CCVII.—*The Interaction of Anilides and Hypochlorous Acid.*

By David Reginald Pryde and Frederick George Soper.

The rate of interaction of chlorine with anilides to form chloroamines indicates that the reaction is bimolecular and simultaneous with the formation of *C*-chloroanilides (Orton, Soper, and Williams, J., 1928, 998). The general method of preparation of chloroamines from anilides by means of hypochlorite in the presence of bicarbonate (Chattaway and Orton, J., 1901, **79**, 244), avoids the simultaneous formation of *C*-chloroanilides and the mechanism of the reaction is therefore quite distinct from that involving chlorine.

The measurement of the rate of formation of *N*-chloroacetanilide from acetanilide and hypochlorous acid is complicated by the fact that both this acid and the product liberate iodine from acidified potassium iodide. *N*-Chloroacetanilide may, however, be estimated by first removing the hypochlorous acid by addition of a phenol and dilute hydrochloric acid, in the presence of which the chloroamine is sufficiently stable.* The iodine then liberated on addition of potassium iodide measures the chloroamine which has been formed.

It was found that an aqueous solution could be prepared which

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* The time of 1% decomposition of *N*-chloroacetanilide in the presence of 0·1*N*-hydrochloric acid is 9 mins.

did not react with acetanilide to give a *C*-chloro-derivative. The presence of a slight concentration of chloride is sufficient, however, to give chlorine, $HCl + HClO = Cl_2 + H_2O$, which reacts rapidly with acetanilide in water ($k = 17{,}000$) to give a mixture of *o*- and *p*-chloroacetanilides. A very high degree of purity of hypochlorous acid is therefore required in order that a fall in iodine titre should not be observed on admixture with acetanilide solution.

On examination, the rate of formation of *N*-chloroacetanilide from hypochlorous acid was found to vary with the method of purification of the acid. This inconsistency in the results was probably due to variations in the hydrogen-ion concentration of the mixture, since experiments in buffered solutions gave reproducible velocity coefficients. The results obtained for the velocity coefficient, *k*, given by the equation

$$d[\text{chloroamine}]/dt = k[\text{HOCl}][\text{anilide}],$$

in solutions where the hydrogen-ion concentration was varied from $0{\cdot}6$ to $2{\cdot}6 \times 10^{-6}$, are given in Table I.

TABLE I.

Initial concentrations : $[:\text{NH}] = 0{\cdot}02M$; $[\text{HOCl}] = 0{\cdot}005M$.
Temp. = 25·0°.

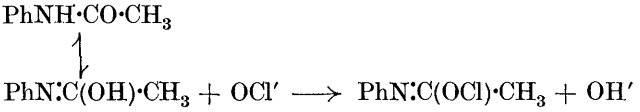
$[H^{\cdot}] \times 10^6$	0·69	1·00	1·35	2·04
k	14·9	10·3	7·3	5·1
$k \times [H^{\cdot}] \times 10^6$	10·3	10·3	9·85	10·4

It will be seen that, within the limits examined, the speed of formation is inversely proportional to the hydrogen-ion concentration of the solution. This relation is also observed for the formation of the chloroamines of the isomeric chloroacetanilides and the acetamidobenzoic acids.

The similar behaviour of hypochlorous acid in its chlorination of phenols (Soper and Smith, J., 1926, 1582) was shown to be due to an interaction of un-ionised hypochlorous acid and the phenoxide ion. Investigation of the formation of chloroamines over the wide range of alkalinity possible in the chlorination of phenols is precluded in the present case, since in neutral and mildly alkaline media the speed is too rapid for measurement, whilst in strongly alkaline solutions the equilibrium, $\text{KOH} + :\text{NCl} \rightleftharpoons \text{KOCl} + :\text{NH}$, favours the production of hypochlorite and little chloroamine is formed. Also in these alkaline solutions, oxidation occurs, the chlorine appearing as chloride and the solution becoming brown.

The observed relation between the speed of formation of the chloroamine and the hydrogen-ion concentration may be due to reaction taking place either between ionised acetanilide, $\text{NPh}:\text{CMe}{\cdot}\text{O}'$, and un-ionised hypochlorous acid, or between the hypochlorite ion and acetanilide. A decision between these alternatives may be possible by a study of the rates of *N*-chlorination of amines in which the acyl group is absent, with consequent lapse of anion-forming ability. Such amines have hitherto been found, however, to react with hypochlorous acid too rapidly for measurement.

A possible view of the mechanism is the replacement of the hydroxyl group of the *aci*-form of the anilide by the hypochlorite ion:



$$\begin{array}{l} \mathrm{PhNH{\cdot}CO{\cdot}CH_3} \\ \quad\updownarrow \\ \mathrm{PhN{:}C(OH){\cdot}CH_3} + \mathrm{OCl'} \longrightarrow \mathrm{PhN{:}C(OCl){\cdot}CH_3} + \mathrm{OH'} \end{array}$$

with the formation of an *O*-chloro-derivative. This formula would afford a ready explanation of the observed formation of carbylamine from *N*-chloroacetanilide in alkaline solution. It might also be related to the fact that the transformation of this substance in the dark into a nuclear chloro-derivative occurs definitely by the intermediate formation of chlorine and not by intramolecular migration of a chlorine atom (Orton and Jones, P., 1909, **25**, 196; *Brit. Assoc. Reports*, 1910, 85). The benzidine and semidine conversions, and the rearrangement of arylhydroxylamines and nitroamines (Orton, Reed, and Thomas, *ibid.*, 1912, 117; Bradfield and Orton, J., 1929, 915), where the migrating group is attached to nitrogen, are apparently true intramolecular changes. Work on the rearrangement of chloroamines in which the acyl group is absent is in progress to examine this suggested cause for the contrasted mechanism of rearrangement of these substances.

The velocity coefficients of *N*-chlorination at 25·0°, defined by the equation $d[\text{chloroamine}]/dt = k_N[\mathrm{OCl'}][{:}\mathrm{NH}]$, and related to the bimolecular coefficients k by the expression $k_N = k[\mathrm{HOCl}]/[\mathrm{OCl'}] = k[\mathrm{H^{\bullet}}]/K_a$, are given, for the anilides examined, in Table II. The figures under $k_N^{\mathrm{Cl_2}}$ refer to the rates of *N*-chlorination by chlorine in 40% acetic acid at 18·0° (J., 1928, 998).

TABLE II.

Temperature 25·0° ± 0·02°.

	$[\mathrm{H^{\bullet}}] \times 10^6$.	k_N.	$k_N^{\mathrm{Cl_2}}$.
N-Chloro-acetanilide	0·69—2·04	1120	96
,, -*o*-acetamidobenzoic acid	0·10—0·16	17	—
,, -*m*- ,, ,, ...	0·63—1·00	44	—
,, -*p*- ,, ,, ...	0·63—1·00	76	—
N : *o*-Dichloroacetanilide	3·98—5·01	6440	286
N : *m*- ,, ...	3·98—5·01	2970	172
N : *p*- ,, ...	1·00—1·35	2700	115

EXPERIMENTAL.

Materials.—The hypochlorous acid was prepared by passing chlorine through water in which was suspended yellow mercuric oxide and distilling the solution at 50° under reduced pressure. In order to test the freedom of the acid from chlorine, the titres were compared of 2 c.c. treated with acidified potassium iodide (*a*) forthwith and (*b*) after 15 minutes' standing in the dark with acetanilide solution. The difference in titres is due to *C*-chlorination of the anilide which is to be attributed to the presence of traces of chlorine. Aspiration of air through hypochlorous acid (Richardson, J., 1903, **83**, 380) reduced the fall of titre from 33·2% to 9·2% in 2 hrs. and to 7·1% in 40 hrs. After 4 hours' aspiration, chlorine and hypochlorous acid appear to be removed from the solution at equal rates.

Treatment of freshly distilled hypochlorous acid with roasted mercurous oxide shortly before use gave a sample of acid which showed no fall in titre on addition to acetanilide solution. It is necessary, however, that water distilled from chromic acid and baryta (Moseley and Myers, *J. Amer. Chem. Soc.*, 1918, **40**, 1409) should be used in making up solutions, for otherwise, oxidation of impurity in the water may occur with the formation of hydrochloric acid.

The acetyl derivatives, except acetanilide, which was recrystallised twice from water, were prepared from the purified amines.

The *p*-cresol was redistilled and used in saturated aqueous solution.

Stability of the Phosphate Buffer Solutions to Hypochlorous Acid.—The phosphate buffer solutions were prepared from potassium dihydrogen phosphate and sodium hydroxide solutions as described by Clark (" Determination of Hydrogen Ions," 1920, 76). No fall in titre of hypochlorous acid in such solutions was observed over a period of 1 hr.

Velocity Measurements.—Sufficient hypochlorous acid solution to make 100 c.c. of 0·005*M*-solution was added at 25·0° to an aqueous mixture of anilide and phosphate buffer also at that temperature. 10-C.c. portions were added at suitable intervals to 10 c.c. of saturated cresol solution and acidified with 1 c.c. of $\frac{1}{2}N$-hydrochloric acid, followed by addition of potassium iodide. The iodine liberated, corresponding to the chloroamine present, was titrated with thiosulphate in the presence of a stream of nitrogen. Portions were also added at intervals directly to acidified iodide. The titres of these show, usually, a slow fall with time, indicating that some *C*-chlorination occurs. The values of the velocity coefficients of *N*-chlorination are calculated as described by Orton, Soper, and Williams (*loc. cit.*).

The details of a typical experiment are given in Table III.

TABLE III.

[Anilide) = 0·002; [HOCl] = 0·002; [NaOH] = 0·00574; [KH_2PO_4] = 0·05*M*.

Time, mins.	1·20	3·00	6·10	9·00	11·3	14·0	18·6
Total titre of 10 c.c.	—	14·30	—	14·18	—	14·10	—
Titre of :NCl, c.c.	0·92	—	3·80	—	5·52	—	7·24
k	27·5		28·5		26·6		26·1

In conclusion, the authors wish to acknowledge their indebtedness to the late Professor K. J. P. Orton, F.R.S., for the interest taken in this work, and one of them (D. R. P.) expresses his thanks to the Advisory Council of the Department of Scientific and Industrial Research for a maintenance grant.

UNIVERSITY COLLEGE OF NORTH WALES,
BANGOR.

[*Received, February* 14*th*, 1931.]