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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

Cleavage Studies of Simple Aromatic Boronic Acids

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Benzeneboronic acid and *o*-hydroxybenzeneboronic acid anhydride were cleaved with *n*-butyllithium and the products characterized by carbonation. Benzeneboronic acid gave either 1-butaneboronic acid, benzoic acid or benzene, or a combination, the products depending upon the temperature at which the cleavage was run. *o*-Hydroxybenzeneboronic acid anhydride gave salicylic acid as one of the products. The cleavage of *o*-hydroxybenzeneboronic acid anhydride with hydrogen peroxide and bromine behaved normally.

A number of cleavage reactions of alkyl- and arylboronic acids are known. Many of these have been summarized by Lappert[1] in his recent review on organoboron chemistry. For example, benzeneboronic acid can be cleaved with water at elevated temperatures (140–150° under pressure for 40 hours) to give benzene and boric acid,[2] or with concentrated sodium hydroxide or hydrochloric acid at a lower temperature (reflux) and at atmospheric pressure to give similar products.[2] Both *p*-bromobenzeneboronic acid and *p*-tolueneboronic acid were also cleaved with water at elevated temperatures under pressure to give bromobenzene and toluene, respectively, and boric acid.[3] These cleavages were accomplished in 6 hours, the first at 140–150° and the second at 130–140°. From this it appears that some substituted boronic acids may be somewhat less stable to these cleavage conditions than the unsubstituted benzeneboronic acid. Both α- and β-naphthaleneboronic acid[4] and some substituted naphthaleneboronic acids (4-dimethylamino-1-naphthaleneboronic acid and 4-methoxy-1-naphthaleneboronic acid)[5] also seem to be less stable to this type of cleavage than benzeneboronic acid. These boronic acid derivatives of naphthalene decomposed on recrystallization from water.

Cleavage with hydrogen peroxide introduces an –OH group in the position previously occupied by the boronic acid group while cleavage with halogen (chlorine water, bromine water or iodine in potassium iodide) gives a halogen in place of the boronic acid group. Additional halogenation may also occur. Thus, phenol was obtained by treating benzeneboronic acid with hydrogen peroxide,[2] bromobenzene by treating benzeneboronic acid with aqueous bromine water[2] and 2-iodothiophene by treating 2-thiopheneboronic acid with an aqueous solution of iodine in potassium iodide.[6]

Cleavage also has been accomplished by salts of B subgroup elements (*e.g.*, Cu, Ag, Zn, Cd, Hg) to give various products depending partially on the salt used. For example, benzeneboronic acid was converted to chlorobenzene when treated with aqueous cupric chloride,[2] but benzene and biphenyl were produced when an aqueous solution of cupric sulfate was used.[2]

Recently a cleavage of an aromatic boronic acid with *n*-butyllithium[7] has been reported.[8] In an attempt to achieve a halogen–metal interconversion on 2-hydroxy-5-bromobenzeneboronic acid, these workers obtained, after carbonation using a Dry Ice–ether slurry and hydrolysis of the reaction mass, a mixture of products. When the reaction was carried out for 1.5 hours in refluxing ether using five equivalents of *n*-butyllithium, 1-butaneboronic acid, 5-bromosalicylic acid and *p*-hydroxybenzoic acid were obtained. When an 18-minute reflux time was used with the same quantities of material, 1-butaneboronic acid and 5-bromosalicylic acid were obtained. No mechanism was postulated.

In the work reported here, some cleavage reactions were carried out on benzeneboronic acid[9] and *o*-hydroxybenzeneboronic acid anhydride[10] with *n*-butyllithium in an effort to gain additional information concerning the possible nature of the cleavage.

With benzeneboronic acid, reactions were carried out at ether reflux, at 20° (room temperature) and at −50 to −60°. The reactions were terminated by pouring jet-wise into an agitated Dry Ice–ether slurry and any acidic products isolated by extraction with base. When five equivalents of *n*-butyllithium was used at reflux for 1.5 hours, no acidic products could be isolated nor any product containing the benzene nucleus. This perhaps indicates complete decomposition. When the reaction was carried out at either reflux or room temperature for 20 minutes with three equivalents of *n*-butyllithium, 1-butaneboronic acid and a small amount of benzene, characterized as the *m*-dinitro compound, were obtained. There was no evidence of benzoic acid in either case. At −50 to −60° for a period of 25 minutes using three equivalents of *n*-butyllithium, benzoic acid was the only product isolated that was identified. Another high melting product, possibly a salt, was also obtained.

When *o*-hydroxybenzeneboronic acid anhydride was treated with three equivalents of *n*-butyllithium at room temperature for 20 minutes, followed by carbonation and hydrolysis in the usual manner, salicylic acid and an unidentified unstable product were isolated.

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(1) M. F. Lappert, *Chem. Revs.*, **56**, 959 (1956).

(2) A. D. Ainley and F. Challenger, *J. Chem. Soc.*, 2171 (1930).

(3) F. Challenger and O. V. Richards, *ibid.*, 405 (1934).

(4) D. L. Yabroff, G. E. K. Branch and B. Bettman, THIS JOURNAL, **56**, 1850 (1934).

(5) H. R. Snyder and F. W. Wyman, *ibid.*, **70**, 234 (1948).

(6) J. R. Johnson, M. G. Van Campen and O. Grummitt, *ibid.*, **60**, 111 (1938).

(7) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn and L. S. Miller, *ibid.*, **71**, 1499 (1949).

(8) L. Santucci and H. Gilman, *ibid.*, **80**, 193 (1958).

(9) Kindly furnished by the American Potash and Chemical Corp.

(10) H. Gilman, L. Santucci, D. R. Swayampati and R. O. Ranck, THIS JOURNAL, **79**, 3077 (1957).

In all of these cleavage reactions, other products resulting directly from the *n*-butyllithium and of no immediate interest were also isolated. These include valeric acid, di-*n*-butyl ketone and possibly *n*-octane.

These cleavages can, in some aspects, be pictured as occurring by processes similar to metalation[11] or halogen–metal interconversion[12] in which an attack by the anion of *n*-butyllithium on either the hydrogen or halogen occurs, a positive hydrogen or halogen being displaced. In the cleavage of boronic acids, the process may occur by the nucleophilic attack of the butyl anion on the boron to give, after displacement, 1-butaneboronic acid (thus explaining the formation of this compound in some of the cleavage reactions) and an aryllithium compound. Carbonation of the aryllithium compound followed by hydrolysis would explain the formation of such products as 5-bromosalicylic acid,[8] benzoic acid and salicylic acid from the respective cleavages of 2-hydroxy-5-bromobenzeneboronic acid, benzeneboronic acid and *o*-hydroxybenzeneboronic acid anhydride. It could also explain the formation of such products as *p*-hydroxybenzoic acid and benzene from the cleavages of 2-hydroxy-5-bromobenzeneboronic acid and benzeneboronic acid if hydrolysis of the aryllithium compound had occurred prior to the carbonation. However, it does not explain why, in the case of benzeneboronic acid, 1-butaneboronic acid, benzoic acid and benzene could not all be isolated from the same experiment; and why a different combination of products was isolated when the reaction was carried out at different temperatures, the isolation step remaining unchanged. It also fails to explain why a different combination of products was isolated from 2-hydroxy-5-bromobenzeneboronic acid when the reaction time was varied.

These experiments do show, however, that the cleavage of the boronic acid group is extremely facile when a strong base such as *n*-butyllithium is used, the cleavage occurring at very low temperatures. There is also some indication that 2-hydroxy-5-bromobenzeneboronic acid is possibly somewhat more resistant to cleavage than benzeneboronic acid. This is based on the experiments run for 1.5 hours at reflux in which *p*-hydroxybenzoic acid, 5-bromosalicylic acid and 1-butaneboronic acid were obtained from the former compound while nothing has been isolated from the latter. When benzeneboronic acid was treated with *n*-butyllithium under milder conditions, reflux or room temperature for 18 minutes, products (1-butaneboronic acid and benzene) somewhat comparable to those obtained from the 2-hydroxy-5-bromobenzeneboronic acid were produced.

Since *o*-hydroxybenzeneboronic acid anhydride is a relatively new compound, some of the more common cleavage reactions were also carried out on it. Treatment with hydrogen peroxide in acetic acid gave catechol and treatment with bromine water in acetic acid gave 2,4,6-tribromophenol. This latter reaction corresponds closely to the cleavage of other *o*-substituted acids containing an amino or hydroxy group. Both *o*- and *p*-aminobenzoic acid gave 2,4,6-tribromoaniline upon treatment with bromine water[13]; sulfanilic acid and arsanilic acid likewise gave 2,4,6-tribromoaniline,[13] and 2,4-dicarboxyphenol gave 2,4,6-tribromophenol.[14]

Acetylation of *o*-hydroxybenzeneboronic acid anhydride was attempted also in pyridine with and without a sulfuric acid catalyst, but none of the desired product was isolated. Only starting material or the cleavage products, phenol and boric acid, could be recovered. The sulfuric acid catalyst was found to be necessary for the acetylation of salicylic acid to destroy the chelation between adjacent groups.[13] The attempted acetylation of 2,4-dicarboxyphenol using sulfuric acid as a catalyst has also been reported.[14]

Experimental[15]

Cleavage of Benzeneboronic Acid with Three Equivalents of *n*-Butyllithium. (a) At Room Temperature for 20 Minutes.—A solution of 0.225 mole of *n*-butyllithium[7] in 200 ml. of ether was added to a mixture of 10.38 g. (0.085 mole) of benzeneboronic acid in 220 ml. of ether over a period of 10–15 minutes at room temperature. Stirring was continued at room temperature for 20 minutes after which the mass was carbonated by pouring into a Dry Ice–ether slurry. The mixture was acidified to a *p*H of 4–5 with 10% hydrochloric acid and the ether layer was extracted with 100 ml. (0.1 mole) of 8% sodium bicarbonate in four portions and 100 ml. (0.131 mole) of 5% sodium hydroxide, also in four portions. Acidification of the sodium bicarbonate extract with 10% hydrochloric acid produced no solid, but acidification of the sodium hydroxide extract gave, after recrystallization from toluene, 2.5 g. (29%) of 1-butaneboronic acid identified by melting point (90–92°), mixed melting point with an authentic sample prepared according to the method of Snyder, Kuck and Johnson,[16] and the infrared spectrum.

Fractionation of the ether layer gave a quantity of impure benzene which was identified by conversion to the *m*-dinitro derivative. *n*-Octane, di-*n*-butyl ketone and valeric acid were also present.

(b) **At Reflux Temperature for 20 Minutes.**—This experiment was carried out as the one described above except that a reflux temperature was used. Two and fifteen-hundredths grams (25%) of 1-butaneboronic acid, a small amount of benzene and the other usual products, valeric acid, di-*n*-butyl ketone and *n*-octane, were isolated. There was no evidence of benzoic acid.

(c) **At −50° to −60° for 25 Minutes.**—Twelve and two-tenths grams (0.1 mole) of benzeneboronic acid in 250 ml. of ether was treated with 0.3 mole of *n*-butyllithium[7] in 218 ml. of ether added over a 20-minute period. The temperature was kept at −50 to −60° during the addition and for 25 minutes following. At this time Color Test I[17] was positive and Color Test II[18] was negative. The mixture was carbonated in the usual manner, acidified with 100 ml. (0.29 mole) of 10% hydrochloric acid and the ether layer extracted four times with 25-ml. portions (0.1 mole) of 8% sodium bicarbonate and four times with 25-ml. portions (0.131 mole) of 5% sodium hydroxide.

Acidification of the sodium bicarbonate layer gave 0.75 g. (6.2%) of benzoic acid identified by melting point and mixed melting point as well as the infrared spectrum. Acidification of the sodium hydroxide extract caused the formation of white needles which did not melt under 350°. No 1-butaneboronic acid was isolated.

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(11) H. Gilman and J. W. Morton, Jr., in "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 258.

(12) R. G. Jones and H. Gilman, in "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 339.

(13) R. Q. Brewster, "Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1949, p. 658.

(14) S. E. Hunt, J. I. Jones and A. S. Lindsey, *J. Chem. Soc.*, 3099 (1956).

(15) All melting points reported herein are uncorrected. Reactions involving organometallic compounds were carried out in an atmosphere of dry, oxygen-free nitrogen.

(16) H. R. Snyder, J. A. Kuck and J. R. Johnson, THIS JOURNAL, **60**, 105 (1938).

(17) H. Gilman and J. A. Schulze, *ibid.*, **47**, 2002 (1925).

(18) H. Gilman and J. Swiss, *ibid.*, **62**, 1847 (1940).

The original ether layer also contained a large amount of insoluble material melting between 160–200° which resisted purification.

Cleavage of *o*-Hydroxybenzeneboronic Acid Anhydride.—Eight grams (0.067 mole) of *o*-hydroxybenzeneboronic acid anhydride in 250 ml. of ether was treated with 0.134 mole of *n*-butyllithium[7] in 97 ml. of ether at room temperature. This addition required 10 minutes. Color Test II[18] was negative immediately upon completion of the addition so another 0.67 mole of *n*-butyllithium in 49 ml. of ether was added. Color Test II[18] was also negative after this addition. Stirring was continued for 20 minutes at room temperature after which the reaction was carbonated in the usual way. The mass was hydrolyzed by the addition of 100 ml. (0.29 mole) of 10% hydrochloric acid and then the ether layer was extracted four times with 25-ml. portions (0.1 mole) of 8% sodium bicarbonate and four times with 25-ml. portions (0.131 mole) of 5% sodium hydroxide. Acidification of the sodium bicarbonate extract with 10% hydrochloric acid gave 1.65 g. (18%) of material melting at 151–155° which was identified as salicylic acid (159°) by the infrared spectrum.

Acidification of the sodium hydroxide extract gave 1.3 g. of material melting over the range of 155–165°. This decomposed before positive identification could be made. No 1-butaneboronic acid was isolated.

***o*-Hydroxybenzeneboronic Acid Anhydride and Bromine.**—To a solution of 0.48 g. (0.004 mole) of *o*-hydroxybenzeneboronic acid anhydride in 10 ml. of acetic acid, prepared by warming the mixture, was added slowly 3 ml. of bromine in 10 ml. of water containing potassium bromide. The mixture was stirred for a period of 15 minutes and was then diluted to 120 ml. by the addition of water. This caused the precipitation of a solid contaminated with the red color of bromine. This color was destroyed by the addition of a sodium bisulfite solution. The cream-colored product was recovered by filtration, washed with 2% hydriodic acid and then with water, and dried to yield 1.1 g. (85%) of 2,4,6-tribromophenol identified by the method of mixed melting point. The infrared spectra of this product and authentic 2,4,6-tribromophenol were identical.

***o*-Hydroxybenzeneboronic Acid Anhydride and Hydrogen Peroxide.**—To a solution of 0.48 g. (0.004 mole) of *o*-hydroxybenzeneboronic acid anhydride in 10 ml. of acetic acid and 5 ml. of water was added 10 ml. of 30% hydrogen peroxide. After allowing the solution to stand for 5 minutes the mixture was diluted with 70 ml. of water. A small amount of shiny white product was deposited upon cooling. A mixed melting point determination showed it to be catechol.

***o*-Hydroxybenzeneboronic Acid Anhydride and Acetyl Chloride.**—To a stirred solution of 2.4 g. (0.02 mole) of *o*-hydroxybenzeneboronic acid anhydride in 25 ml. of pyridine was added 5 ml. of acetyl chloride dropwise. The mixture was allowed to stand for 20 minutes and was then treated with 100 ml. of water. A reddish-brown oil separated and hardened somewhat upon standing. The crude product was recovered by filtration and dissolved in a mixture of hot acetone and benzene, treated with Norit A for a few minutes, filtered and allowed to cool. The cream-colored solid which separated melted over the range of 165–170° and was identified as metaboric acid, HBO_2, by determination of its neutralization equivalent and comparison of its infrared spectrum with that of an authentic specimen. The presence of phenol was indicated by odor.

Other attempts of acetylation of the anhydride using acetyl chloride or acetic anhydride with and without a sulfuric acid catalyst were unsuccessful.

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[CONTRIBUTION FROM THE STAMFORD LABORATORIES, RESEARCH DIVISION, AMERICAN CYANAMID CO.]

Organoboron Compounds. I. A New Synthesis of B-Trialkyl and Triaryl-N-triphenylborazoles[1]

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A new method for the preparation of B-trialkyl- and triaryl-N-triphenylborazoles is described. B-Trichloro-N-triphenylborazole has been found to react smoothly at room temperature with the appropriate Grignard or lithium reagents to give the desired products in yields of 65–84%. All the compounds prepared are colorless crystalline solids which are easily purified by recrystallization and are stable to moisture.

Substituted borazoles comprise one of the more stable classes of organoboron compounds. The relatively few known substituted borazoles and the limitations of the synthetic methods employed for their preparation[2-6] prompted us to investigate alternate routes to this class of compounds. The availability of a variety of substituted borazoles is of particular interest in studying effects of substituents on the properties of the borazole ring.

Many of the preparative methods for substituted borazoles have relied largely on vacuum line techniques where products were obtained in only small quantities. Recently, however, Ruigh and his associates[7-10] have found that sizable quantities of several B-substituted borazoles can be prepared by the reaction of a substituted boron dichloride and ammonia.[11]

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(1) A preliminary account of this work was presented at the 131st National Meeting of the American Chemical Society, Miami, Fla., April, 1957.

(2) H. I. Schlesinger and A. B. Burg, *Chem. Revs.*, **31**, 1 (1942).

(3) E. Wiberg, *Naturwiss.*, **35**, 182, 212 (1948).

(4) F. G. A. Stone, *Quart. Revs.*, **9**, 174 (1955).

(5) E. M. Smolin and L. Rapoport, "1,3,5-Triazines and Derivatives," Chapter entitled, "*s*-Triazaborane and Derivatives," Interscience Publishers, Inc., New York, N. Y., to be published.

(6) G. E. Coates, "Organo-metallic Compounds," Methuen and Co., Ltd., London, 1956.

(7) W. L. Ruigh and C. E. Erickson, WADC Technical Report 55-26, "Research on Boron Polymers," Part I, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio, March, 1955.

(8) W. L. Ruigh, C. E. Erickson, F. C. Gunderloy and M. Sedlak, *ibid.*, Part II, May, 1955.

(9) W. L. Ruigh, F. C. Gunderloy, M. Sedlak and P. A. Van Der Meulen, *ibid.*, Part III, May, 1956.

(10) W. L. Ruigh, A. D. Olin, M. G. Steinberg and P. A. Van Der Meulen, *ibid.*, Part IV, September, 1956.

(11) The reaction of $BuBCl_2$ and NH_3 was first studied by R. B. Booth and C. A. Kraus, THIS JOURNAL, **74**, 1415 (1952). Ruigh has proposed the borazole structure for the product of this reaction.