, prepared from 14.6 g. of magnesium and 105 g. of 2-ethylbromobenzene in 200 ml. of ether, was cooled to 0° and added slowly to a well stirred solution containing 183 g. of *n*-butyl borate in 100 ml. of ether at −75°. After 2 hr. of stirring the mixture was allowed to warm to room temperature, hydrolyzed with 200 ml. of dilute sulfuric acid, worked up as usual, and dried at 80° to give 64 g. (85% based on bromobenzene) of 2-ethylbenzeneboronic anhydride, m.p. 117–117.5°. The absence of a band between 2.8 and 3.2 μ and the presence of a strong band at 14.45 μ in the infrared spectrum showed that the product was an anhydride.[13]

Anal.[14] Calcd. for C_8H_9OB: H, 6.87; B, 8.20. Found: H, 6.61; B, 7.92.

A dihydrobenzoboradiazole derivative melted sharply at 75°.

Anal. Calcd. for $C_{14}H_{15}N_2B$: N, 12.62. Found: N, 12.90.

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[7] The 2,2′-stilbenediboronic acid described in this paper must be preponderantly, if not exclusively, the *trans* isomer, as it was prepared from *trans*-2,2′-dibromotolan (ref. 4) and exhibited an absorption band at 10.36 μ, which is characteristic of *trans*-stilbene compounds. With respect to a concerted addition involving the alkene bond and groups in the 2,2′-positions, however, it should be noted that the aromatic rings must be twisted out of the plane of the —CH=CH-atoms in order for the reaction to occur. The consequent loss in resonance energy could be reflected in a relatively high activation energy for the process.

(8) H. Normant and J. Braun, *Compt. rend.*, **248**, 828 (1959). See also J. Cazes, *Compt. rend.*, **247**, 2019 (1958), for the preparation of 4-vinylbenzeneboronic acid by means of a Grignard reaction.

(9) A. K. Hoffman and W. M. Thomas, *J. Am. Chem. Soc.*, **81**, 580 (1959).

(10) R. G. Jones and H. Gilman, *Org. Reactions*, **6**, 352 (1951).

(11) R. L. Letsinger and S. B. Hamilton, *J. Am. Chem. Soc.*, **80**, 5411 (1958).

(12) P. Ruggli and R. E. Meyer, *Helv. Chim. Acta*, **5**, 28 (1922).

(13) H. R. Snyder, M. S. Konecky, and W. J. Lennarz, *J. Am. Chem. Soc.*, **86**, 3611 (1958).

2-Vinylbenzeneboronic acid (IV) (T. S.). A mixture of 20 g. of 2-ethylbenzeneboronic anhydride, 26.7 g. of *N*-bromosuccinimide, and 0.15 g. of benzoyl peroxide in 350 ml. of carbon tetrachloride was refluxed for 3.5 hr., then cooled, and filtered. The filtrate was concentrated and the solid which separated was recrystallized twice from heptane to give 11.7 g. (42%) of 2-(1-bromoethyl)benzeneboronic anhydride; m.p. 148.5–150°; λ_{max} 7.4, 14.43 μ (anhydride band).

Anal. Calcd. for $(C_8H_8OBrB)_3$: B, 5.13%. Found. B, 4.84%.

A mixture of 10 g. of this anhydride and 20 g. of freshly distilled quinoline was heated at 130–135° with occasional stirring for 30 min. Following hydrolysis and acidification the boronic acid was taken up in ether and subsequently recrystallized from water. There was obtained 3.7 g. (54% based on the bromoethylbenzeneboronic anhydride) of 2-vinylbenzeneboronic acid; m.p. 108–109°; λ_{max} 3.05 (v. strong, O—H), 5.5 (weak, $=CH_2$), 6.12 (weak, C=C), 7.42 (v. strong, B—O), and 10.05 and 10.9 μ (weak and strong, respectively, vinyl hydrogens; $\lambda_{max}^{50\%\ C_2H_5OH}$ 247 mμ (log ϵ 4.14).

Anal.[14] Calcd. for $C_8H_9O_2B$: H, 6.13; B, 7.31. Found: H, 6.15; B, 6.89.

The dihydrobenzoboradiazole derivative melted sharply at 93.5°.

Anal. Calcd. for $C_{14}H_{13}N_2B$: N, 12.73. Found: N, 13.01.

2-Vinylbenzeneboronic acid was also prepared *via* a Grignard reaction. In this case 6.9 g. of 2-chlorostyrene in 15 ml. of tetrahydrofuran (dried by distillation from lithium aluminum hydride) was added dropwise over a 10-min. period to 2.3 g. of magnesium and 1 ml. of bromoethane in 3 ml. of tetrahydrofuran. After 35 min. of refluxing the mixture was cooled to about −70°, whereupon 23 g. of *n*-butyl borate in 50 ml. of tetrahydrofuran was rapidly added. After 30 min. of stirring the mixture was warmed to room temperature and worked up as in the previous cases to give 0.20 g. (3%) of 2-vinylbenzeneboronic acid, identical in melting point and infrared spectrum to the product obtained from the dehydrobromination reaction.

For polymerization, a solution of 0.390 g. of 2-vinylbenzeneboronic acid and 0.0039 g. of azobisisobutyronitrile in 5 ml. of benzene was heated at 75° for 14 hr. The resulting white gel was washed with several 15-ml. portions of ether to give 0.290 g. (74%) of ether insoluble polymer. The polymer did not soften below 300°.

2-Bromostilbene dibromide (T.F.). 2-Bromobenzaldehyde (90 g.) in 150 ml. of ether was added dropwise to a solution of benzylmagnesium chloride, prepared from 22.4 g. of magnesium and 93 g. of benzyl chloride, in 700 ml. of ether. After standing overnight the mixture was hydrolyzed with aqueous acetic acid. The ether layer was separated, washed with 10% sodium bicarbonate solution, dried, and evaporated to give 105 g. of a liquid alcohol ($\lambda_{max}^{CHCl_3}$ 2.8 μ). A 40-g. portion of this product was dehydrated by heating with 80 g. of potassium acid sulfate for 7 hr. Following hydrolysis the ether layer was filtered to remove a small amount of insoluble material and evaporated. The residual oil (23.4 g.) did not absorb in the 2 to 3 μ region of the infrared. It was taken up in carbon tetrachloride and treated with 5 ml. of bromine in 20 ml. of carbon tetrachloride. After 30 min. at reflux temperature, the solvent was removed at reduced pressure. The residual brownish solid (24.5 g., m.p. 130–140°) was washed with sodium bisulfite solution, decolorized with Norite, and recrystallized from chloroform to give colorless, crystalline 2-bromostilbene dibromide, m.p. 179–181°.

Anal. Calcd. for $C_{14}H_{11}Br_3$: C, 40.13, H, 2.65. Found: C, 40.63; H, 2.61.

2-Bromotolan (T. F.). An attempt to dehydrobrominate the bromostilbene dibromide by a solution of potassium hydroxide in ethylene glycol at 160–170° was not promising since the product showed an infrared band at 10.4 μ, indicative of some debromination to a bromostilbene. Application of Nazy's procedure[4] for purification of 2,2′-dibromotolan to this material did not yield a pure alkyne. As an alternative the dehydrobromination was accomplished by means of potassium *t*-butoxide. In this case 13.7 g. of 2-bromostilbene dibromide was added to a solution of potassium *t*-butoxide prepared from 4.1 g. of potassium and 500 ml. of *t*-butyl alcohol. After the mixture had been refluxed for 4 hr. it was poured into 700 ml. of water and extracted with ether. Distillation of the extract afforded 5.33 g. (63%) of 2-bromotolan; b.p. 155–160° (0.7 mm.); $\lambda_{max}^{CHCl_3}$ 4.5 μ (—C≡C—).

Anal. Calcd. for $C_{14}H_9Br$: C, 65.39; H, 3.53. Found: C, 65.65; H, 4.18.

2-Tolanboronic acid. (V) (T. F.). Butyllithium (150 ml. of 0.118*N* ether solution) was added over an hour to 2.0 g. of 2-bromotolan dissolved in 50 ml. of ether at 0°. The solution was then cooled to −75° and 2.44 g. of *n*-butyl borate in 20 ml. of ether was rapidly added. After two additional hours the mixture was allowed to warm up and was hydrolyzed and worked up as usual to give 0.70 g. of colorless boronic acid, m.p. 126–130°; after recrystallization from ethanol-water the sample weighed 0.53 g. (31% yield) and melted at 158–160°. Subsequent recrystallizations yielded the analytical sample, m.p. 160–161°; $\lambda_{max}^{ethanol}$ 279 mμ (log ϵ 3.36), 297 mμ (log ϵ 3.28).

Anal. Calcd. for $C_{14}H_{11}O_2B$: H, 4.98; B, 4.87. Found: H, 4.69; B, 4.56.

Oxidation of 2-tolanboronic acid (T. F.). Hydrogen peroxide (5 ml. of 30% solution) was added to a solution of 92 mg. of 2-tolanboronic acid in an acetic acid (5 ml.), ethanol (5 ml.), and water (2 ml.) mixture. After 30 min. the solution was poured into 80 ml. of water. White crystals of the hydroxytolan slowly separated when the solution was allowed to stand in the cold; weight, 45 mg. (56%); m.p. 69–70°; λ_{max}^{KBr} 2.95 μ (sharp); no band between 5 and 6 μ; $\lambda_{max}^{C_2H_5OH}$ 296 mμ, log ϵ 4.18.

Anal. Calcd. for $C_{14}H_{10}O$: C, 86.57; H, 5.19. Found: C, 86.62; H, 5.47.

Attempted isomerizations. The boronic acids were heated in 20 ml. of 50 to 60% ethanol-water solutions at reflux temperature; then the solutions were cooled, acidified, concentrated at reduced pressure, and filtered. The precipitates were dried and analyzed by their infrared spectrum. In every case the spectrum of the product was essentially the same as that of the reactant. By contrast, 2,2′-tolandiboronic acid was converted to compound II (70% recovery of an organoboron compound, 90% isomerization) by heating in 50% alcohol-water for 3 hr. at *p*H 9.

Compound	Weight, Mg.	Reflux Time (hr.)	*p*H	% Recovery
III	200	7	10[a]	65
IV	150	3	9	84
V	190	3	10	80
V	152	6.5	9.5[b]	79

[a] The solution also contained sodium tartrate—from 0.836 g. of tartaric acid. [b] From 0.72 g. of tartaric acid.

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(14) As characteristic of aromatic boronic acids, the boron compounds reported in this paper left a black ash after analysis, indicating incomplete carbon combustion. Consequently, all carbon analyses were 1–6% lower than the theoretical value and were of no diagnostic value.