Nucleophilic Addition to Olefins. 11.[1] Kinetics of the Reversible Hydrolysis of Benzylidenemalononitrile in Water

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Abstract: The hydrolysis of benzylidenemalononitrile (BMN) to form benzaldehyde and malononitrile (or its anion) is significantly reversible, with an equilibrium constant $K_h = [PhCH{=}O][CH_2(CN)_2]/[BMN] = 3.36 \times 10^{-3}$ M in water at 25 °C. It involves the following steps (see Scheme III): (1) nucleophilic attack by OH^- or by water to form the adduct T_{OH}^-; (2) carbon protonation of T_{OH}^- to form T_{OH}^0; (3) oxygen deprotonation of T_{OH}^0 to form T_O^-; and (4) collapse of the tetrahedral intermediate, T_O^-, to form benzaldehyde and malononitrile anion, which is in rapid equilibrium with malononitrile. There is also a direct, water-catalyzed breakdown of T_{OH}^0 to products. The pH–rate profile for the hydrolysis reaction has four phases, with the following rate-limiting steps: at pH >8, OH^- attack on BMN; at pH 5–8, water attack on BMN which is subject to non-enforced general base catalysis; at pH 1–5, collapse of T_O^-; at pH <1, collapse of T_{OH}^0. Rate and equilibrium constants for all steps are calculated or estimated and compared with the same parameters in the hydrolysis of a β-nitrostyrene and benzylidene Meldrum acid. They provide new evidence that the nucleofugality of carbanions is relatively high in carbonyl-forming but low in olefin-forming eliminations. They also confirm previous observations according to which the intrinsic barriers in carbanion-forming reactions are much higher for nitro-stabilized than for cyano-stabilized carbanions.

The hydrolysis of benzylidenemalononitrile (BMN) and of phenyl-substituted benzylidenemalononitriles has been studied before.[2] The most elaborate kinetic investigations have been reported by Patai and Rappoport[3] and by Pritchard et al.[4] Patai and Rappoport's studies, carried out in 95% ethanol, were mainly directed toward an elucidation of the mechanism, for which Scheme I was proposed.

On the basis of several observations, they concluded that water attack, to form $T_{OH}^{\pm}$, is rate limiting in neutral and acidic solution, while OH^- attack, to form T_{OH}^-, is rate limiting in basic solutions. Their observations included the following:

(1) In the presence of base the rate of hydrolysis is second order, first order with respect to the olefin and first order with respect to OH^- concentration.

(2) The same rate is observed when monitoring reactants or products which shows that no intermediate accumulates during the reaction.

(3) There is a large substituent effect on the rate constant.

(4) In the presence of $HClO_4$, there is a large decrease in the rate, and at high acid concentration the reaction can be stopped altogether.

(5) The reaction is not subject to general acid–base catalysis; a slight rate enhancement in triethylamine buffers was attributed to a medium effect.

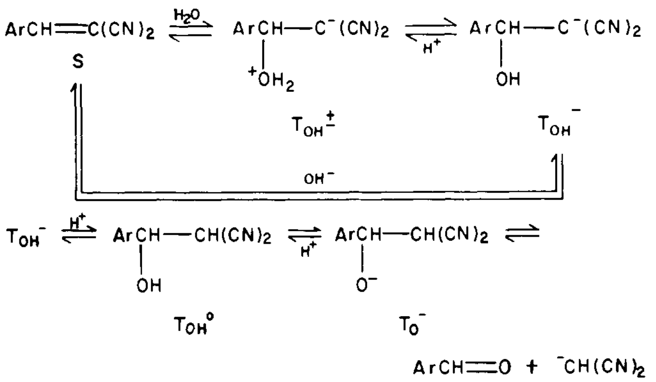
The conclusions reached by Patai and Rappoport for the reactions conducted in basic solution are hardly challengeable, and our own work supports them. On the other hand, with respect to the reactions in neutral and acidic solution, there seem to exist some ambiguities which need clarification.

(1) First, and perhaps most importantly, the nature of the rate-limiting step(s) in acidic solution needs to be more firmly established.

(2) In view of the many known cases of general base catalysis of water attack on electrophiles,[5] we are reluctant to accept the conclusion that the reaction of BMN with water is not subject to such catalysis.

(3) The observation that the reactions are not clearly first order with respect to the substrate, with the apparent first order rate constants decreasing with time,[3] indicates that there are complications which need to be resolved.

Scheme I



We now report a kinetic study of the hydrolysis of BMN in aqueous solution, which addresses these questions and which will allow us to resolve all ambiguities noted above. We were also able to evaluate or estimate the rate constants of most of the steps in Scheme I. We shall show that the rate constants for steps $S + OH^- \rightleftharpoons T_{OH}^-$ and $T_O^- \rightleftharpoons PhCH{=}O + {}^-CH(CN)_2$ are much higher than those for the same steps in the hydrolysis of a β-nitrostyrene.[6] This indicates that the intrinsic barrier for the formation of a cyano-stabilized carbanion is much lower than that for a nitro-stabilized carbanion. This is in agreement with previously established patterns.[1,7]

Results

General Features and Definitions. It is useful to start with some definitions. Depending on the pH, one may define the hydrolysis equilibrium by eq 1 or 2. Note that neither eq 1 or 2 imply any

$$S + H_2O \overset{K_{H_2O}}{\rightleftharpoons} PhCH{=}O + CH_2(CN)_{2)} \quad (1)$$

$$S + OH^- \overset{K_{OH}}{\rightleftharpoons} PhCH{=}O + {}^-CH(CN)_2 \quad (2)$$

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[1] Part 10: Bernasconi, C. F.; Murray, C. J. *J. Am. Chem. Soc.* **1983**, *105*, 3257.

[2] For a recent review on reactions of ylidene malononitriles, see: Freeman, F. *Chem. Rev.* **1980**, *80*, 329.

[3] Patai, S.; Rappoport, Z. *J. Chem. Soc.* **1962**, 383, 392.

[4] Pritchard, R. B.; Lough, C. E.; Reesor, J. B.; Holmes, H. L.; Currie, D. J. *Can. J. Chem.* **1967**, *45*, 775.

[5] Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5133 and numerous references cited therein.

[6] Crowell, T. I.; Kim, T.-R. *J. Am. Chem. Soc.* **1973**, *95*, 6781.

[7] For a recent review, see: Bernasconi, C. F. *Pure Appl. Chem.* **1982**, *54*, 2335.

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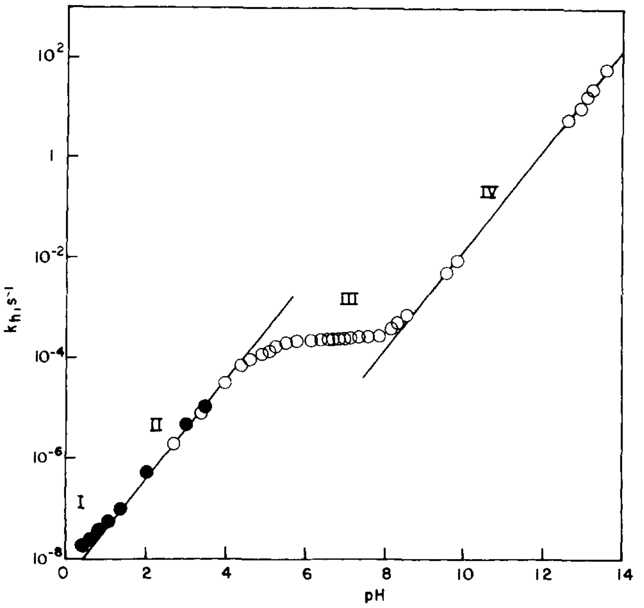

Figure 1. pH–rate profile for the hydrolysis of benzylidenemalononitrile in water at 25 °C: (●) k_c from measurements in the condensation direction; (○) k_h from measurements in the hydrolysis direction.

particular mechanism or rate-limiting step. In this paper we shall frequently use apparent equilibrium constants, K_h, for hydrolysis and apparent rate constants, k_h in the hydrolysis direction and k_c in the condensation direction. Under our experimental conditions there is no accumulation of any intermediate to detectable levels. We define K_h, k_h, and k_c as

$$K_h = \frac{k_h}{k_c} = \frac{[\mathrm{PhCH{=}O}][\mathrm{CH_2(CN)_2}]_{tot}}{[\mathrm{S}]} \qquad (3)$$

with $[\mathrm{CH_2(CN)_2}]_{tot} = [\mathrm{CH_2(CN)_2}] + [^{-}\mathrm{CH(CN)_2}]$ being the total malononitrile concentration, and with the apparent rate constants being defined by the rate law

$$-\frac{d[\mathrm{S}]}{dt} = k_h[\mathrm{S}] - k_c[\mathrm{PhCH{=}O}][\mathrm{CH_2(CN)_2}]_{tot} \qquad (4)$$

The pH dependence of K_h is then given by

$$K_h = K_{H_2O}\left(1 + \frac{K_a^{CH_2(CN)_2}}{a_{H^+}}\right) \qquad (5)$$

with $K_a^{CH_2(CN)_2}$ being the acidity constant of malononitrile ($pK_a^{CH_2(CN)_2} = 11.19$).[8] At pH $\ll pK_a^{CH_2(CN)_2}$ eq 5 simplifies to

$$K_h = K_{H_2O} \qquad (6)$$

while at pH $\gg pK_a^{CH_2(CN)_2}$ one obtains

$$K_h = K_{H_2O}K_a^{CH_2(CN)_2}/a_{H^+} = K_{OH}a_{OH^-} \qquad (7)$$

The pH dependence of k_h and k_c cannot be predicted because they depend on the mechanism, but their ratio, k_h/k_c, must always obey eq 5–7.

Rates were measured in buffered solution, or in dilute KOH or HCl at 25 °C. The runs were conducted under pseudo-first-order conditions, and the ionic strength was always kept at 0.5 M with KCl. The reactions were monitored spectrophotometrically at, or near, λ_{max} of BMN (309 nm, ϵ 2.16×10^4) and/or near λ_{max} of benzalehyde (250 nm, ϵ 1.4×10^4).

Very good agreement was found between the rates determined at 309 nm and at 250 nm. This shows that no intermediate is present at measureable concentrations under our conditions.

Figure 1 shows the dependence of k_h on pH from pH 0.4 to 13.5. There are four phases in the pH–rate profile of k_h: phases I and III are pH independent while phases II and IV are inversely proportional to a_{H^+} (or proportional to a_{OH^-}). Reversibility, side reactions, and buffer catalysis in certain pH ranges made the determination of k_h less than straightforward, as detailed in the following sections.

pH 2.69–4.60. In a first series of experiments, the rate of hydrolysis of BMN was measured in carboxylate buffers. When an initial olefin concentration, $[\mathrm{S}]_0$, of 5×10^{-5} M was used, the plots of log ΔOD vs. time showed slight upward curvature after about 1 half-life, just as had been reported by Patai and Rappoport.[3] We suspected the cause to be the reversibility of the reaction: as the concentration of the products (benzaldehyde and malononitrile) increases with the progress of reaction, the k_c term (eq 4) which refers to a bimolecular process becomes increasingly important and distorts the first-order rate law.

The hypothesis of reversibility is supported by the following additional observations.

(1) When $[\mathrm{S}]_0$ is lowered to $\leq 2 \times 10^{-5}$ M, good first-order plots were obtained over several half-lives. The pseudo-first-order rate constants, $k_{obsd} = k_h$, obtained under these conditions are summarized in Table S1, part A (Supplementary Material).[9]

(2) Addition of benzaldehyde in concentrations at least 20-fold higher than $[\mathrm{S}]_0$ also leads to good first-order plots, even at $[\mathrm{S}]_0 > 2 \times 10^{-5}$ M, and has a rate-enhancing effect. This can be understood in terms of eq 8 which applies under these conditions.

$$k_{obsd} = k_h + k_c[\mathrm{PhCH{=}O}]_0 \qquad (8)$$

The results, obtained at pH 3.98, are summarized in Table S1, part B.[9] They yield $k_h = 3.75 \times 10^{-5}$ s^{-1}, $k_c = 1.04 \times 10^{-2}$ M^{-1} s^{-1}, and $K_h = k_h/k_c = 3.60 \times 10^{-3}$ M. Similar observations were made when an excess of malononitrile was added to the reaction solution. The results of a limited series of experiments are summarized in Table S1, part C.[9]

(3) Spectra of infinity solutions showed residual absorption by BMN, indicating that the reaction does not go to completion. In the presence of added benzaldehyde or malononitrile K_h could be determined by standard spectrophotometric procedures. These spectrophotometric K_h values are included in Table S1. The average from eight determinations is 2.77×10^{-3} M, in good agreement with the kinetic value of 3.60×10^{-3} M.

(4) When the equilibrium is approached from the product side, consistent results are obtained, as detailed in the next section.

Condensation Reaction, pH 0.42–4.07. The hydrolysis reaction becomes extremely slow at very low pH ($k_h < 10^{-7}$ s^{-1} at pH <1.4), making it impractical for kinetic study. However, by using high concentrations of malononitrile and approaching the equilibrium from the product side, k_{obsd} could be enhanced sufficiently as to make it measurable by the method of initial rates.

In a first series of experiments at pH 4.07 we determined rates as a function of excess malononitrile concentration. The results are in Table S2;[9] they yield, according to

$$k_{obsd} = k_h + k_c[\mathrm{CH_2(CN)_2}]_0 \qquad (9)$$

$k_h = 3.70 \times 10^{-5}$ s^{-1}, $k_c = 1.10 \times 10^{-2}$ M^{-1} s^{-1}, and $K_h = k_h/k_c = 3.36 \times 10^{-3}$ M. The K_h value is in excellent agreement with that obtained by hydrolyzing BMN (3.60×10^{-3} M).

In a second series of experiments the dependence of k_{obsd} on pH was determined in the presence of 0.04 M malononitrile. k_h was calculated as

$$k_h = \frac{k_{obsd}K_h}{K_h + [\mathrm{CH_2(CN)_2}]_0} \qquad (10)$$

with use of $K_h = 3.36 \times 10^{-3}$ M. These results are summarized in Table S3;[9] they are shown as filled circles in Figure 1.

pH 4.91–9.79. The hydrolysis was measured at 22 pH values in acetate, cacodylate, phosphate, and borate buffers. The buffer concentration was kept low (buffer base ≤ 0.02 M), in order to minimize buffer catalysis which becomes significant at higher

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(8) Bernasconi, C. F.; Zitomer, J. L.; Fox, J. P.; Howard, K. A. *J. Org. Chem.* **1983**, *49*, 482.

(9) See paragraph concerning supplementary material at the end of this paper.

Table I. Hydrolysis of BMN at 25 °C; Dependence on Buffer Concentration[a]

pH	buffer (pK_a^{BH})	[BH], M	$[B^-]$, M	$[BH]/B^-]$	10^4k_{obsd}, s^{-1}	k_h^B, M^{-1} s^{-1}
3.45	$CH_3OCH_2COO^-$ (3.45)	0.00093	0.00102	0.91	1.42	
		0.00473	0.0052	0.91	1.40	
		0.0946	0.0104	0.91	1.37	
		0.0182	0.020	0.91	1.41	
		0.191	0.210	0.91	1.39	
4.00	AcO^- (4.61)	0.10	0.025	4.0	0.310	
		0.20	0.05	4.0	0.313	
		0.40	0.10	4.0	0.306	
		0.80	0.20	4.0	0.310	
6.38		0.0017	0.0983	0.017	2.49	2.50×10^{-4}
		0.0051	0.295	0.017	2.95	
		0.0085	0.492	0.017	3.48	
6.46	$Me_2AsO_2^-$ (6.13)	0.0188	0.0412	0.46	2.41	1.03×10^{-3}
		0.0565	0.123	0.46	3.29	
6.60[b]		0.169	0.371	0.46	5.90	
6.77		0.0093	0.0407	0.23	2.50	
		0.0280	0.122	0.23	3.34	
6.90[b]		0.093	0.407	0.23	6.20	
6.63	$Cl_2CHPO_3^{2-}$ (5.46)	0.0020	0.0310	0.0645	2.33	6.74×10^{-4}
6.65		0.0041	0.0619	0.0645	2.49	
6.65		0.074	0.113	0.0645	2.88	
6.64		0.0094	0.142	0.0645	3.06	
6.63	HPO_4^{2-} (6.61)	0.0195	0.0205	0.95	2.33	1.08×10^{-3}
6.63		0.0586	0.0614	0.95	2.77	
6.64		0.0879	0.0921	0.95	3.18	
6.69		0.122	0.128	0.95	3.47	

[a] $[S]_0 \approx 2 \times 10^{-5}$ M, $\mu = 0.5$ M. [b] Higher pH for same buffer ratio indicates dependence of pK_a^{BH} on concentration, see text.

Table II. Hydrolysis of BMN in Strongly Basic Solution[a]

no.	pH	k_{obsd} (309 nm), s^{-1}	k_{obsd} (250 nm), s^{-1}
1	13.53	59.2	61.5
2	13.21	23.4	22.0
3	13.09	17.4	16.9
4	12.91	11.0	11.3
5	12.61	≈ 6.7[b]	≈ 6.4[b]
6	12.57	≈ 38[c]	

[a] $[S]_0 = 6.6 \times 10^{-6}$ M, $\mu = 0.5$ M. [b] Slightly biphasic plots, see text. [c] In the presence of 1.12×10^{-4} M $^-CH(CN)_2$; biphasic plot.

concentrations, as detailed below. The results are summarized in Table S4.[9]

Buffer Catalysis. The dependence of $k_{obsd} = k_h$ on buffer concentration was investigated in phases II and III of the pH–rate profile. The results are summarized in Table I. The following points are noteworthy.

(1) In the pH-dependent phase II no catalysis is observed by either methoxyacetate or acetate buffer. However, at pH 6.38 which is in the pH-*in*dependent phase III, catalysis by acetate ion *is* observed. Cacodylate, phosphate, and dichlorophosphonate buffers are also catalytic in phase III.

(2) The results with cacodylate buffer at two different buffer ratios show that it is the basic component which is catalytic. Plots (not shown) of k_{obsd} vs. buffer base concentration are linear; rate constants, k_h^B, for base catalysis are summarized in the last column of Table I.

(3) With cacodylate, and, to a lesser extent, with phosphate, the pH increases significantly at the highest concentrations, despite a constant buffer ratio. This indicates a specific salt effect on the buffer pK_a. Since k_{obsd} is pH independent in this range, no significant error in k_{obsd} is introduced by this pH variation.

pH 12.57–13.53. Rates were determined in KOH solutions. At the highest pH values (≥12.91) excellent first-order plots were obtained at both 309 and 250 nm, with $k_{obsd} = k_h$ being the same at both wavelengths (Table II). At pH 12.61 the log ΔOD vs. time plot shows some nonlinearity in the initial phase and slight upward curvature after about 3 half-lives while at pH ≤12.61 these distortions from linearity become more pronounced.

The upward curvature is reminiscent of our observations at relatively high BMN concentrations in acidic solution, which was shown to be a consequence of the reversibility of the reaction. However, the following points argue against the same interpretation in the present case.

(1) The deviation from first-order behavior occurs at $[S]_0$ as low as 6.6×10^{-6} M while in acidic solution upward curvature was only detectable at $[S]_0 > 2.0 \times 10^{-5}$ M. This result would require K_h to be smaller at high pH than in acidic solution, but eq 5 shows that K_h actually becomes larger at pH > $pK_a^{CH_2(CN)_2}$. For example, at pH 12.2 K_h is 11-fold larger than in acidic solution.

(2) Addition of a large excess of malononitrile does not straighten out the log ΔOD vs. time plots, although it does accelerate the reaction (entry no. 6 in Table II).

Our observations are consistent with a reaction of $^-CH(CN)_2$ with unreacted BMN as shown in Scheme II. The rate constants for this latter reaction have recently been determined to be $k_1^{CH} = 3.44 \times 10^5$ M^{-1} s^{-1} and $k_{-1}^{CH} = 7.69$ s^{-1} under the same conditions.[8] This reaction will interfere with the hydrolysis when the k_1^{CH} step is faster than, or of comparable rate as, the k_h step. For example, at pH 12 $k_h \approx 1.5$ s^{-1}; after 50% reaction 3.3×10^{-6} M of $^-CH(CN)_2$ has been formed, giving $k_1^{CH}[^-CH(CN)_2] \approx 1.1$ s^{-1}. As the pH is increased, a point will be reached where $k_h \gg k_1^{CH}[^-CH(CN)_2]$ and interference by $^-CH(CN)_2$ addition to BMN stops, as evidenced by the excellent first-order kinetics at pH ≥12.91. At very low pH interference also ceases because malononitrile is present in its protonated form.

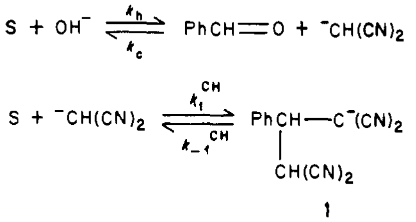
It should be noted that the large value of k_{obsd} in the presence of 1.12×10^{-4} M added malononitrile (entry no. 6 in Table II) reflects the fact that, under these conditions, $^-CH(CN)_2$ addition to BMN becomes the dominant (fast) process, with $k_{obsd} \approx k_1^{CH}[^-CH(CN)_2] + k_{-1}^{CH}$, as discussed in more detail elsewhere.[8]

Discussion

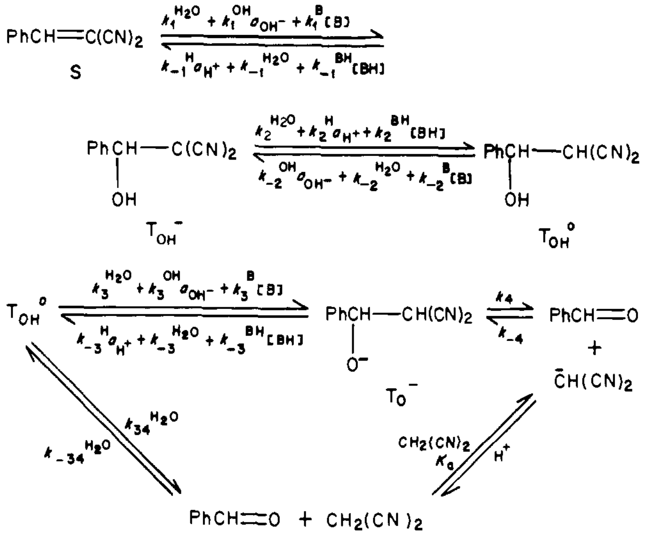
Mechanism. Our results are best discussed with reference to Scheme III. This scheme differs slightly from that suggested by Patai and Rappoport[3] in that we believe it more likely that water addition ($k_1^{H_2O}$) is concerted and bypasses $T_{OH}^{\pm}$, with a second water molecule acting as general base catalyst, as discussed in more detail below. Our scheme also includes a direct pathway from T_{OH}^{0} to products ($k_{34}^{H_2O}$) which will be shown to become important at very low pH.

In the ensuing discussion we shall make frequent use of the

Scheme II



Scheme III



following equilibrium constants: $K_1^{H_2O} = k_1^{H_2O}/k_{-1}^{H}$, $K_1^{OH} = k_1^{OH}/k_{-1}^{H_2O}$, $K_2^{H_2O} = k_2^{H}/k_{-2}^{H_2O} = 1/K_a^{CH}$, $K_3^{H_2O} = k_3^{H_2O}/k_{-3}^{H} = K_a^{OH}$, and $K_4 = k_4/k_{-4}$. Note that $K_2^{H_2O}$ is equivalent to the reciprocal C–H acidity constant of $T_{OH}{}^{\circ}$ (K_a^{CH}) while $K_3^{H_2O}$ is equivalent to the OH acidity constant of $T_{OH}{}^{\circ}$ (K_a^{OH}).

We make the following assignments of rate-limiting steps.

Phase IV. As discussed by Patai and Rappoport, the most likely rate-limiting step for k_h at high pH is OH^- attack on BMN (k_1^{OH}). The most direct evidence for this assignment comes from results in the Me_2SO–water mixtures where the formation of $T_{OH}{}^-$ and its conversion to products can be measured separately.[10] The assignments of rate-limiting steps in the other phases of the pH–rate profile are also consistent with rate-limiting OH^- addition in phase IV, and would be difficult to reconcile with any alternative. Thus k_h is given by

$$k_h = k_1^{OH} a_{OH^-} \tag{11}$$

Phase III. We agree with Patai and Rappoport that water attack ($k_h = k_1^{H_2O}$) must be rate limiting in the pH-independent region from pH 5 to 8. Alternatives which, in principle, are consistent with the rate law include rate-limiting carbon protonation of $T_{OH}{}^-$ by H_3O^+ (eq 12), or the combined $k_3^{H_2O}$ and $k_{34}^{H_2O}$ steps. (eq 13).

$$k_h = K_1^{H_2O} k_2^{H} \tag{12}$$

$$k_h = (K_1^{H_2O}/K_a^{CH})(k_3^{H_2O} + k_{34}^{H_2O}) \tag{13}$$

If the k_2^H step were rate limiting (eq 12), one would expect strong buffer catalysis (k_2^{BH}[BH] term). The estimated $pK_a^{CH} \approx 8.7$ (see below) implies that carbon protonation of $T_{OH}{}^-$ is thermodynamically favored with all the buffers used. From Hibbert et al.[11] one thus estimates $k_2^{BH}/k_2^{H} \approx 0.05$. At a cacodylic acid concentration of 0.1 M at pH 6.5 this would lead to $k_2^{BH}[BH]/k_2^{H}a_{H^+} \approx 1.5 \times 10^4$. This contrasts with an observed $k_2^{BH}[BH]/k_2^{H}a_{H^+} < 2$ under these conditions (Table I), clearly excluding eq 12. On the other hand, the observed weak general *base* (see Results) catalysis is typical for water addition to electrophiles (k_1^B step) and is consistent with water attack being rate limiting.

Equation 13 can be excluded on the grounds that in the pH range under consideration $k_3^{OH}a_{OH^-} \gg k_3^{H_2O} + k_{34}^{H_2O}$. This means that if one of the components of step 3 were rate limiting, it would have to be k_3^{OH} rather than $k_3^{H_2O} + k_{34}^{H_2O}$. That $k_3^{OH}a_{OH^-} \gg k_3^{H_2O} + k_{34}^{H_2O}$ can be justified as follows: k_3^{OH} is estimated to be $\approx 2 \times 10^9$ M^{-1} s^{-1},[10] while $k_3^{H_2O}$ is estimated to be $\approx 3.16 \times 10^{-1}$ s^{-1}, based on an estimated $pK_a^{OH} \approx 11.1$ (see below) and $k_{-3}^{H} \approx 4 \times 10^{10}$ M^{-1} s^{-1}.[10,12] Since $k_{34}^{H_2O} \ll k_3^{H_2O}$ (see below) we have, at pH 7, $k_3^{OH}a_{OH^-}/(k_3^{H_2O} + k_{34}^{H_2O}) \approx 1.74 \times 10^3$.

It should be noted that rate-limiting OH^- attack in phase IV is the natural continuation of water attack in phase III, i.e., for phases III and IV we have

$$k_h = k_1^{H_2O} + k_1^{OH} a_{OH^-} \tag{14}$$

Phase II. The pH dependence of phase II is consistent with either eq 15, 16, or 17. Rate-limiting carbon protonation of $T_{OH}{}^-$ by water (eq 15) can be excluded because strong buffer catalysis (k_2^{BH}[BH] term) should be observed. Specifically $k_2^{BH}[BH]/k_2^{H_2O} \approx 2 \times 10^6$ is expected at [BH] = 0.1 M, on the basis of Hibbert et al.[11] This contrasts with the fact that no buffer catalysis was observed.

$$k_h = K_1^{H_2O} k_2^{H_2O}/a_{H^+} \tag{15}$$

$$k_h = \frac{K_1^{H_2O}}{K_a^{CH}} k_3^{OH} a_{OH^-} \tag{16}$$

$$k_h = \frac{K_1^{H_2O}}{K_a^{CH}} \frac{K_a^{OH}}{a_{H^+}} k_4 \tag{17}$$

If oxygen deprotonation of $T_{OH}{}^{\circ}$ by OH^- (eq 16) were rate limiting, as is the case in the hydrolysis of benzylidene Meldrum's acid[13] and 1,1-dinitro-2,2-diphenylethylene,[14] one would also expect to see buffer catalysis (k_3^B[B] term), although the catalytic effect would be relatively small.[13,14] For this to be the case the relationship $k_4 > (\gg)\ k_{-3}^{H_2O} + k_{-3}^{H}a_{H^+} + k_{-3}^{BH}[BH]$ would have to hold. With $pK_a^{OH} \approx 11.1$ (see below) and $k_3^{OH} \approx 2 \times 10^9$ M^{-1} s^{-1} [13] one estimates $k_{-3}^{H_2O} \approx 3.5 \times 10^6$ s^{-1}, $k_{-3}^{H} \approx 4 \times 10^{10}$ M^{-1} s^{-1},[12] and $k_{-3}^{BH} \approx 2 \times 10^8$ M^{-1} s^{-1}.[10] Thus, at pH 3.45 and in the presence of 0.00093 M methoxyacetic acid (first entry in Table I) one calculates $k_{-3}^{H_2O} + k_{-3}^{H}a_{H^+} + k_{-3}^{BH}[BH] \approx 3.5 \times 10^6 + 1.42 \times 10^7 + 1.86 \times 10^5 = 1.79 \times 10^7$ s^{-1}. This means that k_4 would have to be $>(\gg) 1.79 \times 10^7$ s^{-1} for proton transfer to be rate limiting. Since we could not detect even a trace of buffer catalysis, we conclude that $k_4 \ll 10^7$ s^{-1}; below k_4 will be estimated to be 4.66×10^4 s^{-1}. Thus the conclusion to be drawn from the preceding analysis is that the breakdown of $T_O{}^-$ to products (k_4) is rate limiting in phase II, i.e., eq 17 holds.

Note that the above estimates of $k_{-3}^{H_2O}$, $k_{-3}^{H}a_{H^+}$, and k_{-3}^{BH}[BH] also show that the absence of buffer catalysis is not due to rapid protonation of $T_O{}^-$ by BH, since the k_{-3}^{BH}[BH] term (1.86×10^5) is much smaller than $k_{-3}^{H_2O} + k_{-3}^{H}a_{H^+} = 1.77 \times 10^7$ s^{-1}. This contrasts with the situation in the hydrolysis of *p*-nitrobenzylidene Meldrum's acid,[13] and also of BMN in Me_2SO–water mixtures,[10] where catalysis is observed at very low buffer concentrations ($k_4 > k_{-3}^{BH}[BH]$) but not at high concentrations ($k_4 \ll k_{-3}^{BH}[BH]$).

Phase I. The pH–rate profile shows the beginning of a leveling off at pH <1.0 although the plateau could not be reached under practical experimental conditions. A plateau value of $k_h = 1.30 \times 10^{-8}$ s^{-1} was obtained by extrapolation. It is attributed to

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(10) Bernasconi, C. F.; Kanavarioti, A.; Killion, R. B., to be published.

(11) (a) Hibbert, F.; Long, F. A.; Walters, E. A. *J. Am. Chem. Soc.* **1971**, *93*, 2829. (b) Hibbert, F. *Compr. Chem. Kinet.* **1977**, *8*, 97.

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

(13) (a) Bernasconi, C. F.; Leonarduzzi, G. D. *J. Am. Chem. Soc.* **1982**, *104*, 5143. (b) *Ibid.* **1980**, *102*, 1361.

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

Table III Parameters from pH-Rate Profile and Equilibrium Measurements

parameter	source (phase)	value
$(K_1^{H_2O}/K_a^{CH})k_{34}^{H_2O}$, s^{-1}	I	1.30×10^{-8}
$K_1^{H_2O}(K_a^{OH}/K_a^{CH})k_4$, $M^{-1}\ s^{-1}$	II	3.70×10^{-9}
$k_1^{H_2O}$, s^{-1}	III	2.45×10^{-4}
k_1^{OH}, $M^{-1}\ s^{-1}$	IV	2.75×10^{2}
K_{H_2O},[a] M		3.36×10^{-3}

[a] At pH < $pK_a^{CH_2(CN)_2}$, $K_h = K_{H_2O}$ (see eq 6).

rate-limiting breakdown of $T_{OH}°$ to products ($k_{34}^{H_2O}$), with k_h given by

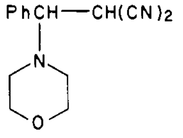
$$k_h = (K_1^{H_2O}/K_a^{CH})k_{34}^{H_2O} \tag{18}$$

Note that eq 18 differs from eq 13 in that there is no $k_3^{H_2O}$ term. Since proton transfer, $T_{OH}° \rightleftharpoons T_O^-$, is never rate limiting (see above), the $k_3^{H_2O}$ term is excluded.

The alternative possibility, rate-limiting carbon protonation by H_3O^+ (eq 12), can be excluded on the basis of the low numerical value of k_h: with $K_1^{H_2O} \approx 2.0 \times 10^{-11}$ M estimated below and $k_2^H \approx 2 \times 10^9\ M^{-1}\ s^{-1}$[11] eq 12 would require k_h to be $\approx 4.0 \times 10^{-2}\ s^{-1}$, which is ($1.54 \times 10^6$)-fold higher than the experimental value.

A referee has suggested that phase I might be due to a medium or specific salt effect. In the context of such an interpretation k_h at the lowest pH used (0.42) would be seen to deviate from the line of phase II by a factor of 2.5, implying a 2.5-fold acceleration by the medium or specific salt effect. Such an acceleration seems much too large. Furthermore, in 50% Me_2SO–50% water and 70% Me_2SO–30% water phase I starts to become significant at pH >2.0[10] where a medium or specific salt effect cannot reasonably be invoked.

Rate and Equilibrium Constants. Table III summarizes the parameters obtained from the four phases of the pH-rate profile. Table IV lists rate and equilibrium constants for the various steps which were either directly determined ($k_1^{H_2O}$, k_1^{OH}) or estimated as detailed in the following sections.



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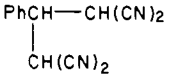


$$\mathrm{PhCH{-}CH(CN)_2}\ (\text{with } \mathrm{CH(CN)_2} \text{ on PhCH})$$

3

pK_a^{CH} and pK_a^{OH}. The pK_a^{CH} of **2** is 9.0 in water at 20 °C.[15] Since the hydroxy group in $T_{OH}°$ is somewhat more electron withdrawing than the morpholine moeity in **2**, one expects pK_a^{CH} of T_{OH}^0 to be somewhat lower, probably closer to 8.7. The same estimate (≈8.7) is obtained from a $\rho_I\sigma_I$ correlation including the pK_a of malononitrile and of **3**.[8]

A Taft correlation (eq 19)[16] for alcohols of the type R′R″R‴COH, using $\sigma_H^* = 0.49$,[17] $\sigma_{Ph}^* = 0.60$,[17] and $\sigma_{CH(CN)_2}^* = 3.42$,[18] yields $pK_a^{OH} = 11.1$.[20]

$$pK_a^{OH} = 17.03 - 1.32(\sigma_{R'}^* + \sigma_{R''}^* + \sigma_{R'''}^*) \tag{19}$$

$K_1^{H_2O}$ and K_1^{OH}. In 50% Me_2SO–50% water the ratio $K_1^{H_2O}/K_a^{CH} \approx 1.53 \times 10^{-2}$.[10] This ratio is essentially an experimental quantity except that it depends on the estimated value of $2 \times 10^9\ M^{-1}\ s^{-1}$ for k_3^{OH}. $K_1^{H_2O}/K_a^{CH}$ is expected to be about 1.5-fold lower in water, i.e., $\approx 1.0 \times 10^{-2}$. This expectation is based on the solvent dependence of $K_1^{H_2O}/K_a^{CH}$ in several Me_2SO–water mixtures.[10] With $pK_a^{CH} \approx 8.7$ (see above) this gives $K_1^{H_2O} \approx 2 \times 10^{-11}$ M.

Table IV Rate and Equilibrium Constants for the Steps of Scheme III

constant	value
Step 1	
$K_1^{H_2O}$, M	$\approx 2.00 \times 10^{-11}$
K_1^{OH}, M^{-1}	$\approx 1.45 \times 10^{3}$[a]
$k_1^{H_2O}$, s^{-1}	2.45×10^{-4}
k_{-1}^{H}, $M^{-1}\ s^{-1}$	$\approx 1.22 \times 10^{7}$
k_1^{OH}, $M^{-1}\ s^{-1}$	2.75×10^{2}
$k_{-1}^{H_2O}$	≈ 0.19
Step 2	
$(K_2^{H_2O})^{-1} = K_a^{CH}(pK_a^{CH})$, M	$\approx 2.0 \times 10^{-9}$ (8.7)
$k_2^{H_2O}$, s^{-1}	≈ 5.5
k_{-2}^{OH}, $M^{-1}\ s^{-1}$	$\approx 8.0 \times 10^{5}$
k_2^{H}, $M^{-1}\ s^{-1}$	$\approx 2.0 \times 10^{9}$
$k_{-2}^{H_2O}$, s^{-1}	≈ 4.0
Step 3	
$K_3^{H_2O} = K_a^{OH}(pK_a^{OH})$, M	$\approx 7.94 \times 10^{-12}$ (11.1)
$k_3^{H_2O}$, s^{-1}	$\approx 3.16 \times 10^{-1}$
k_{-3}^{H}, $M^{-1}\ s^{-1}$	$\approx 4.0 \times 10^{10}$
k_3^{OH}, $M^{-1}\ s^{-1}$	$\approx 2.0 \times 10^{9}$
k_{-3}^{w}, s^{-1}	$\approx 3.48 \times 10^{6}$
Step 34	
$K_{34}^{H_2O}$	≈ 0.33
$k_{34}^{H_2O}$, s^{-1}	$\approx 1.30 \times 10^{-6}$
$k_{-34}^{H_2O}$, $M^{-1}\ s^{-1}$	$\approx 3.88 \times 10^{-6}$
Step 4	
K_4, M	$\approx 2.74 \times 10^{-1}$
k_4, s^{-1}	$\approx 4.66 \times 10^{4}$
k_{-4}, $M^{-1}\ s^{-1}$	$\approx 1.70 \times 10^{5}$

[a] $K_w = 1.38 \times 10^{-14}\ M^2$ at $\mu = 0.5$ M.

Rate Constants for Proton Transfer. k_2^H and k_{-2}^{OH} were taken from Hibbert et al.,[11] and $k_2^{H_2O}$ and $k_{-2}^{H_2O}$ were then calculated from pK_a^{CH}. The rate constants for step 3 are based on Eigen's[12] work and, for k_3^{OH}, on our own.[13,14]

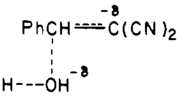
k_4 and $k_{34}^{H_2O}$. With the above estimates for $K_1^{H_2O}/K_a^{CH}$ and K_a^{OH}, k_4 is obtained from eq 17 and $k_{34}^{H_2O}$ from eq 18.

K_4 and $K_{34}^{H_2O}$. These constants were obtained from the following equations (definition of K_{H_2O} is in eq 6):

$$K_4 = \frac{K_{H_2O}K_a^{CH_2(CN)_2}K_a^{CH}}{K_1^{H_2O}K_a^{OH}} \tag{20}$$

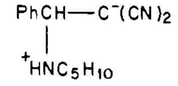
$$K_{34}^{H_2O} = \frac{K_a^{OH}K_4}{K_a^{CH_2(CN)_2}} \tag{21}$$

General Base Catalysis and Mechanism of Water Addition. The most likely mechanism for general base catalysis is an n-type reaction,[22] with a transition state **4**. This mechanism is very common in reactions of electrophiles with water.[5,22]



$$\mathrm{PhCH{=\!=}\overset{-\delta}{C}(CN)_2} \quad \overset{+\delta}{B}\cdots H\cdots \overset{-\delta}{OH}$$

4



$$\mathrm{PhCH{-}C^-(CN)_2}\quad \mathrm{{}^+HNC_5H_{10}}$$

5

The catalytic rate constants for the various bases are summarized in Table I ($k_h^B \equiv k_1^B$), and Figure 2 shows a Brønsted plot which includes points for $k_1^{H_2O}/55.5$ M and k_1^{OH}. Owing to the heterogeneous group of catalysts it is difficult to obtain an accurate Brønsted β value for this catalysis. Two, somewhat arbitrarily chosen, lines have been drawn in Figure 2. One goes through the OH^- point (dashed line) and has a $\beta = 0.55$, and the other is drawn through the two monoanions AcO^- and $Me_2AsO_2^-$ (circles) and has a $\beta = 0.40$.

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(15) Bernasconi, C. F.; Killion, R. B., to be published.

(16) Takahashi, S.; Cohen, L. A.; Miller, H. K.; Peake, E. G. *J. Org. Chem.* **1971**, *36*, 1205.

(17) Taft, R. W. In "Steric Effects in Organic Chemistry;" Newman, M. W., Ed.; Wiley: New York, 1956; Chapter 13.

(18) $\sigma_1 = 0.55$;[19] σ^* is obtained as $2.8\sigma_1/0.45$.[19]

(19) Exner, O. In "Correlation Analysis in Chemistry"; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439.

(20) The pK_a^{OH} of $PhCH(OH)CF_3$ calculated from eq 19 is 12.1 which is close to the experimental $pK_a^{OH} = 11.9$.[21] This good agreement enhances our confidence that our estimated pK_a^{OH} for $T_{OH}°$ is fairly reliable.

(21) Stewart, R.; Van der Linden, R. *Can. J. Chem.* **1960**, *38*, 399.

(22) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425; **1980**, *13*, 161.

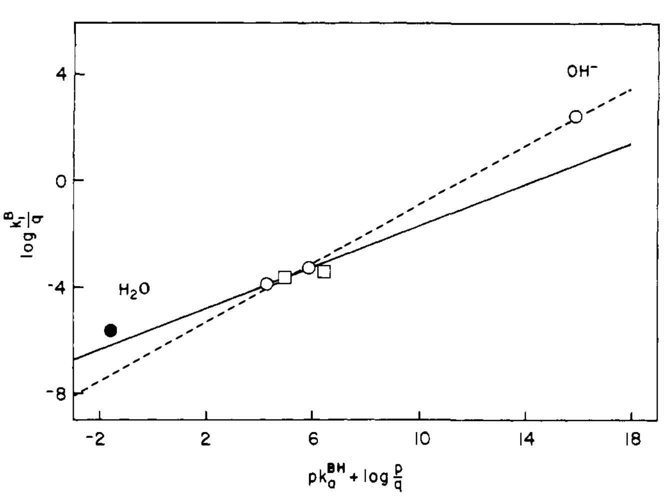


Figure 2. Brønsted plot for general base catalyzed water addition to benzylidenemalononitrile: (○) monoanions; (□) dianions; (●) neutral base (H_2O).

The dashed line implies that the OH^- reaction occurs by the same mechanism as the general base reaction, i.e., it represents OH'catalyzed water addition. There are some precedents for such an interpretation.[5,23,24] However, it is difficult to explain why water catalysis which should proceed by the same mechanism as general base catalysis would be nearly 100-fold faster than predicted by the Brønsted plot. We therefore prefer the solid line. The large positive deviation for the OH^- is easily explained by assuming a different mechanism, namely direct nucleophilic attack by OH^-.

The small positive deviation of the water point and the small negative deviation of the HPO_4^{2-} point may have electrostatic origins.[25] A possible interpretation is that proton transfer is somewhat ahead of C–O bond formation, which would create a $-\delta$ on the OH oxygen, as indicated in **4**. This could explain the stabilization of the transition state with a neutral catalyst (water, $B^{+\delta}$) and the progressive destabilization from a monoanion ($B^{-\delta}$) to a dianion ($B^{-1-\delta}$). It is of course possible that we are simply witnessing an interaction between the $-\delta$ on *carbon* and the charge on the catalyst. Whatever the fine points are, though, it is unclear why $Cl_2CHPO_3^{2-}$ does not deviate negatively from the Brønsted line.

With regard to the water-catalyzed water addition ($k_1^{H_2O}$) it should be noted that the concerted mechanism is probably not enforced by an impossibly short lifetime of the zwitterionic intermediate $T_{OH}^{\pm}$ (Scheme I). This lifetime can be estimated as follows.

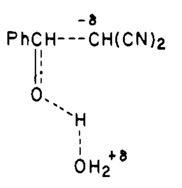
$$T_{OH}^- \underset{K_a^{\pm}}{\overset{H^+}{\rightleftharpoons}} T_{OH}^{\pm} \underset{k_1}{\overset{k_{-1}}{\rightleftharpoons}} S + H_2O \qquad (22)$$

If the k_{-1}^H process were to occur in two steps (eq 22), k_{-1}^H would take on the meaning of $k_{-1}^H = k_{-1}/K_a^{\pm}$. $pK_a^{\pm}$ can be estimated by two different methods. The first gives $pK_a^{\pm} \approx -2.3$; it is based on the observation that the pK_a of the zwitterion **5** is 0.6 units lower than that of piperidinium ion[15] and the assumption that the same pK_a difference exists between $pK_a^{\pm}$ of $T_{OH}^{\pm}$ and the pK_a of H_3O^+. The second yields $pK_a^{\pm} \gtrsim -2.3$ and can be justified as follows. The pK_a of protonated benzyl alcohol ($PhCH_2OH_2^+$) can be estimated to be −2.99;[26] the $^-C(CN)_2$ moiety in $T_{OH}^{\pm}$ will increase this value because it is somewhat electron donating owing to the negative charge. This is evident from the pK_a of **5** which is only 0.6 units lower than that of the piperidinium ion (see above) while the pK_a of $PhCH_2NH_3^+$ is 1.3 units lower than that of $CH_3NH_3^+$.[28] These considerations suggest that the $^-C(CN)_2$ moiety increases $pK_a^{\pm}$ by at least[29] 1.3 − 0.6 = 0.7 units over that of $PhCH_2OH_2^+$, i.e., $pK_a^{\pm} \gtrsim -2.3$.

Using $pK_a^{\pm} = -2.3$, one calculates $k_{-1} = k_{-1}^H K_a^{\pm} = 2.44 \times 10^9$ s^{-1}, a value which is more than 3 orders of magnitude lower than the limit of $\approx 10^{13}$ s^{-1} usually associated with a meaningful rate constant of a dissociative chemical process.[22,30] If a higher estimate for $pK_a^{\pm}$ is used, k_{-1} becomes still smaller. Also, if the k_{-1}^H process does not proceed via $T_{OH}^{\pm}$, but is concerted as implied by the Brønsted plot, this would mean that the actual k_{-1} is lower still.

Similar conclusions have been reached recently for the dehydration of carbinolamines[27b] and the breakdown of Meisenheimer complexes.[25b] This suggests that the coexistence of a stepwise and a concerted pathway is not uncommon, at least for n-type reactions, a conclusion of considerable current interest.[30]

Direct Breakdown of $T_{OH}°$. Just as in the hydrolysis of 1,1-dinitro-2,2-diphenylethylene[14] and of benzylidene Meldrum acid[13] we find that the direct breakdown of $T_{OH}°$ into products ($k_{34}^{H_2O}$ step) becomes the dominant pathway in strongly acidic solution. The relative merits of several mechanistic possibilities for this step have been discussed previously.[13,14] We favor one in which C–C bond cleavage and proton removal by water is concerted (**6**), possibly coupled with an intramolecular proton transfer (**7**) in some type of bifunctional catalysis by water.



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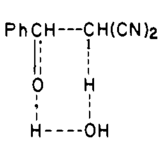

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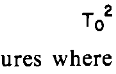
Conversion of T_{OH}^- to Products. At the highest pH used (13.53) formation of T_{OH}^- occurs at a rate given by $k_1^{OH}a_{OH^-} = 137$ s^{-1}. Since at this pH T_{OH}^- is thermodynamically favored over the substrate and there is no indication of an accumulation of T_{OH}^-, one must conclude that conversion of T_{OH}^- to products is much faster than its formation. According to Scheme III this requires $k_2^{H_2O} \gg 137$ s^{-1} which contrasts with an estimated $k_2^{H_2O} \approx 3.4$ s^{-1}. This inconsistency indicates that there must be an alternative pathway to products which is more rapid than protonation of T_{OH}^- by water.

There are two possibilities. One is an intramolecular proton switch which leads directly to T_O^- ($T_{OH}^- \rightarrow T_O^-$). The other is a reaction via the dianion T_O^{2-}, as has been observed in the hydrolysis of 1,1-dinitro-2,2-diphenylethylene.[14]



$$PhCH-\bar{C}(CN)_2,\ \text{with } O^- \text{ on } CH$$

T_O^{2-}

In Me_2SO—water mixtures where the conversion of T_{OH}^- to products can be measured directly there is evidence that both of these alternative pathways contribute to the rate.[10]

Carbon Basicities of $^-CH(CN)_2$ vs. OH^-. The equilibrium constant for OH^- addition to BMN, $K_1^{OH} = 7.25 \times 10^2$ M^{-1}, is 62-fold smaller than the equilibrium constant for $^-CH(CN)_2$ addition to BMN ($K_1^{CH} = 4.47 \times 10^4$ M^{-1}).[8] After taking into

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(23) (a) Ritchie, C. D. *J. Am. Chem. Soc.* **1975**, *97*, 1170. (b) Ritchie, C. D. *Ibid.* **1972**, *94*, 3275.

(24) Ride, J. N.; Wyatt, P. A. H.; Zochowski, Z. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1188.

(25) (a) Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803. (b) Bernasconi, C. F.; Howard, K. A. *Ibid.* **1983**, *105*, 4690. (c) McClelland, R. A.; Coe, M. *Ibid.* **1983**, *105*, 2718.

(26) Based on $pK_a = -1.98$ for $MeOH_2^+$ and a $\rho_I\sigma_I$ relationship with σ_I(phenol) = 0.12[19] and $\rho_I = -8.4$.[27]

(27) (a) Fox, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 1436. (b) Palmer, J. L.; Jencks, W. P. *Ibid.* **1980**, *102*, 6466.

(28) Perrin, D. D. "Dissociation Constants of Organic Bases in Aqueous Solution"; Butterworths: London, 1965.

(29) Since conversion of piperidine into **5** changes the amine from a secondary to a tertiary this should have the effect of lowering the pK_a, suggesting that the pK_a-enhancing effect of the $^-C(CN)_2$ moiety is actually larger than 0.7 units.

(30) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.

Table V Rate and Equilibrium Constants for Steps 1 and 4 in the Hydrolysis of Olefins in Water at 25 °C

	$PhCH{=}C(CN)_2$	$ArCH{=}CHNO_2$[a,b]	$PhCH{=}C(COO)_2C(CH_3)_2$
k_1^{OH}, $M^{-1}\ s^{-1}$	2.75×10^2	0.30	7.45×10^2
$k_{-1}^{H_2O}$, s^{-1}	≈ 0.19	6.0×10^{-7}	3.73×10^{-6}
K_1^{OH}, M^{-1}	$\approx 1.45 \times 10^3$	5.0×10^5 (2.5×10^6)	2.00×10^8
$K_1^{H_2O}$ ($pK_1^{H_2O}$)	$\approx 2.0 \times 10^{-11}$ (10.7)		3.75×10^{-6} (5.43)
k_4, s^{-1}	$\approx 4.66 \times 10^4$	$\approx 6.33 \times 10^2$	$\approx 5.0 \times 10^8$
k_{-4}, $M^{-1}\ s^{-1}$	$\approx 1.70 \times 10^5$	0.2	
K_4, M	$\approx 2.74 \times 10^{-1}$	$\approx 3.16 \times 10^3$ (3.16×10^2)[f]	$>(\gg) 1.09 \times 10^8$
pK_a^{OH}	≈ 11.1	≈ 13.5 (13.35)[f]	≈ 12.8
$pK_a^{CH_2XY}$	11.19	10.2[d]	4.83[e]

[a] Ar = 3,4-methylenedioxyphenyl. [b] Reference 6. [c] References 5 and 13. [d] Reference 55. [e] Reference 13a. [f] Estimated value for β-nitrostyrene, see text.

account the pK_a difference between the two bases, one obtains a corrected K_1^{CH}/K_1^{OH} ratio of 2.91×10^4 which is equivalent to Hine's K_{HA}^{RA}.[31] This high ratio is consistent with numerous observations showing that carbon bases have considerably higher carbon basicities than oxygen bases of comparable proton basicity.[31,32]

A similar comparison can be made for the addition of bases to benzaldehyde. The inverse of K_4, $1/K_4 = K^{CH} = 3.65$, represents the equilibrium constant for $^-CH(CN)_2$ addition to benzaldehyde. This compares with $K^{OH} = 0.18$ for the addition of OH^-.[33] The corrected K^{CH}/K^{OH} ratio is 9.52×10^3.

The somewhat higher K^{CH}/K^{OH} ratio for the addition to BMN (2.91×10^4) compared to that for addition to benzaldehyde (9.52×10^3) is consistent with the notion that BMN is a softer Lewis acid than benaldehyde, thus more strongly favoring the soft carbon base $^-CH(CN)_2$ over the hard OH^-.[34]

The Effect of the Activating Substituent(s). A. Equilibrium Constants. In Table V we have summarized rate and equilibrium constants of steps 1 and 4 for BMN, a substituted β-nitrostyrene,[6] and benzylidene Meldrum's acid.[13] The K_4 and k_4 values for the substituted β-nitrostyrene and for benzylidene Meldrum's acid are somewhat different from those given in the original papers. This is because both K_4 and k_4 depend on the estimated value for pK_a^{OH} which appears to have been overestimated in both cases. Using the same equation (eq 19) as for pK_a^{OH} of T_{OH}^0 derived from BMN, we obtain $pK_a^{OH} = 13.5$ for the β-nitrostyrene (original estimate 14.0) and $pK_a^{OH} = 12.8$ for benzylidene Meldrum's acid (original estimate 14.45).[35]

The values $K_1^{OH} = 2.5 \times 10^6\ M^{-1}$[36] and $K_4 = 3.16 \times 10^2$ M[38] given in parentheses for $ArCH{=}CHNO_2$ are those estimated for the parent β-nitrostyrene.

The lower limit, $K_4 > 1.09 \times 10^8$ M for benzylidene Meldrum's acid, was estimated from an equation analogous to eq 20 ($K_a^{CH_2(CN)_2}$ replaced by K_a of Meldrum's acid) and assuming that K_{H_2O} is larger than $K_{H_2O} = 3.36 \times 10^{-3}$ for BMN. The justification for this assumption is that no evidence of reversibility (such as non-linear first-order plots) was found during the investigation of the hydrolysis of benzylidene Meldrum's acid.[13]

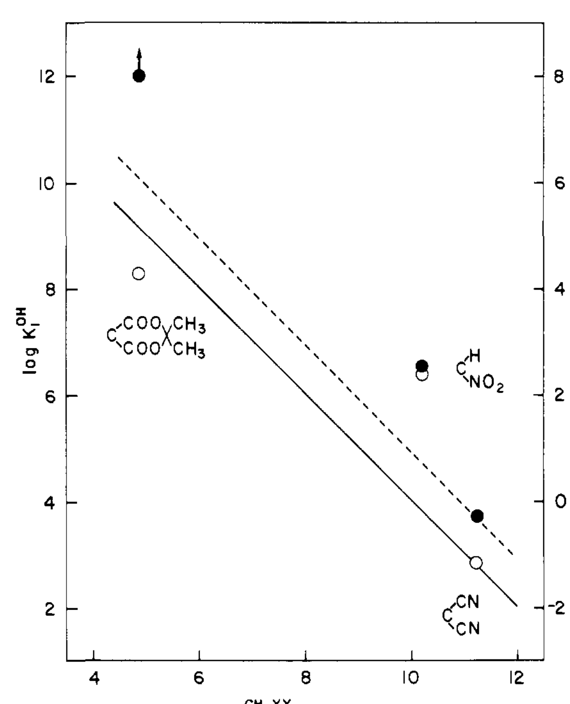

Figure 3. Correlation of K_1^{OH} (○, left ordinate) and K_4 (●, right ordinate) with $pK_a^{CH_2XY}$. Lines through the dicyano points have unit slope, see text.

K_1^{OH} for $PhCH{=}CXY$ increases with increasing acidity of the corresponding CH_2XY, as one might expect, but the correlation is not linear (Figure 3, open circles). We have drawn a line of unit slope through the point for BMN; K_1^{OH} for benzylidene Meldrum's acid is seen to deviate negatively by about one log unit from the line, while β-nitrostyrene shows a positive deviation of nearly three log units. In view of the uncertainty in K_1^{OH} for BMN, not too much significance should be attached to the small negative deviation of benzylidene Meldrum's acid; if real it could represent a steric effect of the bulkier benzylidene Meldrum's acid. However, the large positive deviation for the nitro compound appears to be well outside this uncertainty and suggests that, relative to its effect on proton acidity, the effect of the nitro group on Lewis acidity is exalted compared to that of the cyano groups or the $C(COO)_2C(CH_3)_2$ moiety.

A similar conclusion is reached when plotting log K_4 vs. $pK_a^{CH_2XY}$ (Figure 3, closed circles, right-hand ordinate); the nitro compound again deviates positively (by 1.75 log units) from the (dashed) line of unit slope drawn through the point of the dicyano compound. Both the K_1^{OH} and the K_4 process lead to the formation of carbanions which are either very similar (K_1^{OH} process) or identical (K_4 process) with those formed in the ionization of CH_2XY. One would thus expect that the relative stabilities of the respective carbanions would be about the same (K_1^{OH}) or identical (K_4) with those of ^-CHXY. Hence, barring steric effects which are probably small, the exalted K_1^{OH} and K_4 values for the nitro derivative must arise from a weaker C=C bond in $PhCH{=}CHNO_2$ (compared to $PhCH{=}C(CN)_2$) and a weaker C–C bond in T_O^- derived from $PhCH{=}CHNO_2$, respectively.

The large positive deviation of the benzylidene Meldrum's acid point in the K_4 correlation is probably mainly due to steric crowding in the T_O^- adduct.

B. Nucleofugality of Carbanions. The rate constant $k_4 = 4.66 \times 10^4\ s^{-1}$ for the collapse of T_O^- into benzaldehyde and $^-CH(CN)_2$ is remarkably high for a moderately basic carbanion as leaving group. It compares with an estimated rate constant of $\approx 5 \times 10^3\ s^{-1}$ for expulsion of a primary amine of equal basicity[40] from **8**,

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(31) Hine, J. "Structural Effects on Equilibria in Organic Chemistry"; Wiley-Interscience: New York, 1975; p 225.

(32) Hine, J.; Weimar, R. D. *J. Am. Chem. Soc.* **1965**, *87*, 3387.

(33) Greenzaid, P. *J. Org. Chem.* **1973**, *38*, 3164.

(34) Pearson, R. G. *Surv. Prog. Chem.* **1969**, *5*, 1.

(35) The rather large discrepancy between the original (14.45) and the new estimate (12.8) in the case of benzylidene Meldrum's acid calls for comment. The original estimate was based on the assumption that k_{-3}^{BH}, the rate constant for oxygen protonation of T_O^- by carboxylic acids, is $10^{10}\ M^{-1}\ s^{-1}$. Recent work[10] has shown that because of steric hindrance k_{-3}^{BH} is probably not higher than $\approx 2 \times 10^8\ M^{-1}\ s^{-1}$.

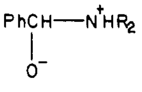
(36) Based on $K_1^{OH} = 5 \times 10^5\ M^{-1}$ for 3,4-methylenedioxy-β-nitrostyrene.[6] A fivefold higher value for β-nitrostyrene is estimated, based on substituent effects on K_1^{Pip} for phenyl-substituted β-nitrostyrenes.[37]

(37) Bernasconi, C. F.; Tia, P. R.; Renfrow, R. A., to be published.

(38) Based on substituent effects on the equilibrium constant of CN^- addition to substituted benzaldehydes.[39]

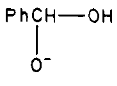
(39) Ching, W.-M.; Kallen, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 6119.

or with the rate constant of ≈5 × 10^3 s^{-1} for the expulsion of OH^- from **9**.[42] Similarly, the loss of Meldrum's acid ($pK_a = 4.83$)



$PhCH(O^-)-\overset{+}{N}HR_2$

8



$PhCH(O^-)-OH$

9

anion from the corresponding T_O^- adduct ($k_4 \approx 5 \times 10^8\ s^{-1}$) is about twofold faster than the expulsion of the equally basic methoxyamine ($pK_a = 4.7$) from **8** ($k = 3 \times 10^8\ s^{-1}$),[41] although the steric effect mentioned above probably contributes to this exceptionally high rate.

Even nitromethane anion leaves at a rate which is not much slower than that of primary amines of the same pK_a. A similar result ($k_4 = 10^3\ s^{-1}$) has been reported for the reaction $PhCH(O^-)C(CH_3)_2NO_2 \rightarrow PhCH{=}O + (CH_3)_2{}^-CNO_2$.[43]

The relatively high nucleofugality of carbanions in carbonyl-forming eliminations contrasts with a relatively lower nucleofugality in olefin-forming eliminations. For example, the loss of $^-CH(CN)_2$ from **1** (Scheme II) has a rate constant of 7.69 s^{-1}[8] which is only about 20-fold higher than $k_{-1}^{H_2O} = 0.38\ s^{-1}$ for the loss of the much more basic OH^- from T_{OH}^-. Or compared to a primary amine of the same basicity the loss of $^-CH(CN)_2$ is about 50-fold slower.[44] These results are consistent with the findings of Stirling.[46]

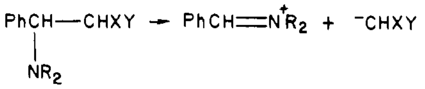
C. **Intrinsic Barriers.** k_1^{OH} for BMN is 916-fold larger than that for the nitro compound even though K_1^{OH} for BMN is 345-fold lower than that for $ArCH{=}CHNO_2$. This suggests that the intrinsic rate constant, k_0,[47] is substantially higher (or the intrinsic barrier, ΔG_0^{*},[47] substantially lower) for OH^- addition to BMN than for OH^- addition to β-nitrostyrene. If one assumes $\alpha = d \log k_1^{OH}/d \log K_1^{OH} = 0.5$ to correct for the different equilibrium constants, one obtains a ratio $k_1^{OH}((CN)_2)/k_1^{OH}(NO_2) = 1.70 \times 10^4$. This ratio may be considered to be an approximate measure of the ratio of the intrinsic rate constants, $k_0^{(CN)_2}/k_0^{NO_2}$.

On the basis of similar considerations for the BMN/benzylidene Meldrum's acid pair, one obtains $k_0^{(CN)_2}/k_0^{(COO)_2C(CH_3)_2} \approx 1.37 \times 10^2$.

It should be noted that even though the assumption of $\alpha = 0.5$ is an arbitrary and crude one, the qualitative conclusion that $k_0^{(CN)_2} \gg k_0^{NO_2}$ is not sensitive to this assumption;[48] on the other hand the rank of $k_0^{(COO)_2C(CH_3)_2}$ may become ambiguous if $\alpha \neq 0.5$.[48] A similar uncertainty in the rank of the $(COO)_2C(CH_3)_2$ moiety was noted for addition of amine nucleophiles to olefins.[5] It arises mainly because the high equilibrium constants necessitate long extrapolations in estimating k_0.

Similar conclusions can be reached with regard to step 4. If one again assumes $\alpha = d \log k_4/d \log K_4 = 0.5$ one obtains $k_0^{(CN)_2}/k_0^{NO_2} \approx 7.9 \times 10^3$ and $k_0^{(CN)_2}/k_0^{(COO)_2C(CH_3)_2} > (\gg)$ 1.86. The former ratio shows again that the intrinsic rate for the dicyano compound is much higher than that for the nitro compound, while the latter ratio leaves some ambiguity about the position of the Meldrum's acid derivative.[49]

Comparison with Other Systems and Conclusions. Our results add new support to the notion that, from a *kinetic* point of view, activation by cyano groups is far superior than activation by a nitro group. This qualitative pattern, which is related to the difference in the amount of resonance stabilization provided to the carbanion by the two kinds of activating groups,[7] seems to be independent of the type of reaction which generates the carbanion. It has been observed in proton transfers,[7] in the addition of amines to olefins,[7] in reactions such as eq 23,[1] in an S_N2 reaction on sulfur,[50] and now in the addition of OH^- to olefins and the breakdown of tetrahedral intermediates such as T_O^- into benzaldehyde and ^-CHXY.



$$PhCH(NR_2)-CHXY \rightarrow PhCH{=}\overset{+}{N}R_2 + {}^-CHXY \qquad (23)$$

There are *quantitative* differences, though, which seem to depend on the type of reaction. On the basis of previous work it appears that $k_0^{(CN)_2}/k_0^{NO_2}$ is largest for proton transfer (10^8 to 10^9),[7] smallest for the addition of amines to olefins (≈10^3),[7] and intermediate for reaction 23 (≈10^4 to 10^5)[51] and for nucleophilic displacement on sulfur (10^3 to 10^5).[50] Possible reasons for these quantitative differences have been discussed in detail elsewhere.[7,50,52] They are, briefly, as follows. In the proton transfers there are three major factors which contribute to the intrinsic barrier and increasingly so when the carbanion is strongly resonance stabilized. They are (a) the diminished hydrogen-bonding capability of the carbon of the carbanion, (b) structural reorganization, and (c) solvent reorientation or, more precisely, its lag behind bond changes.

For the reaction in which the carbanion acts as a nucleophile or nucleofuge (eq 23, S_N2) only factors b and c can contribute and hence the difference in $k_0^{(CN)_2}/k_0^{NO_2}$ is smaller.

In nucleophilic addition to olefins factor a is again inoperative. Furthermore, structural reorganization b is a much less significant factor because the carbanionic site is already sp^2 hydribized in the olefin. Thus $k_0^{(CN)_2}/k_0^{NO_2}$ should essentially reflect the difference in solvational reorientation only and be smallest.

The results of the present study, which lead to a slightly larger $k_0^{(CN)_2}/k_0^{NO_2}$ ratio for OH^- addition to the olefins (≈1.70×10^4) than for the k_4 process (≈7.9×10^3), seem to be at variance with these earlier quantitative findings. However, it needs to be realized that the $k_0^{(CN)_2}/k_0^{NO_2}$ ratios obtained in the present study have a considerably higher uncertainty than the ones obtained earlier, and thus the present result might be an artifact. One source of uncertainty in the present ratios is the fact that our equilibrium constants are based on estimates. The other, more serious, one is that the $k_0^{(CN)_2}/k_0^{NO_2}$ ratios had to be calculated by rather long extrapolations, making them quite sensitive to the choice of α. For example, if $\alpha = 0.3$ were assumed for step 1 and $\alpha = 0.7$ for step 4, the $k_0^{(CN)_2}/k_0^{NO_2}$ ratios would change to 5.29×10^3 for step 1[48] and 5.12×10^4 for step 4,[49] i.e., they would be in the "correct" rank order.

Experimental Section

Materials. Benzylidenemalononitrile was available from a previous study.[54] Malononitrile (Aldrich) was either recrystallized from ethanol or distilled and stored over P_2O_5, mp 31–33 °C (lit. 32 °C).[55] Pyridine was refluxed over BaO for 12 h and distilled under nitrogen. An attempt to synthesize dichlorophosphonic acid according to Kinnear and Perrin[56] failed. The following procedure was successful. In a 500-mL round-bottom flask containing 66 g (0.495 mol) of anhydrous $AlCl_3$ and 39 mL

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(40) This estimate is based on $k = 3 \times 10^8\ s^{-1}$ for the expulsion of methoxyamine ($pK = 4.7$) and a $\beta_{lg} = 0.8$.[41]

(41) Rosenberg, S.; Silver, S. M.; Sayer, J. M.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7986.

(42) Bell, R. P.; Sorensen, P. E. *J. Chem. Soc. Perkin Trans. 2* **1976**, 1594.

(43) Guanti, G.; Petrillo, G.; Thea, S.; Cevasco, G.; Stirling, C. J. M. *Tetrahedron Lett.* **1980**, 4735.

(44) Based on $k = 2 \times 10^4\ s^{-1}$ for piperidine expulsion[15] and an estimated 50-fold lower rate for a primary amine.[45]

(45) See, e.g.: Bernasconi, C. F.; Carré, D. J.; Fox, J. P. In "Techniques and Applications of Fast Reactions in Solution"; Gettins, W. J., Wyn-Jones, E., Eds.; Reidel: Dordrecht, Holland, 1979; p 453.

(46) (a) Varma, M.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1981**, 553. (b) Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198.

(47) k_0 (ΔG_0^{*}) is defined as $k_1^{OH} = k_{-1}^{H_2O}$ when $K_1^{OH} = 1$ ($\Delta G° = 0$).

(48) For example, if $\alpha = 0.3$ (0.7) were assumed, one would obtain $k_0^{(CN)_2}/k_0^{NO_2} = 5.29 \times 10^3$ (5.48×10^4) and $k_0^{(CN)_2}/k_0^{(COO)_2C(CH_3)_2} = 12.8$ (1.46×10^3).

(49) If $\alpha = 0.3$ (0.7) one obtains $k_0^{(CN)_2}/k_0^{NO_2} = 1.22 \times 10^3$ (5.12×10^4) and $k_0^{(CN)_2}/k_0^{(COO)_2C(CH_3)_2} > (\gg)$ 3.54×10^{-2} (9.75×10^1).

(50) Gilbert, H. F. *J. Am. Chem. Soc.* **1980**, *102*, 7059.

(51) Estimated, based on a comparison between $^-CH(CN)_2$ and $^-CH(CN)C_6H_4$-4-NO_2.[1]

(52) Bernasconi, C. F.; Fox, J. P.; Murray, C. J.; Carré, D. J. *J. Am. Chem. Soc.* **1983**, *105*, 4349.

(53) Ritchie, C. D. *J. Am. Chem. Soc.* **1969**, *91*, 6749.

(54) Bernasconi, C. F.; Fox, J. P.; Fornarini, S. *J. Am. Chem. Soc.* **1980**, *102*, 2810.

(55) Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439.

(56) Kinnear, A. M.; Perrin, E. A. *J. Chem. Soc.* **1952**, 3437.

(0.445 mol) of PCl_3 were placed 75 mL (0.422 mol) of purified $CHCl_3$ and the mixture was refluxed for 7 h. The white solid formed was dissolved in approximately 600 mL of CH_2Cl_2 and cooled to −25 °C with the addition of dry ice. Water was added dropwise, with continuous swirling, while the aluminum products coagulated, leaving a clear liquid. The liquid was decanted, filtered twice, dried over $CaCl_2$, and refiltered. The solvent was removed on a flash evaporator, leaving $\approx$50 mL of a pale yellow, clear liquid, which was fractionally distilled at 1-2 mm. The fraction distilling at 61-64 °C ($Cl_2CHP(O)Cl_2$) was collected (41.8 g) and added to 100 mL of water with stirring. A large fraction of water was then removed with a flash evaporator and the product dried for 9 days in vacuo over P_2O_5, mp 110-114 °C (lit. 113-116 °C).[56]

All other materials were reagent grade commercial products.

Kinetics. The slow reactions were measured in a temperature-controlled Gilford Model 2000 or a Perkin-Elmer Model 559 spectrophotometer. Cuvettes containing buffer solutions were equilibrated at 25 °C and BMN or malononitrile/benzaldehyde added by injecting a few μL of concentrated stock solution. pH measurements were performed with a Corning Model 110 pH meter thermostated at 25 °C.

The fast reactions were monitored in a Durrum stopped-flow apparatus with computerized data handling. BMN solutions for mixing experiments were prepared in slightly acidic solution, to prevent hydrolysis in the reservoir syringe of the stopped-flow apparatus. pH measurements were performed on mock mixing solutions outside the stopped-flow apparatus.

Acknowledgment. This research was supported by Grant CHE80-24261 from the National Science Foundation.

Registry No. BMN, 2700-22-3.

Supplementary Material Available: Kinetic data, Tables S1-S4 (6 pages). Ordering information is given on any current masthead page.

Communications to the Editor

Inversion of the Electronic Reactivity of Allyl Acetates Using an Aluminum-Tin Reagent

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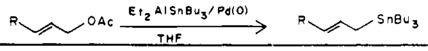
Recently, allylstannanes have emerged as valuable tools in organic synthesis, coupling with electrophiles such as carbonyl compounds under mild conditions and in a highly chemoselective and regioselective manner.[1,2] Allylstannanes also serve as a very soft source of allyl anion, making them ideal substrates for reaction with allyl[3] and arylpalladium(II) complexes.[4] However, their use in synthesis has been restricted to reactions involving relatively simple allyl systems, since current methods of synthesis of allylstannanes suffer from the often poor chemoselectivity and regioselectivity exhibited by the stannylating reagent.[5-13]

Table I. Conversion of Allyl Acetates to Alkylstannanes



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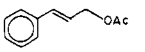
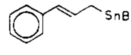
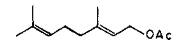
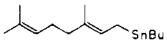
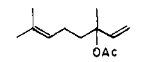
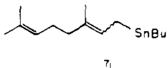
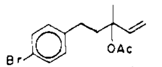
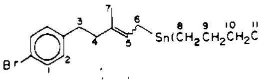
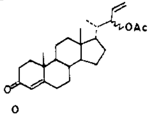
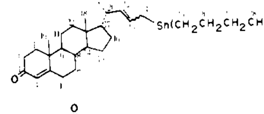
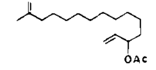
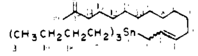
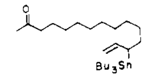
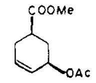
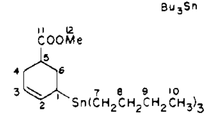
1		25 °C/6 hr		72[g]
2		35 °C/6 hr		68[h]
3		25 °C/20 hr		74[b]
4		25 °C/20 hr		61[c,i]
5		25 °C/20 hr		70[d,i]
6		25 °C/20 hr	 A  B	71[e,i]
7		25 °C/20 hr		73[f,i]

[a] The yields are of chromatographed samples and are homogenous by TLC analysis. [b] The product was obtained as a 1:1 mixture of *E*/*Z* isomers. [c] The product was obtained as a 6:4 mixture of *E*/*Z* isomers. [d] The product was obtained as a 9:1 mixture of trans/cis olefin isomers. [e] The ratio A:B = 82:18. Product B was not isolable, but treatment of the reaction mixture with trifluoroacetic produced an 82:18 mixture of terminal/internal olefin isomers. [f] The product was obtained as a 70:30 mixture of trans/cis isomers. [g] Reference 22. [h] Reference 23. [i] The numbering of carbons corresponds to spectral data for new compounds reported in the supplementary material.

We were prompted to undertake a study of the reaction of an aluminum-tin species with allylic acetates in the presence of a catalyst to overcome existing limitations.[14] Nevertheless, such

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(1) Sawyer, A. K. In "Organotin Compounds"; Marcel Dekker: New York, 1971; Vol. III.

(2) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555-566.

(3) (a) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2595-2598. (b) Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599-2602.

(4) Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, J. *Chem. Lett.* **1977**, 301-302.

(5) For coupling of (trialkylstannyl)lithium reagents with allylic halides, see: Wickham, G.; Young, D.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 4884-4895.

(6) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481-1487.

(7) San Filippo, J., Jr.; Silbermann, J.; Fagan, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 4834-4842.

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