The Stabilities of Meisenheimer Complexes. Part 25.[1] Kinetic Studies of the Reaction of 1,3,5-Trinitrobenzene with Aliphatic Amines in Dimethyl Sulphoxide

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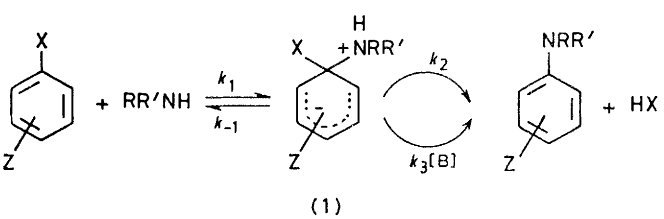
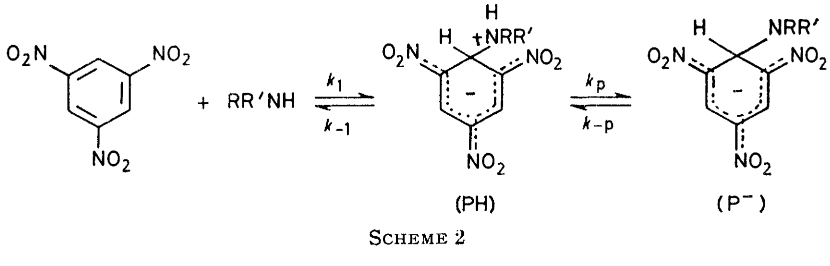
Kinetic studies by stopped-flow spectrophotometry are reported for the reactions of 1,3,5-trinitrobenzene with n-butylamine, benzylamine, isopropylamine, or piperidine in dimethyl sulphoxide. These reactions lead to the formation of anionic σ-adducts *via* zwitterionic intermediates and it is shown that proton-transfer may be kinetically significant. Reduction below the values expected for diffusion-control in the values of rate constants for proton-transfer between the zwitterions and amines is attributed to a steric effect which is more pronounced in the reaction involving piperidine than in the reactions of primary amines.

EVIDENCE derived from kinetic studies of the reactions of amines with aromatic substrates has provided one of the cornerstones for the intermediate complex mechanism of nucleophilic substitution.[2-4] The base catalysed step, k_3[B] in Scheme 1, may involve rate-limiting proton transfer from the zwitterionic intermediate (1), or rapid interconversion of (1) into its deprotonated form followed by general acid-catalysed leaving-group departure (SB-GA mechanism). The former process generally applies in protic solvents while in aprotic solvents, where leaving group expulsion is more difficult the latter mechanism holds.[4-6] The uncatalysed step generally involves intramolecular proton-transfer from nitrogen to the leaving group.



(1)

SCHEME 1



(PH) (P$^-$)

SCHEME 2

This paper is concerned with the related reaction of 1,3,5-trinitrobenzene (TNB) with aliphatic amines in dimethyl sulphoxide (DMSO) where it is well established that σ-adducts are formed.[7] The likely mechanism is shown in Scheme 2. In 1970 Bernasconi reported a kinetic study[8] of the reaction in 90 : 10 v/v water–dioxan in which the data were interpreted on the assumption that proton transfer between (PH) and (P$^-$) is always rapid. More recently, and while our work was in progress, new results relating to mixed aqueous solvents have been published[9] showing that proton-transfer may be rate limiting. Our results show that in DMSO proton transfer is kinetically significant and enable a useful comparison of the solvent effect on the reaction to be made. Data obtained with the secondary amine piperidine indicate significant steric effects to proton-transfer between nitrogen atoms in DMSO. The related reaction of TNB with aniline in DMSO has been studied by Buncel and Eggimann[10] who showed that in the presence of the tertiary amine diazabicyclo-octane (DABCO) the anilide adduct is formed; again proton transfer is rate-limiting.

EXPERIMENTAL

G.P.R. grade DMSO was dried by refluxing over calcium hydride, fractionally distilled under reduced pressure and subsequently protected from moisture. TNB was rerecrystallised to constant m.p., 123°. A commercial sample of DABCO was used as supplied. n-Butylamine (G.P.R. grade) was fractionated at 1 atm pressure, the fraction boiling at 77.5° being collected. Isopropylamine (reagent grade), was fractionated at 1 atm pressure using a Fischer–Spaltrohr column, the fraction boiling at 32.5—33° being collected. Benzylamine and piperidine were AnalaR grade reagents used as supplied. Tetraethylammonium perchlorate was a commercial specimen recrystallised twice from toluene and dried by warming in vacuum. Benzylammonium perchlorate was prepared by reaction of benzylamine with aqueous perchloric acid in ethanol and was recrystallised twice from ethanol. Isopropylammonium perchlorate was prepared as a concentrated stock solution in DMSO from weighed amounts of amine and perchloric acid. n-Butylamine hydrochloride was prepared from the amine and gaseous hydrogen chloride in ether and was recrystallised from acetonitrile. Piperidine hydrochloride was a commercial ' pure ' specimen used as supplied.

Kinetic measurements were made using a Canterbury stopped-flow spectrophotometer with freshly prepared solutions of reagents. In most cases quoted rate constants are the mean of five separate determinations and are precise to ±5%.

trations of amine and salt in large excess of the stoicheiometric TNB concentration both forward and reverse reactions are first order so that the observed rate coefficient, $k_{\text{obs.}}$, is given by equation (8). Again making the assumption that (PH) is a steady-state intermediate we obtain equation (9), which will apply [8] in the absence of any base other than the amine or solvent.

$$k_{\text{obs.}} = (k_f)_1 + (k_r)_1 \tag{8}$$

$$k_{\text{obs.}} = \{k_1[\text{Am}](k_{\text{Am}}[\text{Am}] + k_s) + k_{-1}(k_{\text{AmH}^+}[\text{AmH}^+] + k_{\text{SH}^+}[\text{SH}^+])\}/(k_{-1} + k_{\text{Am}}[\text{Am}] + k_s) \tag{9}$$

RESULTS

In agreement with previous work [7] it was found that mixing a dilute solution of TNB with a solution of an aliphatic amine in DMSO resulted in rapid formation of the σ-adduct (P^-) with visible maxima at 450 and 530—540 nm.

Kinetic Analysis.—Proton transfer from (PH) in Scheme 2 may be expected to involve either the amine (Am), or any general base such as DABCO (B) or the solvent, while proton transfer to (P^-) will correspondingly involve the protonated amine (AmH^+), protonated base (BH^+), or protonated solvent (SH^+). Hence we obtain equations (1) and (2).

$$k_p = k_{\text{Am}}[\text{Am}] + k_B[\text{B}] + k_S \tag{1}$$

$$k_{-p} = k_{\text{AmH}^+}[\text{AmH}^+] + k_{\text{BH}^+}[\text{BH}^+] + k_{\text{SH}^+}[\text{SH}^+] \tag{2}$$

Colour-forming Reaction.—Rates of colour formation were made by stopped-flow spectrophotometry with amine and base (if present) in large excess of TNB. In some cases the neutral salt, tetraethylammonium perchlorate, was present, but no protonated amine was initially present. Under these conditions we may write equation (3) where XH^+ is the species in solution carrying the proton and will be equal in concentration to P^-. This equation represents a

$$\text{TNB} + \text{Am} \underset{(k_r)_2}{\overset{(k_f)_1}{\rightleftharpoons}} P^- + \text{XH}^+ \tag{3}$$

mixed first-order (forward) and second-order (reverse) equilibrium for which the standard solution [11] is equation (4) in which $[\text{TNB}]_0$ is the stoicheiometric concentration and $[P^-]$ and $[P^-]_e$ represent the concentrations during the reaction and at equilibrium respectively. When conversion of TNB to P^- goes to virtual completion equation (4)

$$\ln\left(\frac{[\text{TNB}]_0[P^-]_0 + [P^-]([\text{TNB}]_0 - [P^-]_e)}{[\text{TNB}]_0([P^-]_e - [P^-])}\right) = \left(\frac{2[\text{TNB}]_0 - [P^-]_e}{[P^-]_e}\right)(k_f)_1 \,.\, t \tag{4}$$

$$\ln\frac{[\text{TNB}]_0}{[\text{TNB}]_0 - [P^-]} = (k_f)_1 \,.\, t \tag{5}$$

reduces to (5). Values of $(k_f)_1$ could thus be evaluated by use of the appropriate expression.

Assuming that (PH) may be treated as a steady-state intermediate [8-10] leads to equation (6). The second order rate coefficient for the forward reaction is related to $(k_f)_1$ by equation (7).

$$(k_f)_1 = \frac{k_1[\text{Am}](k_{\text{Am}}[\text{Am}] + k_B[\text{B}] + k_s)}{k_{-1} + k_{\text{Am}}[\text{Am}] + k_B[\text{B}] + k_s} \tag{6}$$

$$(k_f)_2 = (k_f)_1/[\text{Am}] \tag{7}$$

Fading Reaction.—In some cases it was possible to preform the σ-adduct (P^-) and then measure the rate of fading when this solution was mixed with a solution containing the appropriate substituted ammonium salt. With concen-

Equilibrium Constants.—We define an equilibrium constant K for the overall conversion of TNB into (P^-) in the presence of amine by equation (10). This equilibrium constant is related by equation (11) to the equilibrium constant K_1 for formation of the zwitterionic intermediate (PH), and to the acid dissociation constants of (PH) and protonated amine, AmH^+. Equation (12) relates the

$$K = \frac{[P^-][\text{AmH}^+]}{[\text{TNB}][\text{Am}]^2} \tag{10}$$

$$K = K_1 \cdot \frac{K_a^{\text{PH}}}{K_a^{\text{AmH}^+}} \tag{11}$$

$$K = \frac{k_1}{k_{-1}} \cdot \frac{k_{\text{Am}}}{k_{\text{AmH}^+}} \tag{12}$$

equilibrium constant K to the rate constants associated with formation of (PH) and its amine catalysed conversion to (P^-).

Reaction with Primary Amines.—The kinetic features of the reactions of TNB with benzylamine, n-butylamine, and isopropylamine have some common characteristics. Thus for the colour-forming reaction plots of the second-order rate coefficient, $(k_f)_2$, *versus* amine concentration are curved and tend to a limiting value at high amine concentration. Data are in Tables 1 and 3 and a representative plot is

TABLE 1

Rate data for the colour-forming reaction of TNB (5×10^{-6}M) with benzylamine in DMSO at 25°

[Benzylamine]/ M	[DABCO]/ M	$(k_f)_1$/s^{-1}	$(k_f)_2$/ l mol^{-1} s^{-1}	OD [b] (450 nm)
0.001		1.7 ± 0.1	1 700	0.022
0.002		5.7	2 850	0.023
0.004		16.3	4.075	0.023
0.006		32	5 300	0.024
0.008		50	6 300	0.024
0.010		65	6 500	0.025
0.001 [a]		1.4 ± 0.1	1 400	0.022
0.002 [a]		4.6	2 300	0.022
0.004 [a]		16.0	4 000	0.023
0.006 [a]		32	5 300	0.025
0.008 [a]		49	6 100	0.025
0.002	0.005	9.5	4 700	0.023
0,002	0.01	12.1	6 000	0.022
0.002	0.02	15.6	7 800	0.022
0.002	0.03	19.5	9 700	0.022
0.002	0.04	21.4	10 700	0.022
0.002	0.07	24.5	12 200	0.022
0.002	0.10	28	14 000	0.022
0.002	0.20	30	15 000	0.023

[a] Solutions contain 0.1M-tetraethylammonium perchlorate.
[b] At equilibrium.

shown in the Figure. Rates were affected very little by the presence of 0.1M-tetraethylammonium perchlorate.

The curvature in the Figure indicates a change in the rate-determining step as the amine concentration is varied. At low amine concentrations proton transfer from (PH) to amine is rate determining ($k_{-1} > k_{\mathrm{Am}}[\mathrm{Am}] + k_s$) while at high amine concentrations the first step is rate limiting ($k_{-1} < k_{\mathrm{Am}}[\mathrm{Am}] + k_s$). It follows that $k_{-1} \gg k_s$ so that at sufficiently low base concentrations equations (6) and (7) reduce to $(k_f)_2 = K_1k_s$. Values of the product K_1k_s could in principle be determined from the intercepts of plots of $(k_f)_2$ *versus* amine concentration. However reference to the Figure or Tables 1 and 3 indicates that such intercepts are small and will have high uncertainty and the best we can do is to find an upper limit for these terms.

TABLE 2

Rate and equilibrium data relating to the fading reaction of the TNB–benzylamine adduct [a] on mixing with benzylammonium perchlorate in DMSO at 25°

[Benzylammonium perchlorate]/M	[Benzylamine]/M	$k_{\mathrm{obs.}}/\mathrm{s}^{-1}$	$k_{\mathrm{calc.}}$ [b]$/\mathrm{s}^{-1}$	OD [c] (450 nm) initial	OD [c] (450 nm) equilibrium	K [d]/l mol^{-1}
0.0001	0.001	3 ± 0.3	3.0	0.022	0.011	102
0.0003	0.001	5.4	5.7	0.023	0.006	107
0.0005	0.001	8.4	8.4	0.021	0.004	118
0.0007	0.001	10.7	11	0.024	0.003	100
0.001	0.001	15	15	0.021	0.003	
0.002	0.001	28	28	0.022	0.002	
0.003	0.001	41	42	0.024	0.001	
0.004	0.001	56	55	0.022	0	
0.005	0.001	73	69	0.022	0	

[a] [TNB] is 5×10^{-6}M. All solutions contain 0.1M-tetraethylammonium perchlorate. [b] Calculated from equation (14) with $(k_f)_1$ 1.7 s^{-1}, k_{Am}/k_{-1} 120 l mol^{-1}, and $k_{\mathrm{AmH^+}}$ 1.5×10^4 l mol s^{-1}. [c] Measured with stopped-flow spectrophotometer (2 mm cell). The initial value corresponds to the OD (corrected for dilution by factor of 2) for the solution containing TNB and amine alone where conversion to the adduct is virtually complete. [d] Calculated from equation (10).

TABLE 3

Rate data for the colour forming reaction of TNB (5×10^{-6}M) with n-butylamine in DMSO at 25°

[n-Butylamine]/ M	[DABCO]/ M	$(k_f)_1/\mathrm{s}^{-1}$	$(k_f)_2$/ l mol^{-1} s^{-1}	OD [a] (450 nm)
0.0001		0.48	4,800	0.013
0.0002		1.73	8,700	0.018
0.0003		3.3	11,000	0.019
0.0005		9.4	18,800	0.021
0.0007		15.2	21,700	0.021
0.001		25.4	25,400	0.024
0.002		65.4	32,700	0.022
0.003		121	40,000	0.021
0.006		250	42,000	0.024
0.0005	0.005	15.5	31,000	0.021
0.0005	0.01	18.2	36,400	0.021
0.0005	0.03	21	42,000	0.021
0.0005	0.05	21	42,000	0.021
0.0005	0.10	22	44,000	0.021

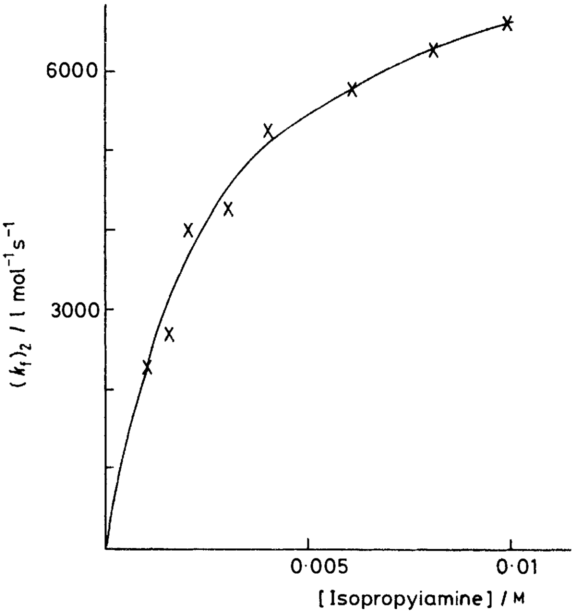
[a] At equilibrium.

Thus under our experimental conditions $k_{\mathrm{Am}}[\mathrm{Am}] > k_s$, so that in the absence of added bases, such as DABCO, we obtain from equations (6) and (7) the reciprocal plot of equation (13). Plots of $1/(k_f)_2$ *versus* $1/[\mathrm{Am}]$ were linear and were used to obtain values for the parameters k_1 and k_{Am}/k_{-1}.

$$\frac{1}{(k_f)_2} = \frac{1}{k_1} + \frac{k_{-1}}{k_1k_{\mathrm{Am}}[\mathrm{Am}]} \qquad (13)$$

Increasing the concentration of the non-nucleophilic base DABCO at constant amine concentration caused an increase in the value of $(k_f)_2$. Data obtained with $[\mathrm{DABCO}] \gg [\mathrm{Am}]$ where the catalytic effects are largely due to DABCO allowed the evaluation of the ratio $k_{\mathrm{DABCO}}/k_{-1}$.

Rate data obtained in the presence of amines and ammonium salts are in Tables 2, 4, and 5. Measurements were made at I 0.1M using tetraethylammonium perchlorate. The same equation, (9), will apply whether the colour-forming or -fading reactions are determined. In practice it was easier to make measurements of the fading reaction since these generally gave larger changes in optical density. We have shown that at the amine concentrations used the contribution to the forward reaction of the term involving solvent, k_s, is small. Similarly for the reverse reaction the contribution from the term involving protonated solvent $k_{\mathrm{SH^+}}[\mathrm{SH^+}]$ will be small compared with that involving protonated amine, $k_{\mathrm{AmH^+}}[\mathrm{AmH^+}]$. Hence in the absence of other bases we can write equation (9) in the form of



Variation with amine concentration of the value of $(k_f)_2$ for reaction of TNB and isopropylamine in DMSO. The full line is the calculated curve from equations (6) and (7) with k_1 8×10^3 l mol^{-1} s^{-1}, k_{Am}/k_{-1} 400 l mol^{-1}, and k_s 0. Since no base other than isopropylamine is present $k_{\mathrm{B}}[\mathrm{B}]$ has a value of 0

Table 4

Rate and equilibrium data for the fading reaction of the TNB–n-butylamine adduct [a] on mixing with n-butylamine hydrochloride in DMSO at 25°

[n-Butylamine hydrochloride]/M	[n-Butylamine]/M	$k_{obs.}/s^{-1}$	$k_{calc.}{}^{b}/s^{-1}$	OD (450 nm) initial	OD (450 nm) equilibrium	K^{c}/l mol^{-1}
0.0025	0.0025	135 ± 10	133	0.023	0.016	900
0.0050	0.0025	170	170	0.023	0.013	1 000
0.0075	0.0025	210	205	0.023	0.013	1 500
0.001	0.0005	52	48	0.022	0.005	1 200
0.001	0.0007	56	50	0.022	0.007	950
0.001	0.0010	57	53	0.022	0.011	1 000
0.001	0.0020	86	83	0.022	0.018	1 100
0.001	0.0030	150	135	0.022	0.020	1 100
0.002	0.0005	87	85			
0.004	0.0005	150	160			
0.006	0.0005	214	230			

[a] [TNB] 5 × 10^{-6}M. [b] Calculated from equation (14) using the value of $(k_f)_1$ appropriate to the amine concentration (Table 2), and with k_{Am}/k_{-1} 1 200 l mol^{-1} and k_{AmH^+} 6 × 10^4 l mol^{-1} s^{-1}. [c] Calculated from equation (10).

equation (14). Also at a given amine concentration the values of $(k_f)_1$ and k_{Am}/k_{-1} are known (Tables 1 and 3) allowing the calculation of k_{AmH^+}.

$$k_{obs.} = (k_f)_1 + \frac{k_{-1}\cdot k_{AmH^+}[AmH^+]}{k_{-1} + k_{Am}[Am]} \qquad (14)$$

Measurements by stopped flow spectrophotometry of optical densities before and after the fading reaction allowed the calculation of the equilibrium constants using equation (10). The value before mixing in solutions where conversion to the adduct (P^-) is virtually complete gives a measure of the stoicheiometric TNB concentration, while the value at equilibrium is proportional to (P^-). The values of the equilibrium constants so calculated were in each case in good agreement with those calculated from kinetic data using equation (12).

Table 5

Rate and equilibrium data for the fading reaction of the TNB–isopropylamine adduct [a] on mixing with isopropylammonium perchlorate in DMSO at 25°

[Isopropylammonium perchlorate]/M	[Isopropylamine]/M	$k_{obs.}/s^{-1}$	$k_{calc.}{}^{b}/s^{-1}$	OD (450 nm) initial	OD (450 nm) equilibrium	K^{c}/l mol^{-1}
0.0005	0.001	6.7	6.7	0.022	0.005	150
0.001	0.001	11.5	12.1	0.024	0.004	200
0.002	0.001	21	23	0.023	0.003	300
0.003	0.001	33	33	0.023	0.002	290
0.004	0.001	43	44	0.023	0.002	380
0.005	0.001	53	54	0.023	0.001	230

[a] [TNB] is 5 × 10^{-6}M. All solutions contain 0.1M-tetraethylammonium perchlorate. [b] Calculated from equation (14) with $(k_f)_1$ 1.4 s^{-1}, k_{Am}/k_{-1} 400 l mol^{-1}, and k_{AmH^+} 1.5 × 10^4 l mol^{-1} s^{-1}. [c] Calculated from equation (10).

Reaction with Piperidine.—Rate data for the forward reaction are in Table 6. A plot of $(k_f)_2$ *versus* piperidine concentration is linear with small intercept. This indicates that $k_{-1} \gg k_{Am}[Am] + k_B[B] + k_s$, so that proton transfer is rate limiting over the entire range of amine concentrations used. The slope gives the value of K_1k_{Am}, and from the absence of curvature we can estimate an upper limit for the ratio k_{Am}/k_{-1} of 10 l mol^{-1}, and hence a lower limit for k_1 of 6 × 10^4 l mol^{-1} s^{-1}.

Data obtained with the concentration of DABCO in large excess of that of piperidine give a value for K_1k_{DABCO}.

Measurements of the rates of the fading reaction in the presence of piperidine hydrochloride allowed the determination of a value for k_{AmH^+} (Table 7). Equilibrium optical densities measured with a conventional spectrophotometer are in Table 8 and were used to calculate a value for K.

Table 6

Rate data for the colour-forming reaction of TNB (5 × 10^{-6}M) with piperidine in DMSO at 25°

[Piperidine]/M	[DABCO]/M	$(k_f)_1/s^{-1}$	$(k_f)_2$/l mol^{-1} s^{-1}	10^{-5} $(k_f)_2$ [piperidine]$^{-1}$/l^2 mol^{-2} s^{-1}	10^{-5} $(k_f)_2$ [DABCO]$^{-1}$/l^2 mol^{-2} s^{-1}
0.002		2.5 ± 0.3	1 250	6.2 [a]	
0.003		5.5	1 840	6.1	
0.004		11	2 800	7.0	
0.006		22	3 700	6.2	
0.008		38	4 800	6.0	
0.010		59	5 900	5.9	
0.002	0.03	11	5 500		1.8 [b]
0.002	0.05	15.5	7 700		1.5
0.002	0.07	20	10 000		1.4
0.002	0.10	29	14 500		1.45
0.002	0.15	41	20 500		1.35
0.002	0.20	53	26 500		1.33

[a] Data in this column give a value for K_1k_{AM}. [b] Data in this column give a value for K_1k_{DABCO}.

DISCUSSION

Our results show that values of $(k_f)_2$, the second-order rate coefficient, increase with increasing concentration of amine or DABCO and, in the case of primary amines, reach a limiting value at sufficiently high base concentration. This clearly indicates that proton transfer between (PH) and (P^-) is kinetically significant. Data are collected in Table 9. Values in the first seven rows are experimentally determined quantities. Other values are based on the assumption that the ratio $K_a^{PH}/K_a^{AmH^+}$ has a value of 500 which is independent of the nature of the amine. That this ratio has a value greater than unity is expected since it is known[12,13] that the trinitrocyclohexadienate group, although negatively charged, is electron-withdrawing relative to hydrogen. Hence the zwitterionic species (PH) will be more acidic than the corresponding substituted ammonium ions, AmH^+. Bernasconi *et al.*[9] report values for the above ratio in 30 : 70 DMSO–water of 370 for n-butylamine and 400 for piperidine. In 10 : 90 dioxan–water[8,9] values are 230 for n-butylamine, 260 for piperidine, 230 for methylamine, and 120 for dimethylamine. These data indicate that the value of the ratio does not vary significantly with the amine. Also we do not expect these values to vary drastically with change in solvent since changes in energy of (PH), for example due to changes in solvation,[14] are likely to be compensated by similar changes in energy of AmH^+. Buncel and Eggimann[10] obtained a value of *ca.* 10^4 for the ratio in the reaction of TNB with aniline in DMSO. However this was based on the assumption that deprotonation of the TNB–aniline zwitterion by DABCO is diffusion-controlled. Present evidence[5,9] suggests that the rate of the proton transfer will be considerably less than diffusion-controlled leading to a lower value for the ratio of acid dissociation constants.

TABLE 7

Rate data for the fading reaction of the TNB–piperidine[a] adduct on mixing with piperidine hydrochloride in DNSO at 25°

[Piperidine hydrochloride]/M	[Piperidine]/M	$k_{obs.}s^{-1}$	$k_{calc.}$[b]$/s^{-1}$
0.01	0.001	2.3 ± 0.2	2.3
0.02	0.001	3.3	3.3
0.04	0.001	5.4	5.3
0.07	0.001	7.8	8.3
0.10	0.001	11.2	11.3

[a] [TNB] is 5×10^{-6}M. Ionic strength 0.1M with tetraethylammonium perchlorate. [b] Calculated from equation (14) with $(k_f)_1$ 1.3 s^{-1}, $k_{-1} \gg k_{Am}[Am]$, and k_{AmH^+} 100 l mol^{-1} s^{-1}.

TABLE 9

Summary of rate and equilibrium constants for reaction of TNB with amines in DMSO at 25° and *I* 0.1M

	n-Butylamine	Benzylamine	Isopropylamine	Piperidine
k_1/l mol^{-1} s^{-1}	(4.5 ± 0.5) × 10^4	(1.3 ± 0.2) × 10^4	(8 ± 1) × 10^3	>6 × 10^4
K_1k_{Am}/l^2mol^{-2} s^{-2}	(5.5 ± 0.5) × 10^7	(1.6 ± 0.2) × 10^6	(3.3 ± 0.3) × 10^6	(6 ± 0.5) × 10^5
k_{Am}/k_{-1}(l mol^{-1})	1 200 ± 200	120 ± 30	400 ± 50	<10
k_{DABCO}/k_{-1}(l mol^{-1})	450 ± 50	60 ± 20	120 ± 20	<2.5
K_1k_s/l mol^{-1} s^{-1}	<1 000	<1 000	<1 000	<500
k_{AmH^+}/l mol^{-1} s^{-1}	(6 ± 1) × 10^4	(1.5 ± 0.1) × 10^4	(1.5 ± 0.1) × 10^4	100 ± 20
K/l mol^{-1}	1 000 ± 100	105 ± 10	200 ± 50	4 500 ± 500
K_1[a]/l mol^{-1}	2	0.2	0.4	9
k_{-1}[b]$/s^{-1}$	2.3 × 10^4	6 × 10^4	2 × 10^4	>7 × 10^3
k_{Am}[c]/l mol^{-1} s^{-1}	3 × 10^7	7.5 × 10^6	7.5 × 10^6	5 × 10^4
k_{DABCO}[d]/l mol^{-1} s^{-1}	1 × 10^7	4 × 10^6	2 × 10^6	1.2 × 10^4
p_aK (AmH^+)[e]	10.6	9.4	10.6	11.2

[a] From equation (11), assuming $K_a^{PH}/K_a^{AmH^+}$ has the value 500. [b] k_1/K_1. [c] 500 k_{AmH^+}, from equation (12). [d] k_{Am} × (ratio of rows 4 and 3). [e] In water.[15]

The basicities of the amines, as reflected by their pK_a values in water,[15] decrease in the order piperidine > n-butylamine, isopropylamine > benzylamine. This order is unlikely to be changed in DMSO.[14] Our calculated values of K_1 which decrease in the order piperidine > n-butylamine > isopropylamine > benzylamine largely reflect these changes in basicity of the amines, although the value for isopropylamine is depressed, probably through unfavourable steric interactions in the zwitterionic adduct. The much smaller value of 13 l mol^{-1} for K obtained previously[7] in the case of diethylamine may reflect a more serious steric effect. The values of k_1, which measure the nucleophilicities of the amines, similarly reflect the basicities although the value for isopropylamine is again somewhat lowered by steric factors. Our reactivity order for the amines parallels that obtained for S_NAr substitution of 1-chloro-2,4-dinitrobenzene in ethanol.[16]

TABLE 8

Equilibrium measurements for the TNB–piperidine[a] adduct in DMSO at 25°

[Piperidine]/M	[Piperidine hydrochloride]/M	OD[b] (450 nm)	K[c]/l mol^{-1}
0.001	0.01	0.160	3 800
0.002	0.02	0.25	3 800
0.003	0.02	0.38	4 200
0.002	0.05	0.17	5 200
0.004	0.05	0.36	5 100
0.006	0.10	0.36	4 500
0.008	0.10	0.44	4 900
0.001	0	0.58[d]	

[a] [TNB] 2×10^{-5}M. *I* 0.1M with tetraethylammonium perchlorate. [b] Measured with SP 500 spectrophotometer using a 1-cm cell. [c] Calculated from equation (10). [d] Corresponds to complete conversion into adduct.

For n-butylamine and piperidine, where data are also available in mixed aqueous media,[9] there is an increase of *ca.* 10^3 in the values of K_1 on transfer from 30 : 70 DMSO–water to pure DMSO. This increase reflects increases in values of k_1 and decreases in values of k_{-1}. These changes are in agreement with much evidence [17] which shows that DMSO has a strong stabilising influence on Meisenheimer complex formation.

Rates of Proton Transfer.—There is no *a priori* reason why proton transfers between nitrogen centres should be appreciably slower in dimethyl sulphoxide than in water. Thus Bianchin and Delpuech [18] have shown that the rate constant for proton transfer from the ammonium ion to ammonia has a value of 1.2×10^9 l mol^{-1} s^{-1}, close to the diffusion-controlled rate. However, in situations where steric hindrance to proton transfer exists then rates may be considerably lower in DMSO than in water,[19,20] since in the latter medium there is the possibility of proton transfer *via* an interstitial water molecule.[21]

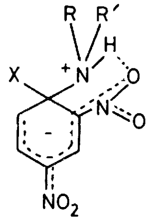
In the present case, since the zwitterionic adducts (PH) are more strongly acidic than the corresponding ammonium ions it might have been expected that the rate of proton transfer between these species would be diffusion-controlled. However, based on the assumption that the ratio $K_a^{PH}/K_a^{AmH^+}$ has the value 500, we obtain values for k_{Am} of *ca.* 10^7 for primary amines and 5×10^4 for piperidine. These values are less than that expected for diffusion-controlled reaction. The fact that catalysis by DABCO is somewhat less efficient than by the respective amines also points to the fact that these proton transfers are not diffusion controlled.

Bernasconi *et al.*[9] obtained values for reaction of the piperidine–TNB zwitterion with piperidine in 30 : 70 DMSO–water of 1.6×10^7 l mol^{-1} s^{-1}, and for the reaction of the dimethylamine–TNB adduct with dimethylamine in 10 : 90 dioxan–water of 1.2×10^7 l mol^{-1} s^{-1}. They attributed the reduction in rate below that expected for diffusion-controlled reaction to steric factors,[5,9] in that the reactive site of (PH) is crowded and cannot be easily approached by bases larger than the hydroxide ion. More generally Bernasconi [9] states that deprotonation of typical (PH)-type Meisenheimer complexes by amines are usually depressed by a factor of 100 or more due to steric hindrance.

Our data are in accord with this hypothesis in that the value of k_{Am} is considerably lower for the system involving the secondary amine piperidine, where steric effects are expected to be larger, than for systems involving primary amines. However our value for k_{Am} for piperidine in anhydrous DMSO is *ca.* 300 times lower than the value obtained for the same amine in 30 : 70 DMSO–water. This decrease can be attributed to the slower rate of proton transfer expected in DMSO relative to aqueous media where proton transfer may occur along hydrogen-bonded networks. We note that if values of k_{Am} for systems involving primary amines are subject to a similar factor (300) on change of solvent then we obtain values of *ca.* 10^9 in aqueous media. This suggests that in aqueous media proton transfer from zwitterionic intermediates (PH) derived from primary amines may be diffusion controlled.

Our experimental data show that the ratio k_{Am}/k_{-1} is considerably reduced for reaction involving the secondary amine, piperidine, compared to reactions involving primary amines. This phenomenon is well documented in the related area of nucleophilic aromatic substitution reactions [3,4] and leads to the much more general observation of base catalysis in reactions of secondary amines than of primary amines. A slightly larger value for k_{-1} in the case of the bulkier secondary amines may partially account for this change,[9] but the smaller value of k_{Am} is the major factor. Zwitterionic adducts derived from secondary amines possess only a single acidic proton and it has been suggested [5,22,23] that the slower rate of proton transfer in these cases is a result of intramolecular hydrogen-bonding as depicted in (2). It is reasonable that in non-polar solvents such hydrogen-bonding should occur. However, DMSO is a very good hydrogen-bond acceptor [24] and may compete for the acidic proton. Our data in Table 9 show that the value of k_{Am} is reduced by a factor of *ca.* 100 for piperidine compared to the primary amines. However, the value of k_{AmH^+} representing proton transfer from the substituted ammonium ion to (P^-) is also reduced by a similar factor for the secondary amine. It is logical that intramolecular hydrogen-bonding should reduce the rate of proton transfer from (PH) to amine but it is not easy to see how such hydrogen-bonding would reduce the rate of the reverse reaction. We think it likely that the lower rates of proton transfer in the case of the secondary amine are due to increased steric interactions which reduce both the rate of attack of amine on (PH) and of ammonium ion on (P^-).

Finally we consider rates of proton transfer to the solvent. Experimentally we find that at the amine concentrations used proton transfer from (PH) to the solvent cannot compete with proton transfer to the amine. Hence we can only set upper limits ont he values of k_s. That values of k_s should be small is in agreement with the values [9] of *ca.* 8—9 expected for $\mathrm{p}K_a^{PH}$. If proton transfer from the protonated solvent to (P^-) is diffusion-controlled then values of k_s will be in the range 1—10 s^{-1}.



(2)

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