Hydrolysis of Imines: Kinetics and Mechanism of Spontaneous Acid-, Base-, and Metal Ion-induced Hydrolysis of *N*-Salicylidene-2-aminothiazole

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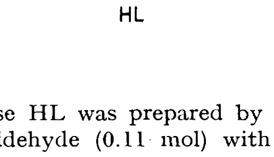
The kinetics of hydrolysis of *N*-salicylidene-2-aminothiazole (HL) have been investigated in aqueous 5% MeOH (I = 0.1 mol dm^{-3}) in the presence and absence of Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II}. The solvent deuterium isotope effect on the rate of spontaneous and hydroxide-catalysed hydrolysis of the Schiff-base anion (L$^-$) is consistent with intramolecular catalysis by the phenoxide anion. Of all the metal ions, only copper(II) retards the rate of hydrolysis of the imine significantly. This is due to the formation of less reactive [CuL]$^+$ species. Such a species, however, undergoes both spontaneous and acid-catalysed hydrolysis of the imine linkage in the pH range 4.22—5.2. The mixed-ligand complex [Zn(im)$_2$L]$^+$ (im = imidazole) is also found to be an effective catalyst. The imine linkage in [Zn(im)$_2$L]$^+$ is hydrolysed about three times faster than that in [CuL]$^+$ and L$^-$ in the pH-independent path.

THE study of the kinetics of formation and hydrolysis of imines has received considerable attention owing to its relevance to the transformation of $>$C=O to $>$C=N and *vice versa* in biochemical processes. Quantitative assessment of the catalytic effect of various metal ions on the condensation of carbonyl compounds with primary amines has been attempted by several workers.[1] It has been shown that imines capable of forming monocyclic chelates are hydrolysed in the presence of metal ions under mild acidic conditions.[2-4] Previous work from our laboratory [3] involved a detailed kinetic study of the hydrolysis of *N*-salicylideneaniline in the presence of Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II}. The (1 : 1) Schiff-base–metal chelates (ML$^+$) were found to undergo acid-catalysed hydrolysis at rates decreasing with the thermodynamic stabilities of the chelates. The acid-independent hydrolysis rate constant of the chelates was, however, too small to be determined. This work presents the results of a thorough kinetic investigation of the spontaneous acid-, base-, and metal ion-induced hydrolysis of *N*-salicylidene-2-aminothiazole (HL).



HL

EXPERIMENTAL

The Schiff base HL was prepared by refluxing freshly distilled salicylaldehyde (0.11 mol) with 2-aminothiazole (0.1 mol) (Koch Light) in ethanol in the presence of a small amount of piperidine. The crude solid obtained by cooling the mixture to 0 °C after reflux was further purified by recrystallisation from ethyl alcohol–acetone (50 : 50, v/v). The light yellow product had m.p. 77 °C (Found: C, 58.3; H, 4.0; S, 15.4; N, 13.7. Calc. for $C_{10}H_8N_2OS$: C, 58.8; H, 3.9; S, 15.7; N, 13.7%). I.r. spectrum (Nujol mull): 3 100 ν(C–OH) (hydrogen-bonded); 1 625 ν(C=N) (imine); 1 605, 1 530, 1 460, 1 430 cm^{-1} (thiazole and phenyl ring).

pH Measurement was made with a digital pH meter model 5651 (ECIL, India, Ltd.). The calomel electrode used saturated sodium chloride solution and the meter was standardised against phthalate, phosphate, and carbonate buffers of pH 4.0, 6.86, and 9.2 respectively. The pH data for the kinetic runs were reduced to concentration of hydrogen ion with $f_{H^+} = 0.74$.[5] D_2O (99.4%) was received from BARC, India. Metal perchlorate solutions were prepared and estimated as described earlier.[6] Sodium perchlorate was used to adjust the ionic strength of the reaction mixture. Acetate, phosphate, imidazole, morpholine (morph), and carbonate buffers were used in the pH ranges 3.9—6.0, 6.0—7.5, 8—9, and 9—10 respectively. Sodium hydroxide solution was used in the range [OH$^-$] = 0.002—0.1 mol dm^{-3}.

Kinetic Measurements.—Hydrolysis of the Schiff base HL was studied in methanol–water (5% v/v) medium at 30—40 °C and I = 0.1 mol dm^{-3}, using [HL] = (6—8) × 10^{-5} mol dm^{-3}. Rate measurements were made in the range pH 3.91—13.0. In a typical run, 3.0 cm^3 of the pre-thermostatted aqueous solution of the buffer (I = 0.105 mol dm^{-3}) was transferred to both the 1-cm quartz cells housed in the thermostatted cell compartment of a Beckman DU 2 spectrophotometer. The reaction was initiated by adding 0.15 cm^3 of a stock solution of HL in methanol to one of the cells. Mixing could be effected by quickly inverting the Teflon-stoppered cell several times. The reaction was monitored by following the decrease of absorbance with time at 370 nm (pH $\leqslant$ 9) or 420 nm (pH 9—13). Plots of log($A_t - A_\infty$) against time were excellent straight lines for at least five half-lives and the pseudo-first-order rate constants were calculated from the slope of such plots. An exactly similar procedure was adopted in the studies of hydrolysis of HL in the presence of the M^{2+} ions (M^{2+} = Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+}); the wavelength of measurement was 370 nm.

Determination of Dissociation Constants.—The equilibria involving HL in the absence of M^{2+} ions may be represented by equations (1) and (2) where H$_2$L$^+$, HL, and L$^-$ stand for

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

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

its protonated, neutral, and anionic (due to deprotonation of the phenolic group) forms respectively (*i.e.*, $H_2L^+ = C_{10}H_9N_2SO^+$, $HL = C_{10}H_8N_2SO$, and $L^- = C_{10}H_7N_2SO^-$). The extrapolated zero-time absorbance data, from the plot of log ($A_t - A_\infty$) *versus* time, were found to be independent of pH ($5 \leqslant \text{pH} \leqslant 7.0$) and wavelength (330—420 nm). In alkaline media ($[\text{OH}^-] = 0.002$—0.1 mol dm^{-3}) the Schiff base exhibits an absorption maximum at 420 nm; the absorption coefficient calculated from the absorbance data extrapolated to zero time was also found to be independent of $[\text{OH}^-]$. Evidently, the Schiff base exists essentially in the anionic form (L^-) at $[\text{OH}^-] \geqslant 0.002$ mol dm^{-3}. With $E_{\text{HL}}^{420} = (1.04 \pm 0.22) \times 10^3$ and $E_{\text{L}^-}^{420} = (1.33 \pm 0.06) \times 10^4$ dm^3 mol^{-1} cm^{-1}, $E_{\text{obs.}}^{420}$ (extrapolated) data at pH 9.15—9.99 were used to calculate K_2 from the relationship $K_2 = (E_{\text{obs.}} - E_{\text{HL}})[\text{H}^+]/(E_{\text{L}^-} - E_{\text{obs.}})$. The value of K_2 at 39.8 °C ($I = 0.1$ mol dm^{-3}) is $(2.7 \pm 0.7) \times 10^{-9}$ mol dm^{-3}.

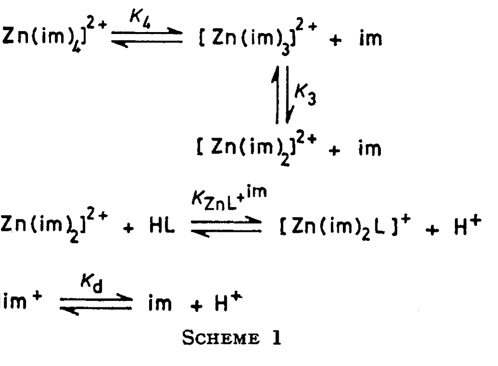
Determination of the Equilibrium Constant K_{ML^+}.—The extrapolated zero-time absorbance data [plot of log $(A_t - A_\infty)$ *vs.* time] at 370 nm for the runs at different Cu$^{\text{II}}$ concentration indicated that copper(II) interacts with the imine. The equilibrium was assumed to be as in equation (3) for $10 \leqslant [\text{Cu}^{2+}]/[\text{HL}]_\text{T} \leqslant 100$ and pH = 4.22—5.33.

$$\text{Cu}^{2+} + \text{HL} \xrightleftharpoons{K_{\text{CuL}^+}} \text{CuL}^+ + \text{H}^+ \qquad (3)$$

The equilibrium constant K_{CuL^+} was calculated from the gradient and intercept of the plot of $(E_{\text{HL}} - E_{\text{obs.}})^{-1}$ against $(1 + [\text{H}^+]/K_1)([\text{H}^+]/[\text{Cu}^{2+}])$, as equation (4) can easily be shown [3] to be true; $E_{\text{obs.}}$ and E_{HL} stand for the

$$(E_{\text{HL}} - E_{\text{obs.}})^{-1} = (E_{\text{HL}} - E_{\text{ML}^+})^{-1} + [(E_{\text{HL}} - E_{\text{ML}^+})K_{\text{ML}^+}]^{-1}(1 + [\text{H}^+]/K_1)([\text{H}^+]/[\text{Cu}^{2+}]) \qquad (4)$$

absorption coefficient of the Schiff base in the presence and absence of Cu$^{\text{II}}$ respectively. At 370 nm the zero-time absorbance data of HL in the absence of Cu$^{\text{II}}$ were found to be independent of pH in the range stated above (*i.e.* $E_{\text{H}_2\text{L}^+} \simeq E_{\text{HL}}$). With $E_{\text{HL}} = (14.0 \pm 0.5) \times 10^3$ dm^3 mol^{-1} cm^{-1} and $K_1 = (7.8 \pm 0.8) \times 10^{-5}$ mol dm^{-3} (as determined from the kinetic data) we obtained $(E_{\text{HL}} - E_{\text{ML}^+})^{-1} = (1.06 \pm 0.03) \times 10^{-4}$ mol cm dm^{-3} and $K_{\text{CuL}^+} = (15.9 \pm 1.4) \times 10^{-3}$ at 39.8 °C, $I = 0.1$ mol dm^{-3}. There was no spectrophotometric evidence of interaction of Zn^{2+}, Co^{2+}, and Ni^{2+} with HL in acetate buffer medium in the range pH 4.8—5.8 and metal ion concentration 0.001—0.015 mol dm^{-3}. For runs in imidazole buffer (im) with Zn^{2+} as catalyst the observed zero-time (extrapolated) absorption coefficient ($E_{\text{obs.}}$) of the Schiff base at 370 nm decreased with $[\text{Zn}^{2+}]_\text{T}$. This is attributed to complexation of L$^-$ with Zn^{2+}. $[\text{im}]_\text{T} > 4[\text{Zn}^{2+}]_\text{T}$ was maintained in the kinetic study. Hence, the equilibria existing under the experimental conditions may reasonably be assumed to be those shown in Scheme 1. The absorbing species being HL and $[\text{Zn(im)}_2\text{L}]^+$, equation (5) can be easily derived, where



$$[\text{Zn(im)}_4]^{2+} \xrightleftharpoons{K_4} [\text{Zn(im)}_3]^{2+} + \text{im}$$
$$[\text{Zn(im)}_3]^{2+} \xrightleftharpoons{K_3} [\text{Zn(im)}_2]^{2+} + \text{im}$$
$$[\text{Zn(im)}_2]^{2+} + \text{HL} \xrightleftharpoons{K_{\text{ZnL}^+}^{\text{im}}} [\text{Zn(im)}_2\text{L}]^+ + \text{H}^+$$
$$\text{Him}^+ \xrightleftharpoons{K_\text{d}} \text{im} + \text{H}^+$$

SCHEME 1

$E_{\text{ZnL}^+}^{\text{im}}$ represents the absorption coefficient of the species $[\text{Zn(im)}_2\text{L}]^+$ and $f = [\text{H}^+] + K_3^{-1}K_\text{d}[\text{Him}^+] + (K_4K_3)^{-1}$

$$(E_{\text{HL}} - E_{\text{obs.}})^{-1} = (E_{\text{HL}} - E_{\text{ML}^+}^{\text{im}})^{-1} + [(E_{\text{HL}} - E_{\text{ML}^+}^{\text{im}})K_{\text{ZnL}^+}^{\text{im}}]^{-1}(f/[\text{Zn}^{2+}]_\text{T}) \qquad (5)$$

$(K_\text{d}^2[\text{Him}^+]^2/[\text{H}^+])$. With $[\text{Him}^+] = [\text{HClO}_4]_\text{T}$, $K_4^{-1} = 52$, $K_3^{-1} = 115$ dm^3 mol^{-1},[7] and $K_\text{d} = 2 \times 10^{-7}$ mol dm^{-3} (determined by pH measurements of imidazole–HClO$_4$ buffer) ($I = 0.1$ mol dm^{-3}, 39.8 °C), a plot of $10^3(E_{\text{HL}} - E_{\text{obs.}})^{-1}$ against $10^4f/[\text{Zn}^{2+}]_\text{T}$ yielded an intercept of 0.07 mol cm dm^{-3} and gradient 0.074 mol cm dm^{-3} from which is obtained $K_{\text{ZnL}^+}^{\text{im}} = 1.0 \times 10^{-4}$.

RESULTS AND DISCUSSION

Hydrolysis in the Absence of the Metal(II) *Ions*.—The rate of hydrolysis of the imine is subject to H$^+$ and OH$^-$ catalysis as depicted by the buffer-corrected pH rate profile (Figure 1). Buffer catalysis was observable above pH 8 with carbonate and morpholine buffers. Rate data are collected in Table 1. The pseudo-first-order rate constant $k_{\text{obs.}}$ tends to attain a limiting value in the neutral region of pH where the Schiff base exists predominantly in the neutral form (HL). The levelling off of the rate profile reflects its spontaneous hydrolysis as well as hydroxide-catalysed hydrolysis of its protonated form, both the processes being kinetically indistinguishable. The value of K_2 suggests that the Schiff base will exist almost entirely in the anionic form at $[\text{OH}^-] = 0.002$—0.1 mol dm^{-3}. Excellent straight-line plots of $k_{\text{obs.}}$ against $[\text{OH}^-]$ with non-vanishing intercepts and gradient, therefore, reveal that the Schiff-base anion undergoes both spontaneous and hydroxide-catalysed hydrolysis. Consistent with these facts, the overall rate of hydrolysis is given by equation (6), where k_i are the specific rate constants of

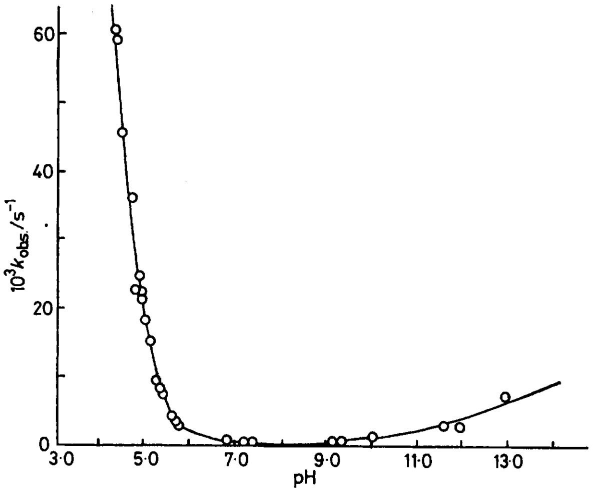


FIGURE 1 The pH–rate profile for the hydrolysis of the Schiff base HL in the absence of metal(II) ions: $10^3k_{\text{obs.}}$ *versus* pH, at 39.8 °C

$$\text{Rate} = k_1[\text{H}_2\text{L}^+] + k_2[\text{H}_2\text{L}^+][\text{OH}^-] + k_3[\text{HL}] + k_4[\text{L}^-] + k_5[\text{L}^-][\text{OH}^-] \qquad (6)$$

hydrolysis of different species as defined below in Scheme 2. On replacement of $[OH^-]$ by $K_w/[H^+]$ the observed pseudo-first-order rate constant takes the form of equation (7).

$$k_{obs.} = \frac{(k_1/K_1)[H^+] + (k_2K_w/K_1 + k_3) + k_4K_2/[H^+] + k_5K_2K_w/[H^+]^2}{1 + [H^+]/K_1 + K_2/[H^+]} \qquad (7)$$

Graphical analysis of the rate data indicated that the dependence of $k_{obs.}$ on $[H^+]$ is best represented by equation (8) up to the neutral region of pH. A plot of $k_{obs.}$ against $[H^+]$ is linear at $5.6 \leqslant pH \leqslant 7.0$ (*i.e.*

$$k_{obs.} = \frac{(k_1/K_1)[H^+] + (k_2K_w/K_1 + k_3)}{1 + [H^+]/K_1} \qquad (8)$$

$1 \gg [H^+]/K_1$). With the value of $(k_3 + k_2K_w/K_1)$ obtained as the intercept of such plot, the rate data at pH <5.6 were utilised to calculate k_1 and K_1 from the intercept and gradient of the plot of $10^{-1}[k_{obs.} - (k_2K_w/K_1 + k_3)]^{-1}$ against $10^{-4}[H^+]^{-1}$ (Figure 2). Values of K_1 were found to be $(9.7 \pm 0.9) \times 10^{-5}$, $(8.3 \pm 0.8) \times 10^{-5}$, and $(7.8 \pm 0.8) \times 10^{-5}$ mol dm^{-3} at 30, 35, and 39.8 °C respectively. pK_1 ($I = 0.1$ mol dm^{-3}, 30—39.8 °C) of the imine (4.0—4.1) is about one unit lower than that of the protonated 2-aminothiazole ($pK_1 = 5.21$—5.09,

TABLE 1

Rate data for the hydrolysis of *N*-salicylidene-2-aminothiazole. In 5% MeOH, $I = 0.1$ mol dm^{-3}, $\lambda = 370$ nm ($pH \leqslant 8.5$) or 420 nm ($pH > 8.5$)

(*a*) pH	$10^3k_{obs.}$/s^{-1} (30.0 ± 0.1 °C)
Acetate buffer	
3.93	55.2 ± 0.1
4.11	40.0 ± 0.5
4.21	35.4 ± 0.2
4.32	31.3 ± 0.4
4.41	28.3 ± 0.6
4.49	23.9 ± 0.1
4.54	22.6 ± 0.2
4.59	20.9 ± 0.4
4.61	19.5 ± 0.1
4.62	18.8 ± 0.1
4.72	15.2 ± 0.2
4.94	11.3 ± 0.1
5.30	6.02 ± 0.1
5.56	3.06 ± 0.03
5.55	2.53 ± 0.05
Phosphate buffer	
5.99	1.55 ± 0.02
6.39	0.71 ± 0.02
6.59	0.50 ± 0.01
7.12	0.300 ± 0.003
7.42	0.225 ± 0.006
7.66	0.212 ± 0.007

pH	$10^3k_{obs.}$/s^{-1} (35.0 ± 0.1 °C)
Acetate buffer	
4.01	54.7 ± 2.2
4.21	44.8 ± 0.4
4.32	41.9 ± 0.5
4.41	36.8 ± 1.3
4.49	32.1 ± 0.2
4.54	28.9 ± 0.1
4.59	28.3 ± 0.2
4.61	25.1 ± 0.1
4.65	23.6 ± 0.6
4.80	18.0 ± 0.6
4.95	13.6 ± 0.4
5.30	6.69 ± 0.30
5.56	3.90 ± 0.06
Phosphate buffer	
5.99	2.88 ± 0.04
6.39	1.35 ± 0.01
6.59	0.808 ± 0.003
6.91	0.603 ± 0.003
7.12	0.403 ± 0.002
7.42	0.362 ± 0.001
7.60	0.338 ± 0.007

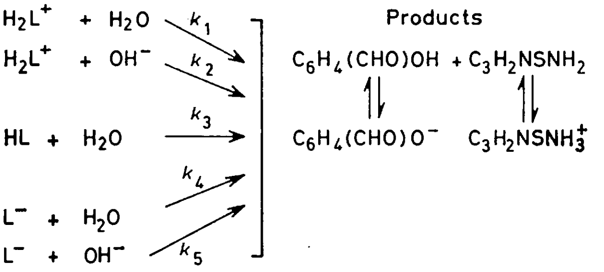
pH	$10^3k_{obs.}$/s^{-1} (39.8 ± 0.1 °C)
Acetate buffer	
4.18	60.7 ± 1.5
4.22	59.1 ± 1.0
4.39	45.6 ± 0.4
4.62	36.1 ± 0.5
4.65	33.6 ± 0.4
4.81	22.7 ± 1.0
4.84	24.7 ± 0.5
4.90	22.6 ± 0.5
4.93	21.1 ± 0.5
5.00	18.3 ± 0.2
5.15	14.0 ± 0.2
5.30	9.23 ± 0.1
5.40	8.02 ± 0.06
5.45	7.60 ± 0.1
5.65	4.20 ± 0.1
5.71	3.70 ± 0.04
5.78	3.35 ± 0.02
5.80	3.36 ± 0.08
Imidazole buffer	
6.87 [e]	0.75 ± 0.02
6.88 [f]	0.74 ± 0.02
Phosphate buffer	
6.95 [g]	0.61
6.94 [g]	0.63
6.95 [g]	0.65
7.24 [h]	0.51
7.45 [h]	0.46

pH	$10^3k_{obs.}$/s^{-1} (39.8 ± 0.1° C)
Morpholine buffer	
8.53 [a]	6.74
8.53 [a]	14.2
8.53 [a]	22.0 ± 3.5
8.53 [a]	28.8
8.53 [a]	35.8 ± 5.2
9.50 [b]	25.6
9.12 [b]	31.2
9.15 [c]	24.3
9.15 [c]	8.4
Carbonate buffer	
9.99	1.16
9.80	1.16
9.73	1.18
9.58	1.15
9.47	1.14
10.05	1.30
9.35	1.01
9.25	0.98
9.19	0.97
10.10 [d]	2.30 ± 0.07
10.10 [d]	1.82 ± 0.10
10.10 [d]	1.56

(*b*) [NaOH]/mol dm^{-3}	$10^3k_{obs.}$/s^{-1}		
	(30.0 ± 0.1 °C)	(35.0 ± 0.1 °C)	(39.8 ± 0.1 °C)
0.002	0.478 ± 0.024	0.73 ± 0.01	1.24 ± 0.02
0.005	0.626 ± 0.008	0.84 ± 0.02	1.32 ± 0.03
0.008		0.98 ± 0.02	
0.01	0.697 ± 0.007	1.08 ± 0.01	1.63 ± 0.05
0.0112			0.825 [i]
0.0206			2.48 ± 0.05
0.0224			1.20 [i]
0.03	1.34 ± 0.01	1.94 ± 0.02	3.1 ± 0.30
0.0448			1.99 [i]
0.05	1.85 ± 0.01	2.90 ± 0.03	4.46 ± 0.05
0.08	2.56 ± 0.02	4.21 ± 0.01	6.20 ± 0.20
0.0897			3.37 [i]
0.10	3.37 ± 0.03	4.98 ± 0.06	7.70 ± 0.15

[a] $[morph]_T = 0.02$, 0.04, 0.06, 0.08, and 0.1 mol dm^{-3}; $[Hmorph^+]/[morph]_f = 1.0$. [b] $[morph]_T = 0.1$; $[HClO_4]_T = 0.01$ and 0.02 mol dm^{-3}. [c] $[morph]_T = 0.075$ and 0.025 mol dm^{-3}; $[Hmorph^+]/[morph]_f = 0.25$. [d] $[Na_2CO_3] = 0.025$, 0.015, and 0.01 mol dm^{-3}; $[CO_3^{2-}]/[HCO_3^-] = 1.0$. [e] $[im]_T = 0.02$; $[HClO_4] = 0.01$ mol dm^{-3}. [f] $[im]_T = 0.1$; $[HClO_4] = 0.05$ mol dm^{-3}. [g] $[Na_2HPO_4]/[NaH_2PO_4] = 1$; $[Na_2HPO_4] = 0.015$, 0.02, and 0.025 mol dm^{-3}. [h] $[Na_2HPO_4] = 0.02$; $[NaH_2PO_4] = 0.01$ and 0.005 mol dm^{-3}. [i] In 90% D_2O–5% MeOH medium.

$I = 0.1$ mol dm^{-3}, 30—40 °C).[8] This is consistent with the earlier observations that basicity of the imine nitrogen is usually lower than that of the corresponding primary amine.[1,9] By comparison, a value of pK 2.7 ($I = 0.5$ mol dm^{-3}, 25 °C) is reported for the protonated thiazole.[10] Evidently, the imine nitrogen is the preferred site for protonation.



SCHEME 2 H+ Involved in the protonation equilibria are not shown

The rate constants for spontaneous and hydroxide-catalysed hydrolysis of the imine anion (L^-) were calculated from the intercept and gradient of the least-squares best line plot of $k_{obs.}$ against [OH^-], as it can be easily shown that equation (7) reduces to equation (9) at [OH^-] = 0.002—0.1 mol dm^{-3}.

$$k_{obs.} = k_4 + k_5[OH^-] \qquad (9)$$

It is worth noting that the ratio $k_{OH}(L^-) : k_{H_2O}(L^-)$ $\{k_{H_2O}(L^-) = k_4/[H_2O]$ and $k_{OH}(L^-) = k_5\} = 3.3 \times 10^3 : 1$ (30—39.8 °C). This is considerably lower than the value ($10^8 : 1$) usually observed in the hydrolysis of esters where direct nucleophilic attack of OH^- or H_2O at the ester carbonyl is expected.[11] A significantly smaller value for this rate ratio has also been observed in the hydrolysis of esters which involve intramolecular general base catalysis.[11] Reactions in which OD^- acts as a nucleophile usually are reported to have rate constants which are 20—40% higher than that for the corresponding reaction with OH^-.[11,12] We observed a significant slowing-down effect of D_2O on the pathways associated with both k_4 and k_5 [$k_4(H_2O)/k_4(D_2O) = 2.2 \pm 0.2$, $k_5(H_2O)/k_5(D_2O) = 2.0 \pm 0.1$ at 39.8 °C, $I = 0.1$ mol dm^{-3}, 90% D_2O medium, see Table 4]. This presumably suggests that hydrolysis of the imine HL *via* k_4 and k_5 pathways involves general base catalysis by the phenoxide ion (Scheme 3). The similarity of the mechanisms is also indicated by the comparable activation parameter data (Table 4) for both the pathways. It is worth mentioning that the mechanism of hydrolysis of the imines is believed to involve the rate-determining attack of H_2O and OH^- at the aldimine carbon of its protonated form in mild acidic and alkaline media.[3,13-15]

TABLE 2

Rate data for copper(II)-catalysed hydrolysis of *N*-salicylidene-2-aminothiazole, in 5% MeOH, $I = 0.1$ mol dm^{-3}, 39.8 ± 0.1 °C

pH	$[Cu^{2+}]_T$/mol dm^{-3}	$10^3k_{obs.}$/s^{-1}	$10^3k'_{obs.}$/s^{-1} [a]	$10^3k_{app.}$/s^{-1} [b]
4.54 (±0.02)	0.001	28.9 ± 0.6	38.6 ±1.1	6.8 ± 1.2
	0.002	23.6 ± 0.8		
	0.003	19.8 ± 0.07		
	0.004	18.3 ± 0.6		
	0.005	16.8 ± 0.7		
	0.006	15.8 ± 0.5		
	0.008	14.5 ± 0.5		
	0.009	14.0 ± 0.5		
	0.010	12.2 ± 0.5		
	0.012	12.0 ± 0.5		
	0.014	10.7 ± 1.3		
4.39	0.014	16.8 ± 0.5	45.5	8.0 ± 2.1
4.27	0.014	25.2 ± 1.1	54.0	11.5 ± 3.5
4.27	0.008	33.7 ± 1.1	54.0	16.8 ± 4.2
4.28	0.006	36.2 ± 1.2	53.5	17.6 ± 5.1
4.22	0.010	33.4 ± 1.5	59.1	13.1 ± 5.2
4.18	0.014	31.7 ± 0.7	60.7	12.8 ± 4.5
4.68	0.014	7.84 ± 0.18	31.7	4.7 ± 0.7
4.86	0.014	4.73 ± 0.12	23.0	3.3 ± 0.4
4.49	0.010	15.2 ± 0.5	41.2	6.8 ± 2.0
5.11	0.010	4.21 ± 0.10	15.6	3.6 ± 0.2
5.13	0.014	3.75 ± 0.15	14.5	3.3 ± 0.2
5.15	0.008	4.25 ± 0.15	14.5	3.6 ± 0.2
5.20	0.009	3.42 ± 0.10	12.8	2.9 ± 0.1
5.20	0.002	3.93 ± 0.06	12.8	1.9 ± 0.5
5.19	0.004	3.57 ± 0.09	13.2	2.4 ± 0.3
5.33	0.001	3.71 ± 0.10	9.2	1.9 ± 0.4

$k_u = (1.9 \pm 0.3) \times 10^{-3}$ s^{-1}, $k_H = (0.12 \pm 0.02) \times 10^3$ dm^3 mol^{-1} s^{-1} [c]

[a] $k'_{obs.} = k_{obs.}$ at $[Cu^{2+}]_T = 0$. [b] See equation (11). [c] See equation (12).

The anion of *o*-hydroxybenzylidene-2-aminopropane [13] undergoes hydroxide-catalysed hydrolysis ($k_5 = 13.3$ dm^3 mol^{-1} s^{-1}, 30 °C, $I = 0.1$ mol dm^{-3}, in 5% MeOH) *ca.* 480 times faster than its 2-aminothiazole amine analogue. This remarkable reactivity difference may be ascribed to the significant stabilising effect of the phenoxide ion on

TABLE 3

Rate data for hydrolysis of *N*-salicylidene-2-aminothiazole in imidazole (im) buffer and in the presence of Zn^{II}, in 5% MeOH, $I = 0.1$ mol dm^{-3}, 39.8 °C

$[Zn^{2+}]_T$/mol dm^{-3}	$[im]_T$/mol dm^{-3}	$[HClO_4]$/mol dm^{-3}	pH	$10^3k_{obs.}$/s^{-1}	$10^3k'_{obs.}$/s^{-1}	$10^3k_{app.}$/s^{-1}
0.005	0.1	0.05	6.70	1.46 ± 0.01	0.68	7.1
0.01	0.1	0.05	6.48	2.80 ± 0.04	0.94	8.3
0.002	0.1	0.02	7.26	0.90 ± 0.02	0.40	5.1
0.001	0.1	0.02	7.47	0.662 ± 0.002	0.365	8.3
0.003	0.1	0.02	7.40	1.13	0.376	6.9
0.001	0.1	0.05	6.75	0.83 ± 0.01	0.64	8.0
0.002	0.1	0.05	6.72	0.90 ± 0.005	0.666	5.3
0.003	0.1	0.05	6.67	1.05 ± 0.02	0.71	5.0
0.004	0.1	0.05	6.64	1.21 ± 0.01	0.74	5.2
0.007	0.1	0.05	6.49	1.82 ± 0.01	0.92	5.6
0.005	0.1	0.05	6.57	1.39 ± 0.06	0.816	5.2

$k_{app.} = (6.2 \pm 1.3) \times 10^{-3}$ s^{-1} based on $K_{ZnL^+}{}^{im} = 1.0 \times 10^{-4}$

TABLE 4

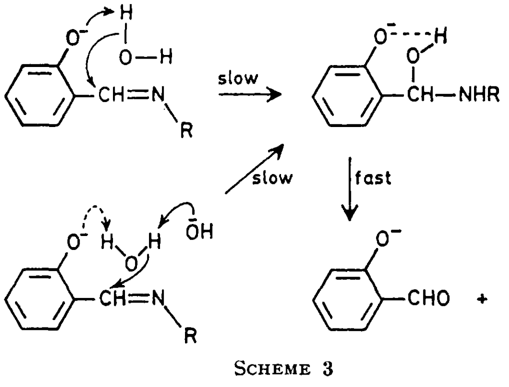
Summary of the calculated rate and activation parameters for hydrolysis of *N*-salicylidene-2-aminothiazole, 5% MeOH, $I = 0.1$ mol dm^{-3}

Reaction	Value of rate constant (30 °C)	(35 °C)	(39.8 °C)	$\Delta H^\ddagger$/ kJ mol^{-1}	$\Delta S^\ddagger$/ J K^{-1} mol^{-1}
$H_2L^+ + H_2O$; $10^2k/s^{-1}$	8.0 ± 0.8	9.1 ± 0.9	11.6 ± 1.1	27.4 ± 5.8	-176 ± 19
$H_2L^+ + OH^-$ $HL + H_2O$ } $10^4k/s^{-1}$ [a]	1.9 ± 0.2	2.9 ± 0.2	4.0 ± 0.2	55.9 ± 3.6	-132 ± 12
$L^- + H_2O$; $10^4k/s^{-1}$	4.6 ± 0.2	6.5 ± 0.1	10.7 ± 0.3 (4.8 ± 0.4) [b]	71.5 ± 12.0	-74 ± 39
$L^- + OH^-$; $10^3k/dm^3\ mol^{-1}\ s^{-1}$	27.5 ± 0.8	44.3 ± 0.5	65.2 ± 1.5 (32.4 ± 0.7) [b]	66.1 ± 4.1	-57 ± 13
$CuL^+ + H_2O$; $10^3k/s^{-1}$			1.9 ± 0.3		
$CuL^+ + H^+ + H_2O$; $10^{-3}k/dm^3\ mol^{-1}\ s^{-1}$			0.12 ± 0.02		
$[Zn(im)_2L]^+ + H_2O$; $10^3k/s^{-1}$			6.2 ± 1.3		

[a] $k_2K_w/K_1 + k_3$, see equation (8). [b] In 90% D_2O–5% MeOH.

the aldimine linkage in the latter arising out of extended charge conjugation (between phenoxide ion and thiazole ring) which is not available to the former. The rate constant of hydrolysis of the protonated form (H_2L^+) of the Schiff base [$k_1 = (8.0 \pm 0.8) \times 10^{-2}$ s^{-1}, 30 °C] is comparable to that for *N*-salicylideneaniline (10.0×10^{-2} s^{-1}, 30.8 °C, $I = 0.2$ mol dm^{-3}, in 10% EtOH) [3] and about 40 times higher than that for *N*-salicylidene-2-aminopropane ($k_1 = 2.1 \times 10^{-3}$ s^{-1}, 30 °C, $I = 0.1$ mol dm^{-3}, in 5% MeOH).[13] This reactivity difference is in keeping with the expected inductive effects of the aliphatic and aromatic moieties of the amine function; the aromatic group of the amine acts as an electron-withdrawing substituent and depletes electron density at the aldimine linkage of the protonated Schiff base (H_2L^+) and hence facilitates nucleophilic attack by H_2O at the aldimine carbon. For the hydrolysis of protonated benzylidene 1,1-dimethylethylamines, the values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are *ca.* 52 kJ mol^{-1} and *ca.* -120 J K^{-1} mol^{-1} respectively.[14] The activation enthalpy for the acid-catalysed path of the Schiff base under investigation (Table 4) is significantly lower. But its effect on the rate is compensated by the large negative value of $\Delta S^\ddagger$. Bimolecular reactions have $\Delta S^\ddagger$ values in the range -20 to -60 J K^{-1} mol^{-1}.[16] A value of $\Delta S^\ddagger$ (k_1) $= -176 \pm 9$ J K^{-1} mol^{-1} in the present case, therefore, is consistent with the fact that considerable entropy loss occurs due to the orientation of solvent molecules around the highly polar transition state.

The apparently pH-independent pseudo-first-order rate constant ($k' = k_3 + k_2K_w/K_1$) compares well with that for *N*-2-pyridylmethyleneaniline ($k' = 2.8 \times 10^{-4}$ s^{-1}, 25 °C, $I = 0.1$ mol dm^{-3}).[4] It is not possible to split k' into k_3 and k_2, but the upper limit of k_3 and k_2 (assuming $k' = k_3$ or k_2K_w/K_1) at 30 °C may be quoted as 1.9×10^{-4} s^{-1} and 8×10^5 dm^3 mol^{-1} s^{-1} respectively taking $K_w = 2.5 \times 10^{-14}$ mol^2 dm^{-6} (ref. 17) and $K_1 = 9.7 \times 10^{-5}$ mol dm^{-3}. This value of k_2 is comparable to the analogous data reported for *N*-benzylidene-2-aminopropane ($k_2 = 12 \times 10^5$ dm^3 mol^{-1} s^{-1}, 30 °C).[13] Presumably hydrolysis *via* the mechanism of k_2 dominates over that of k_3.



SCHEME 3

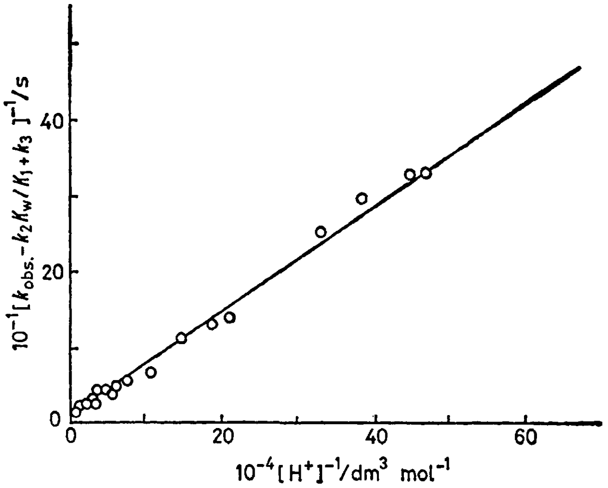


FIGURE 2 Plot of $10^{-1}[k_{obs.} - (k_2K_w/K_1 + k_3)]^{-1}$ *versus* $10^{-4}[H^+]^{-1}$, at 39.8 °C

Metal Ion Catalysis.—The effect of Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II} on the rate of hydrolysis of the imine was examined at 39.8 °C. Rate data presented in Table 2 and Figure 3 indicate that only Cu^{II} retards the rate of hydrolysis of the Schiff base to any significant extent. The observed dependence of the pseudo-first-order rate constant on [Cu^{2+}] at constant pH is consistent with equation (10), where $k_{obs.} = k'_{obs.}$ at $[Cu^{2+}] = 0$ and

$$k_{obs.} = \frac{k'_{obs.}(1 + [H^+]/K_1) + k_{app.}K_{CuL^+}[Cu^{2+}]/[H^+]}{1 + [H^+]/K_1 + K_{CuL^+}[Cu^{2+}]/[H^+]} \quad (10)$$

$k_{app.}$ is the overall pseudo-first-order rate constant of hydrolysis of the metal chelate, [CuL]$^+$. Values of $k'_{obs.}$ at different pH were taken from the plot of $k_{obs.}$

against pH for the hydrolysis reaction in the absence of Cu^{2+}. At constant pH and varying $[Cu^{2+}]$, equation (10) can be linearized. The plot of $(k'_{\text{obs.}} - k_{\text{obs.}})^{-1}$ against $[Cu^{2+}]^{-1}$ for the rate data at pH 4.54 ± 0.02 and $[Cu^{2+}] = 0.001$—0.014 mol dm^{-3} yielded a straight line with gradient $\{(K_1[H^+] + [H^+]^2)/[(k'_{\text{obs.}} - k_{\text{app.}})K_1K_{\text{CuL}^+}]\} = 0.070 \pm 0.003$ mol dm^{-3} s and intercept $[1/(k'_{\text{obs.}} - k_{\text{app.}})] = 31.8 \pm 0.4$ s, from which we obtain $k_{\text{app.}} = (6.8 \pm 1.2) \times 10^{-3}$ s^{-1} and $K_{\text{CuL}^+} = (2.6 \pm 0.3) \times 10^{-2}$ utilizing $K_1 = (7.8 \pm 0.8) \times 10^{-5}$ mol dm^{-3}. With the average value of $K_{\text{CuL}^+} = (2.1 \pm 0.5) \times 10^{-2}$ obtained from kinetic and equilibrium measurements, $k_{\text{app.}}$ (see Table 2) was then calculated from equation (11).

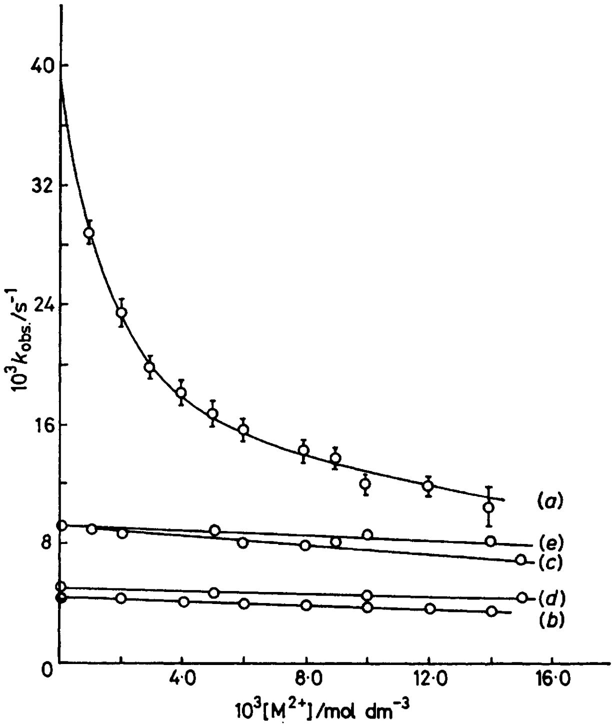


FIGURE 3 Plot of $10^3k_{\text{obs.}}$ *versus* $10^3[M^{2+}]$, at 39.8 °C: (*a*) Cu^{2+}, pH 4.54 ± 0.02, (*b*) Ni^{2+}, pH 5.57 ± 0.02, (*c*) Ni^{2+}, pH 5.32 ± 0.02, (*d*) Co^{2+}, pH 5.60 ± 0.02, (*e*) Zn^{2+}, pH 5.33 ± 0.02

$$k_{\text{app.}} = k_{\text{obs.}} - (k'_{\text{obs.}} - k_{\text{obs.}})(K_1[H^+] + [H^+]^2)/(K_1K_{\text{CuL}^+}[Cu^{2+}]) \quad (11)$$

It is interesting to note that $k_{\text{app.}}$ increases with $[H^+]$. A least-squares best-line (Figure 4) fit of the values of $k_{\text{app.}}$ to equation (12) yielded the rate constants for

$$k_{\text{app.}} = k_u + k_H[H^+] \quad (12)$$

uncatalysed (k_u) and proton-catalysed (k_H) hydrolysis of the chelate as $(1.9 \pm 0.3) \times 10^{-3}$ s^{-1} and $(0.12 \pm 0.02) \times 10^3$ dm^3 mol^{-1} s^{-1} respectively. Noteworthy is the fact that $[CuL]^+$ and L^- hydrolyse at comparable rates ($k_4/k_u = 0.6 \pm 0.1$ at 39.8 °C) in the spontaneous mechanism. Hydrolysis of *N*-salicylideneanilinecopper(II) chelate *via* the uncatalysed path was not observed earlier but such a species and its 2-aminothiazole analogue are found to hydrolyse at comparable rates in the k_H path [$k_H = 0.29 \times 10^3$ dm^3 mol^{-1} s^{-1} at 30.8 °C for *N*-salicylideneanilinecopper(II)[3]]. The 2-pyridylmethyleneanilinecopper(II) imine complex [k_u (calc.) $= 1.7 \times 10^{-4}$ s^{-1}, 25 °C, $I = 0.1$ mol dm^{-3}, k_H not reported[4]] appears to be kinetically more stable to hydrolysis than the *N*-salicylidene-2-aminothiazolecopper(II) imine complex. The protonated imine (H_2L^+) undergoes hydrolysis 60 times faster than $[CuL]^+$ (k_1/k_u *ca.* 61 ± 11). This is indicative of the stabilising action of Cu^{II} relative to H^+ on the aldimine linkage towards hydrolytic splitting.

Rate data for the Zn^{II}-catalysed reaction in imidazole buffer are presented in Table 3. The value of $k_{\text{obs.}}$ increases with $[Zn^{2+}]_T$ at a given pH. In the pH range 6.49—7.49, the mixed-ligand complex $[Zn(im)_2L]^+$ (see Experimental section for equilibrium constant data) is assumed to undergo spontaneous, proton-, and hydroxide-catalysed hydrolysis. The overall rate of hydrolysis is given by Rate $= k'_{\text{obs.}}[HL]_f + k_{\text{app.}}[Zn(im)_2L^+]$, which can be rewritten as equation (13) where $k_{\text{obs.}} = k'_{\text{obs.}}$ at $[Zn^{2+}]_T = 0$. Replacing $[Zn(im)_2]/[H^+]$ by $[Zn]_T/f$ (f is defined earlier in the Experimental section) and rearranging equation (13) gives equation (14). Since $k_{\text{obs.}}$ and $K_{\text{ZnL}^+}{}^{\text{im}}$ are known, $k_{\text{app.}}$ could be calculated; it was found to be virtually independent of pH and $[Zn^{2+}]_T$ and averaged to $(6.3 \pm 1.3) \times 10^{-3}$ s^{-1}. Evidently, the mixed-ligand complex $[Zn(im)_2L]^+$ undergoes both proton- and hydroxide-independent hydrolysis in the neutral zone of pH investigated {*i.e.*, $k_{\text{app.}} = k_u$ for $[Zn(im)_2L]^+$ at pH 6.49 − 7.49}. It is interesting to note that $[Zn(im)_2L]^+$ undergoes pH-independent hydrolysis about three times faster than $[CuL]^+$ and L^- species.

$$\text{Rate} = k_{\text{obs.}}[HL]_T = \frac{(k'_{\text{obs.}} + k_{\text{app.}}K_{\text{ZnL}^+}{}^{\text{im}}[Zn(im)_2]/[H^+])[HL]_T}{1 + K_{\text{ZnL}^+}{}^{\text{im}}[Zn(im)_2]/[H^+]} \quad (13)$$

$$k_{\text{app.}} = \frac{k_{\text{obs.}}(1 + K_{\text{ZnL}^+}{}^{\text{im}}[Zn]_T/f) - k'_{\text{obs.}}}{K_{\text{ZnL}^+}{}^{\text{im}}[Zn]_T/f} \quad (14)$$

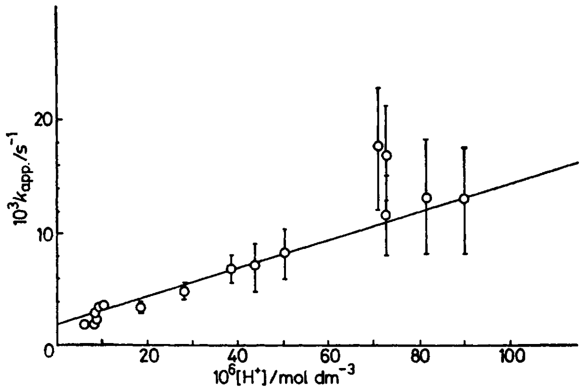


FIGURE 4 Plot of $10^3k_{\text{app.}}$ *versus* $10^6[H^+]$ for the hydrolysis of $[CuL]^+$ species at 39.8 °C

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