Hydrolysis of Imines. Part 2.† Kinetics and Mechanism of Hydrolysis of *N*-Salicylidene-2-aminopyridine in the Presence and Absence of Copper(II) Ion. A Study of the Catalytic Effect of some Mixed-ligand Complexes of Copper(II)

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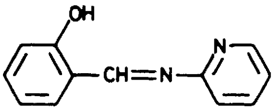
The kinetics of hydrolysis of *N*-salicylidene-2-aminopyridine (HL) have been investigated in aqueous 5% MeOH (I = 0.1 mol dm^{-3}) in the presence and absence of Cu^{II}. The Schiff-base anion is found to undergo hydroxide-independent hydrolysis with $k = (3.5 \pm 0.2) \times 10^{-2}$ s^{-1} at 35 °C, $\Delta H^{\ddagger} = 59.7 \pm 1.0$ kJ mol^{-1}, $\Delta S^{\ddagger} = -79 \pm 3$ J K^{-1} mol^{-1}; the observed solvent deuterium isotope effect [$k(H_2O)/k(D_2O)$ = 1.6 at 35 °C] on this path is consistent with intramolecular catalysis by the phenoxide ion. The possibility of the intramolecular general base-catalysed hydration of the imine linkage by pyridine ring nitrogen of the imine is investigated. The copper(II) chelate, [CuL]$^+$ undergoes acid-catalysed hydrolysis of the imine linkage with $k = (4.4 \pm 0.3) \times 10^{2}$ dm^3 mol^{-1} s^{-1} at 35 °C. The mixed-ligand complexes [Cu(bipy)L]$^+$, [Cu(phen)L]$^+$, and [Cu(im)$_2$L]$^+$ (bipy = 2,2'-bipyridyl, phen = 1,10-phenanthroline, and im = imidazole) have also been found to be effective catalysts.

In the preceding paper in this series,[1] we reported a kinetic study on the hydrolysis of *N*-salicylidene-2-aminothiazole (HL'), both in the presence and absence of Cu^{II}, Ni^{II}, and Zn^{II} ions. The results of this study revealed that the alkaline hydrolysis of the imine anion involves intramolecular general base catalysis; the basic phenoxide group of the iminate anion is presumed to facilitate the attack of H_2O at the aldimine carbon. The metal ions cited above, however, stabilize the aldimine linkage to hydrolytic splitting, the effect being maximum for Cu^{II}. The (1 : 1) Cu^{II}–Schiff-base *N,O*-chelate ([CuL']$^+$) was, however, found to undergo both spontaneous and acid-catalysed hydrolysis in the range pH 4.2—5.2. Also, a mixed-ligand chelate [Zn(im)$_2$L']$^+$ (im = imidazole, L'$^-$ = imine anion) was also found to be an effective catalyst for the hydrolysis of the imine linkage.

These observations prompted us to extend our work to *N*-salicylidene-2-aminopyridine (HL), a Schiff base possessing multiple potential bonding sites for H$^+$ and M^{n+} ions which may presumably impart some novel kinetic features to its hydrolysis reaction. Furthermore it is reasonable to expect that both the pyridine nitrogen and the phenoxide group of the imine anion may in some way facilitate the hydration of the aldimine linkage. In order to clarify these points we undertook this study.



HL

Rate measurements for the Cu^{II}-induced hydrolysis of the imine in the presence of 1,10-phenanthroline (phen), 2,2'-bipyridyl (bipy) and imidazole were made in order to (*i*) explore the possibilities of the formation of the mixed-ligand complexes, [CuL^{1}L]$^+$ (L^1 = phen, bipy, 2im), and (*ii*) examine the sensitivity of the hydrolysis rate of the co-ordinated imine to the variation of the ligand environment of Cu^{II}.

Experimental

The Schiff base HL was prepared by refluxing 2-aminopyridine (2.0 g, 0.1 mol) and salicylaldehyde (2.4 g, 0.1 mol) in dehydrated ethanol in the presence of a small amount of piperidine. The crude solid obtained after cooling the mixture to 0 °C was further recrystallised from methanol. The product was a light yellow solid, m.p. 64 °C (Found: C, 72.25; H, 4.9; N, 14.0%. Calc. for $C_{12}H_{10}N_2O$: C, 72.7; H, 5.05; N, 14.15%). $\lambda_{max.}$/nm (E/dm^3 mol^{-1} cm^{-1}): 270 (9 091), 310 (11 288), 348 (8 750) in methanol medium. ν(C=N) (imine), 1 610 cm^{-1}; pyridine and phenyl group, 1 595, 1 575 (sh), 1 555, 1 500 cm^{-1} (Nujol mull).

The i.r. spectrum was recorded on a Perkin-Elmer 337 i.r. spectrophotometer. Ultraviolet–visible spectra were measured with a Beckman DU 2 spectrophotometer. pH Measurements were made with a Systronics (India) pH meter model 324; the meter was standardised using acetate, phosphate, and carbonate buffers of pH 4.64, 6.86, and 9.97 respectively. The pH data for the kinetic runs were reduced to concentration of hydrogen ion with $f_{H^+} = 0.77$.[2] D_2O (99.4%) was received from BARC, India. Copper(II) perchlorate was prepared and estimated as described previously.[3] AnalaR or extra pure reagents were used; solutions were prepared in freshly distilled water and sodium perchlorate was used to adjust ionic strength. Acetate, imidazole, and carbonate buffers were used in the pH ranges 5.0—6.0, 6.0—8.0, and 9.0—11.0 respectively. Sodium hydroxide solution was used in the range [OH$^-$] = 0.002—0.3 mol dm^{-3}.

Kinetic Measurements.—The hydrolysis of the Schiff base was studied in methanol–water (5% v/v) medium at 29—39.6 °C and I = 0.1 mol dm^{-3} in (*i*) basic buffers and NaOH solution (pH 9—13), (*ii*) acid buffers (5.8 ⩽ pH ⩽ 7.85), (*iii*) acid buffers (pH 5.2—5.8) to which Cu^{II} was added both with and without added phen or bipy, (*iv*) imidazole–HClO$_4$ buffer (pH 6.1—7.0) in the presence of Cu^{II}. The concentration of the Schiff base was varied in the range $(1.15\text{—}3.00) \times 10^{-4}$ mol dm^{-3}. Rate measurements were made spectrophotometrically at 350 nm (pH ⩽ 8) and 420 nm (pH ⩾ 8) as described earlier.[1] Runs were made under pseudo-first-order conditions. Under the experimental conditions, hydrolysis of the Schiff base was complete. The observed rate constants were calcu-

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† Part 1 taken as ref. 1.

Table 1. Rate data for the hydrolysis of *N*-salicylidene-2-aminopyridine in 5% MeOH, $I = 0.1$ mol dm^{-3}, $\lambda = 350$ (pH $\leqslant 8$) or 420 nm (pH $\geqslant 8$)

(*a*)

pH	$10^2k_{obs.}$[a]/ s^{-1}	pH	$10^2k_{obs.}$[a,b]/ s^{-1}	pH	$10^2k_{obs.}$[a]/ s^{-1}
(*i*) 29.0 ± 0.1 °C					
5.79	4.23	6.07	2.25	6.31	1.50
6.51	1.10	6.71	0.86	6.82	0.69
7.09	0.54	7.25	0.49	7.54	0.44
(*ii*) 39.6 ± 0.1 °C					
6.07	4.92	6.31	3.12	6.51	2.23
6.71	1.73	6.82	1.44	7.09	1.20
7.25	1.01	7.54	1.09		

(*b*)

[NaOH]/ mol dm^{-3}	$10^2k_{obs.}$[a]/s^{-1} (*i*) 29.0 ± 0.1 °C	(*ii*) 39.6 ± 0.1 °C
0.005	2.28	5.37
0.01	2.15	5.14
0.02	2.19	5.40
0.0365		5.40
0.10	2.31	5.54
0.20	2.31[c]	5.47[c]

[a] Average of a least two duplicate runs. [b] Imidazole buffer. [c] I = 0.2 mol dm^{-3}.

lated from the gradients of the plots of log ($A_t - A_\infty$) against time (t/s). The kinetic plots yielded good straight lines up to four half-lives and replicate runs reproduced the pseudo-first-order rate constants to ±5%.

Equilibrium Constants.—The protonation/deprotonation equilibria of the imine (HL) may be represented by equations (1) and (2).

$$H_2L^+ \xrightleftharpoons{K_1} HL + H^+ \qquad (1)$$

$$HL \xrightleftharpoons{K_2} L^- + H^+ \qquad (2)$$

For a given concentration of the imine, the extrapolated zero-time absorbance data from the log ($A_t - A_\infty$) against time plots at 330—420 nm were virtually pH independent in the range 5.8 $\leqslant$ pH $\leqslant$ 7.0 (29 °C). Hence the protonated species H_2L^+ is not detectable in the range of pH stated above. The Schiff-base anion (L^-), however, exhibits an absorption maximum at 420 nm with $E = (6.1 \pm 0.6) \times 10^3$ dm^3 mol^{-1} cm^{-1} (extrapolated data) at [OH$^-$] = 0.002—0.3 mol dm^{-3}. With $E_{HL}{}^{420} = (1.02 \pm 0.04) \times 10^3$ dm^3 mol^{-1} cm^{-1}, the $E_{obs.}{}^{420}$ (extrapolated) data at pH 9.0—10.3 were used to compute K_2 from the relationship $K_2 = (E_{obs.} - E_{HL})[H^+]/(E_{L^-} - E_{obs.})$. The value of K_2 at 35 °C (I = 0.1 mol dm^{-3}) was obtained as $(3.1 \pm 1.0) \times 10^{-10}$ mol dm^{-3}.

The determination of pK_1 was attempted by glass-electrode pH measurement. The glass calomel combination electrode was standardised at 5 °C with standard buffers of pH 4.0 and 7.0 and then equilibrated in $NaClO_4 + HClO_4$ solution (I = 0.105 mol dm^{-3}) of known hydrogen ion concentration. The temperature was maintained at 5.5 ± 0.5 °C by using an ice-water bath. A portion (2 cm^3) of a freshly prepared, precooled (*ca.* 5 °C) methanolic solution of the Schiff base was added. The solution was magnetically stirred to effect rapid mixing. The meter reading was noted as a function of time. The pH of the reaction mixture increased with time indicating slow hydrolysis of the Schiff base. pH Data of all sets were extrapolated to 20 s, *i.e.* the assumed time of mixing. Five sets of such measurements were made with $[HL]_T = 9.52 \times 10^{-4}$ and $[HClO_4]_T = (4.76—1.43) \times 10^{-4}$ mol dm^{-3} for which the extrapolated pH ranged from 5.22 to 5.82. The value of pK_1, calculated assuming $[H_2L^+] = [HClO_4]_T - [H^+]_f$, with $[H^+]_f = a_{H^+}/f_{H^+}$, was found to be 4.8 ± 0.2 at 5.5 ± 0.5 °C (I = 0.1 mol dm^{-3}, 5% MeOH).

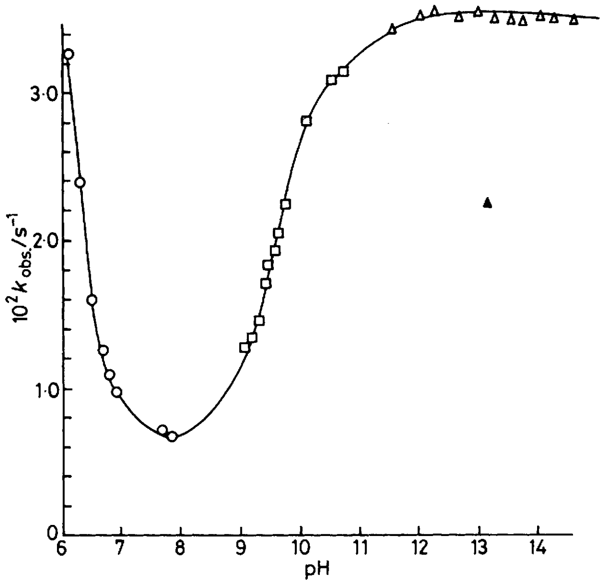


Figure 1. Plot of $10^2k_{obs.}$ *versus* pH at 35 °C for the hydrolysis of Schiff base (HL) in the absence of Cu^{II} ion: (○) imidazole buffer (6.07 $\leqslant$ pH $\leqslant$ 7.85); (□) carbonate buffer (9.13 $\leqslant$ pH $\leqslant$ 10.72); (△) [NaOH] = 0.002—0.3 mol dm^{-3}; (▲) [NaOH] = 0.0365 mol dm^{-3}, 92% D_2O

Results and Discussion

Hydrolysis of Imine in the Absence of Copper(II).—The rate of hydrolysis of the imine was studied over the pH range 5.8—13 at 29.0, 35.0, and 39.6 °C (I = 0.1 mol dm^{-3}). Buffer catalysis was not observable over the entire pH range. Rate data at 29 and 39.6 °C are collected in Table 1. The observed pH *versus* rate profile at 35 °C (Figure 1) exhibits the rate minimum in the neutral zone of pH (7—8); $k_{obs.}$ attains the plateau value at pH > 11.

The observed rate constant ($k_{obs.}$) varies linearly with [H$^+$] in the range pH 5.79—7.85 (Figure 2). This behaviour is reconciled with the fact that the imine is not appreciably protonated at pH $\geqslant$ 5.8 (pK_1 < 5). In the range pH 5.8—13 the imine may be assumed to undergo hydrolysis *via* four rate-limiting pathways:[4] (*i*) acid-catalysed path involving addition of H_2O to the imine linkage of the protonated imine, H_2L^+; (*ii*) spontaneous paths involving addition of H_2O to the imine linkage of the neutral imine, HL, and its anion L^-; and (*iii*) a path involving addition of OH$^-$ to the imine carbon of the protonated imine. Consistent with these facts the overall rate law of hydrolysis will have the form of equation (3) and $k_{obs.}$ is given by equation (4).

$$\text{Rate} = k_1[H_2L^+] + k_2[H_2L^+][OH^-] + k_3[HL] + k_4[L^-] \qquad (3)$$

$$k_{obs.} = \frac{(k_1/K_1)[H^+] + (k_2K_w/K_1 + k_3) + k_4K_2/[H^+]}{1 + [H^+]/K_1 + K_2/[H^+]} \qquad (4)$$

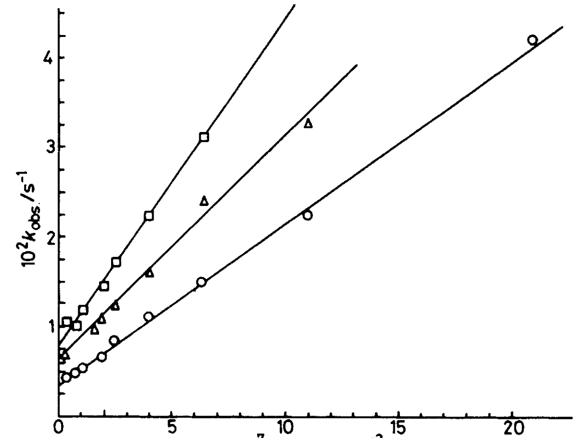
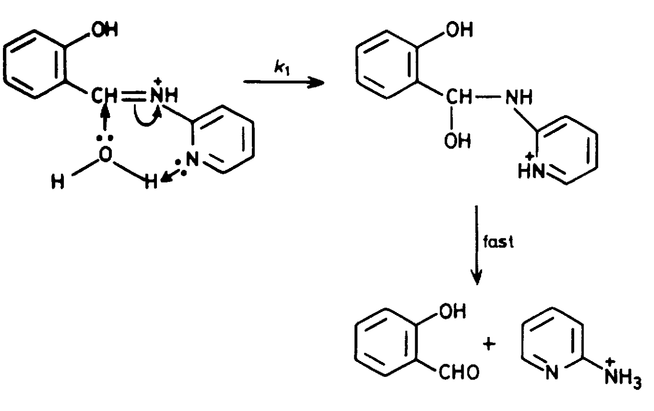


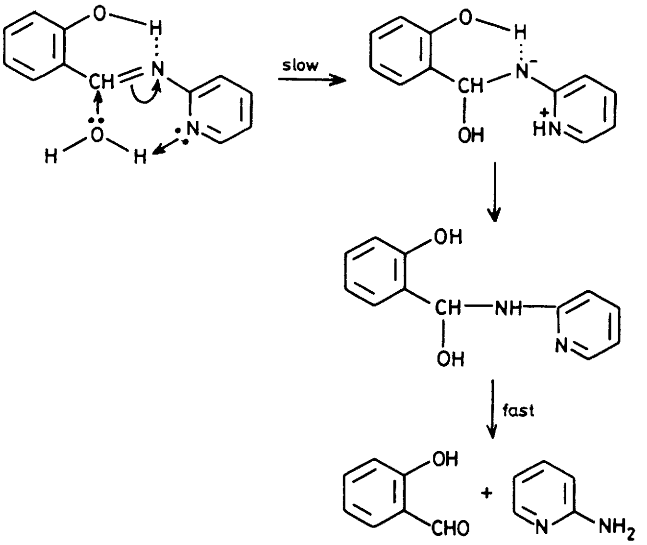
Figure 2. Plot of $10^2k_{obs.}$ *versus* $10^7[H^+]$ at (○) −29 °C, (△) −35 °C, and (□) −39.6 °C

Hydrolysis of the Schiff base in the Mild Acidic and Neutral Range of pH.—In the range pH 5.8—7.8, equation (4) will reduce to equation (5), as the imine will exist predominantly

$$k_{obs.} = k_1/K_1[H^+] + k_2K_w/K_1 + k_3 \qquad (5)$$

in the neutral form ($pK_1 < 5$, $pK_2 = 9.5$). Accordingly, $k_{obs.}$ *versus* $[H^+]$ plots were linear (Figure 2) and the values of k_1/K_1 and $k_2K_w/K_1 + k_3$ were obtained from the least-squares gradients and intercepts of such plots. The value of K_1 is 1.6×10^{-5} mol dm^{-3} at 5.5 °C. Neglecting the temperature effect on K_1 we obtain a value of 0.4 s^{-1} at 35 °C for the lower limit of the rate constant k_1. The value of k_1 for *N*-salicylidene-2-aminothiazole has been reported to be 0.09 s^{-1} at 35 °C. This reflects at least four times higher reactivity of the former as compared to the latter. The apparently pH-independent rate constant k' ($= k_3 + k_2K_w/K_1$) is also *ca.* 20 times larger than the same for *N*-salicylidene-2-aminothiazole [$k' = (2.9 \pm 0.2) \times 10^{-4}$ s^{-1} at 35 °C, $I = 0.1$ mol dm^{-3}][1] under comparable conditions. The activation parameters calculated from the temperature dependence of k' for both the imines are, however, comparable. Intramolecular general base catalysis due to the pyridyl nitrogen is a likely possibility in the hydrolysis of the protonated imine if the site of protonation is the imine nitrogen (see below). Both intramolecular acid catalysis of the phenolic group and base catalysis of the pyridyl nitrogen may be involved in the neutral hydrolysis of the imine (see above).





It is interesting to note that hydrolysis of *N*-salicylidene-2-aminopyridine is not subject to buffer catalysis unlike its 2-aminothiazole analogue. This lends further support to the proposed intramolecular general base catalysis due to the pyridyl nitrogen which predominates in the case of the former imine. It is also pertinent to note that strong intramolecular catalysis of the pyridine nitrogen has been observed in the hydrolysis of the imine derived from benzophenone and 2-aminomethylpyridine; catalysis by the added buffers is also not observed in this system.[5]

Hydrolysis in the Basic Medium.—The rate-limiting effect observed at pH > 11 is worth mentioning. This is in contrast with the behaviour exhibited by *N*-salicylidene-2-aminothiazole [1] and *N*-2-pyridylmethyleneaniline [6] for which $k_{obs.}$ was found to increase with $[OH^-]$ in the alkaline range of pH. The limiting pseudo-first-order rate constant at pH > 11 is also independent of ionic strength ($0.05 \leqslant I \leqslant 0.3$ mol dm^{-3}) (see Figure 1). The Schiff base will exist exclusively in the phenoxide form at pH > 11 ($pK_2 = 9.5$). Hence the limiting rate constant (k_4) can justifiably be attributed to the reaction of the imine anion (L^-) with water, equation (6). The value of k_4

$$L^- + H_2O \xrightarrow{k_4} C_6H_4(CHO)O^- + NC_5H_4NH_2\text{-}2 \qquad (6)$$

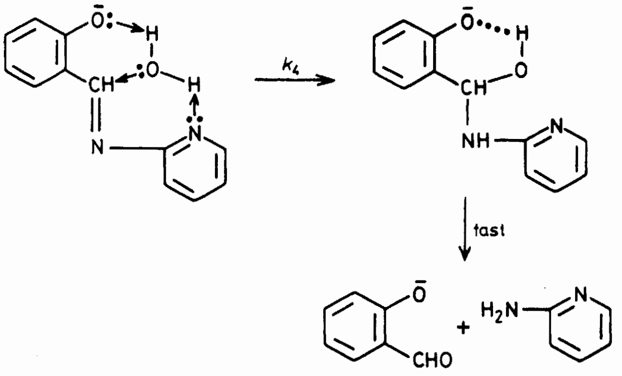
for this imine anion (3.5×10^{-2} s^{-1} at 35 °C) is *ca.* 50 times higher than for its 2-aminothiazole analogue (6.5×10^{-4} s^{-1} at 35 °C) under comparable conditions. This reactivity difference is attributed to the lowering of the activation enthalpy by *ca.* 12 kJ mol^{-1} when the amine residue is changed from the weakly basic thiazole to relatively more basic pyridine moiety. For both the Schiff bases, $\Delta S^\ddagger$ (k_4 path) is highly negative (*ca.* −70 J K^{-1} mol^{-1}) and corresponds closely to the loss of partial molar aqueous entropy of water [S^-(aq) (H_2O) = 68 J K^{-1} mol^{-1}].[7] The solvent isotope effect $k_4(H_2O)/k_4(D_2O)$ is 1.60 ± 0.03 (35 °C, 92% D_2O at $[OH^-] = 0.0365$ mol dm^{-3}) as against 2.2 ± 0.2 (90% D_2O, 39.8 °C) and 1.5 (99% D_2O, 25 °C) for the corresponding reactions of *N*-salicylidene-2-aminothiazole [1] and *N*-salicylidene(*p*-*N'*-trimethylammonio)aniline cation [8] respectively. A solvent isotope effect of this magnitude also has been observed in the hydrolysis of the phenoxide forms of *o*-hydroxyphenyl benzoate [$k(H_2O)/k(D_2O) = 1.8$], phenylsalicylate [$k(H_2O)/k(D_2O) = 1.8$] and the related substrates which have been suggested to undergo spontaneous hydrolysis *via* intramolecular general base catalysis of the ionized phenolic group.[9] Thus the results

Table 2. Rate data for hydrolysis of *N*-salicylidene-2-aminopyridine in the presence of Cu^{II} in 5% MeOH, I = 0.1 mol dm^{-3} at 35.0 ± 0.1 °C, λ = 350nm

pH	$[Cu^{2+}]_T$/ mol·dm^{-3}	$10^2k_{obs.}$/ s^{-1}	$10^2k_{app.}$/ s^{-1}	$10^{-2}k_{app.}/[H^+]$ * dm^3 mol^{-1} s^{-1}
5.19 ± 0.03	0.001	2.44	0.38 ± 0.03	4.5 ± 0.5
	0.002	1.59		
	0.005	0.62		
	0.006	0.53		
	0.009	0.39		
	0.010	0.34		
	0.012	0.41		
	0.014	0.37		
5.61 ± 0.04	0.001	0.90	0.19 ± 0.01	6.0 ± 1.3
	0.002	0.45		
	0.003	0.28		
	0.004	0.24		
	0.006	0.20		
	0.008	0.19		
	0.010	0.18		
5.76 ± 0.05	0.008	0.093 ± 0.001	0.093 ± 0.001	4.1 ± 0.4

* k_4 = (4.4 ± 0.3) × 10^2 dm^3 mol^{-1} s^{-1} (weighted average of the values of $k_{app.}/[H^+]$).

at hand support the intramolecular participation of the phenoxide group in the hydration of the aldimine linkage. The fact that the imine anion L^- did not exhibit a hydroxide-dependent hydrolysis path, unlike *N*-salicylidene-2-aminothiazole, although both are structurally similar, leads us to believe that the pyridine ring nitrogen might be involved in this intramolecular general base catalysis path (see below).



This would also explain the observed 50-fold difference in reactivity of the two closely related imine anions stated above. Evidence for intramolecular general base catalysis due to the pyridine nitrogen also exists in the aminolysis of 2-pyridyl acetate by n-butylamine in chlorobenzene.[10]

Effect of Copper(II) *on the Hydrolysis Rate*.—The effect of copper(II) on the rate of hydrolysis of the imine was examined at 35 °C under varying conditions of pH and $[Cu^{2+}]_T$ ($10 \leqslant [Cu^{2+}]_T \leqslant 100$). Rate data in Table 2 and Figure 3 indicate the retarding influence of Cu^{II}. The kinetic stability of the imine in the presence of Cu^{II} may be qualitatively assessed as follows. Assuming equation (5), $k_{obs.}$ is calculated to be 0.22 s^{-1} at 35 °C, pH = 5.19, and $[Cu^{2+}]_T$ = 0. Under similar conditions of pH and temperature, $k_{obs.}$, however, drastically falls to 0.016 s^{-1} and 0.0062 s^{-1} at $[Cu^{2+}]_T$ = 0.002 and 0.005 mol dm^{-3} respectively. The observed $k_{obs.}$ *versus* $[Cu^{2+}]_T$ profile (Figure 3) at pH 5.19 and 5.61 suggests that the Cu^{II}–Schiff-base chelate, $[CuL]^+$, which is formed by the equilibrium (7) is hydrolysed in an inverse hydrogen ion dependent path. The observed pseudo-first-order rate constant is given by equation (8) where $k_{obs.}' = k_{obs.}$ at $[Cu^{2+}]_T$ = 0 and $k_{app.}$ is the pH-dependent hydrolysis rate constant of the $[CuL]^+$ species. $k_{app.}$ at pH 5.61 and 5.19 were taken to be the limiting value of $k_{obs.}$ at $[Cu^{2+}]_T \geqslant 0.008$ (see Figure 3). $k_{obs.}'$ was calculated from equation (5). The value of K_{CuL} calculated from equation (8) using the rate data at $[Cu^{2+}]_T \leqslant 0.003$ mol dm^{-3} is (7 ± 2) × 10^{-2}. The stability constant of the $[CuL]^+$ species ($K_s = K_{CuL}/K_2$) is then calculated to be 2.2 × 10^8 dm^3 mol^{-1} at 35 °C (I = 0.1 mol dm^{-3}) taking the acid dissociation constant (K_2) of the imine HL to be 3.1 × 10^{-10} mol dm^{-3} (pK_2 = 9.5). This value is *ca.* 36 times larger than the value of the stability constant (K_S = 6 × 10^6 dm^3 mol^{-1}, 39.8 °C, I = 0.1 mol dm^{-3}) of the analogous Cu^{II} complex of *N*-salicylidene-2-aminothiazole; the stability difference for $[CuL]^+$ species may be partly due to the relatively lower pK_2 of the latter ligand (pK_2 = 8.6, 39.8 °C, I = 0.1 mol dm^{-3}).[1] Although multiple potential bonding sites exist for *N*-salicylidene-2-aminopyridine, the preferred sites of co-ordination are the phenolic oxygen and the imine nitrogen. The basic pyridyl nitrogen, however, might be involved in the formation of a six-membered proton solvation bridge (A).

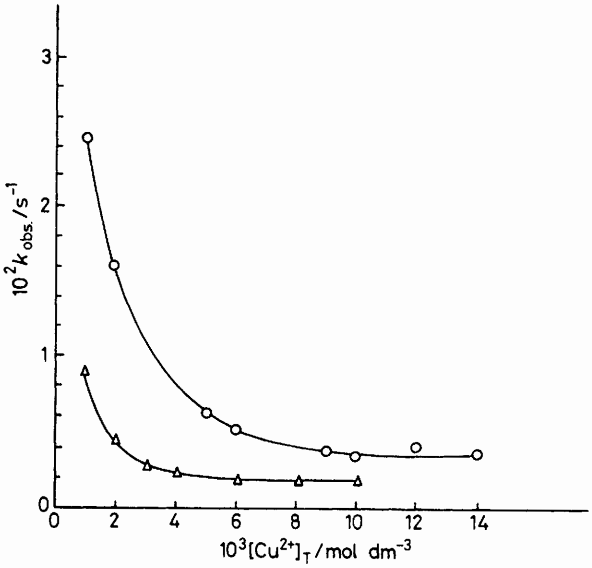
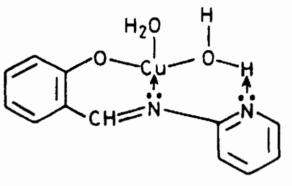


Figure 3. Plot of $10^2k_{obs.}$ *versus* $10^2[Cu^{2+}]_T$ at 35 °C and (○) pH 5.19; (△) pH 5.61

$$Cu^{2+} + HL \overset{K_{CuL}}{\rightleftharpoons} [CuL]^+ + H^+$$

$$K_{CuL} = [CuL^+][H^+]/[Cu^{2+}][HL] \qquad (7)$$

$$k_{obs.} = \frac{k_{obs.}' + k_{app.}K_{CuL}[Cu^{2+}]/[H^+]}{1 + K_{CuL}[Cu^{2+}]/[H^+]} \qquad (8)$$



(A)

Table 3. Rate data for hydrolysis of *N*-salicylidene-2-aminopyridine in the presence of Cu^{II}, phen, and bipy in 5% MeOH, $I = 0.1$ mol dm^{-3} at 35.0 ± 0.1 °C, pH = 5.46 ± 0.01, $[Cu^{2+}]_T = 2.00 \times 10^{-3}$ mol dm^{-3}

$10^3[L^1]_T{}^a$/mol dm^{-3}	$10^2k_{obs.}{}^b/s^{-1}$ phen	$10^2k_{obs.}{}^b/s^{-1}$ bipy
0.10	0.45	0.61
0.20	0.55	0.72
0.30	0.60	0.84
0.50	0.75	1.09
0.60	0.80	1.20
0.80	0.90	1.51
1.00	1.10	1.64
1.20	1.20	1.98
1.40	—	2.23
1.60	—	2.60

[a] L^1 = phen or bipy. [b] λ = 350 nm.

The value of $K_{CuL} \simeq 0.07$ indicates that the imine is virtually completely bound to Cu^{II} at pH ≃ 5.76 and $[Cu^{2+}] \geqslant 0.008$ mol dm^{-3} $\{K_{CuL}[Cu^{2+}]/[H^+] \simeq 248$, see equation (8)$\}$. Therefore, $k_{obs.}$ under these conditions can be taken as $k_{app.}$ for $[CuL]^+$. Using this assumption it is noted that the value of $k_{app.}$ given in Table 2 satisfies equation (9) with k_H =

$$k_{app.} = k_H[H^+] \qquad (9)$$

$(4.4 \pm 0.3) \times 10^2$ dm^3 mol^{-1} s^{-1}; k_H represents the acid-catalysed hydrolysis rate constant of the $[CuL]^+$ species.* For the *N*-salicylidene-2-aminothiazole copper(II) complex, we have reported [1] $k_U = (1.9 \pm 0.3) \times 10^{-3}$ s^{-1} (spontaneous path) and $k_H = (0.12 \pm 0.02) \times 10^3$ dm^3 mol^{-1} s^{-1} (at 39.8 °C, $I = 0.1$ mol dm^{-3}). In contrast, relatively stronger proton catalysis (k_H) and also insignificant spontaneous hydrolysis is observed for the *N*-salicylidene-2-aminopyridine copper(II) complex. The bicyclic structure (A) of $[CuL]^+$(aq) presumably imparts kinetic stability to the imine linkage and renders pyridine nitrogen unavailable for intramolecular general base catalysis. Such a bicyclic proton-bridged structure may not be possible for the corresponding Cu^{II} chelate of *N*-salicylidene-2-aminothiazole due to significantly weaker hydrogen-bonding interaction between the thiazole ring nitrogen and the Cu^{II} bound aqua-ligands. In this context it is also worth mentioning that imines capable of forming bicyclic chelate rings with metal ions (such as *N*-salicylideneglycine) have been reported to be strongly stabilized to hydrolysis under mild acidic conditions.[11]

Effect of 2,2′-*Bipyridyl*, 1,10-*Phenanthroline*, *and Imidazole on the Copper*(II)-*induced Hydrolysis of the Imine*.—Rate data for the system (phen or bipy)–Cu^{II}–imine at constant pH (5.46 ± 0.01) and $[Cu^{2+}]_T$ (0.002 mol dm^{-3}), and varying concentration of the auxiliary ligand are collected in Table 3. Both phen and bipy ligands will be fully bound to Cu^{II} as 1 : 1 complex species [log K_1 = 7.4 (phen) and 6.3 (bipy) at 25 °C, $I = 0.1$ mol dm^{-3}] under the present experimental conditions.[12] If it is assumed that the observed rate enhancement in the presence of these ligands is due to the depletion of Cu^{II} as unreactive $[Cu(bipy)]^{2+}$ and $[Cu(phen)]^{2+}$ species, then according to equation (8), the plot of $k_{obs.}\{1 + K_{CuL}([Cu^{2+}]_T - [L^1]_T)/[H^+]\}$ against $\{[Cu^{2+}]_T - [L^1]\}/[H^+]$ should yield a straight line with intercept = $k_{obs.}'$ and slope = $k_{app.}K_{CuL}$, where $[L^1]$ = $[phen]_T$ or $[bipy]_T$ and $k_{obs.}' = k_{obs.}$ at $[Cu^{2+}]_T = [L^1]_T = 0$. This analysis fails totally. The plots of $k_{obs.}$ against $[L^1]_T$, however, yielded excellent straight lines with positive slopes and extrapolate to a common intercept which agrees with the value of $k_{obs.}$ (see Figure 4) under identical conditions of pH and $[Cu^{2+}]_T$ but $[L^1]_T = 0$. These facts are reconciled with the formation of the catalytically active mixed-ligand complex $[CuL^1L]^+$, equation (10). Assuming $[L^1]_T$ =

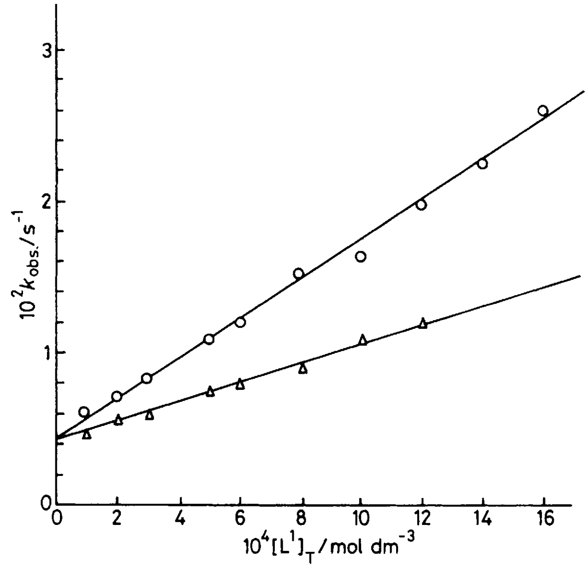


Figure 4. Plot of $10^2k_{obs.}$ *versus* $10^4[L^1]_T$ at 35 °C, pH 5.46 ± 0.01: (○) bipy, (△) phen

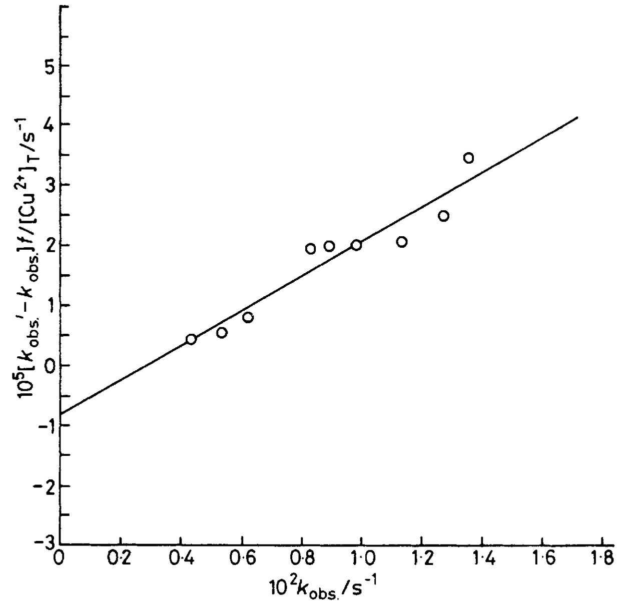


Figure 5. Plot of $10^5[k_{obs.}' - k_{obs.}]f/[Cu^{2+}]_T$ *versus* $10^2k_{obs.}$ for the hydrolysis of the species $[Cu(im)_2L]^+$ at 35 °C

$$[CuL^1]^{2+} + HL \overset{K_{[CuL^1L]}}{\rightleftharpoons} [CuL^1L]^+ + H^+ \qquad (10)$$

$$K_{[CuL^1L]} = [CuL^1L^+][H^+]/[(CuL^1)^{2+}][HL]$$

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* The H^+ catalysis of the hydrolysis of $[CuL]^+$ may involve the formation of $[CuHL]^{2+}$ *via* protonation of the co-ordinated phenoxide group or the pyridine nitrogen which could allow intramolecular proton transfer to the imine nitrogen in the transition state of H_2O addition.

Table 4. Rate data for hydrolysis of *N*-salicylidene-2-aminopyridine in imidazole buffer and in the presence of Cu^{II} in 5% MeOH, I = 0.1 mol dm^{-3} at 35.0 ± 0.1 °C

$[Cu^{2+}]_T$/ mol dm^{-3}	$[im]_T$/ mol dm^{-3}	$[HClO_4]_T$/ mol dm^{-3}	pH	$10^2k_{obs.}$/ s^{-1} *	$10^2k_{obs.}'$/ s^{-1}
0.001	0.10	0.05	6.38	1.36	1.98
0.002	0.10	0.05	6.31	1.28	2.22
0.003	0.10	0.05	6.28	1.14	2.33
0.004	0.10	0.05	6.23	0.98	2.54
0.005	0.10	0.05	6.16	0.89	2.87
0.006	0.10	0.05	6.11	0.83	3.15
0.001	0.10	0.02	7.03	0.62	0.93
0.002	0.10	0.02	6.99	0.54	0.96
0.003	0.10	0.02	7.00	0.43	0.95

$(k_{app.}.K)_{Cu(im)_2L} = (0.8 \pm 0.3) \times 10^{-5}\ s^{-1}$

$K_{Cu(im)_2L} = (0.29 \pm 0.03) \times 10^{-2}$

$k_{app.} = (2.8 \pm 1.0) \times 10^{-3}\ s^{-1}$

* λ = 350 nm.

Table 5. Summary of the calculated rate and activation parameters for hydrolysis of *N*-salicylidene-2-aminopyridine in 5% MeOH, I = 0.1 mol dm^{-3}

Reaction	Value of rate constant (29.0 °C)	(35.0 °C)	(39.6 °C)	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/ J K^{-1} mol^{-1}
$HL + H^+ + H_2O$; $10^{-4}k$/dm^3 mol^{-1} s^{-1} [a]	1.80 ± 0.03	2.5 ± 0.1	3.7 ± 0.1	50.5 ± 1.0	+4 ± 3
$H_2L^+ + OH^-$ $HL + H_2O$ } 10^2k/s^{-1} [b]	0.35 ± 0.02	0.63 ± 0.05	0.80 ± 0.04	60.8 ± 2.1	−91 ± 6
$L^- + H_2O$; 10^2k/s^{-1}	2.26 ± 0.07	3.50 ± 0.18	5.38 ± 0.16	59.7 ± 1.0	−79 ± 3
$[CuL]^+ + H^+ + H_2O$; $10^{-3}k$/dm^3 mol^{-1} s^{-1}		0.44 ± 0.03			
$[Cu(im)_2L]^+ + H_2O$; 10^3k/s^{-1}		2.8 ± 1.0			
$[Cu(bipy)L]^+ + H_2O$; 10^3k/s^{-1}		*ca.* 33 [c]			
$[Cu(phen)L]^+ + H_2O$; 10^3k/s^{-1}		*ca.* 16 [d]			

[a] k_1/K_1. [b] $k_2K_w/K_1 + k_3$; see equation (5). [c] Estimated value at pH 5.46. [d] Estimated value at pH 5.46 assuming $(k_{app.})_{Cu(phen)L}/(k_{app.})_{Cu(bipy)L} = (k_{app.}K)_{Cu(phen)L}/(k_{app.}K)_{Cu(bipy)L} = 0.5$.

$$\begin{tikzcd}
{[\mathrm{Cu(im)_4}]^{2+}} \arrow[r, shift left] & {[\mathrm{Cu(im)_3}]^{2+}} \arrow[l, shift left, "K_4"] \arrow[d, shift left] & {+\ \mathrm{im}} \arrow[d, shift left] \\
{\mathrm{H^+} + [\mathrm{Cu(im)_2L}]^+} \arrow[r, shift left, "K_{\mathrm{Cu(im)_2L}}"] & {\mathrm{HL} + [\mathrm{Cu(im)_2}]^{2+} + \mathrm{im}} \arrow[l, shift left] \arrow[u, shift left, "K_3"'] & {\mathrm{Him^+}} \arrow[u, shift left, "K_d"', "\mathrm{H^+}"]
\end{tikzcd}$$

Scheme.

$[(CuL^1)^{2+}]$, $[Cu^{2+}]_T = [Cu^{2+}] + [(CuL^1)^{2+}]$ and $[CuL^1L]^+$ as the reactive species, equation (8) can be easily transformed to equation (11) where $k_{obs.}' = k_{obs.}$ at $[Cu]_T = [L^1]_T = 0$,

$$k_{obs.} = \frac{k_{obs.}' + k[Cu^{2+}]_T/[H^+] + k'[L^1]_T/[H^+]}{1 + K_{CuL}[Cu^{2+}]_T/[H^+] + \Delta K[L^1]_T/[H^+]} \quad (11)$$

$k = k_{app.}K_{CuL}$, $k' = k_{app.}'K_{CuL^1L} - k_{app.}K_{CuL}$, $\Delta K = K_{CuL^1L} - K_{CuL}$, and $k_{app.}'$ is the apparent hydrolysis rate constant of the mixed-ligand complex $[CuL^1L]^+$ at the experimental pH (5.46). $\Delta K[L^1]_T/[H^+] \ll (1 + K_{CuL}[Cu^{2+}]_T/[H^+])$ is satisfied for $[L^1]_T \leqslant 0.016$ mol dm^{-3} (see Figure 4).

The relationship proposed by Sigel[13] for the difference in stability, $\Delta \log K$, between the binary and ternary complexes of a given metal ion may be recast in the present case as equation (12). For the mixed-ligand complexes $[Cu(bipy)L^2]^+$ (L^2 =

$$\Delta \log K = \log K_{CuL^1L} - \log K_{CuL} \quad (12)$$

N,*O*-chelating agent), $\Delta \log K$ [equal to $\log K^{Cu(bipy)}_{Cu(bipy)L^2} - \log K^{Cu}_{CuL^2}$] has been found to be negative and close to zero.[13] A value of $\Delta \log K = -0.1$ appears reasonable in the present context to satisfy the observed straight-line relationship between $k_{obs.}$ and $[L^1]_T$. The value of $K_{Cu(bipy)L}$ is then calculated from equation (12) to be 62 × 10^{-3}. The slope of plots of $k_{obs.}$ against $[L^1]_T$ yielded $k_{app.}'K_{CuL^1L} = (1.08 \pm 0.04) \times 10^{-3}$ and $(2.1 \pm 0.1) \times 10^{-3}$ s^{-1} for L^1 = phen and bipy respectively; the value of $k_{app.}K_{CuL}$ was taken to be 1.3 × 10^{-4} s^{-1}. Using the calculated value of $K_{Cu(bipy)L}$ as stated above the apparent hydrolysis rate constant of $[Cu(bipy)L]^+$ turned out to be 3.3 × 10^{-2} s^{-1} which is *ca.* 10 times greater than the value for the species $[CuL]^+$ at the same pH. The available data, however, suggest that phen has a weaker rate-accelerating effect than does bipy $\{k_{app.}'K_{Cu(phen)L}/k_{app.}'K_{Cu(bipy)L} \simeq 0.5\}$ on the hydrolysis of the co-ordinated imine.

Rate data for the Cu^{II}-induced hydrolysis of the imine in imidazole buffer (pH 6.11—7.03) are collected in Table 4. A comparison of $k_{obs.}$ data in the presence and absence of Cu^{II} clearly reveals the rate-decelerating effect of this metal ion which we attribute to the formation of the less reactive mixed-ligand complex of Cu^{II}, imidazole, and the imine anion. Under the experimental conditions $\{[im]_T > (4[Cu^{2+}]_T + [HClO_4])\}$, the complexation equilibria of Cu^{II} may be depicted as shown in the Scheme. Based on this, $k_{obs.}$ is given by equation (13) where $k_{obs.} = k_{obs.}'$ at $[Cu]_T = 0$ and $k_{app.}$ is the apparent

$$k_{obs.} = \frac{k_{obs.}' + k_{app.}K_{Cu(im)_2L}[Cu(im)_2{}^{2+}]/[H^+]}{1 + K_{Cu(im)_2L}[Cu(im)_2{}^{2+}]/[H^+]} \quad (13)$$

hydrolysis rate constant of the species $[Cu(im)_2L]^+$. Replacing $[Cu(im)_2{}^{2+}]/[H^+]$ by $[Cu^{2+}]_T/f$ ($f = [H^+] + K_3K_d[Him^+] + K_4K_3K_d{}^2[Him^+]^2/[H^+]$),[1] equation (13) can be rearranged to give equation (14). The value of f was calculated using K_3 =

$$(k_{obs.}' - k_{obs.})f/[Cu^{2+}]_T = K_{Cu(im)_2L}k_{obs.} - k_{app.}K_{Cu(im)_2L} \quad (14)$$

569, $K_4 = 87$ dm^3 mol^{-1} [14] and $K_d = 1.0 \times 10^{-7}$ mol dm^{-3} and taking $[\mathrm{Him}^+] = [\mathrm{HClO}_4]_T$. The rate data over the entire pH range fitted reasonably well to equation (14). The least-squares slopes and intercept of the straight line plot of $(k_{obs.}' - k_{obs.})f/[\mathrm{Cu}^{2+}]_T$ against $k_{obs.}$ (Figure 5) yielded $K_{\mathrm{Cu(im)_2L}} = (2.9 \pm 0.3) \times 10^{-3}$ and $k_{app.}.K_{\mathrm{Cu(im)_2L}} = (0.8 \pm 0.3) \times 10^{-5}$ s^{-1} from which we obtained $k_{app.} = (2.8 \pm 1.0) \times 10^{-3}$ s^{-1}. The value of $K_{\mathrm{Cu(im)_2L}}$ suggests that the thermodynamic stability of the species $[\mathrm{Cu(im)_2L}]^+$ is *ca.* 20 times less than that of $[\mathrm{CuL}]^+$. This is the usual trend observed for the mixed-ligand complexes of Cu$^{\mathrm{II}}$ for *N,O*-chelation.[13] The value of $k_{app.}$ for $[\mathrm{Cu(im)_2L}]^+$ appears to be pH independent in the neutral zone of pH and is less (by a factor of two) than the overall rate constant of hydrolysis of the imine ($k = 6.3 \times 10^{-3}$ s^{-1} at 35 °C) under comparable conditions. It is, however, interesting to note that the value of $k_{app.}$ for $[\mathrm{Cu(im)_2L}]^+$ is *ca.* 10 times less than the rate constant of hydrolysis of the imine anion in the alkaline range of pH. This is in keeping with the fact that the intramolecular general base catalysis path due to the involvement of the phenoxide group is rendered inaccessible when the imine anion is co-ordinated to $[\mathrm{Cu(im)_2}]^+$.

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