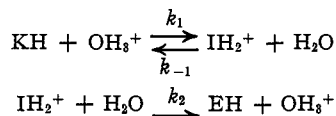


[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

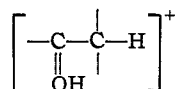
## The Mechanism of the Acid Catalyzed Enolization of Acetophenone Derivatives

BY LOIS ZUCKER<sup>1</sup> AND LOUIS P. HAMMETT

The rate determining step in the enolization of ketones is probably a proton transfer, one of the two necessary to convert ketone to enol. The mechanism of this reaction when catalyzed by oxonium ion is<sup>2</sup>



where KH is the keto form of the ketone, EH is the enol form, and  $\text{IH}_2^+$  is the intermediate ion



In this reaction, as in most others subject to acid or base catalysis, more than one proton transfer is involved, and the question as to which of these is the rate determining step is an important one. Its significance is especially emphasized by the recent work of Bonhoeffer<sup>3</sup> on the relative rates of proton and deuteron transfer in the enolization reaction, and of Cohn and Urey<sup>4</sup> in the oxygen exchange of ketones with solvent.

A possible method of attack upon the mechanism problem is based upon the quantitative correlation which must exist between the rate of proton transfer to or from the substrate in a catalyzed reaction, and the acid or base strength of the substrate. The necessity of the correlation follows from the following considerations. A linear relation is quite generally observed between the logarithms of the ionization constants of a series of catalysts and the logarithms of the specific catalytic rate constants for a reaction with a single substrate.<sup>2</sup> All these specific rates are equal to, or proportional to, the specific rates of transfer of a proton either from acidic substrate to basic catalyst, or from acid catalyst to basic substrate.<sup>2</sup> Consequently, the observed linear relation must be based on a more general linear relation between the logarithms of the ionization constants of any

series of bases (acids), and the logarithms of the specific rates of transfer of a proton between a given acid (base) and the series of bases (acids). Applying this generalization to the case of variable catalyst-fixed substrate gives the observed relation between rates and strengths of catalysts; applying it to the case of variable substrate-fixed catalyst, allows the prediction of a linear relation between the logarithms of the appropriate basic (acidic) ionization constants of a series of substrates which can undergo the same acid (base) catalyzed reaction, and the logarithms of the specific catalytic rate constants for the reaction with a single catalyst.<sup>5</sup>

Thus for the enolization catalyzed by oxonium ion, as outlined above, the following should be true equations when the ketone is varied

$$\log k_1 = -\alpha \log K_{\text{KH}} + \beta \quad (1)$$

$$\log k_2 = \alpha' \log K_{\text{EH}} + \beta' \quad (2)$$

where

$$K_{\text{KH}} = \frac{a_{\text{H}^+} a_{\text{KH}}}{a_{\text{IH}_2^+}}$$

and

$$K_{\text{EH}} = \frac{a_{\text{H}^+} a_{\text{EH}}}{a_{\text{IH}_2^+}} = K_{\text{KH}} K_{\text{Enolization}}$$

and  $\alpha$ ,  $\beta$ ,  $\alpha'$ ,  $\beta'$  are constants for the series of ketones with oxonium ion. If step 1 in the enolization is rate determining, it should be true that

$$\log k = \log k_1 c_{\text{OH}_3^+} = -\alpha \log K_{\text{KH}} + \beta'' \quad (3)$$

where

$$k = -\frac{1}{c_{\text{KH}}} \frac{dc_{\text{KH}}}{dt}$$

$c_{\text{OH}_3^+}$  is constant for all the ketones, and no other catalyst is present in the solution. If step 2 is rate determining

$$\log k = \log k_2 c_{\text{OH}_3^+} / K_{\text{KH}} = (\alpha' - 1) \log K_{\text{KH}} + \alpha' \log K_{\text{Enol.}} + \beta'''$$

and no linear relation is to be expected between  $\log k$  and  $\log K_{\text{KH}}$ , unless all changes in structure concerned have quantitatively similar effects on both equilibrium constants.

There are some limitations on the applicability of these rate-equilibrium constant relationships concerned with allowable differences in structure of the bases (acids) being compared, which can be

(1) Part of a thesis submitted by Lois Zucker in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University. The material was presented at the Milwaukee meeting of the American Chemical Society, September, 1938.

(2) Pedersen, *J. Phys. Chem.*, **38**, 581 (1934).

(3) Bonhoeffer, *Trans. Faraday Soc.*, **34**, 252 (1938).

(4) Cohn and Urey, *THIS JOURNAL*, **60**, 679 (1936).

(5) Pedersen, Dissertation, Copenhagen, 1932; Hammett and Pfuger, *THIS JOURNAL*, **55**, 4079 (1933); Bell, *Proc. Roy. Soc. (London)*, **164**, 414 (1936).

deduced from the results of comparing specific rates obtained for a series of catalysts and the acid (base) strengths of the catalysts. Acids with varying numbers of acidic hydrogens, or their conjugate bases, can be compared only if statistical corrections are applied to their experimentally determined ionization constants.<sup>2</sup> Acids or bases differing largely in structure cannot be compared; substitution on the same atom which carries or can receive the acidic hydrogen,<sup>6</sup> and changes in charge type appear to be such large changes in structure.

Lack of quantitative information about any basic or acidic ionization constants of typical substrates or their conjugate acids or bases, has prevented the practical application of these expectations. Recently, however, a method has been developed for measuring the basic ionization constants of extremely weak bases by the changes in their ultraviolet absorption spectra on ionization in various sulfuric acid-water solutions<sup>7a</sup>;  $pK$ 's are already available for acetophenone,<sup>7a</sup>  $p$ -bromoacetophenone<sup>7b</sup> and  $p$ -methylacetophenone,<sup>7b</sup> and to these we have now added propiophenone,  $n$ -butyrophenone and isobutyrophenone. The rates of enolization of these ketones, the catalyst being oxonium ion, already have been reported.<sup>8</sup> Equation (1) should apply for all these acetophenone derivatives. They are all monoacid bases, so there is no necessity for statistical corrections. When substrate is fixed and catalyst changed, points for alpha substituted aliphatic carboxylic acids or their ions fall on the same line as points for substituted benzoic acids or their ions<sup>2</sup>; it is therefore very improbable that any of the substitutions involved with these ketones is sufficiently drastic to invalidate equation (1). (This set of ketones would not be suitable for a comparison involving the use of equation (2), because of the substitution on the carbon carrying the acidic hydrogen.) Then if step 1 is rate determining, equation (3) is a true equation and a plot of  $\log k$  against  $\log K_{KH}$  should be a straight line. If step 2 is rate determining, equation (3) is not a true equation, because the relative effects of side chain substitution and of ring substitution cannot be expected to be the same on  $\log k_2$  as on  $\log K_{KH}$ ; in this case

the plot of  $\log k$  against  $\log K_{KH}$  will not be a straight line.

The rates actually measured were the rates of iodination of the ketones, which should equal the rates of enolization.<sup>9,2</sup> Before making the comparison between these rates and the base strengths of the ketones, we investigated the nature of the acid catalysis of the iodination of acetophenone, since if general acid catalysis as distinguished from specific hydrogen ion catalysis<sup>2</sup> is not proved definitely, there is the possibility of an iodination mechanism differing fundamentally from that outlined. General acid catalysis has been established for the halogenation of acetone alone among ketones.<sup>10</sup>

### Experimental

**Materials.**—The physical constants and details of purification of the ketones used were given in the preceding paper.<sup>8</sup>

Chloroacetic acid was recrystallized four times from benzene, m. p. 63.0–63.2°; acid titration 99.83% of theoretical.

**Method:  $pK'$  Measurements.**—The method of Flexser, Hammett and Dingwall<sup>7a</sup> was used. In this technique the temperature of the solution was  $22 \pm 5^\circ$ ; closer temperature control was considered unnecessary because of the very small temperature coefficients characteristic of absorption of ultraviolet and visible light, and of the ionization equilibrium. However, the few cases known with very large temperature coefficients of light absorption, all involve ions.<sup>11</sup> We have measured the absorption of isobutyrophenone in 89.7% sulfuric acid, in which it is nearly completely ionized, at room temperature, and at  $45 \pm 0.2^\circ$ . Since the results agreed within the error of measurement, and since the water jacketing is extremely troublesome in the small space available around the absorption cell, all the other measurements reported here were made without temperature control, as previously.

The sodium salicylate treatment<sup>12</sup> of photographic plates for increasing contrast at very short wave lengths was found very useful for determining extinction coefficients from 2100 to 2300 Å.

The "isobestic point" method<sup>7a</sup> of calculating the  $pK'$ 's was used. The use of areas under the curves representing extinction coefficients as a function of wave length, over intervals of 100 Å., gave only slightly better results than the use of the extinction coefficients themselves at wave lengths in the centers of these intervals.

(9) Lapworth, *J. Chem. Soc.*, **85**, 30 (1904).

(6) Pflüger, Abstracts of papers presented before the Division of Phys. and Inorg. Chem., Am. Chem. Soc., April, 1939, p. 23; Brønsted and Pedersen, *Z. physik. Chem.*, **108**, 185 (1924); Junell, Dissertation, Uppsala, 1935.

(7) (a) Flexser, Hammett and Dingwall, *This Journal*, **57**, 2103 (1935); (b) Flexser and Hammett, *ibid.*, **60**, 885 (1938).

(8) Zucker and Hammett, *ibid.*, **61**, 2779 (1939).

(10) (a) Dawson and Carter, *ibid.*, 2282 (1926); Dawson and Spivey, *ibid.*, 2180 (1930); (b) Dawson and Key, *ibid.*, 1239, 1248 (1928); Dawson, Hoskins and Smith, *ibid.*, 1884 (1929); Dawson and Smith, *ibid.*, 2530 (1929); 79 (1930); Dawson and Spivey, *ibid.*, 2612 (1932).

(11) Scheibe, *Z. Elektrochem.*, **35**, 701 (1929); Kortüm, *Z. physik. Chem.*, **B30**, 315 (1935); Mukerji, *J. Phys. Chem.*, **32**, 1834 (1928).

(12) Tien Kui, *Compt. rend.*, **201**, 1348 (1935); Terrien, *ibid.*, **203**, 211 (1935); Tien Kui, *ibid.*, **203**, 1144 (1936); Montague and Ricard, *ibid.*, **202**, 477 (1936).

**Rate Measurements.**—The reaction was studied by the colorimetric technique previously described.<sup>8</sup> Differences in technique arise from two features of these experiments, the low acidity of the solutions and the necessity for maintaining constant ionic strength. The rate of the oxidation of iodide ion to iodine, produced by potassium iodate in all cases, is too slow in this range of hydrogen ion concentration when only a slight excess of iodate is present. The concentration of potassium iodate necessary to prevent any accumulation of iodide ion could be calculated from the known rate of the iodide-iodate reaction,<sup>13</sup> the hydrogen ion concentration of the solution, and an approximate figure for the rate of the iodination reaction. In all runs except 18, 0.01 molar potassium iodate was more than sufficient; in run 18, with a hydrogen ion concentration of 0.001, the concentration of iodate used was 0.08. Because of the necessity of having known concentrations of potassium iodate it was not possible to start the reaction by the addition of an excess of solid potassium iodate as previously; instead, 0.1 cc. of an aqueous potassium iodide solution was added to a known volume of solution containing known concentrations of ketone, catalyst, potassium iodate, and sodium perchlorate.

The decrease in hydrogen ion concentration due to making up the iodine solution from iodide and iodate, equal to twice the initial iodine concentration (and most usually in the neighborhood of 0.0004) is just appreciable in the most dilute perchloric acid solutions; the calculated hydrogen ion concentration was corrected for this effect wherever necessary. The change in hydrogen ion concentration during a run, equal to half the change in iodine concentration, was negligible for all runs.

The ionic strength was maintained at 0.21 by the addition of the appropriate amount of sodium perchlorate. Buffer mixtures were made up from standard carbonate-free sodium hydroxide solution, and chloroacetic acid solution standardized against the sodium hydroxide. The composition of the buffer mixtures was calculated by the use of the value 0.0025 for the ionization constant of chloroacetic acid.<sup>14</sup>

The identity of the principal reaction product was checked by running a large scale bromination of acetophenone in 0.5 molar hydrochloric acid. The mechanism of the bromination should be identical with that of the iodination, and phenacyl bromide has the advantage over phenacyl iodide of being a solid at room temperature, and quite stable away from contact with the solution from which it is prepared. Bromine was added to five liters of a saturated solution of acetophenone (about 0.045 molar) in 0.5 molar hydrochloric acid, the bromine being at approximately a fifth the concentration of the acetophenone. By the time the solution was colorless (about twenty-four hours), a large portion of the product had come out of solution in well-formed crystals (about 6.5 g.). The melting point of the crystals after thorough washing was 47.5–50°. One recrystallization from petroleum ether brought the melting point to 49–50°.

**Rate Calculations.**— $k$ , the first order specific rate, could in all cases be obtained from the slope of a plot of colorimeter settings against time, using

the simplified form<sup>8</sup> which the integrated rate equation takes if only a few per cent. of the ketone present is allowed to react. The slope of the plot of the various values of  $k$  for perchloric acid solutions against concentration of perchloric acid is the specific catalytic constant for oxonium ion. The results in the buffer solutions were fitted to the equation

$$k - k_{\text{OH}_3^+} c_{\text{OH}_3^+} = k_{\text{HC}} c_{\text{HC}} + k_{\text{C}^-} c_{\text{C}^-}$$

by the method of least squares, using the value of  $k_{\text{OH}_3^+}$  determined in perchloric acid solutions. HC refers to chloroacetic acid, C<sup>-</sup> to chloroacetate ion.

## Results

The results of the rate measurements are presented in Table I. The calculated  $k$ 's were obtained by the use of the specific catalytic constants listed. Water catalysis is too small to measure. The effect of chloroacetate ion is small: only in experiment 18 does the calculated contribution of the chloroacetate catalysis amount to more than 4% of the total rate. While further iodination of

TABLE I  
RATES OF IODINATION IN PERCHLORIC ACID SOLUTIONS AND IN BUFFER MIXTURES AT 25.00°

Expt.	Stoichiometric concentrations			$k \times 10^4$ (min. <sup>-1</sup> )	
	HClO <sub>4</sub>	NaOH	HC	Obsd.	Calcd.
1	0.1916			1.410	1.423
2	.2076			1.597	1.550
3	.2108			1.548	1.572
9	.2004			1.491	1.490
10	.1037			0.773	0.772
11	.0502			.372	.374
12		0.1284	1.028	.465	.466
13		.1940	0.679	.245	.243
14		.1840	1.472	.625	.624
15	.0494			.367	.368
17		.0705	0.564	.296	.297
18		.1273	.1820	.0356	.0363

Least squares constants in units of (min.  $\frac{\text{mol}}{\text{liter}}$ )<sup>-1</sup>

$k_{\text{HC}}$	$0.388 \times 10^{-4}$
$k_{\text{C}^-}$	$.06 \times 10^{-4}$
$k_{\text{OH}_3^+}$	$7.45 \times 10^{-4}$

the initial product, phenacyl iodide, by means of the acid catalyzed mechanism is so slow as to be negligible with these high constant acetophenone concentrations, iodine substitution very much favors further iodination by the basic mechanism.<sup>15</sup> The effect of a basic catalyst consequently is determined by a competition between the reaction with acetophenone, the reaction with  $\omega$ -iodoacetophenone, with maximally one-fiftieth the con-

(13) "International Critical Tables," Vol. VII, p. 149.

(14) Randall and Failey, *Chem. Rev.*, **4**, 291 (1927).

(15) Hughes, Watson and Yates, *J. Chem. Soc.*, 3318 (1931); Watson and Yates, *ibid.*, 1207 (1932); Pedersen, *J. Phys. Chem.*, **38**, 601, 999 (1934).

TABLE II  
 EXTINCTION COEFFICIENTS AND BASE STRENGTH OF PROPIOPHENONE

$\lambda$	% H <sub>2</sub> SO <sub>4</sub>								
	0	62.4	69.9	73.7	75.3	77.5	79.8	88.2	95.8
3800		(2)	(7)	13	18	32	48	100	178
3700		(4)	20	48	75	122	164	330	460
3600		9	60	150	210	330	460	790	1050
3500		19	126	330	450	670	960	1450	1700
3400		42	230	550	760	1100	1440	2020	2250
3300		86	380	780	1070	1470	1880	2390	2550
3200		178	560	1080	1480	2000	2460	3200	3520
3100	110	460	1150	2240	2930	4400	5800	8700	10300
3000	290	1060	2730	5800	7400	11000	14000	19800	21500
2900	810	1890	4370	7800	9600	13600	16100	19800	19900
2800	1140	2430	4900	7600	8700	11400	12200	11400	10500
2700	1330	4100	6100	6900	7500	7600	7400	5200	4150
2600	4070	8600	8900	7600	7100	6100	4800	1900	1270
2500	10500	10800	9200	7000	5800	4700	2800	690	400
2400	11000	8200	6000	4200	3200	2500	1500	460	410
2300	6000	3650	2360	1700	1240	1000	780	500	630
2200	2130	1350	1450	1450	1900	2350	3000	3000	3500
$H_0$		-4.58	-5.52	-6.01	-6.21	-6.46	-6.79	-8.00	-8.84
$pK'$			-6.28	-6.29	-6.32	-6.25	-6.25		
			$\pm 0.05$	$\pm 0.06$	$\pm 0.05$	$\pm 0.03$	$\pm 0.06$		

Average value of  $pK'$   $-6.28 \pm 0.06$ . Isobestic point,  $\lambda$  2680, ext. coeff. 7300. Reference curves, 62.4%, 88.2%.

 TABLE III  
 EXTINCTION COEFFICIENTS AND BASE STRENGTH OF *n*-  
 BUTYROPHENONE

$\lambda$	% H <sub>2</sub> SO <sub>4</sub>					
	64	73.5	75.2	76.6	78.1	89.7
3800		(15)	25	32	40	109
3700		60	88	123	149	450
3600		190	270	350	430	980
3500	(6)	420	580	700	870	1570
3400	20	700	950	1100	1300	2300
3300	85	1040	1320	1530	1770	2580
3200	185	1430	1800	2100	2410	3610
3100	450	3070	3970	4700	5500	10100
3000	1070	7200	9400	10800	13400	21100
2900	1900	9800	12200	13600	15100	18800
2800	2420	9000	9900	10700	11200	10200
2700	4100	7700	7500	7300	7000	4370
2600	8600	7500	6200	5500	4680	1590
2500	11200	6200	5000	3960	2980	800
2400	8300	3600	2870	2270	1710	780
2300	3650	1480	1220	1050	940	960
2200	1500	2210	2500		3000	
$H_0$		-5.99	-6.19	-6.36	-6.54	
$pK'$		-6.21	-6.22	-6.23	-6.20	
		$\pm 0.07$	$\pm 0.06$	$\pm 0.07$	$\pm 0.08$	

Average value of  $pK'$   $-6.21 \pm 0.06$ . Isobestic point,  $\lambda$  2710, ext. coeff. 7650. Reference curves, 64%, 89.7%.

centration of the acetophenone but with a much higher specific reaction rate, and the reaction with  $\omega,\omega$ -diiodoacetophenone, maximum concentration unknown, but with a still very much higher specific reaction rate. Any appreciable amount of secondary iodination should produce curvature in the time curves (although possibly too small a

curvature to be apparent), and a definite lack of constancy of the apparent specific catalytic rates with varying buffer concentration. Neither of these effects appeared in the results. The calculated  $k_c$  is probably not a correct value for the specific catalytic constant for the introduction of the first iodine, but the whole effect of chloroacetate ion is so small that the calculated  $k_{HC}$  is undoubtedly quite good. The reaction is certainly subject to general acid catalysis.

The results of the absorption measurements are presented in Tables II-IV. Figures in parentheses are somewhat less reliable than the others. Methyl substitution in the side chain is much more effective in changing the base strength than it is in changing the absorption spectra of the ketone and its conjugate acid formed by the addition of a proton to the oxygen. The spectra of these ketones are practically identical with that of acetophenone within the error of measurement,<sup>7a</sup> (average deviation of the extinction coefficient from the mean 5%). Comparison of the spectra of the conjugate acids cannot be made so directly because data are not available for all the compounds in the same highly acid medium, and there is a medium effect on the absorption distinct from the effect of changing acidity on the ionization equilibrium<sup>7a</sup>; however, specific differences between the spectra of the conjugate acids of the various ketones are certainly small. Alpha

TABLE IV  
 EXTINCTION COEFFICIENTS AND BASE STRENGTH OF ISOBUTYROPHENONE

$\lambda$	% H <sub>2</sub> SO <sub>4</sub>											
	0	65	69.7	73.6	75.3	77.4	78.6	79.6	81.5	83.0	89.7	96
3800				(8)	(12)	(23)	(40)	48	73	89	145	178
3700			(6)	(28)	46	88	130	155	230	268	440	540
3600			(19)	77	115	220	298	385	540	600	930	1110
3500		(6)	46	150	223	435	580	710	990	1090	1570	1760
3400		(22)	81	247	367	610	810	1080	1400	1530	2100	2290
3300	62	59	143	400	520	820	1130	1450	1850	1970	2600	2760
3200	91	149	298	650	830	1280	1710	2200	2820	3050	4000	4500
3100	140	405	760	1600	2000	3300	4230	5250	7500	8300	11500	13350
3000	310	920	1630	3510	4110	6800	9300	10700	13500	15100	20300	21000
2900	840	1610	2660	4650	5600	8300	10000	11800	13800	14600	16900	18400
2800	1120	2140	3200	4970	5600	6800	8200	8600	9900	9200	9500	8700
2700	1400	3950	5300	6400	6500	6600	6500	6400	6100	4900	3850	3480
2600	4800	8400	9200	9600	8600	7000	6700	5900	4770	3350	1500	1120
2500	10500	10400	10000	9600	8100	6200	5800	4570	3550	2230	750	550
2400	10200	7800	7200	5800	4440	3730	3290	2830	2050	1390	600	620
2300	5200	3400	2910	2380	1910	1570	1400	1280	1100	880	760	950
2200	(1730)	(1350)	(1490)	(1650)	(1620)	(1870)	(2200)	(2800)	(2960)		(3650)	(3650)
$H_0$			-5.50	-6.00	-6.20	-6.45	-6.61	-6.76	-7.07	-7.32	-8.15	
$pK'$				-6.76	-6.79	-6.68	-6.69	-6.67	-6.65	-6.74		
				$\pm 0.07$	$\pm 0.06$	$\pm 0.04$	$\pm 0.03$	$\pm 0.06$	$\pm 0.08$	$\pm 0.07$		

Average value of  $pK'$   $-6.72 \pm 0.07$ . Isobestic point,  $\lambda$  2710, ext. coeff. 6500. Reference curves, 65%, 89.7%.

methyl substitution definitely reduces the base strength—compare acetophenone, with a  $pK'$  of  $-6.03$ ,<sup>7a</sup> with the figures for propiophenone and isobutyrophenone. The difference between the  $pK'$ 's of propiophenone and *n*-butyrophenone is within the error of measurement.

### Discussion

The comparison of the rates of enolization of these ketones with their base strengths is shown in Fig. 1; the rectangle about each point indicates the precision measures of the two measurements. There is obviously no simple functional relationship between the two sets of data, so that step 1 cannot be exclusively rate determining. Other possibilities which must be considered are (a) step 2 is rate determining, (b) steps 1 and 2 both affect the rate, (c) the enolization is a one step, termolecular reaction rather than two separate bimolecular reactions. Pedersen<sup>2</sup> objects to c, because product terms of the type  $kc_{HA}c_A$  should be of much greater magnitude than terms  $kc_{HA}$  or  $kc_A$  in the rate equation. This is definitely not the case, although some of Dawson's experiments<sup>10a</sup> may be interpreted to indicate the presence of small product terms.

Both an acid and a base are necessary for any of these mechanisms. Mechanism c was rejected because both the acid and the base appear in the rate determining step and should therefore appear

in the rate equation. But it would seem that mechanism b as well as mechanism c, should call for first order specific rates varying with the concentrations of two catalysts; the concentrations of one acid and one basic catalyst are certainly concerned in rate determining processes, and, in general, if more than one catalyst is present, catalyst pairs which are not conjugate are no less probable than catalyst pairs which are conjugate.

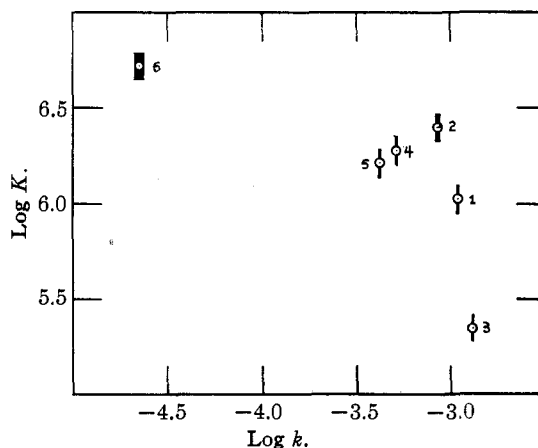


Fig. 1.—1, Acetophenone; 2, *p*-bromoacetophenone; 3, *p*-methylacetophenone; 4, propiophenone; 5, *n*-butyrophenone; 6, isobutyrophenone.

The general rate equation for the two step mechanism, assuming only that the ketonium ion is a kinetically unstable intermediate, is, as Pedersen has shown<sup>2</sup>

$$-\frac{1}{c_{\text{KH}}} \frac{dc_{\text{KH}}}{dt} = k = \frac{\sum k_{1\text{BH}^+} c_{\text{BH}^+} + \sum k_{2\text{B}} c_{\text{B}}}{\sum k_{1\text{B}} c_{\text{B}} + \sum k_{-1\text{B}} c_{\text{B}}} = \frac{\sum k_{1\text{BH}^+} c_{\text{BH}^+}}{1 + \frac{\sum k_{-1\text{B}} c_{\text{B}}}{\sum k_{2\text{B}} c_{\text{B}}}}$$

where  $\text{BH}^+$  represents any acid, B any base, and summation is to be taken over all acids and bases in the solution. These designations are not intended to specify the charge type of the acids and bases. Let

$$F = \frac{\sum k_{-1\text{B}} c_{\text{B}}}{\sum k_{2\text{B}} c_{\text{B}}}$$

When  $F \ll 1$ , step 1 is rate determining and  $k = \sum k_{1\text{BH}^+} c_{\text{BH}^+}$ ; when  $F \gg 1$ , step 2 is rate determining, and since

$$k_{1\text{BH}^+} c_{\text{BH}^+} = c_{\text{H}^+} k_{-1\text{B}} c_{\text{B}} / K_{\text{KH}} \quad (4)$$

for every acid-base pair present,  $k$  reduces to

$$\frac{\sum k_{2\text{B}} K_{\text{BH}^+} c_{\text{BH}^+}}{K_{\text{KH}}}$$

which is in the proper experimental form. When  $F \sim 1$ , we have mechanism b, and it is usually assumed that  $k$  reduces to the observed form because  $F$  is independent of the relative concentrations of the various catalysts, and hence a constant. This would be true in general only if

$$\frac{k_{2\text{B}}}{k_{-1\text{B}}} = \frac{k_{2\text{C}}}{k_{-1\text{C}}} = \frac{k_{2\text{D}}}{k_{-1\text{D}}} = \dots \quad (1)$$

for all bases which might be present, but this is highly improbable. Application of the log-log relation between rates and equilibrium constants for protolytic reactions yields the following:

$$\begin{aligned} \log k_{-1\text{B}} &= \alpha \log K_{\text{B}} + \beta \\ \log k_{2\text{B}} &= \alpha' \log K_{\text{B}} + \beta' \\ k_{-1\text{B}} &= b k_{2\text{B}} (K_{\text{B}})^{(\alpha - \alpha')} \\ F &= \frac{b \sum K_{\text{B}}^{(\alpha - \alpha')} k_{2\text{B}} c_{\text{B}}}{\sum k_{2\text{B}} c_{\text{B}}} \end{aligned}$$

The requirement (1) and the constancy of  $F$  with changing relative catalyst concentrations are equivalent to the requirement that  $\alpha = \alpha'$ , *i. e.*, that the linear relation between the logarithms of the ionization constants of a series of bases and the logarithms of the rates of acceptance of one proton of the dibasic acid  $[\text{RC}(\text{OH})\text{CH}_2]^+$  shall have the same slope as that for the same set of bases and the other proton of the dibasic acid, the one hydrogen being bound to carbon, the other to oxygen. This is definitely not the case for the entirely equivalent example of two monobasic acids even for much smaller differences in structure. A statement equivalent to requirement (1), and one which is manifestly incorrect, is this: the log-log relations between rates and base

strengths of a given series of catalysts should have the same slope for all general base catalyzed reactions.

In special cases  $F$  can still be constant; it is constant if there is only one catalyst present, or if only one base out of several present is effective in steps 2 and -1. That is,  $F$  is constant only if it is true for all the solutions studied that

$$\begin{aligned} k_{-1\text{B}} c_{\text{B}} &\gg k_{-1\text{C}} c_{\text{C}} + k_{-1\text{D}} c_{\text{D}} + \dots \\ k_{2\text{B}} c_{\text{B}} &\gg k_{2\text{C}} c_{\text{C}} + k_{2\text{D}} c_{\text{D}} + \dots \end{aligned}$$

But equation (4), which applies whether there is equilibrium in step 1 or not, shows that the first inequality is identical with

$$k_{1\text{BH}^+} c_{\text{BH}^+} \gg k_{1\text{CH}^+} c_{\text{CH}^+} + k_{1\text{DH}^+} c_{\text{DH}^+} + \dots$$

If  $F$  is constant for these reasons, then

$$k = \frac{k_{1\text{BH}^+} c_{\text{BH}^+}}{1 + \frac{k_{-1\text{B}}}{k_{2\text{B}}}}$$

In other words, if  $F$  is constant with varying relative concentrations of two or more catalysts, it is because a single acid-base pair is causing practically all the reaction, and no other catalyst is very effective, either as acid in step 1, or as base in steps 2 and -1. Conversely, if it is possible to detect large catalytic effects of two or more catalysts present in the same solution, and to calculate specific catalytic constants for each which are truly constant as the relative concentrations are varied, then mechanism b, with neither step solely rate determining, can be rejected. In the particular case in question, the acid catalyzed enolization of acetophenone, the ratio of the contributions of chloroacetic acid and oxonium ion to the rate ranges from 1.5 to 4 in the buffer solutions, and is of course 0 in the perchloric acid solutions.

Since we have eliminated all other suggested mechanisms, it seems highly probable that mechanism a, in which step 2 is rate determining, is the correct one. The same conclusion is a necessary corollary of the mechanism proposed by Cohn and Urey<sup>4</sup> for the isotopic oxygen exchange between acetone and water. Thus two independent types of evidence strongly support both the proposed mechanism for the enolization and the proposed mechanism for the oxygen exchange reaction.

### Summary

The basic ionization constants of propiophenone, *n*-butyrophenone and isobutyrophenone have been measured.

The iodination of acetophenone exhibits a general acid catalysis.

Direct evidence is offered to show that the pro-

ton removal is the rate determining step in the acid catalyzed enolization of ketones.

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## Kinetics of the Iodination of Acetophenone in Sulfuric and Perchloric Acid Solutions

BY LOIS ZUCKER<sup>1</sup> AND LOUIS P. HAMMETT

The acidity function  $H_0^2$  for sulfuric acid-water solutions (and for aqueous solutions of some other strong acids) combines in one functional representation all effects of continuing increase in acid concentration on the ionization equilibria of electrically neutral monoacid bases. These effects are presumably two—the result of increasing the acidity *per se*, and the result of changing the thermodynamic nature of the medium. There is also excellent correlation between the rates of some acid catalyzed reactions in increasingly acid solutions, and the acidity function for these solutions<sup>2,3</sup> and consequently between the effects of increasing acid concentration on the rates of these acid catalyzed reactions, and on the ionization equilibria of electrically neutral monoacid bases. This is simply explained in terms of the transition state theory of reaction velocity if the equilibrium between reactants and activated complex, whose position determines the rate of the reaction, is or approximates an ionization equilibrium of the correct charge type.

On the other hand, the bromination of *m*-nitroacetophenone in moderately concentrated solutions of sulfuric acid in acetic acid-water mixtures shows no such correlation of rate with acidity function.<sup>4</sup> This might be a property of the acetic acid medium or it might be a characteristic property of the enolization reaction. We have therefore studied the rate of iodination of acetophenone in sulfuric acid-water and perchloric acid-water solutions.

### Experimental

**Rate Measurements.**—The colorimetric method used was that previously described.<sup>5</sup>

(1) Part of a thesis submitted by Lois Zucker in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University.

(2) Hammett and Deyrup, *THIS JOURNAL*, **54**, 272 (1932); Hammett and Paul, *ibid.*, **56**, 827 (1934).

(3) Hammett and Paul, *ibid.*, **56**, 830 (1934); Hammett, *Chem. Rev.*, **16**, 67 (1935).

(4) Paul and Hammett, *THIS JOURNAL*, **58**, 2182 (1936).

(5) Zucker and Hammett, *ibid.*, **61**, 2779 (1939).

The color of iodine in sulfuric acid solutions changes in hue from brown in the most dilute solutions to rose in 95% solution, and the effective extinction coefficient for the blue-violet light used slowly decreases. The change becomes perceptible with 46% sulfuric acid solution; for 46 and 51% solutions a pinker colorimetric standard is necessary to get a good match, and is supplied conveniently by an aqueous solution of methyl orange of the same concentration as that used for more dilute acid solutions, but buffered at pH 3.8 with 0.05 molar acetate buffer. The effective extinction coefficient of the iodine decreases by about 2% from 39.5 to 45.9% sulfuric acid, and by another 3% from 45.9 to 51% sulfuric acid. No hue which can be obtained from methyl orange at any reasonable acidity is sufficiently like that of iodine in 66% sulfuric acid solution with light of the spectral composition used to allow precise matching. The one experiment in 66% sulfuric acid was very crudely done by measuring the times at which the reacting solution matched, to the eye, various standard iodine solutions all in bottles of closely similar shape and color.

Both potassium iodate and sodium nitrite were satisfactory oxidizing agents for the more dilute acid solutions, up to and including 25% sulfuric acid. Potassium iodate could not be used in 39.5% sulfuric acid; iodine solutions made up from potassium iodide and excess potassium iodate increase steadily in depth of color for several minutes after mixing, although the iodine production should be practically instantaneous. If a large excess of potassium iodate is present, the color then decreases slowly over a period of days to weeks. In 70% sulfuric acid an iodine solution saturated with potassium iodate takes only a few days for complete decolorization. These two phenomena (production of more intense color, and decolorization) are instantaneous in 95% sulfuric acid with suitable relative concentrations of iodine and potassium iodate and are ascribed by Masson, *et al.*,<sup>6</sup> to the formation of stabilized ions on the oxidative level of  $I^+$  (dark brown) and  $I^{+++}$  (colorless), respectively. One or both of these ions seems to be kinetically active in 39.5% sulfuric acid. No difficulties were observed with sodium nitrite which was used exclusively for all the sulfuric acid solutions more concentrated than 25%. The innocuousness of this oxidizing agent could not be tested by comparing results obtained with it with those obtained with some other agent, because no other suitable oxidizing agent was found. Nor could rates in the presence of

(6) (a) Masson and Race, *J. Chem. Soc.*, 1718 (1937); (b) Masson and Hanby, *ibid.*, 1699 (1938); (c) Masson and Argument, *ibid.*, 1702 (1938); (d) Masson, *ibid.*, 1708 (1938).