

10 hr. at 5°. After drying at room temperature for 6 hr. the orange precipitate (6 g.) was dissolved in 125 ml. of water at 29°, stirred for 10 min. with Celite, and filtered. The filtrate was again diluted to 1 l. with acetone and allowed to stand at 5° for 15 hr. The bright yellow precipitate was filtered, washed with acetone, and finally with ether. The product was dried and stored over solid sodium hydroxide in a vacuum desiccator.

*Anal.* Calcd. for  $C_9H_{12}N_8Cl_2 \cdot \frac{1}{2}H_2O \cdot HCl$ : C, 31.0; H, 4.0; N, 32.1. Found: C, 31.2; H, 4.5; N, 31.7.

**8-[(2-Hydroxyethyl)-thioazo]-hypoxanthine.**—The preparation of this compound is illustrative of the preparation of the compounds listed in Table II.

Ten grams of 8-amino-6-hydroxypurine<sup>11</sup> was diazotized<sup>9</sup> and the 8-diazohypoxanthine added to a flask containing 100 ml. of methanol and 5 g. of 2-mercaptoethanol. The solution was stirred at room temperature for 6 hr.; then 150 ml. of benzene was added and the reaction mixture cooled overnight. The precipitate was filtered, washed with benzene, and dried to yield 7.8 g. of yellow-green powder. For purification the product was reprecipitated from very dilute potassium hydroxide solution with acetic acid.

**Propionic Acid(3)-[(6-hydroxypurine-8-yl)-azothio].**—Ten grams of 8-amino-6-hydroxypurine<sup>11</sup> was diazotized<sup>9</sup>

and the damp diazohypoxanthine transferred to a flask containing 100 ml. of methanol and 5.0 g. of 3-mercaptopropionic acid. The reaction mixture was stirred for 6 hr.; then 150 ml. of benzene was added and the solution cooled overnight. The precipitate was filtered, washed with acetone, and dried to give 9.5 g. of crude product. This compound was purified by dissolving in hot sodium bicarbonate solution followed by precipitation with hydrochloric acid. The compound exhibited at *pH* 1,  $\lambda_{max}$  272, 358  $m\mu$ ,  $\epsilon$  8,000, 8,000.

*Anal.* Calcd. for  $C_8H_8N_6O_3S$ : C, 35.8; H, 3.0. Found: C, 35.6; H, 3.0.

**Propionic Acid(3)-[theophylline-8-yl-thioazo].**—8-Diazothetheophylline<sup>9</sup> (5 g.) was suspended in 250 ml. of acetone. Then 5 g. of 3-mercaptopropionic acid was added and the solution stirred for 3 hr. The yellow precipitate was filtered, washed with acetone, and dried to yield 6.7 g. The product was purified by reprecipitation from warm sodium bicarbonate solution with dilute hydrochloric acid; m.p. 162° dec. The compound exhibited at *pH* 1,  $\lambda_{max}$  293, 370  $m\mu$ ,  $\epsilon$  8,700, 7,200.

*Anal.* Calcd. for  $C_{10}H_{12}N_6O_4S$ : C, 38.4; H, 3.8; N, 26.8. Found: C, 38.4; H, 4.0; N, 26.5.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, N. C.]

## Kinetics of the Acid-catalyzed Hydrolysis of 4-(*p*-Sulfophenylazo)-1-naphthyl Methyl Ether and 4-(*p*-Sulfophenylazo)-anisole<sup>1</sup>

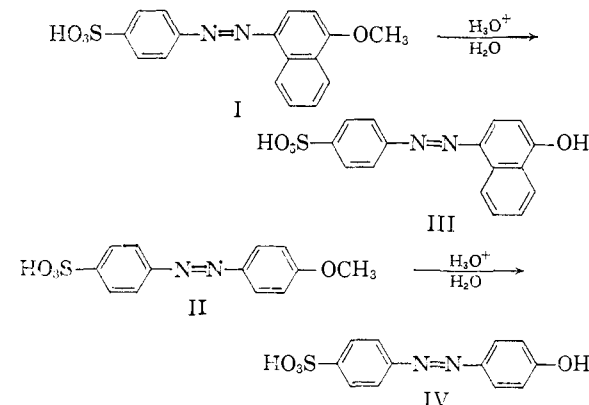
BY J. F. BUNNETT<sup>2</sup> AND ERWIN BUNCEL

RECEIVED MARCH 11, 1960

Azonaphthyl ether I is readily hydrolyzed to azonaphthol III. In dilute acid, the reaction is first order in oxonium ion concentration and is specific oxonium ion catalyzed. In concentrated acids, there is a rate maximum at about 2.5 *M* but suitable treatment of the data reveals correlation of rate with oxonium ion concentration. Alternatively, hydrolysis rate is related to the activity of water in concentrated acids by a new procedure. The resulting *w*-values indicate a mechanism in which the slow step is general acid-catalyzed detachment of a methoxy group from intermediate complex VIII. Azophenyl ether II is much less sensitive to hydrolysis. A rate maximum is again observed in concentrated acids, but rate cannot be correlated either with *h*<sub>0</sub> or with oxonium ion concentration. It is, however, easily related to the activity of water, the *w*-value being +3.1. This suggests a mechanism in which water effects an *SN*<sub>2</sub> displacement on the methyl carbon of protonated II. Incident to the kinetics, *pK*<sub>a</sub> values for I and II have been determined.

The facile acid-catalyzed hydrolysis of azonaphthyl ethers is described in an earlier paper.<sup>3</sup> A kinetic study of this reaction is now presented.

We have studied the kinetics of the hydrolytic cleavage of 4-(*p*-sulfophenylazo)-1-naphthyl methyl ether (I) and of its benzene-series analog, 4-(*p*-sulfophenylazo)-anisole (II). These sulfo compounds were chosen because of their solubility in water.



(1) This research was supported by the National Science Foundation (Grant No. NSF-G2359).

(2) Department of Chemistry, Brown University, Providence, R. I.

(3) J. F. Bunnett and G. B. Hoey, *THIS JOURNAL*, **80**, 3142 (1958).

The kinetics were followed by photometric measurements, advantage being taken (as previously<sup>3</sup>) of the great difference in spectra of the azo-ethers I and II and the corresponding azo-phenols III and IV in alkaline solution. In all cases, the acid catalyst was present in large excess over I or II and the kinetics were first order in the azo compound.

### 4-(*p*-Sulfophenylazo)-1-naphthyl Methyl Ether (I)

**Dependence of Rate on Acid Concentration, Dilute Range.**—First-order rate coefficients in hydrochloric acid solutions representing a thousand-fold variation in oxonium ion concentration, but in which ionic strength was maintained constant by compensation with potassium chloride, are displayed in Table I. The constancy of the second-order coefficients,  $k_2/[H_3O^+]$ , indicates that the reaction is first order in oxonium ion concentration within this range.

### Specific Oxonium Ion vs. General Acid Catalysis.

—The rate of cleavage was studied as a function of buffer concentration in two series of phosphate buffers. In one series (Table II, part A) the ratio  $[H_2PO_4^-]:[NaH_2PO_4]$  was 1:3 and ionic strength was held constant by compensation with sodium perchlorate; *pH* was virtually constant within this series (the *pH* as measured by a glass electrode was constant, but one reckons a decrease in  $[H_3O^+]$  of

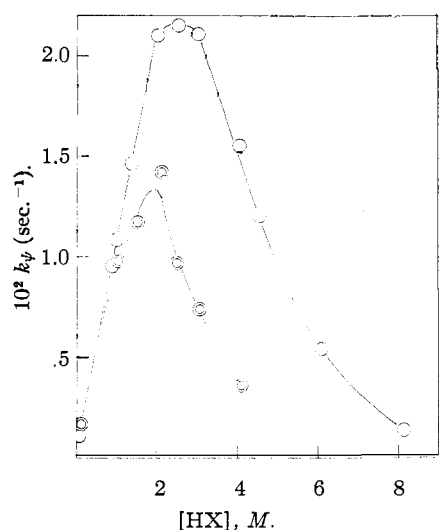


Fig. 1.—Rate of hydrolysis of I in concentrated aqueous acids: O, HCl; ⊙, HClO<sub>4</sub>.

2.5% between the first and last entries in part A) and the hydrolysis rate was constant within experimental error. The second-order rate coefficient  $k_p/[H_3O^+]$  is essentially the same as that derived from measurements in dilute hydrochloric acid solutions (Table I). In the other series of buffers

TABLE I  
HYDROLYSIS OF AZONAPHTHYL ETHER I, DILUTE ACID RANGE (46.0°)

[HCl], M	[KCl], M	$k_p$ , sec. <sup>-1</sup>	$k_p/[HCl]$ , l. mole <sup>-1</sup> sec. <sup>-1</sup>
9.25 × 10 <sup>-1</sup>	...	9.70 × 10 <sup>-3</sup>	1.03 × 10 <sup>-2</sup>
		9.37 × 10 <sup>-3</sup>	
9.25 × 10 <sup>-2</sup>	0.832	1.11 × 10 <sup>-3</sup>	1.20 × 10 <sup>-2</sup>
9.25 × 10 <sup>-3</sup>	0.916	1.33 × 10 <sup>-4</sup>	1.37 × 10 <sup>-2</sup>
		1.21 × 10 <sup>-4</sup>	
9.25 × 10 <sup>-4</sup>	0.925	1.11 × 10 <sup>-5</sup>	1.20 × 10 <sup>-2</sup>

<sup>a</sup> Average of two determinations where appropriate.

TABLE II  
HYDROLYSIS OF AZONAPHTHYL ETHER I, BUFFERED SOLUTIONS (46.0°)

[H <sub>3</sub> PO <sub>4</sub> ], M	[NaH <sub>2</sub> PO <sub>4</sub> ], M	[NaClO <sub>4</sub> ], M	$k_p$ , sec. <sup>-1</sup>	[H <sub>3</sub> O <sup>+</sup> ] <sup>a</sup>	$k_p/[H_3O^+]$ , l. mole <sup>-1</sup> sec. <sup>-1</sup>
Part A					
0.0893	0.2680	...	4.19 × 10 <sup>-3</sup>	3.02 × 10 <sup>-3</sup>	1.39 × 10 <sup>-2</sup>
.0670	.2010	0.0670	4.09 × 10 <sup>-3</sup>	3.02 × 10 <sup>-3</sup>	1.36 × 10 <sup>-2</sup>
.0447	.1340	0.1340	3.99 × 10 <sup>-3</sup>	3.02 × 10 <sup>-3</sup>	1.32 × 10 <sup>-2</sup>
Part B					
0.2680	0.0893	...	2.80 × 10 <sup>-4</sup>	2.09 × 10 <sup>-2</sup>	1.34 × 10 <sup>-2</sup>
.2010	.0670	0.0223	2.52 × 10 <sup>-4</sup>	1.91 × 10 <sup>-2</sup>	1.32 × 10 <sup>-2</sup>
.1340	.0447	.0447	2.14 × 10 <sup>-4</sup>	1.66 × 10 <sup>-2</sup>	1.29 × 10 <sup>-2</sup>
.0670	.0223	.0670	1.62 × 10 <sup>-4</sup>	1.20 × 10 <sup>-2</sup>	1.35 × 10 <sup>-2</sup>
.0268	.0089	.0804	1.05 × 10 <sup>-4</sup>	0.76 × 10 <sup>-2</sup>	1.38 × 10 <sup>-2</sup>

<sup>a</sup> From the pH as measured by a glass electrode.

(Table II, part B) the ratio [H<sub>3</sub>PO<sub>4</sub>]:[NaH<sub>2</sub>PO<sub>4</sub>] was 3:1 and again ionic strength was maintained constant. The composition of these buffers was not such as to maintain constant pH as the absolute buffer concentration was varied and it is not surprising that the pseudo-first-order rate coefficient,  $k_p$ , varied within this series. The second-order rate coefficient,  $k_p/[H_3O^+]$ , was, however, constant

at the same value as in the other series (Table I and Table II, part A). Thus, the acid-catalyzed rate is dependent only on a general property of the medium, the pH, and not on the specific identity or concentration of the various acids present. This is the phenomenon known as specific oxonium ion catalysis.<sup>4</sup>

**Dependence of Rate on Acid Concentration, Concentrated Range.**—As the hydrochloric acid concentration was increased, the reaction rate rose linearly up to 2 M but then it went through a maximum and decreased steadily between 3 and 8 M. The data are set forth in Table III and are plotted in Fig. 1. Qualitatively the same effect was observed in strong solutions of perchloric acid (Table III and Fig. 1).

TABLE III  
HYDROLYSIS OF AZONAPHTHYL ETHER I IN CONCENTRATED ACID SOLUTIONS AT 46.0°

[HX], M	10 <sup>3</sup> $k_p$ , sec. <sup>-1</sup>	$h_0$	$[\log k_p - \log (h_0 / (h_0 + K_{SH}^+))]^a$	$\log a_{H_2O}$
Hydrochloric acid				
1.02	1.08	1.66	-1.33	-0.017
1.39	1.46	2.63	-1.35	-.025
2.03	2.10	5.01	-1.36	-.040
2.54	2.15	7.76	-1.44	-.054
3.05	2.11	11.8	-1.51	-.071
4.06	1.55	26.3	-1.73	-.110
4.56	1.20	39.8	-1.86	-.133
6.09	0.537	141	-2.25	-.216
8.12	0.142	1150	-2.85	-.368
Perchloric acid				
0.134	0.166			
1.07	0.975	1.82	-1.40	-0.019
1.54	1.167	3.55	-1.52	-.030
2.14	1.421	6.92	-1.59	-.047
2.51	0.965	11.26	-1.84	-.060
3.08	.740	18.6	-2.02	-.085
4.10	.357	59.0	-2.41	-.143

<sup>a</sup> Based on  $K_{SH}^+ = 5.50$ .

**Salt Effects.**—Several runs were performed in which the concentration of hydrochloric acid was held constant at 0.00925 M and various amounts of potassium chloride or sodium perchlorate were added. Results are shown in Fig. 2. Small concentrations of potassium chloride caused a decrease in rate while larger concentrations caused the rate to recover to its salt-free value or higher. The minimum is at about 0.15 M potassium chloride. Sodium perchlorate appears to have the same sort of effect.

Some attention was given to the kinetic effects of large concentrations of lithium chloride. At 0.0101 M hydrochloric acid,  $k_p$  in the presence of 2.0 M lithium chloride was  $1.68 \times 10^{-4}$  sec.<sup>-1</sup> which is 32% higher than in the absence of salts. This observation continues the pattern shown in Fig. 2. At 1.014 M hydrochloric acid,  $k_p$  in the presence of 2.0 M lithium chloride was  $1.03 \times 10^{-2}$  sec.<sup>-1</sup> which is slightly less than the salt-free value. At 3.0 M hydrochloric acid,  $k_p$  in the presence of 5.0 M lithium chloride was  $2 \times 10^{-3}$  sec.<sup>-1</sup> which is about one-tenth its value in the absence of salts. Thus

(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 220.

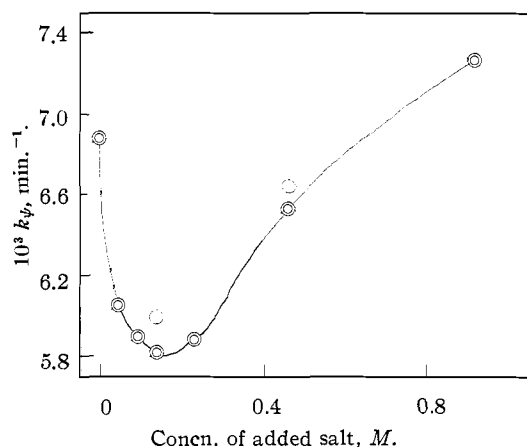


Fig. 2.—Rate of hydrolysis of I in  $9.25 \times 10^{-3} M$  HCl containing various concentrations of added salts:  $\circ$ ,  $\text{NaClO}_4$ ;  $\odot$ ,  $\text{KCl}$ . The point at zero concentration of added salt is the mean of three measurements with an average deviation of 2%.

the kinetic effect of a large concentration of lithium chloride changes from positive to negative as the hydrochloric acid concentration is changed from the dilute to the concentrated range.

#### 4-(*p*-Sulfophenylazo)-anisoie (II)

This benzene-series azo-ether is much less sensitive to acid catalyzed hydrolysis. At  $46.2^\circ$  in 1.015  $M$  hydrochloric acid,  $k_p$  for its hydrolysis is only  $1.570 \times 10^{-6} \text{ sec.}^{-1}$ . Under these conditions, naphthalene-series azo-ether I hydrolyzes 6890 times faster.

The rate of hydrolysis of II was studied as a function of hydrochloric acid concentration in the concentrated range only. Most determinations were made at  $97.0^\circ$  at which temperature the rates are conveniently measured. Again the phenomenon of a rate maximum, at about 5  $M$  hydrochloric acid, was encountered. The data are given in Table IV.

TABLE IV  
HYDROLYSIS OF AZOPHENYL ETHER II IN CONCENTRATED HYDROCHLORIC ACID SOLUTIONS AT  $97.0^\circ$

[HCl] $M$	$10^4 k_p$ , $\text{sec.}^{-1}$	$h_0$	$[\log k_p - \log (h_0 / (h_0 + K_{SH}^+))]^a$	$\log a_{H_2O}$
1.01	1.49	1.62	-1.42	-0.017
2.03	4.31	5.01	-1.42	-0.040
3.04	8.65	11.8	-1.42	-0.071
4.06	11.7	26.3	-1.53	-0.110
4.66	12.3	43.6	-1.63	-0.138
5.08	12.6	60.3	-1.68	-0.159
6.09	10.6	141	-1.87	-0.216
7.24	6.93	457	-2.12	-0.298
9.30	2.23	3020	-2.65	-0.472

<sup>a</sup> Based on  $K_{SH}^+ = 40$ .

The Arrhenius energy of activation in 1.01  $M$  hydrochloric acid is reckoned, from rate coefficients at  $46.2$  and  $97.0^\circ$ , as 20.6 kcal./mole.

#### $pK$ Determinations

The kinetics suggested that I and II were strong enough bases to be extensively protonated in concentrated acid solutions. Determination of their  $pK$  values was therefore undertaken. Since protonation of I or II is accompanied by color changes, the use of a photometric procedure<sup>5</sup> was fea-

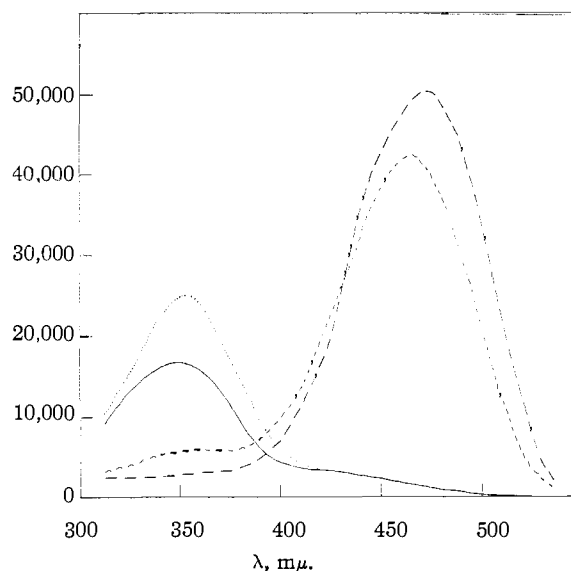


Fig. 3.—Spectra of 4-(*p*-sulfophenylazo)-anisoie (I): —, in water;  $\cdots$ , in 5.0%  $\text{H}_2\text{SO}_4$ ; - - - -, in 36.4%  $\text{H}_2\text{SO}_4$ ; - · - ·, in 79.5%  $\text{H}_2\text{SO}_4$ .

ible. The simple yet rigorous procedure of Davis and Geissman<sup>6</sup> was used.

Photometric measurements on acidic solutions of II were essentially straightforward. However, acidic solutions of I underwent rapid hydrolysis at room temperature and it was therefore necessary to record light absorption by acid solutions of I as a function of time and to extrapolate back to the time of mixing. The extrapolation could be done with precision, but this required a separate solution for each absorbance measurement at each wave length. The determination of complete spectra for I in acidic solutions would consequently be tedious and in fact was not attempted.

Solutions of I or II as their sodium salts in pure water or in weakly acidic aqueous solutions showed a modest variation in absorbance, at the absorption maximum, as a function of time in the light beam of the spectrophotometer. This change in absorbance evidently has to do with *trans*→*cis* isomerization brought about by irradiation.<sup>7</sup> No such variation was observed in strongly acidic solutions, apparently because equilibration between the stereoisomers is acid catalyzed.

4-(*p*-Sulfophenylazo)-anisoie (II).—Spectra of the sodium salt of II in water and in various concentrations of sulfuric acid are displayed in Fig. 3. Several features are of interest. The strong band at  $350 \text{ m}\mu$  in water increases in intensity but remains essentially fixed in wave length as the sulfuric acid concentration is increased to 4.99% (about 1  $N$ ). It is tempting to consider this as a consequence of transformation of the sodium salt of II to the free sulfonic acid; indeed, if this were the explanation,  $pK_a$  for the sulfo group of II could be roughly estimated as +1. This is not vastly different from the  $pK_a$  of -0.3 estimated by King<sup>8</sup> for the sulfo group of  $\text{H}_3\text{N}^+-\text{CH}_2-\text{CH}_2-\text{SO}_3\text{H}$ . Also Bascombe and Bell<sup>9</sup> have estimated  $pK_a$  for methanesulfonic acid to be -0.6. However, doubt is cast on this interpretation by the fact that qualitatively similar changes in intensity on addition of sulfuric acid have been observed for azobenzenes lacking sulfo groups.<sup>10</sup>

Increasing the sulfuric acid concentration to 36.4% causes absorption at  $350 \text{ m}\mu$  to dwindle and a strong new band at

(5) L. A. Flexser, L. P. Hammett and A. Dingwall, *THIS JOURNAL*, **57**, 2103 (1935).

(6) C. T. Davis and T. A. Geissman, *ibid.*, **76**, 3507 (1954).

(7) M. N. Inscoe, J. H. Gould and W. R. Brode, *ibid.*, **81**, 5634 (1959); E. Fischer and Y. F. Frei, *J. Chem. Soc.*, 3159 (1959).

(8) E. J. King, *THIS JOURNAL*, **75**, 2204 (1953).

(9) K. N. Bascombe and R. P. Bell, *J. Chem. Soc.*, 1096 (1959).

(10) H. H. Jaffé, S. J. Yeh and R. W. Gardner, *Molecular Spectroscopy*, **2**, 120 (1958). It should be noted, though, that the maximum change noted by these authors was only 8% in contrast to the 48% change we observed.

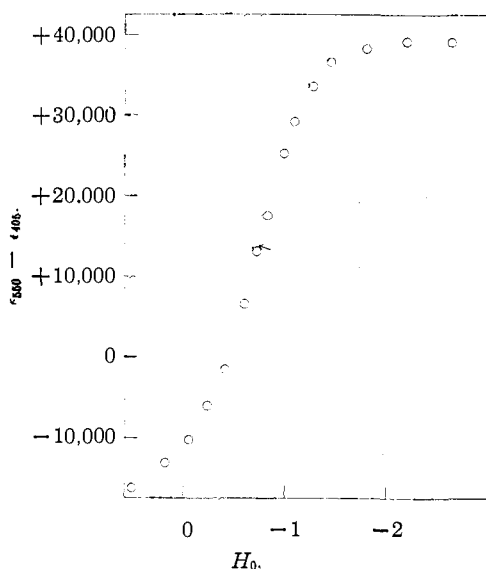
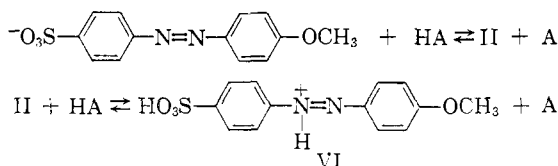


Fig. 4.—Davis-Geissman plot for evaluation of the  $pK_a$  of I. The mid-point (indicated by the arrow) of the portion of steepest slope falls at the  $H_0$ -value equal to  $pK_a$  of V, the conjugate acid of I; data of Table VI.

465  $m\mu$  to appear; the spectrum in 36.4% sulfuric acid is believed to be substantially that of the cationic species VI.<sup>11</sup>

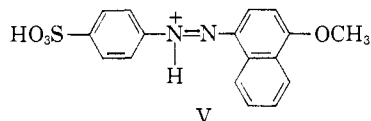
Further increase in sulfuric acid concentration to 79.5% causes small further changes in absorbance and in wave



length of maximum absorption. The latter is a medium effect of a type which has been noted before.<sup>5,12</sup>

The  $pK_a$  of VI was determined from measurements at 353  $m\mu$  and at 462.5  $m\mu$  in both hydrochloric and sulfuric acid solutions at 25°. The relevant data for the determination in sulfuric acid are given in Table V. The key plots of ( $A_{462.5} - A_{353}$ ) vs.  $H_0$  are withheld to save space; it suffices to say that they resembled Fig. 4. The  $pK_a$  of VI was -1.45 from measurements in hydrochloric acid and -1.68 from measurements in sulfuric acid. The average of these two values is -1.56, best rounded off to -1.6.

This evaluation of  $pK_a$  for VI involves the assumption that the sulfonate group of the sodium salt of II is protonated before the azo group is. This is reasonable in view of estimates<sup>9,10</sup> that  $pK_a$  for sulfonic acids is close to zero. If the sulfonate group resisted protonation until  $H_0$  of -2.0, the  $pK_a$  for VI would have to be regarded as approximate because of the inequality of  $H_0$  and  $H_-$ .<sup>13</sup> If both stages of protonation occur within the same  $H_0$  range, this evaluation of  $pK_a$  is also approximate.



**4-(*p*-Sulfophenylazo)-1-naphthyl Methyl Ether (I).**—The sodium salt of I in water has a strong absorption band at 405  $m\mu$  but no other features of interest above 350  $m\mu$ . The spectrum has been recorded.<sup>14</sup> Small concentrations of

(11) Cf. H. Zollinger, "Chemie der Azofarbstoffe," Birkhauser Verlag, Basel, Switzerland, 1958, p. 221.

(12) H. H. Jaffé and R. W. Gardner, *THIS JOURNAL*, **80**, 319 (1958).

(13) Reference 4, p. 269.

TABLE V  
DETERMINATION OF  $pK_a$  OF II<sup>a</sup>; MEASUREMENTS IN SULFURIC ACID AT 25°

$\text{H}_2\text{SO}_4$ , %	$H_0$	Absorbance		
		at 353 $m\mu$	at 462.5 $m\mu$	$A_{462.5} - A_{353}$
4.99	+0.12	0.809	0.056	-0.753
9.24	- .25	.792	.070	- .722
14.82	- .66	.775	.121	- .654
17.66	- .86	.742	.182	- .560
20.33	-1.03	.693	.269	- .424
23.14	-1.22	.622	.403	- .219
25.95	-1.44	.531	.574	+ .043
28.59	-1.62	.435	.795	.360
31.20	-1.79	.334	1.020	.686
33.87	-1.97	.236	1.226	.990
36.39	-2.15	.165	1.367	1.202
48.81	-3.26	.075	1.536	1.461
63.75	-4.90	.070	1.572	1.502
79.47	-6.92	.070	1.572	1.502

<sup>a</sup> Total concentration of II (all stages of protonation) in all solutions:  $3.26 \times 10^{-5} M$ .

hydrochloric acid (e.g., 0.02 *M*) cause an increase in intensity of absorption but no other changes except those due to slow hydrolysis. A solution of I in 2 *M* hydrochloric acid, observed 20 sec. after mixing, showed strong absorption at 550  $m\mu$  but little absorption at 405  $m\mu$ . As time passed, a strong peak developed at 475  $m\mu$  and the peak at 550  $m\mu$

TABLE VI  
DETERMINATION OF  $pK_a$  OF I; MEASUREMENTS IN HYDROCHLORIC ACID AT 25°

$[\text{HCl}]$ , <i>M</i>	$H_0$	Absorbance <sup>a</sup>		$A_{550} - A_{405}$
		at 405 $m\mu$	at 550 $m\mu$	
0.26	+0.52	0.736	0.069	-0.667
.52	.19	.711	.147	- .541
.77	-0.04	.664	.240	- .424
1.03	- .22	.638	.358	- .250
1.34	- .40	.575	.509	- .066
1.75	- .59	.500	.766	+ .266
2.06	- .71	.458	.968	.539
2.36	- .82	.391	1.114	.723
2.78	- .98	.329	1.370	1.041
3.09	-1.08	.296	1.490	1.207
3.60	-1.26	.249	1.633	1.384
4.12	-1.45	.228	1.732	1.510
5.15	-1.80	.210	1.787	1.579
6.18	-2.20	.210	1.824	1.616
7.21	-2.65	.209	1.821	1.612

<sup>a</sup> Details of procedure are in the Experimental section.

dwindled to a slight shoulder. These observations indicate that V, the azo-protonated form of I, has an absorption maximum at 550  $m\mu$ . The strong absorption at 475  $m\mu$  is derived from III.<sup>14,15</sup>

The  $pK_a$  of V was evaluated from measurements at 25° in hydrochloric acid solutions at 405 and 550  $m\mu$ . As mentioned, each absorption value was obtained by an extrapolation back to zero time. Data are presented in Table VI, and the resulting Davis-Geissman plot is given in Fig. 4.  $pK_a$  of V from this plot is -0.74. As in the determination of  $pK_a$  of VI, this value is somewhat uncertain owing to lack of firm knowledge of  $pK_a$  of the sulfo group.

## Discussion

**Hydrolysis of 4-(*p*-Sulfophenylazo)-1-naphthyl Methyl Ether (I).**—Our kinetic study has shown

(14) J. B. Müller, I. Blangey and H. E. Pierz-David, *Helv. Chim. Acta*, **35**, 2579 (1952).

(15) It is interesting that in 6 *M* hydrochloric acid the spectrum of I was nearly time-independent. This is no doubt because the protonated form of III has nearly the same spectrum as V. Only at intermediate acidities, sufficient to protonate I but not III, is hydrolysis accompanied by a great change in spectrum.

that this reaction: (a) is first order in oxonium ion in the dilute acid region, (b) is specific oxonium ion catalyzed in the same region, (c) is subject to some curious salt effects, and (d) goes through a rate maximum at about 2.5*M* in concentrated solutions of hydrochloric and perchloric acids. Observations (a) and (b) are important but not very specific as evidence of mechanism. Observations (d) are more unusual and more significant.

Presuming that the slow step or steps of the hydrolysis mechanism involve reaction of V with water, one can readily comprehend in qualitative terms the phenomenon of the rate maximum. One must take into account the considerable basicity of I. At low acidity, increased acid concentration causes increased hydrolysis rate by raising the concentration of protonated substrate. But as the acidity becomes sufficient to convert a large fraction of the substrate into its protonated form, increased acid concentration can do little more. A new factor now becomes important: decrease in the activity of water with increasing acid concentration. As water becomes progressively less available, hydrolysis rate diminishes steadily.

The kinetic effects of large concentrations of added lithium chloride are also in accord with this explanation. Before the rate maximum, this salt accelerates hydrolysis because it increases  $h_0$ <sup>16</sup> and therefore the concentration of V. Beyond the maximum, lithium chloride is decelerating because it binds water of hydration and thereby decreases the activity of water.

Traditionally, hydrolysis rates in the moderately concentrated acid region have been related either to the Hammett acidity function,<sup>13,17</sup>  $h_0$ , or to oxonium ion concentration. When the substrate is appreciably basic, a simple plot of  $\log k_\psi$  against  $H_0$  or  $\log [H_3O^+]$  no longer suffices. Schubert and Latourette<sup>18</sup> have shown that one must instead plot  $\log (k_\psi[S]_{st}/[S])$ <sup>19</sup> against  $-H_0$  or  $\log [H_3O^+]$ . When the data for hydrolysis of I in perchloric acid were plotted in this way against  $\log [H_3O^+]$ , an excellent straight line of slope unity was obtained. The corresponding plot for hydrochloric acid approximated a straight line of slope unity over its middle portion but was definitely curved at both ends. In the usual phraseology, reaction rate may be said to correlate with oxonium ion concentration rather than with  $h_0$ .

According to the Zucker-Hammett hypothesis,<sup>13,16</sup> this result indicates that the vital transition state contains a molecule of water. Such is indeed called for by the mechanism proposed by Bunnett and Hoey.<sup>3</sup>

Recently a new procedure for the interpretation of reaction rates in moderately concentrated aqueous acids has been developed.<sup>20</sup> This procedure relates reaction rate to the activity of water. When

$$\left[ \log k_\psi - \log \left( \frac{h_0}{h_0 + K_{SH^+}} \right) \right]^{21}$$

(16) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

(17) M. A. Paul and F. A. Long, *ibid.*, **57**, 1 (1957).

(18) W. M. Schubert and H. K. Latourette, *THIS JOURNAL*, **74**, 1829 (1952).

(19) [S] represents concentration of unprotonated substrate, and  $[S]_{st}$  the stoichiometric substrate concentration:  $[S]_{st} = [S] + [SH^+]$ .

(20) I. F. Bunnett, *THIS JOURNAL*, **82**, 499 (1960).

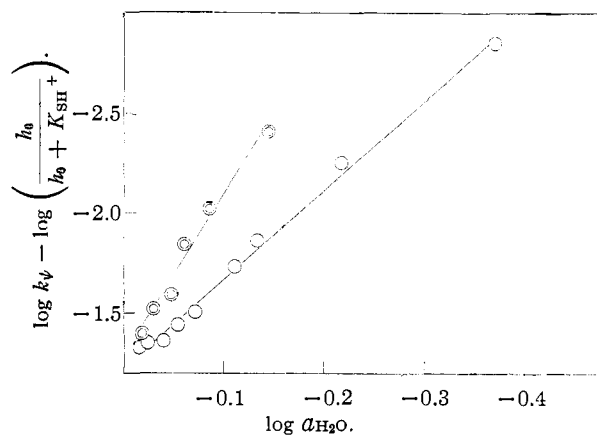


Fig. 5.—Relation of hydrolysis rate of I to activity of water: O, HCl; ⊙, HClO<sub>4</sub>; least squares lines are drawn.

is plotted against  $\log a_{H_2O}$ , in general a linear plot is obtained, and the slope constitutes a parameter,  $w$ , characteristic of the reaction.

When the data for hydrolysis of I in hydrochloric and perchloric acids (Table III) were plotted in this new fashion, straight lines were obtained. The plots are shown in Fig. 5.<sup>22</sup> The slopes ( $w$ -values) are +4.5 in hydrochloric acid and +8.2 in perchloric acid. It is normal for the  $w$ -value to be considerably higher in perchloric than in hydrochloric acid. To illustrate,  $w$  for hydrolysis of  $\gamma$ -butyrolactone<sup>23</sup> is +5.9 in hydrochloric acid and +8.5 in perchloric acid.

Bunnett<sup>20</sup> has shown that reactions of rate-determining proton transfer (e.g., enolization of acetophenone<sup>24</sup>) have high  $w$ -values in the vicinity of +6. Reactions in which water acts as a nucleophile in the slow step (e.g., hydrolyses of carboxamides, of diethyl ether,<sup>25</sup> of ethyleneimmonium ion<sup>26</sup>) have, in contrast,  $w$ -values of about +1 to +3. It is reasoned, then, that a  $w$ -value of about +6 indicates that water is involved in the rate-determining transition state as a proton transfer agent.

The  $w$ -values for hydrolysis of I are indicative of rate-determining proton transfer. The mechanism shown in Chart I, which is an elaboration of that of Bunnett and Hoey,<sup>3</sup> is proposed to accommodate this conclusion.

In this mechanism the hydrated proton is depicted as  $H(H_2O)_n^+$  in recognition of the likelihood that there are several water molecules of hydration.<sup>27</sup> Water is represented as attacking aromatic

(21)  $(h_0/(h_0 + K_{SH^+}))$  is approximately equal to  $[SH^+]/[S]_{st}$ , that is, to the fraction of the substrate which is protonated. Thus, what is plotted against  $\log a_{H_2O}$  is the logarithm of the observed rate coefficient divided by the fraction of the substrate which is protonated. With very weakly basic substrates, one plots  $(\log k_\psi + H_0)$  against  $\log a_{H_2O}$ . With very strongly basic substrates, one plots  $\log k_\psi$  directly against  $\log a_{H_2O}$ .

(22) That the plots show some scatter is not alarming. One must bear in mind that a difference between two large quantities is being plotted, with consequent magnification of random disturbances.

(23) F. A. Long, F. B. Dunkle and W. F. McDevit, *J. Phys. Colloid Chem.*, **55**, 829 (1951).

(24) L. Zucker and L. P. Hammett, *THIS JOURNAL*, **61**, 2791 (1939).

(25) J. Koskikallio and E. Whalley, *Can. J. Chem.*, **37**, 788 (1959).

(26) J. F. Bunnett and F. Olsen, *Absts. Am. Chem. Soc. Meeting*, Cleveland, Ohio, April, 1960, p. 77-O.

(27) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p. 81.

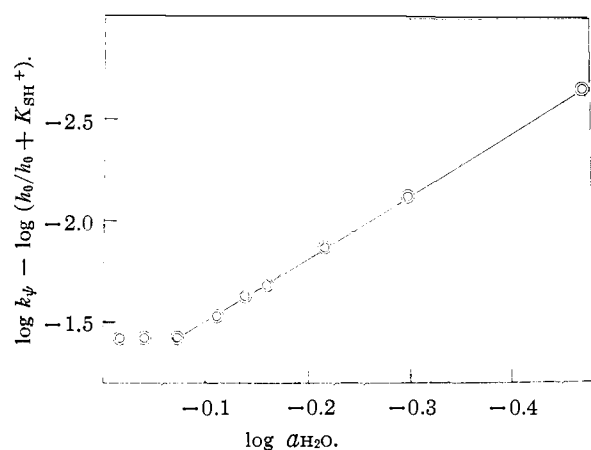
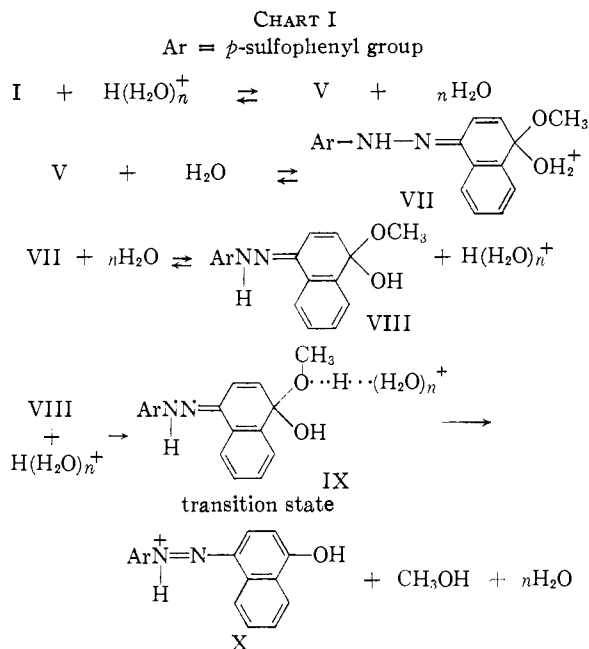


Fig. 6.—Relation of hydrolysis rate of II to activity of water; reactions in HCl solutions; the line drawn ignores the first two points.

carbon in V, leading to intermediate VII, for several reasons which have been cited<sup>3</sup> and particularly because hydrolysis of 4-phenylazo-1-naphthyl methyl ether by  $\text{H}_2\text{O}^{18}$  gives  $\text{O}^{18}$ -labeled azonaphthol.<sup>28</sup>



An additional important consideration is that if water attacked the methyl carbon of V, effecting a synchronous  $\text{S}_{\text{N}}2$  displacement, a  $w$ -value of about +2 would be expected.

The slow step in this mechanism is a general acid-catalyzed detachment of the methoxy group from intermediate VIII. This is reminiscent of a mechanism recently proposed for the aminolysis of esters.<sup>29</sup> An alternate possibility, differing slightly from the mechanism of Chart I, is that removal of a proton from VII may be concerted with general acid-catalyzed detachment of the methoxy group. The two steps,  $\text{VII} \rightarrow \text{VIII}$  and  $\text{VIII} \rightarrow \text{X}$ , may merge into one. A concerted set of proton trans-

(28) J. F. Bunnett, E. Buncel and G. B. Hoey, unpublished work.

(29) J. F. Bunnett and G. T. Davis, *THIS JOURNAL*, **82**, 665 (1960).

fers may occur within a cluster of water molecules grouped about the oxonio ( $-\text{OH}_2^+$ ) and methoxy groups of VII.

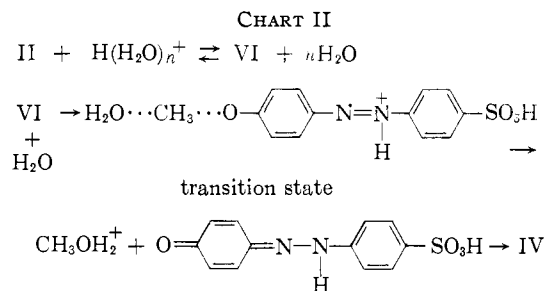
One feature of this mechanism might appear inconsistent with some of our own results. This is the postulate of general acid catalysis in the slow step. As described above, our experiments in the dilute acid region indicated specific oxonium ion catalysis. The conflict can be reconciled if the parameter  $\alpha$  (of the Brønsted catalysis law,<sup>4,30</sup>) for this reaction is close to unity. In such a case general acid catalysis would be difficult to detect by the standard experiment in buffered solutions such as we performed.

**Hydrolysis of 4-(*p*-Sulfophenylazo)-anisole (II).**—Our only kinetic measurements were in moderately concentrated hydrochloric acid solutions. A rate maximum was again observed (Table IV). Plots of  $\log(k_{\psi}[\text{S}]_{\text{st}}/[\text{S}])$  against both  $-H_0$  and  $\log[\text{H}_3\text{O}^+]$  were definitely curved; in traditional phraseology, reaction rate is correlated neither with  $h_0$  nor with oxonium ion concentration.

When the new procedure of plotting

$$\left[ \log k_{\psi} - \log \left( \frac{h_0}{h_0 + K_{\text{SH}^+}} \right) \right]$$

against  $\log a_{\text{H}_2\text{O}}$  was tried, a satisfactory straight line of slope ( $w$ ) + 3.1 was obtained (the first two points being ignored).<sup>31</sup> The plot is shown in Fig. 6. This  $w$ -value is considerably lower than for the hydrolysis of I in hydrochloric acid solutions. Indeed, it is in the range of  $w$ -values characteristic of reactions in which water acts as a nucleophile in the slow step. A mechanism different from that of Chart I therefore seems indicated. The mechanism of Chart II is suggested.



The essence of this mechanism is that it calls for cleavage by nucleophilic attack on the alkyl carbon instead of on the aromatic carbon as in Chart I. Both modes of cleavage of alkyl aryl ethers are known<sup>32</sup> and the balance between the two is sometimes delicate. The two modes of cleavage may be directly competitive<sup>33</sup> or a modest change in the structure of the ether may cause a shift in the sense of cleavage. A change from aryl-oxygen scission (Chart I) to alkyl-oxygen scission (Chart II) with change from the naphthalene series to the benzene series seems not unreasonable.

(30) Reference 27, p. 155.

(31) The least squares slope, considering all points, is +2.8.

(32) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 286 (1951).

(33) The action of the sodium amide-piperidine reagent on methyl *p*-biphenyl ether forms products representing nucleophilic attack both on aromatic carbon (4-piperidinobiphenyl, 68%) and on aliphatic carbon (4-hydroxybiphenyl, 14%); unpublished observations by J. F. Bunnett, T. K. Brotherton, R. Eisenthal and S. W. Williamson.

One would desire confirmation of the sense of cleavage by an oxygen-18 tracer experiment. Also, confirmation of the  $w$ -value by rate measurements in sulfuric or perchloric acid solutions would increase confidence in this interpretation.

### Experimental

**Materials.**—Compound III was prepared by coupling diazotized sulfanilic acid with  $\alpha$ -naphthol in acidic medium according to Slotta and Franke<sup>34</sup>;  $\epsilon$  for the disodium salt at 510  $m\mu$  was 32,960; this compares with 33,000 at 508  $m\mu$  as reported by Müller, Blangey and Fierz-David.<sup>14</sup> Compound III was converted to I (isolated as the dihydrate of its sodium salt) by methylation with methyl sulfate in alkaline medium according to Pfister.<sup>35</sup> At the absorption maximum (405  $m\mu$ )  $\epsilon$  was about 14,200, being a function of the time of residence in the spectrophotometer light beam.

*Anal.* Calcd. for  $C_{17}H_{13}N_2O_4SNa \cdot 2H_2O$ : N, 7.00. Found<sup>36</sup>: N, 6.68, 6.90.

Compound IV was prepared by coupling diazotized sulfanilic acid with phenol in acetate-buffered medium according to Engel.<sup>37</sup> The sodium salt was purified by crystallization from water and dried to constant weight in a vacuum oven. In 0.1  $M$  sodium hydroxide, the absorption maximum was at 435  $m\mu$ ,  $\epsilon$  25,700.

*Anal.* Calcd. for  $C_{12}H_9N_2O_4SNa$ : N, 9.33. Found<sup>36</sup>: N, 9.22, 9.17.

Compound IV was converted to II by methylation with methyl sulfate in alkaline medium.<sup>34,36</sup> The sodium salt was purified by repeated crystallization from water and dried to constant weight in a vacuum oven.

*Anal.* Calcd. for  $C_{13}H_{11}N_2O_4SNa$ : N, 8.91. Found<sup>36</sup>: N, 8.90, 8.91.

**$pK$  Measurements on I.**—Solutions of I in various concentrations of hydrochloric acid were prepared by the rapid mixing of predetermined quantities of an aqueous solution of I (sodium salt) and of hydrochloric acid solutions. The time of mixing was recorded and the solution was quickly introduced into the cell of a Cary recording spectrophotometer. Absorption was measured as a function of time at a pre-set wave length (405 or 550  $m\mu$ ). In most cases measurement was started about 20 sec. after mixing; the maximum time lag was 46 sec. The tracings of absorbance *versus* time were nearly linear and extrapolation to zero time could be done precisely. In no case did the extrapolated value differ from the first recorded value by more than 7%. Zero time (extrapolated) values are given in Table VI. The stoichiometric concentration of I in all solutions was  $4.12 \times 10^{-5} M$ .

**Rate Measurements on Hydrolysis of I.**—For runs in the dilute acid region, appropriate amounts of thermostated standard solutions of I, of the requisite acid and/or salt or buffer were combined in a volumetric flask in the thermostat at 46°. The concentration of I in the reaction solutions was about  $2.3 \times 10^{-4} M$ . Aliquots (5 cc.) were withdrawn at recorded times by pipet and immediately quenched in 0.1  $M$  sodium hydroxide solution in a 50-cc. volumetric flask; the flasks were then filled to the mark with sodium hydroxide. The absorbance at 510  $m\mu$  for each sample was measured by means of a Beckman model B spectrophotometer. Plots of  $\log(A_\infty - A_t)$  against time were good straight lines; the negative of the slope was multiplied by 2.303 to get  $k\psi$ , the pseudo-first order rate coefficient. Occasionally the entire spectrum of an infinity solution was recorded; it was found to match, both qualitatively and quantitatively, the spectrum of III in 0.1  $M$  sodium hydroxide.

Data from a typical run are presented in Table VII.

(34) K. H. Slotta and W. Franke, *Ber.*, **64B**, 86 (1931).

(35) K. H. T. Pfister, *THIS JOURNAL*, **64**, 1521 (1932).

(36) Analysis by Miss Betty Jean Pegram, Venereal Disease Experimental Laboratory, U. S. Public Health Service, through the courtesy of Dr. Leon Freedman.

(37) K. H. Engel, *THIS JOURNAL*, **51**, 2986 (1929).

TABLE VII

### HYDROLYSIS OF I; A TYPICAL RUN

Initial concentrations: I,  $2.30 \times 10^{-4} M$ ; HCl, 0.00925  $M$ ; KCl, 0.138  $M$ ; temperature, 46.1°

Time, min.	Absorbance at 510 $m\mu$	$A_\infty - A_t$	$\log(A_\infty - A_t)$	$\frac{1}{A_\infty - A_t}$
5.00	0.054	0.691	0.840	
20.00	.112	.633	.801	
36.0	.168	.577	.761	
52.0	.217	.528	.723	
65.0	.260	.485	.686	
80.0	.299	.446	.649	
95.0	.335	.410	.613	
110.0	.369	.376	.575	
1080( $\infty$ )	.747			
1080( $\infty$ )	.743			

The slope of the plot of  $\log(A_\infty - A_t)$  against time was  $-0.002529 \text{ min.}^{-1}$  and  $k\psi$  is then  $0.00582 \text{ min.}^{-1}$ .

For runs in the concentrated acid region, 10 cc. of a  $2.30 \times 10^{-3} M$  solution of I was combined with exactly 90 cc. of a strongly acidic solution of known concentration, all solutions and operations being at thermostat temperature. The vessel was shaken quickly to ensure thorough mixing, and samples were withdrawn at recorded times by means of a 5-cc. all-glass syringe fitted with a brass stop to assure constant volume on each filling. Use of this syringe enabled samples to be withdrawn at intervals as short as 3 seconds; such speed was necessary in dealing with reactions having half-lives as short as 33 sec. The samples were quenched by addition to 50-cc. portions of 1  $M$  sodium hydroxide in erlenmeyer flasks, and the photometric measurements and calculations were performed as before.

**Rate Measurements on Hydrolysis of II.**—Reaction solutions were prepared quantitatively at room temperature. The concentration of II was always about  $3.1 \times 10^{-4} M$ . Aliquots (5 cc.) were sealed (at room temperature) into ampoules, and all the ampoules for a run were placed in the thermostat at the same time. Single ampoules were removed at recorded times and stored in a refrigerator until all the ampoules from a run could be opened at once. Each 5-cc. aliquot was diluted to 50 cc. with 1  $M$  sodium hydroxide, and the absorbances of the resulting solutions were read at 435  $m\mu$ . Rate coefficients were reckoned as before, and then were corrected to take account of expansion of the solvent between 25 and 97°. The values reported in Table IV are so corrected.

The spectrum between 360 and 700  $m\mu$  of a quenched infinity sample was identical with that of a mock infinity solution (a solution of IV in the concentration expected if hydrolysis were quantitative). Also, the spectrum of an infinity aliquot diluted with *ca.* 9  $M$  hydrochloric acid was identical with that of a mock infinity aliquot similarly treated. (The latter spectrum showed a maximum at 468  $m\mu$ .) These observations confirm that hydrolysis of II forms IV.

**Data in Tables III and IV from the Literature.**—Activity of water data for hydrochloric acid are from Randall and Young<sup>38</sup> and Åkerlöf and Teare,<sup>39</sup> and for perchloric acid from Pearce and Nelson<sup>40</sup> and Robinson and Baker.<sup>41</sup>  $h_0$  values are by interpolation of data given by Paul and Long.<sup>17</sup> These data are all for 25°; unfortunately data for higher temperatures are largely unavailable.

**Acknowledgment.**—The counsel of Professor W. M. Schubert in interpretation of our results is greatly appreciated.

(38) M. Randall and L. E. Young, *THIS JOURNAL*, **50**, 989 (1928).

(39) G. Åkerlöf and J. W. Teare, *ibid.*, **59**, 1855 (1937).

(40) J. N. Pearce and A. F. Nelson, *ibid.*, **55**, 3075 (1933).

(41) R. A. Robinson and O. J. Baker, *Trans. Roy. Soc. New Zealand*, **76**, 250 (1946).