Kinetics of the Reactions of Phenyl 2,4,6-Trinitrophenyl Ether with Piperidine, n-Butylamine, Aniline, Benzylamine, and Morpholine in Benzene

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The kinetics of the reactions of phenyl 2,4,6-trinitrophenyl ether with piperidine, n-butylamine, benzylamine, and morpholine have been investigated as a function of the amine concentration in benzene and the results compared with that of aniline. Base-catalysis was observed with all the amines except n-butylamine. The overall reaction with morpholine was wholly base-catalysed. Mechanisms are proposed for the uncatalysed and the catalysed decomposition of the intermediate formed in nucleophilic aromatic substitution.

In an earlier paper [1] we investigated the effect of solvent basicity on the reaction of phenyl 2,4,6-trinitrophenyl ether with aniline. The reaction was base-catalysed in all the solvents studied. The second-order rate constants varied linearly with the amine concentration except in the least basic solvent, benzene, where the linearity was with the square of the aniline concentration. A different mechanism was therefore proposed for this amine in benzene. In order to establish how widespread this phenomenon is, we have studied the reaction of this substrate with two other primary amines, n-butylamine and benzylamine, as well as two secondary amines, piperidine and morpholine, all of different basicities in the same solvent, benzene.

TABLE 1

Rate constants (l mol^{-1} s^{-1}) for the reactions of phenyl 2,4,6-trinitrophenyl ether with piperidine, n-butylamine, aniline, benzylamine, and morpholine in benzene at 25°

Amine							
Piperidine	10^3[Piperidine]/M	2.5	3.0	3.5	4.0	4.5	5.0
	$10k_A$	3.30	3.72	4.20	4.50	4.90	5.29
n-Butylamine	10^4[n-Butylamine]/M	2.0	3.0	4.0	5.0	6.0	7.0
	k_A	52.0	51.0	52.5	52.0	52.0	52.5
Aniline [a]	10[Aniline]/M	1.8	2.0	2.2	2.4	2.6	2.8
	10^4k_A	6.98	8.67	10.50	12.34	14.20	16.21
Benzylamine	10^4[Benzylamine]/M	5.0	6.0	7.0	8.0	9.0	10.0
	k_A	17.54	18.67	19.43	20.37	21.55	22.10
Morpholine	10^2[Morpholine]/M	1.5	2.0	2.5	3.0	4.0	5.0
	10^2k_A	1.90	2.61	3.22	3.86	5.16	6.50
	$k = \frac{dx/dt}{[\text{Ether}][\text{Morpholine}]^2}$	1.27	1.30	1.29	1.29	1.29	1.30

[a] Data from our previous paper.[1]

The reactions were followed spectrophotometrically with the amines in sufficient excess to give pseudo-first-order kinetics and the absorbance readings at infinity agreed with the calculated ones. The observed second-order rate constants k_A are listed in Table 1.

DISCUSSION

The variation of the observed second-order rate constants (Table 1) with change in amine does not follow the usual pattern [2,3] found in nucleophilic aromatic substitution reactions. If steric factors are not dominant, there is generally a higher nucleophilic reactivity of secondary than of primary amines [4,5] and for both primary and secondary amines the rates should decrease with decrease in the basicity of the amines. Observation of the second-order rate constants in Table 1 shows that primary amines are sometimes more reactive than secondary amines of comparative strength and the variation of the rate constants with change in amine is independent of base strength (Table 2) in the region of strongly to moderately basic amines while in the region of moderately to weakly basic amines the variation in rate constants with amine basicity follows the usual pattern referred to above.

Comparing amines of approximately the same basicity, piperidine should be more nucleophilic than n-butylamine, being a secondary amine and having a slightly higher pK_a (Table 2) but in fact the observed second-order rate constants for the reaction of these amines with phenyl 2,4,6-trinitrophenyl ether in benzene (Table 1) shows n-butylamine to be faster. Besides, the reaction of piperidine is base-catalysed while that of n-butylamine is not. Similarly, benzylamine is much faster than morpholine in its reaction with the same substrate, both reactions being base-catalysed. Examination of

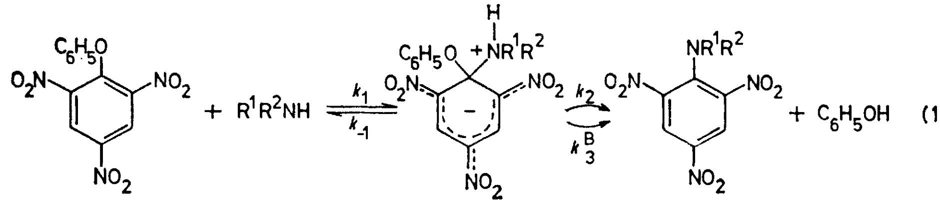
TABLE 2

The pK_a values of the amines in benzene [6]

Amine	pK_a
Piperidine	11.06
n-Butylamine	10.59
Benzylamine	9.73
Morpholine	8.36
Aniline	4.60

the results for morpholine (Table 1) shows that the second-order rate constants increase linearly (r 0.9999) with increasing amine concentration and extrapolate to zero at zero amine concentration, while those for piperidine and benzylamine (r 0.9986 and 0.9966, respectively) give intercepts of 0.136 and 13.0 l mol^{-1} s^{-1}. The reaction with morpholine is therefore third order overall (second order in morpholine) as shown by the constancy of the third-order rate constant k (Table 1). Thus the reaction with morpholine is wholly base-catalysed. Aniline, which is the least basic of all the amines studied, follows the usual pattern of reactivity by being the least nucleophilic as shown by the second-order rate constants in Table 1.

The results are interpreted in terms of the mechanism for nucleophilic aromatic substitution [7] represented by equation (1).



(I)

The rate expression [equation (2)] for the system can be derived from steady-state approximation. One

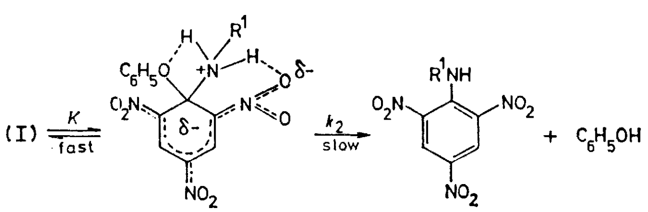
$$\mathrm{Rate}/[\mathrm{ArOC_6H_5}][\mathrm{R^1R^2NH}] = k_A = k_1(k_2 + k_3{}^{B}[\mathrm{B}])/(k_{-1} + k_2 + k_3{}^{B}[\mathrm{B}]) \quad (2)$$

salient feature of the mechanism is the fact that the intermediate (I) can proceed to products by two distinct pathways: (i) spontaneously (k_2) and (ii) through general base catalysis ($k_3{}^{B}$). If no base catalysis is observed, the inference can be made that the formation of the intermediate (k_1) is the rate-determining step and that $k_2 \gg k_{-1}$. In this case, the measured second-order rate constant k_A is equal to k_1. When base catalysis is observed, on the other hand, it means that the decomposition of the intermediate (I) is the rate-determining step and that $k_{-1} \gg k_2$.

Piperidine and n-butylamine have comparable base strengths in benzene but the rate-determining steps in their reactions with the substrate are different, this being the decomposition of the intermediate for piperidine, while for n-butylamine it is the formation of the intermediate. A possible explanation for this difference is the steric strain in the intermediate (I) [7b] when piperidine is the nucleophile, giving a greater value for k_{-1} in equation (2) for piperidine than n-butylamine. This, in fact, is the reason adduced for methylamine being less nucleophilic than aniline.[6] A more plausible explanation, however, is the occurrence of intramolecular hydrogen bonding between the ammonium proton and the oxygen of the phenoxide ion in the intermediate complex (I), resulting in intramolecular acid catalysis of the leaving-group departure through a cyclic transition state (II) (Scheme 1) in line with a suggestion by Kirby and Jencks.[4] n-Butylamine being the nucleophile in this case, there are two amino-hydrogen atoms present in the intermediate; one can take part in the proposed cyclic transition state while the other participates in intramolecular hydrogen bonding (involving the *o*-nitro-group) which is known to occur [8, 9] when the intermediate (I) is first formed.

This mechanism is similar to the one earlier proposed by us [1] for the base-catalysed reaction of aniline with the substrate under study, except that in the present case, no extra amine molecule is involved in the cyclic transition state involving the intermediate complex (I) as the reaction is not base-catalysed.

We explain the wholly third-order kinetics observed in the case of morpholine along similar lines. Here a second morpholine molecule is involved, this time, in intermolecular acid catalysis of leaving-group departure through hydrogen bonding with the oxygen of the phenoxide ion. A second hydrogen bond between this morpholine molecule and the ammonium proton of the amine moiety of the intermediate (I) then results in a cyclic transition state (III) (Scheme 2) followed by rapid decomposition into products.

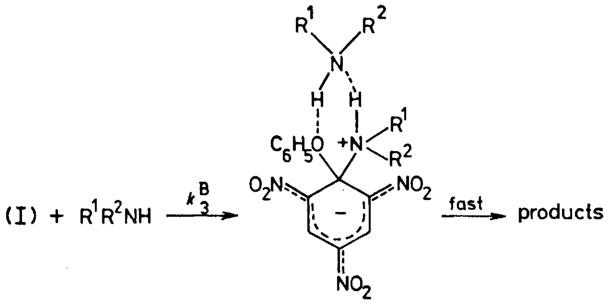


(II)

$k_A = k_2K$; K = [(II)]/[(I)]

Scheme 1

In this case of secondary amine, however, since there is only one hydrogen in the amine moiety of the intermediate (I), the initially formed hydrogen bond to the *o*-nitro-group has to be broken before the new one to the morpholine molecule can be formed in the proposed cyclic transition state. This would also be the case for the uncatalysed decomposition of the intermediate (I) discussed in Scheme 1 if a secondary amine were to be the nucleophile. The breaking of this bond is made easier by the fact that the stabilizing interaction between the ammonium proton and the oxygen of the *o*-nitro-group is relatively small for the substrate under study (as compared with substrates with only one or two nitro-groups) owing to the dispersal of the negative charge over three nitro-groups (Scheme 1) coupled with the fact that the solvent is non-polar. However, since the breaking of this bond requires some extra activation energy, the values of k_2 and k_3^{B} (k_2 for morpholine in this case, however, being zero as the reaction is wholly base-catalysed) are reduced relative to those of the corresponding primary amine which are little affected. This in part at least accounts for the sometimes observed faster rates of primary over secondary amines.



(III)

SCHEME 2

EXPERIMENTAL

Materials.—The preparation of phenyl 2,4,6-trinitrophenyl ether was described previously.[1] The amines used were purified by standard methods and the products of their reactions with the substrate prepared by methods described in the literature.[10] AnalaR benzene was further purified by first drying with calcium chloride, then over sodium wire, and then distilled.

Kinetic Procedure.—The rates of formation of the products of the reactions were determined spectrophotometrically by the pipette procedure previously described.[1] Those for n-butylamine and benzylamine were measured on a PMQ recording spectrophotometer.

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