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paratus was of the Durrum-Gibson type, interfaced with a Tarbell computer.

pK_a Determinations. The pK_a values of the various amines were determined at μ = 0.5 M by classical potentiometric procedures. A standard spectrophotometric method was used for the determination of p$K_a^{\pm}$ values (eq 9) and of K_1 and p$K_a^{\pm}$ for the (cyanomethyl)amine adduct (eq 7).

Acknowledgment. This research was supported by Grants CHE 80-24262 and CHE 83-15374 from the National Science Foundation.

Registry No. BuNH$_2$, 109-73-9; MeOCH$_2$CH$_2$NH$_2$, 109-85-3; H$_2$NCOCH$_2$NH$_2$, 598-41-4; NCCH$_2$NH$_2$, 540-61-4; H$_2$NNH$_2$, 302-01-2; MeONH$_2$, 67-62-9; Sem, 57-56-7; benzylidene Meldrum's acid, 1214-54-6.

Supplementary Material Available: Kinetic and equilibrium data, Tables S1–S5 (8 pages). Ordering information is given on any current masthead page.

Brønsted Coefficients for Intramolecularly Assisted Carbon Protonation of Amine Adducts of Benzylidene Meldrum's Acid

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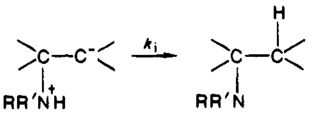
Contribution from the Thimann Laboratories of the University of California, Santa Cruz, California 95064. *Received December 9, 1985*

Abstract: The conversion of the anionic amine adducts of benzylidene Meldrum's acid, PhCH(RR′N)C$^-$(COO)$_2$C(CH$_3$)$_2$ (T$_A^-$), into benzaldehyde and Meldrum's acid anion is subject to general acid catalysis, indicating that carbon protonation of T$_A^-$ to form PhCH(RR′N)CH(COO)$_2$C(CH$_3$)$_2$ (T$_A^0$) is rate limiting. The rate constants for hydronium ion catalysis (k_H) are higher than those expected from simple, unassisted protonation of T$_A^-$ by H$_3$O$^+$ or for the kinetically equivalent protonation of the zwitterionic adduct, PhCH(RR′N$^+$H)C$^-$(COO)$_2$C(CH$_3$)$_2$ (T$_A^{\pm}$), by water. Furthermore, for the adducts derived from *n*-butylamine, 2-methoxyethylamine, glycinamide, (cyanomethyl)amine, and methoxyamine, k_H depends on the basicity (p$K_a^{\pm}$) of the amine nitrogen, with a Brønsted β_N = 0.29 ± 0.05; with the semicarbazide adduct the Brønsted plot levels off. These observations demonstrate that there is intramolecular assistance by the amine nitrogen in all but the semicarbazide adduct. Several kinetically equivalent mechanisms are proposed: (1) concerted intramolecular proton transfer (T$_A^{\pm}$ → T$_A^0$) with a water molecule in the transition state; (2) protonation of T$_A^-$ by H$_3$O$^+$ with transition-state stabilization by hydrogen bonding between nitrogen and H$_3$O$^+$; and (3) protonation of T$_A^{\pm}$ by water with transition-state stabilization by hydrogen bonding between the protonated nitrogen and the incipient hydroxide ion and/or by electrostatic interactions. The third mechanism is easily ruled out, while a distinction between the first and second is more difficult. The β_N value of 0.29 ± 0.05 is in somewhat better agreement with concerted intramolecular proton transfer. For the adducts derived from piperidine and morpholine k_H is also enhanced but shows little dependence on p$K_a^{\pm}$($\beta_N \approx$ 0.01 ± 0.05). Possible reasons for this low β_N value are discussed.

In a recent paper[1] we posed the question, "When is intramolecular proton transfer between carbon and nitrogen or oxygen observable?" We were particularly interested in examples where the donor and acceptor sites are separated by only one carbon atom, as is the case in amine adducts of electron-deficient olefins (1).



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(1)

The major problem with the detectability of intramolecular proton transfer (k_i) is competition from intermolecular reactions which involve the solvent, the lyonium, and the lyate ion. A mathematical model was proposed[1] to deal with various factors such as the pK_a of the donor and acceptor sites, the pH, the Brønsted α and β values for inter- and intramolecular proton transfer, the solvent, and others. Two of the major predictions of the model were as follows:

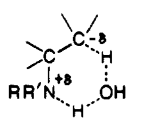
(1) The detectability of the intramolecular pathway and the pH range within which it is detectable are very sensitive to the pK_a of the heteroatom (NH$^+$ in 1) and to the Brønsted α value which relates carbon protonation rates to this pK_a. pK_a values near the midpoint of the scale (7 in aqueous solution) and α values close to 0.5 are optimal.

(2) The detectability depends only little or not at all on the pK_a of the carbon. Similarly, the Brønsted β value which relates carbon protonation rates to the carbon pK_a has a minor influence except for extreme β values as in the case of the nitroalkanes.

These and other predictions were compared with experimental results for nine systems, and agreement between theory and experiment was found for eight of them.

Some of the assumptions underlying the model were necessarily crude. For example, since no relevant experimental data existed, it was assumed that the Brønsted α value which refers to the variation in k_i with the pK_a of the NH$^+$ group in 1 is the same as α for the protonation of carbanionic sites similar to those in 1 by a series of RR′NH$_2^+$. If the two α values were significantly different, this would, for example, lead to a shift in the pK_a range of the NH$^+$ groups which are most suitable for the detection of k_i. An experimental determination of α values for k_i would therefore be desirable.

Another point which needs clarification is the mechanism of the intramolecular proton transfer. In the past we have usually assumed that the reaction is a concerted process, with a transition state that includes one (or several) water molecule(s) as shown in 2.[1] However, other kinetically equivalent mechanistic possibilities exist, as will be discussed below.



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

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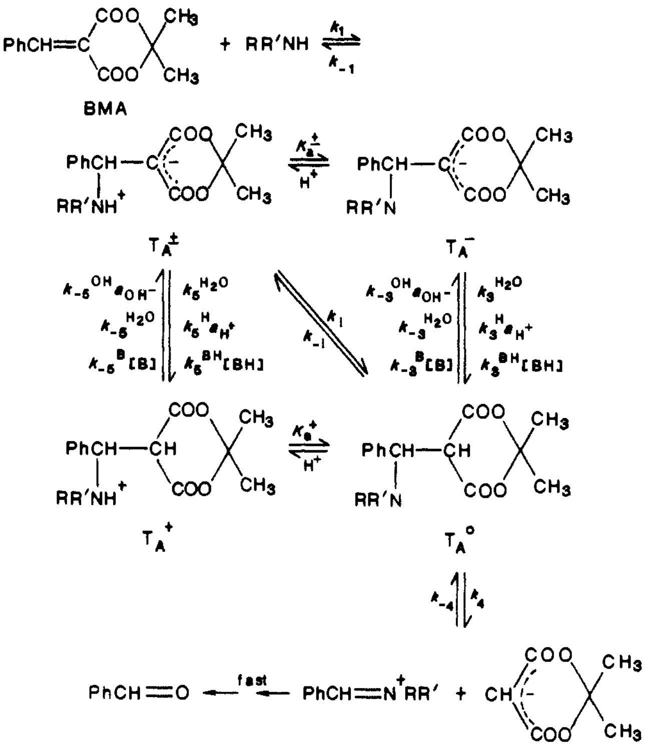
Scheme I



In this paper a first attempt to deal with these questions is being made. The system we have studied is the hydrolysis of benzylidene Meldrum's acid (BMA) in the presence of a series of primary aliphatic amines and also in the presence of piperidine and morpholine. As shown before,[2,3] this reaction proceeds by the mechanism outlined in Scheme I.

The reaction is characterized by two well-separated kinetic processes. The first is on the stopped-flow time scale; it refers to the steps in eq 2 and has been thoroughly studied.[2,3] The second

$$\mathrm{BMA} + \mathrm{RR'NH} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{T_A}^{\pm} \underset{\mathrm{H}^+}{\overset{K_a^{\pm}}{\rightleftharpoons}} \mathrm{T_A}^- \qquad (2)$$

is quite slow; it is associated with the transformation of T_A^- and/or $T_A^{\pm}$ into products and is the object of the present study. In a limited previous investigation it was found that with RR'NH = morpholine, formation of T_A^0 is rate limiting.[2]

There are numerous pathways which can lead to T_A^0, with the rate of conversion of T_A^- to T_A^0 being given by[4] eq 3.

$$\frac{\mathrm{d}[\mathrm{T_A}^0]}{\mathrm{d}t} = \left(k_3^{\mathrm{H_2O}} + k_{\mathrm{H}} a_{\mathrm{H}^+} + \frac{k_5^{\mathrm{H}}}{K_a^{\pm}} a_{\mathrm{H}^+}{}^2 + k_3^{\mathrm{BH}}[\mathrm{BH}] + \frac{k_5^{\mathrm{BH}}}{K_a^{\pm}} a_{\mathrm{H}^+}[\mathrm{BH}] \right) [\mathrm{T_A}^-] \qquad (3)$$

with $$k_{\mathrm{H}} = k_3^{\mathrm{H}} + k_{\mathrm{i}}/K_a^{\pm} + k_5^{\mathrm{H_2O}}/K_a^{\pm} \qquad (4)$$

From the pH and buffer dependence of the rate the relative importance of the five terms in eq 3 is easily assessed. However, since the k_3^{H}, k_{i}, and $k_5^{\mathrm{H_2O}}$ terms (eq 4) all have the same pH dependence, the contribution of each of these terms to k_{H} is more difficult to evaluate. In our previous study with the morpholine adduct we concluded that the k_{i} pathway (or some kinetically equivalent alternative mechanism,see Discussion section) is a major contributor, because the value obtained for k_{H} was significantly higher than expected for direct carbon protonation of T_A^- by the hydronium ion (k_3^{H}). The present study will confirm this conclusion for most (but not all) amine adducts of BMA.

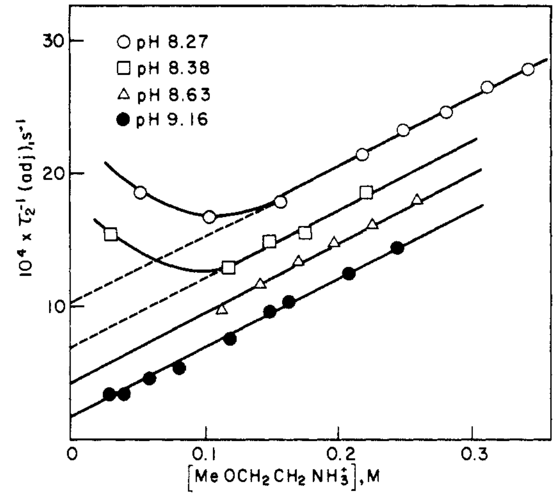


Figure 1. Plots of τ_2^{-1}(adj) vs. [RR'NH$_2^+$] for the conversion of the 2-methoxyethylamine adduct of BMA into benzaldehyde and Meldrum's acid anion. Results obtained from experiments using increasing buffer concentrations at the indicated pH values and data analyzed by means of eq 6.

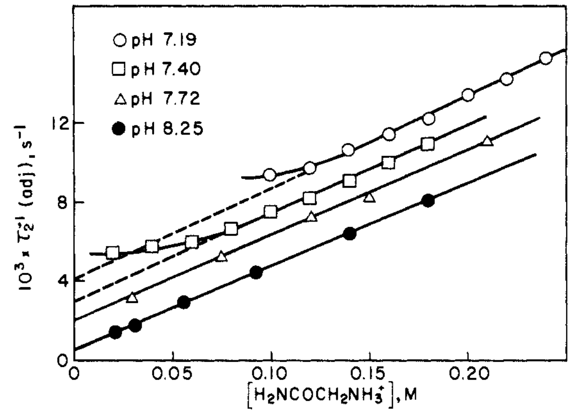


Figure 2. Plots of τ_2^{-1}(adj) vs. [RR'NH$_2^+$] for the conversion of the glycinamide adduct of BMA into benzaldehyde and Meldrum's acid anion. Results obtained and analyzed in a similar way as those in Figure 1.

Results

General Features. All kinetic experiments were conducted in aqueous solution at 25 °C. Pseudo-first-order conditions were used throughout with the amine in large excess over BMA. The ionic strength was kept at 0.5 M with KCl.

Conversion of T_A^- to Benzaldehyde. (A) Strongly Basic Amines. With the strongly basic amines glycinamide, 2-methoxyethylamine, n-butylamine, morpholine, and piperidine, we have K_1[RR'NH] $\gg$ 1 and/or $K_1K_a^{\pm}$[RR'NH]$/a_{\mathrm{H}^+} \gg 1$ under all practical conditions.[3] Hence $T_A^{\pm}$ and/or T_A^- are the initial states of the reaction.

Rates were measured by monitoring the formation of benzaldehyde and Meldrum's acid anion at 255 nm. Just as with the morpholine adduct studied previously,[2] the reactions were all found to be general acid catalyzed, indicating that carbon protonation of T_A^- is rate limiting. The reciprocal relaxation time, τ_2^{-1} (τ_1^{-1} refers to reaction 2),[3] is given by eq 5. Note that the k_5^{H} and k_5^{BH} terms (eq 3) have been omitted because they were negligible under our reaction conditions (see below); k_{H} is defined in eq 4, while the symbol AH is used when BH = RR'NH$_2^+$.

$$\tau_2^{-1} = \frac{K_a^{\pm}}{K_a^{\pm} + a_{\mathrm{H}^+}} (k_3^{\mathrm{H_2O}} + k_{\mathrm{H}} a_{\mathrm{H}^+} + k_3^{\mathrm{AH}}[\mathrm{RR'NH_2}^+]) \qquad (5)$$

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[2] Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329.

[3] Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.*, preceding article in this issue.

[4] Equation 3 implies that T_A^- is the reference state; if $T_A^{\pm}$ is chosen as the reference state, we have $\mathrm{d}[\mathrm{T_A}^0]/\mathrm{d}t = (k_3^{\mathrm{H_2O}}K_a^{\pm}/a_{\mathrm{H}^+} + k_{\mathrm{H}}K_a^{\pm} + k_5^{\mathrm{H}}a_{\mathrm{H}^+} + k_3^{\mathrm{BH}}K_a^{\pm}[\mathrm{BH}]/a_{\mathrm{H}^+} + k_5^{\mathrm{BH}}[\mathrm{BH}])[\mathrm{T_A}^{\pm}]$.

Table I. Slopes (k_3^{AH}) and Intercepts ($k_3^{H_2O} + k_H a_{H^+}$) for Carbon Protonation of T_A^- According to Equations 6 and 8[a]

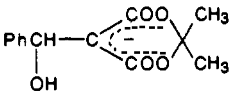
pH	10^3(intercept)[b]	10^2(slope)[b]
	Piperidine	
10.61	0.185 ± 0.018	
10.70	0.150 ± 0.015	
10.83	0.107 ± 0.011	
11.08	0.050 ± 0.005	0.0325 ± 0.0030
	Morpholine	
8.78	0.940 ± 0.023	0.0654 ± 0.0035
9.05	0.506 ± 0.010	0.0707 ± 0.0075
9.27	0.321 ± 0.008	0.0689 ± 0.0040
	n-Butylamine	
10.38	0.025 ± 0.007	0.114 ± 0.008
9.81	0.062 ± 0.010	0.150 ± 0.004
9.43	0.179 ± 0.041	0.120 ± 0.008
	2-Methoxyethylamine	
9.16	0.106 ± 0.059	0.543 ± 0.016
8.63	0.365 ± 0.097	0.557 ± 0.025
8.38	0.663 ± 0.181	0.532 ± 0.054
8.27	0.954 ± 0.081	0.537 ± 0.011
	Glycinamide	
8.25	0.581 ± 0.120	4.16 ± 0.08
7.72	1.60 ± 0.40	4.26 ± 0.15
7.70	1.81 ± 0.20	4.94 ± 0.08
7.40	3.22 ± 0.30	4.25 ± 0.09
7.19	4.76 ± 0.83	4.29 ± 0.17
	(Cyanomethyl)amine	
6.19	10.4 ± 2.0	126 ± 2
5.82	19.0 ± 2.0	136 ± 2
5.47	31.6 ± 2.5	174 ± 2
5.21	53.9 ± 6.0	127 ± 2
5.03	85.0 ± 8.0	
	Methoxyamine	
3.50	1150 ± 100	*c*
2.97	4150 ± 300	*c*
	Semicarbazide	
3.25	3090 ± 300	*c*
3.15	3560 ± 300	*c*
2.79	8400 ± 700	*c*

[a] At 25 °C, μ = 0.5 M (KCl). [b] Intercepts and slopes were determined by least-squares analysis using points at high enough amine concentrations so that interference with the reaction of T_{OH}^- is negligible; see text. Error limits are standard deviations. [c] Too small to be determined.

The raw data are summarized in Tables S1–S5[5] (119 rate constants). Figures 1 and 2 show representative plots according to the rearranged eq 6.[6] The data obey eq 6 well at high pH

$$\tau_2^{-1}(\text{adj}) = \tau_2^{-1}\frac{K_a^+ + a_{H^+}}{K_a^\pm} = k_3^{H_2O} + k_H a_{H^+} + k_3^{AH}[\text{RR'NH}_2^+] \quad (6)$$

and/or at high $[\text{RR'NH}_2^+]$. At low pH and low $[\text{RR'NH}_2^+]$ τ_2^{-1}(adj) deviates positively from the straight line. This behavior was noted previously[2] and attributed to competing formation of the hydroxide ion adduct T_{OH}^-.



T_{OH}^-

Slopes (k_3^{AH}) and intercepts ($k_3^{H_2O} + k_H a_{H^+}$) according to eq 6 are summarized in Table I. The slopes are seen to be pH independent, showing that the k_5^{BH} (or k_5^{AH}) term in eq 3 is indeed negligible. Plots of the intercepts vs. a_{H^+} (not shown) give straight lines with slope = k_H and negligible intercepts ($k_3^{H_2O}$). The linearity of the plots indicates that the k_5^H term in eq 3 is negligible.

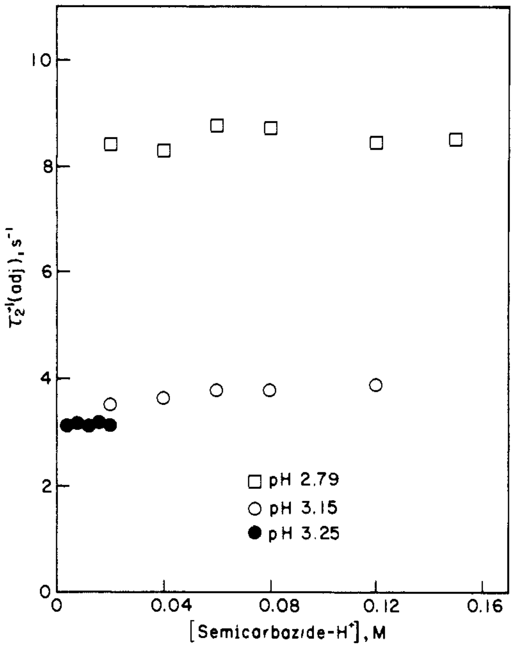


Figure 3. Plots of τ_2^{-1}(adj) vs. $[\text{RR'NH}_2^+]$ for the conversion of the semicarbazide adduct of BMA into benzaldehyde and Meldrum's acid anion. Results obtained in a similar way as those in Figure 1 and analyzed by means of eq 8 without the $K_1^{H_2O}/a_{H^+}$ term.

(B) (Cyanomethyl)amine. With (cyanomethyl)amine the equilibrium does not always favor adduct formation. Furthermore, the presence of T_{OH}^- in equilibrium with BMA, $T_A^\pm$ and T_A^- cannot be neglected.[7] Hence the expression for τ_2^{-1} becomes eq 7, with $K_1^{H_2O}$ being the equilibrium constant for BMA + $H_2O \rightleftharpoons T_{OH}^- + H^+$.[9]

$$\tau_2^{-1} = \frac{K_1K_a^\pm[\text{RR'NH}]/a_{H^+}}{1 + K_1^{H_2O}/a_{H^+} + (K_1 + K_1K_a^\pm/a_{H^+})[\text{RR'NH}]} \times (k_3^{H_2O} + k_H a_{H^+} + k_3^{AH}[\text{RR'NH}_2^+]) \quad (7)$$

Rearranging eq 7 affords eq 8. The data are summarized in

$$\tau_2^{-1}(\text{adj}) = \tau_2^{-1}\frac{1 + K_1^{H_2O}/a_{H^+} + (K_1 + K_1K_a^\pm/a_{H^+})[\text{RR'NH}]}{K_1K_a^\pm[\text{RR'NH}]/a_{H^+}} = k_3^{H_2O} + k_H a_{H^+} + k_3^{AH}[\text{RR'NH}_2^+] \quad (8)$$

Table S6[5] (24 rate constants), while slopes (k_3^{AH}) and intercepts ($k_3^{H_2O} + k_H a_{H^+}$), according to eq 8, are included in Table I.

(C) Semicarbazide and Methoxyamine. The data are summarized in Table S7 (29 rate constants).[5] As with the (cyanomethyl)amine adduct, $T_A^\pm$ and T_A^- formation is not always strongly favored. However, because K_1 is abnormally high relative

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

[6] Note that $K_a^\pm$ is known from ref 3.

[7] The interference by T_{OH}^- in this case but not with the more basic amines might seem paradoxical since at a given pH and amine concentration the equilibrium favors T_{OH}^- over $T_A^\pm$ and T_A^- relatively more with strongly basic amines. For example, for the *n*-butylamine adduct at pH = $pK_a^\pm$ = 10.60[3] and an amine concentration of 0.02 M we have $[T_A^\pm]:[T_A^-]:[T_{OH}^-]$ = 1:1:2.17;[8] for the (cyanomethyl)amine adduct at pH = $pK_a^\pm$ = 5.46[3] and the same amine concentration we have $[T_A^\pm]:[T_A^-]:[T_{OH}^-]$ = 1:1:0.30.[9] The difference in behavior arises from the fact that with strongly basic amines the *rate* of formation of T_{OH}^- is slow[3,10] on the time scale of τ_2, and hence T_{OH}^- does not build up to its equilibrium concentration.

[8] $K_1 = 3.41 \times 10^6$ M^{-1},[3] $K_1^{H_2O} = 3.75 \times 10^{-6}$ M for BMA + $H_2O \rightleftharpoons T_{OH}^- + H^+$.[10]

[9] $K_1 = 1.93 \times 10^2$ M^{-1},[3] $K_1^{H_2O} = 3.75 \times 10^{-6}$ M.[10]

[10] Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1980**, *102*, 1361.

Table II. Summary of Rate Constants for Carbon Protonation of T_A^- in Water at 25 °C[a]

adduct	catalyst	pK_{AH}	$pK_a^{\pm}$	k_3^{AH}, $M^{-1}\ s^{-1}$	k_H, $M^{-1}\ s^{-1}$	$k_i = k_H K_a^{\pm}$,[c] s^{-1}	k_i/k_3^{AH},[d] M
piperidine	$pipH^+$	11.40	11.64	3.25×10^{-5}	7.50×10^5	1.72×10^{-6}	5.29×10^{-2}
morpholine	$morH^+$	8.78	8.90	6.83×10^{-4}	5.66×10^5	7.12×10^{-4}	1.04
n-$BuNH_2$	n-$BuNH_3^+$	10.87	10.60	1.21×10^{-3}	4.52×10^5	1.13×10^{-5}	9.34×10^{-3}
$MeOCH_2CH_2NH_2$	$MeOCH_2CH_2NH_3^+$	9.64	9.44	5.42×10^{-3}	1.73×10^5	6.28×10^{-5}	1.16×10^{-1}
$H_2NCOCH_2NH_2$	$H_2NCOCH_2NH_3^+$	8.20	8.00	4.28×10^{-2}	6.49×10^4	6.49×10^{-4}	1.62×10^{-2}
$NCCH_2NH_2$	$NCCH_2NH_3^+$	5.50	5.46	1.28	8.67×10^3	3.01×10^{-2}	2.35×10^{-2}
$MeONH_2$	$MeOHN_3^+$	4.70	4.35	*b*	3.94×10^3	1.76×10^{-1}	
semicarbazide	semicarbazide-H^+	3.82	3.42	*b*	5.02×10^3	*e*	

[a] μ = 0.5 M (KCl). [b] Catalysis too weak to be measurable. [c] Assuming that the mechanism of intramolecular assistance involves the intramolecular proton transfer $T_A^{\pm} \rightarrow T_A^0$; see text. [d] $k_i/k_3^{AH} \approx$ EM, see text. [e] No k_i observed, see text.

to the pK_a^{AH} of these α-effect nucleophiles,[3] interference by T_{OH}^- is negligible and no $K_1^{H_2O}/a_{H^+}$ term is needed in eq 7 and 8.

More interestingly, τ_2^{-1}(adj) is virtually independent of $[RR'NH_2^+]$ as shown in Figure 3 for the semicarbazide example. This raises the question as to whether there may be a change in the rate-limiting step from formation of T_A^0 to its breakdown. We shall show in the Discussion section that no change in the rate-limiting step occurs.

Discussion

Rate-Limiting Step for Methoxyamine and Semicarbazide Adducts. As pointed out in the Results section, the absence of clear-cut evidence for catalysis by the protonated amine (Figure 3) is open to two different interpretations. It could simply be a manifestation of the increasing difficulty to detect general acid catalysis at low pH because the hydronium ion pathway becomes dominant. Our systems are good candidates for this type of behavior because general acid catalysis is subject to substantial steric hindrance (see below) and the k_H pathway is accelerated by intramolecular assistance.

An alternative explanation is that with the methoxyamine and semicarbazide adducts breakdown of T_A^0 (k_4) rather than its formation is rate limiting, eq 9, with $K_a^0 = k_{-3}^{H_2O}/k_3^H$. Such

$$\tau_2^{-1}(\text{adj}) = k_4 a_{H^+}/K_a^0 \tag{9}$$

a change in the rate-limiting step would imply that for these two adducts $k_4 \ll k_{-H}$, while for all the others $k_4 \gg k_{-H}$; k_{-H} is the reverse of k_H (eq 4) and is given by eq 10, where K_w is the ionic product of water. There are two lines of reasoning which demonstrate that this alternative interpretation cannot be correct.

$$k_{-H} = k_{-3}^{H_2O} + k_{-i} + k_{-5}^{OH}K_w/K_a^+ \tag{10}$$

(1) Approximate k_4 values are known for the glycinamide ($\approx 1.6 \times 10^4\ s^{-1}$) and the 2-methoxyethylamine ($\approx 5.8 \times 10^4\ s^{-1}$)[3] adducts. On the basis of these values we estimate, by extrapolation, $k_4 \approx 6.1 \times 10^2\ s^{-1}$ for the methoxyamine and $k_4 \approx 3.1 \times 10^2\ s^{-1}$ for the semicarbazide adduct. If τ_2^{-1}(adj) were indeed given by eq 9, the kinetic data would yield $k_4/K_a^0 = 3.94\ M^{-1}\ s^{-1}$ and hence $K_a^0 \approx 1.55 \times 10^{-1}$ M ($pK_a^0 \approx 0.81$) for the methoxyamine adduct and $k_4/K_a^0 = 5.02$ and $K_a^0 \approx 6.17 \times 10^{-2}$ M ($pK_a^0 \approx 1.21$) for the semicarbazide adduct. These pK_a^0 values are not only in the wrong order (one expects pK_a^0 for the semicarbazide adduct to the lower one) but at least 1.5–2.0 units below what one expects for pK_a^0 (see below). The discrepancy would become even greater if k_4 for the methoxyamine and semicarbazide adducts were enhanced by a greater "push", owing to the fact that methoxyamine and semicarbazide are α-effect nucleophiles.[3,11]

(2) From the relationship $k_{-H}/k_H = k_{-3}^{H_2O}/k_3^H = K_a^0$ one can estimate k_{-H} as follows. The (cyanomethyl)amine adduct is the least basic for which unambiguous buffer catalysis was observed. Its k_H value of $8.67 \times 10^3\ M^{-1}\ s^{-1}$ thus provides an upper limit for k_H for the methoxyamine and semicarbazide adducts, because k_H decreases with decreasing $pK_a^{\pm}$ (Table II). By use of a conservative estimate of 3.0 for pK_a^0 (see below), this affords $k_{-H} \lesssim 8.7\ M^{-1}\ s^{-1}$ for these latter adducts. This value is several orders of magnitude too low for the condition $k_4 \ll k_{-H}$ to be met, as is apparent from the above estimates for k_4.

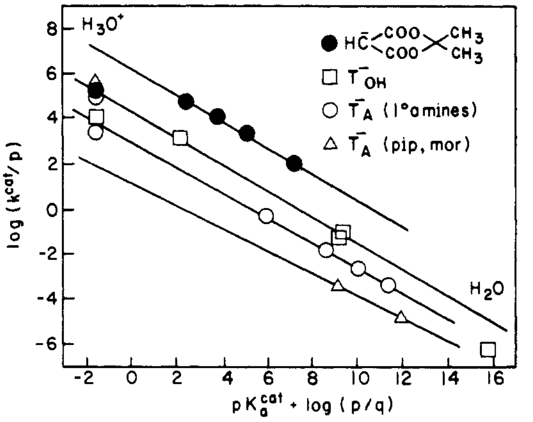

Figure 4. Brønsted plots for the carbon protonation of MA^-, T_{OH}^-, and T_A^-.

Protonation by $RR'NH_2^+$. The rate constants, k_3^{AH}, for carbon protonation of the amine adducts of BMA by their respective $RR'NH_2^+$ are summarized in Table II. Figure 4 shows Brønsted plots. Included in the figure are Brønsted plots for the protonation of Meldrum's acid anion (MA^-) by H_3O^+, chloroacetic acid, benzoic acid, pyridinium ion, and imidazolium ion at 15 °C[12] and for the protonation of the OH^- adduct (T_{OH}^-) by H_3O^+, chloroacetic acid, morpholinium ion, bicarbonate ion, and water at 25 °C.[13]

The Brønsted α_{AH} values (we shall use the symbol α_{AH} irrespective of whether BH = $RR'NH_2^+$ or any buffer acid) determined without including the H_3O^+ points are quite similar for all the systems: 0.50 ± 0.03 for T_A^- derived from piperidine and morpholine, 0.55 ± 0.03 for T_A^- derived from the primary amines, and 0.58 ± 0.05 for MA^- and T_{OH}^-. In view of the somewhat heterogeneous group of catalysts, especially for MA^- and T_{OH}^-, and their small number (T_{OH}^- and T_A^- for piperidine and morpholine), the somewhat higher α_{AH} values for MA^- and T_{OH}^- may not be mechanistically significant. This becomes even more apparent when it is realized that the observed α_{AH} values for T_A^- underestimate the true α_{AH} values because in the protonation of T_A^- the change in catalyst is always accompanied by a change in the amine substituent in T_A^-. Thus the rate-increasing effect of a more acidic $RR'NH_2^+$ is attenuated by a slight decrease in the basicity of the carbon in T_A^-.

This attenuation can be expressed as eq 11, with $-(\partial \log k_3^{AH}/\partial pK_a^{AH})_{pK_a^0}$ being the true α_{AH} value, i.e., the α_{AH} value that would prevail if the C–H acidity of T_A^0 (pK_a^0) were constant.

$$\alpha_{AH,\text{obsd}} = -\partial \log k_3^{AH}/\partial pK_a^{AH} = -(\partial \log k_3^{AH}/\partial pK_a^{AH})_{pK_a^0} - (\partial \log k_3^{AH}/\partial pK_a^0)_{pK_a^{\pm}}(\partial pK_a^0/\partial pK_a^{\pm}) \tag{11}$$

On the basis of Bell and Grainger's[14] data we estimate $(\partial \log k_3^{AH}/\partial pK_a^0)_{pK_a^{\pm}}$ to be ≈ 0.56 while $\partial pK_a^0/\partial pK_a^{\pm}$ is estimated at

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(11) (a) Fina, N. J.; Edwards, J. O. *Int. J. Chem. Kinet.* **1973**, *5*, 1. (b) Hoz, S.; Buncel, E. *Isr. J. Chem.* **1985**, *26*, 313.

(12) Eigen, M.; Ilgenfritz, G.; Kruse, W. *Chem. Ber.* **1965**, *98*, 1623.

(13) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5143.

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

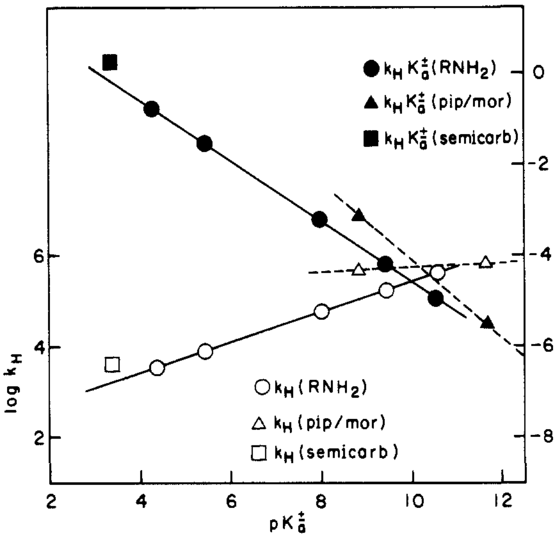

Figure 5. Brønsted plots for k_H (open symbols, left *y* axis) and $k_H K_a^\pm$ (filled symbols, right *y* axis).

0.07 ± 0.035.[15] Hence the true α_{AH} values for T_A^- are approximately 0.56 × (0.07 ± 0.035) ≈ 0.04 ± 0.02 higher, i.e., 0.54 ± 0.05 and 0.59 ± 0.05, respectively.

The relative position of the Brønsted lines in Figure 4 appears to be the result of two factors: the basicity of the carbon and steric hindrance. MA^- is the most basic (pK_a^0 = 4.83)[12] and T_{OH}^- the least basic (pK_a^0 = 2.95);[10] pK_a^0 values for T_A^- are not known but have been estimated to be between 3.75 and 4.0 for the more basic amine adducts.[2] For the least basic ones we estimate pK_a^0 ≈ 3.0–3.5.

The Brønsted line for T_{OH}^- is displaced downward from that of MA^- by approximately 2 log units. Using our above estimate of ≈0.56 for $(\partial \log k_3^{AH}/\partial pK_a^0)_{pK_a^\pm}$, we can attribute about 1.0 log unit of the negative displacement to the lower basicity of T_{OH}^- and ≈1.0 log unit to the steric hindrance of the PhCH(OH) moiety.

The Brønsted line for T_A^- derived from the primary amines is displaced negatively from the MA^- line by ≈3 log units, that for T_A^- derived from piperidine and morpholine by ≈4.5 units. The contribution by the reduced basicity is ≈0.6, assuming an average pK_a^0 ≈ 3.8; hence most of the negative displacements (≈2.4 and ≈3.9 log units, respectively) are of steric origin. Note that the significantly larger steric effect with the piperidine and morpholine adducts is the consequence of increasing the bulk of both T_A^- *and* the catalyst.[16]

Protonation by H_3O^+. Evidence for Intramolecular Assistance. Figure 4 includes the k_H values (from Table II) for T_A^- derived from 2-methoxyethylamine (high ○), semicarbazide (low ○),[18] and piperidine (△), as well as the rate constants for protonation of MA^- (●) and T_{OH}^- (□) by H_3O^+. We now demonstrate that for all but one of the adducts k_H can refer neither to simple, i.e., unassisted protonation of T_A^- by H_3O^+ (k_3^H) nor to unassisted protonation of $T_A^\pm$ by water ($k_5^{H_2O}/K_a^\pm$). In other words, k_H must refer to carbon protonation that is in some way or another intramolecularly assisted by the amine moiety in $T_A^\pm$ or T_A^-. We first disprove the hypothesis $k_H = k_3^H$.

One piece of evidence, at least with primary amine adducts, is that k_H shows a fairly strong dependence on p$K_a^\pm$; it amounts to an approximately 100-fold variation in k_H (Table II); i.e., k_H for the *n*-butylamine adduct is 100-fold larger than that for the methoxyamine or semicarbazide adducts. Such a dependence is inconsistent with the simple, unassisted k_3^H process, because it implies that the amine moiety is not just a spectator but is somehow involved in the reaction. A Brønsted plot of log k_H vs. p$K_a^\pm$ (Figure 5, open symbols, left *y* axis) yields an excellent straight line from which only the semicarbazide adduct deviates positively. From the slope, excluding the semicarbazide adduct, one obtains β_N = 0.33 ± 0.03 or, after correction[19] for the effect of p$K_a^\pm$ on pK_a^0, β_N ≈ 0.29 ± 0.05.

The positive deviation of the semicarbazide point must be a consequence of the leveling off in the intramolecular assistance by the amine nitrogen. As the plot in Figure 5 implies, this assistance becomes weaker with decreasing basicity of the nitrogen, and a point must be reached where the basicity is too low for such assistance to be effective. It appears that this point is reached or approached for a p$K_a^\pm$ somewhere between that of the methoxyamine adduct (4.35) and that of the semicarbazide adduct (3.62). At and below this point k_H becomes k_3^H.

For the piperidine and morpholine adducts the dependence of k_H or p$K_a^\pm$ is too small (observed β_N = 0.05 ± 0.03, corrected[19] β_N ≈ 0.01 ± 0.05) to provide evidence for intramolecular assistance. However, this assistance can be inferred from the larger than expected magnitude of k_H. The k_H values (5.66 × 10^5 M^{-1} s^{-1} for the morpholine and 7.50 × 10^5 M^{-1} s^{-1} for the piperidine adduct) are more than 100-fold higher than $k_H = k_3^H$ = 5.02 × 10^3 M^{-1} s^{-1} for the semicarbazide adduct. One factor which may contribute to a higher k_3^H value for the piperidine and morpholine adducts is their enhanced basicity at carbon, pK_a^0. However, this enhancement is unlikely to be very large. Using againg $\partial pK_a^0/\partial pK_a^\pm$ = 0.07 ± 0.035 and assuming $\partial \log k_3^H/\partial pK_a^0 \approx$ 0.5 gives an approximately 2-fold increase in k_3^H for the piperidine over that for the semicarbazide adduct. This increase is likely to be overcompensated for by the greater steric hindrance of the piperidine and morpholine adducts.

Turning now to the hypothesis $k_H = k_5^{H_2O}/K_a^\pm$ (unassisted protonation of $T_A^\pm$ by water), we note the following. (1) Figure 5 includes plots of log ($k_H K_a^\pm$) vs. p$K_a^\pm$ (filled symbols) according to $k_5^{H_2O} = k_H K_a^\pm$. Both plots show a strong dependence on p$K_a^\pm$, with a corrected[21] α_N = 0.71 ± 0.05 for the primary amine adducts and an α_N = 0.99 ± 0.05 for the piperidine and morpholine adducts.[22] This strong dependence is contrary to what we would expect for unassisted protonation of $T_A^\pm$. Indeed, k_5^H for the protonation of $T_A^\pm$ by H_3O^+ is virtually independent of p$K_a^\pm$,[3] except for the slight effect of increasing pK_a^0 with increasing p$K_a^\pm$.

(2) k_H is much larger than expected for $k_5^{H_2O}/K_a^\pm$. This is most dramatically seen with the weakly basic adducts. For example, for the (cyanomethyl)amine adduct one calculates $k_5^{H_2O} = k_H K_a^\pm$ = (8.67 × 10^3)(3.47 × 10^{-6}) = 3.01 × 10^{-2} s^{-1}. This value is 600-fold higher than the rate constant for protonation of T_{OH}^- by water[13] even though the positive charge on $T_A^\pm$ should make the carbon much less basic than that in T_{OH}^-, and the steric hindrance is greater in $T_A^\pm$ than in T_{OH}^-. Both factors should make $k_5^{H_2O}$ smaller than the rate constant for protonation of T_{OH}^-. Similarly, for the morpholine adduct one calculates $k_5^{H_2O}$ = 7.13 × 10^{-4} s^{-1}, which is 14.3-fold higher than $k_5^{H_2O}$ for water protonation of T_{OH}^-.

As p$K_a^\pm$ increases $k_H K_a^\pm$ decreases, and one would expect that above a certain p$K_a^\pm$ intramolecular assistance becomes negligible. At this point $k_H K_a^\pm$ should indeed become equal to $k_5^{H_2O}$ and the plots in Figure 5 should level off, just as the plot of log k_H vs. p$K_a^\pm$ levels off at low p$K_a^\pm$. Inspection of Figure 5 shows that the leveling off does not occur within the p$K_a^\pm$ range covered in our study.

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(15) Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1984**, *106*, 3257.

(16) The steric effect on these latter adducts is probably even somewhat larger than the numbers indicate because proton transfers involving secondary amines are usually somewhat faster than those involving primary amines.[17]

(17) (a) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1973; Chapter 10. (b) Spencer, T. A.; Kendall, M. C. R.; Reingold, I. D. *J. Am. Chem. Soc.* **1972**, *94*, 1250. (c) Bernasconi, C. F.; Hibdon, S. A. *Ibid.* **1983**, *105*, 4343. (d) Hine, J.; Mulders, J. J. *J. Org. Chem.* **1967**, *32*, 2200. (e) Terrier, F.; Lelievre, J.; Chatrousse, A.-P.; Farrell, P. G. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1479.

(18) These are representative examples for a high and a low k_H value. The others have not been included in the figure because of crowding.

(19) Note that in contrast to the protonation by $RR'NH_2^+$ where α_{obsd} underestimates the true α_{AH}, the observed β_N overestimates the true β_N. We have assumed that the absolute magnitude of the correction is the same as for α_{AH}, i.e., 0.04 ± 0.02.

(20) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475.

(21) Corrected for $\partial pK_a^0/\partial pK_a^\pm$ as for β_N and α_{AH} for k_3^{AH}.

(22) Note that $\alpha_N = 1 - \beta_N$.

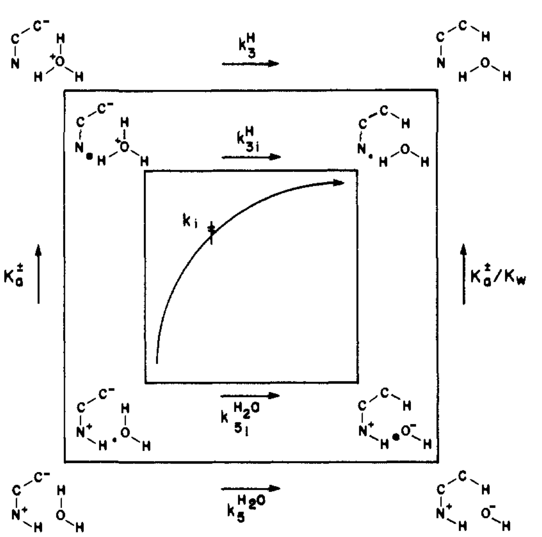


Figure 6. More O'Ferrall–Jencks diagram. The outer square refers to the unassisted pathways of Scheme I. The inner square shows the three possible mechanisms for intramolecular assistance. The reaction through the inside of the square is the concerted intramolecular proton transfer (k_i). The pathways along the edges of the inner square involve hydrogen-bonding stabilization of the respective transition states (4 for k_{3i}^H, 5 for $k_{5i}^{H_2O}$); the large dots indicate strong, the small dots weak, hydrogen bonding in the corner states of the inner square.

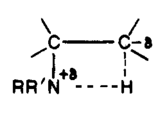
Relevance to Theoretical Model. An examination of the above observations in the context of the previously proposed model[1] is revealing. One of the major conclusions that were drawn from this model is that the range within which the intramolecularly assisted pathway is operative and detectable strongly depends on the pK_a of the heteroatom ($pK_a^{\pm}$ in our example) and on α_N.[23] For example, if everything else is equal, the $pK_a^{\pm}$ range for maximum effectiveness of the intramolecular pathway is slightly higher than 7 for $\alpha_N \approx 0.5$; for $\alpha_N < 0.5$ this range shifts to lower $pK_a^{\pm}$ values, for $\alpha_N > 0.5$ to higher values. This is illustrated in Figure 6 of ref 1.

In the absence of relevant data on α_N it was assumed that its value is the same as α_{AH} for intermolecular protonation by a series of buffer acids.[1] The results of the present study show that $\alpha_N > \alpha_{AH}$. Hence the intramolecular pathway should be operative in a $pK_a^{\pm}$ range which is shifted upwards from that predicted by the specific model for carbonyl compounds (Figure 2 in ref 1). Our observations that one of our plots of log k_H vs. $pK_a^{\pm}$ levels off around $pK_a^{\pm} \approx 4$ (where $k_H = k_3^H$) while the plots of log ($k_H K_a^{\pm}$) vs. $pK_a^{\pm}$ do not level off at a $pK_a^{\pm}$ as high as 11.6 (limit where $k_H = k_5^{H_2O}/K_a^{\pm}$ is not reached) appear thus entirely consistent with the model's predictions.

It is interesting that in the 9-((dimethylamino)methyl)fluorene system the unassisted pathway involving water protonation of $T_A^{\pm}(k_5^{H_2O}/K_a^{\pm})$ appears to be completely dominant[24] even though the $pK_a^{\pm}$ must be quite similar to that of the piperidine adduct of BMA. This indicates that the leveling off in the log ($k_H K_a^{\pm}$) vs. $pK_a^{\pm}$ plot has already occurred and suggests that α_N is relatively small in that system. This suggestion is supported by the fact that $\alpha_{AH} = 0.35$ for carbon protonation by tertiary ammonium ions[25] is much lower than our $\alpha_{AH} = 0.59$ for protonation by $RR'NH_2^+$.

Another system where no intramolecular pathway could be observed is the imine–enamine tautomerism of 2- and 4-phenacylquinolines.[26] A possible explanation for this absence is the strong resonance between the acid and base center in the enamine which may create an unfavorable geometry for the intramolecular proton transfer.[26]

Mechanism of Intramolecular Assistance. In this section we examine which might be the most likely mechanism for intramolecular assistance. Apart from the concerted intramolecular proton transfer (k_i) with a transition state such as **2** or perhaps **3**, at least two alternative possibilities seem reasonable. This is most easily seen by placing the reaction on a More O'Ferrall–Jencks[27] type diagram (Figure 6). The outer square in the figure refers to the unassisted pathways k_3^H (top horizontal axis) and $k_5^{H_2O}$ (bottom horizontal axis). The inner square shows the catalytic pathways.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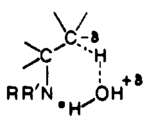
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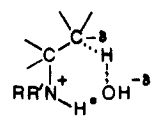
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One nonconcerted catalytic pathway is represented by the rate constant k_{3i}^H (top horizontal axis, *inner* square) and involves transition state **4**. The energetic advantage of the k_{3i}^H over the unassisted k_3^H pathway is that the transition state is able to benefit from some of the hydrogen-bonding stabilization between H_3O^+ and the amine nitrogen that is present in the intermediate at the upper left corner. Note that the hydronium ion either could come from the solvent and react with T_A^- (top left outer corner ⇄ top left inner corner) or could be generated by a loss of a proton from $T_A^{\pm}$ (lower left outer corner ⇄ lower left inner corner ⇄ top left inner corner), but in either case it is likely to be in equilibrium with the bulk solvent. Jencks[28] prefers this mechanism over the concerted intramolecular proton transfer (k_i).

The second alternative nonconcerted catalytic pathway (bottom horizontal axis, inner square, $k_{5i}^{H_2O}$ involves reaction of $T_A^{\pm}$ with water and proceeds through transition state **5**. Here the special transition-state stabilization arises from hydrogen bonding of the NH^+ group to the incipient OH^-.[28b] Note that electrostatic stabilization of the negative charge on the incipient OH^- and on the carbanionic site by the positive charge on nitrogen[29] may add to the lowering of the free energy of **5**. It is again assumed that there is rapid equilibrium between the inner and outer corners.

Transition state **3** has not been seriously advocated because of the unfavorable geometry of the four-membered ring. In fact, most transition states proposed for intramolecular proton transfer between two centers separated by very few atoms have included at least one or sometimes several water molecules.[1,30,31] On the other hand, Menger[32] has recently questioned the common assumption of linearity in the transition state of proton transfer which implies that **3** may not be as unfavorable as has been assumed. The present results do not provide conclusive evidence for or against **3**. However, a recent proton inventory study[33] has shown that a water molecule is definitely included in the transition state, which is consistent with **2**, **4**, and **5** but excludes **3**.

Transition state **5** is also easily eliminated: if **5** was correct, we would have $k_H = k_{5i}^{H_2O}/K_a^{\pm}$ or $k_{5i}^{H_2O} = k_H K_a^{\pm}$, and $\alpha_N = 0.71 \pm 0.05$ (1° amines) and 0.99 ± 0.05 (pip/mor) determined from Figure 5 would be a measure of the hydrogen-bonding interaction between NH^+ and the incipient hydroxide ion in **5**. These α_N values appear to be much too high to be realistic. Typical α values

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[23] In the model[1] it was assumed that the mechanism of intramolecular assistance represents concerted intramolecular proton transfer (k_i). Hence $k_i = k_H K_a^{\pm}$ and α for k_i is equal to α_N.

[24] (a) Kelly, R. P.; More O'Ferrall, R. A. *J. Chem. Soc., Perkin Trans. 2* **1979**, 681. (b) Larkin, F.; More O'Ferrall, R. A. *Aust. J. Chem.* **1983**, *36*, 1831.

[25] The reaction was measured in the reverse direction with $\beta = 0.65$ for general base catalysis. Kelly, R. P.; More O'Ferrall, R. A.; O'Brien, M. *J. Chem. Soc., Perkin Trans. 2* **1982**, 211.

[26] Carey, A. R. E.; Fukata, G.; More O'Ferrall, R. A.; Murphy, M. G. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1711.

[27] (a) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274. (b) Jencks, W. P. *Chem. Rev.* **1972**, *72*, 705.

[28] (a) Tapuhi, E.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 5758. (b) Bednar, R. A.; Jencks, W. P. *Ibid.* **1985**, *107*, 7126.

[29] (a) Cox, B. G.; De Maria, P.; Fini, A.; Hassan, A. F. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1351. (b) Cox, B. G.; De Maria, P.; Fini, A. *Ibid.* **1984**, 1647.

[30] Gandour, R. D. *Tetrahedron Lett.* **1974**, 295.

[31] Kirby, A. L.; Lloyd, G. J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1762.

[32] (a) Menger, F. M.; Chow, J. F.; Kaiserman, H.; Vasquez, P. C. *J. Am. Chem. Soc.* **1983**, *105*, 4996. (b) Menger, F. M. *Tetrahedron* **1983**, *39*, 1013.

[33] Bernasconi, C. F.; Murray, C. J.; Fairchild, D. R., unpublished results.

for hydrogen-bonding stabilizations of transition states are in the range 0.05–0.2,[13,34-39] with only one reported example as high as 0.26.[37] We can therefore safely reject **5**. Note that if the main source of transition-state stabilization were of electrostatic origin,[29] α_N should also be small, probably even smaller than for hydrogen bonding.[40]

In discussing the remaining possibilities, **2** and **4**, we shall first deal with the adducts derived from the primary amines which appear to display a more "normal" behavior than those derived from piperidine and morpholine.

(A) Primary Amine Adducts. If the reaction proceeds through **4**, we have $k_H = k_{3i}{}^H$; $\beta_N = 0.29 \pm 0.05$ obtained from Figure 5 thus measures the hydrogen-bonding interaction between the amine nitrogen and the hydronium ion which delivers the proton to the carbon.

The value of β_N is significantly higher than most Brønsted coefficients for transition-state stabilization by hydrogen bonding (0.05–0.2)[13,34-39] but close to the value of 0.26 reported for the reaction of acetaldehyde with thiolate ions.[37] Hence, even though it is questionable whether our high β_N could still be interpreted in terms of hydrogen bonding, the value is hardly large enough to exclude **4** outright.

A comparison of our experimental results with predictions based on the Hine[41] equation leads to the same conclusion. This equation expresses the association constant of a hydrogen-bonded complex AH·B as

$$\log K_{AH\cdot B} = \tau(pK_{H_3O^+} - pK_{BH})(pK_{AH} - pK_{H_2O}) - \log [H_2O] \quad (12)$$

The first term on the right represents the enhancement of $K_{AH\cdot B}$ over a situation where AH·B is simply an encounter complex without hydrogen bonding and has a $\log K_{AH\cdot B} = -\log [H_2O]$.

Applying this to $T_A^-\cdot H_3O^+$ (upper left inner corner in Figure 6) derived from *n*-butylamine ($pK_{AH} = pK_{H_3O^+} = -1.74$; $pK_{BH} = pK_a{}^{BH} = 10.60$, Table II) and using Jencks'[42] value of 0.013 for τ, one calculates $K_{AH\cdot B} = 11.5$. This value represents a 638-fold enhancement over $K_{AH\cdot B}$ in the absence of hydrogen bonding. If this effect were entirely carried over into the transition state (**4**), the enhancement of $k_{3i}{}^H$ over $k_3{}^H$ would thus be 638-fold. This would be more than enough to account for the *observed* rate enhancement of about 50-fold ($k_H = k_{3i}{}^H$ for the *n*-butylamine adduct compared to unassisted $k_H = k_3{}^H$ for the semicarbazide adduct, after correction for the changing $pK_a{}^0$).

It is likely, though, that in **4** hydrogen bonding is weaker. This is because the reduced charge on oxygen is tantamount to a higher pK_{AH} value (eq 12), and the reduced negative charge on carbon also lowers pK_{BH} somewhat. We shall assume that pK_{BH} decreases by no more than 2 pK_a units. This allows us to estimate pK_{AH} for the transition state on the basis of the experimentally observed rate enhancement (eq 13). This yields $pK_{AH} \geq 3.13$, which is

$$\log \left(\frac{k_{3i}{}^H(n\text{-BuNH}_2)}{k_3{}^H(\text{semi})} \right)_{pK_a{}^0} = 1.7 = \tau(pK_{H_3O^+} - pK_{BH})(pK_{AH} - pK_{H_2O}) \quad (13)$$

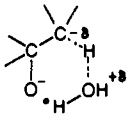
not an unreasonable value. However, it leads to an inconsistency with respect to β_N. According to eq 12, β_N is given by eq 14. This yields $\beta_N \leq 0.16$, which is far below our corrected experimental value of 0.29 ± 0.05.

$$\frac{\partial}{\partial pK_{BH}}[\tau(pK_{H_3O^+} - pK_{BH})(pK_{AH} - pK_{H_2O})] = -\tau(pK_{AH} - pK_{H_2O}) \quad (14)$$

This above analysis does not rigorously disprove the hydrogen-bonding mechanism, but it renders it unattractive. Its appeal is further diminished in view of recent results for reaction 15. In

$$\text{Ph(OH)CH–C(CN)}_2{}^- \rightarrow \text{Ph(O)}^-\text{CH–CH(CN)}_2 \quad (15)$$

this case transition state **6**, which is the analogue of **4** could be unambiguously excluded on the basis of the high value of the rate constant.[43]



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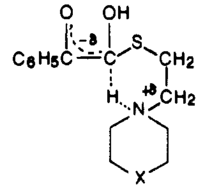
With respect to the remaining alternative (**1**, $k_H = k_i/K_a{}^{\pm}$ or $k_i = k_H K_a{}^{\pm}$), we interpret $\alpha_N = 0.71 \pm 0.05$ as the Brønsted coefficient for intramolecular proton transfer from NH^+ to carbon. This value is somewhat higher than the (corrected) $\alpha_{AH} = 0.59$ for protonation of T_A^- by $RR'NH_2^+$. One would hardly expect the two α values to be the same, though, since the transition states of the two reactions are so different: in the intermolecular proton transfer there is no water molecule in the transition state[44] and the C--H--N axis is likely to be linear.[45]

A possible interpretation of the high α_N value is in terms of a transition state which is imbalanced in the sense that proton transfer from nitrogen to water has made more progress than proton transfer from water to the carbon. This is indicated by the curved reaction coordinate in Figure 6 and the location of the transition state near the upper left corner. This would mean that the energetics of the reaction are to a considerable extent governed by the proton transfer from NH^+ to water, and the high α_N value would be understood as approaching the limiting value of unity for a thermodynamically unfavorable proton transfer between nitrogen and oxygen.[46]

By way of contrast we have estimated an $\alpha_N \approx 0.21$ for the intramolecular proton transfer in a hemithioacetal (**7**), on the basis of data by Okuyama et al.[47] It is possible that the much lower α_N values in this case could indicate the absence of a water molecule from the transition state which is indeed not required in **7** to avoid strain.



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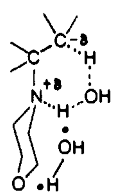

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(B) Piperidine/Morpholine Adducts. The β_N value for **4** is 0.01 ± 0.05, which implies essentially no hydrogen-bonding interaction; the α_N value for **2** is 0.99 ± 0.05, which suggests that the loss of the proton from the nitrogen is virtually complete. Neither interpretation seems very satisfactory. These extreme Brønsted

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coefficients are not an artifact of the BMA system since similar values were obtained for the piperidine/morpholine adducts of α-cyano-2,4-dinitrostilbene.[15]

The most "obvious" explanation of these results, namely, that k_H simply refers to unassisted protonation of T_A^- by H_3O^+ (k_3^H), has been ruled out in a previous section by showing that k_H is much higher than expected for k_3^H.

A possible cause for the extreme Brøsted coefficients is that the morpholine adduct displays enhanced reactivity akin to an α effect in nucleophilic reactions.[3,11] This effect could arise from a stabilizing interaction with a lone pair of the morpholine oxygen, possibly by hydrogen bonding if two water molecules were involved in the transition state (**8**). Note that with 2-methoxyethylamine, which also has an ether oxygen, such a transition state would be entropically disfavored because of the greater conformational flexibility of the noncyclic amine. A similar but more dramatic enhancement in reactivity by a ring oxygen has recently been reported by Bordwell and Hughes[48] in an S_N2 reaction of phenoxazine.

A more remote possibility is that our α_N (or β_N) values include a component for the solvation of the amine nitrogen. In the reaction of quinuclidines with phosphates Jencks[49] has attributed the extremely low or even negative β_{nuc} values to the requirement for desolvation of the amine before nucleophilic attack. If the same effect were operative in proton-transfer reactions, this would imply that the commonly reported Brønsted α values in the protonation direction overestimate the true α or the observed β values in the deprotonation direction underestimate the true β. The problem with this interpretation as applied to our k_H is that in both **2** and **4** the solvent is an active participant in the reaction; i.e., there is no need for solvation/desolvation of the amine nitrogen. We therefore disfavor this interpretation.

Effective Molarities. It is common practice to measure the effectiveness of an intramolecular reaction by its effective molarity (EM).[50] In our system EM is defined as $k_i/k_3^{AH}(pK_a^{\pm})$ with $k_3^{AH}(pK_a^{\pm})$ referring to a $RR'NH_2^+$ whose pK_a^{AH} is equal to $pK_a^{\pm}$. Since for a given amine $pK_a^{\pm}$ and pK_a^{AH} are very similar (Table II), the ratios k_i/k_3^{AH} obtained by using the experimental k_3^{AH} values are good approximations for EM. These ratios are included in Table II.

Except for the morpholine adduct the k_i/k_3^{AH} ratios are all in the range $\approx 10^{-2}$ to $\approx 5 \times 10^{-2}$ M. Such low EMs are typical for intramolecular proton transfers.[50] The fact that k_i/k_3^{AH} is much higher for the morpholine adduct than for all the others is a further indication that the morpholine adduct displays abnormally high reactivity with respect to the intramolecular process.

Experimental Section

All reagents were available in pure form from a previous investigation.[3] The kinetic experiments were performed in a temperature-controlled Perkin-Elmer 559A UV-vis spectrophotometer. In most cases the rates were measured at 255 nm, where $\epsilon_{products}$ (benzaldehyde and Meldrum's acid anion) is higher than $\epsilon_{T_A^-}$.[2] With the methoxyamine and semicarbazide adducts the decrease of [BMA] at 320 nm was monitored, since conversion to $T_A^{\pm}$ or T_A^- was not extensive.

A typical kinetic run was initiated by injecting 3-10 μL of a 0.05 M stock solution of BMA in Me_2SO (which contained traces of HCl to suppress hydrolysis) into a spectrophotometric cuvette that contained the thermally equilibrated amine buffer. First-order plots were linear over at least 3-4 half-lives.

With the piperidine adduct the rates were very slow, with half-lives up to 20 h or more. Here the reaction was only followed to 2-5% completion, and τ_2^{-1} was obtained by the method of initial rates, i.e., by dividing dOD/dt by $[BMA]_0(\epsilon_{products} - \epsilon_{T_A^-})$.

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Registry No. T_A^- (RR'N = piperidine), 103150-39-6; T_A^- (RR'N = morpholine), 103191-55-5; T_A^- (RR'N = $BuNH_2$), 103150-40-9; T_A^- (RR'N = $MeO(CH_2)_2NH_2$), 103150-41-0; T_A^- (RR'N = $H_2NCOCH_2NH_2$), 103191-56-6; T_A^- (RR'N = $NCCH_2NH_2$), 103150-42-1; T_A^- (RR'N = $MeONH_2$), 103191-57-7; T_A^- (RR'N = semicarbazide), 103150-43-2.

Supplementary Material Available: Kinetics of conversion of the amine adducts into benzaldehyde, Tables S1-S7 (7 pages). Ordering information is given on any current masthead page.

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Liquid-Crystalline Solvents as Mechanistic Probes. 21. Control of Norrish II 1,4-Biradical Reactivity by the Phase and Molecular Dimensions of an Ordered Solvent[1]

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Abstract: The fates of four triplet 1,4-biradicals (produced as Norrish II intermediates during the irradiations of *n*-decanophenone, 2-cyclohexyl-1-(4-ethylphenyl)-1-ethanone, 4-cyclohexyl-1-phenyl-1-butanone, and 5-cyclohexyl-1-phenyl-1-pentanone) have been explored in crystalline-, smectic B-like-, nematic-, and isotropic-phase solutions of *trans,trans*-4'-*n*-butyl[1,1'-bicyclohexyl]-4-carbonitrile (BCCN). The experimental probe is the ratio of elimination to cyclization products. The results indicate that the ordered phases of BCCN behave as a molecular ruler with regard to solute conformations; the micromorphology of each phase imposes a different set of constraints upon the shapes of the 1,4-biradicals. A rationalization for the seemingly bizarre phase-dependent changes in product ratios, based upon the shapes and labilities of the 1,4-biradicals, is presented.

During the last several years, others and we have observed that the rates and reactivities of a wide variety of solutes can be influenced by the solvent order of liquid-crystalline phases.[2-17] In spite of the considerable attention given the effects, few conclusions of general applicability have emerged. This is largely a conse-

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