Metal-ion-promoted Hydrolysis of Methyl 8-Hydroxyquinoline-2-carboxylate

By **Robert W. Hay** * and **Charles R. Clark**, Chemistry Department, University of Stirling, Stirling FK9 4LA

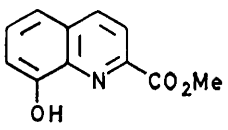
Base hydrolysis of the title compound (EH) has been studied over the range pH 9.18—12.1 and values of k_{OH} determined for EH (k_{OH} 4.0 dm^3 mol^{-1} s^{-1}) and for the anion E$^-$ (k_{OH} 0.485 dm^3 mol^{-1} s^{-1}) at 25 °C and I = 0.1 mol dm^{-3}. Formation constants K_{ME^+} have been obtained at 25 °C and I = 0.1 mol dm^3 for the equilibrium $M^{2+} + E^- \rightleftharpoons [ME]^+$ using both spectrophotometric and kinetic methods. Rate constants for the base hydrolysis of the [ME]$^+$ complexes (M^{II} = Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, or Zn^{II}) have been determined together with the values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ at 298 K. Quite large rate accelerations are observed (10^3—10^6) when comparisons are made with the base hydrolysis of E$^-$. The origin of the rate accelerations is discussed in terms of the thermodynamic activation parameters obtained and possible mechanisms for the reaction are considered.

In recent years a number of studies have been made of metal-ion-promoted ester hydrolysis and the topic is the subject of a current review.[1] Many of these reactions are difficult to study in detail as the formation constants of the metal complexes involved are rather low, and in addition a number of different catalytically active species may be present in solution. In the present paper we

---

[1] R. W. Hay and P. J. Morris, in 'Metal Ions in Biological Systems,' vol. 5, ed. H. Sigel, Marcel Dekker, New York, 1976, ch. 4.

have studied the effect of a variety of metal ions (Mn^{II}, Co^{II}, Ni^{II}, Cu^{II}, and Zn^{II}) on the hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate (1). This ligand binds



(1) = EH

quite strongly to metals and it is possible, using high metal-to-ligand ratios, to completely form the 1 : 1 complex $[ME]^+$ and hence study the base-hydrolysis rates of these complexes. A further aim of the present work was to determine the requisite activation parameters for base hydrolysis of the $[ME]^+$ species so that the relative effects of various metal ions in promoting ester hydrolysis could be more thoroughly understood.

EXPERIMENTAL

2-Cyanoquinolin-8-ol was prepared as previously described.[2]

8-Hydroxyquinoline-2-carboxylic Acid.—2-Cyanoquinolin-8-ol (3.40 g, 0.02 mol) in water (50 cm^3) was heated under reflux with sodium hydroxide (6.0 g) until ammonia was no longer evolved (4—5 h). The solution was cooled to room temperature and hydrochloric acid (5 mol dm^{-3}) was added until the yellow acid was completely precipitated (pH *ca.* 4). The crude *product* was recrystallised from aqueous dimethylformamide to give large yellow-brown crystals, m.p. 217—218 °C (Found: C, 63.2; H, 3.9; N, 7.5. Calc. for $C_{10}H_7NO_3$: C, 63.5; H, 3.7; N, 7.4%). Irving and Pinnington [3] prepared 8-hydroxyquinoline-2-carboxylic acid (m.p. 211 °C) by catalytic demethylation of 8-methoxyquinoline-2-carboxylic acid. A subsequent report,[4] where the same preparative procedure was employed, gives the m.p. as 216—217 °C.

Methyl 8-Hydroxyquinoline-2-carboxylate Hemihydrate.—Dry hydrogen chloride gas was bubbled continuously through a suspension of powdered 8-hydroxyquinoline-2-carboxylic acid (2.5 g, 0.137 mol) in anhydrous methanol (35 cm^3) until all the solid had dissolved. The resulting solution was then poured into dry diethyl ether (500 cm^3) and the precipitated yellow ester hydrochloride was filtered off, washed with ether, and dried *in vacuo*. A suspension of the *product* in water (100 cm^3) was titrated to pH 6 with 2,6-dimethylpyridine and the free-base form of the ester was recovered by filtration. After treatment with decolourising charcoal, the ester was recrystallised from methanol–water to give fine golden needles, m.p. 105—106 °C, ν(C=O) 1 715 cm^{-1} (Found: C, 62.2; H, 4.9; N, 6.6. Calc. for $C_{11}H_9NO_3 \cdot 0.5H_2O$: C, 62.2; H, 4.75; N, 6.6%). The i.r. and n.m.r. spectra both confirmed the presence of water of crystallisation.

Deuterium oxide (99.8%) was supplied by Fluorochem Ltd. Piperazine-*NN'*-bis(ethane-2-sulphonic acid) (pipes) and *N*-(2-hydroxyethyl)piperazine-*N'*-ethane-2-sulphonic acid (hepes) were B.D.H. biochemical reagents. Morpholine (b.p. 128 °C) and triethylamine (b.p. 89 °C) were redistilled prior to use. Zinc(II) perchlorate hexahydrate was prepared by reaction of perchloric acid with 'basic' zinc carbonate and its solutions were standardised by titration with ethylenediamine tetra-acetic acid. All the other metal salts were AnalaR grade.

Kinetic Measurements.—The reactions were followed spectrophotometrically using a Gilford 2 400S instrument. The ionic strength of the solutions was 0.1 mol dm^{-3}. Normally a methanolic solution of the ester (5—10 μl) was injected into the appropriate temperature-equilibrated reaction mixture (3.0 cm^3) in a cell of 1-cm pathlength. The cell contents were then mixed by rapidly inverting the stoppered cell three or four times before measurements were begun.

The base hydrolysis was monitored by following the decrease in absorbance at 420 nm. In the range pH 9.2—11.5, borate and triethylamine buffers were used to effect pH control. No significant catalysis by buffer species was observed. At pH > 11.5, reactions were carried out using sodium hydroxide solutions. The concentration of hydroxide ion or buffer species was at least 70 times that of the substrate (initial concentration, 1.33×10^{-4} mol dm^{-3}) so that first-order kinetics were observed.

The metal-ion-catalysed hydrolyses were studied using solutions of metal perchlorate salts with the exception of the manganese(II) reactions where manganese(II) chloride was employed. In each case the appearance of the product acid (or the metal ion–acid complex) was monitored in the 257—280 nm region, at the wavelength where the absorbance change was greatest under the particular conditions employed. The initial concentration of the ester in the metal-promoted reactions was in the range 1×10^{-5}—5×10^{-5} mol dm^{-3}.

The observed first-order rate constants ($k_{obs.}$) for the hydrolyses in both the presence and absence of metal ions were obtained from plots of $\log(A_t - A_\infty)$ or $\log(A_\infty - A_t)$ against time, where A = absorbance. Kinetic runs giving plots which were not linear over at least three half-lives were rejected. The temperature of the cell compartment was monitored periodically during the course of a kinetic run. A deviation of $> \pm 0.2$ °C was considered unacceptable. The pH of the solutions used in the kinetic runs was determined prior to reaction and periodic checks were made at the end of the reaction to ensure that no significant pH drift occurred. Measurements of pH were made with a Radiometer 26 pH meter equipped with a G202B high-alkalinity glass electrode and a K401 calomel electrode. The electrode assembly was standardised with both 10^{-2} mol dm^{-3} $Na_2[B_4O_7] \cdot 10H_2O$ and 5×10^{-2} mol dm^{-3} oven-dried (110 °C) potassium hydrogenphthalate (pH 9.180 and 4.008 at 25 °C, respectively). Hydroxide-ion concentrations at 25 °C were obtained from the pH using a value of 0.772 for the mean molar activity coefficient at $I = 0.1$ mol dm^{-3} and $pK_w = 13.997$; concentrations at other temperatures were obtained using the values of pK_w listed by Robinson and Stokes [5] and molar activity coefficients (γ) obtained from the Davies equation [6] (1). Pronounced but reversible poisoning of the

$$-\log \gamma = Az_1z_2\{[I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}})] - 0.2I\} \qquad (1)$$

glass electrode occurred with certain solutions of Mn^{II} which ultimately precipitated manganese(II) hydroxide on storage. In these cases the pH measurements were made on solutions lacking the metal ion but containing all the other reagents. The pD values were taken as the pH meter

---

[2] C. R. Clark and R. W. Hay, *J.C.S. Dalton*, 1974, 2148.

[3] H. Irving and A. R. Pinnington, *J. Chem. Soc.*, 1954, 3782.

[4] W. R. Turner and J. T. Stock, *J. Chem. Soc.*, 1965, 1506.

[5] R. A. Robinson and R. H. Stokes, 'Electrolyte Solutions,' 2nd edn., Butterworths, London, 1959.

[6] C. W. Davies, *J. Chem. Soc.*, 1938, 2093.

readings plus the appropriate correction factor for the liquid-junction potential given by Fife and Bruice[7] [equation (2)]. At 25 °C, pD = pH(meter reading) + 0.40. Values

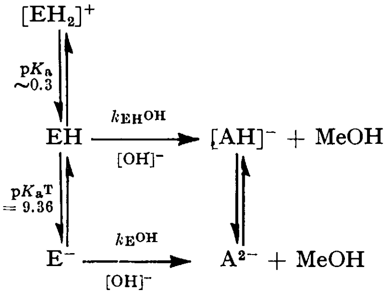
$$\text{pD} = \text{pH(meter reading)} + 1\,429\,(T/K) - 1.04 \qquad (2)$$

of pOD at 25 °C were calculated from pD using a value for D_2O of pK 14.81.[8,9] Deuteroxide concentrations were obtained from pOD using a value of 0.772 for the mean molar activity coefficient at 25 °C and $I = 0.1$ mol dm^{-3}. A recent study has confirmed that at low ionic strengths the activity coefficients of alkali-metal deuteroxides in D_2O are closely comparable with those of the corresponding hydroxides in water.[10]

pK_a *Measurements.*—The pK_a (phenolic group ionisation) of methyl 8-hydroxyquinoline-2-carboxylate was determined spectrophotometrically at 25 °C and $I = 0.1$ mol dm^{-3} by the method of Albert and Serjeant.[11] Measurements were made by mixing a solution of the ester with an equal volume of the appropriate buffer and recording the absorbance of the resulting solution at 399 nm. Hydrolysis of the substrate was negligible in the time scale (*ca.* 20 s) of the measurement except in the case where the solution pH was sufficiently high (>11.5) to fully generate the ester anion. In this case the problem of hydrolysis was overcome by the choice of the analytical wavelength, an isosbestic point for the conversion of the ester anion into the corresponding carboxylate dianion. The relevant experimental data are in Table 1. The mean value of pK_a^M is 9.25 ± 0.03 (pK_a^M = the mixed constant involving the hydrogen-ion activity and the concentrations of the other species). The proton-ionisation constant for the dissociation of the conjugate base ($\overset{+}{N}$H ionisation) was not determined with precision. Spectroscopic measurements indicated *ca.* 50% protonation of the quinoline nitrogen in 0.3 mol dm^{-3} HCl at 25 °C.

RESULTS

Base Hydrolysis of the Ester.—The kinetic scheme for the base hydrolysis of methyl 8-hydroxyquinoline-1-carboxylate can be summarised:



Here A^{2-} = the dianion of 8-hydroxyquinoline-2-carboxylic acid.

The ionisation of the phenolic hydroxy-group of the ester can be represented as $EH \rightleftharpoons E^- + H^+$ with pK_a^M 9.25 at 25 °C and $I = 0.1$ mol dm^{-3} (pK_a^T 9.36), Table 1.

In the range pH 9.2—12.2 used in the kinetic measurements, equations (3) and (4) are obeyed where $k_{\text{obs.}}$ is the

$$\text{Rate} = k_{EH}^{OH}[EH][OH^-] + k_{E^-}^{OH}[E^-][OH^-] \qquad (3)$$

$$= k_{\text{obs.}}([EH] + [E^-]) \qquad (4)$$

observed first-order rate constant at constant pH. The concentration of E^- is given by the expression $[E^-] = K_a^M[EH]/a_{H^+}$ where a_{H^+} is the hydrogen-ion activity. It can be readily shown by substituting in equations (3) and (4) that (5) also applies. A plot of the left-hand side of

$$k_{\text{obs.}}/[OH^-](a_{H^+} + K_a^M) = k_{EH}^{OH}a_{H^+} + k_{E^-}^{OH}k_a^M \qquad (5)$$

equation (5) against a_{H^+} should be linear of gradient k_{EH}^{OH} and intercept $k_{E^-}^{OH}K_a^M$. The data in Table 2 give a linear plot with $k_{EH}^{OH} = 4.0$ dm^3 mol^{-1} s^{-1} and $k_{E^-}^{OH} = 0.485$ dm^3 mol^{-1} s^{-1} at 25 °C and $I = 0.1$ mol dm^{-3}. The second term of equation (3) can only be attributed to specific base hydrolysis of E^-; however, the first term of equation (3) could be assigned to specific base hydrolysis of EH or to the kinetically equivalent pH-independent reaction of E^-. The ionised phenolic group is too far removed from the reaction centre to influence the reaction by intramolecular general base catalysis; we therefore conclude that specific base hydrolysis of EH occurs.

TABLE 1

Spectrophotometric determination of the pK_a of methyl 8-hydroxyquinoline-2-carboxylate (EH) at 25 °C and $I = 0.1$ mol dm^{-3}

pH	A (399 nm)	pK_1^M
7.0	0.196 (EH)	
8.510	0.307	9.24
8.750	0.358	9.28
8.940	0.427	9.26
9.130	0.504	9.25
9.320	0.583	9.24
9.576	0.687	9.23
9.770	0.749	9.25
11.5	0.909 (E^-)	

Mean 9.25 ± 0.03

pK_1^M 9.25 ± 0.03, pK_1^T 9.36.

TABLE 2

Rate constants for the base hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate at 25.0 °C and $I = 0.1$ mol dm^{-3} (KCl)

pH	$10^4k_{\text{obs.}}/\text{s}^{-1}$	$10^4k_{\text{calc.}}{}^a/\text{s}^{-1}$
9.185 [b]	0.447	0.447
9.610 [b]	0.753	0.787
9.980	1.27	1.27
10.360	2.10	2.22
10.715	4.20	4.00
11.095	8.78	8.33
11.490	18.3	19.8
11.895 [c]	48.7	49.2
12.195 [c]	97.2	97.3

[a] Calculated according to equation (5). Reaction media, 10^{-2} mol dm^{-3} in triethylamine buffer unless otherwise stated. [b] Reaction media, 10^{-2} mol dm^{-3} in borate buffer. [c] Sodium hydroxide solutions.

The value of k_{EH}^{OH} is 1.9 times greater than the value of k_{OH} for the base hydrolysis of ethyl 1,10-phenanthroline-2-carboxylate (2) (k_{OH} 2.1 dm^3 mol^{-1} s^{-1} at 25 °C).[12] Steric

---

[7] T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, 1961, **65**, 1079.

[8] R. W. Kingerley and V. K. La Mer, *J. Amer. Chem. Soc.*, 1941, **63**, 3256.

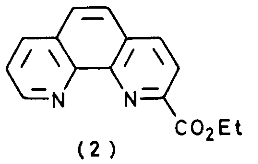
[9] E. Abel, E. Bratu, and O. Redlich, *Z. phys. Chem.*, 1953, **A173**, 353.

[10] R. P. Marshall and J. J. Katz, *J. Inorg. Nuclear Chem.*, 1974, **36**, 1589.

[11] A. Albert and E. P. Serjeant, 'The Determination of Ionisation Constants,' 2nd edn., Chapman and Hall, 1971.

[12] K. H. Gerber and R. G. Wilkins, Amer. Chem. Soc. Meeting, Dallas, Texas, 1973, abstract 173.

and electronic effects at the carbonyl carbon should be similar in the two compounds. The observed rate ratio is expected on the basis of the increased $+I$ effect of the Me relative to the Et group.[13] Methyl esters normally undergo base hydrolysis twice as rapidly as ethyl esters.[14] The ratio $k_{EH}{}^{OH} : k_{E^-}{}^{OH} \sim 10:1$ is also as expected on the basis of electrostatic considerations.[1]


(2)

Formation Constants.—The formation constants for the 1 : 1 metal complexes of the ester, $[ME]^+$ ($M^{II} = Mn^{II}$, Zn^{II}, or Ni^{II}), in aqueous solution were obtained by spectrophotometric titration of solutions 3.0×10^{-5} mol dm^{-3} in methyl 8-hydroxyquinoline-2-carboxylate and 2×10^{-3}—8×10^{-3} mol dm^{-3} in the metal ion over the range pH 3.4—6.5 at 25 ± 0.5 °C and $I = 0.1$ mol dm^{-3} (Na[ClO$_4$]). Under these conditions only the 1 : 1 complexes $[ME]^+$ are formed and any uncomplexed ester is present as the neutral species EH ($\lambda_{max.}$ 254 nm, ε 4.2×10^4 dm^3 mol^{-1} cm^{-1}). The 1 : 1 complexes with Mn^{II}, Zn^{II}, and Ni^{II} all have $\lambda_{max.}$ 275 ± 1 nm and $\varepsilon_{max.}$ of 3.3×10^4, 3.1×10^4, and 3.2×10^4 dm^3 mol^{-1} cm^{-1} respectively.

The formation constants K_{ME^+} refer to the equlibrium $M^{2+} + E^- \rightleftharpoons [ME]^+$ and are given by equation (6). The

$$K_{ME^+} = \frac{[ME^+]}{[M^2][E^-]} = \frac{[ME^+]a_{H^+}}{k_a{}^M[EH][M^{2+}]} \qquad (6)$$

concentration quotients $[ME^+]/[EH]$ were obtained from measurements at 275 nm using the absorption coefficients of $[ME]^+$ and EH (ε 3.2×10^3 dm^3 mol^{-1} cm^{-1}) at this wavelength. Hydrolysis of $[NiE]^+$ was troublesome at pH > 6. In this case the concentration quotients were estimated from absorbance values extrapolated to zero time. The constants K_{NiE^+} and K_{CoE^+} were also determined at 25 °C and $I = 0.1$ mol dm^{-3} using kinetic techniques (see later). No attempt was made to accurately determine the formation constant for $[CuE]^+$ since this species underwent rapid hydrolysis at pH < 5. Kinetic measurements made at pH 5.6 suggested that, in the presence of 4.0×10^{-4} mol dm^{-3} Cu^{II} at 25 °C and $I = 0.1$ mol dm^{-3}, the fraction of ester (initial concentration, 3.3×10^{-5} mol dm^{-3}) present as $[CuE]^+$ was at least 0.95. The value of K_{CuE^+} is therefore $> 2 \times 10^8$ dm^3 mol^{-1}. The various constants obtained are summarised in Table 3.

TABLE 3

Formation constants for $[ME]^+$ complexes at 25 °C and $I = 0.1$ mol dm^{-3}

Complex	K_{ME^+}/dm^3 mol^{-1}
$[MnE]^+$	$(4.9 \pm 0.4) \times 10^4$
$[ZnE]^+$	$(3.8 \pm 0.4) \times 10^6$
$[NiE]^+$	$(5.9 \pm 0.5) \times 10^5$, $(5.3 \pm 0.4) \times 10^5$ *
$[CoE]^+$	$(3.4 \pm 0.2) \times 10^5$ *
$[CuE]^+$	$> 2 \times 10^8$ *

* Determined kinetically; all the other values were determined spectrophotometrically.

Metal-ion-promoted Hydrolysis.—In the presence of bivalent metal ions the ester is hydrolysed rapidly to the corresponding acid at pH values close to those of neutrality. The cobalt(II)- and nickel(II)-promoted reactions were studied at 25 °C and $I = 0.1$ mol dm^{-3} (Na[ClO$_4$]) using hepes buffer. Experiments were carried out at constant substrate concentration and pH with increasing concentration of the metal ion. At high metal ion : ligand ratios the reaction rate becomes independent of the metal-ion concentration. Under these conditions (metal ion : ligand ratio > 500 : 1) the substrate is fully complexed as the 1 : 1 complex $[ME]^+$. Generally, the total concentration of hepes was comparable with the concentration of the metal ions. However, even when large buffer : metal ion ratios were employed [*e.g.* up to 50 : 1 in some of the nickel(II)-catalysed reactions] no detectable buffer effects were observed. There is therefore negligible binding between the buffer base and both Co^{II} and Ni^{II} under the conditions of the experiments. Removal of free M^{2+} species should significantly decrease the observed hydrolysis rate due to perturbation of the $M^{2+} + E \rightleftharpoons [ME]^+$ equilibrium. Goode *et al.*[15] showed by potentiometric measurements that Cu^{II}, Mn^{II}, Ca^{II}, and Mg^{II} do not bind significantly to the buffer base form of pipes and hepes. In the present investigation, the metal-ion-promoted reactions were studied using hepes [nickel(II)-, cobalt(II)-, and manganese(II)-promoted reactions] and pipes [copper(II)- and zinc(II)-catalysed hydrolyses] as buffers. Buffer effects were absent in each case.

At pH < 7.25 the uncomplexed ester is present as EH^+ (p$K_a{}^M$ 9.25). This species hydrolyses at a negligible rate in neutral or slightly acidic solution. With large metal to ligand ratios only 1 : 1 complexes are formed, so that the rate law (7) or (8) can be written for the metal-promoted hydrolysis, where $k_{lim.}$ is the observed first-order rate

$$\text{Rate} = k_{obs.}([ME^+] + [EH]) \qquad (7)$$

$$= k_{lim.}[ME^+] \qquad (8)$$

constant for the fully complexed substrate at a specific pH. Equating (7) and (8) and rearranging gives (9). Substitution of equation (9) into (6) gives (10). The kinetic data

$$\frac{[ME^+]}{[EH]} = \frac{k_{obs.}}{(k_{lim.} - k_{obs.})} \qquad (9)$$

$$K_{ME^+} = \frac{k_{obs.}}{(k_{lim.} - k_{obs.})} \cdot \frac{a_{H^+}}{K_a{}^M[M^{2+}]} \qquad (10)$$

obtained for the cobalt(II)- and nickel(II)-promoted reactions (Table 4) were substituted in equation (10) to give the values $K_{CoE^+} = (3.4 \pm 0.2) \times 10^5$ and $K_{NiE^+} = (5.3 \pm 0.4) \times 10^5$ dm^3 mol^{-1} at 25 °C and $I = 0.1$ mol dm^{-3} (Table 3). The values for K_{NiE^+} determined spectrophotometrically and kinetically are in reasonable agreement.

Attempts to determine K_{CuE^+} by the kinetic method were unsuccessful. Full complex formation of the ester was achieved at pH 5.62 and 25 °C when the metal ion was present in greater than a 12-fold excess over the substrate (Table 5). However, when lower metal ion to ligand ratios were used plots of log $(A_\infty - A_t)$ against time deviated from linearity. This behaviour could be due to one or both of the following: (*a*) [CuE(AH)] is produced in appreciable

---

[13] J. Clark and D. D. Perrin, *Quart. Rev.*, 1964, **18**, 295.

[14] R. W. Hay and L. J. Porter, *J. Chem. Soc.* (*B*), 1967, 1261; R. W. Hay and P. J. Morris, *ibid.*, 1970, 1577.

[15] N. E. Goode, G. D. Winget, W. Winter, T. N. Connolly, S. Izawa, and R. M. Singh, *Biochemistry*, 1966, **5**, 467.

concentration as the reaction proceeds (AH^- = 8-hydroxyquinoline-2-carboxylate anion), or (*b*) the copper(II)–ester equilibrium is increasingly perturbed when Cu^{II} is bound as $[Cu(AH)]^+$ or $[CuA]$.

The manganese(II)-catalysed reaction was studied at pH 7.88 (25 °C, I = 0.1 mol dm^{-3}) using an initial ester concentration of 3.3 × 10^{-5} mol dm^{-3} (Table 5). Increase in the concentration of the metal ion from 5 × 10^{-3} to 3.0 × 10^{-2} mol dm^{-3} increased the fraction of ester present as $[MnE]^+$ from 0.92 to 0.984 [fractions calculated using the spectrophotometrically determined value of K_{MnE^+} = (4.9 ± 0.4) × 10^4 dm^3 mol^{-1} at 25 °C and I = 0.1 mol dm^{-3}].

The metal-ion dependence of the zinc(II)-promoted reaction was studied at 35 rather than 25 °C, since at 25 °C the rates of hydrolysis at pH values where precipitation of zinc(II) hydroxide was not a problem were very slow. At

TABLE 4

Nickel(II)- and cobalt(II)-promoted hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate.[a] Metal-ion dependence at 25 °C and I = 0.1 mol dm^{-3}

(*i*) Cobalt(II)-promoted hydrolysis at pH 7.005 [b]

$10^3[Co^{II}]$ / mol dm^{-3}	10^2[hepes] / mol dm^{-3}	$10^3k_{obs.}$ / s^{-1}	$10^3k_{calc.}$[b] / s^{-1}
0.15	0.50	0.381	0.342
0.30	0.50	0.547	0.558
0.60	0.50	0.797	0.817
0.60	1.00	0.815	0.817
1.00	1.00	0.959	1.00
2.00	1.00	1.13	1.21
5.00	1.00	1.34	1.38
10.0	1.00	1.39	1.44
20.0	1.00	1.44	1.48
20.0	2.00	1.48	1.48
30.0	1.00	1.52	1.49

(*ii*) Nickel(II)-promoted hydrolysis at pH 7.020

$10^3[N^{II}]$ / mol dm^{-3}			$10^3k_{calc.}$[c] / s^{-1}
0.10	0.50	0.365	0.338
0.20	0.50	0.590	0.546
0.20	1.00	0.570	0.546
0.30	1.00	0.633	0.686
0.40	1.00	0.725	0.788
0.50	1.00	0.837	0 862
1.00	1.00	1.08	1.07
2.00	1.00	1.16	1.22
4.00	1.00	1.32	1.31
6.00	1.00	1.36	1.35
10.0	1.00	1.44	1.38
10.0	2.00	1.40	1.38
20.0	1.00	1.44	1.40

[a] Initial ester concentration used in the range 1.0 × 10^{-5}—5.0 × 10^{-5} mol dm^{-3}. Supporting electrolyte, $Na[ClO_4]$. [b] Obtained assuming $k_{lim.}$ = 1.52 × 10^{-3} s^{-1} at pH 7.005 and K_{CoE^+} = 3.4 × 10^5 dm^3 mol^{-1}. [c] Obtained assuming $k_{lim.}$ = 1.42 × 10^{-3} s^{-1} at pH 7.02 and K_{NiE^+} = 5.3 × 10^5 dm^3 mol^{-1}

TABLE 5

Copper(II)-, manganese(II)-, and zinc(II)-promoted hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate. Metal-ion dependence at I = 0.1 mol dm^{-3} ($Na[ClO_4]$) [a]

(*i*) Copper(II)-promoted hydrolysis at pH 5.616 and 25 °C [b]

$10^4[Cu^{II}]$/mol dm^{-3}	$10^3k_{obs.}$/s^{-1}
4.00	3.30
6.00	3.33
8.00	3.32

(*ii*) Manganese(II)-promoted hydrolysis at pH 7.88 and 25 °C [c]

$10^2[Mn^{II}]$/mol dm^{-3}	$10^4k_{obs.}$/s^{-1}	Fraction of $[MnE]^+$
0.50	4.63	0.92
1.00	4.74	0.954
1.00	4.81	0.954
1.50	4.83	0.969
2.00	4.90	0.976
3.00	4.81	0.984

(*ii*) Zinc(II)-promoted hydrolysis at pH 6.13 and 35 °C [b]

$10^2[Zn^{II}]$/mol dm^{-3}	$10^4k_{obs.}$/s^{-1}
0.50	1.93
1.00	1.92
1.50	1.95

[a] Initial ester concentration 3.3 × 10^{-5} mol dm^{-3} with $Na[ClO_4]$ as the supporting electrolyte. [b] Solutions 5 × 10^{-3} mol dm^{-3} in pipes. [c] Solutions 5 × 10^{-3} mol dm^{-3} in hepes.

TABLE 6

Metal-ion promoted hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate. pH dependence studies at I = 0.1 mol dm^{-3}

(*i*) Copper(II)-promoted hydrolysis at 25.0 °C [a]

pH	$10^3k_{obs.}$ / s^{-1}	$10^9[OH^-]$ / mol dm^{-3}	$10^{-5}k_{OH}$ / dm^3 mol^{-1} s^{-1}
5.615	3.30	5.34	6.18
5.850	5.98	9.18	6.51
6.120	10.8	17.1	6.32
6.240	14.4	22.5	6.40
6.390	19.8	31.7	6.26
6.48	25.0	39.1	6.40

(*ii*) Nickel(II)-promoted hydrolysis at 25.0 °C [b]

pH	$10^3[Ni^{II}]$ / mol dm^{-3}	$10^3k_{obs.}$ / s^{-1}	$10^7[OH^-]$ / mol dm^{-3}	$10^{-4}k_{OH}$ / dm^3 mol^{-1} s^{-1}
7.020	10.0	1.42	1.36	1.04
7.460	10.0	4.02	3.74	1.07
7.740	5.0	7.42	7.45	0.96
7.930	3.0	11.1	11.0	1.01
8.070	2.0	15.3	15.3	1.00
8.340	1.0	30.0	28.4	1.06

(*iii*) Cobalt(II)-promoted hydrolysis at 25.0 °C [c]

pH	$10^3[Co^{II}]$ / mol dm^{-3}	$10^3k_{obs.}$ / s^{-1}	$10^7[OH^-]$ / mol dm^{-3}	$10^{-4}k_{OH}$ / dm^3 mol^{-1} s^{-1}
7.005	30.0	1.52	1.31	1.15
7.310	20.0	3.03	2.64	1.14
7.500	10.0	4.49	4.09	1.10
7.720	5.0	7.35	6.79	1.08
8.035	3.0	15.3	14.0	1.09

(*iv*) Manganese(II)-promoted hydrolysis at 25.0 °C [d]

pH	$10^3[Mn^{II}]$ / mol dm^{-3}	$10^3k_{obs.}$ / s^{-1}	$10^{-6}[OH^-]$ / mol dm^{-3}	$10^{-2}k_{OH}$ / dm^3 mol^{-1} s^{-1}
7.880	20.0	0.483	0.983	4.91
8.080	15.0	0.716	1.55	4.62
8.265	10.0	1.20	2.38	5.04
8.265	10.0	1.20	2.38	5.04
8.390	5.0 †	1.56	3.17	4.92
8.565	5.0 †	2.40	4.75	5.05

(*v*) Zinc(II)-promoted hydrolysis at 35.0 °C [e]

pH	$10^3[Zn^{II}]$ / mol dm^{-3}	$10^4k_{obs.}$ / s^{-1}	$10^8[OH^-]$ / mol dm^{-3}	$10^{-3}k_{OH}$ / dm^3 mol^{-1} s^{-1}
6.15	15.0	1.95	3.69	5.29
6.37	6.0	3.18	6.38	4.98
6.52	3.0	4.51	8.93	5.05
6.78	3.0	8.19	16.4	4.99
7.01	2.0	1.42	27.9	5.10

[a] Solutions 4 × 10^{-4} mol dm^{-3} in $Cu[ClO_4]_2$ and 10^{-2} mol dm^{-3} in pipes. Initial ester concentration 2.1 × 10^{-5} mol dm^{-3}, λ 268 nm. [b] Solutions 10^{-2} mol dm^{-3} in hepes. Initial ester concentration 3.3 × 10^{-5} mol dm^{-3}, λ 270 nm. [c] Solutions 10^{-2} mol dm^{-3} in hepes. Initial ester concentration 4.2 × 10^{-5} mol dm^{-3}, λ 275 nm. [d] Solutions buffered with 10^{-2} mol dm^{-3} hepes except for those designated † where morpholine (5 × 10^{-3} mol dm^{-3}) was used as buffer. Initial ester concentration 3.3 × 10^{-5} mol dm^{-3}, λ 275 nm. [e] Solutions 5 × 10^{-3} mol dm^{-3} in pipes. Initial ester concentration 3.3 × 10^{-5} mol dm^{-3}, λ 266 nm.

pH 6.135 essentially constant values of $k_{obs.}$ were obtained when the zinc(II) concentration was increased from 5 × 10^{-3} to 1.5 × 10^{-2} mol dm^{-3} (Table 5).

TABLE 7

Reactions in deuterium oxide as solvent

Complex	$[M^{II}]$/mol dm^{-3}	pD	$10^3k_{obs.}$/s^{-1}	$10^7[OD^-]$/mol dm^{-3}	10^4k_{OD}/dm^3 mol^{-1} s^{-1}
$[CuE]^+$	4.0 × 10^{-4}	6.850	11.3 ±0.03	0.142	79.5 ± 2.5
$[NiE]^+$	5.0 × 10^{-3}	8.085	2.51 ±0.07	2.41	1.04 ± 0.03
$[CoE]^+$	2.0 × 10^{-2}	8.085	3.67 ±0.10	2.41	1.52 ± 0.05

TABLE 8

Temperature dependence of the base and metal-ion-promoted hydrolyses of methyl 8-hydroxyquinoline-2-carboxylate (I = 0.1 mol dm^{-3}) [a]

(*i*) Copper(II)-promoted hydrolysis [b]

θ_c/°C	pH	$10^2k_{obs.}$/s^{-1}	$10^8[OH^-]$/mol dm^{-3}	$10^{-5}k_{OH}$/dm^3 mol^{-1} s^{-1}
15.0	5.890	0.169	0.452	3.74
25.0	5.820	0.552	0.856	6.44
35.0	5.750	1.51	1.53	9.89

(*ii*) Nickel(II)-promoted hydrolysis [c]

		$10^3k_{obs.}$/s^{-1}	$10^7[OH^-]$/mol dm^{-3}	$10^{-4}k_{OH}$/dm^3 mol^{-1} s^{-1}
15.0	7.100	0.497	0.725	0.684
25.0	6.980	1.31	1.24	1.06
35.0	6.860	3.24	1.97	1.65

(*iii*) Cobalt(II)-promoted hydrolysis [d]

15.0	7.490	1.11	1.46	0.587
25.0	7.360	3.22	2.29	1.08
35.0	7.230	8.41	3.55	1.82

(*iv*) Manganese(II)-promoted hydrolysis [e]

		$10^4k_{obs.}$/s^{-1}	$10^6[OH^-]$/mol dm^{-3}	$10^{-2}k_{OH}$/dm^3 mol^{-1} s^{-1}
15.0	8.170	2.19	0.861	2.54
25.0	8.055	7.43	1.48	5.03
35.0	7.930	23.3	2.32	10.0

(*v*) Zinc(II)-promoted hydrolysis [f]

			$10^7[OH^-]$/mol dm^{-3}	$10^{-3}k_{OH}$/dm^3 mol^{-1} s^{-1}
15.0	6.980	0.614	0.550	1.12
25.0	6.890	2.58	1.005	2.57
35.0	6.810	8.91	1.757	5.07
45.0	6.730	29.6	2.801	10.6

(*vi*) Base hydrolysis in 10^{-2} mol dm^{-3} Na[OH] [g]

θ_c/°C	$10^3k_{obs.}$/s^{-1}	k_{OH}/dm^3 mol^{-1} s^{-1}
15.0	2.32	0.232
25.0	4.80	0.480
35.0	9.02	0.902

[a] Supporting electrolyte Na[ClO_4] unless otherwise stated. Initial concentration of ester and monitoring wavelengths were identical to those used in Table 6. [b] Solution 4 × 10^{-4} mol dm^{-3} in Cu[ClO_4]$_2$ and 5 × 10^{-3} mol dm^{-3} in pipes. [c] Solutions 10^{-2} mol dm^{-3} in Ni[ClO_4]$_2$ and 10^{-2} mol dm^{-3} in hepes. [d] Solutions 2.0 × 10^{-2} mol dm^{-3} in Co[ClO_4]$_2$ and 10^{-2} mol dm^{-3} in hepes. [e] Solutions 10^{-2} mol dm^{-3} in $MnCl_2$ and 5 × 10^{-3} mol dm^{-3} in morpholine. [f] Solutions 3 × 10^{-3} mol dm^{-3} in Zn[ClO_4]$_2$ and 5 × 10^{-3} mol dm^{-3} in pipes. [g] Supporting electrolyte KCl.

pH *Dependence*.—The pH dependence of the hydrolysis of the $[ME]^+$ complexes (M = Cu^{II}, Ni^{II}, Co^{II}, or Mn^{II}) was studied at 25 °C and I = 0.1 mol dm^{-3}. Conditions were chosen such that at least 97% of the substrate was present as $[ME]^+$ throughout the pH range investigated. These conditions were realised for the cobalt(II)-, nickel(II)-, and manganese(II)-promoted reactions. For the reasons previously discussed, the copper(II)-promoted reaction was studied using a metal-ion concentration of 4.0 × 10^{-4} mol dm^{-3}. For each complex the pH dependence was studied over *ca.* 1 pH unit. Studies over a wider pH range were not possible due to the dual requirements of full complex formation of the substrate and the avoidance of precipitation of the metal hydroxide. Values of $k_{obs.}$ increased with increasing pH and values of $k_{obs.}/[OH^-] = k_{OH}$ were sensibly constant (Table 6).

Provided the concentration of the metal ion was sufficiently high to ensure essentially complete conversion into $[ZnE]^+$, constant values of k_{OH} were also observed in the zinc(II)-promoted reaction over the range pH 6.14—7.01 at 35 °C. At pH > 7.1, however, values of k_{OH} increased. Precipitation of zinc(II) hydroxide was not observed in the kinetic solutions and the anomalous reactivity may be due to catalysis by a hydroxozinc(II) complex. The reaction was not investigated further; metal-bound hydroxide-ion attack on carbonyl substrates has recently been studied in detail.[16,17]

A limited study of the hydrolysis of $[CuE]^+$, $[NiE]^+$, and $[CoE]^+$ at 25 °C and I = 0.1 mol dm^{-3} was carried out using D_2O as solvent (Table 7). The pH control in these reactions was effected with the buffer systems used for the corresponding studies in water. The quoted rate constants are mean values (errors ±3%) derived from duplicate determinations.

The temperature dependence of the metal-promoted hydrolysis and of the base hydrolysis of E^- was also studied and the requisite kinetic data obtained are in Table 8. In the metal-promoted reactions sufficient metal ion was added to ensure complete conversion of the substrate into the 1 : 1 complex $[ME]^{2+}$. The quoted rate constants are mean values obtained from a minimum of two kinetic runs. No attempt was made to determine the thermodynamic parameters for the base hydrolysis of EH, as this reaction could not be studied in isolation. Linear plots of log k_{OH} against T^{-1} were obtained in each case. The uncertainties in the derived values of $\Delta H^‡$ (±1.3—1.7 kJ mol^{-1}) and $\Delta S^‡$ (±3.3—6.3 J K^{-1} mol^{-1}) at 298 K are in accord with the uncertainties (*ca.* 4%) in the second-order rate constants. Values of the various parameters are in Table 9.

TABLE 9

Thermodynamic parameters for the hydrolysis of the ester and its metal complexes *

Substrate	k_{OH}^{25}/dm^3 mol^{-1} s^{-1}	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$ at 298 K/J K^{-1} mol^{-1}
EH	4.0		
E^-	0.485	47.7	−90.8
$[MnE]^+$	4.9 × 10^2	47.7	−33.1
$[CoE]^+$	1.12 × 10^4	38.1	−39.7
$[NiE]^+$	1.01 × 10^4	30.5	−65.3
$[CuE]^+$	6.3 × 10^5	33.1	−22.6
$[ZnE]^+$	2.6 × 10^3	54.4	2.9

* The uncertainties in $\Delta H^‡$ are ±1.3—1.7 kJ mol^{-1} and in $\Delta S^‡$ are ±3.3—6.3 J K^{-1} mol^{-1}.

---

[16] D. A. Buckingham and L. M. Engelhardt, *J. Amer. Chem. Soc.*, 1975, **97**, 5915.

[17] M. A. Wells, G. A. Rogers, and T. C. Bruice, *J. Amer. Chem. Soc.*, 1976, **98**, 4338.

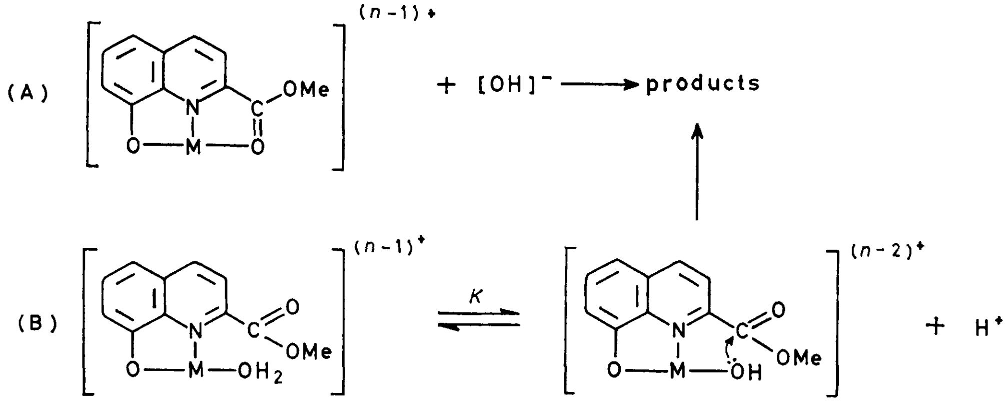
DISCUSSION

The metal-promoted hydrolysis of methyl 8-hydroxyquinoline-2-carboxylate can be represented by Scheme 1.

$$M^{2+} + E^- \overset{K_{ME^+}}{\rightleftharpoons} [ME]^+ \xrightarrow[{[OH]^-}]{k_{OH}} \text{products}$$

Scheme 1

The observed first-order dependence of the hydrolysis rates on the hydroxide-ion concentration is consistent with two possible mechanisms (Scheme 2). Mechanism (A) involves attack by external hydroxide ion on a complex in which the ester group is bound to the metal ion *via* the carbonyl oxygen atom. Mechanism (B) involves rapid pre-equilibrium formation of a hydroxo-complex followed by intramolecular hydroxide-ion attack. In principle these two mechanisms can be differentiated by measurements at high pH since in mechanism (B) the reaction should become independent of $[OH^-]$ when complete conversion into the hydroxo-complex has occurred. Unfortunately this type of experiment cannot be carried out with the present system as high metal : ligand ratios are required for complete conversion of the substrate into $[ME]^+$ and precipitation of the metal hydroxide occurs at high pH.



Scheme 2 Possible mechanisms for hydrolysis of the metal complexes. For the sake of clarity, additional co-ordinated water molecules have been excluded

Table 10

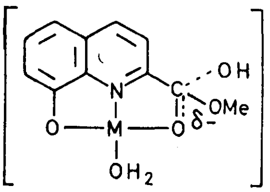
Comparison of the log K_1 values for metal complexes of quinolin-8-ol and methyl 8-hydroxyquinoline-2-carboxylate

	log K_1	
Metal ion	quinolin-8-ol [a]	methyl 8-hydroxyquinoline-2-carboxylate [b]
Cu^{II}	12.6 [c]	>8.3
Ni^{II}	9.9 [d]	5.7
Co^{II}	9.1 [d]	5.5
Zn^{II}	8.6 [c]	6.6
Mn^{II}	6.8 [d]	4.7
pK_{NH^+}	4.91 [e]	<1
pK_{OH}	9.81 [e]	9.36

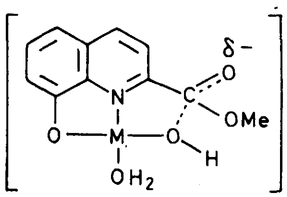
[a] At 20 °C and $I = 0.01$ mol dm^{-3} unless otherwise stated. [b] This work; 25 °C and $I = 0.1$ mol dm^{-3}. [c] At 20 °C and $I \rightarrow 0$ (R. Nasanen and U. Penttinen, *Acta Chem. Scand.*, 1952, **6**, 837. [d] A. Albert, *Biochem. J.*, 1953, **54**, 646; A. Albert, M. I. Gibson, and S. D. Rubbo, *Brit. J. Exp. Pathology*, 1953, **34**, 9. R. Nasanen, P. Lumme, and A. L. Mukula, *Acta Chem. Scand.*, 1951, **5**, 1199.

In 1 : 1 complexes of the ester the rigid nature of the ligand places the CO_2Me group in close proximity to the metal ion. An examination of molecular models suggests that if this group is not bonded to the metal ion there should be severe steric crowding between it and a water molecule in the co-ordination sphere of the metal. Steric compression of this type might be expected to be reflected in the formation constants of 1 : 1 complexes. Table 10 lists the formation constants of the ester complexes and those of the parent ligand quinoline-8-ol. The CO_2Me group is strongly electron withdrawing and thus markedly lowers the basicity of the quinoline nitrogen; the pK_{NH^+} of the ester is at least 4 pK units below that of quinolin-8-ol. The data in Table 10 suggest that, when due allowance is made for the lower basicity of the pyridine nitrogen atom, the formation constants of the metal–ester complexes are not abnormally low. The results provide some support for the view that metal–carbonyl bonding does occur with the complexes.

Deuterium solvent-isotope effects in the metal-ion-promoted reactions were also investigated as a possible probe of mechanism. Such effects depend on the free-energy differences between the ground and transition states in water and D_2O. The two transition states, (3) and (4), are not exactly identical, but differ only in the positioning of a single proton. The two paths are thus very similar, except that for one a pre-equilibrium step occurs while for the other it does not. Reactions in which $[OD]^-$ acts as a nucleophile usually have rate



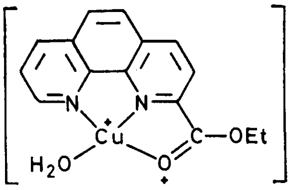
(3)



(4)

constants which are 20—40% higher than the corresponding reactions with $[OH]^-$.[18] For the base hydrolysis of organic substrates k_{OH}/k_{OD} is usually in the range 0.71—0.83.[19] The values of k_{OH}/k_{OD} obtained for the base hydrolysis of the copper(II), cobalt(II), and nickel(II) complexes are 0.79, 0.72, and 0.97 respectively. Few studies have been made of the ionisation of aquametal complexes in D_2O solution. Tobias and his co-workers [20] reported that for the two equilibria $[Co(NH_3)(OH_2)]^{3+} + H_2O \rightleftharpoons [Co(NH_3)_5(OH)]^{2+} + [H_3O]^+$ and $[Co(NH_3)_5(OD_2)]^{3+} + D_2O \rightleftharpoons [Co(NH_3)_5(OD)]^{2+} + [D_3O]^+$ the pK values are 6.22 and 6.75 respectively, the deuterium derivative being a somewhat weaker acid. Values of $k_{OH}/k_{OD} > 1$ might therefore be expected for an intramolecular process since a smaller proportion of the active hydroxo-species would be present in solution.

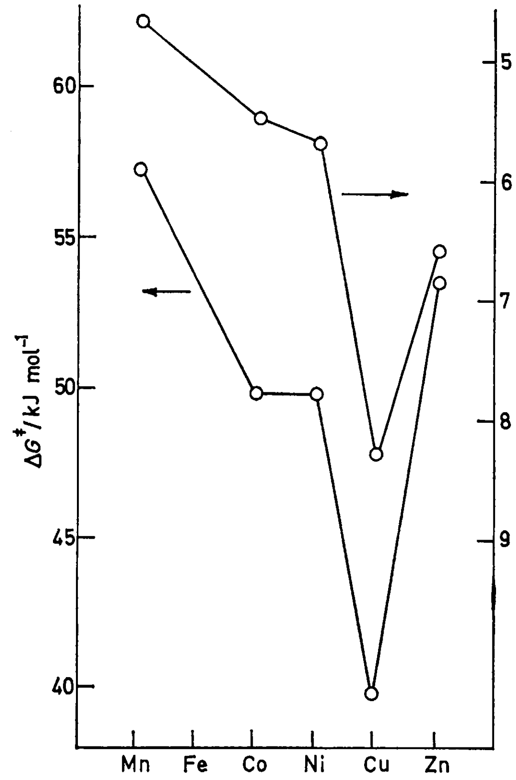
The order of decreasing reactivity of the various ester species towards nucleophilic attack by hydroxide ion at 25 °C is $[CuE]^+ > [CoE]^+ \sim [NiE]^+ > [ZnE]^+ > [MnE]^+ > EH > E^-$. There is a wide variation in the reactivity of the various complexes towards hydroxide ion; thus $[CuE]^+$ undergoes base hydrolysis 1.3×10^6 times faster than E^- while the rate acceleration with $[MnE]^+$ is *ca.* 10^3. The total charge carried by the complex does not appear to be a major factor in determining the hydrolysis rates. Thus at 25 °C the complex $[CuE]^+$ undergoes base hydrolysis (k_{OH} 6.3×10^5 dm^3 mol^{-1} s^{-1}) at a very similar rate to the corresponding complex of ethyl 1,10-phenanthroline-2-carboxylate (5) which carries a dipositive charge (k_{OH} 5×10^5 dm^3 mol^{-1} s^{-1}).[12]



(5)

If the reaction proceeded by the intramolecular path (B) the reactivity of the metal complexes towards hydrolysis might be expected to be reflected in the K_a values for the ionisation [21] of the aqua-ions [21] $\{[M(OH_2)_n]^{2+} \rightleftharpoons [M(OH_2)_{n-1}(OH)]^+ + H^+\}$ since the ionisation constants of water molecules in the co-ordination sphere of the 1 : 1 complex should follow a similar trend. On this basis the order of reactivity would be $[CuE]^+ > [ZnE]^+ \sim [CoE]^+ > [NiE]^+ \sim [MnE]^+$ which is markedly different from that observed.

The thermodynamic parameters for the hydrolysis of the various ester species (Table 9) show that the rate enhancements in the metal-ion-promoted reactions arise from more positive values of $\Delta S^\ddagger$ and, in general, lower enthalpies of activation. Base hydrolysis of the deprotonated ligand E^- has $\Delta H^\ddagger = 47.7$ kJ mol^{-1} and $\Delta S^\ddagger = -90.8$ J K^{-1} mol^{-1} at 298 K. The large negative entropy of activation is typical of a bimolecular reaction involving two anions.[22] In the Figure, values of $\Delta G^\ddagger$ and log K_{ME^+} are plotted against atomic number. Both plots display similar trends. The values of log K_{ME^+} provide a measure of the polarising power of the metal ion. The close correspondence of the two plots is strong evidence for a path involving metal-ion–carbonyl bonding in the ground state of the reaction.



Relation between $\Delta G^\ddagger$ for the base hydrolysis of $[ME]^+$ and log K_{ME^+}

Metal ions providing more significant polarisation of the carbonyl oxygen bond should lead to a lower value of $\Delta G^\ddagger$ for nucleophilic attack. Hay and Morris [23] noted that the enthalpies of activation for hydrolysis of the free ligand and the metal complexes of methyl 2,3-diaminopropionate do not vary by more than 5 kJ mol^{-1}. In this case the metal-ion-promoted reactions do not involve direct interaction between the metal ion and the ester function of the ligand. Thus variations in $\Delta H^\ddagger$ (as observed in the present case) may well provide a useful probe for metal–carbonyl bonding.

In the present reactions the nickel(II)-promoted hydrolysis has the most favourable enthalpy (30.5 kJ mol^{-1}), but the least favourable entropy of activation

---

[18] W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, p. 272.

[19] F. A. Long and J. Bigelensen, *Trans. Faraday Soc.*, 1959, **55**, 2077.

[20] R. C. Splinter, S. J. Harris, and R. S. Tobias, *Inorg. Chem.*, 1968, **7**, 897.

[21] F. Basolo and R. G. Pearson, 'Mechanisms of Inorganic Reactions,' 2nd edn., Wiley, London, 1967, p. 32.

[22] A. A. Frost and R. G. Pearson, 'Kinetics and Mechanism,' 2nd edn., Wiley, New York, 1961.

[23] R. W. Hay and P. J. Morris, *J.C.S. Dalton*, 1973, 56.

(-65.3 J K^{-1} mol^{-1}). The situation is reversed with Zn^{II}, in this case $\Delta H^‡$ is large (54.4 kJ mol^{-1}) while the value of $\Delta S^‡$ (2.9 J K mol^{-1}) is clearly very favourable. A general feature of the present reactions is the tendency for the two contributions to the free energy of activation to partially compensate each other. Bender [24] discussed the importance of metal-ion stabilisation of the transition state relative to ground-state stabilisation. In ester hydrolysis, stabilisation of the transition state appears to be of primary importance when the metal ion can interact directly with the developing negative charge on the ester carbonyl group. The orientation of the solvent molecules around charges, or developing charges, 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 transition state thus leading to a more positive (*i.e.* less negative) entropy of activation. The bimolecular reaction of a positively charged metal complex with hydroxide ion gives rise to an overall neutral transition state where less solvent is contained than in the initial state. As a result a more positive entropy of activation for hydrolysis would be expected than occurs with the unpromoted reactions, as is observed.

The general trends in $\Delta H^‡$ and $\Delta S^‡$ in the metal-promoted reactions can be rationalised in terms of ground- and transition-state interactions between the metal ion and the carbonyl group of the ester. Where a strong interaction occurs between the metal ion and the ester function in the ground state of the reaction, as appears to occur in the nickel(II)-promoted reaction, the value of $\Delta H^‡$ is significantly lowered due to polarisation of the carbonyl group, but $\Delta S^‡$ remains quite negative since there is little change in solvation on moving to the transition state. If ground-state interactions are weak but a significant interaction occurs in the transition state, as appears to be the case with Zn^{II}, $\Delta H^‡$ remains quite large but $\Delta S^‡$ is significantly lowered since the metal ion is able to ' solvate ' the developing negative charge on the carbonyl group and desolvation is thus more extensive.

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

[6/1969 *Received, 25th October, 1976*]

---

[24] M. L. Bender, ' Mechanisms of Homogeneous Catalysis from Protons to Proteins,' Wiley–Interscience, New York, 1971.