Kinetic and Equilibrium Studies on Copper(II) Complexes of a 9-Membered Macrocyclic Triamine, 1,4,7-Triazacyclononane, and a 14-Membered Macrocyclic Tetra-amine, 1,4,8,11-Tetra-azacyclotetradecane

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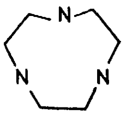
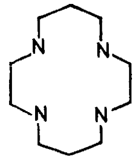
The thermodynamics and kinetics of formation of copper(II) complexes of 1,4,7-triazacyclononane (L^1) and 1,4,8,11-tetra-azacyclotetradecane (L^2) have been studied. The stability constants and thermodynamic parameters have been determined by a polarographic method for L^1 and by the potentiometric method of Bjerrum and Nielson for L^2. The complex $[CuL^2]^{2+}$ has log K_{CuL} 27.2 (ΔH − 30.4 kcal mol^{-1} and ΔS 22.4 cal K^{-1} mol^{-1}) at I 0.20 mol dm^{-3} and 25 °C, which represents stability enhancement over the complex of the corresponding linear tetra-amine by three orders of magnitude due to more favourable entropy and enthalpy contributions. The higher frequency of the maximum of the visible absorption band indicates that the favourable ΔH term derives from an increase in Cu–N bond energy. On the other hand, the cyclization poses severe steric constraints on the complex of the triamine ligand, as manifested by a large enthalpy loss. This destabilization is barely compensated by the favourable entropy term: log K_{CuL} 16.2, ΔH − 13.0 kcal mol^{-1}, and ΔS 30.5 cal K^{-1} mol^{-1}. Kinetic studies in acetate buffers using the stopped-flow method have given the following rate laws for the complex formation at 25 °C and I 0.20 mol dm^{-3}: for L^1, $d[CuL^{2+}]/dt = k_H[Cu(O_2CMe)^+][HL^+]$, where $k_H = 10^{6.8}$ dm^3 mol^{-1} s^{-1}; for L^2, $d[CuL^{2+}]/dt = k_H[Cu(O_2CMe)^+][HL^+] + k_{2H}[Cu(O_2CMe)^+][H_2L^{2+}]$, where $k_H = 10^{6.7}$ and $k_{2H} = 10^{0.9}$ dm^3 mol^{-1} s^{-1}. The rate law for the formation of $[CuL^2]^{2+}$ at pH 1.8—2.5 (unbuffered) and 25 °C has been determined by the polarographic method: $d[CuL^{2+}]/dt = k_H'[Cu^{2+}][HL^+] + k_{2H}'[Cu^{2+}][H_2L^{2+}]$, where $k_H' = 10^{6.9}$ and $k_{2H}' = 10^{-1.1}$ dm^3 mol^{-1} s^{-1}.

CYCLIZATION of saturated polyamine ligands has remarkable thermodynamic and kinetic effects on complex formation. However, most studies have focused on tetra-amine complexes [1-18] and there are few studies on complexes containing cyclic triamines.[19,20] This paper presents stability constants, thermodynamic parameters, rate constants, and activation parameters for the complex formation between 1,4,7-triazacyclononane (L^1) and Cu^{II}, in order to understand the effects of cyclization of the linear triamine 3-azapentane-1,5-diamine (L^3).

Meanwhile for cyclic tetra-amines there remains the question of what causes the ' macrocyclic effect '[1] by 14-membered ligands, such as 1,4,8,11-tetra-azacyclotetradecane (L^2). Hinz and Margerum [9,10] concluded from a study of nickel(II) complexes that the macrocyclic effect is due to fewer degrees of solvation for cyclic relative to linear tetra-amines such as 3,7-diazanonane-1,9-diamine (L^4), resulting in an exceptionally favourable enthalpy. On the other hand, in recent studies on copper(II) complexes of a 12-membered homologue, 1,4,7,10-tetra-azacyclododecane (L^5),[12,13] and of a 13-membered homologue, 1,4,7,10-tetra-azacyclotridecane (L^6),[14,15] we have found that the major contributory term to the macrocyclic effect is entropy, although its importance relative to the enthalpy term decreases with increasing ring size. An extrapolation suggests that the entropy term may play a role in the high stability of the complexes of 14-membered macrocycles. Moreover, based on a study of a linear relation between the enthalpy of complex formation and the energy of the electronic-absorption maxima, Fabbrizzi *et al.*[21] predicted that the enthalpy contribution



L^1



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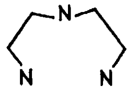
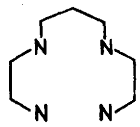


L^3



L^4

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due to the ligand desolvation claimed by Hinz and Margerum may be overestimated and that the extra stability of macrocyclic complexes arises from the entropy term. In order to settle this question, we have undertaken an equilibrium study for $[Cu^{II}L^2]^{2+}$. We have also examined the kinetics of formation of this complex in acid and acetate buffers. Comparison of the present kinetic results with those for the nickel(II) system [3] might be expected to be helpful in deducing the reaction mechanisms for these metal ions.

EXPERIMENTAL

Materials.—The macrocyclic triamine ligand L^1 was prepared as the *NN'N''*-tris(toluene-*p*-sulphonyl) derivative by the method of Yang and Zompa,[20] m.p. 223 °C (lit.,[20] 222—223 °C). The trihydrochloride of L^1 was purified by twice recrystallizing from an aqueous solution of 6 N HCl and dried *in vacuo* at room temperature, m.p. *ca.* 240 °C (decomp.). Its mass and n.m.r. spectra confirmed the purity and structure. The macrocyclic tetra-amine L^2 was prepared by the method of Martin *et al.*[22] Its tetrahydrochloride was purified by twice recrystallizing from an aqueous solution of 6 N HCl and dried *in vacuo* at room temperature, m.p. 253—255 °C (Found: N, 12.75. Calc. for $C_{10}H_{24}N_4\cdot 4HCl\cdot 5H_2O$: N, 12.8%). Its mass and n.m.r. spectra confirmed the purity and structure. Copper amalgam used for e.m.f. measurements was prepared by saturating mercury with pure copper metal (99.999%) in an atmosphere of nitrogen to prevent oxidation. The preparation of the other reagents was described earlier.[13,15]

Apparatus and Procedures.—The polarographic measurements for equilibrium studies were identical to those used previously.[12-16] The complex-formation equilibrium between Cu^{II} and L^2 was studied by measuring the e.m.f. of the following cell using the four-necked vessel to be described below:

$$\begin{array}{l|c|c|c|l} \mathrm{Cu(Hg)} & \text{Test solution} & 1.00\ \mathrm{mol\ dm^{-3}} & \mathrm{KCl\ (saturated)} & \mathrm{Hg} \\ & c_{\mathrm{Cu}}, c_{\mathrm{L}} & \mathrm{KCl\ solution} & \mathrm{Hg_2Cl_2} & \end{array}$$

The four-necked vessel [23] allowed the insertion of a J-type amalgam electrode,[24] a saturated calomel electrode (s.c.e.), a glass electrode, and a glass tube for entry and exit of nitrogen gas. The vessel was filled with pure nitrogen gas before introduction of the deaerated test solution and the copper-amalgam electrode. A stream of nitrogen gas was passed through the test solution during the course of e.m.f. measurement. Potentials were determined by using a digital pH/mV meter (Orion Research, model 701) or a Shimazu model K-2 precision potentiometer, with an accuracy of ±0.1 mV. Two hours were required after the introduction of the test solution for the e.m.f. of the amalgam electrode to become constant. The response of the electrode was checked with copper(II) solution containing an excess of ethylenediaminetetra-acetic acid (H_4edta) or L^4. The amalgam-electrode potentials agreed satisfactorily with those calculated from the reported equilibrium constants for $[Cu(edta)]^{2-}$ (ref. 25) and $[CuL^4]^{2+}$ (ref. 26) by using the Nernst equation at pH <4.0 for the edta and 5.0 for the L^4 system. The potentials of the copper-amalgam electrode conformed to the Nernst relation at pCu <11.0.

The kinetics of formation of $[CuL^1]^{2+}$ and $[CuL^2]^{2+}$ in acetate buffer solutions were studied by the stopped-flow method, using an Union Giken RA-401 stopped-flow spectrophotometer. The formation of the complexes was followed at 640 and 510 nm, respectively, by measuring the increase in absorbance. The apparent formation rate constant, k_f, was determined from the gradient of linear second-order plots of $\log(a-x)/(b-x)$ against time [Supplementary Publication No. SUP 22062 (4 pp.)] * as done for $[CuL^6]^{2+}$.[15] The kinetics of formation of $[CuL^2]^{2+}$ at lower pH 1.8—2.5 (unbuffered) were measured polarographically using the initial-gradient method described earlier.[13,15]

RESULTS

Equilibrium Study of $[CuL^1]^{2+}$.—The copper(II) complex of L^1 in acetate buffers (pH < 4.0) gave a well defined wave, diffusion-controlled at the dropping mercury electrode (d.m.e.).† The polarographic behaviour of the complex was unaffected by variation of the acetate concentration from 0.03 to 0.10 mol dm^{-3}, indicating no mixed-ligand complex formation within this range. Plots of log $i/(i_d - i)$ against d.c. potential, E, were linear with a reciprocal gradient of −34 mV, corresponding to a reversible two-electron reaction at the d.m.e. The half-wave potentials, $(E_{\frac{1}{2}})_{CuL}$, shifted with a change in concentration of the ligand, $[L]_F$, and pH according to equation (1). Typical results at 25 °C are shown in Table 1.

$$\Delta E_{\frac{1}{2}} = (E_{\frac{1}{2}})_{Cu} - (E_{\frac{1}{2}})_{CuL} = 0.0296\left\{\log\frac{K_{CuL}\cdot[L]_F}{(\alpha_H)_L} + \log\frac{k_{CuL}}{k_{Cu}}\right\} \qquad (1)$$

TABLE 1

Effects of ligand, copper(II), and acetate concentrations and pH on the half-wave potentials of $[CuL^1]^{2+}$ at I 0.20 mol dm^{-3} and 25 °C

10^3[L]	$10^3[Cu^{II}]$	$[MeCO_2^-]$		$E_{\frac{1}{2}}$	$\Delta E_{\frac{1}{2}}$/mV	
mol dm^{-3}			pH	V *versus* s.c.e.	calc.*	obs.
2.50	0.20	0.05	4.00	−0.097 5	0	0
5.00	0.20	0.05	4.00	−0.107 6	−8.9	−10.1
10.00	0.20	0.05	4.00	−0.117 8	−17.8	−19.7
5.00	0.20	0.03	4.00	−0.107 4		
5.00	0.20	0.10	4.00	−0.107 5		
5.00	0.40	0.05	4.00	−0.106 8		
5.00	0.20	0.05	3.50	−0.075 6	0	0
5.00	0.20	0.05	4.00	−0.107 6	−29.6	−32.0

* Using equation (1).

For a definition of the symbols, see refs. 13 and 15. Here, $\log(k_{Cu}/k_{CuL}) = 0.040$.

With the aid of equation (1), the stability constants K_{CuL} at 35.0, 25.0, and 15.0 °C were determined as 15.92, 16.23, and 16.56 dm^3 mol^{-1} (I 0.20 mol dm^{-3}), respectively. The linear plot of log K_{CuL} against T^{-1} afforded ΔH −13.0 ±

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* For details, see Notices to Authors No. 7, *J.C.S. Dalton*, 1976, Index issue (items less than 10 pp. are supplied as full-size copies).

† At pH >4 in acetate buffers there was a second reduction wave, although very minor in relative height, which was irreversible. This complex species was unidentified. The first reduction wave (major) was reversible in nature and had the $E_{\frac{1}{2}}$ value expected from the reported K_{CuL} (ref. 20) and the pK_i values of L^1.

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0.5 kcal mol^{-1} and ΔS 30.5 ± 3.0 cal K^{-1} mol^{-1}.* The values of pK_1 (mixed mode) used at these temperatures are 10.48, 10.59, and 10.80, respectively, and of pK_2 are 6.64, 6.88, and 7.09. These were experimentally determined by potentiometric titrations.[15]

Equilibrium Study of [CuL^2]$^{2+}$.—The polarograms of [CuL^2]$^{2+}$ consistently exhibited two reduction waves, both of which were diffusion controlled but irreversible. Their half-wave potentials were almost independent of the concentration of the buffer reagents (acetate, phosphate, or valinate), but they shifted to more negative potentials with increases in the solution pH and in $[L]_F$. For instance, the first wave moved according to the relations $\Delta E_{\frac{1}{2}}/\Delta\log(\alpha_H)_L = 0.0296/\alpha$ and $\Delta E_{\frac{1}{2}}/\Delta\log\,[L]_F = -0.0296/\alpha$ V, where α is *ca.* 0.3. The $E_{\frac{1}{2}}$ difference (0.15 V) and the wave-height ratio (2 : 1) between the two waves were almost unchanged irrespective of pH 3.7—10.5 and $[L]_F$, which indicates that in solution there are two kinds of [CuL^2]$^{2+}$ complexes having the same Cu^{II} : L^2 molar ratio. However, because of the irreversibilities of their reduction waves, further study using the d.c. polarographic technique was not attempted.

We then turned to a potentiometric method developed by Bjerrum and Nielson,[27] and later by Oyama *et al.*[28] whereby K_{CuL} was determined through measurement of the e.m.f. of the cell containing the solution of [CuL^2]$^{2+}$. At pH <2.5 (unbuffered) the e.m.f. of the cell (described in the Experimental section) changed linearly to more negative potentials as [CuL^{2+}], $[L]_F$, and pH changed according to relations (2) and (3). Typical results at 25 °C are shown in Table 2.

TABLE 2

Equilibrium data for [CuL^2]$^{2+}$ at I 0.20 mol dm^{-3} and 25 °C

$\frac{10^3[CuL^{2+}]}{mol\ dm^{-3}}$	$\frac{10^3[L]_F}{mol\ dm^{-3}}$	pH	log $(\alpha_H)_L$	$\frac{E - \varepsilon_{Cu(Hg)}}{V}$	ΔE/mV	
					calc.*	obs.
1.0	4.0	2.07	17.79	0.297 3	0	0
1.0	4.0	2.26	17.35	0.307 2	6.7	9.9
1.0	4.0	2.45	16.96	0.318 4	24.5	21.1
1.0	2.0	2.26		0.297 0	0	0
1.0	4.0	2.26		0.307 2	8.9	10.2
0.5	2.0	2.26		0.306 0	8.9	9.0

* Using equation (4).

$$\Delta E/\Delta\log([CuL^{2+}]/[L]_F) = -30\ \text{mV} \quad (2)$$

$$\Delta E/\Delta\log(\alpha_H)_L = -30\ \text{mV} \quad (3)$$

Therefore, we concluded that Cu^{II} forms only a 1 : 1 complex with L^2, and that the potential of the copper-amalgam electrode, E, is given by (4), where $\varepsilon_{Cu(Hg)}$ is the normal oxidation potential evaluated by measuring the e.m.f. of the cell containing only Cu^{2+}. With the aid of (4), the stability

$$E = \varepsilon_{Cu(Hg)} + 0.0296\left\{\log K_{CuL}\cdot\frac{[L]_F}{[CuL^{2+}]}\cdot\frac{1}{(\alpha_H)_L}\right\} \quad (4)$$

constants at 35, 25, and 15 °C were determined as 26.44, 27.15, and 27.94 dm^3 mol^{-1}, respectively, which afforded ΔH -30.4 ± 0.3 kcal mol^{-1} and ΔS 22.4 ± 1.0 cal K^{-1} mol^{-1}. The values of the protonation constants for L^2 are listed in ref. 18. All the equilibrium data are in Table 3.

Kinetic Study of [CuL^1]$^{2+}$ *Formation.*—The reaction of Cu^{II} with L^1 (present as protonated forms) at pH 3.6—4.6 in acetate buffer was second order. By examining the variation of the observed second-order rate constant (k_f) with [MeCO$_2^-$] (typical results at 25 °C are in Table 4), it is possible to assess, with the aid of the appropriate plot,[13,15] the contributions of the various forms of copper ions and of the ligand to the rate. The rate equation was of the form (5) where k_H is the rate constant for reaction of monoprotonated ligand species [HL]$^+$ with [Cu(O$_2$CMe)]$^+$ ion. For a

$$k_f(\alpha_H)_L\frac{\beta_{MeCO_2}}{K_{Cu(O_2CMe)}[MeCO_2^-]} = \frac{k_H[H^+]}{K_1} \quad (5)$$

definition of the other terms see refs. 13 and 15. The appropriate plots at 35.5, 28, 25, and 20 °C are shown in Figure 1. The value of the gradient and K_1 lead to k_H values of (6.8 ± 0.5) × 10^6 dm^3 mol^{-1} s^{-1} at 25 °C. The activation parameters were determined from an Arrhenius plot (Figure 2).

TABLE 3

Comparison of stability constants, and enthalpy and entropies of formation, of 1 : 1 copper complexes at 25 °C

Ligand	log K_{CuL}	$\frac{-\Delta H}{kcal\ mol^{-1}}$	$\frac{\Delta S}{cal\ K^{-1}\ mol^{-1}}$	Remarks
L^1 [a]	16.2	13.0	30.5	9-Membered cyclic triamine
L^3 [b]	16.0	18.0	12.0	Linear triamine
L^2 [a]	27.2	30.4	22.4	14-Membered cyclic tetra-amine
L^4 [c]	23.9	27.7	16.5	Linear tetra-amine
L^5 [d]	24.8	18.3	51.4	12-Membered cyclic tetra-amine
L^6 [e]	29.1	29.2	33.7	13-Membered cyclic tetra-amine
L^7 [f]	24.4	26.5	22.7	15-Membered cyclic tetra-amine

[a] This work. [b] M. Ciampolini, P. Paoletti, and L. Sacconi, *J. Chem. Soc.*, 1961, 2994. [c] Ref. 26. [d] Ref 13. [e] Ref. 15. [f] Ref 16.

TABLE 4

Experimental rate data for [CuL^1]$^{2+}$ formation at I 0.20 mol dm^{-3} and 25 °C

(*a*) Effect of reactant concentrations on the rate at [MeCO$_2^-$] = 0.10 mol dm^{-3} and pH 3.81

$\frac{10^3[L^1]_I}{mol\ dm^{-3}}$	$\frac{10^3[Cu]_I}{mol\ dm^{-3}}$	Gradient *	$\frac{10^3 k_f}{dm^3\ mol^{-1}\ s^{-1}}$
8.66	7.50	1.66	3.29
8.66	5.00	5.20	3.27
8.66	2.50	8.83	3.30
13.09	5.00	11.25	3.24

(*b*) Effect of [MeCO$_2$]$^-$ on the rate at [Cu] = 5.00 × 10^{-3} and [L^1] = 8.66 × 10^{-3} mol dm^{-3}, and pH 3.81

$\frac{[MeCO_2^-]}{mol\ dm^{-3}}$	$\frac{\beta_{MeCO_2}}{K_{Cu(O_2CMe)}[MeCO_2^-]}$	Gradient *	$\frac{Gradient\cdot\beta_{MeCO_2}}{K_{Cu(O_2CMe)}[MeCO_2^-]}$
0.05	1.38	4.48	6.18
0.10	1.19	5.20	6.19
0.20	1.10	5.62	6.15

* From the second-order plot, see Figure 1 of SUP 22062.

Kinetic Study of [CuL^2]$^{2+}$ *Formation.*—The observed second-order rate constants for the reaction of Cu^{II} with L^2 at pH 4.2—5.0 in acetate buffer were treated similarly (see Table 5). The rate equation was of the form (6) where k_H and k_{2H} are the rate constants for the reaction of [Cu(O$_2$CMe)]$^+$ ion with [HL]$^+$ and [H$_2$L]$^{2+}$, respectively. The appropriate plots at 35, 30, and 25 °C are shown in Figure

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* Throughout this paper: 1 cal = 4.184 J.

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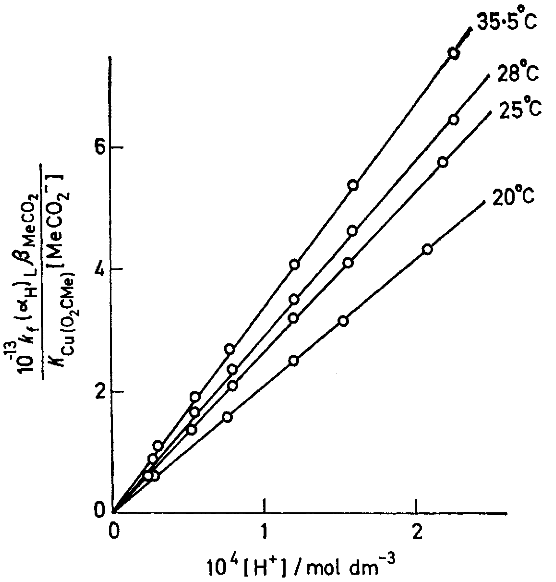

FIGURE 1 Plot of $10^{-13}k_f(\alpha_H)_L\beta_{MeCO_2}(K_{Cu(O_2CMe)}[MeCO_2^-])^{-1}$ against $10^4[H^+]$ for reaction of Cu^{2+} with L^1 in acetate buffer

3. The value of the intercept and K_1 lead to a k_H value of $(5.3 \pm 0.5) \times 10^6$ dm^3 mol^{-1} s^{-1}, and the value of the gradient and K_1 and K_2 lead to a k_{2H} value of 8.1 ± 1.0 dm^3 mol^{-1} s^{-1} at 25 °C. The activation parameters were determined as before (see Figure 1).

The reaction of Cu^{II} with L^2 at pH 1.8—2.5 (unbuffered)

$$\frac{k_f(\alpha_H)_L\beta_{MeCO_2}}{K_{Cu(O_2CMe)}[MeCO_2^-]} = \frac{k_H[H^+]}{K_1} + \frac{k_{2H}[H^+]^2}{K_1K_2} \quad (6)$$

$$k_f(\alpha_H)_L = \frac{k_H'[H^+]}{K_1} + \frac{k_{2H}'[H^+]^2}{K_1K_2} \quad (7)$$

was studied polarographically. The rate equation was of the form (7) where k_H' and k_{2H}' are the rate constants for the reaction of Cu^{2+} (aq) with $[HL]^+$ and $[H_2L]^{2+}$, respectively. The k_H' and k_{2H}' values were determined as $(8.0 \pm 0.5) \times 10^6$ and $(7.6 \pm 0.5) \times 10^{-2}$ dm^3 mol^{-1} s^{-1}, respectively, from the plot in Figure 4. All the kinetic results are in Table 6.

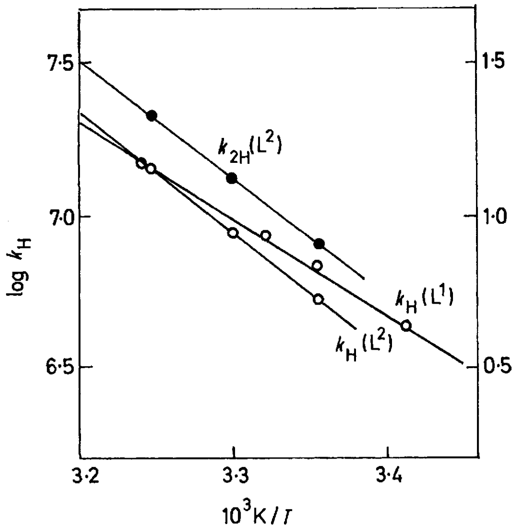

FIGURE 2 Arrhenius plots of copper(II) reactions with L^1 (k_H) and L^2 (k_H and k_{2H})

DISCUSSION

Stability of $[CuL^1]^{2+}$.—The stability constant of the 1 : 1 complex was recently determined by a potentiometric-titration method.[20] Our value obtained from an entirely separate approach agrees well with the previous value of log K_{CuL} 15.5 (in 0.1 mol dm^{-3} $K[NO_3]$ at 25 °C). Comparison with the stability constant of the complex $[CuL^3]^{2+}$ (see Table 3) indicates that the cyclization of the linear triamine has seemingly little influence on the complex formation. More insight is obtained by comparing the thermodynamic parameters and visible spectra. Evidence for the presumed weaker co-ordination bonds due to the steric constraint and possible change in the co-ordination from *meridional* to *facial* [20] is provided by the large enthalpy loss [$\Delta(\Delta H)$ *ca.* 5 kcal mol^{-1}] and by a shift to lower frequency of the maximum of the visible band, $\nu(d\text{–}d)$ ($\Delta\nu$ 1 000 cm^{-1}).[21] The experimental ΔH value of -13 kcal mol^{-1} for $[CuL^1]^{2+}$ formation in aqueous solution satisfactorily agrees with the theoretical value of -13.3 kcal mol^{-1} obtained by substituting $\nu(d\text{–}d) = 15\ 600$ cm^{-1} into the equation $-\Delta H = 54.43 + 4.33\ \nu(d\text{–}d)$. The linear relation between ΔH and $\Delta(d\text{–}d)$ was well established for copper–polyamine complexes including $[CuL^3]^{2+}$.[21] This strongly suggests that the

TABLE 5

Experimental rate data for $[CuL^1]^{2+}$ formation at I 0.20 mol dm^{-3} and 25 °C

(a) Effect of reactant concentrations on the rate at $[MeCO_2^-]$ = 0.10 mol dm^{-3} and pH 4.59

$10^3[L^2]_I$ / mol dm^{-3}	$10^3[Cu]_I$ / mol dm^{-3}	10^2 Gradient *	k_f / dm^3 mol^{-1} s^{-1}
8.80	7.50	0.960	17.0
8.80	5.00	2.80	17.0
8.80	2.50	4.66	17.1
13.20	5.00	6.05	17.0
5.87	2.50	2.46	16.8

(b) Effect of $[MeCO_2]^-$ on the rate at [Cu] = 5.00×10^{-3} and $[L^2] = 8.80 \times 10^{-3}$ mol dm^{-3}, and pH 4.28

$[MeCO_2^-]$ / mol dm^{-3}	β_{MeCO_2} / $K_{Cu(O_2CMe)}[MeCO_2^-]$	10^2 Gradient *	10^2 Gradient·β_{MeCO_2} / $K_{Cu(O_2CMe)}[MeCO_2^-]$
0.05	1.38	1.58	2.18
0.10	1.19	1.85	2.19
0.20	1.10	1.99	2.18

* From the second-order plot, see Figure 2 of SUP 22062.

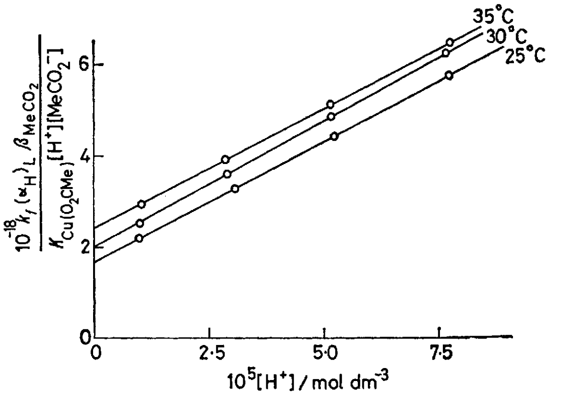

FIGURE 3 Plot of $10^{-18}k_f(\alpha_H)_L[H^+]^{-1}\beta_{MeCO_2}(K_{Cu(O_2CMe)}[MeCO_2^-])^{-1}$ against $10^5[H^+]$ for reaction of Cu^{2+} with L^2 in acetate buffer

smaller $-\Delta H$ value for $[CuL^1]^{2+}$ relative to $[CuL^3]^{2+}$ is solely attributed to the weaker Cu–N bond energy in the former complex. The enthalpic destabilization is barely offset by the favourable entropy contribution [$\Delta(\Delta S)$ *ca.* 20 cal K^{-1} mol^{-1}] also caused by the cyclization. A similar ΔS contribution to the macrocyclic complexes was reported for tetra-amine systems, whose interpretation could be applied here, too.[12–16]

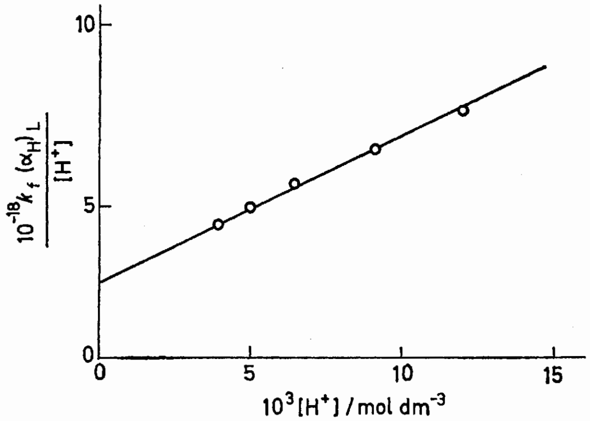

FIGURE 4 Plot of $10^{-18}k_f(\alpha_H)_L[H^+]^{-1}$ against $10^3[H^+]$ for reaction of Cu^{2+} with L^2

Stability of $[CuL^2]^{2+}$.—At the employed pH 2—5, only the formation of a red complex ($\lambda_{max.}$ 510 nm) was observed, which corresponds to a stable red isomer ($\lambda_{max.}$ 520 nm) of the 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetra-azacyclotetradecane complex described by Cabbiness and Margerum.[1] However, its polarograms indicate a mixture of two isomers having the same Cu^{II} : L^2 composition. This and the irreversible nature of the reduction waves of the complex ions are exceptional among the copper(II) complexes of 12- to 15-membered macrocyclic tetra-amines.[12–16] It might be that, with the 14-membered complex, rapid isomerizations such as configurational or conformational changes occur to perturb the electron-transfer step at the electrode. The stability constant log K_{CuL} 27.2 estimated using the second method should be a composite of those for the two possible isomers. Our value is in fair agreement with log K_{CuL} 28 (I 0.1 mol dm^{-3}) reported for the hexamethyl-substituted L^2 complex.[1] The extra stability of the L^2 complex arises from the cyclization, with the formation constant being three orders of magnitude larger than that for the linear L^4 complex.[26,29] The macrocyclic effect for the 14-membered tetra-amine arises from both enthalpy (*ca.* 60%) and entropy (*ca.* 40%) contributions, as distinct from the solely enthalpy-governed macrocyclic effect for the nickel(II) system.[9,10]

The stability constants are slightly larger for the 13- and smaller for the 12- and 15-membered homologues (see Table 3). It is of interest that the heat of formation reaches a maximum value at the 14-membered system, while entropy term peaks at the 12-membered system. Thus the 13-membered ring forms the most stable complex. That the 14-membered tetra-amine results in the largest heat of complex formation may be rationalized in terms of the least steric constraint imposed in planar chelation (*i.e.* the best fit to the macrocyclic cavity).[22] That the 12-membered tetra-amine results in the most favourable entropy term may reflect the most restricted freedom of the free ligands and hence the least entropy loss on co-ordination, and this effect has also been observed in other complexes of Zn^{II} (ref. 18) or Hg^{II} (ref. 17).

Here again the *d–d* absorption maximum (19 600 cm^{-1}) and the ΔH value (−30.4 kcal mol^{-1}) strictly obey the linear relation between ν(*d–d*) and ΔH as do the values for $[CuL^4]^{2+}$.[21] This indicates that the more favourable enthalpy term for L^2 relative to L^4 is primarily attributed to greater Cu–N bond energy (probably due to the nitrogen-donor atom being forced into a more favourable position for co-ordination by the cyclization) and not to other contributions such as the ligand-solvation effect postulated for the nickel(II) system.[9,10] The order of the decreasing $-\Delta H$ values for 14- (30.4), 13- (29.2), 15- (26.5), and 12-membered complexes (18.3 kcal mol^{-1}) parallels the decreasing ν(*d–d*) values (19 600, 18 200, 17 400, and 16 800 cm^{-1}), although the relation is not perfectly linear.

Kinetics of $[CuL^1]^{2+}$ *Formation.*—Only the monoprotonated species $[HL]^+$ contributed to the rate of the reaction with Cu^{II} in acetate buffer. The rate constant for the diprotonated species is negligible despite its greater abundance in the acid conditions of the experiments. This is apparently because of the electrostatic repulsion caused by the dipositive charge. The rate constant (k_H) is quite similar to those found for the monoprotonated tetra-amine macrocycles,[12–16] suggesting that a similar mechanism (*i.e.* dissociative) operates here. If more associative nature is involved in the rate-determining step, it is no wonder that the smaller size of the 9-membered ring retards the reaction rate. It is to be noted that the reaction of the monoprotonated species of the linear triamine L^3 with copper ion has entirely different activation parameters,[30]

TABLE 6

Summary of rate constants and associated activation parameters for copper species with protonated macrocyclic ligands L^1 and L^2 in aqueous solution at I 0.20 mol dm^{-3} and 25 °C *

Reaction	Rate constant dm^3 mol^{-1} s^{-1}	$\Delta H^‡$ kcal mol^{-1}	$\Delta S^‡$ cal K^{-1} mol^{-1}
$[Cu(O_2CMe)]^+$–$[HL^1]^+$	$(6.8 \pm 0.5) \times 10^6$	13.7 ± 0.3	19 ± 1
$[Cu(O_2CMe)]^+$–$[HL^2]^+$	$(5.3 \pm 0.5) \times 10^6$	16.9 ± 0.3	29 ± 1
$[Cu(O_2CMe)]^+$–$[H_2L^2]^{2+}$	8.1 ± 1.0	16.3 ± 0.3	0 ± 1
$Cu^{2+}(aq)$–$[HL^2]^+$	$(8.0 \pm 0.5) \times 10^6$		
$Cu^{2+}(aq)$–$[H_2L^2]^{2+}$	$(7.6 \pm 0.5) \times 10^{-2}$		

* Uncertainties are standard deviations.

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[29] R. Barbucci, L. Fabbrizzi, and P. Paoletti, *Co-ordination Chem. Rev.*, 1972, 8.

[30] T. R. Roche and R. G. Wilkins, *J. Amer. Chem. Soc.*, 1974, **96**, 5082.

although a direct comparison may not be appropriate because the effect of acetate ions used as buffer on the $[CuL^3]^{2+}$ formation rate was not reported. The L^1 reaction kinetics without acetate ions were not investigated due to the difficulty in complex formation in unbuffered solution at $pH < 3$.

Kinetics of $[CuL^2]^{2+}$ *Formation.*—The rate laws are identical to those found for the 12- and 13-membered homologues.[12-15] Since the rate constants and the activation parameters are also very similar, the discussion will not be repeated. However, there are two points to emphasize from the present study. First, the rate constants involving $[HL]^+$ species are nearly the same with (k_H) or without (k_H') the presence of the acetate anion. Although the exact nature of the $[Cu(O_2CMe)]^+$ species is unknown, it is clear that the acetate ion included in the rate equation has little influence on the kinetics, as shown [15] for the 13-membered homologue, and that accordingly the mechanism of the rate-determining step will not change with or without the buffer. On the other hand, acetate ion accelerates the rate of reaction of the diprotonated species by 10^2-fold. This is also true for the 13-membered homologue.[15] This supports the earlier postulate that proton transfer from the highly protonated macrocyclic ligand aided by $[MeCO_2]^-$ could be rate determining.[13,15] Secondly, the complex formation between Ni^{2+} and L^2 occurs with the same rate expression [3,*] where k_H' is $10^{5.6}$ times and k_H' $10^{1.4}$ times greater for the copper(II) (unbuffered) reaction. The ratio of rate constants for reaction of $Cu^{2+}(aq)$ and $Ni^{2+}(aq)$ with a common ligand is *ca.* $10^5 : 1$ for a large number of uni- and multidentate linear ligands.[30] Using this criteria for the normal dissociative mechanism, one can conclude that if formation of the first bond is rate determining for Cu^{2+}–$[HL]^+$, so it is for the Ni^{2+}–$[HL]^+$ reactions. The ratios $k_{Cu} : k_{Ni}$ for the $[H_2L]^{2+}$ reactions are far removed from $10^5 : 1$, suggesting other mechanisms such as proton transfer may be operative for both metal ions, or less likely that formation of the first bond is not rate determining for one of the two metal ions.

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[*] Kinetically indistinguishable expressions involving hydrolyses of aquated copper species {*e.g.* $[Cu(OH)]^+ + [H_2L]^{2+}$} appear to contribute significantly only at a pH range above those included in this study (see D. B. Moss, C. Lin, and D. B. Rorabacher, *J. Amer. Chem. Soc.*, 1973, **95**, 5179).