Kinetics of the Reactions of Piperidine, n-Butylamine, Morpholine, and Benzylamine with 2,4-Dinitrophenyl Phenyl Ether

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The kinetics of the reactions designated in the title have been studied as a function of amine concentration in acetonitrile, dimethyl sulphoxide, and (for piperidine and n-butylamine only) methanol. In all the solvents studied, the reactions of the secondary amines are base-catalysed; those of the primary amines are not. The results are interpreted in terms of the generally accepted mechanism of nucleophilic aromatic substitution.

RECENTLY,[1] we examined the effect of amine basicity and the change from primary to secondary amine on the mechanism of aminodehalogenation of 1-fluoro- and 1-chloro-2,4-dinitrobenzenes in acetonitrile. Morpholine and benzylamine have identical basicities in this solvent, but the reaction of the former with the fluoro-substrate is base-catalysed, whereas that of the latter is not. We wished to see how widespread this phenomenon is, and in particular to study the effects of change in basicity of the primary–secondary amine pair and change of solvent. For this purpose we required a substrate whose reactions with strongly basic amines were likely to be base-catalysed in a range of solvents. Bunnett and Bernasconi[2] have reported that the reaction of 2,4-dinitrophenyl phenyl ether with piperidine in 1 : 9 dioxan–water is base-catalysed, and Pietra[3] has shown that in benzene the reaction is second-order in piperidine; hence we chose this as the substrate. To examine the effect of basicity we used the amine pairs piperidine–n-butylamine [pK_a(H_2O)[4] 11.20, 10.65: pK_a(acetonitrile)[5] 18.92, 18.26] and morpholine–benzylamine [pK_a(H_2O)[4] 8.61, 9.38: pK_a(acetonitrile)[5] 16.62, 16.76] and studied the reactions in acetonitrile, dimethyl sulphoxide, and (piperidine and n-butylamine only) methanol containing 0.2M-amine hydrochloride to prevent solvolysis. We have been unable to find a complete set of data for the pK_a values of the amines in dimethyl sulphoxide and methanol, and have assumed that the similarities in basicities of the pairs observed in water and acetonitrile also hold in these solvents.

The reactions were followed spectrophotometrically with the amine in large excess. In all cases good first-order kinetics were observed and the absorbances at infinity agreed with the calculated ones. As the reactions in methanol at 30 °C of even piperidine and n-butylamine were slow, and to obtain meaningful comparisons the kinetics had to be studied at the same temperature, the reactions of morpholine and benzylamine were not investigated in this solvent. The

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[1] D. Ayediran, T. O. Bamkole, and J. Hirst, *J.C.S. Perkin II*, 1976, 1396.

[2] J. F. Bunnett and C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1965, **87**, 5209.

[3] F. Pietra, *Tetrahedron Letters*, 1975, 2405.

[4] D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' Supplement, 1972, IUPAC, Butterworths, London.

[5] J. F. Coetzee, *Progr. Phys. Org. Chem.*, 1967, **4**, 45.

results are given in the Table, together with other relevant information. Bernasconi[6] has found that the reaction of this substrate with benzylamine in 1 : 9 dioxan–water is not base-catalysed, and Bernasconi and Schmid[7] have shown that in the same solvent when the nucleophile is morpholine the reaction is base-catalysed.

Rate constants (l $\mathrm{mol^{-1}\,s^{-1}}$) for the reactions of 2,4-dinitrophenyl phenyl ether with piperidine, n-butylamine, morpholine, and benzylamine in various solvents

Solvent	Amine	t/°C								k_3/k_2
Dimethyl sulphoxide	Piperidine	30.2	10^3[amine]/M:	5.00	10.0	20.0		30.0		461
			10^3k_A:	6.86	11.5	21.0		29.5		
	n-Butylamine	30.2	10^3[amine]/M:	5.00	10.0	20.0				
			10^2k_A:	5.61	5.48	5.60				
	Morpholine [a]	30.5	10^2[amine]/M:	4.00	6.00	8.00	10.0	12.0	16.0	86
			10^3k_A:	1.00	1.40	1.73	2.24	2.43	3.26	
	Benzylamine	30.2	10^2[amine]/M:		6.38			15.91	25.5	
			10^2k_A:		1.37			1.35	1.38	
Acetonitrile	Piperidine	30.6	10^3[amine]/M:	8.6	15.0	20.6	30.0	36.0	41.3	542
			10^3k_A:	6.90	11.9	15.0	21.0	26.6	28.9	
	n-Butylamine	30.6	10^2[amine]/M:		4.0	5.0	8.15	10.0		
			10^3k_A:		5.64	5.61	5.64	5.55		
	Morpholine [a]	30.5	10^2[amine]/M:	4.00	6.00	8.00	10.0	12.0	16.0	185
			10^4k_A:	3.38	4.57	6.50	7.58	9.42	12.26	
	Benzylamine	30.6	10^2[amine]/M:	2.88		6.21	8.00	13.88	16.0	
			10^3k_A:	1.26		1.26	1.28	1.25	1.27	
Methanol containing 0.2M-amine hydrochloride	Piperidine	30.6	10^2[amine]/M:	4.00	6.00	8.00	12.0	16.0	20.0	74.5
			10^5k_A:	8.6	11.9	17.4	23.7	29.8	35.8	
	n-Butylamine		10^2[amine]/M:	5.0	10.0	16.0		20.0		
			10^4k_A:	3.61	3.62	3.62		3.61		
Dioxan–water (3 : 2)	Piperidine	29.4								53 [b]
Dioxan–water (1 : 9)	Piperidine	29.4								475 (114) [c]
	Morpholine	29.4								86.5 [d]

[a] Data of present authors.[13] [b] Data of J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 1965, **87**, 3879. [c] Data of Bunnett and Bernasconi.[2] The plot of k_A against piperidine concentration is curvilinear and these authors evaluate k_2/k_{-1} as 0.02 and k_3/k_{-1} as 9.5, giving k_3/k_2 as 475. In a later paper (J. F. Bunnett and C. F. Bernasconi, *J. Org. Chem.*, 1970, **35**, 70), however, the values are given as k_2/k_{-1} 0.069, k_3/k_{-1} 7.86, giving k_3/k_2 as 114. Using the value of $k_1 = 31.3 \times 10^{-3}$ given in ref. 2, by purely graphical procedures we obtained values of k_2/k_{-1} and k_3/k_{-1} giving k_3/k_2 *ca.* 143, reasonably close to the figure (114) obtained by linear regression analysis. The value of k_3/k_2, however, seems very sensitive to the magnitude of k_1, as a 15% reduction in the value quoted gives k_3/k_2 as *ca.* 450. [d] Data of Bernasconi and Schmid.[7]

dinitrobenzene in acetonitrile is base-catalysed, and we[1] have utilised this result to show that for primary amines if the basicity is reduced sufficiently the reaction changes from a non-catalysed to a base-catalysed one. It is also independent of the solvents used, which are all of moderately high dielectric constant and range from protic to

DISCUSSION

In all the solvents investigated the reactions of n-butylamine and benzylamine are not base-catalysed, but for piperidine and morpholine the observed second-order rate constant increases linearly with amine concentration, *i.e.* the kinetic form is that given in equation (1). Hence

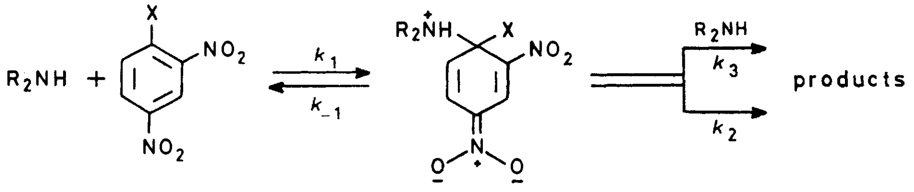
$$k_A = k' + k''[\text{amine}] \ldots \qquad (1)$$

over the range of basicities investigated the phenomenon we originally noted is independent of base strength. This independence, though, must be restricted to the range of moderately to strongly basic amines, as Kavalek *et al.*[8] have shown that the reaction of aniline with 1-fluoro-2,4-dinitrobenzene in acetonitrile is base-catalysed, and we ... both very weak and moderately basic dipolar aprotic solvents.

The results are interpreted in terms of the mechanism of nucleophilic aromatic substitution given in Scheme 1. Application of the steady state theory gives equation (2), where k_A is the observed second-order rate constant.

$$k_A = k_1(k_2 + k_3[\text{amine}])/(k_{-1} + k_2 + k_3[\text{amine}]) \quad (2)$$

For the condition $k_{-1} \ll k_2 + k_3[\text{amine}]$, $k_A = k_1$, the formation of the intermediate is rate-determining, and no base-catalysis is observed. For the condition $k_{-1} \gg k_2 + k_3[\text{amine}]$, $k_A = k_1(k_2 + k_3[\text{amine}])/k_{-1}$, the reaction is base-catalysed, and a comparison with equation



(A)

Scheme 1

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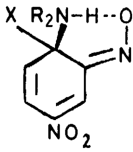
[6] C. F. Bernasconi, *J. Org. Chem.*, 1967, **32**, 2947.

[7] C. F. Bernasconi and P. Schmid, *J. Org. Chem.*, 1967, **32**, 2953.

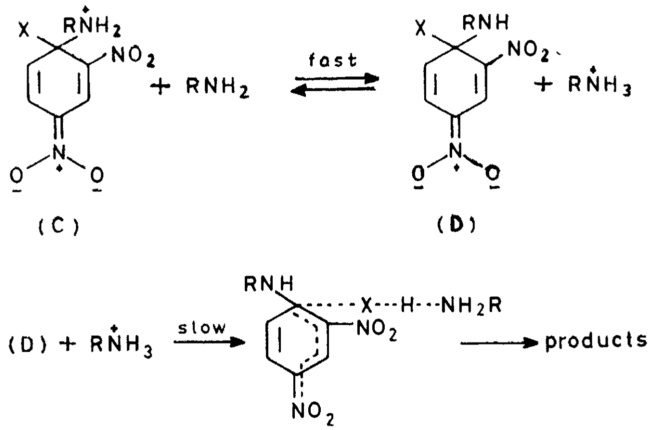
[8] J. Kavalek, J. Haasova, and V. Sterba, *Coll. Czech. Chem. Comm.*, 1972, **37**, 3333.

(1) shows that $k''/k' = k_3/k_2$. Values of this are given in the last column of the Table.

In our previous publication,[1] we gave reasons for rejecting differential steric effects in the intermediate (A) to explain the difference in kinetic form of the reactions of primary and secondary amines of the same basicity, and based our arguments on the strong hydrogen bonding, as illustrated in (B), which is known [9,10] to occur when (A) contains an *ortho*-nitro-group. Orvik and Bunnett [11] have shown that in dimethyl sulphoxide the mechanism of the base-catalysed decomposition of the intermediate is as shown in Scheme 2, *i.e.* a rapidly established equilibrium between the first formed intermediate (C) and a second molecule of the nucleophile, followed by slow electrophilically catalysed decomposition of the conjugate base of (C). Bunnett's demonstration however utilised primary amines, and we pointed out that when the nucleophile was a secondary amine, the existence of hydrogen bonding to the *ortho*-nitro-group would make the initial abstraction of the proton an activated process which could be rate-limiting.

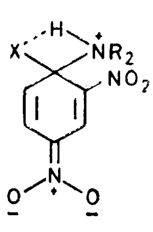


(B)



Scheme 2

A modification of our original proposal is as follows.* In Scheme 1, hydrogen-bonding to the *ortho*-nitro-group will stabilise the intermediate (A) and hence reduce k_{-1} irrespective of whether the nucleophile is a primary or secondary amine. If the nucleophile is a primary amine, then a second hydrogen atom is available which can be removed by a base and hydrogen bonding will have little effect on the magnitude of k_3. If the nucleophile is a secondary amine, then the hydrogen bond has to be broken before the proton can be abstracted and hence the value of k_3 is reduced. Little is known about the mechanism of the uncatalysed path, but Bernasconi [12] has shown for hydroxylic solvents and we have shown for dipolar aprotic solvents [13] that it does not take place by a Bunnett-type mechanism in which a solvent molecule replaces the base. For poor leaving groups the decomposition most likely takes place *via* the internally hydrogen-bonded intermediate (E) as first proposed by Jencks.[14] If this is the case, when the nucleophile is a primary amine, the initially formed hydrogen bond to the *ortho*-nitro-group will have little effect on k_2, but for secondary amines the initially formed hydrogen bond has to be broken before the new one can be formed; hence k_2 is reduced. Thus hydrogen bonding to an *ortho*-nitro-group reduces k_{-1} for both primary and secondary amines, but while for primary amines it has little effect on k_2 and k_3, for secondary amines the magnitudes of k_2 and k_3 are decreased. Hence the values of $(k_2 + k_3[\text{amine}])/k_{-1}$ are greater for primary amines than for secondary ones, and the decomposition of the intermediate is more likely to be rate-determining for secondary than for primary amines of the same basicity. On this view, the transfer of the proton when the nucleophile is a secondary amine is an activated but not necessarily rate-limiting process.



(E)

Recently [13] we have shown that the hypothesis that the uncatalysed pathway proceeds by the same mechanism as the catalysed one with the solvent taking the part of the base requires that there should be a large variation in the magnitude of k_3/k_2 when the reaction is carried out in solvents of widely ranging basicity. As this was not observed, we rejected the hypothesis. Further confirmation is obtained from the reactions of piperidine. There is a variation [15] of *ca.* 10^{10} in the basicity of the dipolar aprotic solvents acetonitrile and dimethyl sulphoxide, yet, as shown in Table 1, there is little difference in the k_3/k_2 values in the two solvents. The basicities of the protic solvents 1 : 9 dioxan–water, 6 : 4 dioxan–water, and methanol would not be expected to

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* Since this manuscript was completed we have had access to an article [12] where an essentially similar explanation is put forward.

[9] C. F. Bernasconi, *J. Phys. Chem.*, 1971, **75**, 3636.

[10] C. F. Bernasconi and F. Terrier, *J. Amer. Chem. Soc.*, 1975, **97**, 7458.

[11] J. Orvik and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 2417.

[12] C. F. Bernasconi, MTP International Reviews of Science, 1973, Series 1, Butterworths, London, vol. 3, p. 33.

[13] D. Ayediran, T. O. Bamkole, J. Hirst, and I. Onyido, *J.C.S. Perkin II*, 1977, 597.

[14] A. J. Kirby and W. P. Jencks, *J. Amer. Chem. Soc.*, 1965, **87**, 3217.

[15] E. M. Arnett, *Progr. Phys. Org. Chem.*, 1963, **1**, 223.

show wide variation, and if we take the k_3/k_2 value in 1 : 9 dioxan–water as 114, there is an approximately 2-fold variation of the value of the ratio in these solvents.

EXPERIMENTAL

Materials.—2,4-Dinitrophenyl phenyl ether, m.p. 69—70° (lit.,[6] 70°), was prepared by the method of Raiford and Colbert.[16] The purification of methanol,[17] acetonitrile,[18] and dimethyl sulphoxide [19] has been described previously. The water content of the solvents was determined by Karl Fischer titration and did not exceed 0.2%. The amines used were commerical samples purified by standard procedures and the products of their reactions with the substrate were prepared by methods described in the literature.

Kinetic Procedure.—The rates of formation of the products of the reactions were determined spectrophotometrically by the pipette procedure already described.[20]

[6/2182 *Received*, 26*th November*, 1976]

[16] L. C. Raiford and J. C. Colbert, *J. Amer. Chem. Soc.*, 1926, **48**, 2652.

[17] C. W. L. Bevan, T. O. Fayiga, and J. Hirst, *J. Chem. Soc.*, 1956, 4284.

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

[19] D. Ayedrian, T. O. Bamkole, and J. Hirst, *J.C.S. Perkin II*, 1974, 1013.

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