Kinetics of the Metal Ion Catalyzed Iodination of 2-Acetylpyridine

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Abstract: The kinetics of the iodination of 2- and 4-acetylpyridine and their corresponding N-methyl derivatives have been investigated. The reactions are general base catalyzed and exhibit large kinetic deuterium isotope effects (acetyl-d_3). This, together with the observed independence of the rates of iodine concentration, shows that the rate-determining step is the enolization or ionization of the C–H bond adjacent to the carbonyl group. Complex formation between 2-acetylpyridine (SH) and Zn^{2+}, Ni^{2+}, and Cu^{2+} leads to large rate increases, the catalytic constants for the acetate catalyzed iodination being between 5×10^3 (for $Zn(SH)^{2+}$) and 2×10^5 (for $Cu(SH)^{2+}$) times larger than that of the uncomplexed substrate. This effect, which is considerably larger than that observed on protonation of 2-acetylpyridine (*ca.* 200-fold rate increase), is consistent with stabilization of the negative charge developing on the carbonyl oxygen during ionization of the C–H bond.

The rate of halogenation of ketones has been shown to be a measure of the rate of enolization or ionization of the active C–H bond adjacent to the carbonyl group except under conditions of low-halogen concentrations, when the halogenation of the enol or enolate ions may become rate determining.[1] The mechanisms of both acid- and base-catalyzed enolization reactions have been extensively studied and in particular general acid catalysis is thought to proceed *via* rate-determining proton removal from the protonated ketone by the conjugate base B of the general acid BH+ (Scheme I).

Scheme I
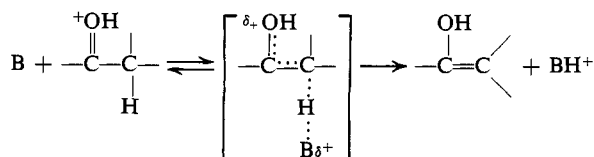
The rates of enolization or ionization of certain keto acids in which the carboxylic acid group is suitably placed to assist the ionization by interaction with the carbonyl oxygen have been found to be considerably higher (by factors of up to 2000) than those of the corresponding keto esters.[2,3] If the carbonyl oxygen can be coordinated to a metal ion, then this should also lead to a considerable enhancement of the rate of ionization of the active C–H bond. Pedersen has in fact observed such a rate enhancement of the acetate-catalyzed halogenation of both ethyl acetoacetate[4] and ethyl 2-oxocyclopentanecarboxylate[5] in the presence of cupric ions. The effects however were not large, presumably because of only weak complex formation between Cu^{2+} and the ketones. More recently Kluger and Wasserstein[6] have shown that complex formation with magnesium can accelerate the rate of deuteration of acetonyl phosphonate by a factor of over 2000 depending upon the catalyzing base. There are also many examples of metal ion catalysis of ester hydrolyses[7] and carbonyl-hydration reactions,[8] in which the catalytic effects are attributed to coordination of the carbonyl group to a metal ion.

In the present paper the effect of added metal ions (Cu^{2+}, Zn^{2+}, and Ni^{2+}) on the rate of halogenation of 2-acetylpyridine in a variety of buffers is reported. Kinetic deuterium isotope effects on the reaction have also been measured. The results are compared with those for 4-acetylpyridine and for the corresponding *N*-

(1) R. P. Bell, "The Proton in Chemistry," 2nd ed, Chapman and Hall, London, 1973.

(2) R. P. Bell and M. I. Page, *J. Chem. Soc., Perkin Trans. 2*, 1681 (1973).

(3) B. G. Cox and R. E. J. Hutchinson, *J. Chem. Soc., Perkin Trans. 2*, 613 (1974).

(4) K. J. Pedersen, *Acta Chem. Scand.*, 2, 385 (1948).

(5) K. J. Pedersen, *Acta Chem. Scand.*, 2, 252 (1948).

(6) R. Kluger and P. Wasserstein, *J. Amer. Chem. Soc.*, 95, 1071 (1973).

(7) D. A. Buckingham, C. E. Davis, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 92, 5571 (1970).

(8) Y. Pocker and J. E. Meany, *J. Phys. Chem.*, 74, 1486 (1970).

methylpyridinium ions. 2-Acetylpyridine is known to form complexes with several metals[9,10] and it has been reported that enolization of the 2-acetylpyridine takes place on complex formation.

Experimental Section

Materials. 2- and 4-acetylpyridine were commercial samples (Aldrich Chemical Co.) purified by distillation under reduced pressure. 2- and 4-acetyl-N-methylpyridinium iodides were prepared by refluxing the acetylpyridines with methyl iodide. They were recrystallized from ethanol and had melting points of 160–162 (lit. 161°) and 167–169°, respectively. Zinc nitrate was prepared by dissolving metallic zinc in nitric acid and evaporating off the excess nitric acid. All other inorganic salts were of AnalaR grade and were used without further purification.

Kinetic Measurements. Rates of loss of bromine or iodine were observed spectrophotometrically at 353 nm (unless otherwise stated), with a Gilford 2400 spectrophotometer. All kinetic measurements were made at $25 \pm 0.2°$.

pK_a Determinations. The pK_a's of 2- and 4-acetylpyridinium ions were determined from pH measurements on solutions prepared by adding known amounts of standard perchloric acid to acetylpyridine solutions. Activity coefficients required to obtain hydrogen ion concentrations from measured pH values were calculated from the expression

$$- \log y^{\pm} = 0.509 I^{1/2}/(1 + I^{1/2})$$

All pH measurements were made at 25°, using a Radiometer 26 pH meter.

Results

(i) pK_a of 2- and 4-Acetylpyridinium Ions. From pH measurements as described above the following results were obtained: 2-acetylpyridinium ion $10^3 K_a = 2.29 \pm 0.04$, i.e., $pK_a = 2.64$; 4-acetylpyridinium ion $10^4 K_a = 3.70 \pm 0.10$, i.e., $pK_a = 3.43$. The pK_a of the 4-acetylpyridinium ion at 25° has recently been reported[11] as 3.60. This value was obtained from measurements of the change in nmr chemical shift on deprotonation of the 4-acetylpyridinium ion. In view of the high ionic strength used in the nmr study (1.0 M) the agreement is probably reasonable.

(ii) Iodination of 2- and 4-Acetylpyridine in Buffer Solutions. Rates of iodination of 2- and 4-acetylpyridine were measured in self-buffered solutions and in acetate and monochloroacetate buffers of varying buffer ratio. Acetylpyridine concentrations were ca. 5×10^{-2} M and initial iodine concentrations were ca. 5×10^{-5} M. All reactions were carried out in the presence of 0.01 M I$^-$ at an ionic strength of 0.2, maintained by the addition of NaClO$_4$.

In all cases the reactions were zero order with respect to iodine for at least 90% of the reaction. Optical density readings were converted to concentrations using an effective extinction coefficient of 2.30×10^4 at 353 nm for iodine in the presence of 0.01 M I$^-$. This value was obtained from quoted values of $\epsilon_{I_3^-}$ and the formation constant of I_3^-.[12] Rates of iodination of 4-acetylpyridine were followed at 370 or 380 nm because of significant absorption due to the 4-acetylpyridinium ion at 353 nm. Optical density measurements at these wavelengths gave effective extinction coefficients of the I_2/I_3^- solutions as 2.02×10^4 and 1.55×10^4, respectively.

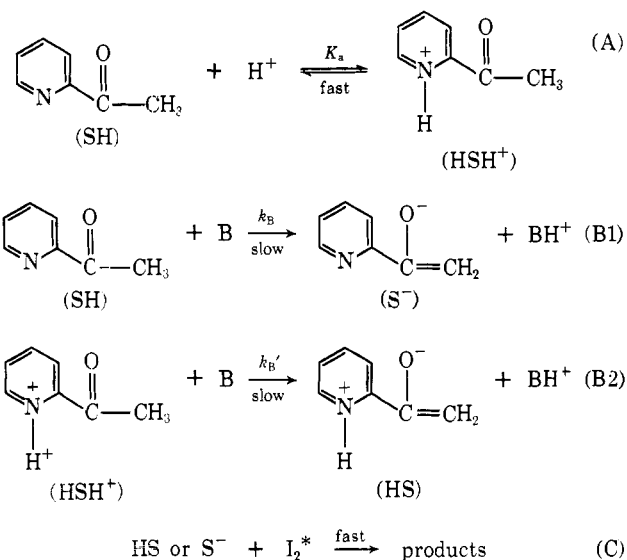(9) B. Kirson, *Isr. J. Chem.*, **6**, 1 (1968).
(10) B. Kirson, *Isr. J. Chem.*, **8**, 709 (1970).
(11) M. R. Chakrabarty, C. S. Handloser, and M. W. Mosher, *J. Chem. Soc., Perkin Trans. 2*, 938 (1973).
(12) J. Awtrey and D. Connick, *J. Amer. Chem. Soc.*, **73**, 1842 (1951).

The observed iodination rates were analyzed in terms of the following kinetic Scheme II (shown for 2-acetyl-

Scheme II

$$\text{HS or S}^- + \text{I}_2^* \xrightarrow{\text{fast}} \text{products} \qquad (C)$$

pyridine). In Scheme II B represents any base present including SH, and $\text{I}_2^* = \text{I}_2 + \text{I}_3^-$. It may be noted that reaction B2 is kinetically equivalent to the reaction between SH and BH$^+$. In principle the iodination of HSH$^+$ may also be acid catalyzed but the rates of iodination were found to be independent of acid concentration once sufficient acid had been added to fully protonate SH. The above scheme leads to the rate law shown in eq 1–3, where it is assumed that only mono iodination occurs under these conditions (i.e., [SH] + [HSH$^+$] $\gg$ [I$_2^*$]).

$$-d[\text{I}_2^*]/dt = -d([\text{SH}] + [\text{HSH}^+])/dt =$$
$$k_e[\text{SH}] + k_e'[\text{HSH}^+] \quad (1)$$

where

$$k_e = k_0 + k_B[\text{B}] + k_{SH}[\text{SH}] \qquad (2)$$

and

$$k_e' = k_0' + k_B'[\text{B}] + k_{SH}'[\text{SH}] \qquad (3)$$

The concentrations of SH and HSH$^+$ in the various buffers were calculated from the known pK_a's of the buffers (acetate or monochloroacetate) together with the measured pK_a's of the acetylpyridines. To do this it was necessary to estimate the activity coefficients of H$^+$ and the acetate and chloroacetate ions at an ionic strength of 0.2 M. These were estimated from the Davies equation (eq 4).[13]

$$\log y^{\pm} = -0.509[I^{1/2}/(1 + I^{1/2}) - 1/_3 I] \qquad (4)$$

The rates of iodination of 4-acetylpyridine in acetate buffers showed evidence of a slight contribution from hydroxide ion catalysis, as the extrapolated rates at zero acetate concentration were slightly higher than those expected purely on the basis of the spontaneous (solvent catalyzed) and self-catalyzed rates. No attempt was made to determine individual hydroxide ion catalytic constants for iodination of SH and HSH$^+$.

(13) C. W. Davies, "Ion Association," Butterworths, London, 1962.

The catalytic constants (eq 3 and 4) for the various bases are listed in Table I. The observed rates of

Table I. Catalytic Constants for the Base-Catalyzed Iodination of 2- and 4-Acetylpyridine at 25°

	2-Acetylpyridine		4-Acetylpyridine	
Base (B)	$10^5 k_B,^a$ l. mol^{-1} sec^{-1}	$10^5 k_B',^b$ l. mol^{-1} sec^{-1}	$10^5 k_B,^c$ l. mol^{-1} sec^{-1}	$10^5 k_B',^d$ l. mol^{-1} sec^{-1}
(H$_2$O)		0.141/55.5		0.053/55.5
Chloroacetate		11.7		3.4
2- or 4-acetyl-pyridine		4.15		27.8
Acetate	0.725	150	3.35	71.0

^{a} 2-Acetylpyridine. ^{b} 2-Acetylpyridinium ion. ^{c} 4-Acetylpyridine. ^{d} 4-Acetylpyridinium ion.

iodination in the various buffer solutions are given, together with those calculated from eq 1–3 using the catalytic constants in Table I, in the microfilm edition (Tables 1(a) and 1(b)). The catalytic constants relating to the unprotonated acetylpyridines were obtained only for the acetate-catalyzed iodination. This is because the unprotonated acetylpyridines are very much less reactive than the corresponding acetylpyridinium ions and their iodination only contributed significantly to the observed iodination rates in acetate buffers where [SH] ≫ [HSH+].

(iii) **Iodination of 2- and 4-Acetyl-N-methylpyridinium Iodides.** The rates of iodination 2- and 4-acetyl-N-methylpyridinium ions were measured in perchloric acid solution as well as in both acetate and monochloroacetate buffers. Experimental conditions were the same as those described above for the iodination of the acetylpyridines except that substrate concentrations were generally lower (0.004–0.01 M). Rates measured in acid solution were found to be independent of acid concentration up to 0.25 M, the highest concentration studied.

For both substrates, the reactions were zero order with respect to iodine, although for the 2-acetyl-N-methylpyridinium ion this was so only during the first 50–70% of reaction. At the lower iodine concentrations the rate became dependent upon iodine concentration. To confirm that during the first 50–70% of reaction the rates were truly independent of both the nature and concentration of the halogen, the rates of bromination of the 2-acetyl-N-methylpyridinium ion were also measured (see below).

For the iodination reactions, the observed rate law was of the form shown in eq 5, where

$$-\mathrm{d}[I_2^*]/\mathrm{d}t = (k_0 + k_B[B])[SH] \qquad (5)$$

SH represents the substrate. The rate of iodination of the 2-acetyl derivative in acetate buffers also showed evidence for a slight contribution from hydroxide ion catalysis.

The catalytic constants are listed in Table II. The observed rates of iodination are listed and compared with rates calculated from eq 5, using the catalytic constants in Table II, in Table 2(a) of the microfilm edition. The rates of bromination of the 2-acetyl-N-methylpyridinium ion were also measured in acetate buffers (r = 1). Acetate concentrations were 0.1 M and the solutions contained 0.2 M NaBr. The re-

Table II. Catalytic Constants for the Iodination of 2- and 4-Acetyl-N-methylpyridinium Iodides at 25°

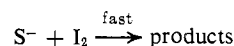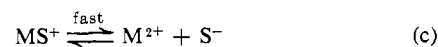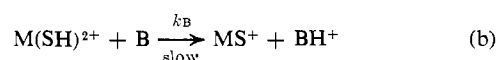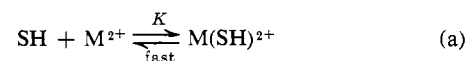| Base B	$10^5 k_B$(2-acetyl), l. mol^{-1} sec^{-1}	$10^5 k_B$(4-acetyl), l. mol^{-1} sec^{-1}
(H$_2$O)	0.80/55.5	0.040/55.5
Chloroacetate	62.2	3.06
Acetate	830	46.0

actions (carried out with excess bromine) were first order with respect to the 2-acetyl-N-methylpyridinium ion and zero order with respect to bromine. In each case 3 mol of bromine were consumed, the observed kinetics indicating that the ionization of the first C–H bond was rate determining with the two remaining bromine atoms entering in rapid subsequent steps.

The observed first-order rate constant was $k_{Br_2} = 7.6 \times 10^{-4}$ sec^{-1}. The corresponding value for the iodination rate obtainable from the iodination reactions in acetate buffers was $k_{I_2} = 8.4 \times 10^{-4}$ sec^{-1}. The agreement between these values confirms that the halogenation rates are independent of the halogen used. The slight difference (10%) may be attributed to the higher ionic strength used during the bromination reactions leading to a negative salt effect as expected for a reaction between an anion (acetate) and a cation (2-acetyl-N-methylpyridinium ion).

(iv) **Metal Ion Catalyzed Iodination of 2-Acetylpyridine.** The effect of Cu^{2+}, Zn^{2+}, and Ni^{2+} on the rates of iodination of 2-acetylpyridine was studied in unbuffered solutions (pH ca. 4.5) and in acetate and chloroacetate buffers. 2-Acetylpyridine concentrations were ca. 3×10^{-3} M and concentrations of I$_2$ and I$^-$ were the same as those for reactions in the absence of metal ions. The ionic strength was 0.1 for all reactions. In the absence of added buffers, rates were measured over a wide range of metal ion concentrations. For each of the metal ions, the observed rates showed a linear increase with increasing metal ion concentration at low metal ion concentration but leveled off and approached a limiting value at higher concentrations. In all cases the reactions were zero order with respect to iodine except at higher Ni^{2+} concentrations (>0.01 M) when the rates showed some dependence on iodine concentration. This limited the Ni^{2+} concentration range over which the reaction was studied. When sufficient acid was added to fully protonate 2-acetylpyridine, no catalysis by M^{2+} was observed, indicating that the free base was the only species involved in the catalytic reaction.

The observed kinetics were analyzed according to Scheme III in which the rate-determining step is the

Scheme III

$$SH + M^{2+} \underset{fast}{\overset{K}{\rightleftharpoons}} M(SH)^{2+} \qquad (a)$$

$$M(SH)^{2+} + B \underset{slow}{\overset{k_B}{\longrightarrow}} MS^+ + BH^+ \qquad (b)$$

$$MS^+ \overset{fast}{\rightleftharpoons} M^{2+} + S^- \qquad (c)$$

$$S^- + I_2 \overset{fast}{\longrightarrow} products$$

loss of a proton from SH coordinated to the metal ion. Step c need not involve dissociation of MS$^+$ but may

Cox / Metal Ion Catalyzed Iodination of 2-Acetylpyridine

Table III. Metal Ion Catalyzed Iodination of 2-Acetylpyridine at 25°

—Cu²⁺ catalysis,[a] K = 750[b]—			—Ni²⁺ catalysis,[c] K = 490[b]—			—Zn²⁺ Catalysis,[a] K = 35.7[b]—		
10^3[Cu²⁺], mol l.⁻¹	10^8rate, mol l.⁻¹ sec⁻¹	10^8rate-(calcd),[d] mol l.⁻¹ sec⁻¹	10^3[Ni²⁺], mol l.⁻¹	10^8rate, mol l.⁻¹ sec⁻¹	10^8rate-(calcd),[d] mol l.⁻¹ sec⁻¹	10^3[Zn²⁺], mol l.⁻¹	10^8rate, mol l.⁻¹ sec⁻¹	10^8rate-(calcd),[d] mol l.⁻¹ sec⁻¹
0.0	0.3		0.0	0.3		0.0	0.3	
0.2	23.9	22.9	0.2	0.97	0.87	1.0	0.60	0.60
0.4	41.7	41.4	0.4	1.50	1.43	2.0	0.80	0.87
0.6	68.7	61.4	0.6	1.96	1.95	5.0	1.75	1.62
0.8	79.1	80.6	0.8	2.69	2.48	7.5	2.09	2.23
1.0	101	99.1	1.0	2.97	2.92	10.0	2.90	2.71
2.0	178	183	1.5	4.12	4.12	15.0	3.43	3.35
4.0	280	299	2.0	5.00	5.13	20.0	4.39	4.22
6.0	348	363	2.5	6.13	5.98	30.0	5.43	5.23
8.0	407	399	3.0	6.65	6.88	40.0	5.93	5.93
10.0	393	422	4.0	7.83	8.19	80.0	7.20	7.46
12.0	443	436	5.0	9.09	9.21	∞		10.4
14.0	427	446	7.0	10.9	10.7			
16.0	457	453	10.0	11.7	11.9			
20.0	470	464	15.0	13.0	13.0			
∞		500	20.0	13.4	13.4			
			∞		15.0			

[a] [2-Acetylpyridine] = 3.38×10^{-3} M. [b] K = [MSH²⁺]/[M²⁺][SH]. [c] [2-Acetylpyridine] = 3.04×10^{-3} M. [d] Rates calculated from eq 6 and 7 using values of K and rates ([M] = ∞) shown in the table.

Table IV. Catalytic Constants[a] for the Iodination of 2-Acetylpyridine (SH) at 25°

Base (B)	SH	HSH⁺	ZnSH²⁺	NiSH²⁺	CuSH²⁺
(H₂O)		1.41×10^{-6}	3.1×10^{-5}	4.9×10^{-5}	1.48×10^{-3}
Chloroacetate		1.17×10^{-4}	2.57×10^{-3}	5.1×10^{-3}	1.46×10^{-1}
Acetate	7.25×10^{-6}	1.50×10^{-3}	3.24×10^{-2}	7.6×10^{-2}	1.47

[a] Catalytic constants in mol⁻¹ l.⁻¹ sec⁻¹ except for spontaneous (solvent catalysed) rate in sec⁻¹. Ionic strength = 0.1 M for MSH²⁺ reactions, otherwise 0.2 M.

involve a direct reaction between I_2 and MS⁺. For such a scheme, the observed kinetics will be of the form shown in eq 6 and 7, where [SH]* represents the total concentration of 2-acetylpyridine.

$$\text{rate} = -d[I_2]^*/dt = -d[SH]^*/dt = k_e[M(SH)^{2+}] \quad (6)$$

where

$$k_e = k_0 + k_B[B] \quad (7)$$

If the equilibrium constant K is known, then [M(SH)²⁺] can be readily determined for any given concentration of M²⁺ and SH. In the absence of equilibrium data, values of K were determined by fitting the observed rates in solutions without added base B to eq 6 and 7 over a wide range of M²⁺ concentrations. The results for catalysis by Cu²⁺, Zn²⁺, and Ni²⁺ are given in Table III.

Rates were then measured in monochloroacetate and acetate buffers to determine catalytic constants for the monochloroacetate and acetate ions. Buffer concentrations were kept relatively low to avoid excessive complex formation between M²⁺ and the carboxylate ions.[14] The catalytic constants for the bases acting on M(SH)²⁺ are listed in Table IV. The corresponding values for HSH⁺ and SH from Table I are included for comparison. In Table 4(a) of the microfilm edition, individual rates of iodination in the various buffers are given, together with rates calculated from eq 6 and 7 using the catalytic constants from Table IV.

(14) L. G. Sillén and A. E. Martell, *Chem. Soc. Spec. Publ.*, No. 17 (1964).

A check was made to see if any metal ion catalysis of the iodination of 4-acetylpyridine in acetate buffers could be detected. It was found that under the same conditions as used for the iodination of 2-acetylpyridine no significant rate acceleration was observed.

(v) **Kinetic Deuterium Isotope Effects.** 2-Acetyl-d_3-pyridine was prepared by allowing a solution of 2-acetylpyridine (ca. 0.2 M) in 10 ml of D₂O containing 1 M CH₃CO₂D and 0.1 M NaCH₃CO₂ to exchange for approximately 1 week at 30°. The exchange was monitored by comparing the relative intensities of the acetyl CH₃ and acetic and acetate CH₃ nmr signals with a Perkin-Elmer R 10 spectrometer. An analogous solution in H₂O was subjected to the same treatment. Reactions were carried out by adding 30 μl quantities of either the protio or deuterio solutions to spectrophotometric cells containing 2 ml of an appropriate reaction solution. Rates were measured in acetate buffers, with and without added metal ion catalysts, and in dilute acid solutions. Catalytic constants were determined as described above. The resulting catalytic constants for the protio substrates were, within experimental error, the same as those previously obtained, except for Zn(SH)²⁺ for which k^H(OAc⁻) was found to be 4.3×10^{-2} l. mol⁻¹ sec⁻¹ (cf. 3.10 l. mol⁻¹ sec⁻¹ from Table IV). The reason for this is not clear, but as the rates of iodination of both the protio and deuterio substrates were measured in the same solutions, any errors in either acetate or Zn²⁺ concentrations leading to such a discrepancy should be reflected equally in the catalytic constants for the two substrates. The observed deuterium isotope effects are listed in Table V.

Table V. Kinetic Deuterium Isotope Effects (k^H/k^D) in the Iodination of 2-Acetylpyridine (SH or SD) at 25°

| Base (B) | k_B^H/k_B^D | | | |
	HSH+	Zn(SH)2+	Ni(SH)2+	Cu(SH)2+
(H₂O)	4.1			
Acetate	7.1	7.1	7.0	7.4

Discussion

The observed independence of the iodination rates of iodine concentrations, together with the large kinetic hydrogen isotope effects, clearly shows that the rate-determining step in the iodination of the ketones is the ionization of the C–H bond adjacent to the carbonyl group.

In the absence of added metal ions, the reactivities of both 2- and 4-acetylpyridine toward base catalysis are similar to those of various acetophenones. Thus the observed catalytic constants for iodination of 2- and 4-acetylpyridine of 0.73×10^{-5} and 3.4×10^{-5} l. mol⁻¹ sec⁻¹ respectively (Table I) may be compared with values for acetophenones varying between 0.1 and 1.5 $\times 10^{-5}$ l. mol⁻¹ sec⁻¹ depending upon the substituents present.[15] The large increase in rate observed on addition of acid indicates a considerably higher reactivity of the acetylpyridinium ions toward base catalysis. Base-catalyzed iodination of the acetylpyridinium ions is however kinetically indistinguishable from general acid-catalyzed iodination of the acetylpyridines (involving rate-determining proton removal from the O-protonated ketone as in Scheme I). The results from Table II, which show similar large increases in rate on N-methylation of the acetylpyridines, suggest that the effect of formation of a positive charge on the nitrogen atom is sufficient to account for the observed rate increases in acid solution in terms of the former mechanism. This mechanism has been assumed in the presentation of results in Table I and subsequent tables.

It is noticeable that the observed rate increase on protonation of 2-acetylpyridine (200-fold) is considerably larger than that for 4-acetylpyridine (20-fold). This, together with the much higher reactivity of the 2-acetyl-N-methylpyridinium ion compared with the corresponding 4-acetyl isomer, suggests that for the 2-acetyl isomer there may be some direct electrostatic stabilization of the negative charge forming on the carbonyl oxygen during proton loss (I). The normal

I
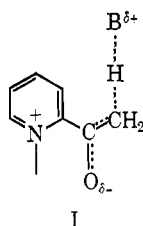
inductive effect of the positive charge however would also have a larger effect on the 2-acetyl group and may be sufficient to account for the relative changes in reactivity.

Complex formation between 2-acetylpyridine and the metal ions leads to very large rate enhancements, varying from ca. 4×10^3 for Zn²⁺ to ca. 2×10^5 for Cu²⁺. In other respects, however, the reactions behave in a

(15) D. W. Earls, private communication.

manner normally expected for enolizations. Thus the reactions are general base catalyzed as shown by the results in acetate and monochloroacetate buffers, and they show large kinetic deuterium isotope effects. The catalytic constants for the acetate-catalyzed iodinations are ca. 10 to 15 times higher than those for chloroacetate, this corresponding to a Brönsted β coefficient of ca. 0.6 for the reactions. These results can most readily be interpreted in terms of transition state II in which the major rate acceleration arises from the

II
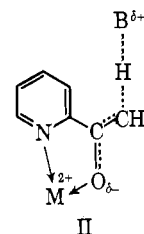
interaction between the metal ion and the carbonyl oxygen. The absence of any significant rate acceleration in the iodination of 4-acetylpyridine indicates that both the nitrogen and oxygen atoms are involved in the coordination. Cu²⁺ is known to interact more strongly than either Ni²⁺ or Zn²⁺ with oxygen ligands,[16] this being consistent with the significantly higher catalytic constants shown by 2-acetylpyridine when complexed to Cu²⁺.

In principle, iodination of the 2-acetylpyridinium ion could also proceed through a transition state analogous to II, but the fact that N-methylation of 2-acetylpyridine causes an even larger rate acceleration than does protonation suggests that such an effect does not play a large part in the reaction.

The alkaline hydrolysis of ethyl picolinate has also been shown to be very strongly catalyzed by Cu²⁺.[17] The formation constant for the Cu²⁺ complex was found to be 150 (cf. 750 for 2-acetylpyridine) and the catalytic constant for the hydroxide-catalyzed hydrolysis of the Cu²⁺ complex ca. 10⁶ larger than the corresponding value for the uncomplexed substrate. The higher stability constant found here for 2-acetylpyridine is consistent with the relative basicities of the two substrates toward N protonation[18] and the expected higher basicity of the carbonyl oxygen of the keto group compared to the ester group.

The rate accelerations observed here for 2-acetylpyridine are somewhat larger than those observed in the Mg²⁺ catalyzed deuteration of acetonyl phosphonate.[6] This may however be misleading, as it is clear from the results in the absence of metal ions that formation of a positive charge on the nitrogen atom leads to quite large rate increases, and this may account for part of the observed rate increase upon complex formation with metal ions. A similar comment would apply to earlier studies of the hydrolysis of ethyl picolinate[17] and the hydration of pyridine aldehydes.[19]

The large rate enhancements resulting from the interaction of both metal ions and suitably placed carboxylic

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acid groups[2,3] with the carbonyl oxygen during enolization reactions contrasts sharply with the results of a number of studies of intramolecular general base catalyzed enolization reactions.[20-23] The observed rates for these reactions were found to be similar to those that could be achieved by the use of only modest concentration of base in the corresponding intermolecular reaction. These results would suggest that to achieve large increases in the rates of enolization or

ionization of simple ketones, it is necessary to stabilize the developing negative charge on the carbonyl oxygen.

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Picosecond Studies of the Excited Charge-Transfer Interactions in Anthracene-(CH₂)₃-N,N-Dimethylaniline Systems

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Abstract: The excited inter- and intramolecular charge-transfer interactions in N,N-dimethyl-4-[3-(9-anthryl)-propyl]aniline systems have been studied using methods of picosecond laser photolysis. The rates of intramolecular rotation about the methylene bonds of the model compound, the rates of orientational relaxation of the excited charge-transfer complex, and the kinetics of electron transfer are determined and discussed.

It has been established for some time that the kinetics of charge-transfer (CT) interaction between an electron donor (D) and an acceptor (A) are determined by the transitional motion of the particles and the inherent characters of the interacting species. These properties may include the ionization potential of the donor, the electron affinity of the acceptor, and the solvation and Columbic interactions.[1] Little is known, however, regarding the molecular geometric requirements for electron-transfer reactions. Recently, Chandross,[2,3] Okada,[4] and their coworkers made a series of studies on the intramolecular exciplex formation to elucidate this problem. Chandross,[2] *et al.*, showed that in the naphthalene-$(CH_2)_n$-$N(CH_3)_2$ system naphthalene and alkylamine readily form an exciplex when electronically excited. The exciplex did not seem to have strong geometrical preferences. In the anthracene-$(CH_2)_n$-dimethylaniline systems, Okada, *et al.*,[4] found that while for $n = 3$ charge-transfer complex formed easily in all solvents, the excited complex could not form for $n = 1$ or 2 in solvents of low polarity, *e.g.*, *n*-hexane and cyclohexane. They, nevertheless, concluded that a parallel

sandwich geometrical structure might be favorable but not necessary for the exciplex formation.

We approach the problem from the molecular dynamic point of view. We choose N,N-dimethyl-4-[3-(9-anthryl)propyl]aniline as a model molecule (A-$(CH_2)_3$-DMA). In the previous report,[5] we established that upon excitation anthracene would accept an electron from N,N-diethylaniline (DEA) with the intermolecular reaction distance of 8 Å. Since dimethylaniline has the same electron donating properties as diethylaniline and the three-methylene bond distance is much less than 8 Å, this model molecule should form an exciplex as rapidly as the free anthracene and dimethylaniline system, if there is no orientational requirement for interaction. On the other hand, if the time courses for exciplex formations are different, then we know molecular motions other than translational modes must be involved. Theoretically, absolute fluorescence quantum yield and radiative lifetime measurements may provide similar information about these systems. Yet, as Okada, *et al.*, have shown, the lifetime and quantum yield varies from system to system and quantitative measurements and interpretation are difficult. Furthermore, time-dependent measurement can reveal the dynamic feature of the molecular process and the measurement is possible for nonfluorescent

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