$\times 10^5$, σ_{n-1} 0.0257 $\times 10^5$; for gly, f_{gly} = 0.501 45 $\times 10^5 \equiv 0.50 \times 10^5$, σ_{n-1} 0.0267 $\times 10^5$; for lan, f_{lan} = 0.6032 $\times 10^5 \equiv 0.60 \times 10^5$, σ_{n-1} 0.0187 $\times 10^5$. In the analysis for cys, the area of gly reported is not the same as the area in the glu-gly-lan study. Therefore, the ratio of f_{cys} to f_{gly} for these analyses was calculated, 1.1549, σ_{n-1}: 0.0556, and applied to the above value of gly to give f_{cys} = 0.58 $\times 10^5$.

The amount of glutathione disulfide and glutathione sulfide (3) was calculated using two glu and two gly for each cys or lan. The millimole values for serine and alanine were used without calibration. The weight of each fraction analyzed was calculated as the sum of the weights of all the amino acids in the fraction and was found to range between 1.2 and 0.8 mg (Table II).

NMR Analysis. The fractions containing glutathione sulfide and glutathione disulfide showed no NMR signals attributable to the bimane moiety. Changes in the NMR spectra were observed in the region of the cysteine proton signals (Figure 2).

Glutathione Sulfide (3) (GSG). ^{1}H NMR (D$_2$O): 2.274–2.503 (m, 4 H, CH$_2$ glu), 2.698–2.874 (m, 4 H, CH$_2$ glu), 2.987–3.488 (m, 4 H, CH$_2$ cys), 3.974–4.081 (2 H, J = 6.0 Hz, CH cys), 4.012 (s, 4 H, CH$_2$ gly), 4.772–4.925 (m, 2 H, CH glu].

The specific chemical shifts δ (intensity ratios) for the lanthionine methylene protons are 2.987 (0.10), 3.015 (0.05), 3.089 (0.15), 3.145 (0.33), 3.171 (0.23), 3.262 (1.00), 3.321 (0.54), 3.425 (0.18), and 3.448 (0.10). The appearance and increasing strength of the signal at δ 3.262 as well as the downfield shift of the lan methyne protons were used as a measure of glutathione sulfide in the sample. The yields of glutathione

disulfide and glutathione sulfide in fractions not analyzed were estimated by interpolation using the results from the GSSG reductase experiments used for the GSSG values and of the amino acid analysis for the GSG. The total yield of glutathione disulfide was estimated as 0.388 g (0.59 mmol) and of glutathione sulfide as 0.416 g (0.665 mmol).

Nucleophilic Addition to Olefins. 16.[1] Unusual Substituent Effects in the Reaction of Amines with β-Nitrostyrenes. Solvent Effect on Intrinsic Rate Constants

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Abstract: A kinetic study of the addition of piperidine and morpholine to β-nitrostyrene in water and in 70% Me$_2$SO–30% water at 20 °C and of piperidine to 4-NO$_2$-, 4-CN-, 3-Cl-, 4-Br-, 4-OMe-, and 4-NMe$_2$-substituted β-nitrostyrenes in water at 20 °C is reported. The reaction leads to a zwitterionic adduct, ArCH(R$_2$NH)$^+$CHNO$_2^-$ (T$^\pm$), which is in rapid equilibrium with its conjugate base, ArCH(R$_2$N)CHNO$_2^-$ (T$^-$). Rate constants for nucleophilic attack (k_1) and its reverse (k_{-1}) both increase slightly along the series H, 4-Br, 3-Cl, 4-CN, and 4-NO$_2$ with Hammett $\rho(k_1)$ = 0.27 ± 0.02 and $\rho(k_{-1})$ = 0.33 ± 0.05, while for the equilibrium constant, $K_1 = k_1/k_{-1}$, $\rho_{eq}(K_1) \approx 0$. The small size of the substituent effects is attributed to the near cancellation of two opposing factors: the combined effect of negative charge development and rehybridization of the α-carbon and the effect of the positive charge of the amine nitrogen. The fact that $\rho(k_1)$ and $\rho(k_{-1})$ are larger than $\rho(K_1)$ indicates a transition-state imbalance which arises from a lag in the resonance stabilization and solvation of the negatively charged CHNO$_2$ moiety. K_1 for the 4-OMe and 4-NMe$_2$ derivatives deviates negatively while k_1 and k_{-1} show positive deviations from the Hammett plots defined by the other substituents. The negative deviation of K_1 is attributed to resonance stabilization of the olefin which is a common phenomenon. The positive deviations for k_1 and k_{-1} are unusual because they suggest an even greater resonance stabilization in the transition state. These observations are attributed to the energetic advantage of having the negative charge delocalized into the nitro group at the transition state. This avoids the problem of the late development of resonance stabilization of the negative CHNO$_2$ moiety which is the main reason for the high intrinsic barriers in nitronate ion forming reactions. A two-point Brønsted plot for the piperidine and morpholine reactions with β-nitrostyrene yields β_{nuc} = 0.26 (β_{nuc}^n = 0.25) and an intrinsic rate constant, log k_0 = 2.10 ($k_0 = k_1 = k_{-1}$ at K_1), in water. In 70% Me$_2$SO β_{nuc} = 0.32 (β_{nuc}^n = 0.37) and log k_0 = 2.90. The increase in log k_0 upon addition of Me$_2$SO is consistent with late solvation of the negative charge being a factor contributing to the high intrinsic barrier of nitronate ion forming reactions. When in the kinetic experiments the equilibrium is approached from the T$^-$ side, protonation of T$^\pm$ on carbon becomes significant at high buffer concentrations, to yield ArCH(R$_2$NH)$^+$CH$_2$NO$_2$ (T$^+$) as a transient. This allowed evaluation of various kinetic and thermodynamic parameters of T$^+$.

The study of substituent effects on the reaction of nucleophiles with activated olefins of the type
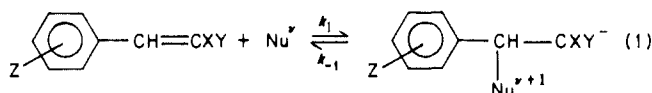
where X and Y are electron-withdrawing groups, has yielded interesting information about the transition states of these reac-

tions. For example with XY = (COO)$_2$C(CH$_3$)$_2$ (benzylidene Meldrum's acids) it was observed that the normalized Hammett ρ-values, $\rho_n(k_1) = \rho(k_1)/\rho(K_1)$, are larger than the normalized β_{nuc}-values, $\beta_{nuc}^n = \beta_{nuc}/\beta_{eq}$, for the addition of amines[2] or aryloxide ions.[3] This disparity in the substituent effects or "imbalance" was attributed to a lag in the charge delocalization into the

(1) Part 15: Bernasconi, C. F.; Fox, J. P.; Kanavarioti, A.; Panda, M. *J. Am. Chem. Soc.* **1986,** *108,* 2372.

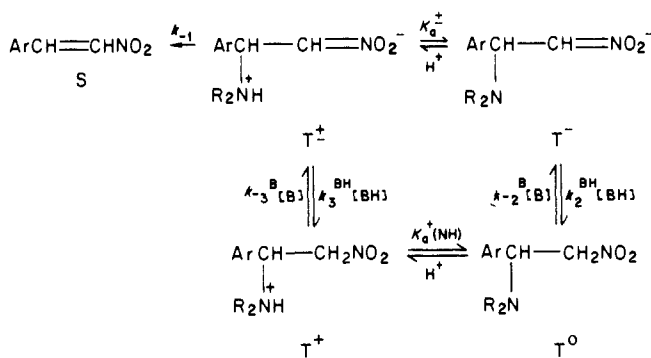(2) Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980,** *102,* 5329.
(3) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982,** *104,* 5133.
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4542 *J. Am. Chem. Soc., Vol. 108, No. 15, 1986*

Bernasconi et al.

$(COO)_2C(CH_3)_2$ moiety behind C–Nu bond formation in the transition state.[3,5]

Similar conclusions have emerged from a study of substituent and solvent effects on the addition of hydroxide ion and amines to benzylidenemalononitriles[7] ($XY = (CN)_2$) and a study of the reaction of amines with α-nitrostilbenes substituted in the α-phenyl group.[8]

A particularly interesting feature of reaction 1 is that the olefin may be subject to substantial resonance stabilization by electron-donating substituents such as 4-OMe and 4-NMe$_2$ (1) if X

$$Z^+ = \!\!\!\!\bigcirc\!\!\!\!= CHCXY^-$$

1

and/or Y are strongly electron-withdrawing. This reduces both k_1 and K_1 and manifests itself by negative deviations of the 4-OMe and 4-NMe$_2$ points from Hammett plots based on the standard σ-values and by better correlations with σ^+-values. The literature until 1973 on this topic has been thoroughly reviewed by Rappoport and Ladkani.[9] More recent examples include the reactions of benzylidene Meldrum's acids with amines in water[2] and acetonitrile,[10] of water and hydroxide ion addition to the same substrates in water,[3] and of benzylidenemalononitriles with piperidine[7] and hydroxide ion[6] in aqueous Me$_2$SO.

The main theme of this paper is an examination of the substituent effects on the reaction of piperidine with substituted β-nitrostyrenes in water. The nitro group represents an extreme in terms of its electronic effect on carbanion-forming reactions, mainly because of its strong resonance stabilization of the negative charge.[5] This has been particularly apparent in the deprotonation of nitroalkanes and the unusual substituent effects observed in these reactions.[11-15] One might therefore expect some extreme behavior with regard to substituent effects in the nucleophilic addition to β-nitrostyrenes, too. The results to be presented will confirm this expectation, particularly with respect to resonance effects.

A second point of major interest is the effect of solvent on the intrinsic barrier (in the Marcus[16] sense) or intrinsic rate constant of amine addition to β-nitrostyrene. To this end we have complemented a previous study[17] in 50% Me$_2$SO–50% water with new data in 70% Me$_2$SO–30% water.

Our previous investigation in 50% Me$_2$SO–50% water[17] showed that the reaction can be described by a two-step scheme, in which the proton transfer between T$^\pm$ and T$^-$ is a rapid equilibrium. In the present study the basic scheme of eq 2 will be confirmed but

$$ArCH{=}CHNO_2 +$$
$$\underset{S}{}$$

$$R_2NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{T^\pm}{ArC(R_2NH^+)HCH{=}NO_2^-} \overset{K_a^\pm}{\underset{H^+}{\rightleftharpoons}}$$

$$\underset{T^-}{ArC(R_2N)HCH{=}NO_2^-} \quad (2)$$

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

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Figure 1. Kinetics of adduct formation. Representative plots of τ_1^{-1} vs. piperidine concentration at pH 11.90.

it will be shown that, under certain experimental conditions, other species which are formed by carbon protonation of T$^\pm$ and T$^-$ can be generated as transients. This allowed us to determine a number of kinetic and thermodynamic parameters for some of these species.

Results

General Features. All kinetic experiments were performed by the stopped-flow technique and monitored at or near λ_{max} of the olefin (λ_{max} = 460, 359, 319, 324, 310, 308, and 315 nm for the 4-NMe$_2$, 4-OMe, unsubstituted, 4-Br, 3-Cl, 4-CN, and 4-NO$_2$ derivatives, respectively). The reactions were conducted in water and in 70% Me$_2$SO–30% water at 20 °C; in the former solvent the ionic strength was maintained, with KCl, at 0.5 M, in the latter at 0.25 M. Pseudo-first-order conditions were used throughout, with substrate concentrations around 2.5 × 10⁻⁵ M except for the poorly soluble 4-NMe$_2$ derivative in water where 5 × 10⁻⁶ M was used.

Kinetics of Adduct Formation. Rates of piperidine and morpholine adduct formation were measured as a function of amine concentration. Excellent first-order behavior was observed in all cases. The reciprocal relaxation time (observed pseudo-first-order rate constant) for equilibration of reaction 2 is given by

$$\tau_1^{-1} = k_1[R_2NH] + k_{-1}\frac{a_{H^+}}{K_a^\pm + a_{H^+}} \quad (3)$$

For each substrate/amine pair two series of runs were conducted. In water the first series with piperidine was at pH 11.90, the second at pH 12.49; the morpholine they were at pH 8.80 and 9.90. In 70% Me$_2$SO the first series with piperidine was at pH 11.38, the second at pH 11.78, and with morpholine at pH 9.69 and in a nonbuffered high-pH solution.

The results are summarized in Tables S1–S5 (supplementary material).[18] Representative plots of τ_1^{-1} vs. amine concentration for piperidine adduct formation are shown in Figure 1. The

Scheme I

intercepts are seen to be indistinguishable from zero which means that eq 3 simplifies to

$$\tau_1^{-1} = k_1[R_2NH] \tag{4}$$

The only reaction for which the $k_{-1}a_{H^+}/(K_a^\pm + a_{H^+})$ is non-negligible is that of β-nitrostyrene with morpholine in 70% Me$_2$SO at pH 9.69. The k_1-values are summarized in Table II for the reaction of β-nitrostyrene with the two amines in different solvents and in Table III for the reaction of piperidine with the substituted β-nitrostyrenes in water.

Kinetics of Adduct Breakdown. In order to evaluate k_{-1} and $K_a^\pm$, τ_1^{-1} was determined by approaching the equilibrium from the T$^-$ side. T$^-$ was generated in a solution containing 0.04 M amine and 10^{-3} M KOH. Under these conditions the substrates were virtually completely converted to T$^-$. These solution were then mixed with a buffer of lower pH ("pH-jump") in the stopped-flow apparatus and the formation of the olefin was monitored. In water, cacodylic acid and Dabco were used as buffers in a range from pH 5.63 to 9.14 with all the piperidine adducts, acetic acid and cacodylic acid in a range from pH 3.99 to 6.47 with the morpholine adduct of β-nitrostyrene. In 70% Me$_2$SO-30% water, Dabco and triethylamine buffers were used in a range from pH 7.90 to 9.61 with the piperidine adduct, acetic acid and Dabco (pH 7.49 to 8.60) with the morpholine adduct.

Piperidine Adducts in Water. A. pH-Jumps with Cacodylic Acid. With the cacodylic acid buffers (pH 5.63–6.87) the return of T$^-$ to the substrate (eq 2) was complicated by the transient formation of other products. The most typical situation was that two kinetic processes were observed. The first (τ_1^{-1}) occurred within a few seconds and led to recovery of the substrate (S) which, however, was not quantitative. The second process (τ_2^{-1}) was complete after 1–2 min and resulted in the recovery of the rest of S. When the experiments were carried out in a conventional spectrophotometer, spectra recorded after about 2 min showed ≈100% recovery of S.

Under certain conditions a third kinetic process could be observed. It led to a slow decrease in olefin concentration, presumably due to hydrolysis. This reaction was not investigated further.

The presence of the two kinetic processes, coupled with other observations to be described, is consistent with the extended Scheme I. As T$^-$ is mixed with acid the equilibrium T$^\pm$ ⇌ T$^-$ is immediately established by diffusion-controlled proton transfer.

In a first approximation the τ_1^{-1}-process then represents concurrent formation of S and of varying amounts of T$^+$ and/or T^0. The τ_2^{-1}-process is associated with conversion of T$^+$ and/or T^0 into substrate, via T$^\pm$ as a steady-state intermediate. This conversion occurs because the substrate is thermodynamically favored over T$^+$ and T^0.

We have determined how τ_1^{-1}, τ_2^{-1}, and the yield of substrate recovery at $\tau_2 \gg t \gg \tau_1$ depend on buffer concentration and pH. Table I summarizes the results for a representative case (S-Br) while the results for S-OMe, S-H, S-Cl, S-CN and S-NO$_2$ are in Tables S6-S10 (supplementary material).[18] With S-NMe$_2$ τ_2^{-1} was not detectable and substrate recovery was always close to 100%.

Table I. pH and Buffer Dependence of τ_1^{-1}, τ_2^{-1}, and the Fraction of Substrate Recovery for 4-Bromo-β-nitrostyrene in Cacodylic Acid Buffer[a]

no.	pH	[BH], M	[B⁻], M	τ_1^{-1}, s⁻¹	100 × τ_2^{-1}, s⁻¹	A_1/A_∞[b]
1	6.14	0.0105	0.0105	1.22	8.70	0.97
2	6.14	0.0505	0.0505	1.62	25.2	0.82
3	5.76	0.0245	0.0105	1.25	6.94	0.92
4	5.74	0.1245	0.0505	1.69	20.2	0.66
5	5.63	0.030	0.010	1.37	7.2	0.92
6	6.12	0.010	0.010	1.24	6.3	0.97
7	6.62	0.010	0.030	1.24	10.1	0.97
8	6.87	0.010	0.050	1.21	11.5	0.97

[a] Reactions in water at 20 °C. [b] Fraction of substrate recovery measured by absorption A_1 after end of τ_1-process and A_∞ after end of τ_2-process, at λ_{max} of the substrate, see text.

According to our interpretation of the fast process, τ_1^{-1} is given by

$$\tau_1^{-1} = k_{-1}\frac{a_{H^+}}{K_a^\pm + a_{H^+}} + k_2^{BH}[BH]\frac{K_a^\pm}{K_a^\pm + a_{H^+}} + k_3^{BH}[BH]\frac{a_{H^+}}{K_a^\pm + a_{H^+}} \tag{5}$$

Carbon protonation of T$^\pm$ and T$^-$ by the solvent or by H$_3$O$^+$ are negligible as seen by the fact that at very low buffer concentrations substrate recovery approaches 100%. Close to 100% recovery under these conditions also indicates that the intramolecular pathway, T$^\pm \rightarrow$ T^0, plays an insignificant role.[19]

If the concentrations of S, T$^+$, and T^0 after completion of the τ_1-process are labeled with a subscript 1, while [S]$_\infty$ designates the substrate concentration after completion of the τ_2-process, we can express the fraction of substrate recovery after the τ_1-process by

$$\frac{[S]_1}{[S]_\infty} = \frac{[S]_1}{[S]_1 + [T^0]_1 + [T^+]_1} = \frac{A_1}{A_\infty} \tag{6}$$

Since S is the only absorbing species, the fraction is also equal to the ratio of the respective absorbances, A_1/A_∞.

An alternative way of expressing this fraction is in terms of

$$\frac{A_1}{A_\infty} = \frac{k_{-1}\dfrac{a_{H^+}}{K_a^\pm + a_{H^+}}}{k_{-1}\dfrac{a_{H^+}}{K_a^\pm + a_{H^+}} + k_2^{BH}[BH]\dfrac{K_a^\pm}{K_a^\pm + a_{H^+}} + k_3^{BH}[BH]\dfrac{a_{H^+}}{K_a^\pm + a_{H^+}}}$$

$$= \frac{k_{-1}}{\tau_1^{-1}}\frac{a_{H^+}}{K_a^\pm + a_{H^+}} \tag{7}$$

Rearranging affords

$$\tau_1^{-1}\frac{A_1}{A_\infty} = k_{-1}\frac{a_{H^+}}{K_a^\pm + a_{H^+}} \tag{8}$$

Since in the cacodylic acid buffers the pH is substantially lower than $pK_a^\pm$ (see below), eq 8 yields k_{-1} according to

$$\tau_1^{-1}\frac{A_1}{A_\infty} \approx k_{-1} \tag{9}$$

while $K_a^\pm$ is obtained from experiments in Dabco buffers as detailed below.

(19) This conclusion does not mean that the intramolecular step is not an important pathway in the conversion of T$^\pm$ to T^0.[20] It only means that it cannot compete with the k_{-1} step.

(20) (a) Bernasconi, C. F.; Hibdon, S. A.; McMurry, S. E. *J. Am. Chem. Soc.* **1982**, *104*, 3459. (b) Bernasconi, C. F.; Murray, C. J. *Ibid.* **1984**, *106*, 3257.
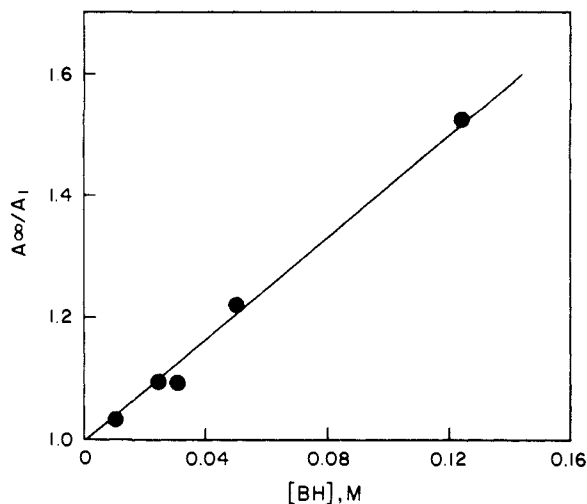
Figure 2. Plot according to eq 12 for 4-bromo-β-nitrostyrene.

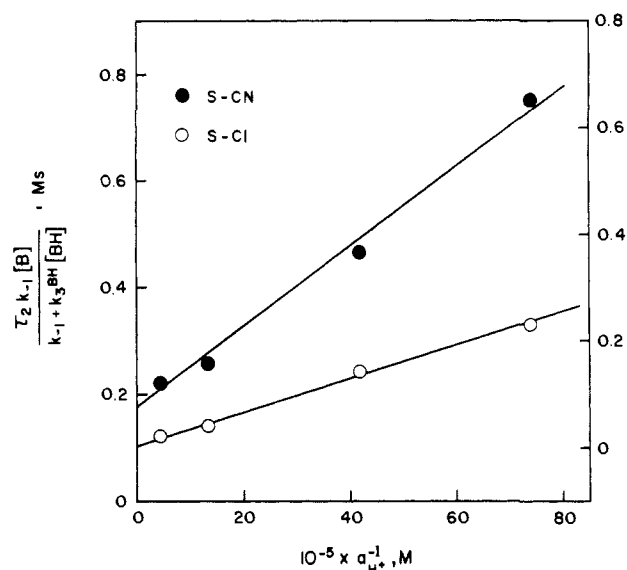**Figure 3.** Plots according to eq 14 for 3-chloro-β-nitrostyrene (left y axis) and 4-cyano-β-nitrostyrene (right y axis).

The pH dependence of A_1/A_∞ allows us to evaluate the relative importance of the k_2^{BH} vs. the k_3^{BH} term as follows. If the k_2^{BH} term were dominant eq 7 would simplify to

$$\frac{A_1}{A_\infty} = \frac{k_{-1}}{k_{-1} + k_2^{BH}K_a^{\pm}[B]/K_a^{BH}} \qquad (10)$$

where K_a^{BH} is the acid dissociation constant of BH. Equation 10 implies that for a given buffer *base* concentration the ratio A_1/A_∞ should be independent of pH. The data in Table I show that this clearly is not the case (entries 1 vs. 3; 2 vs. 4; 5 vs. 6).

If alternatively the k_3^{BH} term were dominant eq 7 would become

$$\frac{A_1}{A_\infty} = \frac{k_{-1}}{k_{-1} + k_3^{BH}[BH]} \qquad (11)$$

and the ratio A_1/A_∞ should be pH independent for given buffer *acid* concentration. The experimental results do indeed display this behavior (entries 1 and 6–8 in Table I). It should be noted, though, that in view of the fact that the A_1/A_∞ values are all relatively close to unity there is considerable experimental uncertainty in these ratios. Hence a small contribution by the k_2^{BH} term may have gone undetected.

Having shown that our data can be (approximately) fit to eq 11 the dependence of A_1/A_∞ on [BH] alows us to evaluate approximate k_3^{BH}/k_{-1} ratios from inversion plots according to

$$\frac{A_\infty}{A_1} = 1 + \frac{k_3^{BH}}{k_{-1}}[BH] \qquad (12)$$

This is shown in Figure 2 for 4-bromo-β-nitrostyrene. In conjunction with k_{-1} we now obtain k_3^{BH}.

Analysis of τ_2^{-1} allows evaluation of additional parameters as follows. Since in the formation of T$^+$ the k_3^{BH} pathway was shown to be dominant, the k_{-3}^{B} step must be the main pathway in the conversion of T$^+$ to S. If T$^{\pm}$ is treated as a steady-state intermediate τ_2^{-1} is given by

$$\tau_2^{-1} = \frac{a_{H^+}}{K_a^+(NH) + a_{H^+}} \frac{k_{-3}^{B}k_{-1}[B]}{k_{-1} + k_3^{BH}[BH]} \qquad (13)$$

with $K_a^+(NH)$ being the nitrogen acidity constant of T$^+$.
Rearranging eq 13 affords

$$\frac{\tau_2 k_{-1}[B]}{k_3^{BH}[BH] + k_{-1}} = \frac{1}{k_{-3}^{B}} + \frac{K_a^+(NH)}{k_{-3}^{B}a_{H^+}} \qquad (14)$$

A representative plot of the left side of eq 14 vs. a_H^{-1} is shown in Figure 3. It provides k_{-3}^{B} and $K_a^+(NH)$.

We now also obtain $K_a^+(CH) = (k_{-3}^{B}/k_3^{BH})K_a^{BH}$ for the carbon acidity constant of T$^+$ and $K_a^0(CH) = K_a^{\pm}K_a^+(CH)/K_a^+(NH)$ for the carbon acidity constant of T^0.
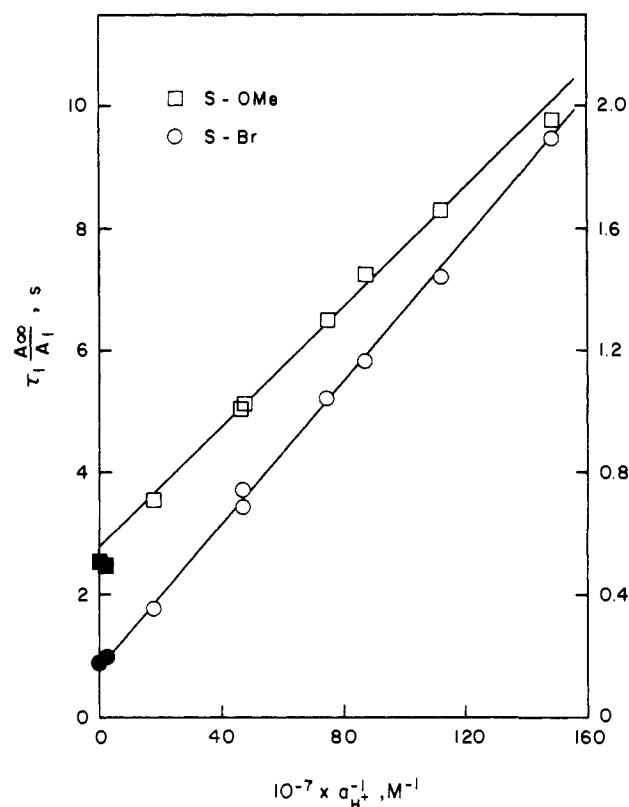
Figure 4. Plots according to eq 15 for 4-methoxy-β-nitrostyrene (right y axis) and 4-bromo-β-nitrostyrene (left y axis). Open symbols, Dabco data; filled symbols, cacodylic acid data.

B. pH Jumps with Dabco. Experiments with Dabco buffers performed between pH 8.24 and 9.17 were aimed at evaluating $pK_a^{\pm}$ on the basis of eq 8 or its inverted form

$$\tau_1 \frac{A_\infty}{A_1} = \frac{1}{k_{-1}} + \frac{K_a^{\pm}}{k_{-1}a_{H^+}} \qquad (15)$$

In these experiments formation of T$^+$ and T^0 was negligible; i.e., only the τ_1-process could be clearly observed (see below, however), substrate recovery was essentially quantitative, and τ_1^{-1} was independent of buffer concentration.

The results are summarized in Tables S11 and S12 (supplementary material)[18] while Figure 4 shows two representative plots according to eq 15. With the 4-Br derivative there is excellent

Table II. Rate and Equilibrium Constants of Equation 2 for the Reactions of Piperidine and Morpholine with β-Nitrostyrene in Different Solvents at 20 °C[a]

amine (p$K_a^{R_2NH_2^+}$)	k_1, M^{-1} s^{-1}	k_{-1}, s^{-1}	K_1(pK_1), M^{-1}	p$K_a^{\pm}$	p($K_1 K_a^{\pm}$)	p$K_a^{CH_3NO_2}$
		H$_2$O				
piperidine (11.53)	6.61 × 10^2	0.84	790 (−2.90)	8.44	5.54	10.28[d]
morpholine (8.90)	1.37 × 10^2	95.0	1.44 (−0.16)	5.87	5.71	
		50% Me$_2$SO–50% H$_2$O[b]				
piperidine (11.0)	1.14 × 10^3	36	31.8 (−1.50)	8.30	6.80	11.32[d]
morpholine (8.72)	2.17 × 10^2	1.0 × 10^3	0.22 (0.66)	6.15	6.81	
		70% Me$_2$SO–30% H$_2$O[c]				
piperidine (10.48)	1.05 × 10^2	6.0 × 10^2	1.75 (−0.24)	8.35	8.11	12.45[d]
morpholine (8.38)	2.26 × 10^2	8.0 × 10^3	2.8 × 10^{-2} (1.60)	6.25	7.85	

[a] μ = 0.5 M (KCl).   [b] Reference 17.   [c] μ = 0.25 M (KCl).   [d] pK_a of CH$_3$NO$_2$, ref 28.

Table III. Summary of Rate and Equilibrium Constants of Scheme I for the Reaction of Piperidine with Substituted β-Nitrostyrenes in Water at 20 °C, μ = 0.5 M

substituent	4-NMe$_2$	4-OMe	H	4-Br	3-Cl	4-CN	4-NO$_2$
σ	−0.83	−0.27	0	0.23	0.37	0.66	0.78
σ^o	−0.32	−0.16	0	0.26	0.37	0.69	0.82
k_1, M^{-1} s^{-1}	790	622	661	796	912	989	1100
k_{-1}, s^{-1}	12.0	2.0	0.84	1.3	1.0	1.3	1.5
K_1, M^{-1}	66	310	790	610	910	760	730
p$K_a^{\pm}$	8.83	8.72	8.44	8.12	8.02	7.68	7.51
$K_1 K_a^{\pm}$	9.8 × 10^{-8}	5.9 × 10^{-7}	2.9 × 10^{-6}	4.6 × 10^{-6}	8.7 × 10^{-6}	1.6 × 10^{-5}	2.25 × 10^{-5}
pK_a^+(NH)	a	a	6.57	6.39	6.53	5.95	6.19
pK_a^+(CH)	a	a	5.96	5.91	5.86	5.63	5.78
pK_a^0(CH)	a	a	7.83	7.64	7.35	7.35	7.10
k_3^{BH}, M^{-1} s^{-1}	a	a	4.5	5.6	4.8	4.3	4.6
k_{-3}^B, M^{-1} s^{-1}	a	a	7.0	9.7	9.5	14.5	10.8

[a] Cannot be determined with meaningful precision, see text.

agreement between the intercept ($1/k_{-1}$) of the plot and k_{-1} determined in cacodylic acid buffers. This is also the case for the 4-NO$_2$ and 4-Me$_2$N compounds. On the other hand, for the 4-CN compound the intercept is somewhat larger than $1/k_{-1}$ found in the cacodylic acid buffer, and similar discrepancies exist with the 4-OMe, 3-Cl, and the parent β-nitrostyrene.

The probable reason for the discrepancies is that the precision of the Dabco data was adversely affected by two problems. One was that some of the first-order log plots displayed slight curvature, especially for substrates with electron-donating substituents. The cause of this curvature is not known although we suspect that it is due to a small contribution of the τ_2-process seen at lower pH. A smaller separation between τ_1^{-1} and τ_2^{-1} would indeed be expected at higher pH since $k_{-1}a_{H^+}/(K_a^{\pm} + a_{H^+})$ is smaller while the reduction in τ_2^{-1} which comes from the disfavoring of T$^{\pm}$ and T$^+$ is partially compensated for by the higher basicity of B.

The second problem is that at the high end of the pH range the $k_1[R_2NH]$ term (eq 3) is no longer negligible; with substrates carrying electron-withdrawing substituents it actually becomes the dominant term. Hence, even if one corrects for this term by subtraction, the resulting value for $k_{-1}a_{H^+}/(K_a^{\pm} + a_{H^+})$ has a large uncertainty.

For the above reasons and because they were obtained at pH $\ll$ p$K_a^{\pm}$ we judge the k_{-1} values determined in the cacodylic acid buffer to be much more reliable than those calculated from the Dabco data. We have therefore used k_{-1} obtained in the cacodylic acid buffers to calculate $K_a^{\pm}$ from the slopes according to eq 15.

Morpholine Adduct of β-Nitrostyrene in Water. pH Jumps with Cacodylic and Acetic Acid. All experiments were performed in buffers where the buffer *acid* concentration was held at 0.01 M. Under these conditions substrate recovery was always around 99% and the τ_2^{-1}-process was not detectable. The results, which are summarized in Table S13 (supplementary material),[18] were evaluated according to eq 15 (A_∞/A_1 = 1).

pH Jumps with Adducts of β-Nitrostyrene in 70% Me$_2$SO–30% Water. All experiments were carried out at low buffer concentrations to assure virtually complete substrate recovery. The results, which are summarized in Table S14 (supplementary material), were evaluated via eq 15 (A_∞/A_1 = 1). With the piperidine adduct the plot (not shown) according to eq 15 yielded a measurable intercept ($1/k_{-1}$) with an uncertainty of ±30%, but

Table IV. β-Values and log k_0 for Nucleophilic Addition of Piperidine and Morpholine to β-Nitrostyrene

	H$_2$O	50% Me$_2$O–50% H$_2$O	70% Me$_2$SO–30% H$_2$O
$\beta_{nuc}(k_1)$	0.26	0.32	0.32
$\beta_{lg}(k_{-1})$	−0.78	−0.63	−0.54
$\beta_{eq}(K_1)$	1.04	0.95	0.86
$\beta_{nuc}^n = \beta_{nuc}/\beta_{eq}$	0.25	0.34	0.37
$\beta_{lg}^n = \beta_{lg}/\beta_{eq}$	−0.75	−0.66	−0.63
log k_0(β-nitrostyrene)	2.10	2.55	2.90
log k_0(CH$_3$NO$_2$)[a]	−0.59	0.73	1.76

[a] Ref. 28.

with the morpholine adduct the intercept was indistinguishable from zero. In this latter case k_{-1} was obtained from the slope ($K_a^{\pm}/k_{-1}$) and a p$K_a^{\pm}$ value estimated from the relation (p$K_a^{\pm}$)$_{pip}$ − (p$K_a^{\pm}$)$_{mor}$ = p$K_a^{PipH^+}$ − p$K_a^{MorH^+}$.

Discussion

Table II summarizes k_1, k_{-1}, K_1, and p$K_a^{\pm}$ for the reactions of piperidine and morpholine with the parent β-nitrostyrene in three different solvents. Table III includes all rate and equilibrium constants for the reaction of piperidine with the various substrates in water.

The values for k_1 are considered to be the most accurate, with a conservatively estimated error limit of ±5%. For k_{-1} and K_1 in water we estimate error limits of ±10% and ±15%, respectively, while for p$K_a^{\pm}$ the probable error is ±0.10 log units; in 70% Me$_2$SO–30% water the respective limits are ±30%, ±35%, and ±0.15 units. The other parameters (Table III) are less certain, mainly because of propagation of errors and some difficulties in obtaining highly accurate data, as detailed in the Results section. Thus, uncertainties exceeding ±50% may affect some of these parameters. With the 4-OMe and 4-NMe$_2$ derivatives these uncertainties are even greater and no meaningful values for pK_a^+(NH), pK_a^+(CH), pK_a^0(CH), k_3^{BH}, and k_{-3}^B could be obtained.

Dependence of k_1, k_{-1}, and K_1 on Amine. From two-point Brønsted plots (not shown) one obtains the structure–reactivity parameters summarized in Table IV. We note that β_{nuc} and β_{nuc}^n
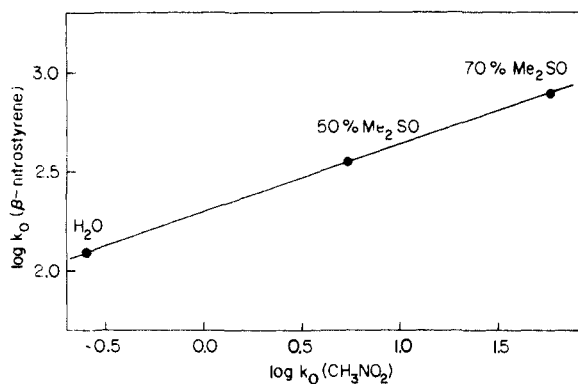
4546 *J. Am. Chem. Soc., Vol. 108. No. 15, 1986*

Bernasconi et al.

Figure 5. Plot of log k_0(β-nitrostyrene) vs. log k_0(CH_3NO_2) in different solvents. Slope of 0.34 indicates attenuation of solvent effect in the nucleophilic addition compared to the proton-transfer reaction.

are somewhat larger in the Me_2SO-containing solvents than in pure water. This is analogous to the trend toward increasing Brønsted β-values in the deprotonation of various carbon acids upon addition of Me_2SO to the solvent.[21] This increase in β was attributed to a solvation effect of the developing ammonium ion.[21b] The increase in β_{nuc} or β_{nuc}^n may be caused by a similar solvation effect of the developing ammonium ion in $T^{\pm}$. A desolvation effect of the free amine as envisioned by Jencks[22] may be a contributing factor.

Solvent Effect on K_1 and $K_1K_a^{\pm}$. The equilibrium for amine addition is significantly less favorable in the Me_2SO-containing solvents than in water. This is reflected both in a decrease in K_1 (higher pK_1) and a decrease in $K_1K_a^{\pm}$ (higher $p(K_1K_a^{\pm})$) with increasing Me_2SO content, as shown in Table II. This effect can be mainly attributed to the reduced solvational stabilization of the negatively charged $CHNO_2$ moiety. The somewhat lower basicity of the amine, particularly in the piperidine reaction, is expected to contribute to the solvent effect on pK_1, but not to the one on $p(K_1K_a^{\pm})$, because of compensation by a lower $pK_a^{\pm}$.

In quantitative terms, the correlation of $p(K_1K_a^{\pm})$ with the pK_a of nitromethane in the three solvents gives a slope of 1.18 ± 0.02 for the piperidine and of 0.99 ± 0.04 for the morpholine adduct. This indicates that the $CHNO_2^-$ moieties in T^- and in $CH_2NO_2^-$ show roughly the same response to the change in solvent;[23] the somewhat smaller slope for the morpholine adduct, if significant at all,[24] may be attributed to the stronger electron-withdrawing effect of the morpholine moiety which lessens the demand for solvation. In the zwitterionic adducts electrostatic stabilization further reduces the demand for solvation, as can be seen from the correlation of pK_1 vs. $pK_a^{CH_3NO_2} - pK_a^{R_2NH_2^+}$[25] which gives a slope of 0.83 ± 0.04 for the piperidine and 0.65 ± 0.01 for the morpholine adduct.

Solvent Effect on Intrinsic Rate Constant. Even though K_1 decreases considerably with decreasing Me_2SO content, k_1 is virtually unchanged or even increases slightly. This indicates that the *intrinsic* rate constant, k_0,[26] increases upon addition of Me_2SO. Values for log k_0, identified as log k_0(β-nitrostyrene) and obtained by interpolation or extrapolation of two-point plots of log k_1 vs. log K_1, are included in Table IV.

The increase in k_0 is consistent with the notion that solvation of the developing negative charge has made little progress in the transition state (see below). Such a lag in solvation has the effect of depressing k_0 the most in solvents that are most effective at
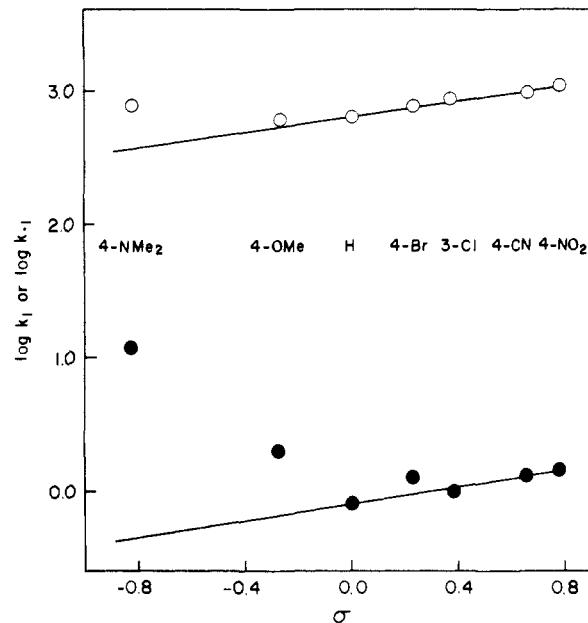
Figure 6. Hammett plots (standard σ-values) for k_1 (open circles) and k_{-1} (filled circles) in the reaction of piperidine with substituted β-nitrostyrenes.

solvating the negative charge, i.e., k_0 in water is more depressed than in the Me_2SO-containing sovlents as discussed in detail elsewhere.[15] It is qualitatively the same phenomenon as the increase in k_0 observed in the deprotonation of nitroalkanes[14,27] and diketones[21] when Me_2SO is added to the solvent.

The *magnitude* of the solvent effect on k_0 for amine addition to β-nitrostyrene is, however, significantly smaller than that for deprotonation of nitromethane by the piperidine/morpholine pair.[28] Values of log k_0(CH_3NO_2) for this deprotonation are included in Table IV while Figure 5 shows a plot of log k_0(β-nitrostyrene) vs. log k_0(CH_3NO_2). Its slope is 0.34 ± 0.01. This reduced solvent effect on k_0 is probably mainly[29] a consequence of a smaller lag in the solvation of the negative charge in the transition state of nucleophilic addition compared to the transition state of the proton transfer; evidence for this smaller lag is discussed below.

Substituent Dependence of k_1, k_{-1}, and K_1. A. Polar Effects. Hammett plots for k_1 and k_{-1}, using standard σ-values, are shown in Figure 6. Both k_1 and k_{-1} are seen to increase slightly for electron-withdrawing substituents. Electron-donating substituents are also rate-enhancing, particularly so for k_{-1}. These latter rate enhancements are caused by an unusual resonance effect discussed below; the slight positive deviation of the 4-Br point in the k_{-1} plot is likely to be due to the same resonance effect.

Omitting 4-OMe and 4-NMe₂ (and 4-Br for k_{-1}) from the correlation one obtains $\rho(k_1) = 0.27 \pm 0.02$ and $\rho(k_{-1}) = 0.33 \pm 0.05$; for K_1 which is virtually substituent-independent this yields $\rho(K_1) = -0.06 \pm 0.07$.

The small ρ-values must be the result of near cancellation of opposing factors: the combined effect of negative charge development on the $CHNO_2$ moiety and rehybridization of the α-carbon,[9] which should be favored by electron-withdrawing substituents, and the development of positive charge on the amine nitrogen, which is disfavored. Apparently the cancellation is just about perfect for K_1 while for k_1 and k_{-1} the effect of the negative charge/rehybridization is somewhat stronger than that of the positive charge.

This enhanced response of k_1 and k_{-1} compared to that of K_1 indicates that the charge *distribution* in the transition state is different from that in $T^{\pm}$. Since the positive charge can only be

(21) (a) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420. (b) Bernasconi, C. F.; Paschalis, *J. Am. Chem. Soc.* **1986**, *108*, 2969.

(22) Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. L. *J. Am. Chem. Soc.* **1986**, *108*, 479.

(23) A more rigorous analysis would have to take into account possible solvent effects on the stability of S, the amine, and nitromethane.

(24) In view of the relatively large uncertainties in $p(K_1K_a^{\pm})$ the indicated standard deviations in the slopes may underestimate the actual error.

(25) In correlating pK_1 with $pK_a^{CH_3NO_2} - pK_a^{R_2NH_2^+}$ rather than with $pK_a^{CH_3NO_2}$ the contribution of the effect on pK_1 which arises from the solvent effect on $pK_a^{R_2NH_2^+}$ is canceled out.

(26) k_0 is defined as $k_1 = k_{-1}$ when $K_1 = 1$.

(27) Cox, B. G.; Gibson, A. *Faraday Symp. Chem. Soc.* **1975**, *10*, 107.

(28) Bernasconi, C. F.; Kliner, D.; Mullin, A. unpublished results.

(29) Electrostatic stabilization by the positive charge on the amine nitrogen occurs in the transition state of both types of reactions and hence should have a minor discriminating effect if any.

Nucleophilic Addition to Olefins

J. Am. Chem. Soc., Vol. 108, No. 15, 1986 4547

localized on the amine nitrogen the implication is that the center of gravity of the negative charge is closer to the aryl group in the transition state than it is in $T^{\pm}$. In other words, delocalization of the negative charge into the nitro group and its concomitant solvation lag behind the development of the positive charge.[30] This is then another example of a transition-state imbalance;[4,5] they are ubiquitous in carbanion-forming reactions.[2-3,5-8,15]

In an attempt to quantify this imbalance we may estimate the contribution to $\rho(k_1)$ or $\rho(k_{-1})$ which can be attributed to the development of negative charge and rehybridization of the α-carbon as follows. For the equilibrium constant we write $\rho(K_1)$ as the sum of two terms

$$\rho(K_1) = \rho_{eq}(C^-) + \rho_{eq}(NH^+) \approx -0.06 \qquad (16)$$

$\rho_{eq}(C^-)$ is the response to the combined effect of the negative charge and the rehybridization of the α-carbon, while $\rho_{eq}(NH^+)$ measures the effect of the positive charge. Equation 16 gives us

$$\rho_{eq}(C^-) = -\rho_{eq}(NH^+) - 0.06 \qquad (17)$$

The ρ-value for $pK_a^{\pm}$ ($\rho(pK_a^{\pm}) = -1.15$, see below) can serve as an approximation for $\rho_{eq}(NH^+)$, and thus $\rho_{eq}(C^-) \approx 1.09$.

In analogy to eq 16 one can express $\rho(k_1)$ as the sum of two contributions

$$\rho(k_1) = \rho_{kin}(C^-) + \rho_{kin}(NH^+) = 0.27 \qquad (18)$$

We can define $\rho_{kin}(NH^+)/\rho_{eq}(NH^+)$ as the progress in the development of positive charge on the amine nitrogen at the transition state as seen by the aryl substituent and $\beta_{nuc}^n = 0.25$ (Table IV) as the progress of the same process as seen by the amine substituent. Assuming that they are equal affords

$$\rho_{kin}(NH^+)/\rho_{eq}(NH^+) = \beta_{nuc}^n = 0.25 \qquad (19)$$

and hence $\rho_{kin}(NH^+) \approx -0.25 \times 1.15 = -0.29$. Inserting into eq 18 leads to $\rho_{kin}(C^-) \approx 0.56$ or to a normalized $\rho_{kin}^n(C^-) = \rho_{kin}(C^-)/\rho_{eq}(C^-) \approx 0.56/1.09 = 0.51$.[31]

The difference $\rho_{kin}^n(C^-) - \beta_{nuc}^n \approx 0.51 - 0.25 = 0.26$ can now be regarded as an approximate measure of the imbalance; it has the same qualitative meaning as the difference $\alpha - \beta > 0$ in the deprotonation of carbon acids by normal bases,[5,12-15,21] with α and β being the Brønsted coefficients obtained by varying the substituent in the carbon acid and that in the base, respectively. However, the magnitude of the imbalance (0.26) is considerably smaller than $\alpha - \beta = 1.29 - 0.55 = 0.74$ for the corresponding deprotonation of 1-aryl-2-nitroethanes.[12a]

The main reason for this quantitative difference must be the fact that in the transition state for nucleophilic addition (2) the

$$\underset{2}{\underset{\overset{|}{R_2NH}^{\delta+}}{ArCH\overset{\delta-}{=\!=\!=}CR\overset{\delta-}{=\!=\!=}NO_2^{\delta-}}} \qquad \underset{3}{\underset{\overset{|}{H}\ \ \underset{\overset{|}{R_2NH}^{\delta+}}{}}{\overset{CH_3}{\underset{\overset{|}{\delta-}}{ArC\!-\!\!-\!NO_2}}}}$$
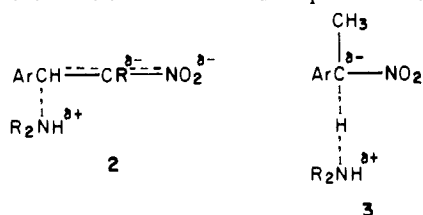
developing negative charge is not as easily localized on the carbon bearing the nitro group as in the transition state of the proton transfer (3). This is because in 2 the carbon is likely to maintain its sp^2 hybridization, thereby facilitating the shift of the negative charge into the nitro group, while in 3 the carbon is more sp^3-like.[12] The reduced delay in the development of resonance in the nitro group[32] must in turn reduce the lag in the solvation of the negative charge.[15] We believe this to be one of the main reasons for the

smaller solvent effect on the intrinsic rate constant for the addition reaction compared to the deprotonation of nitromethane, as discussed earlier. It is noteworthy that the slope (0.34) of the plot of $\log k_0(\beta$-nitrostyrene) vs. $\log k_0(CH_3NO_2)$ in Figure 5 is virtually the same as the ratio of the respective imbalances, $(\rho_{kin}^n(C^-) - \beta_{nuc}^n)/(\alpha - \beta) = 0.26/0.74 = 0.35$.

B. Resonance Effects. For the 4-OMe and 4-NMe$_2$ substrates both k_1 and k_{-1} deviate positively from their respective Hammett plots (Figure 6). This deviation is much more pronounced for k_{-1} and, as a consequence, K_1 is lower than for the other five β-nitrostyrenes (Table III).

As mentioned in the introduction, reduced equilibrium constants for nucleophilic addition to 4-OMe- and 4-NMe$_2$-substituted olefins are common[2,3,6,7,9,10] and are most easily understood as an effect of resonance stabilization of the substrate (4).[33]

4

5
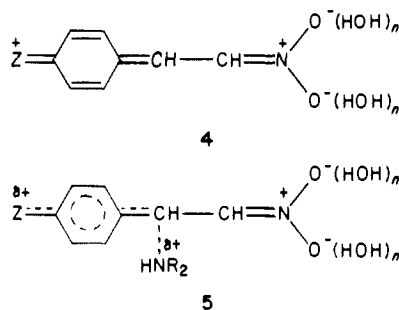
In general the *rate* constants for nucleophilic attack on the 4-OMe- and 4-NMe$_2$-substituted olefins also deviate negatively from Hammett plots. In some cases this deviation is nearly as large as for the equilibrium constant, particularly in the addition of hydroxide ion[3] and amines[7,10] to benzylidene Meldrum's acids, and in the addition of amines to benzylidene-N,N'-dimethyl-barbituric acids.[10] This manifests itself most clearly in Brønsted type plots of $\log k_1$ or $\log k_{-1}$ vs. $\log K_1$ where, for example, the 4-NMe$_2$ point falls well below the line.[7] In the context of the principle of imperfect synchronization (PIS)[34] these observations are examples in which the early loss of a reactant stabilizing factor (resonance) leads to a reduction of the intrinsic rate constant of the reaction.

Since early loss is just the microscopic reverse of late development in the opposite direction of a reaction, these findings of early loss of resonance in the olefin must have the same quantum mechanical origin as the ubiquitously observed late development of resonance or carbanion-forming reactions.[15,35] It is therefore surprising that the k_1-values as well as the k_{-1}-values for piperidine addition to 4-methoxy- and 4-(dimethylamino)-β-nitrostyrene deviate *positively* from the Hammett plot:[36] it suggests, in keeping with the PIS, that here the resonance stabilization of the olefin is lost *late* along the reaction coordinate in the k_1 direction, or develops early in the k_{-1} direction.

A possible way to understand these unusual results is in terms of a transition state which, in exaggerated form, may be represented by 5. The major difference between 5 and 2 is the fact that the negative charge is already extensively delocalized and solvated in the nitro group. Such a transition state could reduce the PIS effect which is ordinarily associated with the late development of resonance and solvation in the anionic portion of the molecule.

(30) Another possible factor that could contribute to $\rho(k_1) > \rho(K_1)$ is that rehybridization of the α-carbon is ahead of positive charge development, as suggested for another system.[2] We believe that this is a less important factor than the lag in the delocalization of the negative charge.

(31) A similar analysis for $\rho(k_{-1})$ affords $\rho_{kin}(NH^+) = 0.86$, $\rho_{kin}(C^-) = -0.53$ and $\rho_{kin}^n(C^-) = -0.49$.

(32) It is conceivable that in 2 there is no significant amount of negative charge on the carbon, and that the imbalance is entirely due to the lag in the solvation of the negative charge in the nitro group.

(33) A strong resonance effect, particularly for the 4-NMe$_2$ derivative, is also indicated by its $\lambda_{max} = 460$ nm which is strongly red-shifted compared to λ_{max} for the other β-nitrostyrenes.

(34) The PIS states that a product (reactant) stabilizing factor which develops early (is lost late) increases the intrinsic rate constant while product (reactant) stabilizing factors which develop late (are lost early) decrease the intrinsic rate constant.[15] "Early" and "late" in a nucleophilic addition reaction is defined in relation to the progress of charge transfer from the nucleophile to the substrate, as approximated by β_{nuc}^n.

(35) (a) Pross, A.; Shaik, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1129. (b) Pross, A. *Adv. Phys. Org. Chem.* **1985**, *21*, 99.

(36) A recent study of OH$^-$ addition to the same series of β-nitrostyrenes revealed similar positive deviations for the 4-OMe and 4-NMe$_2$ derivatives: Bernasconi, C. F.; Zitomer, J. L., unpublished results.

Why would a transition state such as **5** be energetically more advantageous in the case of say 4-(dimethylamino)-β-nitrostyrene but not with 4-(dimethylamino)benzylidene Meldrum's acid or 4-(dimethylamino)benzylidene-N,N'-dimethylbarbituric acid? It is believed that the delayed development of resonance and solvation has a more adverse effect on the intrinsic rates of nitronate ion than on other carbanion-forming reactions.[5,15] This is because resonance and solvation have the greatest stabilizing effect on the *product* ion.[15] Hence these should also be the reactions which benefit the most from a situation where this resonance and solvation is already partially built into the reactant. Our results indicate that for the β-nitrostyrenes this benefit outweighs the loss in through-conjugation (**4**), while for the other olefins this is not the case.

There is a certain analogy between our present observations and the abnormally high intrinsic rate constants for *water* addition (in contrast to OH⁻ addition) to benzylidene Meldrum's acid and benzylidene-1,3-indandione.[37] This high intrinsic rate constant was explained by intramolecular hydrogen bonding between the attacking water molecule and one of the carbonyl oxygens (**6**)

$$
\mathrm{ArCH} = \mathrm{C} \underset{\substack{\\ \mathrm{HO}}}{\overset{\substack{O \\ C \\ \delta - \\ C \\ O}}{\Big\langle}} \!\!\!\!\!\!
$$

6
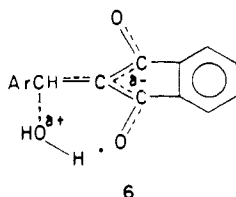
which represents another way of circumventing or reducing the PIS effect associated with the late solvation of the negative charge.

p$K_a^{\pm}$, pK_a^+(NH), pK_a^0(CH), and pK_a^+(CH). The p$K_a^{\pm}$ values (Table III) are all considerably lower than p$K_a^{R_2NH_2^+}$ = 11.53 for the piperidinium ion, indicating that the ArCHCHNO$_2^-$ moiety is strongly electron-withdrawing, despite its negative charge. The negligible effect of the negative charge is undoubtedly due to its strong delocalization into the nitro group. Similar effects have been observed for the amine adduct of 1,1-dinitro-2,2-diphenylethylene[38] and in Meisenheimer complexes derived from nitro aromatics and amines.[39] In cases where the negative charge is not as effectively delocalized, e.g., in the piperidine adduct of benzylidenemalononitrile, the p$K_a^{\pm}$-value is only slightly lower than p$K_a^{R_2NH_2^+}$.[7,40]

The substituent dependence of p$K_a^{\pm}$ is shown in Figure 7. Since there is no possibility of conjugation between the amine nitrogen and the aryl substituent, σ^0[41] instead of σ was used for the 4-OMe and 4-NMe$_2$ derivatives. The correlation affords ρ(p$K_a^{\pm}$) = -1.15 ± 0.05; the ρ-value is reasonable and is consistent with ρ = -1.06 for the pK_a of benzylammonium ions.[42]

For the other pK_a-values calculation of ρ-values is not warranted because the error limits are too large. Nevertheless, the fact that pK_a^+(NH) < p$K_a^{\pm}$ and pK_a^+(CH) < pK_a^0(CH) and the qualitative trends with changing substituent seen for these values are again reasonable. Thus all pK_a-values decrease for more electron-withdrawing substituents but less so for pK_a^+(NH) and pK_a^+(CH) than for p$K_a^{\pm}$ and pK_a^0(CH), respectively. This attenuation of the substituent effects on pK_a^+(NH) and pK_a^+(CH), if real, may be understood as a saturation effect: the positive charge on the amine nitrogen and the neutralization of the negative charge on the nitro group are both acidifying effects which lower the sensitivity of pK_a^+(NH) and pK_a^+(CH) to the aryl substituent.

k_3^{BH} **and** k_{-3}^B. k_{-3}^B for carbon deprotonation of T⁺ increases with the electron-withdrawing strength of the substituent as expected, but k_3^{BH} for protonation of T⁺ is independent of the
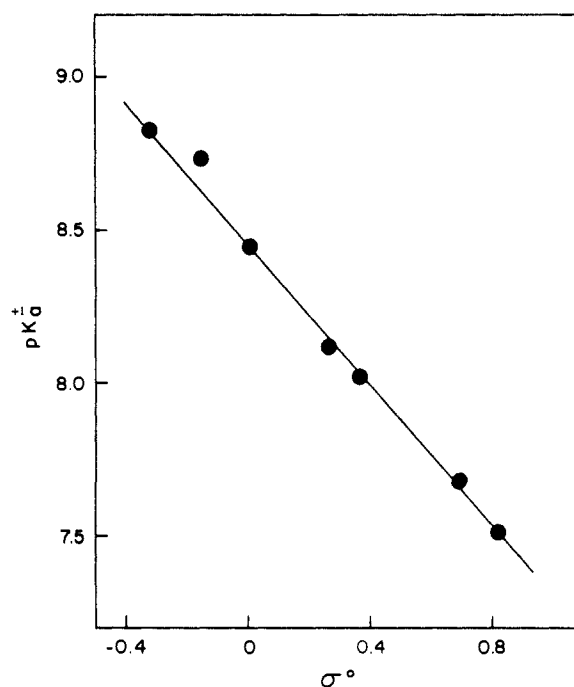

Figure 7. Hammett plot (σ^0) for p$K_a^{\pm}$ of the piperidine adducts of the substituted β-nitrostyrenes.

substituent. This situation is tantamount to a Brønsted α-value for k_{-3}^B near unity and a Brønsted β-value for k_3^{BH} of about zero. The large α- and small β-value is reminiscent of the large α = 1.29 and small β = -0.29 for the proton transfer between 1-phenylnitroethane and morpholine;[12a] in view of the considerable uncertainty in our k_3^{BH}, k_{-3}^B, and pK_a^+(CH) values we cannot be sure whether the fact that our α-value (β-value) is somewhat lower (higher) than Bordwell's[12a] is significant or not. The presence of the positive charge on T⁺ could possibly lead to an attenuation of the substituent effect on the transition state, and hence a reduced α- (enhanced β-) value would not be unreasonable.

The fact that under our experimental conditions (pH < p$K_a^{\pm}$) only the k_3^{BH} pathway could be observed is also consistent with the low β-value. In systems where β is larger, the equivalent to the k_2^{BH} pathway in Scheme I is observable even at pH < p$K_a^{\pm}$ because $k_2^{BH} \gg k_3^{BH}$. This is, e.g., the case in the reaction of amines with benzylideneacetylacetone.[43]

Experimental Section

Materials. β-Nitrostyrene was obtained from Aldrich and recrystallized from ethanol. The remaining β-nitrostyrenes were literature compounds prepared by the method of Worrall[44] and recrystallized from ethanol or ethanol/acetic acid. All β-nitrostyrenes have trans stereochemistry.

Piperidine, morpholine, and N-methylmorpholine were refluxed over calcium hydride and distilled. Dabco was recrystallized from hexanes. Cacodylic acid (free acid and sodium salt) and potassium acetate were used without further purification. KOH and HCl solutions were "Dilut-It" (Baker) diluted to appropriate volumes with deionized distilled water.

Methods. All kinetic experiments were carried out in a Durrum stopped-flow spectrophotometer with computerized data acquisition and analysis.[45] Kinetics in the forward direction were determined by mixing a KCl solution of the substrate with the appropriate amine/amine hydrochloride solution. In the pH-jump experiments the T⁻ species was generated by dissolving the substrate in 0.04 M amine and 0.001 M KOH; this solution was then mixed with the appropriate acidic buffer in the stopped-flow apparatus to give the final pH. Reactions were monitored near λ_{max} of the substrate. Solution pH's were determined from mock mixing experiments with an Orion 611 digital pH meter calibrated with commercial buffers.

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Swain–Scott Correlations for Reactions of Nucleophilic Reagents and Solvents with Secondary Substrates[1]
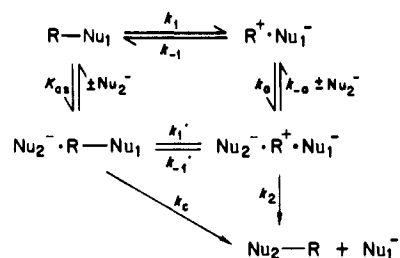
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Abstract: The reactions of 1-(4-nitrophenyl)-2-propyl derivatives with nucleophilic reagents in 50% trifluoroethanol–water follow Swain–Scott correlations with slopes *s* = 0.27, 0.34, and 0.43 for tosylate, bromide, and iodide leaving groups, respectively. The rate constants for reaction of this simple secondary system with the solvent components, trifluoroethanol and water, do not show positive deviations from these Swain–Scott correlations. This suggests that the reactions with solvent occur by the same mechanism as the reactions with other nucleophiles. Azide and cyanide ions show positive and negative deviations, respectively. However, linear correlations of log k_n are observed for reactions of nucleophiles, including azide and cyanide, with two compounds that have different leaving groups. These correlations include nucleophiles of both larger and smaller nucleophilic reactivity than the leaving group. The larger sensitivity toward nucleophiles of the iodo compound compared with the tosylate shows that there is an interaction, or "symbiosis", between the attacking and leaving groups in the transition state. It is difficult or impossible to describe a mechanism for these reactions that proceeds through an intermediate between two very similar transition states, with significant barriers for collapse of the intermediate. The results are consistent with a concerted S_N2 or A_ND_N reaction mechanism that proceeds through a single, carbocation-like transition state for the bond-forming and bond-breaking steps.

In spite of extensive investigation, the mechanism of substitution reactions at simple secondary alkyl carbon centers is still not understood. The reactions of secondary substrates exhibit behavior that is characteristic of both the S_N1 and S_N2 mechanisms, or both the D_N + A_N and the A_ND_N mechanisms according to recently proposed nomenclature for reaction mechanisms.[2] The sensitivity of simple secondary substrates toward solvent ionizing power is larger than that of primary and smaller than that of tertiary substrates, while the sensitivity toward solvent nucleophilicity is smaller than that of primary and larger than that of tertiary substrates.[3,4] The solvolysis of 2-butyl tosylate in trifluoroacetic acid occurs with partial racemization,[5] and the 2-propyl and 2-butyl cations have been observed directly in superacid solutions.[6] Substitution reactions of secondary substrates with substituted pyridine leaving groups in solvents of low nucleo-

Scheme I

philicity at high temperature have been shown to occur by both S_N1 and S_N2 mechanisms.[7] Furthermore, the solvolysis of secondary substrates with labeled oxygen atoms in the leaving sulfonate is accompanied by scrambling of the oxygen atoms in recovered starting material.[8,9] For these and other reasons it has been suggested that the solvolysis of secondary substrates occurs through an intermediate carbocation, possibly through ion-pair intermediates,[10,11] an "S_N2 intermediate",[3,4,9,12,13] or an "ion-sandwich" mechanism.[14]

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(2) A and D refer to associative and dissociative processes, respectively, and N refers to a nucleophilic or nucleofugic process. A + sign and a * refer to stepwise processes in which the intermediate does or does not exist long enough to become diffusionally equilibrated with the solvent, respectively, while the absence of punctuation refers to a concerted process with no intermediate. Commission on Physical Organic Chemistry, IUPAC, Pure and Applied Chemistry, in press.

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