

Hydrogen-ion driven molecular motions in Cu²⁺-complexes of a ditopic phenanthrolinephane ligand†

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One of the first kinetic evaluations of a metal ion interchange between the two coordination sites of a ditopic macrocycle is presented.

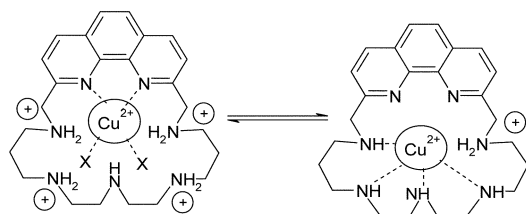
Oriented molecular motions and reorganisations are a key feature in living systems. ATP hydrolysis and proton-motive sources power these movements. Examples of movements coupled to proton gradients are, for instance, the rotation of γ protein that acts as an axle of the $\alpha_3\beta_3$ hexamer in the F₀/F₁ ATP-synthase¹ or the molecular gear generating the propulsive force that induces flagellar rotation in bacteria.² The regulatory role of many proteins is also related to conformational changes induced by protonation processes. In spite of this interest, the number of examples in which oriented molecular motions have been identified in small molecules is still not very large.³

Mononuclear metal complexes of ligands containing two different coordination sites can provide nice examples for elementary molecular motions. For this to occur, the metal ion has to interchange between the two coordination sites following a chemical input and in doing so has to produce a measurable change in a physical property of the system.

Here we report on a phenanthrolinephane receptor (L) consisting of a 1,10-phenanthroline unit linked to the ends of the pentaamine 4,7,10-triazatridecane-1,13-diamine (L1).⁴

We show that, as a consequence of a change in the protonation degree of the macrocycle, the Cu²⁺ metal ion leaves the phenanthroline site and moves to a coordination site exclusively formed by the amine nitrogens (see Scheme 1). Such a movement produces very important changes in the UV-visible spectra and we report one of the first studies on the kinetics of one of such processes.

pH-metric titrations⁵ of the system Cu²⁺-L show formation of the mono- and dinuclear Cu²⁺ complexes with stoichiometries CuH_xL^{(2+x)+} ($x = 4-0$) and Cu₂H_xL^{(4+x)+} ($x = 1,0,-1$), respectively. While for 1:1 M:L molar ratios the main species in solution are mononuclear complexes, for 2:1 M:L molar ratios the binuclear complexes are the only species present in solution

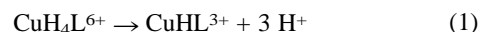


Scheme 1 H⁺-Driven molecular motion in the Cu²⁺-complexes of L.

† Electronic supplementary information (ESI) available: experimental details. See <http://www.rsc.org/suppdata/cc/b3/b309721h/>

(Fig. S1 in the ESI†). UV-Vis titrations of solutions containing a 1:2 M:L molar ratio show a blue-shift of the absorption band from 770 to 584 nm on going from acidic pH (pH = 2.5) where the species CuH₄L⁶⁺ predominates ($\epsilon = 194 \text{ M}^{-1} \text{ cm}^{-1}$) to pH values above 6 where the CuHL³⁺ species is the only one in solution ($\epsilon = 149 \text{ M}^{-1} \text{ cm}^{-1}$) (Fig. 1). The spectrum of CuHL³⁺ is very close to those recorded for the Cu²⁺ complexes of the open-chain polyamine 4,7,10-triazatridecane-1,13-diamine (L1) which constitutes the bridge of L. These spectral changes are reversible and reveal that the Cu²⁺ ions move from the phenanthroline to the polyamine site following the deprotonation of the amino groups. Such intense spectral changes were not observed for Cu²⁺ complexes of a similar pentaazaphenanthrolinephane containing all ethylene chains in the bridge.⁶ The spectra obtained for molar ratios M:L 2:1 do not show such a change and the colour remains green throughout all the pH range due to the fact that in the binuclear complexes the phenanthroline nitrogens will be always involved in the coordination of one of the two metal ions.

In order to obtain some information about the dynamics of the Cu²⁺ switch between the polyamine and the phenanthroline sites, kinetic experiments were carried out by mixing solutions containing the CuH₄L⁶⁺ species with MES (2-(4-morpholino)ethanesulfonic acid) solutions buffered at pH values at which the formation of the CuHL³⁺ species is favoured. These experiments showed that reaction (1) is established within the mixing time of the stopped-flow instrument (*ca.* 1 ms),⁷ *i.e.* the pH-induced switch of Cu²⁺ from the phenanthroline (phen) site to the polyamine site is very fast.



The dynamics of the reverse process were studied by mixing solutions containing CuHL³⁺ with an excess of acid. According

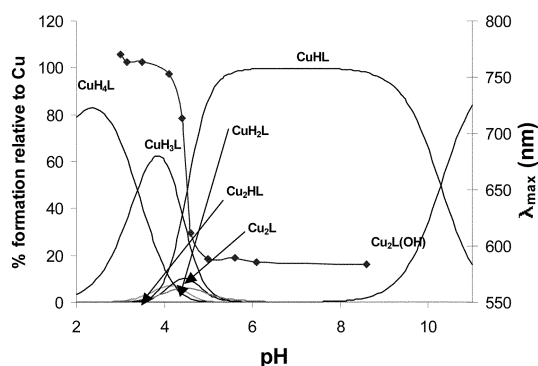
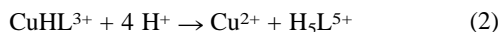


Fig. 1 Distribution diagram for the system Cu²⁺-L determined for 1:2 molar ratio ([Cu²⁺] = 1 × 10⁻³ M). The points represent the wavelengths at which the maximum is found as a function of pH. Charges omitted for clarity.

to the species distribution diagram in Fig. 1, if the acid excess is large enough, complete decomposition of the complex will occur (eqn. 2), although significant amounts of $\text{CuH}_4\text{L}^{6+}$ will be also formed when the pH of the final solution is greater than 2.



Stopped-flow experiments revealed two kinetically resolvable steps with rate constants $k_{1\text{obs}}(\text{CuHL}^{3+})$ and $k_{2\text{obs}}(\text{CuHL}^{3+})$ for the acid promoted decomposition of the CuHL^{3+} species in eqn. 2. The dependence of both rate constants with the acid concentration is illustrated in Fig. 2 and the data can be fitted by eqn. 3 to give the following values of the kinetic parameters: $a_1 = 82 \pm 3$, $b_1 = 52 \pm 5$, $a_2 = 11 \pm 1$, $b_2 = 24 \pm 4$ (a values in units of s^{-1} and b values in M^{-1}). In contrast, upon addition of an excess of acid, the $\text{CuH}_4\text{L}^{6+}$ species decomposes more slowly in a single kinetic step (see Fig. 2), the rate constants $k_{\text{obs}}(\text{CuH}_4\text{L}^{6+})$ changing with the acid concentration according to eqn. 4 with $c = 18 \pm 2 \text{ s}^{-1}$ and $d = 1.34 \pm 0.08 \text{ M}^{-1} \text{ s}^{-1}$. Despite the different rate laws observed for the decomposition of both species, eqns 3 and 4 can be considered simplified forms of the general eqn. 5, which is usually observed for the decomposition of Cu^{2+} -polyamine complexes, although for the case of the $\text{CuH}_4\text{L}^{6+}$ species the b value is very small and only the product $a \times b = d$ can be derived from the experimental data.

$$k_{\text{obs}} = \frac{a b [\text{H}^+]}{1 + b [\text{H}^+]} \quad (3)$$

$$k_{\text{obs}} = c + d [\text{H}^+] \quad (4)$$

$$k_{\text{obs}} = \frac{c + a b [\text{H}^+]}{1 + b [\text{H}^+]} \quad (5)$$

The mechanistic meaning of the a , b and c parameters has been comprehensively discussed in the literature⁸ and the actual values for the L complexes will be compared with related compounds in a future work. At this time, the most important observation is that complete decomposition of the CuHL^{3+} species occurs faster than decomposition of the more acidic $\text{CuH}_4\text{L}^{6+}$ species, which shows that the latter species is not an intermediate during the decomposition of CuHL^{3+} . Nevertheless, stopped-flow experiments using a diode array detector

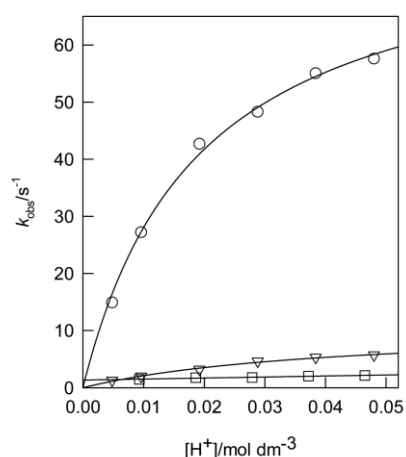


Fig. 2 Kinetic data for the acid-promoted decomposition of the $\text{CuH}_4\text{L}^{6+}$ and CuHL^{3+} species (25.0 °C, 0.15 M NaCl). The symbols \circ and Δ correspond to the first and second steps observed for CuHL^{3+} , whereas \square corresponds to the single step observed for $\text{CuH}_4\text{L}^{6+}$.

confirmed the expected formation of significant amounts of $\text{CuH}_4\text{L}^{6+}$ at the lowest concentrations of acid used in the decomposition of CuHL^{3+} . This kind of experiment also showed that the detectable intermediate formed during the decomposition of CuHL^{3+} has an absorption band centred at 690 nm, a position intermediate between those of CuHL^{3+} and $\text{CuH}_4\text{L}^{6+}$, which suggests the simultaneous coordination of the phen unit and some of the aliphatic amine groups, *i.e.* the shift of the metal ion from the polyamine to the phen site occurs through an intermediate containing the metal ion partly coordinated by both donor subunits. The same intermediate is probably also formed in reaction (1), although the rapidity of the reaction precludes its detection. In the presence of a large excess of acid, the intermediate decomposes rapidly and $\text{CuH}_4\text{L}^{6+}$ is not detected. However, if the acid excess is not large enough, the intermediate evolves to $\text{CuH}_4\text{L}^{6+}$. Although the nature of this intermediate is not clear, the equilibrium results suggest that it is probably $\text{CuH}_3\text{L}^{5+}$ or $\text{CuH}_2\text{L}^{4+}$. Unfortunately, Fig. 1 shows that the latter compounds always exist as a complex mixture of species in solution and their kinetics of decomposition could not be studied to compare the data with those corresponding to the second step in the decomposition of CuHL^{3+} . In any case, the whole set of kinetic experiments clearly show that the pH-induced switch of Cu^{2+} between the two different donor sites of L occurs rapidly and reversibly in both directions: the shift from the phen site to the polyamine unit occurs in the sub-ms time scale and the reverse shift always requires less than 1 s (Scheme 1). These results clearly show the basic principle and kinetics of a proton driven molecular reorganisation and can provide light into the mechanisms of such processes.

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- Compound L has been carried out by reacting 4,7,10-tris(*p*-tolylsulfonyl)-4,7,10-triazatridecane-1,13-diamine and 1,10-phenanthroline-2,9-dicarboxaldehyde in a CHCl_3 :MeOH (1:5 v/v) mixture. The formed imine was then reduced with NaBH_4 . Synthetic details are included in the ESI†.
- Potentiometric measurements were carried out at 298.1 K in 0.15 mol dm^{-3} NaCl. The program HYPERQUAD P. Gans, A. Sabatini and A. Vacca, *Talanta*, 1996, **43**, 1739 was used to compute the stability constants of L. Protonation constants are as follows: $\log K_{\text{H}_1/\text{H}_1\text{L}} = 10.01(1)$, $\log K_{\text{H}_2/\text{H}_2\text{L}} = 9.15(1)$, $\log K_{\text{H}_3/\text{H}_3\text{L}} = 7.81(1)$, $\log K_{\text{H}_4/\text{H}_4\text{L}} = 6.42(1)$, $\log K_{\text{H}_5/\text{H}_5\text{L}} = 2.97(2)$. System Cu^{2+} -L: $\text{Cu}^{2+} + 4\text{H}^+ + \text{L} = \text{CuH}_4\text{L}^{6+}$, $\log K = 38.48(4)$, $\text{Cu}^{2+} + 3\text{H}^+ + \text{L} = \text{CuH}_3\text{L}^{5+}$, $\log K = 35.08(8)$, $\text{Cu}^{2+} + 2\text{H}^+ + \text{L} = \text{CuH}_2\text{L}^{4+}$, $\log K = 29.9(1)$, $\text{Cu}^{2+} + \text{H}^+ + \text{L} = \text{CuHL}^{3+}$, $\log K = 26.26(6)$, $\text{Cu}^{2+} + \text{L} = \text{CuL}^{2+}$, $\log K = 15.98(6)$, $2\text{Cu}^{2+} + \text{L} + \text{H}^+ = \text{Cu}_2\text{HL}^{4+}$, $\log K = 31.64(8)$, $2\text{Cu}^{2+} + \text{L} = \text{Cu}_2\text{L}^{4+}$, $\log K = 27.5(1)$, $2\text{Cu}^{2+} + \text{L} + \text{H}_2\text{O} = \text{Cu}_2\text{L}(\text{OH})^{3+} + \text{H}^+$, $\log K = 18.1(1)$.
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