[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NEW HAMPSHIRE]

Electrophilic Displacement Reactions. II. Rates of Brominolysis of Substituted Benzeneboronic Acids[1,2]

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The rates of brominolysis of ten substituted benzeneboronic acids have been measured in "20%" acetic acid at 25.0°. The absence of correlation by the Hammett equation is discussed.

In a previous paper an examination of several kinetic characteristics of the brominolysis of benzeneboronic acid was described.

$$C_6H_5B(OH)_2 + Br_2 \xrightarrow[HOAc]{H_2O} C_6H_5Br + HBr + H_3BO_3$$

The results indicate that molecular bromine attacks a quadricovalent boron intermediate in the rate-determining step. The present paper describes an extension of this work to a study of the effect of meta and para substituents on the rate of the reaction. Two related primary objectives are involved. One of these is to gain more information concerning the mechanism of the reaction. The second deals with the general problem of the correlation of the rates of electrophilic displacement reactions in the aromatic series. This includes the question of whether the Hammett equation[3] or any other simple relation correlates these reactions.

This problem has been considered[4] with regard to the rates of nitration of substituted benzenes[5] with the observation that a parallel trend exists between log k and σ leading to a ρ value of about -5. McDuffie and Dougherty[6] have determined the relative rates of acetylation of several benzene derivatives. For the four substituents which could be compared they found a linear relation between the logarithms of the *total* rates of acylation and nitration in the meta and para positions. The Hammett equation was said to apply to acetylation.[7] More recently McEwen and Mehta[8] have reported that the rates of reaction of unsymmetrical diarylethylenes and benzoic acids with hydrazoic acid obey the Hammett equation.

Experimental

Boronic Acids.—The boronic acids were prepared by methods described in literature references indicated in Table I. Esterification of the carboxy substituted acids was carried out by the ternary azeotrope method using benzene as the third component and sulfuric acid as catalyst. Addition of water brought about hydrolysis of the diethyl carbethoxyboronate to the carbethoxyboronic acid.

TABLE I

DATA ON BENZENEBORONIC ANHYDRIDES

Substituent	Preparation Acid	Preparation Anhydride	M.p., °C[a]	Neutral equivalent Calcd.	Neutral equivalent Found
H	*c*	*i*	214–216[g]	103.9	104.3
p-OCH_3	*c*	*i*	204–207	134.0	134.4
m-NO_2	*d*	*h*	280–281	148.9	149.1
p-Cl	*c*	*h*	261–262.5	138.4	139.6
m-Cl	*c*	*h*	178–179	138.4	138.4
p-CH_3	*c*	*h*	246–248	118.0	117.8
m-CH_3	*c*	*i*	160–161.5	118.0	118.7
p-$COOC_2H_5$	*e*	*i*	198–200	174.8	175.9
m-$COOC_2H_5$[b]	*e*		136–138	193.9	194.4
p-Br[b]	*c*		279–282[f]	200.8	199.5

[a] All melting points are uncorrected. [b] Free boronic acid. [c] F. R. Bean and J. R. Johnson, THIS JOURNAL, **54**, 4415 (1932). [d] W. Seaman and J. R. Johnson, *ibid.*, **53**, 711 (1931). [e] A. Michaelis, *Ann.*, **315**, 19 (1901). [f] Lit. 286–289°; reference in note *c* above. [g] Lit. 190°; A. Michaelis and P. Becker, *Ber.*, **15**, 181 (1882). [h] Acid dried to constant weight in vacuum desiccator over sulfuric acid. [i] Acid dried to constant weight in oven at 110°.

Because of the great ease of dehydration of some of the acids reliable melting points are rather difficult to obtain.[9] Therefore, in most cases the acid was converted to the anhydride whose melting point could be easily reproduced. Dehydration was effected by drying either in a desiccator over sulfuric acid or in the oven at 110°. Contrary to previous experience[10] with the acids, titration in the presence of mannitol yielded neutralization equivalents in excellent agreement with theory.

Pertinent data are listed in Table I.

Kinetic Experiments.—The rate measurements were all carried out in "20%" acetic acid containing 0.4 M sodium bromide at 25.0 ± 0.03° by a procedure previously described.[1]

Benzeneboronic acid and its anhydride yielded the same specific rate constants within the experimental error (±3%). This fact is presented as justification for the use of acid in some cases (*p*-Br and *m*-COOEt) and the anhydride in others.

The acid liberated in the reaction has a tendency to decrease its rate. This effect can be minimized by the use of low concentrations of reactants.[1] Therefore, in all cases but one (*m*-nitro) the initial concentrations of bromine and boronic acid were 0.008 and 0.010 M, respectively, or smaller. With *m*-nitro the concentration of boronic acid was 0.080 M. Conventional second-order plots of the data were made and the rate constants calculated from initial slopes. Precipitation of the brominated product, which occurred in several instances, did not appear to affect the rate.

A typical plot is shown in Fig. 1.

At least two runs were made with each compound. Rate constants agreed within ±3%.

Reaction Product from *m*-Chlorobenzeneboronic Acid.—A possible explanation of the location of the point for *m*-chloro in Fig. 3 would be that the rate for brominolysis is spuriously high due to intrusion of bromination (replacement of hydrogen) in the positions ortho and para to the chlorine. In such a case the number of moles of boric acid

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(1) For preceding paper in this series see THIS JOURNAL, **73**, 4629 (1951).

(2) Taken in part from the Master's thesis of Alfred R. Hendrickson, August, 1950.

(3) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

(4) Reference 3, pp. 198–199.

(5) C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *J. Chem. Soc.*, **1959** (1931); M. L. Bird and C. K. Ingold, *ibid.*, 918 (1938); C. K. Ingold and M. S. Smith, *ibid.*, 905 (1938); G. A. Benford and C. K. Ingold, *ibid.*, 929 (1938).

(6) H. F. McDuffie, Jr., and Gregg Dougherty, THIS JOURNAL, **64**, 297 (1942).

(7) However, the statistical correction for the fact that there are six vulnerable positions in benzene appears to have been neglected.

(8) W. E. McEwen and N. Mehta, THIS JOURNAL, **74**, 526 (1952).

(9) W. Seaman and J. R. Johnson, *ibid.*, **53**, 711 (1931).

(10) G. E. K. Branch, D. L. Yabroff and B. Bettman, *ibid.*, **56**, 1865 (1934).

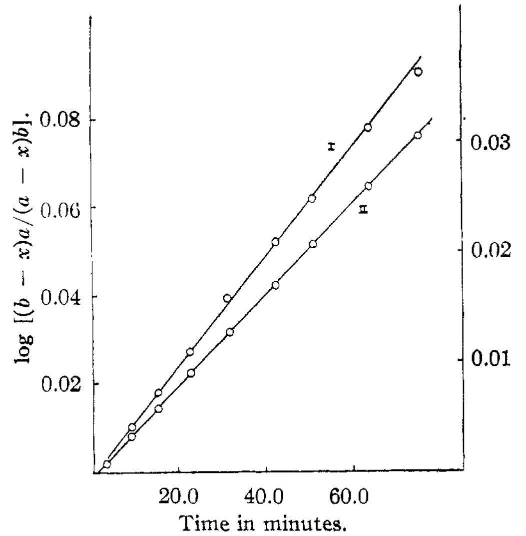

Fig. 1.—Brominolysis of *p*-chlorobenzeneboronic acid: $[C_6H_5B(OH)_2]_0$, 0.0100 *M*; I, $[Br_2]_0$, 0.00805 *M*, left ordinate; II, $[Pr_2]_0$, 0.00391 *M*, right ordinate.

formed in the reaction would be smaller than the number of moles of bromine consumed.

To test this possibility a "20%" acetic acid solution 0.0289 *M* in *m*-chlorobenzeneboronic acid, 0.0197 *M* in bromine and 0.40 *M* in sodium bromide was allowed to react at 25.0° for 16 days whence the bromine concentration had dropped to 0.00319 *M*. The excess bromine was destroyed by addition of thiosulfate and analysis for boric acid made on an aliquot. The aliquot was made basic and evaporated almost to dryness on the steam-bath. Methanol was added and the distillation procedure of Chapin[11] followed for the determination of boric acid. In a sample which should contain 0.189 meq. of boric acid, assuming only replacement of boron, 0.195 meq. were found. In a synthetic mixture containing 0.168 meq. of boric acid and 0.0902 meq. of the boronic acid, 0.178 meq. of boric acid was found.

TABLE II

RATES OF BROMINOLYSIS OF SUBSTITUTED BENZENEBORONIC ACIDS IN "20%" ACETIC ACID 0.40 *M* IN SODIUM BROMIDE AT 25.0°

Substituent	$k \times 10^5$, l.m.$^{-1}$ sec.$^{-1}$	$\log k/k_0$	$\log k/k_0$ nitration[5]
H	484	0	0
p-OCH_3	>7 × 10^8	>6	
p-CH_3	38000	1.88	1.74
p-Cl	261	−0.268	−0.876
p-Br	200	−0.383	−1.00
p-$COOC_2H_5$	5.04	−1.98	−3.05
m-CH_3	1610	0.523	0.477
m-Cl	16.9	−1.46	−3.5
m-$COOC_2H_5$	21.0	−1.36	−2.11
m-NO_2	1.46	−2.52	

Results and Discussion

In Table II are listed the rate constants and values of $\log k/k_0$ obtained in this investigation along with those for nitration.[5] It will be of interest to discuss the former in terms of the Hammett equation.

Although the equation correlates the rates or equilibria of a large number of reactions, exceptions have been noted. Walling and Mayo[12] observed that the reactivities of substituted styrenes toward radicals derived from styrene follow the equation, but the relationship is quite lost with radicals derived from methyl methacrylate or maleic anhydride. Swain and Langsdorf[13] have examined the data for a number of reactions, particularly nucleophilic displacements on benzyl halides, revealing separate non-linear relations between log *k* and σ for meta and para substituents.

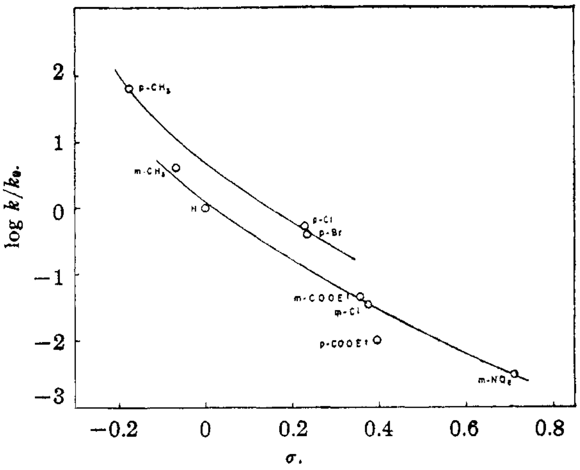

Fig. 2.—Hammett plot for brominolysis.

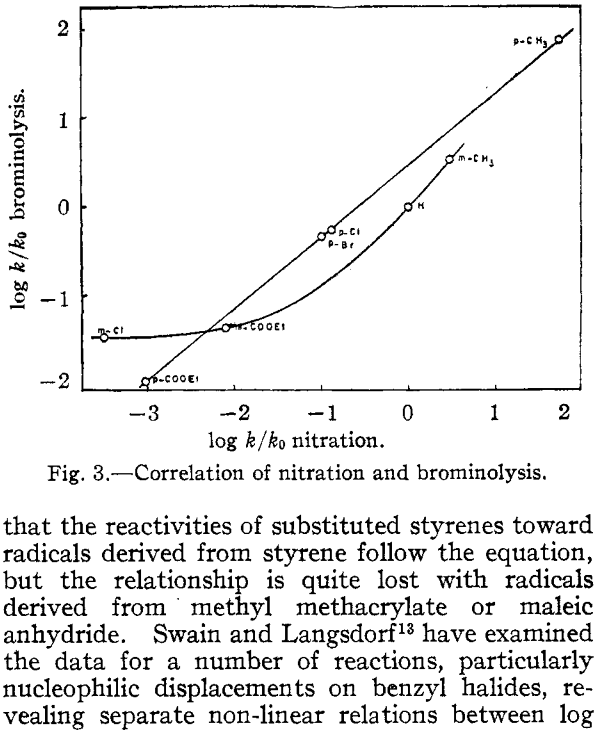

Fig. 3.—Correlation of nitration and brominolysis.

These deviations are attributed to differing capacities of the substituents for resonance stabilization of a charged activated complex.[12,13] They have been interpreted as lending support to the concept of unity of mechanism in nucleophilic displacement reactions.[13]

A plot of $\log k/k_0$ from our data *vs.* σ is reproduced in Fig. 2. It is evident that the meta substituents yield a relatively smooth non-linear plot. Of the para substituents methoxy (not shown), methyl, chloro and bromo fall above the meta curve whereas carbethoxy[14] falls below. These observations are consistent with the assumption that the rate-determining step leads to the formation of a dis-

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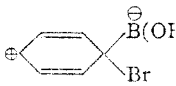
[11] "Scott's Standard Methods of Analysis," N. H. Furman, Ed., D. Van Nostrand Co., Inc., New York, N. Y., Vol. I, p. 176.

[12] C. Walling and F. R. Mayo, *Faraday Society Discussion*, No. 2, 295 (1947).

[13] C. G. Swain and W. P. Langsdorf, Jr., THIS JOURNAL, **73**, 2813 (1951).

[14] The σ-value (for derivatives other than phenols or amines) used is that for the carboxyl group estimated from data on the dissociation constants of benzoic acids given by R. Kuhn and A. Wassermann, *Helv. Chim. Acta*, **11**, 44 (1928).

crete intermediate which may be represented by structure I.



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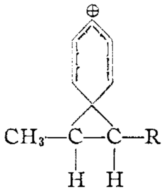
The σ-value of a substituent can be regarded as a measure of electron availability which it creates due to a combination of inductive and resonance effects.[15] The fact that the curves are concave upward is the result of the ability of electron-releasing groups to increase through resonance the capacity for positive charge. This is especially true for the para substituents, which therefore produce higher rates than do the meta. The discontinuity in the para curve between the halogens and carbethoxy reflects the inability of the latter to stabilize a cation to such an extent that it falls below the meta curve. Now if cleavage of the carbon–boron bond were important in the rate-determining step it would be facilitated by electron withdrawing groups, particularly when in the ortho or para positions. In this event one would expect the point for *p*-carbethoxy to fall above the meta curve.

The fact that one of the reacting species in the rate-determining step is probably a quadricovalent boron derivative does not alter the argument. It would be expected that the electron-releasing groups would decrease the concentration of such an intermediate. In such a case the effect on the brominolysis rate would be the reverse of that actually observed. Thus this factor must be relatively unimportant in determining the relative rates.

Convincing evidence for a discrete intermediate in aromatic electrophilic displacement reactions has been obtained by other investigators. In aromatic nitration tritium is replaced at the same rate as hydrogen.[16] The stereochemistry of the acetolysis of the tosylates of 3-phenyl-2-butanol (II) and 2-phenyl-3-pentanol (III) has been shown by Cram to require the assumption of an intermediate such as II.[17]



II, R = CH_3
III, R = C_2H_5

Figure 3 is a log–log plot of our rate constants *versus* those for aromatic nitration. It is apparent that, whereas the para substituents fall on a straight line, the meta substituents do not.[18] The probable similarity of the transition state complexes in the two reactions might lead one to anticipate a linear relation for both meta and para substituents. However, a number of other factors, such as over-all mechanism and solvent, for example, intrude to make prediction difficult. An extension of this work which is in progress may make possible a delineation of the important factors.

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[15] Reference 3, p. 196.

[16] L. Melander, *Acta. Chem. Scand.*, **3**, 95 (1949); *Nature*, **163**, 599 (1949); *Arkiv. Kemi*, **2**, 213 (1950).

[17] D. J. Cram, THIS JOURNAL, **71**, 3863, 3875 (1949).

[18] The rate constant for the *m*-chloro substituent in nitration is estimated on the basis of about 0.3% meta nitration of chlorobenzene; A. Hollemann, *Rec. trav. chim.*, **19**, 304 (1900). This has been confirmed by the isotopic dilution method of analysis (private communication from Dr. J. D. Roberts).

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF WASHINGTON]

The Isolation of Dipalmitoleyl-L-α-glycerylphosphorylcholine from Yeast. A New Route to (Dipalmitoyl)-L-α-lecithin[1]

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An individual, completely unsaturated lecithin, dipalmitoleyl-L-α-glycerylphosphorylcholine, has been isolated for the first time from fresh baker's yeast. A reproducible, modified adsorption technique, which uses aluminum oxide as the adsorbent, is described for the isolation of this lecithin. Catalytic hydrogenation of this unsaturated compound gives the corresponding individual, saturated lecithin, (dipalmitoyl)-L-α-lecithin.

In a previous report from this Laboratory,[3] it was shown that the lecithins of egg could be isolated by passage of an ethanol solution of the mixed phospholipides through a column of aluminum oxide. The ethanolic eluates contained only the lecithins, with approximately 25% of their fatty acids being unsaturated. As a supply of a more highly unsaturated lecithin was also desired for enzyme studies, other sources of phospholipides were considered. A very promising source appeared to be yeast (*Saccharomyces cerevisiae*). Salisbury and Anderson[4] reported that the phospholipides obtained from yeast, grown under conditions designed to prevent the production of hydrocarbon impurities, were composed of 4 parts lecithin and 1 part cephalin. Approximately 86% of the fatty acids of these lecithins were unsaturated. In confirmation of these observations, we have found a similar composition of the fatty acids in the mixed phospholipides of commercial baker's yeast.

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[1] This work was performed under Contract No. N8-onr-52004 between the University of Washington and the Office of Naval Research, United States Navy Department.

[2] A portion of this paper formed the thesis submitted by Michael E. Jayko to the Graduate School, University of Washington, January, 1952, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Biochemistry.

[3] D. J. Hanahan, M. B. Turner and M. E. Jayko, *J. Biol. Chem.*, **192**, 623 (1951).

[4] L. F. Salisbury and R. J. Anderson, *ibid.*, **112**, 541 (1936).