

# MECHANISM OF NUCLEOPHILIC SUBSTITUTION OF 2,4-DINITROHALOGENOBENZENES WITH N-METHYLANILINES

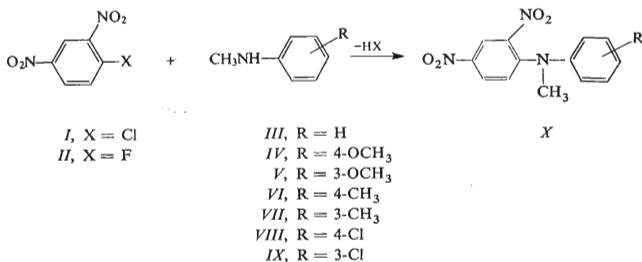
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The reactions of 3- and 4-substituted N-methylanilines with 2,4-dinitrochlorobenzene resp. 2,4-dinitrofluorobenzene have been followed in methanol and acetonitrile. The splitting of the addition complex is the rate-determining step of the reaction of 2,4-dinitrofluorobenzene, the reaction being, however, not base catalyzed in contrast to 3- and 4-substituted anilines.

In a previous paper<sup>1</sup> we studied the mechanism of the reaction of 3- and 4-substituted anilines with 2,4-dinitrochlorobenzene (*I*) and 2,4-dinitrofluorobenzene (*II*) in methanol and acetonitrile. The both solvents are polar with roughly the same dielectric constant, the former being protic and the latter being aprotic. During the reactions of the chloro derivative *I*, the reaction order with respect to aniline was unity in the both media, the reaction being about 3 times slower in acetonitrile. In the case of the fluoro derivative *II* the reaction in methanol was again 1. order in the amine, but in acetonitrile aniline acted catalytically on the reaction, and the overall reaction rate was far lower than that in methanol. The catalytic influence diminished with increasing base concentration. The presence of the base catalysis is explained as a consequence of the decreased velocity of the transformation of the intermediate into the products, so that this velocity becomes comparable with the rate of the reverse transformation of the intermediate into the starting substances. The substitution of N-hydrogen of aniline by a methyl group increases the steric requirements of the nucleophilic reagent which makes itself felt first of all in the lowering of the rate of transformation of the intermediate into the final reaction products.



The aim of the present work was to ascertain how the N-substitution would make itself felt in the mechanism of the nucleophilic substitution eventually in the extent of base catalysis, too. We studied the reaction of 3- and 4-substituted N-methylanilines *III*–*IX* with the fluoroderivative *II* in methanol and acetonitrile, the corresponding reactions of the chloro derivative *I* being measured for comparison.

## RESULTS AND DISCUSSION

As it could be expected<sup>2</sup>, the reaction of the chloroderivative *I* in methanol was 1. order in each of the reaction components (Table I). N-Methylaniline (*III*) reacted about 3 times more slowly than aniline under the same conditions<sup>1</sup>. This retardation is probably due to steric influence of the N-alkylation. The Hammett correlation for a series of substituted N-methylanilines was linear, the value of  $\rho$  being  $-2.9$ . In acetonitrile medium the reaction was studied with methylanilines *III* and *IV*. The reaction was again 1. order in base and in the case of the amine *III* it proceeded 2 times more slowly than that with aniline. The results obtained and the comparison with the aniline derivatives<sup>1</sup> indicate that the formation of intermediate is the rate-determining step of the reaction of the chloroderivative *I* in both the media. The reaction of the fluoro derivative *II* in methanol was also 1. order in the amine (Table I), but the N-methyl derivative *III* reacted more slowly than aniline by 2 orders of magnitude. This difference in reactivities was very exacting as to the purity of the N-methylanilines *III*–*IX*. The large retardation of the reaction and the relatively small value of  $k_F/k_{Cl} = 11$  for the amine *III* indicate that the second reaction step becomes rate-determining. However, this is in contrast with that we failed in finding base catalysis for this reaction. A still lower ratio  $k_F/k_{Cl} = 1$  was obtained for this reaction in ethanol at 20°C, and in this case the reaction was not catalyzed by N-methylaniline either<sup>3</sup>. The authors<sup>3</sup> succeeded in finding the catalysis by a stronger base (acetate), but the yield of the expected reaction product  $X(R = H)$  was only maximum 20%.

The second reaction step (decomposition of the intermediate) is undoubtedly rate-determining for the reaction of the fluoro derivative *II* in acetonitrile. This step was becoming rate-determining in the case of the less sterically hindered aniline, too, as it could be proved by the overall reaction rate and the base catalysis found<sup>1</sup>. In spite of this we did not find base catalysis for this reaction in this medium (Table I). All the other experimental facts found indicate, however, that the second reaction step is rate-determining; the ratio  $k_F/k_{Cl}$  is only 2.5. The ratio of the rate constants of reactions of the compounds  $II + III$  and  $II + \text{aniline}$ <sup>1</sup> is 1 : 30 whereas the ratio of the corresponding rate constants of the chloroderivative *I* is only 1 : 2. As the steric effect is the same for the above chloro and fluoro derivatives<sup>4</sup>, this large difference in the ratios must be due to the fact that the rate constants corresponding to various rate-determining steps are being compared.

TABLE I

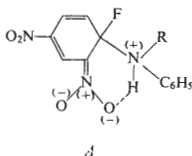
Reaction Rate Constants of Chloro Derivative I ( $k_{Cl}$ ) and Fluoro Derivative II ( $k_F$ ) in Methanol (Acetonitrile) at 20°C

$$[I]_0 = 1 \cdot 10^{-4} \text{M}; [II]_0 = 1 \cdot 10^{-2} \text{M}.$$

Substituted N-methylaniline	$k_{Cl}$	$k_F$
	$\text{l mol}^{-1} \text{min}^{-1}$	$\text{l mol}^{-1} \text{min}^{-1}$
III	$4.3 \cdot 10^{-4}$ ( $1.8 \cdot 10^{-4}$ )	$4.8 \cdot 10^{-3}$ ( $4.4 \cdot 10^{-4}$ ) <sup>a</sup>
IV	$(3.7 \cdot 10^{-3})$	$(2.5 \cdot 10^{-2})$ <sup>a</sup>
IV	—	1.1
V	—	$8.5 \cdot 10^{-4}$
VI	$1.8 \cdot 10^{-3}$	$3.5 \cdot 10^{-1}$
VII	$6.0 \cdot 10^{-4}$	$7.5 \cdot 10^{-3}$
VIII	$9.7 \cdot 10^{-5}$	$4.9 \cdot 10^{-5}$
IX	$2.8 \cdot 10^{-5}$	—

$$^a [II]_0 = 5 \cdot 10^{-6} \text{M}.$$

The reaction of the fluoro derivative II proceeds in methanol 11 times more rapidly than in acetonitrile, because methanol facilitates the splitting of the C—F bond in the second (rate-determining) step owing to hydrogen bond formation. There remains a question why this reaction is not base catalyzed. The structure of the intermediate of the reaction of the fluoro derivative II with aniline resp. N-methylaniline can be expressed approximatively as follows (R = H or CH<sub>3</sub>):



In the case of the reaction of N-methylaniline the base can react only with the hydrogen atom bound by intramolecular hydrogen bond to nitro group, which is very exacting energetically. In addition to it the hydrogen bond to the nitro group stabilizes the intermediate and thereby the activated complex, too, even though to a lesser extent. From this point of view the breaking of the hydrogen bond would be disadvantageous. Therefore *e.g.* during the reaction of 4-nitrofluorobenzene with secondary amines the found catalytic influence of bases was much greater than that during the analogous reaction with 2-nitrofluorobenzene<sup>5</sup>. In the case of the reaction with aniline only one of the both hydrogen atoms of the intermediate A is bound to the nitro

group by a hydrogen bond. Hence, the second hydrogen atom can react with a further aniline molecule whereby the reaction is catalyzed.

It holds for a nucleophilic aromatic substitution proceeding by the addition-elimination mechanism that the experimentally found bimolecular rate constant  $k$  is generally given<sup>6</sup> by Eq. (1).

$$v/([\text{RX}][\text{Amine}]) = k = (k_1k_2 + k_1k_3[\text{Amine}])/(k_{-1} + k_2 + k_3[\text{Amine}]) \quad (1)$$

We found that  $k_2 \gg k_3[\text{Amine}]$  and  $k_{-1} \gg k_2$  for the reaction of the fluoro derivative *II* and, therefore, Eq. (1) can be simplified to Eq. (2):

$$k = k_1k_2/k_{-1} \quad (2)$$

The values of the Hammett  $\rho$  constants were about  $-3$  for those reactions of the halogeno derivatives *I* and *II* with anilines<sup>1</sup> and *N*-methylanilines, where the first step was rate-determining. For the reaction of the fluoro derivative *II* having the second step rate-determining we found the value  $\rho -6.5$  in methanol (an estimate for acetonitrile was about  $-6$ ). In the case of the first step being rate-determining the substituents of the amine influence the course only until the formation of the first activated complex, whereas in the second case this influence extends up to the formation of the second activated complex. The Hammett equation can be modified in this case as follows:

$$\begin{aligned} \log k &= \rho\sigma + \text{const.} = \log k_1 + \log k_2 - \log k_{-1} + \text{const.} = \\ &= (\rho_1 + \rho_2 - \rho_{-1})\sigma + \text{const.} \end{aligned} \quad (3)$$

As  $\rho_1$  and  $\rho_2$  have negative values and  $\rho_{-1}$  has a positive value, all the three partial  $\rho$  constants sum up. The far greater absolute value of the  $\rho$  constant for the reaction of the fluoroderivative *II* stands in accord with the Eq. (3) discussed and represents a piece of evidence for our statement that the second step is rate-determining in this reaction.

## EXPERIMENTAL

**Reagents.** 2,4-Dinitrochlorobenzene *I*, p.a. (Reanal, Budapest) m.p. 53–54°C. 2,4-Dinitrofluorobenzene *II*, p.a. (Lachema, Brno) was distilled, and a fraction boiling at 151 °C/8 Torr was used. The substituted methylanilines *III–IX* were prepared either by methylation of the respective tosylanilines<sup>7</sup> or acetanilides<sup>8</sup> or by reduction of formylanilides with lithium aluminium hydride<sup>9</sup>. Each of the three procedures gave a methylaniline containing 3–8% of non-methylated substance. Therefore, these raw amines were purified as tosyl derivatives first by washing with 30% NaOH and then crystallization from acetic acid. The hydrolysis of the purified tosyl derivatives gave the amines *III–IX* of 99.9% purity. The purity was checked by gas chromatography.

graphy (GV apparatus, Carlo Erba; column packed with elastomer SE; temperature 250°C) which could detect 0.1% aniline in its N-methyl derivative. Methanol and acetonitrile were purified as in the previous work<sup>1</sup>.

*Kinetic measurements.* In the case of experiments having the initial concentration of the halogeno derivative *I* resp. *II*  $10^{-4}$  to  $10^{-5}$  mol/l (Table I), the increasing concentration of the compound *X* was followed photometrically at 370 nm in a thermostated cell compartment of a VSU-2P apparatus (Zeiss, Jena). In the case of the reactions having the initial concentration of the fluoro derivative *II*  $10^{-2}$  mol/l in methanol (Table I), 0.1 ml samples were withdrawn by means of a microdosing apparatus MD 100 (Labora) and analyzed photometrically after a 250 fold dilution. The rate constant *k* was calculated in the same way as in the previous work<sup>1</sup>.

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