ORGANIC AND BIOLOGICAL CHEMISTRY

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Electrophilic Displacement Reactions. IX. Effects of Substituents on Rates of Reactions between Hydrogen Peroxide and Benzeneboronic Acid[1-3]

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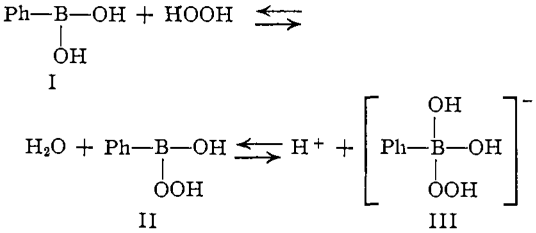
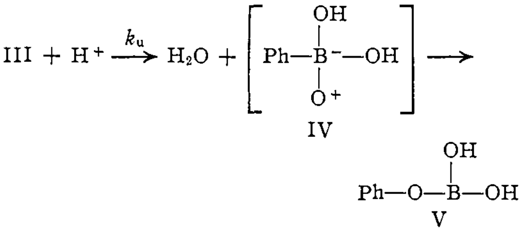
The effects of *meta* and *para* substituents on the rates of reactions between benzeneboronic acid and hydrogen peroxide have been measured. Ten substituents and five different reaction paths are included in the study. The Hammett equation correlates the rates for each reaction path suggesting that the mechanisms involved do not have in detail the characteristics of aromatic electrophilic substitution in the slow steps.

The reaction between hydrogen peroxide and benzeneboronic acid in aqueous solutions produces quantitative yields of phenol and boric acid. Formally this would appear to be either a homolytic or an electrophilic substitution in the benzene ring, in which the boronic acid group rather than the usual hydrogen is replaced. Homolytic reactions involving hydrogen peroxide and organic compounds are usually complex.[4] Electrophilic hydroxylation of arenes is unknown. These considerations led to a series of investigations on the kinetics of the reaction between hydrogen peroxide and benzeneboronic acid[5] which have revealed that the reaction proceeds by several mechanisms each of which can be shown to predominate under appropriate conditions. Those which were studied in the present investigation are depicted below[5c] in postulated forms which are consistent with the kinetic information now available[5a,b] though not necessarily unique in this regard.



$$\underset{\mathrm{I}}{\mathrm{Ph{-}\underset{\substack{|\\ OH}}{B}{-}OH}} + \mathrm{HOOH} \rightleftarrows$$

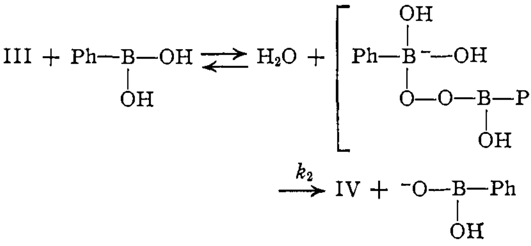
$$\mathrm{H_2O} + \underset{\mathrm{II}}{\mathrm{Ph{-}\underset{\substack{|\\ OOH}}{B}{-}OH}} \rightleftarrows \mathrm{H^+} + \underset{\mathrm{III}}{\left[\mathrm{Ph{-}\overset{\substack{OH\\ |}}{\underset{\substack{|\\ OOH}}{B}}{-}OH}\right]^-} \quad (1)$$



$$\mathrm{III} + \mathrm{H^+} \xrightarrow{k_u} \mathrm{H_2O} + \underset{\mathrm{IV}}{\left[\mathrm{Ph{-}\overset{\substack{OH\\ |}}{\underset{\substack{|\\ O^+}}{B^-}}{-}OH}\right]} \longrightarrow$$

$$\underset{\mathrm{V}}{\mathrm{Ph{-}O{-}\overset{\substack{OH\\ |}}{B}{-}OH}} \quad (2)$$

$$\mathrm{III} \xrightarrow{k_1} \mathrm{HO^-} + \mathrm{IV} \quad (3)$$



$$\mathrm{III} + \mathrm{Ph{-}\underset{\substack{|\\ OH}}{B}{-}OH} \rightleftarrows \mathrm{H_2O} + \left[\mathrm{Ph{-}\overset{\substack{OH\\ |}}{\underset{\substack{|\\ O{-}O{-}\underset{\substack{|\\ OH}}{B}{-}Ph}}{B^-}}{-}OH}\right]$$

$$\xrightarrow{k_2} \mathrm{IV} + {}^-\mathrm{O{-}\underset{\substack{|\\ OH}}{B}{-}Ph} \quad (4)$$

$$\mathrm{II} \xrightarrow[\text{catalysis}]{\text{acid}} \mathrm{V} \quad (5)$$

The rates of all of these reactions depend on the concentrations of both peroxide and boronic acid. It is assumed that the equilibria (1) are maintained at all times. Reaction 2 represents a *p*H-independent reaction leading to monophenyl borate which is presumed to hydrolyze rapidly to phenol and boric acid. This is the predominating reaction in the *p*H range 1–3. Reaction 3 has as its distinguishing characteristic a first power dependence of rate on hydroxide ion concentration.[6] Reaction 4 shows the same *p*H dependence but is complicated by the fact that its rate depends on the square of the boronic acid concentration. Since it has the same stoichiometry as the other reactions, one molecule of boronic acid must function as a catalyst. The acid-catalyzed reaction[5] shows different characteristics in perchloric, sulfuric and phosphoric acids[5b] and is discussed separately below.

Results and Discussion

In addition to benzeneboronic acid, four *para* and five *meta* substituted acids were included in this investigation. The experimental methods used have been described earlier.[5a,b]

The *p*H-dependent Reactions.—A minimum of four runs with varying initial boronic acid concentration were carried out in 25% ethanol with each

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[1] Preceding paper in this series, H. G. Kuivila and L. E. Benjamin, THIS JOURNAL, **77**, 4834 (1955).

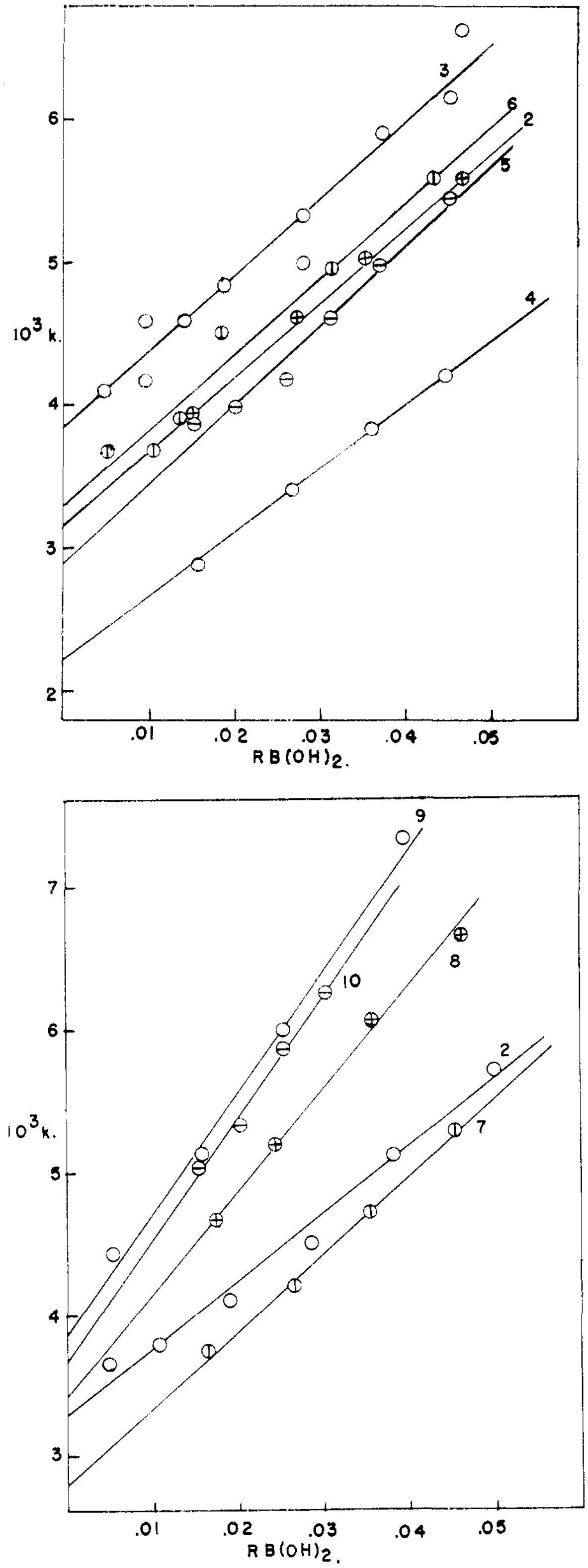
[2] Substantial support of this work by the Office of Naval Research is gratefully acknowledged.

[3] Taken in part from the senior thesis of A. G. Armour, June, 1955. Presented in part at the 130th Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956.

[4] For example the iron salt catalyzed reaction between benzene and hydrogen peroxide produces a complex mixture of products including phenol and other products of further oxidation (A. Kraus, *Roczniki Chem.*, **27**, 9 (1953); *C. A.*, **48**, 5624 (1954)).

[5] (a) H. G. Kuivila, THIS JOURNAL, **76**, 870 (1954); (b) H. G. Kuivila, *ibid.*, **77**, 4014 (1955); H. G. Kuivila and R. A. Wiles, *ibid.*, **77**, 4830 (1955); (c) H. G. Kuivila, paper presented at the 130th Meeting of the American Chemical Society, Atlantic City, N. J., September 20, 1956, Abstracts p. 58-O.

[6] The structure III for the intermediate is preferred over a conventional conjugate base of II (*e.g.*, $\mathrm{Ph{-}\underset{\substack{|\\ OOH}}{B}{-}O^-}$, VIII). The path III → IV → V appears to be a more probable one in aqueous solution than one proceeding from VIII to PhOB=O with loss of a hydroxide ion. Further evidence for III comes from the effects of *ortho* chloro and methyl groups on the acidity of benzeneboronic acid. The acid-weakening effect of these groups has been interpreted as evidence for a quadricovalent anionic species $\mathrm{PhB^-(OH)_3}$ rather than the tercovalent species $\mathrm{PhB(OH)O^-}$; D. H. McDaniel and H. C. Brown, THIS JOURNAL, **77**, 3756 (1955).



Figs. 1 and 2.—Plots of second-order rate constants *vs.* initial benzeneboronic acid concentrations. Numbers correspond to those in Table I.

boronic acid in an acetate buffer at *p*H 5.45 with ionic strength adjusted to 0.02 with sodium perchlorate. A plot of the apparent rate constants thus obtained *versus* initial boronic acid concentration was then made. The intercept obtained by the method of least squares provided k_1, the rate constant for the reaction first order in boronic acid, and the slope provided the value of k_2, the rate constant for the reaction second order in boronic acid. These plots are shown in Figs. 1 and 2, and the rate constants are listed in Table I.

It remains to demonstrate that the uncatalyzed reaction makes no significant contribution to the rate constants obtained in this way. To do so two runs were made with each boronic acid at *p*H 5.90 with different initial boronic acid concentrations (usually 0.015 and 0.030 molar). It was shown in an earlier paper[5a] that the rate constants k_1 and k_2 increase linearly with hydroxide ion activity. As a result the over-all rate constant, $[k_1 + k_2\,(\mathrm{ArB(OH)_2})]_0$, at *p*H 5.90 can be computed from the values obtained at *p*H 5.42. When this was done the observed and computed values agreed within 5%. If the reaction characterized by k_u were making a significant contribution to the rate at *p*H 5.42, the absolute magnitude of this contribution would be the same at *p*H 5.90, but this would constitute a smaller fraction of the total rate constant. As a result the observed rate constant would be smaller than the calculated one. Since this was not the case it can be concluded that only the two *p*H dependent reactions were important in this range. (The values of k_u obtained in this work cannot be used in this case because they were obtained in aqueous solution, whereas k_1 and k_2 were obtained in 25% aqueous ethanol. In this solvent rates are about a tenth as fast as in water at the same *p*H.)

The values of k_1 and k_2 show very little variation. Hammett plots as shown in Fig. 2 have least squares slopes (ρ-values) of 0.071 for k_1 and 0.28 for k_2. This lack of dependence of over-all rate on the electron density at the carbon bearing the boron is undoubtedly an indication of complexity in the reaction. The concentration of IV at a given *p*H obviously will increase as the electron density on the boron decreases (positive ρ). On the other hand, ionic cleavage of the peroxide bond with departure of a hydroxide ion as well as migration of the aryl group to oxygen should be favored by high electron density (negative ρ). It seems clear that the formation of III and its subsequent transformation to products have essentially equal but opposite electronic demands.

In recent years it has become apparent that the Hammett equation does not correlate the rates of reactions involving electrophilic substitution in the benzene ring when the original σ-values are used.[7] The greatest deviation observed in the brominolysis of benzeneboronic acids is due to the *p*-methoxy group.[7c] In the present data this substituent appears to be "normal." Therefore it seems quite probable that carbon–oxygen bond for-

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[7] (a) J. D. Roberts, J. K. Sanford, F. L. J. Sixma, H. Cerfontain and R. Zagt, This Journal, **76**, 4525 (1954). (b) C. W. McGary, Jr., Y. Okamoto and H. C. Brown, *ibid.*, **77**, 3037 (1955). (c) H. G. Kuivila and A. R. Hendrickson, *ibid.*, **74**, 5068 (1952); H. G. Kuivila and L. E. Benjamin, *ibid.*, **77**, 4834 (1955). (d) See H. C. Brown and Y. Okamoto, *ibid.*, **79**, 1913 (1957), concerning sigma constants for aromatic electrophilic substitution.

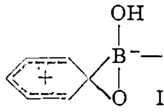
TABLE I

SUMMARY OF RATE CONSTANTS FOR THE REACTIONS OF SUBSTITUTED BENZENEBORONIC ACIDS WITH HYDROGEN PEROXIDE BY FIVE MECHANISMS[a]

Substituent	Number	σ	$10^3 \times k_1^{b,d}$	$k_2^{c,d}$	$10^3 \times k_u^{b}$	$100k_{\text{pe}}^{b,e}$	$100k_{\text{ph}}^{b,}$
p-CH_3O	1	−0.268	3.15	0.053	1.08	18.77	40.43
p-CH_3	2	−0.170	3.30	.0468	0.842	12.98	17.45
H	3	0	3.84	.055	.771	6.47	12.41
p-F	4	0.062	2.21	.0468	.718	4.64	8.75
m-CH_3O	5	.115	2.90	.0565	.891	4.96	9.55
p-Cl	6	.227	3.30	.054	.857	4.23	8.09
m-F	7	.337	2.81	.0545	.758	2.27	5.35
m-Cl	8	.373	3.43	.0730	.940	2.53	6.10
m-Br	9	.391	3.87	.086	1.06	2.63	6.33
m-NO_2	10	.710	3.69	.0851	0.739	0.827	2.13

[a] All data at 25.0°. [b] Units, l. mole^{-1} sec.$^{-1}$. [c] Units, l.^{2} mole^{-2} sec.$^{-1}$. [d] pH 5.42 ± 0.03, μ 0.02. [e] $HClO_4$, 4.77 M. [f] H_3PO_4, 5.29 M.

mation leading to a pentadienate intermediate IX is not energetically important in the slow step of the reaction. Thus, at this stage the available



IX

information can be embraced in a mechanism which assumes cleavage of the peroxide bond as the dominating feature of the slow step in each of these two reactions.

The pH-independent Reaction.—The rate constants for this reaction were obtained as follows: Rates (at 25°) were determined at several acidities in the pH range 1 to 3 with perchloric acid as the only electrolyte present. Values of specific rate constants for the ten boronic acids are assembled in Table II. It is noteworthy that the minimum values in all cases occur in a pH range probably no broader than one-half unit. The lowest value observed was taken as k_u, the specific rate constant for the pH-independent reaction, and is repeated in Table I.

The plot of these values *versus* sigma in Fig. 3 with slope −0.044 reveals a lack of dependence on substituent. In terms of the mechanisms under discussion this means that the electronic effects on equilibrium 1 and k_u balance each other almost exactly. The equilibrium must be shifted to the right by electron withdrawal from boron. Subsequently a proton must add to the hydroxyl oxygen of the peroxide group, the peroxide bond must be ionized to give IV and the aryl group must migrate to give V. All of these steps will be retarded by electron-withdrawing substituents in the benzene ring. Regardless of which is rate determining or whether two or more are simultaneous, the net result is a very nearly exact counterbalancing of the electronic effect on the equilibrium by that on the rate-determining step.

The Phosphoric and Perchloric Acid Catalyzed Reactions.—Before discussing our results on these reactions, an error made in an earlier paper[5b] should be corrected. It was reported that the rate constants for the reaction in perchloric acid solutions were correlated by the product $(a_{\mathrm{H_2O}})(a_{\mathrm{HClO_4}})$. However, the activities used for perchloric acid were those defined by the product $m\gamma_\pm$, where $\gamma_\pm$ is the mean ionic activity coefficient[8] and not activities of molecular perchloric acid. Since $m\gamma_\pm = (a_{\mathrm{HClO_4}})^{1/2}$, the rate constants in perchloric acid are actually proportional to $(a_{\mathrm{H_2O}})(a_{\mathrm{HClO_4}})^{1/2}$. A similar situation exists for the sulfuric acid data where $m\gamma_\pm = {}^1/_4\,(a_{\mathrm{H_2SO_4}})^{1/3}$. As a result the rate constants in this medium are actually proportional to $(a_{\mathrm{H_2O}}\cdot a_{\mathrm{H_2SO_4}})^{1/3}$. The activities for phosphoric acid were correct as used.

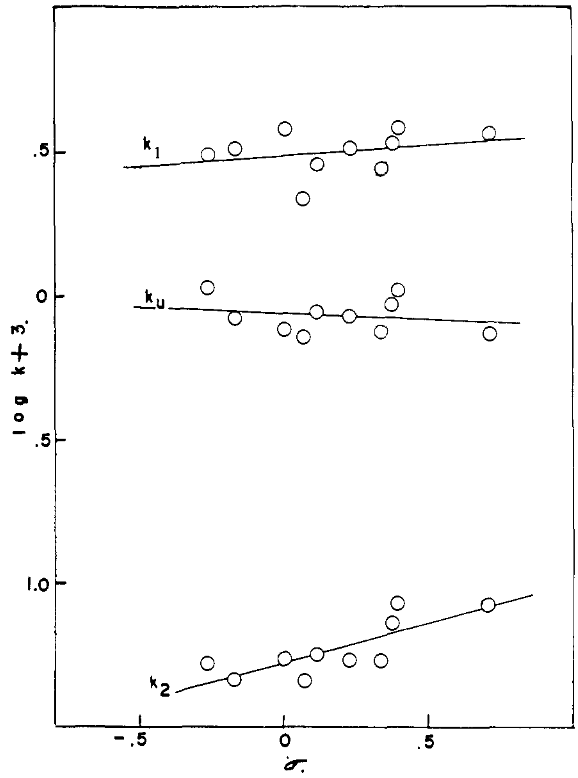


Fig. 3.—Hammett plots for the pH independent reaction (k_u) and for the pH dependent reactions first order (k_1) and second order (k_2) in boronic acid. Order of points from left to right follows the order 1–10 in Table I.

Each of the three acids still shows a different correlation of rate with acidity but the earlier discus-

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[8] This error was kindly pointed out by Dr. F. A. Long who discovered it in another paper (H. G. Kuivila, *J. Phys. Chem.*, **59**, 1028 (1955)) in which the same activities were used.

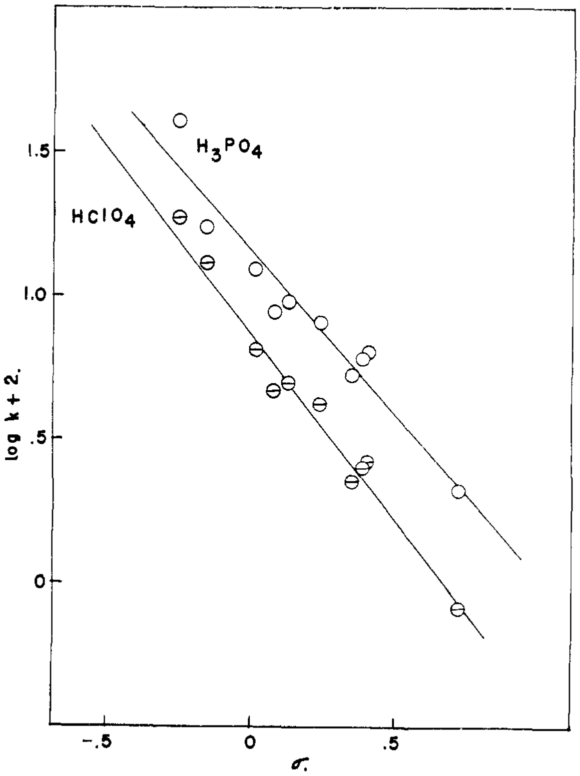

Fig. 4.—Hammett plots for the perchloric and phosphoric acid catalyzed reactions. Order of points from left to right follows the order 1–10 in Table I.

sion concerning perchloric acid catalysis is invalid.

TABLE II

SUMMARY OF RATE CONSTANTS USED TO DETERMINE VALUES FOR THE UNCATALYZED REACTION BETWEEN SUBSTITUTED BENZENEBORONIC ACIDS AND HYDROGEN PEROXIDE AT 25.0°

Substituent	pH	10^3k, l. mole^{-1} sec.$^{-1}$	Substituent	pH	10^3k, l. mole^{-1}, sec.$^{-1}$
p-CH$_3$O	3.04	1.27	p-Cl	2.99	0.883
	2.54	1.08		2.46	.874
	1.95	1.12		1.93	.857
p-CH$_3$	3.02	0.923	m-F	2.93	.827
	2.48	.842		2.45	.764
	1.95	.893		1.96	.758
H	2.62	.781	m-Cl	2.90	1.05
	2.32	.771		2.53	0.967
	2.15	.773		1.98	.940
	2.00	.793		1.48	.973
p-F	2.97	.778	m-Br	3.00	1.14
	2.51	.718		2.53	1.07
	1.97	.729		2.00	1.06
m-CH$_3$O	3.01	.973	m-NO$_2$	3.04	0.915
	2.51	.895		2.52	.819
	1.99	.891		2.03	.739
				1.49	.795
				0.95	.854

In the present work kinetic runs were carried out in 5.29 *M* phosphoric acid. At this concentration the uncatalyzed reaction makes a small contribution to the over-all rate. Consequently a correction for this was made on the assumption that this rate constant was not altered by the change in medium. In this way rate constants for the phosphoric acid catalyzed reaction were obtained from at least two runs for each boronic acid. Mean values are listed in Table I under k_{ph}. The Hammett plot from these data in Fig. 4 has a slope of −1.12 as determined by the method of least squares. Thus electron release by the substituent in the benzene ring is the dominating factor in determining the over-all reaction rate.

Runs also were carried out in 4.77 *M* perchloric acid. The data thus obtained were treated similarly and are gathered under k_{pe} in Table I. A Hammett plot, Fig. 4, has slope of −1.27 as determined by the method of least squares.

There appears to be only a random scatter of points about the least squares line in each of these two cases. It can therefore be concluded that electromeric electron release is not brought into play to any significant extent in the transition state of the slow step; *i.e.*, it has little of the pentadienate character of a structure such as IX.

It is interesting that under the conditions imposed these two reactions have very nearly the same electronic requirements as reflected in the similar ρ-values.

DURHAM, N. H.