

The Studies of Substituent Effect in Reactivity and Orientation in Some *N*-Chloro- *N*(4'-Chlorobenzoyl) Anilines in 99% v/v Acetic Acid Media

Batoul Bashir Sirag, Abdel Rahman H. El Nadi and Iftikhar Ahmad

Department of Chemistry, University of Khartoum, Khartoum, Sudan

ABSTRACT. Rates and isomer distribution for the transformation of four *N*-chloramines to the nuclear substituted chloroanilides have been studied in acetic acid (99% v/v), containing hydrochloric acid or toluene-*p*-sulphonic acid as promoters of the change. The reaction was found to be first order with respect to toluene-*p*-sulphonic acid and also first order with respect to *N*-chloro compound. The effect of hydrochloric acid concentration has also been studied and an explanation is put forward to account for the details of the course of the reaction.

In our previous paper (Sirag *et al.*) the kinetics and activation energy for the rearrangement of some *N*-chloramines to the corresponding nuclear substituted anilides have been investigated under the influence of hydrochloric acid as a promoter of the change. These results were in agreement with the results obtained by other workers (Hughes and Ingold 1952, Abdel Rahman *et al.* 1970) for the rearrangement of *N*-chloramines. The accepted mechanism for these transformations in the presence of hydrochloric acid involves formation of free molecular chlorine and free anilide according to equation (1)



Other workers (Atkins *et al.* 1968, Coulson *et al.* 1967) studied the rearrangement of *N*-chloroacetanilide under different free radical conditions and proposed mechanisms to describe the course of the change in different conditions. They suggested (i) autocatalysis of hydrogen chloride generated during the reaction, (ii) homolytic reaction followed by faster heterolytic reaction catalysed by hydrogen chloride and (iii) contribution to the overall reaction by hypochlorites.

In the present paper, the rearrangement products of four *N*-chloramines (namely *N*-chloro-*N*(4'-chlorobenzoyl)aniline (I); *N*-chloro-*N*(4'-chlorobenzoyl)-2,5-dimethylaniline (II); *N*-chloro-*N*(4'-chlorobenzoyl)-2,4-dichloroaniline (III); and *N*-chloro-*N*(4'-chlorobenzoyl)-2-chloroaniline (IV) were analysed quantitatively and the results have been discussed in terms of substituent effect in reactivity and orientation.

Experimental

a) Preparation and Purification of Material

The following compounds were prepared and purified by standard methods described elsewhere (Vogel 1958, Effenberger and Gleiter 1964).

(i) 4-Chlorobenzoyl chloride was obtained as pale yellow liquid, b.p. 220°C (lit. b.p. 220-222°C, Harris 1965).

(ii) *N*-(4'-chlorobenzoyl) aniline was obtained as colourless needles, m.p. 194-195°C (lit. m.p. 194-195°C, Harris 1965).

(iii) *N*-(4'-chlorobenzoyl)-2,5-dimethylaniline was obtained as colourless needles, m.p. 160°C.

Mass spectra: $M/Z = 259, 261 (M^+); 139, 141 (ClC_6H_4-CO^-); 120 (C_6H_3-(CH_3)_2-NH^-); 111, 113 (C_6H_4Cl)$.

Elemental analysis: Found: C, 69.09; H, 5.38%
 $C_{15}H_{14}ClNO$ requires: C, 69.36; H, 5.39%.

(iv) *N*-(4'-chlorobenzoyl)-2,4-dichloroaniline was obtained as colourless needles, m.p. 156-157°C (lit. m.p. 156-157°C, Effenberger and Gleiter 1964).

(v) *N*-(4'-chlorobenzoyl)-2-chloroaniline was obtained as colourless needles, m.p. 129-130°C.

Mass spectra: $M/Z = 265, 267, 269 (M^+); 104 (-C_6H_4CO^-); 139, 141 (Cl-C_6H_4-CO^-); 167 (-C_6H_4-NH-C_6H_4^-)$.

b) Preparation of *N*-Chloro compounds

N-chloro compounds were prepared by the method described by Hickinbottom (1968) and percentage active chlorine was determined iodometrically which was 100 percent active.

(i) *N*-Chloro-*N*-(4'-chlorobenzoyl) aniline was obtained as colourless needles, m.p. 87-88°C (lit. m.p. 87-88°C).

(Found active chlorine, 13.31%; $C_3H_9Cl_2NO$ requires active chlorine 13.33%).

(ii) *N*-Chloro-*N*-(4'-chlorobenzoyl)-2,5-dimethylaniline was obtained as colourless needles, m.p. 202-205°C.

(Found active chlorine, 12.04%; $C_{15}H_{13}Cl_2NO$ require active chlorine 12.06%).

(iii) *N*-Chloro-*N*-(4'-chlorobenzoyl)-2,4-dichloroaniline was obtained as colourless needles, m.p. 104°C.

(Found active chlorine, 10.57%; $C_{13}H_7Cl_4NO$ requires active chlorine 10.59%).

(iv) *N*-Chloro-*N*-(4'-chlorobenzoyl)-2-chloroaniline was obtained as colourless needles, m.p. 121-122°C.

(Found active chlorine, 11.80%; $C_{13}H_8Cl_3NO$ requires active chlorine, 11.80%).

c) *Method of Kinetic Measurement*

All the reactions were carried out in a darkened flask. Measured quantities of the reactants were thermostated in the water bath at 40°C unless mentioned otherwise. The reaction was started by adding hydrochloric acid or toluene-p-sulphonic acid. The aliquot (5 cm³) portions were withdrawn at definite time intervals and quenched in the titration flask which contained 10 cm³ of 10% potassium iodide solution. The liberated iodine was determined by titration against sodium thiosulphate solution using starch as indicator.

Identification of Products

The products were identified under the same conditions chosen for the kinetic measurements. The anilides which were obtained as reaction products, were hydrolysed by boiling the anilide under reflux with 100 cm³ of hydrochloric acid (2 *M*) for about an hour. The products were extracted with diethyl ether, washed in turn with water, sodium carbonate solution, water and dried over sodium sulphate. The solvent was removed under reduced pressure and the remaining crude products were dissolved in chloroform/petroleum ether (97 : 3 v/v). The chloroanilines were analysed by thin layer chromatography and high performance liquid chromatography by running reaction mixtures against authentic samples of the expected products.

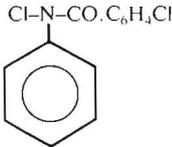
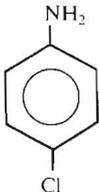
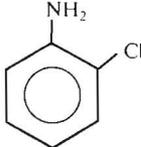
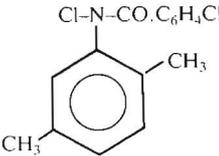
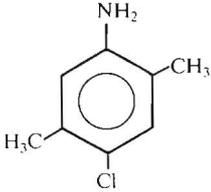
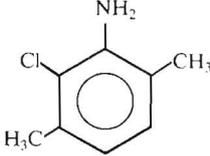
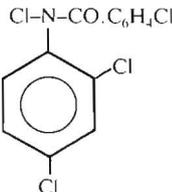
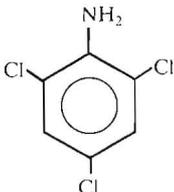
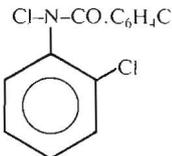
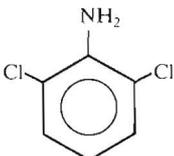
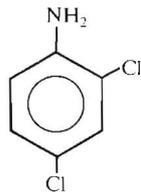
1. *Thin Layer Chromatography*

The stationary phase was silica gel for chromatography with chloroform and petroleum ether (97 : 3 v/v) as moving phase.

II. High Performance Liquid Chromatography

The chloroanilines were also confirmed by high performance liquid chromatography using model Pye Unicam PU 4020 u.v. detector at 272 nm attached to PM 8251 recorder. The moving phase was chloroform/petroleum ether (97:3 v/v) with flow rate 1.0 cm min^{-1} . The yields obtained are given in Table 1.

Table 1. The Quantitative Analysis of Rearrangement of N-Chloramines

<i>N-Chloramines</i>	<i>Products obtained after hydrolysis</i>	
 <p>(I)</p>	 <p>(62.5%)</p>	 <p>(37.5%)</p>
 <p>(II)</p>	 <p>(71%)</p>	 <p>(29%)</p>
 <p>(III)</p>	 <p>(100%)</p>	
 <p>(IV)</p>	 <p>(18.75%)</p>	 <p>(81.25%)</p>

The acid part of the hydrolysis for all the reaction mixtures was identified as p-chlorobenzoic acid (m.p. $238-239^\circ\text{C}$; lit. m.p. $238-239^\circ\text{C}$).

Results and Discussion

The progress of the reaction was observed by measuring the disappearance of *N*-chlorocompound iodometrically. The concentration of *N*-chlorocompound was varied from 0.01 to 0.05 *M* keeping other variables constant. The first order rate constants have been calculated by applying the following equation:

$$k_1 = \frac{2.303}{t} \log \frac{a}{a-x}$$

where *a* is the initial concentration of *N*-chlorocompound and (*a* - *x*) is its concentration at time *t*. The values of *k*₁ as calculated at different times during a single kinetic run were consistent.

The effect of concentration of hydrochloric acid was studied by changing its concentration and keeping other variables constant. The results are given in Table 2. The plot of rate constant versus concentration of hydrochloric acid was a straight line (Fig. 1). This shows first order dependence of rate on hydrochloric acid concentration. The reaction was also studied in the absence of chloride ions by using toluene-*p*-sulphonic acid as promoter. Toluene-*p*-sulphonic acid is known to give protons. The rate of reaction was observed at different toluene-*p*-sulphonic acid concentration and keeping other variables constant. The plot of rate constant versus the concentration of toluene-*p*-sulphonic acid was a straight line passing through origin (Fig. 2). This shows first order dependence of rate on toluene-*p*-sulphonic acid concentration and it also confirms that there is no reaction in the absence of protons.

Table 2. Variation of rate with the variation of concentration of hydrochloric acid

[<i>N</i> -chloro- <i>N</i> -(4'-chlorobenzoyl)-2-chloroaniline] = 2.00 × 10 ⁻² <i>M</i> Acetic acid, 99% v/v; Temp, 40°C	
[HCl] × 10 ³ (<i>M</i>)	<i>k</i> ₁ × 10 ⁵ (sec ⁻¹)
1.00	1.11
1.50	1.68
1.80	2.00
2.00	2.22
5.00	5.55
10.00	11.10
20.00	22.20

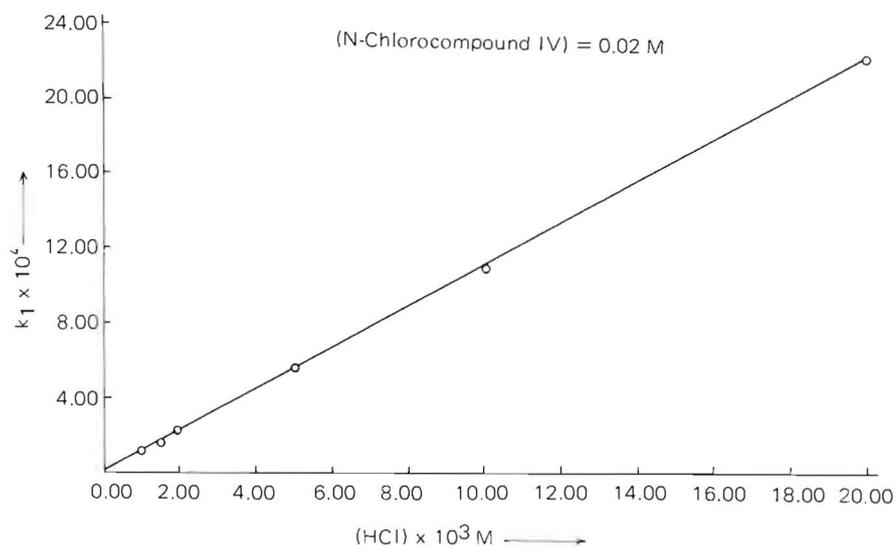


Fig. 1. Variation of rate on hydrochloric acid concentration [[*N*-chloro-*N*-(4'-chlorobenzoyl)-2-aniline] = $2.00 \times 10^{-2}M$ Acetic acid, 99% v/v; Temp., 40°C].

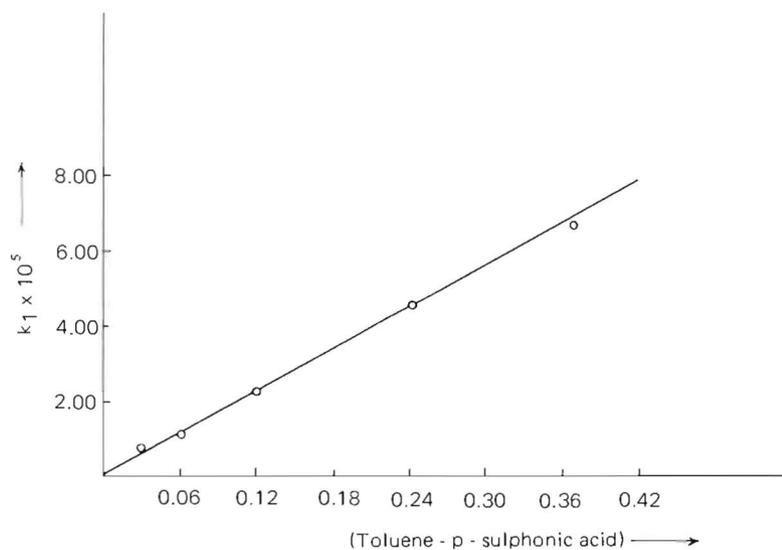
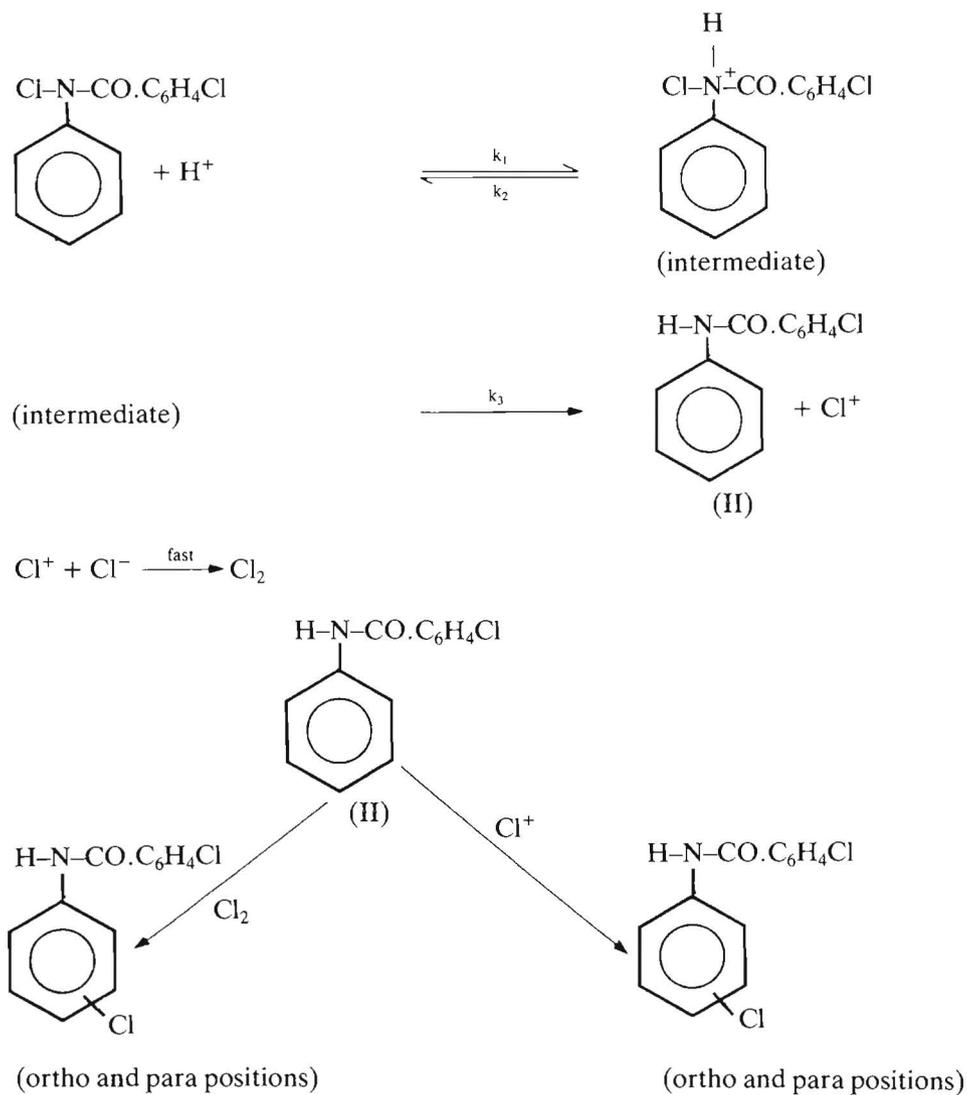
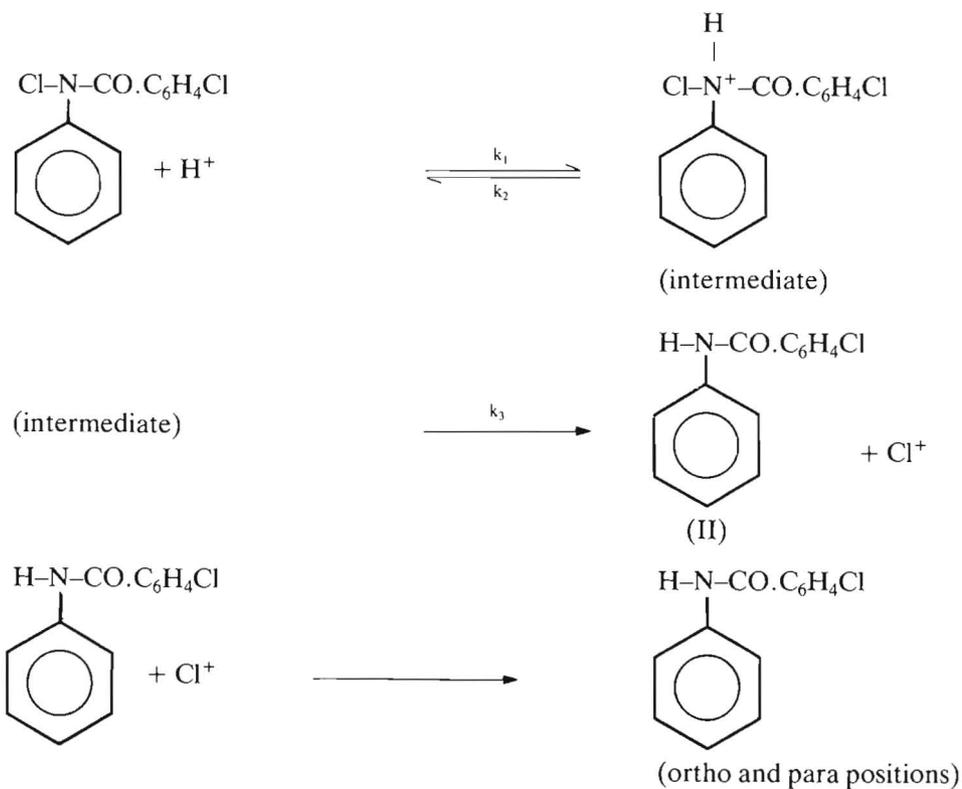


Fig. 2. Variation of rate on toluene-p-sulphonic acid concentration [[*N*-chloro-*N*-(4'-chlorobenzoyl)-2-aniline] = $2.00 \times 10^{-2}M$; Acetic acid, 99% v/v; Temp., 40°C].

In view of the above consideration, the probable mechanism of the rearrangement of *N*-chlorocompound under the influence of hydrochloric acid is represented in Scheme 1, and the probable mechanism of the change under the influence of toluene-*p*-sulphonic acid is represented in Scheme 2.

Scheme 1.



Scheme 2.

$$\text{Rate of reaction} = k_3 [\text{intermediate}] \quad (2)$$

By applying the steady-state approximation for the concentration of intermediate, we obtain equation (3)

$$[\text{intermediate}] = \frac{k_1[\text{N-chlorocompound}][\text{H}^+]}{k_2 + k_3} \quad (3)$$

Substituting the value of intermediate from equation (3) into equation (2), we get,

$$\text{Rate of reaction} = \frac{k_1 k_3 [\text{N-chlorocompound}][\text{H}^+]}{k_2 + k_3} \quad (4)$$

or,

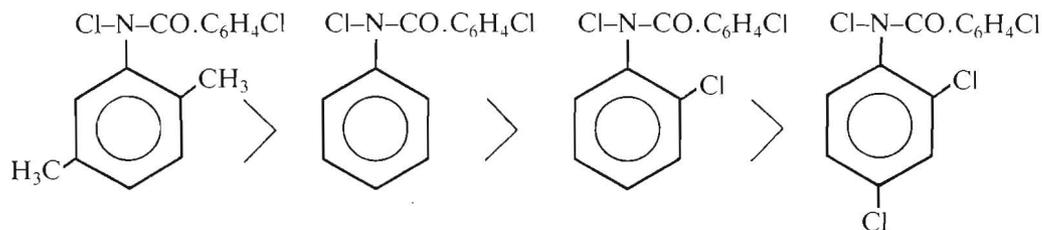
$$\text{Rate of reaction} = k' [\text{N-chlorocompound}][\text{H}^+] \quad (5)$$

$$k' = \frac{k_1 k_3}{k_2 + k_3}$$

The equation (5) explains the order of reaction with respect to *N*-chlorocompound and hydrogen ions.

The rate of rearrangement under the influence of hydrochloric acid is higher than that brought about by toluene-*p*-sulphonic acid. The reason being that in case of hydrochloric acid, in addition to the reaction of Cl^+ with compound (II) to give the rearrangement products, there is a possibility of a reaction of molecular halogen with compound (II), since molecular halogen can be formed by the union of Cl^+ and Cl^- from hydrochloric acid. On the other hand, in case of toluene-*p*-sulphonic acid clearly this can not be the case when no chloride ion is present. This is in agreement with rate values obtained for these transformations under the influence of these acids.

The rate of rearrangement of different *N*-chlorocompounds are given in Table 3. They are in the following order:



Comparison of the rates of rearrangement of these *N*-chlorocompounds, given in Table 3, clearly indicate that their order of basicity of the anilides, *i.e.*, anilides with electron releasing substituents rearrangement faster than those with electron withdrawing substituents. The most reactive compound of the series has two electron donating (methyl groups) and the least reactive of the series has two electron withdrawing substituents (chlorine atoms). This emphasises an electrophilic nature

Table 3. Variation of rate of rearrangement of *N*-chlorocompounds with varying the substituents

**[*N*-chlorocompound] = 2.00×10^{-2} M; [HCl] = 2.00×10^{-2} M;
Acetic acid, 99% v/v**

<i>N</i> -Chlorocompound	$k_1 \times 10^4$ (sec ⁻¹)				
	30°C	40°C	45°C	50°C	60°C
Compound I	1.89	3.75	5.50	7.24	14.10
Compound II	3.71	7.58	11.00	15.50	29.60
Compound III	0.73	1.43	2.27	3.09	5.82
Compound IV	1.11	2.22	3.34	4.45	8.70

of the reaction which confirms the attack of proton obtained from hydrochloric acid or toluene-*p*-sulphonic acid on nitrogen of the *N*-chlorocompound shown in the first step of the given schemes.

The quantitative isomer product distribution is given in Table 1. This clearly shows that in isomer distribution the directive influence is governed by *p*-chlorobenzamide group which is known to direct incoming substituents to the ortho and para positions. Since this group is bulky, it is expected to exert mechanical hinderance to substitution at a position ortho to it. Thus, the para isomer predominates in all products identified for these rearrangements (Table 1). The ortho substitution is decreased markedly when one of the ortho position is already occupied by a methyl or chloride substituent (compound II and compound IV). However, in compound III there is only one free ortho position thus only 2,4,6-trichloroaniline was obtained as a rearrangement product.

It can reasonably be concluded that the electron releasing substituent (like methyl group) which avail electrons on the ring as well as on nitrogen as an exocyclic atom facilitate the course of the reaction and the steric hinderance has a great influence on isomer distribution.

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دراسة تأثير بعض المتبادلات في سرعة
تفاعلات بعض الـ N كلور - بنزالييدات
وتوجيه شق الكلور إلى موضع في حلقة
البنزين في وسط يتكون من حمض الخليك
(٩٩٪ بالحجم)

بتول بشير سراج - عبدالرحمن حسن النادى - وافتخار
احمد

قسم الكيمياء - كلية العلوم - جامعة الخرطوم - الخرطوم - السودان

يتناول هذا البحث دراسة آلية إعادة تنظيم شق الكلور في
بعض مشتقات الـ N - كلوربنزانيلايد ذات الصيغة العامة
 $C_6H_4NCICOC_6H_4Cl$ (حيث $\times =$ متبادل) لتنتج الكلور -
بنزانيلايد المناظر بانتقال ذرة الكلور من ذرة النيتروجين إلى
ذرة الكربون التي تنتمى إلى نواة حلقة البنزين. تتم هذه
العملية في وسط يتكون من حمض الخليك (٩٩٪ بالحجم)
تحت تأثير مقادير مختلفة من حمض الهيدروكلوريك أو حمض
التلويين - p - سلفونيك عند درجات حرارة مختلفة.

لقد أُجريت دراسة لحركيات تفاعلات إعادة تنظيم
شق الكلور المتبادل وتم التعرف على النواتج وتم التوصل إلى
أن السرعة التي تتم بها هذه التفاعلات، تحت تأثير
الأحماض التي ورد ذكرها آنفاً، تخضع للترتيب الأولى من

حركيات التفاعل بالنسبة لـ N - كلوربنزانيايلايد وأيضا تخضع للرتبة الأولى لحمض التلويين p - سلفونيك . وقد درس أيضا تأثير حامض الهيدروكلوريك وقد رسم سير التفاعل حيث إنه أقوى من تأثير حمض السلفونيك .