hold bleach) was reacted by procedures analogous to those used for 1′, yielding 0.42 g (0.0017 mol, 40%) of *trans-N,N′*-bis(1-bicyclo[2.2.2]octyl)diazene (4′): mp 130–131 °C (lit.[15] mp 132–134 °C); ^{1}H NMR (CDCl$_3$) δ 1.60 (m), 1.49 (m), 0.82 (m); ^{13}C NMR (CDCl$_3$) δ 67.5, 33.4, 32.2, 30.8, 29.8, 8.2; UV, λ_{max} 368 nm (lit.[4a] λ_{max} 369 nm).

Solvents. The alkane solvents were purified by stirring over sulfuric acid for 24–48 h, washed with water and 10% aqueous sodium bicarbonate, and then distilled from phosphorus pentoxide and stored over potassium carbonate. Ethanol (95%) was used as supplied; its UV spectrum was free of interfering absorbances between 330 and 700 nm. *tert*-Butylamine and triethylamine, used to eliminate traces of acid in the reaction mixtures,[2b,4a] were stirred over potassium hydroxide for 12 h, distilled in vacuo, and stored in brown bottles.

Kinetics. General Procedures. All glassware, reaction cells, droppers, and syringes that came in contact with the diazene reaction mixtures were carefully washed with dilute ammonium hydroxide and air-dried.

Pressure Apparatus. Kinetic studies were conducted in a thermostated optical high-pressure bomb that has been described.[2a,18] Degassed solutions of reactants were transferred to the high-pressure sample cell with use of a glovebag with a nitrogen atmosphere.

Photolysis of *trans*-Diazenes. The photolysis apparatus has been described.[5] Solutions of *trans*-diazenes were photolyzed in the thermostated high-pressure optical cell that was then transferred to the UV–vis spectrometer for kinetic measurements.

Kinetic Studies of *cis*-Diazene Decompositions. The procedures used were essentially the same as those recently reported by us for a viscosity study of a series of *cis*-diazenes.[5] Values of $k(\mathrm{O})$ were calculated from the decrease with time in the *cis*-diazene absorbance at λ_{max} by standard procedures and appropriate base-line corrections. Values of $k(\mathrm{I})/k(\mathrm{O})$ were obtained from eq 8 as previously described.[5]

$$k(\mathrm{I})/k(\mathrm{O}) = [A_{\mathrm{trans}(t=\infty)} - A_{\mathrm{trans}(t=0)}]/[A_{\mathrm{trans(pre\text{-}}h\nu)} - A_{\mathrm{trans}(t=0)}] \quad (8)$$

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[18] (a) Ertley, E. Ph.D. Dissertation, University of California, Riverside, 1973. (b) Lockyer, G. Ph.D. Dissertation, University of California, Riverside, 1975.

Kinetics of Reactions of Amines with α-Nitro-β-substituted-stilbenes in 50% Me$_2$SO–50% Water. Search for the Intermediate in Nucleophilic Vinylic Substitution Reactions

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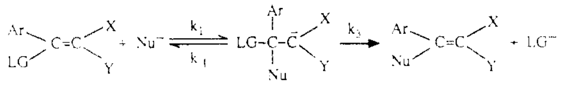
The kinetics of the reaction of Ph(OMe)C=CPh(NO$_2$) with piperidine, morpholine, pyrrolidine, and *n*-butylamine, and of the reactions of piperidine with Ph(Cl)C=CPh(NO$_2$), Ph(I)C=CPh(NO$_2$), and Ph(SEt)C=CPh(NO$_2$) where measured in 50% Me$_2$SO–50% water at 20 °C. The reactions are discussed within the framework of the multistep mechanism of nucleophilic vinylic substitutions with amines. Nucleophilic attack is rate limiting in the reactions of piperidine with Ph(LG)C=CPh(NO$_2$) when LG = Cl, I, EtS, and in the reactions of Ph(OMe)C=CPh(NO$_2$) with all the amines at high pH. At low pH, methoxide departure becomes partially rate limiting in the reactions with piperidine, morpholine, and pyrrolidine. The intermediate Ph(OMe)(NRR′)CCPh(NO$_2$)$^-$ could not be directly observed. The failure to detect the intermediate is not caused by a thermodynamic stability of the intermediate with respect to reactants that is too low, but by a rate of conversion to products that is too fast compared to its rate of formation.

Over the last 25 years a large body of evidence has accumulated in favor of the addition–elimination mechanism of nucleophilic vinylic substitution with strongly activated substrates.[1] Equation 1 shows this mechanism for the reaction of a benzylidene type vinylic substrate with an anionic nucleophile:



(1)

1 2 3

X and Y are the activating (electron-withdrawing) groups, while LG is the nucleofuge. For consistency with Scheme I (see below) we shall use the symbol k_3 for leaving-group departure from an anionic intermediate and reserve the symbol k_2 for the breakdown of a zwitterionic intermediate.

The evidence in support of the two-step nature of the mechanism has been mainly indirect and has been based on ratios of rate constants for different leaving groups,[1a,d,e] rate laws showing a change in rate-limiting step in base-catalyzed reactions with amine nucleophiles,[2] stereochemical arguments,[1d,3] and analogies with systems without a leaving group in which adducts of the type **2** (LG = H) could be detected.[4]

In recent papers we reported the first examples of reactions in which intermediates such as **2** could be *directly* observed spectrophotometrically and whose rates of formation and of transformation to products could be measured separately.[5] The successful systems were the re-

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[†] University of California.

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[1] For reviews, see: (a) Rappoport, Z. *Adv. Phys. Org. Chem.* **1969**, *7*, 1. (b) Modena, G. *Acc. Chem. Res.* **1971**, *4*, 73. (c) Miller, S. I. *Tetrahedron* **1977**, *33*, 1211. (d) Rappoport, Z. *Acc. Chem. Res.* **1981**, *14*, 7. (e) Rappoport, Z. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 309. (f) Shainyan, B. A. *Usp. Khim.* **1986**, *55*, 942.

[2] (a) Rappoport, Z.; Ladkani, D. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1045. (b) Rappoport, Z.; Peled, P. *J. Am. Chem. Soc.* **1979**, *101*, 2682. (c) Rappoport, Z.; Topol, A. *J. Org. Chem.* **1989**, *54*, 5967.

[3] (a) Rappoport, Z.; Avramovitch, B. *J. Am. Chem. Soc.* **1988**, *110*, 911. (b) Lodder, G.; van Dorp, J. W. J.; Avramovitch, B.; Rappoport, Z. *J. Org. Chem.* **1989**, *54*, 2574.

[4] For reviews, see: (a) Patai, S.; Rappoport, Z. In *The Chemistry of the Alkenes*; Patai, S., Eds.; Wiley-Interscience: New York, 1964; p 469. (b) Rappoport, Z.; Ladkani, D. *Chem. Scr.* **1974**, *5*, 124. (c) Bernasconi, C. F. *Tetrahedron* **1989**, *45*, 4017.

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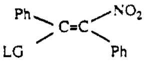
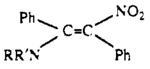
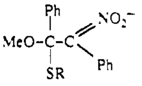
actions of alkyl thiolate ions ($CH_2CH_2S^-$, $HOCH_2CH_2S^-$, $CH_3O_2CCH_2CH_2S^-$, $CH_3O_2CCH_2S^-$) with **4-OMe** and **4-SR** (R = $CH_3CH_2CH_2$, $HOCH_2CH_2$, $CH_3O_2CCH_2CH_2$) in 50% Me_2SO–50% water (v/v).



4-LG (LG=MeO, RS, EtS, Cl, I, H)



4-NRR′



5-(OMe, SR)$^-$

There are three conditions that need to be met for an intermediate to be observable in a reaction such as eq 1. (1) The equilibrium for intermediate formation from the reactants must be favorable, i.e. $K_1[Nu^-] > (\gg) 1$.[6] (2) The conversion of the intermediate to products must be slower than its formation, i.e. $k_1[Nu^-] > (\gg) k_3$. (3) The absolute magnitude of k_3 must be low enough to allow the detection of **2** by a suitable technique, e.g. by conventional or stopped-flow spectrophotometry. The intermediates, **5-(OMe, SR)$^-$**, derived from reaction of **4-OMe** with thiolate ions are actually remarkably stable, both thermodynamically (with respect to reactants) and kinetically (with respect to conversion to products). For example, with RS^- = $HOCH_2CH_2S^-$, $K_1 = 7.65 \times 10^3$ M^{-1}, $k_1 = 3.90 \times 10^2$ M^{-1} s^{-1}, and $k_3 = 9.6 \times 10^{-6}$ s^{-1}.[5] Thus, even at $[RS^-]$ as low as 10^{-3} M we still have $K_1[RS^-] = 7.65 \gg 1$ and $k_1[RS^-] = 3.9 \times 10^{-1}$ s^{-1} $\gg k_3$, i.e. 88% of the substrate is converted to the intermediate with a half-life of approximately 1.5 s, while conversion of the intermediate to the product occurs with a half-life of approximately 19 h.

In view of the ease with which **5-(OMe, SR)$^-$** was detected,[5] it did not seem unreasonable to expect that an intermediate may also be observed in the reaction of **4-OMe** with strongly basic amines, despite their lower nucleophilicity compared to thiolate ions. In this paper we report a kinetic study of the reaction of **4-OMe** with pyrrolidine, piperidine, morpholine, and *n*-butylamine and of the reactions of **4-SEt**, **4-Cl**, and **4-I** with piperidine, all in 50% Me_2SO–50% water. Somewhat surprisingly, no intermediate could be observed in any of the reactions, not even the reactions of **4-OMe**. The possible reasons for this failure will be analyzed in detail.

Results

General Features. All kinetics were run under pseudo-first-order conditions, with a large excess of amine over the substrate. The solutions were prepared in 50% Me_2SO–50% water (v/v) at 20 °C, with the ionic strength maintained at 0.5 M with KCl. The reactions of **4-OMe** with piperidine, pyrrolidine, and morpholine, and the reactions of **4-SEt**, **4-Cl**, and **4-I** with piperidine, afforded the substitution product, **4-NRR′**, in quantitative yield, as evidenced by the UV spectra of infinity solution which matched those of authentic synthetic samples of the products. In the reaction of **4-OMe** with *n*-butylamine, the observed product was the hydroxide ion adduct of **4-NHBu**, $PhC(NHBu)(OH)C(Ph){=}NO_2^-$ **5-(NHBu, OH)$^-$**, which forms in a rapid postequilibrium.[7] Acidification of the reaction solution generated **4-NHBu**.

Rates were usually measured at or near λ_{max} of **4-NRR′** (420 nm for piperidine and morpholine, 410 nm for pyrrolidine) except for the *n*-butyl reaction where the "product", **5-(NHBu, OH)$^-$**, has a λ_{max} = 305 nm. In the piperidine, morpholine, and pyrrolidine reactions with **4-OMe**, a number of determinations were also made at 350 nm, where most of the absorption is due to **4-OMe**; within experimental error the results were the same as at 420 or 410 nm, indicating that there is no accumulation of an intermediate to detectable levels.

Reactions of 4-OMe with Piperidine and Morpholine. Rates were measured as a function of amine concentration at various pH values. At any given pH, 4–5 or more different amine concentrations were used. The results for piperidine (15 pH values ranging from pH 8.80 to 14.27) are summarized in Table S1 of the supplementary material,[9] the ones for morpholine (11 pH values ranging from pH 7.25 to 13.6) in Table S2 of the supplementary material.[9] Plots of k_{obsd}, the observed pseudo-first-order rate constants, versus free amine concentration were all linear. Some representative plots are shown in Figures 1 and 2. The slope of these plots are reported in Tables I

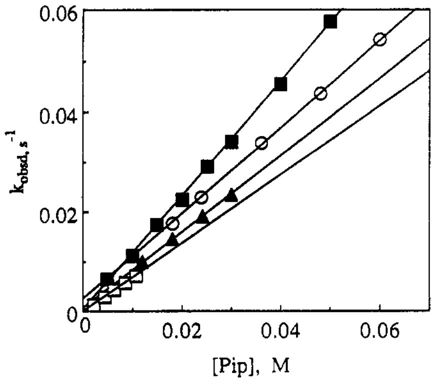


Figure 1. Reaction of **4-OMe** with piperidine. Representative plots of k_{obsd} vs piperidine concentration. (■) pH 12.02; (○) pH 10.10; (▲) pH 9.80; (□) pH 9.35. Data from Table S1 of the supplementary material.[9]

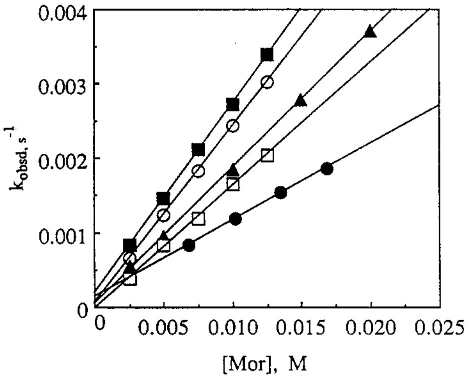


Figure 2. Reaction of **4-OMe** with morpholine. Representative plots of k_{obsd} vs morpholine concentration. (■) pH 11.18; (○) 10.91; (▲) 10.51; (□) pH 10.20; (●) pH 7.25. Data from Table S2 of the supplementary material.[9]

Table I. Slopes of Plots of k_{obsd} vs [Piperidine] for the Reaction of 4-OMe with Piperidine

pH	slope, M^{-1} s^{-1}	pH	slope, M^{-1} s^{-1}
14.27	1.01 ± 0.03	9.65	0.732 ± 0.020
12.02	1.02 ± 0.03	9.63	0.747 ± 0.005
10.26	0.950 ± 0.021	9.58	0.713 ± 0.015
10.10	0.862 ± 0.010	9.51	0.711 ± 0.005
9.97	0.807 ± 0.019	9.45	0.720 ± 0.012
9.80	0.764 ± 0.016	9.35	0.686 ± 0.013
9.72	0.746 ± 0.034	8.80	0.672 ± 0.013
9.69	0.741 ± 0.012		

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[5] Bernasconi, C. F.; Fassberg, J.; Killion, R. B., Jr.; Rappoport, Z. *J. Am. Chem. Soc.* (a) **1989**, *111*, 6862; (b) **1990**, *112*, 3169.

[6] It is assumed that the nucleophile is in large excess over the olefin.

[7] The evidence for the formation of **6-(NHBu, OH)$^-$** is discussed elsewhere.[8]

[8] Bernasconi, C. F.; Fassberg, J., to be published.

[9] See paragraph concerning supplementary material at the end of this paper.

Table II. Slopes of Plots of k_{obsd} vs [Morpholine] for the Reaction of 4-OMe with Morpholine

pH	slope, M^{-1} s^{-1}	pH	slope, M^{-1} s^{-1}
13.6	0.282 ± 0.008	10.20	0.165 ± 0.003
13.2	0.277 ± 0.005	9.72	0.110 ± 0.003
12.2	0.265 ± 0.005	8.72	0.101 ± 0.001
11.18	0.255 ± 0.002	7.46	0.102 ± 0.001
10.91	0.237 ± 0.002	7.25	0.102 ± 0.002
10.51	0.183 ± 0.002		

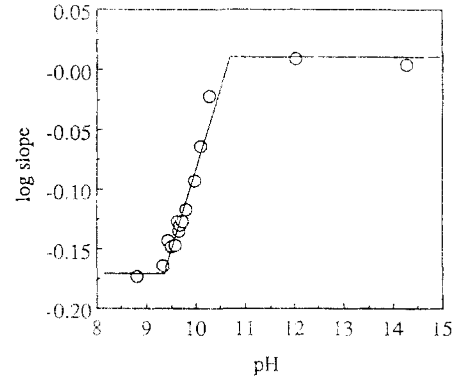
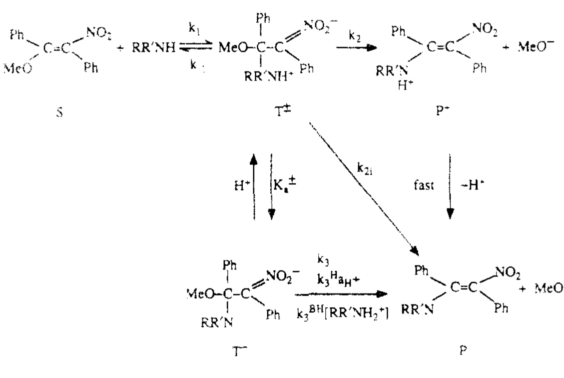


Figure 3. Reaction of **4-OMe** with piperidine. Slopes of the plots of k_{obsd} vs piperidine concentration (Table I) as function of pH.

Scheme I



and II while plots of log (slope) vs pH are shown in Figures 3 and 4.

The results may be discussed with reference to Scheme I. This scheme differs from similar schemes reported previously in three ways.[2] (1) The acid–base equilibrium between $T^{\pm}$ and T^- is assumed to be fast relative to the other steps, particularly with respect to leaving group departure. In view of the low nucleofugality of methoxide and the relatively slow rates of nitronate ion consuming reactions,[4c,10] this seems to be a reasonable assumption. (2) The possibility of general acid catalysis of leaving group departure from T^- ($k_3^{H}a_{H^+}$, $k_3^{BH}[RR'NH_2^+]$) is allowed for. (3) Allowance is also made for the possibility of an intramolecularly catalyzed pathway from $T^{\pm}$ to products (k_{2i}).

Applying the steady state assumption to $T^{\pm}$ and T^- yields eq 2 for the slope = k_{obsd}/[RR'NH],

$$\text{slope} = \frac{k_1[k_2' + (K_a^{\pm}/a_{H^+})(k_3^{H}a_{H^+} + k_3 + k_3^{BH}[RR'NH_2^+])]}{k_{-1} + k_2' + (K_a^{\pm}/a_{H^+})(k_3^{H}a_{H^+} + k_3 + k_3^{BH}[RR'NH_2^+])} \quad (2)$$

with

$$k_2' = k_2 + k_{2i} \quad (3)$$

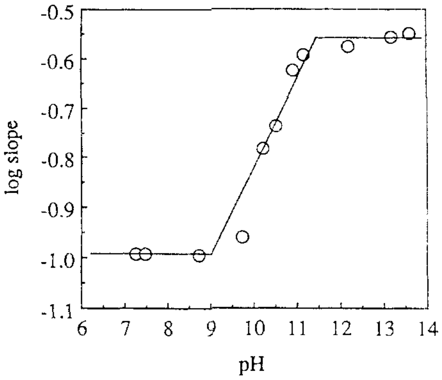


Figure 4. Reaction of **4-OMe** with morpholine. Slopes of the plots of k_{obsd} vs morpholine concentration (Table II) as a function of pH.

Table III. Parameters from Analysis of Eq 4 for the Reactions of 4-OMe with Piperidine and Morpholine

	piperidine	morpholine
k_1, M^{-1} s^{-1}	1.01 ± 0.03	0.27 ± 0.01
$K_1K_a^{\pm}k_3$, s^{-1}	(4.2 ± 1.1) × 10^{-10}	(1.7 ± 0.2) × 10^{-11}
$K_a^{\pm}k_3/k_{-1}$, M	(4.15 ± 1.1) × 10^{-10}	(6.3 ± 0.6) × 10^{-11}
$(k_2' + K_a^{\pm}k_3^{H})/k_{-1}$	1.82 ± 0.09	0.606 ± 0.030
$K_a^{\pm}k_3/(k_2' + K_a^{\pm}k_3^{H})$, M	(2.3 ± 0.7) × 10^{-10}	(1.04 ± 0.15) × 10^{-10}
pH^a	~9.64	~9.98

[a] pH at which $K_a^{\pm}k_3/a_{H^+} \approx k_2' + K_a^{\pm}k_3^{H}$.

The linearity of the plots of k_{obsd} vs [RR'NH] indicates that the $k_3^{BH}[RR'NH_2^+]$ term is negligible; if it were important, upward curvature should have been observed. This allows simplification of eq 2 to eq 4

$$\text{slope} = \frac{k_1[k_2' + K_a^{\pm}k_3^{H} + (K_a^{\pm}/a_{H^+})k_3]}{k_{-1} + k_2' + K_a^{\pm}k_3^{H} + (K_a^{\pm}/a_{H^+})k_3} \quad (4)$$

The variations in the slopes with pH (Tables I and II, Figures 3 and 4) are determinated by the size of the $K_a^{\pm}k_3/a_{H^+}$ term relative to k_{-1} and $k_2' + K_a^{\pm}k_3^{H}$ and can be understood by considering the following three special cases of eq 4.

Case I. At very high pH, $K_a^{\pm}k_3/a_{H^+} \gg k_{-1}$ which makes $k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+} \gg k_{-1}$ and simplifies eq 4 to slope $= k_1$.

This situation in which nucleophilic attack is rate limiting seems to prevail at pH values above ≈11.0 in the piperidine reaction, above ≈11.5 in the morpholine reaction. The resulting k_1 values are reported in Table III.

Case II. Below pH ~11.0 for piperidine and below pH ~11.5 for morpholine, the slopes become smaller than k_1. This implies $k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+} \leq k_{-1}$ and eq 4 cannot be simplified unless it is assumed that $K_a^{\pm}k_3/a_{H^+} \gg k_2' + K_a^{\pm}k_3^{H}$ so that eq 4 reduces to

$$\text{slope} = \frac{k_1(K_a^{\pm}/a_{H^+})k_3}{k_{-1} + (K_a^{\pm}/a_{H^+})k_3} \quad (5)$$

As our calculations show, $K_a^{\pm}k_3/a_{H^+} \approx k_2' + K_a^{\pm}k_3^{H}$ at pH ≈9.64 for the piperidine reaction and at pH ≈9.98 for the morpholine reaction. Hence eq 5 becomes a reasonable approximation above pH ~10.3 for the piperidine reaction and above pH ~10.6 for the morpholine reaction. We have therefore applied this equation in these pH ranges which, after inversion, becomes

$$\text{slope}^{-1} - k_1^{-1} = \frac{a_{H^+}}{K_1K_a^{\pm}k_3} \quad (6)$$

with $K_1 = k_1/k_{-1}$. The resulting $K_1K_a^{\pm}k_3$ values from plots according to eq 6 (not shown) are reported in Table III.

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(10) (a) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.

The large experimental error in $K_1K_a^{\pm}k_3$ for the piperidine reaction reflects the small range in slope values, due to a relatively large ratio $(k_2' + K_a^{\pm}k_3^{H})/k_{-1}$ (see below).

Case III. At low pH one eventually reaches the point where $K_a^{\pm}k_3/a_{H^+} \ll k_2' + K_a^{\pm}k_3^{H}$. The slope is no longer pH dependent and eq 4 becomes

$$\text{slope} = \frac{k_1(k_2' + K_a^{\pm}k_3^{H})}{k_{-1} + k_2' + K_a^{\pm}k_3^{H}} \tag{7}$$

This limiting situation is reached at pH ≤ 9 in both reactions. Rearranging eq 7 leads to

$$\left(\frac{k_1}{\text{slope}} - 1\right)^{-1} = \frac{k_2' + K_a^{\pm}k_3^{H}}{k_{-1}} \tag{8}$$

Values of the ratio $(k_2' + K_a^{\pm}k_3^{H})/k_{-1}$ are summarized in Table III.

There are three additional entries in Table III. One is $K_a^{\pm}k_3/k_{-1}$, obtained from $K_1K_a^{\pm}k_3$ after dividing by k_1. Another is the ratio $K_a^{\pm}k_3/(k_2' + K_a^{\pm}k_3^{H})$, calculated as $(K_a^{\pm}k_3/k_{-1})/[(k_2' + K_a^{\pm}k_3^{H})/k_{-1}]$. The third, derived from this latter ratio, is the pH for which $K_a^{\pm}k_3/a_{H^+} \approx (k_2' + K_a^{\pm}k_3^{H})$ holds.

Reactions of 4-OMe with Pyrrolidine and *n*-Butylamine. Only a limited number of experiments were performed with pyrrolidine and *n*-butylamine reacting with **4-OMe**. It was hoped that the somewhat higher nucleophilicity of pyrrolidine compared to that of piperidine might enhance the likelihood of detecting an intermediate. Rates were determined at pH 13.9 and 11.22, with the k_{obsd} values summarized in Table S3 of the supplementary material.[9] The linearity of the plots of k_{obsd} vs pyrrolidine concentration, and the fact that k_{obsd} values measured at 410 nm (product) were the same as those measured at 350 nm showed that no intermediate accumulates to detectable levels. The slope = 3.95 M^{-1} s^{-1} of the plot of k_{obsd} vs pyrrolidine concentration at pH 13.9 is assumed to be k_1 while the slightly lower slope (3.19 M^{-1} s^{-1}) at pH 11.22 indicates that $k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+} \le k_{-1}$ (eq 4), as for the piperidine and morpholine reactions.

The reaction of **4-OMe** with *n*-butylamine was only studied at pH 14.6 (Table S3[9]); it yielded k_1 = 1.45 M^{-1} s^{-1}.

Reactions of 4-Cl, 4-I, and 4-SEt with Piperidine. The reactions of **4-Cl** and **4-I** were studied at pH 11.02 and that of **4-SEt** at pH 11.02 and 10.50. The results are reported in Table S4 of the supplementary material;[9] they afford $k_1 = 1.81 \times 10^{-2}$ M^{-1} s^{-1} (**4-Cl**), 7.40×10^{-4} M^{-1} s^{-1} (**4-I**), and 9.08×10^{-5} M^{-1} s^{-1} (**4-SEt**). At piperidine concentrations above 0.3 M the plots of k_{obsd} vs piperidine concentration in the reactions of **4-Cl** and particularly of **4-I** showed some downward curvature (Figure 5). Since the rates were measured by monitoring product formation, such curvature could, in principle, indicate the presence of an accumulating intermediate. However, since no such accumulation was observed in the reactions of **4-OMe**, which has a much poorer leaving group, the curvature is attributed to a medium effect due to the high concentration of the amine. We shall return to this point in the Discussion.

Discussion

Why Has No Intermediate Been Detected? In the reactions of **4-Cl**, **4-I**, and **4-SEt** with piperidine there was no expectation that an intermediate would be detectable because of the high nucleofugality of the leaving groups, especially that of chloride and iodide. On the other hand, based on the precedent of the reaction of thiolate ions with **4-OMe**,[5] it seemed quite possible that an intermediate would accumulate to detectable levels in the reaction of **4-OMe** with amines. However, no such intermediate was observed, i.e. both intermediates that are part of the reaction scheme ($T^{\pm}$ and T^- in Scheme I) appear to remain at the steady-state level under all reaction conditions.

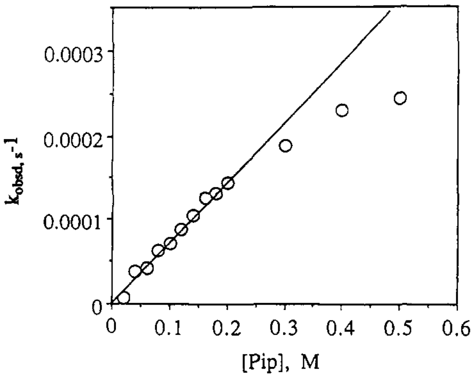


Figure 5. Reaction of **4-I** with piperidine. Plot of k_{obsd} vs piperidine concentration at pH 11.02. Data from Table S4 of the supplementary material.[9]

In order to understand this result it is useful to define the conditions that are necessary for the detection of $T^{\pm}$ and/or T^-. They are conceptually the same as for the detection of **2** in the simpler system of eq 1, i.e. (1) the equilibrium of intermediate formation must be favorable, (2) the conversion of the intermediate(s) to products must be slower than their formation, and (3) the absolute rate of the product forming process(es) must be low enough to allow detection by a suitable technique.

Condition 1 can be expressed as

$$\left(K_1 + \frac{K_1K_a^{\pm}}{a_{H^+}}\right)[\text{RR'NH}] > (\gg)\ 1 \tag{9}$$

while condition 2 takes on the form of eq 10

$$k_1[\text{RR'NH}] > (\gg)\ \frac{k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+}}{1 + K_a^{\pm}/a_{H^+}} \tag{10}$$

At pH ≫ $pK_a^{\pm}$ eqs 9 and 10 simplify to eqs 11 and 12, respectively.

$$(K_1K_a^{\pm}/a_{H^+})[\text{RR'NH}] > (\gg)\ 1 \tag{11}$$

$$k_1[\text{RR'NH}] > (\gg)\ (k_2' + K_a^{\pm}k_3^{H})(a_{H^+}/K_a^{\pm}) + k_3 \tag{12}$$

At sufficiently high pH we have $(k_2' + K_a^{\pm}k_3^{H})a_{H^+}/K_a^{\pm} \ll k_3$ so that eq 12 further simplifies to

$$k_1[\text{RR'NH}] > (\gg)\ k_3 \tag{13}$$

Note that under the conditions of pH ≫ $pK_a^{\pm}$ it would be the T^- form of the intermediate that is detectable.

At pH ≪ $pK_a^{\pm}$ eqs 9 and 10 are reduced to eqs 14 and 15, respectively.

$$K_1[\text{RR'NH}] > (\gg)\ 1 \tag{14}$$

$$k_1[\text{RR'NH}] > (\gg)\ k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H}^{+} \tag{15}$$

Under these conditions it would be $T^{\pm}$ which is the dominant form of the intermediate. At low enough pH to render $k_2' + K_a^{\pm}k_3^{H} \gg K_a^{\pm}k_3/a_{H^+}$, eq 15 becomes

$$k_1[\text{RR'NH}] > (\gg)\ k_2' + K_a^{\pm}k_3^{H} \tag{16}$$

The chances to meet the requirements of eq 14 are slim because of too low a value of K_1 (see below). On the other hand the conditions for eq 11 can be achieved because $K_a^{\pm}/a_{H^+} \gg 1$ in eq 11, i.e. the equilibrium for adduct formation can be pulled toward T^- at high pH, even if K_1

is relatively low. Depending on the pH this feature may either partially or completely compensate for the fact that the Lewis basicity of amines towards Lewis acids is lower than that of thiolate ions of the same pK_a.[4c,11]

The following calculations illustrate the point. The equilibrium constant, K_1, for $HOCH_2CH_2S^-$ addition to PhCH=CPh(NO_2) (**4-H**) is 8.16 × 10^6 M^{-1},[12] while K_1 for piperidine addition to **4-H** is 45 M^{-1}.[13] If one assumes that the ratio $K_1^{Pip}/K_1^{RS^-}$ for addition to **4-OMe** is the same as for addition to **4-H**, one calculates $K_1^{Pip} = 4.22 \times 10^{-2}$ M^{-1} for piperidine addition to **4-OMe**. The $pK_a^{\pm}$ value is expected to be lower than $pK_a^{\pm} = 9.73$[13] for the piperidine adduct of **4-H** by approximately 2 units. This estimate is based on an estimated acidifying effect of 1.88 pK_a units[14] for the change from $(CH_3)_2NH_2^+$ to $HOCH_2N^+H_2CH_3$, and the fact that σ_I for MeO is slightly larger than for HO.[15] With $pK_a^{\pm} \approx 7.73$ and $K_1 \approx 4.22 \times 10^{-2}$ M^{-1}, $K_1K_a^{\pm} \approx 7.86 \times 10^{-10}$ and thus the $K_1K_a^{\pm}[RR'NH]/a_{H^+}$ term should be ≈5.27 × 10^4 under the most favorable conditions used in this study ([RR'NH] = 0.36 M, pH 14.27). K_1 and $pK_a^{\pm}$ for the morpholine reaction may be estimated by assuming that the K_1^{Mor}/K_1^{Pip} and $K_a^{\pm}(\mathrm{Mor})/K_a^{\pm}(\mathrm{Pip})$ ratios for the adducts derived from **4-OMe** are the same as those derived from **4-H**, i.e. 7.56 × 10^{-3} and 2.95 × 10^2, respectively. This affords $K_1 \approx 3.19 \times 10^{-4}$ M, $pK_a^{\pm} \approx 5.26$, $K_1K_a^{\pm} \approx 1.75 \times 10^{-9}$ and the $K_1K_a^{\pm}[RR'NH]/a_{H^+}$ term should be ≈2.84 × 10^4 under the most favorable conditions used in our study ([RR'NH] = 0.408 M, pH 13.60).

Even though further analysis discussed under Estimates of Rate Constants indicates that K_1 for the piperidine and morpholine adducts ($T^{\pm}$) must be lower than the above estimates of 4.22 × 10^{-2} and 3.19 × 10^{-4} M by at least a factor of 57, presumably because of stronger steric crowding in the piperidine and morpholine adducts than in the $HOCH_2CH_2S^-$ adduct, it is virtually inconceivable that this steric effect could reduce K_1 by a large enough factor that $K_1K_a^{\pm}[RR'NH]/a_{H^+}$ is no longer ≫ 1. And for the reaction of *n*-butylamine the crowding in the adduct is unlikely to be more severe than in the $HOCH_2CH_2S^-$ adduct and could actually be less.

We can draw two conclusions from the above considerations. (1) K_1 is too small for the conditions of eq 14 to be met, even for pyrrolidine whose K_1 value is expected to be somewhat larger than for piperidine. Hence the zwitterionic adduct, $T^{\pm}$, will not be detectable irrespective of possible adherence to eq 16. (2) The reason why the *anionic* adduct, T^-, is not detectable is not that it is thermodynamically insufficiently stable relative to reactants. It is because its conversion to products is too fast, i.e. the conditions for eq 13 are not achieved. If we assume that traces of T^- would have been detected if $k_1[RR'NH]/k_3$ were at least 0.2, we can set a lower limit for the k_1/k_3 ratios based on the highest amine concentrations used: $k_1/k_3 \leq 0.56$ M^{-1} for piperidine ($[\mathrm{Pip}]_{max}$ = 0.36 M) and $k_1/k_3 \leq 0.49$ M^{-1} for morpholine ($[\mathrm{Mor}]_{max}$ = 0.408 M).

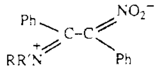
In the reaction of **4-OMe** with $HOCH_2CH_2S^-$ the k_1/k_3 ratio is 4.06 × 10^7 M^{-1}. Hence the k_1/k_3 ratios for the piperidine and morpholine reactions are seen to be at least 10^8-fold lower than for the thiolate ion reaction.

Table IV. Upper and Lower Limits of Equilibrium and Rate Constants for Reactions of 4-OMe with Piperidine and Morpholine in 50% Me$_2$SO–50% Water at 20 °C (μ = 0.5 M)

	piperidine	morpholine
K_1, M^{-1}	≤7.44 × 10^{-4}	≤5.62 × 10^{-6}
$pK_a^{\pm}$	≈7.73	≈5.26
$K_1K_a^{\pm}$	≤1.38 × 10^{-11}	≤3.09 × 10^{-11}
k_1, M^{-1} s^{-1}	1.01 ± 0.03	0.27 ± 0.01
k_3, s^{-1}	≥30.4	≥0.55
k_1/k_3, M^{-1}	≤3.32 × 10^{-2}	≤0.49
k_{-1}, s^{-1}	≥1.36 × 10^3	≥4.80 × 10^4
$k_2' + K_a^{\pm}k_3^H$, s^{-1}	≥2.48 × 10^3	≥2.91 × 10^4
k_2',[a] s^{-1}	≥2.48 × 10^3	≥2.91 × 10^4
k_3^H,[b] M^{-1} s^{-1}	≥1.31 × 10^{11}	≥5.30 × 10^9

[a] Assuming $k_2' \gg K_a^{\pm}k_3^H$. [b] Assuming $k_2' \ll K_a^{\pm}k_3^H$.

One relatively minor factor responsible for the low k_1/k_3 ratios is the lower nucleophilicity of amines compared to thiolate ions of comparable pK_a.[4b,c,16] For example, k_1 = 1.01 M^{-1} s^{-1} for piperidine addition to **4-OMe** is nearly 400-fold lower than k_1 = 3.90 × 10^2 M^{-1} s^{-1} for $HOCH_2CH_2S^-$ addition.[5] However, the *major* factor in making the k_1/k_3 ratios small must be a very much faster methoxide ion expulsion from T^- (k_3 in Scheme I) than from the corresponding thiolate adduct **5-(OMe, SR)**$^-$ (k_3 in eq 1). We attribute the accelerated methoxide ion expulsion to a stronger "push". This stronger push seems to be a consequence of both a stronger resonance stabilization of the amine product (**6**) compared to the thiolate product (**7**), and a transition state in which this push is nearly fully developed (β_{push} = 0.71, see below).[17] A contributing factor in the reactions with secondary amines may be the greater steric crowding in T^- compared to **5-(OMe, SR)**$^-$, but this effect cannot be invoked for reactions with primary amines (*n*-butylamine). On the other hand, the reduced crowding in the *product* derived from primary amines should allow better π-overlap and lead to a stronger resonance effect (**6**).



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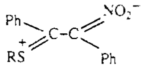

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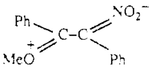

8

Estimates of Rate and Equilibrium Constants. Even though k_{-1}, k_2, k_{2i}, k_3, and k_3^H in Scheme I cannot be determined directly, limits for most of them can be estimated. One starting point is the upper limit for the k_1/k_3 ratio estimated above for the morpholine reaction (≤0.49 M^{-1}). Since k_1 is known (0.27 M^{-1} s^{-1}), this affords a lower limit for k_3 (≥0.55 s^{-1}). From $K_1K_a^{\pm}k_3$ (Table III) we now obtain $K_1K_a^{\pm} \leq 3.09 \times 10^{-11}$. Assuming our estimate for $pK_a^{\pm}$ (≈5.26) is reliable, this affords $K_1 \leq 5.62 \times 10^{-6}$ M^{-1}, a value that is ≥56.7-fold lower than the estimate (3.19 × 10^{-4} M^{-1}) based on the comparison with the reactions of **4-H**. Our calculation thus indicates that the steric reduction of K_1 is at least 56.7-fold. We can now also estimate lower limits for k_{-1} and $k_2' + K_a^{\pm}k_3^H$ (from $(k_2' + K_a^{\pm}k_3^H)/k_{-1}$ in Table III). The various parameters are summarized in Table IV.

In principle, one may go through a similar exercise for the piperidine reaction, i.e. start with $k_1/k_3 \leq 0.56$ based on the criterion that, if $k_1[RR'NH]/k_3$ were ≥0.2, T^- should have been detected. However, the upper limit of the K_1 value (≤1.25 × 10^{-2} M^{-1}) that is obtained from this procedure is only 3.4-fold lower than K_1 ≈4.22 × 10^{-2} M^{-1}

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[11] (a) Sander, E. G.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *90*, 6154. (b) Hine, J.; Weimar, R. D., Jr. *Ibid.* **1965**, *87*, 3387. (c) Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; p 225. (d) Pearson, R. G. *Surv. Prog. Chem.* **1969**, *5*, 1. (e) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827.

[12] Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506.

[13] Bernasconi, C. F.; Renfrow, R. A. *J. Org. Chem.* **1987**, *52*, 3035.

[14] Fox, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 1436.

[15] Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum: New York, 1978; p 439.

[16] For a recent review, see: Rappoport, Z. *Adv. Chem. Ser.* **1987**, *215*, 399.

[17] When the pushing group is a thiolate, β_{push} appears to be quite small, e.g. for Ph(RS, R'S)C—CPh(NO_2^-) → Ph(RS)C=CPh(NO_2) + $R'S^-$ β_{push} values of ≈0.18 to 0.29 may be estimated from data in ref 5b.

Table V. Rate Constants for Nucleophilic Attack (k_1) by Amines on Ph(LG)C═CPh(NO_2) in 50% Me_2SO–50% Water at 20 °C (μ = 0.5 M)[a]

LG	piperidine	morpholine	pyrrolidine	n-$BuNH_2$
H[b]	117	17.6		
OMe	1.01 ± 0.03	0.27 ± 0.01	3.95 ± 0.16	1.45 ± 0.02
Cl	1.81×10^{-2}			
I	7.40×10^{-4}			
SEt	9.08×10^{-5}			

[a] In units of $M^{-1}\ s^{-1}$. [b] Reference 13.

estimated from the comparison with **4-H**, suggesting a much smaller steric effect than in the morpholine reaction. Since the steric effects in the two reactions should be very similar, the above procedure for estimating limits of rate and equilibrium constants appears to greatly underestimate the steric effect on the piperidine reaction. A better procedure is therefore to assume that the steric reduction of K_1 in the piperidine reaction is equal to that in the morpholine reaction (≥56.7-fold), i.e. to assume a $K_1 \leq 7.44 \times 10^{-4}$ M and to calculate the limits for k_{-1} from K_1, and then obtain the limits for k_3 from $K_1 K_a^{\pm} k_3$, etc. The parameters reported in Table IV for the piperidine reaction are based on this latter procedure.

Note that there is another advantage to using the above procedure for estimating limits for the various rate and equilibrium constants for the piperidine reaction. It assures that the numerical factor by which these limits differ from their actual values is the same for the piperidine and the morpholine reactions. This means that all *ratios* that are calculated from these limits such as $K_1^{\mathrm{Pip}}/K_1^{\mathrm{Mor}}$, $k_{-1}^{\mathrm{Pip}}/k_{-1}^{\mathrm{Mor}}$, $k_3^{\mathrm{Pip}}/k_3^{\mathrm{Mor}}$, etc. represent the true ratios.

Structure–Reactivity Relationships. A. Nucleophilic Attack. k_1 values for the various reactions determined in this study are summarized in Table V, along with previously measured rate constants for piperidine and morpholine addition to **4-H**. The most important factor affecting k_1 appears to be steric crowding in the adduct. This is seen, e.g., in the fact that k_1 for n-$BuNH_2$ is larger than for piperidine, which contrasts with the usual reactivity order piperidine >(≫) n-$BuNH_2$ ($k_1^{\mathrm{Pip}}/k_1^{n\text{-}\mathrm{BuNH_2}}$ = 14.7 for α-cyano-4-nitrostilbene,[18] 4.82 for benzylidene Meldrum's acid,[19] 36.8 for β-nitrostyrene[20]). It is also seen in the large decrease in k_1 with increasing size of the leaving group, i.e. H < OMe < Cl < I, although part of the reason why **4-OMe** is less reactive than **4-H** must be due to resonance stabilization of **4-OMe** (**8**). A small degree of resonance stabilization of **4-SEt** (**7**) may also be partially responsible for the fact that k_1 for **4-SEt** is lower than for **4-I**.

These steric effects on k_1 are consistent with the conclusion reached in the previous section that the equilibrium constants for piperidine and morpholine addition to **4-OMe** are reduced at least 56.7-fold (relative to K_1 for $HOCH_2CH_2S^-$ addition) by steric crowding in the intermediate.

A β_{nuc}(d log k_1/d$\mathrm{p}K_a^{\mathrm{R_2NH_2^+}}$) of 0.25, and a normalized $\beta^{\mathrm{n}}_{\mathrm{nuc}}$(d log k_1/d log K_1) of 0.27 can be calculated from k_1 for the piperidine and morpholine reaction with **4-OMe**. For the k_{-1} step the corresponding parameters are β_{lg}(d log k_{-1}/d $\mathrm{p}K_a^{\mathrm{R_2NH_2^+}}$) = −0.67[21] and $\beta^{\mathrm{n}}_{\mathrm{lg}}$(d log k_{-1}/d log K_1) = −0.73.[21] Our β_{nuc} value compares with β_{nuc} = 0.35 for the reaction of **4-H** with the same amines[13] under identical conditions. It is noteworthy that β_{nuc} for thiolate ion addition to **4-OMe** (0.09)[5] is also lower than β_{nuc} for thiolate addition to **4-H** (0.16);[12] the possible relevance (or lack thereof) of these findings to the reactivity–selectivity principle[22] have been discussed previously.[5]

B. Intrinsic Rate Constant for Piperidine and Morpholine Addition to 4-OMe. If one assumes that the lower limits for K_1 in Table IV are the *actual* K_1 values, one may determine an intrinsic rate constant ($k_0 = k_1 = k_{-1}$ when $K_1 = 1$) for addition of piperidine and morpholine to **4-OMe** by extrapolating a plot of log k_1 vs log K_1 to log K_1 = 0 (plot not shown). This procedure yields log k_0 = 0.85. Since the K_1 values in Table IV are upper limits, this means that 0.85 is a lower limit for log k_0, i.e. log $k_0 \geq 0.85$. This compares with log k_0 = 1.43 for the reaction of piperidine and morpholine with **4-H**.[13] In the reaction of thiolate ions with the same substrates we found that log k_0 for **4-OMe** (2.16)[5] is also lower than log k_0 = for **4-H** (3.43).[12] The lower intrinsic rate constants for the reaction of nucleophiles with **4-OMe** compared to **4-H** is consistent with resonance stabilization (**7**) in **4-OMe**. Resonance effects typically reduce k_0 because their development (in a product) generally lags behind bond formation, or their loss (from a reactant) is ahead of bond formation.[10]

C. Expulsion of Methoxide from $T^{\pm}$ and T^-. The processes of expulsion of methoxide from $T^{\pm}$, to form P^+ (k_2), expulsion of methoxide from $T^{\pm}$ with *intra*molecular general acid catalysis (k_{2i}), and expulsion of methoxide from T^- with hydronium ion catalysis (k_3^{H}), are kinetically indistinguishable. However, the following considerations demonstrate that the k_{2i} pathway must be the preferred one, i.e., $k_2' \gg K_a^{\pm} k_3^{\mathrm{H}}$ and $k_{2i} \gg k_2$.

There are three arguments that show the lower limits for k_3^{H} (Table IV), calculated under the assumption that $K_a^{\pm} k_3^{\mathrm{H}} \gg k_2'$, to be unreasonable. (1) The hydronium ion catalyzed expulsion of methoxide ion from Ph(OMe)(OMe)C(Ph)═NO_2^- (**5-(OMe, OMe)$^-$**) has a statistically corrected[24] k_3^{H} value of 373 $M^{-1}\ s^{-1}$.[8] This value is ($\geq 3.5 \times 10^8$)-fold lower than the k_3^{H} value in Table IV for hydronium ion catalyzed methoxide loss from T^- derived from piperidine. Even though T^- derived from piperidine is expected to expel methoxide ion faster than **5-(OMe, OMe)$^-$** because it is more crowded and resonance stabilization of the product **4-NRR′** (**6**) should be appreciably stronger than in **4-OMe** (**8**), it is difficult to see how these two factors could lead to a ($\geq 3.5 \times 10^8$)-fold acceleration of leaving group departure.[25] (2) The absolute value of k_3^{H} in the piperidine reaction ($\geq 1.31 \times 10^{11}\ M^{-1}\ s^{-1}$) seems

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(18) Bernasconi, C. F.; Murray, C. J.; Fox, J. P.; Carré, D. J. *J. Am. Chem. Soc.* **1983**, *105*, 4349.

(19) (a) Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329. (b) Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 5251.

(20) (a) Bernasconi, C. F.; Carré, D. J.; Fox, J. P. In *Techniques and Applications of Fast Reactions in Solution*; Gettins, W. J.; Wyn-Jones, E., Eds.; Reidel: Dordrecht, Holland, 1979; p 453. (b) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. *J. Am. Chem. Soc.* **1986**, *108*, 4541.

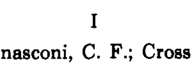
(21) As mentioned under Estimates of Rate and Equilibrium Constants the *ratios* $K_1^{\mathrm{Pip}}/K_1^{\mathrm{Mor}}$, $k_{-1}^{\mathrm{Pip}}/k_{-1}^{\mathrm{Mor}}$, $k_3^{\mathrm{Pip}}/k_3^{\mathrm{Mor}}$ are accurate because the limits for K_1, k_{-1}, k_3, etc. in Table IV differ from their true values by a constant factor which is independent of the amine. Hence the $\beta_{\mathrm{lg}}(\beta^{\mathrm{n}}_{\mathrm{lg}})$ and β_{push} values derived therefrom are also accurate.

(22) (a) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *16*, 69. (b) Reactivity–Selectivity issue of *Isr. J. Chem.* **1985**, *26*, (4).

(23) (a) Johnson, C. D. *Tetrahedron* **1980**, *36*, 3461. (b) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288. (c) Arnett, E. M.; Reich, R. *Ibid.* **1980**, *102*, 5892. (d) Bordwell, F. G.; Hughes, D. H. *J. Org. Chem.* **1980**, *45*, 3314; **1982**, *47*, 3224.

(24) Experimental rate constant divided by 2.

(25) In a somewhat comparable case, the alkoxide ion departure from the spiro Meisenheimer complexes I and II, the rate for the *N*-methylethanolamine derivative was 5.35-fold faster (after statistical correction) than for the ethylene glycol derivative.[26]



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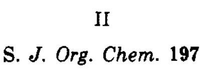

II

(26) Bernasconi, C. F.; Cross, H. S. *J. Org. Chem.* **1974**, *39*, 1054.

to be higher than what is commonly accepted to be a diffusion limited rate constant.[27] (3) No general acid catalysis by piperidinium or morpholinium ion (k_3^{BH}[RR′NH$_2^+$] term in Scheme I) was detected, which contrasts with the observation of substantial general acid catalysis of methoxide loss from **5-(OMe, OMe)**$^-$.[8] Hence we conclude that $k_2' \gg K_a^{\pm}k_3^{H}$.

Regarding k_2', if it referred to k_2 ($k_2 \gg k_{2i}$), one would obtain k_2/k_3 ratios of 81.7 (piperidine) and 5.28 × 10^4 (morpholine). These ratios would imply that leaving group expulsion from T$^-$ (k_3), which occurs with push by the developing resonance (**6**) is slower than expulsion from T$^{\pm}$(k_2) without such push, a nonsensical result. It would also be hard to understand why k_2 for the morpholine reaction is 11.8-fold larger than for the piperidine reaction, since the stronger electron withdrawing effect of the morpholine moiety should lead to a *lower* k_2. On the other hand, if k_2' refers to k_{2i}, ($k_{2i} \gg k_2$) the fact that k_{2i} is larger than k_3 is easily understood in terms of intramolecular acid catalysis which assists the departure of the leaving group. The larger k_{2i} value for the morpholine reaction compared to that of the piperidine reaction also finds a natural explanation since the more acidic ammonium proton in the morpholine adduct provides stronger intramolecular catalysis than the ammonium proton in the piperidine adduct. The $k_{2i}^{Mor}/k_{2i}^{Pip}$ ratio of 11.8 is equivalent to a Brønsted α value of 0.43 for intramolecular acid catalysis.

The results obtained by Rappoport and Peled[2b] for the reaction of piperidine and morpholine with 1,1-dicyano-2-[*p*-(dimethylamino)phenyl]-2-(trifluoroethoxy)ethylene in acetonitrile permit a similar conclusion. The reaction was found to obey the rate law of eq 17

$$k_{obsd} = k' + k''[\mathrm{RR'NH}] \qquad (17)$$

with k_{obsd} being the observed *second*-order rate constant. The relatively small k'(Pip)/k'(Mor) ratios (e.g. 7.38 at 30 °C) are consistent with the reaction following Scheme I and the assumption that $k_{2i} \gg k_2$. This assumption implies that $k' = k_1k_{2i}/k_{-1}$. The small k'(Pip)/k'(Mor) ratios arise from a partial compensation of a large $(k_1/k_{-1})^{Pip}/(k_1/k_{-1})^{Mor}$ ratio by $k_{2i}^{Pip}/k_{2i}^{Mor} <(\ll) 1$.

Turning to the k_3 process, we note that $k_3^{Pip}/k_3^{Mor} = 55.3$ which corresponds to a $\beta_{push} = 0.71$.[21] This high value of β_{push} indicates that the resonance effect (**6**) has made very substantial progress at the transition state. This is consistent with our earlier conclusion regarding the importance of this push in accounting for the large acceleration of the k_3 step relative to that of the reaction of **4-OMe** with HOCH$_2$CH$_2$S$^-$.[17]

It is interesting that β_{push} (0.71) is so much larger than β_{nuc} (0.25). It implies that the k_1/k_3 ratio increases as the amine becomes less basic. Thus k_1/k_3 for the morpholine reaction is 14.7-fold larger than for the piperidine reaction. This surprising result leads to the prediction that the best chances of detecting the intermediate T$^-$ will be in reactions with very *weakly* rather than strongly basic amines. Work aimed at checking this prediction is in progress in our laboratory.

D. Could the Intermediate Possibly Accumulate in the Reactions of 4-Cl or 4-I or Could Leaving Group Departure Be Rate Limiting? In the reactions of **4-Cl** and **4-I** with piperidine the plots of k_{obsd} vs amine concentration display downward curvature. Such a plot is shown in Figure 5 for the reaction of **4-I**. Since the reactions were monitored at λ_{max} of the product, this curvature is, in principle, consistent with the accumulation of an intermediate. According to this interpretation the plateau values that may be calculated by extrapolation would correspond to k_3 in a scheme analogous to Scheme I. They are $k_3 \approx 2 \times 10^{-2}$ s^{-1} for **4-Cl**, $\approx 3 \times 10^{-4}$ s^{-1} for **4-I**. These k_3 values are several orders of magnitude lower than k_3 in the reaction of piperidine with **4-OMe** ($k_3 \geq 30.4$). Since Cl and I are generally known to be much better leaving groups than methoxide for the expulsion from $\bar{\mathrm{C}}$-C-LG carbanions,[28] the above analysis cannot possibly be correct and the curvature in the plots of k_{obsd} vs amine concentration must be attributed to a medium effect.

A related question is whether in the reactions of **4-Cl** and **4-I** with piperidine and morpholine, leaving-group departure could possibly be rate limiting without leading to the accumulation of an intermediate. Rappoport and Topol[2c] have raised this possibility on the basis of the high k_{Cl}/k_I ratios (20.1 to 23.7) in these reactions in ethanol which, incidentally, are very close to the k_{Cl}/k_I ratio of 24.5 for the piperidine reaction in the current study and which we have equated with k_1(Cl)/k_1(I) (see Table V). In view of the fact that k_{Cl}/k_I ratios in nucleophilic vinylic substitutions are usually close to unity, Rappoport and Topol suggested that the high ratios might possibly be explained if k_{Cl}/k_I were given by eq 18 instead of k_1(Cl)/k_1(I). The absence of base catalysis typical for reactions of amines in which leaving group departure is rate limiting would have to be explained by assuming that $k_2' \gg K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+}$.

$$k_{Cl}/k_I = [k_1(\mathrm{Cl})/k_1(\mathrm{I})][k_2(\mathrm{Cl})/k_2(\mathrm{I})][k_{-1}(\mathrm{I})/k_{-1}(\mathrm{Cl})] \qquad (18)$$

The results of the present study render such an interpretation unattractive. According to eq 4, leaving group departure is rate limiting (or partially so) if $k_{-1} >(\gg) k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+}$. The $k_2' + K_a^{\pm}k_3^{H} + K_a^{\pm}k_3/a_{H^+}$ term is smallest at low pH where $K_a^{\pm}k_3/a_{H^+}$ becomes negligible. Under these conditions $(k_2' + K_a^{\pm}k_3^{H})/k_{-1} = 1.82$ and 0.606 (Table III) in the reactions of **4-OMe** in 50% Me$_2$SO–50% water with piperidine and morpholine, respectively. These ratios show that even with the very poor nucleofuge methoxide, leaving group departure is only partially rate limiting. The change from 50% Me$_2$SO–50% water to ethanol should not have a large effect on these ratios since the charge type of the reactions to be compared is the same.[29] Hence with the much better leaving groups Cl and I it is unlikely that leaving group departure could be rate limiting, and the large k_{Cl}/k_I ratios simply reflect a large steric effect on k_1 as discussed earlier.

Conclusions. (1) In view of the great ease with which the intermediate in the reaction of **4-OMe** with HOCH$_2$CH$_2$S$^-$ was observable, it is somewhat surprising that no intermediate could be observed in the reaction of **4-OMe** with amines. We have shown that this failure cannot be attributed to an insufficient thermodynamic stability of T$^-$ relative to reactants, but that it is a consequence of a relatively low rate of formation of T$^{\pm}$ (k_1), coupled with a fast conversion of T$^-$ to products (k_3). This high value of k_3 compared to that in the thiolate ion reaction is mainly due to a strong push by the developing resonance in the product (**6**). This push is associated with a $\beta_{push} = 0.71$ and is so strong that the k_1/k_3 ratio, and with it the chance

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[27] Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1.

[28] (a) Marshall, D. R.; Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1898. (b) Thomas, P. J.; Stirling, C. J. M. *Ibid.* **1978**, 1130. (c) Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198. (d) Issari, B.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1982**, 684.

[29] They all refer to the reaction of a zwitterion being converted to neutral products except for the k_2 process, but it was shown above that k_2 is negligible compared to k_{2i}, at least with methoxide as the leaving group.

to observe T^-, increases with *decreasing* basicity of the amine.

(2) Nucleophilic attack (k_1) is strongly affected by steric hindrance in the intermediate which, e.g., leads to the unusually large $k_1(\mathrm{Cl})/k_1(\mathrm{I})$ ratio of 24.5. It is shown that a possible alternative interpretation of this high ratio in terms of rate-limiting leaving-group departure is unattractive. It is also shown that the downward curvature in the plots of k_{obsd} vs amine concentration in the reactions of piperidine with **4-Cl** and **4-I** cannot possibly be due to the accumulation of an intermediate.

(3) β_{nuc} for piperidine and morpholine attack on **4-OMe** is 0.25, while for the intrinsic rate constant $\log k_o \le 0.87$ is estimated. This intrinsic rate constant is lower than $\log k_o$ for piperidine and morpholine addition to **4-H**, which is consistent with the loss of the resonance stabilization of **4-OMe** (**8**) being ahead of bond formation in the transition state.

(4) Among the kinetically equivalent competing pathways k_2, k_{2i}, and $K_a^{\pm}k_3^{\mathrm{H}}$, the intramolecularly acid catalyzed leaving group departure from $\mathrm{T}^{\pm}$ (k_{2i}) is shown to be dominant.

Experimental Section

Materials. **4-Cl**, **4-I**, and **4-OMe** were available from a previous study.[5] **4-SEt** was synthesized by adding 94 μL (1.27 mmol) of ethanethiol to a solution of 0.038 g (0.127 mmol) of **4-Cl** in 5 mL of acetonitrile. Upon addition of 177 μL (1.27 mmol) of triethylamine, a color change from pale yellow to bright yellow occurred. The solution was stirred for 1.5 h, poured into 25 mL of water, and extracted with 2 × 15 mL of dichloromethane. The dichloromethane layers were combined and washed with 5 × 25 mL water, dried over Na_2SO_4, and evaporated under reduced pressure. Recrystallization of the resulting yellow solid from 95% ethanol gave 7.7 mg (18%, first crop, mp 84–86 °C), 7.8 mg (18%, second crop, mp 84–87 °C): ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.10 (t, 3 H, *J* = 7.2 Hz), 2.27 (q, 2 H, *J* = 7.2 Hz), 7.13 (s, 10 H); MS *m/e* 285 (M^+); UV/vis $\lambda_{\max}$ 365 nm (ε 1.08×10^4).

The piperidine and *n*-butylamine substitution products, **4-NRR′** were prepared as described by Rappoport and Topol.[2c] **4-Piperidine**: mp 140–141 °C; ^{1}H NMR ($CDCl_3$) δ 1.70 (s, 6 H), 3.00 (s, 4 H), 7.17, 7.37, 7.53 (Ar-H, 10 H); MS *m/e* 308 (M^+); UV/vis $\lambda_{\max}$ 420 nm (ε 1.2×10^4). **4-*n*-BuNH$_2$**: mp 92–93 °C; ^{1}H NMR (CD_3CN) δ 0.79–0.84 (t, CH_3, 3 H), 1.24–1.33 (sextet, CH_3CH_2, 2 H), 1.47–1.56 (quintet, $CH_3CH_2CH_2$, 2 H), 3.08–3.10 (quartet, CH_2NH, 2 H); MS *m/e* 296 (M^+); UV/vis $\lambda_{\max}$ 368 nm (ε 2.17×10^4).

Piperidine, morpholine, pyrrolidine, *n*-butylamine, and triethylamine were refluxed over calcium hydride, distilled and stored at 4 °C in the dark. Dabco (1,4-diazabicyclooctane)[2.2.2] was recrystallized from hexane.

Kinetics. The fast rates were measured in a Durrum-Gibson stopped-flow spectrophotometer, the slow ones in a Perkin-Elmer 559A UV/vis spectrophotometer, both thermostatted and equipped with computerized data acquisition and analysis. The procedures, including the method of preparing solutions and pH measurements, were similar to the ones described in previous work.[30]

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Registry No. 4-OMe, 96746-56-4; 4-SET, 85296-22-6; 4-Cl, 57337-95-8; 4-I, 55902-54-0; piperidine, 110-89-4; pyrrolidine, 123-75-1; morpholine, 110-91-8.

Supplementary Material Available: Tables S1–S4 listing kinetic data (10 pages). Ordering information is given on any current masthead page.

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[30] Bernasconi, C. F.; Killion, R. B., Jr. *J. Org. Chem.* **1989**, *54*, 2878.

Pyrolysis of 9-Methylenespiro[3.5]nona-5,7-diene: A Route to Benzo-2-hexene-1,6-diyl, a Putative Intermediate in the Retro-Diels–Alder Reaction of Tetralin

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A precursor to the 1,6-biradical potentially formed in the retro-Diels–Alder reaction of tetralin, namely, 5-methylenespiro[bicyclo[2.2.1]hept-2-ene-6,1′-cyclobutan]-7-one (**9**) has been prepared and found to give tetralin and *o*-allyltoluene upon pyrolysis in solution below 100 °C and upon flash vacuum pyrolysis around 250 °C. The product ratio changes from 1:1 to 6:1 at higher temperatures. Rate-determining loss of CO from **9** to give 9-methylenespiro[3.5]nona-5,7-diene, **2**, has been demonstrated by trapping the triene with *N*-methyl- and *N*-phenyltriazolinedione in a reaction whose rate is independent of trapping agent concentration. The kinetics for loss of ketone, **9**, gave $\log k\ (\mathrm{s}^{-1}) = 14.628 \pm 0.038 - (30.554 \pm 0.064)/2.3RT$. Pyrolysis of *cis-syn*(to methylene)- and *trans*-1,2-dimethyl-9-methylenespiro[3.5]nona-5,7-diene gives the vinylcyclobutane rearrangement product, 2,3-dimetyltetralin, with a 4:1 and 2.7:1, respectively, preference for retention over inversion at the migrating carbon. Hydrogen shift products are also formed and by highly ordered transition states. One of these hydrogen shifts involves an unprecedented shift from the carbon remote from the vinyl group.

In tetralin pyrolyses, much attention has been focused on the intermediacy of the 1,6-biradical, **1**, that could result from benzylic C–C bond cleavage in tetralin. Thus, for example, in the SiF_4-sensitized laser pyrolysis of tetralin, benzocyclobutene and *o*-allyltoluene were observed as principal products.[1] Indene, styrene, and 1,2-dihydronaphthalene were also formed. The observation of *o*-allyltoluene and energetic considerations led authors to propose biradical **1** as an intermediate. Possible involve-

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[1] Comita, P. B.; Berman, M. R.; Moore, C. B.; Bergman, R. G. *J. Phys. Chem.* **1981**, *85*, 3266.

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