m/z (rel intens) 221 (15, $M^+ + 1$), 163 (56, $M^+ - t$-Bu), 105 (100, $C_6H_5CO^+$), 57 (91, t-Bu^+). Analysis of the original product mixture by ^1H NMR showed **12** and **13** as the only detectable products in the ratio of 28/72. Further heating of the crude reaction product in CH_3OH for 48 h led to no apparent change in the product composition as indicated by ^1H NMR.

Ethynyl benzoate (**9**; 0.0425 g, 0.29 mmol) was kept in 1 mL of CH_3OH at 60 °C for 4.5 h. Examination of the reaction mixture by TLC showed methyl benzoate as the only detectable product. Part of the CH_3OH was distilled, and the ^1H NMR spectrum showed the presence of methyl benzoate, methanol, and possibly methyl acetate. The methyl benzoate was isolated by radial chromatography and its identity confirmed by ^1H NMR.

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Equilibration of *N*-(2-Cyanoethyl)pyridinium Cations with Substituted Pyridines and Acrylonitrile. A Change in Rate-Determining Step in an E1cb Reaction

John W. Bunting,* Andrea Toth, Christina K. M. Heo, and Rodney G. Moors

Contribution from the Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada. *Received April 18, 1990*

Abstract: The rates of equilibration of *N*-(2-cyanoethyl)pyridinium cations (**1**) with the corresponding pyridines and acrylonitrile have been measured in aqueous solutions of ionic strength 0.1 at 25 °C. Second-order rate constants (k_{OH}) have been obtained for the hydroxide ion catalyzed elimination reactions of 16 ring-substituted **1** having pyridine leaving groups of pK_{BH} in the range 1.5–9.7. Brønsted plots of log k_{OH} vs pK_{BH} are "concave down" with two distinct linear regions having $\beta_{lg} = -0.30$ (for $pK_{BH} < 5.8$) and $\beta_{lg} = -0.93$ (for $pK_{BH} > 5.8$). This observation is consistent with a change in rate-determining step within an E1cb reaction mechanism from rate-determining deprotonation of **1** (i.e., $(E1cb)_{irrev}$) for $pK_{BH} < 5.8$ to rate-determining leaving-group expulsion from the carbanionic intermediate (i.e., $(E1cb)_{rev}$) for $pK_{BH} > 5.8$. This interpretation is supported by ^1H NMR spectral observations in basic D_2O, which show no incorporation of deuterium into the acrylonitrile product for $pK_{BH} < 5.8$ but do show D for H exchange of the methylene protons that are α to the cyano group at a rate that is faster than elimination for $pK_{BH} > 5.8$. Rates of nucleophilic attack of pyridines and pyridinone anions ($pK_{BH} > 6$) upon acrylonitrile have also been measured. These display a linear Brønsted plot of $\beta_{nuc} = 0.20$. Combination of β_{lg} and β_{nuc} gives $\beta_{eq} = 0.13$ for the Michael-type addition of pyridinium cations to acrylonitrile to produce **1**. Although the rates of the addition of pyridines of $pK_{BH} < 6$ are too slow for convenient measurement in the current study, the combination of the measured rate and equilibrium Brønsted parameters allows the demonstration of the change in rate-determining step in these addition reactions from rate-determining nucleophilic attack (carbanion formation) with $\beta_{nuc} = 0.20$ for pyridines of $pK_{BH} > 5.8$ to rate-determining protonation of the carbanionic intermediate with $\beta_{nuc} = 0.83$ for pyridine nucleophiles of $pK_{BH} < 5.8$. General-base catalysis of the elimination reactions is observable in the $(E1cb)_{irrev}$ region but is extremely weak under the current experimental conditions.

In 1972, Bordwell presented[1] a tabular summary of the variety of mechanistic possibilities that have been recognized for base-catalyzed 1,2-elimination reactions. This table and variations upon it have now been widely reproduced[2] in review articles on this important general class of organic reactions. Experimental criteria for distinguishing between most of the mechanistic possibilities are generally available; however, a simple experimental test to allow the distinction between the E2 ($A_{xh}D_HD_N$ in IUPAC mechanistic nomenclature[3]) and $(E1cb)_{irrev}$ ($A_{xh}D_H^* + D_N$) mechanisms remains quite elusive, although second-derivative p_{xy} cross-correlation coefficients have been used to distinguish between these two mechanistic possibilities.[4] In principle, the demonstration of the $(E1cb)_{irrev}$ mechanism should be possible by the extension of structure–reactivity relationships until a change in rate-determining step is observed. This would effectively represent the conversion of the $(E1cb)_{irrev}$ ($A_{xh}D_H^* + D_N$) mechanism into the $(E1cb)_{rev}$ ($A_{xh}D_H + D_N^*$) case and allow a distinction between the E1cb mechanism and the formal E2 concerted elimination reaction in which no change in rate-determining step is possible.

Despite the common occurrence[1,5] of the carbanionic E1cb mechanism in eliminations involving activated carbon acids, there appear to have been only relatively few demonstrations of a change in rate-determining step from deprotonation ($(E1cb)_{irrev}$) to leaving-group expulsion ($(E1cb)_{rev}$) in any one reaction series. The only clear demonstrations of such a change in rate-determining step that we have been able to locate are the data of Jencks and co-workers for eliminations from *N*-(4-nitrophenethyl)-quinuclidinium cations[6] and from 2-cyanoethyl sulfides[7] in predominantly aqueous media, the study of Fedor and Glave[8a] on the elimination reactions of 4-phenoxy-2-butanones in aqueous solution, and the studies of Stirling and co-workers[8b] on the eliminations of β-activated ethylammonium cations in ethanolic solution. In these cases, the change in rate-determining step involves the demonstration of a kinetic saturation effect at high concentrations of the general-base catalyst species. A change in rate-determining step that results from structural variation in the elimination substrate itself does not seem to have been clearly demonstrated, although there was an indication of such a phe-

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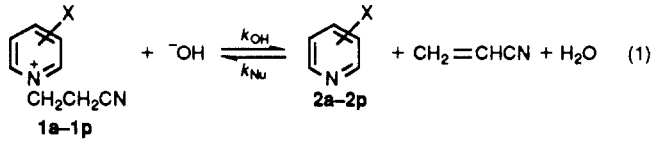
Table I. Characterization of *N*-(2-Cyanoethyl)pyridinium Bromides (**1**·Br^-)

pyridinium cation	X	mp (°C)	^{1}H NMR[a] (δ)
1a	3-CN	204–206	3.68 (2 H, t), 5.43 (2 H, t), 8.57 (1 H, dd), 9.05 (1 H, d), 9.50 (1 H, d), 9.77 (1 H, s)[b]
1b	3-Cl	121–122	3.42 (2 H, t), 5.07 (2 H, t), 6.73 (1 H, dd), 7.30 (1 H, d), 7.55 (1 H, d), 7.80 (1 H, s)[c]
1c	3-$CONH_2$	164–166	3.39 (2 H, t), 5.09 (2 H, t), 8.32 (1 H, dd), 9.03 (1 H, d), 9.19 (1 H, d), 9.49 (1 H, s)[c]
1d	4-$CONH_2$	224–225	3.39 (2 H, t), 5.08 (2 H, t), 8.48 (2 H, d), 9.19 (2 H, d)[c]
1e	3-CH_2CN	140–142	3.50 (1 H, t), 4.38 (2 H, s), 5.17 (2 H, t), 8.30 (1 H, dd), 8.83 (1 H, d), 9.13 (1 H, d), 9.33 (1 H, s)[b]
1f	H	148–150	3.40 (2 H, t), 5.03 (2 H, t), 8.20 (2 H, dd), 8.70 (2 H, t), 9.00 (1 H, d)[c]
1g	3-CH_3	115–117	2.70 (3 H, s), 3.47 (2 H, t), 5.10 (2 H, t), 8.12 (1 H, dd), 8.57 (1 H, d), 8.73 (2 H, br s)[b]
1h	4-CH_3	146–148	2.77 (3 H, s), 3.42 (2 H, t), 5.03 (2 H, t), 8.03 (2 H, d), 8.92 (2 H, d)[b]
1i	3,5-$(CH_3)_2$	160–161	2.57 (6 H, s), 3.33 (2 H, t), 4.88 (2 H, t), 8.38 (1 H, s), 8.72 (2 H, s)[c]
1j	3,4-$(CH_3)_2$	132–134	2.48 (3 H, s), 2.60 (3 H, s), 3.32 (2 H, t), 4.83 (2 H, t), 8.00 (1 H, d), 8.72 (1 H, d), 8.78 (1 H, s)[c]
1k	3-NH_2	141–143	3.29 (2 H, t), 4.79 (2 H, t), 7.76 (2 H, m), 8.13 (1 H, m), 8.19 (1 H, s)[c]
1l	4-OCH_3	145–146	3.40 (2 H, t), 4.23 (3 H, s), 4.97 (2 H, t), 7.53 (2 H, d), 8.40 (2 H, d)[b]
1m	3-Br, 4-NH_2	231–232	3.33 (2 H, t), 4.72 (2 H, t), 7.28 (1 H, d), 8.30 (1 H, d), 8.57 (1 H, s)[b]
1n	4-morpholino	231–233	3.23 (2 H, t), 3.87 (4 H, br m), 4.08 (4 H, m), 4.62 (2 H, t), 7.12 (2 H, d), 8.18 (2 H, d)[b]
1o	4-NH_2	215–217	3.18 (2 H, t), 4.52 (2 H, t), 6.90 (2 H, d), 8.07 (2 H, d)[c]
1p	4-$N(CH_3)_2$	189–190	3.13 (2 H, t), 3.21 (6 H, s), 4.45 (2 H, t), 6.87 (2 H, d), 8.00 (2 H, d)[c]

[a] In CF_3CO_2H relative to $(CH_3)_4Si$ or in D_2O relative to $(CH_3)_3Si(CH_2)_3SO_3^-Na^+$. [b] In CF_3CO_2H. Spectra are unstable in this solvent due to a reaction between the cyano group and CF_3CO_2H. [c] In D_2O.

nomenon in one case when a one-point deviation was observed in a Brønsted plot for leaving-group expulsion.[7a]

We have recently reported[9] a detailed kinetic analysis of the hydroxide ion catalyzed elimination of isoquinolines from *N*-(2-cyanoethyl)isoquinolinium cations in aqueous solutions. The pH dependences of these eliminations are complicated by competing hydroxide ion addition and deprotonation equilibria. In an attempt to obtain a clearer expression of leaving-group substituent effects in these reactions, we have now extended this study to a series of 16 ring-substituted *N*-(2-cyanoethyl)pyridinium cations (**1**),



since pyridinium cations are much less prone to hydroxide ion addition (pseudobase formation) than are isoquinolinium cations.[10] These pyridinium cations also had the further advantage of providing a much broader range of leaving groups than those that are readily available in the isoquinoline series. The current study includes pyridine leaving groups with pK_{BH} in the range 1.5–9.7 and reveals a nonlinear Brønsted plot that is only readily interpretable in terms of a change in rate-determining step from deprotonation (at low pK_{BH}) to leaving-group departure (at high pK_{BH}) within an E1cb reaction mechanism.

A further extension of this study became possible upon the observation that in some cases an equilibrium mixture between these *N*-(2-cyanoethyl)pyridinium cations and the corresponding pyridine and acrylonitrile could be established and readily observed spectroscopically. This observation lead us to also investigate the rates and equilibria for the Michael-type addition[11] of a number of pyridinium cations and pyridinones to acrylonitrile. This addition process, the microscopic reverse of the above elimination, must also undergo a change in rate-determining step with changing nucleophilicity of the pyridine. We have found that the rate constants for the addition of the less nucleophilic pyridines are sufficiently small that it is inconvenient to use rate measurements to directly demonstrate this change in rate-determining step from the addition direction. Nevertheless, we have been able to conclusively demonstrate its existence from the combination of linear free energy relationships for the rates of the elimination reaction with those for the overall equilibrium that is established.

Experimental Section

Materials. Most of the substituted pyridines, 4-methoxypyridine 1-oxide, 1-(4-pyridyl)pyridinium chloride, 2(1*H*)- and 4(1*H*)-pyridinone, 3-bromopropanenitrile, and acrylonitrile are commercially available. 4-Morpholinopyridine was synthesized as described by Jameson and Lawlor,[12] and 3-bromo- and 3,5-dibromo-4(1*H*)-pyridinone were prepared by the method of Tee and Paventi.[13] 4-Methoxypyridine was prepared by the deoxygenation of its *N*-oxide with PCl_3 in chloroform by the method of Ochiai.[14] 4-Amino-3-bromopyridine[13] was a gift from Professor O. S. Tee of Concordia University, Montreal, Quebec. Pyridine nucleophiles for use in the kinetic studies of the addition reactions were purified by recrystallization or distillation; acrylonitrile (99+%) was used as received from Aldrich Chemical Co., Milwaukee, WI.

1-(2-Cyanoethyl)pyridinium Bromides (1·Br^-). These salts were prepared by the treatment of the appropriate substituted pyridine with 3-bromopropanenitrile in a mixture of methanol and acrylonitrile as solvent by the following general method, which is described for **1b**. Yields varied from 20% to 90%, depending upon the nucleophilicity of the substituted pyridine. Crude salts were crystallized several times from either ethanol–ethyl acetate or 2-propanol–ethyl acetate mixtures.

A solution containing 3-chloropyridine (4 mL), 3-bromopropanenitrile (5.6 mL), acrylonitrile (5 mL), and methanol (10 mL) was refluxed for 48 h. After cooling, the addition of diethyl ether (30 mL) produced a thick clear oil. The ethereal layer was decanted off, and the oil was repeatedly washed with fresh ether until a solid product was obtained. The salt was recrystallized three times from 2-propanol–ethyl acetate to yield cream white needles (2.8 g).

All bromide salts were characterized by ^{1}H NMR spectroscopy (Table I), and their purities were checked by Volhard titration of the bromide ion. All titrations indicated molecular weights of 100 (±1)% of the theoretical values.

Kinetic Studies. All kinetic data were obtained in aqueous solutions of ionic strength 0.1 (buffer + KCl) at 25 °C. Reactions with half-times less than 10 s were studied on the Durrum–Gibson stopped-flow spectrophotometer. Slower reactions were investigated on a Cary 210 spectrophotometer. In each case, digital data recording and rate constant analysis were carried out as previously described.[15] All solution pH values were measured on a Radiometer PHM82 pH meter with a GK2401B combination electrode, and calibration was with BDH Colourkey standard buffer solutions in a cell thermostated at 25 °C. The pH of each reaction solution from studies on the Cary 210 spectrophotometer was measured at the completion of each run. The pH measurements of solutions in the stopped-flow studies employed 1:1 dilutions of the original reaction solutions. Buffer solutions consisted of ethanolamine–hydrochloric acid, sodium carbonate–sodium bicarbonate, or standard KOH solutions adjusted to ionic strength 0.1 with KCl.

Both elimination and addition reactions were investigated at wavelengths that were chosen for each pyridine derivative so as to maximize the absorbance change between the neutral pyridines and the pyridinium cations (**1**). Pyridine (in addition reactions) and pyridinium cation (in elimination reactions) concentrations were in the range 0.05–0.2 mM in the spectrophotometric kinetic studies. Acrylonitrile concentrations in the addition reactions were in the range 0.1–0.5 M.

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pK_{BH} values were measured spectrophotometrically at 25 °C, ionic strength 0.1, in buffered aqueous solutions by the general method of Albert and Serjeant[16] but with the computation of pK_{BH} via a curve-fitting program for the pH dependence of the measured absorbances. ^1H NMR spectra were obtained on either Varian T60 (preliminary studies) or Varian Gemini 200 spectrometers.

Results

Eliminations. Each of the 16 ring-substituted *N*-(2-cyanoethyl)pyridinium cations (**1**) that we have examined cleanly undergoes elimination in basic aqueous solutions to give the substituted pyridine and acrylonitrile. We have identified the reaction products by both ^1H NMR and UV spectroscopies. For each **1**, the reaction products have spectroscopic properties identical with those of an equimolar mixture of the appropriate pyridine and acrylonitrile. The only exceptions to these general observations are in the ^1H NMR spectra of the reactions of **1n–1p** in basic D_2O, as discussed in case 3 below. With these cations, the methylene protons α to the cyano group in **1** undergo exchange much faster than the elimination reaction occurs, and the resulting acrylonitrile contains complete deuterium label at C-2.

The elimination reactions of **1** (at 0.2 M) were followed by ^1H NMR spectroscopy in three different basic reaction media in D_2O. The more reactive **1** were examined in 0.5 M K_2HPO_4 in D_2O (pD ≈ 9) and 0.5 M Na_2CO_3 in D_2O (pD ≈ 11), while the less reactive cations were examined in this carbonate solution and also in 0.5 M KOD in D_2O. Three general classes of experimental results were obtained:

1. For **1** having pyridine leaving groups of $pK_{BH} < 5.5$, elimination is complete in both the phosphate and carbonate solutions, with no incorporation of deuterium into the acrylonitrile product.

2. For $pK_{BH} \approx 6.5$, elimination does not go to completion in either phosphate or carbonate solutions, but rather an equilibrium mixture of **1** and the appropriately substituted pyridine and acrylonitrile is obtained. Elimination is always more complete in the more basic carbonate solutions than in the phosphate solutions. It was this observation that originally encouraged us to examine the nucleophilic addition reactions of pyridines to acrylonitrile that are described below. Initially, the acrylonitrile that is formed in these reactions contains no deuterium; however, at longer reaction times exchange of the C-2 hydrogen for deuterium becomes evident.

3. For **1** having pyridine leaving groups of $pK_{BH} > 8$, the elimination is too slow to be readily observed in the carbonate solution. In such solutions, exchange of the methylene protons adjacent to the cyano group occurs rapidly and results in the disappearance of the triplet for these hydrogen atoms at δ 3.2 and the conversion of the triplet at δ 4.5 for the adjacent methylene group into a singlet. In KOD solutions, the elimination occurs cleanly, with the elimination product being entirely $CH_2{=}CDCN$.

We have also established that acrylonitrile does not undergo exchange in these basic solutions on the same time scale as these elimination reactions. Lengthy incubations (several days) of acrylonitrile in these basic media do lead to the gradual disappearance of the signals due to the acrylonitrile and the growth of a singlet at δ 3.85, which we assign to the methylene protons of $DOCH_2CD_2CN$.

A typical time-dependent UV spectrum, showing the elimination reaction of **1d**, is shown in Figure 1. All such reactions are characterized by a significant reduction in the intensity of the $\pi \rightarrow \pi^*$ absorption maximum, but with little change in λ_{max}, upon conversion of the pyridinium cation into the neutral pyridine product. The only exceptions to these general spectral observations are found for the derivatives **1k–1p**, which show a more significant spectral change as a result of the resonance interactions of the substituted amino and methoxy substituents with the pyridine and pyridinium chromophores (e.g., Figure 2).

All reactions proved to be strictly first-order in pyridinium cation (**1**). Reaction rates are both pH and X-substituent dependent, with a total range of 4 × 10^5-fold in pseudo-first-order rate

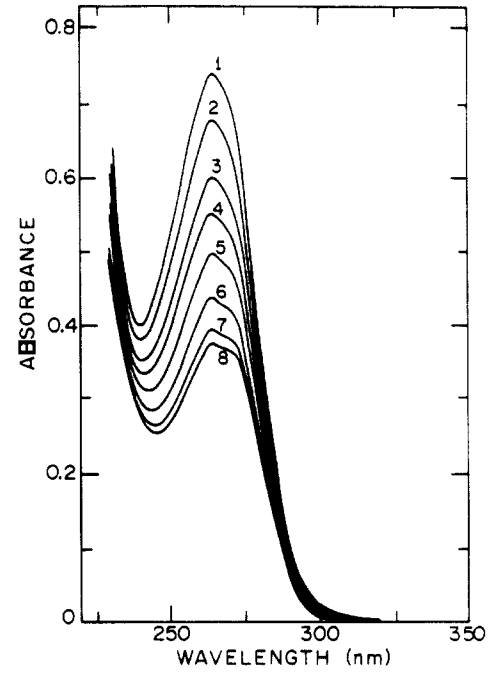

Figure 1. Time-dependent spectrum of **1d** (0.21 mM) in aqueous solution at pH 9.57: curve 1, 0 s; 2, 90; 3, 195; 4, 270; 5, 375; 6, 555; 7, 855; 8, 1620.

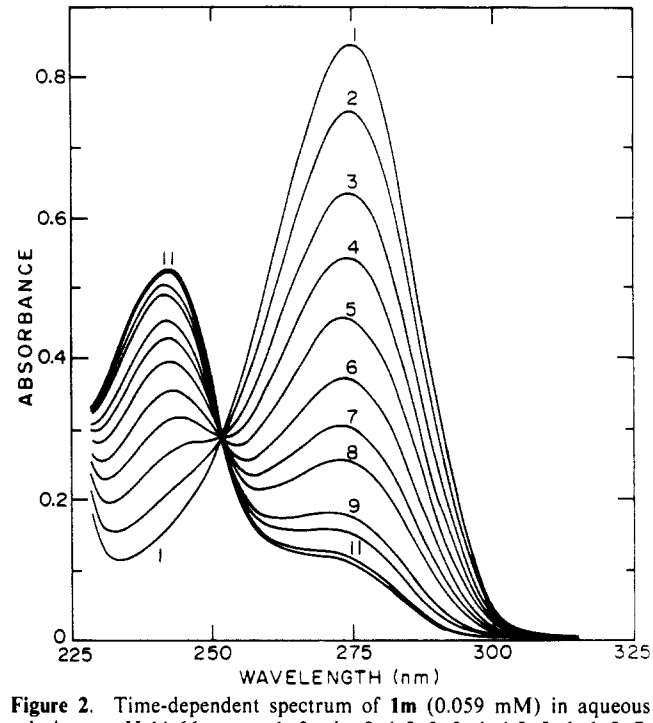

Figure 2. Time-dependent spectrum of **1m** (0.059 mM) in aqueous solution at pH 11.66: curve 1, 0 min; 2, 1.5; 3, 3; 4, 4.5; 5, 6; 6, 8; 7, 10; 8, 13; 9, 18; 10, 20; 11, 50.

constants, covering reaction half-times from 60 ms (measured by the stopped-flow technique) to 6 h, as measured in the current study. The pH dependences of the pseudo-first-order rate constants (k_{obs}) for elimination are summarized in Figures 3 and 4.

For most **1**, the log k_{obs} vs pH profiles in Figure 3 appear to be linear and of approximately unit slope. However, least-squares fitting of these linear profiles in most cases gave slopes that were slightly greater than 1.0 (Table II). These deviations from unit slope appear to be experimentally significant and are probably attributable to specific ion effects upon replacement of hydroxide ion by chloride ion in these constant ionic strength solutions. Similar specific ion effects have been reported previously by Jencks and co-workers[6] in their studies of elimination reactions of quinuclidinium cations in basic aqueous solutions and are presumably

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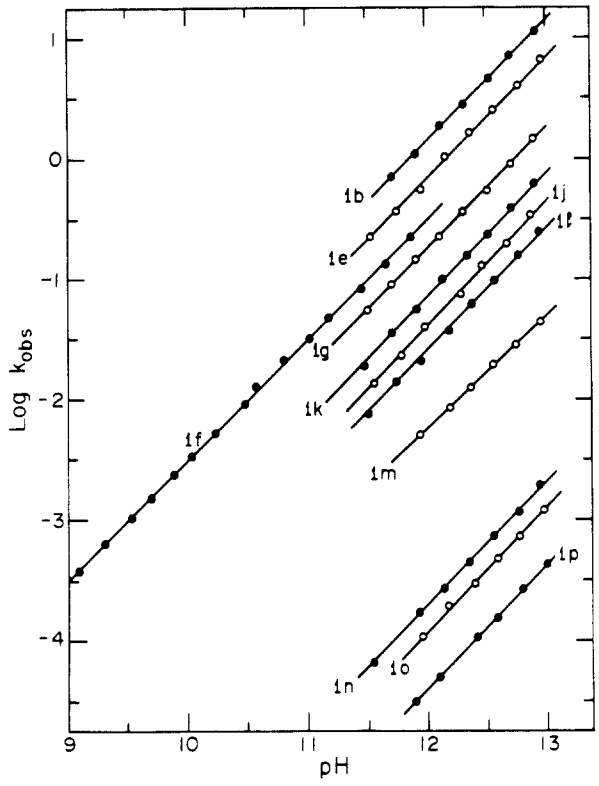


Figure 3. pH dependence of k_{obs} for various **1**. Lines are least-squares lines with slopes given in Table II.

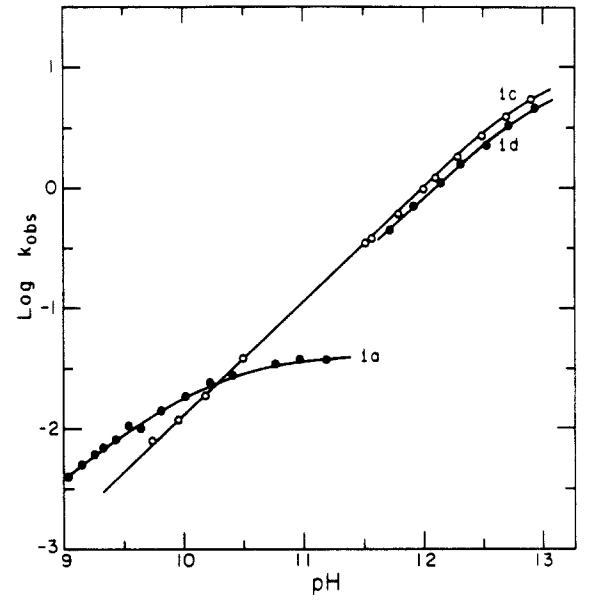


Figure 4. pH dependence of k_{obs} for **1a**, **1c**, and **1d**. Curves are calculated according to eq 2 with k_{OH} and pK_a parameters from Table II.

the result of weak ion-pairing phenomena between the cationic substrates and the background anions. Such deviations from unit slope lead to slightly pH-dependent second-order rate constants (k_{OH}) for hydroxide ion catalyzed elimination. We have, therefore, chosen to report second-order rate constants for all cations by interpolation to pH 12.0. These second-order rate constants are listed in Table II.

Deviations from linear pH–rate profiles are observed for the 3-CN (**1a**),[17] 3-$CONH_2$ (**1c**), and 4-$CONH_2$ (**1d**) cations. In each

(17) A complicated base-catalyzed decomposition of **1a** occurs above pH 11.5. We have not examined this reaction in detail but assume that it is similar to the competing hydrolytic and disproportionation processes that have been reported[18] for the 3-cyano-1-methylpyridinium cation in basic aqueous solutions.

Table II. Kinetic Parameters for the Hydroxide Ion Catalyzed Elimination Reactions of **1**[a]

pyridinium cation	X	slope	k_{OH} (M^{-1} s^{-1})	pK_a	pK_{BH}
1a	3-CN	*b*	324	10.11	1.50
1b	3-Cl	1.03	154		2.84[c]
1c	3-$CONH_2$	*b*	115	13.16	3.30
1d	4-$CONH_2$	*b*	90	13.30	3.58
1e	3-CH_2CN	1.06	66.9		4.08
1f	H	1.03	29.6		5.16
1g	3-CH_3	1.03	17.8		5.82[d]
1h	4-CH_3	1.07	8.45		6.15[e]
1i	3,5-$(CH_3)_2$	1.06	8.36		6.14[d]
1j	3,4-$(CH_3)_2$	1.06	4.23		6.45[d]
1k	3-NH_2	1.08	6.94		6.14
1l	4-OCH_3	1.06	2.42		6.66[e]
1m	3-Br, 4-NH_2	0.94	0.567		7.15
1n	4-morpholino	1.02	0.0194		8.82
1o	4-NH_2	1.02	0.0119		9.21
1p	4-$N(CH_3)_2$	1.05	0.00417		9.68[f]

[a] In aqueous solution, ionic strength 0.1, at 25 °C. Slopes are of plots of log k_{obs} vs pH. pK_a is obtained by fitting nonlinear plots to eq 2. All k_{OH} are obtained from $k_{obs}/[^-OH]$ upon interpolation to pH 12.0 (except **1a**, **1c**, and **1d**, which are evaluated with eq 2). [b] Nonlinear plot requires eq 2. [c] Brown, H. C.; McDaniel, D. H. *J. Am. Chem. Soc.* **1955**, *77*, 3752. [d] Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 3040. [e] Battye, P. J.; Ihsan, E. M.; Moodie, R. B. *J. Chem. Soc., Perkin Trans. 2* **1980**, 741. [f] Bunting, J. W.; Stefanidis, D. *J. Am. Chem. Soc.* **1990**, *112*, 779.

Table III. General-Base Catalysis of the Elimination Reactions of **1**[a]

pyridinium cation	base	pH	base concn (M)	k_{obs} (10^{-3} s^{-1})	k_B (M^{-1} s^{-1})
1e	$HOCH_2CH_2NH_2$	9.66	0.025	3.50	
			0.050	3.51	
			0.075	3.57	1.2×10^{-3}
1f	$HOCH_2CH_2NH_2$	9.66	0.025	1.29	
			0.050	1.30	
			0.10	1.34	6×10^{-4}
1g	$HOCH_2CH_2NH_2$	9.66	0.025	0.707	
			0.050	0.723	
			0.075	0.729	
			0.10	0.734	2×10^{-4}
1c	CO_3^{2-}	9.98	0.0065	11.8	
			0.0130	12.0	
			0.0195	12.4	
			0.0260	12.9	0.058

[a] In aqueous solution, ionic strength 0.1, at 25 °C.

of these cases, k_{obs} appears to approach a limiting value in the most basic solutions and can be expressed by eq 2. Values of k_{OH} and pK_a, which are obtained by analysis of the pH–rate profiles for each of these cations according to eq 2, are included in Table II.

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

For **1a**, we assign $pK_a = 10.11$ as pK_{R^+} for pseudobase formation by hydroxide ion addition at C-4 of this cation. This assignment seems reasonable in view of $pK_{R^+} = 12.2$ for the 3-cyano-1-methylpyridinium cation[19] and $\Delta pK_{R^+} \approx 2$ that has been observed[9] for the difference in pK_{R^+} between *N*-methyl- and *N*-(2-cyanoethyl)isoquinolinium cations. For each of **1c** and **1d**, we ascribe the pK_a values of Table II to the deprotonation of the amide functional group of each of these cations. For **1c**, $pK_a = 13.16$ is similar to $pK_a = 13.2$, which has been assigned[20] to amide

(18) Kosower, E. M.; Patton, J. W. *Tetrahedron* **1966**, *22*, 2081. (b) Blanch, J. H.; Fretheim, K. *J. Chem. Soc. C* **1971**, 1892. (c) Moracci, F. M.; Casini, A.; Liberatore, F.; Carelli, V. *Tetrahedron Lett.* **1976**, 3723. (d) Moracci, F. M.; Tortorella, S.; Di Rienzo, B.; Liberatore, F. *Tetrahedron* **1979**, *35*, 2591.

(19) Bunting, J. W. *Tetrahedron* **1987**, *43*, 4277.

Table IV. Kinetic Data for the Nucleophilic Attack of Pyridines and Pyridinones upon Acrylonitrile[a]

nucleophile	X	pK_{BH}	k_{Nu} (10^{-3} M^{-1} s^{-1})	k_{OH} (M^{-1} s^{-1})	K	K_{HNu} (10^4 M^{-1})
2i	3,5-$(CH_3)_2$	6.14[b]	0.90	8.9	1.03×10^{-4}	0.75
2j	3,4-$(CH_3)_2$	6.45[b]	1.21	4.02	2.8×10^{-4}	0.97
2m	3-Br, 4-NH_2	7.15[b]	0.81	0.50	1.5×10^{-3}	1.08
2n	4-morpholino	8.78	2.34	0.025	0.120	2.0
2o	4-NH_2	9.24	2.90	0.0121	0.24	1.4
2p	4-$N(CH_3)_2$	9.73	4.03	0.0042	0.98	1.83
5a[c]	4-O^-	11.12	8.5	0.00019[d]	45	3.4
5b[c]	3-Br, 4-O^-	9.4	3.5	0.0083	0.42	1.7
5c[c]	3,5-Br_2, 4-O^-	7.73	1.47	0.150	0.0098	1.8
3[c]	2-O^-	11.74	5.0	*e*		

[a] In aqueous solution, ionic strength 0.1, at 25 °C. pK_{BH} and k_{Nu} are obtained from curve-fitting to eq 4, unless otherwise indicated. [b] From Table II. Addition reactions for this nucleophile have only been studied at a single pH. [c] Anion. [d] Calculated from eq 8. [e] Very small; experimentally indistinguishable from zero.

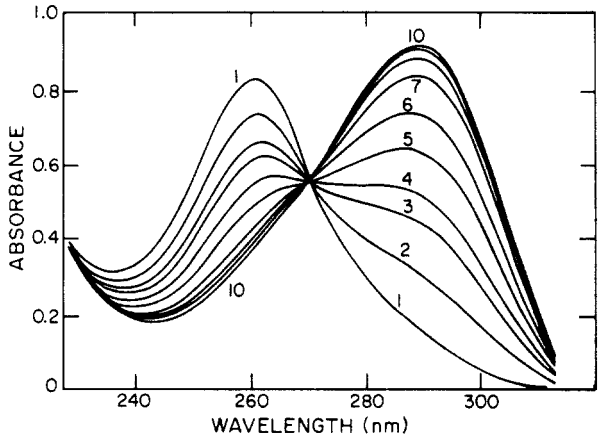


Figure 5. Time-dependent spectrum of an aqueous solution containing acrylonitrile (0.4 M) and 4-(dimethylamino)pyridine (0.052 mM) at pH 12.92: curve 1, 0 min; 2, 3; 3, 6; 4, 8; 5, 12; 6, 17; 7, 26; 8, 23; 9, 45; 10, 57.

deprotonation in the 1-methylnicotinamide cation.

We have investigated the possibility of catalysis by buffer species for several **1**. We have established that such catalysis is present in a number of cases; however, it is extremely weak. The clearest expressions of such catalysis are summarized in Table III.

Additions. Figure 5 shows the time-dependent electronic absorption spectrum of 4-(dimethylamino)pyridine in the presence of a large excess of acrylonitrile at pH 12.92. These spectral changes proved to be cleanly kinetically first-order in the pyridine concentration, and pseudo-first-order rate constants (k_{add}) were measured as a function of both acrylonitrile concentration (0.1–0.5 M) and pH (9–13). These pseudo-first-order rate constants can be expressed by eq 3, where AN represents acrylonitrile.

$$k_{add} = k_f[AN] + k_{OH}[^-OH] \quad (3)$$

The apparent second-order rate constants (k_f) that are defined by eq 3 proved to be pH-dependent (Figure 6). This pH dependence is consistent with eq 4. Values of k_{Nu}, which represents the second-order rate constant for reaction of the neutral pyridine with acrylonitrile, are listed in Table IV. Values of k_{OH} obtained

$$k_f = k_{Nu}/[1 + [H^+]/K_{BH}] \quad (4)$$

from ordinate intercepts in the data for the addition reactions according to eq 3 are included in Table IV. In general, the k_{OH} values in Table IV are in excellent agreement with the k_{OH} values in Table II that were obtained in the study of the elimination reactions, and the pK_{BH} values obtained from fitting the kinetic data to eq 4 agree with the independently determined pK_{BH} values of these nucleophiles. Pyridines less basic than $pK_{BH} = 6$ proved to react too slowly to be readily investigated in these addition reactions.

(20) Martin, R. B.; Hull, J. G. *J. Biol. Chem.* **1964**, *239*, 1237.

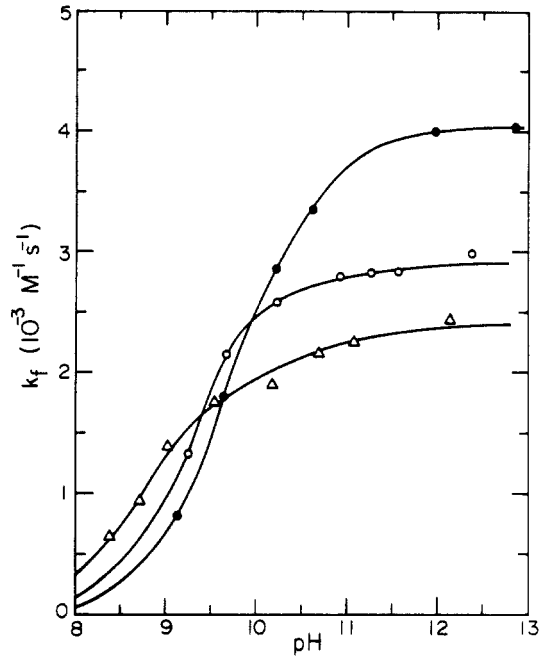
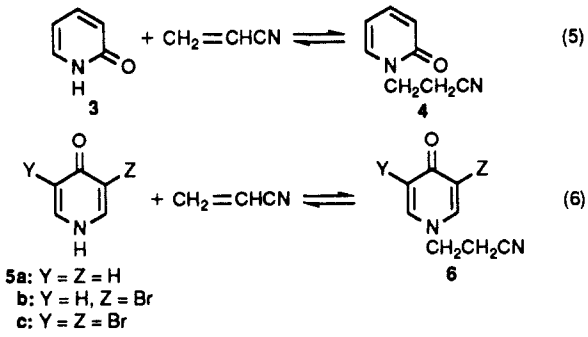


Figure 6. pH dependence of k_f for the reaction of 4-(dimethylamino)-pyridine (filled circles), 4-aminopyridine (open circles), and 4-morpholinopyridine (triangles) with acrylonitrile in aqueous solution. Curves are calculated according to eq 4 with k_{Nu} and K_{BH} from Table IV.

The additions of the pyridines to acrylonitrile (each 0.3 M) were also studied by ^1H NMR spectroscopy in 0.5 M Na_2CO_3 in D_2O. Under these conditions, the product spectra were identical with **1** bearing an *N*-(CH_2CD_2CN) substituent (**1**-d_2). The spectrum of acrylonitrile collapses to that of $CH_2{=}CDCN$ before the addition process is complete, consistent with a dynamic equilibrium in which exchange of deuterium into acrylonitrile is catalyzed via the formation of **1**-d_2 and its subsequent elimination. At very long reaction times (3–12 h at pD 11), the methylene singlet at δ 4.45 from **1p**-d_2 is gradually replaced by another singlet at δ 4.40 and then by another at δ 4.35 at extremely long reaction time (1–2 days at pD 11). We interpret these observations as the hydrolysis of the nitrile group of **1**-d_2 first to the amide and then ultimately to the carboxylate anion. Small singlets at δ 3.85 and 3.80 also slowly appear, and we attribute these to the formation of $DOCH_2CD_2CN$ and $DOCH_2CD_2COND_2$, respectively.

2(1*H*)-Pyridinone (**3**), 4(1*H*)-pyridinone (**5a**), and its 3-bromo (**5b**) and 3,5-dibromo (**5c**) derivatives also readily reacted with acrylonitrile under basic conditions. For each of these pyridinones, k_{add} was consistent with eq 3, while the pH dependence of k_f was similar to Figure 6. The kinetic parameters for these pyridinones are included in Table IV.

The occurrence of N-alkylation rather than O-alkylation in the reactions of **3** and **5** is established by a comparison of the electronic absorption spectra of the reaction products with those of the



corresponding *N*-methyl and *O*-methyl derivatives that have been reported by Mason.[21] These data are collected in Table V and are consistent only with the formation of the *N*-(2-cyanoethyl) derivatives. These product assignments are also consistent with the observed ^{1}H NMR spectra of these reaction products. We have also shown that O-alkylation is unlikely in these reactions by the observation that phenoxide ion does not react with acrylonitrile at any significant rate under the current reaction conditions.

Discussion

The current study shows that the equilibrium of eq 1 is cleanly established in aqueous solutions. Under appropriate conditions, this equilibrium may be investigated from both the elimination reaction of the *N*-(2-cyanoethyl)pyridinium cation (**1**) and the addition of the pyridine to acrylonitrile, although with less nucleophilic pyridines the rate constants are such that it is inconvenient to investigate the addition reaction.[22]

The only reactions that compete with the reaction of eq 1 are the hydrolysis of the nitrile group in **1** to amide and carboxylate anion after lengthy reaction times in very basic solutions and also the slow base-catalyzed addition of water to acrylonitrile under these same reaction conditions. Our ^{1}H NMR spectral observations establish that both of these types of reaction occur very much more slowly than either the addition or elimination processes, so that the establishment of the equilibrium of eq 1 is readily investigated without complications from these alternative processes. By extrapolation of the higher temperature data of Wronski and Bogdanski,[23] we estimate a second-order rate constant of 1.5×10^{-4} M^{-1} s^{-1} for hydroxide ion attack at the β-carbon atom of acrylonitrile at 25 °C. This is smaller than the range of k_{Nu} = $(8.1-85) \times 10^{-4}$ M^{-1} s^{-1} that is observed for the second-order rate constants for nucleophilic attack by the substituted pyridines in Table IV. The pseudo-first-order rate constants for pyridine attack and hydroxide ion attack show an even greater difference when it is realized that the former are studied under conditions of [AN] $\geq$ 0.1 M while the latter have [$^-$OH] < 0.1 M. In fact, the addition of the less nucleophilic pyridines is always studied at low pH so as to minimize the rate of the elimination reaction. All of these considerations indicate that hydroxide ion attack on acrylonitrile in the current studies never exceeds 2% of the rate of pyridine attack, and in most experiments this rate ratio is $\ll$1%. The much slower nucleophilic attack of hydroxide ion on acrylonitrile than of the attack by the more basic pyridines is consistent with Bernasconi's demonstration[24] that the second-order rate constant for nucleophilic attack of hydroxide ion on benzylidenemalononitrile is over 100-fold smaller than the second-order rate constant for the attack of piperidine upon this same species.

The Brønsted plot for the dependence of k_{OH} for the elimination reaction upon leaving-group basicity is shown in Figure 7. The data in Figure 7 describe two distinct linear relationships with a break appearing near pK_{BH} = 6. The data are described by the correlation eqs 7 and 8 for pyridinium cations having $pK_{BH} \leq 5.82$ and $pK_{BH} > 5.82$, respectively.

$$\log k_{OH} = -0.30\ (\pm 0.01)pK_{BH} + 3.00\ (\pm 0.03) \qquad r = 0.997 \tag{7}$$

$$\log k_{OH} = -0.93\ (\pm 0.02)pK_{BH} + 6.6\ (\pm 0.1) \qquad r = 0.997 \tag{8}$$

Two of the data points in Figure 7 (3-Br, 4-O$^-$ and 3,5-Br_2, 4-O$^-$) were obtained during our study of the addition of these pyridinone anions to acrylonitrile. Note that these anionic pyridine leaving groups seem to fit the same Brønsted correlation as neutral pyridines of similar basicity. Figure 7 also includes data points for four isoquinoline leaving groups from our recent study[9] of the elimination reactions of *N*-(2-cyanoethyl)isoquinolinium cations. It is clear that these isoquinolines behave as substituted pyridines in terms of their reactivities in these elimination reactions. The reported β_{lg} = −0.43 for these isoquinolines is somewhat greater than β_{lg} = −0.30, which is indicated by eq 7. In retrospect, we note that the slope of the Brønsted plot for the isoquinoline data alone is relatively uncertain since three of the isoquinolines have quite similar basicities.

Table V. Electronic Absorption Spectral Data of the Cyanoethylation Products of **3** and **5**

compound	λ_{max} (ϵ)[a]
4	296 (6400)
1-methyl-2(1*H*)-pyridinone	297 (5700)[b]
2-methoxypyridine	269 (3230)[b]
6a	262 (19000)
6b	275 (>8400)[c]
6c	279 (13800)
1-methyl-4(1*H*)-pyridinone	260 (18900)[b]
4-methoxypyridine	222 (9300)[b]

[a] In aqueous solution. [b] From ref 21. [c] Because of low solubility, studies were in a saturated solution of uncertain concentration.

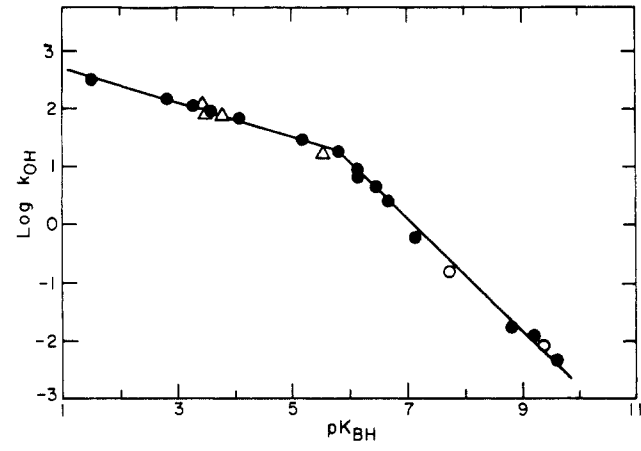
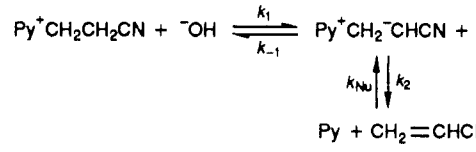


Figure 7. Brønsted plot for the hydroxide ion catalyzed elimination reaction of **1a–1p** (filled circles), data from Table IV for **6b** and **6c** (open circles), and data for *N*-(2-cyanoethyl)isoquinolinium cations (triangles) from ref 9.

Scheme I



(21) Mason, S. F. *J. Chem. Soc.* **1959**, 1253.

(22) For instance, from the linear free energy relationships that are developed in the present work, we estimate a half-time of 135 h for the pseudo-first-order addition of 3-chloropyridine in the presence of 0.5 M acrylonitrile, which is the highest concentration used in the current study. The rate of the addition of the pyridinium cation to acrylamide has been studied by ^{1}H NMR spectroscopy in D_2O under second-order kinetic conditions, with concentrations of ≥1 M in each reagent. Under these conditions, the first half-time of this reaction is about 20 h: Le Berre, A.; Delacroix, A. *Bull. Soc. Chim. Fr.* **1973**, 647. A similar method should be applicable to the study of the reactions of acrylonitrile with pyridines of $pK_{BH} < 6$.

(23) Wronski, M.; Bodganski, J. *Zesz. Nauk. Uniw. Lodz. Ser. 2* **1963**, *14*, 153; *Chem. Abstr.* **1965**, *62*, 3903.

(24) (a) Bernasconi, C. F.; Howard, K. A.; Kanavarioti, A. *J. Am. Chem. Soc.* **1984**, *106*, 6827. (b) Bernasconi, C. F.; Killion, R. B., Jr. *J. Org. Chem.* **1989**, *54*, 2878.

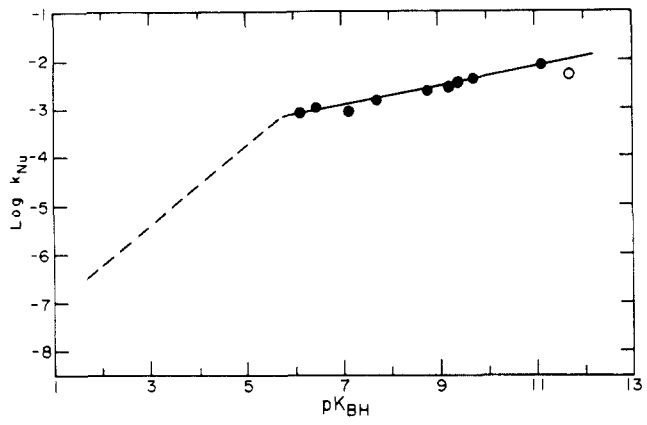


Figure 8. Brønsted plot for the nucleophilic attack of pyridines and pyridinone anions upon acrylonitrile in aqueous solution. The broken line represents eq 12, which is calculated as described in the text. The open circle represents the 2-pyridinone anion.

The "concave down" linear free energy relationship of Figure 7 is characteristic of a change in rate-determining step within a common reaction mechanism. Stirling has established[8b,25] that eliminations from cyano-activated substrates in basic ethanol usually occur via E1cb mechanisms, and Fishbein and Jencks have also established[7] this carbanionic mechanism for eliminations from (arylthio)propanenitriles in aqueous base. Consistent with these results, the only simple interpretation of a change in rate-determining step in the current reaction is in terms of an E1cb mechanism (Scheme I) in which deprotonation (k_1) with β_{lg} = −0.30 is rate-determining for $pK_{BH} < 6$ and leaving-group departure (k_2) from the carbanionic intermediate (β_{lg} = −0.93) is rate-determining for $pK_{BH} > 6$. This formally represents a change from an $(E1cb)_{irrev}$ mechanism for good leaving groups to an $(E1cb)_{rev}$ mechanism for the poorer leaving groups in the current study. To the best of our knowledge, this work represents the most dramatic demonstration that is currently available of a change in rate-determining step within a common series of leaving groups in an E1cb reaction.

The above interpretation is consistent with the lack of any observable incorporation of deuterium into the acrylonitrile product in basic D_2O for pyridine leaving groups of $pK_{BH} < 6$ (i.e., $(E1cb)_{irrev}$), while the less reactive *N*-(2-cyanoethyl)pyridinium cations having β_{lg} = −0.93 undergo hydrogen–deuterium exchange in the methylene group adjacent to the cyano group much faster than they undergo elimination under these same conditions.

The Brønsted plot for the addition of substituted pyridines to acrylonitrile is shown in Figure 8 and can be described by the correlation eq 9. The anions of the 4(1*H*)-pyridinones (**5**) appear to fit well with the data for the other substituted pyridines, and this is a further demonstration (see Results) that the ring nitrogen atom, rather than the exocyclic oxyanion, is the nucleophilic center in these species. The anion of 2(1*H*)-pyridinone reacts at only

$$\log k_{Nu} = 0.20\ (\pm 0.02)pK_{BH} - 4.3\ (\pm 0.1) \qquad r = 0.962 \qquad (9)$$

45% of the rate that is predicted by eq 9. This result is presumably a reflection of steric and solvation effects that arise from the proximity of the C-2 oxyanion substituent to the nucleophilic nitrogen atom in this case.

The β_{nuc} = 0.20 of eq 9 represents rate-determining nucleophilic attack upon acrylonitrile for these substituted pyridines. This represents the microscopic reverse of rate-determining departure of the pyridine with β_{lg} = −0.93 in the elimination reactions of **1** bearing these same pyridine substituents. Combination of these two Brønsted slopes allows the prediction of $\beta_{eq} = \beta_{nuc} - \beta_{lg}$ = 1.13 for the equilibrium constant $K = k_{Nu}/k_{OH}$ = $[Py^+CH_2CH_2CN][^-OH]/[Py][AN]$ for the addition reaction according to eq 10.

$$Py + CH_2{=}CHCN + H_2O \rightleftharpoons Py^+CH_2CH_2CN + {}^-OH \qquad (10)$$

Alternatively, one may write the addition reaction as the addition of the pyridinium cation to acrylonitrile as in eq 11, with $K_{HNu} = (k_{Nu}K_{BH})/(k_{OH}K_w) = [Py^+CH_2CH_2CN]/[Py^+H][AN]$, and β_{eq} = 0.13. Values of K and K_{HNu} are collected in Table IV. The magnitude of β_{eq} indicates that this addition reaction is somewhat more sensitive to pyridine basicity than is the standard protonation equilibrium.

$$Py^+H + CH_2{=}CHCN \rightleftharpoons Py^+CH_2CH_2CN \qquad (11)$$

The observed β_{eq} = 1.13 must apply to all substituted pyridines, including those that are not readily experimentally accessible ($pK_{BH} < 6$) as a result of a small rate constant for the addition reaction. Combination of β_{eq} with β_{lg} = −0.30 for $pK_{BH} < 6$ then allows the prediction of β_{nuc} = 0.83 for pyridines of $pK_{BH} < 6$ (eq 12). Equation 12 is represented by the broken line in Figure 8.

$$\log k_{Nu} = 0.83pK_{BH} - 7.9 \qquad (12)$$

The change in rate-determining step that is experimentally observed in the elimination reaction requires a similar change in rate-determining step in the Michael addition of these pyridines to acrylonitrile. Thus, whereas nucleophilic attack of the substituted pyridine with β_{nuc} = 0.20 is rate-determining for the more basic pyridines, the protonation of the carbanion intermediate by water becomes the rate-determining step for the addition of pyridines of $pK_{BH} < 6$ (β_{nuc} = 0.83 in Figure 8).

Such a rate-determining protonation of a carbanion intermediate in a Michael addition reaction has been observed by Alunni and Jencks[6a] in their studies of the reversible addition of quinuclidinium ions (QH^+) to 4-nitrostyrene (eq 13). For this reaction, Brønsted plots are linear for quinuclidines of pK_{BH} in the range 3–11, with β_{nuc} = 0.69, β_{lg} = −0.18, and β_{eq} = 0.89. All of these Brønsted

$$Q + CH_2{=}CHC_6H_4NO_2 + H_2O \rightleftharpoons Q^+CH_2CH_2C_6H_4NO_2 + {}^-OH \qquad (13)$$

parameters are somewhat smaller than what we find in the current study for the reaction of eq 1. It should be noted, however, that the normalized $\beta_{nuc}^n = \beta_{nuc}/\beta_{eq}$ = 0.73 and $\beta_{lg}^n = \beta_{lg}/\beta_{eq}$ = −0.27 for $pK < 6$ in the current study are reasonably similar to β_{nuc}^n = 0.78 and β_{lg}^n = −0.20 for the reaction of eq 13. The β_{lg} = −0.30 for the more reactive **1** is also similar to β_{lg} = −0.25, which has been found[7] for the hydroxide ion catalyzed elimination reactions of the thiophenol adducts of fumaronitrile ($ArSCH(CN)CH_2CN$). These latter reactions also occur via rate-determining deprotonation.

Friedman and co-workers[26] have reported extensive studies of the addition of primary amines to acrylonitrile and a variety of other simple Michael acceptors in aqueous solution at 30 °C. In all cases, they find β_{nuc} = 0.43 for amines of $pK_{BH} > 7.6$, which is considerably larger than β_{nuc} = 0.20 that we find for pyridines of similar basicity reacting with acrylonitrile. Despite this difference in selectivity, the reactivities of pyridines of $pK_{BH} \approx 10$ are quite similar to those of primary amines that are of similar basicity to these pyridines, provided these amines do not have multiple substitution at the α-carbon atom.

Apart from the reaction of eq 13 that is discussed above, we have been unable to locate any other examples of quantitative measurements of equilibria between a Michael addition reaction and its microscopic reverse elimination. There seems to be no precedent for the change in rate-determining step within a reaction series that is cleanly demonstrated by Figure 7 for an E1cb elimination and Figure 8 for a Michael addition. Apart from the nitrogen nucleophiles discussed above and a limited amount of data for other nitrogen,[23,27] sulfur,[7a,23,26b,27g,29] and oxygen[23,27c,g,28]

(25) Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1909.

(26) (a) Friedman, M.; Wall, J. S. *J. Am. Chem. Soc.* **1964**, *86*, 3735. (b) Friedman, M.; Cavins, J. F.; Wall, J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3672. (c) Friedman, M.; Wall, J. S. *J. Org. Chem.* **1966**, *31*, 2888. (d) Friedman, M. *J. Am. Chem. Soc.* **1967**, *89*, 4709.

Table VI. Rate Constants for the Deprotonation of Cyano-Activated Carbon Acids by Hydroxide Ion in Aqueous Solution

acid	k_1 (M^{-1} s^{-1})	pK_a	ref
CH_3CN	4×10^{-5}	≈28	34
$C_6H_5SCH_2CH_2CN$	0.04	26.7	7b
$C_6H_5SCH(CN)CH_2CN$	36	23.2[a]	7b
$C_5H_5N^+CH_2CH_2CN$ (**1f**)	29.6	≈23	*b*
$NCCH_2CH{=}CHCH_2CN$	5.89	≈21	33
$(CH_3)_3CCH(CN)_2$	4.32×10^5	13.1	35
$O_2NC_6H_4CH_2CN$	26	13.4	36

[a] pK_a for $CH_3SCH(CN)CH_2CN$. [b] Current work; k_1 is from Table II.

nucleophiles, there is a paucity of kinetic data for additions to simple monoactivated Michael acceptors such as acrylonitrile. The extensive investigations of nucleophilic additions to much more highly activated Michael acceptors have recently been reviewed by Bernasconi.[30]

Various synthetic procedures have been reported[31] for the addition of the conjugate acids of heterocyclic bases to Michael acceptors. Although the stoichiometry of these reactions involves the protonated heterocyclic cations, mechanistically such reactions are expected to proceed via nucleophilic attack by the heterocyclic base followed by protonation of a carbanionic intermediate. Our attempts to use some of these published synthetic procedures have resulted in capricious yields after the stated reaction times. Such results are probably a result of the presence of variable small amounts of neutral heterocyclic base, which is the reactive nucleophile, as contaminants in the prepared samples of the acid halide salts of these bases.

Proton-Transfer Reactions. Equation 7 represents a linear free energy relationship for the deprotonation of a series of cyano-activated carbon acids by hydroxide ion, with second-order rate constant $k_1 = k_{OH}$. These rate constants are reasonably sensitive to substituents in the pyridine ring. Since the equilibrium Hammett $\rho = 5.9$ for pK_{BH} for ring-substituted pyridinium cations,[32] eq 7 implies $\rho = 1.8$ for the influence of X substituents in **1** upon k_1. This sensitivity is presumably an indication of a significant variation in the effective positive charge on the pyridinium nitrogen atom with substitution on the pyridine ring carbon atoms.

Equation 7 may be extrapolated to $pK_{BH} > 6$ to predict the deprotonation rate constants for those members of the series **1** for which leaving-group departure is rate-determining. For leaving groups of $pK_{BH} > 6$, the observed k_{OH} for elimination is k_1k_2/k_{-1}, and the ratio k_{-1}/k_2 can, thus, be calculated. Combination of eqs 7 and 8 gives eq 14, which must hold for all pK_{BH} of the present study. This equation predicts that k_{-1}/k_2 is quite sensitive to pK_{BH}, and this ratio varies from 0.007 for $pK_{BH} = 2$ to 500 for $pK_{BH} = 10$. Values of $k_{-1}/k_2 < 1$ are consistent with rate-determining deprotonation in the elimination reaction, while $k_{-1}/k_2 > 1$ is required for rate-determining loss of the leaving group from the carbanionic intermediate. Fishbein and Jencks[7] reported $k_{-1}/k_2 \approx 0.1$ for hydroxide ion catalyzed elimination from $C_6F_5SCH_2CH_2CN$ for which deprotonation was rate-determining, but $k_{-1}/k_2 \approx 10$ for more basic thiophenoxide leaving groups for which leaving group expulsion was rate-determining. Equation 14 predicts $k_{-1}/k_2 = 1$ for $pK_{BH} = 5.7$, which is consistent with the experimentally observed change in rate-determining step.

$$\log (k_{-1}/k_2) = 0.63pK_{BH} - 3.6 \qquad (14)$$

Table VI compares the rate constants for the deprotonation of **1f** with literature data for the hydroxide ion catalyzed deprotonation of a variety of other cyano-activated carbon acids. As expected, the cationic **1** react with hydroxide ion considerably faster than the neutral β-thio-substituted propanenitriles ($ArSCH_2CH_2CN$) that have recently been extensively studied.[7] However, k_1 for **1f** is quite similar to k_1 for the thiophenol adducts of fumaronitrile ($ArSCH(CN)CH_2CN$), which also eliminate via rate-determining deprotonation. For the *N*-(2-cyanoethyl)-pyridinium cation (**1f**), k_1 is 5-fold greater than for 1,4-dicyano-2-butene[33] and 7×10^5-fold greater than $k_1 \approx 4 \times 10^{-5}$ M^{-1} s^{-1}, which appears to be the only value available[34] for the deprotonation of acetonitrile by hydroxide ion. Deprotonation of **1** is much slower than hydroxide ion catalyzed deprotonation of $(CH_3)_3CCH(CN)_2$ ($pK_a = 13.1$)[35] but very similar to the rate constant for deprotonation of $4\text{-}NO_2C_6H_4CH_2CN$ ($pK_a = 13.4$),[36] even though this latter species is approximately 10^{10}-fold more acidic than **1f** ($\Delta pK_a \approx 10$). These seem to be the only cyano-activated carbon acids for which both k_1 and pK_a are available in aqueous solutions. All of these considerations suggest that the pK_a values for the deprotonation of **1** are probably in the vicinity of 23, which is similar to the acidity of $ArSCH(CN)CH_2CN$.[7]

General-base catalysis of the elimination reactions of **1** is extremely weak (Table III). The relative efficiency of ethanolamine to hydroxide ion catalysis for **1** is, however, quite similar to that reported[7] in the elimination reactions of (arylthio)propanenitrile derivatives. From the data in Tables II and III, we can compare k_B for ethanolamine with k_{OH} for each of **1e**, **1f**, and **1g**. The ratio k_B/k_{OH} falls in the range $(1\text{–}2) \times 10^{-5}$. A similar comparison of the data[7] for a number of (arylthio)propanenitrile derivatives gives k_B/k_{OH} in the range $(2\text{–}6) \times 10^{-5}$. The use of ionic strength 1.0 in that earlier study[5] allowed an easier demonstration of general-base catalysis since the conditions permitted experiments at higher base concentrations. Since general-base catalysis of the deprotonation of cyano-activated carbon acids usually displays[37] Brønsted β values close to 1, general-base catalysis is particularly difficult to establish with these derivatives in most cases.

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