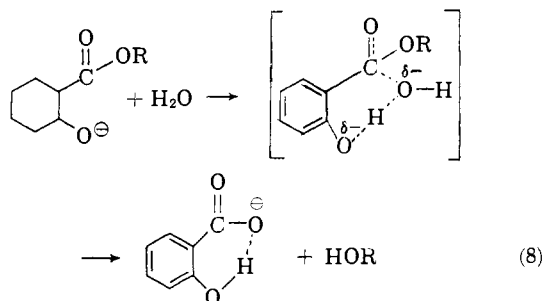


droxide ion with an ester, it would appear in the reaction of other nucleophiles with that ester. Since the special effect of the *o*-hydroxyl group does not appear in the latter reactions, it must be concluded that it also does not operate in the former reaction and further that the former reaction must be interpreted as the reaction of water with the ionized form of the ester.

If one interprets the pH-independent reaction in the alkaline region in terms of the reaction of water with the ionized form of the ester, the question may be raised as to the reason for the facile reaction of this species. The most straightforward explanation is that the phenoxide ion may act as an intramolecular general basic catalyst for the reaction of water with the ester group, as suggested above. The mechanism may be depicted as in eq. 8, or alternatively as the corresponding mechanism



in which the internal base removes a proton from the addition compound of water and the ionized ester, as discussed by Jencks and Carriuolo for general basic catalysis.³⁷ It appears, however, that in this instance one

can rule out those mechanisms which are kinetically general basic catalysis, but which are mechanistically general acid-hydroxide ion reactions.³⁷

Previous results in the literature concerning catalysis by neighboring hydroxyl groups can all be interpreted according to the above mechanism.⁴⁻⁹ Bruice and Fife⁶ considered eq. 8 as the mechanism for the effect of a neighboring hydroxyl group, but discarded this mechanism on the grounds of an argument involving deuterium oxide solvent isotope effects.³⁸ The deuterium oxide isotope effects in our hands are compatible with both possible mechanisms of general acid-specific hydroxide-catalyzed hydrolysis and general base-catalyzed hydrolysis (see above).

It is not mandatory, of course, that all examples of neighboring hydroxyl group catalysis occur by the same mechanism. Some may operate *via* eq. 8 involving general basic catalysis by the alkoxide ion while others may operate *via* general acidic catalysis by the un-ionized hydroxyl group. However, since the hydrolysis of salicylate esters, which when calculated as the hydroxide ion reaction of the un-ionized ester has the most significant neighboring hydroxyl group catalysis, appears to involve the phenoxide ion and not the phenolic group, it would appear that the other examples of neighboring hydroxyl group participation should be re-examined in this light.

(37) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **83**, 1743 (1961).

(38) The equation of Bruice and Fife⁶ for calculating the isotope effect does not agree with eq. 5, but a revised equation from Professor T. C. Bruice (personal communication) does agree with eq. 5. When their isotopic data are calculated according to eq. 5, the resulting isotope effect does not support general base catalysis. Their isotopic data are, however, in accord with nucleophilic catalysis by hydroxide ion.

COMMUNICATIONS TO THE EDITOR

Electrophilic Substitution. Electronic Effects in SE2 Reactions

Sir:

There are many reactions in which a carbon-Y bond is broken by the attack of an electrophilic group or atom where the usual result is retention of configuration at the center of displacement. Examples are: base catalyzed H-D exchange in carbon acids,¹ electrophilic cleavage of organometal bonds,² oxidation of organoboron compounds with hydrogen peroxide,³ and Beckmann, Lossen, and hydroperoxide rearrangements.⁴ All these reactions can be represented⁵ by

(1) D. J. Cram, D. A. Scott, and W. D. Nielsen, *J. Am. Chem. Soc.*, **83**, 3696 (1961).

(2) (a) S. Winstein, T. G. Traylor, and C. S. Garner, *ibid.*, **77**, 3741 (1955); (b) H. B. Charman, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2523 (1959); (c) F. R. Jensen and L. H. Gale, *J. Am. Chem. Soc.*, **81**, 1261 (1959).

(3) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, p. 67.

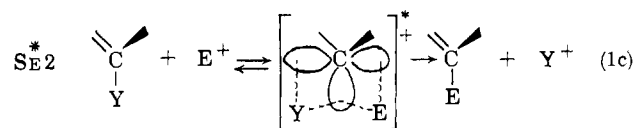
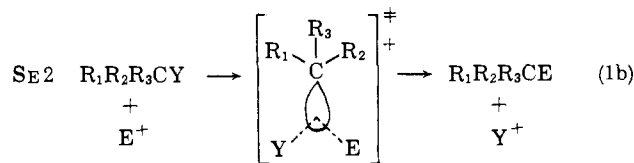
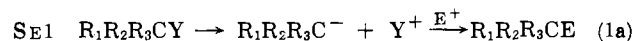
(4) See, e.g., J. A. Berson and S. Suzuki, *J. Am. Chem. Soc.*, **81**, 4088 (1959) for references.

(5) The term⁶ SE1 refers to dissociations into ions or ion pairs; SE2 is conceived to have a transition state in which two electrophiles are attached to the carbon orbital without appreciable rehybridization or development of charge on carbon. In this respect it is analogous to the SN2 mechanism. The term S^{*}E2, representing what is usually called aromatic substitution, is introduced to specify an intermediate of the Pfeifer-Wizinger⁷ type (*i.e.*, σ -complex) denoted by * instead of ‡ to differentiate an intermediate from a transition state. This terminology allows for SE1 and SE2 aromatic substitution, the latter demonstrated herein, and for the nonaromatic Pfeifer-Wizinger intermediates which are required to explain some accelerated electrophilic reactions at vinyl and cyclopropyl groups.^{3d}

(6) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 244 (1935).

(7) P. Pfeifer and R. Wizinger, *Ann.*, **461**, 132 (1928).

mechanisms intermediate between the limiting cases 1a, 1b, and 1c.



These formulations represent rearrangement to an electron-deficient E if an E-Y bond is present in the reactant and typical electrophilic substitutions otherwise. When a ligand connects E with Y in the transition state

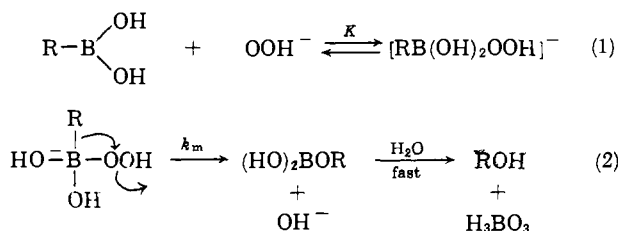
(the mechanism is generally

called SEi. However, since this process differs so little from SE2 we are including it in the designation SE2.

The electronic effects can be predicted for such formulations. Electron supply by R will accelerate

SE2 and S*E2 and retard SE1 reactions.⁶ Such effects have been amply demonstrated for mechanisms near SE1¹ and S*E2.⁸ However, there is wide disagreement concerning effects of structure on rates of reactions which are reported to be SE2 (or SEi).⁹

We have therefore sought a type of carbon-metal bond sufficiently polar ($\bar{C}-\bar{Y}$) that the SE2 reaction could be studied over a full range of structure without contribution from S*E2 while still avoiding the SE1 mechanism. Such a system is shown in eq. 2.



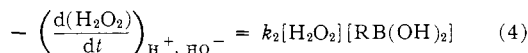
This reaction is not accompanied by protolysis and it occurs with retention of configuration in water. The oxidation is therefore not an SE1 reaction. Kuivila and Armour^{10a} have inferred from kinetic studies that the reaction of arylboronic acids with hydrogen peroxide is not S*E2. Our work confirms their proposal that no π -participation is involved.

Reaction 2, whose rate k_m reflects the effect of structure on this "SE2" process, is preceded by a rapidly established equilibrium.¹¹ Therefore, K must be estimated in order to convert k_{obsd} into relative k_m . We have measured the acidities of our subject boronic acids (eq. 3) and, with the reasonable assumption¹²



that $K \propto K_a$, have obtained relative k_m from the relation $k_m^{\text{rel}} = k_{\text{observed}}/K_a$.

The reactions of alkylboronic acids with hydrogen peroxide are clearly second order over the observed H_0 range (-1.5 to 6).



The pH-rate profile for *n*-butylboronic acid is like that published for phenylboronic acid,^{10b} exhibiting both specific acid and base catalysis and a rate minimum at pH ~ 3 . Unlike arylboronic acids it has no term that is second order in alkylboronic acid, and the rate minimum is much deeper.

Typical rate data for both acid (k_2') and base (k_2) catalyzed reactions are shown in Table I along with the acidities and relative values of k_m which appear as k_2/K_a or k_2'/K_a .

The first striking result in Table I is that *t*-butylboronic acid is a stronger acid than *n*-butylboronic acid. This is the reverse of the order expected from electronic

(8) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt-Dryden, New York, N. Y., 1959, Chapter 11.

(9) (a) C. S. Marvel and H. O. Calvery, *J. Am. Chem. Soc.*, **45**, 820 (1923); (b) S. Winstein and T. G. Traylor, *ibid.*, **77**, 3747 (1955); (c) M. M. Kreevoy and R. L. Hansen, *ibid.*, **83**, 626 (1961); (d) R. E. Dessy, G. F. Reynolds, and J. Y. Kim, *ibid.*, **81**, 2683 (1959); (e) G. A. Russell and K. L. Nagpal, *Tetrahedron Letters*, 421 (1961).

(10) (a) H. G. Kuivila and A. G. Armour, *J. Am. Chem. Soc.*, **79**, 5659 (1957); (b) H. G. Kuivila, *ibid.*, **77**, 4014 (1955).

(11) J. O. Edwards, *ibid.*, **75**, 6154 (1953).

(12) Some justification of this assumption is available. J. H. Polevy¹³ has used literature rate^{10b} and acidity¹⁴ data for arylboronic acids to plot $\log(k_{\text{obsd}}/K_a)$ vs. σ obtaining an excellent line with $\rho = -2.03$. Also, we have observed that relative over-all rates of reaction of cyclohexylboronic acid and *n*-butylboronic acid are the same with hydrogen peroxide or *t*-butylhydroperoxide.

(13) J. H. Polevy, Ph.D. Thesis, University of New Hampshire, 1960, p. 63.

(14) D. L. Yabroff, G. E. K. Branch, and J. J. Almquist, *J. Am. Chem. Soc.*, **55**, 2940 (1933).

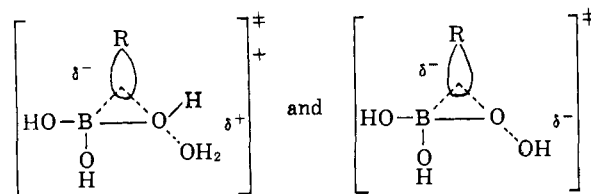
TABLE I
RATES OF REACTIONS OF BORONIC ACIDS WITH HYDROGEN PEROXIDE AND RELATIVE RATES OF MIGRATION FROM BORON TO OXYGEN

R	k_2 , 1./mole sec., $H_0 = 5.23^a$	k_2' , 1./mole sec., $H_0 = 1.48^b$	$10^{10}K_a$	k_2/K_a (rela- tive)	k_2'/K_a (rela- tive)
CH ₃ -	0.000127	0.00024	2.52 ^d	(1)	(1)
<i>n</i> -Bu-	.00480	.00724	1.83	52	42
<i>sec</i> -Bu-	.0233	...	2.5	185	...
<i>t</i> -Bu-	.0718	.094	4.32	330	229
1-Bicycloheptyl	.11	...	3.05	680	...
C ₆ H ₅ -	.016 ^c	.0319 ^c	138 ^d	2.3	2.4
Vinyl	.0068	...	32	4.2	...
C ₆ H ₅ CH ₂ -	.0875	...	73	24	...

^a A buffer 0.158 *M* in sodium acetate and 0.042 *M* in acetic acid. ^b 3.77 *M* perchloric acid. ^c Data of Kuivila. Other kinetics were determined by his method⁶. See ref. 10b. ^d Determined by the method of Yabroff, Branch, and Almquist. See ref. 14. ^e All data at 25.0°.

considerations and therefore implies that less steric compression is experienced in tetrahedral boron [RB(OH)₃⁻] than in trigonal boron [RB(OH)₂]. Consequently, the observed rate sequence, bridgehead > 3° > 2° > 1°, is not due to relief of steric strain as was suggested for a similar rate order in the Baeyer-Villiger reaction.^{15a,16} Both SE1 and S*E2 mechanisms are excluded by the extreme sluggishness of the cleavage of aryl-, vinyl-, and cyclopropyl-boron bonds. Thus, even in this very polar carbon-metal bond the R group does not migrate as a "free" R⁻ as has been suggested.¹⁶ The third suggestion for this rate sequence in the Baeyer-Villiger reaction, *i.e.*, development of carbonium ion character in the migrating group,^{15b} is considered very unlikely in the present reaction because the group departs from a negatively charged boron atom.

The transition states for the acid and base catalyzed reactions can therefore be formulated for all structures:



in R. This is the first instance of electrophilic substitution or migration of R to an electron-deficient center in which no change in mechanism occurs when R is varied. This reaction is therefore considered to be a good model for an SE2 reaction (including SEi) and the order observed, *t*-Bu > *sec*-Bu > *n*-Bu > vinyl \sim phenyl > Me, is suggested to be the electronic sequence for the SE2 process.¹⁷

Recently, reports of the opposite sequence, 1° > 2° > 3°, for electrophilic substitution have appeared.^{9c-e} In these cases, additional factors such as changes in the leaving group,^{9d} interfering side reactions, and stringent steric requirements^{9e} make the extrapolation of their results to other electrophilic substitutions tenuous.

We, therefore, conclude that purely SE2 (or SEi) reactions will show the rate sequence 3° > 2° > 1° > C₆H₅, vinyl, cyclopropyl \geq Me and that the extent of involvement of the S*E2 mechanism can be measured by the observed position of phenyl, vinyl, and cyclopropyl groups in this series.

(15) (a) M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *ibid.*, **80**, 6393 (1958); (b) W. D. Emmons and G. B. Lucas, *ibid.*, **77**, 2287 (1955).

(16) S. L. Friess and N. Farnham, *ibid.*, **72**, 5518 (1950).

(17) The structural effects in this reaction are small. We shall demonstrate a similar order with large effects on C-B bond cleavage rates in the following communication.

Acknowledgment.—We are grateful to Professor Henry G. Kuivila for enlightening discussions and to the National Science Foundation for financial support (Grant GP-242).

(18) International Christian University, Mitaka, Tokyo, Japan.

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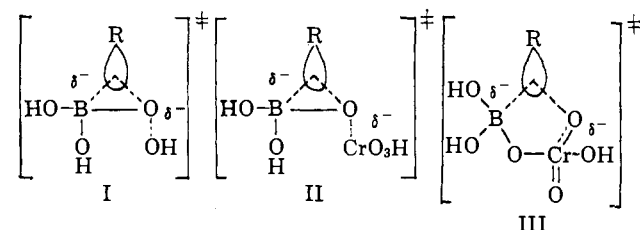
HIROSHI MINATO¹⁸
JUDITH C. WARE
T. G. TRAYLOR

RECEIVED AUGUST 16, 1963

Electrophilic Substitution. Chromic Acid Cleavage of Carbon-Boron Bonds

Sir:

In the previous communication¹ we indicated the effect of structure in R on the stability of the three-center transition state I.



The general behavior of chromic acid oxidation of alcohols^{2a-f} caused us to believe that chromic acid

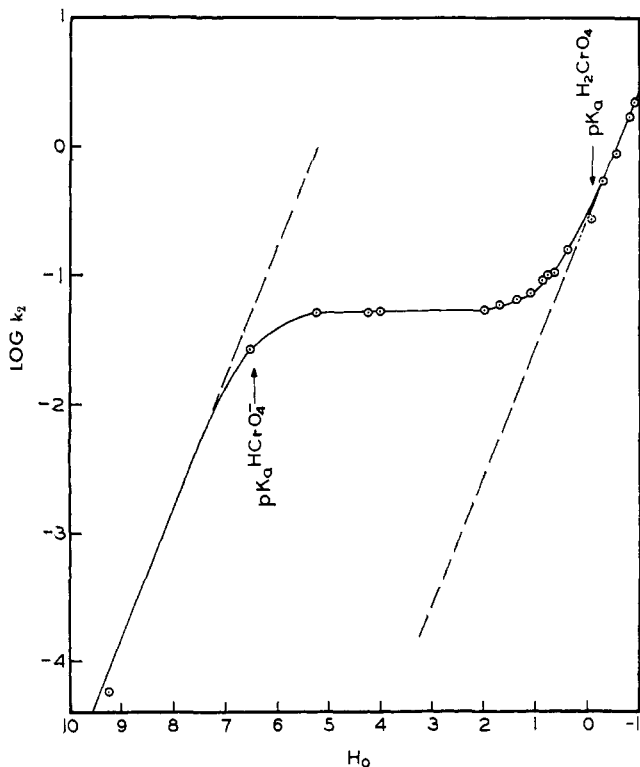


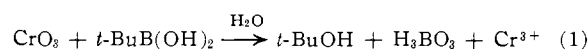
Fig. 1.—Plot of $\log k_2$ at 30.0° vs. H_0 (or pH) for the rate expression $d[\text{Cr}^{\text{VI}}]/dt = k_2[t\text{-BuB}(\text{OH})_2][\text{Cr}^{\text{VI}}]$. Circles are experimental points. The solid line represents eq. 3 and the dashed lines indicate unit slope. The H_0 values for the perchloric acid solutions were taken from Long and Paul.⁶

(1) H. Minato, J. C. Ware, and T. G. Traylor, *J. Am. Chem. Soc.*, **85**, 3024 (1963).

(2) (a) F. H. Westheimer, *Chem. Rev.*, **45**, 419 (1949); (b) F. Holloway, M. Cohen, and F. H. Westheimer, *J. Am. Chem. Soc.*, **73**, 65 (1951); (c) G. T. E. Graham and F. H. Westheimer, *ibid.*, **80**, 3030 (1958); (d) R. Brownell, A. Leo, Y. W. Chang, and F. H. Westheimer, *ibid.*, **82**, 406 (1960); (e) J. Roček and F. H. Westheimer, *ibid.*, **84**, 2241 (1962); (f) Y. W. Chang and F. H. Westheimer, *ibid.*, **82**, 1401 (1960); (g) H. G. Kuivila and W. J. Becker, *ibid.*, **74**, 5329 (1952); (h) J. Roček and J. Krupicka, *Chem. Listy*, **52**, 1735 (1958); (i) F. H. Westheimer and A. Novick, *J. Chem. Phys.*, **11**, 506 (1943).

cleavage of boronic acids might attain the five-membered transition state III rather than the three-membered II. Structural effects on transition states such as I (and we imply II) are not strongly dependent on the nature of the leaving group.^{1,3} Therefore, from the effects of the structure of R on the rate of chromic acid cleavage of boronic acids, we might distinguish between II and III. This is possible only if one mechanism is operating. However, several species of chromic acid in aqueous solution could bring about oxidation. Among the species H_3CrO_4^+ , H_2CrO_4 , HCrO_4^- , CrO_4^{2-} , $\text{H}_2\text{Cr}_2\text{O}_7$, HCr_2O_7^- , and $\text{Cr}_2\text{O}_7^{2-}$, only the first two have been definitely associated with oxidation in dilute solutions and these two usually are in competition. This competition of mechanisms greatly complicates studies of structural effects.⁴

We wish to report an oxidation by HCrO_4^- in a reaction which promises important application both in synthesis and in mechanism studies. This finding also points the way to studies of reactions of the remaining Cr^{VI} species. The reaction of chromic acid with *t*-butylboronic acid



is first order in each reagent over a wide range of pH (-1 to 9) and has a very small salt effect (5% increase at $1.0 M \text{NaClO}_4$) on rate.

$$-\frac{d[\text{Cr}^{\text{VI}}]}{dt} = k_2[\text{RB}(\text{OH})_2][\text{Cr}^{\text{VI}}] \quad (2)$$

The pH-rate profile is shown in Fig. 1.^{5,6}

The shape of this curve has three important implications. First, the oxidation of boronic acids at pH 3–7 where alcohols are relatively stable to Cr^{VI} makes possible the *synthesis* of alcohols using chromic acid. Thus, oxidation with chromic acid at pH *ca.* 5 will produce alcohols⁷ and at higher acidities, *e.g.*, $2 N$ acid, will produce ketones.⁸ Further, this reagent makes possible selective alkylborane cleavage because its reaction rate is much more sensitive to structure than that of hydrogen peroxide.¹ Thus, the k_2 values for various R are *t*-Bu, 7.5×10^{-2} ; Et, 6.6×10^{-4} ; Me, 2.4×10^{-7} l./mole sec. in $0.114 M$ perchloric acid at 30.0° .

Secondly, the pH-rate profile is unusually informative about the mechanism of the reaction. This curve is accurately described by the equation

$$[\text{Cr}^{\text{VI}}] \times k = 0.054(\text{HCrO}_4^-) + 0.36(\text{H}_2\text{CrO}_4) + 0.32(\text{H}_2\text{CrO}_4)h_0 \quad (3)$$

using the recorded⁹ values of $K_{\text{H}_2\text{CrO}_4} = 1.21$ and $K_{\text{HCrO}_4^-} = 3.2 \times 10^{-7}$. (Dimeric species are precluded by the low Cr^{VI} concentrations.) Therefore the oxidants in this reaction are HCrO_4^- and H_3CrO_4^+ ; CrO_4^{2-} and H_2CrO_4 are relatively ineffective¹⁰ (*i.e.*, H_2CrO_4

(3) H. G. Kuivila, *J. Am. Chem. Soc.*, **77**, 4014 (1955).

(4) H. Kwart and P. S. Francis, *ibid.*, **77**, 4907 (1955).

(5) All rate data were obtained by the spectrophotometric method of Westheimer and Novick.²¹ Borate buffer was used at pH 9, phosphate at pH 6.5, and acetate at pH 4–5. At higher acidities perchloric acid was used. At pH 6.5, the reaction is pseudo first order ($\text{RB}(\text{OH})_2$ in excess) for about one-half life and then accelerates rather sharply. Similar acceleration was noted with other buffers (except borate) above pH 5.

(6) M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

(7) The chromic acid cleavage appears to proceed with the same stereochemistry and yield as the hydrogen peroxide cleavage (unpublished results).

(8) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

(9) J. T. Long and E. L. King, *ibid.*, **75**, 6180 (1953).

(10) This preference of boronic acids for the anions is seen in other cases. The ^{11}B n.m.r. of ethylboronic acid¹¹ indicates it to be entirely trigonal¹² in water (*i.e.*, not complexed with water) and tetrahedral in $0.8 N$ sodium hydroxide.

(11) We are indebted to H. Landesman, J. Ditter, and T. Burns, of the National Engineering Science Co., Pasadena, California, who very generously determined the ^{11}B chemical shifts.

(12) T. P. Onak, H. Landesman, R. E. Williams, and I. Shapiro, *J. Phys. Chem.*, **63**, 1533 (1959).