Hz, C1H), 4.89 (dd, 1 H, J = 4.4, 8.3 Hz, C2H), 3.93–4.2 (m, 4 H, C3H, C4H, C5H's). Anal. Calcd for $C_5H_9P_2O_{10}\cdot(C_2H_5)_3NH^+\cdot0.5H_2O$: C, 32.84; H, 6.76. Found: C, 33.05; H, 6.27.

Synthesis of α-D-Ribofuranosyl 1,5-Bisphosphate 3 and D-Ribofuranosyl 2,5-Bisphosphate 4 by Alkaline Hydrolysis of Compound 2. 2 (40 mg, 0.1 mmol) was dissolved in 2 mL of 0.1 N NaOH, and the course of hydrolysis was monitored by ^{31}P NMR. After the hydrolysis of 2 was completed (ca. 2.5 h), the solution was lyophilized. The residue was dissolved in 2.5 mL of cyclohexylammonium bicarbonate (0.2 M, pH 8.0) and applied to a polyacrylamide boronate column[8] (Affigel 601, 0.5 × 9 cm), which had been previously washed with 25 mL of doubly distilled water, followed by 6 mL of cyclohexylammonium bicarbonate. The first fraction to elute with 12 mL of cyclohexylammonium bicarbonate contained ribose 2,5-bisphosphate. Compound 3 was eluted with a further 20 mL of water. The pH of the aqueous solution containing compound 3 was immediately adjusted to 8.0 with 0.1 N NaOH. Lyophilization of both eluates yielded white fluffy powders. Compound 3 was isolated as a hygroscopic tetra sodium salt (10 mg, 25%): R_f (7:1:2 isopropyl alcohol/NH_3/H_2O) 0.05–0.1. Anal. Calcd for $C_5H_8P_2O_{11}\cdot4Na\cdot2.5H_2O$: C, 13.55; H, 2.38. Found: C, 13.20; H, 2.14. Compound 4 was isolated as a hygroscopic tetrakis(cyclohexylammonium) salt (25 mg, 44.64%): R_f (7:1:2 isopropyl alcohol/NH_3/H_2O) 0.05–0.1. Anal. Calcd for $C_5H_8P_2O_{11}\cdot4C_6H_{11}NH_3^+\cdot2H_2O$: C, 46.89; H, 9.22; N, 7.54. Found: C, 46.68; H, 8.92; N, 7.72.

Synthesis of D-Ribofuranosyl 2,5-Bisphosphate 4 by Acid Hydrolysis of Compound 2. Compound 2 (20 mg, 0.05 mmol) was dissolved in 2.5 mL of 0.1 N HCl. The time course of hydrolysis was monitored to completion by ^{31}P NMR spectroscopy. Next, the solution was lyophilized, and the residue was treated as above by chromatography on the Affigel 601 column in cyclohexylammonium bicarbonate and then lyophilized. Recovery of D-ribofuranosyl 2,5-bisphosphate ranged from 90% to 95% of the theoretical yield.

Determination of the Rate of Alkaline Hydrolysis of Compound 2. The alkaline hydrolysis of compound 2 was carried out in triplicate in 0.1 N NaOH. Solutions were prepared by dissolving the appropriate amounts of material in 1.4 mL of standard base solution. D_2O (0.1 mL) was added, and the resulting mixture was transferred to a 10-mm NMR tube, which then was fitted with a Teflon vortex suppressor. The tube was placed in the probe, and spectra were accumulated at the times indicated using an automated program. The reaction was monitored at 21 °C, the ambient temperature of the probe. The hydrolysis was allowed to proceed until all starting material was consumed. Electronic integration was employed to determine the fraction of starting material remaining at different time intervals. First-order kinetics were obeyed to at least three half-lives.

Acknowledgment. Financial support by the Rutgers University Busch Fund and the Rutgers University Research Council is gratefully acknowledged, as are the elemental analyses performed by Dr. F. J. Scheidl of Hoffmann-LaRoche Inc., Nutley, NJ.

Registry No. 1·4Na, 87372-47-2; 2·Et_3N, 113599-16-9; 3·4Na, 113599-17-0; 4·4(c-$C_6H_{11}NH_2$), 113599-19-2; 5, 90275-35-7.

Nucleophilic Addition to Olefins. 22.[1] Kinetics of Hydrolysis of the Piperidine and Morpholine Adducts of Benzylideneacetylacetone in 50% Me_2SO–50% Water

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Benzylideneacetylacetone reacts with piperidine and morpholine to form a pH-dependent mixture of anionic adducts, $PhCH(R_2N)C(COCH_3)_2^-$ (T_A^-), and zwitterionic adducts, $PhCH(R_2NH^+)C(COCH_3)_2^-$ ($T_A^\pm$), which slowly hydrolyze to benzaldehyde, acetylacetone (or its anion), and R_2NH. A kinetic study of this hydrolysis in 50% Me_2SO–50% water shows that at high pH carbon protonation of T_A^-, to form $PhCH(R_2N)CH(COCH_3)_2$ (T_A^0), is rate-limiting while at intermediate pH carbon protonation of $T_A^\pm$, to form $PhCH(R_2NH^+)CH(COCH_3)_2$ (T_A^+), is co-rate-limiting with intramolecular proton transfer, $T_A^\pm \rightarrow T_A^0$ (Scheme I). At low pH the enol form of T_A^+ becomes an important intermediate (Scheme II). Rate and equilibrium constants for the various elementary steps leading from $T_A^\pm$ and T_A^- to T_A^0 were determined or estimated and a lower limit for the rate constant of breakdown of T_A^0 into $PhCH{=}N^+R_2$ and $CH(COCH_3)_2^-$ was estimated. Comparison of the kinetic behavior of benzylideneacetylacetone adducts with that of amine adducts of four other PhCH=CXY-type olefins shows both similarities and important differences which are discussed in detail. It appears that there are two major factors that determine whether formation of T_A^0 or its breakdown is rate-limiting. One is crowding, which enhances breakdown and slows proton transfer. The other is the sensitivity of the intrinsic barriers to resonance effects in the carbanion that is formed in the breakdown of T_A^0 on the one hand and that which is formed in the deprotonation of T_A^0 on the other. The smaller sensitivity to this factor in the breakdown reaction tends to make breakdown rate-limiting for systems where resonance in the carbanion is modest and to make proton-transfer rate-limiting where this resonance is strong.

The reaction of benzylideneacetylacetone (BAA) with piperidine and morpholine in aqueous Me_2SO leads to hydrolytic cleavage of the olefin into benzaldehyde, acetylacetone (AA) or its anion (AA^-), and the respective amine. The mechanism comprises a number of steps with some of the intermediates accumulating to measurable concentrations. The first two steps occur on a relatively rapid time scale (stopped-flow) and involve the nucleophilic addition of the amine, to form a zwitterionic adduct ($T_A^\pm$), which is in rapid acid–base equilibrium with its anionic form (T_A^-). At high amine concentration and high pH the equilibrium favors $T_A^\pm$ and T_A^- over the substrate, and $T_A^\pm$ and T_A^- can be characterized by their UV spectra.[2] A kinetic study of reaction 1 has been reported recently.[2]

The present paper describes the kinetics of the conversion of $T_A^\pm$ and T_A^- into benzaldehyde, acetylacetone or its anion, and amine. This is a much slower reaction

(1) Part 21: Bernasconi, C. F.; Panda, M. *J. Org. Chem.* **1987**, *52*, 3042.

(2) Bernasconi, C. F.; Kanavarioti, A. *J. Am. Chem. Soc.* **1986**, *108*, 7744.

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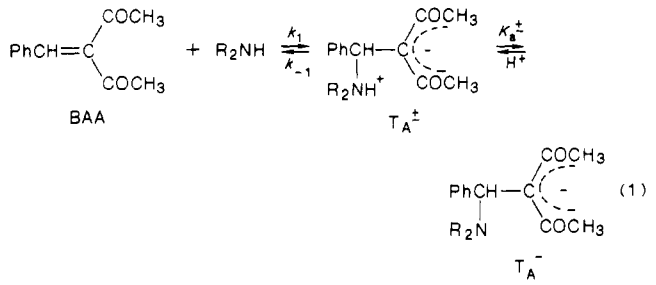


than the formation of $T_A^{\pm}$ and T_A^- and thus is easily studied as a separate kinetic process. As will be shown this conversion can be described by the mechanism of Scheme I. Our interest in this reaction, and particularly in the determination of the rate and equilibrium constants shown in Scheme I, was motivated by the following questions.

(1) Is there a significant contribution by the intramolecular proton transfer that leads directly from $T_A^{\pm}$ to T_A^0 (k_i), as has been observed for a number of amine adducts of benzylidene Meldrum's acid,[3] the morpholine and piperidine adducts of α-cyano-2,4-dinitrostilbene,[4] and the morpholine adduct of 1,1-dinitro-2,2-diphenylethylene?[5] And if so, does the Brønsted α coefficient for the k_i step show the kind of abnormally high value that was observed in some of these systems?[3a,4]

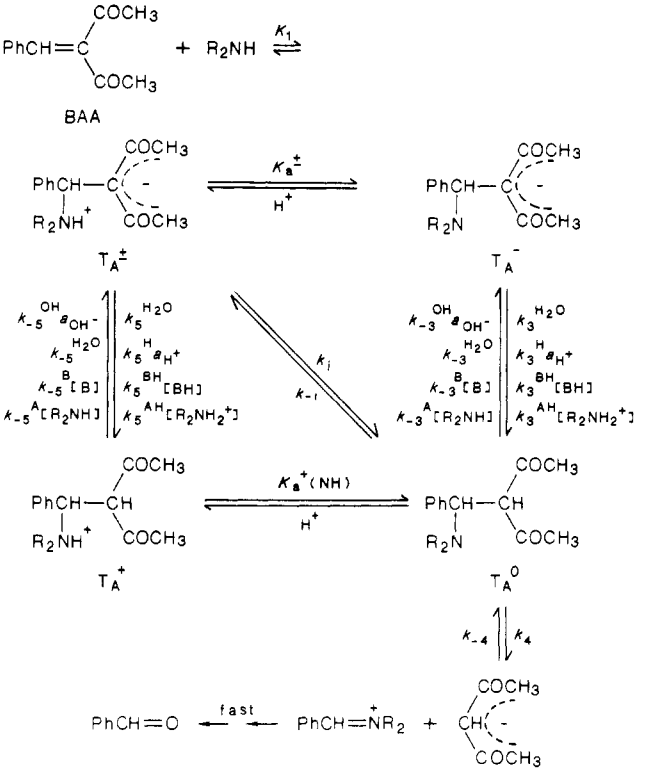
(2) The *intrinsic* rate constant (k for $K = 1$) for nucleophilic addition to BAA (k_1 and k_{-1}, eq 1) was found to be abnormally low when compared to the intrinsic rate constant for the deprotonation of acetylacetone.[2] If this were a consequence of some special feature associated with the formation of acetylacetonate type ions via reactions *not* involving a proton transfer, one might expect that the intrinsic rate constant of the k_4 process (Scheme I) is similarly depressed. On the other hand, if the reasons for the low intrinsic rate of nucleophilic addition to BAA have to do with special factors arising from steric hindrance to coplanarity and intramolecular hydrogen bonding in $T_A^{\pm}$, as we believe to be the case,[2] the k_4 step should not be abnormally slow. One aim of the present study was therefore to evaluate, or at least estimate, the magnitude of k_4.

(3) Since a substantial fraction of AA exists in the enol form, one might expect that the enol form of either T_A^0 or T_A^+ could be playing an important role as additional intermediate(s) in Scheme I, at least under certain reaction conditions. Part of our investigation involving work at low pH was aimed at this question.

Results

General Features. All kinetic determinations were made in 50% Me_2SO–50% water at 20 °C and at an ionic strength of 0.5 M maintained with KCl. Pseudo-first-order conditions with the amine in large excess were used throughout. Two types of kinetic experiments were performed. In the first, "conventional" type, reaction was initiated by mixing BAA with morpholine or piperidine either acting as their own buffers, or in a KOH solution. The reaction was monitored in a conventional UV–vis spectrophotometer, usually at around 250 or 294 nm. Except at very high pH (see below) the reactions lead to quantitative conversion into benzaldehyde and AA (AA^-) as established by UV–vis spectroscopy.

Scheme I



In the second type of experiment T_A^- was first generated in a 0.2 M piperidine (morpholine), 0.1 M KOH solution. This solution was then mixed with various acidic buffers or HCl (pH-jump experiments) in the stopped-flow apparatus. Depending on the conditions these experiments led to the formation of mixtures of BAA, benzaldehyde, and AA. We discovered that it was important to carry out the pH-jump experiments within a few seconds after generating T_A^-, which necessitated the use of a special multimixing stopped-flow system. If the pH jump was delayed more than a few seconds there was enough hydrolysis products formed that the protonation of one of these products, AA^-, by the acidic buffer seriously interfered with the measurement of the pH-jump kinetics.

The pseudo-first-order rate constant, k_{obsd}, for the reaction of BAA with morpholine was measured as a function of amine concentration at pH 7.69, 7.99, 8.72, 11.00, and 14.2. The data are summarized in Table S1 (supplementary material).[7] k_{obsd} shows a greater than first-order dependence on amine concentration which reflects the fact that one amine molecule is used to form $T_A^{\pm}$ or T_A^- (rapid preequilibrium, eq 1) while a second molecule acts as a proton-transfer catalyst (k_3^{BH} and/or k_5^{BH} in Scheme I). The data can be fit to the following expression which was derived under the assumption that T_A^0 breaks down (k_4) much faster than it reverts to T_A^- or $T_A^{\pm}$.

$$k_{obsd} = [k_3 + (k_5 + k_i)a_{H^+}/K_a^{\pm}]/Z \quad (2)$$

with

$$k_3 = k_3^{H_2O} + k_3^{H}a_{H^+} + k_3^{AH}[R_2NH_2^+] \quad (3)$$

$$k_5 = k_5^{H_2O} + k_5^{H}a_{H^+} + k_5^{AH}[R_2NH_2^+] \quad (4)$$

$$Z = \frac{1 + (K_1 + K_1K_a^{\pm}/a_{H^+})[R_2NH]}{K_1K_a^{\pm}[R_2NH]/a_{H^+}} \quad (5)$$

$$K_1 = k_1/k_{-1} \quad (6)$$

(3) (a) Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 5257. (b) Bernasconi, C. F.; Fairchild, D. E.; Murray, C. F. *Ibid.* **1987**, *109*, 3409.
(4) Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1984**, *106*, 3257.
(5) Bernasconi, C. F.; Carré, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 2698.
(6) Omitting the intercept from the triethylamine data since here the intercept contains a contribution from triethylamine catalysis.
(7) See paragraph concerning supplementary material at the end of this paper.

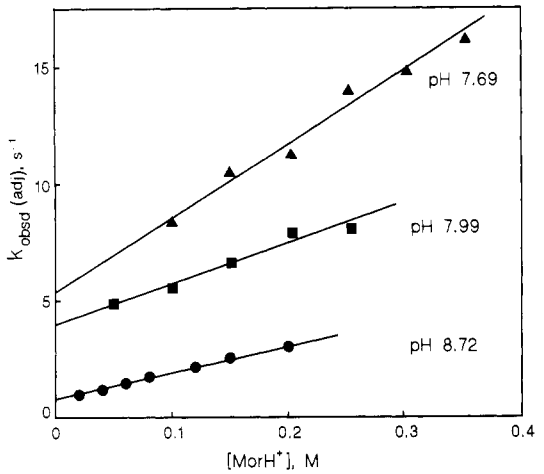


Figure 1. Representative plots of k_{obsd}(adj) vs morpholinium ion concentration for the hydrolysis of the morpholine adduct. Data from Table S1.

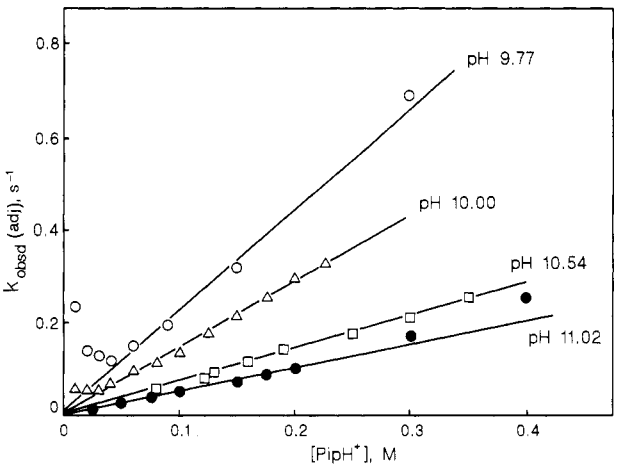


Figure 2. Representative plots of k_{obsd}(adj) vs piperidinium ion concentration for the hydrolysis of the piperidine adduct. Data from Table S2.

By rearranging eq 2 we can define an "adjusted" k_{obsd} as

$$k_{obsd}(adj) = k_{obsd}Z = k_3 + (k_5 + k_i)a_{H^+}/K_a^{\pm} = k_3^{H_2O} + \frac{k_3^{H}K_a^{\pm} + k_5^{H_2O} + k_i}{K_a^{\pm}}a_{H^+} + \frac{k_5^{H}}{K_a^{\pm}}a_{H^+}^2 + \frac{k_3^{AH}K_a^{\pm} + k_5^{AH}a_{H^+}}{K_a^{\pm}}[R_2NH_2^+] \quad (7)$$

Table S1 lists k_{obsd}(adj) values calculated on the basis of $K_1 = 0.64$[2] and $pK_a^{\pm} = 11.24$.[2] Representative plots of k_{obsd}(adj) versus $[R_2NH_2^+]$ are shown in Figure 1. These plots are consistent with eq 7 in that there is a linear dependence on $[R_2NH_2^+]$, and the increase in the slopes with decreasing pH shows that the pathway through T_A^+ (k_5^{AH} term) makes a significant contribution to k_{obsd}(adj). These slopes are given by eq 8

$$\text{slope} = k_3^{AH} + k_5^{AH}a_{H^+}/K_a^{\pm} \quad (8)$$

from which we obtain $k_3^{AH} = 9.46\ M^{-1}\ s^{-1}$ and $k_5^{AH} = 5.16 \times 10^{-3}\ M^{-1}\ s^{-1}$.

The intercepts of Figure 1 are given by eq 9

$$\text{int} = k_3^{H_2O} + \frac{k_3^{H}K_a^{\pm} + k_5^{H_2O} + k_i}{K_a^{\pm}}a_{H^+} + \frac{k_5^{H}}{K_a^{\pm}}a_{H^+}^2 \quad (9)$$

A plot (not shown) of these intercepts versus a_{H^+} does not show upward curvature and, within experimental error, passes through the origin. This indicates that neither the k_5^{H} term nor the $k_3^{H_2O}$ term contribute significantly; a value of $2.9 \times 10^{-4}\ s^{-1}$ for $k_3^{H_2O}$ could be obtained from the experiment at pH 14.2 (Table S1), though.

From the slope of the plot of int versus a_{H^+} (eq 9) one calculates $k_3^{H} + k_5^{H_2O}/K_a^{\pm} + k_i/K_a^{\pm} = 3.72 \times 10^8\ M^{-1}\ s^{-1}$ or $k_3^{H}K_a^{\pm} + k_5^{H_2O} + k_i = 2.0 \times 10^{-3}\ s^{-1}$. In the Discussion section it will be shown that k_i is the dominant term, i.e., $k_i \approx 2.0 \times 10^{-3}\ s^{-1}$.

k_{obsd} for the reaction of BAA with piperidine was measured as a function of amine concentration at pH 9.25, 9.78, 10.00, 10.54, 11.02, 11.72, and 13.30. The data are summarized in Table S2[7] while Figure 2 shows some representative plots. At high *free* amine concentration there is slight upward curvature which we attribute to a nonspecific medium effect.

The plots at low pH also show upward curvature at very *low* concentrations. This behavior has been noted previously in the reaction of amines with benzylidene Meldrum's acid[8] and has been attributed to competing formation of the hydroxide ion adduct. In analyzing the data according to eq 7 the deviating points at very low and very high amine concentrations have been excluded. This analysis[9] which is based on eq 8 affords $k_3^{AH} = 4.85 \times 10^{-1}\ M^{-1}\ s^{-1}$ and $k_5^{AH} = 2.59 \times 10^{-4}\ M^{-1}\ s^{-1}$. The intercepts of the plots of k_{obsd}(adj) versus $[R_2NH_2^+]$ were indistinguishable from zero except at pH 9.25 and 9.78. They afford $k_3^{H} + k_5^{H_2O}/K_a^{\pm} + k_i/K_a^{\pm} = 1.85 \times 10^8\ M^{-1}\ s^{-1}$ or $k_3^{H}K_a^{\pm} + k_5^{H_2O} + k_i = 5.2 \times 10^{-6}\ s^{-1}$, with k_i being the dominant term as is the case for the morpholine adduct (see Discussion).

From experiments in 0.05 and 0.1 M KOH, [piperidine] = 0.06–0.20 M, which yielded constant k_{obsd} values, a $k_3^{H_2O} = 3.7 \times 10^{-4}\ s^{-1}$ was determined. The identification of this process with $k_3^{H_2O}$ was confirmed by running the reaction in a Me_2SO–D_2O mixture which yielded $k_3^{D_2O} = 8.0 \times 10^{-5}\ s^{-1}$, for a kinetic isotope effect $k_3^{H_2O}/k_3^{D_2O} = 4.63$.

At very high pH ([KOH] = 0.05–0.1 M) the $k_3^{H_2O}$ process is followed by a further reaction which is about ten times slower and which leads to a final spectrum somewhat different from that of a mixture of benzaldehyde and AA^-. We were not able to identify the nature of this process, but we could exclude the possibility of nucleophilic attack of AA^- on unreacted BAA by observing the same behavior at different initial concentrations of BAA.

pH-jump experiments with the piperidine adducts were performed in acetate (pH 6.06, 5.74), chloroacetate (pH 3.23), and dichloroacetate buffers (pH 2.15), as well as in HCl solutions (pH 2.30, 1.90, 1.60, 1.12). The results are summarized in Table I. We offer the following interpretation.

(1) At pH 6.06 and 5.74 the observed pseudo-first-order rate constant, which we shall call τ_1^{-1}, is independent of buffer concentration and pH, and the reaction leads to a 100% recovery of BAA. This must therefore correspond to the k_{-1} step in eq 1. The average value of $0.152\ s^{-1}$ for $\tau_1^{-1} = k_{-1}$ is identical with k_{-1} observed previously from conventional stopped-flow mixing experiments.[2]

(2) At pH 3.23 and 2.15 there is substantial buffer catalysis, indicating that protonation of $T_A^{\pm}$, to form T_A^+, competes significantly with the k_{-1} step and becomes the main reaction at low pH and/or high buffer concentration.

(3) Closer inspection of the buffer data shows that the chloroacetate buffer is more effective than the dichloro-

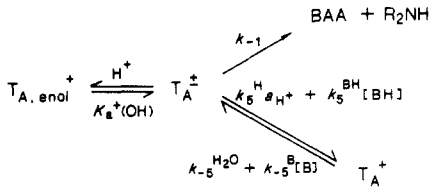
(8) Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329.
(9) Z in eq 5 is based on $K_1 = 54.7$,[2] $pK_a^{\pm} = 13.5$.[2]

Table I. pH Jump Data for the Piperidine Adduct of Benzylideneacetylacetone in 50% Me_2SO–50% Water (v/v) at 20 °C

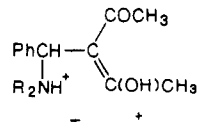
pH	[BH], M	[B⁻], M	τ_1^{-1}, s^{-1}
	BH = Acetic Acid		
6.06	2.50×10^{-2}	5.00×10^{-2}	0.151
5.74	2.50×10^{-2}	2.50×10^{-2}	0.156
5.74	5.00×10^{-2}	5.00×10^{-2}	0.150
	BH = Chloroacetic Acid		
3.23	6.00×10^{-2}	2.00×10^{-2}	0.509
	1.20×10^{-1}	4.00×10^{-2}	0.934
	1.80×10^{-1}	6.00×10^{-2}	1.23
	2.40×10^{-1}	8.00×10^{-2}	1.60
	3.00×10^{-1}	1.00×10^{-1}	1.89
	BH = Dichloroacetic Acid		
2.15	1.00×10^{-2}	1.00×10^{-2}	0.233
	2.00×10^{-2}	2.00×10^{-2}	0.256
	4.00×10^{-2}	4.00×10^{-2}	0.332
	5.00×10^{-2}	5.00×10^{-2}	0.378
	6.00×10^{-2}	6.00×10^{-2}	0.418
	7.00×10^{-2}	7.00×10^{-2}	0.454
	8.00×10^{-2}	8.00×10^{-2}	0.477
	9.00×10^{-2}	9.00×10^{-2}	0.515
	1.00×10^{-1}	1.00×10^{-1}	0.565
	BH = $PipH^+$ in HCl		
2.30	5.00×10^{-2}		0.133
2.30	1.00×10^{-1}		0.143
2.30	1.50×10^{-1}		0.146
1.90	5.00×10^{-1}		0.132
1.90	1.00×10^{-1}		0.145
1.90	1.50×10^{-1}		0.145
1.60	5.00×10^{-2}		0.130
1.60	1.00×10^{-1}		0.146
1.60	1.50×10^{-1}		0.149
1.12	5.00×10^{-2}		0.126
1.12	1.00×10^{-1}		0.141
1.12	1.50×10^{-1}		0.149
1.24[a]	1.00×10^{-1}		0.016

[a] In Me_2SO–D_2O mixture.

Scheme II



acetate buffer. This is typical behavior for general *base* catalysis and may seem surprising since protonation of $T_A^{\pm}$ (k_5^{BH}[BH]) should manifest itself as general *acid* catalysis. The general *base* catalysis can be attributed to the presence of rapid preequilibrium protonation of $T_A^{\pm}$ on oxygen which leads to the enol form of T_A^+



The relevant reactions are shown in Scheme II. τ_1^{-1} is thus given by eq 10

$$\tau_1^{-1} = \frac{K_a^+(OH)}{K_a^+(OH) + a_{H^+}}(k_{-1} + k_5^H a_{H^+} + k_5^{BH}[BH]) \quad (10)$$

In the acetate buffers (pH 6.06 and 5.74) we have $K_a^+(OH) \gg a_{H^+}$ as well as $k_{-1} \gg k_5^H a_{H^+} + k_5^{BH}[BH]$, and hence

$$\tau_1^{-1} = k_{-1}$$

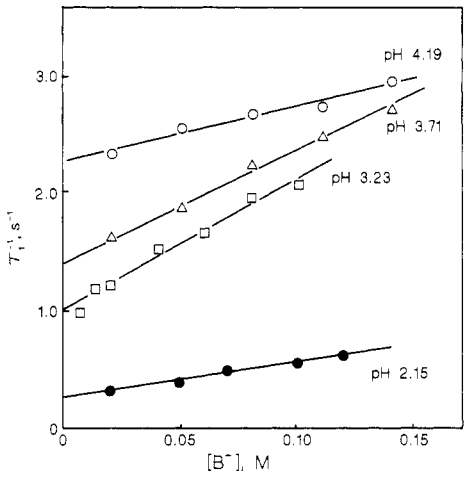


Figure 3. Buffer catalysis of the τ_1^{-1} process in the pH-jump experiments with the morpholine adduct: open symbols, chloroacetate buffer; filled symbols, dichloroacetate buffer. Data from Table S3.

as shown above.

In the more acidic chloroacetate (pH 3.23) and dichloroacetate buffers (pH 2.15) as well as in the HCl solutions (pH 1.12 to 2.30) the opposite relations hold; i.e., $K_a^+(OH) \ll a_{H^+}$ and $k_{-1} \ll k_5^H a_{H^+} + k_5^{BH}[BH]$, and thus eq 10 simplifies to

$$\tau_1^{-1} = K_a^+(OH)k_5^H + \frac{K_a^+(OH)}{a_{H^+}}k_5^{BH}[BH] = K_a^+(OH)k_5^H + \frac{K_a^+(OH)}{K_a^{BH}}k_5^{BH}[B^-] \quad (11)$$

with K_a^{BH} being the acid dissociation constant of the buffer.

One point worthy of note is that τ_1^{-1} in the HCl solutions has nearly the same value (0.130 ± 0.003 s^{-1}) as $k_{-1} = 0.15$ s^{-1}. That the near sameness of these values is purely coincidental can be seen from the last entry in Table II which reports τ_1^{-1} in a Me_2SO–D_2O mixture. The value of this latter mixture indicates a large kinetic solvent isotope effect of 8.1, which is clearly incompatible with $\tau_1^{-1} = k_{-1}$ but consistent with $\tau_1^{-1} = K_a^+(OH)k_5^H$.

In the chloroacetate, dichloroacetate, and HCl experiments the τ_1^{-1} process is followed by a much slower reaction that leads to recovery of BAA. This process was not studied in detail for the piperidine adduct but was investigated thoroughly for the morpholine adduct as discussed in the following section.

pH-jump experiments with the morpholine adduct were performed in acetate (pH 5.74), chloroacetate (pH 4.19, 3.71, 3.23) and dichloroacetate buffers (pH 2.40, 2.15), and also in HCl solutions (pH 2.11, 1.80, 1.39, 1.06). The results are summarized in Table S3.[7] There are both similarities and differences in the behavior of the morpholine as compared to the piperidine adduct. Thus in the acetate buffer there is again virtually 100% recovery of BAA by the k_{-1} step: the buffer independent average value of τ_1^{-1} = 3.08 s^{-1} agrees well with k_{-1} = 2.78 s^{-1} determined previously.[2]

At pH 1.06 to 4.19 *two* kinetic processes were observed. The faster one, τ_1^{-1}, is linearly dependent on buffer concentration. Figure 3 shows the buffer plots. Just as for the piperidine adduct, this process can be understood in terms of Scheme II. However, there are some differences. For one, the slopes of the chloroacetate buffer plots increase with decreasing pH, indicating that $K_a^+(OH) \sim a_{H^+}$ in these buffers. Furthermore, k_{-1} = 3.08 s^{-1} (2.78 s^{-1})[2] is

Table II. Rate and Equilibrium Constants of Reactions of Equation 1 and Schemes I and II in 50% Me_2SO–50% Water at 20 °C

	morpholine adduct	piperidine adduct	$CH(COCH_3)_2^-$[b]
k_1, M^{-1} s^{-1}	1.79[a]	8.20[a]	
k_{-1}, s^{-1}	2.78[a]	0.15[a]	
K_1, M^{-1}	0.64[a]	54.7[a]	
$k_3^{H_2O}$, s^{-1}	$(2.9 \pm 0.2) \times 10^{-4}$	$(3.6 \pm 0.1) \times 10^{-4}$	1.06×10^{-2}
k_{-3}^{OH}, M^{-1} s^{-1}	$\approx 2.5 \times 10^3$ (est)[c]	$\approx 2.2 \times 10^3$ (est)[c]	6.26×10^4
k_3^{H}, M^{-1} s^{-1}	$\approx 4 \times 10^5$ (est)[c]	$\approx 5 \times 10^5$ (est)[c]	1.56×10^7
$k_{-3}^{H_2O}$, s^{-1}	$\approx 4.5 \times 10^{-4}$ (est)[c]	$\approx 5.6 \times 10^{-4}$ (est)[c]	1.18×10^{-2}
k_3^{AH}, M^{-1} s^{-1}	9.5 ± 1.5	$(4.9 \pm 0.3) \times 10^{-2}$	1.29×10^3 (mor); 6.06×10^1 (pip)
k_{-3}^{A}, M^{-1} s^{-1}	≈ 5.56 (est)[c]	$\approx 3.68 \times 10^1$ (est)[c]	5.07×10^2 (mor); 4.81×10^3 (pip)
$k_3^{BH}(Cl_2CHCOOH)$, M^{-1} s^{-1}			1.09×10^6
$k_{-3}^{B}(Cl_2CHCOO^-)$, M^{-1} s^{-1}			1.58×10^{-1}
$k_3^{BH}(ClCH_2COOH)$, M^{-1} s^{-1}			4.37×10^5
$k_{-3}^{B}(ClCH_2COO^-)$, M^{-1} s^{-1}			1.70
$k_5^{H_2O}$, s^{-1}	$\leq 3 \times 10^6$	$\leq 4 \times 10^{-6}$	
k_5^{H}, M^{-1} s^{-1}	$(5.2 \pm 2.0) \times 10^2$	$\approx 8.5 \times 10^2$	
$k_{-5}^{H_2O}$, s^{-1}	$(1.38 \pm 0.13) \times 10^{-2}$	$\approx 1.40 \times 10^{-2}$	
k_5^{AH}, M^{-1} s^{-1}	$(5.2 \pm 0.8) \times 10^{-3}$	$(2.6 \pm 0.5) \times 10^{-4}$	
k_{-5}^{A}, M^{-1} s^{-1}	$(7.1 \pm 3.0) \times 10^1$	$\approx 7.1 \times 10^2$	
$k_5^{BH}(Cl_2CHCOOH)$, M^{-1} s^{-1}	$(9.3 \pm 3.5) \times 10^1$	$\approx 1.3 \times 10^2$	
$k_{-5}^{B}(Cl_2CHCOO^-)$, M^{-1} s^{-1}	$(3.5 \pm 1.4) \times 10^{-1}$	$\approx 3.0 \times 10^{-1}$	
$k_5^{BH}(ClCH_2COOH)$, M^{-1} s^{-1}	20 ± 8	≈ 21	
$k_{-5}^{B}(ClCH_2COO^-)$, M^{-1} s^{-1}	3.0 ± 1.2	≈ 1.8	
k_i, s^{-1}	$(2.0 \pm 0.6) \times 10^{-3}$	$(5.0 \pm 2.0) \times 10^{-6}$	
k_{-i}, s^{-1}	≈ 0.41 (est)[c]	≈ 0.14 (est)[c]	
K_i	$\approx 4.8 \times 10^{-3}$ (est)[c]	$\approx 3.7 \times 10^{-5}$ (est)[c]	
$pK_a^{\pm}$	11.27[a]	13.55[a]	
pK_a°	≈ 8.95 (est)[c]	≈ 9.12 (est)[c]	
pK_a^{+}(CH)	4.58 ± 0.15	≈ 4.75	
pK_a^{+}(OH)	3.75 ± 0.15	≈ 3.67	
pK_a^{+}(NH)	≈ 6.90 (est)	≈ 9.18 (est)[c]	

[a] Reference 2. [b] Reference 12. [c] Estimates based on an estimated pK_a°, see Discussion section.

considerably larger than in the piperidine system and hence cannot be neglected in eq 10. Applying eq 10 to our data allows the evaluation of several parameters as follows. At pH 1.39 (HCl) and 2.15 (dichloroacetate) it is safe to assume $K_{a,enol}^{+} \ll a_{H^+}$. Hence τ_1^{-1} in HCl as well as the intercept of the dichloroacetate buffer plot is given by

$$\tau_1^{-1}(\text{HCl}) \text{ or } \text{int}(Cl_2CHCOO^-) = K_a^{+}(\text{OH})(k_5^{H} + k_{-1}/a_{H^+}) \quad (12)$$

Since k_{-1} is known one can solve eq 12 at pH 1.37 and 2.15 and obtain $k_5^{H} = 5.2 \times 10^2$ M^{-1} s^{-1} and $K_a^{+}(\text{OH}) = 2.69 \times 10^{-5}$ ($pK_a^{+}(\text{OH})$) = 3.57). $k_5^{BH} = 93.4$ M^{-1} s^{-1} for dichloroacetic acid is obtained from the slope of the buffer plot which is given by $K_a^{+}(\text{OH})k_5^{BH}/K_a^{BH}$ (eq 11).

In view of the limited data available to calculate k_5^{H} and pK_a^{+}(OH) we estimate the uncertainty in these parameters to be a factor of 2. A different method for the determination of pK_a^{+}(OH) can be based on the pH dependence of the slopes of the chloroacetate buffer plots. The inverse of these slopes is given by eq 13

$$(\text{slope})^{-1} = K_a^{BH}/k_5^{BH}a_{H^+} + K_a^{BH}/K_a^{+}(\text{OH})k_5^{BH} \quad (13)$$

from which we calculate $k_5^{BH} = 20$ M^{-1} s^{-1} for chloroacetic acid and $pK_a^{+}(\text{OH}) = 3.87$. This latter value is in reasonable agreement with the value of 3.57 determined above.

A third check for the internal consistency of our analysis is provided by the intercepts of the chloroacetate buffer plots. According to eq 10 they are given by

$$\text{int} = \frac{K_a^{+}(\text{OH})}{K_a^{+}(\text{OH}) + a_{H^+}}(k_{-1} + k_5^{H}a_{H^+}) \quad (14)$$

By rearranging eq 14 one obtains

$$\text{int}(K_a^{+}(\text{OH}) + a_{H^+})/K_a^{+}(\text{OH}) = k_{-1} + k_5^{H}a_{H^+} \quad (15)$$

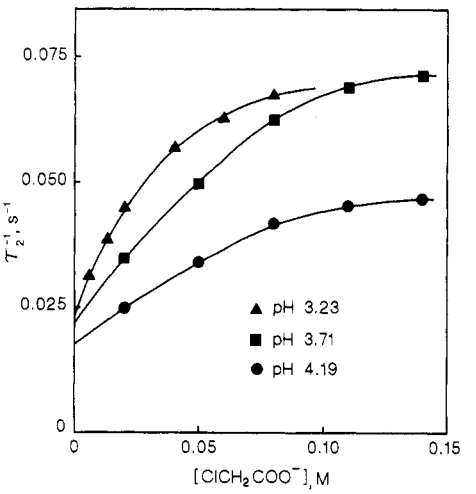


Figure 4. Chloroacetate buffer catalysis of the τ_2^{-1} process in the pH-jump experiments with the morpholine adduct. Data from Table S3.

A plot (not shown) of the left side of eq 15 vs a_{H^+} affords $k_{-1} = 3.0 \pm 1.0$ s^{-1} and $k_5^{H} = 9.2 \pm 4.0 \times 10^2$ M^{-1} s^{-1}, in good agreement with k_{-1} 3.08 s^{-1} obtained in HCl solution and $k_5^{H} = 5.2 \times 10^2$ M^{-1} s^{-1} calculated from eq 12, respectively.

Turning to the second kinetic process (τ_2^{-1}) we note the following. (1) The infinity spectrum shows virtually 100% BAA recovery, based on the original amount of BAA that was used to generate T_A^- before the pH jump. (2) In the dichloroacetate buffers τ_2^{-1} is independent of buffer concentration (Table S3). (3) In the chloroacetate buffer τ_2^{-1} shows a curvilinear dependence on buffer concentration (Figure 4).

These observations are consistent with the conversion of the equilibrium mixture of T_A^+ and $T_{A,enol}^+$, formed during the τ_1^{-1} process, into BAA via $T_A^{\pm}$. At low pH (HCl and dichloroacetate buffers) we apparently have $k_5^{H}a_{H^+}$

Table III. $pK_a°$ and k_4 Values of Amine Adducts of Activated Olefins in 50% Me_2SO–50% Water at 20 °C

PhCH=CXY	$pK_a^{CH_2XY}$	$pK_a°$(mor)	$pK_a°$(pip)	$k_4(T_{pip}°)$, s^{-1}
PhCH=C(COO)$_2$C(CH$_3$)$_2$[a,c]	4.83	≈3.75	≈3.90	>8.3 × 10^5 [b]
PhCH=C(CN)C$_6$H$_3$-2,4-(NO$_2$)$_2$[d]	8.06	≈8.65	≈8.80	≈9.4
PhCH=C(COCH$_3$)$_2$[e]	9.12	≈8.95	≈9.12	≥200
PhCH=C(CN)$_2$[f]	10.05		8.43	66
PhCH=C(CN)C$_6$H$_4$NO$_2$[d]	12.62	11.65	11.82	4.5 × 10^{-2}

[a] In water at 25 °C. [b] Based on $k_4 = 5.8 \times 10^4$ for the 2-methoxyethylamine adduct and β_N = d log k_4/d $pK_a^{\pm} = 0.39$, $k_4 = 8.3 \times 10^5$ is obtained. Increased steric hindrance in the piperidine adduct compared to the 2-methoxyethylamine adduct is likely to increase this value further. [c] Reference 3a, 8. [d] Reference 4. [e] This work. [f] Reference 15.

$\gg k_{-1}$ as indicated by the absence of buffer catalysis. This implies that k_{-1} is rate-limiting and τ_2^{-1} is given by

$$\tau_2^{-1} = k_{-1}\frac{K_a^+(CH)K_a^+(OH)}{K_a^+(CH)K_a^+(OH) + [K_a^+(CH) + K_a^+(OH)]a_{H^+}} \quad (16)$$

with $K_a^+(CH)$ being the CH-acidity constant of T_A^+. At pH ≤2.40 the first term in the denominator of eq 16 is negligible and eq 16 simplifies to

$$\tau_2^{-1} \approx k_{-1}\frac{K_a^+(CH)K_a^+(OH)}{[K_a^+(CH) + K_a^+(OH)]a_{H^+}} \quad (17)$$

A plot (not shown) of τ_2^{-1} versus $(a_{H^+})^{-1}$ gives an excellent straight line with a slope of 7.35×10^{-5} M^{-1} s^{-1}. In conjunction with the known values of k_{-1} and $pK_a^+(OH)$ we obtain $pK_a^+(CH) = 4.58$.

In the chloroacetate buffers the relation $k_5^H a_{H^+} \gg k_{-1}$ no longer holds and deprotonation of T_A^+ on carbon becomes partially rate-limiting. Since the above results show that $pK_a^+(CH)$ is significantly larger than $pK_a^+(OH)$, τ_2^{-1} can be approximated by the steady-state expression

$$\tau_2^{-1} = \frac{k_{-1}(k_{-5}^{H_2O} + k_{-5}^B[B^-])}{k_{-1} + k_5^H a_{H^+} + k_5^{BH}[BH]} \quad (18)$$

This equation accounts for the curvilinear buffer dependence in Figure 4.

Discussion

All rate and equilibrium constants pertaining to Schemes I and II, as well as eq 1, are summarized in Table II. Some of the parameters listed in Table II are estimates. This is indicated in the table (est), while the procedures used to arrive at these estimates are described below. It should also be noted that the evaluation of a number of proton-transfer rate constants depends on the determination of the pK_a of the OH group of $T_{A,enol}^+$ ($pK_a^+(OH)$). This pK_a could be determined for the morpholine adduct but not for the piperidine adduct. However, it is reasonable to assume that $pK_a^+(OH)$ should depend very little on the amine moiety in $T_{A,enol}^+$. We have assumed that the pK_a is 0.1 units higher for the piperidine adduct compared to the morpholine adduct. The values for the proton transfer rate constants of the piperidine adduct are based on this assumed $pK_a^+(OH)$.

Table II also lists proton transfer rate constants for acetylacetone under the same reaction conditions.

Protonation of T_A^- and $T_A^{\pm}$ by Water and General Acids. In discussing the various rate constants for proton transfer it is useful to use acetylacetone as a reference point. There is a direct correspondence between the rate constants for carbon protonation of T_A^- and of acetylacetonate ion (k_3), and for deprotonation of T_A^0 and of acetylacetone (k_{-3}). We note that carbon protonation by water ($k_3^{H_2O}$) of the adducts is 36.5-fold (morpholine adduct) and 29.4-fold (piperidine adduct), respectively, slower than protonation of acetylacetonate ion. For protonation by $R_2NH_2^+$ (k_3^{AH}), the rate reductions relative to acetylacetonate ion are 130-fold (morpholine adduct) and 125-fold (piperidine adduct), respectively.

There are two factors which may contribute to these rate reductions: a lower carbon pK_a (pK_a^0) due to the electron-withdrawing effect of the PhCH(R_2N) moiety and a steric effect. The greater reduction in k_3^{AH} compared to $k_3^{H_2O}$ can be regarded as direct evidence for a steric effect in the k_3^{AH} process, to be attributed to the larger size of $R_2NH_2^+$ compared to water. The following considerations suggest that for the water reaction ($k_2^{H_2O}$) the steric effect is dominant, too. We start by estimating pK_a^0, based on pK_a^0 values of similar adducts and on how they relate to the pK_a of the parent carbon acid. Table III lists such values for four other systems.

With the adducts of benzylidene Meldrum's acid and α-cyano-4-nitrostilbene the pK_a^0 values are 0.8 to 1.1 units lower than the pK_a of the respective parent carbon acids ($pK_a^{CH_2XY}$), reflecting the expected electron withdrawing effect of the PhCH(NRR′) moiety. However, for the adducts of α-cyano-2,4-dinitrostilbene pK_a^0 is higher than $pK_a^{CH_2XY}$. This reflects the strong steric hindrance of π-overlap in T_A^- caused by the ortho nitro group.[4] Since in T_A^- derived from benzylideneacetylacetone there is also evidence of steric hindrance to π-overlap[2] we expect a similar effect, although one which is perhaps not as strong. We shall assume that the electronic and steric effects just about cancel each other in the piperidine adduct, i.e., pK_a^0 ≈ 9.12 for the piperidine adduct, and a slightly lower value of ≈8.95 for the morpholine adduct, taking into account the slightly stronger electron withdrawing effect of the morpholine moiety.

The following reasoning suggests that these estimates cannot be far off the mark. In comparing k_5^{AH} ($T_A^{\pm} + R_2NH_2^+ \rightarrow T_A^+ + R_2NH$) with k_3^{AH} ($T_A^- + R_2NH_2^+ \rightarrow T_A^0 + R_2NH$) we note that k_5^{AH} for the morpholine adduct is (1.83×10^3)-fold lower than k_3^{AH}, while for the piperidine adduct this factor is 1.87×10^3. These reductions must be mainly a consequence of the lower basicity of the carbon caused by the positive charge on nitrogen although the electrostatic repulsion between this positive charge and that on $R_2NH_2^+$ in the transition state is expected to contribute to this reduction.[10] With $pK_a^0 - pK_a^+(CH) \approx 4.38$ and a d log k^{AH}/d $pK_a = 0.58$ based on Bell and Grainger's[11] data, one calculates a factor of ≈3.5×10^2 for the reduction due to the lower pK_a. This leaves a factor of ≈5.3 for the electrostatic effect which is in the expected range.[10]

From the k_3^{AH} values of the two adducts one can calculate an apparent Brønsted α value of 0.56 ± 0.03, defined as d log k_3^{AH}/d pK_a^{AH}, for protonation by piperidinium and morpholinium ion. However, since changing the catalyst is accompanied by a change in amine moiety of the adduct and thus by a slight change in pK_a^0 (see above), correction for this change in pK_a^0 affords a true α of 0.60

(10) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475.
(11) Bell, R. P.; Grainger, S. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1367.

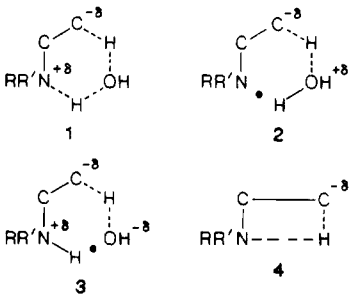
± 0.04. This value is, within experimental error the same as α for morpholinium/piperidinium protonation of acetylacetonate ion (α = 0.58 ± 0.03).[12]

In a similar way one can calculate an apparent α = 0.57 ± 0.03 for k_5^{AH}, which yields a true α = 0.61 ± 0.04 after correction for the changing pK_a^+(CH). For the protonation of $T_A^\pm$ by chloro- and dichloroacetic acid (k_5^{BH}) one obtains α = 0.43 ± 0.04 for the morpholine adduct and 0.48 ± 0.04 for the piperidine adduct. This compares with α = 0.31 ± 0.04 for acetylacetonate ion.[12]

Protonation of T_A^- by H_3O^+. Evidence for Intramolecular Assistance. As indicated in the Results section, carbon protonation of T_A^- by H_3O^+ (k_3^H) is kinetically indistinguishable from the two pathways $T_A^- + H^+ \rightleftarrows T_A^\pm \rightarrow T_A^0$ ($k_i/K_a^\pm$) or $T_A^- + H^+ \rightleftarrows T_A^\pm \rightarrow T_A^+ + OH^-$ ($k_5^{H_2O}/K_a^\pm$) shown in Scheme I. From the intercepts according to eq 9 one obtains $k_3^H + k_i/K_a^\pm + k_5^{H_2O}/K_a^\pm$ = 3.72×10^8 M^{-1} s^{-1} for the morpholine adduct, 1.85×10^8 M^{-1} s^{-1} for the piperidine adduct. These values are considerably larger than $k_3^H = 1.56 \times 10^7$ M^{-1} s^{-1} for acetylacetonate ion protonation.[12] If one assumes that the steric effect in the adduct lowers k_3^H relative to acetylacetone by the same factor as they lower $k_3^{H_2O}$, k_3^H should be in the order of (4–5) $\times 10^5$ M^{-1} s^{-1}, i.e., $k_3^H + k_i/K_a^\pm + k_5^{H_2O}/K_a^\pm$ is about (3–9) $\times 10^2$ fold larger than the expected value for k_3^H. This means that $(k_i + k_5^{H_2O})/K_a^\pm \gg k_3^H$ from which we calculate $k_i + k_5^{H_2O} = 2.0 \times 10^{-3}$ s^{-1} for the morpholine adduct, 5.2×10^{-6} s^{-1} for the piperidine adduct.

We now show that $k_i \gg k_5^{H_2O}$ for the morpholine adduct. On the basis of $pK_a^0 - pK_a^+(CH) \approx 4.37$, d log k/d pK_a = 0.58 based on data by Bell and Grainger,[11] and $k_3^{H_2O} = 2.9 \times 10^{-4}$ s^{-1} one estimates $k_5^{H_2O} \approx 8.4 \times 10^{-7}$ s^{-1}, which is (2.38 $\times 10^3$)-fold lower than $k_i + k_5^{H_2O}$. A similar calculation for the piperidine adduct affords $k_5^{H_2O} \approx 1.04 \times 10^{-6}$ s^{-1}, which is about 5-fold lower than $k_5^{H_2O} + k_i = 5.2 \times 10^{-6}$ s^{-1}. It appears that for both adducts the k_i pathway is dominant and for the morpholine adduct overwhelmingly so.

A detailed investigation of the k_i step in amine adducts of benzylidene Meldrum's acid has shown that the most likely mechanism of this process is an intramolecular proton-transfer mediated by a water bridge (**1**).[3] Several alternatives



1 **2** **3** **4**

including protonation of T_A^- by H_3O^+ with hydrogen bonding stabilization of the transition state (**2**), protonation of $T_A^\pm$ by water with hydrogen bonding and electrostatic stabilization of the incipient OH^- by the ammonium ion (**3**), and direct intramolecular proton transfer between nitrogen and carbon (**4**) were excluded.[3] We believe that the same mechanism (**1**) is operative for the amine adducts of benzylideneacetylacetone.

Just as for the piperidine/morpholine adduct pairs derived from benzylidene Meldrum's acid[3a] and α-cyano-2,4-dinitrostilbene,[4] the Brønsted α value for the k_i step is, within experimental error, unity or even slightly higher (~1.1). As discussed in more detail in a previous report,[3a] this unusually high α value is most reasonably interpreted as an enhanced reactivity of the morpholine adduct, which is akin to an α effect[13] in nucleophilic reactions.

Estimate of Lower Limit for k_4. As shown in the Results section benzaldehyde and acetylacetone formation occurs only in experiments initiated by mixing benzylideneacetylacetone with amine solution; in the pH-jump experiments reversion to the substrate is observed, either immediately (acetate buffers) or in the second relaxation process. Furthermore, under all experimental conditions where product formation is observed, the rate-limiting step is carbon protonation, either inter- or intramolecular. This implies

$$k_4 \gg k_{-i} + k_{-3}^A[R_2NH] + k_{-3}a_{OH^-} + k_{-3}^{H_2O} + \frac{a_{H^+}}{K_a^+(NH)}(k_{-5}^A[R_2NH] + k_{-5}^{H_2O})$$

The quantity on the right of the inequality sign is largest for the piperidine adduct, at high pH, and at high piperidine concentrations. Its maximum value (at pH 13.3 and [pip] = 0.7 M) is 32 s^{-1}, and thus $k_4 \gg 32$ s^{-1}, which means k_4 is probably at least 200 s^{-1}.

It is interesting to compare our estimate with the k_4 values summarized in Table III for some other adducts. There appear to be three main factors which determine k_4: the pK_a of the departing carbanion ($pK_a^{CH_2XY}$), the intrinsic barrier as a function of XY, and release of steric strain. Increased nucleofugality with decreasing $pK_a^{CH_2XY}$ is clearly seen in comparing benzylidene Meldrum's acid with benzylideneacetylacetone and α-cyano-2,4-dinitrostilbene with α-cyano-4-nitrostilbene. The disproportionately high k_4 value (relative to $pK_a^{CH_2XY}$) for the benzylidenemalononitrile adduct reflects the much smaller intrinsic barrier typically observed in the formation of carbanions with relatively little resonance stabilization.[14] Release of steric strain is the likely cause for the disproportionately high k_4 value for the benzylideneacetone adduct and, as pointed out before,[4] for the high ratio of $k_4(CN)(C_6H_3\text{-}2,4\text{-}(NO_2)_2)/k_4((CN)C_6H_4\text{-}4\text{-}NO_2)$; this ratio is too high to be accounted for only in terms of the $pK_a^{CH_2XY}$ difference because the intrinsic barrier for the loss of (2,4-dinitrophenyl)acetonitrile anion should be higher than for the loss of (4-nitrophenyl)acetonitrile anion.[4,14]

In the Introduction the possibility was raised that k_4 for the benzylideneacetylacetone adducts might be abnormally low in comparison with other systems. The above comparisons show clearly that this is not the case; if anything k_4 is *higher* than one might have anticipated. This conclusion thus adds further support to the interpretation offered[2] for the unusually low intrinsic rate constant for piperidine and amine addition to benzylideneacetylacetone (eq 1).

Comparisons with Other Systems. Mechanistically the breakdown of the amine adducts of the five activated olefins listed in Table III is quite similar in that they all can be described by a scheme such as Scheme I. There exist important differences between the various systems, though, and in particular between the benzylideneacetylacetone system and the others. One unique feature of the benzylideneacetylacetone adducts is that even at relatively high pH the pathway through T_A^+ becomes important and even dominant while in the other systems this

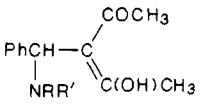
(12) Bernasconi, C. F.; Bunnell, R. D. *Isr. J. Chem.* **1985**, *26*, 420.

(13) (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.

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

pathway was undetectable under comparable conditions. This feature can be attributed to the unusually high $pK_a^{\pm}$ values (11.27 for the morpholine adduct, 13.55 for the piperidine adduct) which makes T_A^- a high-energy intermediate even at moderate pH values.

The high $pK_a^{\pm}$ values are also the reason why the enol form of T_A^0, **5**, cannot be observed: the nitrogen of T_A^- is more basic than the oxygen. On the other hand no such competition between nitrogen and oxygen exists in $T_A^{\pm}$, and hence the enol form of T_A^+ was easily observed (Scheme II).



5

It is also interesting to note that because with the benzylideneacetylacetone adducts the k_4 step is relatively fast, carbon protonation is rate-limiting under all reaction conditions. This is similar to the behavior of the benzylidene Meldrum's acid adducts[3a,8] but contrasts with the behavior of the benzylidenemalononitrile[15] and α-cyano-4-nitrostilbene adducts,[4] where the k_4 step was found to be rate-limiting throughout, and the α-cyano-2,4-dinitrostilbene adducts,[4] where carbon protonation is rate-limiting at low buffer concentration, while the k_4 step becomes rate-limiting at high concentrations. Whether carbon protonation or the k_4 step is rate-limiting depends on the relative magnitude of k_4 and the *de*protonation rate of T_A^0 whose largest component is $k_{-3}^A[R_2NH]$. As discussed earlier, k_4 increases with decreasing $pK_a^{CH_2XY}$, decreasing resonance stabilization of $CHXY^-$, and increasing steric crowding. On the other hand, k_{-3}^A *de*creases with steric crowding but shows the same qualitative dependence on $pK_a^{CH_2XY}$ and resonance stabilization as k_4, because pK_a^0 is roughly correlated with $pK_a^{CH_2XY}$ and the carbanion in T_A^- is related to $CHXY^-$.[14] There is reason to believe, though, that the sensitivity of k_{-3}^A to changes in resonance stabilization of $CHXY^-$ is substantially greater than for k_4.[14b,16,17] This would tend to make k_{-3}^A particularly large for the benzylidenemalononitrile and, to a lesser degree, also for the α-cyano-4-nitrostilbene adducts, offering a simple rationalization for the small $k_4/k_{-3}^A[R_2NH]$ ratios (rate-limiting k_4 step) in these systems; the more intermediate $k_4/k_{-3}^A[R_2NH]$ ratios for the α-cyano-2,4-dinitrostilbene adducts (change in rate-limiting step with changing $[R_2NH]$) may be the result of a substantially less exalted k_{-3}^A due to the greater resonance effect, combined with the sterically accelerated k_4 (see above). The large $k_4/k_{-3}^A[R_2NH]$ ratios for the benzylidene Meldrum's acid and benzylideneacetylacetone adducts may mainly reflect steric accelerations of the k_4 step coupled with substantial steric hindrance in the k_{-3}^A step.

(15) Bernasconi, C. F.; Fox, J. P.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 2810.
(16) Bernasconi, C. F. *Adv. Chem. Ser.* **1987**, *215*, 115.
(17) Bernasconi, C. F.; Laibelman, A.; Zitomer, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 6563.

Experimental Section

Materials. Benzylideneacetylacetone was available from a previous study.[2] Piperidine and morpholine were purified as described previously.[5] Triethylamine (Aldrich) was distilled over BaO prior to use. Dichloroacetic acid (Aldrich) was distilled under reduced pressure; chloroacetic acid (Aldrich) was recrystallized from ligroine; reagent grade acetic acid and KCl (Mallinckrodt) were used without further purification. Stock solutions of HCl and KOH were prepared from "dilute it" (Baker Analytical) stock solutions. Me_2SO (Mallinckkrodt) was stored over molecular sieves. D_2O (Norell Inc.) was 99.9% pure.

Reaction Solutions and Kinetic Measurements. Reaction solutions were prepared as described before.[5] The slow reactions were run in thermostated cuvettes of a Perkin-Elmer 559A UV–vis spectrophotometer. The fast reactions (pH-jump experiments) were monitored in a Durrum-Gibson stopped-flow spectrophotometer. pH measurements were made in the reaction solution for the slow reaction, in mock mixing experiments for the stopped-flow runs. The wavelength to monitor the reaction varied with the pH range and amine concentration. This is because most absorbing species in the reaction scheme (BAA, T_A^-, $T_A^{\pm}$, PhCH=O, AA^-) have overlapping spectra,[2] but their relative contributions to the absorption of the reaction solution change with changing experimental conditions. The best wavelength was determined empirically: 255 nm for all pH-jump experiments; 250 nm for k_{obsd} with the morpholine adduct at pH 7.69, 7.99, and 8.72, and with the piperidine adduct at pH 9.25, 9.78, 10.00, and 10.54; 324 nm for k_{obsd} with the morpholine adduct at pH 11.0 and 14.02; 294 nm with the piperidine adduct at pH 11.02.

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Supplementary Material Available: Kinetic data on the reaction of benzylideneacetylacetone with morpholine, Tables S1–S3 (8 pages). Ordering information is given on any current masthead page.