Reactions of Co-ordinated Imines. Part I. Kinetics and Mechanism of Hydrolysis of *N*-2-Pyridylmethyleneaniline both in the Presence and Absence of Copper(II) Ions

By **Robert W. Hay** * and **Kevin B. Nolan**, Chemistry Department, University of Stirling, Stirling FK9 4LA

The hydrolysis of *N*-2-pyridylmethyleneaniline (L) has been studied at 25 °C and $I = 0.1$ mol dm^{-3} over the pH range 6.6—13.5. The observed rate constants ($k_{obs.}$) at constant pH pass through a minimum at pH 10.5. The reaction is subject to specific acid and base catalysis. Rate constants have been obtained for the reactions (i) and

$$\mathrm{HL^+ + H_2O \longrightarrow Products},\ k = 1.26 \times 10^{-1}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}} \qquad \text{(i)}$$

$$\mathrm{L + [OH]^- \longrightarrow Products},\ k = 2.17 \times 10^{-2}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}} \qquad \text{(ii)}$$

(ii) and for the kinetically indistinguishable processes (iii) and (iv) where $k = 2.8 \times 10^{-4}$ s^{-1}. The effect of

$$\mathrm{L + H_2O \longrightarrow Products} \qquad \text{(iii)}$$

$$\mathrm{HL^+ + [OH]^- \longrightarrow Products} \qquad \text{(iv)}$$

copper(II) ions on the hydrolysis has been studied at 25 °C and $I = 0.1$ mol dm^{-3}, under conditions where the 1 : 1 complex $[\mathrm{CuL}]^{2+}$ is the predominant species in solution. Evidence for an equilibrium of the type $[\mathrm{CuL(OH_2)_2}]^{2+} \overset{K_a}{\rightleftharpoons} [\mathrm{CuL(OH)(OH_2)}]^+ + \mathrm{H^+}$ for which pK_a is *ca.* 7.2 has been obtained from the kinetic measurements. Rate constants have been derived for the hydrolytic reactions (v)—(vii). Base hydrolysis of $[\mathrm{CuL(OH_2)_2}]^2$ is some 4.4 ×

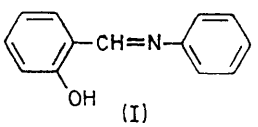
$$\mathrm{[CuL(OH)_2]^{2+} + H_2O \longrightarrow Products},\ k = 3.15 \times 10^{-6}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}} \qquad \text{(v)}$$

$$\mathrm{[CuL(OH_2)_2]^{2+} + [OH]^- \longrightarrow Products},\ k = 9.72 \times 10^{3}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}} \qquad \text{(vi)}$$

$$\mathrm{[CuL(OH)(OH_2)]^{+} + [OH]^- \longrightarrow Products},\ k = 2.75 \times 10^{3}\ \mathrm{dm^3\ mol^{-1}\ s^{-1}} \qquad \text{(vii)}$$

10^5 times faster than base hydrolysis of L at 25 °C and $I = 0.1$ mol dm^{-3}. Possible mechanisms for the reactions are discussed.

THE catalytic effect of metal ions has been recognised in a wide variety of reactions involving organic substrates. One important reaction of biological interest is the effect of metal ions on the hydrolysis of imines. A number of papers have discussed the effect of metal ions on the formation and hydrolysis of such compounds.[1-10] Dash and Nanda [9] made a detailed kinetic study of the hydrolysis of *N*-salicylideneaniline, (I), in the presence and absence of cobalt(II), nickel(II), copper(II), and zinc(II) ions using 10% ethanol–water as solvent. The reactivity of the chelates towards hydrolysis was found to follow the reverse sequence of their stability constants, the most thermodynamically stable complexes undergoing the slowest rate of hydrolysis. Imines capable of forming bicyclic chelate rings as in (III) [3] are known to be stabilised towards hydrolysis under mildly acidic conditions. However, imines which can form monocyclic chelates such as *N*-salicylideneaniline, (I), and *NN*′-ethylenebis(2-thienylmethyleneimine) [2] [as in (IV) where the S atoms do not act as donors] are rapidly hydrolysed in the presence of copper(II) and nickel(II) ions. Hydrolysis of a bicyclic metal complex such as (III) involves the rupture of chelate rings, a process which is not normally favoured.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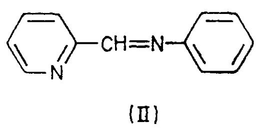
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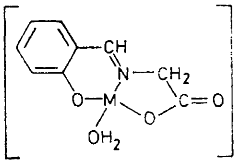
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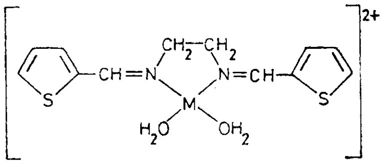
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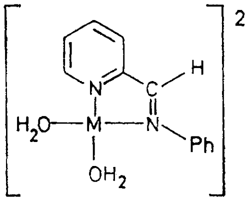
It would be expected that at high metal to ligand ratios *N*-2-pyridylmethyleneaniline, (II), would form 1 : 1 complexes, (V), which would be susceptible to nucleophilic attack by water or hydroxide ion. The present paper discusses kinetic measurements on the hydrolysis of this imine in the presence and absence of copper(II) ions.


(V)

EXPERIMENTAL

N-2-Pyridylmethyleneaniline, (II), was prepared as follows. Freshly distilled pyridine-2-carbaldehyde (10.7 g, 0.10 mol) was added to a solution of aniline (9.3 g, 0.10 mol) in ethanol (30 cm^3). The mixture was heated under reflux

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[2] G. L. Eichhorn and I. M. Trachtenberg, *J. Amer. Chem. Soc.*, 1954, **76**, 5183.

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[9] A. C. Dash and R. K. Nanda, *J. Amer. Chem. Soc.*, 1969, **91**, 6944.

[10] L. F. Lindoy, *Quart. Rev.*, 1971, **25**, 379.

(*ca.* 0.5 h) and the ethanol removed *in vacuo*. The resulting yellow oil was stored *in vacuo* overnight and then chilled to 0 °C. Crystallisation was induced by scratching the container with a glass rod. The solid yellow *product* was recrystallised from the minimum volume of light petroleum (b.p. 40—60 °C), m.p. 32—33 °C, ν(CN) (imine) 1 630 cm^{-1}, ν(CN) (pyridine ring) 1 595 cm^{-1} in $CHCl_3$ solution (Found: C, 78.9; H, 5.6; N, 15.5. Calc. for $C_{12}H_{10}N_2$: C, 79.1; N, 5.5; N, 15.4%). The imine has previously been reported as a yellow oil,[11] b.p. 101—103 °C.

Kinetic Measurements.—The hydrolysis of the Schiff base was studied in the pH range 6.66—13.54 using a Schiff base concentration of 6×10^{-5} mol dm^{-3}. The reaction was monitored by observing the decrease in absorption at 310 nm. Plots of $\log(A_\infty - A_t)$ against time were linear for at least 4 half-lives. Hepes [4-(2-hydroxyethyl)piperazine-1-ethanesulphonic acid] buffer (5×10^{-3} mol dm^{-3}) was employed in the pH range 6.66—8.74 and borax buffer (2.5×10^{-3} mol dm^{-3}) in the pH range 9.04—9.83. Sodium hydroxide solutions were used for the pH range 10.20—13.54. The ionic strength was maintained at 0.1 mol dm^{-3} using $Na[ClO_4]$, except for the measurements at pH 13.26 and 13.54 where I was 0.25 and 0.5 mol dm^{-3} respectively. All kinetic measurements were carried out at 25.0 ± 0.1 °C.

In a typical run an aqueous solution of the buffer (Hepes or borax) was adjusted to the desired ionic strength with $Na[ClO_4]$ solution and the pH adjusted to the requisite value (pH meter) by adding concentrated acid or base by means of a syringe. The solution was equilibrated in a 1 cm cell at 25 °C and the reaction was initiated by adding 15 μl of the Schiff base dissolved in acetonitrile (1.2×10^{-2} mol dm^{-3}). The final concentration of the imine in the cell was 6×10^{-5} mol dm^{-3}.

The copper(II)-promoted reactions were studied at $I = 0.1$ mol dm^{-3}. Hepes Buffer (5×10^{-3} mol dm^{-3}) was used to maintain the pH since Hepes does not complex significantly with metal ions. The concentration of the imine was 1.6×10^{-5} mol dm^{-3} at pH < 8.0 and 0.8×10^{-5} mol dm^{-3} at pH > 8.0. The concentration of copper(II) perchlorate was varied between 8×10^{-4} mol dm^{-3} at pH 5.9 and 2×10^{-5} mol dm^{-3} at pH 8.4. Each kinetic run was made at three different copper(II) concentrations and at a constant ligand concentration. All reactions were independent of the metal-ion concentration, confirming that the ligand was fully complexed as the 1 : 1 species $[CuL]^{2+}$. Reactions were monitored at 310 nm on a Gilford 2400S spectrophotometer. Plots of $\log(A_t - A_\infty)$ against time were linear for at least 3 half-lives. The general technique employed was as follows. A solution containing 0.1 mol dm^{-3} $Na[ClO_4]$, 5×10^{-3} mol dm^{-3} Hepes, and the requisite concentration of copper(II) perchlorate was adjusted to the desired pH by addition of minute quantities (syringe) of concentrated sodium hydroxide solution. The solution was equilibrated in a 1 cm cell at 25 °C and 30 (or 15) μl of a stock solution of the imine (1.6×10^{-3} mol dm^{-3} in acetonitrile) were added using a microsyringe. Values of the hydrogen-ion and hydroxide-ion concentrations were obtained from the pH by using a molar activity coefficient of 0.775 [12] and a value of $pK_w = 14.00$ [13] at 25 °C.

RESULTS AND DISCUSSION

Hydrolysis in the Absence of Metal Ions.—The hydrolysis of (II) was studied over the pH range 6.66—13.54 (Table 1). The observed rate constants ($k_{obs.}$) at constant pH increased markedly in both acidic and basic solution and passed through a minimum at pH *ca.* 10.5 (Figure 1).

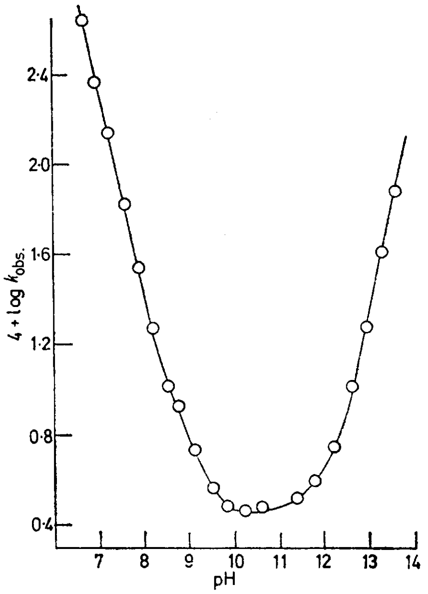

FIGURE 1 pH–Rate profile for the hydrolysis of *N*-2-pyridylmethyleneaniline

TABLE 1

pH Dependence of Schiff base hydrolysis at $I = 0.1$ mol dm^{-3} and 25 °C

pH	$10^4k_{obs.}/s^{-1}$
6.660	442
6.945	237
7.235	140
7.583	66.8
7.883	35.0
8.192	18.5
8.495	11.44
8.742	8.41
9.043	5.37
9.488	3.61
9.833	3.01
10.200	2.90
10.62	2.99
11.37	3.21
11.78	3.94
12.20	5.56

[NaOH] [a]/mol dm^{-3}	I/mol dm^{-3}	pH [b]	$10^4k_{obs}/s^{-1}$
0.050	0.10	12.59	10.95
0.100	0.10	12.89	18.83
0.250	0.25	13.26	41.2
0.500	0.50	13.54	77.0

[a] This is a reaction of hydroxide ion with a neutral substrate; the rate should be independent of ionic strength, and this was shown experimentally to be the case. [b] Calculated using activity coefficients obtained from ref. 13.

The reaction is subject to specific acid and specific base catalysis. Base catalysis in the hydrolysis of benzylideneaniline is not observable below pH 12,[14] but base catalysis occurs with salicylideneaniline at pH > 7.[15]

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N-2-Pyridylmethyleneaniline (L) is a diacidic base since protonation can occur at both the pyridine nitrogen and at the imine nitrogen atom. The ionisation equilibria can be represented by equations (1) and (2). The complete rate expression for the hydrolysis of the imine would be expected to take the form (3), so that $k_{obs.}$ is given by equation (4). At low pH (<8.5) plots of log $k_{obs.}$ against pH were linear with unit gradient, confirming a first-order dependence on the hydrogen-ion activity, so that expression (4) can be simplified to (5). Since the concentration of H_2L^{2+} at pH > 7 must be exceedingly small (pK_1 would be expected to be *ca.* 2), it is reasonable to assume expression (6), so that a plot of $k_{obs.}$ against $[H^+]$

$$H_2L^{2+} \overset{K_1}{\rightleftharpoons} HL^+ + H^+ \qquad (1)$$

$$HL^+ \overset{K_2}{\rightleftharpoons} L + H^+ \qquad (2)$$

$$\text{Rate} = k_{H_2O}'[H_2L^{2+}] + k_{OH}'[H_2L^{2+}][OH^-] + k_{H_2O}''[LH^+] + k_{OH}''[HL^+][OH^-] + k_{OH}'''[L][OH^-] + k_{H_2O}'''[L] \qquad (3)$$

$$k_{obs.} = ([H^+]^2k_{H_2O}'/K_1K_2) + ([H^+]K_wk_{OH}'/K_1K_2) + ([H^+]k_{H_2O}''/K_2) + (K_wk_{OH}'/K_2) + k_{H_2O}''' + [OH^-]k_{OH}''' \qquad (4)$$

$$k_{obs.} = ([H^+]K_wk_{OH}'/K_1K_2) + ([H^+]k_{H_2O}''/K_2) \qquad (5)$$

$$k_{obs.} = [H^+]k_{H_2O}''/K_2 \qquad (6)$$

should be linear with gradient k_{H_2O}''/K_2. Such plots were in fact linear with a gradient of 2.34×10^5 dm^3 mol^{-1} s^{-1}. A reasonable value for pK_2 for the Schiff base would be *ca.* 4.5 (*cf.* 4.7 for salicylideneaniline),[9] giving a value of *ca.* 7.0 s^{-1} for k_{H_2O}''. The requisite second-order constant obtained by dividing k_{H_2O}'' by the molar concentration of water is 1.26×10^{-1} dm^3 mol^{-1} s^{-1}. The constant k_{H_2O}'' refers to the process (7). (It should be noted that the reaction of OH^- with H_2L^{2+} will be rapid, so that although the concentration of H_2L^{2+} will be very small it could make some contribution to the reaction; the quoted value of k_{H_2O}'' is therefore an upper limit.)

$$HL^+ + H_2O \longrightarrow \text{Products} \qquad (7)$$

Dash and Nanda[9] reported a constant of 1.8×10^{-3} s^{-1} for the analogous reaction of salicylideneaniline. The monoprotonated form of *N*-2-pyridylmethyleneaniline thus undergoes hydrolysis some 4×10^3 times faster than *N*-salicylideneaniline. A lower value of pK_2 would lead to an increased value for k_{H_2O}''. At high pH (>12.5) a plot of log $k_{obs.}$ against pH was linear with a gradient of unity. At these pH values, the only kinetically significant process is the reaction $L + [OH]^- \longrightarrow$ Products. At higher pH values the rate expression can be simplified to (8), so that in this case we obtain (9) for $k_{obs.}$. A plot of $k_{obs.}$ against $[OH^-]$

$$\text{Rate} = k_{OH}''[HL^+][OH^-] + k_{H_2O}'''[L] + k_{OH}'''[L][OH^-] \qquad (8)$$

$$k_{obs.} = (k_{OH}''K_w/K_2) + k_{H_2O}''' + k_{OH}'''[OH^-] \qquad (9)$$

should be linear with gradient k_{OH}''' and intercept $((k_{OH}''K_w/K_2) + k_{H_2O}''')$. A plot of $k_{obs.}$ against $[OH^-]$ at pH > 12.5 was indeed linear with a gradient of 2.17×10^{-2} dm^3 mol^{-1} (= k_{OH}''') and intercept 2.8×10^{-4} s^{-1}. The last constant represents a pH-independent process due to one or both of the kinetically indistinguishable reactions (10) and (11).

$$L + H_2O \longrightarrow \text{Products} \qquad (10)$$

$$HL^+ + [OH]^- \longrightarrow \text{Products} \qquad (11)$$

Hydrolysis in the Presence of Copper(II).—Under the conditions of the experiments the ligand was fully complexed as the 1 : 1 complex $[CuL]^{2+}$, which presumably exists as the diaqua-species $[CuL(OH_2)_2]^{2+}$, (V), in solution. If ionisation of one of the water molecules occurs, $[CuL(OH_2)_2]^{2+} \longrightarrow [CuL(OH)(OH_2)]^+ + H^+$, the rate expression takes the form (12). It can be readily shown that $k_{obs.}$ is given by equation (13). At high pH, $[H^+]/K \longrightarrow 0$, so that expression (13) simplifies to (14).

$$\text{Rate} = k_{H_2O}'[CuL(OH_2)_2{}^{2+}] + k_{OH}'[CuL(OH_2)_2{}^{2+}][OH^-] + k_{H_2O}''[CuL(OH)(OH_2)^+] + k_{OH}''[CuL(OH)(OH_2)^+][OH^-] \qquad (12)$$

$$k_{obs.} = \{([H^+]k_{H_2O}'/K) + (K_wk_{OH}'/K) + k_{H_2O}'' + k_{OH}''[OH^-]\}\left\{\frac{1}{1 + ([H^+]/K)}\right\} \qquad (13)$$

$$k_{obs.} = (K_wk_{OH}'/K) + k_{H_2O}'' + k_{OH}''[OH^-] \qquad (14)$$

A plot of $k_{obs.}$ against $[OH^-]$ should be linear with gradient k_{OH}'' and intercept $(K_wk_{OH}'/K) + k_{H_2O}''$. The gradient of such a plot (Figure 2) gives $k_{OH}'' = 2.75 \times 10^3$ dm^3 mol^{-1} s^{-1} and an intercept of 2.58×10^{-3} s^{-1}.

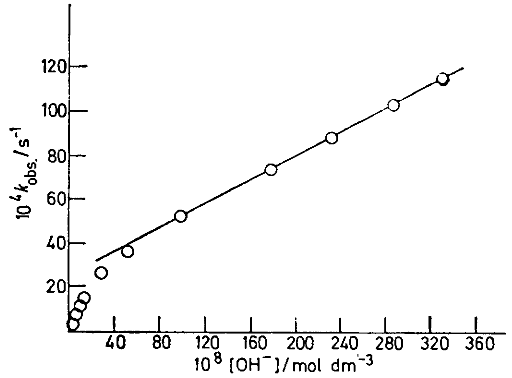


FIGURE 2 Plot of $k_{obs.}$ against hydroxide-ion concentration for the hydrolysis of the 1 : 1 copper(II)–Schiff base complex, (V)

At low pH, $[H^+]/K$ becomes very large so that $\{1 + ([H^+]/K)\}$ can be approximated to $[H^+]/K$ and in this case $k_{obs.} = k_{H_2O}' + k_{OH}'[OH^-]$. A plot of $k_{obs.}$ against $[OH^-]$ was linear (Figure 3) with a gradient of 9.72×10^3 dm^3 mol^{-1} s^{-1} (= k_{OH}') and intercept 1.75×10^{-4} s^{-1} (= k_{H_2O}'). The last constant can be converted into the second-order constant by dividing by the molar concentration of water (55.5 mol dm^{-3}) giving 3.15 × 10^{-6} dm^3 mol^{-1} s^{-1}. Water hydrolysis of $[CuL(OH)_2)_2]^{2+}$ is *ca.* 3 × 10^9 times slower than base hydrolysis at 25 °C, a result consistent with the relative nucleophilicities of water and hydroxide ion.

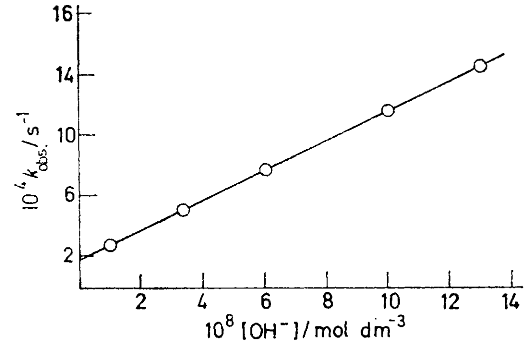


FIGURE 3 Plot of $k_{obs.}$ against hydroxide-ion concentration for the hydrolysis of the 1 : 1 copper(II)–Schiff base complex (V), at pH < 7.0

TABLE 2

Copper(II)-promoted hydrolysis at 25 °C and I = 0.1 mol dm^{-3}

pH	$10^8[OH^-]$/mol dm^{-3}	$10^4 k_{obs.}/s^{-1}$
5.888	1.00	2.75
6.410	3.33	5.05
6.672	6.09	7.67
6.890	10.00	11.57
7.000	12.95	14.45
7.325	27.38	26.7
7.597	51.22	36.1
7.880	98.25	52.2
8.136	177.2	73.3
8.248	230.0	87.9
8.344	286.0	103.3
8.405	329.1	115.2

In ester hydrolysis, the quotients k_{OH}/k_{H_2O} usually fall within the range [16] 10^9—10^{11}.

It would be expected that $k_{H_2O}'' \ll k_{H_2O}'$, *i.e.* $k_{H_2O}'' \ll 1.75 \times 10^{-4}$ s^{-1}. Since $(K_w k_{OH}'/K) + k_{H_2O}'' = 2.58 \times 10^{-3}$ s^{-1}, $K_w k_{OH}'/K \sim 2.58 \times 10^{-3}$ s^{-1} and $K_w/K = 2.65 \times 10^{-7}$ mol dm^{-3}. The constant K_w in the present scheme is defined as the product $[H^+][OH^-] = 1.0 \times 10^{-14}/(0.772)^2 = 1.68 \times 10^{-14}$ mol^2 dm^{-6}. (The activity coefficient of a 1 : 1 electrolyte at I = 0.1 mol dm^{-3} was calculated from the Davies equation.[12]) Thus $K = 1.68 \times 10^{-14}/2.65 \times 10^{-7} = 6.34 \times 10^{-8}$ mol dm^{-3} giving pK_a = 7.20. The kinetic value of pK_a falls well within the range of pK_a values of aquacopper(II) species determined by direct measurement and supports the various assumptions made in the calculation.

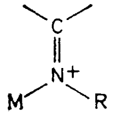
Conclusions.—The kinetic data obtained are summarised in Table 3. Base hydrolysis of $[CuL(OH_2)_2]^{2+}$ is some 4.4 × 10^5 times faster than base hydrolysis of L and some 3.5 times faster than the aquahydroxo-species $[CuL(OH)(OH_2)]^+$. The rate accelerations are very similar to the value of 10^6 observed in the metal-ion promoted base hydrolysis of carboxylic esters,[17] a result not totally unexpected in view of the similarity of the structures (VI) and (VII). Entropy effects have been shown to be the prime source of the large rate accelerations for carboxylic esters. Bimolecular reactions have $\Delta S^\ddagger$ values in the range −20 to −60 J K^{-1} mol^{-1}.[18] The orientation of solvent molecules around charges or developing charges in the transition state results in a negative entropy change and the effect may be as large or larger than that resulting from the molecularity of the reaction. The metal ion can be regarded as solvating the developing negative charge on the nitrogen atom when attack by hydroxide occurs at the carbon centre. Such an effect leads to more positive entropies of activation and accelerated reaction rates.

TABLE 3

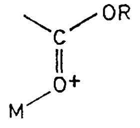
Summary of kinetic data at 25 °C and I = 0.1 mol dm^{-3}

Reaction	k/dm^3 mol^{-1} s^{-1}
$HL^+ + H_2O$	1.26 × 10^{-1}
$L + [OH]^-$	2.17 × 10^{-2}
$\left\{\begin{matrix} L + H_2O \\ HL^+ + OH^- \end{matrix}\right\}$	2.8 × 10^{-4} *
$[CuL(OH_2)_2]^{2+} + H_2O$	3.15 × 10^{-6}
$[CuL(OH_2)_2]^{2+} + [OH]^-$	9.72 × 10^3
$[CuL(OH)(OH_2)]^+ + [OH]^-$	2.75 × 10^3

* Units are s^{-1}.



(VI)



(VII)

We thank the S.R.C. for support.

[5/1543 *Received, 5th August*, 1975]

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