Catalysis by Amine Salts of the Reactions of 1-Chloro- and 1-Fluoro-2,4-dinitrobenzene with *N*-Methylaniline in Acetonitrile

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The second-order rate constant k_A for the reaction of 1-chloro-2,4-dinitrobenzene with *N*-methylaniline increases slightly with the addition of quaternary ammonium salts according to the equation $k_A = k' + k''$ [salt]. Values of k''/k' of 8.9 for the chloride and 4.1 for the perchlorate are much less than the value of 240 obtained previously for the chloride when the nucleophile was aniline. Any acceleration produced by the hydrochlorides of *N*-methylaniline, trimethylamine, or triethylamine is less than those given by the quaternary ammonium perchlorate. The results agree with a recently proposed mechanism for the halide ion catalysis of the anilinodechlorination reaction in acetonitrile.

The reaction of 1-fluoro-2,4-dinitrobenzene with *N*-methylaniline has a curvilinear dependence on the concentrations of tetraethylammonium chloride and the hydrochlorides of *N*-methylaniline and trimethylamine; the accelerations observed are greater than that produced by tetraethylammonium perchlorate. The results are interpreted as due to base catalysis by chloride ion at the intermediate stage.

The mechanism of aromatic nucleophilic substitution when the nucleophile is a primary or secondary amine is given in Scheme 1. Application of the stationary-state hypothesis gives equation (1), where k_A is the observed second-order rate constant and ' B ' is either an added base or a second molecule of the nucleophile. When the condition $k_{-1} \ll k_2 + k_3$ [B]

$$k_A = \frac{k_1(k_2 + k_3\,[B])}{k_{-1} + k_2 + k_3\,[B]} \qquad (1)$$

does not hold, decomposition of the intermediate is rate-limiting and the reaction is base-catalysed. When $k_1 \sim k_2 + k_3$ [B] a curvilinear dependence of k_A on the concentration of base is observed, and when $k_{-1} \gg k_2 + k_3$ [B] a linear equation of the form (2) is obtained. As $k''/k' = k_3/k_2$ this ratio can be

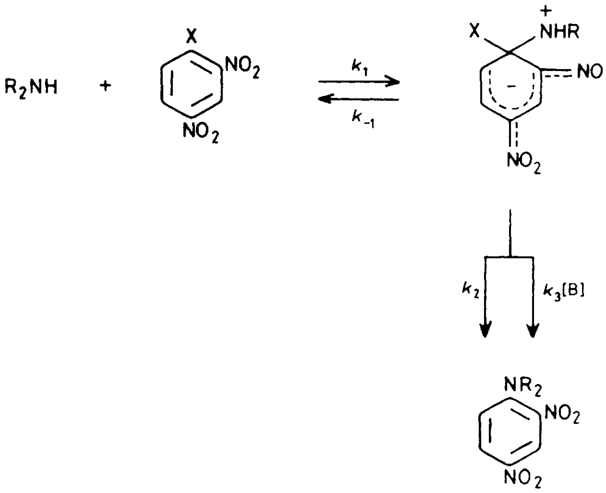
$$k_A = k' + k''\,[B] \qquad (2)$$

taken as a measure of the catalytic efficiency of the base. In many reactions the addition of several substances leads to a small linear increase in k_A similar to that represented by equation (2), but the values of k''/k' are small and bear no relationship to the base strength of the additives. These mild accelerations are not regarded as due to true base catalysis, but to some unspecified effect.[1]

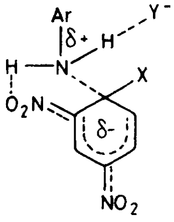
Recently [2] we have identified an additional form of catalysis. The reaction of 1-chloro-2,4-dinitrobenzene with aniline in acetonitrile has a strong linear dependence on the concentration of added halide ions. We have demonstrated that this is due to hydrogen bonding of the halide ions with an amino hydrogen atom in the transition state of the reaction as shown in (A), giving a rate equation of the form (3). When the

$$k_A = k_0 + k\,[Y^-] \qquad (3)$$

substrate was changed to 1-fluoro-2,4-dinitrobenzene, for which the decomposition of the intermediate is known [3] to be rate-limiting, a curvilinear dependence of k_A on chloride ion was observed. This was ascribed to the effect of chloride ion acting as a base in Scheme 1, superposed on its hydrogen-bonding effect.



Scheme 1.



(A)

The catalysis of the first step of the reaction depends on the availability of a relatively acidic hydrogen atom attached to nitrogen in the transition state. It is known that when the substrate contains an *ortho*-nitro group, strong hydrogen bonding occurs between it and the amino hydrogen atoms in the formation of the transition state. When a primary amine is the nucleophile there is still one amino hydrogen left for interaction with halide ions, but when the amine is secondary this is not the case: for secondary amines the catalytic effect would be expected to be considerably reduced, if not eliminated. Consequently we have investigated the effect of amine salts on the reactions of *N*-methylaniline with 1-chloro- and 1-fluoro-2,4-dinitrobenzene in acetonitrile: the results are given in the Table.

Kavàlek, Kubias, and Sterba [4] have shown that for the reaction of 1-chloro-2,4-dinitrobenzene with *N*-methylaniline in acetonitrile the formation of the intermediate is rate-

Table. The effect of the addition of amines and amine salts on the rate constants (l mol^{-1} s^{-1}) at 30 °C of the reactions of 1-fluoro- and 1-chloro-2,4-dinitrobenzene with *N*-methylaniline in acetonitrile

(1) Reaction of 1-fluoro-2,4-dinitrobenzene [a]

(A) Effect of *N*-methylaniline (NMA)

(i) No added salt

10^2[NMA]/M	4.0	8.0	16	24	40
10^7k_A	7.28	7.99	13.9	19.2	29.8

(ii) In the presence of 1.0×10^{-1}M-*N*-methylaniline hydrochloride

10^2[NMA]/M	16	24	40
10^7k_A	24.2	31.8	44.0

(B) Effect of DABCO ([PhNHMe] = 8.0×10^{-2}M)

10^3[DABCO]/M	5	10	15	20	30
10^5k_A	2.01	4.03	5.19	7.78	12.3
10^3[DABCO]/M	40	50			
10^5k_A	15.8	18.3			

(C) Effect of tetraethylammonium perchlorate (Et_4NClO_4) ([PhNHMe] = 1.6×10^{-1}M)

10^3[Et_4NClO_4]/M	0.00	5.0	10.0	20.0	25
10^7k_A	13.9	15.7	16.7	18.2	18.0
10^3[Et_4NClO_4]/M	35				
10^7k_A	19.4				

(D) Effect of tetraethylammonium chloride (Et_4NCl)

(i) [PhNHMe] = 8.0×10^{-2}M

10^3[Et_4NCl]/M	0	4	8	16	24
10^7k_A	7.90	12.2	15.3	18.4	20.5
10^3[Et_4NCl]/M	40				
10^7k_A	24.8				

(ii) [PhNHMe] = 1.6×10^{-1}M

10^3[Et_4NCl]/M	0	5.0	10.0	20.0	25.0
10^7k_A	13.9	23.3	27.2	33.1	33.4
10^3[Et_4NCl]/M	35.0				
10^7k_A	40.1				

(E) Effect of *N*-methylaniline hydrochloride (NMAH) ([PhNHMe] = 8.0×10^{-2}M)

10^3[NMAH]/M	0	5	10	12.5	16.0
10^7k_A	7.90	9.09	9.81	11.4	12.0
10^3[NMAH]/M	20.0	25.0	28.0	32.0	37.5
10^7k_A	12.0	13.1	13.8	14.3	15.3
10^3[NMAH]/M	85				
10^7k_A	17.7				

(F) Effect of trimethylamine hydrochloride (Me_3NHCl) ([PhNHMe] = 8.0×10^{-2}M)

10^3[Me_3NHCl]/M	0	5	10	20	25
10^7k_A	7.90	8.66	9.55	12.0	12.3
10^3[Me_3NHCl]/M	30	40	50	70	85
10^7k_A	13.5	15.8	13.6	18.0	17.3

(G) Effect of triethylamine hydrochloride (Et_3NHCl) ([PhNHMe] = 8.0×10^{-2}M)

10^3[Et_3NHCl]/M	0	5	10	20	30
10^7k_A	7.90	10.2	10.2	11.5	11.5
10^3[Et_3NHCl]/M	40	50	60		
10^7k_A	12.8	12.6	13.8		

Table (*continued*)

(2) Reaction of 1-chloro-2,4-dinitrobenzene [a]

(A) Effect of *N*-methylaniline (NMA)

10^2[NMA]/M	8	16	24	40
10^6k_A	4.82	4.86	4.83	4.90

(B) Effect of DABCO ([PhNHMe] = 8.0×10^{-2}M)

10^3[DABCO]/M	0	5	10	20	30
10^6k_A	4.82	5.48	6.60	8.73	9.65
10^3[DABCO]/M	90				
10^6k_A	13.6				

(C) Effect of tetraethylammonium perchlorate (Et_4NClO_4) ([PhNHMe] = 1.6×10^{-1}M)

10^3[Et_4NClO_4]/M	0.00	5.0	10	20	35
10^6k_A	4.86	5.14	5.25	5.44	5.64

(D) Effect of tetraethylammonium chloride (Et_4NCl) ([PhNHMe] = 8.0×10^{-2}M)

10^3[Et_4NCl]/M	0	3.5	7.0	14.0	38.5
10^6k_A	4.82	4.91	4.97	5.29	6.39

(E) Effect of *N*-methylaniline hydrochloride (NMAH) ([PhNHMe] = 8.0×10^{-2}M)

10^2[NMAH]/M	0	1.25	2.5	3.75	7.0
10^6k_A	4.82	4.90	4.80	5.00	5.17

(F) Effect of trimethylamine hydrochloride (Me_3NHCl) ([PhNHMe] = 8.0×10^{-2}M)

10^3[Me_3NHCl]/M	0	5	10	25	50
10^6k_A	4.82	4.74	4.99	5.06	5.26
10^3[Me_3NHCl]/M	70				
10^6k_A	5.32				

(G) Effect of triethylamine hydrochloride (Et_3NHCl) ([PhNHMe] = 8.0×10^{-2}M)

10^3[Et_3NHCl]/M	0	5	10	20	30
10^6k_A	4.82	4.68	4.99	5.02	5.00
10^3[Et_3NHCl]/M	40	50			
10^6k_A	4.93	4.99			

[a] Substrate concentration 1.0×10^{-3}M.

limiting; in agreement with this we find that *N*-methylaniline does not catalyse the reaction. The second-order rate constant does however increase with increasing concentration of 1,4-diazabicyclo[2.2.2]octane (DABCO) and at the higher DABCO concentrations, good kinetics could not be obtained, the rate constants drifting downwards as the reaction proceeded. Ross, Bruno, and Petersen [5] give the second-order rate constant for the reaction of the chloro compound with DABCO in acetonitrile as 11.3×10^{-5} l mol^{-1} s^{-1} at 50.8 °C. This gives an approximate value of 3×10^{-5} for the reaction at 30 °C to be compared with 4.85×10^{-6} l mol^{-1} s^{-1} when the nucleophile is *N*-methylaniline. Hence the observed increments in k_A with increasing DABCO concentration are not due to its catalytic effect as a base, but to its competition as a nucleophile with *N*-methylaniline.

Additions of tetraethylammonium chloride and perchlorate give slight linear increases in the observed second-order rate constant as shown in Figure 1, with k''/k' values of 8.9 and 4.1, respectively. Whether the approximately two-fold increase of k''/k' of the chloride over the perchlorate is a genuine catalytic effect or not is difficult to say, but if it is, its magnitude is greatly reduced in comparison with that when the nucleophile is aniline, for which k''/k' is 240.[2] Hence the original reasoning is justified and the results provide additional evidence for the proposed mechanism of halide catalysis of

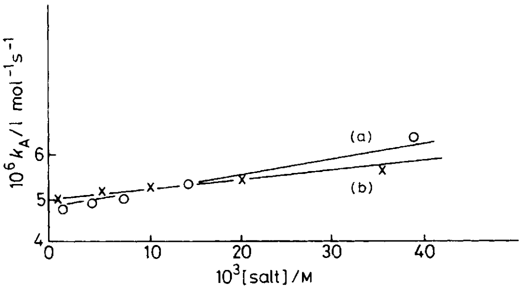


Figure 1. Plots illustrating the effect of the addition of tetraethylammonium salts on the reaction of 1-chloro-2,4-dinitrobenzene with *N*-methylaniline in acetonitrile: (a) chloride; (b) perchlorate

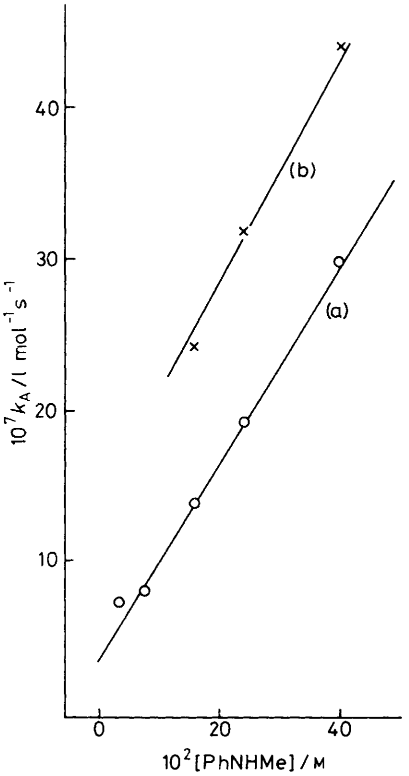


Figure 2. Plots illustrating the variation of the rate constant with *N*-methylaniline concentration for the reaction of 1-fluoro-2,4-dinitrobenzene with *N*-methylaniline in acetonitrile: (a) no salt present; (b) in the presence of 1.0×10^{-1}M-*N*-methylaniline hydrochloride

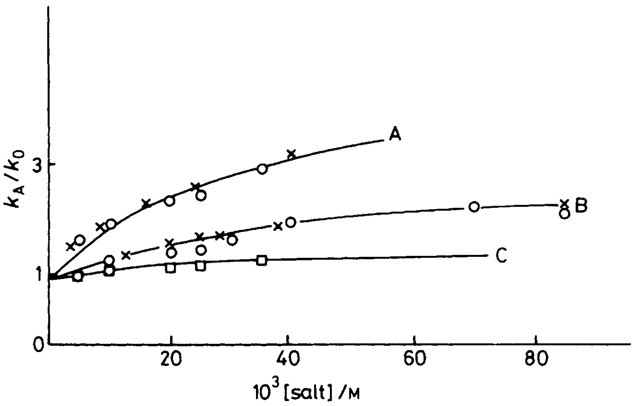


Figure 3. Plots illustrating the effect of added amine salts on the reactions of 1-fluoro-2,4-dinitrobenzene with *N*-methylaniline in acetonitrile: (A) salt Et_4NCl: × [PhNHMe] 8.0×10^{-2}M, ○ [PhNHMe] 1.6×10^{-1}M; (B) × salt *N*-methylaniline hydrochloride, ○ salt trimethylamine hydrochloride; (C) salt Et_4NClO_4

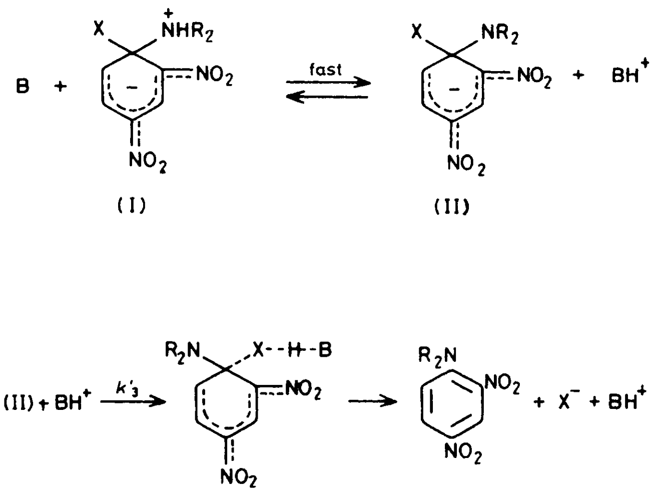
anilinodechlorination. Any small increases in the rate constant which occur on the addition of the hydrochlorides of *N*-methylaniline, trimethylamine, or triethylamine are less than those occurring with the perchlorate, and cannot be ascribed to catalysis.

Bunnett and Randall[6] observed small increases in the second-order rate constant with increasing amine concentration for the reaction of 1-fluoro-2,4-dinitrobenzene with *N*-methylaniline in ethanol, but because of the high nucleophile concentrations used (up to 0.4M) they could not tell whether this represented a minor participation of a third-order term or a medium effect. Kaválek, Kubias, and Sterba,[4] who studied the reaction in acetonitrile at 20 °C, provided convincing evidence that under these conditions the decomposition of the intermediate is rate-limiting. They state however that the reaction is not catalysed by *N*-methylaniline, but do not give any details of the concentration ranges employed. The present results as illustrated in Figure 2 show that there is a slight linear increase of k_A with amine concentration, giving k''/k' 17.3. Although normally this would be regarded as in the ' mild acceleration ' category, because of the evidence of the Czech workers as to the mechanism of the reaction and the effect of DABCO discussed later, we interpreted the increase as due to true base catalysis.

A plot of k_A against DABCO concentration is linear, passing through the origin. We believe that this is due to base catalysis of the reaction by DABCO and not to nucleophilic attack by DABCO on the substrate for the following reason. The absorbance of a solution, containing the fluoro compound and DABCO only was monitored at 380 nm, the wavelength used in all these measurements. When these results were used to calculate an apparent rate constant using the same infinity value as for k_A, a value of 3.26×10^{-6} l mol^{-1} s^{-1} was obtained. A solution of the chloro substrate and DABCO was left until there was no further change in absorbance, and when this value was used in the calculation, a rate constant value of 6.0×10^{-6} l mol^{-1} s^{-1} was obtained. Both these figures are substantially less than the lowest value of k_A measured in the presence of DABCO (20.1×10^{-6}) and very much less than the highest (183×10^{-6}).

The pK_a value of *N*-methylaniline in acetonitrile is not known, but it will not be substantially different from that of aniline, which is 10.65,[7] whereas that of DABCO is 18.3.[7] Not only is DABCO a much stronger base in acetonitrile than *N*-methylaniline, but its steric requirements are less; consequently it is a much better base catalyst than *N*-methylaniline. The kinetic form indicates that in the presence of DABCO the condition $k_{-1} > k_3[B] > k_2$ holds in equation (1). This is in line with the anilinodefluorination reaction in acetonitrile, for which a plot of k_A against aniline concentration is curvilinear and passes through the origin,[3] indicating that the base-catalysed path is much more important than the uncatalysed one. The greater steric requirement of *N*-methylaniline as compared with aniline is probably responsible for both its inefficiency as a base catalyst and also the change from the condition $k_{-1} \simeq k_3[B]$ to $k_{-1} \gg k_3[B]$; relief of steric compressions in the transition state for the decomposition of the intermediate to reactants giving an increase in k_{-1}.

Figure 2 shows that the addition of *N*-methylaniline hydro-



Scheme 2.

chloride accelerates the reaction between *N*-methylaniline and 1-fluoro-2,4-dinitrobenzene, and Figure 3 shows that there is curvilinear dependence of the rate constant on the concentrations of tetraethylammonium chloride and the hydrochlorides of *N*-methylaniline and trimethylamine. The accelerations are greater than those produced by tetraethylammonium perchlorate, and as amine hydrochlorides are highly associated in acetonitrile, the accelerations cannot be due to a salt effect.

The detailed mechanism of the base-catalysed step of aromatic nucleophilic substitution reactions is believed to be that proposed by Bunnett and Davies [8] and is given in Scheme 2. As $d[\text{Products}]/dt = k_3'[(\text{II})][\text{BH}] = k_3'K[(\text{I})][\text{B}]$, where $K = [(\text{II})][\text{BH}]/[(\text{I})][\text{B}]$, catalysis by *N*-methylaniline hydrochloride cannot be due to the cation and must be due to the chloride ion, and as the catalytic effect of trimethylamine hydrochloride is identical, this must be the case for the trimethylamine salt too. In Scheme 1, values of k_1 are invariably much higher for fluoro than for the corresponding chloro compounds, indicating that the transition state occurs earlier for the fluoro substrate. Hence its amino hydrogen atoms in the transition state will be less acidic and less prone to hydrogen bond to halide ions than those of the chloro compound. As we have just shown that neither hydrochloride catalyses the reaction with the chloro compound, the accelerations observed for the fluoro substrate must be due to chloride ion acting as a base in Scheme 1. We believe that this is the first unambiguous example of the base-catalysed decomposition of the intermediate formed in aromatic nucleophilic substitution reactions in dipolar aprotic solvents where the base is not an amine.

It is known [9] that dilute solutions of quaternary ammonium chlorides are almost completely dissociated in acetonitrile, unlike amine hydrochlorides where considerable association occurs; this accounts for the greater catalytic effect of tetraethylammonium chloride as compared with *N*-methylaniline and trimethylamine hydrochlorides. The fact that the points for the plots of k_A/k_0 against tetraethylammonium chloride concentration lie on the same curve for both concentrations of *N*-methylaniline (8×10^{-2} and 1.6×10^{-1}M) shows that the magnitude of the chloride ion catalysis is insensitive to nucleophile concentration. This is in contrast to the large decrease in catalytic activity of chloride ion with increasing methanol concentration found in the methanolysis of *p*-nitrobenzoyl chloride in acetonitrile.[10] The difference is due to *N*-methylaniline being a much more ineffectual catalyst of aminodefluorination than methanol is of methanolysis.

Experimental

The purification of the substrates,[11] solvent,[12] tetraethylammonium chloride [13] and perchlorate,[3] and trimethylamine hydrochloride,[14] and the method of following the reactions by the spectrophotometric determination of the products [11] at 380 nm, have been described previously. Samples of *N*-methylaniline purified *via* either the nitroso or the acetyl compound gave identical kinetic results. *N*-Methylaniline hydrochloride was prepared by passing dry hydrogen chloride gas through a solution of purified *N*-methylaniline in sodium-dried ether and purified by precipitation with dry ether from its solution in methanol–ethanol. Trimethylamine and triethylamine hydrochlorides were commercial samples purified by precipitation from a solution in methanol by sodium-dried ether.

The reactions are extremely slow at 30 °C; consequently most rate constants were calculated using theoretical values of the absorbance at infinite time. Occasionally reactions were allowed to go to completion and good agreement was found between the experimental and calculated values of the final absorbance. A blue colour developed in all reactions carried out in the presence of *N*-methylaniline hydrochloride. In the case of the chloro substrate this did not interfere with the kinetic determination and final values of the absorbance agree with the calculated ones. With 1-fluoro-2,4-dinitrobenzene, when the nucleophile concentration was 4×10^{-2}M, serious interference occurred and the kinetics could not be determined. When the nucleophile concentration was increased to 8×10^{-2}M, rate constants could be determined in the presence of up to 8.5×10^{-2}M-hydrochloride and when the nucleophile concentration was 16×10^{-2}M good kinetics were obtained in the presence of 1.0×10^{-1}M-hydrochloride.

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