Kinetics and Mechanism of Displacement of Zinc(II) by Copper(II) in Complexes of Saturated Macrocyclic Tetra-amines

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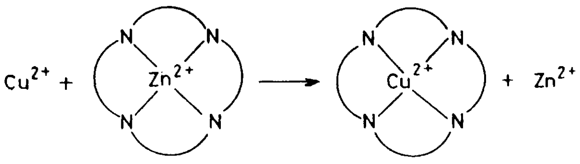
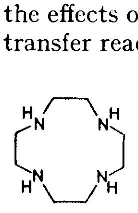
The kinetics of displacement of Zn^{2+} by Cu^{2+} from complexes of saturated 12- to 15-membered macrocyclic tetra-amines have been investigated in acetate-buffer solutions. Kinetic data support a common mechanism: $[ZnL]^{2+} + MeCO_2H \rightleftharpoons [Zn(O_2CMe)]^+ + HL^+$ (k_1, k_{-1}); $HL^+ + [Cu(O_2CMe)]^+ \longrightarrow [CuL]^{2+} + MeCO_2H$ (k_2), where the dissociation of L from Zn^{2+} is the slowest step. Values for k_1 and k_{-1}/k_2 show good agreement with previous values obtained independently. The activation parameters for k_1 and k_{-1} are discussed. The pre-dissociation mechanism is the same as that recently proposed for similar metal-exchange reactions in porphyrin complexes in dimethylformamide solutions.

The kinetic effects by which cyclic ligands convey unusual properties on metal complexation and decomplexation have gradually been disclosed by use of saturated macrocyclic polyamine ligands possessing only the most fundamental structures. The knowledge thus accumulated is expected to be extremely useful in discerning the kinetic chelate effects of natural macrocyclic tetra-amine porphyrins. Despite intensive studies,[1] these chelate effects are still far from clarified due to the complexity of the structures of these compounds and their solubilities.

We have now undertaken a kinetic study of the replacement of zinc(II) by copper(II) in complexes of 12- (L^1), 13- (L^2), 14- (L^3), and 15-membered macrocyclic tetra-amines (L^4) in acetate buffers [reaction (1)]. Ring size, an inseparable parameter of the cyclic structure, controls the equilibrium and kinetics of metal incorporation into the homologous macrocyclic tetra-amines. Hence, the use of a range of sizes from the smallest and the most rigid (L^1) through to the largest and the most flexible homologue (L^4)[2-18] might help in understanding the effects of the cyclic structures on tetra-amine ligand-transfer reactions.[19]

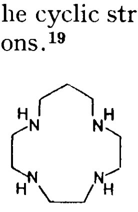


(1)



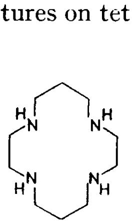
L^1

1,4,7,10-Tetra-aza-cyclododecane



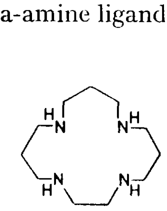
L^2

1,4,7,10-Tetra-aza-cyclotridecane



L^3

1,4,8,11-Tetra-aza-cyclotetradecane



L^4

1,4,8,12-Tetra-aza-cyclopentadecane

Most interestingly, the results of the present study ould shed light on the disputed mechanisms of the same type of metal-exchange reactions involving porphyrins: on the one hand an associative electrophilic mechanism has been proposed by Hambright and co-workers,[20-22] and on the other a dissociative mechanism has been proposed by Das [23] and Lavallee *et al.*[24]

EXPERIMENTAL

The macrocyclic tetra-amines L^1—L^4 were prepared as described before.[7,8,10,11] The first and second mixed protonation constants log K_1 and K_2 used for calculation were 10.70 and 9.70 for L^1,[7] 11.10 and 10.10 for L^2,[8] 11.50 and 10.30 for L^3,[11] and 11.20 and 10.10 for L^4.[10] When stock solutions of $Zn[NO_3]_2$ and L, both in acetate buffers ($MeCO_2H$–$Na[O_2CMe]$), were mixed the relatively stable $[ZnL]^{2+}$ complex (log K_{ZnL} 16.2, 15.6, 15.5, and 15.0 for L^1, L^2, L^3, and L^4, respectively) [12] was formed within a few minutes. Zinc ions were always used in excess to suppress dissociation of $[ZnL]^{2+}$. Under the acetate-buffer conditions uncomplexed Zn^{2+} is in equilibrium with $[Zn(O_2CMe)]^+$ (the equilibrium constant $K_{Zn(O_2CMe)}$ used was $10^{0.66}$ dm^3 mol^{-1}).[25] The degree of $[ZnL]^{2+}$ dissociation expressed by (2) is estimated as $10^{-5.1}$, $10^{-2.0}$, $10^{-2.0}$, and $10^{-3.8}$ for L^1 (pH 4.8), L^2 (pH 4.9), L^3 (pH 5.3), and L^4 (pH 5.2) respectively, at $[Zn^{2+}]_{app.} = 10^{-2}$ mol dm^{-3} and $[MeCO_2^-] = 10^{-1}$ mol dm^{-3}. Here $[L]_f$ is the concentration of uncomplexed macrocyclic ligand, and the last term in

$$\frac{[L]_f}{[ZnL^{2+}]} = \frac{(\alpha_H)_L \beta_{Zn(O_2CMe)}}{K_{ZnL}[Zn^{2+}]_{app.}} \qquad (2)$$

$$(\alpha_H)_L = [L]_f/[L] = 1 + K_1[H^+] + K_1K_2[H^+]^2 \qquad (3)$$

$$[Zn^{2+}]_{app.} = [Zn^{2+}] + [Zn(O_2CMe)^+] \qquad (4)$$

$$\beta_{M(O_2CMe)} = [M^{2+}]_{app.}/[M^{2+}] = 1 + K_{M(O_2CMe)}[MeCO_2^-] + K_{M(O_2CMe)}K_{M(O_2CMe)_2}[MeCO_2^-]^2 \qquad (5)$$

equation (5) is neglected for Zn because of the negligible concentration of $Zn[O_2CMe]_2$.[25]

The acidity constant pK_a of acetic acid used was 4.67. A stock solution of $Cu[NO_3]_2$ was prepared as described previously.[7] Uncomplexed Cu^{2+} is in equilibrium with $[Cu(O_2CMe)]^+$ and $Cu[O_2CMe]_2$, *i.e.* $[Cu^{2+}]_{app.} = [Cu^{2+}] + [Cu(O_2CMe)^+] + [Cu(O_2CMe)_2]$, with the corresponding equilibrium constants $K_{Cu(O_2CMe)} = 10^{1.72}$ dm^3 mol^{-1} and $K_{Cu(O_2CMe)_2} = 10^{0.25}$ dm^3 mol^{-1}.[25] The complex stability constants log K_{CuL} used were 24.8 (L^1),[7] 29.1 (L^2),[8] 27.1 (L^3),[11] and 24.4 (L^4).[10] Ionic strength was maintained at

0.20 mol dm^{-3} with Na[ClO$_4$]. All the work was at 25.0 ± 0.1 °C. The pH meter was calibrated to read hydrogen-ion concentration directly.

The metal-exchange kinetics were followed spectrophotometrically for the L^1 system by the increase in absorption intensity at 590 nm due to [CuL]$^{2+}$ formation, and polarographically for systems L^2—L^4 by the decrease in wave height at the reduction potential of uncomplexed Cu^{2+} [−0.25 V *vs.* the saturated calomel electrode (s.c.e.)] which was adequately separated from the reduction waves of [ZnL]$^{2+}$ (< −1.0 V) or [CuL]$^{2+}$ (< −0.5 V). The reaction rates were all determined four times by the initial-gradient method (*ca.* 25% of the reaction courses). Average values (±8% for 95% confidence limits) for the rates at 25.0 ± 0.1 °C are given in Table 1. The exchange rates were also measured at 15.0, 35.0, and 45.0 °C (all the parameters needed for the calculations are given in the references cited) to determine the activation parameters.

Table 1

Rate data for the Cu^{II}–[ZnL]$^{2+}$ reactions at 25 °C and *I* 0.2 mol dm^{-3}

Ligand	[ZnL^{2+}] (mmol dm^{-3})	[Zn^{2+}]$_{app.}$ (mmol dm^{-3})	[Cu^{2+}]$_{app.}$ (mmol dm^{-3})	[MeCO$_2^-$] (mmol dm^{-3})	pH	10^2 [MeCO$_2$H] * / mol dm^{-3}	Initial rate / mol dm^{-3} s^{-1}	
L^1	2.0	8.0	2.5	100	4.80	7.4_1	9.2	× 10^9
	2.0	18.0	2.5	100	4.80		7.1	
	2.0	28.0	2.5	100	4.80		6.0	
	2.0	8.0	5.0	100	4.80		$10._2$	
	2.0	8.0	7.5	100	4.80		$10._8$	
	2.0	8.0	2.5	100	5.00	4.8_6	5.9	
	2.0	8.0	2.5	100	5.20	2.9_5	3.7	
	2.0	8.0	2.5	100	5.70	0.93_3	1.1_6	
	1.0	8.0	2.5	100	4.80		4.7	
	4.0	8.0	2.5	100	4.80		$18._0$	
	2.0	8.0	2.5	50	4.80		5.1	
	2.0	8.0	2.5	200	4.80		$16._0$	
L^2	1.0	19.0	2.0	100	4.90	5.8_9	1.7_5	× 10^7
	1.0	39.0	2.0	100	4.90		1.1_0	
	1.0	59.0	2.0	100	4.90		0.88	
	1.0	19.0	1.2	100	4.90		1.3_2	
	1.0	19.0	3.4	100	4.90		2.1_0	
	1.0	19.0	2.0	100	5.20	2.9_5	0.90	
	1.0	19.0	2.0	100	5.60	1.1_8	0.35	
	2.0	19.0	2.0	100	4.90		3.6	
	3.0	19.0	2.0	100	4.90		5.5	
	5.0	19.0	2.0	100	4.90		8.8	
	1.0	19.0	2.0	50	4.90	2.9_5	1.1	
	1.0	19.0	2.0	200	4.90	$11._8$	2.5	
L^3	2.0	18.0	2.0	100	5.31	2.2_9	4.5	× 10^8
	2.0	38.0	2.0	100	5.31		4.2	
	2.0	58.0	2.0	100	5.31		4.0	
	2.0	18.0	1.0	100	5.31		4.3	
	2.0	18.0	3.2	100	5.31		4.6	
	2.0	18.0	2.0	100	5.57	1.2_6	2.4_6	
	2.0	18.0	2.0	100	5.80	0.72_5	1.4_2	
	4.0	18.0	2.0	100	5.31		9.0	
	6.0	18.0	2.0	100	5.31		$13._6$	
	2.0	18.0	2.0	50	5.31	1.1_5	2.3	
	2.0	18.0	2.0	200	5.31	4.5_8	8.8	
L^4	0.5	10.0	0.64	100	5.20	2.9_5	1.2_6	× 10^6
	0.5	10.0	1.28	100	5.20		1.2_9	
	0.5	10.0	1.92	100	5.20		1.3_1	
	0.5	20.0	0.64	100	5.20		1.1_8	
	0.5	30.0	0.64	100	5.20		1.0_3	
	0.5	50.0	1.28	100	5.20		1.1_2	
	0.5	10.0	0.64	100	5.40	1.8_6	0.80	
	0.5	10.0	0.64	100	5.70	0.93_3	0.40	
	0.25	10.0	0.64	100	5.20		0.64	
	1.0	10.0	0.64	100	5.20		2.5_0	
	1.5	10.0	0.64	100	5.20		3.9	
	0.5	10.0	0.64	50	5.30	1.4_8	0.67	
	0.5	10.0	0.64	200	5.20	5.9_0	2.3_7	

* Calculated using [MeCO$_2$H] = [H$^+$][MeCO$_2^-$]/10$^{-pK_a}$ with pK_a = 4.67.

RESULTS AND CALCULATION

The metal-exchange reactions are thermodynamically very favourable, as predicted from the log of the conditional equilibrium constants $K_{app.}$ for (6) * estimated as 8.0 (with L^1), 12.9 (L^2), 11.0 (L^3), and 8.8 (L^4) using equations (5) and (7) at [MeCO$_2^-$] = 0.1 mol dm^{-3} and 25 °C.

$$[ZnL]^{2+} + Cu^{2+}_{app.} \xrightleftharpoons{K_{app.}} [CuL]^{2+} + Zn^{2+}_{app.} \quad (6)$$

$$K_{app.} = K_{CuL}\beta_{Zn(O_2CMe)}/K_{ZnL}\beta_{Cu(O_2CMe)} \quad (7)$$

As shown in Table 1, the initial rates (when other conditions were the same) were: (*i*) linearly dependent (for L^1 and

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* Cu$^{2+}_{app.}$ represents all forms of Cu^{II} not complexed to L.

TABLE 2

Rate constants for the substitution of Cu^{2+} for Zn^{2+} in macrocyclic tetra-amine complexes, at 25.0 °C and I 0.2 mol dm^{-3}

		Activation parameters					
		For k_1		For k_{-1}[b]			
Ligand	k_1[a] / dm^3 mol^{-1} s^{-1}	$\Delta H^\ddagger$/ kcal mol^{-1}	$\Delta S^\ddagger$/ cal K^{-1} mol^{-1}	$\Delta H^\ddagger$/ kcal mol^{-1}	$\Delta S^\ddagger$/ cal K^{-1} mol^{-1}	K[c]	k_{-1}/k_2[d]
L^1	$(7.9 \pm 0.8) \times 10^{-5}$ $[4.1 \times 10^{-5}]$	12.3 ± 1.1	-36 ± 4	14.3	9	3.4×10^9	$(2.1 \pm 0.2) \times 10^{-1}$ $[1.8 \times 10^{-1}]$[e]
L^2	$(5.5 \pm 0.8) \times 10^{-3}$ $[3.7 \times 10^{-3}]$	9.9 ± 1.1	-36 ± 4	13.0	9	3.2×10^8	$(2.2 \pm 0.2) \times 10^{-1}$ $[2.1 \times 10^{-1}]$[f]
L^3	$(1.0 \pm 0.2) \times 10^{-3}$ $[7.3 \times 10^{-4}]$	11.4 ± 1.1	-34 ± 4	14.9	10	1.0×10^8	*ca.* 0 $[1.4 \times 10^{-2}]$[g]
L^4	$(9.2 \pm 1.5) \times 10^{-2}$ $[7.3 \times 10^{-2}]$	7.4 ± 1.0	-38 ± 5	13.7	14	6.5×10^7	*ca.* 0 $[2.0 \times 10^{-2}]$[h]

[a] Observed second-order rate constants for reaction (8); calculated second-order rate constants (dm^3 mol^{-1} s^{-1}) for the reverse reaction of (14) with M = Zn, using data given in ref. 12, are shown in square brackets. [b] Taken from k_f data of equation (14) with M = Zn.[12] [c] Calculated using equilibrium data given in ref. 12. [d] Observed values for reactions (8) and (9). The ratio of second-order rate constant for the forward reaction of (14) for Zn to that of Cu is given in square brackets. [e] Calculated using data given in refs. 7 and 12. [f] Calculated using data given in refs. 8 and 12. [g] Calculated using data given in refs. 11 and 12. [h] Calculated using data given in refs. 10 and 12.

L^2) or almost independent (for L^3 and L^4) of $[Cu^{2+}]_{app.}/[Zn^{2+}]_{app.}$; (*ii*) proportional to $[MeCO_2H]$; and (*iii*) proportional to $[ZnL^{2+}]$. We suggest the general mechanism in (8) and (9) for all the macrocyclic tetra-amine systems. A

$$[ZnL]^{2+} + MeCO_2H \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [Zn(O_2CMe)]^+ + HL^+ \quad (8)$$

$$HL^+ + [Cu(O_2CMe)]^+ \xrightarrow{k_2} [CuL]^{2+} + MeCO_2H \quad (9)$$

$$dc/dt = k_2[HL^+][Cu(O_2CMe)^+] = \frac{k_1k_2[ZnL^{2+}][MeCO_2H][Cu(O_2CMe)^+]}{k_{-1}[Zn(O_2CMe)^+] + k_2[Cu(O_2CMe)^+]} \quad (10)$$

steady-state approximation on $[HL^+]$ gives the initial rate in (10) which rearranges to (11). Substituting the relation (12) derivable from (5) into equation (11) and calling the left-hand side R^{-1}, one obtains (13). Plots of R^{-1} *vs.* $[Zn^{2+}]_{app.}/[Cu^{2+}]_{app.}$ were linear (see Figure 1 for L^1 and L^2),* and were used to find k_1 (the reciprocal of the intercept multiplied by $[MeCO_2H]^{-1}$) and k_{-1}/k_2 [calculable from (gradient/intercept)]. For L^3 and L^4, the gradients were almost zero, *i.e.* $k_{-1}/k_2 \approx 0$. All plots of log k_1 against T^{-1} gave straight lines permitting an estimation of $\Delta H^\ddagger$ and $\Delta S^\ddagger$. The results are listed in Table 2.

$$\left(\frac{dc}{dt}\right)^{-1}[ZnL^{2+}] = \frac{1}{k_1[MeCO_2H]}\left\{1 + \frac{k_{-1}[Zn(O_2CMe)^+]}{k_2[Cu(O_2CMe)^+]}\right\} \quad (11)$$

$$[M(O_2CMe)^+] = K_{M(O_2CMe)}[MeCO_2^-][M^{2+}]_{app.}/\beta_{M(O_2CMe)} \quad (12)$$

$$R^{-1} = \frac{1}{k_1[MeCO_2H]}\left\{1 + \frac{k_{-1}\beta_{Cu(O_2CMe)}K_{Zn(O_2CMe)}[MeCO_2^-][Zn^{2+}]_{app.}}{k_2\beta_{Zn(O_2CMe)}K_{Cu(O_2CMe)}[MeCO_2^-][Cu^{2+}]_{app.}}\right\} \quad (13)$$

DISCUSSION

To our knowledge this is the first kinetic study of the metal-exchange reactions involving complexes of saturated macrocyclic polyamines. In earlier independent kinetic studies we had determined the rates for incorporation of copper(II)[7,8,10,11] and zinc(II)[12] into the macrocyclic tetra-amines L^1—L^4 under the same acetate-buffer conditions, where the second-order reactions (14) between the major reactive species, the

$$[M(O_2CMe)]^+ + HL^+ \underset{k_r}{\overset{k_f}{\rightleftharpoons}} [ML]^{2+} + MeCO_2H,\ K = k_f/k_r \quad (14)$$

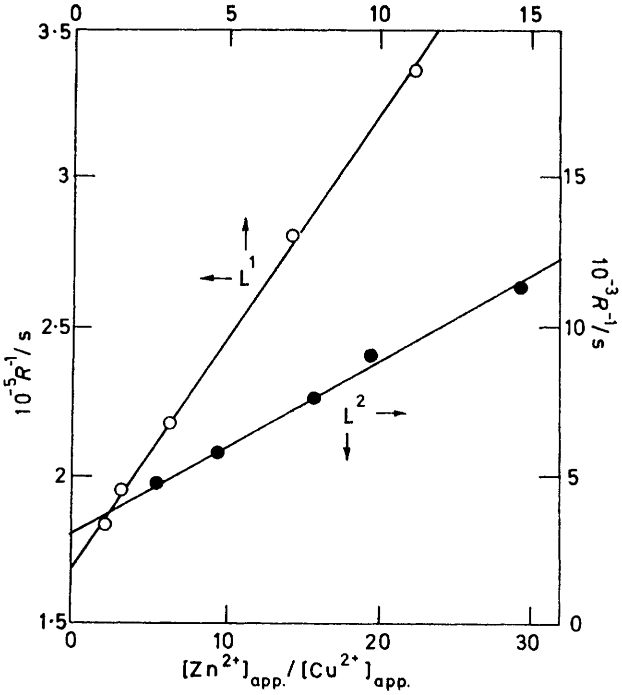

FIGURE 1 Plots of R^{-1} *vs.* $[Zn^{2+}]_{app.}/[Cu^{2+}]_{app.}$ at 25.0 °C [see equation (13)]. Data at $[ZnL^{2+}] = 2 \times 10^{-3}$, $[MeCO_2^-] = 10^{-2}$ mol dm^{-3}, and pH 4.80 for L^1, and at $[ZnL^{2+}] = 2 \times 10^{-3}$, $[MeCO_2^-] = 10^{-2}$ mol dm^{-3}, and pH 4.90 for L^2

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* A referee has suggested that the rates be measured under pseudo-first order conditions, *i.e.* $[Zn(O_2CMe)^+] \ll [Cu(O_2CMe)^+]$ and $[MeCO_2H]$ = constant. To ascertain that Zn^{2+} is in the form of $[ZnL]^{2+}$ in the acetate buffer, we employed $[Zn^{2+}]_{app.} > 10^{-2}$ mol dm^{-3}. This necessitates $[Cu^{2+}]_{app.} > 10^{-1}$ mol dm^{-3}, which is unsuitable for polarographic measurements of $[Cu^{2+}]_{app.}$.

monoprotonated ligand HL$^+$ and the monoacetatometal ion $[\mathrm{M(O_2CMe)}]^+$, were all observed. The reverse rate constants k_r were calculable using the reported stability constants K. Thus calculated k_r values for Zn are in good agreement with the k_1 values derived for the present reaction (8). Further, by dividing the reported k_f values for Zn by k_f values for Cu, we can assess the values for k_{-1}/k_2 for the reactions (8) and (9), which are close to the values experimentally derivable with L^1 and L^2 (see Table 2). These agreements support the mechanism involving dissociation of the $[\mathrm{ZnL}]^{2+}$ complex promoted by the attack of the acid $\mathrm{MeCO_2H}$, followed by $\mathrm{Cu^{2+}}$ incorporation into the freed L.*

We can now rule out an associative reaction pathway for metal-exchange reactions in the macrocyclic tetra-amine complexes. The associative mechanism prevalent to complexes of the homologous linear polyamines supposed binuclear intermediates in which both outgoing and incoming metal ions are co-ordinated to sites on the flexible ligands.[19] An associative mechanism[22] proposed for porphyrin systems comprises an intermediate where the entering and leaving metal ions lie on the same side of the porphyrin plane. However, the rigid co-ordination requirements of macrocycles whether folded or planar would not allow stepwise dissociation of bimetallated intermediates. Also, the steric crowding and lack of π electrons would not facilitate access of the incoming metal ion. Complete loss of the leaving metal ion assisted by acetic acid would be the alternative preferred by saturated macrocyclic systems. Even the most flexible 15-membered system L^4 would be no exception, although the demetallation rate from it is the fastest among the macrocycles tested. The subsequent incorporation of $\mathrm{Cu^{2+}}$ is also fastest with L^4.[10]

Our reaction mechanism is reminiscent of the predissociation mechanism (15) and (16) recently proposed by Lavallee *et al.*[24] for the substitution of $\mathrm{Cu^{2+}}$ for $\mathrm{Cd^{2+}}$ in *N*-methyltetraphenylporphyrinatocadmium, $[\mathrm{Cd(mtpp)}]^+$, in dimethylformamide solution (where the

$$[\mathrm{Cd(mtpp)}]^+ + \mathrm{H_2O} \underset{k_{-2}'}{\overset{k_1'}{\rightleftharpoons}} \mathrm{Cd^{2+}} + \mathrm{mtpp^-} \tag{15}$$

$$\mathrm{Cu^{2+}} + \mathrm{mtpp^-} \xrightarrow{k_2'} [\mathrm{Cu(mtpp)}]^+ \tag{16}$$

monoanionic form of the porphyrin, mtpp$^-$, is in rapid equilibrium with neutral Hmtpp). The reaction observed was first order in $[\mathrm{Cd(mtpp)^+}]$ and $[\mathrm{H_2O}]$, but was independent of $[\mathrm{Cu^{2+}}]$ or $[\mathrm{Cd^{2+}}]$.[24] However, Lavallee noted that the apparent lack of $[\mathrm{Cd^{2+}}]$ effects cannot be considered to be definitive support for an associative mechanism as was stated by Hambright and coworkers.[20-22] Provided that the rate of incorporation of $\mathrm{Cu^{2+}}$ into the mtpp$^-$ is much greater than the $\mathrm{Cd^{2+}}$ incorporation rate and that the ratio of $[\mathrm{Cd^{2+}}]$ to $[\mathrm{Cu^{2+}}]$ is not extremely large, the experimental rate would be expressed by $k_1'[\mathrm{Cd(mtpp)^+}][\mathrm{H_2O}]$ and the effects of $[\mathrm{Cu^{2+}}]$ or $[\mathrm{Cd^{2+}}]$ would not be detected. However, there were no individual experimental data in support of this supposition.

The mechanism in (8) and (9) for substitution of $\mathrm{Cu^{2+}}$ for $\mathrm{Zn^{2+}}$ in our macrocyclic system may provide a model for the postulated mechanism for the porphyrin system in (15) and (16). Incorporation of $\mathrm{Cu^{2+}}$ into L^3 and L^4 [k_2 in reaction (9) is equal to k_f for $\mathrm{Cu^{2+}}$ in (14), *i.e.* 5.3×10^6 and 2.2×10^8 dm^3 mol^{-1} s^{-1} respectively][10,11] is 50—70 times faster than of $\mathrm{Zn^{2+}}$ [k_{-1} in (8) equals k_f for $\mathrm{Zn^{2+}}$ in (14), *i.e.* 7.5×10^4 and 4.5×10^6 dm^3 mol^{-1} s^{-1}][12] and so the rate expression (10) can be approximated to the form (17) when $[\mathrm{Zn(O_2CMe)^+}]/[\mathrm{Cu(O_2CMe)^+}] = 6.71$ at $[\mathrm{Zn^{2+}}]_{\mathrm{app.}} = 10^{-2}$, $[\mathrm{Cu^{2+}}]_{\mathrm{app.}} = 6.4 \times 10^{-4}$, and $[\mathrm{MeCO_2^-}] = 10^{-1}$ mol dm^{-3}. The theoretical rate expression (17), on one hand, explains the present experimental

$$\mathrm{d}c/\mathrm{d}t \approx k_1[\mathrm{ZnL^{2+}}][\mathrm{MeCO_2H}] \tag{17}$$

results for L^3 and L^4, and on the other hand it is similar to the observed relation for the mtpp$^-$ system. For the smaller systems L^1 and L^2, k_2 [1.8×10^6 (L^1) and 5.6×10^6 (L^2) dm^3 mol^{-1} s^{-1}][7,8] is not much greater than k_{-1} [1.3×10^5 (L^1) and 1.2×10^6 (L^2) dm^3 mol^{-1} s^{-1}],[12] and consequently the rates are more sensitive to variation of $[\mathrm{Zn^{2+}}]_{\mathrm{app.}}$ or $[\mathrm{Cu^{2+}}]_{\mathrm{app.}}$ It is of interest that in the displacement of $\mathrm{Zn^{2+}}$ by $\mathrm{Cu^{2+}}$ in a water-soluble porphyrin complex in acetate buffers, the rate-determining step was found to be the protolytic dissociation of the zinc complex with the rates showing a slight suppression by added $\mathrm{Zn^{2+}}$ and enhancement by $\mathrm{Cu^{2+}}$.[23], †

Comparison of the activation parameters for the L^1—L^4 systems shows that the fastest dissociation rate (of L^4) from $\mathrm{Zn^{2+}}$ corresponds to the smallest $\Delta H^\ddagger$, which probably reflects the most flexible conformation for dissociation. The constantly large and negative $\Delta S^\ddagger$ term regardless of the ring size may indicate appreciable solvation of the transition state. The activation parameters for k_1 allow one to draw energy profiles of reaction (8); these had previously been constructed in part from the parameters for k_{-1}[12] and the equilibrium constants K.[12] Figure 2 shows the L^4 case, and the energy parameters for all the profiles are listed in Table 2. From the independently observed activation parameters for the forward and reverse steps of each reaction, the overall enthalpy and entropy changes are calculable, *e.g.* $\Delta H = -6.3$ kcal mol^{-1} and $\Delta S = -52$ cal K^{-1} mol^{-1} for the dissociation of L^4.‡ The calculated total free-

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* Within the technical limitation of the kinetic studies, no more data were obtained that would permit an elaborate mechanistic analysis of the k_1 step of equation (8). Hence we were confined to a simple description of the dissociative mechanism (as against the associative mechanism). It is not inconceivable that, as a referee has suggested, equation (8) [hence also (9)] may be a composite of multi-stage processes involving an acid-base equilibrium. The activation parameters presented below would then also be composite.

† It should be added that a porphyrin-metallation mechanism whereby solvent dissociation from the metal ion is rate-determining (P. H. Hambright and P. B. Chock, *J. Amer. Chem. Soc.*, 1974, **96**, 3123; M. J. Bain-Ackerman and D. K. Lavallee, *Inorg. Chem.*, 1979, **18**, 3358) is also related to the L^1—L^4 metallation mechanism.[3,4,7,8,10-12]

‡ Throughout this paper: 1 cal = 4.184 J.

energy changes (*ca.* 12, 10, 10, and 9 kcal mol^{-1} with L^1, L^2, L^3, and L^4, respectively) are reasonably close (within experimental error) to values (13, 12, 11, and 11 kcal mol^{-1}) derived from independently determined K.[12] We are now fairly certain that the equilibrium (8) is entropy-governed in all the macrocyclic systems L^1—L^4. The large negative $\Delta S^{\ddagger}$ may imply that the transition state lies nearer to the product $\{[Zn(O_2CMe)]^+ + HL^+\}$ than to the starting state ($[ZnL]^{2+} + MeCO_2H$). That is the complexation of L with $[Zn(O_2CMe)]^+$ must overcome the highest energy barrier at a fairly early stage, in accord with the solvent-dissociation mechanism.[12]

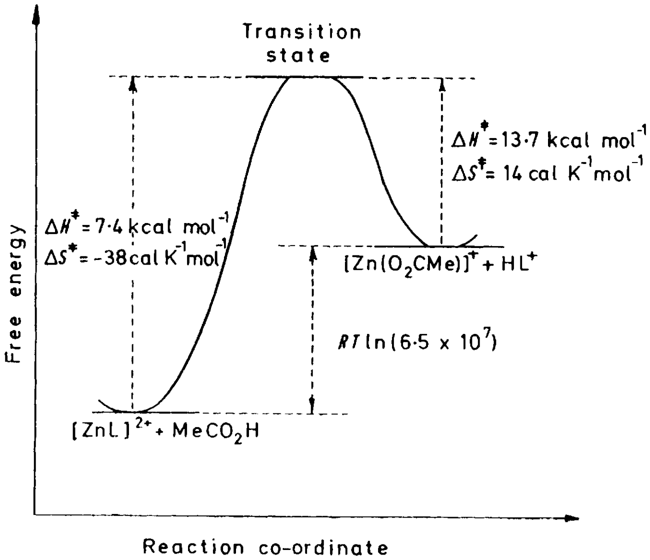

FIGURE 2 Energy profile for reaction (8) with L^4 at 25 °C

The ring size of the tetra-amine macrocycles can seriously affect the metal complex geometry depending on the size of the metal ions to be included: *e.g.* the 14-membered L^3, while adopting a planar (or square-pyramidal) *trans* configuration with relatively small cations Ni^{2+},[26] Cd^{2+},[27] or Hg^{2+},[27] forms a folded *cis* configuration with the larger cation Pb^{2+}.[28] Although there has been no report on the geometries of complexes of Zn^{2+} with L^1—L^4, a similar ring size–cation size relationship probably holds: the relatively large rings L^3 and L^4 would adopt a square-planar configuration, while the small L^1 could not accommodate Zn^{2+} in a planar fashion and must assume a folded *cis* configuration. In fact, 1,4,8,11-tetramethyl-1,4,8,11-tetra-azacyclotetradecane exhibits a square-pyramidal geometry around Zn^{2+} with four N atoms in the basal plane.[29] The present kinetic study, however, has revealed little of the effects of the complex geometries on the pre-dissociation reaction mechanism.

[9/921 *Received, 15th June,* 1979]

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