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Electrophilic Displacement Reactions. XII. Substituent Effects in the Protodeboronation of Areneboronic Acids[1-3]

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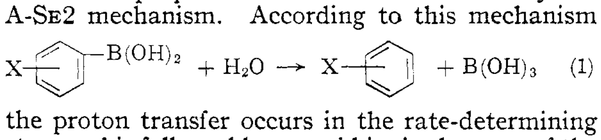
Kinetic studies on the hydrolysis of nine areneboronic acids in aqueous sulfuric and phosphoric acids are described. Dependence of rate on acidity has been examined in each case, and activation parameters and solvent hydrogen isotope effects have been determined in certain cases. Conventional H_0 plots reveal the presence of two kinetically distinct regions separated by the H_0 range 5.0–5.5. The behavior of activation parameters and solvent isotope effects bear out this dichotomy. Consideration of these facts, coupled with the effect of substituents on reactivity, leads to an interpretation of the data in terms of the existence of at least two mechanisms for the reaction.

In the preceding papers[1a,4] it was established that the hydrolysis of *p*-methoxybenzeneboronic acid (eq. 1, X = *p*-OCH_3) and of 2,6-dimethoxybenzeneboronic acid are subject to general acid catalysis, and it was proposed that the reaction occurs by the A-SE2 mechanism. According to this mechanism



the proton transfer occurs in the rate-determining step, and is followed by a rapid ionic cleavage of the boron–carbon bond. Because of its intrinsic interest and the likelihood that it would provide further insights into the mechanism, a kinetic study of the hydrolysis of eight additional areneboronic acids in aqueous sulfuric acid has been made. For seven of these substrates (X = *p*-CH_2, *p*-F, H, *p*-Br, *m*-F, *m*-Cl and *m*-NO_2) the dependence of rate on the acidity function, H_0, has been determined, and for four (X = *p*-CH_3, *p*-F, H and *m*-F) the dependence on temperature. The solvent hydrogen isotope effect has been measured for four of the substrates (X = *p*-CH_3, *p*-OCH_3, *p*-F and *m*-F). Rate measurements for the hydrolysis of *p*-tolueneboronic acid in aqueous phosphoric acid at two temperatures have also been made.

Experimental

Reagents.—The preparation and properties of all but one of the areneboronic acids have been referred to previously.[5]

***m*-Trifluoromethylbenzeneboronic anhydride** was prepared by the method of Bean and Johnson[6] in 30% yield; m.p. sinter 60°, m. 160–162° (acid), 160–162° (anhydride).

Anal. Calcd. for $C_7H_4BF_3O$: C, 48.91; H, 2.35; neut. equiv., 171.9. Found: C, 49.03; H, 2.59; neut. equiv., 171.8.

The preparation of deuteriosulfuric acid has been described.[1a]

All of the other reagents were of the best grade available commercially.

Kinetic Procedure.—Since each of the boronic acids has an ultraviolet absorption spectrum substantially different from that of its hydrolysis product, the concentration of unreacted boronic acid could be determined spectrophotometrically, a Beckman DU spectrophotometer being used. The absorptivities of the boronic acids and their hydrolysis products at the wave lengths used for analysis are listed in Table I. In all cases but one (X = *m*-NO_2) the absorptivities of boronic acids are much greater than those of the hydrolysis products. Therefore the absorbance of the kinetic sample could be taken as a direct measure of boronic acid concentration, C, of the sample. For X = *m*-NO_2 the difference is small; therefore absorbances were converted to concentrations using the relationship $C = (\text{absorbance} - 2210 C_0)/(4250-2210)$, where C_0 is the initial concentration of the substrate. Initial concentrations of boronic acid were in the range 10^{-3}–10^{-4} M. The procedure was essentially that described previously.[1a]

TABLE I

SPECTRAL DATA USED FOR ANALYSIS OF KINETICS SOLUTIONS

X	Wave length, mμ	Absorptivity[a] $XC_6H_4B(OH)_2$	Absorptivity[a] XC_6H_5
H	218	8450	55[b]
m-NO_2	228	4250	2210
p-Br	232	13700	50
m-F	218	7300	25
p-F	218	7380	25
p-CH_3	226	10800	30
p-OCH_3	236	28200[c]	
	238	12000[d]	70[d]
m-Cl	228	3000	63
m-CF_3	220	5200	40

[a] In 10–14% sulfuric acid unless otherwise stated. [b] In 75% sulfuric acid. [c] In water. [d] In 1% formic acid.

Results and Discussion

A. Kinetic Order of the Reaction.—Except for the one run mentioned below, all of the rate experiments reported here showed first-order kinetics; that is, the data fit the rate equation

$$kt = 2.303 \log C + \text{constant}$$

where k is the pseudo-first-order rate coefficient and C is the concentration of areneboronic acid at time t. Figure 1 shows a typical rate plot for *m*-nitrobenzeneboronic acid and Tables II and III list experimental values of log k obtained in aqueous sulfuric and phosphoric acids, respectively.

B. Course of the Reaction.—In aqueous sulfuric acid, especially in the more concentrated solutions, sulfonation is a possible side reaction. Gold and Satchell[7] have reported that at 25° the pseudo-first-order rate coefficient for the sulfonation of benzene in 77.5% H_2SO_4 is 2.6×10^{-7} sec.$^{-1}$.

(1) (a) Preceding paper in this series: H. G. Kuivila and K. V. Nahabedian, *J. Am. Chem. Soc.*, **83**, 2164 (1961). (b) Presented in part at the 12th Meeting of the American Chemical Society, Chicago, Ill., September, 1958, Abstracts, p. 37p.

(2) Based on the doctoral dissertation of K. V. Nahabedian, June, 1959.

(3) This research was supported by the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command, under Contract No. AF 49 (638)-312. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(4) H. G. Kuivila and K. V. Nahabedian, *J. Am. Chem. Soc.*, **83**, 2159 (1961).

(5) (a) H. G. Kuivila and E. K. Easterbrook, *ibid.*, **73**, 4629 (1951); (b) H. G. Kuivila and A. R. Hendrickson, *ibid.*, **74**, 5068 (1952); H. G. Kuivila and A. G. Armour, *ibid.*, **79**, 5659 (1957).

(6) F. R. Bean and J. R. Johnson, *ibid.*, **54**, 4415 (1932).

(7) V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 1635 (1956).

Table II

Pseudo-first-order Rate Coefficients, k, for Aqueous Sulfuric Acid

Run	Temp., °C.	% H_2SO_4	$-H_0$	$\log k + 7$
		X = H (I)		
I_s-21	60	71.1	5.65	3.842
22		70.9	5.64	3.864
23		60.0	4.14	2.558
24		60.0	4.14	2.558
25		67.4	5.15	2.399
26		67.5	5.16	3.407
27		74.4	6.11	4.434
28		74.6	6.13	4.427
29		62.6	4.46	2.849
30		62.6	4.46	2.843
31		54.7	3.59	2.076
32		54.4	3.57	2.046
33		49.8	3.15	1.657
34		50.3	3.19	1.674
35		44.8	2.72	1.383
36		44.8	2.72	1.355
39		46.6	2.87	1.466
40		45.3	2.76	1.303
41		42.9	2.56	1.123
42		41.0	2.40	0.967
43	25	74.8	6.34	3.067
44		72.4	6.00	2.674
45		70.3	5.70	2.316
46	40	75.0	6.28	3.632
47		72.6	5.96	3.310
48		70.8	5.72	3.014
		X = m-NO_2 (II)		
II_s- 3	60	92.1	8.30	2.783
4		91.6	8.26	2.772
5		89.3	8.04	2.601
6		89.4	8.05	2.601
7		97.0	8.86	3.138
8		96.7	8.83	3.162
9		88.5	7.97	2.515
10		88.5	7.97	2.508
11		83.0	7.37	1.887
12		82.7	7.33	1.874
13		78.8	6.74	1.458
14	60	78.5	6.69	1.423
15		73.7	6.00	0.839
16		73.6	5.99	0.883
		X = p-Br (III)		
III_s- 1	60	74.5	6.12	3.789
2		69.4	5.43	3.085
3		65.2	4.83	2.538
5		77.0	6.47	4.111
6		61.2	4.27	2.122
7		53.4	3.47	1.375
8		47.7	2.96	0.953
		X = m-F (IV)		
IV_s- 1	60	83.8	7.48	4.196
2		78.5	6.70	3.423
3		74.1	6.06	2.739
4		68.5	5.30	2.007
5		62.2	4.41	1.403
6		55.2	3.64	0.821
19		69.4	5.43	2.152
20		70.3	5.55	2.193
7	25	83.3	7.64	2.817
8		80.9	7.29	2.318
9		79.0	7.00	1.960
10	40	84.2	7.67	3.520
11		82.4	7.42	3.180
12		80.4	7.11	2.884
13	69.4	64.9	4.76	2.068
14		61.0	4.23	1.720
15		56.9	3.80	1.399
16	79.4	[illegible]5.4	4.78	2.499
17		[illegible]1.3	4.24	2.136
18		[illegible]7.4	3.83	1.821
		X = m-CF_3 (V)		
V_s- 6	60	[illegible]5.4	3.66	0.499
		X = p-F (VI)		
VI_s- 1	60	6[illegible].7	4.76	3.455
2		6[illegible].1	4.14	2.938
3		5[illegible].9	3.62	2.492
4		4[illegible].5	3.11	2.039
8	40	5[illegible].3	3.49	1.462
9		5[illegible].0	4.00	1.826
10		6[illegible].7	4.48	2.236
5	25	5[illegible].1	3.48	0.641
6		5[illegible].4	4.02	1.148
7		6[illegible].0	4.63	1.629
		X = p-CH_3 (VII)		
VII_s 1	60	5[illegible].5	3.67	3.641
2		4[illegible].6	3.13	3.100
3		4[illegible].7	2.38	2.363
4		2[illegible].6	1.53	1.455
8	40	4[illegible].9	2.55	1.612
9		4[illegible].8	2.98	2.042
10		5[illegible].9	3.45	2.574
5	25	4[illegible].1	2.57	0.923
6		4[illegible].3	3.02	1.419
7		5[illegible].5	3.52	1.916
		X = m-Cl (IX)		
IX_s- 1	60	59.3	4.05	1.094
2		62.9	4.51	1.411
3		66.3	4.99	1.686
4		69.9	5.50	2.075
5		74.5	6.11	2.748
6		79.9	6.91	3.523

Table III

Pseudo-first-order Rate Coefficients, k, for Hydrolysis of p-Tolueneboronic Acid in Aqueous Phosphoric Acid

Run	Temp., °C.	% H_3PO_4	$-H_0$	$\log k + 7$
VII_{Ph}-1	60	72.4	2.22	4.641
2		66.6	1.76	4.044
3		56.3	1.16	2.998
4		42.7	0.61	1.945
5	25	71.3	2.40	3.273
6		68.3	2.11	2.887
7		63.9	1.75	2.379
8		60.7	1.55	2.054
9		56.3	1.32	1.574
10		73.5	2.63	3.657
11		76.7	2.92	4.133

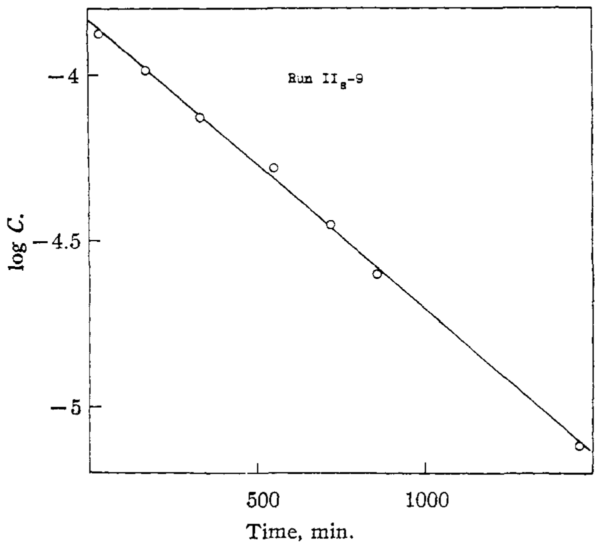


Fig. 1.—Rate plot for *m*-nitrobenzeneboronic acid; 60°, 97.0% H_2SO_4.

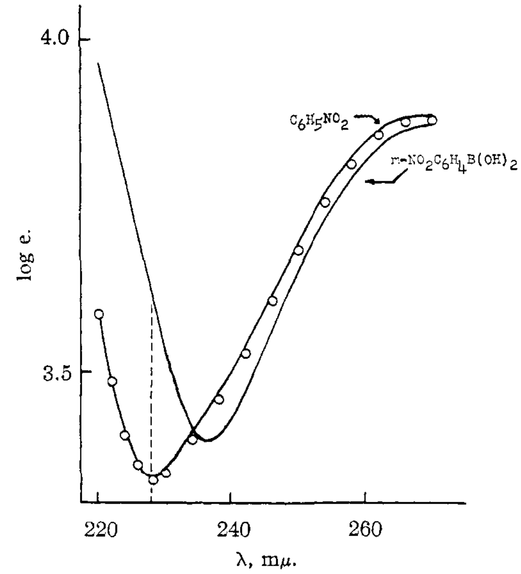


Fig. 2.—Absorption spectra of nitrobenzene and *m*-nitrobenzeneboronic acid. The dotted line is at 228 mμ.

The rate coefficient at 25° for the hydrolysis of benzeneboronic acid in 75% H_2SO_4 is 1.2×10^{-4} $sec.^{-1}$. Clearly, then, the sulfonation of benzene is at least 500 times slower than the hydrolysis of benzeneboronic acid, and, since the boronic acid group is deactivating ($\sigma_m = 0.006$, $\sigma_p = 0.454$),[8] sulfonation of benzeneboronic acid should be even slower. Indeed, the spectrum of a kinetic sample taken after twenty half-lives showed that the extent of sulfonation was less than 1%.

Sulfonation was found to interfere with the kinetics of hydrolysis in only one experiment: with *m*-fluorobenzeneboronic acid in 83.9% H_2SO_4 at 60° the absorbances of kinetic samples taken after a half-life began to level off and then, after two half-lives, began to increase. Because every position available for sulfonation in this boronic acid is *ortho* or *para* to the boronic acid group, or *meta* to the fluorine atom ($\sigma_m = 0.337$),[8] sulfonation of fluorobenzene, rather than the boronic acid, must be the side reaction. Hence the initial slope of a log *C versus* time plot was assumed to be a measure of the hydrolysis rate of *m*-fluorobenzeneboronic acid under the conditions of the experiment.

That the hydrolysis of the areneboronic acids in aqueous sulfuric acid media is quantitative is illustrated in Fig. 2, which shows the spectra of nitrobenzene and *m*-nitrobenzeneboronic acid. The circles represent the spectrum of a kinetic sample taken after essentially infinite time from a rate experiment in 97% H_2SO_4; the curve represents the expected spectrum for nitrobenzene.

Table I lists only one rate coefficient for *m*-(trifluoromethyl)-benzeneboronic acid determined in 55.4% H_2SO_4. Experiments at higher acidities showed erratic kinetics. Evolution of hydrogen fluoride was detected, and flasks containing the kinetic solutions became etched. Therefore the erratic kinetics were attributed to hydrolysis of the trifluoromethyl group in the substrate. With the one experiment reported, first-order kinetics was observed through 30% reaction, and the observed rate coefficient was assumed to be a measure of the hydrolysis rate of the boronic acid group in the substrate.

C. Dependence of Rate on Acidity.—Figures 3, 4 and 5 show representative plots of log *k versus* the acidity function, H_0.[9] Subject to the qualifications described and discussed below, these plots establish the correlation of rate by the acidity function. A similar correlation was found to obtain for the

TABLE IV
VALUES OF LOG *k versus* $-H_0$ SLOPES FOR AQUEOUS SULFURIC ACID

X	Temp., °C.	Acid region % H_2SO_4	log *k vs.* $-H_0$ slope
p-CH_3O	60	3–30	1.10
	40	20–30	1.15
	25	16–55	1.15
p-CH_3	60	29–56	1.03
	40	43–54	1.06
	25	43–54	1.05
p-F	60	50–65	0.86
	40	53–62	.85
	25	53–63	.86
H	60	41–75	0.90
	40	71–74	1.10
	25	70–74	1.16
p-Br	60	48–70	0.87
		70–84	1.0
m-F	79.4	57–65	0.71
	69.4	57–65	.69
	60	55–70	.72
		70–84	1.0
	40	80–84	1.14
	25	79–83	1.35
m-Cl	60	59–70	0.65
		70–80	1.0
m-NO_2	60	75–97	0.84

(8) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(9) The H_0 values for aqueous sulfuric and phosphoric acid solutions are for the appropriate temperatures and are taken from the data of A. I. Gelbshtein, G. G. Sheglova and A. I. Temkin, *Zhur. Neorg. Khim.*, **1**, 282 506 (1956).

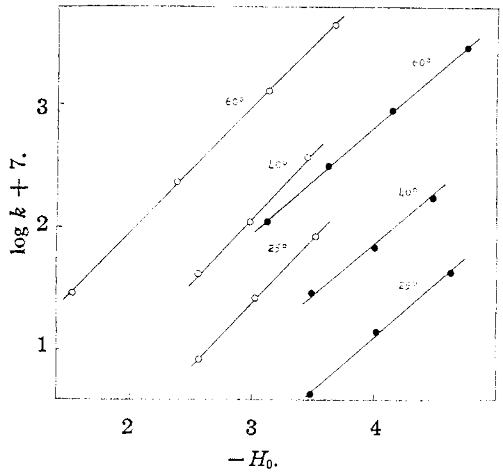


Fig. 3.—log k *vs.* $-H_0$ for sulfuric acid solutions of *p*-tolueneboronic (open circles) and *p*-fluorobenzeneboronic (solid circles) acids.

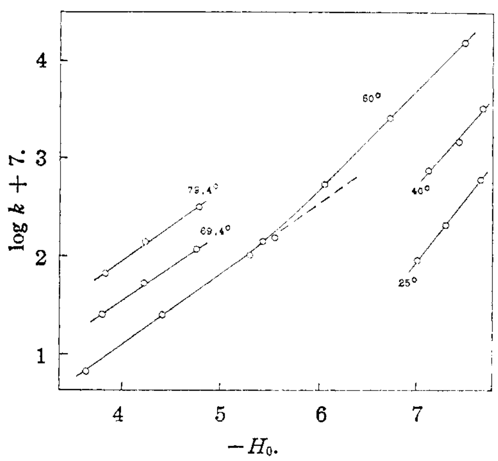


Fig. 4.—log k *vs.* $-H_0$ for sulfuric acid solutions of *m*-fluorobenzeneboronic acid.

hydrolysis of *p*-methoxybenzeneboronic acid[4] in sulfuric and perchloric acids.

To simplify further discussion, slopes of the plots of log k *versus* $-H_0$ are shown in Table IV. These slopes are generally different from unity. At 60°, and for solutions weaker in acidity than about 70% H_2SO_4, the values of the slopes appear to be decreasing with decreasing reactivity of the substrate.

Other characteristics of the correlation for this reaction are perhaps unique among those studied thus far. For a given substrate (*i.e.*, X = *m*-Cl, *m*-F or *p*-Br) a substantial change in slope occurs on passing from solutions weaker to solutions stronger in acidity than 70% H_2SO_4. In the case of *m*-Cl the change is from 0.65 to 1.0. This change in slope is emphasized by the dependence of slope on temperature. In the lower acid region the slope is independent of temperature, while in the higher acid region the slope appears to decrease with increasing temperature (for example see X = *m*-F). These characteristics suggest that, for this reaction, there are two kinetically distinguishable regions of acidity in aqueous sulfuric acid solutions.

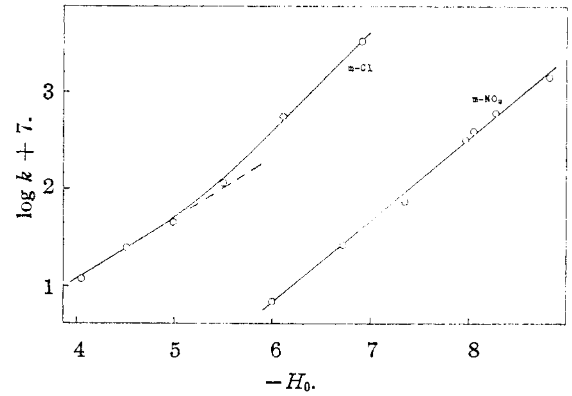


Fig. 5.—log k *vs.* $-H_0$ for sulfuric acid solutions of *m*-chloro- and *m*-nitrobenzeneboronic acids at 60°.

Inasmuch as the nitro group is known to show specific properties[10] in concentrated sulfuric acid, no significance is attached to the abnormally low slope for *m*-nitrobenzeneboronic acid. It will not be considered in the discussion of the results.

D. Dependence of Rate on Temperature.—Rate measurements at different temperatures have been made for a total of five substrates (X = *p*-CH_3O, *p*-CH_3, *p*-F, H and *m*-F). With each of these substrates the slope of a log k *vs.* $1/T$ plot for a given medium composition was used to calculate an activation energy, $\Delta E^{\ddagger}$, and from the intercept an activation entropy, $\Delta S^{\ddagger}$. Table V lists the values obtained.

TABLE V

ACTIVATION PARAMETERS

X	Medium	ΔE^*	ΔS^*
p-CH_3O[a]	30% $HClO_4$	23.6	− 5.2
	30% H_2SO_4	21.1	−12.0
	38% H_3PO_4	18.1	−23.9
	48% H_3PO_4	17.5	−22.6
	58% H_3PO_4	15.0	−26.1
p-CH_3	30% H_2SO_4	21.1	−22.6
	55% H_2SO_4[b]	20.2	−15.5
	58% H_3PO_4	18.2	−23.8
	68% H_3PO_4	17.1	−22.3
	72% H_3PO_4	15.7	−25.1
p-F	30% H_2SO_4[b]	22.3	−22.4
	55% H_2SO_4	21.7	−16.2
m-F	55% H_2SO_4[b]	23.1	−19.5
	64% H_2SO_4	23.0	−18.7
	81% H_2SO_4	18.4	−20.3
	83% H_2SO_4	17.1	−22.9
H	72% H_2SO_4	18.3	−19.8
	74% H_2SO_4	18.1	−18.7

[a] Data from ref. 4. [b] Values of log k obtained by extrapolating log k *vs.* $-H_0$ plots.

The data in Table V allow two kinds of comparison to be made. For a given substrate values for the different media, and for a given medium values for the different substrates, may be compared.

The first kind of comparison can be made using the data for *m*-fluorobenzeneboronic acid in sulfuric acid. In the weaker acid region (below 70%

(10) N. C. Deno and C. Perizzolo, *J. Am. Chem. Soc.*, **79**, 1345 (1957).

H_2SO_4) the values of $\Delta E^\ddagger$ are remarkably greater than those in the higher acid region (above 70% H_2SO_4). Also, because of the inverse dependence of log *k versus* $-H_0$ slopes on temperature in the acidic media above 70% H_2SO_4, it is obvious that above 70% H_2SO_4 the value of $\Delta E^\ddagger$ continues to decrease as the acidity is increased. These changes in $\Delta E^\ddagger$, combined with the change in the value of log *k versus* H_0 slopes, clearly indicate that two kinetically distinguishable regions exist in aqueous sulfuric acid solutions for the hydrolysis of at least the less reactive areneboronic acids.

Also amenable to this first kind of comparison are the activation parameters for *p*-methoxybenzeneboronic acid in perchloric, sulfuric and phosphoric acid media. The data clearly indicate that as the medium is changed from perchloric (30%, 3.6 *M*) through sulfuric (30%, 3.7 *M*) to phosphoric (38%, 4.8 *M*) acid both $\Delta E^\ddagger$ and $\Delta S^\ddagger$ decrease substantially. On the other hand, in phosphoric acid solutions $\Delta E^\ddagger$ decreases and $\Delta S^\ddagger$ remains unaffected as the acidity increases. This latter result is also evident in the data for phosphoric acid solutions of *p*-tolueneboronic acid. In sulfuric acid media, however, $\Delta S^\ddagger$ increases with increasing acidity both with *p*-tolueneboronic and with *p*-fluorobenzeneboronic acid.

The other kind of comparison, in which ΔE^* and $\Delta S^\ddagger$ for different substrates in a given medium are compared, can be made in three different media. In 55% H_2SO_4, the values of $\Delta E^\ddagger$ increase markedly and those of $\Delta S^\ddagger$ decrease slightly (if at all) in the order *p*-CH_3, *p*-F, *m*-F; that is, in the order of decreasing substrate reactivity. It would appear, then, that differences in reactivity are attributable primarily to differences in the activation energies. However, in 30% H_2SO_4 the values of $\Delta E^\ddagger$ and $\Delta S^\ddagger$ for X = *p*-CH_3O and *p*-CH_3, when compared, present a different situation. Now it is found that although *p*-methoxybenzeneboronic acid is substantially more reactive than *p*-tolueneboronic acid, these two substrates have the same value of $\Delta E^\ddagger$, the difference in reactivity resulting from the large difference in $\Delta S^\ddagger$. Finally, in 58% H_3PO_4 the former pattern appears to be re-established; that is, the greater reactivity of *p*-methoxybenzeneboronic acid is due primarily to its lower activation energy.

E. The Solvent Hydrogen Isotope Effect.—Rates of hydrolysis of four areneboronic acids (X = *p*−CH_3O, *p*-CH_3, *p*-F and *m*-F) have been measured in solutions of deuterium sulfate in deuterium oxide at a temperature of 60°. Values of the solvent hydrogen isotope effect, k_H/k_D, for a given percentage by weight acid, are shown in Table VI. All of the values are greater than unity.

An interesting feature is illustrated by the data for X = *m*-F. Above 68% H_2SO_4 the values of k_H/k_D increase and then, above 72% H_2SO_4, appear to level off. This is the region of acidity in which the break in the correlation of rate by H_0 and the large change in the value of $\Delta E^\ddagger$ occur. Therefore the solvent hydrogen isotope effect further substantiates the existence of two kinetically distinguishable acid regions.

F. The Effect of Substituents on Reactivity.—The data obtained at 60° allow discussion of the relative areneboronic acid reactivities. However, inasmuch as the degree of rate dependence on acidity changes with substrate, the relative rates will be acid dependent. This fact is amply illustrated in Table VII which lists logarithms of the relative rate coefficients for two different acidic solutions, 55.4% H_2SO_4 and 74.5% H_2SO_4. Figure 6 shows plots of these values *versus* the σ^+-constants

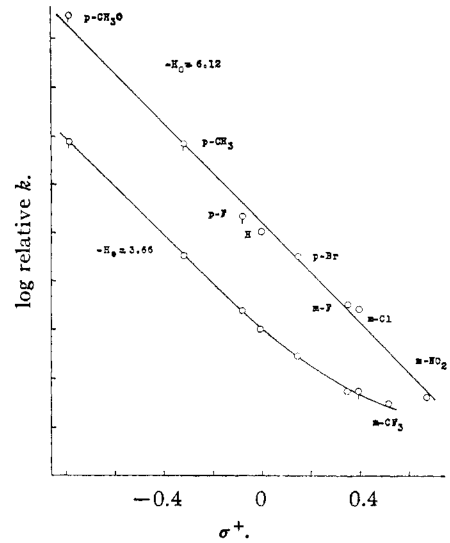


Fig. 6.—The effect of substituents.

TABLE VI

THE SOLVENT HYDROGEN ISOTOPE EFFECT

X	% H_2SO_4	k_H/k_D
p-CH_3O	22.4	2.02
	32.5	1.93
p-CH_3[a]	40	1.60
	45	1.64
	50	1.69
	55	1.74
p-F	60.6	2.16
	65.4	2.27
m-F[b]	64	2.40
	68	2.48
	72	2.68
	76	2.99
	80	2.99

[a] *k*'s interpolated from log *k vs.* $-H_0$ plots. [b] *k*'s interpolated from log *k vs.* % acid plots.

TABLE VII

THE EFFECT OF SUBSTITUENTS ON REACTIVITY

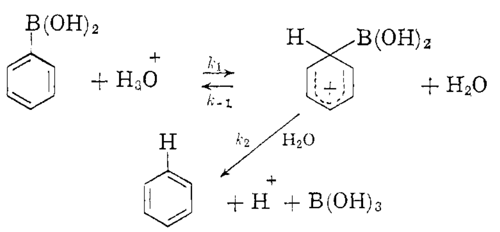
X	σ^+	log relative rate $-H_0 = 3.66$	$-H_0 = 6.12$
p-CH_3O	−0.778	3.88[a]	4.35[a]
p-CH_3	− .311	1.51	1.82[a]
p-F	− .073	0.39	0.32[a]
H	0	0	0
p-Br	0.150	−0.57	−0.53
m-F	.352	−1.27	−1.50
m-Cl	.399	−1.28[a]	−1.60
m-CF_3	.520	−1.52	....
m-NO_2	.674	....	−3.39

[a] Obtained by extrapolation of log *k vs.* $-H_0$ plots.

of Brown and Okamoto.[11] The values of ρ are, respectively, -5.0 (p-substituents only) and -5.2.

G. Discussion of Mechanism.—In the preceding paper it was suggested that the A-SE2 mechanism was the simplest one which would account for the results presented. The additional experimental facts summarized above create a pattern of such complexity that this simple interpretation must clearly be embellished or modified. In particular, the trends in the activation parameters, the kinetic isotope effects and the slopes of the log k *vs.* H_0 plots, as well as the apparently unique breaks in these plots in the region near 72% sulfuric acid, need to be explained. A mechanistic hypothesis which accounts for all of the facts, semi-quantitatively at least, is outlined below. In view of the existence of a kinetic isotope effect it is first assumed that proton transfer is always involved in the rate-determining step. Furthermore, the high sensitivity of the reaction to substituents, with electron release facilitating reaction, leads to the conclusion that substantial positive charge is developed in the aromatic ring in the transition state.

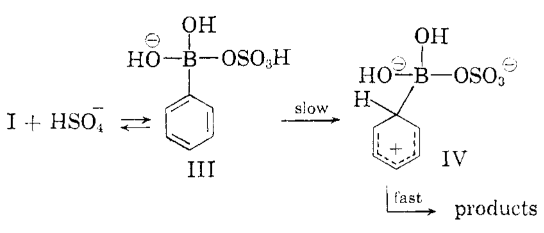
The protodeboronation of p-methoxybenzeneboronic acid in 30% perchloric acid is taken to proceed by way of a simple A-SE2 reaction (eq. 2) in which the hydronium ion is the major electrophile and $k_2 > k_{-1}$. The small negative entropy indicated in Table V is in accord with expectation: entropy changes due to differences in solvation and



(2)

in translational motion between ground and transition states should be small. When the solvent is changed to 30% sulfuric acid both the energy and entropy of activation decrease. These changes are due to replacement of perchlorate as anion by bisulfate, and is attributed to the incursion of an A-SE2 reaction involving the latter ion as proton donor. In this case an increase in charge takes place, and a more negative entropy results from greater ordering of solvent in the transition state. Furthermore, the isotope effect k_H/k_D, is 1.65 (for 2,6-dimethoxybenzeneboronic acid) in 0.1 M perchloric acid[4] and 3.67 (for p-methoxybenzeneboronic acid) in 6.3 M sulfuric acid,[1a] consistent with the expectation that a larger kinetic isotope effect would be observed with the weak acid bisulfate ion than with the more strongly acidic hydronium ion. Long and Watson,[12] for example, have observed that in proton transfer to the anion of 2,4-pentanedione the corresponding isotope effects for hydronium ion and acetic acid are 1.1 and 5.6, respectively. Since a considerably different substrate is involved in the present case the relative change in going from a strong acid to a weak acid might be somewhat different in magnitude, but in the same direction.

Now, in 30% H_2SO_4, when the substrate is changed from p-methoxybenzeneboronic acid to p-tolueneboronic acid the rate constant is decreased by nearly 2.5 powers of ten. This decrease is reflected entirely in a decrease in the activation entropy by ten units. On the other hand, the change in rate from p-tolueneboronic acid to the less reactive p-fluorobenzeneboronic acid is due only to an increase in activation energy, the entropy remaining essentially constant. In order to rationalize these observations, we bear in mind the fact that p-methoxybenzeneboronic acid is the least discriminating of the substrates and, therefore, the one with which participation in a simple A-SE2 reaction by bisulfate is most likely to compete with lyonium ion. With the less reactive substrates reaction involving bisulfate can be facilitated in another way: the boron atom is more electrophilic and can become coordinated to bisulfate ion either before the rate-determining proton transfer or simultaneously. Let us assume a pre-equilibrium attack on the boron by bisulfate, by analogy with those proposed in reactions of areneboronic acids with bromine,[5a,13] iodine,[14] arylmercuric hydroxides[15] and hydrogen peroxide.[16] The formation of intermediate III (eq. 3) will tend to facilitate reaction in two ways: a negative charge on the boron atom will increase the susceptibility to electrophilic attack of the carbon to which it is attached by virtue of its inductive effect, and attachment of the bisulfate ion to the boron will increase its ability to transfer a proton because of the fact that the negative charge originally on oxygen (now on boron) is one atom further removed from the hydrogen. A six-membered cyclic transition state would intervene between III and the pentadienate ion IV; this might be called an



(3)

A-SEi mechanism by analogy with the SNi mechanism postulated by Ingold for some nucleophilic substitution. The species IV can also result from a direct protonation of the boronic acid by bisulfate, if the sulfate ion, instead of diffusing away, remains to bond with the boron. Either mode of reaction will be accompanied by a larger decrease in entropy than the simple protonation by lyonium ion.

The data of Table V show that, below 80% sulfuric acid, the activation energy decreases and the entropy increases as the acid strength increases. This is attributed to a greater sensitivity of the

(11) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

(12) F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958).

(13) H. G. Kuivila and E. J. Soboczenski, *J. Am. Chem. Soc.*, **76**, 2675 (1954).

(14) H. G. Kuivila and R. M. Williams, *ibid.*, **76**, 2679 (1954).

(15) T. Muller, Ph.D. thesis, University of New Hampshire, June, 1960.

(16) H. G. Kuivila, *J. Am. Chem. Soc.*, **76**, 870 (1954).

lyonium ion reaction to sulfuric acid concentration than of those in which bisulfate ion is the proton donor.

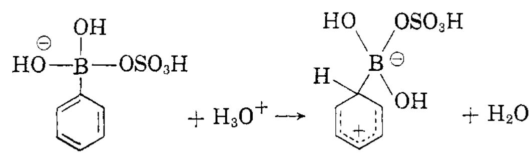
Turning now to the slopes of the plots of log k *vs.* H_0 listed in Table IV we can account first for the decreases noted as the reactivity of the boronic acid decreases. As the substituent becomes more electron withdrawing, rendering the boron atom more electrophilic, the concentration of species III will increase, and the mechanism of eq. 3 becomes more important at any given acidity, relative to that of eq. 2.

The change in slopes of the H_0 plots occurs in the region 66–70% sulfuric acid, and might be attributed to a change in the character of the substrate. For example, the greater dehydrating power of the medium as the acidity is increased would tend to convert the boronic acids to their anhydrides, this conversion being complete when the plots resume linearity beyond 70% acid. No experiments have been conducted to test this possibility explicitly. However, no complications were noted in the first-order kinetic plots in any of the experiments. This means that if the boronic anhydride is participating in large degree under any conditions, it must be monomeric. Boronic acids normally exist as cyclic trimers (boroxines).

An alternative explanation is suggested by the dramatic changes in the structure of the solvated proton which must occur in the region of sulfuric acid concentration under consideration. In recent years there has been an increasing amount of evidence supporting the view that, in aqueous solutions, protons are hydrated by four water molecules, provided that these are available.[17–19] It may be significant that 64.5% sulfuric acid has the stoichiometric composition $H_2SO_4 \cdot 3H_2O$ and 73.1% acid has the composition $H_2SO_4 \cdot 2H_2O$. This means that the maximum average degree of hydration of protons in this region decreases from three to two. A structural change of this type will lead to a greater acidity of the proton, and a decrease of rather substantial magnitude in the activation energy for protonation by lyonium ion as observed in the case of *m*-fluorobenzeneboronic acid. As a result this reaction becomes predominant as we pass through this region of acidity. Unit slopes are observed for all substrates now because all are reacting by the simple A-SE2 mechanism. A decrease in entropy of activation occurs on passage through this region. This can be accounted for (and should be compared with those for *p*-methoxybenzeneboronic acid) on the ground that the positive contribution to the entropy which results from desolvation of the proton on going from ground to transition states is markedly diminished. This is characteristic of changes expected in going from solvents of lower to those of higher dielectric constant, as is the case here.

It was suggested above that *p*-methoxybenzeneboronic acid reacts primarily by the A-SE2 mechanism with both lyonium ion and bisulfate functioning as general acids; *p*-tolueneboronic acid, on the other hand, reacts to some significant extent by the A-SEi mechanism (eq. 3). In the latter case a more reactive ring carbon atom is protonated in the slow step, and the degree to which this has occurred in the transition state is expected to be smaller than in the former case.[20] The smaller solvent isotope effect observed for *p*-tolueneboronic acid is consistent with this argument. As shown by the numbers in Table VI, there is an increase in the isotope effect as the substituent in the benzene ring is changed from *p*-methyl to *p*-fluoro to *m*-fluoro. This is consistent with a decrease in the reactivity of the substrate, provided no material change in mechanism takes place. The small increase with acid strength for a given substituent, to the extent that it is real, could be a reflection of a trend toward the A-SE2 mechanism, which is complete beyond about 72% acid. A substantial increase on passing into this region is revealed by the data for *m*-fluorobenzeneboronic acid, but could not have been foreseen. The change in substrate from III to the free boronic acid would suggest an increase in isotope effect, but the change in proton donor to lyonium ion would argue for a decrease.

A third mechanism, one in which III is protonated by hydronium ion (eq. 4), can be envisioned. However the participation of this mechanism to



(4)

any appreciable extent is eliminated by the observed isotope effects. As the acidity increases, the amount of III relative to that of free boronic acid increases; hence we would expect this mechanism to become more dominant relative to either the simple A-SE2 or the SEi mechanisms. We would anticipate, then, that the magnitude of k_H/k_D would decrease with increasing acidity, rather than increase.

Because of the variations in slopes of the plots of log k *vs.* H_0 it is obvious that the character of a Hammett plot will depend on the composition of the solvent. The data in Table VII and Fig. 6 were arbitrarily chosen to represent conditions of acidity below the region of the breaks in the plots, H_0 -3.66, and above the breaks, H_0 -6.12. The fact that the data for the higher acidity fall very nicely on a line of slope -5.24 is of doubtful significance, because of the large extrapolations needed for *p*-methoxy and *p*-methyl, which are the crucial ones in a test of a σ^+-correlation. The data for the lower acidity required an extrapolation of any magnitude only for the *p*-methoxybenzeneboronic acid. Consequently the shape of the plot bears discussion. Even though σ^+-values are used, there is a pronounced tendency toward a decrease in slope with the less reactive substituents. If a lower acidity had been chosen for the plot this effect would be even more pronounced and, in the extreme, there would be a change from a simple curve as shown to one containing a minimum. This behavior is in complete accord with the

(17) K. N. Bascombe and R. P. Bell, *Disc. Faraday Soc.*, 158 (1957).
(18) P. A. H. Wyatt, *ibid.*, 162 (1957).
(19) D. G. Tuck and R. M. Diamond, *Proc. Chem. Soc.*, 236 (1958).
(20) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

mechanistic picture developed above. As substituents make the benzene ring less susceptible to electrophilic attack, the alternative SEi mechanism becomes energetically the more favored one. This is more pronounced the lower the acidity, but when the acidity becomes high enough the A-SE2 mechanism returns to favor.

Gold and Satchell[21] have determined the rates of protodedeuteration of 4-*d*-anisole, 4-*d*-toluene and deuteriobenzene in sulfuric acid at 25°. Thus direct comparisons can be made with the rates of protodeboronation of benzeneboronic acid and the *p*-methoxy and *p*-methyl derivatives. The results are given in Table VIII. In each case deboronation is faster than dedeuteration, but the ratio decreases with increasing acidity, except for the marked increase in going from the *p*-methoxy to the *p*-methyl substituent. This latter fact is consistent with the above discussion.

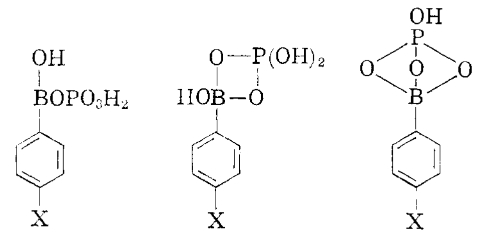
TABLE VIII

RELATIVE RATES OF DEBORONATION AND DEDEUTERATION

X	$-H_0$	Deboronation / Dedeuteration
p-CH_3O	1.60	36
	3.40	20
p-CH_3	3.02	66
	3.52	51
H	5.60	18
	6.40	15

(21) V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 3619 (1955); 2743, 3911 (1956).

In contradiction to the differences in mechanism outlined above for the hydrolysis of *p*-methoxybenzeneboronic and *p*-tolueneboronic acids in sulfuric acid, the activation parameters for these substrates in H_3PO_4 strongly suggest that both are reacting by the same mechanism. The contradiction vanishes, however, if in phosphoric acid essentially all of either substrate is present as any one of the anhydride species V, VI or VII. In



V VI VII

view of the ease with which molecular phosphoric acid forms anhydrides, this possibility is at least conceivable.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES 24, CALIF.]

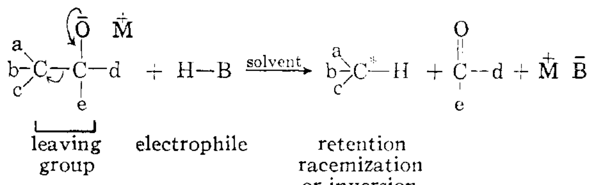
Electrophilic Substitution at Saturated Carbon. VIII. Mixed Solvents and Steric Course[1]

BY DONALD J. CRAM AND W. DAVID NIELSEN

RECEIVED OCTOBER 4, 1960

The base-catalyzed cleavage of (−)-2,3-diphenyl-3-methyl-2-pentanol to (+)- or (−)-2-phenylbutane has been used to study the effect of solvent compositions and temperature on the stereochemical course of electrophilic substitution at saturated carbon. Three kinds of steric courses have been observed with lithium *n*-propoxide as base, and different proportions of 1-propanol and dimethyl sulfoxide as solvent. Pure propanol gives 13% net retention, pure dimethyl sulfoxide gives 100% racemization, whereas 80 mole % 1-propanol–20 mole % dimethyl sulfoxide gives 14% net inversion. A qualitatively similar picture is observed with *t*-butyl alcohol–dimethyl sulfoxide solvent mixtures. Three kinds of steric courses have been observed in 36 mole % diethylene glycol, 64 mole % dioxane with potassium diethylene glycoxide as catalyst. At 140°, 16% net inversion, at about 175°, 100% racemization, and 220°, 12% net retention was observed. These results are interpreted in terms of mechanisms in which carbanions in an asymmetric environment are captured by proton donors at varying relative rates either from the side of, or the side remote from, the leaving group.

Earlier studies[2] of carbon as leaving group in electrophilic substitution at saturated carbon revealed that by proper control of solvent and cation, a number of systems that fit the general formulation could be induced to give product that ranged from 99% net retention to 100% racemization to 60% net inversion. A large body of results was accommodated[2f] by a mechanistic scheme which in all cases involved carbanion intermediates. The



exact composition of the solvent-leaving group envelope determined the stereochemical fate of this intermediate.

This paper reported the results of a study of the steric course of cleavages of 2,3-diphenyl-3-methyl-2-pentanol (I) to give 2-phenylbutane. The relative configurations of these compounds were established earlier.[2c] The alcohol had previously been found to cleave with net retention in solvents such as dioxane or *t*-butyl alcohol,[2b,2c] with net inversion in methanol or diethylene gly-

(1) This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to donors of said fund.

(2) (a) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 570 (1959); (b) D. J. Cram, A. Langemann and F. Hauck, *ibid.*, **81**, 5750 (1959); (c) D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *ibid.*, **81**, 5754 (1959); (d) D. J. Cram, A. Langemann, W. Lwowski and K. R. Kopecky, *ibid.*, **81**, 5760 (1959); (e) D. J. Cram, F. Hauck, K. R. Kopecky and W. D. Nielsen, *ibid.*, **81**, 5767 (1959); (f) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959).