Kinetics of Hydrolysis of Benzylideneacetylacetone

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The hydrolysis of the title compound occurs by the four-step mechanism typical for the hydrolysis of olefins PhCH=CXY where X and/or Y are electron-withdrawing groups. These steps are nucleophilic attack by OH^- or water on the olefin to form $PhCH(OH)\bar{C}(COMe)_2$ (T_{OH}^-); carbon protonation of T_{OH}^- to form $PhCH(OH)CH(COMe)_2$ (T_{OH}^0); oxygen deprotonation of T_{OH}^0 to form $PhCH(O^-)CH(COMe)_2$ (T_O^-); and collapse of T_O^- to $PhCH=O$ and acetylacetonate anion. In strongly basic solution two kinetic processes were observed. To a good approximation the fast one can be assigned to reversible OH^- addition to the substrate (k_1^{OH}, $k_{-1}^{H_2O}$) to form T_{OH}^- and the slow one to irreversible conversion of T_{OH}^- to final products with rate-limiting carbon protonation of T_{OH}^- by water ($k_2^{H_2O}$). This latter interpretation is at variance with one offered earlier by Calmon and Calmon. In acidic solution only one kinetic process was observed; it corresponds to rate-limiting water addition to the substrate ($k_1^{H_2O}$). Rate constants for hydronium ion catalyzed reversion of T_{OH}^- to reactants (k_{-1}^H) and for carbon protonation of T_{OH}^- by H_3O^+ (k_2^H), acetic acid, and DABCOH$^+$ (k_2^{BH}) were also obtained from pH-jump experiments on T_{OH}^-. Approximate *intrinsic* rate constants for water and OH^- addition to benzylideneacetylacetone were calculated from $k_2^{H_2O}$ and k_1^{OH}, respectively, and compared with those for the corresponding reactions of benzylidenemalondialdehyde and benzylidene Meldrum's acid as well as other olefins. This comparison indicates that the intrinsic reactivity of benzylideneacetylacetone toward OH^- and water is "normal," and sheds more light on its "abnormal" intrinsic reactivity toward secondary alicyclic amines reported earlier.

Introduction

As part of an ongoing inquiry into the structure–reactivity behavior of activated olefins toward nucleophiles, reactions of substrates of structure **1** with OH^-, water, amines, thiolate ions, and carbanions have been investigated.[1–7] The main focus has been the nucleophilic attack step, eq 1, and the dependence of the *intrinsic* rate constant, k_o,[8] on X and Y.
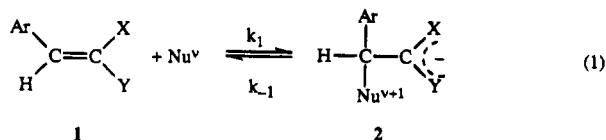
In the reaction of **1** with OH^- or water in aqueous solutions the adduct **2** typically reacts further and leads to ArCHO and CH_2XY ($CHXY^-$ at high pH).[1,9] The complete mechanism of this hydrolysis is well established

and is shown in Scheme 1. Step 1 may be subject to general base catalysis of water addition ($k_1^B[B]$ term), although this catalysis is usually negligible at low buffer concentrations. Steps 2 and 3 are proton transfers at carbon and oxygen, respectively, while step 4 represents C—C bond cleavage. The step labeled $k_{34}^{H_2O}$ involves C—C bond cleavage concerted with deprotonation of the OH-group by water, or intramolecularly, by the leaving carbanion; this step may become important in strongly acidic solution.[1,10,11]

Even though Scheme 1 applies quite generally, there are marked differences among substrates regarding rate-limiting steps at a given pH and concerning detectability of the intermediates T_{OH}^-, T_{OH}^0, and T_O^-. T_{OH}^-, the intermediate of greatest interest, is directly observable when both of the following conditions are met. (1) The equilibrium constant for the first step must be large enough that $K_1^{H_2O}/a_{H^+} = K_1^{OH}[OH^-] > 1$ ($K_1^{H_2O} = k_1^{H_2O}/k_{-1}^H$; $K_1^{OH} = k_1^{OH}/k_{-1}^{H_2O}$). (2) The rate of formation of T_{OH}^-($k_1^{H_2O} + k_1^{OH}[OH^-] + k_1^B[B]$) must be larger than the rate by which T_{OH}^- proceeds to T_{OH}^0 or to final products.

The first condition is met by the following compounds: benzylidenemalononitrile (**3**, $pK_1^{H_2O} = 10.7$ in water,[10] $pK_1^{H_2O} = 9.5$ in 50% Me_2SO–50% water[12]), benzylidene-1,3-indandione (**4**, $pK_1^{H_2O} = 7.79$ in 50% Me_2SO–50% water),[11] 1,1-dinitro-2,2-diphenylethylene (**5**, $pK_1^{H_2O} = 6.09$ in 50% Me_2SO–50% water),[13] β-nitrostyrene (**6**, $pK_1^{H_2O} = 10.37$ in 50% Me_2SO–50% water),[2] α-nitrostil-

[@] Abstract published in *Advance ACS Abstracts,* June 15, 1994.

(1) For a recent review summarizing our work prior to 1989, see: Bernasconi, C. F. *Tetrahedron* **1989,** *45,* 4017.

(2) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1989,** *111,* 5893.

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(6) Bernasconi, C. F.; Zitomer, J. L.; Schuck, D. F. *J. Org. Chem.* **1992,** *57,* 1132.

(7) Bernasconi, C. F.; Schuck, D. F. *J. Org. Chem.* **1992,** *57,* 2365.

(8) The intrinsic rate constant of a reaction with a forward rate constant k_f and a reverse rate constant k_r is defined as $k_o = k_f = k_r$ when the equilibrium constant is unity. The intrinsic barrier, $\Delta G_o^\ddagger$, is the free energy of activation that corresponds to k_o.

(9) For earlier reviews, see: (a) Patai, S.; Rappoport, Z. In *The Chemistry of the Alkenes*; Patai, S., Ed.; Wiley-Interscience: New York, 1964; p 469. (b) Fyfe, C. A. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Wiley-Interscience: New York, 1971; p 51. (c) Rappoport, Z.; Ladkani, D. *Chem. Scripta* **1974,** *5,* 124.
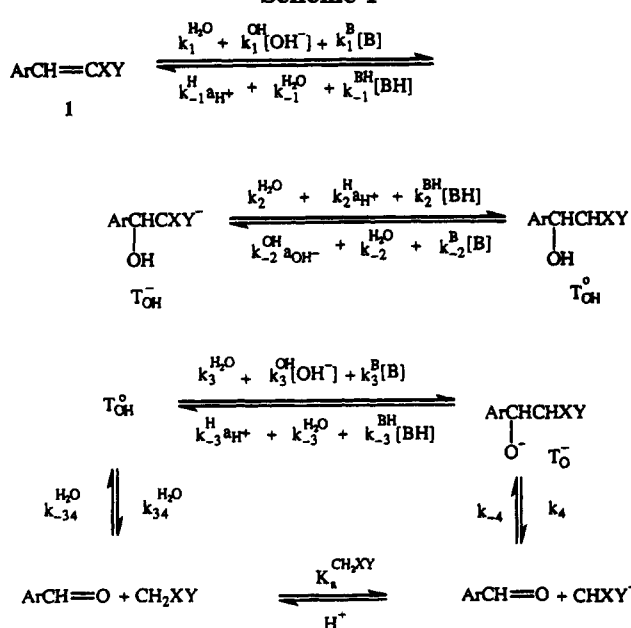
(10) Bernasconi, C. F.; Howard, K. A.; Kanavarioti, A. *J. Am. Chem. Soc.* **1984,** *106,* 6827.

(11) Bernasconi, C. F.; Laibelman, A.; Zitomer, J. L. *J. Am. Chem. Soc.* **1985,** *107,* 6563.

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

(13) Bernasconi, C. F.; Carré, D. J.; Kanavarioti, A. *J. Am. Chem. Soc.* **1981,** *103,* 4850.

Scheme 1

bene (**7**, $pK_1^{H_2O}$ = 9.53 in 50% Me$_2$SO−50% water),[14] benzylidene Meldrum's acid (**8**, $pK_1^{H_2O}$ = 5.43 in water),[15] and benzylidenemalondialdehyde (**9**, $pK_1^{H_2O}$ = 4.79 in water).[16] The second condition is not met for **3** in water at any pH and hence T_{OH}^- is not observable in this solvent. However in 50% and 70% Me$_2$SO the rate
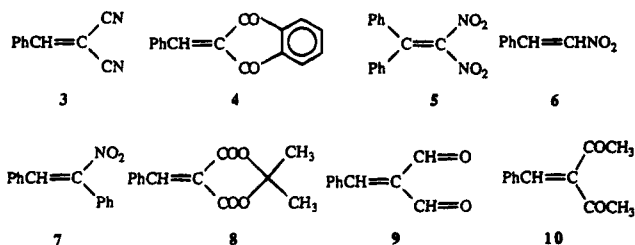
of formation of T_{OH}^- at high pH is enhanced while conversion of T_{OH}^- to products is slowed down, resulting in direct detectability of T_{OH}^-.[12] For **4−9**, the second condition *is* met but in most cases a higher pH is required than that needed to fulfill the first condition.

Under conditions where T_{OH}^- accumulates to detectable levels, carbon protonation of T_{OH}^- by water ($k_2^{H_2O}$) has invariably been found to be rate limiting for product formation. The only exception is the hydrolysis of **10**[17] and substituted benzylideneacetylacetones,[18] where collapse of T_{OH}^-, concerted with deprotonation of the hydroxyl group by OH⁻ (with transition state **11**), was proposed to be rate limiting. This represents a highly unorthodox proposal which warrants scrutiny and is one of the reasons that led us to reinvestigate this reaction.

We also hoped that determination of $k_1^{H_2O}$ and k_1^{OH} in Scheme 1, which would allow an estimate of the *intrinsic* rate constant (k_o)[8] for nucleophilic addition by OH⁻ and
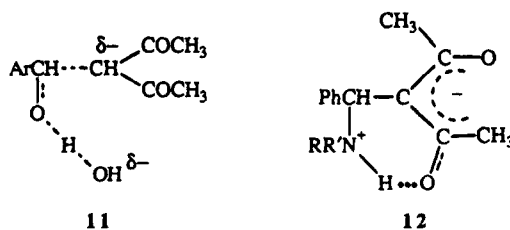
water, could shed more light on possible reasons for the abnormally low k_o value for *amine* addition to **10**.[19] The low k_o value for this latter reaction has been attributed to a combination of two factors. The first is that the zwitterionic adduct is strongly stabilized by intramolecular hydrogen bonding (**12**), but in the transition state this hydrogen bonding is too weak to produce a rate enhancement commensurate with the enhanced equilibrium constant. This has the effect to decrease k_o and is a manifestation of the principle of nonperfect synchronization (PNS).[20,21] The second factor is steric crowding in the adduct which reduces its stability. This steric effect appears to be virtually fully developed in the transition state, and hence, it decreases the rate of nucleophilic attack almost as much as the equilibrium constant. The result is again a lowering of k_o in accordance with the PNS.[20,21]

Inasmuch as T_{OH}^- lacks the relatively acidic NH⁺-proton and positive charge of **12** and is also less crowded than **12**, k_o for nucleophilic addition of OH⁻ to **10** should be "normal" if the hydrogen bonding and steric explanation of the abnormally low k_o for amine addition is valid. Our results will show that this is indeed the case.

Results

Measurements in Strongly Basic Solution. The hydrolysis of **10** in basic solution generates benzaldehyde and acetylacetonate ion, as confirmed by the UV spectrum of an infinity solution that is identical to that of an authentic mixture of the reaction products. In strongly basic solutions ([KOH] = 0.01−0.5 M) two kinetic processes are observed. In a first approximation, the more rapid process, with the reciprocal relaxation time $1/\tau_1$, corresponds to reversible conversion of **10** into T_{OH}^-, and the slower one ($1/\tau_2$) to irreversible appearance of products. The dependence of $1/\tau_1$ and $1/\tau_2$ on [OH⁻] is displayed in Figure 1.

As will be shown below, under these conditions, the rate-limiting step for product formation is, to a good approximation, carbon protonation of T_{OH}^- while conversion of T_{OH}^o to products is fast, i.e., faster than carbon deprotonation of T_{OH}^o. Hence, Scheme 1, as applied to benzylideneacetylacetone, simplifies to eq 2.

In evaluating the concentration dependence of the two relaxation times we shall first assume that $1/\tau_1$ refers

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(15) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1980**, *102*, 1361.

(16) Bernasconi, C. F.; Stronach, M. W. *J. Org. Chem.* **1986**, *51*, 2144.

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(18) Calmon, M.; Arnaud-Lehujeur, B.; Calmon, J.-P. *Bull. Soc. Chim. Fr.* **1972**, 174.

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

(20) According to the PNS a product-stabilizing factor (e.g., resonance, solvation, intramolecular hydrogen bonding) lowers k_o if its development at the transition state lags behind bond formation; a product-*de*stabilizing factor (e.g., steric crowding) also lowers k_o if its development is ahead of bond formation. The opposite is true for product-stabilizing factors that develop early or product-destabilizing factors that develop late.[21,22]

(21) (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Acc. Chem. Res.* **1992**, *25*, 9. (c) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **1992**, *27*, 119.

(22) Bernasconi, C. F. *Relaxation Kinetics*; Academic Press: New York, 1976; p 25.
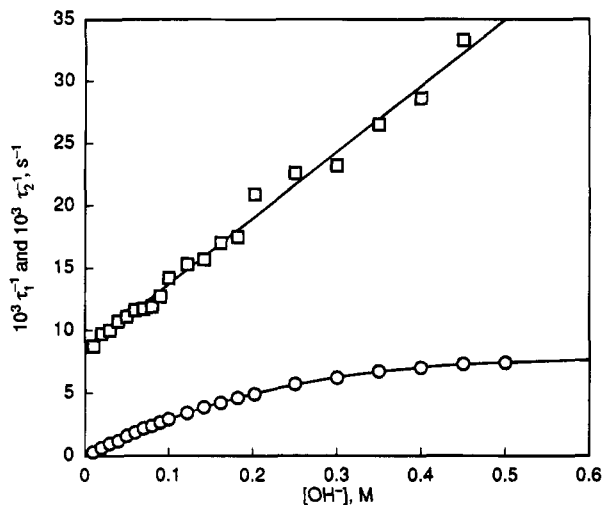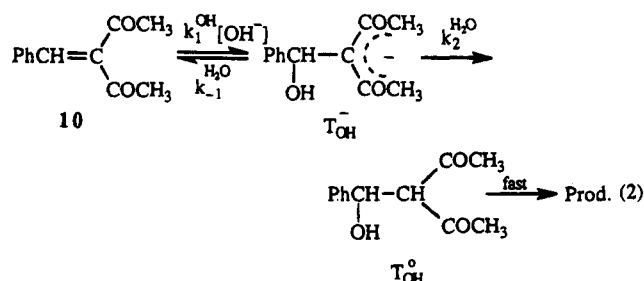
Figure 1. Data in strongly basic solution. Dependence of $1/\tau_1$ ($\square$) and $1/\tau_2$ ($\bigcirc$) on [OH$^-$]. $1/\tau_1$ obtained at 275 nm, $1/\tau_2$ at 250 nm.

strictly to the **10** $\rightleftharpoons$ T$_{OH}^-$ equilibrium while $1/\tau_2$ represents slow conversion of T$_{OH}^-$ to T$_{OH}^\circ$, with **10** $\rightleftharpoons$ T$_{OH}^-$ acting as fast preequilibrium. $1/\tau_1$ and $1/\tau_2$ are thus given by eqs 3 and 4, respectively. The plot of $1/\tau_1$ vs [OH$^-$]

$$\frac{1}{\tau_1} = k_1^{OH}[OH^-] + k_{-1}^{H_2O} \tag{3}$$

$$\frac{1}{\tau_2} = \frac{K_1^{OH}[OH^-]}{1 + K_1^{OH}[OH^-]} k_2^{H_2O} \tag{4}$$

yields $k_1^{OH} = 5.0 \times 10^{-2}$ M^{-1} s^{-1}, $k_{-1}^{H_2O} = 8.1 \times 10^{-3}$ s^{-1}, and $K_1^{OH} = k_1^{OH}/k_{-1}^{H_2O} = 6.17$ M^{-1}, while the plot of $1/\tau_2$ vs [OH$^-$] yields $k_2^{H_2O} = 8.2 \times 10^{-3}$ s^{-1} and $K_1^{OH} = 4.04$ M^{-1}.

The following considerations suggest that the rate constants determined from Figure 1 are only approximate. (1) The agreement between the K_1^{OH} values obtained from $1/\tau_1$ and $1/\tau_2$ is only fair. (2) $k_{-1}^{H_2O}$ and $k_2^{H_2O}$ have nearly identical values; this violates the assumption that **10** $\rightleftharpoons$ T$_{OH}^-$ is a rapid equilibrium compared to the T$_{OH}^-$ $\rightarrow$ T$_{OH}^\circ$ step. (3) Except at very low base concentrations, $1/\tau_1$ and $1/\tau_2$ differ by less than 5-fold, indicating that the two steps are substantially coupled, as one would expect if $k_{-1}^{H_2O}$ and $k_2^{H_2O}$ had similar values. In such situations the best procedure for evaluating the rate constants is to plot the sum, $1/\tau_1 + 1/\tau_2$, and the product, $(1/\tau_1)(1/\tau_2)$, vs [OH$^-$] instead of $1/\tau_1$ and $1/\tau_2$ individually.[22] The appropriate expressions for the sum and the product

(23) We have refrained from including standard deviations for the various parameters determined from eqs 3–6 because they do not take into account the problems discussed in the preceding paragraphs and hence vastly underestimate the true error in the rate constants; this true error is unknown but probably at least ±25%; see Table 2.
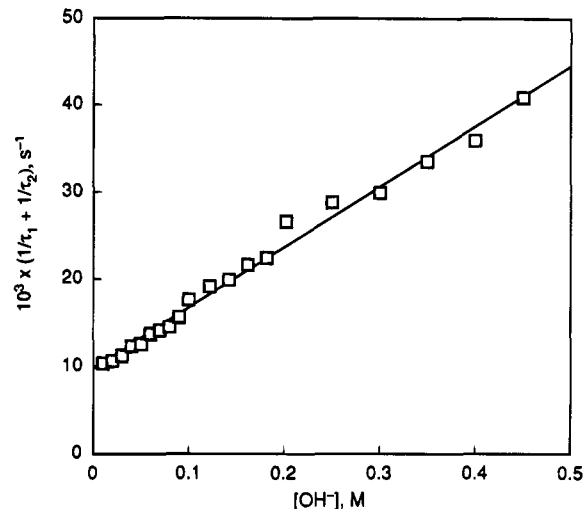

Figure 2. Data in strongly basic solution. Plot according to eq 5.
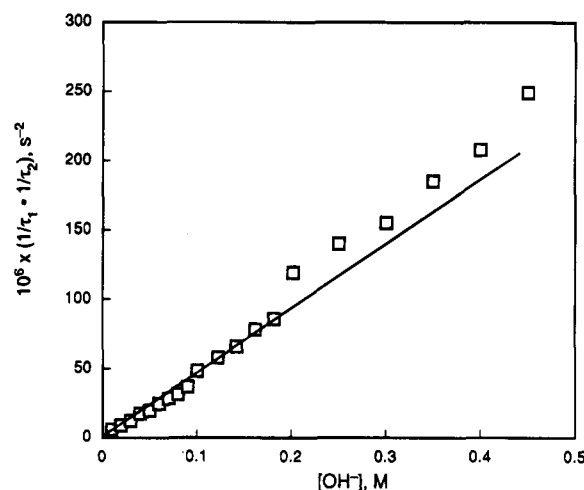

Figure 3. Data in strongly basic solution. Plot according to eq 6.

are given by eqs 5 and 6, respectively.

$$\frac{1}{\tau_1} + \frac{1}{\tau_2} = k_1^{OH}[OH^-] + k_{-1}^{H_2O} + k_2^{H_2O} \tag{5}$$

$$\frac{1}{\tau_1}\frac{1}{\tau_2} = k_1^{OH}k_2^{H_2O}[OH^-] \tag{6}$$

Plots according to eqs 5 and 6 are shown in Figures 2 and 3. The slight upward trend of the $(1/\tau_1)(1/\tau_2)$ plot at [KOH] > 0.2 M is most likely due to a salt effect; in calculating the slope of the line the points at the five highest concentrations were therefore omitted. Figure 2 yields $k_1^{OH} = 7.15 \times 10^{-2}$ M^{-1} s^{-1} and $k_{-1}^{H_2O} + k_2^{H_2O} = 8.5 \times 10^{-3}$ s^{-1} while from Figure 3 we obtain $k_1^{OH}k_2^{H_2O} = 3.5 \times 10^{-4}$ M^{-1} s^{-2}. This allows calculation of $k_2^{H_2O} = 4.9 \times 10^{-3}$ s^{-1} and $k_{-1}^{H_2O} = 3.6 \times 10^{-3}$ s^{-1}. k_1^{OH} from eq 5 is about 40% higher, while $k_{-1}^{H_2O}$ and $k_2^{H_2O}$ are both roughly 2-fold lower than those based on eqs 3 and 4; $K_1^{OH} = 19.9$ M^{-1} is about 3-fold higher than that obtained from $1/\tau_1$. In the following text, the values derived from eqs 5 and 6 will be adopted.[23]

Table 1. Hydrolysis of Benzylideneacetylacetone in HCl Solutions and Acetate Buffers[a]

buffer	[BH], M	[B$^-$], M	pH	$10^6 k_{obsd}$,[b] s^{-1}
HCl	0.01			0.99 ± 0.12
	0.005			0.81 ± 0.12
	0.001			0.75 ± 0.15
CH$_3$COOH	0.05	0.01	3.88	1.35 ± 0.05
	0.01	0.01	4.59	1.41 ± 0.06
	0.005	0.05	5.58	1.73 ± 0.02
	0.025	0.25	5.58	1.76 ± 0.03
	0.20	0.20	4.61	1.86^c

[a] In water at 25 °C, μ = 0.5 M (KCl). [b] Measured at 252 nm. [c] Reference 24.

Measurements in Acidic Solution. Calmon et al.[24] have determined the rate of hydrolysis of **10** in acetate and formate buffers at pH 3.33–4.95. They found that k_{obsd}, the pseudo-first-order rate constant, was independent of pH and buffer concentration and had a value between 1.79×10^{-6} and 1.95×10^{-6} s^{-1} at 25 °C and an ionic strength of 1 M. This process was attributed to rate-limiting water addition to **10**, i.e., $k_{obsd} = k_1^{H_2O}$.

We performed a few experiments in HCl solutions and acetate buffers that essentially confirmed Calmon's results, but also revealed a subtlety not seen under the conditions used in Calmon's study. Our results are summarized in Table 1. The k_{obsd} values in HCl solution are pH-independent and give an average of $(0.85 \pm 0.15) \times 10^{-6}$ s^{-1}. In the acetate buffers there is a slight non-linear increase in k_{obsd} with increasing buffer base concentration which levels off around 1.75×10^{-6} s^{-1}. This plateau value is very close to Calmon's at pH 4.61 (last entry in Table 1) and is representative of the nine acetate buffer experiments in Calmon's study.

The fact that k_{obsd} levels off indicates that the buffer catalysis cannot be attributed to a class n[25] general base-catalyzed water addition (k_1^B[B] in Scheme I); in fact, our results and those of Calmon show that the k_1^B[B] term is negligible.[26] The most reasonable interpretation of the buffer catalysis is that, in the absence of buffer, water addition ($k_1^{H_2O}$) to the substrate and carbon protonation of T_{OH}^- by the hydronium ion ($k_2^H a_{H^+}$ in Scheme 1) are co-rate limiting, because k_{-1}^H and k_2^H are of comparable magnitude. Hence, treating T_{OH}^- as a steady-state intermediate yields a k_{obsd} given by eq 7. In the presence
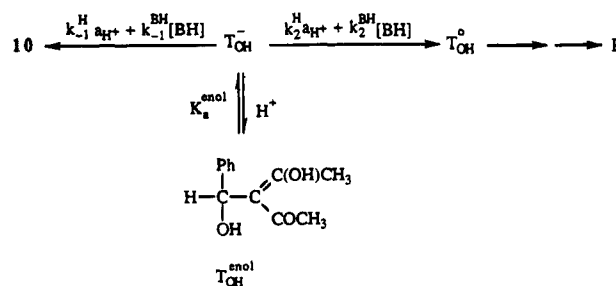
$$k_{obsd} = \frac{k_1^{H_2O} k_2^H}{k_{-1}^H + k_2^H} \qquad (7)$$

$$k_{obsd} = \frac{k_1^{H_2O}(k_2^H a_{H^+} + k_2^{BH}[BH])}{(k_{-1}^H + k_2^H) a_{H^+} + k_2^{BH}[BH]} \qquad (8)$$

of buffer eq 7 becomes eq 8 which, for high buffer concentrations (k_2^{BH}[BH] + $k_2^H a_{H^+} \gg k_{-1}^H a_{H^+}$) simplifies to eq 9. From k_{obsd} = $(0.85 \pm 0.10) \times 10^{-6}$ (eq 7) and k_{obsd} =

$$k_{obsd} = k_1^{H_2O} \qquad (9)$$

$(1.75 \pm 0.05) \times 10^{-6}$ (eq 9) one obtains k_2^H/k_{-1}^H = 0.94 ± 0.25.

Scheme 2

In conjunction with K_1^{OH} determined above, k_{-1}^H = 4.70×10^6 M^{-1} s^{-1} can now be calculated as k_{-1}^H = $k_1^{H_2O}/K_1^{H_2O}$ with $K_1^{H_2O}$ = $K_1^{OH} K_w$[27] = 3.72×10^{-13} M.

pH-Jump Experiments. 10 was allowed to react with 0.2 M KOH for about 2 min[29] to form T_{OH}^-. This solution was then subjected to pH-jumps by mixing it with HCl, acetic acid, or DABCO (1,4-diazobicyclo[2.2.2]-octane) buffers. The ensuing reactions are represented in Scheme 2. For pH-jumps into HCl solutions, we have $K_a^{enol} \ll a_{H^+}$, and Scheme 2 predicts a single kinetic process with a reciprocal relaxation time given by eq 10.

$$\frac{1}{\tau} = K_a^{enol}(k_{-1}^H + k_2^H) \qquad (10)$$

The results are in agreement with this expectation: pH 1.02, $1/\tau$ = 0.14 ± 0.04 s^{-1}; pH 1.26, $1/\tau$ = 0.11 ± 0.01 s^{-1}; pH 1.44, $1/\tau$ = 0.11 ± 0.02 s^{-1}; pH 1.74, $1/\tau$ = 0.11 ± 0.01 s^{-1}. With pK_a^{enol} = 7.75 (see below) and using the average value of 0.12 s^{-1} for $1/\tau$, we now obtain k_{-1}^H + k_2^H = 6.75×10^6 M^{-1} s^{-1}. In combination with the k_2^H/k_{-1}^H ratio of 0.94 (see above) this yields k_{-1}^H = 3.48×10^6 M^{-1} s^{-1} and k_2^H = 3.27×10^6 M^{-1} s^{-1}. The k_{-1}^H value obtained by this method is remarkably close to k_{-1}^H = 4.70×10^6 M^{-1} s^{-1} calculated on the basis of $k_1^{H_2O}$ and $K_1^{H_2O}$ (see above).

For pH-jumps into acetate buffers, $1/\tau$ was measured as function of acetate ion concentration at pH 3.56, 4.50, and 5.30. A representative plot is shown in Figure 4. The results are consistent with Scheme 2 for which $1/\tau$ is now given by eq 11 (K_a^{enol} is still $\ll a_{H^+}$ and k_{-1}^{BH} is

$$\frac{1}{\tau} = \frac{K_a^{enol}}{a_{H^+}}[(k_{-1}^H + k_2^H) a_{H^+} + (k_2^{BH}[BH])] =$$

$$K_a^{enol}(k_{-1}^H + k_2^H) + \frac{K_a^{enol}}{K_a^{BH}} k_2^{BH}[B] \qquad (11)$$

negligible). The slopes of the lines are, within experimental error, the same (19.2, 23.0, and 22.4 M^{-1} s^{-1} at pH 3.56, 4.50, and 5.30, respectively) and give an average value of 21.5 M^{-1} s^{-1}. They correspond to $K_a^{enol} k_2^{BH}/K_a^{BH}$; with p$K_a^{BH}$ = 4.59 and pK_a^{enol} = 7.75 (see below) we obtain k_2^{BH} = 3.1×10^4 M^{-1} s^{-1}. The intercept in the plots of $1/\tau$ vs [AcO$^-$] are too small for accurate determination at pH 4.50 and 5.30, but at pH 3.56 the intercept is seen to be approximately 0.11 s^{-1} (Figure 4), in excellent agreement with the HCl data.

(24) Calmon, M.; Arnaud-Lehujeur, B.; Calmon, J.-P. *Bull. Soc. Chim. Fr.* **1972**, 2314.

(25) (a) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425. (b) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.

(26) As stated in the introduction, the k$_1^B$[B] term is usually negligible at low buffer concentrations.[10–16]

(27) K_w = 1.87×10^{-14} M^2 at μ = 0.5 M.[28]

(28) Harned, H. S.; Owen, B. B. *The Physical Chemistry of Electrolyte Solutions*; Pergamon Press: Elmsford, NY, 1968; p 50.

(29) At longer times decomposition to benzaldehyde and acetylac-etonate ion becomes significant.
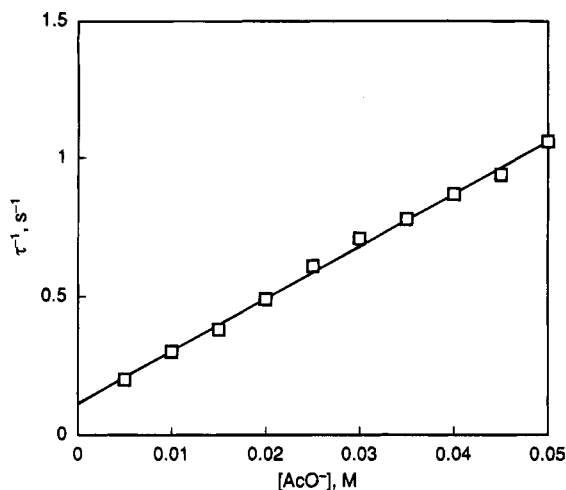
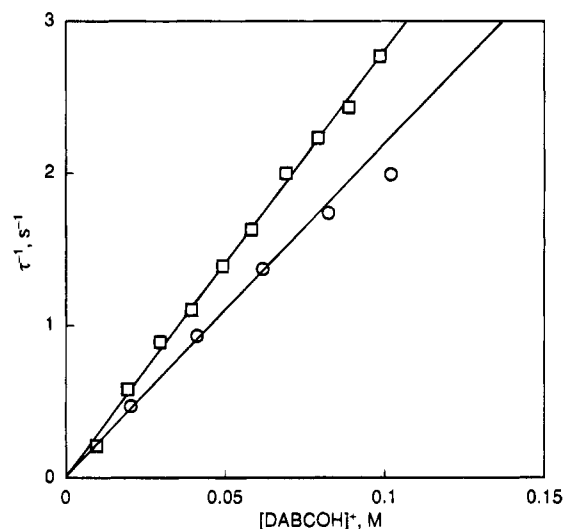**Figure 4.** Data from pH-jump experiments into acetate buffers. Plot of $1/\tau$ vs $[AcO^-]$ according to eq 11.

Figure 5. Data from pH-jump experiments into DABCO buffers. Plot of $1/\tau$ vs $[DABCOH^+]$ according to eq 12. ○: pH 8.39. □: 9.36.

The pH-jump experiments into DABCO buffers were conducted between pH 7.80 and 9.39. In one series of experiments, $1/\tau$ was determined as function of buffer concentration at constant pH. Figure 5 shows two representative plots of $1/\tau$ vs $[DABCOH^+]$. The plots have intercepts that are indistinguishable from zero, which implies that $(k_{-1}^H + k_2^H)a_{H^+} \ll k_2^{BH}[BH]$. At these pH values we can no longer assume that $K_a^{enol} \ll a_{H^+}$, and hence, $1/\tau$ is given by eq 12. The slopes of the plots at

$$\frac{1}{\tau} = \frac{K_a^{enol}}{K_a^{enol} + a_{H^+}} k_2^B[BH] \qquad (12)$$

pH 8.39 (Figure 5), 8.73 (plot not shown), 9.04 (plot not shown), and 9.33 (Figure 5) are only slightly pH-dependent, indicating that $K_a^{enol} > a_{H^+}$ in all experiments. By plotting the reciprocal slopes vs a_{H^+} according to eq 13

$$\frac{1}{slope} = \frac{1}{k_2^{BH}} + \frac{a_{H^+}}{K_a^{enol}k_2^{BH}} \qquad (13)$$

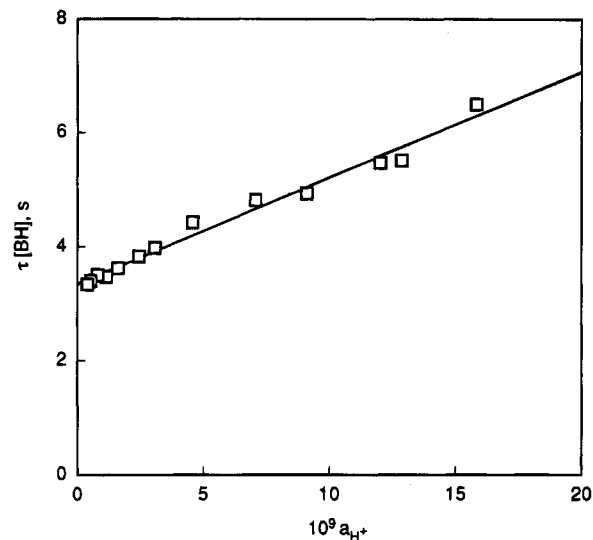(plot not shown) one obtains $k_2^{BH} = 31.1 \pm 1.6$ M^{-1} s^{-1}; since the dependence of slope^{-1} on a_{H^+} is very weak, only

Figure 6. Data from pH-jump experiments into DABCO buffers. Plot according to eq 14.

a very approximate value for pK_a^{enol} ($\sim$8) can be calculated from these data. A more accurate pK_a^{enol} was obtained from a second series of pH-jump experiments in which the concentration of DABCOH$^+$ was held constant at 0.10 M while the pH was varied from 7.80 to 9.39. These data can be described by eq 14. A plot

$$\tau[BH] = \frac{\tau}{10} = \frac{1}{k_2^{BH}} + \frac{a_{H^+}}{K_a^{enol}k_2^{BH}} \qquad (14)$$

according to eq 14 is shown in Figure 6. It provides $k_2^{BH} = 29.9 \pm 0.5$ M^{-1} s^{-1}, in excellent agreement with the result from eq 13, and $pK_a^{enol} = 7.75 \pm 0.02$.

Discussion

Mechanism. The mechanism shown in Scheme 1 is well accepted for the hydrolysis of substrates of the general structure $1^{1,2,9-16}$ and also specifically for the hydrolysis of 10.[17,18,24] Our results indicate that in a strongly basic solution of 10, T_{OH}^- accumulates to a detectable concentration. This gives rise to two measurable kinetic processes ($1/\tau_1$ and $1/\tau_2$).

To a good approximation, $1/\tau_1$ (eq 3) represents reversible formation of T_{OH}^- by OH$^-$ addition to 10, while $1/\tau_2$ (eq 4) refers to conversion of T_{OH}^- to benzaldehyde and acetylacetonate ion; the fact that there is some coupling between these two processes that necessitates the use of eqs 5 and 6 to determine the rate constants more accurately does not alter this conclusion in a major way. The rate-limiting step for the conversion of T_{OH}^- to products is carbon protonation of T_{OH}^-. This contention is supported by two lines of evidence. (1) Our pH-jump experiments show that in DABCO as well as in acetate buffers the rate of conversion of T_{OH}^- to products is dominated by the buffer terms (k_2^{BH} in Scheme 1 or Scheme 2), which is indicative of carbon protonation.[30] (2) In strongly basic solution Calmon and Calmon[17] have shown that conversion of T_{OH}^- to products is 7-fold slower in D$_2$O than in H$_2$O, consistent with a primary kinetic isotope effect[34,35] on carbon protonation of T_{OH}^- by water ($k_2^{H_2O}$ in Scheme 1 or eq 2).

Alternative interpretations of $1/\tau_2$ that are, in principle, consistent with its pH-dependence are rate-limiting

Table 2. Summary of Rate and Equilibrium Constants for the Hydrolysis of Benzylideneacetylacetone in Water at 25 °C, $\mu = 0.5$ M. Comparison with Benzylidenemalondialdehyde and Benzylidene Meldrum's Acid

parameter	PhCH=C(COCH$_3$)$_2$ **10**	PhCH=C(CHO)$_2$[a] **9**	PhCH=C(COO)$_2$(CH$_3$)$_2$[b] **8**
k_1^{OH}, M^{-1} s^{-1}	7.15×10^{-2} [c]	223	745
$k_{-1}^{H_2O}$, s^{-1}	3.6×10^{-3} [c]	2.57×10^{-7}	3.37×10^{-6}
$K_1^{OH} = k_1^{OH}/k_{-1}^{H_2O}$, M^{-1}	19.9^d	8.66×10^8	2.00×10^8
$K_1^{H_2O} = K_1^{OH}K_w^j$	3.72×10^{-13} [d]	1.62×10^{-5}	3.75×10^{-6}
$k_1^{H_2O}$, s^{-1}	1.75×10^{-6} [c]	0.068	0.55
k_{-1}^{H}, M^{-1} s^{-1}	4.70×10^6 [c]	4.2×10^3	1.47×10^5
$pK_a^{CH_2XY}$	9.01^e	$\ll 4.43^f$	5.43^g
$K_1^{R_2NH}K_a^{\pm k}$	1.73×10^{-12} [h]		4.77×10^{-5} [i]

[a] Reference 16. [b] Reference 15. [c] Estimated error ±25%. [d] Estimated error ±40%. [e] Reference 41. [f] Reference 42. [g] Reference 43. [h] Reference 19. [i] Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329. [j] $K_w = 1.87 \times 10^{-14}$ M^2, ref 28. [k] Refers to formation of T_A^- by amine addition, see text.

collapse of T_O^- (eq 15;[36] eq 16 for $K_1^{OH}[OH^-] \gg 1$), and

$$\frac{1}{\tau_2} = \frac{K_1^{OH}K_2^{H_2O}K_3^{OH}k_4[OH^-]}{1 + K_1^{OH}[OH^-]} \quad (15)$$

$$\frac{1}{\tau_2} = K_2^{H_2O}K_3^{OH}k_4 \quad (16)$$

rate-limiting oxygen deprotonation of T_{OH}^- by OH$^-$ (eq 17; eq 18 for $K_1^{OH}[OH^-] \gg 1$). However, the first alter-

$$\frac{1}{\tau_2} = \frac{K_1^{OH}K_2^{H_2O}k_3^{OH}[OH^-]}{1 + K_1^{OH}[OH^-]} \quad (17)$$

$$\frac{1}{\tau_2} = K_2^{H_2O}k_3^{OH} \quad (18)$$

native is inconsistent with buffer catalysis and the large kinetic isotope effect. The second alternative is also inconsistent with the isotope effect, because k_3^{OH} refers to an oxygen to oxygen proton transfer that is expected to be diffusion controlled.[37] Furthermore, if the acetic acid- and DABCOH$^+$-catalyzed conversion of T_{OH}^- to products is interpreted in terms of rate-limiting oxygen deprotonation of T_{OH}^- by DABCO and AcO$^-$, respectively, one calculates a $k_3^{DABCO}/k_3^{AcO^-}$ ratio of 19.9 which is much smaller than the ratio of ~3.55 × 10^4 expected for a thermodynamically unfavorable diffusion-controlled proton transfer.[38] Thirdly, the following consideration shows that the numerical values obtained for $1/\tau_2$ are much too low to be consistent with eq 18. Assuming that the pK_a of T_{OH}^- (loss of carbon proton) is somewhat lower than that of acetylacetone, 9.03, say by one unit (for justification see below), this makes $K_2^{H_2O} \approx 10^{-6}$ M. With a k_3^{OH} values of $\geq 10^9$ M^{-1} s^{-1}[37] this yields $K_2^{H_2O}K_3^{OH} \geq 10^3$ which is at least 5 orders of magnitude higher than the experimental $1/\tau_2$ values at high [OH$^-$].

Calmon and Calmon[17] originally proposed rate-limiting collapse of T_O^- (eqs 15 and 16) to account for the observed rate law but, in order to explain the large kinetic isotope effect, modified their proposal and postulated rate-limiting collapse of T_{OH}^- concerted with oxygen deprotonation by OH$^-$ (transition state 11). However, since oxygen deprotonation of T_{OH}^0 by OH$^-$ must be a thermodynamically favored diffusion-controlled process,

the proposed mechanism violates Jenck's libido rule[39,40] and is therefore untenable.

In moderately acidic solution, the pH and buffer independence of k_{obsd} at high buffer concentrations is consistent with rate-limiting $k_1^{H_2O}$, as already proposed by Calmon et al.[24] However, in the absence of buffer or at very low buffer concentrations, carbon protonation of T_{OH}^- is co-rate limiting with the $k_1^{H_2O}$ step, as manifested by somewhat lower rate constants and a leveling off of k_{obsd} at high buffer concentrations.

Structure–Reactivity Relationships. A. Nucleophilic Addition. Table 2 summarizes the rate and equilibrium constants determined in this work along with the corresponding parameters for benzylidenemalondialdehyde (9) and benzylidene Meldrum's acid (8). Among the three compounds, 10 is by far the least electrophilic. This is not surprising since the acidity of CH$_2$XY which should be an approximate measure of the activating strength of the XY group is much lower for CH$_2$(COCH$_3$)$_2$ (pK_a 9.03)[41] than for CH$_2$(CHO)$_2$ (p$K_a \ll 4.39$)[42] and CH$_2$-(COO)$_2$C(CH$_3$)$_2$ (pK_a 5.43).[43] In fact, the Lewis acidity of 10 is more strongly depressed than the comparison of the

(30) Rates of proton transfer at carbon involving H$_3$O$^+$, H$_2$O, or OH$^-$ are typically strongly depressed compared to what they would be if they followed the Brønsted plots defined by buffer acids or bases.[31] This means that in buffer solutions at pH values in the midrange of the scale the rates are usually dominated by the buffer contribution, especially if the Brønsted coefficients are in the midrange, e.g., $k_2^{BH}[BH] \gg k_2^{H_2O} + k_2^{H}a_{H^+}$ in our system. When buffer catalysis is due to processes other than proton transfer at carbon the relative contribution of the buffer to the overall rate is typically much smaller.[25a,31,32]

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

(32) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969; p 229.

(33) Keeffe, J. R.; Kresge, A. J. In *Investigation of Rates and Mechanisms of Reactions, Part I*; Bernasconi, C. F., Ed.; Wiley-Interscience: New York, 1986; p 747.

(34) More O'Ferrall, R. A. In *Proton Transfer Reactions*; Caldin, E., Gold, V., Eds.; Wiley & Sons: New York, 1975; p 201.

(35) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980; p 152.

(36) $K_2^{H_2O} = k_2^{H_2O}/k_{-2}^{OH}$; $K_3^{OH} = k_3^{OH}/k_{-3}^{H_2O}$.

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

(38) For an unfavorable diffusion-controlled proton transfer $k_3^{DABCO}/k_3^{AcO^-}$ should be approximately equal to $K_a^{AcOH}/K_a^{DABCOH^+}$.[37]

(39) The rule states that "concerted general acid–base catalysis of complex reactions in aqueous solution can occur only (a) at sites that undergo a large change in pK_a in the course of the reaction and (b) when this change in pK_a converts an unfavorable to a favorable proton transfer with respect to the catalyst, i.e., the pK_a of the catalyst is intermediate between the initial and final pK_a values of the substrate site."[40] It is clear that transition state 11 violates part b of the rule.

(40) Jencks, W. P. *J. Am. Chem. Soc.* **1972**, *94*, 4731.

(41) Calmon, J.; Maroni, P. *Bull. Soc. Chim. Fr.* **1965**, 2525.

(42) The pK_a of the enol form of CH$_2$(CHO)$_2$ is 4.33 in 50% Me$_2$SO–50% water.[5] Since malonaldehyde is virtually 100% in the enol form,[44] p$K_a^{CH_2XY}$ must be $\ll 4.33$.[33]

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

$pK_a^{CH_2XY}$ values suggests: K_1^{OH} for **10** is about 10^7-fold lower than for **8** and about 4×10^7-fold lower than for **9**, while the acidity of acetylacetone is only about 4×10^3-fold lower than that of Meldrum's acid; no direct comparison is available with malondialdehyde since it exists virtually exclusively in the enol form.[44]

The additional loss of Lewis acidity of **10** relative to **8** and **9** may be attributed to steric effects. One problem is that the PhCH(OH) moiety interferes with the coplanarity of the carbonyl groups of the acetylacetonate anion in T_{OH}^-, which prevents full resonance development; another is F-strain.[45] T_{OH}^- derived from **9** should be much less subject to either steric effect while the steric effect that interferes with resonance in T_{OH}^- derived from **8** should be relatively inconsequential because resonance plays a minor role in benzylidene Meldrum's acid anions.[46,47] The difference in the equilibrium constants for piperidine addition to **10** vs **8** ($K_1 K_a^\pm$ for formation of T_A^-)[48] ($\sim 3 \times 10^7$) is somewhat larger than for OH^--addition ($\sim 10^7$). This is consistent with a still larger steric effect, due to the larger size of the PhCH(NR_2) moiety.
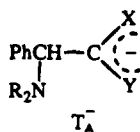
Turning to the rate constants for OH^- addition, k_1^{OH} for **10** is much lower than for **8** or **9**, as expected based on the much smaller K_1^{OH} value. An interesting question is whether the low k_1^{OH} and $k_1^{H_2O}$ values for **10** can be entirely accounted for by the smaller thermodynamic driving force or whether there is a kinetic effect contributing in the form of a reduced intrinsic rate constant (k_o).[8] This question is also relevant with respect to the abnormally low k_o value for amine addition to **10**[19] mentioned in the Introduction.

A quantitative answer to the above questions cannot be given because, in contrast to the reactions with amines, k_o for OH^- or water addition can only be estimated. Nevertheless, a *qualitative* answer is possible. Approximate intrinsic barriers, $\Delta G_o^\ddagger$ may be calculated by solving the Marcus[49] equation, eq 19, for $\Delta G_o^\ddagger$; $\Delta G^\ddagger$ is

$$\Delta G^\ddagger = \Delta G_o^\ddagger + 0.5\Delta G^o + \frac{(\Delta G^o)^2}{16\Delta G_o^\ddagger} \quad (19)$$

the free energy of activation that corresponds to k_1^{OH} or $k_1^{H_2O}$, respectively, while ΔG^o is the free energy that corresponds to $K_1^{H_2O}$ or K_1^{OH}, respectively. The log k_o values obtained by applying the Eyring equation to the calculated $\Delta G_o^\ddagger$ values are summarized in Table 3. The log k_o values for water and OH^- addition to **3** and **6** are

(44) (a) Hüttel, R. *Chem. Ber.* **1941**, *74*, 1825. (b) Bothner-By, A. A.; Harris, R. K. *J. Org. Chem.* **1965**, *30*, 254. (c) Dersch, R.; Reichardt, C. *Synthesis* **1980**, 940.

(45) (a) Brown, H. C.; Taylor, M. D.; Gerstein, M.; Bartholomay, H. *J. Am. Chem. Soc.* **1944**, *66*, 431. (b) Brown, H. C. *Science* **1946**, *103*, 385.

(46) Arnett, E. M.; Maroldo, S. G.; Schilling, S. L.; Harrelson, J. A. *J. Am. Chem. Soc.* **1984**, *106*, 6759.

(47) (a) Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 1870. (b) Wilberg, K. B.; Laidig, K. E. *Ibid.* **1988**, *110*, 1872.

(48) $K_1 K_a^\pm$ refers to the reaction $PhCH{=}CXY + R_2NH \overset{K_1 K_a^\pm}{\rightleftharpoons} T_A^- + H^+$.

(49) Marcus, R. A. *J. Chem. Phys.* **1965**, *43*, 679.

Table 3. Intrinsic Rate Constants Expressed as log k_o for Nucleophilic Addition of OH^-, H_2O, and Secondary Alicyclic Amines to Various Olefins in Water at 25 °C

PhCH=CXY	log k_o^{OH}	log $k_o^{H_2O}$	log $k_o^{R_2NH a}$
Dicarbonyl Activated			
PhCH=C(COCH₃)₂ (**10**)	-1.81^b	1.35^b	0.30^c
PhCH=C(CHO)₂ (**9**)	-1.79^d	1.34^d	3.60^e
PhCH=C(COO)₂C(CH₃)₂ (**8**)	-0.98^f	2.63^f	4.10^g
Others			
PhCH=C(CN)₂ (**3**)	0.96^h	2.42^h	4.94^i
ArCH=CHNO₂ (**6**)	$-3.14^{j,k}$	$-0.63^{j,k}$	2.55^l

^{a} R_2NH = piperidine and morpholine in 50% Me_2SO–50% water at 20 °C. ^{b} This work. ^{c} Reference 19. ^{d} Based on data from ref 16. ^{e} Reference 5. ^{f} Based on data from ref 15. ^{g} Bernasconi, C. F.; Panda, M. *J. Org. Chem.* **1987**, *52*, 3042. ^{h} Based on data from ref 10. ^{i} Bernasconi, C. F.; Killon, R. B. *J. Org. Chem.* **1989**, *54*, 2878. ^{j} Ar = 3,4-methylenedioxyphenyl. ^{k} Based on data from: Crowell, T. K.; Kim, T.-R. *J. Am. Chem. Soc.* **1973**, *95*, 6781. ^{l} Ar = phenyl: Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *108*, 4541.

also reported in Table 3, as are the intrinsic rate constants for nucleophilic addition of piperidine and morpholine to **3, 6, 8, 9,** and **10**. The latter were obtained in 50% Me_2SO–50% water at 20 °C as log $k_o^{R_2NH}$ = log $k_1^{R_2NH} - \beta_{nuc}^n$ log $K_1^{R_2NH}$, with β_{nuc}^n being the experimental normalized Brønsted coefficient.[21a,c]

The results in Table 3 can be summarized as follows. (1) With respect to OH^- addition, k_o^{OH} is highest for the dicyano derivative **3**, lowest for the nitroolefin **6**, and intermediate for the dicarbonyl-activated substrates **8–10**. This order reflects the relative π-acceptor abilities of the activating groups (strongest for nitro, intermediate for dicarbonyl, and weakest for dicyano) in accordance with the PNS.[20,21] Within the family of dicarbonyl activated olefins, k_o^{OH} for **9** and **10** are essentially the same but lower than for **8** by approximately 1 order of magnitude. The fact that log k_o^{OH} for **9** is lower than for **8** was already commented upon earlier;[16] it can be explained in terms of a greater resonance contribution to the stability of T_{OH}^- derived from **9**, which depresses log k_o^{OH}. The similarity in the log k_o^{OH} values for **10** and **9** suggests that there may be a cancellation of two opposing factors. One is the steric hindrance of the π-overlap in T_{OH}^- derived from **10** inferred from the low K_1^{OH} value. This should reduce the k_o^{OH}-lowering resonance PNS effect and hence increase k_o^{OH} relative to that of **9**. The other factor is the large F-strain in T_{OH}^- derived from **10**. If this strain is strongly developed in the transition state, it should lower k_o.

(2) The log $k_o^{H_2O}$ values follow the same pattern as log k_o^{OH} except that their absolute values are all substantially higher than log k_o^{OH} for all five compounds. One likely reason for the difference between $k_o^{H_2O}$ and k_o^{OH} is that k_o^{OH} is depressed by the strong solvation of OH^-;[31,50,51] another is enhancement of $k_o^{H_2O}$ for the water reaction with **6, 8, 9,** and **10**, due to transition-state stabilization by intramolecular hydrogen bonding to a carbonyl or nitro oxygen,[11] e.g., **13**. Support for this view comes from the fact that Δlog k_o = log $k_o^{H_2O}$ – log k_o^{OH} is substantially larger for these compounds (Δlog k_o 2.5–3.5) than for benzylidenemalononitrile (Δlog k_o = 1.46) where no hydrogen bonding is possible.

(50) (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Pohl, E. R.; Wu, D.; Hupe, D. J. *Ibid.* **1980**, *102*, 2759.

(51) Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc.* **1982**, *104*, 7045.
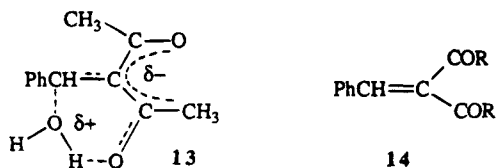
(3) The *relative* intrinsic reactivities toward piperidine and morpholine ($k_o^{R_2NH}$) are approximately the same as toward OH$^-$ (k_o^{OH}) for **3, 6, 8,** and **9,** but log $k_o^{R_2NH}$ for **10** is abnormally low: it is about 3 orders of magnitude lower than for **9** (while **9** and **10** have about equal log k_o^{OH} values) and even substantially lower than for **6.** The same conclusion was reached based on a correlation of $k_o^{R_2NH}$ for amine addition to a series of olefins of the type **1,** with intrinsic rate constants for the deprotonation of carbon acids of the type CH$_2$XY by the same amines.[19,21a,c] $k_o^{R_2NH}$ for the reaction of **10**[19] as well as analogs such as **14** with R = CH$_3$CH$_2$, (CH$_3$)$_2$CH, and Ph[4] showed a negative deviation of about 2.5 log units from the correlation.[4,19,21] The results of the present study thus provide independent confirmation of our earlier inference that $k_o^{R_2NH}$ for **10** is abnormally low. As discussed in the Introduction, this depression of $k_o^{R_2NH}$ has been attributed to a combination of late development of intramolecular hydrogen bonding and early development of steric strain in the transition state leading to **12.**[19] With respect to intramolecular hydrogen bonding, it is important to understand the contrast between its k_o-lowering effect in the amine reaction and its k_o-enhancing effect on the water reaction. In both reactions there is stabilization of the transition state. In the water reaction , this is the only effect since in the product (T$_{OH}^-$) the proton responsible for hydrogen bonding in the transition state (**13**) is no longer present.[52] In the amine reaction there is also stabilization of the product (**12**) which completely overshadows the stabilization of the transition state and therefore leads to a lower k_o.

B. Carbon Protonation of T$_{OH}^-$ and pK_a^{enol}. Our results are reported in Table 4 along with rate constants for the protonation of acetylacetonate ion (acac$^-$) by water, H$_3$O$^+$, and acetic acid.[53] All rate constants are somewhat lower than for the protonation of acac$^-$ despite the higher temperature.[54] This is reasonable because the basicity of T$_{OH}^-$ is expected to be lower than that of

Table 4. Rate Constants, k_2^{BH}, for the Carbon Protonation of T$_{OH}^-$ by Various Acids and pK_a^{enol} of T$_{OH}^{enol}$

BH	T$_{OH}^-$ (25 °C)[c]	acac$^-$ (20 °C)[c]
H$_3$O^{+a}	3.0×10^6	1.42×10^7
AcOH^a	3.1×10^4	7.87×10^4
DABCOH^{+a}	31.1	
H$_2$O^b	4.9×10^{-3}	1.26×10^{-1}
pK_a^{enol}	7.75	8.37

^{a} In units of M^{-1} s^{-1}. ^{b} In units of s^{-1}. ^{c} $\mu = 0.5$ M (KCl), ref 53.

acac$^-$, due to the electron-withdrawing effect of the PhCH(OH) moiety. In the case of T$_{OH}^-$ derived from **8,** the pK_a^{CH} of T$_{OH}^-$ is 1.9 units lower than that of Meldrum's acid,[15] while the pK_a^{CH} of T$_{OH}^-$ derived from **4** is 0.5 units lower than that of 1,3-indandione.[11] The electron-withdrawing effect of the PhCH(OH) moiety on T$_{OH}^-$ derived from **10** can be seen indirectly in the pK_a of T$_{OH}^{enol}$ which is 0.6 units lower than that of the enol form of acac.[53] Apparently, this electron-withdrawing effect outweighs the reduction in the resonance stabilization of T$_{OH}^-$ caused by the steric effect of the PhCH(OH) moiety.

Experimental Section

Materials. Benzylideneacetylacetone was available from a previous study.[19] Acetylacetone and benzaldehyde were distilled under dry nitrogen before use. DABCO was recrystallized from hexanes. Reagent grade acetic acid was used without further purification. KOH and HCl were "dilut it" from Baker Analytical.

pH Measurements. All pH measurements were made at 25 °C using an Orion 611 Research pH meter equipped with a Corning AgCl (No. 476022) and Beckman D-8U glass electrode. For the stopped-flow pH-jump experiments the pH was measured in mock mixing solutions.

Kinetic Measurements. Most kinetic experiments in strongly basic solutions were monitored in a Perkin-Elmer 559A UV–vis spectrophotometer, although a few runs were conducted in a Durrum D-110 stopped-flow spectrophotometer. Typically, a substrate concentration of 5×10^{-5} M was used. The reaction was followed at 270 or 275 nm for $1/\tau_1$ and at 250 nm for $1/\tau_2$. All the pH-jump experiments were carried out in the stopped-flow apparatus and monitored at 295–300 nm (DABCO) or 270–275 nm (AcOH). The very slow reactions of **10** in HCl and acetic acid buffers were run in thermostated volumetric flasks with absorbance readings taken every 24 to 48 h for 15–30 days, corresponding to about 2.5–5 half-lives. k_{obsd} for these reactions was evaluated by means of a curve fit computer program that does not require the infinity value as input parameter.

(52) As mentioned in the Introduction, since T$_{OH}^-$ lacks the relatively acidic NH$^+$ proton and the positive charge of **12,** intramolecular hydrogen bonding is expected to be too weak to noticeably affect k_o for OH$^-$ addition to **10.**

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

(54) Data obtained at 27.5 °C at $\mu = 0.1$ M yielded very similar rate constants,[55] suggesting that the temperature effect is quite small or compensated for by the difference in ionic strength.

(55) Ahrens, M.-L.; Eigen, M.; Kruse, W.; Maass, G. *Ber. Bunsenges* **1970,** *74,* 380.