ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Arylboronic Acids. III. Preparation and Polymerization of *p*-Vinylbenzeneboronic Acid[1]

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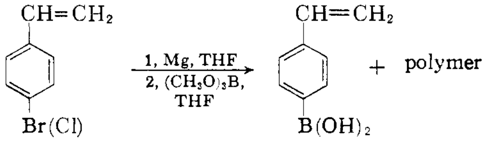
RECEIVED AUGUST 10, 1959

The preparation of *p*-vinylbenzeneboronic acid by means of the Grignard reaction is discussed. Poly-*p*-vinylbenzeneboronic acid is obtained upon free radical initiated polymerization of *p*-vinylbenzeneboronic acid in aqueous solution.

In an earlier paper dealing with the boronic acid–boronic anhydride transformation, several features of the infrared spectra of *p*-vinylbenzeneboronic and *p*-vinylbenzeneboronic anhydride, compounds not previously reported in the literature, were discussed.[3] Since that time four papers dealing with the acid and its derivatives have appeared.[4–7] In this paper we wish to report our findings concerning the preparation and polymerization of *p*-vinylbenzeneboronic acid.

At the start of our studies the only report of the successful preparation of a Grignard reagent from a halostyrene was that of Bachman, Carlson and Robinson.[8] In that work the Grignard reagent of *p*-bromostyrene was prepared in ethyl ether by the entrainment method, an equimolar amount of ethyl bromide being used; after carbonation a 15% yield of *p*-vinylbenzoic acid was obtained, along with a large amount of polymeric material which was not characterized. Despite the low yield in the Grignard reaction it appeared worthwhile to study this direct route for the preparation of *p*-vinylbenzeneboronic acid.[9] When the Grignard reagent was prepared under the conditions described by Bachman, *et al.*,[8] and was added to methyl borate maintained at −70 to −60°, *p*-vinylbenzeneboronic acid (I) was obtained in 12% yield. A large amount of polymeric material was also isolated. It was found that if tetrahydrofuran was employed instead of ethyl ether, the yield of I was increased to 20%.



I

At this point in our studies there appeared an account of the preparation of *p*-vinylphenylmagnesium chloride.[10] It was reported that carbonation of the Grignard reagent, which was prepared in tetrahydrofuran, afforded *p*-vinylbenzoic acid in high yield. Therefore, we undertook the preparation of *p*-vinylbenzeneboronic acid *via* the magnesium chloride derivative. Unfortunately, the Grignard solution prepared by this procedure was very viscous, and it was necessary to carry out the second stage of the reaction in the "normal" rather than the "inverse" manner, that is, by adding the methyl borate solution to the Grignard solution. The yield of *p*-vinylbenzeneboronic acid averaged 20%, and again a large amount of polymer was obtained.

Examination of the polymer revealed that it was insoluble in benzene or xylene and hence probably crosslinked, and that it contained chlorine and boron. The polymer was suspended in benzene to remove any benzene-soluble monomers and then subjected to combustion analysis. From the results of the analysis and from infrared studies it was concluded that the polymer consisted of *p*-vinylbenzeneboronic acid and *p*-chlorostyrene units in a 3 to 1 ratio. In this connection it is interesting to note that Letsinger and Hamilton[7] obtained a copolymer from *p*-vinylbenzeneboronic acid and *p*-chlorostyrene (with a small amount of dialkyl maleate added as a crosslinking agent) in 50% yield.

After the completion of our studies Cazes[4] reported the preparation of *p*-vinylbenzeneboronic acid *via* the Grignard reaction. He employed *p*-bromostyrene in tetrahydrofuran and obtained *p*-vinylbenzeneboronic acid in 75% yield. A short time later Normant and Braun[5] reported the preparation of *p*-vinylbenzeneboronic acid in a like manner from *p*-chlorostyrene in 80% yield. Neither paper contains any mention of polymer formation. More recently, Letsinger and Hamilton[7] described the preparation of I from *p*-chlorostyrene in 60% yield. They obtained a 38% yield of polymer. Thus, it appears that the extent of polymerization during the preparation of *p*-vinylbenzeneboronic acid *via* the Grignard reaction is governed by rather subtle variations in the reaction conditions and/or in the purity of the reagents.

Most of the salient physical and spectral properties of *p*-vinylbenzeneboronic acid have been described previously.[3,4,6] Further support for the assigned structure was obtained by reduction of I to the known *p*-ethylbenzeneboronic acid (II). In connection with the various melting points of *p*-

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[1] Part of this work was supported by a grant [AT(11-1)-314] from the Atomic Energy Commission.

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[3] H. R. Snyder, Milton S. Konecky and W. J. Lennarz, THIS JOURNAL, **80**, 3611 (1958).

[4] Joë Cazes, *Compt. rend.*, **247**, 2019 (1958).

[5] H. Normant and J. Braun, *ibid.*, **248**, 828 (1959).

[6] A. K. Hoffmann and W. B. Thomas, THIS JOURNAL, **81**, 580 (1959).

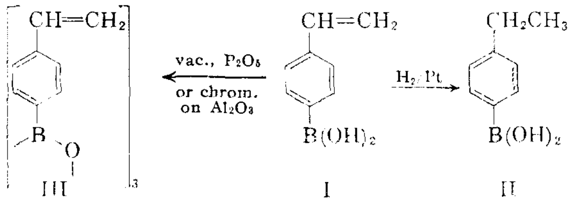
[7] R. L. Letsinger and S. B. Hamilton, *ibid.*, **81**, 3009 (1959).

[8] G. B. Bachman, C. L. Carlson and M. Robinson, *ibid.*, **73**, 1964 (1951).

[9] For a less direct route see ref. 6.

[10] J. R. Leebrick and H. E. Ramsden, *J. Org. Chem.*, **23**, 935 (1958).

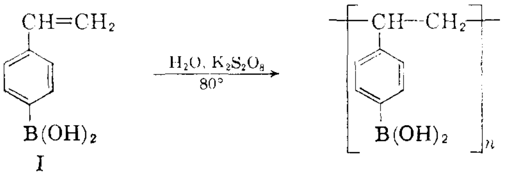
vinylbenzeneboronic acid that have been reported,[4-7] it should be pointed out that the acid is readily converted to its anhydride III and that for this reason the melting point is very difficult to reproduce. It has been found that a convenient method for the one-step purification and dehydration of *p*-vinylbenzeneboronic acid to its anhydride is chromatography on neutral alumina. This method also has been employed in the purification and dehydration of *p*-methylbenzeneboronic acid and it is hoped that the technique may be generally applicable in boronic acid chemistry.



Attention was next directed to the homopolymerization of *p*-vinylbenzeneboronic acid in aqueous systems. Hoffmann and Thomas[6] have reported the polymerization of *p*-vinylbenzeneboronic anhydride in toluene, and Letsinger and Hamilton[7] have studied the preparation of "popcorn" copolymers of *p*-vinylbenzeneboronic acid and its esters with styrene derivatives. We were interested in the preparation of a homopolymer of *p*-vinylbenzeneboronic acid for two reasons. First, it was thought that the polymer might possess unusual properties because of its ability to undergo dehydration to the boronic anhydride. Such a transformation should result in the formation of a highly crosslinked polymer. Second, it was hoped that there could be obtained a polymer possessing some of the properties of several azo dyes that have shown promise in boron-disintegration cancer therapy.[11,12]

In the initial polymerization experiments *p*-vinylbenzeneboronic acid was dissolved in dilute sodium hydroxide containing a small amount of benzoyl peroxide or potassium persulfate, and the solution was irradiated with ultraviolet light. If oxygen was present, no polymerization was observed. However, when the reaction was carried out under nitrogen, the solution gradually became opaque and upon acidification polymeric material precipitated. Polymerization in basic solution also could be effected by ultraviolet light without the use of a peroxide initiator.

The polymer initially obtained by either of these methods was a white solid, but it rapidly turned brown in the air. The amount of boron found by analysis of the polymer was somewhat lower than the theoretical value. Boronic acids are known to undergo oxidative cleavage to phenols in the presence of hydrogen peroxide.[13] In view of these facts, it was concluded that the polymer probably contained some deboronated, phenolic units produced by the action of hydrogen peroxide liberated upon decomposition of potassium persulfate. It was found that either ultraviolet light or potassium persulfate alone was sufficient to initiate the polymerization of *p*-vinylbenzeneboronic acid in basic solution. With persulfate, the polymerization was carried out at *ca.* 80°. Unfortunately, with either method of initiation, the polymer manifested the same instability in air as that prepared in the earlier experiments. Since *p*-vinylbenzeneboronic acid is moderately soluble in water at 80°, it was decided to repeat the polymerization experiments without the use of added base. Thus, a simplified polymerization procedure was developed whereby *p*-vinylbenzeneboronic acid was dissolved in hot water and, after deoxygenation of the solution, was treated with a small amount of potassium persulfate. Polymerization commenced almost immediately and proceeded in a virtually quantitative manner. The polymer formed a colloidal dispersion and was isolated by lyophilization.



The white, air-stable powder obtained did not melt below 300°; in the range 300–350° it softened somewhat and became brown. It was insoluble in water and dilute acid, and slightly soluble in 3% potassium hydroxide. A dispersion of the polymer in water could be prepared by dissolving the polymer in dilute potassium hydroxide and then carefully adjusting the *p*H to 8 with dilute hydrochloric acid.

The infrared spectrum of the polymer was consistent with a structure of the polystyrene type. The strong C–H deformation bands of the vinyl group present in the monomer were absent. In addition, the ultraviolet spectrum of a solution of the polymer in dilute base no longer had the maximum near 257 mμ that is typical of the styrene chromophore,[14] but instead was quite similar to the spectrum of a solution of *p*-ethylbenzeneboronic acid in base.

A sample of poly-*p*-vinylbenzeneboronic acid was dried under conditions that were sufficient to convert most boronic acids to their anhydrides. From the results of a combustion analysis on the dried sample it was found that the polymer still contained *ca.* 25–50% of the boronic acid groups. This approximate degree of dehydration was also obtained in other samples that were dried under varying conditions. These results are not surprising in view of the fact that the phenyl groups containing the boronic acid function are, in the polymer, constrained to a much higher degree than a normal boronic acid, and it might be expected that formation of the cyclic anhydride function could not proceed to completion.

The infrared spectrum of the "dehydrated" polymer has a band at 3400 cm.$^{-1}$ which is attributable to the hydroxyl group of the boronic acid. Furthermore, there is no anhydride band in the 700 cm.$^{-1}$ region, whereas *p*-ethylbenzeneboronic anhydride[3] has a strong band at 680 cm.$^{-1}$. It there-

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[11] H. R. Snyder and S. L. Meisel, THIS JOURNAL, **70**, 774 (1948).

[12] P. G. Kruger, *Radiation Research*, **3**, 1 (1955).

[13] A. D. Ainley and F. Challenger, *J. Chem. Soc.*, 2171 (1930); *cf.* H. G. Kuivila, THIS JOURNAL, **76**, 870 (1954).

[14] H. A. Laitinen, F. A. Miller and T. D. Parks, *ibid.*, **69**, 2707 (1947).

fore appears that most of the dehydration that occurs is incomplete, so far as the formation of anhydride rings is concerned.

Poly-*p*-vinylbenzeneboronic acid was found to be insoluble in dry, hot dimethyl sulfoxide but soluble in wet, hot dimethyl sulfoxide. (Addition of a large amount of water causes the polymer to precipitate.) These observations may be explained in terms of the crosslinking caused by anhydride formation. In dry dimethyl sulfoxide any anhydride linkages between different chains remain intact and effectively crosslink the polymer. When a small amount of water is added, the anhydride links are broken and the polymer becomes soluble.

These results brought to mind the possibility that *p*-vinylbenzene-boronic anhydride might be a powerful crosslinking agent if it were copolymerized with styrene. Several exploratory experiments were carried out to study this possibility. Styrene was bulk polymerized in the presence of α,α'-azodiisobutyronitrile with varying amounts of *p*-vinylbenzeneboronic anhydride, and the solubility of the polymer obtained was studied. It was found that the addition of as little as 0.4 mole % of *p*-vinylbenzeneboronic anhydride to the polymerization mixture resulted in the formation of a benzene-insoluble polymer. When styrene was polymerized under the same conditions without added *p*-vinylbenzeneboronic anhydride, the resulting polymer readily dissolved in benzene.

Experimental[15]

***p*-Vinylbenzeneboronic Acid.**—A solution of 1.5 ml. of redistilled ethyl bromide in 2.5 ml. of dry tetrahydrofuran was added to 3.88 g. (0.160 g. atom) of magnesium under nitrogen; reaction commenced almost immediately. After most of the ethyl bromide had been consumed, a solution of 11.8 g. (0.080 mole) of *p*-chlorostyrene[16] in 20 ml. of dry tetrahydrofuran was added at such a rate that the solution gently refluxed. The addition was complete in *ca.* 20 min. The solution was heated to reflux for 15–20 min. and then stirred at room temperature for 45 min. At this point the Grignard solution was very viscous. The solution was stirred and cooled to 0°, and then a solution of 10.5 ml. (0.160 mole) of methyl borate in 25 ml. of tetrahydrofuran cooled to $-50°$ was added. A white semi-solid mixture resulted. The mixture was cooled to $-80°$ and stirred at this temperature for 4 hr. It was allowed to warm up to 0° during a 2-hour period, and then maintained at room temperature overnight. The white suspension was poured into a stirred mixture of 50 ml. of water, 50 ml. of ice and 10 ml. of concentrated sulfuric acid. The resulting mixture was extracted several times with ether. The combined ether extract was evaporated under a stream of nitrogen, and the resulting solid residue was dissolved in *ca.* 50 ml. of 10% potassium hydroxide. Acidification of this solution to *p*H 2–3 with 10% hydrochloric acid resulted in the precipitation of a pale pink solid, which was collected, mixed with 150 ml. of 33% ethanol and heated to boiling. A considerable amount of insoluble, polymeric material was present. The gums were removed by filtration through glass wool and the filtrate was concentrated *in vacuo* to *ca.* 50 ml. The crystals which deposited on storage in the refrigerator overnight were collected and air-dried. The crystals weighed 2.00 g. (17% yield). Concentration of the mother liquors gave an additional 0.50 g. (3% yield). Recrystallization from water afforded white, crystalline *p*-vinylbenzeneboronic acid, m.p. 176–180°, $\lambda_{\max}$ 257mμ (ϵ 23,850) in ethanol. The acid may be converted to the anhydride by drying the former *in vacuo* over phosphorus pentoxide.

An analytically pure sample of *p*-vinylbenzeneboronic acid could not be obtained by repeated crystallization from water. When *ca.* 300 mg. of the acid was chromatographed on a 20-g. alumina column, an analytically pure sample of *p*-vinylbenzeneboronic anhydride, m.p. 197–200°, was obtained. The alumina column was prepared in ether and eluted according to the schedule: ethyl ether, 50% ethyl ether–chloroform, chloroform, 50% chloroform–ethanol, absolute ethanol. The anhydride was eluted in the absolute ethanol fraction.

Anal. Calcd. for C_8H_7OB: C, 73.92; H, 5.43; B, 8.34. Found: C, 74.09; H, 5.81; B, 8.65.

Verification of the Structure of *p*-Vinylbenzeneboronic Acid.—To a mixture of pre-reduced Adams catalyst in several milliliters of absolute ethanol was added a solution of 0.2677 g. (0.00181 mole) of *p*-vinylbenzeneboronic acid in 50 ml. of absolute ethanol. The mixture was hydrogenated at 33° and 741 mm.; the theoretical amount of hydrogen was consumed in 35 min. The platinum was removed by gravity filtration and the ethanol was evaporated from the filtrate *in vacuo*. The resulting white solid was recrystallized from water to give white crystals, m.p. 142–150°. After a second recrystallization from water, the crystals were dried *in vacuo* over phosphorus pentoxide and sublimed at 130–140° (0.05–0.1 mm.) The analytically pure *p*-ethylbenzeneboronic anhydride obtained melted at 153–156°. The mixed melting point with an authentic sample (m.p. 155–157°) was 152–157°. The infrared spectrum was identical with that of an authentic sample of *p*-ethylbenzeneboronic anhydride.

Anal. Calcd. for C_8H_9OB: C, 72.80; H, 6.81. Found: C, 72.77; H, 7.07.

Properties of the Polymer Isolated in the Preparation of *p*-Vinylbenzeneboronic Acid.—In an experiment where 0.1 mole of *p*-chlorostyrene was used, there was isolated, in addition to the expected *p*-vinylbenzeneboronic acid, 7.7 g. of polymeric material. This material was dried overnight *in vacuo* at 55° and then crushed to a powder. The powder was mixed with 125 ml. of benzene and the resulting suspension was stirred at room temperature under nitrogen for 2 days. The solid was collected by filtration. Evaporation of the filtrate afforded *ca.* 100 mg. of white solid which was identified as *p*-vinylbenzeneboronic anhydride. The precipitate was dried *in vacuo*; the resulting tan powder weighed 6.1 g. It did not melt or soften appreciably below 300°, and was insoluble in refluxing *o*-xylene. A flame test indicated the presence of boron. The infrared spectrum (Nujol) of this material had no bands that were indicative of the presence of a vinyl group. The spectrum was very similar to that of a known sample of poly-*p*-vinylbenzeneboronic acid.

A sample of the polymer was dried *in vacuo* over phosphorus pentoxide for 12 hr. and submitted for microanalysis.

Anal. Calcd. for C_8H_7Cl: C, 69.33; H, 5.08; Cl, 25.58. Calcd. for $C_8H_9O_2B$: C, 64.94; H, 6.12; B, 7.28. Found: C, 67.00; H, 6.91; B, 5.44, 5.61; Cl, 5.88.

Poly-*p*-vinylbenzeneboronic Acid.—A mixture of 800 mg. of *p*-vinylbenzeneboronic acid and 60 ml. of water was heated to 80°; the boronic acid dissolved. Nitrogen was bubbled into the solution for several minutes and a nitrogen atmosphere was maintained in the system. Potassium persulfate (22 mg.) was added, and the solution soon became milky in appearance and heat was evolved. The mixture was stirred and maintained at 60° for 20 hr. The water was removed from the opaque mixture by lyophilization. The remaining white, voluminous powder weighed 820 mg. This material did not melt below 300°; in the range 300–350° it softened slightly and darkened.

The infrared spectrum of poly-*p*-vinylbenzeneboronic acid contains none of those bands found in *p*-vinylbenzeneboronic acid that are attributable to the vinyl group. The spectrum is similar to that of *p*-ethylbenzeneboronic acid. The ultraviolet spectrum of a solution of the polymer in dilute base resembles that of *p*-ethylbenzeneboronic acid.

An analytical sample was prepared by drying a sample of the lyophilizate at 100° *in vacuo* for 3 days. From the results of the analysis, which were corrected for the small percentage of potassium hydrogen sulfate present, it was concluded that the sample was *ca.* 50–75% dehydrated.

Anal. Calcd. for C_8H_7OB: C, 73.92; H, 5.43; B, 8.34. Calcd. for $C_8H_9O_2B$: C, 64.93; H, 6.12; B, 7.28. Found: C, 69.0; H, 6.0; B, 7.0.

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(15) Microanalyses were carried out by Mr. Josef Nemeth and his associates. Infrared spectra were determined by Mr. Paul McMahon and his associates. Capillary melting points are corrected.

(16) C. S. Marvel and G. L. Schertz, THIS JOURNAL, **65**, 2054 (1943).