

Effects of Ring Size on Thermodynamic and Kinetic Properties of Copper(II)-Diaminodiamide Complexes in Aqueous Solution †

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In order to study the effects of ring size on the thermodynamic and kinetic properties of copper(II)-diaminodiamide complexes, a new quadridentate ligand, *N,N'*-bis(carbamoylmethyl)-trimethylenediamine (L^{131}), was synthesized. The log K values for the protonation constants of the ligand at 25.0 °C and 0.1 mol dm⁻³ NaClO₄ are 8.22 and 6.33. The log K value for the formation constant of $[Cu(L^{131})]^{2+}$ is 13.68, and the log K values for the deprotonation constants of $[Cu(L^{131})]^{2+}$ and $[Cu(H_{-1}L^{131})]^+$ are -6.94 and -8.25, respectively. The complexation kinetics of copper(II) with this ligand has been studied under the same conditions using the stopped-flow technique. The resolved formation rate constants (in 0.10 mol dm⁻³ NaClO₄ at 25.0 °C) for copper(II) reacting with the unprotonated and monoprotinated ligand, L^{131} and $[HL^{131}]^+$, are 1.88×10^9 and 1.79×10^6 dm³ mol⁻¹ s⁻¹ respectively. Two possible pathways for the complexation reaction are discussed.

Recently we have reported the thermodynamic and kinetic properties of copper(II) complexes of four closely related diaminodiamides, *N,N'*-bis(2-carbamoylethyl)ethylenediamine, *N,N'*-bis(2-carbamoylethyl)trimethylenediamine, *N,N'*-bis(2-carbamoylethyl)-1,2-propylenediamine, and *N,N'*-bis(2-carbamoylethyl)-2-hydroxytrimethylenediamine.^{1,2} In the current investigation, we have attempted to study the effects of chelate ring size on the thermodynamic and kinetic properties of copper(II) complexes of linear diaminodiamides of the type $NH_2CO(CH_2)_lNH(CH_2)_mNH(CH_2)_nCONH_2$, which are denoted by the symbol L^{lmn} . To accomplish this we have synthesized a new ligand, *N,N'*-bis(carbamoylmethyl)trimethylenediamine (L^{131}), which reacts with copper(II) to form a 1:1 complex containing linked 5,6,5-membered chelate rings, and have studied the thermodynamic and kinetic parameters of the complex. Comparing these results with those for the copper-diaminodiamide complexes containing 6,5,6- and 6,6,6-membered chelate ring systems, we find the sizes of the chelate rings of these complexes have significant effects on their thermodynamic and kinetic properties.

Experimental

Reagents.—The ligand, L^{131} , was prepared from 1,3-diaminopropane (41.5 cm³, 0.5 mol) and 2-chloroacetamide (55.8 g, 0.6 mol) in dimethylformamide (250 cm³) by heating under reflux for 2 h. The white crystals of the chloride salt of diprotonated 1,3-diaminopropane were removed by filtration. The solution was reduced to 120 cm³ in volume and was cooled in an ice-bath. Dichloromethane (180 cm³) was added dropwise and the solution was stirred until white crystals of the product were obtained. The crystals were isolated, recrystallized from methanol-water (75:25, w/w), filtered off, washed with cold methanol-water mixture (50:50, w/w), and then dried *in vacuo*, m.p. 254–255 °C (Found: C, 32.20; H, 6.85; N, 21.35. Calc. for C₇H₁₈Cl₂N₄O₂: C, 32.20; H, 6.95; N, 21.45%).

Measurements.—For pH measurements a Radiometer PHM64 instrument equipped with a GK2401B combined electrode was used. The kinetics of the formation of the copper(II) complex with L^{131} were studied spectrophotometrically at 294 nm with a Union Giken RA-401 stopped-flow

Table 1. Protonation constants of diaminodiamides and equilibrium constants of their copper(II) complexes at 25.0 ± 0.1 °C and $I = 0.10$ mol dm⁻³ (NaClO₄)

log K^a	L^{131}	L^{222b}	L^{232b}
log K_1^H	8.22 ± 0.04	8.78 ± 0.04	9.22 ± 0.06
log K_2^H	6.33 ± 0.03	5.82 ± 0.03	6.89 ± 0.04
log K_f	13.68 ± 0.08	12.58 ± 0.07	10.20 ± 0.08
log K_A	-6.94	-8.08	-8.62
log K_B	-8.25	-9.33	-10.10

^a $K_1^H = [HL^+]/[H^+][L]$, $K_2^H = [H_2L^{2+}]/[H^+][HL^+]$, $K_f = [CuL^{2+}]/[Cu^{2+}][L]$, $K_A = [Cu(H_{-1}L)^+][H^+]/[CuL^{2+}]$, $K_B = [Cu(H_{-2}L)][H^+]/[Cu(H_{-1}L)^+]$. ^b Data from ref. 1.

spectrophotometer equipped with a Union RA-415 rapid-scan attachment. For the spectrophotometric experiments the pH was controlled with a borate-mannitol buffer,³ which was also incorporated into the reference solution. Kinetic studies were carried out under pseudo-first-order conditions by using at least a 13-fold excess of copper(II). The concentrations of ligand and metal ion employed were in the range of 2.44×10^{-4} – 7.23×10^{-3} mol dm⁻³.

Results and Discussion

Protonation Constants.—A potentiometric titration of the perchlorate salt of diprotonated L^{131} with standard base yielded experimental data which have been deposited as SUP. The values of the protonation constants of L^{131} obtained by using Schwarzenbach's method⁴ are listed in Table 1. For comparison, the corresponding values for the protonation constants of the homologous linear diaminodiamides L^{232} and L^{222} are also given in the table.

For each stage of protonation, the constants K_1^H and K_2^H lie in the order $L^{131} < L^{232}$. This sequence can be related to the different inductive effects of the amide groups in these ligands. The side chains for L^{131} are shorter than those for L^{232} . In a

† Supplementary data available (No. SUP 56779, 7 pp.): observed rate constants, titration curves. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1990, Issue 1, pp. xix–xxii.

Table 2. Rate constants for formation (k_f) of $[\text{Cu}(\text{L}^{131})]^{2+}$ at 25.0 ± 0.1 °C and $I = 0.10$ mol dm⁻³ (NaClO_4)

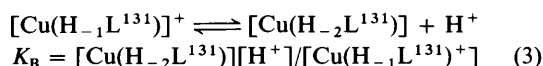
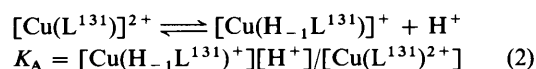
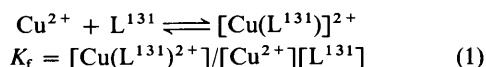
pH	$k_f/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
5.33	2.45×10^5
5.20	1.73×10^5
5.11	1.32×10^5
5.00	8.55×10^4
4.92	7.38×10^4
4.83	5.72×10^4
4.73	4.32×10^4
4.68	3.78×10^4
4.60	2.99×10^4

saturated system, inductive effects fall off rapidly with distance, so that the base-weakening effect of the amide groups makes the secondary amines in L^{131} less basic than those of L^{232} .

It is interesting that the value of K_1^{H} varies in the order $\text{L}^{131} < \text{L}^{222}$, while the order of K_2^{H} value is exactly reversed. As reported by Perrin and co-workers,^{5,6} the base-weakening effect of the substituent in aliphatic amines increases in the order $-\text{NHR}$, $-\text{CONH}_2$, and $-\text{NH}_2\text{R}^+$. The effects are attenuated with increasing chain length, decreasing by a factor of about 0.4 across each CH_2 . Thus, for the protonation of the neutral ligand, inductive effects fall off more rapidly with the length of the side chain than with that of the central chain. On the other hand, for the protonation of the monoprotated ligand, inductive effects fall off more rapidly with the length of the central chain than with that of the side chain. Consequently, K_1^{H} for L^{131} is smaller than that for L^{222} , while K_2^{H} for L^{131} is larger than that for L^{222} .

The Composition of the Copper(II) Complex.—Job's method⁷ of continuous variations was adopted for the determination of the composition of the complex. The results (SUP) indicated that copper(II) forms a 1:1 complex with L^{131} .

Equilibrium Constants for the Interactions of Copper(II) with L^{131} .—The titration curves for the 1:1 and 1:2 copper(II)– L^{131} systems are available as SUP. The equilibria (1)–(3) were found to describe the reactions of copper(II) with this ligand. The equilibrium constants obtained are given in Table 1 together with the corresponding values for $[\text{Cu}(\text{L}^{222})]^{2+}$ and $[\text{Cu}(\text{L}^{232})]^{2+}$.



Comparison of the values of $\log K_f$ shows that the stability order for the copper(II) complexes of diaminodiamides is $[\text{Cu}(\text{L}^{232})]^{2+} < [\text{Cu}(\text{L}^{222})]^{2+} < [\text{Cu}(\text{L}^{131})]^{2+}$. These results indicate that the three linked six-membered rings become sterically constrained on co-ordination to copper(II) and that the replacement of the two terminal six-membered rings by two five-membered rings or the replacement of the middle six-membered ring by a five-membered ring to make an alternating sequence of five- and six-membered rings can reduce the steric constraints, leading to a considerable increase in the stability of the copper(II) complex. For complexes containing an alternating sequence of five- and six-membered rings the formation

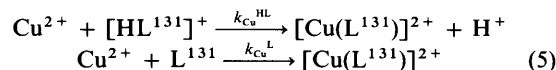
constants increase as the number of five-membered rings increases, so that K_f for $[\text{Cu}(\text{L}^{131})]^{2+}$ is larger than that for $[\text{Cu}(\text{L}^{222})]^{2+}$.

For each of these complexes, the value of K_B is less than that of K_A as might have been expected on the basis of both electrostatic effects and statistical factors.⁸ Comparison of the results listed in Table 1 indicates that K_A and K_B increase in the order $[\text{Cu}(\text{L}^{232})]^{2+} < [\text{Cu}(\text{L}^{222})]^{2+} < [\text{Cu}(\text{L}^{131})]^{2+}$ and $[\text{Cu}(\text{H}_{-1}\text{L}^{232})]^{+} < [\text{Cu}(\text{H}_{-1}\text{L}^{222})]^{+} < [\text{Cu}(\text{H}_{-1}\text{L}^{131})]^{+}$, respectively. There are two important factors influencing these sequences: one is the steric strains among the linked chelate rings,^{9,10} and the other, the inductive or acid-strengthening effects of the adjacent co-ordinated amino group.⁵ It is interesting that the steric strains in the three consecutive six-membered rings hinder not only the formation of the complex $[\text{Cu}(\text{L}^{232})]^{2+}$ but also the Cu–O to Cu–N bond rearrangements at the two amide sites. Similar steric effects were also found in the analogous deprotonation reactions of nickel(II) complexes of diaminodiamides.¹¹ As mentioned above, the large steric constraints in the three linked six-membered chelate rings distort the planar structures of $[\text{Cu}(\text{L}^{232})]^{2+}$, $[\text{Cu}(\text{H}_{-1}\text{L}^{232})]^{+}$, and $[\text{Cu}(\text{H}_{-2}\text{L}^{232})]$. In the copper(II) complex of a diaminodiamide, the crystal-field stabilization energy increases in the order $[\text{CuL}]^{2+} < [\text{Cu}(\text{H}_{-1}\text{L})]^{+} < [\text{Cu}(\text{H}_{-2}\text{L})]$. Thus, the effect attributed to the distortion from a square-planar structure on the stability of the copper(II) complex increases in the order $[\text{CuL}]^{2+} < [\text{Cu}(\text{H}_{-1}\text{L})]^{+} < [\text{Cu}(\text{H}_{-2}\text{L})]$. Consequently, the values of K_A and K_B for copper(II)– L^{232} system are smaller than those for the corresponding L^{222} or L^{131} system.

Kinetic Results.—The kinetics of the complexation reaction of copper(II) and L^{131} were studied at 25 °C, $I = 0.10$ mol dm⁻³ (NaClO_4), and pH 4.60–5.33. Under these conditions, the complex formation reaction was found to proceed to completion. Kinetic studies were carried out under pseudo-first-order conditions by using at least a 13-fold excess of copper(II). The observed pseudo-first-order rate constants are available as a SUP. Plots of k_{obs} vs. $[\text{Cu}^{2+}]$ give good straight lines according to equation (4) where $[\Sigma(\text{L}^{131})]$ represents the total concentration of all species of the uncomplexed ligand. The slopes of these plots give the values of the formation rate constants as a function of pH (Table 2).

$$d[\text{Cu}(\text{L}^{131})]^{2+}/dt = k_{\text{obs}}[\Sigma(\text{L}^{131})] = k_f[\text{Cu}^{2+}][\Sigma(\text{L}^{131})] \quad (4)$$

In the pH range of this study the reactive species are the unprotonated L^{131} and the monoprotated $[\text{HL}^{131}]^{+}$. Reactions of these species with Cu^{2+} to produce the chelate $[\text{Cu}(\text{L}^{131})]^{2+}$ is then considered to occur as in equation (5).



The rate law for the formation of $[\text{Cu}(\text{L}^{131})]^{2+}$ is described by equation (6). Combination of this and equation 4 yields (7). A

$$d[\text{Cu}(\text{L}^{131})]^{2+}/dt = k_{\text{Cu}}^{\text{HL}}[\text{Cu}^{2+}][\text{HL}^{131}]^{+} + k_{\text{Cu}}^{\text{L}}[\text{Cu}^{2+}][\text{L}^{131}] \quad (6)$$

$$\frac{k_f[\Sigma(\text{L}^{131})]}{[\text{L}^{131}]} = k_{\text{Cu}}^{\text{HL}}K_1^{\text{H}}[\text{H}^{+}] + k_{\text{Cu}}^{\text{L}} \quad (7)$$

plot of equation (7) gives a very good straight line and the resolved rate constants obtained are listed in Table 3 along with the corresponding values for the L^{222} and L^{232} systems.¹

Table 3. Resolved rate constants for the formation of copper(II) complexes of diaminodiamides in aqueous solution at 25.0 ± 0.1 °C and $I = 0.10$ mol dm⁻³ (NaClO₄)

Ligand	$k_{\text{Cu}}^{\text{L}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	$k_{\text{Cu}}^{\text{HL}}/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
L ¹³¹	1.88×10^9	1.79×10^6
L ²²² *	3.35×10^8	4.75×10^4
L ²³² *	1.48×10^8	9.21×10^4

* Data from ref. 1.

Pathways for the Formation Reactions.—The rate constants for the complex formation reactions of the aquated copper(II) ion with the unprotonated diaminodiamides are very large because of the internal conjugate-base effect.^{12–14} The two possible pathways for the complexation of copper(II) with each of these diaminodiamides are shown in the Figure. In the reaction path I, initial bonding to an amino nitrogen donor, the rate-determining step is the formation of the first co-ordination bond, (c) → (d).¹ There are two important factors which affect the formation rate constants of this path: one is the basicity of the amino group, and the other the size of the central chelate ring. As shown in the Figure, a strongly basic donor atom of the multidentate ligand can bond to a co-ordinated water molecule to give a stronger outer-sphere complex (larger K_{OS}) and to labilize subsequent water exchange (larger $k^{\text{M-H}_2\text{O}}$) from an adjacent position on the metal ion, leading to a large formation rate constant. Turan¹⁵ has observed a linear relationship between the $\text{p}K_{\text{a}}$ of the basic nitrogen atom and the degree of internal conjugate-base enhancement. On the basis of the proximity effect, the reaction *via* this path for the ligand containing the ethylenediamine moiety is expected to be faster than that *via* this path for the ligand containing the trimethylenediamine moiety. The magnitude of this proximity effect can be estimated from the relative distribution of the free end of bidentate ligands of varying chain length when one end is bonded to a co-ordinated water molecule [species (c) in the Figure]. Cotton and Harris¹⁶ have calculated a distribution of this type for bidentate ligands with four to seven links..

The basicity of the unprotonated ligand (K_1^{H}) increases in the order $\text{L}^{131} < \text{L}^{222} < \text{L}^{232}$. In addition, the proximity effect strongly favours the formation of the five-membered relative to the six-membered chelate ring.¹⁷ Based on these two factors, we expect that the rate for this pathway increases in the order $\text{L}^{131} < \text{L}^{232} < \text{L}^{222}$. The observed sequence for k_{Cu}^{L} , $\text{L}^{232} < \text{L}^{222} < \text{L}^{131}$, indicates this mechanism may be the main reaction path for the reactions of copper(II) with L^{222} and L^{232} , but not for the reaction with L^{131} .

In the reaction path II, initial bonding to an amide oxygen-donor atom, the rate-determining step is the formation of the second co-ordination bond, step (g) → (h) in the Figure.¹ For the same reasons mentioned above, the rate constant for this path increases with the basicity of the amino groups, and decreases with the size of the terminal or lateral chelate ring. Based on these two factors, we expect that the rate for this path increases in the order $\text{L}^{222} < \text{L}^{232} < \text{L}^{131}$. The observed sequence for k_{Cu}^{L} , $\text{L}^{232} < \text{L}^{222} < \text{L}^{131}$, indicates this mechanism may be the main reaction path for reactions of copper(II) with L^{131} and L^{232} , but not with L^{222} . In conclusion, path I is the main reaction path for the reaction of copper(II) with L^{222} , while path II is the main reaction path for the reaction of copper(II) with L^{131} ; both paths I and II make significant contributions in the reaction of copper(II) with L^{232} .

For the reactions of copper(II) with monoprotonated diaminodiamides the reaction path I is strongly hindered because of the electrostatic repulsion and the loss of internal conjugate-base enhancement. Thus, path II is the main reaction

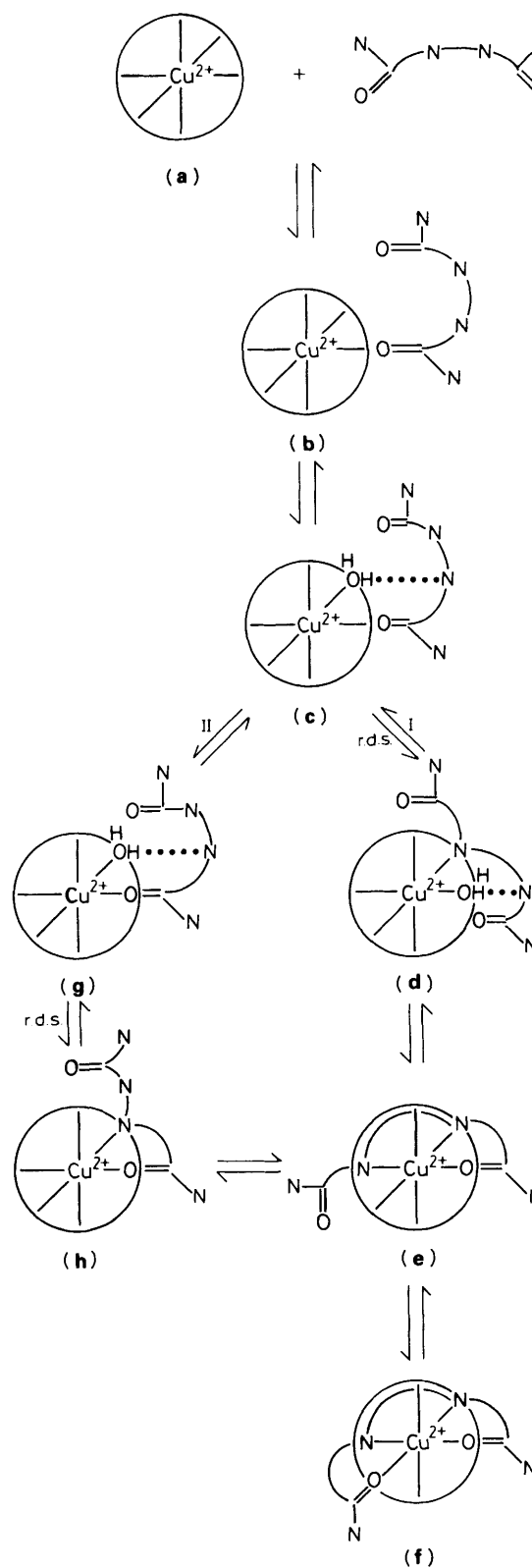


Figure. Possible pathways for the reaction of copper(II) with the unprotonated diaminodiamide. The circles represent the division between inner- and outer-sphere association; r.d.s. = rate-determining step

path for these three monoprotonated ligands. This conclusion is strongly supported by the fact that the sequence of the rate constants, $[\text{HL}^{222}]^+ < [\text{HL}^{232}]^+ < [\text{HL}^{131}]^+$, which is

expected for reaction *via* only path II, is actually found experimentally as listed in Table 3.

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