The Kinetics of the Reactions of Piperidine, n-Butylamine, Morpholine, and Benzylamine with 1-Fluoro- and 1-Chloro-2,4-dinitrobenzenes in Acetonitrile

By **Dapo Ayediran, Titus O. Bamkole,** and **Jack Hirst,*** Department of Chemistry, University of Ibadan, Ibadan, Nigeria

The kinetics of the reactions designated in the title have been studied as a function of amine concentration. The only system to show base catalysis is the reaction of morpholine with 1-fluoro-2,4-dinitrobenzene. The results are analysed in terms of the effects of nucleophile basicity and the change from primary to secondary amine on the mechanism of nucleophilic aromatic substitution.

In aromatic bimolecular nucleophilic substitution reactions when either primary or secondary amines are the nucleophiles the accepted mechanism is reaction (1).

$$\begin{tikzcd} R_2NH + \text{Substrate} \arrow[r, shift left, "k_1"] & \text{(I)} \arrow[l, shift left, "k_{-1}"] \arrow[r, "R_2NH,\ k_3"] \arrow[dr, "k_2"'] & \text{Products} \\ & & \text{Products} \end{tikzcd} \qquad (1)$$

Application of the steady state hypothesis to this mechanism gives equation (2) where k_A is the observed second-order rate constant. Two criteria have been used to

$$k_A = (k_1k_2 + k_1k_3[R_2NH])/(k_{-1} + k_2 + k_3[R_2NH]) \quad (2)$$

determine whether the rate of formation of the intermediate complex or its decomposition to products is rate determining. The first is a kinetic criterion. If $k_{-1} \ll k_2 + k_3[R_2NH]$ then equation (2) reduces to $k_A = k_1$, the formation of the intermediate is rate determining, and the reaction is not base catalysed. If either (a) $k_{-1} \gg k_2 + k_3[R_2NH]$, when equation (2) reduces to the form $k_A = k' + k''[R_2NH]$ or (b) no simplifying conditions can be made, then base catalysis is observed and the decomposition of the intermediate is rate limiting. Condition (a) however requires further amplification. In many aromatic bimolecular substitution reactions small, linear increases of the second-order rate constant with increasing amine (or more generally, added base) concentration are observed. The values of the ratio k''/k' ($\equiv k_3/k_2$) are small, and the accelerating effect of the bases bears no relationship to their base strength. According to Bunnett [1] this does not represent true base catalysis, the formation of the intermediate is rate determining in these reactions, and the small increases observed are due to some unspecified effect. In other reactions increase in base concentration has a powerful accelerating effect, the value of k''/k' is high (>50) and the catalytic effect increases with increase in strength of the base. These reactions are regarded as base catalysed and the decomposition of the intermediate as rate limiting.

The second criterion applies only when the substrates are halogens. If the rate-constant sequence F $\gg$ other halogens is observed, then breaking of the carbon–fluorine bond is not involved in the rate-determining step.[2] We have used these two criteria to examine the effect on the mechanism of the change of nucleophile from primary to secondary amine, using amines of approximately the same basicity and also to examine the

---

[1] J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 1965, **87**, 3875.

[2] J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1.

effect of the basicity of the nucleophile on the mechanism, in the dipolar aprotic solvent acetonitrile. In all cases the rates of the reactions were followed spectrophotometrically with the amine in large enough excess to ensure first-order kinetics and the experimental values of the absorbance at infinity agreed with the calculated one. The results are given in Table 1 and the pK_a of the amines in acetonitrile in Table 2. The reactions of 1-fluoro- and 1-chloro-2,4-dinitrobenzenes with aniline[3] and *N*-methylaniline[4] in this solvent have already been studied by Kavalek and his co-workers.

TABLE 1

Rate constants (l mol^{-1} s^{-1}) for the reactions of 1-fluoro- and 1-chloro-2,4-dinitrobenzenes with n-butylamine, piperidine, benzylamine, and morpholine in acetonitrile

Amine	Substrate	t/°C								
n-Butylamine	Chloro	30.10	10^2[amine]/M	2.02	4.01	6.02	8.06	10.1	12.1	
			10^2k_2	1.05	1.17	1.24	1.34	1.43	1.53	
	Fluoro	29.90	10^4[amine]/M	5.03	7.54	10.0	25.1	50.3	75.4	
			k_2	8.67	8.71	8.89	9.17	9.46	9.13	
Piperidine	Chloro	30.10	10^4[amine]/M		5.0	10	20	26.4		
			$10\ k_2$		6.06	6.21	6.10	6.24		
	Fluoro	29.80	10^4[amine]/M	1.50	2.50	4.0	5.0	7.5		
			k_2	138	152	129	141	141		
Benzylamine	Chloro	30.35	10^2[amine]/M	4.0	8.0	10	12	16		
			10^3k_2	2.46	2.46	2.43	2.50	2.47		
	Fluoro	30.25	10^4[amine]/M	5.0	10.0	30.0	50.0	60.0	80.0	
			k_2	1.99	2.14	2.08	2.17	2.09	2.13	
Morpholine	Chloro	29.90	10^3[amine]/M	4.0	12.0	16.0	20.0			
			10^2k_2	4.73	4.73	4.74	4.74			
	Fluoro	29.80	10^4[amine]/M	4.80	6.15	7.20	10.4	41.6	62.8	83.2
			$10\ k_2$	7.86	8.03	8.03	9.35	12.7	14.0	15.2

When the substrate is 1-chloro-2,4-dinitrobenzene, the only nucleophile whose second-order rate constants increase with increasing nucleophile concentration is n-butylamine. For this amine a plot of the second-order rate constant against amine concentration is linear with a slope of 4.61×10^{-2} l^2 mol^{-2} s^{-1} and intercept 9.68×10^{-3} l mol^{-1} s^{-1}. As the value of k''/k' is 4.77 l mol^{-1} we do not regard this reaction as being base catalysed and conclude that in all the aminodechlorinations studied the formation of the intermediate is rate-determining. The variation of the rate constants with change of amine follows the usual[5] pattern found in aromatic nucleophilic substitution reactions. For both the primary and secondary amines the values decrease with decrease in basicity of the amine and comparing amines of approximately the same basicity, piperidine is more nucleophilic than n-butylamine and morpholine more nucleophilic than benzylamine.

TABLE 2

The pK_a * of amines in acetonitrile

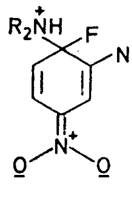
Amine	n-Butylamine	Piperidine	Benzylamine
pK_a	18.26	18.92	16.76
	Morpholine	Aniline	
pK_a	16.61	10.56	

* Values taken from J. F. Coetzee, *Progr. Phys. Org. Chem.*, 1967, **4**, 45.

The reactions of n-butylamine and benzylamine with 1-fluoro-2,4-dinitrobenzene are not base catalysed, the $k^{\mathrm{F}}/k^{\mathrm{Cl}}$ ratios are high (n-butylamine **931**, benzylamine **854**), and the n-butylamine : benzylamine rate constant ratio is approximately the same for the fluoro- (4.29) and chloro-substrates (3.94). Thus for both these nucleophiles the formation of the intermediate is rate determining. Kavalek *et al.*[3] however have shown that the reaction of this substrate with the much less basic nucleophile aniline is base catalysed.

The reaction of piperidine with 1-fluoro-2,4-dinitrobenzene is not base catalysed and the $k^{\mathrm{F}}/k^{\mathrm{Cl}}$ ratio is high (228), hence the formation of the intermediate is rate determining. With the weaker base morpholine, the rate constants increase in a curvilinear fashion with increase in amine concentration and the $k^{\mathrm{F}}/k^{\mathrm{Cl}}$ ratio is only *ca.* 13.5 and we conclude that in this reaction the decomposition of the intermediate is rate determining. Thus in both the primary and secondary amine series, reduction in the basicity of the nucleophile results in a change in the rate-determining step from formation of the intermediate to its decomposition to products.

Benzylamine and morpholine have almost identical base strengths in acetonitrile but the rate-determining stage in their reactions with 1-fluoro-2,4-dinitrobenzene are different. This could be ascribed to steric strain in the intermediate (A) when morpholine is the nucleophile, giving a greater value for k_{-1} in equation (2) for morpholine than benzylamine. Bernasconi[5] however has measured the rate constants for the decomposition to reactants of



(A)

---

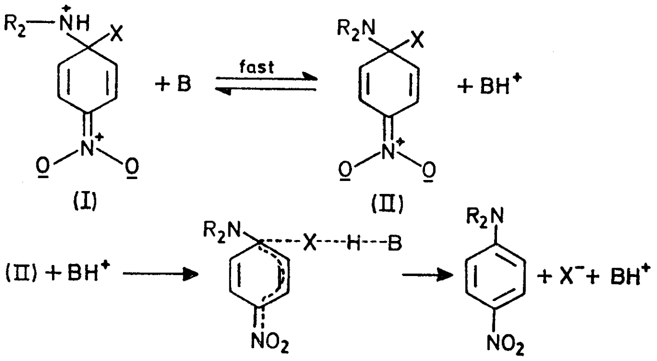
[3] J. Kavalek, J. Haasova, and V. Sterba, *Coll. Czech. Chem. Comm.*, 1972, **37**, 3333.

[4] J. Kavalek, J. Kubias, and V. Sterba, *Coll. Czech. Chem. Comm.*, 1972, **37**, 4041.

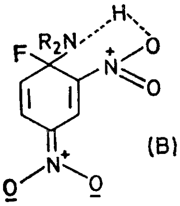
[5] C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1970, **92**, 129.

the Meisenheimer complexes formed from 1,3,5-trinitrobenzene and n-butylamine, piperidine, and pyrrolidine and found them to be approximately the same, and on this basis has specifically rejected the above hypothesis.

Several mechanisms have been put forward[6] to account for the base catalysed step in aromatic nucleophilic substitution, the most acceptable one being due to Bunnett.[7] In this mechanism the first-formed intermediate is rapidly and reversibly transformed into its conjugate base from which the slow, electrophilically catalysed expulsion of the leaving group takes place (Scheme). Bernasconi and Gehriger[8] however have shown that under certain conditions the proton transfer in the Scheme can be rate determining and Kavelek *et al.*[4] have demonstrated that for the reaction of *N*-methylaniline with 1-fluoro-2,4-dinitrobenzene in acetonitrile, the decomposition of the intermediate is rate determining, but the reaction is not base catalysed. These authors explained their results as due to strong hydrogen bonding of the amino-hydrogen atom with an oxygen of the *o*-nitro-group in the intermediate complex (B). Removal of the hydrogen atom is ' very exacting energetically ' and the intermediate decomposes to products unimolecularly.



SCHEME



In the present investigation when benzylamine is the nucleophile, two amino-hydrogen atoms are present in the intermediate complex. One can hydrogen-bond to an *o*-nitro-group, and the other participate in the normal Bunnett mechanism. Provided the condition $k_{-1} \ll k_2 + k_3$[amine] holds, no base catalysis will be observed and the formation of the intermediate complex will be rate determining. When morpholine is the nucleophile, only one amino-hydrogen atom is present in the intermediate complex and this is hydrogen-bonded to the *o*-nitro-group. The intermediate can only decompose either by a unimolecular process or a Bunnett-type mechanism involving the destruction of the hydrogen bond. If this latter process is slow the condition $k_{-1} \ll k_2 + k_3$[amine] no longer applies and the reaction will be base catalysed.

EXPERIMENTAL

Materials.—The purification of acetonitrile[9] and 1-fluoro- and 1-chloro-2,4-dinitrobenzenes[10] have been described elsewhere. The water content of the acetonitrile was determined by Karl Fischer titration and did not exceed 0.02%. The amines used were commercial samples purified by standard procedures and the products of their reactions with the two substrates were prepared by methods described in the literature.

Kinetics Procedure.—The reactions of 1-chloro-2,4-dinitrobenzene were followed spectrophotometrically using the pipette procedure already described.[10] The rates of the reactions of 1-fluoro-2,4-dinitrobenzene were measured on a Guildford 2000 recording spectrophotometer with the exception of those of piperidine. The rates of this reaction were measured on a Durrum stopped flow apparatus and we thank Dr. G. B. Ogunmola for his assistance with these measurements.

[5/2372 *Received, 8th December,* 1975]

---

[6] J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 1965, **87**, 3879.

[7] J. F. Bunnett and G. T. Davies, *J. Amer. Chem. Soc.*, 1960, **82**, 665.

[8] C. F. Bernasconi and C. L. Gehriger, *J. Amer. Chem. Soc.*, 1974, **96**, 1092.

[9] J. Hirst and Khali-Ur-Rahman, *J.C.S. Perkin II*, 1973, 2119.

[10] T. O. Bamkole, C. W. L. Bevan, and J. Hirst, *Nigerian J. Sci.*, 1968, **2**, 11.