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Is There a Transition-State Imbalance in Malononitrile Anion Forming Reactions? Kinetics of Piperidine and Morpholine Addition to Substituted Benzylidenemalononitriles in Various Me_2SO–Water Mixtures[1]

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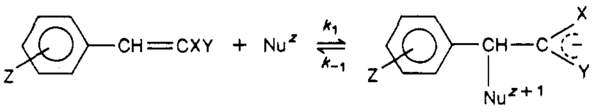
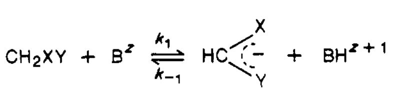
Piperidine and morpholine add to substituted benzylidenemalononitriles ($Z\text{-}C_6H_4CH{=}C(CN)_2$) to form a zwitterionic adduct, $Z\text{-}C_6H_4CH(R_2NH^+)C(CN)_2^-$ ($T^{\pm}$), which is in rapid acid–base equilibrium with the anionic adduct, $Z\text{-}C_6H_4CH(R_2N)C(CN)_2^-$ (T^-). Rate constants for amine addition (k_1) were determined by direct rate measurements while equilibrium constants for addition (K_1) as well as $pK_a^{\pm}$ values of the zwitterions were obtained spectrophotometrically. The bulk of the measurements was carried out in 50% Me_2SO–50% water with piperidine, while a smaller number of experiments were performed with morpholine, and with both amines in water and in 70% Me_2SO–30% water. The reactions show the typical behavior of a carbanion-forming process in which the carbanion derives a good part of its stabilization from polar effects while resonance effects play a more modest role. This behavior includes a high intrinsic rate constant ($k_0 = k$ when $K = 1$), a small transition-state imbalance, and a relatively small solvent effect on the intrinsic rate constant. The observation of an imbalance suggests that the deprotonation of malononitrile derivatives by carboxylate ions should also have an imbalanced transition state. The fact that none has been observed is attributed to a solvation effect of the carboxylic acid, which enhances the Brønsted β_B value, as recently suggested by Murray and Jencks. The 4-Me_2N substituent leads to strong resonance stabilization of the olefin as indicated by a low K_1 value. Contrary to expectation of a lowered intrinsic constant, this resonance stabilization has little effect on k_0. This suggests the operation of a compensating factor which increases k_0 and which can be understood as an attenuation of the reduction in k_0 caused by late development of resonance at the carbanionic center of the adduct.

In our recent work on structure–reactivity relationships in carbanion-forming reactions we have been interested in similarities between nucleophilic additions to activated olefins, eq 1, and proton transfers from activated carbon, eq 2. Both reactions lead to the formation of a carbanion



(1)



(2)

of nearly identical structure except that in eq 1 the hydrogen attached to the central carbon is replaced by the group $Z\text{-}C_6H_4CH(Nu^{z+1})$. It is therefore not surprising that both reactions show a qualitatively similar dependence of the intrinsic rate constant ($k_0 = k_1 = k_{-1}$ when $K_1 = 1$) on the activating groups X and Y. This dependence is such that k_0 decreases with increasing resonance stabilization of the carbanion, i.e., $(CN)_2 > (COO)_2C(CH_3)_2 > CN(C_6H_4\text{-}4\text{-}NO_2) > CN(C_6H_3\text{-}2,4\text{-}(NO_2)_2) > H(NO_2) > Ph(NO_2)$.[2,3]

The observed trend can be understood in terms of transition-state structures in which resonance development and concomitant solvation of the negative charge lag behind bond formation. As a consequence of the principle of nonperfect synchronization (PNS),[2-4] this lag leads to a reduction in k_0 relative to a system in which there is no such resonance. This reduction becomes larger with increasing resonance in the carbanion which explains the observed trend in k_0 with XY.

Another manifestation of the lag in resonance development behind bond formation is the disparity or imbalance in the Brønsted coefficients of these reactions. In the proton transfers this imbalance is measured by $I = \alpha_{CH}$[5] $- \beta_B$[5] > 0, in the nucleophilic addition reactions by $I = \alpha_{nuc}^{n}$[6] $- \beta_{nuc}^{n}$[6] > 0. The imbalances are large for reactions that lead to carbanions with strong resonance stabilization and small when resonance plays only a minor role.

Quantitative comparisons of the effect of XY on intrinsic rate constants and imbalances show significant differences between reactions 1 and 2 though. k_0 for the nucleophilic additions is less sensitive to XY than k_0 for proton transfers: a plot of log k_0 (eq 1) vs log k_0 (eq 2) gives a fairly good linear correlation with a slope of ≈0.45.[3] Similarly, the imbalances observed for the nucleophilic additions are generally smaller than for the corresponding proton transfers. For example, $I = 0.67 - 0.37 = 0.30$ for $PhCH{=}C(Ar)NO_2 + R_2NH$[7] while $I = 1.29 - 0.55 = 0.74$ for $ArCH_2NO_2 + R_2NH$;[8] or $I = 0.22 - 0.07 = 0.15$ for $ArCH{=}C(COO)_2C(CH_3)_2 + R_2NH$[9] while $I = 0.76 - 0.44 = 0.32$ for $ArCH_2CH(COMe)COOEt + RCOO^-$.[10]

There is one proton-transfer reaction, the deprotonation of malononitrile derivatives, that seems to have an abnormally small imbalance. For example, for the reaction of $ArCH_2CH(CN)_2$ with $RCOO^-$, $\alpha_{CH} \approx \beta_B \approx 1.0$ and thus $I \approx 0$.[10a] Similar results[10b] were reported for the detritiation of *tert*-butylmalononitrile by $RCOO^-$ where $\beta_B = 0.98$ while an $\alpha_{CH} = 1.06 \pm 0.05$ was calculated from the rates of detritiation of *tert*-butylmalononitrile and malononitrile by formate ion. A somewhat lower $\beta_B = 0.8$ was found for the deprotonation of *tert*-butylmalononitrile by primary amines[10c] but in the absence of an experimental α_{CH} value

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(1) This is Part 24 in the series Nucleophilic Addition to Olefins. Part 23: Bernasconi, C. F.; Killion, R. B., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 7506.

(2) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301.

(3) Bernasconi, C. F. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Advances in Chemistry 215; American Chemical Society: Washington, DC, 1987; p 137.

(4) Bernasconi, C. F. *Tetrahedron* **1985**, *41*, 3219.

(5) $\alpha_{CH} = d \log k_1/d \log K_a^{CH}$, e.g., when pK_a^{CH} is varied by varying Z in $Z\text{-}C_6H_4CHXY$; $\beta_B = d \log k_1/dpK_a^{BH}$.

(6) $\alpha_{nuc}^{n} = d \log k_1/d \log K_1$, e.g., by varying Z in eq 1; $\beta_{nuc}^{n} = d \log k_1/d \log K_1$ by varying Nu.

(7) Bernasconi, C. F.; Renfrow, R. A. *J. Org. Chem.* **1987**, *52*, 3035.

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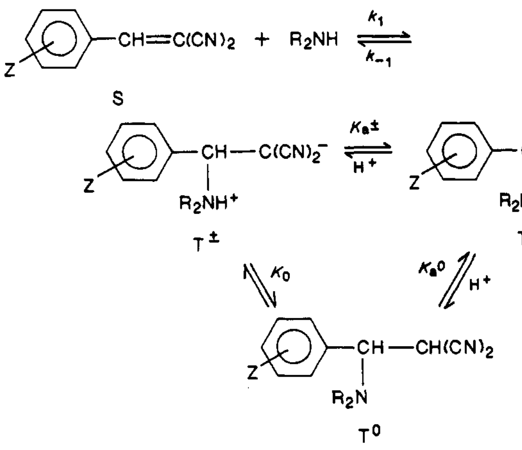
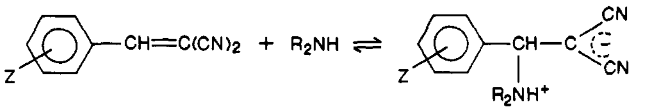
0022-3263/89/1954-2878$01.50/0

Scheme I



it is not clear whether these results imply a larger imbalance for the amine reactions. We shall return to this point in the Discussion.

Even if one assumes a rather modest resonance effect in the malononitrile type anion,[11-13] a modest imbalance that is larger than zero would seem to fit better with the pattern established by the other examples. It occurred to us that one way to demonstrate that the above zero imbalance is indeed abnormal and probably caused by special factors coming into play in the malononitrile deprotonation would be to show that the imbalance in the nucleophilic addition to a dicyano activated olefin is larger than zero. To this end we have studied the reaction of piperidine and morpholine with substituted benzylidenemalononitriles, eq. 3.



(3)

A second motivation for our study was to examine the effect of π-donor substituents (Z = 4-Me_2N, 4-MeO) on the intrinsic rate constant of reaction 3. Two interaction mechanisms of the π-donors have recently been identified which can affect k_0.[9,14] The first one leads to a *decrease* in k_0 and can be visualized as a loss of the resonance stabilization of the olefin running ahead of bond formation. The second leads to an *increase* in k_0 and can be understood as an attenuation of the decrease in k_0 caused by the late development of the resonance effect at the *carbanionic center of the product ion.* For systems where carbanion resonance is strong the second factor dominates, leading to a net increase in k_0,[14] while for systems where the resonance effect in the adduct is weak one might expect that the first interaction mechanism may override the second one, resulting in a net decrease in k_0. Among the reactions studied in this context, reaction 3 involves the smallest degree of resonance stabilization in the adduct and hence should provide a good test case for the above prediction.

A third point of interest is the effect of increasing the Me_2SO content of the solvent on the intrinsic rate constant of the reaction. We therefore determined k_0 for piperidine and morpholine addition to benzylidenemalononitrile in water and in 70% Me_2SO, which complements an earlier investigation in 50% Me_2SO.[15]

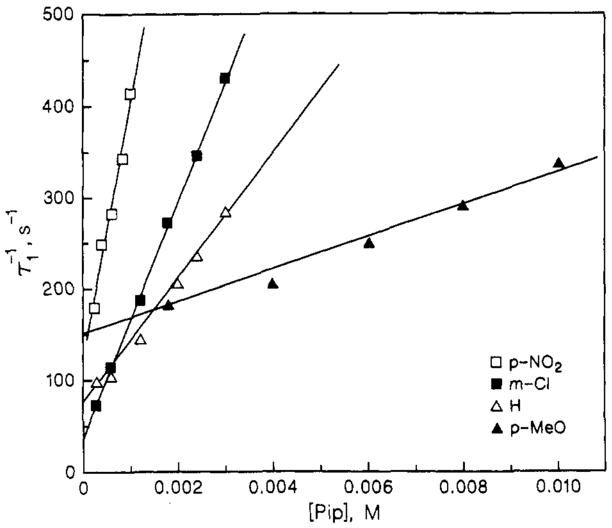


Figure 1. Kinetics of piperidine addition to substituted benzylidenemalononitriles in water at 20 °C. The slopes provide k_1 according to eq 5.

Results

General Features. The reactions of piperidine and morpholine with benzylidenemalononitrile (Z = H) have been previously studied in 50% Me_2SO–50% water, μ = 0.5 M (KCl), T = 20 °C.[15] Two kinetic processes were observed. The first process, shown in Scheme I, was attributed to formation of a zwitterionic addition complex ($T^\pm$) and subsequent rapid deprotonation to form the anionic complex (T^-). With morpholine, a T^0 species was also formed in equilibrium with $T^\pm$ and T^-. The second process was shown to represent a multi-step breakdown of T^0 into benzaldehyde and malononitrile.

In the present study, the rate and equilibrium constants for the following reactions were determined: piperidine and morpholine with variously substituted benzylidenemalononitrile (BMN-Z) where Z = 4-MeO, H, 3-Cl and 4-NO_2, in water; piperidine with BMN-Z where Z = 4-Me_2N, 4-MeO, 4-Me, H, 4-Cl, 4-Br, 3-Cl, 4-CN, 4-NO_2, in 50% Me_2SO–50% water (v/v); piperidine and morpholine with BMN-H in 70% Me_2SO–30% water (v/v). The temperature was 20 °C in all solvents, the ionic strength 0.5 M in water and 50% Me_2SO, 0.25 M in 70% Me_2SO, maintained with KCl.

Kinetics of Piperidine Addition. In our previous report[15] it was shown that with piperidine $pK_a^\pm \gg pK_a^0$, implying $K_0 \ll 1$, so that Scheme I simplifies to eq 4.

$$S + R_2NH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} T^\pm \underset{H^+}{\overset{K_a^\pm}{\rightleftharpoons}} T^- \tag{4}$$

Under the pseudo-first-order conditions used throughout this study the reciprocal relaxation time for eq 4 is given by eq 5. Because k_{-1} is very high and outside the time range of the stopped-flow technique, the kinetics of piperidine addition were measured at pH $\gg pK_a^\pm$, which reduces the size of the $k_{-1}a_{H^+}/(K_a^\pm + a_{H^+})$ term. At these

$$\tau^{-1} = k_1[R_2NH] + k_{-1}\frac{a_{H^+}}{K_a^\pm + a_{H^+}} \tag{5}$$

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[11] Bell, R. P. *The Proton in Chemistry*; Cornell University Press: Ithaca, NY, 1973; p 105.

[12] Hine, J. *Adv. Phys. Org. Chem.* **1977**, *15*, 1.

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[14] Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *108*, 4541.

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Table I. Rate and Equilibrium Constants for the Reactions of Substituted Benzylidenemalononitriles with Piperidine and Morpholine in Water, μ = 0.5 M (KCl), at 20 °C

parameter	4-MeO	H	3-Cl	4-NO$_2$
		Piperidine (pK_a = 11.53)		
$10^{-4}k_1$, M^{-1} s^{-1}	1.72 ± 0.25	7.02 ± 0.39	13.2 ± 0.1	28.2 ± 1.8
$10^{-4}k_{-1}$,[a] s^{-1}	1.10	1.56	0.863	0.502
K_1, M^{-1}	1.60[b]	4.50 ± 1.32[c]	15.3 ± 2.6[c]	56.2 ± 16.8[c]
$10^{11}K_1K_a^{\pm}$	0.880 ± 0.119	5.44 ± 0.37	43.5 ± 1.9	636 ± 19
p$K_a^{\pm}$	11.26[d]	10.92[e]	10.55[e]	9.95[e]
		Morpholine (pK_a = 8.90)		
$10^{-4}k_1$, M^{-1} s^{-1}	0.291 ± 0.009	1.22 ± 0.03	2.48 ± 0.04	4.87 ± 0.34
$10^{-5}k_{-1}$,[a] s^{-1}		4.27	6.58	2.50
K_1,[b] M^{-1}		0.0286	0.0377	0.195
$10^{10}K_1K_a^{\pm}$		1.61 ± 0.18	7.95 ± 1.16	102 ± 1
$K_1 + K_1K_a^{\pm}/K_a^0$, M^{-1}		0.146 ± 0.074	0.585 ± 2.46	4.56 ± 0.16
p$K_a^{\pm}$[f]		8.29	7.92	7.32
pK_a^0[g]		≈8.86	≈8.84	≈8.63

[a] k_{-1} calculated as k_1/K_1. [b] $K_1 = K_1K_a^{\pm}/K_a^{\pm}$, see text. [c] K_1 extrapolated from intercept of plot of slope vs $a_{H^+}^{-1}$ according to eq 6. [d] p$K_a^{\pm}$ extrapolated from Hammett plot in Figure 3. [e] $K_a^{\pm} = K_1K_a^{\pm}/K_1$. [f] p$K_a^{\pm}$ from eq 9. [g] pK_a^0 from $K_1 + K_1K_a^{\pm}/K_a^0$, see text.

Table II. Rate and Equilibrium Constants for the Reactions of Piperidine (pK_a = 11.02) with Substituted Benzylidenemalononitriles in 50% Me$_2$SO–50% Water, μ = 0.5 M (KCl), at 20 °C

parameter	4-Me$_2$N	4-MeO	4-Me	H	4-Cl	4-Br	3-Cl	4-CN	4-NO$_2$
$10^{-5}k_1$, M^{-1} s^{-1}	0.056 ± 0.010	0.98 ± 0.01	2.14 ± 0.02	3.57 ± 0.03	4.54 ± 0.05	5.08 ± 0.12	6.67 ± 0.14	10.8 ± 0.7	14.9 ± 0.9
$10^{-4}k_{-1}$,[a] s^{-1}	5.28	2.60	1.91	2.20			0.93	1.07	
K_1,[b] M^{-1}	0.106	3.77	11.2	16.2 ± 1.95[c]			71.8	101	
$10^{11}K_1K_a^{\pm}$	0.040 ± 0.002	8.05 ± 0.59	32.3 ± 1.5	75.8 ± 2.7			968 ± 144	3120 ± 220	
p$K_a^{\pm}$[d]	11.42	10.67	10.54	10.33 ± 0.13[e]			9.87	9.52	

[a] k_{-1} calculated as k_1/K_1. [b] $K_1 = K_1K_a^{\pm}/K_a^{\pm}$, see text. [c] K_1 from intercept of plot of slope vs $a_{H^+}^{-1}$ according to eq 6. [d] p$K_a^{\pm}$ from p$K_a^{\pm}$ (Z = H) and $\rho = -1.25$, see text. [e] $K_a^{\pm} = K_1K_a^{\pm}/K_1$.

Table III. Rate and Equilibrium Constants for the Reactions of Benzylidenemalononitrile with Piperidine and Morpholine in 70% Me$_2$SO–30% Water, μ = 0.25 M (KCl), at 20 °C

	piperidine (pK_a = 10.48)	morpholine (pK_a = 8.38)
k_1, M^{-1} s^{-1}	(1.29 ± 0.06) × 10^6	(1.58 ± 0.03) × 10^5
k_{-1},[a] s^{-1}	5.18 × 10^4	1.83 × 10^5
K_1, M^{-1}	24.9 ± 9.2[b]	0.86[c]
$K_1K_a^{\pm}$	(2.28 ± 0.28) × 10^{-9}	(9.93 ± 1.53) × 10^{-9}
p$K_a^{\pm}$	10.04 ± 0.39[d]	7.94

[a] $k_{-1} = k_1/K_1$. [b] K_1 from intercept of plot of slope vs $a_{H^+}^{-1}$ according to eq 6. [c] $K_1 = K_1K_a^{\pm}/K_a^{\pm}$. [d] $K_a^{\pm} = K_1K_a^{\pm}/K_1$. [e] $K_a^{\pm}$ from eq 9, see text.

pH values, corresponding to ~0.1 M KOH, hydrolysis of the substrate became competitive with amine addition at low amine concentrations. This added a $k_1^{OH}a_{OH^-}$ term to the intercepts of the plots of τ^{-1} vs [R$_2$NH]. However, this was of no consequence because no numerical information was extracted from the intercepts.

The kinetic experiments were performed by mixing a solution of BMN-Z with a solution of piperidine in the stopped-flow apparatus, and monitoring the disappearance of the substrate at or near λ_{max} of BMN-Z. The raw data are summarized elsewhere.[16] Some representative plots of τ^{-1} vs piperidine concentration are shown in Figure 1. k_1 values are summarized in Tables I–III.

Equilibrium Constants for Piperidine Addition. The equilibrium constants for adduct formation were determined spectrophotometrically by using eq 6 where A_0 is the absorbance of the substrate in the absence of amine,

$$\frac{A_0 - A_\infty}{A - A_\infty} = 1 + \left(K_1 + \frac{K_1K_a^{\pm}}{a_{H^+}}\right)[R_2NH] \qquad (6)$$

A_∞ is the absorbance of T$^-$ at high amine concentration and high pH, and A is the absorbance in the presence of moderate concentrations of piperidine such that [T$^-$] and/or [T$^{\pm}$] are of comparable magnitude with [S]. Equation 6 is strictly valid only if $\epsilon_{T^-} = \epsilon_{T\pm}$. For all substrates except BMN-4-NO$_2$, $\epsilon_{T^-} = \epsilon_{T\pm} = 0$, which reduced the left side of eq 6 to A_0/A. For BMN-4-NO$_2$ ϵ_{T^-} and $\epsilon_{T\pm}$ were nonnegligible but nearly identical.

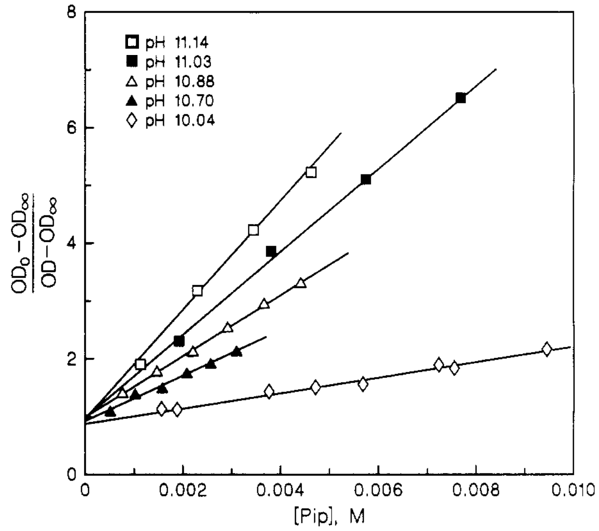

Figure 2. Equilibrium determination for the addition of piperidine to 4-nitrobenzylidenemalononitrile in water at 20 °C. Data plotted according to eq 6.

Since T$^-$ is fairly rapidly converted to benzaldehyde and malononitrile the absorbance had to be measured in the stopped-flow apparatus and extrapolated to "zero time" on the time scale of the conversion into benzaldehyde.

For a given pH, absorbance values at five amine concentrations were determined and slopes = $K_1 + K_1K_a^{\pm}/a_{H^+}$ determined. For each compound such measurements were performed at four to five different pH values. The raw

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(16) Killion, R. B., Jr. Ph.D. Thesis, University of California, Santa Cruz; 1988; Chapter 2.

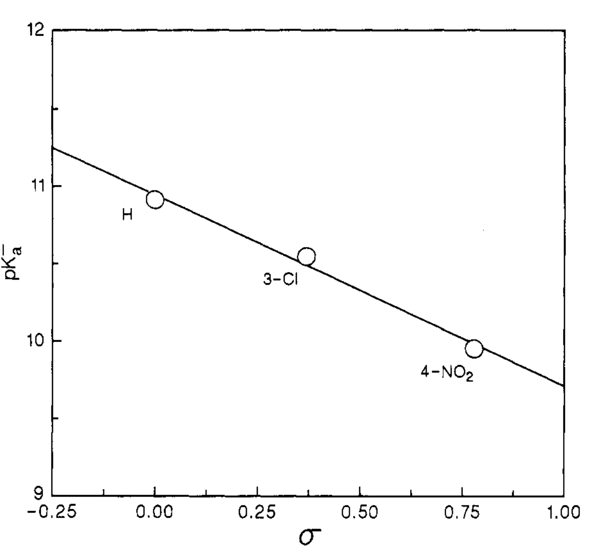

Figure 3. Hammett plot of $pK_a^{\pm}$ for the piperidine adducts of three benzylidenemalononitriles in water at 20 °C.

data are summarized elsewhere.[16] Representative plots according to eq 6 are shown in Figure 2. Plots of the slopes of such plots vs $a_{H^+}^{-1}$ (not shown) provided good values for $K_1K_a^{\pm}$ in all cases; with Z = H, 3-Cl, 4-NO_2 in water, Z = H in 50% Me_2SO, and Z = H in 70% Me_2SO reliable K_1 values could also be obtained (intercepts).

With the other substituents the experimental uncertainty in K_1 was quite large and hence the following method was used to obtain K_1. First, $K_a^{\pm}$ for Z = H, 3-Cl, and 4-NO_2 was calculated as $K_1K_a^{\pm}/K_1$. A Hammett plot of $pK_a^{\pm}$ vs σ is shown in Figure 3. It has a $\rho = -1.25$. The $pK_a^{\pm}$ for Z = 4-MeO was then calculated from this plot, and K_1 for Z = 4-MeO obtained as $K_1K_a^{\pm}/K_a^{\pm}$. In 50% and 70% Me_2SO $pK_a^{\pm}$ for Z ≠ H was calculated on the basis of $pK_a^{\pm}$ for Z = H and assuming the same $\rho = -1.25$ as in water. $|\rho|$ values for ion-forming equilibria generally become larger when changing from water to a less polar solvent,[17] but the superior ability of Me_2SO to accept hydrogen bonds from ammonium ions[18] should roughly compensate for the reduced polarity. Be it as it may, the major conclusions from this work are not affected by a potential small error in the assumed ρ value. The various K_1 and $pK_a^{\pm}$ values are summarized in Tables I–III.

Kinetics of Morpholine Addition. For the morpholine adduct $pK_a^{\pm} < pK_a^{0}$,[15] implying $K_0 > 1$, and hence T^0 cannot be ignored. The rate equation is given by

$$\tau^{-1} = k_1[R_2NH] + k_{-1}\frac{a_{H^+}}{K_a^{\pm} + (1 + K_a^{\pm}/K_a^{0})a_{H^+}} \qquad (7)$$

However, k_{-1} being even higher than for the piperidine reaction, all measurements were performed at high enough pH values that the k_{-1} term in eq 7 becomes small and insignificant. Representative plots of τ^{-1} vs morpholine concentration are shown in Figure 4, with the k_1 values summarized in Tables I–III; the raw data are summarized elsewhere.[16]

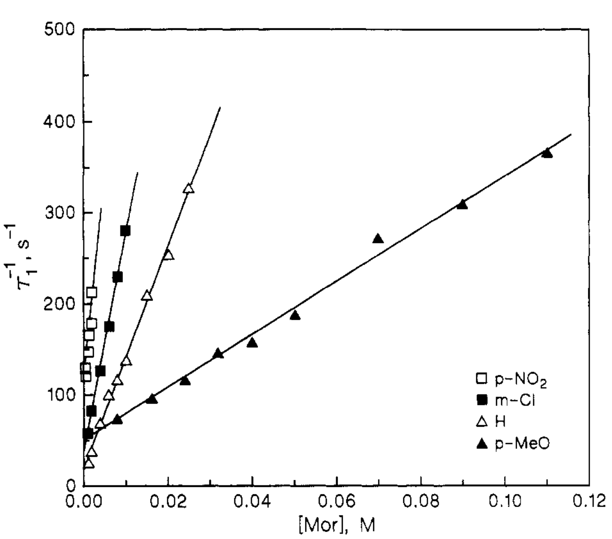

Figure 4. Kinetics of morpholine addition to substituted benzylidenemalononitriles in water at 20 °C. The slopes provide k_1 according to eq 7.

Table IV. Brønsted β Values and log k_0 for the Nucleophilic Addition of Piperidine and Morpholine to Substituted Benzylidenemalononitriles in Water, 0.5 M (KCl), at 20 °C

parameter	4-MeO	H	3-Cl	4-NO_2
$\beta_{nuc}(k_1)$	0.29 ± 0.03	0.29 ± 0.01	0.28 ± 0.01	0.29 ± 0.03
$\beta_{lg}(k_{-1})$		−0.55 ± 0.06		
$\beta_{eq}(K_1)$		0.84 ± 0.05		
$\beta_{nuc}^{n} = \beta_{nuc}/\beta_{eq}$		0.35 ± 0.03		
$\beta_{lg}^{n} = \beta_{lg}/\beta_{eq}$		−0.65 ± 0.03		
log k_0		4.62	4.79	4.91

Equilibrium Constants for Morpholine Addition. Since T^0 is an important species in the morpholine reactions, eq 6 takes on the form

$$\frac{A_0 - A_\infty}{A - A_\infty} = 1 + \left(K_1 + \frac{K_1K_a^{\pm}}{K_a^{0}} + \frac{K_1K_a^{\pm}}{a_{H^+}}\right)[R_2NH] \qquad (8)$$

The experiments, summarized elsewhere,[16] were performed in a similar way as for the piperidine reaction, with slopes according to eq 8 yielding $K_1 + K_1K_a^{\pm}/K_a^{0} + K_1K_a^{\pm}/a_{H^+}$, and plots of these slopes vs $a_{H^+}^{-1}$ yielding $K_1K_a^{\pm}$. $K_a^{\pm}$ was calculated from $K_a^{\pm}$ of the piperidine adducts by means of the relationship

$$pK_a^{\pm}(\text{mor}) \approx pK_a^{\pm}(\text{pip}) + pK_a^{\text{MorH}^+} - pK_a^{\text{PipH}^+} \qquad (9)$$

K_1 and $pK_a^{\pm}$ values are summarized in Table I and III.

pK_a^{0} values could also be obtained by solving $K_1 + K_1K_a^{\pm}/K_a^{0}$ (intercepts of plots of the slopes according to eq 8 vs $a_{H^+}^{-1}$) for K_a^{0}. Due to a large experimental error in $K_1 + K_1K_a^{\pm}/K_a^{0}$ (Table I) these pK_a^{0} values are rather crude with an estimated uncertainty of ±0.3 pK units.

Discussion

All rate and equilibrium constants determined in this study are summarized in Tables I–III. Error limits which correspond to standard deviations are indicated for all parameters that were directly determined from experimental quantities (all k_1 and $K_1K_a^{\pm}$ values, some K_1 values). For the various parameters calculated indirectly by the procedures described in the Results, the error limits are not known and not given in the tables. They are estimated to be ±20% to ±30% except for pK_a^{0}, which may have error limits as high as ±0.3 log units.

Dependence of k_1, k_{-1}, and K_1 on Amine. For the cases where rate and equilibrium constants with both

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(17) Lewis, E. S. In *Investigation of Rates and Mechanisms of Reactions*, 4th ed.; Bernasconi, C. F., Ed.; Wiley: New York, 1986; Part II, p 871.

(18) This is reflected in negative log ${}^{W}\gamma_{R_2NH_2^+}^{D}$ values[19] where ${}^{W}\gamma_{R_2NH_2^+}^{D}$ represents the solvent activity coefficient[20] for the transfer of $R_2NH_2^+$ from water to a Me_2SO–water solution.

(19) Wells, C. F. In *Thermodynamic Behavior of Electrolytes in Mixed Solvents*; Furter, W. F., Ed.; Advances in Chemistry 177, American Chemical Society: Washington, DC, 1979; p 53.

(20) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1.

Table V. Brønsted β Values and log k_0 for the Nucleophilic Addition of Piperidine and Morpholine to Benzylidenemalononitrile in Different Solvents at 20 °C

parameter	H_2O^a	50% Me_2SO^a	70% Me_2SO^b
$\beta_{nuc}(k_1)$	0.29 ± 0.01	0.34 ± 0.02	0.43 ± 0.02
$\beta_{lg}(k_{-1})$	−0.55	−0.47	−0.26
$\beta_{eq}(K_1)$	0.84 ± 0.04	0.81 ± 0.04	0.70 ± 0.15
$\beta_{nuc}{}^n = \beta_{nuc}/\beta_{eq}$	0.35 ± 0.03	0.42 ± 0.04	0.61 ± 0.13
$\beta_{lg}{}^n = \beta_{lg}/\beta_{eq}$	−0.65 ± 0.03	−0.58 ± 0.05	0.39 ± 0.13
log k_0	4.62	5.04	5.24

$^a \mu$ = 0.5 M (KCl). $^b \mu$ = 0.25 M (KCl).

Table VI. Structure-Reactivity Coefficients for the Reaction of Piperidine with Substituted Benzylidenemalononitriles in Water and in 50% Me_2SO at 20 °C

parameter	H_2O	50% Me_2SO
$\rho(K_1)$	≈0.98	1.03 ± 0.08
$\rho(k_1)$	0.78 ± 0.01	0.74 ± 0.02
$\rho(k_{-1})$	≈−0.20	−0.29
$\rho(pK_a{}^{\pm})$	−1.25 ± 0.02	-1.25^a ± 0.02
$\alpha_{nuc}{}^n = \rho(k_1)/\rho(K_1)$	≈0.80	0.72 ± 0.07
$\rho_{eq}(C^-)^b$	≈2.23	2.28 ± 0.10
$\rho_{kin}(C^-)^b$	≈1.22	1.27 ± 0.07
$\alpha_{nuc,corr}{}^n = \rho_{kin}(C^-)/\rho_{eq}(C^-)$	≈0.55	0.56 ± 0.03
$\alpha_{nuc,corr}{}^n - \beta_{nuc}{}^n$	≈0.20	0.14 ± 0.07

^{a}Assumed to be the same as in water; for justification, see Results. $^b \rho_{eq}(C^-)$ corresponds to $\rho(K_1)$ after correction for the effect of the positive charge on the amine nitrogen in $T^{\pm}$, $\rho_{kin}(C^-)$ corresponds to $\rho(k_1)$ after a similar correction in the transition state, see text and ref 14.

piperidine and morpholine were obtained, various Brønsted β values were calculated and summarized in Table IV (as a function of the substituent) and Table V (as a function of the solvent). The following points are noteworthy.

(1) β_{nuc} is, within experimental error, independent of the substituent. A similar constancy of β_{nuc} was observed in the reactions of substituted α-nitrostilbenes with piperidine and morpholine,[7] although a slight substituent dependence was reported in the reactions of substituted benzylidene Meldrum's acids.[9]

(2) For Z = H, β_{eq} and $\beta_{nuc}{}^n$ are also given in the tables; for the other substituents these parameters may, in principle, be calculated but, due to the relatively large uncertainty in K_1, the uncertainty in these parameters is correspondingly high. Since β_{nuc} is substituent independent it is likely that β_{eq} and hence $\beta_{nuc}{}^n$, β_{lg} and $\beta_{lg}{}^n$ also show little substituent dependence, as was found to be the case with the substituted α-nitrostilbenes.[7]

(3) β_{nuc} (and $\beta_{nuc}{}^n$) increases with increasing Me_2SO content of the solvent. Similar increases have been observed in the reactions of the same amines with β-nitrostyrene[14] and benzylidene Meldrum's acid.[9] Brønsted β_B values for the deprotonation of various carbon acids by amines also show increasing values upon addition of Me_2SO to the solvent.[21-23] It is likely that these increases in the Brønsted β values for the two types of reactions are related and hence have a common origin. They have been attributed to a solvation effect of the developing ammonium ion, as described in detail elsewhere.[22]

Substituent Effects. Hammett plots for k_1, k_{-1} and K_1, using σ^+ substituent constants, are shown for the reaction of piperidine with substituted benzylidenemalononitriles in water (Figure 5) and in 50% Me_2SO–50% water (Figure 6). The ρ values are summarized in Table VI. Only a small number of substituents could be investigated in water because many of the substrates were not sufficiently water soluble. We shall therefore focus our discussion mainly on the results in 50% Me_2SO. As observed for the reactions of piperidine with benzylidene Meldrum's acid,[9] the point for Z = Me_2N shows a negative deviation from the plots of k_1 and K_1 (Figure 6), suggesting that there is a π-donor effect that is even stronger than in the system used to define σ^+.[24,25] This effect may be attributed to resonance stabilization of the olefin, as shown in **1b**, which reduces k_1 and K_1. The ρ values were therefore calculated by excluding the 4-Me_2N substituent.

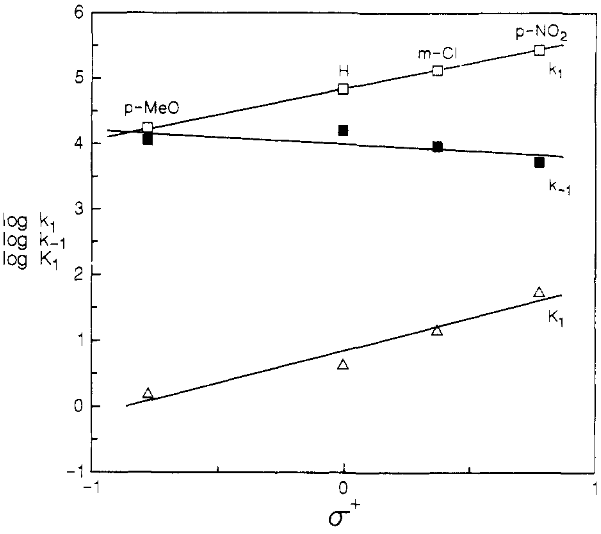


Figure 5. Hammett plots of log k_1, log k_{-1}, and log K_1 for piperidine addition in water at 20 °C.

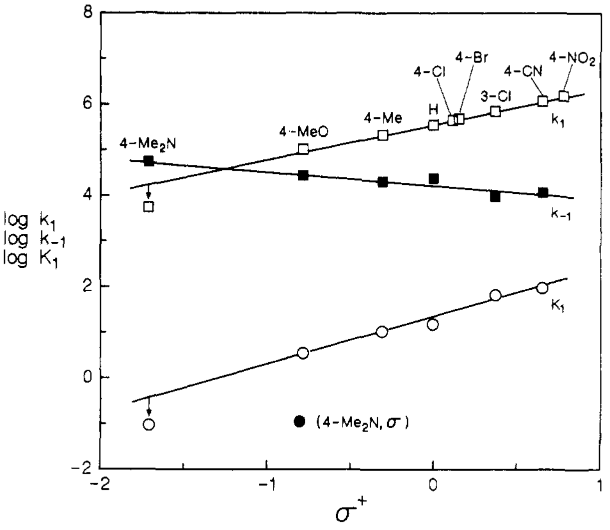
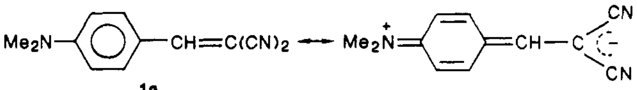


Figure 6. Hammett plots of log k_1, log k_{-1}, and log K_1 for piperidine addition in 50% Me_2SO–50% water at 20 °C. The 4-Me_2N substituent deviates from the k_1 and K_1 lines.



1a **1b**

Due to scatter the best correlation lines for k_{-1} and K_1 in water are not as well defined as in 50% Me_2SO–50%

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[21] Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420.
[22] Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969.
[23] Bernasconi, C. F.; Kliner, D. A. V.; Mullin, A. S.; Ni, J. X. *J. Org. Chem.* **1988**, *53*, 3342.
[24] Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.
[25] Hoefnagel, A. J.; Wepster, B. M. *J. Am. Chem. Soc.* **1973**, *95*, 5357.

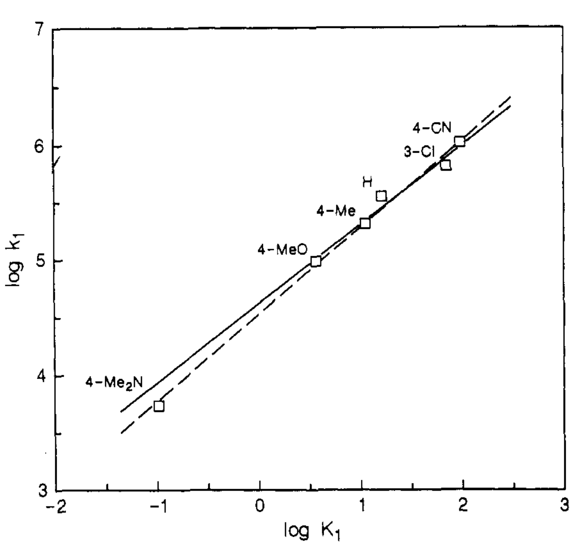


Figure 7. Brønsted plot for piperidine addition in 50% Me$_2$SO–50% water at 20 °C. Dashed line is least-squares line through all points, solid line is least-squares line omitting the 4-Me$_2$N point, see text.

water. Since the point for Z = 4-MeO lies on the lines in 50% Me$_2$SO, and the same is also true for k_1 in water, it seems reasonable to include the 4-MeO point into the correlation for K_1 and k_{-1}, even though a line through Z = H, 3-Cl, and 4-NO$_2$ with 4-MeO as a deviating point would be an alternative possibility. This alternative is rejected because it would yield a ρ value in water that is about twice as large as in 50% Me$_2$SO, which is clearly unreasonable.[17]

A question of considerable interest is how the resonance effect (**1b**) affects the *intrinsic* rate constant of the reaction. A decrease in k_0 would manifest itself by a negative deviation, an increase in k_0 by a positive deviation of the 4-Me$_2$N point from a Brønsted type plot of log k_1 vs log K_1. Figure 7 shows such a plot in 50% Me$_2$SO. The data can be interpreted in two ways. The solid line is the least-squares line through all the points except for Z = 4-Me$_2$N. The point for 4-Me$_2$N deviates negatively from this line by 0.2 log units, suggesting a reduction in log k_0 by the same amount. The second interpretation is based on the dashed line, which represents a least-squares line through all points, including 4-Me$_2$N. According to this second interpretation the π-donor effect of the 4-Me$_2$N group leaves k_0 unaffected.

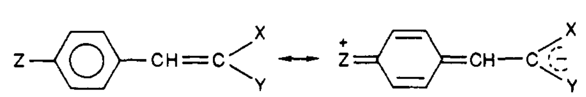
Regardless of which interpretation is preferred, we conclude that the π-donor effect is either quite small or possibly nonexistent. A similar conclusion was reached for the reaction of piperidine with 4-Me$_2$N-benzylidene Meldrum's acid.[9]

The simplest explanation why the 4-Me$_2$N group does not significantly affect k_0 would be that the loss of the resonance stabilization of the olefin occurs (almost) synchronously with bond formation along the reaction coordinate. Despite the virtue of its simplicity, this explanation is not very satisfactory. There is mounting evidence that whenever a reaction leads to a resonance stabilized species, or involves the destruction of such a species, the developing resonance lags behind bond formation at the transition state or, by virtue of the principle of microscopic reversibility, the loss of the resonance runs ahead of bond cleavage.[2-4] This lack of synchronization of the two events always leads to a lowering of k_0. The evidence for this phenomenon is strongest for carbanions with π-acceptor substituents *directly attached* to the central carbon,[2-4] but several cases are known where *remote* π-acceptor substituents show a qualitatively similar effect.[26-29] It is therefore reasonable to expect that the resonance stabilization of the type shown in **1b** with a *π-donor* should follow the same pattern, i.e., lower k_0.

A crude estimate of the expected magnitude of this decrease may be based on a comparison with the effect of π-acceptors. For example, in the deprotonation of substituted phenylnitromethanes by benzoate ion in Me$_2$SO[26] the negative deviation from the Brønsted plot, Δ(log k_0) is $\approx$–0.8 for the 4-nitro, $\approx$–0.36 for the 4-cyano group. Similar Δ(log k_0) value for these substituents have been observed in the deprotonation of 2-nitro-4-X-phenylacetonitriles by glycinamide in 90% Me$_2$SO–10% water.[30] For the phenylnitromethanes the extra stabilization of the carbanion which may be attributed to the resonance effect of the 4-nitro group is estimated[31] to be equivalent to $\Delta pK_a \approx 1.4$, the effect of the 4-cyano group to $\Delta pK_a \approx 0.9$. Thus, for the 4-nitro group $\Delta(\log k_0)/\Delta pK_a \approx 0.8/1.4 = 0.57$, for the 4-cyano group $\Delta(\log k_0)/\Delta pK_a \approx 0.36/0.9 = 0.40$.

We now assume that in the amine addition to benzylidenemalononitriles the lowering of k_0 (Δ(log k_0)) for a given degree of resonance stabilization of the olefin would be about the same as in the above-mentioned proton transfer reactions. Using the reduction in K_1 (Δ(log K_1)) by the 4-Me$_2$N group as a measure of this resonance stabilization, our assumption is equivalent to setting $(\Delta(\log k_0)/\Delta(\log K_1))_{\mathrm{BMN}} \approx (\Delta(\log k_0)/\Delta pK_a)_{\mathrm{ArCH_2NO_2}}$, i.e., $\approx$0.40–0.57.

A lower limit of $\sim$1.4 for Δ(log K_1) can be estimated from the Hammett plot shown in Figure 6 by using the standard σ rather than σ^+ for 4-Me$_2$N (filled circle). Since σ for 4-Me$_2$N already contains a substantial resonance contribution,[32] an alternative and probably more realistic method for estimating Δ(log K_1) is from a Hammett plot (not shown) based on σ^n values.[32] This provides $\Delta(\log K_1) \approx 2.0$. With $\Delta(\log k_0)/\Delta(\log K_1) \approx 0.40$–$0.57$ and $\Delta(\log K_1) \approx 1.4$–$2.0$ one thus expects a Δ(log k_0) in the range from 0.56 to 1.14. The 0.2 log units deviation from the solid line in Figure 7 is significantly smaller than even the lower limit of the estimated range expected for Δ(log k_0). This suggests a compensating factor that enhances k_0. Direct evidence for a k_0-enhancing effect by strong π-donors was found in the reaction of substituted β-nitrostyrenes with piperidine in 50% Me$_2$SO–50% water,[14] where the point for 4-Me$_2$N deviated *positively* from the respective structure–reactivity plots. This increase in k_0 may be understood by viewing **1b**, or **2b** for the general case, as already having part of the product carbanion resonance built in.[33] In other words, the usual k_0-lowering effect of



2a **2b**

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[26] Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1295.

[27] (a) Bunting, J. W.; Stefanidis, D. In *Physical Organic Chemistry 1986*; Kobayashi, M., Ed.; Elsevier: New York, 1987; p 383. (b) Bunting, J. W.; Stefanidis, D. *J. Am. Chem. Soc.* **1988**, *110*, 4008.

[28] Bernasconi, C. F.; Hibdon, S. A. *J. Am. Chem. Soc.* **1985**, *105*, 4343.

[29] Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224.

[30] Bernasconi, C. F.; Wenzel, P. J., unpublished results.

[31] These estimates are based on a Hammett plot of the pK_a values using standard σ values and measuring the deviation from the line for the 4-NO$_2$ and 4-CN substituents.

[32] (a) van Bekkum, H.; Verkade, P. E.; Wepster, B. M. *Recl. Trav. Chim. Pays-Bas* **1959**, *78*, 815. (b) Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; Wiley: New York, 1975; p 71.

[33] An alternative explanation for the increase in k_0 by π-donors in terms of radicaloid character of the transition state has recently been suggested by Hoz.[34]

Table VII. Imbalances for Piperidine and Morpholine Addition to Activated Olefins

olefin	solvent	$\alpha_{\mathrm{nuc,corr}}^{\mathrm{n}}$	$\beta_{\mathrm{nuc}}^{\mathrm{n}}$	$I = \alpha_{\mathrm{nuc,corr}}^{\mathrm{n}} - \beta_{\mathrm{nuc}}^{\mathrm{n}}$
$ArCH{=}C(CN)_2$[a]	H_2O	0.55	0.35	0.20
	50% Me_2SO	0.56	0.42	0.14
$ArCH{=}C(COO)_2$-$C(CH_3)_2$[b]	H_2O	0.24	0.08	0.17
	50% Me_2SO	0.25	0.15	0.10
$ArCH{=}CHNO_2$[c]	H_2O	0.51	0.25	0.26
$PhCH{=}C(A)NO_2$[d]	50% Me_2SO	0.67	0.37	0.30

[a] This work. [b] Reference 9. [c] Reference 14. [d] Reference 7.

delayed carbanion resonance development is circumvented, or at least attenuated. This factor should be particularly important where delayed carbanion resonance development has a very strong effect on k_0, as is the case in the piperidine addition to β-nitrostyrenes.

Imbalance and Intrinsic Rate Constants. As mentioned in the Introduction, a major goal of this study was to determine the imbalance, $I = \alpha_{\mathrm{nuc}}^{\mathrm{n}} - \beta_{\mathrm{nuc}}^{\mathrm{n}}$ for the BMN reaction. In principle, $\alpha_{\mathrm{nuc}}^{\mathrm{n}}$ which is also equal to $\rho(k_1)/\rho(K_1)$, could be obtained from the slope of the plot of log k_1 vs log K_1 in Figure 7. However, the developing positive charge on the amine nitrogen distorts the substituent effect that arises from the developing negative charge. Since this distortion affects $\rho(k_1)$ and $\rho(K_1)$ differently, the result is a distorted $\alpha_{\mathrm{nuc}}^{\mathrm{n}}$. One may correct for these distortions by a procedure developed earlier.[14] This leads to ρ values ($\rho_{\mathrm{eq}}(\mathrm{C}^-)$ and $\rho_{\mathrm{kin}}(\mathrm{C}^-)$) that measure only the effect of the negative charge and to a corrected $\alpha_{\mathrm{nuc}}^{\mathrm{n}}$, defined as $\alpha_{\mathrm{nuc,corr}}^{\mathrm{n}} = \rho_{\mathrm{kin}}(\mathrm{C}^-)/\rho_{\mathrm{eq}}(\mathrm{C}^-)$. Table VI includes these corrected parameters.

The imbalances calculated from these parameters are summarized in Table VII, along with imbalances for amine addition to other activated olefins. We note that the imbalances for addition to benzylidenemalononitrile are quite small and of comparable magnitude with those for addition to benzylidene Meldrum's acid.[9] This contrasts with the much higher imbalances in the reactions of α-nitrostilbene and β-nitrostyrene. These results are consistent with the notion that imbalances should be small for reactions that lead to carbanions whose main source of stabilization is a polar rather than resonance effect.[2-4]

Our results also provide more evidence for the notion that large imbalances/low intrinsic rates (or small imbalances/high intrinsic rates) are just two different manifestations of the same phenomenon, namely a lag in resonance development and concomitant solvation of the carbanion at the transition states. Thus log k_0 = 5.04 for piperidine/morpholine addition to BMN in 50% Me_2SO (Table V), even though the highest value measured in the series of $PhCH{=}CXY$, is not much different from log $k_0 \approx 4.10$ for piperidine/morpholine addition to benzylidene Meldrum's acid in the same solvent,[9] just as the imbalances for these two systems are of comparable magnitude. On the other hand, log k_0 for piperidine/morpholine addition to α-nitrostilbene (log k_0 = 1.43 in 50% Me_2SO at 20 °C),[7] or to β-nitrostyrene (log k_0 = 2.55 in water at 25 °C)[14] are much lower, consistent with the much larger imbalances in these reactions.

Imbalances in Proton Transfers vs Nucleophilic Addition. In all cases studied previously the imbalances in the nucleophilic additions (eq 1) are smaller than in the corresponding proton transfers (eq 2). Based on the demonstration that the imbalance in the BMN system, even though small, is definitely larger than zero, one should expect that the imbalance in the deprotonation of malononitrile is also substantially larger than zero. Hence, the observed zero imbalance in the reaction of $ArCH_2CH(CN)_2 + RCOO^-$,[10a] and in the detritiation of *tert*-butylmalononitrile/malononitrile by $RCOO^-$[10b] clearly suggests an anomaly in these reactions. One factor that is likely to contribute to this anomaly is the β_B value, which overestimates the degree of proton transfer at the transition state. Murray and Jencks[35] have shown that the solvation of RCOOH which is formed in the deprotonation of a carbon acid by $RCOO^-$ (or the desolvation of RCOOH in the protonation direction) tends to enhance β_B and that this effect becomes increasingly important for large β_B values. Applying the suggested correction of −0.2[35] to an observed $\beta_B = 1.0$ leads to $\beta_B^{\mathrm{corr}} = 0.8$. Interestingly, this is the same as β_B for the deprotonation of *tert*-butylmalononitrile by *primary amines*.[10c] The true imbalance in the proton transfers involving malononitriles seems therefore to be closer to $I \approx 1.0-0.8 \approx 0.2$ than to zero, a much less anomalous value in light of the imbalances in the amine addition to benzylidenemalononitrile ($I \approx 0.20$ in water, ≈ 0.14 in 50% Me_2SO–water, Table VI).

Substituent and Solvent Dependence of log k_0. log k_0 values are summarized in Table IV as a function of the Z substituent in water, and in Table V as a function of the solvent for the reaction of the unsubstituted BMN. There is a slight trend toward increasing log k_0 with increasing electron-withdrawing strength Z. This is a general phenomenon observed with polar substituents[36] in carbanion-forming reactions; it is a consequence of the imbalance rather than caused by the substituent itself. The effect can be described by eq 10 where $\delta(\log k_0(\mathrm{Z}))$ is the difference between log k_0(Z) and log k_0(H), and $\delta(\log K_1(\mathrm{Z}))$ is the difference between log K_1(Z) and log K_1(H).

$$\delta(\log k_0(\mathrm{Z})) = (\alpha_{\mathrm{nuc}}^{\mathrm{n}} - \beta_{\mathrm{nuc}}^{\mathrm{n}})\delta(\log K_1(\mathrm{Z})) \qquad (10)$$

The intrinsic rate constant is also seen to increase with increasing Me_2SO content of the solvent (Table V). This increase, too, is a general phenomenon in carbanion-forming reactions.[37] It results from the fact that the carbanion is less solvated in the Me_2SO-rich solvents, which reduces the rate-lowering impact of the late development of the carbanion solvation on k_0.[2,4] According to this notion the solvent effect on k_0 should be large when the solvation energy of the carbanion differs strongly from one solvent to another, as is the case with nitronate ions.[38] On the other hand, the effect should be smaller for malononitrile type anions because of smaller solvational differences in the various Me_2SO–water mixtures.[38] This prediction is borne out by the slope of 0.74 of a plot of log k_0(BMN) vs log k_0(β-nitrostyrene) in the three solvents water, 50% Me_2SO and 70% Me_2SO (Figure 8).

pK_a^0. pK_a^0 values for the carbon acidity of T^0 derived from morpholine and BMN with Z = H, 3-Cl, and 4-NO_2 in water are summarized in Table I. The value of ≈8.86 for Z = H compares with p$K_a^0 \approx 8.43$ for the same compound in 50% Me_2SO.[15] The corresponding pK_a values of malononitrile are 11.39 in water, 10.21 in 50% Me_2SO,[39]

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(34) Gross, Z.; Hoz, S. *J. Am. Chem. Soc.* **1988**, *110*, 7489.

(35) Murray, C. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1988**, *110*, 7561.

(36) This polar effect contrasts with the effects of π-acceptors that can interact with the carbanionic center, or π-donors that can lead to resonance forms such as **1b** or **2b**, as discussed in previous sections of this paper.

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

(38) Bernasconi, C. F.; Bunnell, R. D. *J. Am. Chem. Soc.* **1988**, *110*, 2900.

(39) Bernasconi, C. F.; Zitomer, J. L.; Fox, J. P.; Howard, K. A. *J. Org. Chem.* **1984**, *49*, 482.

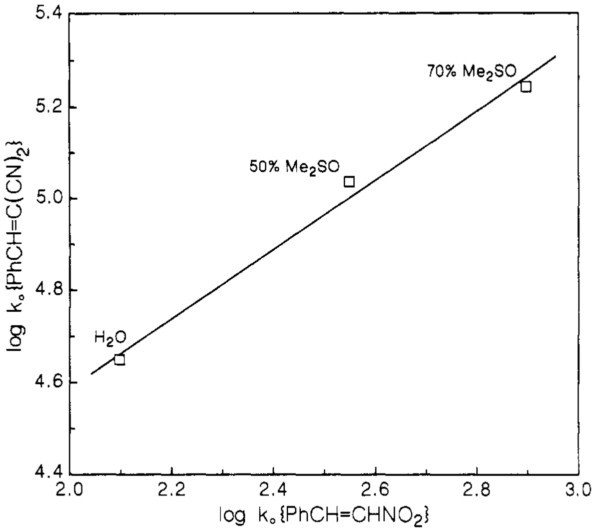

Figure 8. Comparison of solvent effect on k_0 for piperidine addition to benzylidenemalononitrile with that for piperidine addition to β-nitrostyrene.

showing the expected acidifying effect of the $PhCH(R_2N)$ moiety.

Conclusions

(1) The intrinsic rate constant for piperidine/morpholine addition to BMN is relatively high ($\log k_0 = 4.62$ in water, 5.04 in 50% Me_2SO, 5.24 in 70% Me_2SO) and in fact higher than for all the $PhCH{=}CXY$ type olefins ($XY = (COO)_2C(CH_3)_2$, $(CN)C_6H_4$-4-NO_2, $(CN)C_6H_3$-2,4-$(NO_2)_2$, $(H)NO_2$, $(Ph)NO_2$) studied thus far. This result is characteristic for a reaction that forms a carbanion with relatively little resonance stabilization. A manifestation of the same phenomenon is the smallness of the imbalance, $I = \alpha_{nuc,corr}{}^{n} - \beta_{nuc}{}^{n} \approx 0.20$ in water, 0.14 ± 0.07 in 50% Me_2SO.

(2) Even though small, the imbalance is not zero, suggesting that the absence of a measurable imbalance in the deprotonation of malononitrile derivatives by $RCOO^-$ is an abnormality caused, at least in part, by the solvation of RCOOH.

(3) Despite its strong resonance effect on the stability of 4-Me_2N-BMN (low K_1), the 4-Me_2N group does not show the expected strong deviation from the Brønsted plot (Figure 7) which should arise because of early loss of the resonance effect (**1b**) along the reaction coordinate. This suggests a compensating effect on the intrinsic rate constant, which can be understood as an attenuation of the decrease in k_0 caused by late development of the resonance stabilization of the carbanionic center in the adduct.

Experimental Section

Materials. The various substituted benzylidenemalononitriles were prepared according to literature procedures,[40] mp 180 °C (lit.[40] mp 179 °C) for 4-Me_2N-BMN; 114–115 °C (lit.[40] mp 115.5–116.5 °C) for 4-MeO-BMN; 83–84 °C (lit.[40] mp 83–84 °C) for BMN; 115–116 °C (lit.[41] mp 116–117 °C) for 3-Cl-BMN; 153–154 °C (lit.[40] mp 152–153 °C) for 4-CN-BMN; 160–161 °C (lit.[40] mp 160 °C) for 4-NO_2-BMN; 132–134 °C for 4-Me-BMN; 160–162 °C for 4-Cl-BMN; 163–164 °C for 4-Br-BMN. UV spectral data have been reported previously.[42] Morpholine and piperidine were purified and stored as in previous work.[43]

Reaction Solutions and pH Measurements. Aqueous solutions were prepared by adding appropriate amounts of aqueous stock solutions to a volumetric flask and then diluting to the mark with water. Solutions in 50% Me_2SO–50% water (v/v) were prepared by adding appropriate amounts of aqueous stock solutions to a volumetric flask containing a measured amount of Me_2SO that would correspond to 50% of the final volume and then diluting to the mark with water. Solutions in 70% Me_2SO–30% water (v/v) were prepared by adding appropriate amounts of aqueous stock solution plus water to a volumetric flask so that the total aqueous component would correspond to 30% (v/v) of the final solution volume and then diluting to the mark with Me_2SO. The ionic strength was maintained at 0.5 M with KCl in water and 50% Me_2SO, at 0.25 M in 70% Me_2SO.

All pH measurements were performed on an Orion Research 611 digital pH meter with a Corning No. 476022 glass electrode and a Beckman No. 39400 calomel reference electrode. The pH meters were calibrated for Me_2SO–water solutions with standard buffer solutions described by Hallé et al.[44] Mallinckrodt standard buffer solutions were used to calibrate the pH meters for aqueous solutions.

Rate and Equilibrium Measurements. A Durrum-Gibson stopped-flow spectrophotometer with computerized data acquisition and analysis was used to monitor the kinetics of all reactions. Due to hydrolysis of T^-, the equilibrium measurements were also performed in the stopped-flow apparatus by determining absorbances extrapolated to "zero" time (on the time scale of the hydrolysis).

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Registry No. p-$Me_2NC_6H_4CH{=}C(CN)_2$, 2826-28-0; p-$MeOC_6H_4CH{=}C(CN)_2$, 2826-26-8; p-$MeC_6H_4CH{=}(CN)_2$, 2826-25-7; Ph-$CH{=}C(CN)_2$, 2700-22-3; p-$ClC_6H_4CH{=}C(CN)_2$, 1867-38-5; p-$BrC_6H_4CH{=}C(CN)_2$, 2826-24-6; m-$ClC_6H_4CH{=}C(CN)_2$, 2972-73-8; p-$CNC_6H_4CH{=}C(CN)_2$, 36937-92-5; p-$NO_2C_6H_4CH{=}C(CN)_2$, 2700-23-4; piperidine, 110-89-4; morpholine, 110-91-8.

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