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

# Arylboronic Acids. V. Methyl-substituted Boronic Acids, Borinic Acids and Triarylborons[1,2]

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A number of arylboron compounds bearing *o*- and *p*-methyl substituents are prepared and studied. Whereas 2,6-dimethylbenzeneboronic anhydride is shown by molecular weight determinations to be a trimer, mesityleneboronic anhydride is a dimer, for which a four-membered boron–oxygen ring is proposed. The former yields a complex with pyridine, but only spectral evidence for a pyridine–mesityleneboronic anhydride complex is noted. Under mild conditions, dimesityleneborinic acid is not dehydrated nor is the anhydride hydrated to the acid. Trimesitylboron is nitrated to yield a hexanitro derivative. 2-Mesityl-1,3-dihydro-2,1,3-benzoboradiazole, prepared from mesityleneboronic acid and *o*-phenylenediamine, is shown to be more resistant to cleavage by hydrochloric acid than is the 2-phenyl homolog. The preparation of 6-methylboronophthalide and some proton magnetic resonance studies of arylboron compounds are reported.

The carbon–boron bonds of most arylboron compounds are cleaved readily by many reagents.[5] Consequently, the reactions that may be carried out on such compounds are limited. For example, attempts to nitrate arylboron compounds have often resulted in deboronation or even more extensive alteration of the molecule.[6] The lack of stability of arylboron compounds also has limited their potential applications. For example, efforts to apply certain arylboron compounds to a tumor therapy based upon the disintegration of boron[7,8] have been hampered by hydrolytic or oxidative deboronation.[9]

Enhanced stability toward hydrolysis or oxidation might be expected of arylboron compounds which carry substituent groups *ortho* to the carbon–boron bond. Accordingly, we have prepared a series of methyl-substituted arylboron compounds and have studied their stabilities as a function of the steric and electronic environment of the boron atom.

Of the many preparative routes used to synthesize areneboronic acids, areneborinic acids and triarylborons, the most widely used has been the reaction of a Grignard reagent with an orthoborate ester or with a boron trihalide.[5] Refinements of the technique have evolved and detailed studies of the preparation of areneboronic acids,[10] specifically benzeneboronic acid,[11] have appeared. Simultaneous addition of the phenyl Grignard reagent and the methyl borate ester to well agitated diluent in a reaction flask maintained at Dry Ice–acetone temperatures provided almost quantitative yields of benzeneboronic acid. Comparable yields of hindered boronic acids, whether by similar or different preparative routes, have not been claimed. For example, yields of mesityleneboronic acid, a boronic acid with *o*-methyl groups, have been much lower ($28^{12}$ and $5\%^{13}$). Furthermore, a recent report mentions the synthesis of mesityleneboron dichloride, the precursor of the acid, in only trace amounts[14] by the reaction of the hydrocarbon with boron trichloride in the presence of aluminum and aluminum chloride, a method which gave benzeneboron dichloride in yields as high as 72%.

When first prepared in the present study, mesityleneboronic acid had not been reported in the literature. Its preparation in low yield and its properties, as well as the preparation of mesityleneboronic anhydride, have since been described.[12] The better yield in the present study can be attributed to the better yield of Grignard reagent.

Bromomesitylene is known to react sluggishly with magnesium in ethyl ether solution, and often requires a catalyst.[15] In the present study, when ether was used as solvent, after eighteen hours at 35–60° (reflux temperatures of the solutions used) the yield of reagent was 66.6% as measured by titration. With ethyl ether and a catalytic amount of ethyl bromide added as promoter, the yield after four and one-half hours was 64.7%. In contrast, when tetrahydrofuran (THF) was used as the solvent,[16] the unpromoted reaction started readily and proceeded rapidly to high yields, particularly when the reaction was initiated at a comparatively high temperature (about 90°). Such a high reflux temperature was conveniently obtained by limiting the amount of THF solvent. Additional THF was added later, as needed, to control the viscosity and aid in handling. When THF was used as solvent, after one and one-half to four hours at about 90°, the yield of reagent was consistently 95 to 98% as measured by titration.

Mesityleneboronic acid was prepared from mesityl Grignard reagent and two different borates, methyl and *n*-butyl. When the technique of simultaneous addition[11] was used, the best yield

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[2] Taken in part from the theses submitted by W. J. Lennarz and R. T. Hawkins in partial fulfillment of the requirements for the degree of doctor of philosophy in the Graduate College of the University of Illinois, 1959.

[3] University of Illinois Fellow, 1956–1957; Phillips Petroleum Co. Fellow, 1957–1959.

[4] Public Health Service Research Fellow of the National Cancer Institute, 1958–1959.

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

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(14) E. L. Muetterties, *ibid.*, **81**, 2397 (1959).

(15) R. C. Fuson, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 131.

(16) H. E. Ramsden, A. E. Balint, W. R. Whitford, J. J. Walburn and R. Cserr, *J. Org. Chem.*, **22**, 1202 (1957).

noted was 72.3%, and there was no appreciable amount of dimesityleneborinic acid in the product. When the technique of reverse addition was used (that is, the Grignard reagent was added to excess methyl borate at Dry Ice–acetone temperatures), the yield of mesityleneboronic acid was almost as great as that cited above, and the ratio of mesityleneboronic acid to dimesityleneborinic acid in the product was estimated to be about 28 to 1. Thus, the equilibria involving a tetracoördinate boronate anion as an intermediate in the reaction of methyl borate with a Grignard reagent, as stressed by Washburn, *et al.*,[10,11] may not be as important when the Grignard reagent is mesityl as when it is phenyl. The steric requirements of the mesityl group may shift the equilibria and minimize the side reactions leading to the diareneborinic acids.

It has been customary to acidify crude reaction mixtures in the preparation of boronic acids either concurrently with the initial hydrolysis or subsequently. In the present study, the possibility of working up the hydrolyzed reaction mass without acidification was explored because of the sensitivity of mesityleneboronic acid to mineral acids. It was shown that the manipulation could be performed either way. No great difference in yield was noted, but mesityleneboronic acid separated from an unneutralized reaction mixture appeared to be of slightly better quality.

The synthesis of 2,6-dimethylbenzeneboronic acid (I) from 2-bromo-*m*-xylene presented no difficulty when the Grignard reagent was prepared in THF (98–100% yield) and converted to the acid (72% yield) by reaction with methyl borate. Attempts to use the iodo compound were less successful, for the Grignard reagent prepared from it was insoluble in THF, and the yield of the Grignard reagent prepared in ether was only 65%.

The difficulty with reproducibility of melting points of boronic acids and the facile conversion of boronic acids to anhydrides are well known and have been commented upon often.[5,11,17–23] Mesityleneboronic acid was observed to lose water on the Kofler hot-stage microscope at temperatures as low as 80° with formation of the anhydride. The observed melting point in a capillary tube was somewhat higher, but not reproducible.

Mesityleneboronic acid proved to be a very weak acid, with an estimated $pK_a$ of 11.8 in aqueous ethanol. Attempts to titrate it in the presence of mannitol or glycerol in aqueous ethanol with standard sodium hydroxide[24] were unsuccessful. The acid was slightly soluble in solutions of sodium hydroxide, but organic material could be extracted with ether from such solutions. Similarly, 2,6-dimethylbenzeneboronic acid was extracted by ether from a basic solution. The solubility of mesityleneboronic acid in water at 28° was found to be 1.05 g./100 ml.

In common with other boronic acids,[5] mesityleneboronic acid was found to be cleaved rapidly by dilute hydrochloric acid, bromine water, sulfuric acid, nitric acid and mercuric chloride.[25] When mesityleneboronic acid was dissolved in refluxing 1:3 hydrochloric acid, the formation of mesitylene was rapid (about two minutes) and almost quantitative. Under the same conditions, benzeneboronic acid required several hours for an equivalent amount of benzene to be evolved. About fifteen minutes was required for the complete deboronation of 2,6-dimethylbenzeneboronic acid. The results are in accord with the observation made by Hawthorne.[12] Mesityleneboronic acid reacted instantaneously with bromine water, to discharge the bromine color within a matter of seconds. Under the same conditions, benzeneboronic acid required about eighteen minutes for a comparable discharge of color, and 2,6-dimethylbenzeneboronic acid required three minutes. The results are in accord with a comment made by Hine.[26] All attempts to effect direct nitration of mesityleneboronic acid were unsuccessful, as was to be expected from the ready cleavage of the boronic acid by electrophilic reagents. Several unsuccessful attempts were made to nitrate mesityleneboronic acid under neutral or alkaline conditions with acetone cyanohydrin nitrate according to the method of Emmons and Freeman.[27]

An attempt was made to couple mesityleneboronic acid with diazotized picramide in view of the fact that mesitylene couples successfully.[28] When mesityleneboronic acid was added to an acidic solution of diazotized picramide, a dark red color developed, but the temperature of the reactants rose suddenly, a gas was evolved (probably nitrogen), and no boron-containing compound was isolated from the reaction mixture.

While mesityleneboronic acid lost some water readily, difficulty was experienced in effecting complete conversion to the anhydride. The initial dehydration of the acid was necessarily carried out under rather mild conditions to avoid hydrolytic cleavage of the carbon–boron bond and also to minimize carry-over of the acid, which was observed to sublime with incomplete dehydration. Azeotropic removal of water from a refluxing benzene solution was effective in preparing small quantities of the anhydride. However, when the same procedure was scaled up, or used with less pure acid, the anhydride was obtained in low yield and was of poor quality, unsuitable for sublimation to the pure anhydride. Another suitable procedure used to dehydrate mesityleneboronic acid initially was long-term desiccation over calcium chloride, preferably in a vacuum desiccator at 35°. Treating the acid with thionyl chloride or heating it to 130° in a drying oven for one-half

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(25) K. Torssell, *Acta Chem. Scand.*, **13**, 115 (1959).

(26) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 353; citing H. G. Kuivila and A. R. Hendrickson, THIS JOURNAL, **74**, 5068 (1952).

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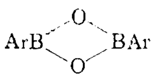
(28) K. H. Meyer and H. Tochtermann, *Ber.*, **54**, 2283 (1921).

hour resulted in extensive decomposition. Desiccation of the acid over phosphorus pentoxide under reduced pressure resulted in crude anhydride of poor quality which could not be sublimed satisfactorily. The xyleneboronic acid showed a similar resistance to dehydration; sublimation was found to be the most convenient method for converting it to the anhydride III.

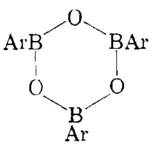
Mesityleneboronic anhydride was converted by boiling water to the acid. Dissolution of the anhydride in water at room temperature required a matter of months. The formation of mesityleneboronic anhydride was shown to be reversible.

The analytical sample of mesityleneboronic anhydride was observed to melt on the hot-stage with decomposition to a yellow glass. This result is not surprising when the reports by McCusker, *et al.*,[29] and Lappert, *et al.*,[30] are considered. The former have mentioned the decompositions of some alkaneboronic anhydrides, when heated over 200°, to boric oxide and trialkylborons. The latter investigators have reported that benzeneboronic acid heated to over 200° in a sealed tube was cleaved to benzene and metaboric acid.

The anhydride of mesityleneboronic acid was shown to be a dimer by molecular weight determinations. Two analyses (ebullioscopic in 2-butanone) on two separate samples of pure anhydride indicated the molecular weight to be within 2 to 4% of the theoretical weight of the dimer. The anhydride showed no unusual absorption in the ultraviolet ($\lambda_{\max}$ 245 m$\mu$, $\epsilon_{\max}$ 8700; $\lambda_{\max}$ 283 m$\mu$, $\epsilon_{\max}$ 800), and no unusual absorption in the infrared. The anhydride of 2,6-dimethylbenzeneboronic acid, in both ebullioscopic (benzene) and cryoscopic (camphor) molecular weight determinations, gave values within about 15% of the theoretical weight of the trimeric anhydride. It thus appears that the mesitylenic anhydride has a four-membered ring (II) whereas the xylene derivative contains the normal six-ring (III).



II



III

An infrared absorption band in the 700 cm.$^{-1}$ region has been assigned to areneboronic anhydrides by Snyder, Konecky and Lennarz.[17] Mesityleneboronic anhydride exhibited this band as a doublet around 705 cm.$^{-1}$. The band was observed in the spectrum of the xylene derivative at 700 cm.$^{-1}$.

When mesityleneboronic anhydride was treated with pyridine in warm benzene, a precipitate slowly appeared in small yield. The precipitate, soft white needles with a faint odor of pyridine, melted sluggishly at 156–166°, after being dried in vacuum. All attempts to recrystallize the material from ether, THF or benzene resulted in loss of the material or decomposition. Microanalytical data on the original precipitate (carbon, hydrogen, nitrogen and boron analyses) indicated it to be a mixture comprised of mesityleneboronic anhydride, pyridine and boric anhydride. The infrared spectrum of the precipitate exhibited many features strikingly similar to those of the infrared spectrum of the complex between benzeneboronic anhydride and pyridine.[17] Most noticeable were two bands between 1605 and 1630 cm.$^{-1}$ in the spectrum of the precipitate as well as the spectrum of the benzeneboronic anhydride complex. Thus, the existence of a complex between mesityleneboronic anhydride and pyridine was indicated by the infrared spectra. However, the complex was not formed readily in the high yields and high purity observed for benzeneboronic anhydride.[17] The pyridine complex of 2,6-dimethylbenzeneboronic anhydride appeared to be much more nearly normal in its properties, but even it could not be obtained in a state of complete analytical purity.

Dimesityleneborinic acid has been reported as the hydrolysis product of dimesityleneboron fluoride,[31] but no data were provided about the facility with which boron trifluoride etherate reacted with two moles of mesityl Grignard reagent. In the present study, it was shown that, at reaction temperatures up to 55°, boron trifluoride etherate reacted with excess mesityl Grignard reagent to afford dimesityleneboron fluoride in 95.5% yield in less than two hours. Undoubtedly, steric factors are responsible for the ease of preparation of this diareneboron halide.

In our independent study, dimesityleneboron fluoride was hydrolyzed in 99% yield to afford an over-all 94.5% yield of dimesityleneborinic acid. The borinic acid showed remarkable resistance to dehydration. Dimesityleneborinic acid was observed to sublime at 160° at 0.3 mm. with no evidence of dehydration. Attempts to remove water azeotropically in refluxing toluene, both at atmospheric and reduced pressures, failed. Heating the acid alone under reduced pressure over calcium chloride also failed to convert it to the anhydride. Only when the acid was heated on the hot-stage to over 200° did it show loss of water. The observed melting behavior was that of the anhydride.

Dimesityleneborinic acid was subjected to the action of hot hydrochloric acid under the same conditions used with mesityleneboronic acid and benzeneboronic acid. The dimesityleneborinic acid was cleaved comparatively slowly by the mineral acid, at an even slower rate than was benzeneboronic acid.

Dimesityleneborinic acid, like other borinic acids, was observed not to be soluble in aqueous caustic[5]; all attempts to nitrate it were unsuccessful.

Dimesityleneborinic anhydride was isolated from attempted preparations of trimesitylboron from the Grignard reagent and methyl borate under forcing conditions. Because of the complexity of the reaction mixtures from which dimesityleneborinic anhydride was isolated, no estimate could be made of the purity or yield of the crystals so obtained. The mechanism for the formation of the

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[29] P. A. McCusker, E. C. Ashby and H. S. Makowski, THIS JOURNAL, **79**, 5179 (1957).

[30] E. W. Abel, W. Gerrard and M. F. Lappert, *J. Chem. Soc.*, 1451 (1958).

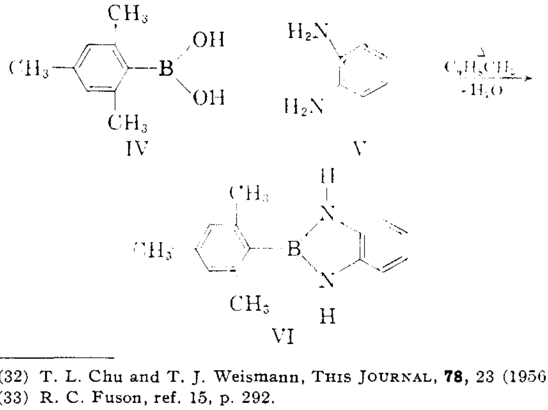
[31] H. C. Brown and V. H. Dodson, THIS JOURNAL, **79**, 2302 (1957).

anhydride was not elucidated. The anhydride could not be hydrated to the acid in refluxing aqueous acetone.

Trimesitylboron was prepared according to the procedure of Brown and Dodson,[31] and also by a convenient modification which consisted of the preparation of the mesityl Grignard reagent in THF solution instead of ether. Some difficulty was noted in causing the trimesitylboron to precipitate from the crude reaction mixture, by the addition of ethanol (95%), probably because of the complex nature of the mixtures. The observed melting point of the pure product was somewhat higher than that cited in the literature (195–197° as compared to 190.5–191.5°[31,32]), possibly because of different ways in which the melting points were taken.

In accord with the observations of Brown and Dodson,[31] the trimesitylboron showed remarkable stability to moisture and oxygen. Trimesitylboron was nitrated by mixed acids at Dry Ice–acetone temperatures, forming the hexanitro derivative in 53% yield. The hexanitration is not surprising when it is considered that tetrasubstituted phenyl rings of trimesitylboron are similar to the tetrasubstituted ring of durene. As with durene,[33] the bulk effect of the methyl groups (as well as the boron atom) presumably forces the first nitro group entering the ring out of the plane of the ring. The nitro group then cannot deactivate the ring by means of a resonance interaction. As a consequence, the ring is still electron-rich and undergoes further nitration. It is noteworthy that each ring of trimesitylboron undergoes dinitration at temperatures as low as −40°. The stability of the nitrated trimesitylboron was such that it could be kept in a desiccator for many months without noticeable change. The nitro derivative showed no color test with sodium.[31,32]

In 1957, the 2-alkyl dihydrobenzoboradiazolo ring system was reported.[34] More recently, reports on the 2-aryl series have appeared.[35–37] 2-Mesityl-1,3-dihydro-2,1,3-benzoboradiazole (VI) was prepared according to the procedure of Letsinger and Hamilton[35] by condensing IV with V in refluxing toluene.



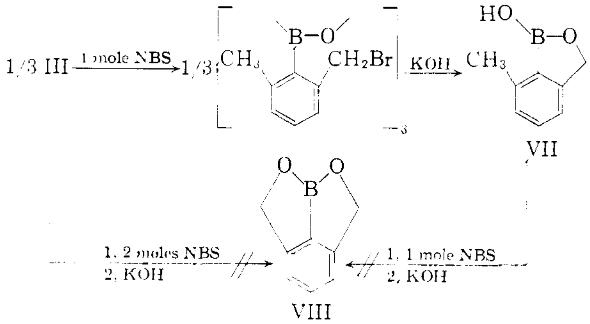
IV V

VI

Compound VI is oxidized readily, but is more resistant to cleavage by hydrochloric acid than the 2-phenyl homolog. Letsinger and Hamilton have reported the cleavage of the latter to benzeneboronic acid and *o*-phenylenediamine when it was shaken with hydrochloric acid for a few minutes at room temperature.[35] Under the same conditions, the 2-mesityl homolog was less affected, and 90% of it was recovered unchanged after ten minutes. Higher temperatures, more concentrated hydrochloric acid and longer times served to cleave the 2-mesityl-1,3-dihydro-2,1,3-benzoboradiazole. The only cleavage product isolated was *o*-phenylenediamine.

All attempts to couple VI with diazotized *p*-aminobenzoic acid in acetic acid solution failed. The products isolated did not contain boron, and were probably diazo compounds from the coupling of the diazonium salt with *o*-phenylenediamine arising from the solvolytic cleavage of the boradiazole.

A successful extension of the reactions utilized in preparing boronophthalide from *o*-methylbenzeneboronic anhydride[38,39] to 2,6-dimethylbenzeneboronic anhydride would lead to 6-methylboronophthalide (VII) and the unique tricyclic compound VIII.



VII

VIII

In several preliminary experiments, 6-methylboronophthalide (VII) was obtained in 11% net yield by free-radical bromination of III with N-bromosuccinimide, followed by hydrolysis of the resulting bromomethyl compound. A considerable amount of I was recovered; it is possible that the crowding caused by three adjacent substituents results in a lowered rate of bromination. The proton magnetic resonance spectrum of 6-methylboronophthalide (VII) (see below) is consistent with the assigned structure.

Preliminary attempts to prepare VIII by the bromination of impure 6-methylboronophthalide and subsequent hydrolysis of the bromide failed. Exploratory experiments on the dibromination of 2,6-dimethylbenzeneboronic anhydride (III) and hydrolysis of the resulting dibromide to VIII were also unsuccessful.

**Proton Magnetic Resonance.**—The proton magnetic resonance spectra of the boronic acids and boronic acid derivatives available in this Laboratory were examined. As a result of this study, it has been found that the protons of the hydroxyl groups of a boronic acid are manifested by a single peak in the same general region as the protons on

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(32) T. L. Chu and T. J. Weismann, THIS JOURNAL, **78**, 23 (1956).

(33) R. C. Fuson, ref. 15, p. 292.

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(37) E. Nyilas and A. H. Soloway, THIS JOURNAL, **81**, 2681 (1959).

(38) H. R. Snyder, A. J. Reedy and W. J. Lennarz, *ibid.*, **80**, 835 (1958).

(39) H. R. Snyder and W. J. Lennarz, *ibid.*, **82**, 2172 (1960).

aromatic nuclei. In instances where it was not possible to differentiate readily between the hydroxylic protons and the aromatic protons, addition of a small amount of acid (usually benzenesulfonic acid) caused the hydroxyl peak to move to a higher field. In this way it was possible to determine which one of the peaks present in the original spectrum was due to the hydroxyl proton resonance.

The movement of the hydroxyl peak to higher field upon addition of acid suggests that the acid caused dehydration of the boronic acid and that the proton peak observed is that of the average of water and the sulfonic acid.[40] Proton magnetic resonance spectroscopy was particularly useful as a means of verifying the structures of boronophthalide and its derivatives.[38,39]

In Table I are listed some compounds studied together with the resonance peaks of the various protons. The measurements were run on *ca.* 20% solutions or, if the compound was not sufficiently soluble, on saturated solutions of the boronic acids or boronophthalides in dioxane. Peroxides were removed from the dioxane by the method of Fieser.[41] The spectra were obtained with a Varian V-4300B NMR spectrometer with super stabilizer at a hydrogen precession frequency of 40 mc. and were calibrated with methylene chloride as the external reference. The peaks are expressed in δ parts per million relative to water as zero and are not corrected for the bulk diamagnetic shielding effect of the solvent. In all cases the relative areas under the various peaks were consistent with the assigned structures.

TABLE I

PROTON MAGNETIC RESONANCE PEAKS OF SOME BORONIC ACIDS AND BORONOPHTHALIDE DERIVATIVES

| Compound | Peak values in δ parts per million[a] |
|---|---|
| Benzeneboronic acid | −2.53(m) ArH; −2.00(s) HO |
| *p*-Tolueneboronic acid | −2.48(q) ArH; −1.87(s) HO; +2.60(s) $CH_3$ |
| *o*-Tolueneboronic acid | −2.20(m) ArH; −1.95(s) HO; +2.55(s) $CH_3$ |
| 2,6-Dimethylbenzeneboronic acid | −2.05(m) ArH; −1.98(s) HO; +2.64(s) $CH_3$ |
| Mesityleneboronic acid | −1.96(s) HO; −1.72(s) ArH; +2.64(s) *o*-$CH_3$; +2.69(s) *p*-$CH_3$ |
| *p*-Vinylbenzeneboronic acid | −2.52(q) ArH; −1.90(s) HO; —CH= and $CH_2$=[b] |
| *p*-Ethylbenzeneboronic acid | −2.45(q) ArH; −1.85(s) HO; +2.43(q) -$CH_2$-; +3.84(t) $CH_3$ |
| Boronophthalide[39] | −2.58(s) HO; −2.55(m) and −2.30(m) ArH; +0.04(s) -$CH_2$- |
| 6-Methylboronophthalide | −2.40(s) HO; −2.02(m) ArH; +0.09(s) -$CH_2$-; +2.48(s) $CH_3$ |
| 5-Nitroboronophthalide[39] | ArH[c]; −2.88(s) HO; −0.10(s) -$CH_2$- |

[a] With multiple peaks due to spin–spin coupling, the mean value is recorded. The abbreviations used in describing the peaks are as follows: (s) is singlet, (d) doublet, (t) triplet, (q) quartet, (m) = unresolved multiplet. [b] Several singlets and doublets between −1.65 and −0.08 p.p.m. [c] Several singlets and a doublet between −3.50 and −2.40 p.p.m.

In Table II are listed some hindered boron compounds and the resonance peaks of the various protons. The spectra were obtained on saturated solutions in deuterated chloroform, except as noted, with methylene chloride as the external reference. The spectra are presented in the same manner as the data in Table I. In all cases, the proton ratios were consistent with the assigned structures.

TABLE II

PROTON MAGNETIC RESONANCE PEAKS OF SOME HINDERED BORON COMPOUNDS

| Compound | Peak values in δ parts per million[a] |
|---|---|
| *o*-Tolueneboronic anhydride | −2.60(m) ArH; +1.93(s) *o*-$CH_3$ |
| 2,6-Dimethylbenzeneboronic anhydride | −2.38(m) ArH; +2.12(s) *o*-$CH_3$ |
| Mesityleneboronic acid | −2.12(s) ArH; +2.35(s) *o*-$CH_3$; +2.42(s) *p*-$CH_3$ |
| Mesityleneboronic anhydride | −2.15(s) ArH; +2.20(s) *o*-$CH_3$; +2.40(s) *p*-$CH_3$ |
| Dimesityleneborinic acid[b] | −2.05(s) ArH; +2.50(s) *o*- and *p*-$CH_3$ |
| Dimesityleneborinic anhydride[c] | −1.88(s) ArH; +2.80(s) *o*-$CH_3$; +2.55(s) *p*-$CH_3$ |
| Trimesitylboron[c] | −1.88(s) ArH; +2.85(s) *o*-$CH_3$; +2.55(s) *p*-$CH_3$ |

[a] See Note *a*, Table I. [b] 20% solution in $CDCl_3$. [c] 20% solution in $CCl_4$.

The data show shifts to higher field with increased shielding and crowding. The aryl protons show shifts to higher field with increased electron density of the rings. Since the *p*-methyl protons change but little, an inductive effect is indicated. The shifts observed for *o*-methyl protons are noteworthy. In the highly hindered compounds, the *o*-methyl protons show peaks at higher field than the *p*-methyl. The exact coincidence of the two peaks in dimesityleneborinic acid illustrates that atoms with the same chemical shift can be nonequivalent.[42]

## Experimental[43]

**Preparation of Mesityl Grignard Reagent.**—To 10.0 g. of dry magnesium turnings heated to about 90° was added slowly, with stirring under nitrogen, a solution of 59.67 g. of bromomesitylene[44] in 60 ml. of dry tetrahydrofuran (THF). Within 2 min. the reaction started, and it was quenched briefly by external cooling. The rate of addition of the halide was then adjusted to maintain the reactants at about 90°. After the addition, the reaction mixture was kept at about 95° for 2 hr. The cooled reaction mixture was diluted with 120 ml. of THF, transferred by nitrogen pressure into a graduated dropping funnel, and an aliquot was analyzed[45] (yield usually about 96%).

**Mesityleneboronic Acid.**—A THF solution of 0.275 mole of mesityl Grignard reagent and a solution of 34.0 ml. of methyl borate (Callery, redistilled and dried over lithium chloride[46]) were added simultaneously[10,11] within about 20 min. to 200 ml. of vigorously stirred dry ether maintained at −60 to −70°. After an additional half-hour at −70°, the reaction mass was allowed to warm to 0° and was stirred

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(40) J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 61.

(41) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1955, p. 285.

(42) S. Brownstein, *Chem. Revs.*, **59**, 463 (1959).

(43) All melting points, unless specified otherwise, were determined on a calibrated Fisher melting-point block apparatus. The symbol (c) designates capillary method. Microanalyses were performed by Mr. Josef Nemeth, Miss Claire Higham, Mrs. Maria Stingl and Miss Jane Liu. Molecular weights were determined by Clark Microanalytical Laboratory, Urbana, Ill. Infrared spectra were determined by Mr. James Brader, Mr. Paul McMahon and their associates using a Perkin-Elmer model 21 infrared spectrophotometer equipped with sodium chloride optics. Ultraviolet spectra were determined by Mr. J. Chiu using a Cary model 14 spectrophotometer. Proton magnetic resonance spectra were determined by Mr. B. E. Shoulders.

(44) L. I. Smith, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 95.

(45) H. Gilman, P. D. Wilkinson, W. P. Fishel and C. H. Meyers, THIS JOURNAL, **45**, 150 (1923).

(46) H. I. Schlesinger, H. C. Brown, D. L. Mayfield and J. R. Gilbreath, *ibid.*, **75**, 213 (1953).

at that temperature for 1 hr. It was hydrolyzed by the addition of 100 ml. of water and allowed to stand overnight.

The organic layer was separated from the pasty aqueous phase and combined with 3 ether extracts of the latter. The ether phase was washed twice with water, thrice with dilute hydrochloric acid, and twice more with water. The ether was removed by dropping the organic phase into a warmed flask with a stirrer in operation. As the head temperature approached 42°, water was added from a funnel. A total of 650 ml. of water was added, and 90 ml. of water was collected as distillate while the temperature of the liquid rose to 103°. The cloudy, light tan mixture was allowed to cool slowly with stirring, and then to stand overnight at room temperature. After cooling in ice-salt, the crystals were collected, washed with ice-water, and allowed to air dry. A second crop was isolated from the combined filtrate and washings by concentration and cooling. The first and second crops came to constant weight (33.5 g., 72%) after 3 days.

The infrared spectrum indicated the mesityleneboronic acid to be of good purity, suitable for many purposes. The pure acid was prepared by recrystallization from water (20 ml. per g.) with 70% recovery. It showed an indefinite melting point on the hot-stage microscope, with loss of water as low as 80°, and formation of the anhydride (lit.[12] loss of water at 143–145°).

*Anal.* Calcd. for $C_9H_{13}BO_2$: C, 65.91; H, 7.99. Found: C, 65.97; H, 8.52.

**Mesityleneboronic Anhydride.**—A sample of pure mesityleneboronic acid was dried in a vacuum desiccator for several days, recrystallized from petroleum ether, dried further by heating under reduced pressure, and finally sublimed at 170° at 1–2 mm. pressure; m.p. 220–222° dec. (lit.[12] 209–210°). It was shown by molecular weight determinations to be a dimer.

*Anal.* Calcd. for $C_{18}H_{22}B_2O_2$: C, 74.04; H, 7.59; mol. wt., 292.0. Found: C, 74.18; H, 7.90; mol. wt. (ebullioscopic in 2-butanone), 298, 307.

**Dimesityleneborinic Acid.**—Crude dimesityleneborinic acid (m.p. 137–143°) was prepared by hydrolysis of dimesityleneboron fluoride in 94.5% yield. The acid was recrystallized from petroleum ether twice to provide pure dimesityleneborinic acid, m.p. 142° (lit.[31] 140–141°).

*Anal.* Calcd. for $C_{18}H_{23}BO$: C, 81.21; H, 8.73. Found: C, 81.14; H, 8.95.

**Dimesityleneborinic Anhydride.**—Dimesityleneborinic anhydride was isolated as a by-product from attempted preparations of trimesitylboron wherein the Grignard reagent and methyl borate were used as reactants.

From the crude reaction mixture, after addition of ethanol, several small crops of crystals were recovered. Portions of these solids were recrystallized from petroleum ether–acetone mixtures, then from petroleum ether. Sublimation at 230° at 0.2 mm. pressure afforded pure dimesityleneborinic anhydride. It proved to be polymorphic, with the more stable modification showing the lower melting point; m.p. 267–268° and 289–290°.

*Anal.* Calcd. for $C_{36}H_{44}B_2O$: C, 84.06; H, 8.62; B, 4.21; mol. wt., 514. Found: C, 84.39; H, 8.71; B, 4.16; mol. wt. (ebullioscopic in benzene), 434.

**Trimesitylboron** was prepared by modification of the procedure of Brown and Dodson[31] (preparation of the Grignard reagent in THF solution instead of in ether). The crude trimesitylboron, which separated upon addition of 95% ethanol to the reaction mixture, was twice recrystallized from ethyl acetate, or from benzene and ethyl acetate, and then sublimed at 140° at 2 mm.; m.p., 195–197° (lit.[31,32] 190.5–191.5°).

*Anal.* Calcd. for $C_{27}H_{33}B$: C, 88.03; H, 9.03; B, 2.94; mol. wt., 368.4. Found: C, 88.43; H, 9.20; B, 3.00, 2.75, 2.76; mol. wt. (ebullioscopic in benzene), 341.

**Tris-(3,5-dinitro-2,4,6-trimethylphenyl)-boron.**—To a mixture of 7.0 ml. of white fuming nitric acid (90%, with a little urea added) and 4.0 ml. of concentrated sulfuric acid, cooled to −70° and vigorously stirred, was added over 10 min. 500 mg. of trimesitylboron. The thick brown slurry was stirred at −70° for 10 min., allowed to warm over about 45 min. to about −40°, and then diluted with 15 ml. of cold water added rapidly. The crude material (750 mg., 85%) obtained by filtration and copious washing with water was recrystallized from ethyl acetate and dried at 165° at 0.8 mm. for 6 hr.; yield, 450 mg. (51.3%). The crystals showed no distinct melting point up to 350°. Decomposition as evidenced by darkening was noted beginning at about 290°.

*Anal.* Calcd. for $C_{27}H_{27}BN_6O_{12}$: C, 50.80; H, 4.26; N, 13.17. Found: C, 51.17; H, 4.08; N, 13.28.

**2-Mesityl-1,3-dihydro-2,1,3-benzoboradiazole.**—A mixture of 3.28 g. of mesityleneboronic acid and 2.16 g. of recrystallized *o*-phenylenediamine in 25 ml. of toluene was heated under reflux for 17 hr. with azeotropic removal of the water formed. The product was concentrated *in vacuo* and diluted with 20 ml. of petroleum ether. The solids that separated were removed by filtration and dried briefly. Unchanged *o*-phenylenediamine was removed by sublimation at 100° and 0.5 mm. pressure for 5 hr. The residue from the sublimation was dissolved in 80 ml. of warm benzene; the solution was filtered, concentrated to 15 ml. and cooled. The yield of boradiazole, m.p. 137–138°, was 2.18 g. (46.4%). The analytical sample (m.p. 141°), was prepared by recrystallization from benzene, with all operations performed under an atmosphere of nitrogen.

*Anal.* Calcd. for $C_{15}H_{17}BN_2$: C, 76.29; H, 7.26; N, 11.87. Found: C, 76.22; H, 7.49; N, 11.94.

**2,6-Dimethylbenzeneboronic Acid.**—2-Bromo-*m*-xylene was prepared from 2-amino-*m*-xylene (Eastman Kodak Co.) by the procedure described for the preparation of *o*-chlorobromobenzene.[47] The only modification was that the crude product was not washed with sulfuric acid. A 37% yield of redistilled bromide, b.p. 201–202°, was obtained.[48]

2,6-Dimethylbenzeneboronic acid was prepared by a modification of the procedure employed in the preparation of mesityleneboronic acid. The Grignard reagent was prepared from 37.0 g. of 2-bromo-*m*-xylene and 5.1 g. of magnesium in 140 ml. of dry tetrahydrofuran at 50°, and was heated to *ca.* 50° overnight. The cooled solution was added to 28.0 ml. of methyl borate (dried over lithium chloride)[46] in *ca.* 175 ml. of absolute ether at a temperature below −60°. After the addition was complete (15 min.) 40 ml. of ether was added, and the stirred suspension was maintained at −75° for 15 min. and then allowed to warm to −15° during 1 hr. With ice-cooling 50 ml. of water was added in three portions, followed by 45 ml. of 10% sulfuric acid added at such a rate that the temperature of the mixture did not rise above 15°, and finally by 60 ml. of water. The ether layer, combined with extracts of the water phase, was washed with 50 ml. of water. Removal of solvent and hydrolysis of any boronic ester present were accomplished by heating with water, much as described for mesityleneboronic acid. The 2,6-dimethylbenzeneboronic acid (21.7 g., in two crops) was recrystallized from 150 ml. of water and dried in the air overnight. The white, needle-like crystals weighed 15.25 g. (50.8%) and melted at 125–130° (c). Concentration of the mother liquors afforded an additional 1.72 g. (5.7% yield) of product, m.p. 125–128° (c).

2,6-Dimethylbenzeneboronic acid was converted to its anhydride by twofold sublimation at 125° (0.05 mm.). The anhydride sintered at 135° and melted at 144–147° (c); mol. wt. calcd. for trimer, 396; mol. wt. found, 349, 358 (ebullioscopic, in benzene); 355 (Rast, in camphor).

*Anal.* Calcd. for $C_8H_9BO$: C, 72.80; H, 6.89. Found: C, 72.78; H, 6.99.

**Pyridine-2,6 dimethylbenzeneboronic Anhydride Complex.**[17]—To 300 mg. of 2,6-dimethylbenzeneboronic anhydride, contained in a 10-ml. flask, was added a solution of 56.8 mg. of reagent grade pyridine in 5.0 ml. of absolute ether. The anhydride appeared to begin to dissolve and new crystals formed. The mixture was allowed to stand overnight. The crystals were washed with 3–4 ml. of ether and then with 3–4 ml. of low-boiling petroleum ether; 271.7 mg. (76%), m.p. 170–175° (c). Evaporation of the filtrate afforded another 70 mg. of product. The large, hexagonal crystals obtained by recrystallization from ether were dried *in vacuo* over phosphorus pentoxide.

*Anal.* Calcd. for $C_{29}H_{32}NO_3B_3$: C, 72.86; H, 6.75; N, 2.93; B, 7.42. Found: C, 73.89; H, 6.93; N, 3.63; B, 7.49.

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(47) J. L. Hartwell, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 185.

(48) H. Conrad-Billroth, *Z. physik. Chem.*, **B25**, 217 (1934).

**6-Methylboronophthalide.**—A solution of 4.00 g. of 2,6-dimethylbenzeneboronic anhydride in 40 ml. of reagent grade carbon tetrachloride was boiled for several minutes, and then stirred while 1.78 g. of recrystallized *N*-bromosuccinimide and 8.3 mg. of benzoyl peroxide were added to the solution. The resulting mixture was heated to reflux and irradiated with a 200-watt, unfrosted lamp. After 15 min. the mixture was pale red in color, and a small amount of succinimide had formed. Heating and irradiation were continued for 1.5 hr. after the addition of 3.56 g. more of N-bromosuccinimide and 16.6 mg. of benzoyl peroxide. The succinimide isolated by filtration weighed 2.87 g. (87%). The crude 2-(bromomethyl)-6-methylbenzeneboronic anhydride obtained by concentrating the filtrate weighed 6.29 g. (99%) and contained 39.4% bromine (calcd., 37.9%). It was added portionwise to a stirred, two-phase mixture of 25 ml. of tetrahydrofuran and a solution of 1.43 g. (0.035 mole) of sodium hydroxide in 25 ml. of water. Sufficient heat was evolved during the addition, which required 20 min., to maintain the mixture at 40–50°; the mixture was then stirred overnight under nitrogen. The *p*H was adjusted to 2–3 with 2.5 ml. of 4 *N* hydrochloric acid, and the aqueous layer was extracted with three 20-ml. portions of ether followed by a fourth extraction after the addition of sodium chloride. The ether extracts were combined with the tetrahydrofuran layer and concentrated *in vacuo* (rotary evaporator). The semisolid residue (4.72 g.) was extracted with 130 ml. of boiling 10% ethanol, and the cooled extract was decanted from the oil which had separated and then seeded and stored in the refrigerator. After two days the crystals (1.14 g.) were collected. A second crop of crystals (0.49 g.) and a third crop (0.20 g.) were obtained by concentrating the mother liquor.

The combined crops were sublimed at 45° (0.05 mm.) for 20 hours in a sublimator equipped with a cold finger condenser. The sublimate, 6-methylboronophthalide, weighed 330 mg. (7.4% yield). The crystals sintered at 110° and melted at 115–125° (c). The residue from the sublimation was identified as 2,6-dimethylbenzeneboronic acid. An analytical sample was prepared by resublimation.

*Anal.* Calcd. for $C_8H_9O_2B$: C, 64.93; H, 6.12; B, 7.32. Found: C, 65.43; H, 6.35; B, 7.09.

URBANA, ILL.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, DAVIS]

# Trifluoroacetic Acid as a Catalyst for the Dissociation of an Iodobenzene Dichloride

BY L. J. ANDREWS AND R. M. KEEFER

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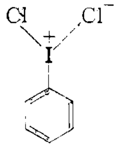
The equilibration of methyl *p*-iodobenzoate dichloride with chlorine and the free iodo compound does not occur at an appreciable rate in carbon tetrachloride, but the reaction in this solvent is markedly catalyzed by trifluoroacetic acid. At relatively low concentrations of the catalyst the reaction is second order with respect to trifluoroacetic acid. The rate of the reaction is not changed when a small quantity of acetic acid, in addition to the catalyst, is included in the medium. In acetic acid solvent the rate of equilibration of the dichloride is markedly enhanced by the addition of trifluoroacetic acid. The order of the catalyzed phase of the reaction is close to unity at 25° and is between one and two at 45°. It is proposed that two molecules of catalyst dimer are incorporated in the activated complex for the reaction in carbon tetrachloride and that these are associated through hydrogen bonding with the two chlorine atoms of the dichloride. It is suggested that when acetic acid is used as the solvent and trifluoroacetic acid is present, any one of three dimers, $(CH_3COOH)_2$, $(CF_3COOH)_2$ and $CF_3COOH \cdot CH_3COOH$, may be coördinated with the two chlorine atoms in the activated complex.

It has been established with considerable certainty that the activation process for the equilibration of iodobenzene dichloride with its components in polar media in the dark is accompanied by a distribution of charge between the iodine and chlorine atoms, as indicated in structure I. Clearly



I

the iodine atom serves as the positive end of the iodine–chlorine dipole since certain substituents (such as $COOCH_3$ and $CH_2OH$), which are potentially nucleophilic in character and which are properly constituted geometrically, sharply enhance the equilibration rate when they are located *ortho* to the trihalide grouping.[1] These substituents may be presumed to function as neighboring groups in stabilizing the activated complex by coordinating with the iodine atom. Although nitromethane has a much higher dielectric constant than does acetic acid, the dissociation of the dichloride occurs somewhat more rapidly in the latter than in the former solvent at room temperature.[2] The efficiency of acetic acid as a medium can be attributed to its capacity to promote the polarization required for activation by hydrogen bonding to the electronegative chlorine atom of the activated complex.

To obtain further information concerning the role of a carboxylic acid in this activation process a study of the kinetics of the trifluoroacetic acid-catalyzed dissociation of methyl *p*-iodobenzoate dichloride in carbon tetrachloride has now been made. Because of its relatively high acidity, trifluoroacetic acid is far superior to acetic acid as a hydrogen bond type solvating agent in polar processes.[2,3] Unlike acetic acid it is a sufficiently effective catalyst at high dilution in carbon tetrachloride so that it has been possible to determine its contribution to the over-all order of the reaction. The iodobenzoic acid derivative rather than iodobenzene dichloride itself has been used to avoid the complication of trifluoroacetic acid-catalyzed chlorination of the aromatic nucleus, a process which can occur rapidly in the absence of substituents which strongly deactivate the ring with respect to electrophilic substitution.[3] A study of the influence of trifluoroacetic acid on the rate of dissociation of methyl *p*-iodobenzoate dichloride in acetic acid, a medium the effective dielectric constant of which should not be strongly dependent on the catalyst concentration, also has been made.

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[1] (a) L. J. Andrews and R. M. Keefer, THIS JOURNAL, **81**, 4218, (1959); (b) R. M. Keefer and L. J. Andrews, *ibid.*, **81**, 5329 (1959).

[2] R. M. Keefer and L. J. Andrews, *ibid.*, **80**, 5350 (1958).

[3] L. J. Andrews and R. M. Keefer, *ibid.*, **81**, 1063 (1959).