The data were adjusted for a 3% decrease in intensity over the course of data acquisition. Lorentzian and polarization corrections as well as an empirical absorption correction based on ψ scan data were applied.

The structure was solved with direct methods (SHELXS). The asymmetric unit consists of one cis isomer and one trans isomer of **6a** in general positions. Anisotropic refinement was carried out by full-matrix least squares on F. Neutral atom scattering factors were obtained from the *International Tables for X-ray Crystallography*, Vol. IV. Non-hydrogen atoms were refined anisotropically, and the hydrogens were refined isotropically for a total of 465 parameters. The refinement converged at $R = 0.051$, $R_w = 0.038$, and EOF = 1.28.

Acknowledgment. We thank J. E. Feaster, L. Lardear, and W. Marshall for expert technical assistance. We also thank J. Lazar for obtaining HRMS spectra, R. S. McLean for magnetic susceptibility data, E. Conaway for ^{31}P and ^{19}F NMR data, and W. Barney for EPR spectra. We are grateful to Dr. M. D. Ward for performing electrochemical experiments, Dr. P. J. Krusic for simulating the EPR spectrum of **12**, and Drs. A. J. Arduengo, III, and B. E. Smart for helpful discussions.

Supplementary Material Available: Tables of final positional and isotropic thermal parameters, anisotropic thermal parameters, complete interatomic bond distances, and complete intramolecular bond angles for **2b**, **3d**, **5**, and **6a**, additional ORTEP plots for **2b**, **3b**, and **5**, and packing diagrams for **2b**, **5**, and **6a** (23 pages); tables of observed and calculated structure factors for **2b**, **3d**, **5**, and **6a** (31 pages). Ordering information is given on any current masthead page.

Kinetics of Amine Addition to Benzylidene-1,3-indandione and Other Vinylic β-Diketones. Effect of Cyclic Structure and Steric Strain on Intrinsic Rate Constants

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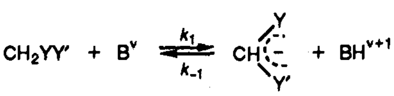
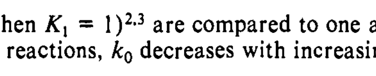
Abstract: The kinetics of the reactions of benzylidene-1,3-indandione (**4**) with piperidine, morpholine, *n*-butylamine, 2-methoxyethylamine, glycinamide, and cyanomethylamine and the reactions of benzylidene-3,5-heptanedione (**5**), benzylidene-2,6-dimethyl-3,5-heptanedione (**6**), and benzylidenedibenzoylmethane (**7**) with piperidine and morpholine have been measured in 50% Me_2SO–50% water (v/v) at 20 °C and 0.5 M ionic strength. The reactions lead, in all cases, to the reversible formation of the zwitterionic adduct $PhCH(RR'NH^+)C(COX)_2^-$ ($T_A^\pm$) that is in fast equilibrium with its anion $PhCH(RR'N)C(COX)_2^-$(T_A^-). Rate constants for nucleophilic addition (k_1) and its reverse (k_{-1}) as well as the pK_a of $T_A^\pm$ were determined for all reactions. The intrinsic rate constant ($k_0 = k_1 = k_{-1}$ when $K_1 = 1$) for amine addition to **4** is abnormally high, whereas k_0 for the reactions of **5**–**7** are abnormally low and similar to k_0 in magnitude for amine addition to benzylideneacetylacetone reported previously. The terms "abnormally high" and "abnormally low" refer to positive and negative deviations, respectively, from a plot of log k_0 for amine addition to a series of electrophilic olefins of the type PhCH═CYY′ vs log k_0 for deprotonation of carbon acids of the type CH_2YY'. The high k_0 for the reaction of **4** is attributed to its cyclic structure, which assures that the π-overlap required for the stabilization of the adduct is strongly developed in the transition state. The low k_0 values for the reactions of **5**–**7** arise from intramolecular hydrogen bonding, which is strong in $T_A^\pm$ but poorly developed in the transition state, and from steric strain in the adduct, which is strongly developed in the transition state. All these effects can be viewed as manifestations of the principle of nonperfect synchronization (PNS).

Previous work has shown that the rates of reversible nucleophilic addition to electrophilic olefins (eq 1) are governed by factors similar to those that govern the rates of deprotonation of carbon acids (eq 2).[1] This becomes especially apparent when, for a given YY′, the *intrinsic* rate constants (k_0) for reactions 1 and 2 ($k_0 = k_1 = k_{-1}$ when $K_1 = 1$)[2,3] are compared to one another. For both types of reactions, k_0 decreases with increasing resonance stabilization of the carbanionic product, i.e., in the order CN, CN ≫ $(COO)_2C(CH_3)_2$[5a] ≫ CN, C_6H_4-4-NO_2 ~ C_4Cl_4[5b] > CN, C_6H_3-2,4-$(NO_2)_2$ > H, NO_2 > C_6H_5, NO_2.



$$PhCH{=}CYY' + Nu^{\nu} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} PhCH(Nu^{\nu+1})\text{—}C^{-}YY' \qquad (1)$$



$$CH_2YY' + B^{\nu} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH^{-}YY' + BH^{\nu+1} \qquad (2)$$

In fact, a plot of log k_0 for piperidine and morpholine addition to PhCH═CYY′ (log $(k_0)_N$) in 50% Me_2SO–50% water vs log k_0 for deprotonation of CH_2YY' by piperidine and morpholine (log $(k_0)_P$) in the same solvent is well-approximated by a straight line of slope 0.46 ± 0.07 (Figure 1). The decrease in $(k_0)_P$ and $(k_0)_N$ with increasing resonance in the carbanion has been interpreted as being primarily a manifestation of the principle of nonperfect synchronization (PNS)[1,6] and linked to imbalanced transition states in which the development of resonance lags behind charge transfer or bond formation. According to the PNS, a product stabilizing factor (in this case, resonance) that develops late along the reaction coordinate always lowers k_0.[7]

Figure 1 shows one strongly deviant point: $(k_0)_N$ for benzylideneacetylacetone (**1**)[8] is about 2.5 log units smaller than ex-

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(1) (a) Bernasconi. C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi. C. F. *Tetrahedron* **1989**, *45*, 4017.

(2) For proton transfers, statistical factors are usually included and log $(k_0)_P$ is defined as log (k_1/q) when log K_1 + log (p/q) = 0, where p is the number of protons on $BH^{\nu+1}$ and q is the number of equivalent basic sites on B^{ν}.

(3) Regarding potential problems with the definition of k_0 for an addition reaction due to different units for k_1 and k_{-1}. see ref 4.

(4) Berrnasconi, C. F. *Adv. Phys. Org. Chem.* **1991**, *27*, in press.

(5) (a) $CH_2(COO)_2C(CH_3)_2$ is Meldrum's acid. (b) $CH_2C_4Cl_4$ is 1,2,3,4-tetrachloro-1,3-cyclopentadiene.

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

(7) A corollary to the original formulation of the PNS is that a product-stabilizing factor that develops early increases k_0. Alternatively, a product-*de*stabilizing factor that develops early decreases k_0; one that develops late increases k_0.

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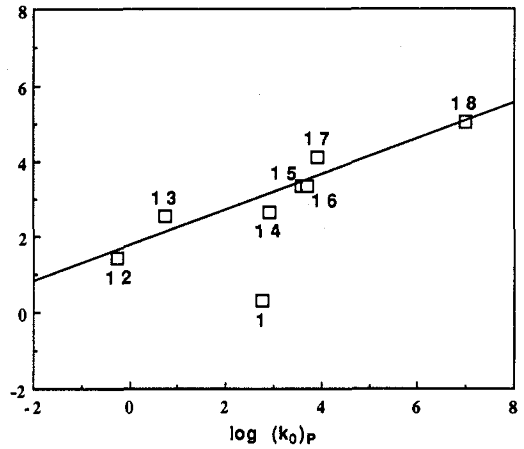
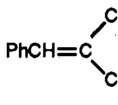


Figure 1. Correlation of log $(k_0)_N$ for nucleophilic addition of piperidine/morpholine to PhCH=CYY′ with log $(k_0)_P$ for deprotonation of CH_2YY' by piperidine/morpholine in 50% Me_2SO–50% water at 20 °C: **1** YY′ = $(COCH_3)_2$; **12** (Ph, NO_2); **13** (H, NO_2); **14** (CN, 2,4-$(NO_2)_2$–C_6H_3); **15** (CN, 4-NO_2–C_6H_4); **16** (C_4Cl_4), 1,2,3,4-tetrachlorocyclopentadiene;[5b] **17** $(COO)_2C(CH_3)_2$, Meldrum's acid;[5a] **18** $(CN)_2$. Data taken from ref 1b.

pected based on $(k_0)_P$ for the deprotonation of acetylacetone. This deviation has been attributed to a combination of two factors.[9]



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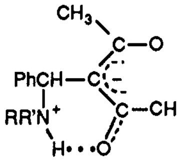

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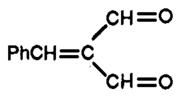

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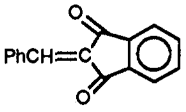


4

The first is that the zwitterionic product of the reaction is strongly stabilized by intramolecular hydrogen bonding (**2**), but in the transition state this hydrogen bonding is too weak to produce a rate enhancement commensurate with the enhanced equilibrium constant. This produces a decrease in k_0.

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 again is a depression of k_0. Both of these effects can be viewed as further manifestations of the PNS.[1,6,7]

It should be noted that there are other points that deviate negatively from the least-squares line in Figure 1. These relatively small negative deviations (as well as the two small positive deviations) might be dismissed as random scatter. However, it is noteworthy that all the points that deviate negatively refer to olefins for which a certain degree of steric hindrance in the adduct is expected and evidenced in depressed equilibrium constants,[8,11,19a] particularly for the most strongly deviating PhCH=C(CN)C_6H_3-2,4-$(NO_2)_2$. This suggests that the negative deviations are not random but due to this steric factor, except that the effects are much smaller than for benzylideneacetylacetone, and not augmented by the k_0-lowering hydrogen-bonding factor.

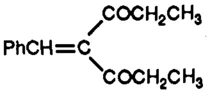
The purpose of the present paper is to further explore the structure–reactivity behavior of olefins activated by keto groups. This is of particular interest since the only such olefin for which there is a corresponding k_0 for proton transfer (benzylideneacetylacetone) has a k_0 for amine addition that deviates negatively from the line in Figure 1. Another dicarbonyl-activated olefin for which the intrinsic rate constant for piperidine/morpholine addition has recently been reported is benzylidenemalonaldehyde (**3**).[12] However, it is difficult to assess how well the log $(k_0)_N$ value of 3.6 would fit on the correlation line of Figure 1 because the corresponding carbon acid (malonaldehyde) only exists as an enol[13] and hence proton-transfer rates at carbon cannot be measured. Nevertheless, it was shown[12] that the reaction of **3** with amines is essentially devoid of the steric and hydrogen-bonding effects that depress k_0 for the reaction of **1**, and hence **3** may be regarded as reference or as a "normal" dicarbonyl-activated olefin.

Table I. Spectral Data of the Piperidine Adducts (T_A^-) of **1** and **4–7** and of the Corresponding $CH(COX)_2^-$ in 50% Me_2SO–50% Water at 20 °C

	S		T_A^-		$CH(COX)_2^-$	
compd	λ_{max}, nm	ε	λ_{max}, nm	ε	λ_{max}, nm	ε
4	343	19 500	435	1800	414[a]	2400[a]
1	289[b]	18 000[b]	308[b]	15 000[b]	291[b]	23 500[b]
5	287	15 600	312	14 300	296	23 500
6	289	18 600	316	19 500	296	14 700
7	322	18 800	351	12 800	351	22 100

[a] Reference 14. [b] Reference 8.

Olefinic substrates for which $(k_0)_P$ for the proton transfers of the corresponding carbon acids are known include benzylidene-1,3-indandione (**4**),[14] benzylidene-3,5-heptanedione (**5**),[15] benzylidene-2,6-dimethyl-3,5-heptanedione (**6**),[15] and benzylidenedibenzoylmethane (**7**).[15] We report here a determination of the intrinsic rate constants for amine addition to **4–7**.



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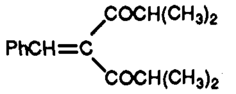

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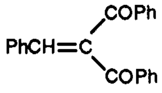

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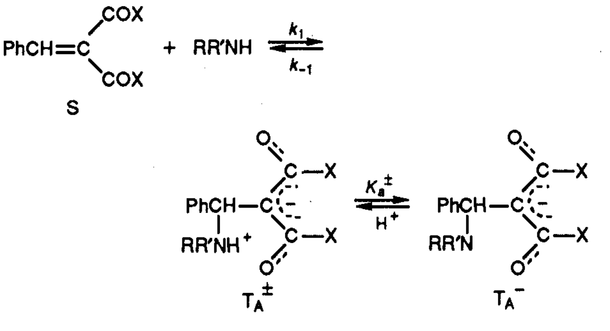
Results

General Features. The reaction of amines with **4–7** can be described by the general scheme of eq 3, which is typical for the reaction of amines with electrophilic olefins.[16] The rates are easily determined spectrophotometrically because of large differences between the UV spectra of substrates and $T_A^{\pm}$ and/or T_A^-.



(3)

Spectral information is summarized in Table I. The spectrum of T_A^- is typically somewhat red-shifted compared to that of the corresponding $CH(COX)_2^-$. Similar spectral patterns have been observed for the amine adducts of benzylidenemalonaldehyde,[12] benzylideneacetylacetone,[8] and benzylidene Meldrum's acid.[17]

The reactions of eq 3, which occur on the stopped-flow time scale, are followed by a much slower process that leads to the

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

(9) This deviation is *not* related to the fact that acetylacetone is in equilibrium with its enol and that $T_A^{\pm}$ and/or T_A^- derived from **1** can undergo protonation on oxygen.[10]

(10) Bernasconi, C. F.; Bunnell, R. D. *J. Org. Chem.* **1988**, *53*, 2001.

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

(12) Bernasconi, C. F.; Stronach, M. W. *J. Org. Chem.* **1991**, *56*, in press.

(13) (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.

(14) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1986**, *108*, 2969.

(15) Bernasconi, C. F.; Ohlberg, D. A. A.; Stronach, M. W. *J. Org. Chem.* **1991**, *56*, in press.

(16) For a recent review, see ref 1b.

(17) Bernasconi, C. F.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 5329.

Table II. Summary of Rate and Equilibrium Constants for the Reaction with Benzylidene-1,3-indandione with Amines in 50% Me_2SO–50% Water at 20 °C[a] and Comparison with Those of Benzylidenemalonaldehyde

amine	k_1, $M^{-1}\ s^{-1}$	k_{-1}, s^{-1}	K_1,[b] M^{-1}	$pK_a^{\pm}$	$K_1K_a^{\pm}$	$pK_a^{RR'NH_2^+}$
Benzylidene-1,3-indandione (4)						
piperidine	$(2.1 \pm 0.1) \times 10^5$	3.34 ± 0.06	$(6.3 \pm 0.4) \times 10^4$	10.34 ± 0.05	$(2.9 \pm 0.6) \times 10^{-6}$	11.02
morpholine	$(6.3 \pm 0.2) \times 10^4$	160 ± 3	394 ± 20	8.03 ± 0.05	$(3.7 \pm 0.6) \times 10^{-6}$	8.72
n-butylamine	$(9.34 \pm 0.35) \times 10^3$	0.126 ± 0.005	$(7.42 \pm 0.50) \times 10^4$	10.2 ± 0.05	$(4.7 \pm 0.8) \times 10^{-6}$	10.65
2-methoxyethylamine	$(3.52 \pm 0.16) \times 10^3$	0.73 ± 0.03	$(4.82 \pm 0.45) \times 10^3$	9.19 ± 0.05	$(3.14 \pm 0.55) \times 10^{-6}$	9.62
glycinamide	$(1.24 \pm 0.06) \times 10^3$	7.1 ± 0.4	175 ± 10	7.99 ± 0.05	$(1.79 \pm 0.36) \times 10^{-6}$	8.27
cyanomethylamine	$(1.06 \pm 0.05) \times 10^2$	200 ± 10	0.53 ± 0.05	~5.2[c]	$\sim 8.2 \times 10^{-7}$[c]	5.39
Benzylidenemalonaldehyde (3)[d]						
piperidine	1.69×10^5	8.2×10^{-5}	2.1×10^9	11.05	1.90×10^{-2}	11.02
n-butylamine	1.19×10^4	1.5×10^{-5}	7.9×10^8	10.63	1.85×10^{-2}	10.65
glycinamide	6.23×10^3	1.14×10^{-3}	5.5×10^6	8.39	2.24×10^{-2}	8.27

[a] $\mu = 0.5$ M (KCl). [b] $K_1 = k_1/k_{-1}$. [c] Estimated from a plot of $pK_a^{\pm}$ vs $pK_a^{RR'NH_2^+}$ for primary amines. [d] Reference 4.

hydrolysis of T_A^- to benzaldehyde and $CH(COX)_2^-$. This slow process was thoroughly investigated in the case of benzylidene Meldrum's acid[17,18] and benzylideneacetylacetone,[10] as well as for the reactions of α-cyano-4-nitrostilbene and α-cyano-2,4-dinitrostilbene[19b] with piperidine and morpholine, but was not a focus of the present study.

All kinetic determinations were made in 50% Me_2SO–50% water (v/v) at 20 °C and constant ionic strength of 0.5 M maintained with KCl. Pseudo-first-order conditions were used throughout, with the nucleophiles or buffers as the excess component. Under these conditions, the kinetics of eq 3 can be described by the reciprocal relaxation time given by eq 4.

$$\frac{1}{\tau} = k_1[RR'NH] + k_{-1}\frac{a_{H^+}}{K_a^{\pm} + a_{H^+}} \qquad (4)$$

Benzylidene-1,3-indandione (4). Kinetic experiments were performed with piperidine, morpholine, *n*-butylamine, 2-methoxyethylamine, glycinamide, and cyanomethylamine. The determination of k_1, k_{-1} and $K_a^{\pm}$ was carried out according to well-established procedures[4,8,11,12,17] and hence is only briefly described here.

For the determination of k_1, the substrate was reacted with an excess of amine acting either as its own buffer or in the presence of KOH. Under these conditions, the equilibrium of eq 3 favors T_A^- and plots of $1/\tau$ vs [RR'NH] at constant pH yield straight lines of slope k_1 and small (or negligible) intercepts. With the least nucleophilic amines, experiments in KOH solution afforded large intercepts and small slopes. The large intercepts were not due to the $k_{-1}a_{H^+}/(K_a^{\pm} + a_{H^+})$ term in eq 4 but due to strong competition by OH^- addition to the substrate, as shown by the *decrease* in the size of the intercept at lower pH. The k_1 values reported in Table II are typically the average of slopes determined at two to four different pH values, with each plot of $1/\tau$ vs [RR'NH] consisting of five to seven points. The raw data are summarized elsewhere.[20]

The k_{-1} and $K_a^{\pm}$ values were obtained from pH-jump experiments. In a first series of runs, T_A^- was generated under conditions similar to those used to measure k_1 and then reacted with an acidic buffer, e.g., acetate around pH 5–6 or dilute HCl. Under these conditions, k_1[RR'NH] becomes negligible, $K_a^{\pm} \ll a_{H^+}$, and eq 4 simplifies to $1/\tau = k_{-1}$. For the determination of $K_a^{\pm}$, pH-jump experiments into buffers of pH in the neighborhood of $pK_a^{\pm}$ were performed. Under these conditions, the k_1[RR'NH] term in eq 4 was not always negligible but could be corrected for according to eq 5. From inversion plots according to eq 6, $K_a^{\pm}$ and k_{-1} were

$$\frac{1}{\tau}(\text{corr}) = \frac{1}{\tau} - k_1[RR'NH] = k_{-1}\frac{a_{H^+}}{K_a^{\pm} + a_{H^+}} \qquad (5)$$

obtained; the agreement between the k_{-1} values determined by the two methods was usually very good. The results are summarized in Table II, while the raw data are reported elsewhere.[20]

$$\tau_{\text{corr}} = \frac{1}{k_{-1}} + \frac{K_a^{\pm}}{k_{-1}a_{H^+}} \qquad (6)$$

The only amine for which $K_a^{\pm}$ could not be determined experimentally is cyanomethylamine. pH-jump experiments into highly acidic buffers were characterized by biphasic kinetics, which led to too much scatter in the data. A more satisfactory method for estimating $pK_a^{\pm}$ for this amine was from extrapolation of a plot of $pK_a^{\pm}$ vs $pK_a^{RR'NH_2^+}$.

Benzylidene-3,5-heptanedione (5), Benzylidene-2,6-dimethyl-3,5-heptanedione (6), and Benzylidenedibenzoylmethane (7). With these substrates, the kinetic determinations were restricted to the reactions with piperidine and morpholine. There are two major differences between these reactions and those of **4**: The equilibrium constants for the formation of T_A^- ($K_1 = k_1/k_{-1}$) are much smaller, and the $pK_a^{\pm}$ values are substantially higher than with **4**. Both of these factors disfavor the $T_A^{\pm}/T_A^-$ side of eq 3, and experiments aimed at measuring k_1 had to be performed at high amine concentrations and high pH in order for the k_1[RR'NH] term in eq 4 to be significant compared to $k_{-1}a_{H^+}/(K_a^{\pm} + a_{H^+})$. Because of the large size of the $k_{-1}a_{H^+}/(K_a^{\pm} + a_{H^+})$ term even at relatively high pH, intercepts of plots of $1/\tau$ vs [RR'NH] could be used in some cases in combination with results from pH-jump experiments to evaluate k_{-1} and $K_a^{\pm}$ from inversion plots according to eq 6.

Raw data are summarized elsewhere,[20] while the k_1, k_{-1}, K_1, and $pK_a^{\pm}$ values are reported in Table III.

Discussion

Benzylidene-1,3-indandione vs Benzylidenemalonaldehyde. The rate and equilibrium constants pertaining to the reaction scheme of eq 3 with **4** are summarized in Table II along with parameters for the reaction of benzylidenemalonaldehyde (**3**) with some representative amines. We note that, for a given nucleophile, the k_1 values are quite comparable for the two substrates, while the k_{-1} values for the reactions of **4** are about 4 orders of magnitude larger than for the reactions of **3** and the K_1 values are about 4 orders of magnitude smaller. For example, with piperidine, $k_1(4)/k_1(3) = 1.24$, $k_{-1}(4)/k_{-1}(3) = 4.07 \times 10^4$, and $K_1(4)/K_1(3) = 3.0 \times 10^{-5}$; for *n*-butylamine, the respective ratios are 0.785, 8.4×10^3, and 9.38×10^{-5}; for glycinamide, they are 0.20, 6.23×10^3 and 3.18×10^{-5}.

These results imply that the reaction of **4** with amines is *kinetically* more facile than that of **3**; i.e., the *intrinsic* rate constant ($(k_0)_N$) for amine addition to **4** is higher than for addition to **3**. $(k_0)_N$ values may be obtained by extrapolation of plots of log k_1 (or log k_{-1}) vs log K_1 as shown in Figure 2 for the reactions with primary amines.[3] The log $(k_0)_N$ for the reactions of **4** and **3** with primary and secondary alicyclic amines are summarized in Table IV, along with β_{nuc}^n and β_{lg}^n.

The extent by which log k_0 for **4** exceeds log k_0 for **3** is smaller than what one might intuitively have expected on the basis of comparing the $k_1(4)/k_1(3)$ ratios with the $K_1(4)/K_1(3)$ ratios.

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(18) Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1986**, *108*, 5257.

(19) (a) Bernasconi, C. F.; Murray, C. J.; Fox, J. P.; Carrĕ, D. J. *J. Am. Chem. Soc.* **1983**, *105*, 4349. (b) Bernasconi, C. F.; Murray, C. J. *Ibid.* **1984**, *106*, 3257.

(20) M. W. Stronach. Ph.D. Thesis, University of California, Santa Cruz, CA, 1990.

Table III. Summary of Rate and Equilibrium Constants for the Reactions of Benzylideneacetylacetone (**1**), Benzylidene-3,5-heptanedione (**5**), Benzylidene-2,6-dimethyl-3,5-heptanedione (**6**), and Benzylidenedibenzoylmethane (**7**) with Piperidine and Morpholine in 50% Me$_2$SO–50% Water (v/v) at 20 °C[a]

substrate	k_1, M^{-1} s^{-1}	k_{-1}, s^{-1}	K_1,[b] M^{-1}	p$K_a^{\pm}$	$K_1K_a^{\pm}$	p$K_a^{CH_2(COX)_2}$[d] keto form	p$K_a^{CH_2(COX)_2}$[d] enol form
				Piperidine (pK_a = 11.02)			
1[c]	8.20	0.15	54.7	13.5	1.07 × 10^{-12}	9.12	8.75
5	2.1 ± 0.1	2.0 ± 0.1	1.05 ± 0.10	13.5 ± 0.1	(3.38 ± 1.18) × 10^{-14}	10.16	9.52
6	1.5 ± 0.06	5.1 ± 0.3	0.29 ± 0.03			10.45	10.23
7	0.98 ± 0.04	2.6 ± 0.1	0.38 ± 0.06			8.72	9.23
				Morpholine (pK_a = 8.72)			
1[c]	1.79	2.78	0.64	11.26	3.55 × 10^{-12}	9.12	8.75
5	0.35 ± 0.03	14.3 ± 0.8	(2.45 ± 0.55) × 10^{-2}	11.20 ± 0.05	(1.31 ± 0.30) × 10^{-13}	10.16	9.52
6	0.31 ± 0.02	45 ± 4	(6.9 ± 1.2) × 10^{-3}	11.38 ± 0.05	(2.89 ± 0.80) × 10^{-14}	10.45	10.23
7	0.43 ± 0.03	47 ± 5	(9.15 ± 1.5) × 10^{-3}	10.64 ± 0.05	(2.11 ± 0.50) × 10^{-13}	8.72	9.23

[a] μ = 0.5 M (KCl). [b] $K_1 = k_1/k_{-1}$. [c] Reference 8. [d] Reference 15.

Table IV. Intrinsic Rate Constants (log $(k_0)_N$) and Normalized Brønsted Coefficients for the Reactions of Benzylidene-1,3-indandione (**4**) and Benzylidenemalonaldehyde (**3**) with Amines[a]

	4		**3**[b]	
	pip/mor	1° amines	pip/mor	1° amines
β_{nuc}^n = d log k_1/d log K_1	0.24	0.38	0.18	0.26
β_{lg}^n = d log k_{-1}/d log K_1	−0.76	0.62	−0.82	−0.74
β_{eq} = d log K_1/dp$K_a^{RR'NH_2^+}$	0.90	0.97	0.85	0.78
log $(k_0)_N$ (nucleophilic addn)	4.2 ± 0.1	2.2 ± 0.1	3.6	1.9
log $(k_0)_P$ (proton transfer)[a]	3.13[c]	2.44[c]	*d*	*d*

[a] Estimated error limits are ±0.03 for β_{nuc}^n and β_{lg}^n and ±0.06 for β_{eq}. [b] Reference 4. [c] Refers to deprotonation of 1,3-indandione.[14] [d] Not available; see text.

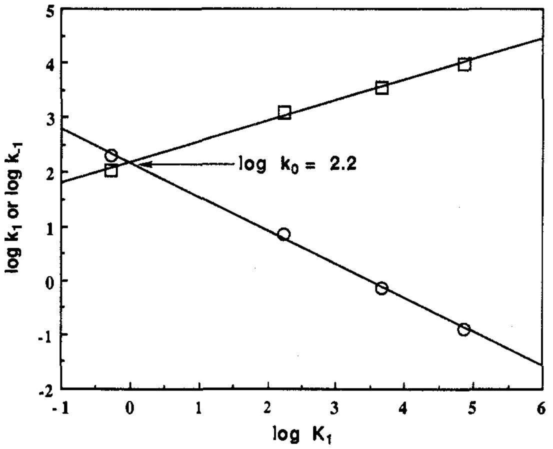

Figure 2. Brønsted-type plots for addition of primary amines to benzylidene-1,3-indandione (**4**).

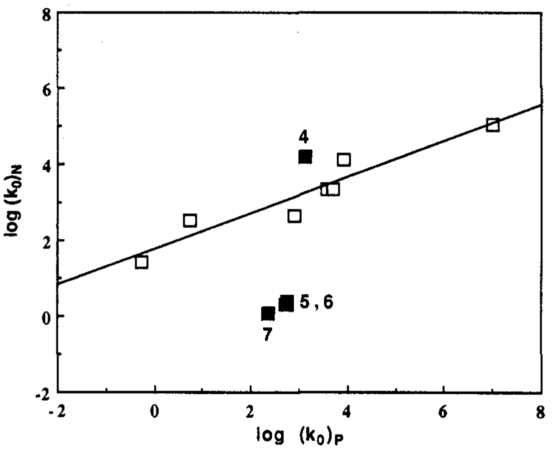

Figure 3. Same as Figure 1 with points for **4**–**7** (filled squares) determined in this study. Note that the point for **1** is invisible since it is the same as for **5** and **6**.

There are two reasons for this. The principal one is the rather small β_{nuc}^n values.[21] The other is the fact that the β_{nuc}^n values for **3** are smaller than for **4**, particularly for the reaction of the primary amines. As elaborated upon elsewhere,[12] such differences in β_{nuc}^n introduce some uncertainties in quantitative comparisons of log $(k_0)_N$ values, especially when log $(k_0)_N$ is obtained by rather long extrapolations as is the case with **3**. Thus, the conclusions to be drawn from our results are that the intrinsic rate constants for amine addition to **4** are indeed higher than for amine addition to **3**, but the extent by which they are higher is somewhat uncertain and may be in the range between 2- and 4-fold.[22]

As stated in the introduction, **3** may be regarded as a "normal" dicarbonyl-activated olefin; i.e., there are no significant k_0-lowering hydrogen-bonding or steric effects in its reactions with amines. The fact that $(k_0)_N$ for the reactions of **4** is not only not depressed relative to that of **3** but even enhanced indicates that, with **4**, steric and hydrogen-bonding effects are not important either. The p$K_a^{\pm}$ values (Table II), which are much lower than for the corresponding adducts of **1** (Table III) and even somewhat lower than for the adducts of **3**, actually demonstrate directly that intramolecular hydrogen bonding in $T_A^{\pm}$ derived from **4** must be quite weak and hence cannot possibly have a large effect on $(k_0)_N$.

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(21) If β_{nuc}^n is the same for **4** and **3**, the relationship between the k_1, K_1, and k_0 ratios and β_{nuc}^n is given by log $[k_0(4)/k_0(3)]$ = log $[k_1(4)/k_1(3)] - \beta_{nuc}^n$ log $[K_1(4)/K_1(3)]$. Thus, when $k_1(4)/k_1(3)$ = 1.0 and $K_1(4)/K_1(3) = 10^{-4}$, one would calculate $k_0(4)/k_0(3)$ = 1.0 for β_{nuc}^n = 0, 10 for β_{nuc}^n = 0.25, 100 for β_{nuc}^n = 0.5, 10^3 for β_{nuc}^n = 0.75, and 10^4 for β_{nuc}^n = 1.0.

(22) As observed in several previous cases,[12,18] log $(k_0)_N$ for the piperidine/morpholine reaction is substantially higher than for the reaction of primary amines. This is consistent with numerous observations according to which the rate of nucleophilic attack by piperidine on a given electrophile is much faster than the rate of attack by primary amines of the same pK_a.[23,24] The same is true for proton transfers where log $(k_0)_P$ for the deprotonation of carbon acids by the piperidine/morpholine pair is typically up to 1 log unit higher than for the deprotonation by primary amines.[25] This reactivity order has generally been understood to be a consequence of the stronger solvation in the order RR'R''NH$^+$ < RR'NH$_2^+$ < RNH$_3^+$, coupled with the assumption that the solvation of the incipient positive charge in the transition state lags behind the development of this charge.[26] This, of course, is again a PNS effect.

(23) (a) Bernasconi, C. F.; Carré, D. J.; Fox, J. P. In *Techniques and Applications of Fast Reactions in Solutions*; Gettins, W. J., Wyn-Jones, E., Eds.; Reidel: Dordrecht, Holland, 1979; p 453. (b) Bernasconi, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 129.

(24) (a) Kirby, A. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1965**, *87*, 3217. (b) Bernasconi, C. F.; de Rossi, R. H.; Schmid, P. *Ibid.* **1977**, *99*, 4090.

(25) Numerous references cited in refs 1a and 6.

(26) (a) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, New York, 1973; Chapter 10. (b) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969; p 178.

Table V. Intrinsic Rate Constants (log k_0) and Normalized Brønsted Coefficients for the Reactions of **1** and **5–7** with Piperidine/Morpholine[a]

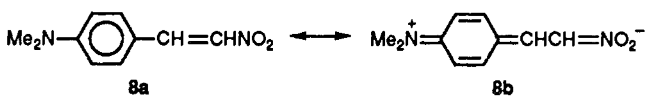
	1[b]	**5**	**6**	**7**
$\beta_{nuc}^{n} = d \log k_1/d \log K_1$	0.33	0.48	0.42	0.22
$\beta_{lg}^{n} = d \log k_{-1}/d \log K_1$	−0.67	−0.52	−0.58	−0.78
$\beta_{eq} = d \log K_1/dpK_a^{RR'NH_2^+}$	0.84	0.71	0.71	0.70
log $(k_0)_N$ (nucleophilic addn)	0.30 ± 0.10	0.31 ± 0.10	0.40 ± 0.10	0.08 ± 0.10
log $(k_0)_P$ (proton transfer)[c]	2.75[d]	2.73[e]	2.76[e]	2.36[b,d]

[a] Estimated error limits are ±0.03 for β_{nuc}^{n} and β_{lg}^{n} and ±0.06 for β_{eq}. [b] Reference 8. [c] Refers to $CH_2(COX)_2 + RR'NH \rightleftarrows CH(COX)_2^- + RR'NH_2^+$.

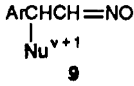
A potential reason why k_0 for **4** is actually higher than for **3** is a smaller degree of resonance stabilization of the carbanionic portion of $T_A^{\pm}$, but there may also be hitherto unidentified factors. A comparison of k_0 for **4** with k_0 for the deprotonation of 1,3-indandione can provide some insight into this question.

Benzylidene-1,3-indandione vs 1,3-Indandione. log $(k_0)_P$ for deprotonation of 1,3-indandione by primary amines in 50% Me_2SO–50% water at 20 °C is 2.44; log $(k_0)_P$ for deprotonation by piperidine and morpholine in the same solvent is 3.13.[14] When the log $(k_0)_N$ values for the piperidine/morpholine reactions are placed on the plot of log $(k_0)_N$ vs log $(k_0)_P$, the point for the **4**/1,3-indandione pair is seen to deviate positively by about 1.05 log units from the line in Figure 3. This deviation confirms our earlier conclusion that k_0 for **4** is larger than expected for a normal dicarbonyl-activated olefin. If there was a smaller degree of resonance stabilization in carbanions derived from the 1,3-indandione moiety than in carbanions derived from malonaldehyde and this were the principal reason why $(k_0)_N$ for **4** is higher than for **3**, then $(k_0)_P$ for the deprotonation of 1,3-indandione should also be enhanced and the point for the **4**/1,3-indandione pair should then lie on, or close to, the line in Figure 3. The fact that it deviates so strongly from the line suggests the presence of a different factor.

We propose that this factor is related to the cyclic structure of **4**. This ring structure assures that the π-overlap needed for the stabilization of $T_A^{\pm}$ is already maximally built into the olefin; i.e., the structural reorganization that may be required to achieve this overlap in noncyclic systems is not necessary here, and this reduces the activation barrier of the reaction. This effect, which enhances $(k_0)_N$ but not $(k_0)_P$ since in the proton transfer the cyclic structure does not provide the same kind of π-overlap in the sp^3-hybridized substrate, may be interpreted as another manifestation of the PNS in which a product stabilizing factor (π-overlap) develops ahead of bond formation.[7] Or one may view the π-overlap as a means to alleviate the k_0-lowering effect of the resonance stabilization, which in noncyclic systems develops late along the reaction coordinate but in the present system develops much earlier. There is a striking similarity of this effect to the enhancement of k_0 in the reaction of nucleophiles with *p*-(dimethylamino)-β-nitrostyrene,[27] where the resonance form **8b** provides some π-delocalization built into the substrate, which facilitates the formation of the adduct (**9**) compared to that for the nonsubstituted β-nitrostyrene.



8a **8b**



$$\underset{\displaystyle Nu^{v+1}}{ArCH}CH{=}NO_2^-$$

9

In further support of our interpretation, we note that the exalted $(k_0)_N$ for nucleophilic addition to **4** is not restricted to amine nucleophiles. For the addition of hydroxide ion, it was shown that $(k_0)_N$ for **4** is comparable to that for benzylidene Meldrum's acid[28] or even slightly exceeds it, even though $(k_0)_N$ for nucleophilic addition to benzylidene Meldrum's acid also seems to be somewhat exalted (Figure 3). The exalted $(k_0)_N$ for benzylidene Meldrum's acid is likely to have a similar explanation, i.e., the ring structure. The effect is smaller here, presumably because resonance is not as important in the stabilization of Meldrum's acid anions[29,30] and/or because the ring structure is less rigid than in **4**.

The fact that $(k_0)_N$ for amine addition to 1,2,3,4-tetrachloro-6-phenylfulvene is not abnormally high may be attributed to the extreme bulk of this olefin, which prevents coplanarity of the cyclopentadiene ring with the CH carbon, an effect that tends to decrease $(k_0)_N$ as discussed below.

Benzylidene-3,5-heptanedione (5), Benzylidene-2,6-dimethyl-3,5-heptanedione (6), and Benzylidenedibenzoylmethane (7). The relevant rate and equilibrium constants are summarized in Table III along with the corresponding parameters for benzylideneacetylacetone (**1**). In a previous report,[8] it was noted that $K_1K_a^{\pm}$ for **1** is strongly depressed compared with $K_1K_a^{\pm}$ for other substrates of the general structure PhCH=CYY′. This conclusion was reached by showing that, on a correlation of log $(K_1K_a^{\pm})$ vs the pK_a of the corresponding carbon acids CH_2YY', the point for **1** was strongly deviant; the same conclusion can be drawn from a comparison of log $(K_1K_a^{\pm})_4$ − log $(K_1K_a^{\pm})_1$ = 6.02 (morpholine reaction) with pK_a(acetylacetone) − pK_a(1,3-indandione) = 2.77, which suggests that $(K_1K_a^{\pm})_1$ is depressed by at least 3 orders of magnitude. This depression was attributed to steric crowding in $T_A^{\pm}$,[31,32] the exact nature of which will be discussed below.

The results for **5–7** show substantial further reductions in $K_1K_a^{\pm}$ compared to **1**. For **5** and **6**, this additional reduction seems to mainly reflect the increased pK_a of the corresponding carbon acid, which is primarily a polar effect,[33] although some additional steric effect also comes into play. This is seen by comparing log $(K_1K_a^{\pm})_1$ − log $(K_1K_a^{\pm})_5$ = 1.43 (morpholine) with pK_a(3,5-heptanedione) − pK_a(acetylacetone) = 1.04 or log $(K_1K_a^{\pm})_1$ − log $(K_1K_a^{\pm})_6$ = 2.08 with pK_a(2,6-dimethyl-3,5-heptanedione) − pK_a(acetylacetone) = 1.33. On the other hand, with **7** the additional reduction appears to be mainly or exclusively steric, judging from log $(K_1K_a^{\pm})_1$ − log $(K_1K_a^{\pm})_7$ = 1.23 and pK_a(dibenzoylmethane) − pK_a(acetylacetone) = −0.30.

The $pK_a^{\pm}$ values for **5** and **6** are about the same as for **1** and just slightly lower for **7**. These high $pK_a^{\pm}$ values, which are 2–2.5 units higher than the pK_a of the corresponding $RR'NH_2^+$, contrast with the $pK_a^{\pm}$ values for **4** that are 0.3–0.7 unit *lower* than $pK_a^{RR'NH_2^+}$ and $pK_a^{\pm}$ values for miscellaneous PhCH=CYY′ that are up to 2.90 units lower than $pK_a^{RR'NH_2^+}$.[8] As argued before,[8] such high $pK_a^{\pm}$ values indicate the presence of a strong intramolecular hydrogen bond as shown in **2**. We conclude that the $T_A^{\pm}$ adducts derived from **1** and **5–7** have all comparable intra-

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

(29) Arnett, E. M.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 809.

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

(31) The depression in $K_1K_a^{\pm}$ which refers to the formation of T_A^-, is a better gauge of steric effects than that of K_1, which refers to the formation of $T_A^{\pm}$, because the latter is also affected by intramolecular hydrogen bonding in $T_A^{\pm}$ (K_1-enhancing), which may not be the same for the various compounds.

(32) It is assumed that, in the absence of steric hindrance, log $(K_1K_a^{\pm})_4$ − log $(K_1K_a^{\pm})_1$ would not be larger than pK_a(acetylacetone) − pK_a(1,3-indandione).

(33) Besides an inductive effect,[34,35] hyperconjugation[34] and steric effects[35,36] have been invoked to explain the changes in pK_a.

(34) Calmon, J.-P.; Maroni, P. *Bull. Soc. Chim. Fr.* **1965**, 2532.

(35) Talvik, A. *Org. React.* (*Tartu*) **1972**, *9*, 233.

(36) Hammond, G. S.; Borduin, W. G.; Guter, G. A. *J. Am. Chem. Soc.* **1959**, *81*, 4682.

molecular hydrogen bonding; i.e., the differences in the steric bulk of these compounds does not seem to affect hydrogen bonding in a major way.

Intrinsic rate constants, along with the Brønsted parameters,[37] are summarized in Table V. Interestingly, log $(k_0)_N$ is the same for **1**, **5**, and **6** and only minimally lower for **7**, reflecting a similar constancy of log $(k_0)_P$ for the deprotonation of the $CH_2(COX)_2$'s (also in Table V). Hence, the points for **1** and **5**–**7** all cluster together on the plot of Figure 3.

The fact that the intrinsic rate constants are so similar for the four olefins suggests that the main factors such as resonance, intramolecular hydrogen bonding, and steric strain that affect $(k_0)_N$ in these reactions are either insensitive to the specific structure of these compounds or that potential changes in one or two of these factors are compensated for by changes in a third one. The first interpretation seems more satisfactory for the following reasons. Judging from the constancy of log $(k_0)_P$ for the proton transfers from $CH_2(COX)_2$ corresponding to **1**, **5**, and **6** (Table V), no substantial changes seem to occur in the resonance stabilization of the corresponding anions. Since we concluded above that the decrease in $K_1K_a^{\pm}$ in going from **1** to **5** to **6** mainly reflects the increased pK_a values of the $CH_2(COX)_2$ acids, which are caused by factors other than changes in the resonance stabilization of $CH(COX)_2^-$, there should not be major changes in the resonance stabilization of the adducts of **5** and **6** compared to those of **1** either. This means that the effect of resonance on $(k_0)_N$ should be about the same for **1**, **5**, and **6**. It was also shown above that the destabilization of the adducts of **5** and **6** by steric crowding is only marginally stronger than for the adducts of **1**, and hence no significant change in $(k_0)_N$ is expected from this factor. Finally, the strength of the intramolecular hydrogen bond in $T_A^{\pm}$ being about the same for these three olefins also implies a constant contribution of this effect to $(k_0)_N$ for **1**, **5**, and **6**.

This situation with **7** is somewhat different. Here the decrease in $K_1K_a^{\pm}$ compared to $K_1K_a^{\pm}$ of **1** is opposite to the change in the acidity of $CH_2(COX)_2$ and reflects strongly enhanced steric crowding in $T_A^{\pm}$. It is possible that this enhanced crowding is responsible for the fact that $(k_0)_N$ is lower than for **1**, **5**, and **6**. However, it is also possible that the low $(k_0)_N$ for **7** is caused by the late development of π-overlap of the phenyl groups with the enolate structure, as shown for the deprotonation of dibenzoylmethane.[15] Such π-overlap is indicated by the strong red shift in λ_{max} of T_A^- derived from **7** compared to λ_{max} of T_A^- derived from **1**, **5**, or **6**, just as was observed with the anion of dibenzoylmethane whose λ_{max} is also red-shifted compared to λ_{max} of the other $CH(COX)_2^-$ anions (Table I).

Conclusions

1. The intrinsic rate constant for amine addition to benzylidene-1,3-indandione (**4**) is higher than that for amine addition to benzylidenemalonaldehyde (**3**). It is also substantially higher than expected on the basis of $(k_0)_P$ for the deprotonation of 1,3-indandione as seen in the strong positive deviation from the correlation line in Figure 3. The exalted $(k_0)_N$ value for nucleophilic addition to **4** is attributed to its cyclic structure, which assures that the π-overlap needed for the stabilization of the adduct is already optimally built into the substrate. This effect can be understood as a manifestation of the PNS whereby $(k_0)_N$ increases because a product-stabilizing factor (π-overlap) develops ahead of bond formation.

2. The equilibrium constants for amine addition to benzylidene-3,5-heptanedione (**5**), benzylidene-2,6-dimethyl-3,5-heptanedione (**6**), and benzylidenedibenzoylmethane (**7**) are further reduced compared to the already depressed values for addition to benzylideneacetylacetone (**1**). For **5** and **6**, this reduction essentially parallels a similar reduction in the acidity of the corresponding carbon acids $CH_2(COX)_2$, but for **7** this reduction is mainly caused by a steric effect.

3. The intrinsic rate constants for the reactions of **5**–**7** are all very low but about the same as for **1**. This implies that the $(k_0)_N$-lowering PNS effects, which are attributed to late development of intramolecular hydrogen bonding and early development of steric hindrance in $T_A^{\pm}$ and which come on top of the "normal" PNS effect caused by late resonance development, are all quite similar. The additional reduction in $(k_0)_N$ in the reaction of **7** may either be a consequence of a further increase in the steric crowding of $T_A^{\pm}$ and/or be caused by late development of π-overlap with the phenyl groups in $T_A^{\pm}$.

Experimental Section

Materials. Benzylidene-1,3-indandione (**4**) was available from a previous study.[28] Benzylidene-3,5-heptanedione (**5**), benzylidene-2,6-dimethyl-3,5-heptanedione (**6**), and benzylidenedibenzoylmethane (**7**) were prepared by modifying a literature procedure[38] as follows. Benzaldehyde (10 mmol), the appropriate carbon acid (10 mmol), and a few drops of pyrrolidine were refluxed in 50 mL of ethanol for 24 h (10 days in the case of benzylidenedibenzoylmethane). The ethanol was evaporated and the crude product dissolved in 75 mL of ether followed by washing (2 × 50 mL) with 5% $NaHSO_3$, 5% $NaHCO_3$, and 0.1 M HCl. The ether layer was dried over anhydrous Mg_2SO_4 and evaporated to give the crude product. Material for kinetics and instrumental analysis was obtained by distilling the crude material under vacuum with use of a short-path distillation flask.

5: clear oil; MS, *m/z* (relative intensity) 216 (12, M^+), 205 (9), 187 (23), 135 (33), 131 (62), 107 (19), 103 (12), 79 (14), 77 (18), 57 (100), 51 (12); FT-IR (film, cm^{-1}) ν_{max} 2978, 1701, 1665, 1614, 1493, 1454, 1377, 1346, 1196, 1119, 1040, 980, 931, 880, 806, 762, 696; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.9–1.2 (6 H, m, CH_3), 2.37 (2 H, q, CH_2), 2.64 (2 H, q, CH_2), 7.1–7.4 (5 H, m, Ar), 7.45 (1 H, s, HC=).

6: slightly yellow oil; MS, *m/z* (relative intensity) 244 (11, M^+), 201 (59), 131 (72), 103 (12), 102 (18), 77 (15), 71 (100), 51 (10); FT-IR (film, cm^{-1}) ν_{max} 2976, 1699, 1660, 1611, 1574, 1495, 1464, 1385, 1288, 1207, 1152, 1084, 1044, 936, 758, 696; ^{1}H NMR (250 mHz, $CDCl_3$) δ 1.03 (6 H, d, CH_3), 1.20 (6 H, d, CH_3), 2.58 (1 H, m, CH), 3.31 (1 H, m, CH), 7.2–7.5 (5 H, m, Ar), 7.60 (1 H, s, HC=).

7: slightly yellow viscous oil; MS, *m/z* (relative intensity) 312 (5, M^+), 207 (18), 105 (100), 77 (92), 69 (12), 51 (34); FT-IR (film, cm^{-1}) ν_{max} 3067, 1963, 1900, 1717, 1667, 1607, 1275, 1215, 1176, 1105, 1026, 934, 869, 746, 613, 686; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.87 (1 H, s, HC=), 7.4–7.7 (10 H, m, Ar), 7.9–8.2 (5 H, m, Ar).

UV Spectra and Kinetic Experiments. The procedures were similar to the ones described before.[8,11,17,27] Spectra were taken on a 559 Perkin-Elmer spectrophotometer. Rates were measured in a Durrum-Gibson stopped-flow spectrophotometer. The pH of the reaction solutions was measured in mock mixing experiments with a pH meter calibrated for 50% Me_2SO–50% water with buffers described by Hallé et al.[39]

Acknowledgment. This research was supported by Grant CHE-8921739 from the National Science Foundation.

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[37] In view of the fact that the Brønsted coefficients are based on just two amines and some of the rate constants may be associated with some experimental error, not much significance should be attached to the differences between them.

[38] McBee, E. T.; Meyer, R. K.; Baranauckas, C. F. *J. Am. Chem. Soc.* **1955**, *77*, 86.

[39] Hallé, J.-C.; Gaboriaud, R.; Schaal, R. *Bull. Soc. Chim. Fr.* **1970**, 2047.