

### 18. *Acid Catalysis in the Formation of Chloroamides from Hypochlorous Acid. N-Chlorination by Hypochlorite Ions and by Acyl Hypochlorites.*

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Further evidence is given for the view that the formation of chloroamides from hypochlorous acid involves the hypochlorite ion as chlorinating agent. *N*-Methylacetamide is *N*-chlorinated in this way and in addition is *N*-chlorinated at a rate dependent on the product of the concentrations of hypochlorous acid and of the free acid used as a component of the buffering solution. This is interpreted in terms of the formation of acyl hypochlorites which act as chlorinating agents. With acetanilides, the latter mechanism appears to be absent, and *N*-chlorination by hypochlorous acid is apparently determined solely by the first mechanism. *N*-Chlorination by hypochlorous acid, by chlorine, by another chloroamine, and by acyl hypochlorites are separate and distinct mechanisms.

THE rate at which chloroamines are formed from chlorine or from hypochlorous acid can be measured by a method (Orton, Soper, and Williams, J., 1928, 998; Pryde and Soper, J., 1931, 1510) which depends on first removing the free chlorinating agent by a phenol with which the chloroamine does not react appreciably. The chloroamine can then be estimated iodometrically. This method has been found of general applicability. Pryde and Soper studied the formation of *N*-chloroanilides from anilides and hypochlorous acid in buffered solutions and over a range of hydrogen-ion concentration of  $0.6$ — $2.6 \times 10^{-6}$  found that the rate of formation was proportional to the hydroxyl-ion concentration. This result was interpreted as indicating that *N*-chlorination by hypochlorous acid occurred *via* the hypochlorite ion. It seemed desirable to examine this conclusion further by studying *N*-chlorination in pH regions where the hypochlorite-ion concentration expressed as a fraction of the total concentration of hypochlorous acid and hypochlorite would not be simply proportional to the hydroxyl-ion concentration. The fraction of the total concentration of hypochlorous acid plus hypochlorite which is present as hypochlorite varies with pH as set out in Table I. These figures are based on the value of the ionisation constant of hypochlorous acid obtained by Ingham and Morrison (J., 1933, 1200), *viz.*,  $3.47 \times 10^{-8}$  at  $18^\circ$ . From the heat absorbed on ionisation of the acid, *i.e.*, 3,970 cal. (I.C.T., Vol. V, p. 176), the value of the constant at  $25^\circ$  may be calculated as  $4.1 \times 10^{-8}$ . Hence, if *N*-chlorination by hypochlorous acid is dependent on the hypochlorite-ion concentration, the specific rate,  $k_2$ , defined by  $v = k_2[\text{HOCl} + \text{OCl}^-][\text{NH}]$ , should increase with alkalinity as set out below, increasing 8-fold from pH 6.0 to 7.0 and 2.8 times from pH 7.0 to 8.0.

TABLE I.

pH .....	5.0	6.0	7.0	8.0	9.0
Percentage of $[\text{HOCl} + \text{OCl}^-]$ as $[\text{OCl}^-]$ .....	0.408	3.94	29.1	80.4	97.6

It was found that *N*-methylacetamide formed a stable chloroamine over the range of pH 3—9 and was therefore suitable for examination. It was not possible to examine satisfactorily the rate of formation of chloroamine from acetamide, owing to the instability of the former. Although *N*-chloroacetamide when pure is reasonably stable in aqueous solution, it becomes very unstable in the presence of hypochlorous acid, owing presumably to the formation of unstable dichloroamine (see Experimental section). A preliminary examination of the results obtained by using *N*-methylacetamide and phosphate buffers (pH 6—8) showed that the rate increased with pH, but at pH 5.0 in presence of an acetate buffer, the rate, instead of being less, was 10 times as great as at pH 6.0 in presence of a phosphate buffer. Velocity coefficients at pH 5.0 and pH 6.0, calculated from the equation  $v = k_2[\text{HOCl} + \text{OCl}^-][\text{amide}]$  for a series of acetate buffers from half to twice the usual concentrations of acid and salt (Walpole, J., 1914, 105, 2501), are given in Table II.

TABLE II.

Fraction of usual buffer concn.	2.	1.67.	1.33.	1.	0.67	0.25
pH = 6.0.						
NaOAc .....	6.3850	0.3208	0.2567	0.1925	0.1283	0.09625
HOAc .....	0.0150	0.0125	0.0100	0.0075	0.0050	0.00375
$k_2$ .....	0.501	0.432	0.351	0.301	0.224	0.193
$k_0$ (= $k_2$ extrapolated to zero concentration of buffer) = 0.085.						
pH = 5.0; $k_0$ 0.05.						
NaOAc .....	0.280	0.233	0.187	0.14	0.0933	—
HOAc .....	0.120	0.100	0.080	0.060	0.040	—
$k_2$ .....	3.381	2.779	2.145	1.640	1.154	—
						0.472

The variation in  $k_2$  with strength of the buffer solution was shown not to be due to an ionic-strength effect, for additions of potassium nitrate up to 0.6M had but slight effect on the specific rate. Variation of sodium acetate concentration from 0.035 to 0.385M at constant acetic acid concentration (0.015M) changed  $k_2$  from 0.472 to 0.501. This alteration in sodium acetate concentration corresponded to a change in pH from 5.0 to 6.0 and showed that pH was of minor effect on the specific rate. A corresponding series of experiments at constant sodium acetate concentrations of 0.0933M and acetic acid concentrations of 0.04M and 0.00375M (pH 5.0 and 6.0, respectively) changed  $k_2$  from 1.154 to 0.193, which indicated that the accelerating effect observed on increasing the concentration of the buffer was due in the main to the change in the concentration

of acetic acid. The increase in  $k_2$  due to an increase in concentration of acetic acid of 0.1M, calculated from a series of experiments at pH 5.0, was found to be 2.78, and from a series at pH 6.0 was 2.77. The accelerating effect of free acetic acid on the rate of *N*-chlorination is thus the same at pH 5.0 as at pH 6.0.

Curves obtained at pH's 3.0—6.0 by plotting  $k_2$  against acid concentration, various weak acids being used as components of the buffering mixtures, are shown in Fig. 1. In these acid solutions where the concentration of hypochlorite ions is small the speed appears to be satisfactorily given by the equation  $v = k_A[HA][HOCl][:NH]$ , *i.e.*, the bimolecular constant  $k_2$  as already defined =  $k_A[HA]$ , and  $k_A$  is given by the slope of the lines in Fig. 1. The catalytic coefficients obtained in this way are given in Table III. The ionisation constants utilised are those obtained respectively by Cohn, Heyroth, and Menkin (*J. Amer. Chem. Soc.*, 1928, 50, 696),

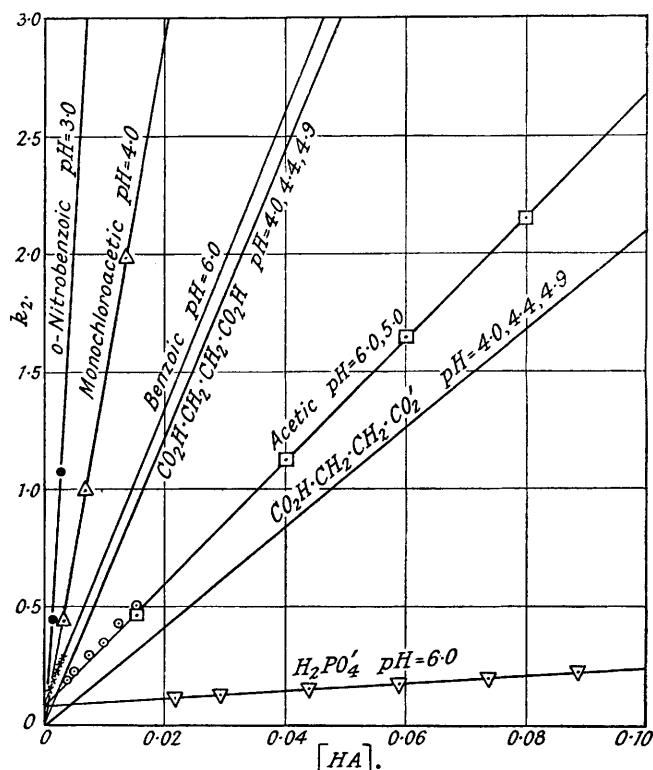


FIG. 1.

TABLE III.

Acid.	Acetic.	Benzoic.	Monochloroacetic.	<i>o</i> -Nitrobenzoic.	Succinic. (1).	(2).
$k_A$ .....	27	62	150	440	61	21
$K_A \times 10^5$ .....	1.86	6.37	155	671	6.89	0.247

Vogel and Jeffrey (*Chem. and Ind.*, 1934, 779), Ostwald (*Z. physikal. Chem.*, 1889, 3, 176), Dippy and Lewis (*J.*, 1937, 1426), and Jones and Soper (*J.*, 1936, 133). The values for  $k_A$  for succinic acid were obtained from experiments in succinate buffers at pH's 4.0, 4.4, and 4.9, which allowed of determination of the separate coefficients for the un-ionised acid and for the acid succinate anion. The relation of the catalytic coefficients,  $k_A$ , to the ionisation constant of the acid is shown in Fig. 2.

Owing to the smallness of  $k_0$  (obtained by extrapolation) in acid solutions, a series of measurements of the rate of *N*-chlorination was made in phosphate buffers from pH 6—9. The results are given in Table IV.

TABLE IV.

N-Chlorination of *N*-methylacetamide.

	pH 6; $k_0$ (by extrapolation) = 0.07.				pH 7; $k_0$ = 0.31.			
$H_2PO_4'$ .....	0.08860	0.06645	0.04430	0.02215	0.04074	0.03055	0.02037	0.01018
$HPO_4''$ .....	0.01140	0.00855	0.00570	0.00285	0.05926	0.04445	0.02963	0.01482
$k_2$ .....	0.231	0.190	0.152	0.111	0.382	0.366	0.343	0.330
	pH 8.0; $k_0$ = 0.72.				pH 9.0; $k_0$ (estimated) = 0.90.			
$H_2PO_4'$ .....	0.00640	0.00480	0.00320	0.00161	—	—	—	—
$HPO_4''$ .....	0.09360	0.07020	0.04680	0.02340	0.100	—	—	—
$k_2$ .....	0.774	0.773	0.738	0.736	0.958	—	—	—

The increase in the value of  $k_0$  defined by the equation  $v = k_0[\text{HOCl} + \text{OCl}'][:\text{NH}]$  obtained by extrapolation to zero acid concentration is closely paralleled by the increasing ionisation of hypochlorous acid. If in the absence of acids the speed is determined by  $v = k_{\text{OCl}'}[\text{OCl}'][:\text{NH}]$ , then  $k_{\text{OCl}'} = k_0[\text{HOCl} + \text{OCl}']/[\text{OCl}']$ . These values of  $k_{\text{OCl}'}$  are given below, and correspond to an increase in the fraction  $[\text{OCl}']/[\text{HOCl} + \text{OCl}']$  from 3.9% at pH 6.0 to 97.6% at pH 9.0.

pH .....	6.0	7.0	8.0	9.0
$k_0$ , mol. <sup>-1</sup> min. <sup>-1</sup> .....	0.07	0.31	0.72	0.90
$k_{\text{OCl}'}$ , mol. <sup>-1</sup> min. <sup>-1</sup> .....	1.78	1.075	0.895	0.922

*N*-Chlorination of Acetanilide.—In view of the effects observed with *N*-methylacetamide, acetanilide was re-examined in a series of phosphate buffers. Unlike that of *N*-methylacetamide, the rate of *N*-chlorination

of acetanilide was not increased by increase of buffer concentration. The specific rate,  $k_2$ , in the case of *N*-methylacetamide is increased at pH 6.0 from 0.152 to 0.231 on doubling the usual concentration of the phosphate buffer (Clark and Lubs, *J. Biol. Chem.*, 1916, 25, 479); the corresponding figures for acetanilide show a decrease from 13.2 to 11.3 (cf. Pryde and Soper, *loc. cit.*, 10.3). Similar experiments on acetanilide in acetate buffers at pH 6.0 gave values for  $k_2$  of 13.7 and 14.1, of similar magnitude to those observed in phosphate at pH 6. In the case of *N*-methylacetamide the change at pH 6.0 from phosphate buffer to acetate buffer increased  $k_2$  by 98%, *i.e.*, from 0.152 to 0.301, the latter value rising by a further 66% to 0.501 on doubling the concentration of the acetate buffer.

It appears therefore that the *N*-chlorination of acetanilide (and other anilides—see Experimental section) by hypochlorous acid is not appreciably catalysed by acids. The values for  $k_2$  observed for acetanilide show a similarity to the coefficients  $k_0$  for *N*-methylacetamide in that they increase with increasing ionisation of the hypochlorous acid. Values of  $k_2$  at pH 5.0–8.0 and of  $k_{\text{OCl}'}$ , defined by  $v = k_{\text{OCl}'}\text{[OCl}'][:\text{NH}]$ , are given below.

#### *N*-Chlorination of acetanilide.

pH .....	5.0	6.0	7.0	8.0
$k_2$ , mol. <sup>-1</sup> min. <sup>-1</sup> .....	1.37	13.2	99	269
$k_{\text{OCl}'}$ , mol. <sup>-1</sup> min. <sup>-1</sup> .....	335.5	335.1	340.4	342.5*

\* If the thermodynamic ionisation constant of hypochlorous acid is used (Ingham and Morrison, *loc. cit.*), *viz.*,  $2.95 \times 10^{-8}$  at 18°, and a calculated value at 25° of  $3.47 \times 10^{-8}$ , the corresponding values of  $k_{\text{OCl}'}$  are 395, 393, 384, and 347.

Thus the *N*-chlorination of acetanilide by hypochlorous acid is satisfactorily explained by interaction of the anilide and hypochlorite ions and apparently there is inappreciable *N*-chlorination by hypochlorous acid molecules. This mechanism applies also to *N*-methylacetamide in low concentrations of acid, but in higher concentrations of acids the chlorination is mainly dependent on the product of the concentrations of the amide, acid, and hypochlorous acid.

In view of the fact that *N*:2:4:6-tetrabromoacetanilide brominates anisole in the presence of an acid such as acetic but not in its absence, Israel, Tuck, and Soper suggested (*J.*, 1945, 547) that an intermediate brominating agent, bromine acetate, was formed from the *N*-bromo-compound and acetic acid. In the formation of *N*-chloromethylacetamide, a similar catalysing effect of acids has been observed and an explanation of the present results is that the acid and hypochlorous acid form a compound analogous to the bromine acetate previously postulated, *i.e.*, a chlorine acetate or, in general, an acyl hypochlorite,  $\text{R}\cdot\text{CO}_2\text{H} + \text{HOCl} \rightleftharpoons \text{R}\cdot\text{CO}\cdot\text{OCl} + \text{H}_2\text{O}$ , which is presumed to be a highly efficient chlorinating agent. Evidence for acyl halogenites has been obtained by Bockemüller and Hoffmann (*Annalen*, 1935, 519, 165), who prepared them in nitrobenzene and in carbon tetrachloride solution by interaction of halogen and silver salts. The effect of increasing concentrations of acid in the present work is to increase proportionally the concentration of the acyl hypochlorite. The fact that *N*-methylacetamide and acetanilide behave differently towards this agent is of interest. Other anilides, *e.g.*, *o*-chloroacetanilide, *o*- and *p*-acetotoluidide, behave similarly to acetanilide in showing no appreciable chlorination by acyl hypochlorite, whereas acetylglycine resembles *N*-methylacetamide in showing an accelerating effect of acids on the *N*-chlorination at constant pH, indicating chlorination by acyl hypochlorite.

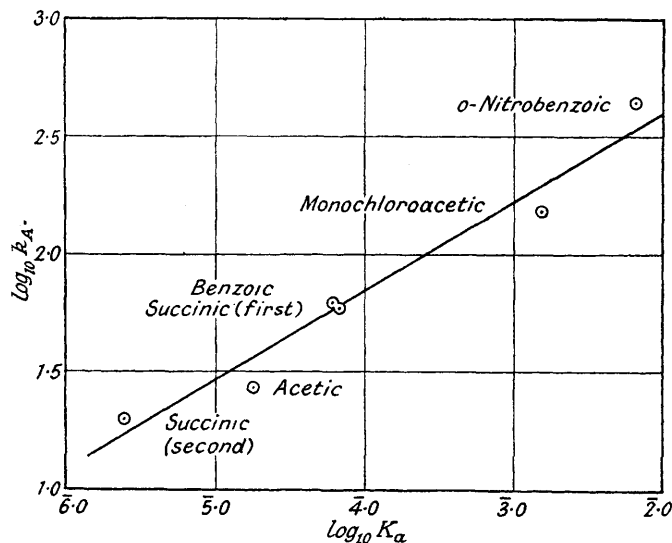
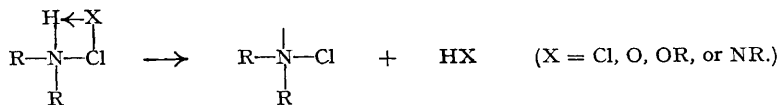


FIG. 2.

*N*-Chlorination may occur by various chlorinating mechanisms of which the following have been studied kinetically: (a) the action of molecular chlorine (Orton, Soper, and Williams, *loc. cit.*), (b) the action of hypochlorite ions (Pryde and Soper, *loc. cit.*; and this paper), (c) the action of another chloroamine (*N*-chloroacetanilide reacts directly with *p*-toluenesulphonamide, Pryde and Soper, J., 1931, 1514), and (d) by the action of acyl hypochlorites (this paper). In all cases the *N*-chlorination may be envisaged as depending on preliminary hydrogen bond formation between the amino-hydrogen and an oxygen, nitrogen, or chlorine atom (in the chlorinating molecule) acting as donor atom:



The specific rate constants for *N*-chlorination by chlorine are rather less than those by hypochlorite ions where comparison is possible [*N*-chlorination of acetanilide by  $\text{Cl}_2$  at  $25^\circ = 130 \text{ mols.}^{-1} \text{ mins.}^{-1}$  (Soper, J. *Physical Chem.*, 1927, 31, 1192), *N*-chlorination of acetanilide by  $\text{OCl}'$  ions (this paper) at  $25^\circ = 338 \text{ mols.}^{-1} \text{ mins.}^{-1}$ ].\*

The removal of halogen from halogenoamine corresponds to the reverse of the above reactions and halogenoamines react directly with halogen acids to form halogens and mixed halogens (Orton and Jones, *Brit. Assoc. Reports*, 1910, 85), with hydroxyl ions to form hypochlorite ions (unpublished work), with alcohols to form alkyl hypochlorite ions (Chattaway and Orton, J., 1899, 75, 1047; Likhosherstov and Sklyarov, *Acta Univ. Voronegiensis*, 1935, 8, 47; *Chem. Abs.*, 1938, 32, 4524), and with acids other than halogen acids to form acyl hypohalogenites accounting for the general acid catalysis of the isomerisation of the *N*-halogenoacetanilides observed by Bell and his co-workers (Bell, J., 1936, 1154).

*N*-Chlorination as envisaged above involves (a) hydrogen bond formation by the amino-hydrogen with the oxygen, nitrogen, or chlorine atom of the halogenating molecule and (b) electron release by the chlorine atom of the halogenating molecule, whereby the chlorine atom becomes a positive chlorine ion. The other stages, *viz.*, the chlorine attachment and proton release by the nitrogen atom are constant factors in the *N*-chlorination of a particular substance.† The greater efficiency in *N*-chlorination of the  $\text{OCl}'$  ion in comparison with molecular chlorine is understandable in view of the greater tendency of the oxygen in the  $\text{OCl}'$  ion to form a hydrogen bond, which is envisaged as the preliminary step. No evidence was obtained for *N*-chlorination by  $\text{HOCl}$ . This fact is due presumably to the decreased electron-donating power of the oxygen in  $\text{HOCl}$  as compared with  $\text{OCl}'$ . It is therefore difficult to understand why an acyl hypochlorite should be such an active chlorinating agent for certain substances such as *N*-methylacetamide and acetyl glycine.

In the acyl hypochlorite the donor properties of the hypochlorite oxygen should be less than in hypochlorous acid (relative inductive effects of O-H and O-C), and its tendency to form hydrogen bonds and cause *N*-chlorination should likewise be less. In view of the fact that the acyl hypochlorite is not apparently an active *N*-chlorinating agent for the anilides, the explanation of its activity in chlorinating *N*-methylacetamide may be due to some constitutional property of the latter. Thus the *isoamide* structure has been advocated for trichloroacetamide (Hantzsch, *Ber.*, 1931, 64, 661) on the basis of a comparison of its absorption spectrum with those of its *O*- and *N*-derivatives. If *N*-methylacetamide is partly in the *isoamide* form,  $\text{CH}_3\text{N}^+\text{C}(\text{OH})\text{CH}_3$ , the acyl hypochlorite may add on across the double bond (Bockemüller and Hoffmann, *loc. cit.*) in a manner analogous also to the way in which phenyl hypochlorite,  $\text{PhOCl}$ , adds on to butylene to give 2-chloro-3-phenoxybutane (Likhosherstov and Arkhangel'skaya, *J. Gen. Chem. U.S.S.R.*, 1937, 7, 1914). Such an explanation would require that the aliphatic amides exist to a much greater extent in the *isoamide* structure than do the anilides; otherwise, the anilides also should be *N*-chlorinated by acyl hypochlorites. The evidence from ultra-violet absorption spectra for the *isoamide* structure of anilides, based on the dissimilarity of the absorption curves of *N*-methylacetanilide and acetanilide (Ramart-Lucas and Wohl, *Compt. rend.*, 1933, 196, 120), is slight, for in the anilides substitution of the amino-hydrogen by methyl would tend to reduce the resonance of the  $\text{NH}\cdot\text{CO}\cdot$  system which, in the contributing form  $\text{NH}^+\text{C}\bar{\text{O}}\cdot$ , is conjugated with the benzene ring and hence might be expected to affect considerably the absorption, independently of any effect due to the possible structure,  $\text{N}^+\text{C}(\text{OH})\cdot$ . The difference in the absorption spectra of acetanilide and *N*-methylacetanilide cannot therefore be regarded as evidence for the *isoamide* structure of the former.

#### EXPERIMENTAL.

*Hypochlorous Acid.*—Hypochlorous acid (Pryde and Soper, *loc. cit.*) was stored over mercuric oxide, and before use was shaken with fresh yellow mercuric oxide and centrifuged.

*N-Methylacetamide.*—A cold solution of freshly distilled acetic anhydride in 3 vols. of dry ether was added slowly to excess of methylamine in dry ether. The reaction mixture was kept below  $-10^\circ$  for an hour. The product was purified by stirring with a little water and potassium carbonate until alkaline to litmus, and the ether portion was then

\* The figures for  $k_{\text{OCl}'}$  ( $k_{\text{N}}$ , Pryde and Soper, *loc. cit.*) were calculated on a limited range of pH using a value for  $K_{\text{HOCl}}$  of  $1.0 \times 10^{-8}$  and are therefore some 3 times too large.

† *C*-Chlorination shows marked contrasts with *N*-chlorination in that  $\text{Cl}_2$  is greatly more efficient than  $\text{HOCl}$  in the chlorination of phenols, and in the *C*-chlorination of anilides there is no evidence that the  $\text{OCl}'$  ion can cause nuclear chlorination at all.

dried with anhydrous potassium carbonate and fractionated, the main portion distilling at 120—125° (column temp.)/40 mm. and solidifying to very hygroscopic colourless needles, m. p. 27.8° (cf. 28°; Hofmann, *Ber.*, 1881, **14**, 2729).

**Buffer Solutions.**—For succinic, benzoic, *o*-nitrobenzoic, and monochloroacetic acids, the buffers were prepared so as to give the desired pH ( $\pm 0.01$  unit) against a Cambridge glass-electrode pH meter standardised with 0.05M-potassium hydrogen phthalate. The stability of hypochlorous acid to the buffer was tested for each experiment.

**Velocity Measurement.**—Hypochlorous acid and amide solutions of twice the required strength were prepared in buffers. When both solutions had attained the temperature of the thermostat, 25.0° ( $\pm 0.02^\circ$ ), the reaction was started by addition of 50 c.c. of the hypochlorous acid solution to an equal volume of the amide solution.

The composition of the reaction mixture was then determined at suitable intervals by transferring 5-c.c. portions to (a) 5 c.c. of 3% freshly distilled phenol, shaking for 10 seconds, followed by the addition of 5 c.c. of 5N-acetic acid then 5 c.c. of 2% potassium iodide, whereby the chloroamide titre was determined, and (b) 5 c.c. of 5N-acetic acid followed by 5 c.c. of 2% potassium iodide, which gives the hypochlorous acid + chloroamide titre, the iodine liberated being titrated against N/200- or N/500-thiosulphate.

The results for a typical experiment are given below.

$$\text{CH}_3\cdot\text{CO}_2\text{H} = 0.0150\text{M}; \text{CH}_3\cdot\text{CO}_2\text{Na} = 0.385\text{M}; \text{CH}_3\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_3 = 0.0200\text{M}; \text{HOCl} = 0.00457\text{M}.$$

Time (mins.)	1.00	10.00	14.25	30.0	50.0	70.0	90.0	93.5	120.0
Titre of :NCl, c.c.	0.17	0.94	—	2.41	3.56	4.52	5.24	—	6.15
Total titre, c.c.	—	—	9.25	—	—	—	—	9.20	—
$k_2$	—	0.499	—	0.505	0.502	0.505	0.497	—	0.497

$k_2 = 0.501 \pm 1\%$ .

In the case of acetamide, the chloroamide formed was unstable in the presence of hypochlorous acid. The stability of this chloroamide to hypochlorous acid in phosphate buffer pH 7.0 is given below.

$$\text{KH}_2\text{PO}_4 = 0.050\text{M}; \text{NaOH} = 0.0296\text{M}; \text{CH}_3\cdot\text{CO}\cdot\text{NHCl} = 0.020\text{M}; \text{HOCl} = 0.010\text{M}. \text{Temp.} = 13^\circ.$$

Time (mins.)	1.00	2.00	20.00	28.50	75.00	85.00	182.5	184.0	1080
Titre of :NCl, c.c.	—	38.28	—	34.05	27.24	—	19.21	—	10.25
Total titre, c.c.	53.62	—	43.90	—	—	29.75	—	21.12	10.56

N-Chloroacetamide in the absence of hypochlorous acid shows only slight decomposition under similar conditions.

**Catalytic Effects of Acids.**—The values of  $k_2$  plotted against the concentration of acid are shown in Fig. 1, and the catalytic coefficients recorded in Table III. For succinic acid buffers, where catalysis is due both to the acid and the acid anion,  $k_2 = k_{\text{H}_2\text{A}}[\text{H}_2\text{A}] + k_{\text{HA}^-}[\text{HA}^-]$ , a series of measurements using different amounts of the buffer mixture were made at pH's 3.96, 4.43, and 4.94;  $k_2$  increased linearly with increase of buffer concentration. Substitution for the acid and acid anion concentrations at two different pH values allows of solution of the separate catalytic coefficients  $k_{\text{H}_2\text{A}}$  and  $k_{\text{HA}^-}$ . The calculated and observed values for  $k_2$ , values of  $k_{\text{H}_2\text{A}}$  and  $k_{\text{HA}^-}$  of 61 and 21 being used, obtained as indicated, are given below.

*Catalytic influence of succinate buffers.*

$$\text{CH}_3\cdot\text{CO}\cdot\text{NHCH}_3 = 0.0200\text{M}; \text{HOCl} = 0.0050\text{M}; \text{temp.} = 25.0^\circ (\pm 0.02^\circ).$$

pH.	$[\text{H}_2\text{A}]$ .	$[\text{Na}_2\text{A}]$ .	$[\text{H}_2\text{A}]$ , calc.	$[\text{HA}^-]$ , calc.	$k_2$ .	$k$ , calc.
3.96	0.1398	0.03612	0.1662	0.0104	9.99	10.36
	0.1049	0.02709	0.1247	0.0078	6.95	7.77
	0.0699	0.01806	0.0831	0.0052	5.03	5.18
	0.0350	0.00903	0.0416	0.0026	2.36	2.59
4.43	0.06085	0.03915	0.0337	0.0623	3.41	3.37
	0.03043	0.01958	0.0169	0.0312	1.81	1.69
	0.01521	0.00979	0.0084	0.0156	1.0	0.84
4.94	0.05209	0.06875	0.01460	0.0875	2.57	2.73
	0.04167	0.05500	0.01168	0.0700	2.08	2.18
	0.02084	0.02750	0.00584	0.0350	1.08	1.09
	0.01042	0.01375	0.00292	0.0175	0.558	0.55

**Absence of Acid Catalysis in the N-Chlorination of Anilides.**—Values of  $k_2$  observed in phosphate and acetate buffers are shown below. The velocity coefficients refer to the following substances: (1) *o*-chloroacetanilide, (2) *o*-acetotoluidide,

*Velocity coefficients of N-chlorination.*

Buffer pH.	Molar concn. of buffer acid.	Molar concn. of buffer salt.	(1).	(2).	(3).	(4).	(5).	(6).
Acetate, 6.0	$\text{CH}_3\cdot\text{CO}_2\text{H}$ .	$\text{CH}_3\cdot\text{CO}_2\text{Na}$ .						
	0.00375	0.0963	155	13.0	—	—	0.356	0.193
	0.00750	0.1925	149	12.5	13.7	10.8	0.387	0.301
Phosphate, 6.0	0.0150	0.3850	148	—	14.1	11.0	0.462	0.501
	$\text{H}_2\text{PO}_4'$ .	$\text{HPO}_4''$ .						
	0.0443	0.00574	145	—	13.2	10.8	0.280	0.152

(3) acetanilide, (4) *p*-acetotoluidide (5), acetyl glycine, (6) *N*-methylacetamide. No acid catalysis is observed for substances (1)—(4), and the velocity coefficients observed in phosphate buffers are similar to those in acetate buffers.

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