518. *The Orton Rearrangement. Part III.* Evidence for the Mechanism Derived from Kinetic Studies of* o-*Substituted* N-*Bromoacetanilides.*

By M. J. S. Dewar and J. M. W. Scott.

The rearrangements of *N*-bromo-2-fluoro-, -2-chloro-, -2-nitro-, -2-phenyl-, -2-methyl-, and -2 : 6-dimethyl-acetanilide in chlorobenzene containing trichloroacetic acid have been studied kinetically, and also the analogous debromination of *N*-bromo-2 : 4 : 6-trichloroacetanilide. In several cases chemical and kinetic evidence was found for the intervention of an intermediate containing active bromine. This supports the mechanism suggested by Israel, Soper, and Tuck,[1] and this mechanism is theoretically preferable to that involving π-complex intermediates.[2]

The Orton rearrangement is a rearrangement of *N*-halogenoacylanilides in which the halogen migrates to a *para*- or occasionally an *ortho*-position in the ring. Such reactions have been effected under conditions of three types: (1) Photochemically or by the action of heat; these reactions probably involve free-radical intermediates. (2) With halogen acids as catalysts, the evidence[3] indicating that these reactions are intermolecular, involving as Orton suggested, free halogens as intermediates. (3) With carboxylic acids or phenols as catalysts in aprotic solvents. The present paper is concerned with reactions of the last type.

Bell and his collaborators[4-6] studied in detail the rearrangement of *N*-bromoacetanilide, *N*-bromobenzanilide, and *N*-iodoformanilide in aprotic solvents, using a variety of carboxylic acid and phenols as catalysts. They found that the rearrangements were of first order with respect to the *N*-halogenoacylanilide and obeyed the Brönsted relation. They also established that the reactions did not take place by the Orton mechanism (involving free halogen as intermediate), and Bell[6] concluded that they were probably intramolecular.

On the other hand Israel, Soper, and Tuck[1] considered the reactions to be intermolecular, proceeding by a variation of the Orton mechanism in which an acyl hypohalite is the intermediate; *i.e.*:

$$\mathrm{Ph{\cdot}NXAc + HOY \longrightarrow Ph{\cdot}NHAc + XOY}$$

$$\mathrm{Ph{\cdot}NHAc + XOY \longrightarrow X{\cdot}C_6H_4{\cdot}NHAc + HOY}$$

where X is the halogen and HOY the acid catalyst. They observed that when *N*-bromoacetanilide was allowed to react with acetic acid in presence of anisole or phenetole, most of the bromine migrated to the ether. This they considered to be evidence for an intermolecular mechanism. It is, however, inconclusive, for two reasons. First, the migration of bromine to the added ether might have involved a direct bromination of the ether by the *N*-bromoamide, and it would then throw no light on the rearrangement since the mechanisms of the two processes would be dissimilar.† Secondly, if the rearrangements are intermolecular, it seems very likely that they take place through a π-complex which

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* Part II, *J.*, 1957, 1445.

† Mr. P. Couzens, in these laboratories, has recently shown that the bromine transfer does take place mainly in this way.

[1] Israel, Soper, and Tuck, *J.*, 1945, 547.

[2] Dewar, "Electronic Theory of Organic Chemistry," Oxford, 1949, p. 168.

[3] For reviews and references see Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 34; Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 604.

[4] Bell, *Proc. Roy. Soc.*, 1934, *A*, **143**, 377; Bell and Levinge, *ibid.*, 1935, *A*, **151**, 211; Bell and Dankwerts, *J.*, 1939, 1774; Bell and Lidwell, *J.*, 1939, 1096.

[5] Bell and Brown, *J.*, 1936, 1520.

[6] Bell, *J.*, 1936, 1154.

would be expected to act as a brominating agent and might well brominate any reactive compound such as anisole that might be present.

The available evidence concerning the mechanism of the Orton rearrangement in aprotic solvents is therefore still inconclusive, and there is not even a general consensus of opinion whether it is intramolecular or intermolecular. We have now obtained definite evidence that the reaction takes place in stages, through the formation of an intermediate brominating agent; this strongly supports the Soper mechanism.

Our evidence comes from a kinetic study of the rearrangements and related reactions of a number of *ortho*-substituted *N*-bromoacetanilides. It could be predicted that the steric effects of *ortho*-substituents would increase the life of the intermediate if the Soper mechanism operated, and we have detected formation of an intermediate in such cases.

EXPERIMENTAL

Materials.—" AnalaR " trichloroacetic acid solutions were prepared as previously described [7] and were standardised by addition of water and titration with sodium hydroxide to phenolphthalein. The 2- and poly-substituted *N*-bromoacylanilides were prepared as before; [7, 8] their purity, determined by estimation of active bromine, ranged from 97 to 100%. The solutions of the *N*-bromoacylanilides were made up by volume, and concentrations checked by estimation of active bromine. The acid solutions were stored in a desiccator over anhydrous calcium chloride or silica gel. The *N*-bromoacylanilide solutions were stored in brown bottles over anhydrous calcium chloride or silica gel in a desiccator in the dark, and were stable for at least a year.

TABLE 1. *Reaction of* N-*bromo-2-nitroacetanilide* (I).

Temp. 25·1°							
Concn. of (I) (N) ...	0·0643	0·0648	0·0455	0·0385	0·0338	0·0134	0·0088
10^5k (sec.$^{-1}$)	2·49	2·49	2·51	2·65	2·70	3·44	3·53
			10^5k_0 = 14·1 sec.$^{-1}$				
Temp. 35·7°							
Concn. of (I) (N) ...	0·0640	0·0471	0·0415	0·0358	0·0299	0·0245	0·0131
10^5k (sec.$^{-1}$)	6·12	6·34	6·50	6·50	6·78	7·15	7·70
			10^5k_0 = 31·2 sec.$^{-1}$.				
Temp. 44·5°							
Concn. of (I) (N)	0·0640	0·0471	0·0415	0·0358	0·0229	0·0245	0·0191
10^5k (sec.$^{-1}$)	13·3	13·3	13·1	14·5	14·9	15·3	15·9

10^5k_0 = 66·5 sec.$^{-1}$.
E = 15·5 kcal. mole^{-1}. log PZ = 6·4.

Rate Measurements.—The conventional thermostat was kept constant within ±0·02°. The reaction vessels were essentially the same as those used by Bell and Levinge.[4] The mercury seal was rarely used. The reaction vessels were covered with tin-foil during the runs. The runs were initiated by mixing equal volumes (25 ml.) of acid and *N*-bromoacylanilide solutions after both had come to equilibrium in a thermostat. The rearrangement was followed by estimation of active bromine. The first-order constants were obtained graphically or by the method of least squares.

N-*Bromo-2-nitroacetanilide.*—Under the conditions used this anilide does not rearrange but brominates the solvent.[8] The reactions were carried out in 0·279N-acid, and followed first-order kinetics with respect to anilide. The first-order constants (k) varied, however, with the initial concentration of anilide, in a manner analogous to that found by Bell and Levinge [4] for *N*-bromoacetanilide. The empirical relation suggested by those authors was used to give a limiting first-order constant, and from this the limiting constant k_0, corresponding to unit acid concentration, was calculated. The values of k and k_0 at three temperatures are given in Table 1, together with the Arrhenius parameters calculated from the values of k_0.

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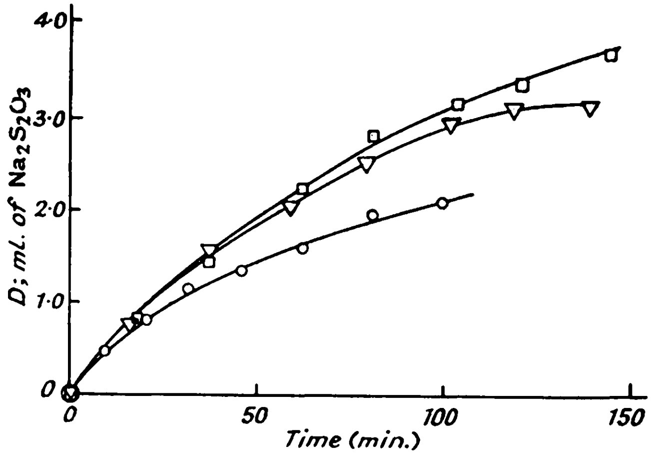
[7] Dewar and Scott, *J.*, 1957, 1445.
[8] *Idem, J.*, 1955, 1845.

N-*Bromo-2-methylacetanilide*.—Rearrangement was carried out in 0·358N-acid. The first-order constants determined graphically did not demonstrate any systematic variation with the initial concentration of the *N*-bromoacylanilide. The variation was shown to be random by recalculating the first-order constants by the method of least squares. These constants are given in Table 2, together with values for k_0 and the Arrhenius parameters.

After the above investigations it was decided to investigate the rates at fewer initial concentrations.

N-*Bromo-2-chloro*- and -*2-phenyl-acetanilide*.—With these compounds the titrations became erratic. Investigation showed that if aliquot parts of reactant were titrated rapidly after addition of iodide solution, reproducible end-points could be obtained; but soon iodine was slowly liberated. After 2—4 hr. a second stable end-point was reached. Clearly the *N*-bromoamides, which react rapidly with iodide, are converted into other oxidising agents which react slowly. That this oxidation was due to some substance in the chlorobenzene layer was shown by titration without agitation; the formation of free iodine took place at the interfaces between the chlorobenzene and the aqueous phase.

FIG. 1. *Concentration of intermediate plotted against time, for* N-*bromo-2-phenylacetanilide.*



Anilide concn. : □ 0·0595N, ▽ 0·0279N, ○ 0·0205N.

These agents accumulated during the reaction as shown in Fig. 1; here *D* represents the

TABLE 2. *Rearrangement of* N-*bromo-2-methylacetanilide* (II).

Temp. : (II) (N)	20·1° 10^5k (sec.$^{-1}$)	35·85° 10^5k (sec.$^{-1}$)	45·25° 10^5k (sec.$^{-1}$)
0·0655	0·247	1·10	2·35
0·0460	0·238	1·02	2·24
0·0410	—	0·990	2·27
0·0361	—	0·983	2·21
0·0305	—	0·986	2·35
0·0241	—	1·02	2·29
0·0180	—	0·998	2·30
0·0131	—	1·05	2·36
10^5k (mean)	0·243	1·02	2·30
10^5k_0	0·679	2·85	6·43

E = 16·6 kcal. mole^{-1}. log *PZ* = 7·1.

TABLE 3.

N-*Bromo-2-phenylacetanilide. Acid,* 0·282N.

Anilide (N)	26·00° 10^5k (sec.$^{-1}$)	34·80° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)
0·0595	1·16	2·26	5·89
0·0279	1·83	4·09; 4·06	9·31
0·0205	2·36	5·22	11·8

E = 14·9 kcal. mole^{-1}. log *PZ* = 6·6.

N-*Bromo-2-chloroacetanilide. Acid,* 0·282N.

Anilide (N)	26° 10^5k (sec.$^{-1}$)	34·8° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)
0·0595	1·58	2·44	5·78
0·0448	1·81	2·63; 2·68	5·35
0·0180	3·28	5·35	13·3

E = 14·7 kcal. mole^{-1}. log *PZ* = 6·3.

difference between the two titres—presumably equal to the concentration of the new oxidising agent. Over a long period, D passed through a maximum, and eventually the solution lost all its oxidising power; the rearrangement product could then be isolated.

Thus the rearrangement occurs in at least two stages, the new oxidising agent being formed as an intermediate.

Logarithmic plots (Fig. 2) showed that the disappearance of *N*-bromo-amide, as measured by the first (rapid) titre, X_0, followed a reaction first order in amide; the kinetics appeared similar to those for the reactions of " normal " *N*-bromoacetanilide derivatives. The corresponding rate constants and Arrhenius parameters are in Table 3. The values for the second titre, X_n, are also indicated in Fig. 2.

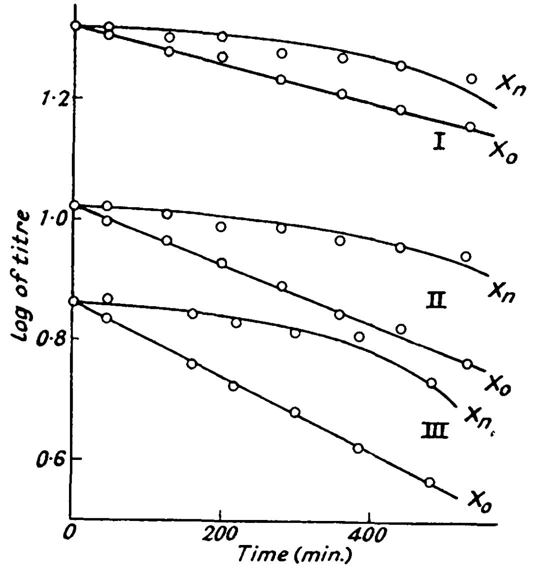


FIG. 2. *First-order plots for* N-*bromo-2-phenylacetanilide.*

Anilide concn.:
I, 0·0595N, II, 0·0279N, IV, 0·0205N.

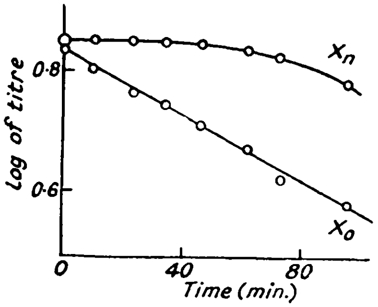


FIG. 3. *First-order plot for* N-*bromo-2 : 4 : 6-trichloroacetanilide.*

N-*Bromo-2-fluoro-* and N : 2-*Dibromo-acetanilide*.—Only the most concentrated solutions of *N*-bromo-2-fluoroacetanilide indicated production of the intermediate. No intermediate was found with *N* : 2-dibromobromoacetanilide. The kinetic results are in Table 4.

TABLE 4.

N-*Bromo-2-fluoroacetanilide. Acid,* 0·358N.

Anilide (N)	25° 10^5k (sec.$^{-1}$)	35·15° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)
0·0569	1·69	3·94	9·09
0·0336	1·66	4·08	9·20
0·0083	—	4·80	9·59

E = 13·9 kcal. mole^{-1}. log PZ = 5·7.

N : 2-*Dibromoacetanilide. Acid,* 0·358N.

Anilide (N)	35·15° 10^5k (sec.$^{-1}$)	45° 10^5k (sec.$^{-1}$)
0·0555	1·25	2·65
0·0323	1·23	2·95
0·0095	1·27	2·96

E = 17·8 kcal. mole^{-1}. log PZ = 7·2.

N-*Bromo*-2 : 4 : 6-*trichloroacetanilide*.—Since this bromo-amide cannot rearrange, it was thought that reaction with trichloroacetic acid in chlorobenzene might lead to a complete conversion into the intermediate, the second titre (X_n) remaining constant. This was approximately true for the first part of the reaction, as shown in Fig. 3; here again the disappearance of *N*-bromo-amide, measured by the first titre (X_0), follows first-order kinetics. Over a long period X_n decreased gradually to zero; *p*-bromochlorobenzene could then be isolated.[7] Then *N*-bromo-2 : 4 : 6-trichloroacetanilide (0·02M) was allowed to react with trichloroacetic acid in chlorobenzene containing acetanilide (0·05M). No intermediate was formed since it presumably rapidly attacked the acetanilide. No attempt was made to investigate this reaction further because of the difficulty of separating mixtures of anilides.

N-*Bromo*-2 : 6-*dimethylacetanilide*.—A single run was carried out with this compound at 45°; no intermediate could be detected. Acid concentration, 0·282N; anilide, 0·040N; $k = 4{\cdot}07 \times 10^{-7}$ (sec.$^{-1}$).

DISCUSSION

We have previously shown [7, 8] that all the substituted *N*-bromoacylanilides discussed in this paper rearrange in chlorobenzene–trichloroacetic acid to the corresponding *p*-bromoacetanilide, except the *p*-nitro- and 2 : 4 : 6-trichloro-derivatives which brominate the solvent. The disappearance of the bromo-amide follows first-order kinetics, and the first-order constants show analogous variations with initial concentrations of the amides; it seems at least probable that all these reactions take place by a common mechanism.

In that case the behaviour of *N*-bromo-2-chloro-, -2-phenyl-, and -2 : 4 : 6-trichloroacetanilide shows that the overall reactions take place in at least two stages. The first step involves the production of a brominating agent which reacts only slowly with iodide solution, together presumably with an equivalent amount of the free acetanilide; the intermediate brominating agent then substitutes either the free acetanilide formed in the first step, or the solvent. Although we have not yet been able to isolate this intermediate, it seems entirely reasonable that it should be trichloroacetyl hypobromite, as required by the Soper mechanism.[1] Certain hypobromites have been reported [9] to react slowly with iodide in a two-phase system, presumably because they are almost insoluble in water.

The intermediate should only accumulate to an appreciable extent in cases where the second step in the Soper mechanism is slow compared with the first. Since the second step is an electrophilic substitution of an acetanilide derivative, it will be inhibited by positive substituents. Moreover *ortho*-substituents should accelerate the first step sterically, in which the bulky group NXAc is replaced by the less bulky NHAc, and sterically inhibit the second step by interfering with the coplanarity and conjugation of the ring and NHAc group. In fact we could detect the intermediate only when bulky *ortho*-substituents were present, and a methyl group ($-I$) was ineffective. Fluorine and bromine were less effective than chlorine; the former is smaller, and the latter less positive, than chlorine.

The behaviour of the 2-nitro-compound was surprising; it did not rearrange, it gave no intermediate, and the rate of acid attack was higher than for the other anilides investigated. It seems quite likely that the *o*-nitro-group increases the electrophilic nature of the bromine to such an extent that direct bromination of the solvent takes place. A similar reaction probably accounts for the bromine transfer observed by Israel *et al.*[1] when *N*-bromoacetanilide reacts in presence of anisole or phenetole.

Bell [6] observed that the rate of rearrangement of *N*-bromoacetanilide varied little with changes in the dielectric constant of the solvent. This suggests very strongly that no ions are formed as intermediates in the reaction. However the rate-determining step must be some reaction of the anilide with the acid catalyst, for otherwise the Brönsted relation would not be obeyed. These observations seem to indicate that the reaction must take

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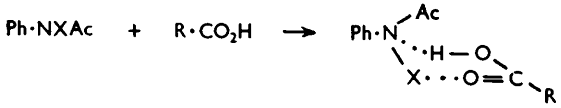
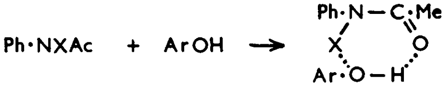
[9] Day and Taggart, *Ind. Eng. Chem.*, 1928, **20**, 545; Scott, *ibid.*, *Anal. Ed.*, 1931, **3**, 67.

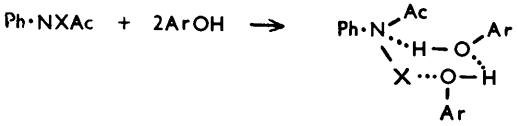
place through a cyclic transition state in which no integral charges need develop; *e.g.*, for a carboxylic acid,



and for a phenol, ArOH, either



or



A similar transition state can be written for hydrogen bromide; this would account for its extreme efficiency as a catalyst in aprotic solvents.[6]

It is not immediately apparent why a reaction of this type should obey the Brönsted relation; this aspect will be discussed in a later paper when it will be shown that the Brönsted relation should hold for such reactions.

It therefore seems highly probable that the rearrangements of all *N*-halogeno-compounds in aprotic solvents with carboxylic acids and phenols as catalysts take place by the Soper mechanism, but a further study of the reaction is in progress.

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