

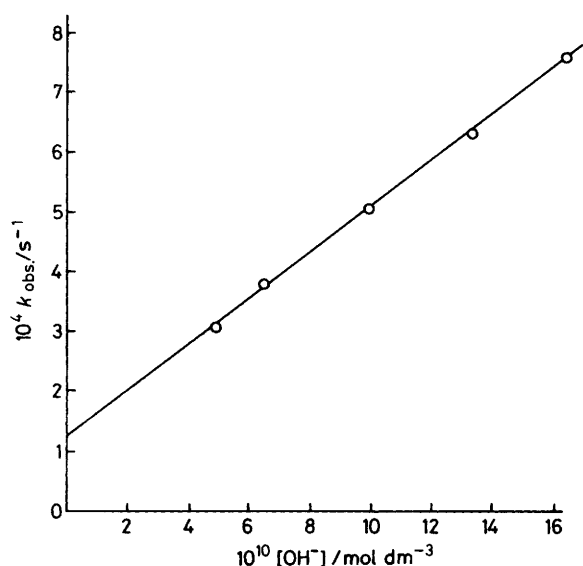
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Spectrophotometric monitoring was carried out using a Gilford 2400S spectrophotometer. A concentrated methanolic solution of the ester (0.05 cm^3) was added to the appropriate acetate buffer and the increase in absorbance due to the release of 4-nitrophenol monitored at 320 nm. Reactions were followed for 5–6 half lives and the A_∞ values recorded after 12–14 half lives. The observed first-order rate constants (k_{obs}) were evaluated from the absorbance data using a desk top computer. The quoted rate constants, k_{obs} , are the mean values of at least three kinetic runs, the experimental spread was normally less than $\pm 5\%$. Derived rate constants were obtained from the least-squares slope and intercept of the linear plots as described in the Results and Discussion section. In all cases the initial ester concentration was $3.67 \times 10^{-4} \text{ mol dm}^{-3}$. Values of the hydroxide ion concentration were determined from the pH using a molar activity coefficient calculated from the Davies' equation¹⁰ (0.768 at 35°C) and a value¹¹ of $\text{p}K_{\text{w}} = 13.680$ at 35°C . Carbon dioxide is known to catalyse the hydrolysis of aryl esters of α -amino acids⁶ and precautions were taken to prevent any CO_2 contamination of solutions.

Table 1. Hydrolysis of HL^+ in acetate buffer at $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3) and 35°C *

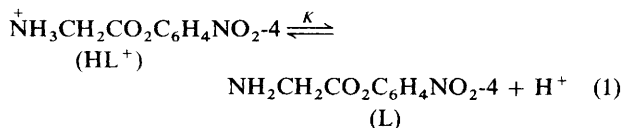
pH	$10^{10}[\text{OH}^-]/\text{mol dm}^{-3}$	$10^4 k_{\text{obs.}}/\text{s}^{-1}$
4.25	4.84	3.05
4.37	6.38	3.81
4.56	9.88	5.04
4.69	13.32	6.30
4.78	16.39	7.58

* Reaction monitored spectrophotometrically at 320 nm. Least-squares analysis gives $k_0 = 1.26 \times 10^{-4} \text{ s}^{-1}$ ($k_{\text{H}_2\text{O}} = 2.27 \times 10^{-6} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) and $k_{\text{OH}} = 3.83 \times 10^5 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$.

**Figure 1.** Hydrolysis of $\text{NH}_3\text{CH}_2\text{CO}_2\text{C}_6\text{H}_4\text{NO}_2\text{-4}$ (HL^+) at 35°C and $I = 0.1 \text{ mol dm}^{-3}$ over the pH range 4.25–4.78

Results and Discussion

The ionization equilibrium of 4-nitrophenyl glycinate can be represented by equation (1). Rapid potentiometric titration of



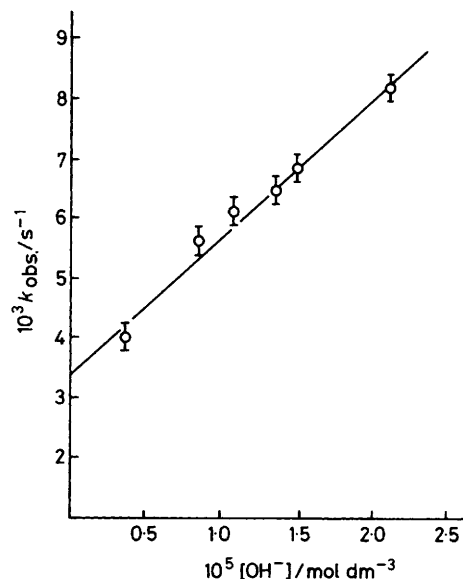
the ester hydrobromide at 25°C and $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3) indicated a $\text{p}K$ of *ca.* 7.1. Base hydrolysis of the ligand is quite rapid, and there is considerable pH drift at higher pH values.

The hydrolysis of the ester was studied in the pH range 4.25–4.78 at 35°C , Table 1. In this pH range all the ester will be essentially present as HL^+ . A plot of $k_{\text{obs.}}$ (the observed first-order rate constant) versus the hydroxide ion concentration is linear with a positive intercept, Figure 1, indicating that $k_{\text{obs.}} = k_0 + k_{\text{OH}}[\text{OH}^-]$. The k_0 term can be assigned to water attack on the protonated ester HL^+ and the k_{OH} term to base hydrolysis of HL^+ . At 35°C least-squares analysis gives $k_0 = 1.26 \times 10^{-4} \text{ s}^{-1}$ and $k_{\text{OH}} = 3.83 \times 10^5 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. The k_0 rate constant can be converted to a second-order rate constant ($k_{\text{H}_2\text{O}}$) using the expression $k_{\text{H}_2\text{O}} = k_0/55.5$, where 55.5 mol dm^{-3} is the molar concentration of water. At 35°C the value of $k_{\text{H}_2\text{O}}$ is $2.27 \times 10^{-6} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. The nucleophilicity ratio

Table 2. Hydrolysis of L at 35°C and $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3) *

pH	$10^5[\text{OH}^-]/\text{mol dm}^{-3}$	$10^3 k_{\text{obs.}}/\text{s}^{-1}$
8.15	0.38	3.99
8.50	0.86	5.60
8.60	1.08	6.13
8.70	1.36	6.44
8.74	1.50	6.82
8.89	2.11	8.18

* Least-squares analysis gives $k_0 = 3.37 \times 10^{-3} \text{ s}^{-1}$ ($k_{\text{H}_2\text{O}} = 6.07 \times 10^{-5} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) and $k_{\text{OH}} = 2.32 \times 10^2 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$.

**Figure 2.** Hydrolysis of $\text{NH}_2\text{CH}_2\text{CO}_2\text{C}_6\text{H}_4\text{NO}_2\text{-4}$ (L) at 35°C and $I = 0.1 \text{ mol dm}^{-3}$ over the pH range 8.15–8.89

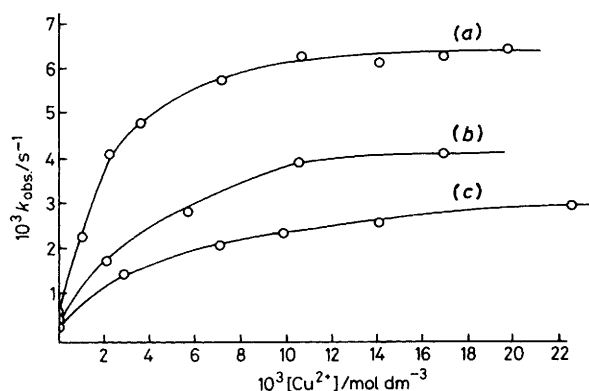
$k_{\text{OH}}/k_{\text{H}_2\text{O}} = 1.7 \times 10^{11}$ at 35°C is of the expected magnitude for the relative nucleophilicity of water and hydroxide ion in ester hydrolysis.^{12,13}

The hydrolysis of the unprotonated ester L was studied by pH-stat at $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3) in the pH range 8.1–8.9. The rate constants obtained at 35°C are summarised in Table 2. In this case plots of $k_{\text{obs.}}$ versus the hydroxide ion concentration are also linear with a positive intercept indicating that $k_{\text{obs.}} = k_0 + k_{\text{OH}}[\text{OH}^-]$, Figure 2. Values of k_0 and k_{OH} were estimated from the least-squares intercept and slope of the plot. At 35°C , $k_0 = 3.37 \times 10^{-3} \text{ s}^{-1}$ and $k_{\text{OH}} = 2.32 \times 10^2 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. The k_0 term is considered to be due to water attack on the ester L with $k_{\text{H}_2\text{O}} = k_0/55.5 = 6.07 \times 10^{-5} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. In this case the nucleophilicity ratio $k_{\text{OH}}/k_{\text{H}_2\text{O}}$ is 3.8×10^7 . Base hydrolysis of HL^+ is some 1.65×10^3 times faster than that of L at 35°C .

The Copper(II) Promoted Reaction.—The reactions in the presence of copper(II) were all studied at a constant ester concentration of $3.67 \times 10^{-4} \text{ mol dm}^{-3}$. Preliminary measurements at pH 4.56 and a total copper(II) concentration of $1.05 \times 10^{-3} \text{ mol dm}^{-3}$ established that the half life of the ester was *ca.* 5.1 min, indicating a significant rate enhancement. The reaction is first order in the ester concentration, and at low copper(II) concentrations, also shows a first-order dependence on the copper(II) concentration. At high metal to ligand ratios,

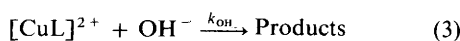
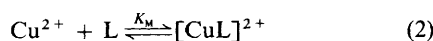
Table 3. Values of k_{obs} for the copper(II) promoted hydrolyses of 4-nitrophenyl glycinate at $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3) at various pH values at 35°C

$10^3[\text{Cu}^{2+}]/\text{mol dm}^{-3}$	$10^3 k_{\text{obs}}/\text{s}^{-1}$	$10^3[\text{Cu}^{2+}]/\text{mol dm}^{-3}$	$10^3 k_{\text{obs}}/\text{s}^{-1}$
(a) pH 4.25 ($[\text{OH}^-] = 4.86 \times 10^{-10} \text{ mol dm}^{-3}$)			
0.0	0.31	9.8	2.41
2.8	1.48	14.0	2.64
7.0	2.14	22.4	3.14
(b) pH 4.37 ($[\text{OH}^-] = 6.44 \times 10^{-10} \text{ mol dm}^{-3}$)			
0.0	0.38	10.5	4.01
2.1	1.77	16.8	4.20
5.6	2.86		
(c) pH 4.56 ($[\text{OH}^-] = 9.79 \times 10^{-10} \text{ mol dm}^{-3}$)			
0.0	0.50	10.50	6.36
1.05	2.28	14.00	6.22
2.10	4.14	16.80	6.39
3.50	4.81	19.60	6.58
7.00	5.76		
(d) pH 4.69 ($[\text{OH}^-] = 13.23 \times 10^{-10} \text{ mol dm}^{-3}$)			
0.0	0.63	5.6	7.49
1.4	3.60	11.2	8.63
2.8	5.22	17.5	8.65
(e) pH 4.78 ($[\text{OH}^-] = 16.2 \times 10^{-10} \text{ mol dm}^{-3}$)			
0.0	0.76	4.20	7.80
0.52	2.90	7.14	10.08
1.05	4.94	10.50	10.78
2.10	6.58	16.80	10.82

**Figure 3.** Plots of k_{obs} versus the total concentration of copper(II) at a total ester concentration of $3.67 \times 10^{-4} \text{ mol dm}^{-3}$ and pH (a) 4.56, (b) 4.37, (c) 4.25; temperature 35°C and $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3)

the reaction rate is independent of the copper(II) concentration, Table 3 and Figure 3.

The copper(II) promoted reaction can be rationalised in terms of equations (2) and (3). There is a rapid pre-equilibrium



formation of $[\text{CuL}]^{2+}$ followed by a slow rate-determining base hydrolysis step. It can be readily shown that equation (4) applies

$$k_{\text{obs}} = k_0 + \frac{k K_M [\text{Cu}^{2+}]}{(1 + K_M [\text{Cu}^{2+}])} \quad (4)$$

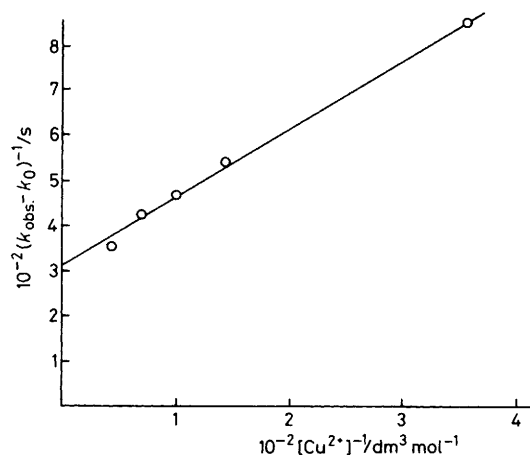
Table 4. Values of k , k_{OH} , and $\log K_M$ obtained from plots of $(k_{\text{obs}} - k_0)^{-1}$ versus $[\text{Cu}^{2+}]^{-1}$ at 35°C and $I = 0.1 \text{ mol dm}^{-3}$ (KNO_3)

pH	$10^{10}[\text{OH}^-]/\text{mol dm}^{-3}$	$10^3 k/\text{s}^{-1}$	$\log K_M$	$10^{-6} k_{\text{OH}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
4.25	4.86	3.23	2.30	6.7
4.37	6.44	4.76	2.30	7.4
4.56	9.79	7.69	2.48	7.9
4.69	13.23	10.53	2.45	7.9
4.78	16.20	12.82	2.61	7.9

Table 5. Plateau values of k_{obs} as a function of the hydroxide ion concentration at 35°C *

pH	$10^{10}[\text{OH}^-]/\text{mol dm}^{-3}$	$10^3 k_{\text{obs}}/\text{s}^{-1}$	$10^{-6} k_{\text{OH}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
4.25	4.84	3.14	6.5
4.37	6.38	4.20	6.6
4.56	9.88	6.58	6.7
4.69	13.32	8.65	6.5
4.78	16.39	10.82	6.6

* Plateau values of k_{obs} taken from Table 3.

**Figure 4.** Double reciprocal plot for the copper(II) promoted hydrolysis of 4-nitrophenyl glycinate at pH 4.25 (35°C and $I = 0.1 \text{ mol dm}^{-3}$). Least-squares analysis gives an intercept of $3.1 \times 10^2 \text{ s}$ and a slope of $1.55 \text{ dm}^3 \text{ mol}^{-1} \text{ s}$ with a correlation coefficient of 0.996

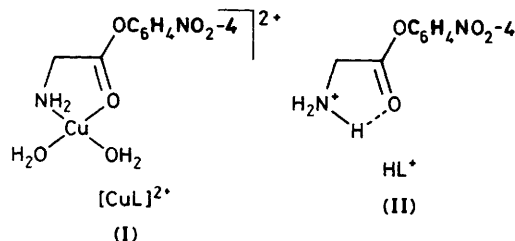
to this system, where k_{obs} is the observed first-order rate constant at constant pH, k_0 is the rate constant due to the background solvolytic reaction in the absence of copper(II), and $k_{\text{OH}} = k/[\text{OH}^-]$. Rearranging equation (4) gives equation (5).

$$1/(k_{\text{obs}} - k_0) = 1/k K_M [\text{Cu}^{2+}] + 1/k \quad (5)$$

A plot of $1/(k_{\text{obs}} - k_0)$ versus $1/[\text{Cu}^{2+}]$ should be linear of slope $1/k K_M$ and intercept $1/k$. Such double reciprocal plots are indeed linear, Figure 4. Values of k and K_M obtained from such plots are summarised in Table 4. The average value of K_M is $270 \text{ dm}^3 \text{ mol}^{-1}$ ($\log K_M = 2.43$) at 35°C which may be compared with $\log K_M = 3.83$ for the chelated copper(II) complex of ethyl glycinate at 25°C .¹⁴ A plot of k versus $[\text{OH}^-]$ is linear, passing through the origin with a least-squares slope of $7.86 \times 10^6 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ which is the value of k_{OH} at 35°C and $I = 0.1 \text{ mol dm}^{-3}$. The individual values of k_{OH} listed in Table 4 indicate the 'clean' first-order dependence on the hydroxide ion concentration and the lack of any solvolytic reaction.

Table 6. Summary of the kinetic data at 35 °C

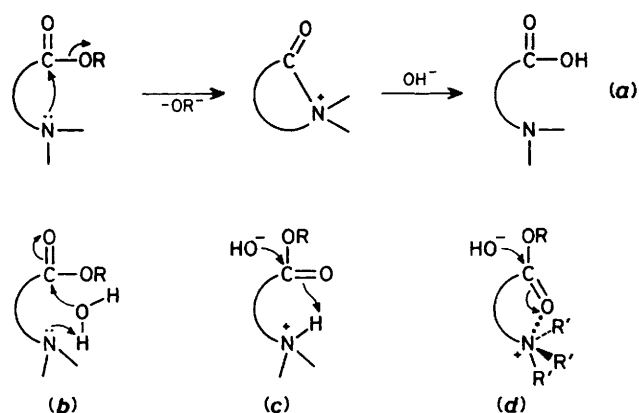
Reaction	$k/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
$\text{HL}^+ + \text{H}_2\text{O}$	2.3×10^{-6}
$\text{HL}^+ + \text{OH}^-$	3.8×10^5
$\text{L} + \text{H}_2\text{O}$	6.1×10^{-5}
$\text{L} + \text{OH}^-$	2.3×10^2
$[\text{CuL}]^{2+} + \text{OH}^-$	6.6×10^6



The rate constant k_{OH} can also be obtained directly from the experimentally determined plateau values of k_{obs} (as all the substrate is present as $[\text{CuL}]^{2+}$). Values of k_{OH} determined by this method are listed in Table 5, giving a least-squares value of $6.6 \times 10^6 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ with a correlation coefficient 0.9997.

The final kinetic data obtained are summarised in Table 6. A direct comparison of values of k_{OH} for $[\text{CuL}]^{2+}$, L, and HL^+ gives: $k_{\text{OH}}^{\text{CuL}^{2+}}/k_{\text{OH}}^{\text{L}} = 3 \times 10^4$, $k_{\text{OH}}^{\text{CuL}^{2+}}/k_{\text{OH}}^{\text{HL}^+} = 18$, and $k_{\text{OH}}^{\text{HL}^+}/k_{\text{OH}}^{\text{L}} = 1.65 \times 10^3$. The rate acceleration of 3.4×10^4 fold observed with $[\text{CuL}]^{2+}$ at 35 °C is consistent with the formation of the chelate (I) in which the aryloxycarbonyl group also acts as a donor, leading to significant polarisation of the carbonyl group.

The species HL^+ is also quite reactive towards base hydrolysis. A variety of mechanisms are available for neighbouring amino group facilitation of ester hydrolysis.¹⁵ These mechanisms (Scheme) include (a) intramolecular nucleophilic catalysis, (b) intramolecular general base catalysis, (c) intramolecular general-acid specific-base catalysis, and (d) electrostatic facilitation due to the formal positive charge on the conjugate acid species. Mechanisms (a), (b), and (c) are kinetically indistinguishable. Base hydrolysis of $\text{Et}_3\text{NCH}_2\text{-CO}_2\text{Et}$ is 200 times faster than that of $\text{CH}_3\text{CO}_2\text{Et}$ due to electrostatic facilitation of the reaction.¹⁶ In the present system intramolecular nucleophilic catalysis (which is favoured where a good leaving group is involved) is unlikely as the formation of a three-membered ring lactam is required. It is probable that a combination of electrostatic facilitation and 'hydrogen bond' catalysis^{17,18} of the type shown in (II) accounts for the relatively high activity of the HL^+ species in base hydrolysis.

**Scheme.**

Acknowledgements

We wish to thank the S.E.R.C. for financial support and the award of a post-doctoral fellowship (to A. K. B.).

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Received 15th January 1985; Paper 5/080