The Kinetics of the Reaction of Phenyl 2,4,6-Trinitrophenyl Ether with Aniline in Methanol, Acetonitrile, Tetrahydrofuran, Ethyl Acetate, and Benzene

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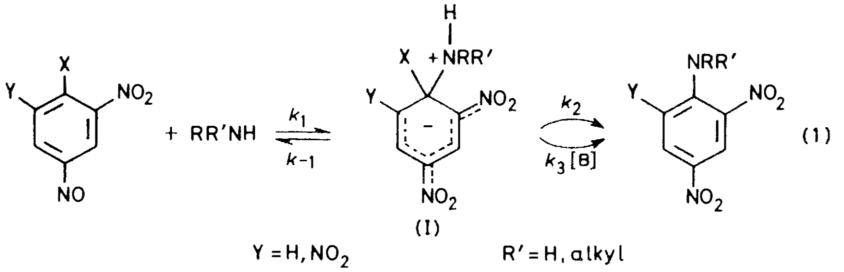
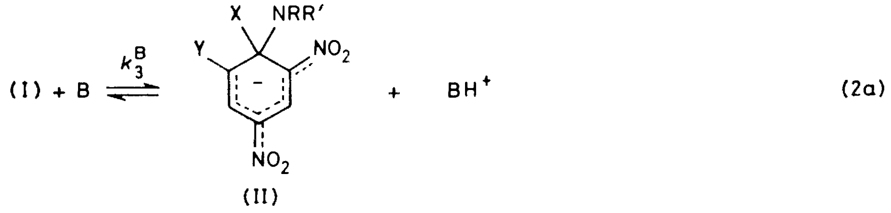
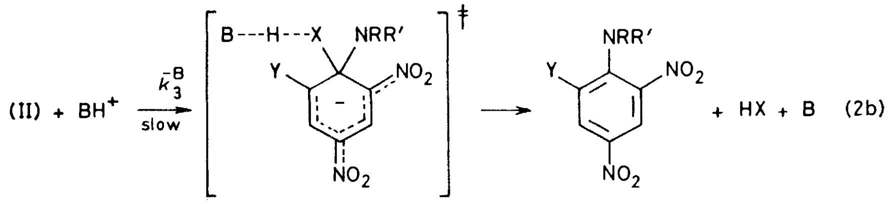
The kinetics of the reaction of phenyl 2,4,6-trinitrophenyl ether with aniline have been investigated as a function of the amine concentration in methanol, acetonitrile, tetrahydrofuran, ethyl acetate, and benzene. Base catalysis was observed in all the solvents. The second-order rate constant k_A shows a linear correlation with the aniline concentration except in benzene where the linearity is with the square of the aniline concentration. The k_3^B/k_2 ratios for the solvents provide information on the mechanism of the uncatalysed decomposition of the intermediate formed in nucleophilic aromatic substitution. A mechanism is proposed for the base-catalysed pathway in solvents of low dielectric constant and basicity.

STUDIES[1-3] of the reactions of primary and secondary amines with nitro-activated aryl halides, ethers, and some other substrates have led to the firm establishment of the intermediate complex mechanism for nucleophilic aromatic substitution reactions. Some of these reactions are base catalysed while others are not.[2,3]



Equation (1) depicts the mechanism of such reactions. According to the two-step mechanism first proposed by Bunnett[4] the reaction is subject to base catalysis only when the expulsion of the leaving group X is at least partially rate determining.[5,6] Whether the expulsion of the leaving group is rate determining or not depends on the relative rates of reversion of the intermediate (I) to reactants and progression to products. Base catalysis is therefore observable in those cases where the leaving group X is slow to separate from the aryl carbon[7] and or when the amine portion of the intermediate complex (I) is easily expelled.[2]





The mechanism of the general base-catalysed step (k_3^B) had been of some controversy for some years,[2] but that shown in equation (2) appears now firmly established due mainly to the work of Orvik and Bunnett.[8] It involves a fast acid–base equilibrium between the initially formed zwitterionic intermediate (I) and its conjugate base followed by a rate-limiting expulsion of the leaving group with general acid catalysis by BH^+. It was also suggested[8] by these authors that the mechanism of the uncatalysed reaction could be similar to that of the catalysed one with a solvent molecule playing the role of base B in equation (2). Bernasconi and de Rossi[9] on one hand, have shown that this mechanism is untenable in hydroxylic solvents while Ayediran *et al.*[10] on the other, have shown that it is not tenable in dipolar aprotic solvents when a secondary amine is the nucleophile; we now show that the mechanism is also not applicable to primary amines in both protic and aprotic solvents.

We have investigated the reaction of phenyl 2,4,6-trinitrophenyl ether with aniline as a function of the aniline concentration in the solvents methanol, acetonitrile, tetrahydrofuran, ethyl acetate, and benzene. The reaction was followed spectrophotometrically with aniline in sufficient excess to give pseudo-first-order kinetics (see Experimental section). The observed second-order rate constants k_A are listed in Table 1.

TABLE 1

Rate constants (l mol^{-1} s^{-1}) for the reaction of phenyl 2,4,6-trinitrophenyl ether [a] with aniline in various solvents at 25°

Solvent									
Methanol	10^2[Aniline]/M	1.0	1.5	2.0	2.5	3.0	4.0		
	10^3k_A	9.06	13.01	17.57	22.0	26.94	34.7		
Acetonitrile	10^2[Aniline]/M	1.0	1.5	2.0	3.0	4.0			
	10^3k_A	3.73	5.83	7.50	11.22	15.15			
Tetrahydrofuran	10^2[Aniline]/M	1.0	1.5	2.0	2.5	3.0	4.0		
	10^3k_A	2.93	4.38	5.83	7.03	8.84	11.52		
Ethyl acetate	10^2[Aniline]/M	6.0	7.0	8.0	10.0	12.0	13.0	14.0	15.0
	10^3k_A	3.80	4.40	5.07	6.24	7.54	8.22	8.81	9.23
Benzene	10^2[Aniline]/M	18.0	20.0	22.0	24.0	26.7	28.0		
	10^4k_A	6.98	8.67	10.50	12.34	14.20	16.21		

[a] Substrate concentration 5.0×10^{-4}M.

In the first four solvents (Table 1) it was observed that the experimental second-order rate constants k_A depend linearly on the aniline concentration. In benzene, however, the experimental second-order rate constants show a linear correlation with the square of the aniline concentration.

DISCUSSION

The kinetic expression derived with reference to the mechanism depicted in equation (1) by means of the steady-state approximation is represented in equation (3). The mechanism assumes that $k_3^{\mathrm{B}} = \bar{k}_3^{\mathrm{B}}K_{\mathrm{B}}$ where

$$\mathrm{Rate}/[\mathrm{ArX}][\mathrm{RR'NH}] = k_A = k_1(k_2 + k_3^{\mathrm{B}}[\mathrm{B}])/(k_{-1} + k_2 + k_3^{\mathrm{B}}[\mathrm{B}]) \quad (3)$$

$K_{\mathrm{B}} = [(\mathrm{II})][\mathrm{BH}^+]/[(\mathrm{I})][\mathrm{B}]$. The non-dependence of k_A on the base concentration means that $k_2 + k_3^{\mathrm{B}}[\mathrm{B}] \gg k_{-1}$ which simplifies equation (3) to (4). According to

$$k_A = k_1 \quad (4)$$

equation (4), the observed rate constant k_A represents the rate of formation of the intermediate. The reaction of 2,4,6-trinitrochlorobenzene with aniline in methanol is not base-catalysed,[12] indicating that equation (4) holds. Our results in the reaction of phenyl 2,4,6-trinitrophenyl ether with aniline in this solvent and the others studied show that it is strongly catalysed by aniline. The phenoxide being a relatively poor leaving group compared with chloride ion, it is not unexpected that the rate-determining step in these solvents would be the decomposition of the intermediate complex (I).

The linear dependence of the second-order rate coefficient k_A with base concentration means that $k_{-1} \gg k_2 + k_3^{\mathrm{B}}[\mathrm{B}]$, a condition which simplifies equation (3) to (5). According to equation (5), a plot of k_A against the

$$k_A = k_1k_2/k_{-1} + k_1k_3^{\mathrm{B}}[\mathrm{B}]/k_{-1} \quad (5)$$

amine concentrations should give a straight line with intercept k_1k_2/k_{-1} and slope $k_1k_3^{\mathrm{B}}/k_{-1}$. The values of the intercepts and slopes obtained for such plots by the least-squares method for the first four solvents in Table 1 are listed in Table 2 with their correlation coefficients.

The values of the intercepts in Table 2 are of the order of 10^{-4} l mol^{-1} s^{-1}. These thus represent very small intercepts and therefore can only be regarded as approximate. Combining the two values of the intercept and slope in each case, the ratio of the catalysed to the uncatalysed pathway k_3^{B}/k_2 for the decomposition of the intermediate can be calculated. The values obtained for the various solvents are listed in Table 3.

TABLE 2

Values of intercepts and slopes of the plot of k_A *versus* amine concentration in various solvents for the reaction of phenyl 2,4,6-trinitrophenyl ether at 25°

Solvent	r	$10^4k_1k_2k_{-1}^{-1}$/ l mol^{-1} s^{-1}	$k_1k_3^{\mathrm{B}}k_{-1}^{-1}/^{-1}$ l^2 mol^{-2} s^{-1}
Methanol	0.9994	2.74	0.869
Acetonitrile	0.9997	0.23	0.377
Tetrahydrofuran	0.9993	0.49	0.287
Ethyl acetate	0.9995	1.10	0.062

TABLE 3

Values of k_3^{B}/k_2 in various solvents for the reaction of phenyl 2,4,6-trinitrophenyl ether at 25°

Solvent	k_3^{B}/k_2
Methanol	3 172
Acetonitrile	16 390
Tetrahydrofuran	5 857
Ethyl acetate	564

The observation of linear variation of the second-order rate coefficient k_A with the square of the amine concentration in benzene is indicative of a change of mechanism in the base-catalysed step in this solvent. This observation necessitates a modification of equation (3) to (6). With $k_{-1} \gg k_2 + k_4^{\mathrm{B}}[\mathrm{B}]^2$, equation (6) will be

$$\mathrm{Rate}/[\mathrm{ArX}][\mathrm{RR'NH}] = k_A = k_1(k_2 + k_4^{\mathrm{B}}[\mathrm{B}]^2)/(k_{-1} + k_2 + k_4^{\mathrm{B}}[\mathrm{B}]^2) \quad (6)$$

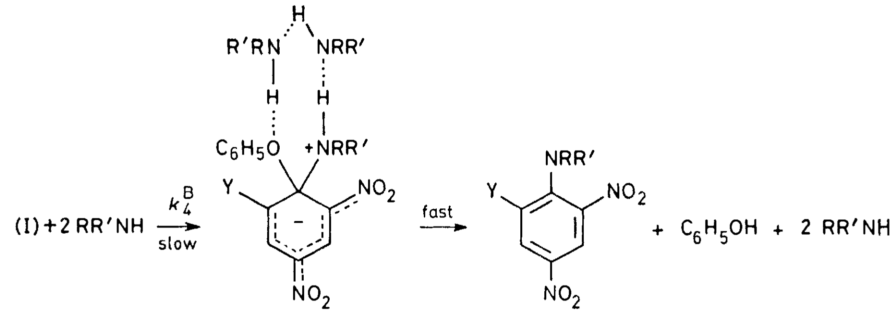
similarly simplified to (7) and a plot of k_A against $[\mathrm{B}]^2$

$$k_A = k_1k_2k_{-1}^{-1} + k_1k_4^{\mathrm{B}}k_{-1}^{-1}[\mathrm{B}]^2 \quad (7)$$

would then give a straight line with intercept k_1k_2/k_{-1} and slope $k_1k_4^{\mathrm{B}}/k_{-1}$.

The value obtained for this intercept by the least-squares method (r 0.999 2) is 0.67×10^{-4} l mol^{-1} s^{-1}. This value like those obtained in the other solvents being very small can only be regarded as approximate. From the slope of the same plot, $k_1k_4^{\mathrm{B}}/k_{-1}$ is 0.02 l^3 mol^{-3} s^{-1} and a combination of the two values gives the ratio of the catalysed to the uncatalysed pathway k_4^{B}/k_2 for the decomposition of intermediate (I) in benzene as 300.

The calculated k_3^{B}/k_2 ratios offer a means of comparing the catalytic effectiveness of the base in question in the various solvents. If we assume that the Bunnett-type mechanism holds for both the catalysed and uncatalysed pathways, then the equilibrium constant K_{B} [equation (2)] refers to the equilibrium between the intermediate (I) and the base B for the base-catalysed pathway, while K_{S} refers to the equilibrium between the same intermediate and the solvent S for the uncatalysed pathway (since it is assumed that S plays the role of B in this pathway) and defines the acid strength of the intermediate (I) in a particular solvent. Since the strength of an acid varies greatly as the solvent is changed, (the acid strengths of the tri-n-butylammonium ion, for example, in dimethyl sulphoxide and in acetonitrile [13] differ by a factor of *ca.* 10^9) one would expect large changes in solvent basicity to give rise to corresponding changes in the values of k_3^{B}/k_2 or k_4^{B}/k_2 as the case may be. Table 3 lists the values obtained for solvents of varying dielectric constant and basicity. Change of solvent does not give a rationalisable trend on these values. For example, while there is *ca.* 5-fold increase in the value of k_3^{B}/k_2 in changing from methanol to acetonitrile, with dielectric constants (ε_{25}) 32.7 and 38.8 respectively,[14] there is only *ca.* 3-fold increase in this ratio in changing from tetrahydrofuran (ε_{25} 7.58) to acetonitrile; the corresponding variation in basicity [15] between the two solvents in each case is *ca.* 10^8. Also, there is *ca.* 10-fold decrease in the k_3^{B}/k_2 ratio in changing from tetrahydrofuran to ethyl acetate (ε_{25} 6.02) and yet the variations in dielectric constant [14] and basicity [15] between these two solvents are only *ca.* 1.5 and 10^4, respectively.



(III)

SCHEME

In changing from solvent S to T say, there is a change in the electrophilic catalyst from SH$^+$ to TH$^+$ [equation (2) where B is replaced by S or T] and if there is a large difference in the catalytic power of these entities, it should reflect a trend in the experimental values of k_3^{B}/k_2 in the various solvents, but as this had not been the case, we presume that the mechanism is untenable as a general postulate. Besides, the k_3^{B}/k_2 ratios for the proposed mechanism are expected to be $\geqslant 10^7$ according to an estimate made by Bernasconi and de Rossi.[9] 10^7 Is a value several orders of magnitude larger than the experimental values (Table 3), these being in the range between 500 and 10^4, with the highest being *ca.* 2×10^4 in acetonitrile. This, thus, lends support to our presumption that for reactions of primary amines in protic and aprotic solvents, the uncatalysed pathway does not proceed by a Bunnett-type mechanism. A plausible alternative is that proposed by Kirby and Jencks [16] involving intramolecular acid catalysis of leaving-group departure by the ammonium proton in intermediate (I).

The dependence of k_{A} on the square of the aniline concentration observed in benzene implies catalysis by two aniline molecules in the rate-limiting base-catalysed step. The first one is easily accommodated in the abstraction of proton from the amine moiety of interdiate (I), but the role of the second aniline molecule is not as easily discernible. We feel it could only be involved in the abstraction of the leaving group X and this is possibly through hydrogen bonding with the oxygen of the phenoxide ion (Scheme). This intermolecular hydrogen bonding is similar to the intramolecular acid catalysis [16] of the leaving-group departure referred to above. Hydrogen bonding between these two bonded amine molecules then results in a cyclic transition state (III) followed by rapid decomposition into products.

This mechanism is a modification of that proposed by Capon and Rees [17] for the reaction of piperidine with 1-fluoro-2,4-dinitrobenzene in benzene, that when nucleophilic substitution reactions take place in solvents of low dielectric constant, the base-catalysed decomposition of the intermediate occurs with a cyclic transition state. The rationale behind the postulate is the need for electrophilic catalysis to assist the departure of poor leaving groups and the inability of such solvents to stabilize the ionic species required by the Bunnett-type mechanism.

The formation of the cyclic transition state involved here (Scheme) is devoid of any conceptual difficulty as it does not require the breaking of the intramolecular hydrogen-bonding (involving the *ortho*-nitro group) which is known to occur [18,19] when the intermediate (I) is first formed. Aniline being the nucleophile in this case, two amino-hydrogen atoms are present in the intermediate complex (I); one can be hydrogen-bonded to the *ortho*-nitro group while the other participates in the proposed cyclic transition state.

EXPERIMENTAL

Materials.—Phenyl 2,4,6-trinitrophenyl ether, m.p. 155° (lit., 155—156°),[20] was prepared by the reaction of potassium phenolate with picryl chloride in alcoholic solution. The product was precipitated from solution with water and recrystallised from alcohol. Aniline was dried with potassium hydroxide and twice distilled from zinc powder. Methanol, tetrahydrofuran, and ethyl acetate were purified by standard methods.

Kinetic Procedure.—The kinetics were determined under conditions of excess of nucleophile over substrate by measuring the increase in absorbance at the absorption maximum (370 nm) of the 2,4,6-trinitrophenylaniline produced during the reaction in accordance with the pipette procedure previously described.[21] In all cases, excellent pseudo-first-order plots were obtained up to at least 70% reaction and the absorption spectrum of the reaction mixture at infinite time corresponded within 2% to the 'mock' infinity prepared by using 2,4,6-trinitrophenylaniline. The second-order rate constants k_A were obtained by dividing the pseudo-first-order rate constants by the amine concentration. All rates were run in duplicate and the rate constants are accurate to within ±2%.

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