J. Am. Chem. Soc. **1983**, *105*, 4349-4359

Nucleophilic Addition to Olefins. 8.[1] Addition of Piperidine, Morpholine, and *n*-Butylamine to α-Cyano-4-nitrostilbene and α-Cyano-2,4-dinitrostilbene. Kinetics and Equilibria in 50% Me_2SO–50% Water

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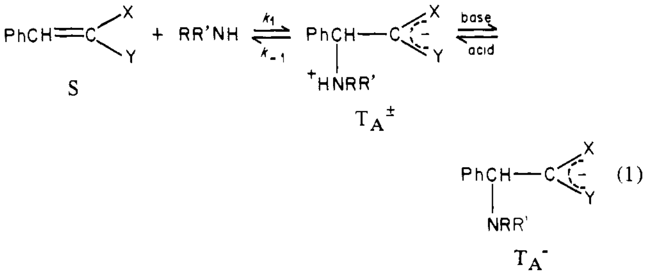
Received November 3, 1982

Abstract: Amines add rapidly to the double bond of α-cyano-4-nitrostilbene (**1**-NO_2) and α-cyano-2,4-dinitrostilbene (**1**-$(NO_2)_2$) to form a zwitterionic Michael adduct, $T_A^{\pm}$, which loses a proton to form the anionic adduct T_A^-. With *n*-butylamine and piperidine nucleophilic attack is rate limiting under all reaction conditions. With morpholine deprotonation is rate limiting at low amine concentration and low pH, but nucleophilic attack becomes rate limiting at high concentration or high pH. Rate and equilibrium constants for nucleophilic addition could be measured or estimated for all reactions, and, for the morpholine adducts, rate constants for proton transfer involving H_3O^+, OH^-, the solvent, morpholine, and several buffers could also be evaluated. There are three major conclusions: (1) The intrinsic rate constants (in the Marcus sense) for piperidine and morpholine addition are lower than those for the analogous reactions of benzylidenemalononitrile but higher than those for β-nitrostyrene. This is the same rank order as for the deprotonation of C–H acids activated by the same substituents ($(CN)_2$ > 4-nitrophenyl and 2,4-dinitrophenyl > NO_2). This result adds further support to our earlier proposal that the intrinsic barrier for nucleophilic addition to olefins and for the deprotonation of C–H acids are governed by similar factors. (2) The average structure–reactivity parameter $\beta_{nuc}{}^{n} = \partial \log k_1/\partial \log K_1 \approx 0.52$ (variation of amine) is larger than the average $\alpha_{nuc}{}^{n} = \partial \log k_1/\partial \log K_1 \approx 0.32$ (variation of olefin). This "imbalance" indicates that C–N bond formation is ahead of negative charge development in the transition state. In the comparable reactions of piperidine and morpholine with arylidene Meldrum's acids (**3**-X) an imbalance in the opposite direction has been reported: $\beta_{nuc}{}^{n} \approx 0.08$ and $\alpha_{nuc}{}^{n} \approx 0.43$; i.e., C–N bond formation appears to lag behind negative charge development. These two types of imbalances are shown to have a common origin, namely, a lag in solvent and electronic/structural reorganization behind C–N bond formation in the transition state. (3) The proton-transfer rates fit the pattern established by Eigen. Thus the rate constants involving the small OH^- and H_3O^+ are near the diffusion-controlled limit while the rate constants for the deprotonation of $T_a^{\pm}$ by morpholine and by buffer bases are considerably below this limit because of steric hindrance. The rate retardation becomes more pronounced as the bulk of the buffer bases increases.

The intrinsic barrier (in the Marcus[2-4] sense) in nucleophilic additions to activated olefins depends markedly on the nature of the activating substituent(s).[5-7] For example, the rate constants (k_1) for the addition of piperidine and morpholine to benzylidenemalononitrile (eq 1, X = Y = CN) are more than 100-fold larger than the corresponding rate constants for addition to β-nitrostyrene (eq 1, X = NO_2, Y = H) in 50% Me_2SO–50% water, even though the respective equilibrium constants (K_1) are virtually the same for the two olefins.[5] By extrapolating to a hypothetical amine for which $K_1 = 1$ we estimated an "intrinsic rate constant" (k_0) of 8.71×10^4 M^{-1} s^{-1} for the cyano-activated olefin and of 3.55×10^2 M^{-1} s^{-1} for the nitro-activated olefin.[5]



We pointed out[5-8] that this difference in k_0 is *qualitatively* similar to that observed in proton transfers involving C–H acids that are activated by the same substituents[9] although *quantitatively* the difference between k_0 for reactions 1 is much smaller than for the corresponding proton transfers.[5] The qualitatively similar behavior of the two types of reactions is not really surprising since the carbanions formed by deprotonation of a C–H acid and that formed by nucleophilic addition to a double bond have essentially the same structure. Hence we explained the lower k_0 (or higher intrinsic barrier) for the nitro compound by the same factor that had been invoked as the principal reason for the much slower deprotonation of nitroalkanes compared to cyanoalkanes, namely, the need for greater solvational reorganization associated with the stronger delocalizing nitro group.[8] The smaller *quantitative* difference in the k_0 for the nucleophilic addition compared to the proton transfer was attributed to the need for a greater *structural* reorganization for the cyano compound in the nucleophilic addition but a greater structural reorganization for the *nitro* compound in the proton transfer.[8]

Simiarly, the intrinsic barrier for nucleophilic attack by water and hydroxide ion on 1,1-dinitro-2,2-diphenylethylene is significantly higher than for the corresponding reactions of benzylidene Meldrum's acid.[6] Again it appears that the more strongly delocalizing nitro groups compared to the $(COO)_2C(CH_3)_2$ moiety are responsible for the higher barrier in the former reaction, just as the deprotonation of 1,1-dinitroethane[10] is intrinsically much slower than that of Meldrum's acid.[11]

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(8) For a recent review see: Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.

(9) See, e.g.: Hibbert, F. *Compr. Chem. Kinet.* **1977**, *8*, 97 and numerous references given in ref. 5 and 8.

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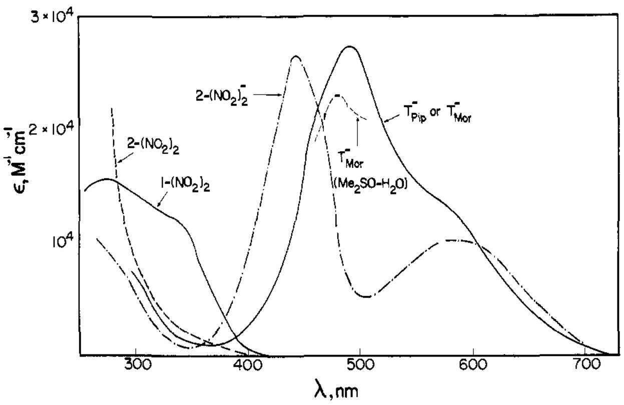
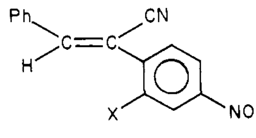
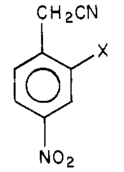


Figure 1. Spectra of **1**-(NO$_2$)$_2$, **2**-(NO$_2$)$_2$, **2**-(NO$_2$)$_2^-$, and T$_A^-$ (piperidine and morpholine adducts of **1**-(NO$_2$)$_2$). All spectra were taken in 50% Me$_2$SO–50% water except for T$_{Pip}^-$ and T$_{Mor}^-$, which were taken in Me$_2$SO. Portion near λ$_{max}$ for T$_{Mor}^-$ is in 50% Me$_2$SO–50% water.

In an attempt to find other examples that might confirm or refute our previous generalizations we have now studied the reactions of α-cyano-4-nitrostilbene (**1**-NO$_2$) and of α-cyano-2,4-dinitrostilbene (**1**-(NO$_2$)$_2$) with *n*-butylamine, piperidine, and morpholine under the same conditions (50% Me$_2$SO–50% water (v/v), 20 °C) as the reactions of β-nitrostyrene and benzylidenemalononitrile. These compounds are of particular interest because they have two types of activating substituents: the cyano group, which leads to low barriers, and the 4-nitroaryl groups, which are strongly delocalizing moieties and should lead to high barriers.



1-NO$_2$, X = H
1-(NO$_2$)$_2$, X = NO$_2$



2-NO$_2$, X = H
2-(NO$_2$)$_2$, X = NO$_2$

In the related deprotonation of (4-nitrophenyl)acetonitrile[12,13] (**2**-NO$_2$) and of (2,4-dinitrophenyl)acetonitrile[13] (**2**-(NO$_2$)$_2$) the intrinsic barriers are much higher than for the deprotonation of dicyanoalkanes, indicating that the barriers are dominated by the 4-nitroaryl groups. Thus, if the suspected analogy between proton transfers and nucleophilic additions is of general validity one would expect the intrinsic barrier for the reactions of **1**-NO$_2$ and **1**-(NO$_2$)$_2$ to be significantly higher than for the reactions of benzylidenemalononitrile. Our results that we now report confirm this expectation.

Results

General Features. When either **1**-NO$_2$ or **1**-(NO$_2$)$_2$ is mixed with a *n*-butylamine, piperidine, or morpholine solution one observes two kinetic processes that can be attributed to reactions of the olefins with the amines. They are described by the relaxation times τ_1 and τ_2, which are quite well separated. Under certain conditions a third process is observed that refers to the reaction of the olefins with hydroxide ion.

This behavior is quite analogous to that of the reactions of amines with β-nitrostyrene,[14] 1,1-dinitro-2,2-diphenylethylene,[15] benzylidene Meldrum's acid,[16] and benzylidenemalononitrile.[5] In this paper we will focus our attention on τ_1, which refers to adduct formation, while in a subsequent paper we shall deal with τ_2, which arises from breakdown of the adduct into benzaldehyde and the anion of **2**-NO$_2$ and **2**-(NO$_2$)$_2$, respectively. All our kinetic and equilibrium measurements were carried out in 50% Me$_2$SO–50% water (v/v) at 20 °C; all data were collected under pseudo-first-order conditions and at an ionic strength of 0.5 M (KCl).

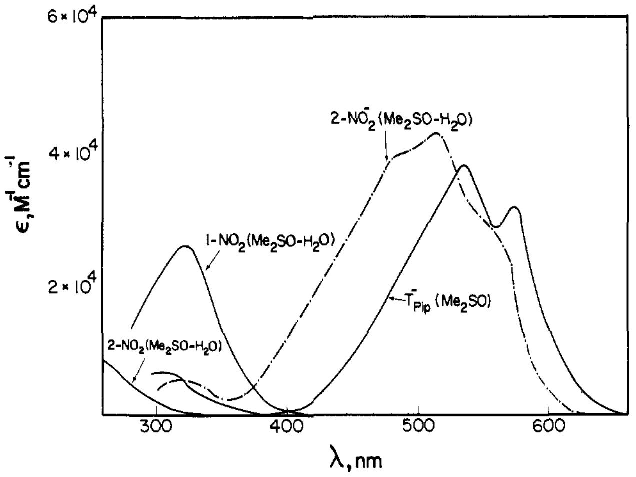


Figure 2. Spectra of **1**-NO$_2$, **2**-NO$_2$, **2**-NO$_2^-$, and T$_A^-$ (piperidine adduct of **1**-NO$_2$). All spectra were taken in 50% Me$_2$SO–50% water except for T$_{Pip}^-$, which is in Me$_2$SO.

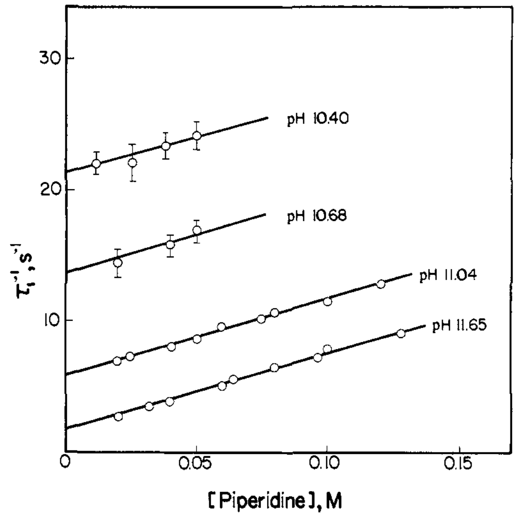


Figure 3. τ_1^{-1} for the reaction of piperidine with **1**-(NO$_2$)$_2$.

Spectra. Figure 1 shows the spectra of **1**-(NO$_2$)$_2$, of T$_A^-$ derived from **1**-(NO$_2$)$_2$ and piperidine and morpholine, of **2**-(NO$_2$)$_2$, and of its conjugate base, (**2**-(NO$_2$)$_2^-$), while Figure 2 shows the corresponding spectra of **1**-NO$_2$, **2**-NO$_2$ and their derivatives. The spectra were obtained in a conventional spectrophotometer except for the one referring to the T$_{Mor}^-$ (of **1**-(NO$_2$)$_2$) in aqueous Me$_2$SO (Figure 1), which had to be taken in the stopped-flow apparatus because of slow decomposition.

As one would expect the spectra of T$_A^-$ are similar to those of the respective **2**-(NO$_2$)$_2^-$ and **2**-NO$_2^-$ anions. More importantly, λ$_{max}$ and ε$_{max}$ are nearly identical with those of the corresponding methoxide ion adducts[17] for which the structures have been confirmed by NMR in some cases.[18] Hence there can be no doubt about the structure of the observed amine adducts.

Reactions of α-Cyano-2,4-dinitrostilbene (1-(NO$_2$)$_2$) with Piperidine and *n*-Butylamine. Kinetics. One type of experiment consisted of mixing the substrate with amine buffers in the stopped-flow apparatus and monitoring the kinetics of adduct (T$_A^-$) formation at 490 nm (piperidine) or 500 nm (*n*-butylamine). At

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Table I. Reactions of α-Cyano-2,4-dinitrostilbene with Piperidine and *n*-Butylamine: pH-Jump Experiments

piperidine		*n*-butylamine	
pH	τ_1^{-1},[a] s^{-1}	pH	τ_1^{-1},[c] s^{-1}
10.30	34.0	9.50	12.3
9.89	79.7	8.80[b]	54.4
9.67	112	8.50[b]	107
9.30	310	8.26[b]	165
9.01[b]	457[e]	7.66[b]	383[e]
8.74[b]	821[f]	5.40[d]	765[f]

[a] Monitored at 490 nm, error limits ±2%. [b] Dabco buffer, $[\text{buffer}]_{\text{tot}} = 0.02$ M. [c] Monitored at 335 and/or 500 nm. [d] Acetate buffer, $[\text{buffer}]_{\text{tot}} = 0.02$ M. [e] Error limits ±10%. [f] Error limits ±25%.

any given pH the reciprocal relaxation time for equilibrium approach, τ_1^{-1}, increases linearly with amine concentration. This is shown in Figure 3 for the piperidine reaction at pH 10.40, 10.68, 11.04, and 11.65 (data in Table S1[19]). Similar plots (not shown) were obtained for *n*-butylamine at pH 11.25, 11.62, and 13.54 (data in Table S1[19]).

These results are consistent with

$$\tau_1^{-1} = k_1[\mathrm{RR'NH}] + k_{-1}\frac{a_{\mathrm{H}^+}}{K_a^{\pm} + a_{\mathrm{H}^+}} \tag{2}$$

Equation 2 refers to the situation where nucleophilic attack (k_1) is rate limiting and proton transfer is a rapid equilibrium as shown in eq 3. The average value of the slopes affords $k_1 = 61.4$ M^{-1} s^{-1} for piperidine and $k_1 = 3.84$ M^{-1} s^{-1} for *n*-butylamine.

$$\mathrm{S} + \mathrm{RR'NH} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{T_A}^{\pm} \underset{\mathrm{H}^+}{\overset{K_A{\pm}}{\rightleftharpoons}} \mathrm{T_A}^{-} \tag{3}$$

At the pH values employed in these experiments the intercepts are proportional to a_{H^+}, implying $K_a^{\pm} \gg a_{\mathrm{H}^+}$ and yielding $k_{-1}/K_a^{\pm} = 6.40 \times 10^{11}$ M^{-1} s^{-1} for piperidine and $k_{-1}/K_a^{\pm} = 3.89 \times 10^{10}$ M^{-1} s^{-1} for *n*-butylamine.

Additional data, aimed at evaluating k_{-1} and $K_a^{\pm}$ individually, were obtained by approaching the equilibrium from the T_A^- side. With piperidine T_A^- was generated in 0.04 M piperidine–0.002 M KOH solutions, conditions under which the equilibrium strongly favors the adduct. These solutions were then mixed with dilute HCl or a Dabco buffer (0.02 M) in the stopped-flow apparatus ("pH jump"). Under these conditions the $k_1[\mathrm{RR'NH}]$ term in eq 2 is negligible and $\tau_1^{-1} \approx k_{-1}a_{\mathrm{H}^+}/(K_a^{\pm} + a_{\mathrm{H}^+})$.

Rates were measured by monitoring either the loss of T_A^- at 490 nm or the formation of substrate at 340 nm. τ_1^{-1} determined at the two wavelengths were very similar but not identical, with τ_1^{-1} at 340 nm being typically about 10–20% smaller than at 490 nm. We attribute the discrepancy to a side reaction that is significantly slower than the τ_1^{-1} process but that nevertheless distorts the kinetic curves of the τ_1^{-1} process somewhat. This side reaction appears to represent protonation of **2**-$(NO_2)_2^-$ [13], which is present because of some hydrolysis of **1**-$(NO_2)_2$ during incubation of **1**-$(NO_2)_2$ in basic solution. Since the distortion of the kinetic curves is less pronounced at 490 nm we shall assume that τ_1^{-1} determined at 490 nm is more reliable, and we shall only use these values in our subsequent analysis. The τ_1^{-1} values are summarized in Table I.

For the *n*-butylamine reaction T_A^- was generated in 0.08 M *n*-butylamine–0.02 M KOH solutions and τ_1^{-1} was measured at 500 and/or 335 nm with equal results at both wavelengths. The results are included in Table I.

For *n*-butylamine τ_1^{-1} is seen to level off at low pH. From an inversion plot (not shown) according to

$$\tau_1 = 1/k_{-1} + K_a^{\pm}/k_{-1}a_{\mathrm{H}^+} \tag{4}$$

Table II. Reactions of α-Cyano-4-nitrostilbene with Piperidine and *n*-Butylamine: pH-Jump Experiments

piperidine[a]		*n*-butylamine[b]	
pH[c]	τ_1^{-1},[a] s^{-1}	pH[d]	τ_1^{-1},[c] s^{-1}
11.37	154[e]	11.10	26.5[e]
11.22	219[e]	10.62	82.7[e]
11.04	336[f]	10.27	197[e]
10.93	432[f]	10.12	235[f]
		9.95	322[f]
		9.82	464[f]
		9.61	561[g]

[a] Monitored at 340 and/or 500 nm. [b] Monitored at 335 nm and/or 500 nm. [c] pH maintained with piperidine buffer. [d] pH maintained with *n*-butylamine buffer. [e] Error limits ±3%. [f] Error limits ±5%. [g] Error limits ±10%.

for the data at pH 9.50–7.76 one calculates $k_{-1} = (6.76 \pm 0.90) \times 10^2$ s^{-1} and $pK_a^{\pm} = 7.76 \pm 0.08$ while for τ_1^{-1} at pH 5.40 where leveling off is complete one obtains $k_{-1} = (7.6 \pm 0.2) \times 10^2$ s^{-1}. This latter value has a relatively large experimental error because it is close to the time resolution of our stopped-flow apparatus, but it nicely confirms the value obtained via eq 4.

In the piperidine reaction the dependence of τ_1^{-1} on a_{H^+} only just begins to deviate from linearity at the lowest pH values, and thus the values of $k_{-1} \approx 2.7 \times 10^3$ s^{-1} and $pK_a^{\pm} \approx 8.37$ obtained via eq 4 must be considered very uncertain. A different method of estimating k_{-1} and $pK_a^{\pm}$ relies on the assumption that the pK_a difference for $T_{\mathrm{pip}}^{\pm}$ and $T_{\mathrm{BuNH_2}}^{\pm}$ is the same as the pK_a difference between PipH^+ and *n*-$\mathrm{BuNH_3}^+$, i.e.,

$$pK_a^{\pm}(\mathrm{Pip}) - pK_a^{\pm}(\mathrm{BuNH_2}) = pK_a^{\mathrm{PipH}^+} - pK_a^{\mathrm{BuNH_3}^+} \tag{5}$$

Indications that eq 5 might be a reasonable approximation come from the study of piperidine and *n*-butylamine adducts of 1,1-dinitro-2,2-diphenylethylene[15] and of 1,3,5-trinitrobenzene[20] where this relationship holds almost perfectly. Additional support for eq 5 comes from proton-transfer rates discussed below. Nevertheless, as has been pointed out by a referee, the validity of eq 5 might appear surprising since coordination of primary amines with a simple alkyl group has the opposite effect on pK_a from that of coordination of a secondary amine with the same alkyl group.[21] This apparent inconsistency is probably due to a steric effect as shown in the Discussion. We shall also show that even if eq 5 were a poor approximation none of the major conclusions of this paper would be affected.

Thus, based on eq 5 we obtain $pK_a^{\pm} = 8.13$ and $k_{-1} = 4.74 \times 10^3$ s^{-1} for the piperidine adduct. These values are not far off from $pK_a^{\pm}$ and k_{-1} estimated from the onset of curvature in the τ_1^{-1} vs. a_{H^+} dependence. In the subsequent analysis we shall use the set based on eq 5.

Incidentally, the major reason we studied the *n*-butylamine reaction was the fact that $pK_a^{\pm}$ (and k_{-1}) could be determined directly and serve as the anchor point to estimate $pK_a^{\pm}$ of the other adducts reported in this study.

Reactions of α-Cyano-4-nitrostilbene (1-NO_2) with Piperidine and *n*-Butylamine. Kinetics. The methodology was essentially the same as for the reactions of **1**-$(NO_2)_2$. τ_1^{-1} was measured at pH 13.16, 13.57, 14.54, and 15.00 for piperdine addition (Table S2[19]), and at pH 13.54 and 13.94 for *n*-butylamine addition (Table S2[19]). We obtained the k_1 values summarized in Table X from the averaged slopes.

We also performed pH-jump experiments, with the results summarized in Table II. In contrast to the reactions of **1**-$(NO_2)_2$ no significant leveling off could be observed, which would allow the determination of k_{-1} and $K_a^{\pm}$ separately. This is because k_{-1} is substantially larger than in the more activated system **1**-$(NO_2)_2$,

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(19) See paragraph at the end of this paper regarding supplementary material.

(20) Bernasconi, C. F.; Muller, M. C.; Schmid, P. *J. Org. Chem.* **1979**, *44*, 3189.

(21) For example, in water the change from *n*-$\mathrm{BuNH_2}$ to *n*-$\mathrm{BuNHCH_3}$ is associated with an increase from $pK_a = 10.64$ to 10.90 (Christensen, J. J.; Izatt, R. M.; Wrathall, D. P.; Hansen, L. D. *J. Chem. Soc. A* **1969**, 1212) while for piperidine → *N*-methylpiperidine the pK_a decreases from 11.12 to 10.08 (Searles, S.; Tamres, M.; Block F.; Quarterman, L. A. *J. Am. chem. Soc.* **1956**, *78*, 4917).

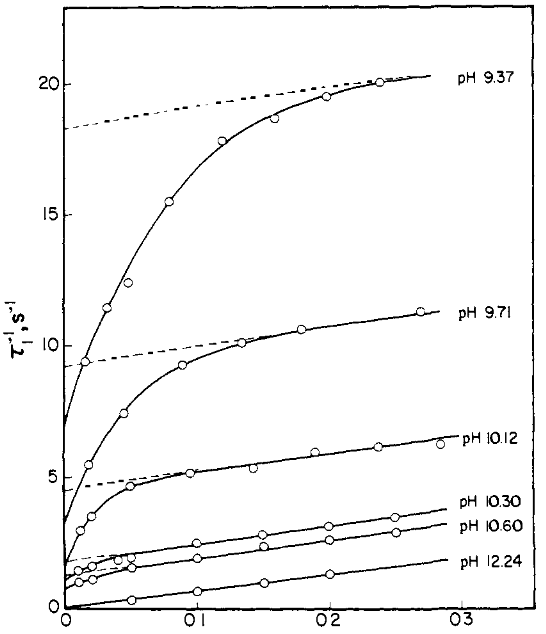


Figure 4. τ_1^{-1} for the reaction of morpholine with **1**-$(NO_2)_2$.

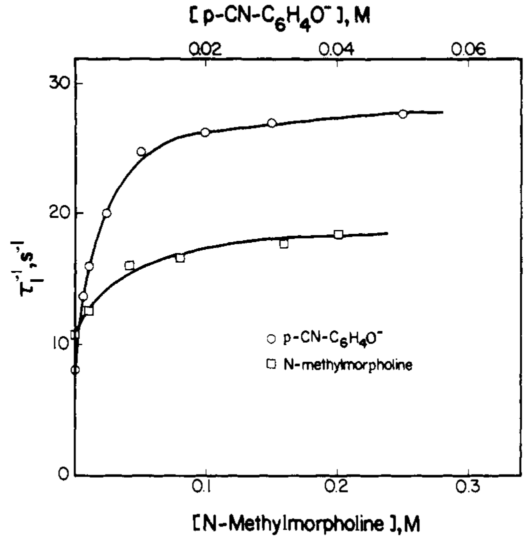


Figure 5. *p*-Cyanophenoxide ion and *N*-methylmorpholine catalysis of the reaction of morpholine with **1**-$(NO_2)_2$.

Table III. Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine: pH-Jump Experiments[a]

pH[b]	τ_1^{-1}, s^{-1}	pH[b]	τ_1^{-1}, s^{-1}
9.45	18.3	8.59	110
9.08	39.8	8.40	130
8.87	60.5	8.18	284
8.71	82.3		

[a] Monitored at 480 nm, $[\text{substrate}]_0 = (2\text{-}3) \times 10^{-5}$ M.
[b] Total buffer concentration 0.8 M, *N*-methylmorpholine buffer.

which prevented us from using pH values approaching $pK_a^{\pm}$. Thus only the ratios $k_{-1}/K_a^{\pm} = 3.57 \times 10^{12}$ M^{-1} s^{-1} for *n*-butylamine and 3.68×10^{13} M^{-1} s^{-1} for piperidine could be obtained. The *n*-butylamine data nevertheless permit an upper limit of ≈9.0 to be set for $pK_a^{\pm}$. If we make the reasonable postulate that $pK_a^{\pm}$ should be higher than for the corresponding **1**-$(NO_2)_2$ adduct (7.76) because of the extra nitro group, we can set $9.0 > pK_a^{\pm} > 7.76$. For the purpose of our further analysis we shall assume an acidifying effect of the extra nitro group of ≈0.55 pK_a unit; i.e., $pK_a^{\pm} \approx 8.3$. As shown in the Discussion this is probably a very good estimate. From eq 5 this leads to $pK_a^{\pm} \approx 8.67$ for the piperidine adduct. From $k_{-1}/K_a^{\pm}$ we now also obtain estimates for k_{-1} (Table X).

Reaction of α-Cyano-2,4-dinitrostilbene (1-$(NO_2)_2$) with Morpholine. Kinetics. Kinetics of adduct formation was monitored at 480 nm as a function of morpholine concentration (a) in morpholine buffers at pH 9.37, 9.71, and 10.12, (b) in 0.01 M triethylamine buffers at pH 10.30 and 10.60, and (c) in a 0.02 M phenol buffer at pH 12.24. Plots of τ_1^{-1} vs. morpholine concentration are shown in Figure 4 while the numerical data are summarized in Table S3.[19]

The plots are characterized by an initial steep portion, whose slope increases with decreasing pH, that then merges into a straight line of much smaller pH-independent slope. This is indicative of a change from rate-limiting proton transfer at low morpholine concentration and low pH to rate-limiting nucleophilic attack at high concentration or high pH. Similar observations have been reported in the reactions of 1,1-dinitro-2,2-diphenylethylene with morpholine and aniline[15] and of benzylidenemalononitrile with morpholine[5] and also in the formation of Meisenheimer complexes between 1,3,5-trinitrobenzene and piperidene or pyrrolidine.[20]

The situation can be described by

$$S + RR'NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} T_A^{\pm} \underset{k_{-2p}}{\overset{k_{2p}}{\rightleftharpoons}} T_A^{-} \qquad (6)$$

with

$$k_{2p} = k_{2p}^{H_2O} + k_{2p}^{OH}a_{OH^-} + k_{2p}^{A}[RR'NH] + k_{2p}^{B}[B] \qquad (7)$$

$$k_{-2p} = k_{-2p}^{H}a_{H^+} + k_{-2p}^{H_2O} + k_{-2p}^{AH}[RR'NH_2^+] + k_{-2p}^{BH}[BH] \qquad (8)$$

where $k_{2p}^{H_2O}$, k_{2p}^{OH}, k_{-2p}^{H}, etc., are the rate constants for deprotonation of $T_A^{\pm}$ (protonation of T_A^-) by the respective bases (acids). Note that B and BH refer to buffers other than the amine as used at pH ≥ 10.30 and in additional experiments described below.

Since K_1 is expected to be smaller than for the piperidine adduct (1.29×10^{-2} M^{-1}) and $pK_a^{\pm}$ to be about 2 units lower than for $T_{Pip}^{\pm}$ (8.13), it is clear that $T_A^{\pm}$ cannot possibly accumulate under the conditions used. Hence the steady-state treatment can be applied, which gives

$$\tau_1^{-1} = \frac{k_1 k_{2p}[RR'NH]}{k_{-1} + k_{2p}} + \frac{k_{-1}k_{-2p}}{k_{-1} + k_{2p}} \qquad (9)$$

At high amine concentration and/or high pH the $k_{2p}^{A}[RR'NH]$ term and/or the $k_{2p}^{OH}a_{OH^-}$ term become so large that $k_{2p} \gg k_{-1}$ and eq 9 reduces to

$$\tau_1^{-1} = k_1[RR'NH] + k_{-1}a_{H^+}/K_a^{\pm} \qquad (10)$$

which is a special case of eq 2 for $K_a^{\pm} \gg a_{H^+}$. Thus eq 10 describes the gently sloping (dashed) straight lines in Figure 4 just as for the piperidine reaction (Figure 3).

Further evidence which shows that proton transfer is (partially) rate limiting at low morpholine concentrations comes from experiments in the presence of *p*-cyanophenoxide and *N*-methylmorpholine buffers, which act as proton-transfer catalysts but are not nucleophilic enough to significantly add to the olefin. The results are summarized in Table S4[19] and shown in Figure 5. τ_1^{-1} is seen to increase with buffer base concentration until it reaches a plateau that agrees well with τ_1^{-1} calculated from eq 10 at the particular pH and morpholine concentration: for *p*-cyanophenoxide at pH 9.20 and [RR'NH] = 0.004 M eq 10 yields 27.3 s^{-1} while the plateau in Figure 5 is ≈28 s^{-1}; for *N*-methylmorpholine at pH 9.37 and [RR'NH] = 0.015 M one calculates $\tau_1^{-1} = 18.7$ s^{-1} while the plateau is at ≈18 s^{-1}.

Additional data referring to the collapse of T_A^- were obtained from pH-jump experiments. The adduct was generated in a 0.04 M morpholine solution at pH 12.3 and then mixed with an acidic solution containing 0.8 M *N*-methylmorpholine. This high buffer concentration was chosen to assure that proton transfer is rapid so that eq 2 or 10 would apply (with negligible k_1[RR'NH] term). The results are summarized in Table III.

Table IV. Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine (Intercepts from Figure 4)

pH	Int, s^{-1}	pH	Int, s^{-1}
9.37	7.0 ± 1.0	10.30	1.1 ± 0.2
9.71	3.3 ± 0.5	10.60	0.75 ± 0.10
10.12	1.6 ± 0.4		

Rate and equilibrium constants were evaluated as follows: (1) From the average slopes of the limiting straight lines at high morpholine concentration (Figure 4) one obtains $k_1 = 6.36$ M^{-1} s^{-1}.

(2) From the intercepts of the extrapolated straight lines in Figure 4, combined with the pH-jump data (Table III), one obtains $k_{-1}/K_a^{\pm} = 4.50 \times 10^{10}$ M^{-1} s^{-1}. No significant nonlinearity of τ_1^{-1} with a_{H^+} is detectable at low pH, and hence k_{-1} and $pK_a^{\pm}$ cannot be obtained directly. However, $pK_a^{\pm}$ can be estimated from the $pK_a^{\pm}$ of the piperidine adduct, based on an equation analogous to eq 5: $pK_a^{\pm} = 5.83$ and $k_{-1} = 6.66 \times 10^4$ s^{-1}.

(3) The intercepts of the curved plots in Figure 4 are approximated by

$$\mathrm{Int} \approx \frac{k_{-1}(k_{-2p}^{H_2O} + k_{-2p}^{H}a_{H^+})}{k_{-1} + k_{2p}^{OH}a_{OH^-}} \tag{11}$$

In eq 11 $k_{2p}^{H_2O}$ has been omitted from the denominator since it is small compared to k_{-1} (see Table XI); the contribution by the $k_{2p}^{B}[B]$ and $k_{-2p}^{BH}[BH]$ terms ($B = Et_3N$) at pH 10.30 and 10.60 has also been assumed to be negligible, an assumption that is reasonable in view of the k_{2p}^{B} and k_{-2p}^{BH} values determined for other buffers (Table XI) and the expected steric hindrance (see Discussion) because of the bulk of Et_3N.

The experimental intercepts are summarized in Table IV. At the two (and probably three) lowest pH values we can safely assume $k_{2p}^{OH}a_{OH^-} \ll k_{-1}$ so that eq 11 further simplifies to

$$\mathrm{Int} \approx k_{-2p}^{H_2O} + k_{-2p}^{H}a_{H^+} \tag{12}$$

A plot (not shown) of Int vs. a_{H^+} at pH 9.37, 9.71, and 10.12 indeed affords straight line with $k_{-2p}^{H_2O} = 0.5 \pm 0.2$ s^{-1} and $k_{-2p}^{H} = (1.50 \pm 0.1) \times 10^{10}$ M^{-1} s^{-1}.

Rearranging eq 11 into

$$\frac{k_{-1}(k_{-2p}^{H_2O} + k_{-2p}^{H}a_{H^+} - \mathrm{Int})}{\mathrm{Int}} = k_{2p}^{OH}a_{OH^-} \tag{13}$$

also provides a method to estimate k_{2p}^{OH} from Int at the two higher pH values. At pH 10.30 eq 13 yields $k_{2p}^{OH} = 3.98 \times 10^9$ M^{-1} s^{-1} and at pH 10.60 $k_{2p}^{OH} = 2.30 \times 10^9$ M^{-1} s^{-1}, for an average of $k_{2p}^{OH} = 3.14 \times 10^9$ M^{-1} s^{-1}. The rather large discrepancy between the two values is caused by the fact that Int and $k_{-2p}^{H_2O} + k_{-2p}^{H}a_{H^+}$ do not differ very much, thus leading to a rather large experimental error. Nevertheless, k_{2p}^{OH} and $k_{-2p}^{H_2O}$ obtained via eq 13 and 12, respectively, appear to be in the right order of magnitude since $K_a^{\pm}$ calculated as $k_{2p}^{OH}/k_{-2p}^{H_2O}K_w = 7.91 \times 10^{-7}$ ($pK_a^{\pm} = 6.10$) is in satisfactory agreement with $pK_a^{\pm} = 5.83$ estimated earlier on the basis of entirely different and independent assumptions.

(4) At very low morpholine concentrations and in the absence of added buffers eq 9 reduces to

$$\tau_1^{-1} \approx \frac{k_{-1}(k_{-2p}^{H_2O} + k_{-2p}^{H}a_{H^+} + k_{-2p}^{AH}[RR'NH_2^+])}{k_{-1} + k_{2p}^{OH}a_{OH^+}} \tag{14}$$

and k_{-2p}^{AH} can be evaluated from initial slopes according to

$$k_{-2p}^{AH} = \mathrm{slope} \times \frac{k_{-1} + k_{2p}^{OH}a_{OH^-}}{k_{-1}}\,\frac{K_a^{AH}}{a_{H^+}} \tag{15}$$

where K_a^{AH} is the acidity constant of morpholinium ion. The initial slopes at four different pH values are summarized in Table V. They yield $k_{-2p}^{AH} = (1.85 \pm 0.30) \times 10^3$ M^{-1} s^{-1}.

(5) The initial slopes in Figure 5 can be used in a similar way to obtain k_{-2p}^{BH} for *N*-methylmorpholinium and *p*-cyanophenol (K_a^{AH} in eq 15 replaced by K_a^{BH}). The results are included in Table V.

Table V. Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine (Initial Slopes from Figures 4 and 5)

pH	initial slope, M^{-1} s^{-1}	k_{-2p}^{AH} [a] or k_{-2p}^{BH}, [a] M^{-1} s^{-1}
	Morpholinium Ion Catalysis	
9.37	≈425	$\approx 1.92 \times 10^3$
9.71	≈187	$\approx 1.88 \times 10^3$
10.12	≈67.5	$\approx 1.82 \times 10^3$
10.30	≈42	$\approx 1.80 \times 10^3$
		av 1.85×10^3
	N-Methylmorpholinium Ion Catalysis	
9.37	≈230	$\approx 1.50 \times 10^4$
	p-Cyanophenol Catalysis	
9.20	$\approx 6.50 \times 10^3$	$\approx 2.07 \times 10^4$

[a] Calculated from eq 15 (k_{-2p}^{AH}) or an equation analogous to eq 15 with K_a^{BH} (k_{-2p}^{BH}) with $k_{-1} = 6.66 \times 10^4$ s^{-1}, $k_{2p}^{OH} = 3.14 \times 10^9$ M^{-1} s^{-1}, $pK_a^{AH} = 8.72$, $pK_a^{BH} = 7.56$ for *N*-methylmorpholinium ion, and $pK_a^{BH} = 8.70$ for *p*-cyanophenol.

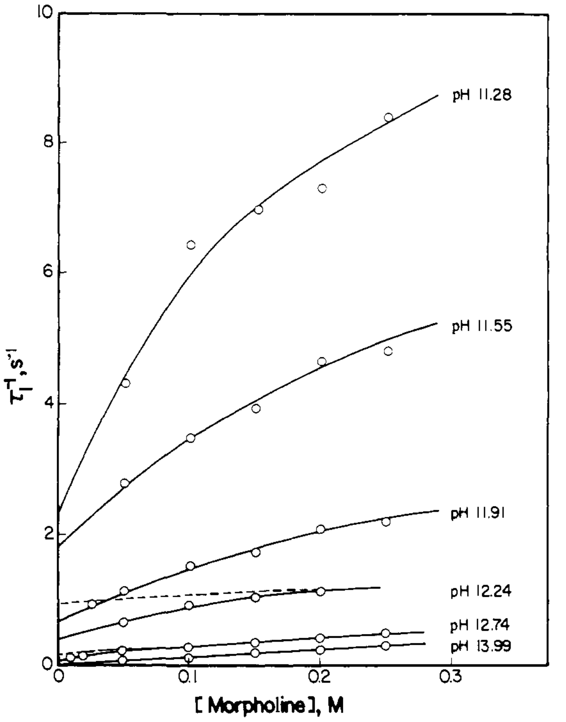


Figure 6. τ_1^{-1} for the reaction of morpholine with **1**-NO_2.

Reaction of α-Cyano-4-nitrostilbene (1-NO_2) with Morpholine. Kinetics. Adduct formation was monitored at 550 nm and the morpholine concentration dependence of τ_1^{-1} was determined in dilute phenol buffers at pH 11.28, 11.55, 11.91, and 12.24, and in dilute 2,4,6-trimethylphenol buffer at pH 12.74 and 13.99. The results are summarized in Table S5,[19] while Figure 6 shows plots of τ_1^{-1} vs. morpholine concentration. The plots are similar to the ones for the reaction of **1**-$(NO_2)_2$ with morpholine, again demonstrating a change from rate-limiting proton transfer to rate-limiting nucleophilic attack. However, leveling off into a straight line of slope k_1, indicating complete transition to rate-limiting nucleophilic attack, does not occur except at pH ≥ 12.74 where $k_{2p}^{OH}a_{OH^-} \gg k_{-1}$. At lower pH virtually complete transition to rate-limiting nucleophilic attack can be achieved by adding high concentrations of *p*-chlorophenol buffer ($k_{2p}^{B}[B] \gg k_{-1}$) as the data in Table VI show; Table VI also includes data on phenol buffer catalysis.

Rate and equilibrium constants were evaluated in a similar way as for the reaction of **1**-$(NO_2)_2$ but with some important differences: (1) k_1 could only be obtained as an average from the slopes

Table **VI**. Reaction of α-Cyano-4-nitrostilbene with Morpholine: Buffer Catalysis

pH	$[B^-]$, M	τ_1^{-1}, s^{-1}
Phenol at [Morpholine] = 0.05 M		
11.22	0.01	6.47
	0.02	7.93
	0.03	9.60
	0.04	10.6
	0.05	12.7
p-Chlorophenol at [Morpholine] = 0.05 M		
11.28	0.02	4.80
	0.05	8.67
	0.10	11.5
	0.15	12.9
	0.20	13.5
	0.25	16.0

Table **VII**. Reaction of α-Cyano-4-nitrostilbene with Morpholine (Intercepts from Figure 6)

pH	Int, s^{-1}	pH	Int, s^{-1}
11.28	2.30	12.24	0.45
11.55	1.80	12.74	0.20
11.91	0.90		

at the two highest pH values (1.10 M^{-1} s^{-1}).

(2) In principle, $k_{-1}/K_a^{\pm}$ could be obtained from the intercepts at pH 13.99 and 12.74 (dashed line) of Figure 6, but owing to the smallness of these intercepts, the experimental error is expected to be large. A more reliable value can be obtained by drawing a straight line of slope k_1 through the highest point at pH 12.24 and equating the intercept of this line with $k_{-1}a_{H^+}/K_a^{\pm}$. This yields $k_{-1}/K_a^{\pm} \approx 1.67 \times 10^{12}$ M^{-1} s^{-1}. Another method is to calculate $k_{-1}a_{H^+}/K_a^{\pm} = \tau_1^{-1} - k_1[RR'NH]$ at pH 11.28, with τ_1^{-1} being the plateau value at high *p*-chlorphenol concentration (Table VI). This yields $k_{-1}/K_a^{\pm} = 2.85 \times 10^{12}$ M^{-1} s^{-1}. A third method is described below.

(3) Again neglecting buffer contributions, the intercepts of the plots in Figure 6, which are summarized in Table VII, are approximated by eq 11. Since the pH range used is higher than for **1**-$(NO_2)_2$ the $k_{-2p}^{H}a_{H^+}$ term is also negligible, which reduces eq 11 to

$$\mathrm{Int} \approx \frac{k_{-1}k_{-2p}^{H_2O}}{k_{-1} + k_{2p}^{OH}a_{OH^-}} \qquad (16)$$

and, after inversion and substitutions, to

$$\mathrm{Int}^{-1} \approx \frac{1}{k_{-2p}^{H_2O}} + \frac{K_a^{\pm}}{k_{-1}}\,\frac{a_{OH^-}}{K_w} \qquad (17)$$

A plot according to eq 17 (not shown) affords $k_{-2p}^{H_2O} = 3.0 \pm 0.5\ k_{-1}/K_a^{\pm}$ and $K_{-1}/K_a^{\pm} = (1.18 \pm 0.20) \times 10^{12}$ M^{-1} s^{-1}. Considering the many potential sources of error in our extrapolations and the approximate nature of eq 16 and 17 the three values for $k_{-1}/K_a^{\pm}$ (1.67×10^{12}, 2.85×10^{12}, and 1.18×10^{12}) are in remarkably good agreement. We shall adopt 1.90×10^{12}, which is the average of the three values. From $k_{-2p}^{H_2O}$ we now calculate $k_{2p}^{OH} = k_{-2p}^{H_2O}K_a^{\pm}/K_w = 1.02 \times 10^{10}$ M^{-1} s^{-1}. In view of $k_{2p}^{OH} \approx 3.14 \times 10^9$ M^{-1} s^{-1} found for **1**-$(NO_2)_2$, the value of 1.02×10^{10} M^{-1} s^{-1} seems rather high. This high value is an artifact caused by the neglect of the buffer terms in eq 13, which is not justified here. Since $k_{-2p}^{BH} = 1.3 \times 10^2$ M^{-1} s^{-1} for phenol (see below) $k_{-2p}^{BH}[BH]$ will contribute significantly to Int at the total buffer concentrations of 0.01–0.02 M used. Thus the actual $k_{-2p}^{H_2O}$, and with it k_{2p}^{OH}, must be significantly lower. The value of 1.02×10^{10} M^{-1} s^{-1} for k_{2p}^{OH} also leads to inconsistencies in the evaluation of the rate constant k_{-2p}^{AH} and thus cannot be correct as shown in the next paragraphs.

(4) Rate constants for protonation of T_A^- by morpholinium ion (k_{-2p}^{AH}) and by phenol and *p*-chlorphenol (k_{-2p}^{BH}) were obtained from initial slopes (eq 15) as with **1**-$(NO_2)_2$; k_{-2p}^{AH} for morpholinium ion was calculated both by assuming $k_{2p}^{OH} = 1.20 \times 10^{10}$ and $k_{2p}^{OH} = 3.14 \times 10^9$, the value obtained for (**1**-$NO_2)_2$. As the results in Table VII show, the assumption of $k_{2p}^{OH} = 1.02 \times 10^{10}$ M^{-1} s^{-1} leads to increasing k_{-2p}^{AH} values. Using the value of 3.14×10^9 M^{-1} s^{-1} found for **1**-$(NO_2)_2$ leads to a great improvement (not shown) but a value of 2×10^9 M^{-1} s^{-1} is more satisfactory still. The same k_{2p}^{OH} value was also used in calculating k_{-2p}^{BH} for phenol and *p*-chlorophenol catalysis (Table VIII).

Table **VIII**. Reaction of α-Cyano-4-nitrostilbene with Morpholine (Initial Slopes from Figure 6)

pH	initial slope, M^{-1} s^{-1}	$k_{-2p}^{AH\,a}$ or $k_{-2p}^{BH\,a}$, M^{-1} s^{-1}
Morpholinium Ion Catalysis		
11.78	≈55.2	$\approx 2.18 \times 10^4$ $(2.60 \times 10^4)^b$
11.55	≈22.0	$\approx 2.03 \times 10^4$ $(2.84 \times 10^4)^b$
11.91	≈11.2	$\approx 2.15 \times 10^4$ $(3.89 \times 10^4)^b$
12.24	≈4.90	$\approx 2.48 \times 10^4$ $(4.99 \times 10^4)^b$
		av 2.21×10^4
Phenol Catalysis		
11.22	≈168	1.31×10^2
p-Chlorophenol Catalysis		
11.38	≈148	9.46×10^2

[a] Calculated from eq 15 (k_{-2p}^{AH}), or an equation analogous to eq 15 with K_a^{BH} (k_{-2p}^{BH}) with $k_{-1} = 8.11 \times 10^5$, $k_{2p}^{OH} = 2.0 \times 10^9$ M^{-1} s^{-1}, $pK_a^{AH} = 8.72$, $pK_a^{BH} = 11.35$ for phenol, $pK_a^{BH} = 10.50$ for *p*-chlorophenol. [b] $k_{2p}^{OH} = 1.02 \times 10^{10}$ M^{-1} s^{-1}, see text.

Table **IX**. Reaction of α-Cyano-2,4-dinitrostilbene with Morpholine: Equilibrium Determinations

pH	slope,[a] M^{-1}	pH	slope,[a] M^{-1}
9.87	0.98	11.73	63.6
11.14	16.0	11.93	96.0
11.45	44.0		

[a] Slopes from plots of $(OD_0 - OD_\infty)/(OD - OD_\infty)$ vs. $[R_2NH]$ according to eq 18; data from Table S6.[19]

Reactions of α-Cyano-2,4-dinitrostilbene with Morpholine. Equilibrium Measurements. In order to have an independent check for consistency at least in one system we determined equilibrium constants spectrophotometrically for the title reaction. OD measurements were performed in the stopped-flow apparatus at 360 nm where $\epsilon_S > \epsilon_{T^-}, \epsilon_T^{\pm}$. Determinations were carried out at pH 9.87, 11.14, 11.45, 11.73, and 11.93 as a function of morpholine concentration (five to six concentrations at each pH). The results are summarized in Tables S6.[19] They were analyzed according to

$$\frac{OD_0 - OD_\infty}{OD - OD_\infty} = 1 + \left(K_1 + \frac{K_1K_a^{\pm}}{a_{H^+}}\right)[RR'NH] \qquad (18)$$

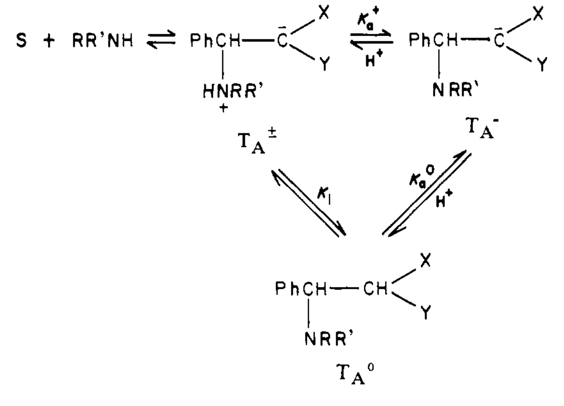
where OD_0 and OD are the optical densities in the absence and in the presence of amine, respectively, and OD_∞ is the optical density in the presence of high enough amine concentration as to quantitatively convert S into T_A^- and/or $T_A^{\pm}$.

Plots (not shown) of the left-hand side of eq 18 vs. morpholine concentration yielded excellent straight lines whose intercepts were unity, within experimental error, and whose slopes are summarized in Table IX. From the pH dependence of these slopes one obtains $K_1K_a^{\pm} = (1.16 \pm 0.04) \times 10^{-10}$, which is in excellent agreement with $k_1/(k_{-1}/K_a^{\pm}) = 1.40 \times 10^{-10}$ determined from rate measurements. K_1 and $K_a^{\pm}$ could not be obtained separately because K_1 is too small for a significant concentration of $T_A^{\pm}$ to build up under any experimental condition.

Discussion

Mechanism. Nitrogen vs. Carbon Protonation. We have interpreted all our observations in terms of the simple scheme of eq 3 (piperidine and *n*-butylamine) or of eq 6 (morpholine). In view of our earlier findings[5] that in the reaction of benzylidenemalononitrile with piperidine and morpholine the carbon-pro-

Scheme I



tonated species T_A^0 is in rapid equilibrium with T_A^- and $T_A^{\pm}$, a possible participation of T_A^0 in the τ_1 process of the present study needs to be considered. The extended reaction scheme is shown in Scheme I. It requires a modification of eq 2 into

$$\tau_1^{-1} = k_1[\mathrm{RR'NH}] + k_{-1}\frac{a_{\mathrm{H}^+}}{K_a^{\pm} + a_{\mathrm{H}^+}(1 + K_a^{\pm}/K_a^0)} \quad (19)$$

As long as $K_a^{\pm} \gg a_H(1 + K_a^{\pm}/K_a^0)$ this is of no consequence because the simplified eq 4 still holds. However, when a leveling off is observed as in the pH-jump experiments for the reaction of *n*-butylamine with **1**-$(NO_2)_2$, implying $K_a^{\pm} \leq a_{H^+}(1 + K_a^{\pm}/K_a^0)$, the meaning of the calculated parameters would change unless $K_a^{\pm}/K_a^0 \ll 1$.[5]

The following arguments show that in the present study T_A^0 is not a participant in the τ_1^{-1} process: (1) For it to be a participant the equilibration of T_A^0 with $T_A^{\pm}$ and T_A^- would have to be rapid compared to $k_{-1} = 6.76 \times 10^2$ s^{-1} (*n*-BuNH$_2$/**1**-$(NO_2)_2$). Based on a Brønsted plot for the deprotonation of **2**-$(NO_2)_2$[13] we can estimate the rate constants for reaction 20 to be $k_f \approx 4 \times 10^3$ M^{-1} s^{-1} and $k_r \approx 10$ M^{-1} s^{-1}.

$$\mathbf{2}\text{-}(NO_2)_2 + n\text{-BuNH}_2 \underset{k_r}{\overset{k_f}{\rightleftharpoons}} \mathbf{2}\text{-}(NO_2)_2^- + n\text{-BuNH}_3^+ \quad (20)$$

If we assume a similar pK_a^0 for T_A^0 as for **2**-$(NO_2)_2$ (8.06) and similar proton-transfer rate constants it is easily seen that under typical reaction conditions (e.g., pH 9.61, [*n*-BuNH$_2$] = 0.008 M, [*n*-BuNH$_3^+$] = 0.072 M) equilibration between T_A^0 and T_A^- would be much slower than k_{-1} ($\tau^{-1} = k_f[n\text{-BuNH}_2] + k_r[n\text{-BuNH}_3^+] \approx 33$ s^{-1}). Since T_A^0 is much more crowded than **2**-$(NO_2)_2$, k_f and k_r would actually most likely be significantly smaller than assumed, reducing τ^{-1} below 33 s^{-1}. Furthermore, pK_A^0 is expected to be higher than the pK_a of **2**-$(NO_2)_2$ because of steric hindrance to coplanarity for the *o*-nitro group (see below). This would reduce k_f and enhance k_r and would decrease τ^{-1} further still. A contribution to the equilibration rate by intramolecular proton transfer ($T_A^{\pm} \rightleftharpoons T_A^0$), even if significant,[22] could not possibly be so large[22,23] as to alter the above conclusions.

(2) The breakdown of the respective piperidine and morpholine adducts (T_A^-) into benzaldehyde and **2**-$(NO_2)_2^-$ is general acid catalyzed,[22] which shows that carbon protonation of T_A^- is rate limiting. This is inconsistent with T_A^0 participating in the τ_1 process.

Reliability of Rate and Equilibrium Constants. All rate and equilibrium constants are summarized in Tables X and XI. k_1 could be determined by direct experiment for all reactions studied and thus should be very reliable. k_{-1} and $pK_a^{\pm}$ could only be obtained directly for the reaction of *n*-butylamine with **1**-$(NO_2)_2$; for the reactions of piperidine nd morpholine with **1**-$(NO_2)_2$ $pK_a^{\pm}$ (and with it k_{-1}) was estimated based on the $pK_a^{\pm}$ of the *n*-butylamine adduct and eq 5 (or equivalent). As mentioned before, despite some questions as to why eq 5 should hold, the $pK_a^{\pm}$ and k_{-1} values derived from it are believed to be quite reliable. In the section entitled "Proton Transfer" we shall discuss additional evidence supporting the validity of eq 5.

Table X. Rate and Equilibrium Constants for Nucleophilic Attack on α-Cyano-4-nitrostilbene (1-NO_2) and α-Cyano-2,4-dinitrostilbene (1-$(NO_2)_2$)

	morpholine ($pK_a^{AH} = 8.72$)	piperidine ($pK_a^{AH} = 11.02$)	*n*-butylamine ($pK_a^{AH} = 10.65$)
		1-NO_2 ($pK_a^{CH} = 12.62$)^b	
k_1, M^{-1} s^{-1}	1.10 ± 0.05	26.0 ± 0.5	1.77 ± 0.05
k_{-1}, s^{-1} ^{a}	≈8.11 × 10^5	≈7.87 × 10^4	≈1.79 × 10^4
K_1, M^{-1} ^{a}	≈1.36 × 10^{-6}	≈3.57 × 10^{-4}	≈9.88 × 10^{-5}
$pK_a^{\pm}$ ^{a}	≈6.37	≈8.67	≈8.30
$K_1K_a^{\pm}$	5.80 × 10^{-13}	7.63 × 10^{-13}	4.95 × 10^{-13}
		1-$(NO_2)_2$ ($pK_a^{CH} = 8.06$)^b	
k_1, M^{-1} s^{-1}	6.36 ± 0.25	61.4 ± 1.0	3.84 ± 0.10
k_{-1}, s^{-1}	6.66 ± 2.00) × 10^4	4.74 ± 1.50) × 10^3	(6.76 ± 1.00) × 10^2
K_1, M^{-1}	(0.95 ± 0.30) × 10^{-4}	(1.29 ± 0.40) × 10^{-2}	(5.70 ± 0.10) × 10^{-3}
$pK_a^{\pm}$	5.83 ± 0.13	8.13 ± 0.13	7.76 ± 0.06
$K_1K_a^{\pm}$	1.40 × 10^{-10} ^{c}	0.96 × 10^{-10}	0.99 × 10^{-10}

^{a} Based on assumed $pK_a = 8.30$ for *n*-BuNH$_2$, see text.
^{b} pK_a^{CH} refers to parent C–H acid 2-NO_2 and 2-$(NO_2)_2$, respectively. ^{c} $K_1K_a^{\pm} = 1.16 \times 10^{-10}$ from equilibrium measurements.

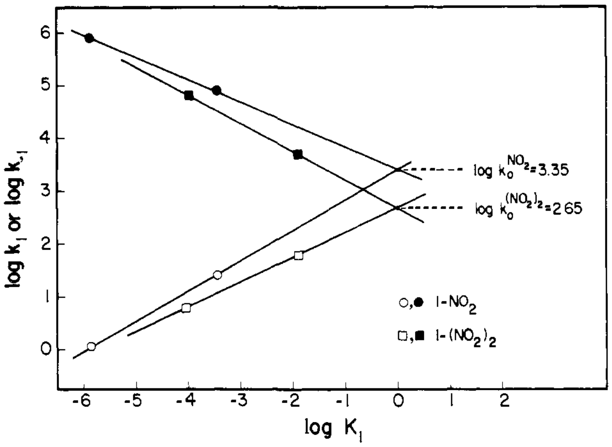


Figure 7. log k_1 (open symbols) and log k_{-1} (filled symbols) vs. log K_1 for the reactions of **1**-NO_2 and **1**-$(NO_2)_2$ with morpholine and piperidine.

For none of the reactions of **1**-NO_2 was $pK_a^{\pm}$ directly measurable, but for the *n*-butylamine adduct at least an upper (9.0) and a lower limit (7.76) can be given. We assumed an acidifying effect of the extra nitro group of ≈0.55 pK_a units giving an estimated $pK_a^{\pm} = 8.3$ for the *n*-BuNH$_2$/**1**-NO_2 adduct. That this value is reasonable is seen from the fact that k_{2p}^{OH} calculated as $k_{-2p}^{H_2O}K_a^{\pm}/K_w$ is of the order expected for a diffusion-controlled reaction as further detailed below.

Intrinsic Rate Constants for Adduct Formation. Figure 7 shows plots of log k_1 (log k_{-1}) vs. log K_1 for the change from morpholine to piperidine. Extrapolation to $K_1 = 1$ ($\Delta G° = 0$) allows estimation of k_0, which is the intrinsic rate constant of the reaction.[2-4] Log k_0 for **1**-NO_2 and **1**-$(NO_2)_2$ along with log k_0 for the reactions of the same amines with benzylidinemalononitrile and with β-nitrostyrene are summarized in Table XII. The table also includes log k_0 values for proton transfers of the corresponding C–H acids.

In terms of the original aim of this work we see from Table XII that **1**-NO_2 and **1**-$(NO_2)_2$ fit very well into the pattern established by the other olefins, namely, that the rank order in log k_0 for nucleophilic additions follows the one for proton transfers. All entries in the table refer to the same solvent except for the deprotonation of RCH(CN)$_2$ and thus constitute the best set yet for comparison purposes. A change from water to 50% Me$_2$SO–50% water in the case of RCH(CN)$_2$ is not expected to change log k_0 drastically; if there is a change it would be toward a slightly higher value[8] and thus the rank order would remain the same.

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[22] Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.*, in preparation.

[23] Bernasconi, C. F.; Hibdon, S. A.; McMurry, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3459.

Table **XI.** Rate Constants for Proton Transfer $T_{Mor}^{\pm} \rightleftharpoons T_{Mor}^{-}$

	1-NO_2 (p$K_a^{\pm}$ = 6.37)		1-$(NO_2)_2$ (p$K_a^{\pm}$ = 5.83)	
B^a (pK_a^{BH})	k_{2p}^{B},^{d} M^{-1} s^{-1}	k_{-2p}^{BH}, M^{-1} s^{-1}	k_{2p}^{B},^{d} M^{-1} s^{-1}	k_{-2p}^{BH}, M^{-1} s^{-1}
H_2O (−1.44)	≈6.40 × 10^3/27.5	≈1.5 × 10^{10} ^{c}	2.22 × 10^4/27.5	(1.50 ± 0.15) × 10^{10}
N-methylmorpholine (7.56)			8.05 × 10^5	(1.50 ± 0.03) × 10^4
p-cyanophenoxide (8.70)			1.53 × 10^7	(2.07 ± 0.70) × 10^4
morpholine (8.72)	4.95 × 10^6	(2.21 ± 0.20) × 10^4	1.44 × 10^6	(1.85 ± 0.20) × 10^3
p-chlorophenoxide (10.50)	1.28 × 10^7	(9.64 ± 2.00) × 10^2		
phenoxide (11.35)	1.25 × 10^7	(1.31 ± 0.26) × 10^2		
OH^- (17.34)	≈2 × 10^9 $(10^{10})^b$	≈0.6 $(3.0)^b$	≈3.14 × 10^9	(0.5 ± 0.2)

^{a} Symbol B includes B = OH^-, H_2O, and morpholine. ^{b} From eq 17, contaminated by buffer catalysis, see text. ^{c} Assumed, ref 24. ^{d} Error limits discussed in text.

Table **XII.** log k_0 for Amine Addition to Olefins and for Proton Transfer of C–H Acids in 50% Me_2SO-50% Water^a

olefin	log k_0	C–H acid	log k_0
$PhCH{=}C(CN)_2$^{b}	4.94	$RCH(CN)_2$^{d}	≈7.0
1-NO_2	3.35	2-NO_2	≈3.95
1-$(NO_2)_2$	2.65^f	2-$(NO_2)_2$	≈2.9
$PhCH{=}CHNO_2$^{c}	2.55	$CH_3CH_2NO_2$^{e}	≈1.14

^{a} Except for proton transfer with $RCH(CN)_2$, which is in water. ^{b} Reference 5. ^{c} Reference 14. ^{d} Reference 9. ^{e} Cox, B. G.; Gibson, A. *J. Chem. Soc., Chem. Commun.* 1974, 638. ^{f} In a preliminary account (ref 8) a log k_0 value of 1.98 was given.

Table **XIII**, β Values for Nucleophilic Addition^a

	1-NO_2	1-$(NO_2)_2$
$\beta_{nuc}(k_1)$	0.60 ± 0.01	0.43 ± 0.01
$\beta_{lg}(k_{-1})$	−0.44 ± 0.03	−0.50 ± 0.03
$\beta_{eq}(K_1)$	1.04 ± 0.04	0.93 ± 0.04
$\beta_{nuc}^n = \beta_{nuc}/\beta_{eq}$	0.58 ± 0.03	0.46 ± 0.03
$\beta_{lg}^n = \beta_{lg}/\beta_{eq}$	−0.42 ± 0.04	−0.54 ± 0.04

^{a} Based on piperidine and morpholine only.

Table **XIV.** α Values for Nucleophilic Addition^a

	morpholine	piperidine	*n*-butylamine
$\alpha_{nuc}(k_1)$	0.17 ± 0.01	0.08 ± 0.01	0.07 ± 0.02
$\alpha_{lg}(k_{-1})$	−0.24 ± 0.08	−0.27 ± 0.08	−0.31 ± 0.07
$\alpha_{eq}(K_1)$	0.40 ± 0.09	0.35 ± 0.09	0.38 ± 0.08
$\alpha_{nuc}^n = \alpha_{nuc}/\alpha_{eq}$	0.41 ± 0.08	0.23 ± 0.08	0.19 ± 0.07
$\alpha_{lg}^n = \alpha_{lg}/\alpha_{eq}$	−0.59 ± 0.04	−0.77 ± 0.04	−0.81 ± 0.03

^{a} $\alpha_{nuc}(k_1) = \Delta \log k_1/\Delta pK_a^{CH}$, $\alpha_{lg}(k_{-1}) = \Delta \log k_{-1}/\Delta pK_a^{CH}$, $\alpha_{eq}(K_1) = \Delta \log K_1/\Delta pK_a^{CH}$, with $\Delta pK_a^{CH} = pK_a^{CH}(2\text{-}NO_2) - pK_a^{CH}(2\text{-}(NO_2)_2)$ and $\Delta \log k_1 = \log k_1(1\text{-}(NO_2)_2) - \log k_1(1\text{-}NO_2)$, etc.

The factors that are responsible for the observed rank orders were briefly mentioned in the introduction and have been discussed at great length elsewhere.[8] We shall not reiterate them here but restrict ourselves to a few comments regarding **1**-NO_2 and **1**-$(NO_2)_2$. In view of the significantly smaller spread in the log k_0 values for the olefin reactions ($\log k_0^{(CN)_2} - \log k_0^{NO_2} = 2.39$) compared to the proton-transfer reactions ($\log k_0^{(CN)_2} - \log k_0^{NO_2} = 5.86$), it appears perhaps surprising that the log k_0 values for **1**-NO_2 and **1**-$(NO_2)_2$ differ by as much as 0.7 while the same difference for the proton transfer involving **2**-NO_2 and **2**-$(NO_2)_2$ is ≈1.05. An enhanced difference in log k_0 for the two olefins might possibly be of steric origin. Steric hindrance for which evidence is presented below is expected to lower K_1, which must come about by a decrease in k_1 and an increase in k_{-1}. Depending on how much of the change in K_1 is caused by the change in k_1 and how much by the change in k_{-1}, k_0 will either be lowered or enhanced. For example, if $\partial \log k_1/\partial \log K_1$ produced by the steric effect is larger than $\partial \log k_1/\partial \log K_1$ produced by changing the basicity of the amine, log k_0 for **1**-$(NO_2)_2$ would be lowered relative to that of **1**-NO_2 as observed.

Incidentally, if our estimate of p$K_a^{\pm}$(pip) based on eq 5 was erroneous and p$K_a^{\pm}$(pip) was in fact lower than assumed,[21] this would imply that the k_{-1} values of all piperidine and morpholine reactions would be higher by a constant factor and all K_1 values would be lower by the same constant factor. This would enhance log k_0 slightly but by approximately the same amount for both substrates and thus our conclusions would remain the same.[24]

Structure–Reactivity Parameters for Adduct Formation. Two-point Brøsted plots of log k_1, log k_{-1}, and log K_1 vs. pK_a^{AH} yield the β parameters summarized in Table XIII. The normalized β values can be obtained either as indicated in the table or more directly from the slopes in Figure 7. Another type of Brønsted relation is obtained by correlating log k_1, log k_{-1}, and log K_1 with the pK_a values of the parent carbon acids **2**-NO_2 and **2**-$(NO_2)_2$. These correlations yield the α values summarized in Table XIV. Here again the normalized parameters could be calculated more directly as $\partial \log k_1/\partial \log K_1$ and $\partial \log k_{-1}/\partial \log K_1$, respectively.

The large experimental uncertainty in α_{lg}, α_{eq}, and α_{nuc}^n stem mainly from the uncertainty in the p$K_a^{\pm}$ for the adducts of **1**-NO_2, which introduces an equivalent uncertainty in k_{-1} and K_1. Note, however, that the uncertainty in p$K_a^{\pm}$(pip) estimated from eq 5 has no effect on any α or β value since all K_1 and k_{-1} values would be equally affected.

Despite these uncertainties in α_{lg}, α_{eq}, and α_{nuc}^n the following points can be made: (1) β_{eq} is close to unity for both olefins; i.e., the relative carbon basicities of the amines are very similar to their relative proton basicities. We note that β_{eq} is slightly lower for **1**-$(NO_2)_2$, but the difference is very close to the experimental error and is therefore probably not significant.[25]

(2) α_{eq} is much smaller than unity for all amines, indicating a strong attenuation of the effect of the *o*-nitro group on K_1 compared to its effect on the acidity of **2**-$(NO_2)_2$. This is most likely a steric effect. One possibility is that increased steric compression in the adduct lowers its stability; an additional and probably more important factor is that the crowding in $T_A^{\pm}$ forces the *o*-nitro group out of the plane of the benzene ring, thereby reducing its mesomeric effect.

(3) The normalized β_{nuc} (or β_{lg}) values are close to 0.5 (−0.5), which indicates that positive charge development on the amine nitrogen, and with it presumably C–N bond formation, is approximately half complete at the transition state. We note that β_{nuc}^n is larger than in the reactions of the same amines with β-nitrostyrene[14] (β_{nuc}^n = 0.34 in 50% Me_2SO-50% water), benzylidenemalononitrile[5] (β_{nuc}^n = 0.30 in 50% Me_2SO-50% water), or benzylidene Meldrum's acid[16] (β_{nuc}^n = 0.08 in water). The unusually low value in this latter reaction can, in part, be accounted for by the different solvent; reducing the water content leads to increases in β_{nuc}^n.[27,28]

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(24) For example if all p$K_a^{\pm}$ values were as much as 1 log unit lower than assumed, k_{-1} would be 10-fold higher and K_1 would be 10-fold lower. This would increase $\log k_0^{NO_2}$ from 3.35 to 3.95 and $\log k_0^{(NO_2)_2}$ from 2.65 to 3.08.

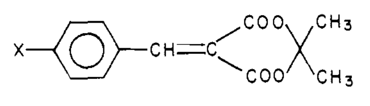
(25) A significantly lower β_{eq} for **1**-$(NO_2)_2$ could be the result of intramolecular hydrogen bonding of the ammonio proton to the *o*-nitro group. Such hydrogen bonding appears to be of some importance in adducts derived from benzylidene Meldrum's acid.[16,7] It it were significant in the adducts of **1**-$(NO_2)_2$ this should manifest itself in a k_{2p}^{OH} value for the deprotonation of $T_A^{\pm}$ by OH^- that is significantly lower for the morpholine adduct of **1**-$(NO_2)_2$ than of **1**-NO_2.[26] This is not the case (Table XI).

(26) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1.

The meaning of the normalized α values is perhaps somewhat less clearly defined than that of the normalized β values (more on this below), but it seems safe to assume that they are some measure of the negative charge developed on the benzene ring attached to the carbon bearing the cyano group, just as α_{CH} in the deprotonation of **2**-NO$_2$ and **2**-(NO$_2$)$_2$ is such a measure.[13] The values for $\alpha_{nuc}{}^{n}$ indicate, particularly for the piperidine and *n*-butylamine reactions, that negative charge development is considerably less than half complete at the transition state.

A comparison of $\alpha_{nuc}{}^{n}$ with $\beta_{nuc}{}^{n}$ suggests then that the transition states are imbalanced in the sense that C–N bond formation seems to be ahead of negative charge development. A quantitative assessment of this imbalance is rendered somewhat difficult because of the relatively large experimental uncertainties in $\alpha_{nuc}{}^{n}$ and by the fact that $\beta_{nuc}{}^{n}$ depends on the olefin and $\alpha_{nuc}{}^{n}$ depends on the amine, a point to which we will return. Nevertheless, if we use an average $\beta_{nuc}{}^{n}$ (0.52) and an average (for piperidine and morpholine) $\alpha_{nuc}{}^{n}$ (0.32) we can crudely quantify the imbalance as $I \approx \beta_{nuc}{}^{n}(av) - \alpha_{nuc}{}^{n}(av) = \beta_{lg}{}^{n}(av) - \alpha_{lg}{}^{n}(av) = 0.20$.

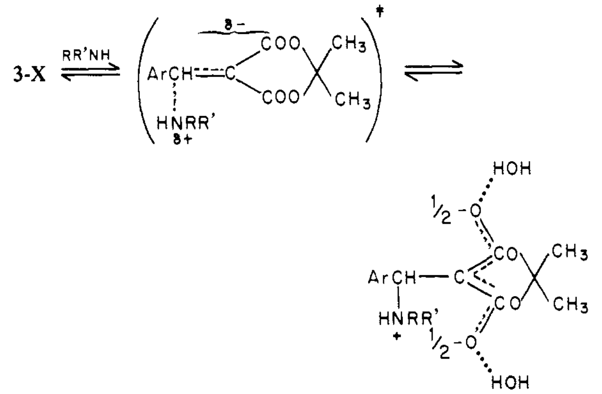
It is revealing to compare the present results with those reported for the reactions of **3**-X with morpholine and piperidine where



3-X, X = H, OMe, NMe$_2$

$\beta_{nuc}{}^{n}(av) = 0.11$ and $\alpha_{nuc}{}^{n}(av) = 0.43$.[16] These numbers indicate an imbalance in the transition states that is of opposite sign since $I \approx \beta_{nuc}{}^{n}(av) - \alpha_{nuc}{}^{n}(av) = -0.32$ is negative. This suggests that here it is the negative charge development (on the (COO)$_2$C(CH$_3$)$_2$ moiety) which is ahead of the C–N bond formation.

Our preferred interpretation[8] of this latter imbalance is illustrated in eq 21. In the adduct the negative charge is essentially



(21)

all concentrated on the carbonyl oxygens where it can be dispersed by hydrogen bonding from the solvent. However, in the transition state the solvent reorganization, which leads to the proper orientation of the water molecules, has not occurred yet or is incomplete. Hence the negative charge is not yet dispersed by the solvent and some of it may be concentrated on carbon, possibly even on the benzylic carbon and/or the phenyl group. The result is an exalted $\alpha_{nuc}{}^{n}$, not because there is a greater amount of charge than that supplied by the entering nucleophile but because the center of gravity of the charge is closer to the phenyl substituent in the transition state than it is in the adduct. An additional factor, discussed in more detail elsewhere,[16] is that loss of resonance stabilization of the olefin might be ahead of C–N bond formation in the transition state. Inasmuch as a large fraction of the substituent effect on the reaction of **3**-X probably arises from this loss of resonance stabilization,[16] this factor would contribute to an exalted $\alpha_{nuc}{}^{n}$ value. We shall return to this factor at the end of this paper.

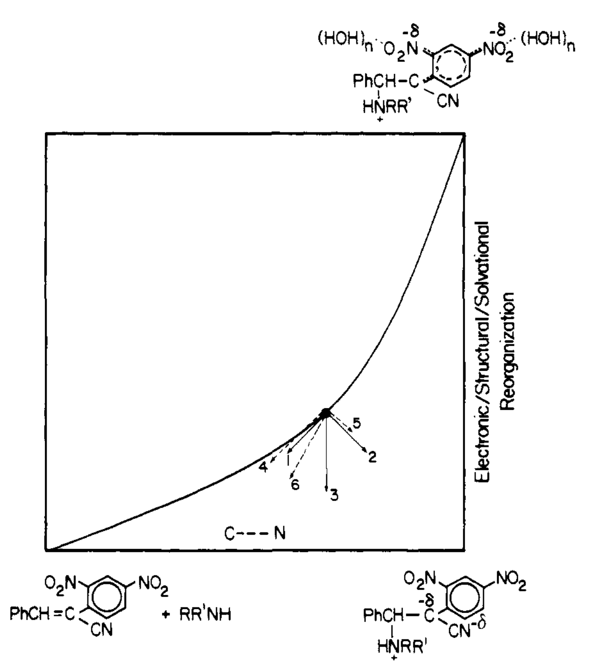
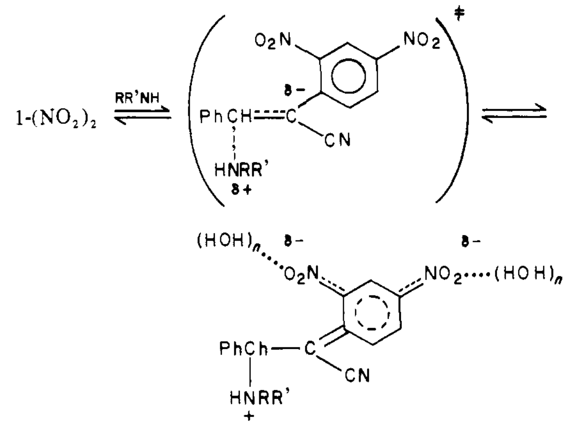


Figure 8. More O'Ferrall–Jencks diagram for the reaction of amines with **1**-(NO$_2$)$_2$ that has separate axes for C–N bond formation/cleavage and for structural/electronic and solvent reorganization. Curved reaction coordinate shows lag of structural/electronic and solvent reorganization behind C–N bond formation. Arrows show the effect of making the amine more basic (arrows 1 and 2 with resulting arrow 3) and the effect of changing from **1**-NO$_2$ to **1**-(NO$_2$)$_2$ (arrows 4 and 5 with resulting arrow 6).

The imbalance in the reactions of **1**-NO$_2$ and **1**-(NO$_2$)$_2$ probably has the same origin, namely, a lag in solvent reorganization and charge dispersion behind C–N bond formation, as illustrated in eq 22 for **1**-(NO$_2$)$_2$. But since here the substituent is in the phenyl



(22)

group that accommodates the negative charge, $\alpha_{nuc}{}^{n}$ is not exalted but reduced because in the transition state the negative charge is *farther away from* (rather than closer to) the substituent than in the adduct. Note that this is essentially the same explanation as that given for a similar imbalance observed in the deprotonation of **2**-NO$_2$ and **2**-(NO$_2$)$_2$.[13]

A convenient way to illustrate these imbalances is to place the reactions on a More O'Ferrall–Jencks diagram[30-33] that has

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(27) Bernasconi, C. F.; Grodzinski, L. J.; Tia, P. R., unpublished observations.

(28) In acetonitrile $\beta_{nuc}{}^{n} = 0.43$.[29]

(29) Schreiber, B.; Martinek, H.; Wolschann, P.; Schuster, P. *J. Am. Chem. Soc.* **1979**, *101*, 4708.

(30) More O'Ferrall, R. A. *J. Chem. Soc. B.* **1970**, 274.

(31) Jencks, W. P. *Chem. Rev.* **1972**, *72*, 705.

(32) Hupe, D. J.; Jenks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451.

(33) Since the imbalances in the olefin reactions and the proton transfers seem to have the same origin[8] it is probably not a coincidence that numerically they are of comparable magnitude for a given activating substituent. Thus $I \approx 0.20$ for nucleophilic addition to **1**-NO$_2$/**1**-(NO$_2$)$_2$ compared with $I = 0.26$ for the deprotonation of **2**-NO$_2$/**2**-(NO$_2$)$_2$,[13] while $I \approx -0.43$ for nucleophilic addition to **3**-X compares with $I \approx -0.37$ for the deprotonation of ArCH$_2$CH(COMe)COOEt by carboxylate ions.[34]

(34) Bell, R. P.; Grainger, S. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1367.

separate axes for C–N bond formation (cleavage) and for solvent reorganization/charge dispersion (Figure 8). The imbalances discussed above imply a curved reaction coordinate as shown in the figure.[33] As discussed in more detail in the preceding paper,[13] these diagrams should of course not be taken too literally but they serve well as a qualitative tool to visualize the observed imbalances.

It should be noted that the interpretation of the imbalances and of the lower intrinsic rate constant in the dinitro derivative is related in a similar way as for the corresponding proton transfers of **2**-NO_2 and **2**-$(NO_2)_2$, as discussed in more detail in the preceding paper.[13]

(4) The dependence of $\beta_{\rm nuc}^{\rm n}$ ($\beta_{\rm lg}^{\rm n}$) on the olefin and the dependence of $\alpha_{\rm nuc}^{\rm n}$ ($\alpha_{\rm lg}^{\rm n}$) on the amine are related by the diagonal interaction coefficient $p_{yy'}$,[35,36] which is given by

$$p_{yy'} = -\frac{\partial\beta_{\rm nuc}^{\rm n}}{(\partial \log K_1)_{\rm RR'NH}} = -\frac{\partial\alpha_{\rm nuc}^{\rm n}}{(\partial \log K_1)_{\rm olefin}} \qquad (23)$$

We obtain an average value $p_{yy'} \approx 0.075$ for the reactions of **1**-NO_2 and **1**-$(NO_2)_2$ while for the reactions of **3**-X $p_{yy'} \approx 0.022$. Note that positive[36] values are consistent with the reactivity–selectivity principle;[38] examples where $p_{yy'}$ is negative (i.e., in violation of the RSP) or zero have been discussed by Young and Jencks[39] (mainly S_N2 reactions). In the light of current views, though, no special significance should be attached to either adherence to or violation of the RSP.[38,39]

$p_{yy'}$ is a measure of how the transition state changes with changing substituent in the reactants.[35,37] A possible way to understand these changes in the reactions of **1**-NO_2 and **1**-$(NO_2)_2$ is based on the diagram of Figure 8. An increase in the basicity of the amine (morpholine → piperidine) has the effect of stabilizing the right edge of the diagram. This introduces a shift of the transition state along the reaction coordinate toward the reactants (arrow 1) and a shift perpendicular to it toward the lower right corner (arrow 2) with a resulting downward displacement (arrow 3). Inasmuch as there must be a relationship between $\alpha_{\rm nuc}^{\rm n}$ and the degree of charge delocalization into the X substituent (see also the preceding paper[13]), this downward displacement of the transition state implies a reduced $\alpha_{\rm nuc}^{\rm n}$ as observed.[40]

The change from **1**-NO_2 to **1**-$(NO_2)_2$ has also the effect of stabilizing the right edge, but stabilization of the upper right corner should be much more pronounced than that of the lower corner (see also preceding paper[13]). This generates the shifts indicated by the arrows 4 and 5 with a net shift as shown by arrow 6. This latter shift is in the direction of less C–H bond formation, which again is consistent with the smaller $\beta_{\rm nuc}^{\rm n}$.

The positive sign of $p_{yy'}$ for the reactions of **3**-X calls for comment. In the deprotonation of C–H acids we noted the following correlations between the signs of $p_{\rm xy} = \partial\beta_{\rm B}/\partial pK_{\rm a}^{\rm CH} = -\partial\alpha_{\rm CH}/\partial pK_{\rm a}^{\rm BH}$ and the signs of the imbalance in I: When the substituent change occurs in the phenyl group that is directly attached to the deprotonated carbon (**2**-NO_2/**2**-$(NO_2)_2$ pair) we have $I > 0$ and $p_{xy} > 0$. When the substituent is in the remote phenyl group (e.g., $ArCH(CH_3)NO_2$) we have the opposite situation, i.e., $I < 0$ and $p_{xy} \leq 0$. These sign reversals can be understood in terms of the location of the substituent with respect to the site of negative charge development in the transition state and product anion.[13]

In view of the close analogy between nucleophilic additions to olefins and deprotonations of C–H acids, one might have expected the same relationships between the signs of I and $p_{yy'}$ ($p_{yy'}$ corresponds to p_{xy} in the proton transfer) and the location of the substituent in the olefin. Indeed for the **1**-NO_2/**1**-$(NO_2)_2$ pair we have $I > 0$ and $p_{yy'} > 0$ as for the **2**-NO_2/**2**-$(NO_2)_2$ pair. For **3**-X, $I < 0$ as expected for a system where the substituent is located on a remote phenyl group but the positive sign of $p_{yy'}$ is contrary to expectation.

This positive value probably results from the fact that in the reaction of **3**-X the substituent effect is not so much related to the stabilization of the developing negative charge in transition state and product but rather to the loss of resonance stabilization of the olefin.[16] This notion is represented in Figure 7 of ref 16, which is a More O'Ferrall–Jencks diagram that has separate axes for C–N bond formation and for rehybridization of the benzylic carbon/loss of resonance stabilization. According to this diagram a change to a more basic amine would have the effect of stabilizing the product (upper right corner) and thus shifting the transition state toward the reactants (lower left corner). This should reduce the degree of rehybridization and decrease $\alpha_{\rm nuc}^{\rm n}$, as observed. A change to a more electron-withdrawing X substituent would mainly reduce the stability of the reactant and thus generate a shift toward the reactant corner. As a consequence the degree of C–N bond formation and with it $\beta_{\rm nuc}^{\rm n}$ should decrease, as observed.

It should be noted that the effects discussed above operate irrespective of whether the reaction coordinate in Figure 7 of ref 16 is curved or diagonal.

Proton Transfers, $T_A^{\pm} \rightleftharpoons T_A^-$. The rate constants for proton transfer are summarized in Table XI. They are consistent with expectations based on the work of Eigen[26,41] and his school.[42] The following points are noteworthy:

(1) $k_{-2p}^{\rm H} = 1.50 \times 10^{10}$ M^{-1} s^{-1} for the protonation of T_A^- is close to the typical values for the diffusion-controlled protonation of tertiary amines by the hydronium ion in water ((1.5–3.0) × 10^{10} M^{-1} s^{-1}[26,43]). However, if one allows for the 3-fold higher viscosity of 50% Me_2SO–50% water,[44] one expects $k_{-2p}^{\rm H}$ to be about 3-fold higher in water,[45] i.e., $\approx 4.5 \times 10^{10}$ M^{-1} s^{-1}. This is slightly higher than the typical rate constants for protonation of tertiary amines, possibly because of an electrostatic effect by the negative charge in T_A^-. The notion of an electrostatic effect is supported by the results for $k_{2p}^{\rm OH}$ discussed next.

(2) The $k_{2p}^{\rm OH}$ values of (2–3) × 10^9 M^{-1} s^{-1} are significantly below the diffusion-controlled rate constants for the deprotonation of tertiary ammonium ions by OH^- in water ((2–3) × 10^{10} M^{-1} s^{-1}[26,41]). However, because $T_A^{\pm}$ is a zwitterion there may be an electrostatic retardation just as is found for $Me_2N^+HCH_2COO^-$ for which $k_{\rm OH} = 7.3 \times 10^9$ M^{-1} s^{-1} in water.[41] After allowance is made for the viscosity difference our $k_{2p}^{\rm OH}$ values would be about (6–9) × 10^9 M^{-1} s^{-1} in water, in excellent agreement with $k_{\rm OH}$ for $Me_2N^+HCH_2COO^-$. This analysis shows that $pK_a^{\pm}$(pip) estimated via eq 5 must be fairly reliable. If $pK_a^{\pm}$(pip) were substantially lower this would lead to an unreasonably high $k_{2p}^{\rm OH}$ value since $k_{2p}^{\rm OH}$ is obtained from eq 13 in which k_{-1} would be larger.

(3) $k_{2p}^{\rm A}$ for the deprotonation of $T_A^{\pm}$ (**1**-$(NO_2)_2$) by morpholine (1.44 × 10^6 M^{-1} s^{-1}) and $k_{2p}^{\rm B}$ for deprotonation by *p*-cyanophenoxide ion (1.53 × 10^7 M^{-1} s^{-1}) and *N*-methylmorpholine (8.05 × 10^5 M^{-1} s^{-1}) are all considerably below the usual limit of ≈6 × 10^8 to ≈3 × 10^9 M^{-1} s^{-1} for thermodynamically favored deprotonations of ammonium ions by normal general bases.[42] This undoubtedly reflects steric hindrance to the approach of the base to the bulky $T_A^{\pm}$. The retardation becomes progressively more pronounced as the bulkiness of the base increases (*p*-cyano-

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(35) Palmer, J. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 6472.

(36) This definition of $p_{yy'}$ is currently preferred[35] over the earlier definition,[37] which had a different sign.

(37) Jencks, D. A.; Jencks, W. P. *J. Am. Chem.* **1977**, *99*, 7948.

(38) See, for example: (a) Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348. (b) Kemp, D. S.; Casey, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 6670. (c) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755. (d) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69. (e) McLennan, D. J. *Tetrahedron* **1978**, *34*, 2331.

(39) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288.

(40) The relationship between $\alpha_{\rm nuc}^{\rm n}$ and charge delocalization is probably not a simple one since X undoubtedly also responds to the negative charge in the hypothetical intermediate of the lower right corner but less so than to the charge in the actual adduct (upper right corner). See also preceding paper[13] for additional comments regarding the use of these diagrams.

(41) Eigen, M.; Kruse, W.; Maass, G.; DeMaeyer, L. *Prog. React. Kinet.* **1964**, *2*, 287.

(42) See, for example: Ahrens, M.-L.; Maass, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 818.

(43) Grunwald, E. *J. Phys. Chem.* **1967**, *71*, 1846.

(44) Janz, G. J.; Tomkins, R. P. T. "Nonaqueous Electrolyte Handbook"; Academic Press: New York, 1972; Vol. 1, p 86.

(45) Crooks, J. E. In "Proton Transfer Reactions"; Caldin, E. F., Gold, V., Eds., Wiley: New York, 1975; p 153.

(46) Bell, R. P. "The Proton in Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1973; Chapter 10.

phenoxide ion < morpholine < *N*-methylmorpholine).

The steric effect is seen to be slightly smaller in the deprotonation of $T_A^{\pm}$ derived from **1**-NO_2, as one would expect for the slightly less crowded mononitro adduct. For example, k_{2p}^{A} is about 3-fold higher for **1**-NO_2 than for **1**-$(NO_2)_2$ despite the slightly more favorable $\Delta pK = pK_a^{AH} - pK_a^{\pm}$ for **1**-$(NO_2)_2$ (2.89) vs. 2.35 for **1**-NO_2. On the other hand there is no significant difference between **1**-NO_2 and **1**-$(NO_2)_2$ with respect to catalysis by phenoxide or substituted phenoxide ions. This could be due, in part, to experimental error in k_{2p}^{B}; k_{-2p}^{BH} was only determined at one pH value (compared to k_{-2p}^{AH}, which is the average from determinations at four different pH values), and k_{2p}^{B}, which is calculated as $k_{-2p}^{BH}K_a^{\pm}/K_a^{BH}$, is very sensitive to the uncertainties in $pK_a^{\pm}$, which are relatively large in the case of **1**-NO_2. It should also be noted that since the phenoxide ions are less bulky than morpholine, discrimination between **1**-NO_2 and **1**-$(NO_2)_2$ should be less pronounced than for k_{2p}^{A} and thus could be masked by the experimental uncertainties.

Other systems where proton-transfer rates are depressed by steric crowding in $T_A^{\pm}$ include the amine adducts of 1,1-dinitro-2,2-diphenylethylene[15] and of 1,3,5-trinitrobenzene.[20] We note that these are the systems where eq 5 appears to hold, i.e., where coordination of *n*-butylamine and piperidine with an electrophile has, surprisingly,[21] the same effect on pK_a. Possibly this is, at least in part, because the stronger solvation of $RR'NH_2^+$ (two H bonds to solvent) compared to $RR'R''NH^+$ (one H bond), which usually leads to $pK_a(RR'NH_2^+) > pK_a(RR'R''NH^+)$, is sterically hindered. This interpretation also fits with the observation that with the less crowded amine adducts of β-nitrostyrene eq 5 breaks down.[47]

Experimental Section

Materials. α-Cyano-4-nitrostilbene (**1**-NO_2) and α-cyano-2,4-dinitrostilbene (**1**-$(NO_2)_2$) were prepared by known procedures.[17,48] **1**-NO_2 was recrystallized from ethanol, mp 177–178 °C (lit.[48] mp 175–176 °C); **1**-$(NO_2)_2$ was recrystallized from glacial acetic acid, mp 161–162 °C (lit.[17] mp 160–161 °C). (4-Nitrophenyl)acetonitrile (**2**-NO_2) and (2,4-dinitrophenyl)acetonitrile (**2**-$(NO_2)_2$) were available from a previous study.[13] Piperidine, morpholine, *n*-butylamine, *N*-methylmorpholine, and *p*-cyanophenol were purified as described before.[15] Reagent grade Me_2SO was stored over 4-Å molecular sieves prior to use. All other chemicals were reagent grade and were used without further purification.

Reaction Solutions, pH Measurements, and Spectra. The procedures used were essentially those described earlier.[15]

Rate and Equilibrium Measurements. We followed the general procedures described earlier[5,15] except that the evaluation of τ_1^{-1} was, in part, performed by direct computer interface with our stopped-flow apparatus. In the pH-jump experiments involving the adducts of **1**-$(NO_2)_2$, the pH jump had to be applied within 1–2 min after generating T_A^- because T_A^- decomposes in strongly basic solution into benzaldehyde and **2**-$(NO_2)_2^-$ and into an additional product with λ_{max} at 360 and 500 nm. The nature of this species was not further investigated but we suspect it is a product of the hydrolysis of the cyano group of **1**-$(NO_2)_2$.

Acknowledgment. This work was supported by Grants No. CHE-77-27998 and CHE-80-24261 from the National Science Foundation. We thank Professor William P. Jencks for comments on this manuscript.

Registry No. **1**-NO_2, 3695-95-2; **1**-$(NO_2)_2$, 19051-22-0; **1**-NO_2 (morpholine adduct), 85613-79-2; **1**-$(NO_2)_2$ (morpholine adduct), 85613-83-8; **1**-NO_2 (anionic piperidine adduct), 85613-82-7; **1**-$(NO_2)_2$ (anionic morpholine adduct), 85613-81-6; **1**-$(NO_2)_2$ (anionic piperidine adduct), 85613-80-5; **3**-H, 1214-54-6; **3**-OMe, 15795-54-7; **3**-NMe_2, 15795-57-0; *n*-butylamine, 109-73-9; piperidine, 110-89-4; morpholine, 110-91-8; morpholinium, 45422-42-2; *N*-methylmorpholinium, 57133-78-5; *p*-cyanophenol, 767-00-0; phenol, 108-95-2; *p*-chlorophenol, 106-48-9; water, 7732-18-5; *N*-methylmorpholine, 109-02-4; *p*-cyanophenoxide, 767-00-0; *p*-chlorophenoxide, 24573-38-4; phenoxide, 3229-70-7; hydroxide, 14280-30-9.

Supplementary Material Available: Kinetic and equilibrium data, Tables S1–S6 (8 pages). Ordering information is given on any current masthead page.

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[47] $pK_a^{\pm}(pip) = 8.30$, $pK_a^{\pm}(n\text{-}BuNH_2) = 8.62$.[14]

[48] Schonne, A.; Braye, E.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1953**, *62*, 155.

α- and β-Carbon Substituent Effect on S_N2 Reactivity. A Valence-Bond Approach

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Abstract: The α- and β-carbon substituent effect, on S_N2 reactivity and reactivity–selectivity, is discussed by using a (previously described) correlation diagram model of S_N2. The reaction barrier (E) is a fraction (f) of the energy gap ($I_{N:} - A_{RX}$) between the two curves which intersect to yield the reaction profile. $I_{N:}$ is the ionization potential of the nucleophile (N:) and A_{RX} is the electron affinity of the substrate (RX). The fraction (f) of $I_{N:} - A_{RX}$ which enters the activation barrier depends inter alia on the degree of delocalization of the three-electron bonds, e.g., $(R\cdots X)^-$. The more delocalized the three-electron bond, the larger the f. Thus, reactivity trends arise from the interplay between the electron surge aspect ($I_{N:} - A_{RX}$) and the bond-interchange aspect (e.g., the degree of delocalization of the three-electron bonds) of the S_N2 transformation. It is shown that α-halo substitution (on R) delocalizes the three-electron bond and effects a small improvement in the acceptor ability of the substrate, and therefore it slows down S_N2 reactivity. The largest delocalization is effected when the α-substituent(s) is (are) identical with the leaving group. In these cases, one observes the strongest rate retardation. π-acceptor α-substituents improve the substrate acceptor ability markedly without greatly delocalizing the three-electron bonds. Therefore, these substituents will enhance reactivity but *mainly toward powerful nucleophiles*. The effects of other α-substituents (e.g., CH_3O, Ph, SiR_3, etc.) and β-substituents (e.g., F, Cl, Br, RO, etc.) are also discussed in this light. The reactivity reversals often reported in the literature are suggested to be manifestations of the gap–slope interplay.

The effect of α- and β-carbon substitution on the S_N2 reactivity of CH_3X derivatives (eq 1) poses a variety of intriguing trends which *in totality* remain enigmatic.

$$N: + YCH_2\text{–}X \rightarrow N\text{–}CH_2Y + :X \qquad (1)$$

Already in the twenties Petrenko-Kritschenko[1] had observed that α-halogenation deactivates the reactivity of various halides toward nucleophilic reagents. Thus, CH_3X (X = Cl, Br, I) was found to be more reactive than its polyhalogenated derivatives, CH_2X_2, CHX_3, and CX_4, and similarly CH_3CH_2X, $PhCH_2Cl$, and HO_2CCH_2X were found to be respectively more reactive than CH_3CHX_2 (X = Cl, Br, I), $PhCH_2Cl_2$, and HO_2CCHX_2 (X = Cl, Br).

In the course of the years several other groups have reported similar trends. Backer and van Mels[2] observed that α-halogenation of potassium bromoacetate results in a diminished reactivity toward potassium sulfite and that α-Br (i.e., KO_2CCHBr_2) tempers S_N2 reactivity better than does α-Cl (i.e., $KO_2CHClBr$). Davies et

0002-7863/83/1505-4359$01.50/0