

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Acid Catalysis in Sulfuric Acid-Acetic Acid Solutions. The Rate of Bromination of *m*-Nitroacetophenone¹

BY MARTIN A. PAUL AND LOUIS P. HAMMETT

Previous papers have given applications of indicator measurements to the study of acid catalysis in solutions containing water.²⁻⁴ Over wide ranges of composition, direct proportionality was found between the acidity of the medium as measured by simple basic indicators² and the speeds of certain reactions. These results led us to make a similar investigation in a solvent, glacial acetic acid, which is of great utility as a medium for organic reactions and in which the pioneer work of Hall and Conant⁵ on super-acid solutions was carried out.

The reaction studied was the bromination of *m*-nitroacetophenone, which proceeds at a rate suitable for measurement in dilute solutions of sulfuric acid in acetic acid. It is a case of the frequently studied acid-catalyzed ketone halogenation.⁶ It is characteristic of this type of reaction that the rate is independent of the halogen concentration, but is proportional to the concentration of ketone. The reaction in dilute aqueous solutions exhibits the phenomena of general acid catalysis in the Brønsted sense and is also subject to a pronounced catalysis by bases.

With this ketone and under the conditions of low ketone concentration necessary to keep the rate within reasonable limits at the high acidities encountered, the method used by previous investigators,⁶ namely, dilution of a sample of the reaction mixture with water containing a small excess of potassium iodide and some sodium acetate and titration with thiosulfate of the liberated iodine, was entirely unsatisfactory. The difficulty arises from the fact that the monobrominated

acetophenone derivative halogenates further in the diluted aqueous solution at a rate which seriously affects the titers obtained. The same phenomenon exists with ω -bromoacetophenone as with its nitro derivative, but the magnitude of the effect is smaller. In the original sulfuric-acetic acid mixtures, the rate of bromination of these brominated ketones is small relative to that of the unbrominated compounds while the latter use up iodine at a negligibly small speed in the solutions diluted with water. Apparently bromine substitution in the methyl group of these compounds shifts the catalytic minimum (the acid concentration separating the region of predominantly acid catalysis from that in which basic catalysis is most important) to quite high acidities, especially for the ketone brominating more slowly. This is in accord with the trend noted by Watson and Yates⁶ⁱ for the brominated acetones. An aqueous acetate buffer acts therefore as a powerful basic catalyst for the halogenation of ω -bromo-*m*-nitroacetophenone. Applied to Watson's data^{6m,n} on halogenation in an acetic acid, water, hydrochloric acid mixture, our observations indicate that, for the ketone *m*-nitroacetophenone, toward the end of a run the rate of disappearance of iodine from the solutions diluted for titration may have been nearly as great as the rate of disappearance of bromine from the undiluted reaction mixture. Unless only initial titers were used in computing rate constants, his value for this ketone may therefore be high.

A colorimetric method of the sort used by Bartlett and Vincent⁷ in the study of the iodination of menthone proved entirely satisfactory and was therefore used throughout this work.

Experimental

Apparatus.—The colorimeter was the Bausch and Lomb instrument used in previous work.⁸ The mirror was replaced by an illuminator similar to that described by Beaver.⁹ The scales were calibrated and had no error exceeding ± 0.1 mm. For indicator measurements in acetic acid solutions, a closed cell with plane parallel ends, described by Hammett and Deyrup,² was employed.

(1) From part of a thesis submitted by Martin A. Paul 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**, 2721 (1932).

(3) Hammett and Paul, *ibid.*, **56**, 830 (1934).

(4) Hammett, *Chem. Rev.*, **16**, 67 (1935).

(5) Hall and Conant, *THIS JOURNAL*, **49**, 3047 (1927); Conant and Hall, *ibid.*, **49**, 3062 (1927).

(6) (a) Lapworth, *J. Chem. Soc.*, **85**, 30 (1904); (b) Dawson with Leslie, *ibid.*, **95**, 1860 (1909); (c) with Wheatley, **97**, 2048 (1910); (d) with Ark, **99**, 1740 (1911); (e) with Carter, 2282 (1926); (f) with Dean, 2872 (1926); (g) with Hoskins, 3166 (1926); 213, 458, 756, 1146, 1290 (1927); (h) *Trans. Faraday Soc.*, **24**, 640 (1928); (i) Hughes and Watson, *J. Chem. Soc.*, 1945 (1929); (j) Watson, *Chem. Rev.*, **7**, 173 (1930); (k) Hughes, Watson and Yates, *J. Chem. Soc.*, 3318 (1931); (l) Watson and Yates, *ibid.*, 1207 (1932); (m) Nathan and Watson, *ibid.*, 217 (1933); (n) Evans, Morgan and Watson, *ibid.*, 1167 (1935); (o) Morgan and Watson, *ibid.*, 1173 (1935).

(7) Bartlett and Vincent, *THIS JOURNAL*, **55**, 4992 (1933).

(8) Hammett and Paul, *ibid.*, **56**, 827 (1934).

(9) Beaver, *J. Opt. Soc. Am.*, **18**, 41 (1929).

For the rate measurements, one cup of the colorimeter was fitted with a jacket having a bottom made of optically clear glass (Fig. 1). Water from a thermostat was circulated through it by means of an air-lift pump and, with suitable insulation, the contents of the cup could be kept at $25.00 \pm 0.01^\circ$. This precision was quite adequate for our purpose, estimating the temperature coefficient of the bromination of acetophenone derivatives in solution to be about 20% per degree.^{6a}

To reduce evaporation of bromine, each cup had a closely fitting glass cap with a hole bored through of diameter slightly larger than that of the plungers. Loss of bromine from the cups so equipped was less than 2% per hour, negligible since no runs lasted longer than an hour.

Method: Indicator Measurements.—Indicator measurements were made essentially according to the method of Hammett and Deyrup.⁹ The reference solution was acetic acid containing enough sodium acetate (about 0.5 molar) to completely convert the bases to their colored uncharged forms. Absorption of water from the atmosphere by this solution during a set of observations was found to be too small to affect readings.

Method: Rate Measurements.—As a reproducible color standard for measuring the concentration of bromine in acetic acid solutions, bromine water prepared freshly as needed from a standard potassium bromate solution by addition of potassium bromide (100% excess) and sulfuric acid (final concentration about 0.5 molar) was adopted. The specific color intensities of bromine in the two media are different due, no doubt, to a shift in the absorption spectrum, but the yellow colors nevertheless may be matched without difficulty.¹⁰ Accordingly, solutions of bromine in acetic acid were made up and their concentrations determined by titration. The apparent concentrations of 0.00500 and 0.00250 molar bromine water were determined against each of these by colorimetric comparison. These experiments tested the constancy of the concentration-color intensity ratio (Beer's law) for bromine dissolved in acetic acid. For six concentrations of bromine covering the range 0.006–0.001 molar, the concentration c_8 of bromine in glacial acetic acid colorimetrically equivalent to 0.00500 molar bromine water was 0.00381 ± 0.00004 molar and to 0.00250 molar bromine water, 0.00191 ± 0.00003 molar. Deviation from Beer's law in the range examined is thus within the precision of matching (2–5%). The 0.00500 molar bromine water was found to be equivalent to 0.00415 molar bromine in the mixed solvent acetic acid–water in the mole ratio 1–1.

The procedure was to make up a solution of ketone, sulfuric acid and acetic acid by weight in a 25-ml. glass-stoppered volumetric flask and to bring to mark with acetic acid at 25° . The flask was then kept in the thermostat for at least fifteen minutes while water was circulated through the jacket of the reaction cup. Standard bromine water was prepared and introduced into the other cup of the colorimeter. A drop of bromine was then added to the flask, a stop watch (calibrated by telephone time) started, the solution thoroughly shaken and a sample poured into the jacketed cup. The latter was immediately racked to a convenient height, r , and left there during the

run. Readings of the length, h , of the standard solution required to balance colorimetrically the "unknown" were taken at times, t , read to the nearest one-tenth minute. The first reading could be made within one and one-half to two minutes after addition of the bromine, while mixing and transfer of the solution took about one-half minute. The initial ketone concentration, c_K^0 , was between 0.005 and 0.05 molar and was always so chosen as to have the run last between twenty and sixty minutes.

Rate Calculations.—Previous investigators have used ketone concentrations so much larger than the bromine concentration that the reaction rate, which is independent of the latter concentration, is essentially constant throughout the run. This procedure would give rates at the higher acidities much too large to be measured, but its abandonment requires some variations in the usual calculation of the rate constant. The fundamental equation is

$$-\frac{dc_K}{dt} = -\frac{dc_{Br_2}}{dt} = kc_K \quad (1)$$

where c_K is ketone concentration and c_{Br_2} is bromine concentration. Using superscript zero to denote initial concentrations at time zero we have

$$-dc_{Br_2}/dt = kc_K = k \{c_K^0 - (c_{Br_2}^0 - c_{Br_2})\} \quad (2)$$

The integrated equation is

$$\ln \left(1 - \frac{c_{Br_2}^0 - c_{Br_2}}{c_K^0} \right) = -kt \quad (3)$$

Experimentally the bromine concentration is given by

$$c_{Br_2} = c_8(h/r) \quad (4)$$

where h and r are the previously defined colorimeter readings. Substituting in (3) we obtain

$$\ln \{ 1 - (h_0 - h) (c_8/rc_K^0) \} = -kt \quad (5)$$

For the initial readings ($h_0 - h$ small) this reduces to

$$(h_0 - h) (c_8/rc_K^0) = kt \quad (6)$$

In calculating the constant for a run, equation 6 was applied to the initial experimental points and the value of h_0 thus obtained was used in equation 5 to obtain the value of k , all experimental points being used. Both calculations were made by the method of least squares. In no case did the mean error in k from a single run exceed 5%. Figure 2, in which h and the quantity $c \equiv -\log \{ 1 - c_8 (h_0 - h)/rc_K^0 \}$ are plotted against t , is a graphical representation of the re-

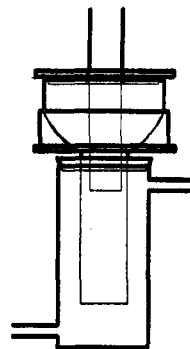


Fig. 1.—Diagram of colorimetric reaction cup.

(10) Flexser, Hammett and Dingwall, *THIS JOURNAL*, **57**, 2111 (1935).

sults of a typical experiment. Conformity of the data with equation (5) for different initial ketone and bromine concentrations establishes the validity of the assumptions that the rate of reaction is independent of the latter and proportional to the former. That ω -bromo- m -nitroacetophenone is the product was proven by obtaining this compound on dilution with water when a run was tried using a relatively high concentration of m -nitroacetophenone. In the range of acidity studied, the rate of bromination of this product is negligibly small at the concentrations at which it was present, but at higher acidities, it is great enough to make independent measurements of the rate for the unbrominated ketone impossible. Lower acidities were not tried for fear of auto-catalysis by hydrobromic acid.

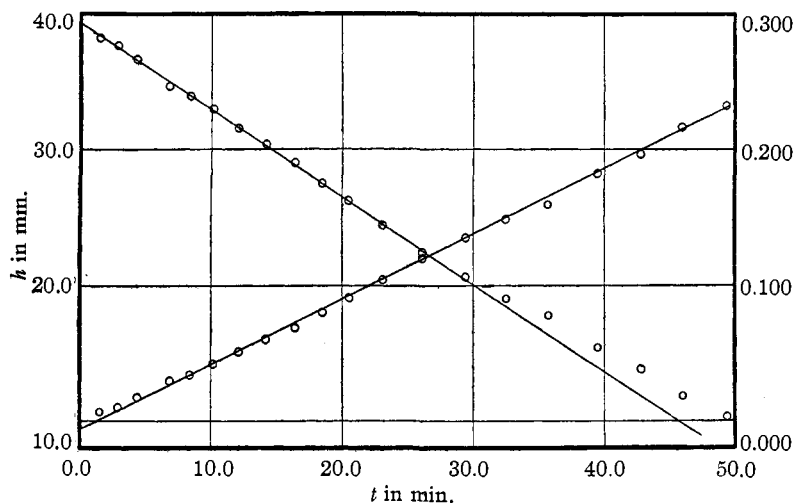


Fig. 2.—Graphical representation of typical bromination experiment: $c^{\circ}\text{K} = 0.01015$ mole/liter; $c_{\text{H}_2\text{SO}_4} = 0.0609$ mole/liter.

Materials.—Acetic acid was prepared from commercial 99.5% reagent by the method of Orton and Bradfield.¹¹ Samples reacting with bromine were rejected. The water content, estimated by the freezing-point method, was between 0.3 and 0.1%. No extraordinary precautions other than rapid manipulation were taken to keep out water from the atmosphere during experiments. No effect on the measurements from this source could be detected. In fact, many of the runs were made with just sufficient acetic anhydride (prepared by fractional distillations of the commercial c. p. reagent) added to react with the quantity of water present. Orton and Jones¹² have shown that this reaction is very rapid in acetic acid in the presence of a small concentration of sulfuric acid. No significant difference could be detected between rates of bromination in this medium and in 99.8% glacial acetic acid. Of course, measurements were impossible on very humid days.

(11) Orton and Bradfield, *J. Chem. Soc.*, 983 (1927).

(12) Orton and Jones, *ibid.*, 101, 1708 (1912).

Sulfuric acid was prepared by distillation of 50% fuming acid into c. p. concentrated reagent and dilution with more of the latter to maximum freezing point.

m -Nitroacetophenone was recrystallized to constant melting point, 77.3° from ethyl alcohol and water.

Bromine was of analytical reagent grade.

Potassium bromate was recrystallized twice from water and dried at 180°. Its equivalent weight was within 0.1% of the theoretical value when checked with that of potassium iodate purified in the same way. The latter was used as primary standard for calibration of thiosulfate solutions. Potassium bromide was recrystallized from water and was bromate free.

Results

Table I contains the results of indicator measurements in sulfuric acid-acetic acid solutions. M is molality of sulfuric acid, c_{BH^+} and c_{B} are concentrations of indicator acid and base, and H_0

is the acidity function. The pK' of -0.17 for o -nitroaniline is from previous work.⁸ The difference in basic strength of the two indicators employed is the same within experimental error as for aqueous solutions of strong acids.^{2,3} Data for solutions containing sodium bisulfate (prepared by mixing an acetic acid solution of sodium acetate with excess of a solution of sulfuric acid in acetic acid) and for solutions of sulfuric acid in the mixed solvent, acetic acid-water in mole ratio 1-1, are included. Table II gives mole fractions of sulfuric acid required to produce the same simple basic indicator acidity in the three media, water, acetic acid and their equimolar mixture.

Table III summarizes the results of measurements of the rate of bromination of the ketone m -nitroacetophenone in sulfuric acid-acetic acid solutions. The unimolecular velocity constants, k , are expressed in natural logarithms and minutes. Measurements in solutions containing the salt sodium bisulfate and in solutions of sulfuric acid in mole-to-mole acetic acid-water are also given. In Fig. 3, $\log k$ is plotted against H_0 of the medium. We have measured the reaction rate in the medium used by Evans, Morgan and Watson,^{6a} 0.5 molar hydrochloric acid in 75% acetic acid-water by volume and our value for m -nitro-

TABLE I
IONIZATION OF INDICATORS IN H₂SO₄-CH₃COOH SOLUTIONS

<i>m</i>	Log <i>m</i> <i>o</i> -Nitroaniline (<i>pK'</i> = -0.17)	Log (<i>c</i> _{BH⁺} / <i>c</i> _B)	<i>H</i> ₀
0.0195	-1.71	+0.71	-0.88
.0262	-1.58	.85	-1.02
.0290	-1.54	.89	-1.06
.0412	-1.38	.98	-1.15
.0506	-1.30	1.16	-1.33
.0591	-1.23	1.20	-1.37
.0680	-1.17	1.26	-1.43
.0837	-1.08	1.34	-1.51
.0901	-1.05	1.37	-1.54
.1132	-0.95	1.44	-1.61
.1273	-.90	1.48	-1.65

<i>m</i>	Log <i>m</i> <i>p</i> -Chloro- <i>o</i> -nitroaniline (<i>pK'</i> = -0.91)	Log (<i>c</i> _{BH⁺} / <i>c</i> _B)	<i>H</i> ₀
0.0721	-1.14	+0.52	-1.43
.1036	-0.98	.64	-1.55
.1197	-.92	.77	-1.68
.1429	-.84	.88	-1.79
.1705	-.77	.94	-1.85
.1981	-.70	1.06	-1.97
.247	-.61	1.15	-2.06
.283	-.55	1.26	-2.17
.348	-.46	1.34	-2.25
.496	-.30	1.58	-2.49
.641	-.19	1.66	-2.57
.756	-.12	1.83	-2.74
.932	-.03	1.95	-2.86
1.110	+.05	2.05	-2.96
1.332	+.12	2.18	-3.09
1.593	+.20	2.27	-3.18

EFFECT OF NaHSO₄ ON *H*₀; INDICATOR-*o*-NITROANILINE

Mole/liter of solution at 25°		Log (<i>c</i> _{BH⁺} / <i>c</i> _B)	<i>H</i> ₀
H ₂ SO ₄	NaHSO ₄		
0.0266	0.0000		-0.99 (interpolated)
.0266	.0266	+0.86	-1.03
.0266	.0797	+1.05	-1.22

IONIZATION OF *o*-NITROANILINE IN SOLUTIONS OF H₂SO₄ IN THE SOLVENT CH₃COOH-H₂O, MOLE RATIO 1-1

Moles of H ₂ SO ₄ per 1000 g. of solvent	Log (<i>c</i> _{BH⁺} / <i>c</i> _B)	<i>H</i> ₀
1.707	+1.09	-1.26
1.912	1.26	-1.43
2.790	1.78	-1.95
2.998	2.00	-2.17

TABLE II

EFFECT OF COMPOSITION OF MEDIUM ON *H*₀ OF H₂SO₄-H₂O-CH₃COOH SOLUTIONS

<i>H</i> ₀	Mole fraction of H ₂ SO ₄ in CH ₃ COOH-H ₂ O Mole ratio 1-1		
	H ₂ O	CH ₃ COOH	CH ₃ COOH
-1.26	0.059	0.063	0.0028
-1.43	.067	.070	.0042
-1.95	.094	.098	.0118
-2.17	.104	.105	.0169

acetophenone is about 20% lower than theirs, a result possibly due to failure of dilution to arrest the reaction in the latter stages of their runs.

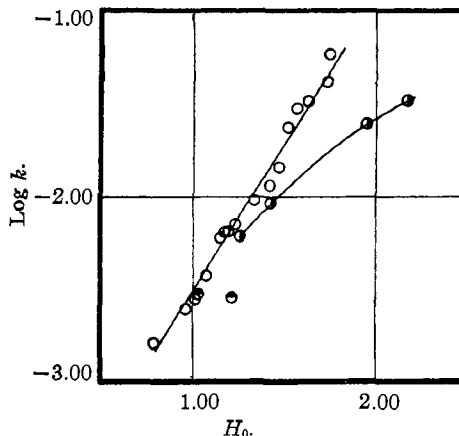


Fig. 3.—Relations between *H*₀ and log *k* in bromination of *m*-nitroacetophenone: ○, H₂SO₄ in CH₃COOH, *M* = 0.0161-0.146; ●, H₂SO₄ in CH₃COOH + H₂O, molar ratio 1-1; ●, H₂SO₄ in CH₃COOH + NaHSO₄ (data taken from Table III).

TABLE III
RATE OF BROMINATION OF *m*-NITROACETOPHENONE IN H₂SO₄-CH₃COOH SOLUTIONS

Concentration of H ₂ SO ₄ in mole/liter	<i>k</i>	Log <i>k</i>
0.0161	0.00160	-2.80
.0251	.00244	-2.61
	.00246	-2.61
.0282	.00268	-2.57
	.00296	-2.53
.0322	.00372	-2.43
.0392	.00567	-2.25
	.00643	-2.19
.0405	.00622	-2.21
	.00666	-2.18
.0434	.00606	-2.22
	.00645	-2.19
	.00682	-2.16
.0484	.00709	-2.15
.0609	.00848	-2.07
	.01089	-1.96
.0731	.0105	-1.98
	.0116	-1.93
	.0120	-1.92
.0786	.0151	-1.82
.0810	.0146	-1.84
.0914	.0237	-1.62
.1032	.0288	-1.54
	.0319	-1.50
.1196	.0297	-1.53
	.0352	-1.45
.1454	.0409	-1.39
	.0421	-1.37
.1462	.0594	-1.23

TABLE III (Concluded)

EFFECT OF NaHSO₄ ON RATE OF BROMINATION OF *m*-NITROACETOPHENONE IN H₂SO₄-CH₃COOH SOLUTIONS

H ₂ SO ₄	Mole/liter NaHSO ₄	<i>k</i>	Log <i>k</i>
0.0266	0.0000	0.00260	-2.58 ^a
.0266	.0266	.00284	-2.55
		.00294	-2.53
.0266	.0797	.00278	-2.56
		.00286	-2.54

^a Interpolated.RATE OF BROMINATION OF *m*-NITROACETOPHENONE IN SOLUTIONS OF H₂SO₄ IN THE SOLVENT CH₃COOH-H₂O, MOLE RATIO 1-1

Concn. of H ₂ SO ₄ in mole/liter	<i>k</i>	log <i>k</i>
1.68	0.00622	-2.21
	.00617	-2.21
1.88	.00868	-2.06
	.01002	-2.00
2.52	.0264	-1.58
	.0243	-1.61
2.82	.0341	-1.47
	.0332	-1.48

RATE OF BROMINATION OF *m*-NITROACETOPHENONE IN 0.5 MOLAR HCl IN THE MEDIUM 75% ACETIC ACID IN WATER BY VOLUME

$$k = 0.000396 \pm 0.000005$$

$$.000395 \pm .000007$$

In terms of "fall of 0.02 *N* thiosulfate titer per minute per 20 cc. of solution containing 0.1 molar ketone concentration," this constant would have the value 0.079. Evans Morgan and Watson⁶ⁿ have reported 0.099.

Discussion

As was to be expected and has been reported by Hall and Spengeman¹³ on the basis of more extensive data than ours, a solution of sulfuric acid in glacial acetic acid is much more acid than one of the same sulfuric acid concentration in water. Our measurements on solutions in the equimolar mixture of the two solvents show that this medium resembles water much more nearly than it does acetic acid. This is true no matter what concentration scale is used, but is especially true, as Table II shows, on the basis of mole fractions. The mole fraction of sulfuric acid necessary to produce a given value of H_0 in the mixed solvent is nearly identical with that required to produce the same acidity in water alone, whereas a much smaller mole fraction of the strong acid is required in glacial acetic acid.

Qualitatively the behavior of the reaction rates

is parallel. The concentration of sulfuric acid required to produce a given rate is much higher in the mixed solvent than in glacial acetic acid, and in either solvent an increase in H_0 is accompanied by an increase in rate. The kind of simple quantitative correlation between reaction rate and indicator acidity which we have previously found in mixtures of strong acids with water is however lacking. In the first place, we note that two solutions, one in glacial acetic acid, the other in the equimolar acetic acid-water mixture, which possess the same value of H_0 , do not necessarily give rise to equal reaction rates. Obviously we have to deal with specific effects of the solvent upon the rate.

Furthermore, the plot (Fig. 3) of log k against H_0 for the experiments in glacial acetic acid, while satisfactorily linear, possesses a slope considerably greater than unity (about 1.6), a phenomenon not susceptible to any simple interpretation. Barring specific solvent effects, a reaction of ketone with solvated hydrogen ion would lead to unit slope in this plot, and unit slope has, indeed, been found for a number of reactions in mixtures of strong acids with water.²⁻⁴ Although the data are too scanty for assurance, our few measurements in the mixed acetic acid-water solvent are not inconsistent with unit slope in this medium also. That the effect is due to catalysis by molecular sulfuric acid seems improbable for two reasons. In the first place, the activity of molecular sulfuric acid in the solvent acetic acid is known from the measurements of Hutchison and Chandlee,¹⁴ and is fairly closely proportional to the molality of the sulfuric acid in dilute solutions. Our reaction rates, on the other hand, increase considerably more rapidly than the first power of the sulfuric acid molality. Furthermore, the magnitude of a catalysis by molecular acid should be increased by the addition of sodium bisulfate, and our results show that the salt has relatively little effect upon the rate.

It follows that specific effects are present in these acetic-sulfuric acid solutions which were absent in the aqueous solutions in which we have found simple proportionality between rate and acidity.²⁻⁴ Further work will be necessary in order to determine the region within which these simple relations apply and to account for the existence of the specific effects.

(13) Hall and Spengeman, reported at the Kansas City meeting of the American Chemical Society, April, 1936.

(14) Hutchison and Chandlee, *THIS JOURNAL*, **53**, 2881 (1931). See also La Mer and Eichelberger, *ibid.*, **54**, 2763 (1932).

Summary

By a colorimetric method the rate of bromination of the ketone *m*-nitroacetophenone has been measured in solutions of sulfuric acid in acetic acid of concentration varying from 0.016 to 0.15 molal. Measurements to establish the effect of sodium bisulfate upon the rate of the reaction in these solutions and a limited series of measure-

ments in solutions in a mixed acetic acid-water solvent have also been made.

It has been found that in the acetic acid solution the rate of reaction increases with increasing sulfuric acid concentration more rapidly than does either the acidity function H_0 , the stoichiometric concentration of sulfuric acid, or the activity of sulfuric acid.

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Energy Levels in Electrochemistry. II

BY WILDER D. BANCROFT AND JAMES E. MAGOFFIN

In aqueous solutions sulfuric acid can only be reduced electrolytically when the concentration is very high. Raising the temperature is equivalent to increasing the concentration. Sodium sulfate and ammonium sulfate solutions cannot be reduced electrolytically at any concentrations and temperatures that can be reached in open vessels.

On the other hand sulfurous acid and sodium sulfite can easily be oxidized electrolytically to sulfuric acid and sodium sulfate. A sulfite-sulfate electrode is therefore a one-way electrode, the reaction being irreversible electrolytically.¹ It was shown in our previous paper² that at constant temperature and constant pH , the potential difference at a sulfite-sulfate electrode should be a function of the concentration of the sulfite and independent of the concentration of the sulfate as an oxidation product. Lewis, Randall and Bichowsky³ found that at constant temperature and constant pH the change of electromotive force with change of concentration of sulfurous acid was described very well by the theoretical formula. They did not find that sulfate concentration had no effect because they varied the pH at the same time. This gap was filled by Noyes and Steinour⁴ who showed that, "provided the hydrogen-ion concentration is nearly the same, hydrochloric acid and sulfuric acid produce (in association with sulfurous acid) substantially the same electromotive force."

Schaum⁵ and von der Linde⁶ found that the

electromotive force of a sodium sulfite electrode varies with the concentration as it should, and that it makes no difference whether one dilutes with water or with sodium sulfate. The addition of a drop of benzyl alcohol was found to shorten the time necessary to reach equilibrium. We have not been able to confirm this effect of benzyl alcohol; but our experiments were made with smooth platinum electrodes and not with platinized electrodes.

The case of the cysteine-cystine electrode is more striking, because the same general results have been obtained by all workers. Dixon and Quastel⁷ found that the electromotive force of this electrode at constant temperature and constant pH is a function of the concentration of cysteine and is independent of the concentration of cystine. This is the more interesting because cystine can be reduced to cysteine with tin and hydrochloric acid. The discrepancy between the potential difference generated by cysteine and that necessary to reduce cystine to cysteine is therefore not very large; but it is sufficient to change the electrode from the reversible to the irreversible class. Dixon thought that cysteine was a stronger reducing agent at a mercury electrode by about 200 mv. than at a gold electrode. He ascribed this, apparently erroneously, to the high hydrogen over-voltage which can be observed at a mercury electrode.

Dixon found that glutathione behaved like cysteine. Michaelis and Flexner⁸ have confirmed Dixon on the important points; but they offer a different and apparently better explanation for

(1) Conant, *Chem. Rev.*, **3**, 4 (1926).

(2) Bancroft and Magoffin, *THIS JOURNAL*, **57**, 2561 (1935).

(3) Lewis, Randall and Bichowsky, *ibid.*, **40**, 356 (1918).

(4) Noyes and Steinour, *ibid.*, **51**, 1418 (1929).

(5) Schaum, *Z. Elektrochem.*, **7**, 483 (1901).

(6) Von der Linde, Inaugural Dissertation, Marburg, 1902.

(7) Dixon and Quastel, *J. Chem. Soc.*, **123**, 2943 (1923); Dixon, *Proc. Roy. Soc. (London)*, **B101**, 57 (1927).

(8) Michaelis and Flexner, *J. Biol. Chem.*, **79**, 689 (1928).