MOLECULAR REARRANGEMENTS—XI

THE ACID-CATALYSED REARRANGEMENT OF N-CHLOROACYLARYLAMIDES

M. Z. A. BADR,† M. M. ALY and S. S. SALEM

Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt, A.R.E.

Abstract—The rearrangement of N-chloroacetanilide in 99% acetic acid is compared with that of the N-chloro-derivatives of propionanilide, butyranilide, α-chloro, α-dichloro and α-trichloroacetanilides in presence of benzoic acid, toluene-*p*-sulphonic acid or hydrochloric acid as promoters.

The rate of change increases progressively with increasing +I effect and decreases with increasing −I effect of substituents on the acyl group.

The rearrangements with different carboxylic acids and sulphonic acid catalysts are best interpreted as intermolecular chlorination, the protonated N-chloro-compounds acting as electrophilic chlorinating agents.

N-Chloroacylarylamides have been reported to rearrange under the influence of acids[1,2] as promoters to mixtures of the corresponding *o*- and *p*-chloroacylarylamines.

The rearrangement of N-halo-acylanilides under the influence of hydrochloric acid[3] depends on the formation of molecular halogen by interaction of the halonium ion with the halogen atom on the protonated N-halo-compounds formed as intermediates.[4] The final stage is halogenation of the N-acylarylamides thus formed changing into the *o*- and *p*-halogeno substitution products.

Rearrangement of N-halo-acylarylamides has also been promoted by carboxylic acid and this was considered to be an intramolecular change,[5] but such view has been excluded.

An alternative to the intramolecular hypothesis was the suggestion that the halogeno-carboxylate salt (R.COOX) was the intermediate responsible[4] for the migration of halogen from nitrogen of N-halo-acylaryl-amides to the nucleus. However, formation of alkyl halides and CO_2 as expected decomposition products of acyl hypohalites, was not observed in the course of rearrangement.

A recent study[6] on the rearrangement of N-chloroanilides brought about by carboxylic acids or toluene-*p*-sulphonic acid had excluded the formation of intermediates of the type $X.O_2CR$ or $Cl.O_2SAr$. On the other hand, the carboxylic acid and sulphonic acid

catalysts[6] had resulted into reversible order of the rearrangement which revealed the difference in the course of their pathways. In the present study the rate measurements for the rearrangements of N-chloroanil-ides in glacial acetic acid (at 50°) promoted by different acid catalysts shows that the reaction is of first order kinetics since dc/dt is constant. On the other hand, the rate constant increases with increasing concentrations of the catalyst (Tables 1 and 2), consequently the reaction can be concluded to be pseudo-unimolecular in character.

The polarity of N–Cl bond is modified by introducing different substituents into the acyl group to observe the probable change of the rate of rearrangement in a predictable manner. The rate of rearrangement is noticed to increase by increasing +I effect of the substituents in the acyl group of the anilide in the order; N-chloroacetanilide ⟨N-chloropropionanilide ⟨N-chlorobu-tyranilide. Similarly, the rate decreases by increasing −I effect of the substituents in the acyl group of the anilide in the following order: N-chloroacetanilide⟩ N-α-dichloro-acetanilide⟩ N-α-trichloroacetanilide⟩ N-α-tetrachloro-acetanilide. The steady change in the rate of anilides rearrangements by gradual change of the inductive effect of the substituents on the acyl group shows a simple relationship between ease of the anilide protonation and the rate constant of its rearrangement.

A comparison of the rate constants of the anilides rearrangements with hydrochloric acid and other acid catalysts (Tables 1 and 2) leads to the obvious conclusion that the rearrangement promoted by toluene-*p*-sulphonic

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†Part X. M. Z. A. Badr, M. M. Aly and A. E. Abdel-Rahman, *Indian J. Chem.* (1977) in press.

Table 1. Relation between +I effect and rate constants of N-chloroanilides rearrangement with different promoters at different concentrations

Ph.NCl.CO.R	Toluene-p-sulphonic acid			Benzoic acid			HCl
	0.05 M	0.10 M	0.15 M	0.15 M	0.30 M	0.45 M	0.001 M
R = −CH₃	2.3×10^{-3}	2.5×10^{-3}	7.00×10^{-3}	3.8×10^{-5}	5.7×10^{-5}	1.7×10^{-4}	6.3×10^{-3}
−C₂H₅	3.0×10^{-3}	3.32×10^{-3}	7.5×10^{-3}	3.3×10^{-4}	4.2×10^{-4}	5.3×10^{-4}	1.01×10^{-2}
−C₃H₇	5.06×10^{-3}	1.07×10^{-2}	1.38×10^{-2}	1.3×10^{-3}	1.6×10^{-3}	4.9×10^{-3}	8.05×10^{-2}

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Table 2. Relation between −I effect and rate constants of N-chloroanilides rearrangement with different promoters at different concentrations

Ph.NCl.CO.R.	Toluene-p-sulphonic acid			Benzoic acid			HCl
	0.05 M	0.10 M	0.15 M	0.15 M	0.30 M	0.45 M	0.001 M
R = −CH₃	2.3×10^{-3}	2.5×10^{-3}	7.0×10^{-3}	3.8×10^{-5}	5.7×10^{-5}	1.7×10^{-4}	6.3×10^{-3}
−CH₂Cl	1.0×10^{-3}	2.0×10^{-3}	6.3×10^{-3}	—	—	— (a)	5.8×10^{-3}
−CHCl₂	1.1×10^{-4}	2.3×10^{-4}	5.3×10^{-4}	—	—	—	1.6×10^{-3}
−C Cl₃	1.0×10^{-4}	2.2×10^{-4}	5.1×10^{-4}	—	—	—	8.0×10^{-4}

(a) The rate is very slow to be measured even at higher acid concentrations.

acid does not follow the same course as that initiated by hydrochloric acid and therefore, after initial protonation, chlorine toluene-p-sulphonate is not an intermediate. Similarly, it can be inferred that the rearrangement brought about by carboxylic acids does not depend on the formation of an intermediate ClO₂C.Ar. However, the rate of change was slowed down on addition of the carboxylate salt,[6] a result that indicates that the carboxylate anion does not participate in the change as would be required if the halogen carboxylates ClO₂.C.Ar were intermediates.

The rearrangement of N-chloroacylarylamides in carboxylic acids or toluene-p-sulphonic acids are best interpreted as an intermolecular chlorination in which the protonated N-chloro-compound acts as an electrophilic chlorinating agent. Since the dissociation constant of carboxylic acids is a measure for the rate to which the acids protonate a given base, it may be expected that the rate constant (k) of a given N-chloroanilide rearrangement increases with increasing dissociation of the carboxylic acid promoters as observed experimentally (Table 3), with the exception of p-aminobenzoic acid which showed a reverse order due to protonation of its amino group in glacial acetic acid medium.

On the other hand, the o/p isomer ratio of the chloro-compounds produced during rearrangement of the different N-chloroanilides are similar to those obtained from chlorination by molecular chlorine (Table 4) and hence it is concluded that the protonated N-chlorocompounds act as electrophilic chlorinating agents.

EXPERIMENTAL

Preparation of N-chloro-anilides[6]

The N-chloro-anilides used in this work were prepared by stirring a soln of the anilide (2g) in chloroform (10 ml) with freshly prepared NaOCl aq (100 ml) containing excess NaHCO₃ (5 g) below 10° for 4 hr. The chloroform layer separated, washed with water, dried over MgSO₄ and evaporated in darkness at low pressure; the residue was crystallised from chloroform/petroleum ether (40-60°) mixture. The following N-chloro-anilides were prepared.

N-Chloroacetanilide, m.p. 91-92° (active Cl; found: 20.92, C₈H₈ClNO requires: 20.94%).

Table 3. Relation between dissociation exponents of acids (pKₐ) in water and rate constants (k) for N-chloroacetanilide rearrangement

Promoter	pKₐ	k
Trifluoroacetic acid	0.30	4.8×10^{-2}
Trichloroacetic acid	0.90	2.1×10^{-2}
Toluene-p-sulphonic acid	2.16	7.0×10^{-3}
p-Nitrobenzoic acid	3.41	2.3×10^{-3}
Benzoic acid	4.19	3.8×10^{-5}
p-Aminobenzoic acid	4.92	3.8×10^{-2}

Table 4. o/p Ratios of the chlorinated products obtained from N-chloro-anilides rearrangements and from direct chlorination

Ph.NCl.CO.R.	Toluene-p-sulphonic	Hydrochloric	Benzoic	Direct chlorination
R = −CH₃	0.42	0.425	0.43	0.45
−C₂H₅	0.40	0.45	0.42	0.40
−C₃H₇	0.45	0.47	—	0.42
−CH₂Cl	0.47	0.42	—	0.51
−CHCl₂	0.48	0.52	—	0.51
−C Cl₃	0.52	—	—	0.53

| Anilide | m.p. C° | |
	o-Cl	p-Cl
Acetanilide	88	179
Propionanilide	91	141
n-Butyranilide	80	104
α-Chloroacetanilide	67	168
α-Dichloroacetanilide	11c	130
α-Trichloroacetanilide	100	150

N-*Chloropropionanilide*, m.p. 77° (active Cl; Found: 19.12 C$_9$H$_{10}$ClNO requires: 19.34%).

N-*Chlorobutyranilide*, m.p. 43° (active Cl; found: 18.17, C$_{10}$H$_{12}$ClNO requires; 18.28).

α-N-*Dichloroacetanilide*, m.p. 70–71° (active Cl; found: 17.34; C$_8$H$_7$Cl$_2$NO requires 17.40%).

α-N-*Trichloroacetanilide*, m.p. 105° (active Cl; found:14.80, C$_8$H$_6$Cl$_3$NO requires 14.88%).

α-N-*Tetrachloroacetanilide*, m.p. 85° (active Cl; found: 12.96, C$_8$H$_5$Cl$_4$NO requires 13.0%).

Preparation of isomeric o-and p-chloroanilides[6]

o- and *p*-Chloroanilines (0.2 mol) were treated with corresponding acid chlorides (0.1 mol). The product washed with water and crystallised from EtOH.

Kinetic measurements. All kinetic measurements were carried out using solns 0.02 M of the anilides in glacial AcOH that are practically stable over a long period at 50° provided that it is shielded from light. The promoter added was in the concentration quoted in specific experiments. The progress of the reaction was followed by utilizing the fact that the N-chlorocompound liberates I$_2$ from KI. The volume of standard thiosulphate soln required to titrate the liberated I$_2$ is a direct measure of the concentration of unchanged reactant.

REFERENCES

[1]C. Beard and W. J. Hickinbottom, *J. Chem. Soc.* 2982 (1958).
[2]F. D. Chattaway and K. J. P. Orton, *Ibid.* 77, 136, 790 (1900).
[3]R. P. Bell *Ibid.* 1154 (1936).
[4]G. C. Israel, A. W. N. Tuck and F. G. Soper, *Ibid.* 547 (1945); S. C. Chan and G. C. Israel, *Ibid.* 196 (1960).
[5]M. J. S. Dewar, *Electronic Theory of Organic Chemistry* p. 225, Oxford University Press (1949).
[6]A. H. El-Nadi, S. Wasif and W. J. Hickinbottom, *J. chem. Soc.* 1131 (1970).