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FULL PAPER

Molecular rearrangements controlled by pH-driven Cu^{2+} motions

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Ligands **1**–**3** contain two coordinatively distinct compartments: AH_2, featuring a bis-amino bis-amido donor set, and B, featuring a bis amino-heterocycle donor set. Their coordinative tendencies towards Cu^{2+} have been studied in dioxane–water solution (4 : 1 v/v) by means of potentiometric titration experiments. The complex species which form in the pH 2–12 range have been individuated and their formation constants calculated. At neutral or slightly acidic pH values, the Cu^{2+} cation forms a 1 : 1 complex with the neutral ligands, residing in the B compartment. If the pH is then raised to distinctly basic values, the AH_2 compartment loses its two amide protons and Cu^{2+} moves inside it, forming neutral complexes with a bis-amino bis-imide donor set. The nature of these complexes has been ascertained by means of UV/Vis spectroscopy and by comparison with results for ligand **5**, which also binds Cu^{2+} by losing its two amide protons, but does not possess further binding groups appended to the amine nitrogens. With ligands **1**–**3**, when Cu^{2+} is coordinated by the bis-amino bis-imide donor set, one of the two appended heterocycles of the B compartment is still bound to it, in one of its apical positions, so that, on changing the pH between neutral and basic values, the Cu^{2+} movement induces an overall molecular rearrangement, which was found to be reversible.

Introduction

The number of systems in which controlled movements at a molecular level are achieved is constantly increasing. These systems have been named *molecular machines*[1] and the use of such molecular scale tools can be envisaged in the fields of logic devices, computation and information storage.[2] Typically, following an external stimulus of a chemical, electrochemical or photochemical nature, a molecular fragment, *i.e.* a component, is made to move with respect to the whole molecular system, to which it is permanently connected either through a covalent bond (like in scorpionates[3]) or thanks to topological constraints (like in rotaxanes[4] and catenates[5]). Some different examples have also been reported in which the switching on or off of an external stimulus is able to control the folding/unfolding of a large molecular system between two different shapes.[6] Beside the perspective of mimicking the folding/unfolding processes of proteins, studies in this field have been devoted particularly to the pH-controlled or redox-driven self-assembly/disassembly of transition metal helicates,[7] also in connection with information storage in solution.[7e,f] Finally, a few examples have also been described in which a monoatomic cationic[8] or anionic[9] particle is made to translocate between two sites of a molecular system, to which it is not permanently connected, but bound through labile metal–ligand coordinative interactions. In particular, we have recently described the pH-driven translocation of a transition metal cation, Ni^{2+}, which can be made to move between the AH_2 and B compartments of ligand **1** thanks to a pH variation, as sketched in Scheme 1.[8c] When the pH is maintained between 7 and 8, the metal cation resides in the bis-aminoquinoline compartment B (form **a**), since the dioxo-tetraamine compartment AH_2 is a very poor donor. However, if the pH is raised to 9.5 or over, the Ni^{2+} cation is able to promote the deprotonation of the two amide nitrogens, and the obtained bis-amino bis-imide donor set, A^{2-}, becomes a much better ligand than B for Ni^{2+}, which thus moves into it (form **b** in Scheme 1).

Ligand **1** is representative, as it possesses the two necessary features for pH-driven cation translocation: (i) two binding sites, one of which has a coordinatively bistable donor set, that can be switched by pH between AH_n and A^{n-}; (ii) a metal–ligand interaction energy which follows the order $AH_n \ll B \ll A^{n-}$. Also the choice of Ni^{2+} as the translocatable cation was not casual: only Co^{2+}, Ni^{2+} and Cu^{2+}, among the first-row dipositive transition metal cations, are able to promote the deprotonation of the two amide nitrogens in a dioxo-tetraamine fragment such as that contained in ligand **1**. Moreover, the dramatically different properties (*e.g.* UV/Vis spectrum and spin state) imparted to the coordinated Ni^{2+} by the two donor sites, B and A^{2-}, allowed easy detection of the translocation process. In the perspective of extending the available set of molecular machines which perform cation translocation, this work reports on the behaviour of Cu^{2+} with three ligands, **1**–**3**, two of which (**2**, **3**) have been synthesized for the first time. All the ligands contain the same dioxo-tetramine fragment as **1** (AH_2 compartment) and different B compartments. The AH_2 compartment is expected to be coordinatively bistable in the presence of Cu^{2+}, and to form, at basic pH, neutral [Cu(A)] complexes, thus allowing pH-driven translocation from B, and *vice versa*. However, as Cu^{2+} prefers five-coordination (differently from the square planar Ni^{2+} in [Ni(A)] complexes) and free donor groups are present in ligands **1**–**3** when the cation is inside A^{2-}, it could be expected that one of the heterocyclic groups coordinating Cu^{2+} when in B remains coordinated when the cation moves to A^{2-}(form **c** in Scheme 1). This would impart the character of an overall molecular rearrangement to the cation movement. In the following, we present potentiometric titration results, which, coupled with mass and UV/Vis spectral studies, allow us to determine which species are present in solution at any pH value. These data confirm that the systems made by ligands **1**–**3** and Cu^{2+} (1 : 1 molar ratio) undergo a pH-controlled molecular rearrangement process, driven by the movement of Cu^{2+} from the B to the AH_2 compartment or *vice versa*.

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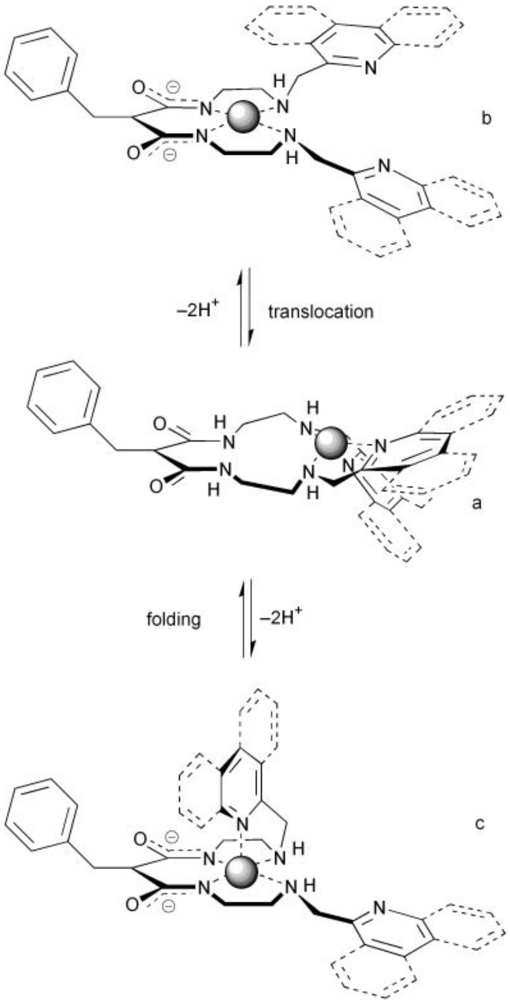
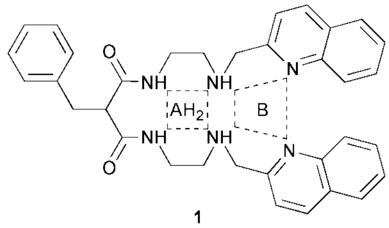


Scheme 1 Sketch of the pH-driven translocation process (form **a** to form **b** and *vice versa*) and of the molecular rearrangement process (form **a** to form **c** and *vice versa*) which could occur in a system made of ligands **1**–**3** and M^{2+} in 1 : 1 molar ratio (M = Ni or Cu). In form **a** the coordination sphere of the metal cation is completed by one (Cu^{2+}) or two (Ni^{2+}) water molecules.



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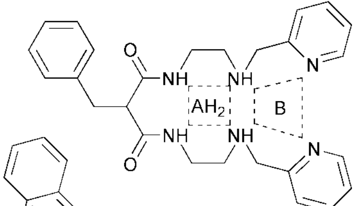

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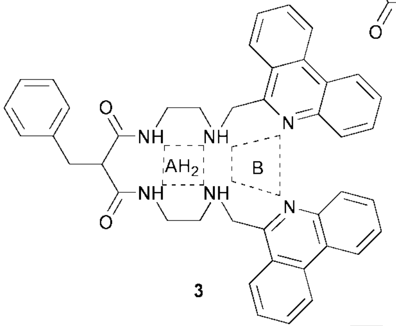

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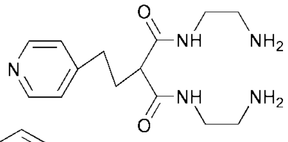

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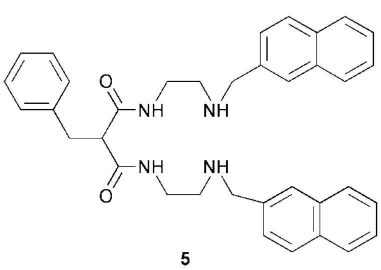

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Results and discussion

(1) Structural features and molecular rearrangement *vs.* translocation

The preference of the Cu^{2+} cation towards five-coordination introduces a new variable for translocation processes inside the ditopic receptor **1**, which has already been proven to be efficient for cation translocation in the case of Ni^{2+}. It is well documented that with ligands containing the same skeleton as **1**, *i.e.* a 1,4,8,11-tetraaza-5,7-dione chain, and which bear no substituents on the amine groups, Cu^{2+} forms, in aqueous solution and at neutral or moderately basic pH values, neutral complexes, due to the release of the two amide protons.[10] In those complexes, the bis-amino bis-imide doubly negative donor set surrounds Cu^{2+} with a square planar geometry, even if a very elongated overall square pyramidal or tetragonal geometry could be a more appropriate description of the metal cation coordination sphere, with water molecule(s) in the apical position(s). Noticeably, the very strong in-plane interactions raise the energy of the d–d transition in the d^9 Cu^{2+} cation, so that an unusually high energy d–d band is observed, *e.g.* at 516 nm for 1,4,8,11-tetraaza-5,7-dione.[10a] However, authentic five-coordination, according to a trigonal bipyramidal or a square pyramidal geometry, which is well known to be feasible for Cu^{2+}, could be in principle obtained if a free pendant arm is available, which could profit from a proper chelate effect. In this connection, it is interesting to note that, in the case of ligand **4**, while the bis-deprotonated copper complex is obviously square planar in solution (the pyridine ring not being able, for geometric reasons, to fold and coordinate Cu^{2+}), in the solid state a five-coordinated square pyramidal copper cation is found, thanks to the intermolecular coordination of the pyridine moiety favoured by crystal packing effects.[10f] In **1**–**3**, N-donor heterocyclic moieties are appended to the amino groups of the (6-benzyl)-1,4,8,11-tetraaza-5,7-dione framework, in such positions that, at least in principle, one of the two heterocycles can fold and coordinate the Cu^{2+} cation when it is in the bis-amino bis-imide bis-negative compartment (as sketched in form **c**, Scheme 1). What would be obtained is a square pyramidal complex, with the coordinating heterocyclic arm forming a very favourable five-membered chelating ring with the Cu^{2+} cation. Heterocycles of different dimensions have been incorporated in the ligands along the **1**–**3** series, in order to evaluate whether their bulkiness could result in unfavourable steric interactions with the benzyl group, thus making apical coordination less favourable.

(2) pH-Controlled molecular folding: potentiometric and spectrophotometric studies

The protonated ligand and copper-containing species present in solution in the pH 2–12 range have been individuated through potentiometric titration experiments.[11] Titrations were carried out by addition of standard base first on solutions containing only the chosen ligand (for the determination of amines and heterocyclic nitrogen protonation constants) and then on solutions containing the ligand plus an equimolar amount of Cu^{II} perchlorate. The results are summarized in Table 1, which reports the logarithm of the formation constants of each species. For the sake of clarity and conciseness, in the Table and

Table 1 Logarithmic formation constants for species relative to systems **1**–**3** and **5** plus Cu^{2+} (1 : 1 molar ratio). LH_2 represents the neutral ligands ($LigandH_2$ in the text). Protonation constants bear a ±0.01 uncertainty. Formation constants of metal-containing species bear a ±0.02 uncertainty

Equilibrium and relative species	Ligand **1**	Ligand **2**	Ligand **3**	Ligand **5**
[0,1]: $LH_2 + H^+ \rightleftharpoons [LH_3]^+$	7.57	7.87	8.33	7.74
[0,2]: $LH_2 + 2H^+ \rightleftharpoons [LH_4]^{2+}$	14.06	14.59	15.36	14.73
[0,3]: $LH_2 + 3H^+ \rightleftharpoons [LH_5]^{3+}$	15.78	17.14	17.21	—
[0,4]: $LH_2 + 4H^+ \rightleftharpoons [LH_6]^{4+}$	—	18.61	—	—
[1,1]: $LH_2 + Cu^{2+} + H^+ \rightleftharpoons [Cu(LH_3)]^{3+}$	13.06	15.39	14.56	—
[1,0]: $LH_2 + Cu^{2+} \rightleftharpoons [Cu(LH_2)]^{2+}$	9.40	11.80	10.49	5.84
[1,−1]: $LH_2 + Cu^{2+} \rightleftharpoons [Cu(LH_2)(OH)]^+ + H^+$	3.21	3.96	4.05	—
[1,−2]: $LH_2 + Cu^{2+} \rightleftharpoons [Cu(L)] + 2H^+$	−4.17	−4.99	−3.65	−6.72

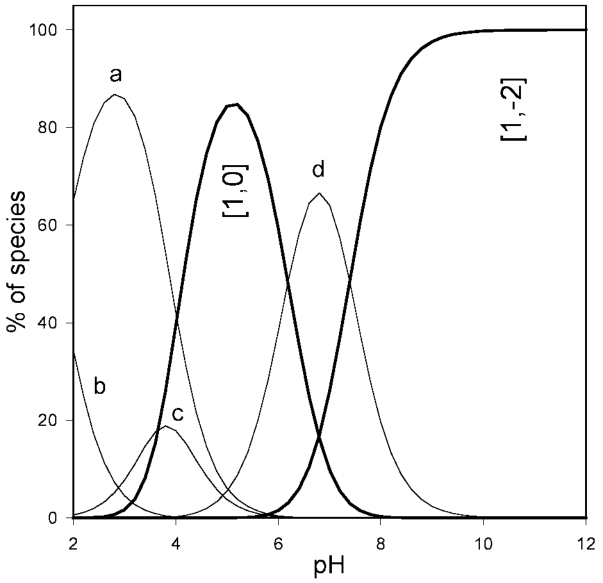

Fig. 1 Distribution diagram (% of species *vs.* pH) for the system **1**/Cu^{2+} (1 : 1 molar ratio), in a 4 : 1 (v/v) dioxane–water mixture. Curves relative to species [1,0] and [1,−2] are evidenced in the figure (bold lines). Curve a refers to [0,2] species; b to [0,3] species; c to [1,1] species and d to [1,−1] species.

throughout the text, for each species a diad of numbers is used which indicates the number of coordinated metal cations (0 or 1) and of protons, respectively. For example, [0,3] represents a species with no metal cations and three protons bound to the ligand. Moreover, as the neutral ligands are to be considered diprotic acids (due to the presence of the two amide groups), *i.e.* $LigandH_2$, the [0,3] species thus corresponds to $[LigandH_5]^{3+}$, while a negative number for the protons indicates that one or more H^+ have been released, so that [1,−2] corresponds to the neutral [Cu(Ligand)] species.

From the values reported in Table 1, distribution diagrams can be drawn, which display the curves relative to the percentage of each species as a function of pH (Figs. 1–3). Four metal-containing species have been individuated in the case of ligands **1**–**3**.

The [1,1] species, which is a one-proton one-metal complex, is of marginal interest for the aims of this work, as one amine group is protonated and the Cu^{2+} cation is thus coordinated by the remaining, unprotonated amino-heterocyclic chelating unit. In each case, it forms at distinctly acidic pH values, reaches only low % values (*e.g.* $\%_{max} = 30$, at pH 4, for ligand **3**), and, most importantly, it does not form in significant amounts at the pH values in which the other metal-containing species exist. The species of interest for the translocation process are [1,0] and [1,−2]. The former is the complex between the neutral ligand, $LigandH_2$, and Cu^{2+}, in which the cation is coordinated by the bis-amino bis-heterocycle compartment B; the latter is the species in which the two amide protons have been released from the AH_2 compartment, and the neutral [Cu(Ligand)] complex is formed, with Cu^{2+} coordinated by the bis-amino bis-imide set A^{2-}. In the representative case of ligand **2** (Fig. 2) the [1,0] species represents over 95% of the species present in solution in

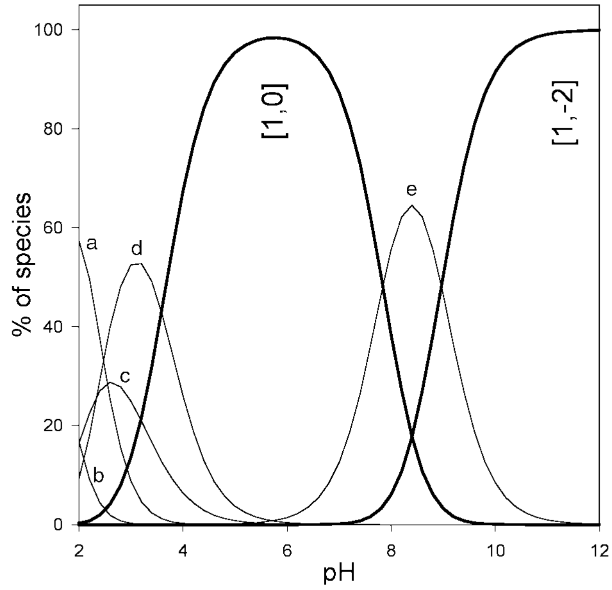

Fig. 2 Distribution diagram (% of species *vs.* pH) for the system **2**/Cu^{2+} (1 : 1 molar ratio), in a 4 : 1 (v/v) dioxane–water mixture. Curves relative to species [1,0] and [1,−2] are evidenced in the figure (bold lines). Curve a refers to [0,3] species; b to [0,4] species; c to [0,2] species; d to [1,1] species and e to [1,−1] species.

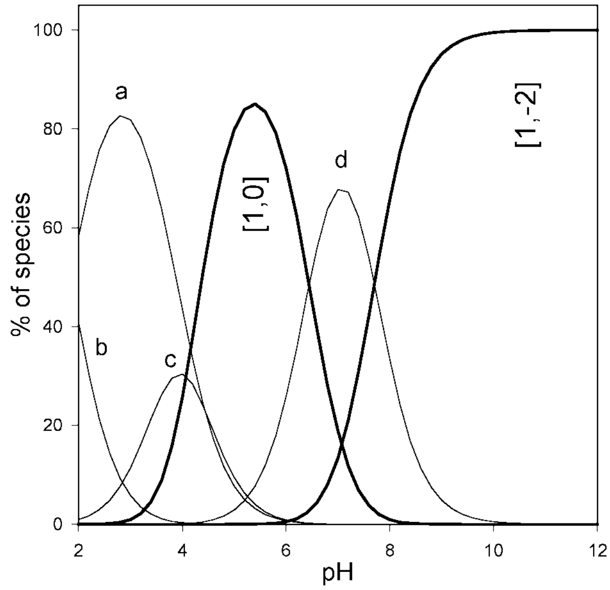

Fig. 3 Distribution diagram (% of species *vs.* pH) for the system **3**/Cu^{2+} (1 : 1 molar ratio), in a 4 : 1 (v/v) dioxane–water mixture. Curves relative to species [1,0] and [1,−2] are evidenced in the figure (bold lines). Curve a refers to [0,2] species; b to [0,3] species; c to [1,1] species and d to [1,−1] species.

the range $5 < pH < 6.5$, while [1,−2] goes over 95% at $pH > 10.2$. In the case of ligands **1** and **3**, the situation is less sharp but [1,0] is still by far the predominant species over the pH ranges of interest (Figs. 1 and 3), while [1,−2] becomes the only species present in solution when the pH is raised sufficiently. Distinct zones can thus be envisaged on the pH axis in which only [1,0] or [1,−2] exist or at least prevail, and it is thus possible to switch from one to the other species by changing the pH of the solution. However, the nature of these two species has to be made clear, in order to assess whether (i) an authentic cation translocation process takes place on changing pH from one value to the other, as sketched in the upper part of Scheme 1 (form **a** transforming into **b**), or (ii) the lower part of Scheme 1 (form **a** transforming into **c**) holds.

Mass spectra, collected by the electrospray ionization (ESI) technique, have been carried out on solutions of each ligand plus Cu^{2+} (1 : 1 stoichiometry), with the pH adjusted by micro-additions of standard perchloric acid or sodium hydroxide at such values that 100% (or the maximum possible percentage) of [1,0] and [1,−2] species was obtained. In all cases, with [1,0] as the prevailing species, peaks relative to $\{[Cu(LigandH_2)](ClO_4)\}^+$ were observed as the main signal,[12] while no heavier mass peaks were detected. This proves that the [1,0] species is authentically monomeric, and it does not represent instead the minimum stoichiometric ratio of multi-ligand multi-metal complexes. UV/Vis spectra taken at the same pH values disclosed bands, for the species [1,0], which suggest that the Cu^{2+} cation is of course coordinated by both aminoquinoline units, with a further water molecule completing the coordination sphere towards a distorted trigonal-bipyramidal geometry. In particular, λ_{max} values were found at 616, 620 and 618 nm, in the case of ligands **1**, **2** and **3**, respectively (see Fig. 4, dashed line, for the representative case of ligand **2**), which compare well with the reported 598 and 586 nm values found for the distorted bis-chelate complexes with the *N*-methyl-2-aminomethylpyridine[13] and 2-aminomethylpyridine[14] ligands, and with the expected red shift found for the coordination of a fifth ligand on the copper centre.[15] These data confirm that the [1,0] species is the expected bis-chelate complex sketched in Scheme 1 as form **a**: Cu^{2+} is contained in the B compartment of ligands **1**–**3**, with a water molecule completing the coordination sphere.

At the pH values at which [1,−2] is the prevalent species, peaks relative to $\{[Cu(ligand)] + Na\}^+$ were observed as the only signal in the ESI experiments (Na^+ comes from the added standard base), indicating that this species is also, as expected, monomeric.[12] The UV/Vis spectra, however, do not support the hypothesis that [1,−2] is, in the case of ligands **1**–**3**, the square planar species depicted in Scheme 1 (form **b**). Instead, the five-coordinated form **c** is obtained. The found λ_{max} values are 552, 590, and 578 nm in the case of the complexes with ligand **1**, **2**, and **3**, respectively (see Fig. 4, solid line, for the case of ligand **2**), which are to be compared with that found in the neutral complex of Cu^{2+} with the bis-deprotonated form of ligand **5**.[16] The [1,−2] species in the case of ligand **5** can be considered as the reference for the complexes with ligands **1**–**3**, as it features the same framework, the same donor set, comparable bulkiness of the substituents on secondary amines, but no B compartment, *i.e.* no further donor groups beside the bis-amine bis-amide AH_2 donor set. Ligand **5**, when deprotonated, is able to exert the strong in-plane interaction typical of the bis-amino bis-imide donor set, and, consequently, the d–d band for the d^9 Cu^{2+} cation is found at 506 nm. This value is comparable with that already found for copper complexes with ligands featuring primary amines such as **4** (λ_{max} = 520 nm) or 1,4,8,11-tetra-aza-5,7-dione (λ_{max} = 516 nm).[10a] The significant shift of λ_{max} towards longer wavelengths in the case of **1**–**3**, which causes the solutions containing [1,−2] to assume a violet-blue color instead of the typical purple-red color of the complexes with the mentioned ligands, can be explained by the coordination of one heterocycle in an apical position of the copper cation, as sketched in form **c** of Scheme 1. Apical coordination of a pendant arm on square planar Cu^{2+} complexes has the well-documented effect of reducing the metal–ligand in-plane interactions and to lower the energy of the d–d transition.[17] Moreover, a very significant example comes from the already mentioned case of ligand **4**, for which a purple solution is obtained for [1,−2] (λ_{max} = 520 nm), while in the solid state, in which square pyramidal five-coordination is preferred, a blue product is obtained, which absorbs at λ_{max} = 590 nm.[10f] In this regard, it has also to be noted that the log*K* of the formation constant for [1,−2] is more than two units lower in the case of ligand **5** with respect to **1**–**3**. This reasonably reflects the lack of further intramolecular coordination on the copper cation encircled by the bis-amino bis-imide donor set. On this basis, it must be concluded that, on changing pH from the range in which [1,0] prevails to that in which [1,−2] prevails, what is obtained is not an authentic translocation of the copper cation, but a more complex movement that involves the whole molecule, which therefore could be better described as a "molecular rearrangement". At any rate, this movement is reversible, as one can make the chosen system rearrange from form **a** to form **c**, and *vice versa*, by simply changing the pH. Up to six folding/unfolding cycles have been carried out with ligands **1**–**3**/Cu^{2+} by addition of microquantities of standard acid and base, obtaining in the final cycle UV/Vis spectra superimposable on those of the first cycle for [1,0] and [1,−2] (neglecting a very moderate decrease in intensity, due to dilution).

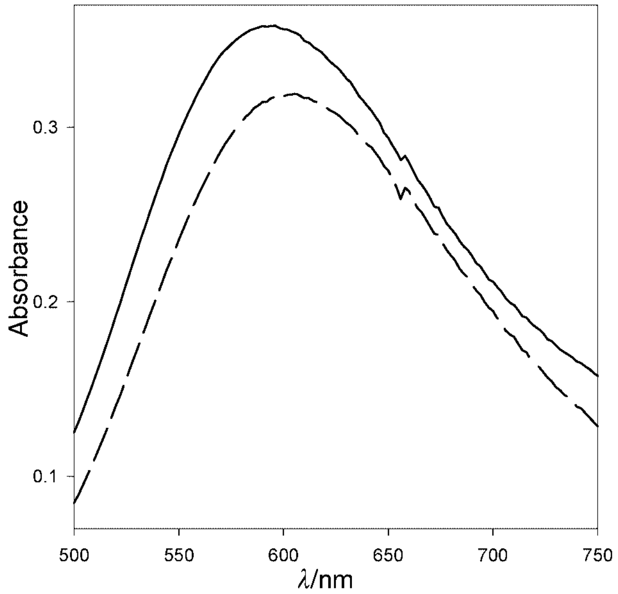

Fig. 4 UV/Vis spectra for the system **2**/Cu^{2+} (1 : 1 molar ratio, concentration = 2.5×10^{-3} M) at pH 5.9 (species [1,0], dashed line) and at pH 11.5 (species [1,−2], solid line).

A final comment is needed for species [1,−1]. The found log*K* values are to be referred to the equilibrium $Cu^{2+} + LigandH_2 + H_2O = [Cu(LigandH_2)(OH)] + H^+$, *i.e.* to the formation of a species in which a hydroxide anion is bound to the Cu^{2+} cation coordinated by the bis-amino bis-heterocycle compartment B. In solution, this species forms on increasing pH with respect to the values at which [1,0] prevails, and is obtained by deprotonation of the water molecule which occupies the fifth coordination position on Cu^{2+}. From the quotient of the formation constant for [1,−1] over that for [1,0] the constant for the deprotonation of the coordinated water molecule can be calculated, from which pK_a values of 6.19, 7.84 and 6.44 can be obtained for complexes with ligands **1**–**3**, respectively. These values fit well with those found for the deprotonation of a copper-coordinated water molecule in analogous five-coordinated copper complexes.[9] A number of papers have already demonstrated that the deprotonation of only one amide group is not observed in complexes of Ni^{2+} or Cu^{2+} with ligands containing the same bis-amido bis-amino framework as **1**–**5**.[18] Moreover, the hypothesis that the [1,−1] species could correspond to a complex of Cu^{2+} with a mononegative and monodeprotonated [LigandH]$^-$ ligand is definitely ruled out by the fact that [1,−1] does not form when the reference ligand **5** is taken into consideration, which does not feature the necessary B compartment.

Conclusions

A reversible double perturbation is obtained in the considered molecular systems, thanks to pH changes, as both translocation of the Cu^{2+} cation and folding of the organic backbone is observed. This work also shows that the coordination preferences of the chosen metal cation can discriminate between simple translocation and translocation + folding: with one of the considered ligands, **1**, a simple cation translocation (without folding) has already been reported with Ni^{2+}, which prefers to be square planar instead of five-coordinated like Cu^{2+}. Moreover, translocation + folding is observed with Cu^{2+} independently of the bulkiness of the heterocycle appended to the 6-benzyl-1,4,8,11-tetraaza-5,7-dione framework. This suggests that simple translocation with Cu^{2+} in this kind of system could be obtained only by significantly changing the nature and geometry of the B site, or by increasing its distance from the AH$_2$ site. Studies along this line are in progress in our laboratories.

Experimental

Synthesis

The preparation of ligand **1** has already been described.[8c] Ligands **2**, **3** and **5** have been synthesized according to the same strategy, *i.e.* by the Schiff-reaction of 6-benzyl-1,4,8,11-tetraazaundecane-5,8-dione[8c] with the appropriate heterocyclic aldehyde (**2**, **3**) or 2-naphthaldehyde (**5**), followed by reduction with sodium borohydride. 2-Pyridinecarbaldehyde and 2-naphthalenecarbaldehyde were purchased from Aldrich or Fluka and used as supplied. 6-Phenanthridinecarbaldehyde[19] was prepared as previously described.

Ligand 2. A 10 ml ethanol solution of 2-pyridinecarbaldehyde (0.187 g, 2.05 mmol) was added dropwise to a stirred solution of 6-benzyl-1,4,8,11-tetraazaundecane-5,8-dione (0.287 g, 1.025 mmol) in 30 ml ethanol, at room temperature, under a nitrogen atmosphere. After 1 hour of stirring, a yellowish solution was obtained, which was left standing for 24 h, after which time a yellow-white microcrystalline precipitate was obtained. The product was filtered, washed with 2 × 5 ml of diethyl ether and then dissolved in 50 ml of refluxing ethanol, to which an excess of solid NaBH$_4$ (0.8 g) was added in small portions, avoiding excessive foaming. When the addition was complete, the mixture was kept at reflux temperature for a further 2 hours, after which time the solvent was removed on a rotary evaporator. The solid product was then dissolved in 20 ml H$_2$O, and the solution extracted with 5 × 20 ml CH$_2$Cl$_2$. The gathered organic layers were dried over MgSO$_4$. Removal of the solvent on a rotary evaporator gave the product as a yellowish oil, which was kept under vacuum (0.1 Torr) at 40 °C for 24 hours, resulting in pure **2** according to NMR and mass analysis. Yield: 42%. Mass (ESI): *m*/*z* 461 (**2** + H$^+$). ^{1}H NMR (CDCl$_3$): δ 8.52 (d, 2H) + 7.65 (t, 2H) + 7.10–7.25 (m, 11H), H of the pyridine and benzene rings + –CONH–; 3.80 (s, 4H, NH–CH_2–pyridine); 3.15–3.35 (m, 7H, CONH–CH$_2$–CH_2– + bz–CH_2–CH–); 2.7 (m, 4H, CONH–CH_2–); 1.85 (broad, CH$_2$–NH–CH$_2$).

A synthetic approach similar to that described for ligand **2** was used for **3** and **5**, which were obtained as yellowish microcrystalline powders.

Ligand 3. Yield: 54%. Elemental analysis calc. (%) for $C_{42}H_{44}N_6O_4$ (**3**·2H$_2$O): C 72.43, H 6.32, N 12.06; found: C 72.41, H 6.27, N 12.09. Mass (ESI): *m*/*z* 661 (**3** + H$^+$). ^{1}H NMR (CDCl$_3$): δ 8.62 (d, 2H), 8.54 (d, 2H), 8.17 (d, 2H), 8.14 (d, 2H), 7.85 (t, 2H), 7.78–7.61 (m, 6H), 7.2 (m, 5H), H of the benzene and phenathridine rings; 7.05 (broad t, 2H, –CONH–); 4.34 (s, 4H, NH–CH_2–phenanthridine); 3.5–2.6 (m, 11H, CONH–CH$_2$–CH_2– + bz–CH_2–CH– + CONH–CH_2–); 1.80 (broad, CH$_2$–NH–CH$_2$).

Ligand 5. Yield: 56%. Elemental analysis calc. (%) for $C_{36}H_{40}N_4O_3$ (**6**·H$_2$O): C 75.02, H 6.94, N 9.71; found C 74.98, H 6.97, N 9.68. Mass (ESI): *m*/*z* 559 (**6** + H$^+$). ^{1}H NMR (CDCl$_3$): δ 7.80 (m, 4H) + 7.69 (s, 2H) + 7.48–7.38 (m, 8H) + 7.20–7.18 (m, 5H), H of the benzene and naphthalene rings; 6.87 (broad t, 2H, CO–NH–CH$_2$); 3.82 (s, 4H, NH–CH_2–naphthalene); 3.32–3.15 (m, 7H, CONH–CH$_2$–CH_2– + bz–CH_2–CH–); 2.67 (m, 4H, CONH–CH_2–); 1.55 (broad, CH$_2$–NH–CH$_2$).

Equilibrium and solution studies

The protonation and Cu^{2+} complex formation equilibria for **1**–**3** and **5** were studied in a dioxane–water solution (4 : 1 v/v) 0.1 M in NaClO$_4$ at 25 °C, by titrating with standard base a solution containing the chosen ligand and excess perchloric acid (to determine protonation constants), and a solution containing the chosen ligand, 1 equiv. of Cu(ClO$_4$)$_2$ plus excess perchloric acid (to determine the complex formation constants). Potentiometric studies were carried out using the fully automated unit described previously.[20] The titration curves were fitted and the equilibrium constants were calculated by using the non-linear least-squares program HYPERQUAD.[21] Absorption spectra were taken on a Hewlett-Packard HP8453 spectrophotometer.

Physical measurements

Mass spectra (ESI) were recorded on a Finnigan MAT TSQ 700 instrument, NMR spectra on a Bruker AMX 400 spectrometer.

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