(2S,3S)-1,4-dimethoxybutane-2,3-diol, 50622-10-1; acetophenone dimethyl acetal, 4316-35-2; (R,R)-N,N,N',N'-tetramethyltartamide, 26549-65-5; 2-methylacetophenone, 577-16-2; diethyl L-tartarate, 87-91-2; 2-methylacetophenone dimethyl acetal, 118719-92-9; o-tolualdehyde dimethyl acetal, 58378-32-8; tricarbonyl[η^6-(4S,5S)-4,5-bis[(N,N-dimethylamino)methyl]-2-methyl-2,6-bis-[2'-(trimethylsilyl)phenyl]-1,3-dioxolane]chromium(0), 141376-31-0.

Supplementary Material Available: Experimental details and spectral data for the preparation of the precursors to compounds 1–4, the preparation of compounds 12–18, and CD spectra of compounds 2, 3, and their immediate precursors (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Rate-Determining Steps in Michael-Type Additions and E1cb Reactions in Aqueous Solution

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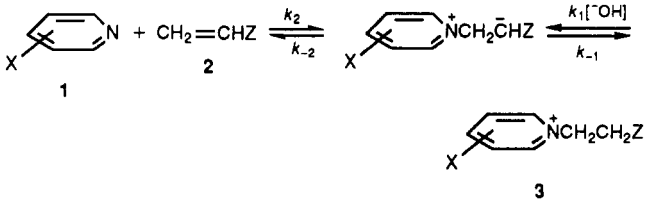
Rates of equilibration of a series of 10 substituted pyridines and five Michael acceptors (CH_2=CHZ, Z = CHO, $COCH_3$, SO_2CH_3, CN, and $CONH_2$) with the corresponding N(ZCH_2CH_2) pyridinium cations have been measured in aqueous solution at ionic strength 0.1 and 25 °C. Analysis of the dependence of the pseudo-first-order rate constants for equilibration as a function of acceptor concentration and of pH allows the evaluation of the second-order rate constants (k_{Nu}) for the nucleophilic attack of each of these pyridines upon each of these acceptors and also the second-order rate constants (k_{OH}) for the hydroxide ion catalyzed E1cb elimination reaction which is the microscopic reverse of each of these Michael-type addition reactions. Brønsted-type plots for each of these processes as a function of the basicity of the substituted pyridine are concave down for each of Z = CHO, $COCH_3$, and CN and are consistent with a change from rate-determining nucleophilic attack for the more basic pyridines to rate-determining protonation of the carbanionic intermediate by a water molecule for less basic pyridines and the corresponding microscopic reverse processes in the elimination reactions. The "break" in these Brønsted-type plots is shown to occur at a pyridine basicity that is a function of the Z-activating substituent. Brønsted β_{lg} and β_{nuc} are evaluated for each rate-determining step (wherever accessible); these two parameters are shown to pass through minima as a function of reactivity. β_{eq} is shown to be a simple linear function of reactivity (as log k_{Nu}) for nucleophilic addition to the acceptor species, although K_{eq} is relatively insensitive to the nature of the Z-activating substituent.

We have recently reported[1] that the rates of equilibration of acrylonitrile and a substituted pyridine with the corresponding *N*-(2-cyanoethyl)pyridinium cation (3, Z = CN) can be readily observed in aqueous solutions for many substituted pyridines (Scheme I).[2] For this Michael-type addition reaction[3] and its E1cb microscopic reverse, we demonstrated a change in rate-determining step as a function of pyridine basicity for pyridines having conjugate acids of pK_{BH} = 5.8. For pyridine nucleophiles of high basicity, rate-determining nucleophilic attack (k_2) was observed in the addition reactions; this assignment corresponds to rate-determining leaving group departure from the carbanionic intermediate (k_{-2}) in the elimination reaction. For weakly basic pyridines, deprotonation of 3 (Z = CN) (k_1) was found to be rate-determining for the elimination reaction, and consequently protonation (k_{-1}) of the carbanionic intermediate by a water molecule is rate-determining in the addition reaction in this case.

The wide range of basicities that is available for simple ring-substituted pyridines is crucial to the demonstration of such a change in the rate-determining step as a function of nucleophile (or nucleofuge) basicity. However, the particular reactivities that are associated with these pyridine nucleophiles (or nucleofuges) are also an important

Scheme I



factor in producing a change in the rate-determining step. In a subsequent study,[4] we demonstrated that a similar change in rate-determining step is apparent for the E1cb reactions of *N*-(2-(4-nitrophenyl)ethyl)pyridinium cations (3, Z = 4-$NO_2C_6H_4$) at pK_{BH} = 6.5, although no such change is observable[5] over a comparable range of nucleofuge basicities in the analogous elimination reactions of *N*-(2-(4-nitrophenyl)ethyl)quinuclidinium cations. This study[4] demonstrated that the ability to observe a change in rate-determining step, as well as the nucleofuge (or nucleophile) basicity at which this change occurs, may be a function of the nature of the carbanion-stabilizing group (i.e., activating group) (Z) as well as of the structure of the nucleofuge (nucleophile).

Electron-deficient monosubstituted alkenes 2 (acrylic acid derivatives, vinyl ketones, etc.) are commonly used as Michael acceptors in synthetic organic chemistry. While many reactivities of Michael acceptors toward nucleophilic addition reactions have been measured, the mechanistic

(1) Bunting, J. W.; Toth, A.; Heo, C. K. M.; Moors, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 8878.

(2) k_1 and k_{-1} of the current Scheme I are defined in the same way as these parameters in Scheme I of ref 1. k_2 and k_{-2} in the current work were defined as k_{Nu} and k_2, respectively, in ref 1. In the current report, k_{Nu} is defined as the observed second-order rate constant for the reaction of 1 with 2 (see eq 2).

(3) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; p 665.

(4) Bunting, J. W.; Kanter, J. P. *J. Am. Chem. Soc* **1991**, *113*, 6950.

(5) (a) Alunni, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 2052. (b) Keeffe, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1983**, *105*, 265.

0022-3263/92/1957-3570$03.00/0

Table I. Rate Data for the Reaction of 4-(Dimethylamino)pyridine with Electrophilic Alkenes 2[a]

alkene	k_{Nu}	k_{OH}	K_{eq}	K_{add}
CH_2=CHCHO	2.39 (9)	5.6 (3)	0.42 (3)	7.9×10^3
CH_2=$CHCOCH_3$	0.55 (1)	0.40 (1)	1.38 (4)	2.6×10^4
CH_2=$CHSO_2CH_3$	8.25 (9) $\times 10^{-2}$	0.024 (3)	3.4 (4)	6.4×10^4
CH_2=$CHC_5H_4NCH_3^+$ [b]	5.2 (1) $\times 10^{-2}$	0.56 (1)	0.093 (2)	1.9×10^3
CH_2=$CHCO_2CH_3$	1.46 (4) $\times 10^{-2}$	[c]		
CH_2=CHCN[d]	4.03 (4) $\times 10^{-3}$	4.2 (3) $\times 10^{-3}$	0.98 (5)	2.0×10^4
CH_2=$CHCONH_2$	6.1 (1) $\times 10^{-4}$	1.9 (4) $\times 10^{-4}$	3.2 (7)	6.0×10^4
CH_2=$CHCON(CH_3)_2$	1.82 (4) $\times 10^{-4}$	7.4 (9) $\times 10^{-5}$	2.4 (3)	4.8×10^4
CH_2=$CHC_6H_4NO_2$[e]	[f]	1×10^{-5} [g]		
(*E*)-CH_3CH=CHCHO	8 (2) $\times 10^{-3}$	25.3 (5)	3.2 (7) $\times 10^{-3}$	60
CH_2=$C(CH_3)$CHO	1.8 (3) $\times 10^{-2}$	9 (1)	2.0 (5) $\times 10^{-3}$	40

[a] In aqueous solution at 25 °C, ionic strength 0.1; k_{Nu} (M^{-1} s^{-1}) and k_{OH} (M^{-1} s^{-1}) are defined by eq 2, and K_{eq} and K_{add} (M^{-1}) by eqs 3 and 5, respectively; integers in parentheses indicate standard errors in the final significant figure of the rate and equilibrium constants. [b] 1-Methyl-4-vinylpyridinium cation. [c] Not directly measurable due to competing hydroxide ion catalyzed ester hydrolysis. [d] Data from ref 1. [e] 4-Nitrostyrene. [f] Extremely slow. [g] Data from ref 4; corrected[4] to ionic strength 0.1.

details of these reactions have rarely been explored in sufficient detail to allow the assignment of the rate-determining step.[1,6] Furthermore, many of these studies have been in organic solvents in which the basicity of the nucleophile is not always readily measurable. Quantitative studies of Michael-type additions are relatively scarce in aqueous solutions in which a quantitative measurement of the nucleophile basicity is readily available.

In the current study, we have taken advantage of the favorable reactivity characteristics that are mentioned above for pyridine nucleophiles to explore the detailed reactivities and rate-determining steps of Michael-type additions in aqueous solution as a function of several common activating Z substitutents in the acceptor species (Z = CHO, $COCH_3$, CN, $CONH_2$, SO_2CH_3). We are now able to demonstrate that the nucleophile basicity at which the change in rate-determining step occurs in these reactions depends upon the nature of the activating Z substituent. Furthermore, since we observe the approach to the overall equilibrium of Scheme I in these reactions, in some cases we have been able to generate Brønsted-type plots for each rate-determining transition state in both the addition and elimination directions. In this way, we have established that, irrespective of rate-determining step, the β_{nuc} and β_{lg} slopes are also quite sensitive to the identity of the Z substituent. The equilibrium Brønsted slopes (β_{eq}) also appear to vary systematically with the nature of this Z substituent, although the individual equilibrium constants for these reactions are relatively independent of Z.

Experimental Section

Materials. The sources and purification of substituted pyridines have been described in an earlier study.[1] 2-(2-Bromoethyl)-1,3-dioxane, 4-vinylpyridine, acrylamide (99+ %) and *N*,*N*-dimethylacrylamide (99%) were obtained from Aldrich Chemical Co. Acrolein, methacrolein, *trans*-crotonaldehyde, methyl vinyl ketone, methyl acrylate, and methyl vinyl sulfone were obtained commercially and distilled before use; acrolein and methyl vinyl ketone were distilled daily during the kinetic studies with these compounds. All buffer species, standardized aqueous solutions of potassium hydroxide and hydrochloric acid, and crystalline potassium chloride were commercial ACS grade materials. Buffer solutions contained *N*-[tris(hydroxymethyl)-methyl]-3-aminopropanesulfonic acid (TAPS from Sigma Chemical Co.) and KOH in the range pH 7.7–9.3, sodium carbonate and sodium bicarbonate in the range pH 9.6–10.8, and KOH + KCl for pH > 11.0.

1-Methyl-4-vinylpyridinium bromide was prepared by stirring 4-vinylpyridine (5.4 mL) and bromomethane (27 mL) in acetone (25 mL) in a pressure bottle overnight at room temperature. The white salt (mp 260–265 °C) that precipitated in >90% yield was filtered and dried under vacuum: ^1H NMR (in D_2O) δ 4.35 (s, 3 H), 5.95–6.45 (m, 2 H), 6.95 (dd, 1 H), 8.05 (d, 2 H), 8.70 (d, 2 H); ^{13}C NMR (in D_2O) δ 50.5, 127.6, 130.4, 135.2, 148.1, 156.3.

The bromide salt of the 4-(dimethylamino)-1-(2-(1,3-dioxan-2-yl)ethyl)pyridinium cation (6·Br^-) was prepared by refluxing 4-(dimethylamino)pyridine (626 mg) and 2-(2-bromoethyl)-1,3-dioxane (699 μL) in ethanol (15 mL) for 26 h. Removal of the solvent gave 6·Br^- (mp 163 °C; 76% yield) which was characterized by ^1H NMR spectroscopy (see Results) and ^{13}C NMR (in D_2O): δ 27.8, 37.5, 42.4, 55.6, 70.0, 102.4, 110.6, 144.9, 159.5.

^1H NMR and ^{13}C NMR spectral data were obtained on a Varian Gemini 200 spectrometer; all chemical shifts are relative to the methyl groups of sodium 4,4-dimethyl-4-silapentane-1-sulfonate. The purity of the above compounds was judged to be >95% by ^1H and ^{13}C NMR spectral characterizations.

Kinetic Studies. All kinetic data were obtained spectrophotometrically on either Varian Cary 210 or GBC 911 spectrophotometers in aqueous solutions of ionic strength 0.1 (buffer or KOH adjusted with KCl) at 25 °C. All absorbance vs. time data were collected on an IBM-compatible PC using 100–300 individual absorbance measurements which were uniformly spread over >90% of the reaction. Data collection on each spectrophotometer employed software that was designed in this department by Mr. George Kretschmann. Pseudo-first-order rate constants (k_{obs}) were calculated by fitting these data via an iterative procedure based upon the Marquardt algorithm. Standard deviations in k_{obs} in individual runs were always less than 1%. Specific experimental conditions for the collection of kinetic data for each reaction are summarized in Tables S1 and S2 and are discussed further in the Results. After each kinetic run, the pH of the reaction solution was measured on a Radiometer PHM82 pH meter using a GK2401B combination electrode with calibration against BDH Colourkey standard buffer solutions in a cell thermostatted at 25 °C.

Results

Addition of 4-(Dimethylamino)pyridine to Electrophilic Alkenes. We initially investigated the kinetics of the reactions of 4-(dimethylamino)pyridine (1, X = 4-$N(CH_3)_2$) with CH_2=CHZ (2) for a variety of Z substituents in order to establish a quantitative scale of relative reactivities of electrophilic alkenes with pyridine nucleophiles in aqueous solution. This nucleophile was chosen because of its relatively high reactivity and also the favorable, and highly characteristic, spectrophotometric change that is observed upon alkylation of the pyridine-ring nitrogen atom.[1] For each 2 in Table I, we have observed the clean formation of the corresponding *N*-(2-(substituted)ethyl)-4-(dimethylamino)pyridinium cation (3, X = 4-$N(CH_3)_2$) in similar spectrophotometric experiments to those which were illustrated for acrylonitrile (2, Z = CN) in our previous study.[1]

Pseudo-first-order rate constants for the equilibration of 1, X = 4-$N(CH_3)_2$, with 3, X = 4-$N(CH_3)_2$, Z = CHO,

(6) (a) Patai, S.; Rappoport, Z. *The Chemistry of Alkenes*; Patai, S., Ed.; Wiley: New York, 1964; Chapter 8. (b) Suminov, S. I.; Kost, A. N. *Russ. Chem. Rev.* **1969**, *38*, 884.

Table II. Substituent Effects upon the Equilibration of Pyridines 1 and Electrophilic Alkenes 2 with *N*-(2-Z-ethyl)pyridinium Cations 3[a]

X	pK_{BH}	k_{Nu}	k_{OH}	K_{eq}	K_{add}
			CH_2=CHCHO		
4-O⁻	11.12	4.3 (1)	1.5 (2)	2.9 (3)	2.2×10^3
4-$N(CH_3)_2$	9.73	2.39 (9)	5.6 (3)	0.42 (3)	7.9×10^3
3-Br,4-O⁻	9.40	1.43 (7)	12.9 (7)	0.110 (8)	4.4×10^3
4-NH_2	9.24	1.65 (3)	18.2 (5)	0.091 (3)	5.2×10^3
4-morpholino	8.78	1.04 (6)	27 (1)	0.038 (3)	6.3×10^3
3,5-Br_2,4-O⁻	7.73	0.156 (5)	39 (1)	$4.1\ (2) \times 10^{-3}$	7.6×10^3
3-Br,4-NH_2	7.15	0.110 (3)	69 (3)	$1.6\ (6) \times 10^{-3}$	1.1×10^4
3,4-$(CH_3)_2$	6.45	0.060 (7)	105 (1)	$5.7\ (7) \times 10^{-4}$	2.0×10^4
3-NH_2	6.14	0.031 (2)	220 (10)	$1.4\ (1) \times 10^{-4}$	1.0×10^4
			CH_2=CHCOCH$_3$		
4-O⁻	11.12	0.96 (5)	(0.073)[b]	13.2	1.0×10^4
4-$N(CH_3)_2$	9.73	0.55 (1)	0.40 (1)	1.38 (4)	2.6×10^4
3-Br,4-O⁻	9.40	0.46 (3)	1.8 (3)	0.26 (5)	1.0×10^4
4-NH_2	9.24	0.42 (3)	1.7 (3)	0.25 (4)	1.4×10^4
4-morpholino	8.78	0.362 (8)	4.4 (8)	0.08 (1)	1.4×10^4
3,5-Br_2,4-O⁻	7.73	0.143 (4)	18.4 (7)	$7.8\ (3) \times 10^{-3}$	1.5×10^4
3-Br,4-NH_2	7.15	0.078 (2)	55 (1)	$1.4\ (4) \times 10^{-3}$	1.0×10^4
3,4-$(CH_3)_2$	6.45	0.079 (6)	110 (20)	$7\ (1) \times 10^{-4}$	2.6×10^4
3,5-$(CH_3)_2$	6.14	0.049 (3)	119 (6)	$4.1\ (3) \times 10^{-4}$	2.9×10^4
3-NH_2	6.14	0.048 (3)	84 (6)	$5.7\ (5) \times 10^{-4}$	4.1×10^4
			CH_2=CHSO$_2$CH$_3$		
4-$N(CH_3)_2$	9.73	0.0825 (9)	0.024 (3)	3.4 (4)	6.4×10^4
3-Br,4-O⁻	9.40	0.077 (1)	0.050 (4)	1.6 (1)	6.2×10^4
4-NH_2	9.24	0.061 (2)	0.045 (7)	1.4 (3)	7.8×10^4
4-morpholino	8.78	0.044 (1)	0.062 (3)	0.72 (4)	1.2×10^5
3,5-Br_2,4-O⁻	7.73	0.0307 (7)	0.9 (1)	0.033 (4)	6.1×10^4
3-Br,4-NH_2	7.15	0.0195 (6)	1.73 (4)	0.0113 (4)	8.0×10^4
3,4-$(CH_3)_2$	6.45	0.0293 (6)	16 (1)	$1.8\ (2) \times 10^{-3}$	6.4×10^4
3,5-$(CH_3)_2$	6.14	0.0269 (6)	29 (1)	$9.2\ (4) \times 10^{-4}$	6.7×10^4
3-NH_2	6.14	0.021 (1)	26 (2)	$8.1\ (7) \times 10^{-4}$	5.9×10^4
			CH_2=CHCONH$_2$		
4-$N(CH_3)_2$	9.73	$6.1\ (1) \times 10^{-4}$	$1.9\ (4) \times 10^{-4}$	3.2 (7)	6.0×10^4
3-Br,4-O⁻	9.40	$5.7\ (2) \times 10^{-4}$	$8.3\ (4) \times 10^{-4}$	0.68 (3)	2.7×10^4
4-NH_2	9.24	$5.3\ (2) \times 10^{-4}$	$1.5\ (8) \times 10^{-3}$	0.4 (2)	2.1×10^4
4-morpholino	8.78	$3.9\ (2) \times 10^{-4}$	$1.6\ (9) \times 10^{-3}$	0.3 (1)	4.1×10^4
3,5-Br_2,4-O⁻	7.73	$1.7\ (7) \times 10^{-4}$	0.0155 (7)	$1.1\ (5) \times 10^{-2}$	2.0×10^4
3-Br,4-NH_2	7.15	$1.0\ (1) \times 10^{-4}$	0.06 (2)	$1.7\ (7) \times 10^{-2}$	1.2×10^4

[a] In aqueous solution at 25 °C, ionic strength 0.1; the experimental k_{OH}, K_{eq}, and K_{add} for aldehydes are uncorrected for hydration of the carbonyl group; see ref 1 for data for reactions of substituted pyridines with CH_2=CHCN. [b] Calculated from the Brønsted plot for other substituted pyridines.

as a function of the concentration of **2**, Z = CHO, in solutions of various pH are shown in Figure 1. This figure is characteristic of the concentration and pH dependences that were commonly observed throughout the current study. The non-zero ordinate intercepts that are present in these plots at high pH are consistent with the approach to an equilibrium mixture of **1** and **3** in these reactions. The measured pseudo-first-order rate constants (k_{obs}) are then the sum of the individual pseudo-first-order rate constants for the addition and elimination processes. At constant pH, the linear dependences of Figure 1 are described by eq 1. The pH dependences that are apparent in the slopes and ordinate intercepts of Figure 1 are consistent with eq 2, where pK_{BH} represents the acidity of the conjugate acid ($1{\cdot}H^+$) of the pyridine nucleophile (**1**), k_{Nu} is the second-order rate constant for the addition of **1** to **2**, and k_{OH} is the second-order rate constant for the hydroxide ion catalyzed elimination reaction of **3**.

$$k_{obs} = k_a[2] + k_e \quad (1)$$

$$k_{obs} = k_{Nu}[2]/(1 + [H^+]/K_{BH}) + k_{OH}[^-OH] \quad (2)$$

In general, the rate constants k_{Nu} and k_{OH} were evaluated by fitting a complete data set (e.g., all data in Figure 1) to eq 2 via an iterative procedure that is based upon the Marquardt algorithm. Values of k_{Nu} and k_{OH} that were obtained in this way for the reaction of 4-(dimethylamino)pyridine with a variety of Z-substituted alkenes **2**, and also several *C*-methyl derivatives of **2**, are listed in Table I.

Reactions of Substituted Pyridines with Electrophilic Alkenes 2. The above kinetic procedure and data analysis were also followed for the investigation of X-substituent effects in pyridine nucleophiles **1** upon the equilibration of **1** and **2** with **3** for four Z-substituted alkenes (**2**, Z = CHO, $COCH_3$, SO_2CH_3, and $CONH_2$). Rate constants for each of these reactions are collected in Table II. Analogous data are also available for **2**, Z = CN, from our previous study.[1]

We define an equilibrium constant for the equilibration reaction of Scheme I in eq 3. This equilibrium constant can be calculated via eq 4 for each pyridine and alkene reactant pair for which both k_{Nu} and k_{OH} are available. Alternatively, this equilibrium may be defined by eqs 5 and 6 in terms of the formal addition of the pyridinium cation ($1{\cdot}H^+$) to the substituted alkene **2**. Values of K_{eq} and K_{add} are included in Tables I and II.

$$K_{eq} = [3][^-OH]/[1][2] \quad (3)$$

$$K_{eq} = k_{Nu}/k_{OH} \quad (4)$$

$$K_{add} = [3]/[1{\cdot}H^+][2] \quad (5)$$

$$K_{add} = k_{Nu}K_{BH}/k_{OH}K_w = K_{eq}K_{BH}/K_w \quad (6)$$

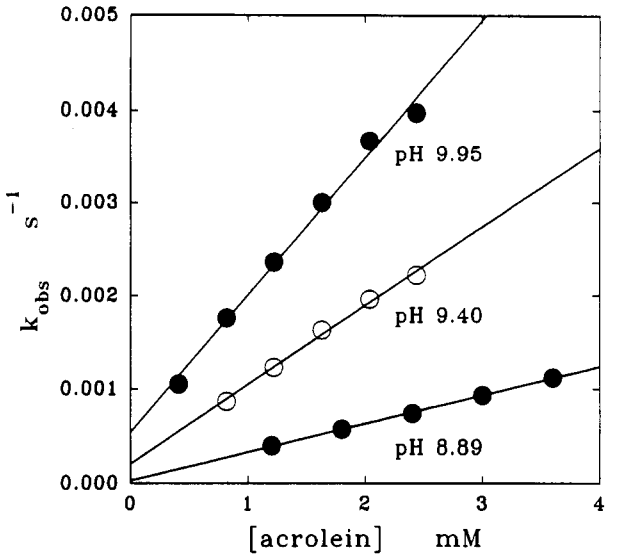


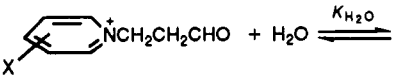
Figure 1. Pseudo-first-order rate constants for the equilibration of 4-(dimethylamino)pyridine and acrolein with the 4-(dimethylamino)-1-(2-formylethyl)pyridinium cation in aqueous solution.

In general, the lower limit to the pK_{BH} range of the pyridines used with each substituted alkene was established by either low reactivity (Z = $CONH_2$) and/or an unfavorable equilibrium for the addition process with the less nucleophilic substituted pyridines. Since the formal equilibrium of Scheme I is pH-dependent and favors the elimination reaction at high pH, the pH range over which rate data for the equilibration could be obtained was also dependent upon X and, to a lesser extent, upon Z. In general, a lower pH range was required in order to observe the addition reaction for the less basic substituted pyridines (see Table I), since these species are the best leaving groups in the hydroxide ion catalyzed E1cb reactions.

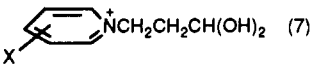
Characterization of *N*-(2-(Substituted)ethyl)-pyridinium Cations 3. In all cases the electronic absorption spectra of the addition products from the reaction of 1 with 2 were typical of the spectra of *N*-alkyl cations of the correspondingly X-substituted pyridines, or of the corresponding *N*-alkylpyridinones in cases where the nucleophile was a 4-pyridinone oxyanion. Typical absorption spectra of these various derivatives were presented in our earlier work.[1]

We have also established the formation of the appropriate *N*-(2-(substituted)ethyl)pyridinium cations and pyridinones in these reactions by ^1H NMR spectroscopic observations of these reactant solutions. In several cases, reactions involving the base-catalyzed interconversion of nitriles, amides, and carboxylate anions of both the acrylic acid derivatives and also the adducts 3, and also the conjugate addition of deuteroxide ion to 2 to give $DOCH_2CD_2Z$, were readily recognized. All such reactions occurred much more slowly than the reactions of the substituted pyridines with 2 that were investigated in the kinetic studies that are discussed above.

The only case in which a complication which interferes in the clean equilibration of 1 and 3 must be taken into consideration occurs for the case of the aldehyde. Whereas there is no evidence for any significant hydration of the carbonyl group of acrolein (^1H NMR (in D_2O): δ 6.25–6.53 (2 H, m), 6.63 (1 H, dd), 9.43 (1 H, d)) in aqueous solution, one does expect[7,20] significant covalent hydration of the aldehydic carbonyl group in 3, Z = CHO (eq 7).



3: Z = CHO

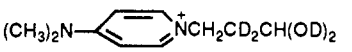


(7)

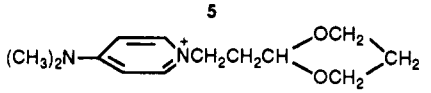
4

The reaction of 4-(dimethylamino)pyridine with acrolein in D_2O gives a product having an ^1H NMR spectrum which is consistent with the deuterated hydrated aldehyde 5 (δ 3.20 (6 H, s), 4.20 (2 H, s), 5.07 (1 H, s), 6.83 (2 H, d), 8.01 (2 H, d)). In addition, there is a small downfield signal at δ 9.48 which has an intensity of 0.07 (±0.02) protons per proton of 5. This signal is assignable to the aldehydic proton in 3, X = 4-$(CH_3)_2N$, Z = CHO, by comparison with the chemical shift of δ 9.45 which has been reported[7] for the aldehydic hydrogen of acetaldehyde in D_2O. The singlet at δ 5.07 in the spectrum of 5 is consistent with the signal from the methine proton in the hydrate of acetaldehyde (δ 5.09 in $CDCl_3$).[7]

The assignment of the spectrum of 5 was further confirmed by the synthesis of the acetal 6 (δ (in D_2O) 1.46 (1 H, m), 1.9–2.2 (3 H, m), 3.20 (6 H, s), 3.85 (2 H, m), 4.05 (2 H, m), 4.22 (2 H, t), 4.75 (1 H, t), 6.85 (2 H, d), 8.00 (2 H, d)). The small upfield shift in the signal (at δ 4.75) for the methine hydrogen in 6 relative to the corresponding hydrogen (at δ 5.07) in 5 is consistent with the reported chemical shifts for the methine hydrogen in the hydrate and acetals of acetaldehyde.[7] In 1 M DCl in D_2O, the spectrum of 6 is gradually converted into that of a 1:1 mixture of 5 and 1,3-propanediol (δ 1.8 (quintet), 3.7 (triplet) in relative intensities 1:2) from the acid-catalyzed hydrolysis of 6. The CD_2 labeling in the hydrolysis product 5 presumably arises via acid-catalyzed enolization of the small amount of the unhydrated aldehyde (3, Z = CHO) that is in equilibrium with 4. Overall, these ^1H NMR spectral observations indicate that 3, Z = CHO, is predominantly hydrated in aqueous solution.



5



6

Discussion

The influence of the Z activating group upon reactivity is summarized in Table III for the addition and elimination reactions which are reported in Table I. Table III also compares the Z substituent effects in the current reactions with selected data from the literature for related reactions. The current Z substituent effects correspond closely to those previously observed for the addition of glycine to 2 in aqueous solution (reaction C in Table III), the addition of morpholine to 2 in methanol (reaction D), and also for the base-catalyzed elimination reactions of eq 8 in ethanol (reaction E). The significant decreases in reactivity that are apparent in Table I upon the introduction of either α- or β-methyl substituents into acrolein are typical of similar substituent effects that have previously been noted for related reactions.[8,15–17] The Z substituent effects in

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Table III. Relative Reactivities in Reactions Having Carbanionic Transition States

	k^{rel}					
Z	A[a]	B[b]	C[c]	D[d]	E[e]	F[f]
CHO	3900	5×10^5[g]	3600		2.3×10^4	8×10^4
$COCH_3$	900	2100	630	3400	2.8×10^4	7000
SO_2CH_3	140	130	50		130	100
CO_2CH_3	25		29	29	54[h]	
CN	6	22	8	16	84	2.4
$CONH_2$	1	1	1	1	1	1

[a] Addition of 4-(dimethylamino)pyridine to CH_2=CHZ in aqueous solution; k_{Nu} from Table I. [b] Elimination from **3** in aqueous solution; k_{OH} from Table I. [c] Second-order rate constants for addition of glycine to CH_2=CHZ in aqueous solution.[8] [d] Second-order rate constants for addition of morpholine to CH_2=CHZ in methanol.[9] [e] Ethoxide ion catalyzed elimination from $C_6H_5OCH_2CH_2Z$ in ethanol.[10] [f] Deprotonation of CH_3Z by deuteroxide ion;[11] relative second-order rate constants for Z = $CONH_2$, CN, SO_2CH_3, and $COCH_3$ from ref 12 are combined with the statistically corrected relative rate constants for the deprotonation of acetone[13] and acetaldehyde[14] by hydroxide ion. [g] After correction by a factor of 16 for hydration of the carbonyl group (see text). [h] Z = $CO_2C_2H_5$.

Table III are typical of those that have been summarized by Rappoport[18] for a variety of reactions that require the stabilization of a carbanionic transition state by the Z substituent.

$$C_6H_5OCH_2CH_2Z + C_2H_5O^- \rightarrow CH_2{=}CHZ + C_6H_5O^- + C_2H_5OH \quad (8)$$

Comparisons of the activating effects of aldehydic and ketonic functional groups are complicated by the much greater tendency for addition to the aldehydic carbonyl group than to ketonic carbonyl groups. This complication is demonstrated in the current study by the ^{1}H NMR spectral observation that the adducts **3**, Z = CHO), from acrolein are thermodynamically less stable than their covalent hydrates (eq 7), whereas no hydration was observed for **3**, Z = $COCH_3$. Hydroxide ion catalyzed hydration of an aldehydic carbonyl group is much faster than the hydroxide ion catalyzed elimination reactions of **3**, Z = CHO; for example,[19] the second-order rate constant for hydroxide ion attack upon the carbonyl group of acetaldehyde is 4.8×10^4 M^{-1} s^{-1}. This value is between 100-fold and 10^4-fold greater than k_{OH} for the elimination reactions for **3**, Z = CHO, in Table II. The hydration equilibrium of eq 7 will be reached much more rapidly than the nucleophilic addition of Scheme I, and consequently the elimination reaction must proceed via the minor amount of nonhydrated aldehyde **3**, Z = CHO, that is in equilibrium with the hydrated aldehyde. The net result of these considerations is that the second-order rate constants (k_{OH}) for the elimination reactions for Z = CHO in Tables I and II underestimate the true reactivities of **3**, Z = CHO, by a factor equal to K_{H_2O}. We have estimated $K_{H_2O} \approx 16$ for eq 7 from the relationship of Greenzaid et al.,[20] by taking $\sigma^*(CH_2CH_2Py^+) = \sigma^*(CH_2CH_2N^+(CH_3)_3) = 0.68$;[21] this estimate is in agreement with the equilibrium ratio of hydrate that was estimated in the ^{1}H NMR spectral observations that are discussed above. Throughout the current work we assume that $K_{H_2O} \approx 16$ and that this ratio is essentially independent of the X substituent on the pyridine ring.

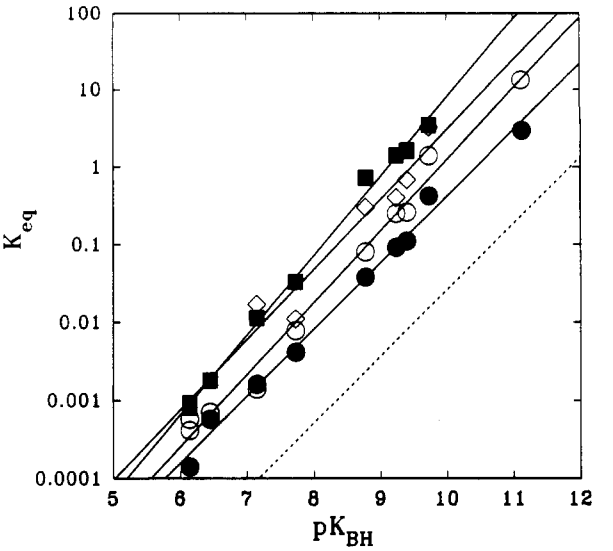

Figure 2. Dependence of K_{eq} (eq 3) upon pyridine basicity for various activating substituents: Z = CHO (filled circles); Z = $COCH_3$ (empty circles); Z = SO_2CH_3 (filled squares); Z = $CONH_2$ (empty diamonds). Broken line represents data for Z = CHO after correction for hydration of the carbonyl group of **3**, Z = CHO.

A similar correction must be considered for all elimination reactions from β-substituted aldehydes in aqueous or alcoholic solution. However, no corresponding correction is required for the second-order rate constants for addition to acrolein since there appears to be no significant amount of hydration of the carbonyl group of this α,β-unsaturated aldehyde at equilibrium (see Results). Thus k_{Nu} for acrolein in Tables I and II represents the true second-order rate constant for the reaction of a substituted pyridine with acrolein. However, $K_{eq} = k_{Nu}/k_{OH}$ will represent the overall equilibrium between acrolein and its hydrated adduct (i.e., in this case, the apparent $K_{eq} = ([^+PyCH_2CH_2CH(OH)_2][^-OH])/([1][acrolein]))$. This value must be divided by K_{H_2O} (≈16) in order to give a value for K_{eq} that is directly comparable with the other equilibrium constants in Tables I and II.

After correction for hydration of the aldehyde, k_{OH} for elimination from **3**, X = 4-$N(CH_3)_2$, Z = CHO, is over 200-fold greater than that for elimination from the corresponding methyl ketone (**3**, X = 4-$N(CH_3)_2$, Z = $COCH_3$) (reaction B in Table III). As discussed below, in this case $k_{OH} = k_{-2}K_a/K_w$ (eq 11a); the relative k_{OH} values for the aldehyde and ketone contain contributions from the influence of Z upon both the thermodynamic acidities (K_a) and also upon k_{-2}. For less basic pyridines for which $k_{OH} = k_1$ (eq 11b), the aldehyde (after correction for hydration) is only approximately 20-fold more reactive than the ketone.

In enolate ion formation from acetone and acetaldehyde in aqueous solution, the second-order rate constant for deprotonation by hydroxide ion is 11-fold greater for the aldehyde than for the ketone (after correction for a statistical effect and for hydration of the aldehyde).[13,14] Furthermore, the thermodynamic acidity of acetaldehyde

(12) Bonhoeffer, K. F.; Geib, K. H.; Reitz, O. *J. Chem. Phys.* **1939**, *7*, 664.
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(20) Greenzaid, P.; Luz, Z.; Samuel, D. *J. Am. Chem. Soc.* **1967**, *89*, 749.

(21) $\sigma^*(CH_2CH_2N^+(CH_3)_3) = 0.36 \times \sigma^*(CH_2N^+(CH_3)_3) = 0.36 \times 1.90 = 0.68$; Clark, J.; Perrin, D. D. *Q. Rev. Chem. Soc.* **1964**, *18*, 295.

Table IV. Brønsted β Values for the Reactions of Scheme I

parameter[a]	Z = CHO	Z = $COCH_3$	Z = SO_2CH_3	Z = CN[b]	Z = $CONH_2$
σ^*	2.15	1.81	3.68	3.30	1.68
σ_p^-	1.04	0.84	1.05	1.00	0.62
β_{eq}	0.86 (±0.03)	0.92 (±0.04)	1.02 (±0.02)	1.13	1.19 (±0.07)
β_{nuc} (k_2)	0.26 (±0.03)	0.18 (±0.01)	0.15 (±0.02)	0.20	0.31 (±0.02)
β_{nuc}^n (k_2)	0.30	0.20	0.15	0.18	0.26
β_{nuc} ($k_{-1}K_2$)	0.54 (±0.06)	0.31 (±0.04)		0.83	
β_{lg} ($k_{-2}K_a$)	−0.56 (±0.06)	−0.77 (±0.09)	−0.87 (±0.04)	−0.93	−0.88 (±0.08)
β_{lg}^n ($k_{-2}K_a$)	−0.65	−0.84	−0.85	−0.82	−0.74
β_{lg} (k_1)	−0.32 (±0.06)	−0.52 (±0.06)		−0.30	

[a] σ^* values are from ref 22; σ_p^- values are from ref 23. [b] β values for Z = CN are from ref 1.

(pK_a = 16.73)[14] is significantly greater than that of acetone (pK_a = 19.27)[13] in aqueous solution, and this difference is clearly dominant in the >200-fold difference in k_{OH} noted in the previous paragraph. The 4-fold greater k_{Nu} for the addition of 4-(dimethylamino)pyridine to acrolein than to methyl vinyl ketone in Table III is also a reflection of the greater stabilization by the formyl group than by the acetyl group of the developing carbanionic character in the transition state for nucleophilic attack. Overall, the enhanced reactivity of acrolein (and its derivatives) in comparison with methyl vinyl ketone (and its derivatives) in the current study is consistent with the greater carbanionic stabilization that is provided by Z = CHO than by Z = $COCH_3$ and contrasts with the similar reactivities that have sometimes been reported for these derivatives (reactions D and E in Table III).

Substituent effects are shown in Figure 2 for the addition equilibrium that is defined by eq 3 in a Brønsted-type plot as a function of the pyridine basicity (defined as pK_{BH} of the pyridinium cation conjugate acid). The addition equilibrium constant (K_{eq}) is quite sensitive to the X substituent on the pyridine ring; Brønsted β_{eq} values are summarized for each 2 in Table IV. However, K_{eq} is relatively independent of the Z activating substituent in 2. For any single substituted pyridine, the rate of nucleophilic attack for Z = $COCH_3$, SO_2CH_3, CN, and $CONH_2$ varies systematically over a 1000-fold range (Table II), whereas K_{eq} for these same four Z groups varies (apparently randomly) by no more than 10-fold. Thus the rates of nucleophilic attack upon these electrophilic alkenes are much more sensitive to the nature of Z than are the equilibrium constants for addition. While acrolein also appears to fit this pattern, correction for K_{H_2O} as discussed above gives the broken line in Figure 2. After this correction, K_{eq} for addition to acrolein is approximately 40-fold smaller than that for addition of the same substituted pyridine to methyl vinyl ketone, despite the fact that the rate constants for nucleophilic attack on the aldehyde are up to 4-fold faster than those for the same reaction with the ketone.

The β_{eq} values in Table IV show a systematic variation with the reactivity (k_{Nu}) of 2. In fact, quite unexpectedly, in most cases the dependence of β_{eq} upon Z in 2 displays a clean linear dependence upon log k_{Nu} for a particular pyridine reacting with 2; this relationship is indicated in Figure 3 and in eq 9 for the case of 4-(dimethylamino)-pyridine.

$$\beta_{eq} = -0.093\ (\pm 0.003)\ \log k_{Nu} + 0.90\ (\pm 0.03)$$

$$r = 0.998 \qquad (9)$$

The slope of the linear relationship in eq 9, $d(\beta_{eq})/d(\log k_{Nu})$ = −0.093, is similar (−0.093 to −0.099) for all of the more basic pyridines (pK_{BH} > 8) in Figure 3. The nonlinear relationship for X = 3-Br, 4-NH_2 in Figure 3 is

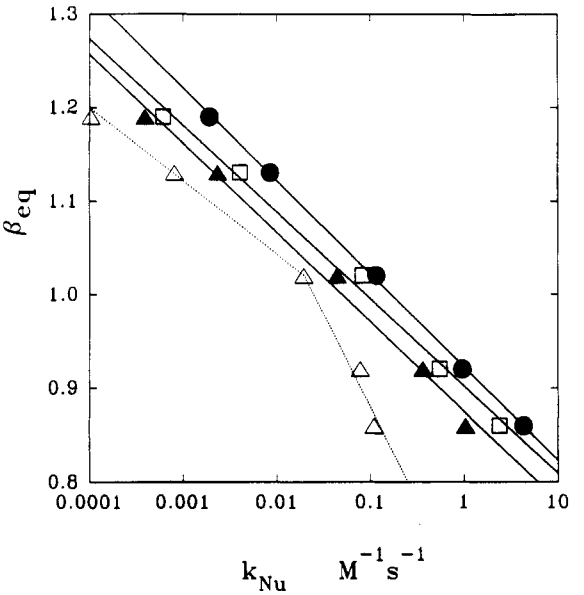

Figure 3. Variation of β_{eq} as a function of reactivity (as log k_{Nu}) for various X-substituted pyridines: X = 4-O^- (filled circles); X = 4-$N(CH_3)_2$ (empty sqares); X = 4-morpholino (filled triangles); X = 3-Br,4-NH_2 (empty triangles).

another manifestation of the change in rate-determining step that is analyzed in more detail below in terms of the Brønsted plots in Figures 4 and 5.

Formally, one can state that the relationship of eq 9 represents the relative X substituent effects upon the equilibrium constants for the *N*-(2-Z-ethylation) and the N-protonation of pyridines as a function of the Z substitutent effect upon the rate constant for nucleophilic attack upon 2. One might have expected a dependence of β_{eq} upon the inductive electronic effect of Z, since the ZCH_2CH_2 substituent would be expected to influence the effective positive charge on the pyridinium nitrogen atom in 3. Since the electronic effect of Z must be transmitted via the saturated two-carbon bridge, a relationship between β_{eq} and σ^* for Z would not be unreasonable. However, it is clear from Table IV that no such relationship exists. Conjugation in 2 might be considered in terms of the resonance contributor 7, which implies the involvement of the electron-withdrawing resonance effect of Z. A similar effect from Z might also be considered to influence the stability of the transition state 8 for nucleophilic attack upon 2. One possible quantitative measure of the electron-withdrawing resonance effect of Z would be in terms of σ_p^- for this substituent. Again, it is clear in Tables I and IV that there is no simple relationship between either k_{Nu} or β_{eq} and σ_p^-.

$$\underset{7}{CH_2CH{=}Z^-} \qquad \underset{8}{Py{\cdots}CH_2{\cdots}CH{\cdots}Z^-}$$

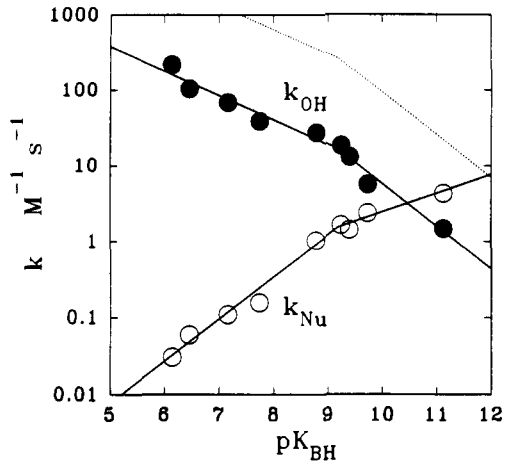

Figure 4. Brønsted-type plots for the addition of pyridines to acrolein (k_{Nu}) and the microscopic reverse elimination from 3, Z = CHO (k_{OH}). Broken lines represent k_{OH} after correction for hydration as discussed in the text.

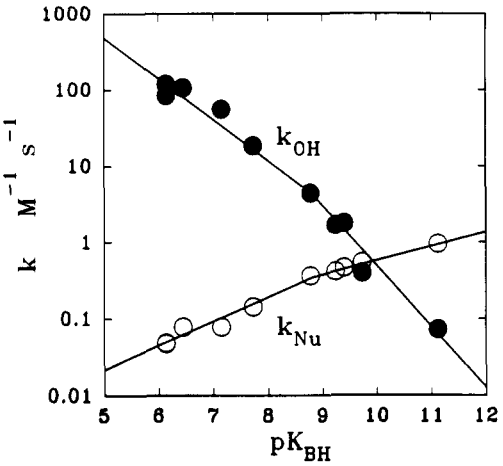

Figure 5. Brønsted-type plots for the addition of pyridines to methyl vinyl ketone (k_{Nu}) and the microscopic reverse elimination from 3, Z = $COCH_3$ (k_{OH}).

The existence of eq 9 is particularly curious when one considers that, as discussed above, there is no clear dependence of K_{eq} upon Z (Figure 2). We know of no precedent for a relationship such as that of eq 9. We have been unable to locate any other Michael-type additions for which extensive rate and equilibrium data are available in the literature, and therefore we are unable to check the applicability of such a relationship to other reactions of this type. It is also unclear in what other classes of reaction one might seek an analogous relationship. At the present time, we can only state that eq 9 appears to be a useful empirical expression of substituent effects upon the addition of pyridines to electron-deficient alkenes. We cannot rule out the possibility that this equation may represent a one-case fortuitous relationship between substituent effects upon equilibrium and rate data.

Brønsted-type plots for the second-order rate constants for nucleophilic addition (k_{Nu}) and hydroxide ion catalyzed elimination (k_{OH}) are shown in Figures 4 (Z = CHO), 5 (Z = $COCH_3$), and 6 (Z = SO_2CH_3 and $CONH_2$). For Z = $CONH_2$ and Z = SO_2CH_3, each of the plots in Figure 6 is linear, and so single β_{nuc} and β_{lg} parameters are only obtainable in these two cases (Table IV). For Z = CHO and Z = $COCH_3$, the plots in Figures 4 and 5 are nonlinear, but they may be divided into two linear "concave down" relationships in each case. The dual β_{nuc} and β_{lg} parameters that are obtained in these cases are given in Table IV.

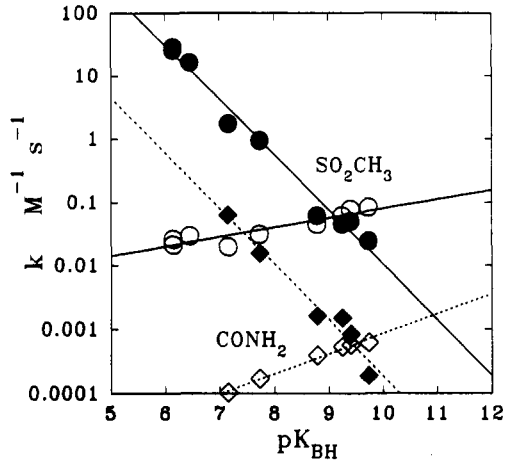

Figure 6. Brønsted-type plots for the addition (k_{Nu}) of pyridines to methyl vinyl sulfone (filled circles) and acrylamide (filled diamonds) and the microscopic reverse elimination reactions (k_{OH}) (empty circles and empty diamonds, respectively).

These "concave down" relationships are similar to the situation which was extensively analyzed for Z = CN in terms of Scheme I in our previous study.[1] Such data are consistent with a change in rate-determining step as the basicity of the substituted pyridine is varied in these reactions.

Analysis of Scheme I in terms of the zwitterionic species as a steady-state intermediate gives the relationships of eqs 10 and 11, which may be simplified to eqs 10a, 10b, 11a, and 11b under the conditions of the indicated inequalities for each of these equations. Equation 10a represents rate-determining nucleophilic attack upon the alkene, which we have shown[1] to occur for the most basic pyridine nucleophiles (high pK_{BH}), while eq 10b represents rate-determining protonation (by water) of the zwitterionic intermediate with the less basic pyridine nucleophiles (low pK_{BH}). The microscopic reverses of each of these processes are defined as rate-determining departure of the pyridine nucleofuge from the intermediate zwitterion in eq 11a and rate-determining deprotonation of the pyridinium cation 3 by hydroxide ion in the case of eq 11b.

$$k_{Nu} = k_2k_{-1}/(k_{-2} + k_{-1}) \quad (10)$$

for $k_{-1} \gg k_{-2}$:

$$k_{Nu} = k_2 \quad (10a)$$

for $k_{-1} \ll k_{-2}$:

$$k_{Nu} = k_2k_{-1}/k_{-2} = k_{-1}K_2 \quad (10b)$$

$$k_{OH} = k_1k_{-2}/(k_{-1} + k_{-2}) \quad (11)$$

for $k_{-1} \gg k_{-2}$:

$$k_{OH} = k_1k_{-2}/k_{-1} = k_{-2}K_a/K_w \quad (11a)$$

for $k_{-1} \ll k_{-2}$:

$$k_{OH} = k_1 \quad (11b)$$

All of the Brønsted slopes that are obtainable from Figures 4, 5, and 6 are summarized in Table IV and are assigned to the appropriate rate-determining steps by analogy with our study[1] of Scheme I for Z = CN and also our investigation[4] of the elimination reaction in Scheme I for Z = 4-$O_2NC_6H_4$ which also shows a change in rate-determining step upon variation of the basicity of the pyridine nucleofuge. Although no clearcut monotonic variations in β_{nuc} and β_{lg} with reactivity are apparent in the data in Table IV, there do appear to be some interesting systematic variations in these parameters as a

function of the Z substituent. These changes will be discussed in terms of the relative reactivities (CHO > $COCH_3$ > SO_2CH_3 > CN > $CONH_2$) that are found for both the addtion and the elimination reactions.

For rate-determining nucleophilic attack of the pyridine upon **2** (eq 10a), β_{nuc} (for k_2) appears to move through a minimum value (at Z = SO_2CH_3) with increasing reactivity of **2**. This observed minimum is unchanged if one compares the normalized β^n_{nuc} ($=\beta_{nuc}/\beta_{eq}$). The relatively small magnitudes of these β_{nuc} values imply a reactant-like transition state species in which relatively little C–N bond formation has occurred.[24] However, any quantitative interpretation of β_{nuc} for k_2, and also of any of the other kinetic β values in Table IV, in terms of transition-state structure is not a simple matter. The major problem in this regard is that there is no known simple relationship between the charge density distributions in carbanionic transition states and in the corresponding Z-stabilized carbanionic species.

All four rate constants (k_1, k_{-1}, k_2, k_{-2}) that are defined in Scheme I are dependent upon the electron density at a developing carbanionic center in the transition state for that step. This same observation applies directly to k_{Nu} of eq 10a and k_{OH} of eq 11b. The k_{Nu} of eq 10b and k_{OH} of eq 11a are dependent upon both a transition-state carbanionic structure and also upon the thermodynamic stability of the intermediate zwitterionic species. Only for Z = CHO and $COCH_3$ are there well-established kinetic and thermodynamic acidities in aqueous solution for carbon acids having conjugate bases that are relevant to the stability of the carbanionic center in the zwitterionic intermediate in Scheme I. However, the data in Table III demonstrate that the relative reactivities of both **2** and **3** as a function of the Z substituent are at least semiquantitatively consistent with the best available data for the hydroxide ion catalyzed deprotonation reactions of CH_3Z in aqueous solution.

The β_{nuc} values for rate-determining nucleophilic attack upon **2** are smaller, and more variable, than the Brønsted slopes that have been reported by Freidman and Wall[8] for the addition of amino acid derivatives to **2** in aqueous solution. These workers report a constant β_{nuc} = 0.43 for a variety of **2**. Since the Z substituent effects in this latter study accurately reflect the same substituent effects that we find for the addition of pyridines to **2** (see Table III), it seems likely that β_{nuc} = 0.43 for these primary amine derivatives also reflects rate-determining nucleophilic attack. The actual rates of attack upon **2** are quite similar if one compares data for a pyridine and a primary amine of the same basicity, so that the differences in the observed β_{nuc} for pyridines and primary amines reacting with **2** are presumably reflections of differences in transition-state solvation phenomena.

The variation of $-\beta_{lg}$ (and especially $-\beta^n_{lg}$) (Table IV) for rate-determining expulsion of the leaving group according to eq 11a shows a broad maximum as a function of Z, in a similar manner to the minimum that is discussed above for β_{nuc} for eq 10a. These two reactions represent the same rate-determining step for processes which are the microscopic reverse of one another. The considerably greater magnitudes of β_{lg} and of β_{nuc} stress the important influence of substituents in the pyridine ring upon the thermodynamic acidity of the β-methylene group in the *N*-(2-(Z-ethyl))pyridinium cations **3**.

The "breaks" which represent the change in rate-determining step in the Brønsted plots for Z = CHO (at $pK_{BH} \approx 9.1$) and for Z = $COCH_3$ (at $pK_{BH} \approx 8.8$) occur at considerably higher pyridine basicity than the corresponding "break" for Z = CN (at pK_{BH} = 5.8).[1] The linearity that is observed for Z = SO_2CH_3 and Z = $CONH_2$ in Figures 4 and 5 requires that the change in rate-determining step in these two cases can only occur for $pK_{BH} \leq 6$ and $pK_{BH} \leq 7$, respectively. As discussed above in the Results, these limits are established experimentally by unfavorable equilibria, and slow reactions, for weakly basic pyridines when the equilibrium is approached from the addition direction. A wider range of pyridine basicities could be examined in these two cases by the synthesis of the adducts **3**, Z = SO_2CH_3 and $CONH_2$, and the direct study of the rates of the elimination reaction, in a similar approach to that which was previously undertaken[1] for **3**, Z = CN.

The limited data that are available at present for the "break" pK_{BH} seem to imply a movement of the change in rate-determining step toward substituted pyridines of greater basicity (i.e., higher pK_{BH}) with increasing reactivity in both the addition and elimination reactions. While the "break" pK_{BH} = 6.5 which was established[4] for the quite slow elimination reactions of **3**, Z = 4-$O_2NC_6H_4$, does not follow this general pattern, it should be noted that the presence of a strongly hydrogen-bonded carbanionic intermediate in this latter case is atypical of the situation that was established for Z = CN and, by inference, for the other cases in the current study.

Our inability to observe the change in rate-determining step for Z = SO_2CH_3 and Z = $CONH_2$ in the current study also limits the acquisition of a full set of β_{nuc} and β_{lg} values corresponding to eqs 10b and 11b. Equation 11b represents rate-determining deprotonation by hydroxide ion in the elimination reaction of **3** for derivatives of pyridines having pK_{BH} less than the "break" pK_{BH}. The limited data for this case in Table IV imply a dependence of $-\beta_{lg}$ upon Z which passes through a maximum value in a similar manner to that which was discussed above for rate-determining nucleofuge departure (eq 11a). In a similar way, β_{nuc} for eq 10b, which represnts rate-determining protonation of the zwitterion intermediate by water, appears to pass rather steeply through a minimum value with increasing reactivity. These latter conclusions, which are based upon a limited number of examples for eqs 10b and 11b, must be considered to be tentative until such time as further data become available.

The current investigations of Michael-type additions to simple monoactivated alkenes can be considered as companion studies to the detailed investigations of related addition reactions of more highly activated electrophilic alkenes which have been proceeding concurrently in Bernasconi's laboratory.[32] The current investigation demonstrates the detailed insights that can be gained into rate-determining steps and transition-state structure via detailed substituent effect studies upon the rates and equilibria of some relatively simple examples of two im-

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portant general classes of addition and elimination reactions. However, it is rather sobering to note that despite the wealth of quantitative data that one can obtain in such a study, the current state of knowledge allows only limited conclusions in terms of the physical significance of the magnitudes of some of the β parameters that are deduced.

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Registry No. 1 (X = 4-N(CH$_3$)$_2$), 1122-58-3; 1 (X = 4-O$^-$), 33630-91-0; 1 (X = 3-Br, 4-O$^-$), 141375-46-4; 1 (X = 4-NH$_2$), 504-24-5; 1 (X = 4-morpholino), 2767-91-1; 1 (X = 3,5-Br$_2$, 4-O$^-$), 141375-47-5; 1 (X = 3-Br, 4-NH$_2$), 13534-98-0; 1 (X = 3,4-(CH$_3$)$_2$), 583-58-4; 1 (X = NH$_2$), 462-08-8; 1 (X = 3,5-(CH$_3$)$_2$), 591-22-0; 2 (Z = CHO), 107-02-8; 2 (Z = COCH$_3$), 78-94-4; 2 (Z = SO$_2$CH$_3$), 3680-02-2; 2 (Z = C$_5$H$_4$NCH$_3$), 45708-76-7; 2 (Z = CO$_2$CH$_3$), 96-33-3; 2 (Z = CONH$_2$), 79-06-1; 2 (Z = CON(CH$_3$)$_2$), 2680-03-7; 3 (X = 4-N(CH$_3$)$_2$, Z = COCH$_3$), 141375-39-5; 3 (X = 4-N(CH$_3$)$_2$, Z = SO$_2$CH$_3$), 141375-40-8; 3 (X = 4-N(CH$_3$)$_2$, Z = CHO), 141375-38-4; 3 (X = 4-N(CH$_3$)$_2$, Z = CONH$_2$), 141375-42-0; 3 (X = 4-N(CH$_3$)$_2$, Z = CON(CH$_3$)$_2$), 141375-43-1; 3 (X = 4-N(CH$_3$)$_2$, Z = C$_5$H$_4$NCH$_3$), 141375-41-9; 3 (X = 4-O$^-$, Z = CHO), 141375-48-6; 3 (X = 3-Br, 4-O$^-$, Z = CHO), 141375-49-7; 3 (X = 4-NH$_2$, Z = CHO), 141375-50-0; 3 (X = 4-morpholino, Z = CHO), 141375-51-1; 3 (X = 3,5-Br$_2$, 4-O$^-$, Z = CHO), 141375-52-2; 3 (X = 3-Br, 4-NH$_2$, Z = CHO), 141375-53-3; 3 (X = 3,4-(CH$_3$)$_2$, Z = CHO), 141375-54-4; 3 (X = 3-NH$_2$, Z = CHO), 141375-55-5; 3 (X = 4-O$^-$, Z = COCH$_3$), 68634-57-1; 3 (X = 3-Br, 4-O$^-$, Z = COCH$_3$), 141375-56-6; 3 (X = 4-NH$_2$, Z = COCH$_3$), 141375-57-7; 3 (X = 4-morpholino, Z = COCH$_3$), 141375-58-8; 3 (X = 3,5-Br$_2$, 4-O$^-$, Z = COCH$_3$), 141375-59-9; 3 (X = 3-Br, 4-NH$_2$, Z = COCH$_3$), 141375-60-2; 3 (X = 3,4-(CH$_3$)$_2$, Z = COCH$_3$), 141375-61-3; 3 (X = 3,5-(CH$_3$)$_2$, Z = COCH$_3$), 141375-62-4; 3 (X = NH$_2$, Z = COCH$_3$), 141375-63-5; 3 (X = 3-Br, 4-O$^-$, Z = SO$_2$CH$_3$), 141375-64-6; 3 (X = 4-NH$_2$, Z = SO$_2$CH$_3$), 141375-65-7; 3 (X = 4-morpholino, Z = SO$_2$CH$_3$), 141375-66-8; 3 (X = 3,5-Br$_2$, 4-O$^-$, Z = SO$_2$CH$_3$), 141375-67-9; 3 (X = 3-Br, 4-NH$_2$, Z = SO$_2$CH$_3$), 141375-68-0; 3 (X = 3,4-(CH$_3$)$_2$, Z = SO$_2$CH$_3$), 141375-69-1; 3 (X = 3,5-(CH$_3$)$_2$, Z = SO$_2$CH$_3$), 141375-70-4; 3 (X = 3-NH$_2$, Z = SO$_2$CH$_3$), 141375-71-5; 3 (X = 3-Br, 4-O$^-$, Z = CONH$_2$), 141375-72-6; 3 (X = 4-NH$_2$, Z = CONH$_2$), 141375-73-7; 3 (X = morpholino, Z = CONH$_2$), 141375-74-8; 3 (X = 3,5-Br$_2$, 4-O$^-$, Z = CONH$_2$), 141375-75-9; 3 (X = 3-Br, 4-NH$_2$, Z = CONH$_2$), 141375-76-0; 5, 141375-78-2; 6-Br, 141375-77-1; (*E*)-CH$_3$CH=CHCHO, 123-73-9; CH$_2$=C(CH$_3$)CHO, 78-85-3; 2-(2-bromomethyl)-1,3-dioxane, 33884-43-4; 3-(4-(dimethylamino)pyridinium)butanal, 141375-44-2; 2-methyl-3-(4-(dimethylamino)pyridinium)propanal, 141375-45-3.

Supplementary Material Available: Experimental conditions for the individual kinetic studies of all 1 with all 2 (Tables S1 and S2) and proton-decoupled ^{13}C NMR spectra referred to in the Experimental Section (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from ACS; see any current masthead page for ordering information.

Hydrogen Bonding between a *N*-Pyridinium Phenolate Betaine and O–H Donors in Acetonitrile

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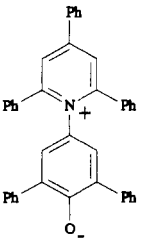
Hydrogen bonding between 4-(2,4,6-triphenylpyridinio)-2,6-diphenylphenolate (1, Dimroth's dye) and water, alcohols, and phenols has been measured spectrophotometrically in acetonitrile at 25 °C. Association constants for 1:1 hydrogen-bonded complexes range from K_{AB} = 2 M^{-1} for water to K_{AB} = 6.06 × 10^3 M^{-1} for *m*-nitrophenol with a Brønsted slope α = 0.38 ± 0.04 for substituted phenols with pK_a > 23. The acidity constant of 4-(2,4,6-triphenylpyridinio)-2,6-diphenylphenol was determined by potentiometric titration: pK_a = 22.1 ± 0.2. Hydrogen bonding of phenols is analyzed within the framework of the Hine equation that describes changes in the strength of the hydrogen bond with changes in the pK_a of the hydrogen-bond donor and acceptor. A value of the Hine interaction coefficient τ = 0.016 ± 0.002 is consistent with a double-minimum potential for the ArOH···1 hydrogen bond.

Introduction

Since the early classification of solvents as "protic" and "aprotic" by Brønsted[1] there have been many attempts to provide a quantitative description of solvent polarity. One of the most widely used scales of solvent polarity is the E_T(30) scale. This scale is based on the increases in the wavelength of the charge-transfer absorption band of 4-(2,4,6-triphenylpyridinio)-2,6-diphenylphenolate, 1, in nonpolar solvents that correspond to decreases in E_T(30) values.[2,3]



1

For example, the absorption maximum of 1 shifts from 453 nm in water to 627 nm in the polar aprotic solvent acetonitrile, with even larger shifts for more nonpolar solvents. These solvent-induced shifts, termed "solvatochromism", are caused by changes in the interac-

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