

THE KINETICS OF SAPONIFICATION OF IODOACETIC ACID
BY SODIUM HYDROXIDE AND BY CERTAIN
ALKALINE BUFFER SOLUTIONS*

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In studying the reaction which takes place between glycine and iodoacetic acid in certain alkaline buffer solutions (1), it was necessary to consider the saponification of iodoacetic acid by hydroxyl ions. This occurs simultaneously as an independent side reaction. By determining the velocity constants for the saponification in the solutions in which glycine was omitted, the rate of the iodoacetic acid-glycine reaction could be obtained. The study of the kinetics of the saponification reaction of iodoacetic acid forms the subject of the present paper. Holmberg (2) investigated this reaction over a limited range of concentration of the reacting constituents. His measurements have been extended in the present paper to regions of greater alkalinity. His paper appeared before the publication of Brönsted's (3) hypothesis, and hence his data were not interpreted on this basis.

The technique employed is essentially the same as that which was described in the previous paper (1). Certain portions of the iodoacetate and hydroxyl ion containing-solution, which was kept in a thermostat at $25^{\circ} \pm 0.01$, were withdrawn during different time intervals during the saponification. In order to stop the reaction they were brought approximately to neutrality by the addition of HCl. The quantitative estimation of the iodoacetic acid in the samples consisted in recording polarographically the horizontal portions of the current-voltage curves. The concentration of iodoacetic acid can be read from these (see Fig. 1).

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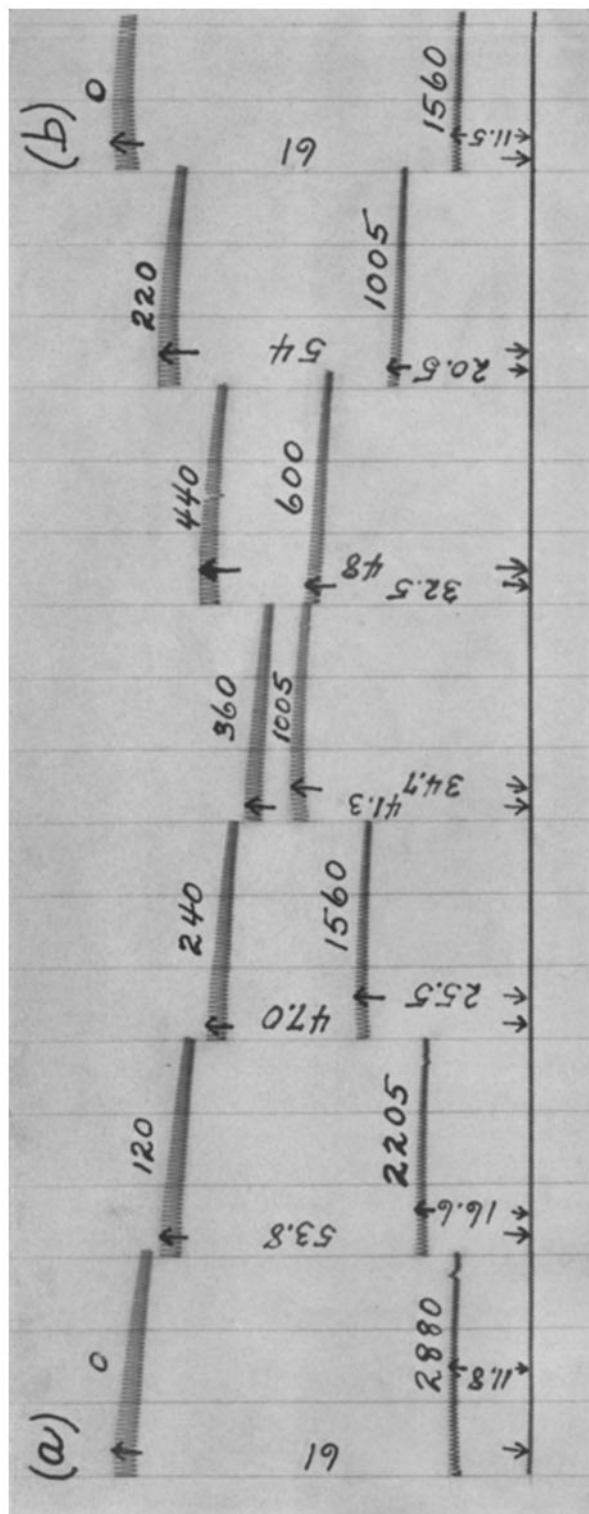


FIG. 1. Limiting current intensities due to electro-reduction of iodoacetates. These are proportional to the values of $(a - x)$, recorded at different times, t , (in minutes), during the course of the saponification of iodoacetate (a) in 0.52 N NaOH (decreasing curves from left to right), and (b) 0.31 N NaOH (decreasing curves from right to left). Sensitivity of galvanometer $\frac{1}{2.5} \mu$.

Since the saponification of the iodoacetic acid by OH ions yielding glycollic acid is an ionic reaction which involves salt effects, it was considered desirable to investigate first the reaction rate using sodium hydroxide instead of the buffer solution. In this case, according to Brönsted's hypothesis (3), only the primary salt effect takes place and a positive salt catalysis for this ionic type is to be expected. This reaction is not complicated by side reactions and the ionic strength of the solution remains unchanged during the reaction.

Brönsted's kinetic equation for this type of reaction has the form,

$$\frac{dx}{dt} = k_0(a-x)(b-x) \frac{f(IAc) \cdot f_{OH^-}}{f_{x^{2-}}}, \quad (1)$$

in which k_0 is the velocity constant independent of salt concentration, a and b are the initial equivalent concentrations of iodoacetate and hydroxyl ions, respectively, x is the decrease in the concentration of reactants at the time t , and $f(IAc)$, f_{OH^-} , and $f_{x^{2-}}$ are the activity coefficients of iodoacetate, hydroxyl ions, and Brönsted's critical complex, respectively. The values for the activity coefficients can be calculated theoretically only in extremely dilute solutions, for which the Debye-Hückel limiting laws (4) can be applied, but they can be determined also in higher concentrations empirically from solubility measurements or by other thermodynamical methods (5). The estimation of the value for $f_{x^{2-}}$ is doubtful since the existence of the critical complex is an hypothetical one. The velocity constant, k , calculated on the basis of the classical bimolecular kinetic equation,

$$k = \frac{2.303}{t(b-a)} \log \frac{a}{b} \cdot \frac{(b-x)}{(a-x)}, \quad (2)$$

involves the factor $\frac{f_{IAc^-} \cdot f_{OH^-}}{f_{x^{2-}}}$ in Brönsted's kinetic equation (1) which used to be denoted simply by F . This factor is expressed by the relationship,

$$k = k_0 F. \quad (3)$$

Knowing the value for F at one ionic strength, for which the value for $f_{x^{2-}}$ was assumed to be equal to a known value of the activity coefficient of a divalent anion at the same ionic strength, other values

for F can be calculated by means of equation (3) when k is determined experimentally.

Table I demonstrates the calculation of the bimolecular velocity constants according to equation (2) for the initial concentrations

(a) $a = 0.0198$ N sodium iodoacetate
 $b = 0.310$ N sodium hydroxide

(b) $a = 0.0198$ N sodium iodoacetate
 $b = 0.520$ N sodium hydroxide.

Since the values for $(a - x)$ represent the reading of the current intensities in millimeters, (which are proportional to the concentrations

TABLE I

(a) NaOH = 0.310 N				(b) NaOH = 0.520 N			
Time	$(a - x)$	$(b - x)$	$k \times 10^4$	Time	$(a - x)$	$(b - x)$	$k \times 10^4$
<i>min.</i>				<i>min.</i>			
0	61	961.2		0	61	1602	
220	54	954.2	18.0	120	53.8	1595	20.2
440	47.7	947.9	18.2	240	47	1588	21.0
1005	34.7	934.9	18.3	360	41.3	1582	21.0
1560	25.5	925.7	18.3	600	32.5	1574	20.4
2205	16.6	916.8	18.3	1005	20.5	1562	21.2
2880	11.8	912.0	18.7	1560	11.5	1553	21.0

Na(I CH₂COO) = 0.0198 N

of iodoacetic acid (see Fig. 1)), the values of b must be expressed in the same arbitrary units; *viz.*, they must be multiplied in this case by the factor $61/0.0198$. The values for $(b - a)$, however, must be expressed in equivalent concentrations.

Table II shows the values for the velocity constants, k , obtained from experiments in which the initial concentration of iodoacetic acid was kept constant ($a = 0.0198$ N), while the initial concentration of sodium hydroxide was gradually increased.

The observed increase of the values of k with the increased concentration of sodium hydroxide must be related to the increase of the factor F , which depends upon the ionic strength. In Fig. 2 the velocity constants, k , are plotted against the ionic strength, μ . Accepting

for F in a solution of ionic strength, $\mu = 0.1$, the value of 1.22, which is given empirically from thermodynamical measurements by La Mer (6), the value, k_0 , can be calculated on the basis of equation (3) and, in this case, is equal to $\frac{14 \times 10^{-4}}{1.22} = 11.5 \times 10^{-4}$. The values for F corresponding to resulting ionic strengths are determined by the ratios k/k_0 . This factor, F , accounts for the primary salt effect, showing a distinct positive salt catalysis. It is worth mentioning that the curve

TABLE II

NaOH normality	$k \times 10^4$	μ	$F = \frac{k}{k_0}$
0.0414	13.0	0.06	1.13
0.083	14.0*	0.103	1.22
0.109	14.7	0.129	1.28
0.310	18.3	0.330	1.59
0.520	21.0	0.540	1.83
0.700	23.3	0.720	2.03
0.873	24.6	0.893	2.14
1.000	26.0	1.020	2.26
1.120	27.7	1.140	2.41
1.36	30.9	1.380	2.69
1.60	35.0	1.62	3.04
2.00	43.0	2.02	3.74
2.40	49.4	2.42	4.30
2.67	52.4	2.69	4.56

*Holmberg (2) found for 0.05 N NaOH + 0.05 Na(I CH₂COO): $10^4 \times k = 13.9$.

in Fig. 2 shows an inflex point at an ionic strength in the neighborhood of 0.8 μ , at which the activity coefficients of alkali hydroxides show minimal values (7).

The positive salt catalysis could be demonstrated also qualitatively by an increased rate of saponification when neutral salts were added to the reacting medium. Thus the presence of 0.5 N KCl in 0.709 N NaOH and 0.0198 N Na(I CH₂COO) increases the velocity constant from the value of 14.7×10^{-4} to a value of 23.5×10^{-4} , and the presence of 0.6 N Na₂SO₄ in 0.083 N NaOH and 0.0198 N Na(I CH₂COO) from the value of 14×10^{-4} to a value of 23.5×10^{-4} .

The measurements of the velocity constants of the saponification of

iodoacetic acid in buffer solutions were carried out by using the same experimental technique. In the set of experiments which are given in Table III, 0.247 M boric acid in 0.1 N KCl, mixed with varying concentrations of NaOH, was used. The pH was determined by means of a standardized hydrogen electrode. The titration curve of 0.247 M boric acid is known (1). For this set of experiments the concentration of iodoacetate was 0.0198 N. The velocity constants,

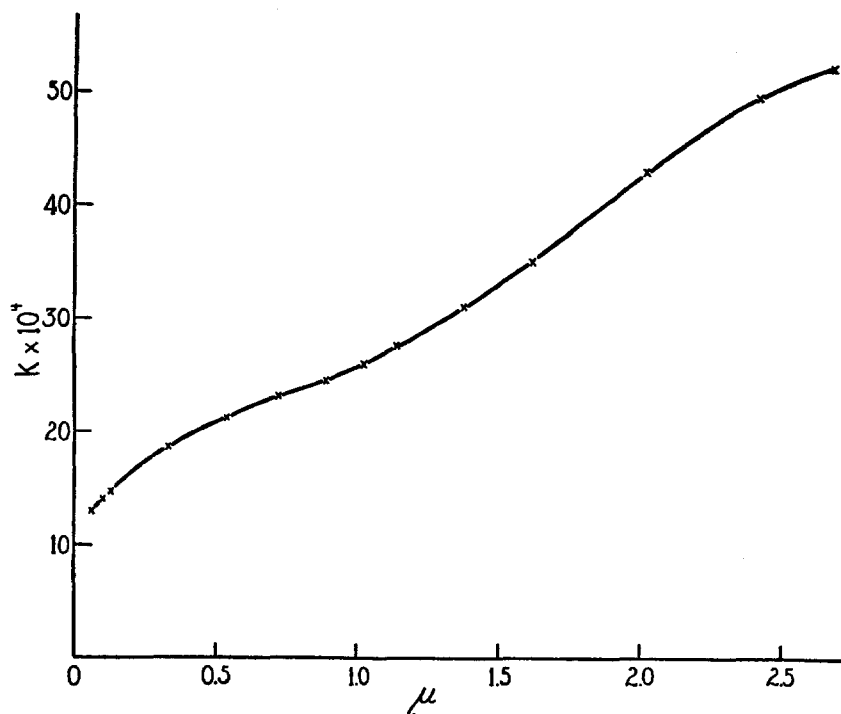


FIG. 2. The relation of the bimolecular velocity constant of the saponification of iodoacetate to the ionic strength of the solution.

denoted by k_s , and related to the given pH, were calculated by using the formula for monomolecular reactions,

$$k_s = \frac{2.303}{t} \log \frac{a}{a-x}, \quad (4)$$

in which a represents the initial concentration of iodoacetate and x its decrease at the time t . The use of this equation was found satis-

factory insofar as the decrease of hydroxyl ions during the reaction did not appreciably affect the pH. At lower values of pH a decrease of k_s was observed, which, nevertheless, permitted its rough estimation. In order to obtain the bimolecular constants which could be compared with the corresponding values of k in Table II, the values of k_s must be divided by the concentration of hydroxyl ions. By determining the pH of the reacting medium, the activity of the hydroxyl ions, ($a_{\text{OH}^-} = f_{\text{OH}^-} \cdot (\text{OH}^-)$), instead of their concentration, can be calculated. If the values of k_s are divided by the activity of OH^- ions, the values of $\frac{k}{f_{\text{OH}^-}}$ are obtained. A comparison between the values of $\frac{k}{f_{\text{OH}^-}}$ and k at the same ionic strength in the first three lines of Table III conforms approximately with the value for

TABLE III

pH	NaOH normality	$k_s \times 10^4$	$f_{\text{OH}^-} \times \text{OH}^-$	$\frac{k_s \times 10^4}{f_{\text{OH}^-} \times \text{OH}^-}$	$k \times 10^4$	μ
12.96	0.415	3.7	0.091	40	21	0.535
12.49	0.311	1.1	0.031	35	20	0.431
12.00	0.269	0.30	0.010	30	19.5	0.389
11.20	0.249	0.10	0.0016	63	19	0.369
9.91	0.208	0.08	0.00008	984	18.3	0.328

f_{OH^-} which, in this case, should be expected to be about 0.6—0.7. The values for k_s at pH = 11.2 and 9.91, on the other hand, do not show any proportionality to the concentration of hydroxyl ions; rather, their proportionality to the concentration of sodium hydroxide or borate anion in the buffer solution seems to be satisfied. This relationship which holds in the pH range below the neutralization of boric acid might be related to the principle of general basic catalysis (8). This principle involves the cases in which the velocity constants are proportional to the anion of the weak acid which, in the sense of Brönsted's interpretation, is to be regarded as a base. In order to apply this principle to the described problem, more detailed experiments must be made.

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SUMMARY

1. The rate of the saponification of iodoacetic acid in sodium hydroxide and alkaline buffer solutions yielding glycollic acid was measured by means of Heyrovský's polarographic method.

2. From the bimolecular velocity constants, increasing with the ionic strength of the solution, the Brönsted factor, F , which characterizes the primary salt effect, was calculated.

3. In the borate buffer solutions the monomolecular constants of the saponification were determined which, at values above the pH of neutralization of boric acid, show a proportionality to the concentration of hydroxyl anions. Below the pH of neutralization of boric acid, they are proportional to the concentration of borate anions.

REFERENCES

1. Brdička, R., *J. Gen. Physiol.*, 1935-36, **19**, 843.
2. Holmberg, B., *Medd. K. Vetenskapsakad. Nobelinst.*, 1919, **5**, No. 11.
3. Brönsted, J. N., *Z. phys. Chem.*, 1922, **102**, 169; 1925, **115**, 337; *Chem. Rev.*, 1928, **5**, 231.
4. Debye, P., and Hückel, E., *Phys. Z.*, 1923, **24**, 185.
5. Brönsted, J. N., and La Mer, V. K., *J. Am. Chem. Soc.*, 1924, **46**, 555.
Brönsted, J. N., *Tr. Faraday Soc.*, 1927, **23**, 416.
6. La Mer, V. K., *Chem. Rev.*, 1932, **10**, 179.
7. Harned, H. S., *J. Am. Chem. Soc.*, 1925, **47**, 676.
8. Brönsted, N. J., *Rec. trav. chim. Pays-bas*, 1923, **42**, 718; *Chem. Rev.*, 1928, **5**, 231.
Kilpatrick, M., and Kilpatrick, M. L., *Chem. Rev.*, 1932, **10**, 213.