Interaction of DL-2,3-Diaminopropionic Acid and its Methyl Ester with Metal Ions. Part II.[1] Hydrolysis Kinetics[2]

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Base hydrolysis of methyl DL-2,3-diaminopropionate (E) has been studied in aqueous solution at $I = 0{\cdot}1$M and three temperatures (25, 37, and 50 °C). Specific rate constants have been obtained for the hydrolysis of the unprotonated ester and its monoprotonated (α-amino-group) form (EH^+), and the corresponding activation parameters determined.

Rate constants for base hydrolysis of the ester function in bis-complexes of copper(II) and mercury(II) with methyl DL-2,3-diaminopropionate have been obtained at 25 °C and $I = 0{\cdot}1$M. The hydrolytic behaviour of the bis-complexes is consistent with equations (i) and (ii), where A^- is the anion of 2,3-diaminopropionic acid and M^{2+} is a bivalent metal ion. The metal complexes undergo base hydrolysis considerably more rapidly than does

$$ME_2^{2+} + OH^- \longrightarrow MEA^+ + MeOH \quad \text{(i)}$$

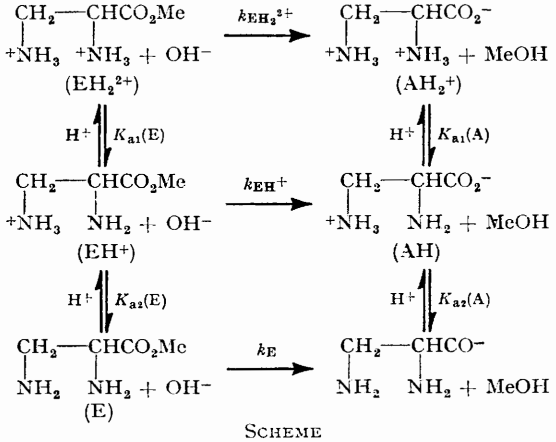
$$MEA^+ + OH^- \longrightarrow MA_2 + MeOH \quad \text{(ii)}$$

the free ligand E. Thermodynamic parameters for hydrolysis of the ester and the copper(II) complexes are compared. Specific rate constants for base hydrolysis of the mono-complex CuE^{2+}, the hydroxy-complexes $CuEOH^+$ and $HgEOH^+$, and the mixed complex $CuE(dae)^{2+}$ (dae = 1,2-diaminoethane) have also been obtained at 25 °C and $I = 0{\cdot}1$M. The relative values of the various rate constants are discussed.

THERE has recently been considerable interest in the hydrolysis of ester ligands in metal complexes. In systems involving labile metal complexes it is necessary to have high formation constants if a rigorous interpretation of the kinetic data is to be attempted, otherwise difficulties arise due to the uncertain nature of the catalytically active species in solution. For this reason we have studied the metal complexes of the methyl esters of L-histidine [3] and L-cysteine.[4] The methyl ester of 2,3-diaminopropionic acid forms complexes with copper(II) and mercury(II) which have very high formation constants,[1] higher than for the analogous histidine complexes [5] which have the same charge. Kinetic measurements on methyl histidinate [3] were essentially limited to the copper(II) complexes [the data for nickel(II) are only approximate] but the present system enables precise measurements to be made of the effect of changing the metal ion. The copper(II) and mercury(II) systems were chosen for the reasons discussed previously.[1]

RESULTS AND DISCUSSION

Base Hydrolysis of Methyl DL-2,3-*Diaminopropionate*.—Base hydrolysis of methyl 2,3-diaminopropionate (E) has previously been studied in detail.[6] The various ionisation equilibria and hydrolytic reactions of the ester are summarised in the following Scheme.



SCHEME

Values of the thermodynamic ionisation constants are $pK_{a1}^T(E) = 4{\cdot}412$ and $pK_{a2}^T(E) = 8{\cdot}250$ at 25 °C and $I = 0{\cdot}1$M. At pH > 8 the only species of kinetic importance are E and EH^+. Values of k_E and k_{EH^+} at 25, 37, and 50 °C are given in Table 1. The ratio $k_{EH^+} : k_E$ is *ca.* 75 : 1 at all three temperatures, a result expected on the basis of electrostatic considerations.

TABLE 1

Rate constants and thermodynamic parameters for base hydrolysis of methyl DL-2,3-diaminopropionate and its copper(II) and mercury(II) complexes at $I = 0{\cdot}1$M

(*a*) Rate constants for the ester species

t/°C	k_E/l mol⁻¹ min⁻¹	k_{EH^+}/l mol⁻¹ min⁻¹
25	43·8	3440
37	93·7	7050
50	214·3	15,440

(*b*) Rate constants for the metal complexes †

Metal ion	t/°C	$10^{-4}k_{M1}$/ l mol⁻¹ min⁻¹	$10^{-4}k_{M2}$/ l mol⁻¹ min⁻¹
Copper(II)	25	1·83	0·532
	37	4·53	1·22
	50	11·1	2·77
Mercury(II)	25	0·69	0·146

(*c*) Thermodynamic parameters

Species	$\Delta H^‡$/kcal mol⁻¹	$\Delta S^‡_{298}$/cal K⁻¹ mol⁻¹
E	11·6 ± 0·5	−20·3 ± 1·7
EH^+	10·9 ± 0·5	−13·9 ± 1·9
CuE_2^{2+}	13·2 ± 0·1	−2·9 ± 0·5
$CuEA^+$	12·1 ± 0·2	−1·4 ± 0·6

† Rate constants k_{M1} and k_{M2} are defined in the text.

Values of the thermodynamic parameters $\Delta H^‡$ and $\Delta S^‡_{298}$ were calculated using standard expressions and are summarised in Table 1. The thermodynamic data has been discussed previously.[6]

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[1] Part I, R. W. Hay and P. J. Morris, *J. Chem. Soc.* (*A*), 1971, 3562.

[2] Preliminary report, R. W. Hay and P. J. Morris, *Chem. Comm.*, 1968, 732.

[3] R. W. Hay and P. J. Morris, *J. Chem. Soc.* (*A*), 1971, 1524.

[4] R. W. Hay and L. J. Porter, *J. Chem. Soc.* (*A*), 1969, 127.

[5] R. W. Hay and P. J. Morris, *J. Chem. Soc.* (*A*), 1971, 1518.

[6] R. W. Hay and P. J. Morris, *J.C.S. Perkin II*, 1972, 1021.

TABLE 2

Time-ratio evaluation of k_{M1} and k_{M2} for the copper(II) and mercury(II) catalysed hydrolysis of the methyl ester of DL-2,3-diaminopropionic acid at 25° C and $I = 0{\cdot}1$M. Cu^{II} : ester = 1 : 2, Hg^{II} : ester = 1 : 6, with correction for uncatalysed hydrolysis

Copper(II) catalysis

(*a*) Time (t_x/min) required to reach x% reaction

pH	t_{10}	t_{20}	t_{30}	t_{40}	t_{50}	t_{60}	t_{70}	t_{80}	t_{90}
8·60		5·00	8·19	12·15	17·15	23·80	33·12	47·21	73·06
8·50	3·13	6·33	10·22	15·11	21·36	29·59	41·08	58·47	90·40
8·40	3·85	7·80	12·73	18·89	26·69	36·97	51·36	73·07	113·0
8·30		9·89	16·02	23·66	33·52	46·50	64·46	91·55	141·1
8·20	5·76	12·13	19·96	26·69	41·95	58·15	80·31	114·2	175·4

(*b*) Selected time-ratios

pH		$t_{90} : t_{60}$	$t_{80} : t_{50}$	$t_{70} : t_{40}$	$t_{70} : t_{20}$	$t_{60} : t_{30}$	$t_{80} : t_{10}$
8·60		3·070	2·753	2·726	6·624	2·906	
8·50		3·055	2·737	2·719	6·490	2·895	9·454
8·40		3·057	2·738	2·719	6·585	2·904	9·603
8·30		3·034	2·731	2·724	6·518	2·903	
8·20		3·016	2·711	2·705	6·621	2·913	10·10
Mean:	Found	3·046	2·736	2·719	6·568	2·904	9·719
	Calc. ($\kappa = 0{\cdot}29$)	3·017	2·729	2·713	6·619	2·899	10·37

(*c*) Values of $10^2\tau/t$ (min^{-1}) at the stated reaction percentages, using $\kappa = 0{\cdot}29$

pH	10%	20%	30%	40%	50%	60%	70%	80%	90%	Mean $10^2\tau/t$ * min^{-1}
8·50		9·365	9·411	9·402	9·407	9·390	9·328	9·328	(9·229)	9·38
8·50	(6·885)	7·397	7·542	7·560	7·553	7·552	7·544	7·531	(7·459)	7·53
8·40	(5·597)	6·003	6·055	6·048	6·045	6·045	6·034	6·027	(5·967)	6·04
8·30		4·734	4·811	4·828	4·813	4·806	4·808	4·810	4·779	4·80
8·20	(3·741)	3·860	3·862	3·848	3·846	3·845	3·859	3·856	3·844	3·85

* Values in parentheses have been excluded in determining the mean.

(*d*) Calculation of k_{M1} and k_{M2}

pH	8·60	8·50	8·40	8·30	8·20
$10^2 k_{M1}$l[OH$^-$] (*i.e.*, $10^2\tau/t$)/min^{-1}	9·38	7·53	6·04	4·80	3·85
$10^{-4}k_{M1}$/l mol^{-1} min^{-1}	1·80	1·82	1·84	1·84	1·86

k_{M1}(mean) = (1·83 ± 0·03) × 10^4 l mol^{-1} min^{-1}; k_{M2}(mean) = κk_{M1} = (5·32 ± 0·09) × 10^3 l mol^{-1} min^{-1}.

Mercury(II) catalysis

(*a*) Times (t_x/min) to reach x% reaction

pH	t_{20}	t_{30}	t_{40}	t_{50}	t_{60}	t_{70}	t_{80}	t_{90}
9·20	3·37	5·87	9·10	13·27	18·77	26·93	39·73	64·10
9·00	4·98	8·60	13·17	19·10	27·41	39·00	57·77	96·60
8·80	8·09	13·89	20·91	30·40	43·80	63·47	94·80	157·1

(*b*) Selected time-ratios

pH		$t_{90} : t_{60}$	$t_{80} : t_{50}$	$t_{70} : t_{40}$	$t_{70} : t_{20}$	$t_{60} : t_{10}$
9·20		3·415	2·994	2·959	7·991	3·198
9·00		3·524	3·024	2·961	7·831	3·187
8·80		3·587	3·118	3·035	7·845	3·153
Mean:	Found	3·509	3·045	2·985	7·889	3·179
	Calc. ($\kappa = 0{\cdot}21$)	3·458	3·131	3·055	7·740	3·178

(*c*) Values of $10^2\tau/t$ (min^{-1}) at the stated reaction percentages, using $\kappa = 0{\cdot}21$

pH	20%	30%	40%	50%	60%	70%	80%	90%	Mean $10^2\tau/t$ min^{-1}
9·20	14·19	13·63	13·32	13·29	13·54	13·74	13·90	13·71	13·7
9·00	9·602	9·301	9·200	9·232	9·274	9·490	9·557	(9·098)	9·38
8·80	5·911	5·789	5·795	5·800	5·804	5·804	5·831	(5·595)	5·82

* Values in parentheses have been excluded in determining the mean.

(*d*) Calculation of k_{M1} and k_{M2}

pH	9·20	9·00	8·80
$10^2 k_{M1}$l[OH$^-$] (*i.e.*, $10^2\tau/t$)/min^{-1}	13·7	9·38	5·82
$10^{-3}k_{M1}$/l mol^{-1} min^{-1}	6·60	7·18	7·06

k_{M1}(mean) = (6·9 ± 0·3) × 10^3 l mol^{-1} min^{-1}; k_{M2}(mean) = κk_{M1} = (1·46 ± 0·07) × 10^3 l mol^{-1} min^{-1}.

The quantity κ is defined as the ratio $k_{M2} : k_{M1}$ (ref. 7). Values of τ, where $\tau = k_{M1}[OH^-]t$ (ref. 7), with which the time-ratios were compared to estimate a value for κ, were obtained using an I.C.T. 1301 computer.

Metal-ion Catalysed Hydrolysis.—It was established in Part I,[1] that formation constants K_1^c and K_2^c for the copper(II) complexes of methyl DL-2,3-diaminopropionate are sufficiently large (log $\beta_{21} = 16{\cdot}75$ at 25°, *cf.* log $\beta_{21} = 14{\cdot}50$ for methyl ester of L-histidine) to allow a fairly rigorous analysis of the kinetics of ester hydrolysis. Thus at a 2 : 1 ratio of ligand to copper(II) at pH *ca.* 6 and total copper(II) concentration of $2{\cdot}5 \times 10^{-3}$M ($I = 0{\cdot}1$M and 25 °C) it can be shown that there is *ca.* 99·5% of CuE_2^{2+} and 0·3% CuE^{2+}. The system is therefore more satisfactory than in the case of the methyl ester of L-histidine.[3] Complications do not arise through formation of protonated complexes or polynuclear species (*cf.* the M^{II} complexes of the methyl ester of L-cysteine [4]) in the pH range used for the kinetic studies.

Mercury(II) complexes of methyl 2,3-diaminopropionate have lower formation constants than those of copper(II), however the dissociation of HgE_2^{2+} can be repressed by increasing the ligand to metal ratio since there is little tendency to form HgE_3^{2+}. At a 6 : 1 ligand to mercury(II) ratio and pH *ca.* 7 it can be shown that some 99·9% of the mercury(II) is present as the HgE_2^{2+} complex.

Precipitation did not occur during the hydrolytic studies at the above ligand to metal ratios. Corrections were applied in the mercury(II) system for hydrolysis of the free ligand. The base consumption data was consistent with the kinetic scheme previously established [3] for the metal-ion catalysed hydrolysis of the methyl ester of L-histidine, *i.e.*, equations (1) and (2). At constant pH, plots of $\log_{10}(V_\infty - V_t)$ against time t showed

$$Me_2^{2+} + OH^- \xrightarrow{k_{M1}} MEA^+ + MeOH \qquad (1)$$

$$MEA^+ + OH^- \xrightarrow{k_{M2}} MA_2 + MeOH \qquad (2)$$

marked initial curvature, becoming linear at high values of t. Moreover, plots of $\log_{10}[(V_\infty/2) - V_t]$ against t were initially linear, curving convexly from the time axis at high values of t (V_∞ and V_t represent the volumes of base consumed at constant pH using a pH-stat). Behaviour of this type is characteristic of two consecutive pseudo-first-order reactions at constant pH corresponding to the stepwise reaction scheme shown in equations (1) and (2). There is initial fast hydrolysis of the bischelate followed by somewhat slower hydrolysis of the mixed ligand complex of the amino-acid and the amino-ester. The rate constants k_{M1} and k_{M2} were evaluated using the Swain time-ratio method as outlined by Frost and Pearson.[7] Table 2 lists a typical analysis of the kinetic data. The various rate constants obtained by this method are shown in Table 3. In all cases values of $\tau/t[OH^-] = k_{M1}$ are essentially independent of pH confirming that the reaction is also first order in hydroxide-ion concentration. The experimental spread of k_{M1} is generally less than ±3% (an error of ±0·01 pH units would lead to an error of *ca.* ±2·3%). Table 1 summarises the various rate constants and lists the thermodynamic parameters for the copper(II) complexes.

TABLE 3

Summary of data for the time-ratio analysis of the copper(II) catalysed hydrolysis of methyl DL-2,3-diaminopropionate at a Cu^{II} : ester ratio of 1 : 2 and $I = 0{\cdot}1$M

37 °C

pH	7·811	7·708	7·608	7·510	7·408	7·308
$10^2\tau/t$ (min^{-1})	8·871	7·333	7·566	4·652	3·675	2·867
$10^{-4}k_{M1}$/l mol^{-1} min^{-1}	4·405	4·615	4·410	4·620	4·614	4·531

k_{M1}(mean) $= (4{\cdot}53 \pm 0{\cdot}13) \times 10^4$ l mol^{-1} min^{-1}; k_{M2}(mean) $= \kappa k_{M1} = (1{\cdot}22 \pm 0{\cdot}04) \times 10^4$ l mol^{-1} min^{-1}

50 °C

pH	7·225	7·125	7·025	6·925	6·820	6·725
$10^2\tau/t$ (min^{-1})	13·60	10·35	8·445	6·760	5·266	4·245
$10^{-5}k_{M1}$/l mol^{-1} min^{-1}	1·127	1·080	1·109	1·118	1·109	1·112

k_{M1}(mean) $= (1{\cdot}11 \pm 0{\cdot}03) \times 10^5$ l mol^{-1} min^{-1}; k_{M2}(mean $= \kappa k_{M1} = (2{\cdot}77 \pm 0{\cdot}07) \times 10^4$ l mol^{-1} min^{-1}

Hydrolysis of Equimolar Mixtures of Metal Ion and Methyl DL-*2,3-Diaminopropionate*.—The kinetics of base hydrolysis of equimolar solutions of methyl DL-2,3-diaminopropionate and a metal ion [copper(II)] or mercury(II)] was also investigated. The formation constant measurements [1] show that at pH *ca.* 8, 25 °C, $I = 0{\cdot}1$M, and a total metal-ion concentration of 5×10^{-3}M at least 90% of the ester ligand is present as a 1 : 1 complex; either ME^{2+} or $MEOH^+$. It should therefore be theoretically possible to carry out a rigorous analysis of the hydrolysis kinetics. As in the analogous histidine methyl ester system,[3] precipitation accompanied hydrolysis of the ester group. The precipitate was presumably the neutral chelate MAOH or its dimer. Reactions were followed at constant pH for at least 12 half-lives and infinity plots were linear for *ca.* one half-life. After one half-life, when precipitation became appreciable, slight upward curvature of the plots occurred. This decrease in rate was possibly due to trapping of the unreacted ester chelates in the precipitate. Rate constants obtained from the initial linear portion of the infinity plots are summarised in Table 4. These rate constants must be regarded as somewhat approximate values.

TABLE 4

Rate constants for the copper(II) and mercury(II) catalysed hydrolysis of the methyl ester of DL-2,3-diaminopropionic acid at a metal ion : ester ratio of 1 : 1, 25 °C, and $I = 0{\cdot}1$M

pH	10^2k_{obs} / min^{-1}	$10^{-3}k_{obs}/[OH^-]$ / l mol^{-1} min^{-1}	k_{M3} / l mol^{-1} min^{-1}	k_{M4} / l mol^{-1} min^{-1}
Copper(II) catalysis				
8·80	6·909	8·381	$3{\cdot}71 \times 10^4$	$8{\cdot}11 \times 10^3$
8·60	4·569	8·786		
8·10	1·581	9·611		
7·90	1·161	11·19		
7·50	0·6060	14·67		
Mercury(II) catalysis				
9·23	6·631	2·988	$4{\cdot}92 \times 10^3$	$3{\cdot}00 \times 10^3$
8·95	3·693	3·171		
8·65	1·832	3·139		
8·43	1·333	3·790		
7·82	0·3516	4·072		

In both the copper(II) and mercury(II) systems, values

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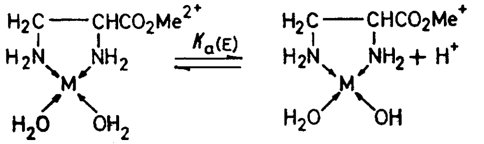
[7] A. A. Frost and R. G. Pearson, ' Kinetics and Mechanism,' John Wiley, New York, 1961. See also C. G. Swain, *J. Amer. Chem. Soc.*, 1944, **66**, 1969.

of $k_{obs}/[OH^-]$ are pH-dependent, a result which can be rationalised in terms of the reactions in (3), where ME^{2+}

$$\begin{tikzcd} ME^{2+} + OH^- \arrow[r, "k_{M3}"] \arrow[d, shift left, "K_a^P(E)"] & MA^+ + MeOH \arrow[d, shift left, "K_a^P(A)"] \\ MEOH^+ + OH^- \arrow[r, "k_{M4}"] \arrow[u, shift left, "H^+"] & MAOH + MeOH \arrow[u, shift left, "H^+"] \end{tikzcd} \qquad (3)$$

and $MEOH^+$ have the structures (I) and (II) respectively.



(4)

(I) 'ME^{2+}'

(II) '$MEOH^+$'

Values of $k_{obs}/[OH^-]$ decrease with increasing pH due to conversion of ME^{2+} into the less-reactive chelate $MEOH^+$. The practical ionisation constants for equilibrium (4), $K_a^P(E) = [MEOH^+]\{H^+\}/[ME^{2+}]$ (braces represent activities), have been determined: at 25 °C and $I = 0\cdot1$M, $pK_a^P(E)$ is 6·81 for copper(II) and 7·81 for mercury(II).[1] For (3) it can readily be shown that expression (5) is applicable, where $\alpha = [ME^{2+}]/([ME^{2+}] + [MEOH^+])$, so that a plot of $k_{obs}/[OH^+]$ against α should be linear, of slope $(k_{M3} - k_{M4})$ and intercept k_{M4}. Plots for both the copper(II) and mercury(II) systems were quite linear and the resulting values of k_{M3} and k_{M4} are shown in Table 4.

$$k_{obs}/[OH^-] = \alpha(k_{M3} - k_{M4}) + k_{M4} \qquad (5)$$

The results obtained for the copper(II) and mercury(II) catalysed hydrolysis of methyl DL-2,3-diaminopropionate are similar to those obtained with the methyl ester of L-histidine.[3] At a 1 : 1 ligand to metal ratio the pH-stat data can be rationalised in terms of a set of parallel pseudo-first-order reactions at constant pH, while at a 2 : 1 ligand to metal ratio, two consecutive pseudo-first-order reactions occur at constant pH. However, the proviso must be added that the time-ratio analysis is only a good approximation to the experimental data because disproportionation of the intermediate complex MEA^+ does occur, a point ignored by the time-ratio treatment. This disproportionation will be somewhat less than that indicated by the formation constants[1] (*viz.*, $CuEA^+ = 56\cdot8$, $CuA_2 = CuE_2^{2+} = 21\cdot6\%$) since, near the beginning of the reaction, the presence of an excess of CuE_2^{2+} will displace the equilibrium $2CuEA^+ \rightleftharpoons CuE_2^{2+} + CuA_2$ towards the left while, towards the end of the reaction, the presence of CuA_2 will also repress the dissociation of $CuEA^+$.

Hydrolysis of Equimolar Mixtures of Copper(II), *Methyl* DL-2,3-*Diaminopropionate, and* DL-2,3-*Diaminopropionic Acid*.—As a check on the time-ratio value of k_{M2} obtained at a 2 : 1 ligand to copper ratio, kinetic measurements were carried out on solutions containing equimolar amounts of copper(II), ester, and amino-acid at a total copper(II) concentration of 5×10^{-3}M and $I = 0\cdot1$M. Infinity plots showed a slight initial curvature, becoming linear after *ca.* one half-life. Such behaviour is expected on the basis of formation constant measurements[1] on solutions of $Cu^{II} : E : A = 1 : 1 : 1$. In the initial stages of reaction the more rapid hydrolysis of CuE_2^{2+} is superimposed on the main reaction, the hydrolysis of $CuEA^+$. As the reaction proceeds formation of CuA_2 represses that of CuE_2^{2+} and so hydrolysis of $CuEA^+$ becomes the only important reaction. Carrying out the reaction in the presence of an excess of CuA_2 decreased the initial curvature but had little effect on the final slope of the plot. The results obtained at pH 8·60 and 25 °C are shown in Table 5(*a*). There was little improvement in the initial curvature of the plots if concentrations of CuA_2 greater than that obtained at $Cu^{II} : E : A = 2\cdot5 : 1 : 4$ were employed. Values of k_{obs} obtained from the final slopes of the plots were pH-dependent, but $k_{obs}/[OH^-]$ (*i.e.* k_{M2}) was essentially constant (Table 5). The resulting mean value of $k_{M2} = (5\cdot26 \pm 0\cdot17) \times 10^3$ l mol^{-1} min^{-1} is in good agreement with that of $(5\cdot32 \pm 0\cdot09) \times 10^3$ l mol^{-1} min^{-1} obtained from the time-ratio analysis.

TABLE 5

Base hydrolysis of mixed ligand complexes of methyl DL-2,3-diaminopropionate, copper(II), DL-2,3-diaminopropionate, and 1,2-diaminoethane at 25 °C and $I = 0\cdot1$M

(*a*) DL-2,3-Diaminopropionate

(i) Effect of varying the copper(II): E : A ratio at pH 8·60

$Cu^{II} : E : A$	10^2k_{obs}/min^{-1}	$\frac{10^{-3}k_{obs}/[OH^-]}{l\ mol^{-1}\ min^{-1}}$
1 : 1 : 1	2·646	5·091
2·5 : 1 : 4	2·750	5·287
3·5 : 1 : 6	2·721	5·232

(ii) Effect of pH at $Cu^{II} : E : A = 2\cdot5 : 1 : 4$

pH	10^2k_{obs}/min^{-1}	$\frac{10^{-3}k_{obs}/[OH^{-1}]}{l\ mol^{-1}\ min^{-1}}$
8·60	2·750	5·287
8·40	1·752	5·338
8·20	1·113	5·374

Mean $k_{obs}/[OH^-] = k_{M2} = (5\cdot26 \pm 0\cdot17) \times 10^3$ l mol^{-1} min^{-1}.

(*b*) 1,2-Diaminoethane; $Cu^{II} : E : dae = 1 : 1 : 1$.†

pH	10^2k_{obs}/min^{-1}	$\frac{10^{-3}k_{obs}/[OH^-]}{l\ mol^{-1}\ min^{-1}}$
8·70	4·883	7·455
8·60	3·889	7·476
8·50	3·139	7·597
8·40	2·945	7·600
8·30	1·947	7·469

Mean $k_{obs}/[OH^-] = (7\cdot52 \pm 0\cdot08) \times 10^3$ l mol^{-1} min^{-1}.

† The results quoted were obtained using a copper(II) : E : dae ratio of 6 : 1 : 11 since this reduced the initial curvative of the infinity plots.

Hydrolysis of Equimolar Mixtures of Copper(II), *Methyl* DL-2,3-*Diaminopropionate, and* 1,2-*Diaminoethane*.—As 1,2-diaminoethane is a ligand closely related to methyl 2,3-diaminopropionate, it was of interest to determine the hydrolysis rate of the mixed ligand chelate $CuE(dae)^{2+}$ (dae = 1,2-diaminoethane). Using the same conditions and procedure described above, it was found that kinetic runs at $Cu^{II} : E : dae = 6 : 1 : 11$ gave infinity plots with little initial curvature and values of $k_{obs}/[OH^-]$ were essentially independent of pH. Table 5(*b*) summarises the rate constants obtained.

Thermodynamic Parameters.—Thermodynamic parameters for base hydrolysis of the species E, EH^+, CuE_2^{2+}, and $CuEA^+$ are summarised in Table 1. The enthalpy of activation, $\Delta H^\ddagger$ is significantly greater for the catalysed than for the uncatalysed reactions. Similar observations were also made with the methyl ester of L-histidine.[3] The reactions are thus best termed ' metal-ion promotions ' rather than true catalytic processes. The rate accelerations observed in the metal complexes arise from more positive (*i.e.* less negative) entropies of activation. The reasons for this behaviour have been considered in detail in a previous paper.[3] The metal complexes of methyl DL-2,3-diaminopropionate are somewhat more reactive towards base hydrolysis than the analogous complexes of methyl histidinate (Table 6), an effect which is due to a more favourable $\Delta S^\ddagger$ term in the former reactions.

TABLE 6

Summary of specific rate constants for base hydrolysis of methyl DL-2,3-diaminopropionate species at 25 °C and $I = 0{\cdot}1$M

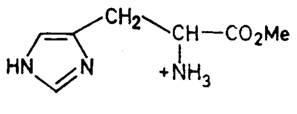
Species	k_{OH} †/l mol⁻¹ min⁻¹	$k_{OH} : k_E$
CuE^{2+}	37,100 (10,500)	850
CuE_2^{2+}	18,300 (19,690)	420
$CuEOH^+$	8100 (2022)	185
$CuE(dae)^{2+}$	7520	170
HgE_2^{2+}	6900	160
$CuEA^+$	5320 (2560)	120
HgE^{2+}	4920	110
EH^+	3440 (2790)	80
$HgEOH^+$	3000	70
$HgEA^+$	1460	30
E	43·8 (37·1)	1

† Values in parentheses are for the corresponding methyl L-histidinate species (ref. 3).

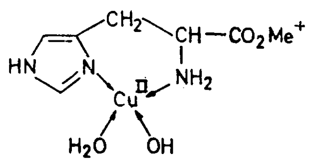
GENERAL CONCLUSIONS

The order of decreasing reactivity of the various methyl 2,3-diaminopropionate species towards nucleophilic attack by hydroxide ion at 25° is $CuE^{2+} > CuE_2^{2+} > CuEOH^+ > CuE(dae)^{2+} > HgE_2^{2+} > CuEA^+ > HgE^{2+} > EH^+ > HgEOH^+ > HgEA^+ > E$. A very similar series was observed in the case of the methyl histidinate complexes *viz.*, $CuE_2^{+} > NiE_2^{2+} > CuE^{2+} > NiE_2^{2+} > EH^+ > CuEA^+ > CuEOH^+ > NiEA^+ > E$. The rate accelerations observed in the methyl 2,3-diaminopropionate system are 10^2—10^3 (Table 6). Recent results obtained by Buckingham and Sargeson [8-13] for inert cobalt(III) systems indicate that a direct interaction between the metal ion and the carbonyl group of the ester should lead to a rate acceleration of *ca.* 10^6. In the present system it therefore seems appropriate to conclude that such interactions are not of great significance. An important factor in determining the reactivity of the complexes towards hydroxide ion is the charge carried by the species. The introduction of a single positive charge near the ester group increases the hydrolysis rate by a factor of *ca.* 50, whilst a dipositive charge produces a rate acceleration of at least 100-fold (Table 6). The reactivity ratios $k_{OH} : k_E$ also include a contribution from the inductive effect of the metal ion (see below) so that the copper(II) complexes are more reactive than the analogous mercury(II) species.

The rate accelerations depend on the relative proximity of the methoxycarbonyl group and the metal ion or proton carrying the positive charge. Thus the EH^+ species of the methyl ester of L-histidine in which the α-amino-group is protonated, (III), is more reactive towards base hydrolysis than the singly charged copper complex, (IV). The reverse effect occurs with methyl 2,3-diaminopropionate as, in this case, the EH^+ species is protonated at the β-amino-group.



(III)



(IV)

The copper(II) complexes of methyl DL-2,3-diaminopropionate are some two—seven fold more reactive towards base hydrolysis than their mercury(II) analogues. This effect is presumably due, in part, to the greater $-I$ effect exerted by copper(II) at the acyl carbon atom which will facilitate nucleophilic attack by hydroxide ion. The influence of the different metal-ion stereochemistries (copper is square planar and mercury tetrahedral) is difficult to assess.

On a statistical basis, bis-complexes having two ester functions should hydrolyse twice as rapidly as mono-complexes carrying the same charge. Thus it is found that $k_{CuE_2^{2+}}/k_{CuE(dae)^{2+}} = 1{\cdot}4$ and $k_{HgE_2^{2+}}/k_{HgE^{2+}} = 2{\cdot}4$; however, the complex CuE_2^{2+} seems abnormally unreactive since $k_{CuE_2^{2+}}/k_{CuE^{2+}} = 0{\cdot}49$. It is also found that CuE_2^{2+} hydrolyses more slowly than its methyl histidinate counterpart (Table 6) although in all other cases the methyl 2,3-diaminopropionate complexes are more reactive towards base hydrolysis than the analogous complexes of methyl histidinate. Thermodynamic data (Table 1) indicate that $\Delta H^\ddagger$ is larger (*ca.* 1 kcal mol⁻¹) and $\Delta S^\ddagger_{298}$ more negative than for $CuEA^+$. In the case of L-histidinate, the values of $\Delta H^\ddagger$ are similar for CuE_2^{2+} and $CuEA^+$, but $\Delta S^\ddagger_{298}$ is more positive (*ca.* 4 cal K⁻¹ mol⁻¹) for CuE_2^{2+}. Steric hindrance in the transition state may be responsible for the anomalous behaviour of CuE_2^{2+}.

The present results confirm that for esters such as

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[11] D. A. Buckingham, D. M. Foster, and A. M. Sargeson, *J. Amer. Chem. Soc.*, 1969, **91**, 3451.

[12] D. A. Buckingham, D. M. Foster, L. G. Marzilli, and A. M. Sargeson, *Inorg. Chem.*, 1970, **9**, 11.

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methyl 2,3-diaminopropionate and methyl histidinate containing two nitrogen donors, metal-ion catalysis at pH > 7 proceeds by a bimolecular reaction of a chelate species and a hydroxide ion; nucleophilic attack by water is unimportant. The magnitude of the rate constants is consistent with the view that a direct interaction between the ester carbonyl group and the metal ion is of limited importance since such interactions should produce much larger rate enhancements. The metal ion in these systems promotes ester hydrolysis mainly by its placement of a positive charge near the reaction centre, thus giving rise to more positive values of $\Delta S^{\ddagger}$.

EXPERIMENTAL

The preparation and purification of DL-2,3-diaminopropionic acid and its methyl ester were described in Part 1.[1] 1,2-Diaminoethane dihydrochloride was prepared by adding an excess of hydrochloric acid (12M) to 1,2-diaminoethane. The dihydrochloride was precipitated by addition of absolute ethanol and was recrystallized from ethanol several times until satisfactory titration data were obtained. Metal salt solutions were prepared and analysed as described in Part 1.[1] The kinetics of base hydrolysis were monitored using a Radiometer pH-stat and associated scale expander, as previously described.[3,4] Pseudo-first-order rate constants were evaluated using infinity plots or the Guggenheim procedure.

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