Kinetics of Formation and Decomposition of the Intermediate Complex in the Reaction of Methyl 4-Methoxy-3,5-dinitrobenzoate with n-Butylamine in Dimethyl Sulphoxide

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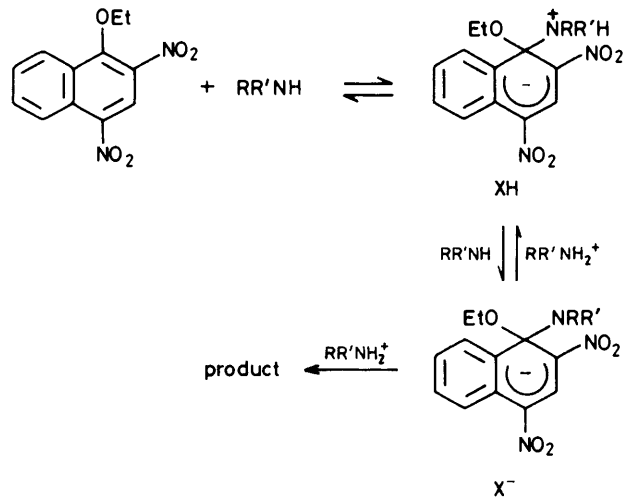
A stopped-flow spectrophotometric study of the reaction of methyl 4-methoxy-3,5-dinitrobenzoate with n-butylamine in dimethyl sulphoxide has confirmed the formation of an intermediate complex, and kinetic and equilibrium constants have been obtained for its formation and decomposition. The observable intermediate is the conjugate base (M^-) of the zwitterionic complex (MH). Proton transfer between MH and M^- is rapid and intermediate formation is not base-catalysed. The decomposition of M^- is first order in n-butylamine hydrochloride. The mechanism of the overall reaction is shown to involve rapid equilibrium deprotonation of MH, followed by general-acid-catalysed leaving group departure.

Bunnett and co-workers have observed an intermediate complex in the reaction of 1-ethoxy-2,4-dinitronaphthalene with primary and cyclic secondary amines in dimethyl sulphoxide (DMSO), and have proposed an overall reaction mechanism (Scheme 1).[1,2] Proton transfer between XH and X^- is rapid, and intermediate formation is not base-catalysed. The decomposition of the intermediate is first order in amine hydrochloride. The mechanism involves general acid catalysis of leaving group expulsion from X^-.

The kinetics of the σ-complex [3] formation from trinitrobenzene and piperidine (Scheme 2) have revealed that proton transfer between YH and Y^- is rate-limiting under certain conditions in aqueous DMSO,[4] and rate limiting over the entire range of piperidine concentrations used in 100% DMSO.[5]

Recently, we have confirmed intermediate formation in the reaction of methyl 4-methoxy-3,5-dinitrobenzoate (MDNB) with piperidine in DMSO (Scheme 3). The kinetic results have shown that proton transfer between ZH and Z^- is rate-limiting and intermediate formation is base-catalysed.[6]

In this paper we report the absorption spectrum of the intermediate complex in the reaction of MDNB with n-butylamine in DMSO, obtained by stopped-flow spectrophotometry, and the kinetics of formation and decomposition of the intermediate.



Scheme 1.

Results

Spectra observed 2.3 and 10 s after mixing of MDNB with n-butylamine in DMSO by stopped-flow spectrophotometry are shown as (a) and (b) in Figure 1, respectively. Spectrum (a) is attributable to MH or M^-, because it resembles that of the 1,1-complex of MDNB with MeO^- [Figure 1(c)].[7] Spectrum (b) is similar to that of a mixture of methyl 4-n-butylamino-3,5-dinitrobenzoate (PH) and n-butylamine in DMSO.[8] The absorption band around 430 nm is due to PH. Spectra of mixtures of PH and bases (MeO^- and OH^-) in DMSO have absorption at 535 nm, assignable to P^-.[8] The band of curve (b) around 540 nm is attributed to P^-.[1,8,9] The likely overall reaction mechanism is shown in Scheme 4.

Kinetic Runs.—The stopped-flow traces exhibited two components, representing the very fast formation and fast decomposition of the intermediate. The rate constants were obtained separately by means of Guggenheim's method.[10] Typical stopped-flow traces and a representative Guggenheim plot are presented in Figure 2.

Equilibrium Constant for Intermediate Formation.—We define an equilibrium constant K for the overall conversion of MDNB into M^- by equation (1). Assuming that k_{Am} is much larger than k_{AmH^+},* equation (1) can be rearranged to give

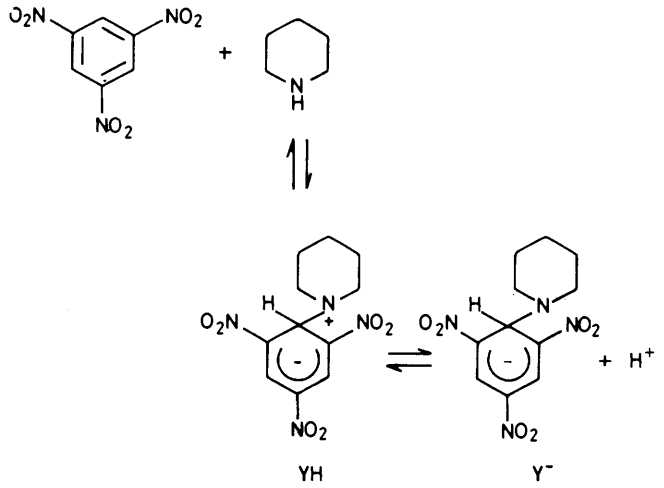
$$K = \frac{[M^-][RNH_3^+]}{[MDNB][RNH_2]^2} \quad (1)$$

$$\frac{[MDNB]_0}{A} = \frac{[RNH_3^+]}{K\varepsilon[RNH_2]^2} + \frac{1}{\varepsilon} \quad (2)$$

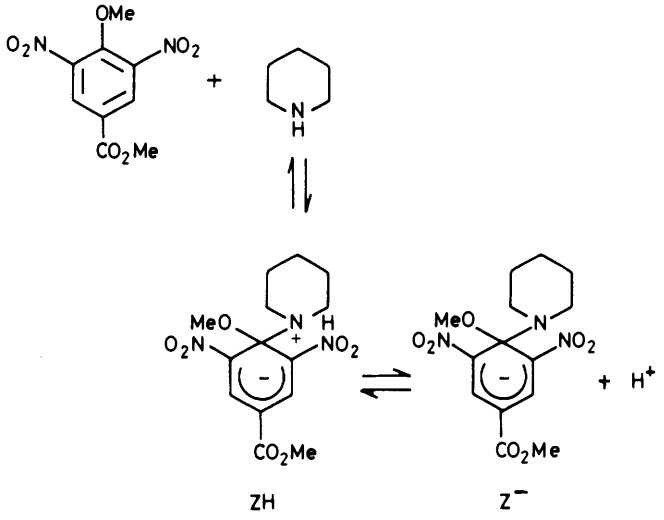
equation (2), where $[MDNB]_0$, A, and ε are the stoicheiometric MDNB concentration, equilibrium absorbance, and molar extinction coefficient, respectively.

Equilibrium measurements were made in the presence of both n-butylamine and n-butylamine hydrochloride in a large excess of MDNB. Because equilibrium absorbance could not be obtained directly from a stopped-flow trace, it was determined that the best linear relationship would be established in a plot of ln $(A_\infty - A_t)$ against time (where A_∞ and A_t are the equilibrium absorbance and the absorbance after time t, respectively). Equilibrium data are displayed in Table 1. A plot of $[MDNB]_0/A$ against $[RNH_2]^{-2}$ in Figure 3 gives a straight line. The K value obtained is 1.36 $dm^3\ mol^{-1}$.

* It is known that the amine complex exists predominantly as its conjugate base rather than as the zwitterionic complex.[1,2,5]



Scheme 2.



Scheme 3.

Kinetics of Intermediate Formation.—Kinetic measurements were made with an excess of n-butylamine and without n-butylamine hydrochloride. Under these conditions we may write equation (3) where AH^+ is the species formed from deprotonation of MH by n-butylamine, and has the same concentration as M^-. Equation (3) represents a mixed first-

$$\text{MDNB} \underset{k_{r2}}{\overset{k_{f1}}{\rightleftharpoons}} M^- + AH^+ \qquad (3)$$

order (forward) and second-order (reverse) equilibrium process. Assuming that MH may be treated as a steady-state intermediate, k_{f1} is given by equation (4).

$$k_{f1} = \frac{k_1[RNH_2]k_{Am}[RNH_2]}{k_{-1} + k_{Am}[RNH_2]} \qquad (4)$$

As shown in Table 2, values of $k_{f1}/[RNH_2]$ are almost constant. This shows that $k_{Am}[RNH_2]$ is much larger than k_{-1}, and so proton transfer between MH and M^- is rapid.

In some cases, kinetic data were obtained in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO), tetrapropylammonium iodide, or water; these results are given in Table 2. As

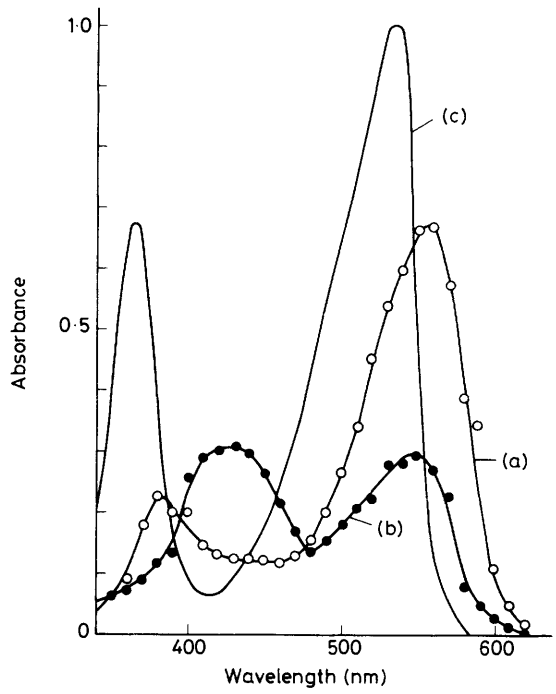


Figure 1. Spectra relevant to reaction of MDNB (6.0×10^{-5}M) with n-butylamine (0.030M) in DMSO: 1(a) and 1(b), 2.3 and 10 s after mixing at 25 °C, respectively; 1(c), spectrum of 1,1-complex of MDNB (4.9×10^{-5}M) with potassium methoxide (8.0×10^{-3}M) in methanolic DMSO (0.8% methanol by volume)

expected, intermediate formation is not catalysed by DABCO. Rates are unaffected by the presence of tetrapropylammonium iodide (0.0051M) or water (0.22M).

Kinetic determinations were carried out under pseudo-first-order conditions with n-butylamine and n-butylamine hydrochloride in a large excess of MDNB. The observed rate constant k_{form} is the sum of the forward and reverse components [equations (5) and (6)]. Again making use of the

$$\text{MDNB} \underset{k_{r1}}{\overset{k_{r1}}{\rightleftharpoons}} M^- \qquad (5)$$

$$k_{form} = k_{f1} + k_{r1} \qquad (6)$$

steady-state approximation with respect to MH, k_{form} is given by equation (7). As $k_{Am}[RNH_2]$ is much larger than k_{-1}, k_{form}

$$k_{form} = \frac{k_1[RNH_2]k_{Am}[RNH_2] + k_{-1}k_{AmH^+}[RNH_3^+]}{k_{-1} + k_{Am}[RNH_2]} \qquad (7)$$

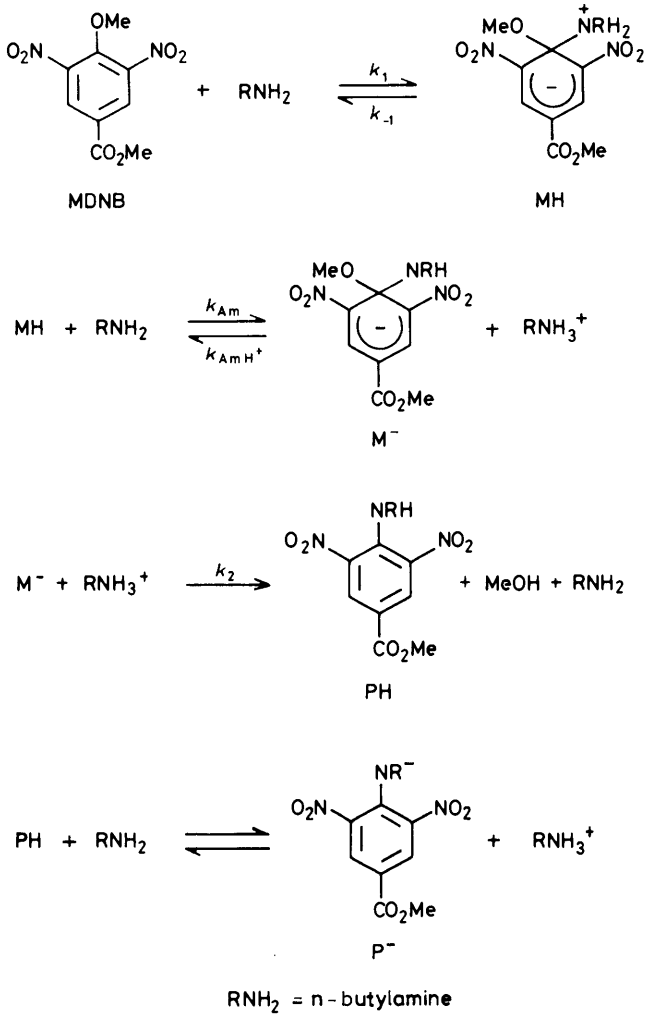
is given by equation (8). Multiplying each side by $[RNH_2]$

$$k_{form} = k_1[RNH_2] + \frac{k_{-1}k_{AmH^+}[RNH_3^+]}{k_{Am}[RNH_2]} \qquad (8)$$

gives equation (9).

$$k_{form}[RNH_2] = k_1[RNH_2]^2 + \frac{k_{-1}k_{AmH^+}[RNH_3^+]}{k_{Am}} \qquad (9)$$

Rate data are presented in Table 1. A plot of $k_{form}[RHN_2]$ against $[RNH_2]^2$ (Figure 4) is linear. The slope, k_1, is 50 dm^3 mol^{-1} s^{-1}. As the intercept, $(k_{-1}k_{AmH^+}[RNH_3^+])/k_{Am}$, is 0.193 mol dm^{-3} s^{-1}, $k_{-1}k_{AmH^+}/k_{Am}$ is 38 s^{-1}. From $K = k_1k_{Am}/(k_{-1}k_{AmH^+})$, K is 1.32 dm^3 mol^{-1}. This agrees well with



Scheme 4.

the K value of 1.36 dm^3 mol^{-1} obtained from a plot of $[MDNB]_0/A$ against $[RNH_2]^{-2}$.

Kinetics of Intermediate Decomposition.—The pseudo-first-order rate constant k_{dec} for decomposition of the intermediate after the equilibrium between MDNB and M^- has been established is given by equation (10).[1] This reduces to equation

$$k_{dec} = \frac{k_2K[RNH_2]^2[RNH_3^+]}{K[RNH_2]^2 + [RNH_3^+]} \quad (10)$$

(11). Under the conditions $K[RNH_2]^2 \gg [RNH_3^+]$ (where the

$$\log k_{dec} + \log (K[RNH_2]^2 + [RNH_3^+]) = \log k_2K + 2 \log [RNH_2] + \log [RNH_3^+] \quad (11)$$

equilibrium between MDNB and M^- lies almost entirely to the right), equation (11) leads to (12).

$$k_{dec} = k_2[RNH_3^+] \quad (12)$$

Kinetic data were obtained in three experiments and are given in Table 3.

The first experiment (Part A) applies to equation (11). Using the K value of 1.32 dm^3 mol^{-1}, a plot of log k_{dec} + log $(K[RNH_2]^2 + [RNH_3^+])$ against log $[RNH_2]$ was constructed. It is linear with slope 2.1 and intercept 0.50; see Figure 5. From log k_2K + log $[RNH_3^+]$ = 0.50, k_2 is 470 dm^3 mol^{-1} s^{-1}.

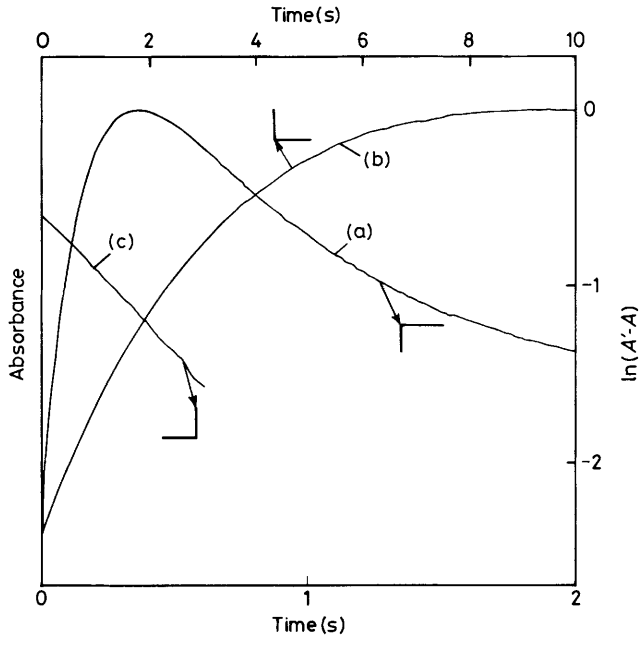


Figure 2. (a), (b) Typical stopped-flow traces at 560 nm and 25 °C with $[MDNB]_0 = 6.0 \times 10^{-5}$M and $[RNH_2] = 0.051$M (vertical scale change in absorbance; full scale = 1); (c) Guggenheim plot of curve (b) (where the constant interval [10b] is taken to be 0.6 s)

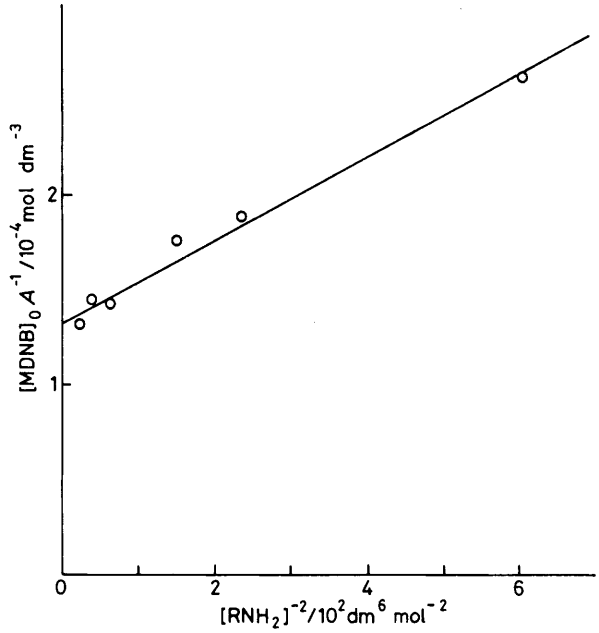


Figure 3. A plot of $[MDNB]_0/A$ against $[RNH_2]^{-2}$

The second (Part B) and third (Part C) experiments are appropriate to equation (12). In the second experiment, n-butylamine concentration was varied, with a constant concentration of n-butylamine hydrochloride, and in the third, n-butylamine hydrochloride concentration was varied, with a fixed n-butylamine concentration. Data from Table 3, Part B, reveal that k_{dec} values are almost constant and so the decom-

Table 1. Equilibrium and rate data for the reaction of MDNB (6.0×10^{-5}M) with n-butylamine in DMSO at 25 °C

$[RNH_2]$/M	$[RNH_3Cl]$/M	A [a]	k_{form}/s^{-1} [b]
0.041	0.0051	0.23	4.9
0.065	0.0051	0.32	6.6
0.081	0.0051	0.34	6.8
0.122	0.0051	0.42	8.5
0.162	0.0051	0.42	9.0
0.20	0.0051	0.46	11.2

[a] Absorbance at 560 nm. [b] Observed rate constant for intermediate formation.

Table 2. Rate data for the reaction of MDNB (6.0×10^{-5}M) with n-butylamine in DMSO at 25 °C [a]

$[RNH_2]$/M	[DABCO]/M	k_{f1}/s^{-1}	$k_{f1}/[RNH_2]$/ $dm^3\ mol^{-1}\ s^{-1}$
0.041		1.18	29
0.051		1.56	31
0.065		1.87	29
0.081		2.4	30
0.122		3.4	28
0.162		4.0	25
0.041	0.042	1.15	
0.041	0.083	1.16	
0.041 [b]		1.16	
0.122 [b]		3.0	
0.041 [c]		1.16	
0.122 [c]		3.2	

[a] Measurements were made at 560 nm. Conversion of MDNB into M^- is almost complete over the entire range of n-butylamine concentrations used; $\varepsilon_{560} = 17\,300\ dm^3\ mol^{-1}\ cm^{-1}$. [b] In the presence of salt; [tetrapropylammonium iodide] = 0.0051M. [c] In the presence of water; $[H_2O] = 0.22$M.

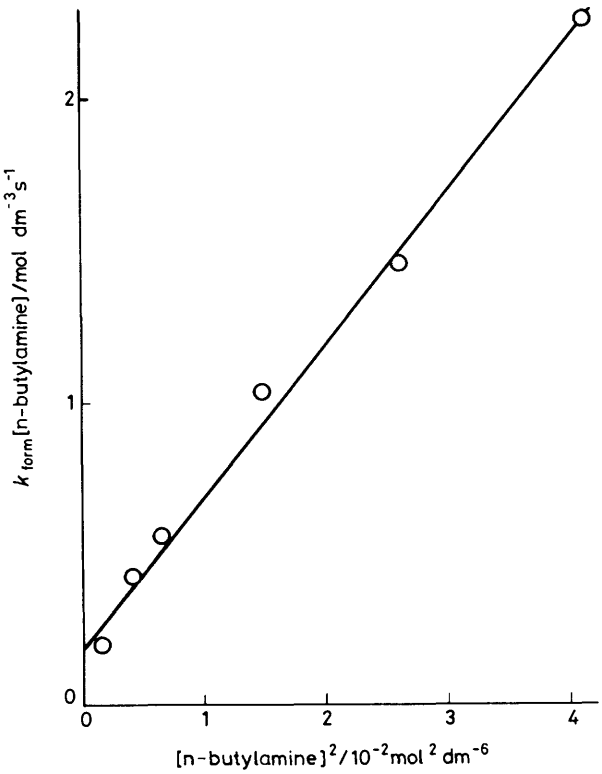


Figure 4. A plot of $k_{form}[RNH_2]$ against $[RNH_2]^2$

Table 3. Rate data for intermediate decomposition in the reaction of MDNB with n-butylamine at 25 °C

$[RNH_2]$/M	$[RNH_3Cl]$/M	k_{dec}/s^{-1}	$k_{dec}/[RNH_3Cl]$/ $dm^3\ mol^{-1}\ s^{-1}$
	Part A [a]		
0.041	0.0051	0.74	
0.065	0.0051	0.87	
0.122	0.0051	1.65	
0.162	0.0051	1.79	
0.20	0.0051	2.4	
	Part B [b]		
0.162	0.000 60	0.66	
0.182	0.000 60	0.64	
0.20	0.000 60	0.63	
0.24	0.000 60	0.72	
	Part C [b]		
0.20	0.000 40	0.48	1 200
0.20	0.000 60	0.63	1 050
0.20	0.000 80	0.76	950
0.20	0.001 20	1.08	900

[a] $[MDNB]_0 = 6.0 \times 10^{-5}$M. [b] $[MDNB]_0 = 1.00 \times 10^{-6}$M.

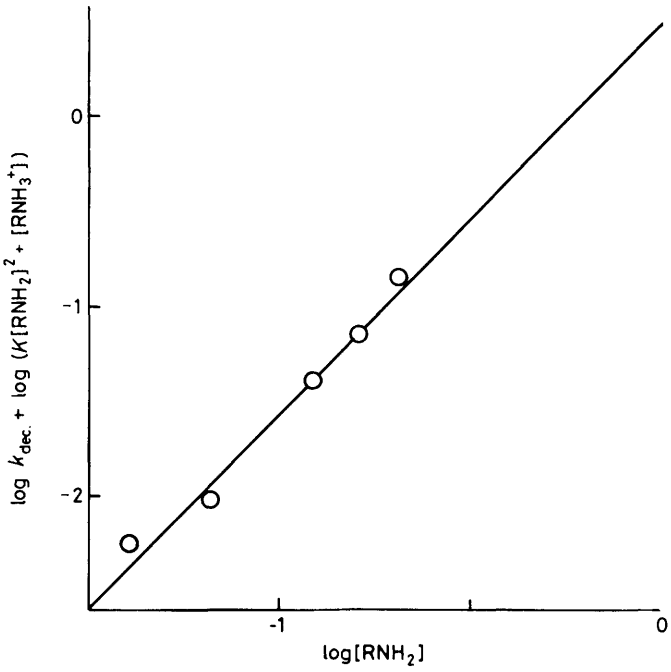


Figure 5. A plot of log k_{dec} + log ($K[RNH_2]^2$ + $[RNH_3^+]$) against log $[RNH_2]$

position of M^- is independent of n-butylamine concentration. However values of $k_{dec}/[RNH_3^+]$ are essentially constant (Part C) and the decomposition of M^- is first order in n-butylamine hydrochloride. The k_2 value obtained is 1 030 $dm^3\ mol^{-1}\ s^{-1}$.

Discussion

Our spectroscopic and kinetic results are consistent with the overall reaction mechanism of Scheme 4. Orvik and Bunnett have observed the intermediate complex in the reaction of 1-ethoxy-2,4-dinitronaphthalene with n-butylamine in DMSO

Table 4. Summary of rate and equilibrium constants at 25 °C

Intermediate	Present work M^-	Reaction of MDNB with piperidine [6] Z^-
k_1/dm^3 mol^{-1} s^{-1}	50	100
K/dm^3 mol^{-1}	1.32	0.083
$k_{-1}k_{AmH^+}/k_{Am}$/s^{-1}	38	1 200
k_2/dm^3 mol^{-1} s^{-1}	470	

and presented the overall reaction mechanism in this case.[1] Our observations are similar to theirs.

Intermediate Formation.—The similarity of the spectra in Figure 1(a) and Figure 1(c) (1,1-complex from MDNB and MeO^-) gives evidence for the formation of the intermediate complex.

The linearity of a plot of $[MDNB]_0/A$ against $[RNH_2]^{-2}$ indicates that the intermediate exists predominantly as its conjugate base rather than the zwitterionic complex.

Proton transfer between MH and M^- is rapid and intermediate formation is not base-catalysed. On the contrary, proton transfer is rate-limiting in the formation of the intermediate complex of MDNB with piperidine.[6] It is likely that the bulk of piperidine prevents it from attacking ZH and causes proton transfer to be rate-limiting. It seems that n-butylamine is not so hindered from attacking the zwitterionic complex.

The value of k_1 (50 dm^3 mol^{-1} s^{-1}) determined in the presence of both n-butylamine and n-butylamine hydrochloride in a large excess of MDNB (Table 1) is somewhat different from that of k_1 ($= k_{f1}/[RNH_2]$) = 29 dm^3 mol^{-1} s^{-1} determined in an excess of RNH_2 without RNH_3Cl (Table 2). This difference can be explained as follows.

Stopped-flow traces showed the very fast formation and fast decomposition of M^-; the rate constants were obtained by Guggenheim's method. Under pseudo-first-order conditions, k_{form}/k_{dec} is between 4.7 and 7.6. However the kinetic traces cannot be completely divided into components of formation and decomposition, and the rate constants obtained are thus approximate. Nevertheless, although the pseudo-first-order rate constants for M^- decomposition cannot be obtained in an excess RNH_2 without RNH_3Cl, M^- decomposes so slowly that the rate constants for M^- formation can be obtained more precisely than in the previous case.

As shown in Table 4, the equilibrium constant K for M^- formation increases by 16-fold, as compared with that for Z^- formation, while k_1 and $k_{-1}k_{AmH^+}/k_{Am}$ decrease by 2- and 32-fold, respectively. This increase in K results mainly from the decrease in $k_{-1}k_{AmH^+}/k_{Am}$.

Intermediate Decomposition.—The k_2 value of 470 dm^3 mol^{-1} s^{-1} determined from Table 3, Part A, differs from that in Part C (1 030 dm^3 mol^{-1} s^{-1}). An explanation * for this discrepancy is that the data in Part C were obtained with very low concentrations of $[RNH_3Cl]$ in order to keep $K[RNH_2]^2 \gg [RNH_3^+]$. We used spectrophotometric grade DMSO as supplied. If the DMSO contained traces of acidic impurities such as H_2SO_4 then the concentrations of RNH_3^+ would be different from the given concentrations of RNH_3Cl.

The decomposition of the intermediate complex is independent of n-butylamine concentration and first-order in n-butylamine hydrochloride concentration. The mechanism of the overall reaction involves rapid equilibrium deprotonation of MH followed by general-acid-catalysed leaving group departure.

* I thank a referee for this explanation.

Experimental

Materials.—MDNB, DABCO, and tetrapropylammonium iodide were prepared as previously described.[6] Spectrophotometric grade DMSO was used as supplied. n-Butylamine was refluxed over sodium and distilled. n-Butylamine hydrochloride was prepared from n-butylamine and concentrated hydrochloric acid and recrystallized. Methyl 4-n-butylamino-3,5-dinitrobenzoate was synthesized by esterification of 4-chloro-3,5-dinitrobenzoic acid followed by nucleophilic substitution of chlorine with n-butylamine. The compound was recrystallized from methanol; $\lambda_{max.}$ (DMSO) 425 nm (ε 6 000 dm^3 mol^{-1} cm^{-1}).

Measurements.—U.v. absorption spectra were recorded with a Hitachi 340 spectrophotometer. Kinetic measurements were carried out using a Union Giken RA 401 stopped-flow spectrophotometer at 25 °C. The mixing cell had a path length of 1 cm. Guggenheim plots were made by means of a Union Giken RA 451 Data Processor.

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