

Oxidation of Aromatic Amines by *N*-Chloroanilides. Direction of Polarity of the Nitrogen–Chlorine Bond

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The effect of substituents in the aromatic ring as well as in the acyl moiety of some *N*-chloroanilides [$\text{XC}_6\text{H}_4\text{N}(\text{Cl})\text{COR}$; X = *m*-Cl, *p*-Br, H, *m*-Me, *p*-Me; R = Me, Prⁱ, Et, PhCH₂, Ph] on the kinetics of oxidation of aniline and *p*-toluidine has been studied in 1:1 ethanol–water (v/v) at various temperatures. The reactivity decreases in the following order: *m*-Cl > *p*-Br > H > *m*-Me > *p*-Me; Ph > PhCH₂ > Me > Et > Prⁱ. For *p*- and *m*-substituted *N*-chloroacetanilides, a correlation with the Hammett σ parameter exists. On the other hand, the Taft equation gives an excellent fit with the rate data for five *N*-chloroacylanilides. The results are interpreted in terms of bimolecular interaction of the positive chlorine of the N–Cl bond and the amino nitrogen.

N-Halogeno compounds are of interest because of the polar nature of halogen in such compounds. The halogen portion of the nitrogen–halogen bond was postulated to bear positive or negative charge, depending on the structure of the remaining moiety. Of all the halogens, chlorine is of most concern in the sense that its electronegativity is similar to that of nitrogen. Based on dipole moment measurements, several reports^{1,2} concerning the direction of polarisation in various *N*-halogeno compounds classify nitrogen as the positive end, $\overset{\delta+}{\text{N}}-\overset{\delta-}{\text{X}}$, whereas in some cases the direction of polarisation has been shown to occur in the opposite way.³ We have studied the kinetics of oxidation of aniline and *p*-toluidine with *N*-chloro-4-acetotoluidide, *N*-chloro-3-acetotoluidide, *N*-chloro-4-bromoacetanilide, *N*-chloro-3-chloroacetanilide, *N*-chloroisobutyranilide, *N*-chloropropionanilide, *N*-chloro- α -phenylacetanilide, and *N*-chlorobenzanilide with particular interest in the N–Cl polarity, the results of which are presented and discussed in this paper.

Experimental

Materials.—*N*-Chloroacetanilide was prepared by the method of Barnes and Porter.⁴ Various substituted *N*-chloroanilides were prepared by the action of Bu^tOCl on the corresponding anilides.^{5–7} The purity of the compounds was checked by iodometric estimation of active chlorine in the molecules.

Kinetic Measurements.—Reactions were carried out in 1:1 ethanol–water (v/v) under pseudo-first-order conditions in well stoppered Pyrex flasks. A typical kinetic run is described below. A measured quantity of the solution (50 ml; 0.01M) of *N*-chloroacetanilide was taken in the reaction flask. In another stoppered vessel, a solution of the aromatic amine of appropriate concentration (0.2M) was taken. Both the solutions were separately thermostatted for ca. 15 min. A known volume of the amine solution (50 ml) was then transferred to the reaction vessel to start the reaction. Immediately, a known volume of the mixture (5 ml) was pipetted into 10% KI solution (5 ml) in an iodine flask and the liberated iodine was titrated using standard thiosulphate solution in a semi-automatic burette. This titre value was taken as the initial concentration of the substrate. Subsequent aliquot portions were similarly drawn and titrated.

The infinite reading taken after ca. 10 half-lives was always zero. The first-order rate constants (k_1) were evaluated by plotting $\log [a/(a-x)]$ versus time. The second-order rate constants (k_2) were obtained by dividing the values of k_1 in the initial stages of the reaction by the concentration of the amine. Results

were found to be reproducible ($\pm 4\%$) within the limits of experimental error.

Product Analysis.—Each reactant solution (100 ml; 0.2M-aniline and 0.01M-*N*-chloroacetanilide) was mixed at room temperature. The reaction mixture gradually turned reddish yellow in colour. After completion of reaction (90 min), it was extracted with ether. The aqueous layer gave a positive test for chloride ion. Evaporation of the ether extract gave a reddish brown viscous mass which contained acetanilide as well. On treatment with dilute HCl and successive washings with hot water and ether, the coloured residue was free from acetanilide. A t.l.c. examination of the residue showed that it consisted of a single component which responded positively to an azo group test. A u.v. spectrum of an ethanolic solution of the sample was identical with that of *trans*-azobenzene.⁸ Analysis of the reaction mixture of *p*-toluidine and *N*-chloroacetanilide gave 4,4'-dimethyl-*trans*-azobenzene as the only azo product; no 4-methylazobenzene could be obtained. Similarly, reaction of aniline with 4-methyl-*N*-chloroacetanilide yielded *trans*-azobenzene; no 4-methyl- or 4,4'-dimethyl-azobenzene could be isolated. Thus the absence of mixed azo compounds clearly indicated that both the phenyl rings in the azo compound are derived from the amine nucleophile and only the N–Cl bond in the *N*-chloro compound is cleaved, the remaining bonds remaining intact.

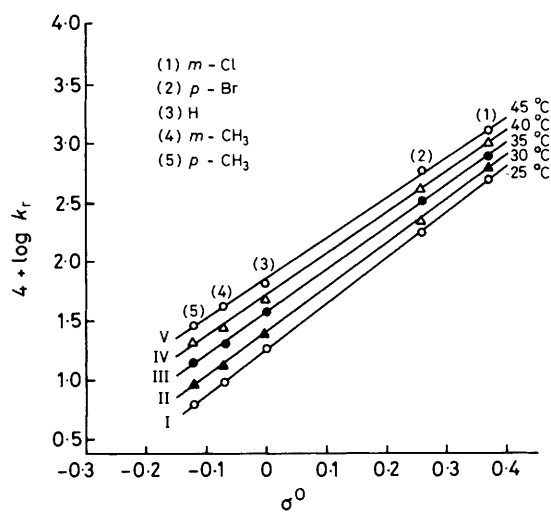
Results and Discussion

The reactions of various *N*-chloroanilides [$\text{XC}_6\text{H}_4\text{N}(\text{Cl})\text{COR}$; X = *m*-Cl, *p*-Br, H, *m*-Me, *p*-Me; R = Me, Et, Prⁱ, Ph, PhCH₂] with aniline and *p*-toluidine have been studied in order to gain more information about the N–Cl bond polarity. These reactions were found to be second order, first order with respect to each reactant. The Arrhenius relationship was obeyed in all cases. The reactions were characterised by a large negative value of ΔS^\ddagger and a rather low value of the energy of activation (Table 1). The close proximity of the values of ΔG^\ddagger for the series is indicative of a similar mechanism operating in each case. An isokinetic relationship was observed in all cases in which the isokinetic temperatures were high and the reaction were enthalpy controlled.

The order of reactivity of *p*- and *m*-substituted *N*-chloroacetanilides toward both aniline and *p*-toluidine decreased in the following order: *m*-Cl > *p*-Br > H > *m*-Me > *p*-Me. The enhancement of reactivity with electron-withdrawing substituents is suggestive of the nature of the transition state. The effect of dielectric constant of the medium on the rate of

Table 1. Activation parameters for the reactions of $\text{XC}_6\text{H}_4\text{N}(\text{Cl})\text{COR}$ with aniline and *p*-toluidine in 1:1 ethanol-water at $40 \pm 0.1^\circ\text{C}$

X	$10^3 k_r / \text{l mol}^{-1} \text{s}^{-1}$	$E(\pm 0.5) / \text{kJ mol}^{-1}$	$-\Delta S^\ddagger / (\pm 1.9) / \text{J mol}^{-1} \text{K}^{-1}$	$\Delta G^\ddagger / (\pm 1.0) / \text{kJ mol}^{-1}$	$\Delta H^\ddagger / (\pm 0.9) / \text{kJ mol}^{-1}$
<i>p</i> -Me	a	2.09	62.3	105.6	92.8
	b	2.96	57.9	117.5	92.0
<i>m</i> -Me	a	2.76	62.1	114.0	92.1
	b	4.41	54.2	126.3	91.0
<i>p</i> -Br	a	42.2	46.8	135.6	85.0
	b	55.8	39.5	150.4	84.3
<i>m</i> -Cl	a	104.9	37.7	155.7	82.7
	b	132.4	35.6	157.8	82.1
H	a	5.08	51.2	128.6	90.5
	b	7.4	51.7	133.9	89.6

a = Aniline, b = *p*-toluidine.**Figure 1.** Hammett equation plot for reactions of aniline with substituted *N*-chloroacetanilides at different temperatures

oxidation of aniline and *p*-toluidine in various ethanol-water mixtures (ethanol content varied from 30 to 70%) was studied. A large increase in the rate with an increase in the dielectric constant of the medium was observed in support of a polar transition state. In the present case, no ionic species were taken and no possibility exists for the ionisation of reactants used under the experimental conditions; hence reactions are likely to involve dipole-dipole interaction. Observation of Laidler-Eyring⁹ and Amis¹⁰ relationships, therefore, supports the above view. Further, there was no effect of ionic strength on the rate of the reaction.

A satisfactory correlation of the rates with the substituent constants denoted by σ^0 indicates that the reaction site is not directly conjugated with the aromatic ring, but some group is interposed.¹¹⁻¹⁴ The Hammett plots for the reactions of aniline with substituted *N*-chloroacetanilides at various temperatures are given in Figure 1. The reaction constant ρ was calculated to be +3.75 at 30°C . The relevant data are given in Table 2. This supports the formation of the polar transition state.

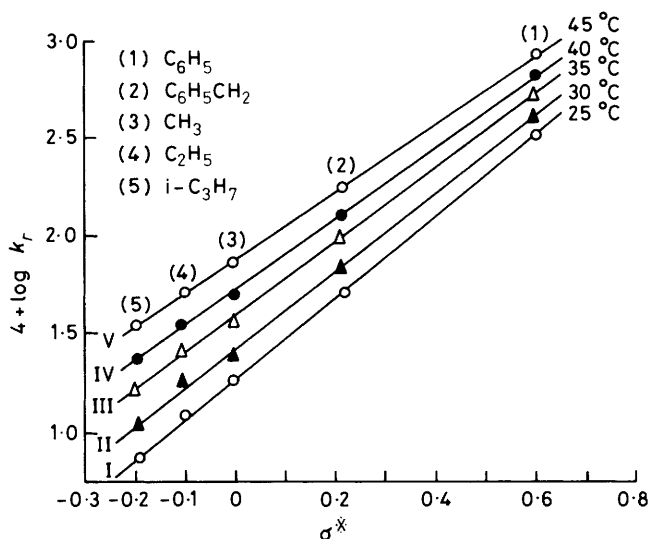
From knowledge of the structure of *N*-chloro compounds, it is clear that the reactivity of the N-Cl bond would be influenced by the nature of the acyl substituent. We studied the kinetics of the reactions of various *N*-chloroacylanilides [$\text{PhN}(\text{Cl})\text{COR}$; R = Me, Et, Prⁱ, Ph, PhCH_2] with aniline and *p*-toluidine. The Arrhenius relationship and isokinetic behaviour were similar to

Table 2. Hammett parameters for reactions of aniline and *p*-toluidine with various *N*-chloroacetanilides [$\text{XC}_6\text{H}_4\text{N}(\text{Cl})\text{COMe}$] in 1:1 ethanol-water at $30 \pm 0.1^\circ\text{C}$. ρ +3.75 for aniline and +3.56 for *p*-toluidine

X	σ^0	$10^4 k_r / \text{l mol}^{-1} \text{s}^{-1}$ (aniline)	$10^4 k_r / \text{l mol}^{-1} \text{s}^{-1}$ (<i>p</i> -toluidine)
<i>p</i> -Me	-0.12	9.6	14.6
<i>m</i> -Me	-0.07	13.2	22.3
H	0.00	25.4	38.4
<i>p</i> -Br	0.26	237.9	337.8
<i>m</i> -Cl	0.37	665.3	844.4

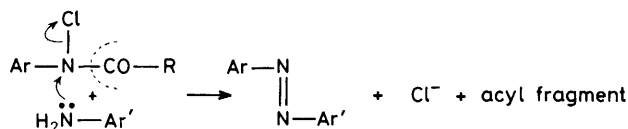
Table 3. Taft parameters for reactions of aniline and *p*-toluidine with various *N*-chloroacylanilides [$\text{C}_6\text{H}_5\text{N}(\text{Cl})\text{COR}$] in 1:1 ethanol-water at $30 \pm 0.1^\circ\text{C}$. ρ^* 1.98 for aniline and 2.41 for *p*-toluidine

R	σ^*	$10^4 k_r / \text{l mol}^{-1} \text{s}^{-1}$ (aniline)	$10^4 k_r / \text{l mol}^{-1} \text{s}^{-1}$ (<i>p</i> -toluidine)
Pr ⁱ	-0.19	11.0	13.2
Et	-0.1	18.6	23.0
Me	0.00	25.4	38.4
PhCH_2	0.22	70.4	118.0
Ph	0.6	409.4	1 023.6

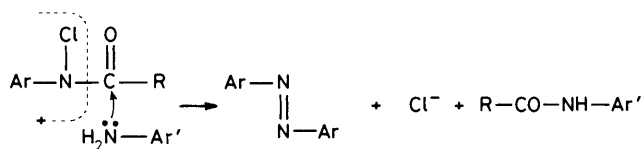
**Figure 2.** Taft equation plots for reactions of aniline with various *N*-chloroacylanilides at different temperatures

those of *p*- and *m*-substituted *N*-chloroacetanilides, *viz.*, large negative values of ΔS^\ddagger , relatively low values of the energy of activation, and near constancy in the values of ΔG^\ddagger . The order of reactivity of various *N*-chloroacylanilides toward both aniline and *p*-toluidine decreased in the following order: Ph > PhCH_2 > Me > Et > Prⁱ. Here also, enhancement of the reaction rate with electron-withdrawing groups shows that the reaction site is electrophilic in nature. For these reactions satisfactory correlation between $\log k_r$ and polar substituent constant, σ^* , exists (Figure 2). The value of ρ^* evaluated for aniline reaction at 30°C was found to be +1.98. The other relevant data are given in Table 3. The positive ρ^* value indicates that electron-withdrawing groups help stabilise the transition state.

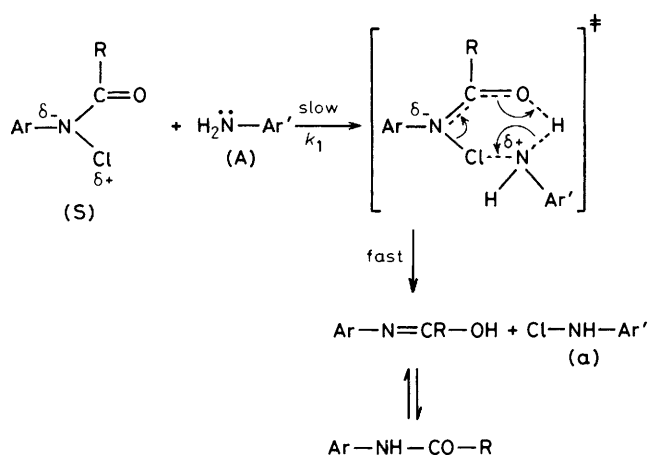
Site of Nucleophilic Attack.—The most probable site of nucleophilic attack is the chlorine of the N-Cl bond. However,



Scheme 1. Nucleophilic attack at the nitrogen of the N-Cl bond



Scheme 2. Nucleophilic attack at the carbonyl carbon

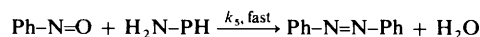
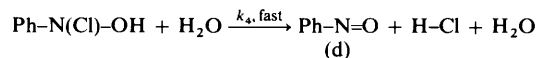
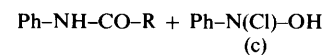
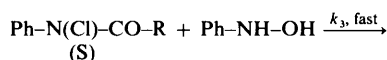
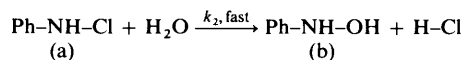


Scheme 3.

there are alternative positions, *viz.*, the nitrogen of the N-Cl bond and the carbonyl carbon of the anilide function. Analysis of the reaction mixture of *N*-chloroacetanilide and *p*-toluidine gave positive tests for chloride ion, acetanilide, and 4,4'-dimethyl-*trans*-azobenzene. As described earlier, in no case would a mixed azobenzene be isolated. Had the nitrogen of the N-Cl bond been the site of nucleophilic attack, the product could not have contained free acetanilide, although formation of a mixed azobenzene could have been possible with the elimination of Cl^- and cleavage of the N-C bond (Scheme 1). On the other hand, nucleophilic attack at the carbonyl carbon would have given rise to the products shown in Scheme 2.

However, in actual practice, Ar-NH-CO-R and $\text{Ar}'\text{N}=\text{NAr}'$ (*trans*) are obtained as products instead of $\text{Ar}'\text{NHCOR}$ and $\text{Ar}'\text{N}=\text{NAr}'$ when $\text{Ar}'\text{N}(\text{Cl})\text{COR}$ and $\text{Ar}'\text{NH}_2$ react. Further, had the carbonyl carbon been the active electrophilic site, the reactions would have been more sensitive to the acyl substituents. A comparison of the values of ρ^* and ρ suggests that sensitivity is rather reduced when substituents are introduced in the acyl component. With all the available information, the chlorine of the N-Cl bond appears to be the most likely site of reaction in the presence of aniline and *p*-toluidine acting as electron donors. On the basis of kinetic studies and product analysis, the reaction pathways in Scheme 3 may be proposed.

Slow nucleophilic attack on the chlorine of the N-Cl bond by the amine results in the formation of the corresponding anilide



Scheme 4.

and the *N*-chloroamine;^{15,16} the latter being unstable, it undergoes fast hydrolysis to produce *N*-phenylhydroxylamine, which being a stronger nucleophile¹⁷ catalyses the reaction at a later stage as experimentally observed. A similar phenomenon has been reported by Behrman in Boyland-Sims oxidation.¹⁸ A series of fast reactions then appear to occur resulting in the formation of a symmetrical *trans*-azobenzene as shown schematically (Scheme 4).

The kinetic expression for the reaction can be derived by assuming a steady-state approximation to the reactive

$$d[\text{a}]/dt = k_1[\text{S}][\text{A}] - k_2[\text{a}] = 0 \quad (\text{i})$$

$$d[\text{b}]/dt = k_2[\text{a}] - k_3[\text{S}][\text{b}] = 0 \quad (\text{ii})$$

$$d[\text{S}]/dt = -k_1[\text{S}][\text{A}] - k_3[\text{S}][\text{b}] = 0 \quad (\text{iii})$$

intermediates. From equations (i) and (ii), (iv) may be derived.

$$k_3[\text{S}][\text{b}] = k_1[\text{S}][\text{A}] \quad (\text{iv})$$

Equation (iii) now takes the form (v). This is in agreement

$$-d[\text{S}]/dt = 2k_1[\text{S}][\text{A}] \quad (\text{v})$$

with the observed kinetic behaviour. Moreover, experimental evidence suggests that these reactions are of the dipole-dipole interaction type and no radicals or ions are involved, in conformity with the observed kinetic expression. There is considerable development of charge in the transition state and the mechanism is explained in terms of the chlorine of the N-Cl bond having electrophilic character.

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