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Nuclear Magnetic Resonance Spectra of Phenylboronic Acids[1a]

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The proton and boron-11 nuclear magnetic resonance spectra of a series of *para*-substituted phenylboronic acids have been investigated. The boron-11 chemical shifts, when calculated relative to the parent compound, phenylboronic acid, gave a linear correlation with corresponding Hammett σ constants for the substituents. The ring proton multiplets were assigned by a rigorous analysis of the group, A_2X_2, using a Royal Precision Model 4000 computer. The chemical shift between the centers of the A and X multiplets was defined as a measure of the inductive effects of the substituents on the electron density of the aromatic ring. Proton chemical shifts calculated for each substituent relative to a reference chemical shift of 0.49 p.p.m. for phenylboronic acid were found to be linear with corresponding σ values for the substituents. The correlations demonstrate that substituent effects on the electron densities of benzenoid rings may be determined by nuclear magnetic resonance.

Introduction

The relationship between nuclear magnetic resonance data and molecular electronic configurations has been the subject of much recent study. Particular interest has been shown concerning the effect of substituents on the n.m.r. parameters of aromatic protons.[2,3] Complex five-spin systems have limited the multiplet analysis of the ring proton spectra of monosubstituted benzenes.[2] The introduction of a second substituent to the ring simplifies the spectrum by increasing the symmetry of the molecule.[3] A rigorous analysis of the multiplet structure in terms of chemical shifts and coupling constants is made possible, in most instances.

Martin and Dailey recently demonstrated a rather straightforward method of analysis for a group of selected *meta*- and *para*-disubstituted benzenes.[4] That method of spin analysis, employed in the present study in a modified form, was developed by Pople, Schneider, and Bernstein.[5]

The transitions may be assigned with confidence for most multiplet structures arising from a symmetric four-spin system, but a difficult problem exists in correlating the shift data with accepted theories of electron density distribution in aromatic systems.[6,7] Richards and Schaeffer discussed the problem in view of their data on *para*-disubstituted benzenes.[3] Martin and Dailey chose to defer any correlation of their data with Hammett σ parameters.[8] Neither paper resolved the data in even the most qualitative sense.

The n.m.r. studies of substituted benzenes, *vide supra*, attempted to assign the chemical shift of each multiplet center from a standard resonance, such as benzene, independent of the chemical shifts of the other equivalent pair of protons on the same ring. It may have been assumed that the "*ortho* effect" of Karplus was the only influence on the screening of the nuclei.[9]

Comparison of their reported n.m.r. shifts reveals that all aromatic protons adjacent to a nitro group, for instance, do not have the same chemical shift from the reference, benzene.[4,7] The shift of the multiplet shows some dependence upon the inductive influence of the second substituent. The difference in shift frequency may be as great as 1 p.p.m. when comparing the *ortho*-proton resonance (*ortho* with respect to the nitro group) of 1-methyl-4-nitrobenzene with 1-iodo-4-nitrobenzene.[7]

A useful method of correlating substituent effects with n.m.r. data for *para*-disubstituted benzenes has been found, however. It entails the use of a standard substituent common to all the compounds under study. Internal chemical shifts between multiplets are calculated relative to a reference shift produced by the common substituent in its monosubstituted counterpart. The usefulness of the method in determining substituent effects will be discussed, as well as its implications.

Experimental

The following *para*-substituted phenylboronic acids were prepared by standard Grignard techniques: 4-methyl-, 4-fluoro-, 4-chloro-, 4-bromo-, and 4-methoxy-. A typical synthesis involved dropwise addition of 0.1 mole of the *para*-substituted bromobenzene to 0.1 g.-atom of magnesium ribbon in a minimum amount of anhydrous ether. The resultant reagent was added dropwise to an equimolar concentration of purified trimethyl borate in ether. Following hydrolysis with 1 N hydrochloric acid, layer separation, extraction of the acid layer with ether, and drying of the combined ether portions with anhydrous magnesium sulfate, the ether was removed *in vacuo*. The crude product was recrystallized from ethanol and hexane alternately until

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[1] (a) Supported in part by a grant from the United States Army Ordnance Corps. (b) Taken in part from a thesis presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry, 1963.

[2] (a) P. G. Corio and B. P. Dailey, *J. Am. Chem. Soc.*, **78**, 3043 (1956); (b) P. Diehl, *Helv. Chim. Acta*, **44**, 829 (1961).

[3] R. E. Richards and T. P. Schaeffer, *Trans. Faraday Soc.*, **429**, 1280 (1958).

[4] J. Martin and B. P. Dailey, *J. Chem. Phys.*, **37**, 2594 (1962).

[5] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Company, Inc., New York, N. Y., 1959.

[6] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1946.

[7] W. Kauzmann, "Quantum Chemistry," Academic Press, Inc., New York, N. Y., 1957.

[8] M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956.

[9] M. Karplus and T. P. Das, *J. Chem. Phys.*, **34**, 1683 (1961).

its anhydride (obtained by heating the acid *in vacuo*) gave a melting point in agreement with literature values.[10,11]

4-N,N-Dimethylaminophenylboronic Acid.—Approximately 0.15 mole of the Grignard reagent was prepared by the method of Davies and Mann.[12] It was filtered through glass wool under nitrogen and added dropwise to 16 g. of trimethyl borate with vigorous stirring. The usual methods of product recovery and purification yielded an orange-yellow crystalline material, m.p. 125°, in 20% yield. The compound was highly soluble in ethanol and ether and moderately soluble in hexane. The corresponding anhydride melted at 191–192° (uncor.).

4-Aminophenylboronic Acid.—A quantity of 4-nitrophenylboronic acid was prepared by the method of Seaman and Johnson.[13] A solution of 4 g. of purified 4-nitrophenylboronic acid in 40 ml. of ether was added dropwise to a solution of 1.2 g. of lithium aluminum hydride in 150 ml. of ether with vigorous stirring. The system was stirred for an additional hour at room temperature with subsequent hydrolysis using 1 *N* HCl. The ether layer was separated and the remaining acid layer washed with two 25-ml. portions of ether. The combined ether solutions were dried over anhydrous magnesium sulfate; the solvent was removed under vacuum. A brown-black crystalline solid remained after 3 weeks of storage under vacuum, yield almost 3 g. The solid was soluble in ether, ethanol, and benzene. The melting point was in excess of 300°. The infrared and n.m.r. spectra of the substance, as well as chemical tests (Table I), confirmed 4-aminophenylboronic acid.

TABLE I

IDENTIFICATION OF COMPOUNDS

Substituent	Neutralization equiv. Obsd.	Neutralization equiv. Calcd.	M.p. of mercuric salt, °C. Obsd.	M.p. of mercuric salt, °C. Lit.[a]
$N(CH_3)_2$			163–164 (OAc)	165
NH_2			165–166 (OAc)	166
OH			162–164 (OAc)	165
OCH_3	154	152	235–236 (Cl)	236.7
CH_3	134	136	238.5 (Cl)	238–239
H	120	122	148–149 (OAc)	149
F	136	140	155–156 (Cl)	
Cl	154	156	223–224 (Cl)	225
Br	191	201	197–198 (OAc)	196
COOH			274–275 (Cl)	273
$COOCH_2CH_3$	187	194		
NO_2	164	167	204–205 (OAc)	202–204

[a] J. M. Heilbron, "Dictionary of Organic Compounds," Eyre and Spottiswoods, London, 1943.

4-Hydroxyphenylboronic Acid.—Approximately 2 g. of 4-aminophenylboronic acid was dissolved in 250 ml. of 50% sulfuric acid. On cooling of the solution to −5° with an ice-salt bath, 20% sodium nitrite solution was added dropwise until no further reaction occurred (about 3 hr.). The system was permitted to warm slowly and stand overnight at ambient temperature. Following neutralization the system was extracted with three 25-ml. portions of ether. The combined ether solutions were dried over anhydrous magnesium sulfate. Removal of the ether under vacuum gave 0.9 g. of crude product. Recrystallization from ether yielded a red crystalline solid which decomposed at 240°. It was soluble in ethanol and was moderately soluble in benzene. The anhydride was prepared by heating a few milligrams at 100° overnight; a red highly-crystalline solid formed, having a melting point in excess of 300°.

(Phenylboronic acid)4-carboxylic Acid.—This compound was prepared by the method of Michaelis.[14] The method entailed the oxidation of 4-methylphenylboronic acid with a saturated solution of potassium permanganate.

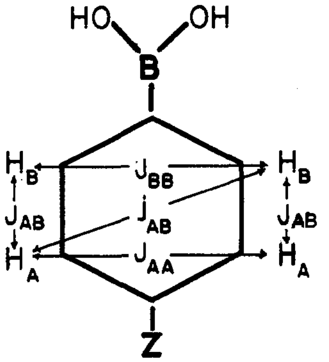

Fig. 1.—Spin coupling constants for four nuclei, A_2B_2, in a *para*-substituted phenylboronic acid.

(Phenylboronic acid)4-ethylcarboxylate.—The ester was prepared from the corresponding carboxylic acid by esterification of the acid with absolute ethanol in the presence of sulfuric acid. Addition of distilled water to the warm solution gave an 89% yield of pale yellow needles. The melting point was in agreement with its reported value.[14]

Phenylboronic Acid.—The reference compound was obtained commercially and was recrystallized from distilled water.

Product Identification.—Product identification was accomplished as follows: neutralization equivalents were found by titration with standard base in the presence of mannitol[15]; cleavage reactions of the B–C bond with either mercuric acetate or mercuric chloride defined the nature of aromatic substitution[16]; the infrared and n.m.r. spectra of the acids and anhydrides were consistent with their molecular structures. These data are summarized in Table I.

Nuclear Magnetic Resonance Measurements.—The proton resonance spectra were obtained with a Varian Model A-60 spectrometer. The standard chart was calibrated with an oscillograph and decade counter to an accuracy of 0.3 c.p.s., the limit of resolution for the instrument. Two scans were made on each chart—one from 500 to 400 c.p.s. shift from tetramethylsilane with a 250-sec. sweep rate, and another from 500 to 400 c.p.s. with the scale expanded to 100 c.p.s. and the sweep offset to 400 c.p.s. to maximize the resolution of the instrument. At least three sets of scans were made on each sample to confirm the band positions and intensities. No variation was permitted (if a variation in either frequency or intensity was noted, the field was reoptimized).

The boron-11 resonance spectra were obtained with a Varian Model HR-60 spectrometer equipped with a 19.3-Mc. radiofrequency unit and probe assembly. Band positions were measured with respect to side bands at 200 c.p.s. from triethyl borate using a Hewlett-Packard oscillator monitored with a Hewlett-Packard Model 521-A decade counter at a 10-sec. gate. Three resonance spectra, without and with side bands, were recorded on a Moseley Model XD-2 recorder. The acceptable shift deviation was ±1 c.p.s. or less.

Samples were prepared in deuteriochloroform; they were 10% in the boronic acid, 10% triethyl borate, and about 0.5% tetramethylsilane. The usual techniques of sample preparation were employed.[3] Previous dilution effect studies were made on selected substituted phenylboronic acids at acid concentrations of 20, 10, and 5%.[17] No variations in band frequencies were noted at acid concentrations of 10 and 5%, showing that at low concentrations solvent effects became constant. Extrapolations of the band frequencies to infinite dilution were unnecessary.

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[10] (a) H. G. Kuivila and A. R. Hendrickson, *J. Am. Chem. Soc.*, **74**, 5068 (1952); (b) H. G. Kuivila and L. E. Benjamin, *ibid.*, **77**, 4014 (1955).

[11] B. Bettman, G. E. K. Branch, and D. L. Yahroff, *ibid.*, **56**, 1865 (1934).

[12] W. C. Davies and F. G. Mann, *J. Chem. Soc.*, 279 (1944).

[13] W. Seaman and J. R. Johnson, *J. Am. Chem. Soc.*, **53**, 711 (1931).

[14] A. Michaelis, *Ann.*, **315**, 19 (1901).

[15] D. D. DeFord, C. A. Lucchesi, and J. M. Thoburn, "Analytical Chemistry of Boron," Department of Chemistry, Northwestern University, Evanston, Ill., 1953.

[16] H. Gilman, "Organic Chemistry," Vol. 1, John Wiley and Sons, Inc., London, 1943.

[17] Unpublished work of the authors.

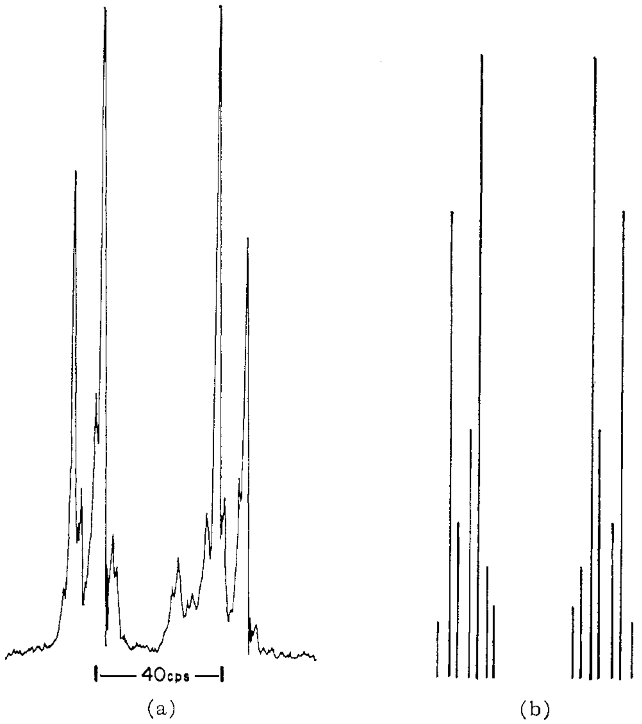

Fig. 2.—A typical A_2X_2 n.m.r. spectrum—4-N,N-dimethylaminophenylboronic acid: (a), ring-proton spectrum; (b), theoretical spectrum; J_{AB} = 9 c.p.s., j_{AB} = 0.0 c.p.s., J_{AA} = J_{BB} = 2.5 c.p.s.

Analysis of Spectra

Proton transitions were assigned with the aid of a Royal Precision Model 4000 computer. The model for the spin system is shown in Fig. 1. The system represents the group, A_2B_2, two pairs of equivalent protons. The spin analysis was based on the complete Hamiltonian for the system discussed by Pople, Schneider, and Bernstein.[5] Transition energies and intensities were calculated on the computer and compared with those found in the spectrum of each boronic acid. Beginning with coupling values of J_{AB} = 8 c.p.s., J_{AA} = J_{BB} = 2 c.p.s., and j_{AB} = 1 c.p.s. and δ determined directly from the spectrum, transition energies and intensities were calculated. The coupling constants were adjusted, and the calculations were reiterated until the best fit was obtained.

In most spectra the analysis could be simplified to A_2X_2, which is proper when the separation of the multiplet centers exceeds 30 c.p.s.[4,5] In that case the number of transitions in each multiplet is reduced from twelve bands to six. An example of the A_2X_2 spectrum and its analysis is shown in Fig. 2.

The parameters which gave the best computer fit for both the transition energies and intensities of the spectra are summarized in Table II.

The spectrum of 4-fluorophenylboronic acid was assigned by assuming that two interacting spin systems were present: A_2X_2 and $A_2'X_2'$. The fluorine nucleus with spin states of $\pm 1/2$ is assumed to split the proton energy levels into both the normal A_2X_2 configuration for four protons plus identical multiplets that are mirror images but opposite in sign with respect to the multiplet centers. The spectrum of the 4-fluorophenylboronic acid and its calculated counterpart are shown in Fig. 3. The agreement is excellent.

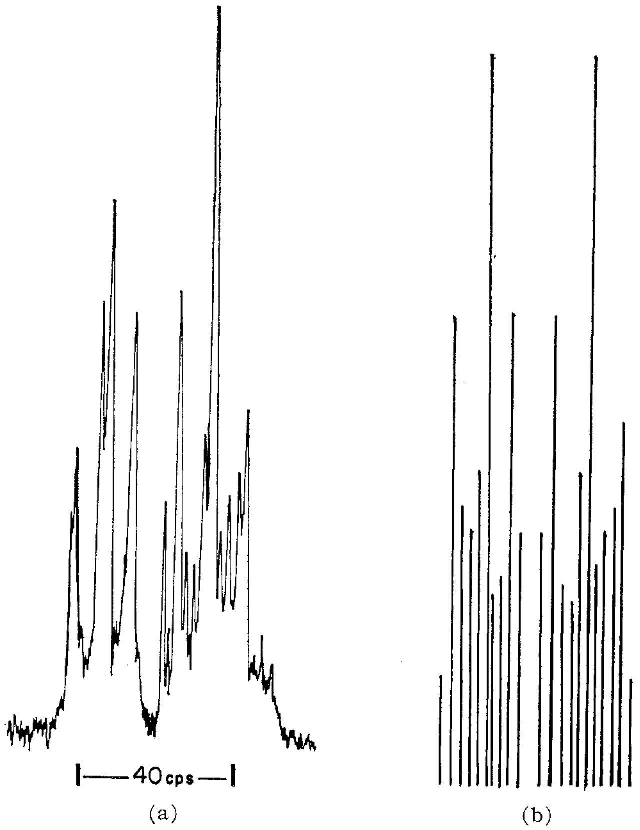

Fig. 3.—4-Fluorophenylboronic acid: (a), ring-proton spectrum; (b), theoretical spectrum; J_{AX} = 8.5 c.p.s., j_{AX} = 0.5 c.p.s., J_{AA} = J_{XX} = 2.2 c.p.s.; $J_{A'X'}$ = 8.5 c.p.s., $j_{A'X'}$ = 0.5 c.p.s., $J_{A'A'}$ = $J_{X'X'}$ = 2.0 c.p.s.

Table II

Observed Shift and Coupling Parameters

Substituent	Chem. shift, p.p.m.	J_{AB}, c.p.s.	j_{AB}, c.p.s.	J_{AA}, c.p.s.	J_{BB}, c.p.s.
$N(CH_3)_2$	0.93	9.0	0.0	2.5	2.5
NH_2	0.74	8.5	0.0	1.5	1.5
OH	0.80	9.5	−0.5	2.0	2.0
OCH_3	0.67	8.5	0.5	2.4	2.4
CH_3	0.57	7.8	0.0	2.4	2.4
H	0.49				
F	0.46	8.5	0.5	2.2	2.2
		8.5	0.5	2.0	2.0
Cl	0.33	7.5	0.5	2.0	2.0
Br	0.26	7.7	0.9	2.6	2.6
COOH	−0.18	8.0	0.0		
$COOC_2H_5$	−0.34	7.5	0.5	2.0	2.0
NO_2	−0.66	6.7	0.5	2.0	2.0

The spectrum of phenylboronic acid was analyzed with the ABX group analysis of Pople, Schneider, and Bernstein.[5] The fit of transition energies was excellent, even though the spin system consists of five protons. The chemical shift between the A and X protons is given under the heading of substituent H in Table III.

Chemical Shift Calculations.—The proton chemical shifts were calculated using the energies of the centers of the A and X multiplets as follows

$$\delta_H = \frac{\nu_X - \nu_A}{60 \text{ Mc.}} \times 10^6 \qquad (1)$$

where 60 Mc. is the frequency of the radiofrequency field. The chemical shift δ_H is found in parts per million (p.p.m.).

The boron-11 chemical shifts were calculated from the relation

$$\delta_B = \frac{\nu_{TEB} - \nu_C}{19.3 \text{ Mc.}} \times 10^6 \qquad (2)$$

where ν_{TEB} is the resonance frequency of the standard, triethyl borate, ν_C is the frequency of boron-11 resonance in the boronic acid, and 19.3 Mc. is the frequency of the radiofrequency field.

The results of the calculations of the chemical shifts using eq. 1 and 2 are summarized in Table III. To correct the chemical shifts for the effect of the boronic acid group, as well as to adjust their magnitudes to a zero relative chemical shift for a *para*-proton substituent, δ_{rel} values were calculated by subtraction using the relation

$$\delta_{rel} = \delta_{disub} - \delta_{PBA} \qquad (3)$$

where δ_{disub} is the chemical shift of the disubstituted molecule and δ_{PBA} is the chemical shift of the parent—phenylboronic acid. The relative chemical shifts are summarized in Table III.

TABLE III

SIGMA ABSOLUTE AND RELATIVE CHEMICAL SHIFTS AND σ CONSTANTS

Substituent	$\delta_{B^{11}}$	δ_{H^1}	$\delta_{rel}B^{11}$	$\delta_{rel}H^1$	σ
$N(CH_3)_2$	5.16	0.93	3.41	0.44	−0.600
NH_2	5.26	0.74	3.51	0.25	−0.660
OH	5.02	0.80	3.75	0.31	−0.357
OCH_3	7.42	0.67	1.35	0.18	−0.268
CH_3	8.21	0.57	0.56	0.08	−0.170
H	8.77	0.49	0.00	0.00	0.000
F	8.72	0.46	−0.05	−0.03	0.062
Cl	9.82	0.33	−1.05	−0.16	0.227
Br	9.63	0.26	−0.86	−0.23	0.232
COOH	10.63	−0.18[a]	−1.86	[b]	
$COOC_2H_5$	10.57	−0.34[a]	−1.80	[b]	0.522
NO_2	11.90	−0.66[a]	−3.32	[b]	0.778

[a] Because the substituent is more electron withdrawing than the boronic acid group, the order of bands is reversed; hence the negative proton shift values. [b] See Discussion.

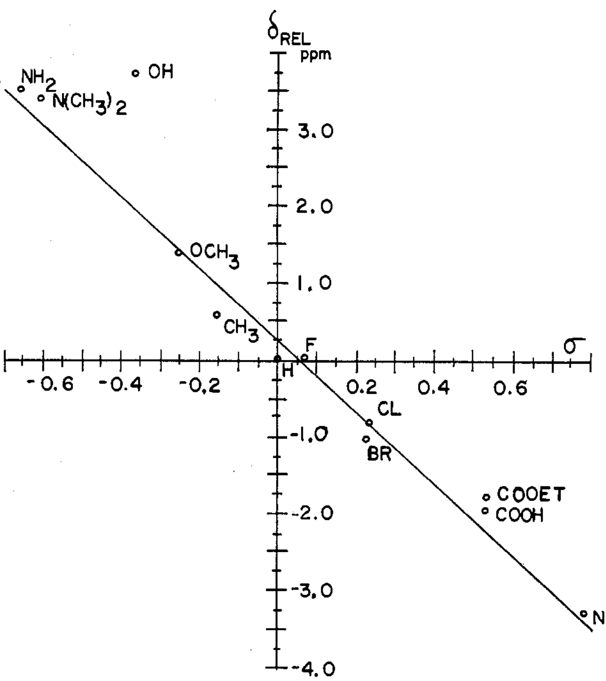

Fig. 4.—Relative boron-11 chemical shifts *vs.* σ.

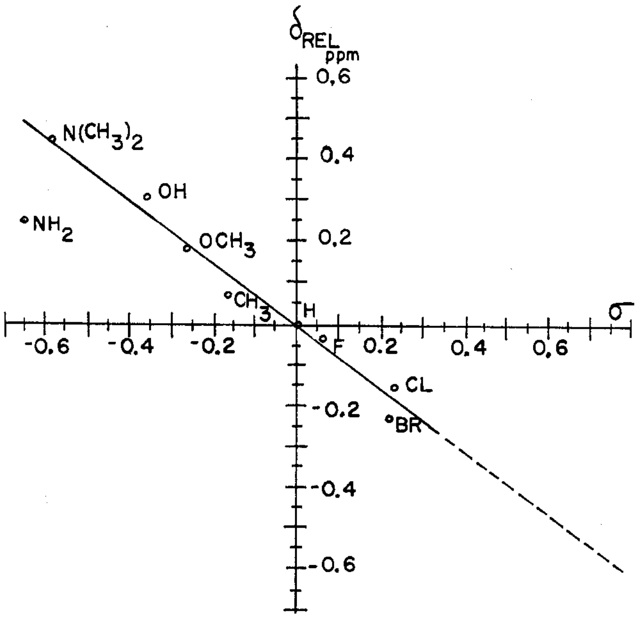

Fig. 5.—Relative proton chemical shifts *vs.* σ.

Discussion

The Hammett σ constants for the *para*-substituents considered in this study are given in Table III. They were listed in the text by Newman.[8] A plot of the relative boron-11 chemical shifts *vs.* σ is shown in Fig. 4. An excellent linear correlation resulted. The point representing the OH group should be considered anomalous, since there is no apparent reason why its electron-donating capability should have been enhanced by intra- or intermolecular interactions.

A plot of the relative proton chemical shifts *vs.* σ is given in Fig. 5. The relative chemical shift of the NH_2 group falls below the otherwise linear correlation. The shift arising from the inductive effect of the $N(CH_3)_2$ group was linear with σ giving an indication that some intermolecular force such as hydrogen bonding may be operating in the 4-aminophenylboronic acid.

A difficulty arose in assigning the relative proton chemical shifts for the COOH, $COOC_2H_5$, and NO_2 groups. The multiplet systems for the compounds represented by the three groups fell well downfield from those of the other boronic acids. In the case of the 4-nitrophenylboronic acid, one of the multiplets was found at a shift of slightly over 500 c.p.s. from tetramethylsilane, about 40-50 c.p.s. toward lower field than was the case for any of the other boronic acids studied.

Comparing the inductive withdrawing capabilities of the three substituents with that expected for the boronic acid group, the only conclusion that could be drawn was that the COOH, $COOC_2H_5$, and NO_2 groups were adjacent to the pair of equivalent protons responsible for the low-field multiplet; *i.e.*, the order of the multiplets was reversed. The fact that the high-field multiplet fell in the region previously ascribed to the pair of protons adjacent to the boronic acid group supports these conclusions. Thus the chemical shifts measured for the compounds containing the three groups were assigned a negative sign.

An inspection of the data reported by Martin and Dailey[4] and Richards and Schaeffer[3] revealed that correlations of substituent effects were possible for the proton spectra of other disubstituted benzenes. Using the method discussed in the present study, internal chemical shifts could be calculated from their data from which relative shifts were derived. The relative shifts for selected compounds were found to be linear with σ provided (a) the same reference substituent was present in each compound in the series, and (b) the substituents *para* to the reference group on the benzene ring were exerting a greater degree of inductive release of electron density than was the reference group.

A future paper will discuss these findings and their implications in detail. For the present it should suffice to state that to be effective in a study of this type the reference group must exert a relatively constant inductive influence on the separation of the multiplets. The principle role of the reference group must be to reduce the number of ring protons so that a complete spin analysis is possible without interacting with the *para* substituents in an inconsistent manner. So long as the inductive effect of the reference group may be classified as electron withdrawing, relative to the *para* substituent, its influence on the separation of the multiplets is virtually constant. The relative chemical shifts within a series of *para* substituents reflect only the electron-donating capabilities of the latter and may be correlated with known substituent phenomena.

The generalization holds for several series in addition to the phenylboronic acids. The series include the benzoic acids and the nitrobenzenes, and, with few exceptions, the relative chemical shifts determined for these series correlate well with σ constants. The chemical shifts of the 4-nitrophenylboronic acid and (phenylboronic acid)4-carboxylic acid correlate well within their respective series when calculated relative to their parent compounds—nitrobenzene and benzoic acid, respectively. That is, they correlate well based on the assumption that the σ constant for the boronic acid group should be slightly less positive than that of the carboxylic acid group; the σ constant for the boronic acid group cannot be determined directly. Their chemical shifts are positive and are of the proper order of magnitude to be treated by the same method given in eq. 3, adjusted for the proper reference shift.

Although much emphasis has been given the correlation of the relative proton chemical shifts with σ, note should be made that the boron-11 shifts for the series of phenylboronic acids correlated surprisingly well with σ. The linear plot fit ten of the eleven relative chemical shifts within the experimental error. Because it may be possible to prepare phenylboronic acids with *para* substituents other than those reported here, future studies may extend the range of the correlation still further. If the appropriate compound could be prepared, it may be possible to use its relative boron-11 chemical shift in conjunction with Fig. 4 to predict the σ constant when no other data are available.

Contribution No. 598 from the Central Research Department,
Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware

Chemistry of Boranes. XV.[1] Synthesis of Diborane from Boric Oxide

By T. A. FORD, G. H. KALB, A. L. McCLELLAND, and E. L. MUETTERTIES

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A direct synthesis of diborane from boric oxide has been achieved by hydrogenation of the oxide in the presence of aluminum and aluminum trichloride. Very pure diborane is obtained from this reaction in 40–50% conversions at temperatures above 150° and hydrogen pressures of 750 atm. This hydrogenation is believed to proceed through an aluminum chlorohydride intermediate. Amine boranes, aminoboranes, and borazines were obtained directly from boric oxide when the hydrogenation was effected in the presence of secondary or tertiary alkylamines.

Diborane Synthesis.—There are a large number of routes to diborane[2] which are based on boron halides or boron esters as starting materials; however, no synthesis of this hydride directly from boric oxide has been described. We have found that the oxide can be converted to diborane in good yields by reaction with aluminum, aluminum chloride (or an $AlCl_3$–NaCl melt), and hydrogen. This reaction, when effected at 175° and 750 atm. hydrogen pressure, gave diborane in conversions as high as 50%. The

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[1] Chemistry of Boranes. XIV: W. R. Hertler and M. S. Raasch, *J. Am. Chem. Soc.*, in press.

[2] For partial review of this subject, see D. T. Hurd, "Chemistry of the Hydrides," John Wiley and Sons, New York, N. Y., 1952, pp. 76–77; N. G. Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publishers, New York, N. Y., 1956, pp. 49–51; Gmelin's "Handbuch Der Anorganischen Chemie," 8th Ed., Verlag Chemie, G.M.B.H., 1954, pp. 97–105.