242. *The Mechanism of the* N-*Halogenoacylanilide Rearrangements.*

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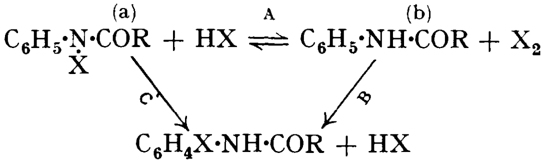
The various possibilities involved in the rearrangement of a *N*-halogenoacylanilide in presence of the corresponding halogen acid may be summarised in the following scheme :



$$\begin{tikzcd} \overset{(a)}{C_6H_5\cdot\underset{X}{N}\cdot COR} + HX \arrow[rr, shift left, "A"] \arrow[dr, "C"'] & & \overset{(b)}{C_6H_5\cdot NH\cdot COR} + X_2 \arrow[ll, shift left] \arrow[dl, "B"] \\ & C_6H_4X\cdot NH\cdot COR + HX & \end{tikzcd}$$

Reaction B is a nuclear halogenation, and reaction C a migration of halogen catalysed by the acid HX. In the case of the rearrangement of *N*-chloroacetanilide in water or dilute acetic acid there is good evidence that the mechanism involves reaction A followed by B, the first step being slow and determining the net rate of the reaction (for a summary of the chief evidence, see Orton, Soper, and Williams, J., 1928, 998). The much slower change in aqueous acid solutions not originally containing halogen acid can be reasonably attributed to the same mechanism, halogen acid being first formed by hydrolysis. It was, however, shown by Orton and Jones (*Brit. Assoc. Rep.*, 1910, 85; J., 1909, **95**, 1456) that in acetic acid of 60% or higher concentration the reversible reaction A is fast compared with the rate of formation of *p*-chloroacetanilide. Under these conditions systems (a) and (b) will be in equilibrium, and it is hence impossible to decide from kinetic data whether the reaction velocity measured is that of the intramolecular rearrangement C or the nuclear halogenation B. The allied migrations of the *N*-nitroamines and the benzidine rearrangement appear to take place intramolecularly (see Ingold and Kidd, J., 1933, 984) and it is therefore of interest to discover whether the migration of halogen can ever take place without the intervention of free halogenating agent.

It has been shown in previous papers (Bell, *Proc. Roy. Soc.*, 1934, *A*, **143**, 377; Bell and Levinge, *ibid.*, 1935, **151**, 211) that the rearrangement *N*-bromoacetanilide ⟶ *p*-bromoacetanilide is catalysed by carboxylic acids and phenols in a number of non-dissociating solvents. With this type of catalyst it is difficult to see how either bromine or hydrogen bromide could be formed in the absence of water. However, since the solutions used sometimes showed a yellow colour resembling that of bromine, attempts were made to detect the presence of free bromine in chlorobenzene solutions undergoing rearrangement. The velocity of the reaction between bromine and acetanilide in chlorobenzene solution was also measured. No free bromine was detected in the first experiment, and the maximum amount which could have escaped detection is quite inadequate to account for the observed rate of formation of *p*-bromoacetanilide. This result indicates strongly that the migration is intramolecular under these conditions.

Some experiments were also carried out with hydrogen bromide as a catalyst in chlorobenzene solution. The equilibrium A is set up instantaneously and results in almost complete formation of acetanilide and free bromine. (This agrees with the results of Orton and Jones, *loc. cit.*, for solutions in acetic acid, chloroform, and carbon tetrachloride.) It is hence impossible to decide whether the formation of *p*-bromoacetanilide in this system is due to a catalysed intramolecular migration or to nuclear bromination. The undissociated hydrogen bromide molecule is a very strong acid (much stronger that the hydrogen ion to which it gives rise in aqueous solution), and in view of the catalytic effect of phenolic and carboxylic acids in general, it would be expected to be a powerful catalyst. The observed reaction velocity is much less than with an equivalent concentration of trichloroacetic acid, but this is consistent with the fact that the actual concentrations of hydrogen bromide and *N*-bromoacetanilide in the solution are very low.

The rearrangement of the allied *N*-iodoformanilide has been studied in this laboratory by Mr. J. F. Brown (to be published shortly), and has also been found to be catalysed by carboxylic acids in inert solvents. In this reaction a small amount of free iodine (detected colorimetrically) is often formed, but its quantity is very variable and its presence has little or no effect on the rate of production of *p*-iodoformanilide. The reaction between iodine and formanilide is in any case much too slow to provide a possible reaction mechanism, and a direct intramolecular migration again seems probable. The production of iodine is probably due to the side reaction $2C_6H_5{\cdot}NI{\cdot}CHO \longrightarrow C_6H_5{\cdot}N(CHO){\cdot}N(CHO){\cdot}C_6H_5 + I_2$. Under the same conditions of catalyst and temperature, *N*-iodoformanilide rearranges about 500 times as fast as *N*-bromoacetanilide. A similar decrease in reaction velocity in passing from *N*-bromo- to *N*-chloro-acetanilide would account for the fact that the rearrangement of the latter does not appear to be catalysed by trichloroacetic acid in inert solvents at ordinary temperatures (cf. Bell, *loc. cit.*).

The available information as to the mechanism of this type of reaction may hence be summed up as follows :

(1) In aqueous hydrochloric acid the rearrangement of *N*-chloroacetanilide takes place chiefly through the chlorination of acetanilide by free chlorine, and its rate is determined by the rate of formation of these substances.

(2) With *N*-chloro- or -bromo-acetanilide and hydrogen chloride or bromide in a number of organic solvents, the equilibrium A is instantaneous. It is therefore impossible to decide whether the rearrangement takes place by the above mechanism or by an acid-catalysed intramolecular migration.

(3) The rearrangement of *N*-bromoacetanilide and of *N*-iodoformanilide is catalysed by carboxylic and phenolic acids in non-dissociating solvents, free halogen playing no part in the process. Under these conditions there is probably intramolecular migration of halogen.

EXPERIMENTAL.

Materials.—Chlorobenzene, trichloroacetic acid, and *N*-bromoacetanilide were obtained as described by Bell and Levinge (*loc. cit.*). The last substance was immediately dissolved in chlorobenzene to give a stock solution about *M*/10, which was kept in a desiccator in the dark. Hydrogen bromide was prepared from phosphorus, bromine, and water, freed from bromine by passing through moist red phosphorus, and dried with phosphoric oxide.

Test for Free Bromine in Catalysis by Trichloroacetic Acid.—All experiments were carried out at room temperature (about 15°) with *M*/50-bromoacetanilide and *M*/2-trichloroacetic acid : in these circumstances the time of half change is about 2 hours (cf. Bell, *loc. cit.*). The reaction took place in a vessel covered with tin foil, and a current of air dried with phosphoric oxide passed first through the reacting solution and then through an absorption vessel containing potassium iodide solution acidified with a little acetic acid. Any iodine formed was titrated with *N*/100-thiosulphate (micro-burette). By means of a parallel experiment with *N*/20-bromine in chlorobenzene, the partition coefficient of bromine between the solution and the gas phase was found to be about 4×10^3 under the conditions of experiment. It is thus possible to calculate the average concentration of free bromine in the reacting solution. The following results were obtained :

Expt.	(a)	(b)	(c)	(d)	(e)
Vol. of air passed, l.	18	27	20	10	42
Time, hrs.	1	2	1·5	0·8	2·5
Bromine concn. in reacting mixture	$<10^{-5}$	5×10^{-5}	$<10^{-5}$	$<10^{-5}$	3×10^{-4}

In experiment (e), 1 c.c. of chlorobenzene saturated with water was added before passage of air. The small amount of bromine found in (b) is hence probably due to hydrolysis by an accidental trace of moisture. A concentration of $< 10^{-5}$ indicates that there was not enough iodine liberated to give a colour with starch.

Rate of Bromination of Acetanilide.—Solutions of bromine and acetanilide in chlorobenzene were mixed at room temperature and 2 c.c. samples estimated at intervals by running into potassium iodide and titrating the liberated iodine. The reaction is roughly unimolecular with respect to each reactant. The following are the data for a typical experiment :

Acetanilide $M/50$, bromine $M/70$; 2 c.c. titrated with $N/100$-$Na_2S_2O_3$.

Time (mins.)	0	10	30	40	60	75	300
Titre (c.c.)	1·54	1·44	1·02	0·95	0·82	0·76	0·33

It is clear that the very small concentrations of bromine present in the first experiment could not react fast enough to account for the observed rate of formation of *p*-bromoacetanilide.

Interaction of N-*Bromoacetanilide and Hydrogen Bromide.*—On mixing chlorobenzene solutions of these two substances a brown colour resembling bromine is produced immediately. The light absorption of these solutions was measured quantitatively by comparison with standard solutions of potassium dichromate in an immersion colorimeter, monochromatic light from a mercury arc being used. The absorption of a solution containing hydrogen bromide and *N*-bromoacetanilide was found to be identical with that of a bromine solution equivalent to the component not present in excess. Similarly, the absorption of a solution of bromine was found to be unaffected by the addition of acetanilide. Finally, the rate of disappearance of oxidising power in a solution prepared from equivalent quantities of hydrogen bromide and *N*-bromoacetanilide is the same as in a solution prepared from equivalent amounts of bromine and acetanilide. These facts taken together establish the fact that the equilibrium $C_6H_5\cdot NBr\cdot CO\cdot CH_3 + HBr \rightleftharpoons C_6H_5\cdot NH\cdot CO\cdot CH_3 + Br_2$ is set up very rapidly and strongly favours the products on the right-hand side of the equation.

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