621. *The Mechanism of Formation of Dialkylchloroamines from Hypochlorous Acid.*

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The specific rate of interaction of dialkylamines and hypochlorous acid is very fast in near-neutral solution, but decreases in acid solution, becoming measurable at pH 3. The kinetic data fit either an interaction of neutral dialkylamine with hypochlorous acid or an interaction of hypochlorite ions with amine cations. The reaction rate is affected by neutral salt, but is not affected at constant pH by the concentration of free acid in the buffer. In this latter respect the reaction resembles the interaction of hypochlorous acid with anilides, whereas with amides believed to exist in an *iso*amide form, acid catalysis is marked.

The kinetics of the formation of *N*-chloroacetanilide from acetanilide and hypochlorous acid in buffered aqueous solution can be expressed over the examined pH range of 5 to 8 by the equation $v = k_2^{\text{OCl}}[\text{OCl}^-][\text{acetanilide}]$ (Mauger and Soper, *J.*, 1946, 71). For certain amides, *e.g.*, *N*-methylacetamide and acetylglycine, an additional mechanism of *N*-chlorination operates which had been explained in terms of a possible structural difference between these amides and the anilides. In the *N*-chlorination of the above amides but not in the case of anilides, a strong catalysing influence is observed owing to the acid component of the buffer mixture, employed in stabilising the pH of the solution, giving an overall rate of *N*-chlorination which can be represented as

$$v = k_2^{\text{OCl}}[\text{OCl}^-][\text{amide}] + k^{\text{AcOCl}}[\text{HOCl}][\text{AcOH}][\text{amide}]$$

Since there is other evidence for the existence of acyl hypochlorites the second term was regarded as due to a reaction of acyl hypochlorite present in small concentration and formed by the reversible reaction $\text{HOCl} + \text{AcOH} \rightleftarrows \text{AcOCl} + \text{H}_2\text{O}$. A similar dependence of the rate of iodination on the free acid concentration of the buffer solution appears in the iodination of phenol (Painter and Soper, *J.*, 1947, 342).

Such acid catalysis cannot be due to a reversible reaction producing positive chlorine, $\text{AcOH} + \text{HOCl} \rightleftarrows \text{Cl}^+ + \text{AcO}^- + \text{H}_2\text{O}$, since the concentration of acylate ion does not affect the catalysis, whereas, if the above equilibrium were established, an increased concentration of acylate ions should decrease the rate. Small concentrations of acyl hypochlorite may, however, be expected to increase the rate of chlorination above that observed when using hypochlorous acid since acyl hypochlorites would tend to release positive chlorine much more easily in the intermediate critical complex. This assertion is based on a comparison of the relative ease of ionisation of acyl hypochlorite and of hypochlorous acid to form positive chlorine ions as given by their relative ionisation constants. Whilst the relative ease of release of positive chlorine by a series of reagents to a nucleophilic centre would not be expected to be strictly parallel to their ionisation constants $[R^-][Cl^+]/[RCl]$ owing, in ionisation equilibria, to stabilising influences on the ions due to hydration and resonance, nevertheless some degree of parallelism might be expected, and a reagent which could ionise relatively easily in water into positive chlorine should, when acting molecularly in substitution, release positive chlorine more easily to the nucleophilic centre than one in which the ionisation into positive chlorine is relatively difficult. The ratio of the ionisation constants of the reactions,

$$\mathrm{AcOCl} \rightleftharpoons \mathrm{AcO^-} + \mathrm{Cl^+} \qquad\qquad \mathrm{HOCl} \rightleftharpoons \mathrm{OH^-} + \mathrm{Cl^+}$$

is given by $[AcO^-][HOCl]/[AcOCl][OH^-]$. But since in a mixture of HOCl and AcOH, the equilibrium amount of the mixed anhydride AcOCl is slight, the ratio of the chlorinating efficiency of a mixture of HOCl and AcOH, based on its AcOCl content, will be less than that of AcOCl by a factor equal to the equilibrium constant $[AcOCl]/[HOCl][AcOH]$. Hence the chlorinating efficiency of a mixture of AcOH and HOCl, compared with that of HOCl alone, will on the above assumption be given by

$$\frac{[\mathrm{AcO^-}][\mathrm{HOCl}]}{[\mathrm{AcOCl}][\mathrm{OH^-}]}\cdot\frac{[\mathrm{AcOCl}]}{[\mathrm{HOCl}][\mathrm{AcOH}]} = \frac{[\mathrm{AcO^-}][\mathrm{H^+}]}{[\mathrm{AcOH}]}\Big/[\mathrm{H^+}][\mathrm{OH^-}] = K_a{}^{\mathrm{AcOH}}/K_w$$

With acetic acid, this ratio is approximately 2×10^9, *i.e.*, a mixture of hypochlorous and acetic acids in presumed equilibrium with a small concentration of acetyl hypochlorite would be expected to act as a more efficient chlorinating agent than molecular hypochlorous acid. This conclusion would refer to substitutions of sufficiently high energy of activation. In a reaction of low energy of activation, the much greater concentration of hypochlorous acid might result in its greater share in the chlorination, overshadowing the effect of the more reactive but less available acyl hypochlorite.

In investigations up to the present, *N*-chlorination by hypochlorous acid molecules has not been observed, the uncatalysed reaction in all cases being due to the reaction of hypochlorite ions. The specific rate of such *N*-chlorination by OCl^- ions may exceed that by molecular chlorine, although the ease of formation of positive chlorine from the latter must be enormously greater. It is for this reason that the formation of chloroamine from OCl^- ions is regarded as involving some different substitution mechanism from that accepted for replacement of a hydrogen attached to a carbon atom. The formation of a hydrogen bridge between the nitrogen atom and the oxygen of the hypochlorite ion has been suggested (Mauger and Soper, *loc. cit.*) and would provide an explanation of the unexpected efficiency of hypochlorite ions, in comparison with that of hypochlorous acid and of chlorine.

The acid catalysis of halogenation by hypohalous acid has also now been observed in the iodination of phenol, in the bromination of benzene by hypobromous acid (unpublished work with W. J. Wilson), and in the addition of hypochlorous acid to allyl alcohol (unpublished work with J. K. Martin). The examples so far obtained appear to have as a common factor the presentation of positive halogen by the acyl hypohalite molecule to a double-bonded atom capable of becoming a nucleophilic centre, the positive halogen being relinquished by the acylate ion. Those amides which show this effect in *N*-chlorination may exist in an *iso*amide form. In no case has any evidence been obtained for addition of acyl hypohalite across the double bond, for in such acid-catalysed reactions there is no disappearance of acid as would occur if there were addition of the acyl hypohalite molecule as a whole.

In conformity with the above hypothesis no acid catalysis has been observed in the present work on the *N*-chlorination of dialkylamines. The action of hypochlorous acid on dialkylamines is practically instantaneous in near neutral solution but decreases in acid solution, becoming measurable about pH 3. In experiments at 25·0° at constant pH and with increasing concentration of the buffer a decrease was observed which could be duplicated by addition of neutral salt such as potassium nitrate and was shown to be an ionic-strength effect. An example of such effect of the concentration of a chloroacetic acid buffer is given in Table I, where $k_2{}^{\mathrm{obs.}}$ is given by $v = k_2{}^{\mathrm{obs.}}[\mathrm{HOCl} + \mathrm{OCl'}][\mathrm{Et_2NH} + \mathrm{Et_2NH_2{}^+}]$.

TABLE I.

pH.	$CH_2Cl{\cdot}CO_2H$.	$CH_2Cl{\cdot}CO_2Na$.	$k_2^{obs.}$ (mol.$^{-1}$ min.$^{-1}$).
2·88	0·0124	0·0124	14·3
2·88	0·0497	0·0497	13·5
2·88	0·0995	0·0995	9·5

No catalysis by the free acid of the buffer was observed.

The dependence of the rate of *N*-chlorination on the pH of the solution was determined in the presence of 0·2M-potassium nitrate to minimise effects due to changes in ionic strength. The values obtained at 25·0° with diethylamine are given in Table II.

TABLE II.

N-Chlorination of diethylamine. Temp. 25·0°, KNO_3 = 0·2M.

Temp. 25·0°, KNO_3 = 0·2M.

pH.	$[OH]^- \times 10^{11}$.	$k_2^{obs.}$.	$10^{-11}k_2^{obs.}/[OH^-]$.	pH.	$[OH^-] \times 10^{11}$.	$k_2^{obs.}$.	$10^{-11}k_2^{obs.}/[OH^-]$.
2·32	0·211	1·99	9·48	2·91	0·822	7·78	9·45
2·47	0·298	2·87	9·64	3·30	2·02	19·4	9·60
2·60	0·404	3·84	9·50	3·51	3·26	29·8	9·14
2·66	0·462	4·55	9·85	2·59 *	0·401	3·81	9·49 *
2·78	0·610	5·83	9·55	3·06 *	1·17	11·5	9·84 *
2·83	0·682	6·55	9·60				

In these experiments the free chloroacetic acid decreases from 0·0933 to 0·249N. from pH 2·32 to pH 3·51, whilst the sodium chloroacetate increases from 0·00622 to 0·0746N. over the same pH range.

In order further to confirm that the speed is independent of the concentration and nature of the free acid in the buffer, two experiments were carried out in a buffer of phosphoric acid and sodium dihydrogen phosphate, the results being shown marked with an asterisk in the above table. In these two experiments the free phosphoric acid was 0·024 and 0·008M.

Similar behaviour was observed in the pH range 2—3 for dimethylamine and dipropylamine, the values of $10^{-11} k_2^{obs.}/[OH^-]$ for dimethylamine being 49·9, 51·8, 50·3, 50·6 and for dipropylamine 25·4, 27·0, 25·7, 24·8. There is no indication of any catalysis by the free acid of the buffer in any of these cases.

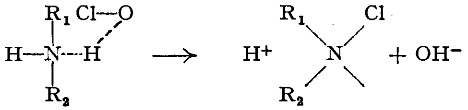
The dependence of the rate of *N*-chlorination on the hydroxyl-ion concentration according to the nature of the reacting species is set out in Table III.

TABLE III.

Reaction.	Reacting species.	$k_2^{obs.}$ propl. to	Reaction.	Reacting species.	$k_2^{obs.}$ propl. to
1	$HOCl + R_2NH$	$[OH']^1$	4	$OCl' + R_2NH_2^+$	$[OH']^2$
2	$HOCl + R_2NH_2^+$	$[OH']^0$	5	$Cl^+ + R_2NH$	$[OH']^0$
3	$OCl' + R_2NH$	$[OH']^2$	6	$Cl^+ + R_2NH_2^+$	$[OH']^{-1}$

Thus either reaction 1 or 4 would agree with observation and in both cases $k_2^{obs.}$ would be expected to show a marked decrease with increase in ionic strength due to Brønsted primary and secondary effects.

The mechanisms cannot be differentiated on the present work; mechanism 4 is favoured by the great donor properties of the OCl^- ion in comparison with HOCl, whilst in mechanism 1 the free electron pair on the amine nitrogen could engage the hydrogen atom of the hypochlorous acid. In each case the same complex would be formed :



In view, however, of the efficiency of hypochlorite ions in other *N*-chlorinations, constants have been evaluated on mechanism 4. The values of k_{OCl}, given by $v = k_{OCl}[OCl^-][R_2NH_2^+]$ are related to $k_2^{obs.}$ by the equation, $k_{OCl} = k_2^{obs.}[H^+]/K_a^{HOCl}$, where K_a^{HOCl}, the ionisation constant of hypochlorous acid, has the value 4×10^{-8}. The mean values of k_{OCl}, the specific rate of interaction of hypochlorite and amine cations, for dimethyl-, diethyl-, and dipropyl-amine are $12·6 \times 10^5$, $2·4 \times 10^5$, and $6·4 \times 10^5$ mol.$^{-1}$ min.$^{-1}$, respectively, whilst the values of their basic ionisation constants are $0·14 \times 10^{-3}$, $1·26 \times 10^{-3}$, and $1·02 \times 10^{-3}$, corresponding to acidic ionisation constants of the amine cations of $1{\cdot}35 \times 10^{-11}$, $0{\cdot}79 \times 10^{-11}$, and $0{\cdot}98 \times 10^{-11}$, respectively.

Experimental.—The chloroamine concentration in the reaction mixtures was determined by addition of 10-c.c. aliquots to 10 c.c. of a 3% solution of freshly distilled phenol, buffered at pH 8, shaking it for 5 seconds, and then adding 10 c.c. of 5N-acetic acid and 10 c.c. of 2% potassium iodide solution. This gives the titre of the chloroamine. The total titre of hypochlorous acid plus chloroamine, determined by addition of 10 c.c. of 2% potassium iodide solution, remained constant over the period examined for the experiment which was of the order of 30 minutes. The chloroacetic acid buffers were made by partial neutralisation of M-monochloroacetic acid and dilution to the required strength, the pH's being checked on a Cambridge glass-electrode pH meter.

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