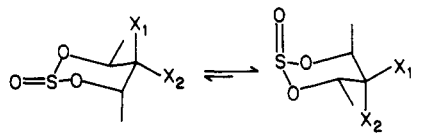
Scheme II



	e		a
25	21%	X_1=CH_3, X_2=H	79%
26	32%	X_1=H, X_2=CH_3	68%
41	15%	X_1=H, X_2=Cl	85%
42	40%	X_1=Cl, X_2=H	60%

cording to the above authors attain chair forms. Changing the solvent from nonpolar to polar did not change the relative intensity of the band although the twist form should be more polar than the chair conformation with an axial S=O group and the relative intensity of the band should increase.[6] Hence we believe that the 1216–1232 cm^{-1} band is due to the C–C(–H) stretching vibrations rather than to isoclinal S=O groups.[6]

Very recently Gorrichon et al.[8] reported that **41** and **42** exist appreciably in twist conformations. Their conclusions are based on a poor correlation of the ^{13}C NMR chemical shift data for these and some model compounds. Using the substituent effects given in Tables II and III, we can estimate chemical shifts for the conformations in Scheme II when $X_1 = X_2 = H$ and from the paper of Gorrichon et al.[8] we obtain the α and β effects due to an equatorial or an axial Cl-atom and a few correction terms due to the gauche interactions. Taking these into account together with our knowledge about the other possible effects we can easily estimate that **41** is about an 85:15 mixture of the S=O axial (a) and S=O equatorial (e) chair forms. In the case of **42** it is more difficult to estimate all of the necessary substituent effects (due to the lack of model compounds[8]) but roughly the proportion of the S=O axial (a) chair form is now about 60%. These estimates are supported by the conformer ratios of **25** and **26** since it can be expected that an axial chlorine atom at C-5 is favored in relation to an axial methyl group at C-5.

In the light of the above discussion we conclude that there is no reason to believe that methyl-substituted 2-oxo-1,3,2-dioxathianes attain other than chair conformations.

Experimental Section

The ^{13}C spectra were recorded at 298 K on Jeol FX-60 NMR spectrometer operating at 15.03 MHz with 8 K data points. Samples were prepared in 10-mm od tubes as 10% w/v solutions in $CDCl_3$ with 2% Me_4Si as a reference. Most shift data (Table I) were extracted from Nikander's dissertation[5] (compounds **1–8**, **10**, **12–21**, **23**, **27–29**, and **31–40**) but those of compounds **9**, **11**, **25**, and **26** were redetermined. Shift data for compounds **22**, **24**, and **30** were taken from Hellier and Phillips.[10] All methyl-substituted 2-oxo-1,3,2-dioxathianes were available from our earlier studies.[3-6] Gorrichon et al.[8] report for **41** and **42** the following ^{13}C chemical shifts. **41**: C-4 77.1, C-5 62.7, and C-6 63.25 ppm. **42**: C-4 72.9, C-5 62.3, and C-6 67.9 ppm.

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Registry No. **1**, 4176-55-0; **2**, 32644-05-6; **3**, 32644-06-7; **4**, 37989-54-1; **5**, 37989-53-0; **6**, 4493-97-4; **7**, 1003-85-6; **8**, 58240-37-2; **9**, 81800-23-9; **10**, 58210-19-8; **11**, 81800-24-0; **12**, 25845-28-7; **13**, 25845-29-8; **14**, 29882-38-0; **15**, 81756-33-4; **16**, 81756-34-5; **17**, 81756-35-6; **18**, 81756-36-7; **19**, 25545-81-7; **20**, 25545-82-8; **21**, 29265-49-4; **22**, 29288-15-1; **23**, 36044-84-5; **24**, 36044-85-6; **25**, 61665-27-8; **26**, 61665-28-9; **27**, 81756-38-9; **28**, 81800-26-2; **29**, 81800-25-1; **30**, 81800-27-3; **31**, 29288-16-2; **32**, 36297-36-6; **33**, 34513-18-3; **34**, 81756-37-8; **35**, 32475-82-4; **36**, 81756-39-0; **37**, 81756-40-3; **38**, 81756-42-5; **39**, 81756-41-4; **40**, 81756-43-6.

Rapid Scan UV Spectroscopic and Kinetic Studies of the Reaction of Methyl 4-Methoxy-3,5-dinitrobenzoate with Pyrrolidine in Dimethyl Sulfoxide

Yoshinori Hasegawa

College of General Education, Tohoku University, Kawauchi, Sendai 980, Japan

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An intermediate complex in the aromatic nucleophilic substitution reaction of methyl 4-methoxy-3,5-dinitrobenzoate with pyrrolidine in dimethyl sulfoxide has been observed by rapid scan UV spectroscopy, and kinetic and equilibrium constants have been obtained for its formation and decomposition. The observable intermediate is the conjugate base (I^-) of the zwitterionic form (IH). The formation of I^- is base catalyzed and the decomposition of I^- is first order in pyrrolidine hydrochloride. The possible mechanism is that proton transfer between IH and I^- is not more rapid than the k_{-1} step and that general acid catalyzed leaving group departure from I^- is rate limiting.

In kinetic studies of the reactions of 1-ethoxy-2,4-dinitronaphthalene with primary and cyclic secondary amines in dimethyl sulfoxide, Bunnett observed that proton transfer is rapid and that the rate-limiting decomposition of X^- is general acid catalyzed (Scheme I).[1,2]

This work provided direct evidence for the specific base–general acid (SB–GA) mechanism of the S_NAr reaction.[3,4] Recently evidence in favor of the SB–GA mechanism has been presented in the reactions of methyl 4-methoxy-3,5-dinitrobenzoate (MDNB)[5] and 2,4,6-trinitrophenetole[6] with *n*-butylamine in Me_2SO.

A series of papers have revealed that the kinetics are greatly different between pyrrolidine and piperidine as nucleophiles.[2,4,7] It has been reported that proton transfer

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(4) Bunnett, J. F.; Cartaño, A. V. *J. Am. Chem. Soc.* **1981**, *103*, 4861.
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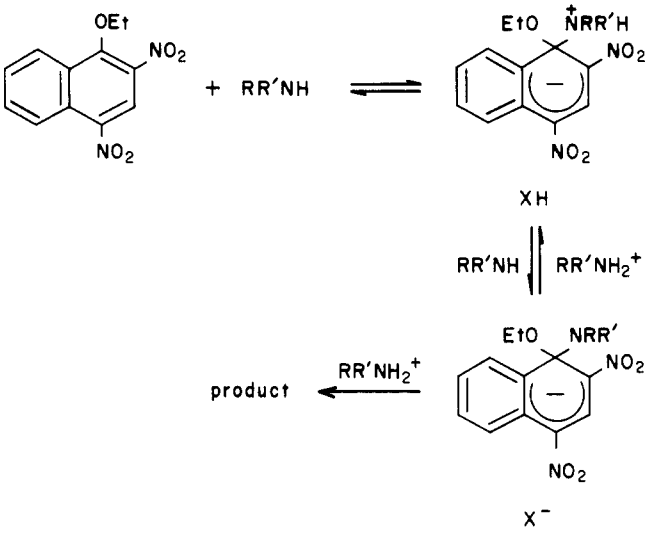
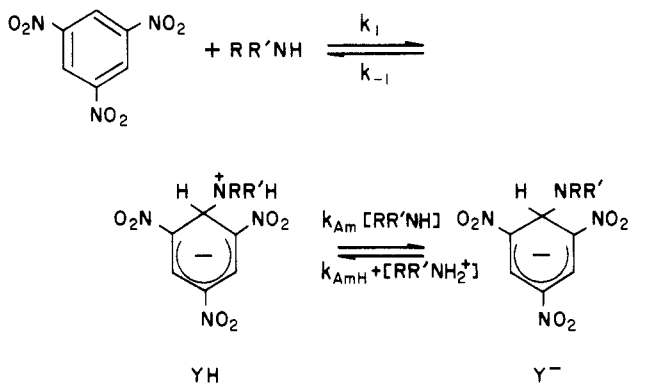
Scheme I



Scheme II



is rate limiting in the formation of the σ-complex Y^- of 1,3,5-trinitrobenzene with piperidine and pyrrolidine in Me_2SO,[8-10] and that the kinetic parameters k_{Am} and k_{AmH^+} are one order of magnitude larger for pyrrolidine than for piperidine (Scheme II).[9]

Our previous kinetic studies have shown that, in the formation of the intermediate complex of MDNB with piperidine, proton transfer between the zwitterionic complex and its conjugate base is rate limiting.[11]

In this paper I wish to report rapid scan UV spectra of the reaction of MDNB with pyrrolidine in Me_2SO and the kinetics of the overall reaction. The reaction mechanism is indicated in Scheme III.

Results

Rapid Scan UV Spectroscopy. Rapid scan UV spectra of the reaction of MDNB with pyrrolidine in the presence of pyrrolidine hydrochloride are shown in Figure

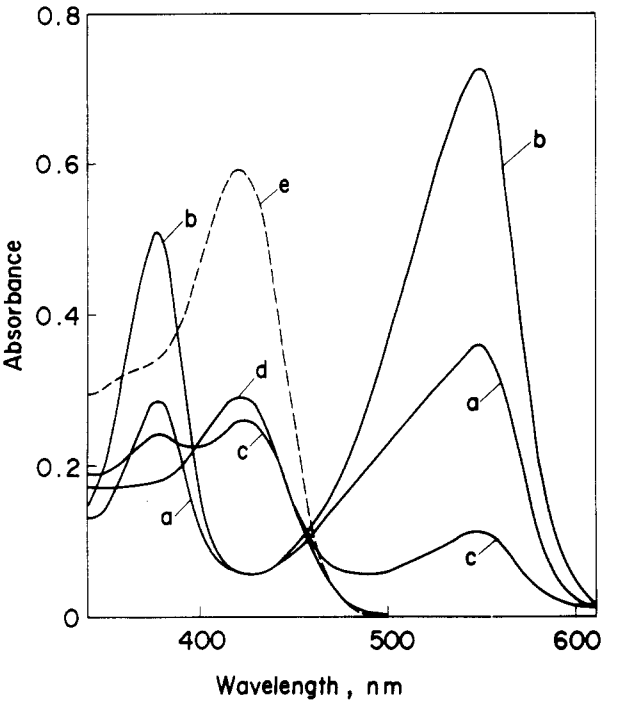
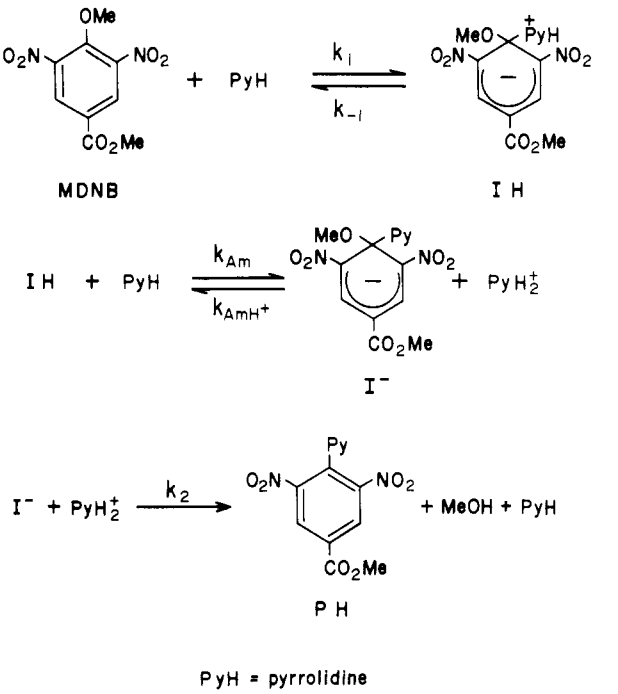


Figure 1. UV spectra relevant to reaction of MDNB (4.0×10^{-5} M) with pyrrolidine (0.29 M) and pyrrolidine hydrochloride (0.0050 M) in Me_2SO at 25 °C: a, 22 ms; b, 142 ms; c, 15.4 s; d, 2 min after mixing; e, spectrum of PH (8.0×10^{-5} M) in Me_2SO.

Scheme III



PyH = pyrrolidine

1. The absorption bands at 377 and 549 nm developed transiently and the complete appearance of these bands was attained within several hundred milliseconds after mixing. At the expense of these bands, the absorption peak at 420 nm developed gradually and appeared completely within about 2 min after mixing. The final spectrum (d) agrees with that (e) of methyl 4-pyrrolidino-3,5-dinitrobenzoate (PH). The absorption bands at λ_{max} 377 and 549 nm observed intially are similar to those of the deprotonated σ-complex intermediate of MDNB with piperidine and *n*-butylamine[5,11] and are attributed to the intermediate complex I^-.

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(9) Crampton, M. R.; Greenhalgh, C. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1175.
(10) For rate-limiting proton transfer in the formation of an anionic σ-complex, see: (a) Terrier, F. *Chem. Rev.* **1982**, *82*, 77. (b) Bernasconi, C. F.; Gehriger C. L. *J. Am. Chem. Soc.* **1974**, *96*, 1092. (c) Bernasconi, C. F.; Terrier, F. *J. Am. Chem. Soc.* **1975**, *97*, 7458. (d) Bernasconi, C. F.; Wang, H. *J. Am. Chem. Soc.* **1976**, *98*, 6265. (e) Bernasconi, C. F.; Gehriger, C. L.; de Rossi, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 8451. (f) Buncel, E.; Eggimann, W. *J. Am. Chem. Soc.* **1977**, *99*, 5958. (g) Bernasconi, C. F.; Muller, M. C.; Schmid, P. *J. Org. Chem.* **1979**, *44*, 3189. (h) Bamkole, T. O.; Hirst, J.; Onyido, I. *J. Chem. Soc. Pkerin Trans. 2* **1981**, 1201. (i) Crampton, M. R.; Routledge, P. J.; Golding, P. *J. Chem. Soc., Perkin Trans. 2* **1984**, 329.
(11) Hasegawa, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1314.

Table I. Rate Data for the Reaction of MDNB with Pyrrolidine in Me_2SO at 25 °C[a]

[pyrrolidine], M	[Dabco], M	k_{f1}, s^{-1}
0.0050		0.031
0.0067		0.063
0.0100		0.133
0.0133		0.23
0.020		0.49
0.024		0.65
0.031		1.14
0.046		2.5
0.052		3.1
0.060		4.1
0.093		5.7
0.123		7.2
0.052	0.029	3.5
0.052	0.057	3.8
0.052	0.086	4.3
0.052	0.112	4.5

[a] $[MDNB]_0 = 4.0 \times 10^{-5}$ M.

Kinetics of Intermediate Formation. As the formation of intermediate I^- is much faster than its decomposition, the formation and decomposition of the intermediate can be treated as an independent system.

Kinetic studies were made in the presence of pyrrolidine and 1,4-diazabicyclo[2.2.2]octane (Dabco) in a large excess of MDNB. Under these conditions, eq 1 may be written

$$\text{MDNB} \underset{k_{r2}}{\overset{k_{f1}}{\rightleftharpoons}} I^- + AH^+ \quad (1)$$

where AH^+ is the species formed from deprotonation of IH and has the same concentration as I^-. Equation 1 represents a mixed first-order (forward) and second-order (reverse) equilibrium process. Assuming that IH can be treated as a steady-state intermediate, k_{f1} is given by eq 2 where k_{Dabco} is the rate constant for deprotonation of IH by Dabco. In the absence of Dabco, eq 2 can be rearranged to give eq 3.

$$k_{f1} = \frac{k_1[PyH](k_{Am}[PyH] + k_{Dabco}[Dabco])}{k_{-1} + k_{Am}[PyH] + k_{Dabco}[Dabco]} \quad (2)$$

$$\frac{[PyH]}{k_{f1}} = \frac{1}{k_1} + \frac{k_{-1}}{k_1 k_{Am}[PyH]} \quad (3)$$

Rate data are shown in Table I, and a plot of $[PyH]k_{f1}^{-1}$ vs. $[PyH]^{-1}$ gives a straight line. The constants k_1 and k_{Am}/k_{-1} were determined to be 230 M^{-1} s^{-1} and 6.0 M^{-1}, respectively.

It is evident that the intermediate formation is catalyzed by Dabco. At a given concentration of Dabco, k_{Dabco}/k_{-1} can be calculated from eq 2. The mean value of k_{Dabco}/k_{-1} thus obtained is 3.1 M^{-1}.

Runs were carried out under pseudo-first-order conditions with pyrrolidine and pyrrolidine hydrochloride in a large excess of MDNB. The observed rate constant k_ψ is the sum of the forward and reverse components (eq 4), and treating IH as a steady-state intermediate yields eq 5. The pseudo-first-order reverse rate constant, k_{r1} is given by eq 6.

$$k_\psi = k_{f1} + k_{r1} \quad (4)$$

$$k_\psi = \frac{k_1[PyH]k_{Am}[PyH] + k_{-1}k_{AmH^+}[PyH_2^+]}{k_{-1} + k_{Am}[PyH]} \quad (5)$$

$$k_{r1} = \frac{k_{-1}k_{AmH^+}[PyH_2^+]}{k_{-1} + k_{Am}[PyH]} \quad (6)$$

Rate data are shown in Table II. At a given concentration of pyrrolidine, k_{AmH^+} can be calculated from eq 6 with $k_{Am}/k_{-1} = 6.0$ M^{-1}. The mean value of k_{AmH^+} thus obtained is 3100 M^{-1} s^{-1}.

Table II. Rate Data for the Reaction of MDNB with Pyrrolidine and Pyrrolidine Hydrochloride in Me_2SO at 25 °C[a]

[pyrrolidine], M	A_{545}[b]	k_ψ, s^{-1}	k_{r1}, s^{-1} [c]	k_{AmH^+}, s^{-1} M^{-1} [d]	k_{calcd}, s^{-1} [e]
0.020	0.028	15.5	15.0	3400	14.9
0.024	0.038	14.5	13.8	3200	14.8
0.031	0.065	14.4	13.3	3200	14.7
0.046	0.136	14.3	11.8	3000	14.9
0.060	0.20	14.6	10.5	2900	15.4
0.072	0.25	15.2			16.1
0.087	0.34	16.5			17.4
0.100	0.38	17.5			18.5
0.118	0.42	19.8			20
0.177	0.59	26			28

[a] $[MDNB]_0 = 4.0 \times 10^{-5}$ M; [pyrrolidine hydrochloride] = 0.0050 M. [b] Equilibrium absorbance at 545 nm. [c] Obtained from $k_{r1} = k_\psi - k_{f1}$. [d] Calculated from eq 6 with $k_{Am}/k_{-1} = 6.0$ M^{-1}. [e] Calculated from eq 5 with $k_1 = 230$ M^{-1} s^{-1}, $k_{Am}/k_{-1} = 6.0$ M^{-1}, and $k_{AmH^+} = 3100$ M^{-1} s^{-1}.

Equilibrium Constant. The equilibrium constant K for the overall conversion of MDNB into I^- is defined by eq 7 and then eq 8.

$$K = \frac{[I^-][PyH_2^+]}{[MDNB][PyH]^2} \quad (7)$$

$$K = \frac{k_1 k_{Am}}{k_{-1}k_{AmH^+}} \quad (8)$$

The equilibrium constant was obtained by the following two methods. (1) A Benesi–Hildebrand type plot[11] of $[MDNB]_0 A_{545}^{-1}$ vs. $[PyH]^{-2}$ gives a straight line; K and ϵ_{545} are determined to be 0.44 M^{-1} and 20 000 M^{-1} cm^{-1}, respectively. (2) From eq 8, K is calculated to be 0.45 M^{-1}, which agrees well with the value obtained above.

Kinetics of the Intermediate Decomposition. The conversion of intermediate I^- into the product PH is rate limiting in the overall reaction of MDNB with pyrrolidine. The pseudo-first-order rate constant k_{obsd} for intermediate decomposition after the equilibrium between MDNB and I^- has been attained and is given by eq 9, which leads to eq 10.

$$k_{obsd} = \frac{k_2 K[PyH]^2[PyH_2^+]}{K[PyH]^2 + [PyH_2^+]} \quad (9)$$

$$\log k_{obsd} + \log (K[PyH]^2 + [PyH_2^+]) = \log k_2 K + 2 \log [PyH] + \log [PyH_2^+] \quad (10)$$

Measurements were made under conditions that $k_{Am}[PyH]$ is not larger than k_{-1}, and stopped-flow data which apply to eq 10 are shown in Table III. When a K value of 0.44 M^{-1} was used, a plot according to eq 10 is linear with slope of 1.91 and intercept of −1.26; k_2 is derived to be 25 M^{-1} s^{-1}.

Rate and equilibrium constants are summarized in Table IV.

Discussion

Intermediate Formation. As shown in Table IV, k_1 decreases in the order of pyrrolidine > piperidine > *n*-butylamine. This order, which reflects amine reactivity, is similar to that for the 1-ethoxy-2,4-dinitronaphthalene–amine system[1,2] and for the 1,3,5-trinitrobenzene–amine system.[10g] Moreover, K decreases in the order *n*-butylamine > pyrrolidine > piperidine, the same order reported for 1-ethoxy-2,4-dinitronaphthalene.[1,2]

Table III. Rate Date for the Intermediate Decomposition in the Reaction of MDNB with Pyrrolidine and Pyrrolidine Hydrochloride in Me_2SO at 25 °C[a]

[pyrrolidine], M	k_{obsd}, s^{-1}	[pyrrolidine], M	k_{obsd}, s^{-1}
0.046	0.028	0.100	0.072
0.060	0.037	0.118	0.081
0.072	0.048	0.123	0.081
0.087	0.068	0.177	0.114

[a] $[MDNB]_0 = 4.0 \times 10^{-5}$ M; [pyrrolidine hydrochloride] = 0.0050 M.

Table IV. Rate and Equilibrium Constants for the Reactions of MDNB with Amines in Me_2SO at 25 °C

	pyrrolidine	piperidine[a]	*n*-butylamine[b]
k_1, M^{-1} s^{-1}	230	100	50
k_{AmH^+}, M^{-1} s^{-1}	3100	340	
k_{Am}/k_{-1}, M^{-1}	6.0	0.28	
$k_{-1}k_{AmH^+}/k_{Am}$, s^{-1}	520	1200	38
k_{Dabco}/k_{-1}, M^{-1}	3.1	0.067	
K, M^{-1}	0.44	0.083	1.32
k_2, M^{-1} s^{-1}	25	very low	470

[a] From ref 11. [b] From ref 5.

The most striking kinetic feature in the reaction of MDNB with the three amines is that the intermediate formation is not base catalyzed for *n*-butylamine[5] but is base catalyzed for pyrrolidine and piperidine.[11] However, a great difference exists between values of the kinetic parameters for pyrrolidine and piperidine. Although the reactivity ratio (2.3) of pyrrolidine to piperidine is similar to that (2.7) reported for 1-ethoxy-2,4-dinitronaphthalene[2] and that (2.2) for 1,3,5-trinitrobenzene,[10g] the k_{AmH^+} value and the k_{Am}/k_{-1} and k_{Dabco}/k_{-1} ratios for pyrrolidine are larger than those of piperidine by factors of 9.1, 21, and 46, respectively.

As Bunnett and Cartaño pointed out,[4] the k_{-1} value for the σ-complex formation of 1,3,5-trinitrobenzene with pyrrolidine is two-thirds that for piperidine.[10g] Assuming that k_{-1} is comparable for the reactions of MDNB with pyrrolidine and piperidine, the discrepancy in k_{Am}/k_{-1} and k_{Dabco}/k_{-1} results from that in k_{Am} and k_{Dabco}, respectively.

The difference in k_{Am} and k_{AmH^+} is similar to that for the σ-complex formation of 1,3,5-trinitrobenzene with pyrrolidine and piperidine,[8,9] and it was suggested that the steric/stereoelectronic/conformational effect is larger for piperidine than for pyrrolidine.[9] The larger steric effect for piperidine than for pyrrolidine will cause less Dabco catalysis for piperidine.

Intermediate Decomposition. Evidence reported for the SB–GA mechanism indicates rapid equilibrium deprotonation of the zwitterionic complex, followed by general acid catalyzed, rate limiting departure of the leaving group.[1,2,5,6] In the present case, the conversion of I^- into PH is surely rate limiting in the overall reaction. Since the plot according to eq 10 is linear with slope of 1.91, the decomposition of I^- is first order in pyrrolidine hydrochloride. The decomposition of I^- was observed under the conditions of $k_{Am}[PyH] \leq k_{-1}$. Hence the proposal mechanism involves MDNB, IH, and I^- in an equilibrium where proton transfer between IH and I^- is not more rapid than the k_{-1} step, and the general acid catalyzed leaving group departure from I^- is rate limiting.

The decomposition of I^- is rapid and so its rate can be obtained only by use of a stopped-flow apparatus. On the contrary, the decomposition of the intermediate from MDNB and piperidine is very slow. This difference is analogous to that reported for the 1-ethoxy-2,4-dinitronaphthalene[2]–amine and 2,4,6-trinitrophenetole[6]–amine systems. This difference may result from steric effect in the piperidine transition state.[2,6]

Experimental Section

MDNB, Me_2SO, and Dabco were prepared as previously described.[11] Pyrrolidine was refluxed over sodium and distilled. Pyrrolidine hydrochloride was prepared from pyrrolidine and concentrated hydrochloric acid and purified by repeated recrystallization from methanol.[4] Methyl 4-pyrrolidino-3,5-dinitrobenzoate was synthesized by esterification of 4-chloro-3,5-dinitrobenzoic acid followed by nucleophilic substitution of chlorine with pyrrolidine. The compound was recrystallized from methanol. Anal. Calcd for $C_{12}H_{13}O_6N_3$: C, 48.82; H, 4.44; N, 14.23. Found: C, 48.90; H, 4.38; N, 14.26.

Rapid scan UV spectra at various stages of the reaction were measured with a Union RA 415 rapid scan spectrophotometer. The apparatus was equipped with an automatically controlled mixing cell with a pass length of 1 cm and controlled by a thermocirculater. The sweep time was taken to be 20 ms for the intermediate formation (Figure 1a,b) and 200 ms for the intermediate decomposition (Figure 1c). Absorption spectra were recorded on a Hitachi 340 Spectrophotometer.

Kinetic measurements were made with a Union RA 401 stopped-flow apparatus and a Union RA 451 data processor. Kinetic traces were obtained after mixing MDNB (4.0×10^{-5} M) and pyrrolidine hydrochloride (0.0050 M) (if present) in Me_2SO at 545 nm and 25 °C. In some cases, Dabco (0.029–0.112 M) was employed as a catalysis. Rate constants obtained are ordinarily averages of three measurements and accurate to within ±3%.

Acknowledgment. I am grateful to Professor Y. Sasaki of Tohoku University for helpful discussions.

Registry No. MDNB, 29544-89-6; pyrrolidine, 123-75-1; pyrrolidine hydrochloride, 25150-61-2.