First assembly of copper(I) naphthyridine-based helicates

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Copper(I) binds to 2,7-diimino-1,8-naphthyridine in solution to form a mixture of equilibrating mono- and polynuclear complexes, as identified by electrospray MS and monitored by UV-visible spectrophotometric titrations, including a binuclear metallo-helicate for which X-ray data are available but whose formation does not require cooperative associations.

Metallo-helicates, being organometallic equivalents of artificial peptides, are formed by coordination of a polytopic ligand around several metal centres providing appropriate binding geometries. Little is known about how the metallo-helicate assembles in solution[1] but, in most cases, yields are remarkably high. The first detailed description of the assembly process stressed the importance of positive cooperativity[2] but later studies found this not to be mandatory for helicate formation.[3,4] Indeed, recent work[5] has shown that certain quarterpyridine ligands bind to copper(I), forming a family of oligomers of type $[Cu(L)]_n^{n+}$, wherein complexes with $n = 2$ and 3, respectively, are double helicates and cyclohelicates. Extending this subject, we now report on the individual steps whereby copper(I) forms a double helicate with a sterically constrained naphthyridine-based polytopic ligand. It is seen that whereas a variety of species co-exist with the metallo-helicate in solution, a single complex crystallises from the mixture.

The 2,7-diimino-substituted 1,8-naphthyridine ligand **NIM** was obtained in excellent yield using standard synthetic methods and was fully characterised.[6] Stoichiometric mixing of **NIM** and $[Cu(CH_3CN)_4]BF_4$ in 4 : 1 $CH_3CN–CH_2Cl_2$ afforded a deep green solution that, upon slow diffusion of ether, gave a crop of green rhombus-shaped crystals (>95% yield).

X-Ray diffractometry of the recovered crystals showed the structure to be a double-stranded helicate in which two ligands are wrapped around each cation, with the two copper(I) centres being separated by 2.915 Å (Fig. 1). Each cation is coordinated to two imino (2.183–2.251 Å) and two naphthyridino (1.955–1.996 Å) N atoms, with the bite angles being typical of a distorted tetrahedral polyhedron (77.6–79.6°). The rigidity and relative planarity of the polytopic ligand, together with the close proximity of the copper(I) cations, seem unfavourable for helicate formation and, in fact, this is the first description of a metallo-helicate formed from such a ligand. Binuclear copper and silver complexes of unsubstituted naphthyridine[9] or pyridine substituted naphthyridine[10] have previously been described but do not
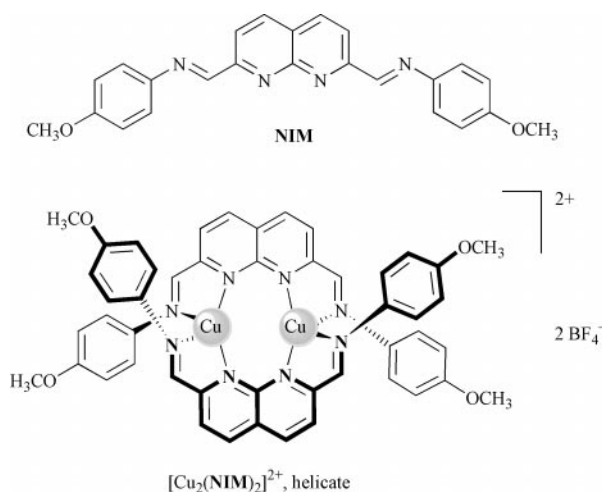

$[Cu_2(NIM)_2]^{2+}$, helicate

exhibit an helicoïdal arrangement of the ligands around the metallic centers.

Dissolving a monocrystal of the helicate in CH_3CN (0.12 mmol dm^{-3}) gave a rich mixture of mononuclear ($[CuNIM]^+$, $[Cu(NIM)_2]^+$ and $[Cu(NIM)_3]^+$), binuclear ($[Cu_2(NIM)_3]^{2+}$ and $[Cu_2(NIM)_6]^{2+}$) and higher-order ($[Cu_3(NIM)_6]^{3+}$) species, as shown by ES-MS (Fig. 2).
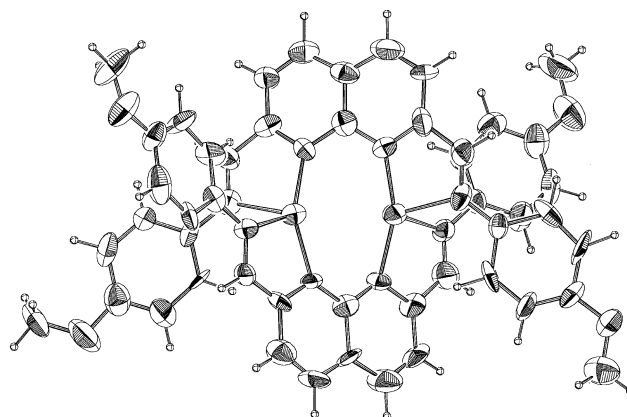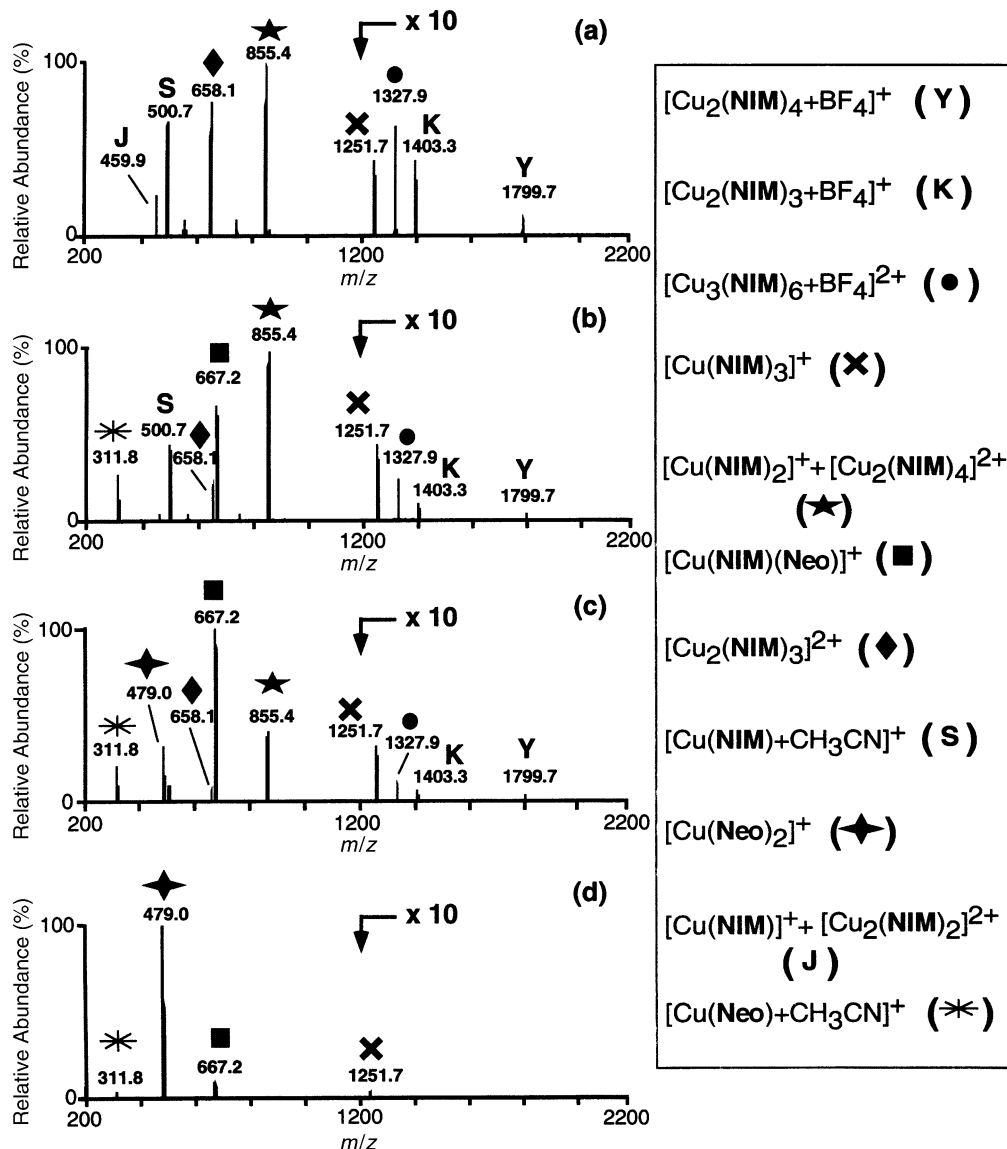

Fig. 1 ORTEP side view (30% probability) of $[Cu_2(NIM)_2](BF_4)_2$.
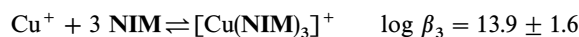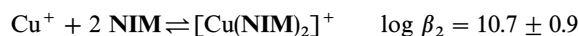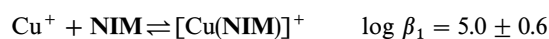
Fig. 2 ES-MS recorded in acetonitrile (a) upon dissolving single crystals of $[Cu_2(NIM)_2](BF_4)_2$ (0.12 mmol dm^{-3}) and after addition of (b) 0.4 equiv. **Neo**, (c) 0.8 equiv. **Neo** and (d) 2 equiv. **Neo**. The extraction cone voltage was set at 20 V. Calc. m/z for $[Cu_2(NIM)_4 + BF_4]^+$ 1799.7; $[Cu_2(NIM)_3 + BF_4]^+$ 1403.3; $[Cu_3(NIM)_6 + BF_4]^{2+}$ 1327.9; $[Cu(NIM)_3]^+$ 1251.8*; $[Cu(NIM)_2]^+ + [Cu_2(NIM)_4]^{2+}$ 855.4*; $[Cu_2(NIM)_3]^{2+}$ 658.2; $[Cu(NIM)(Neo)]^+$ 667.2*; $[Cu(NIM) + CH_3CN]^+$ 500.7*; $[Cu(Neo)_2]^+$ 479.0*; $[Cu(NIM)]^+ + [Cu_2(NIM)_2]^{2+}$ 459.9; $[Cu(Neo) + CH_3CN]^+$ 311.8*. **Neo** stands for 2,9-dimethyl-1,10-phenanthroline. * These values correspond to the monoisotopic m/z peak of the isotopic distribution and contain only the lighter isotopes of each element.

Although the helicate ($[Cu_2(NIM)_2]^{2+}$) remains an important constituent of this mixture it is clear that dissolution sets up a complex chain of equilibria. Similarly, ES-MS profiles show that addition of sub-stoichiometric amounts of Cu$^+$ to **NIM** in CH$_3$CN (1.0 mmol dm^{-3}; [Cu$^+$]/[**NIM**] < 0.2) forms a variety of mononuclear ($[Cu(NIM)]^+$, $[Cu(NIM)_2]^+$ and $[Cu(NIM)_3]^+$) and binuclear ($[Cu_2(NIM)_3]^{2+}$) species without apparent involvement of the metallo-helicate (Fig. 3). Increasing the molar ratio of Cu$^+$ favours formation of $[Cu(NIM)]^+$, although never as a single product, until, under equimolar conditions, the helicate begins to appear.

These qualitative studies, by confirming the existence of the helicate and by identifying important alternative species, provide the foundation from which to launch a quantitative investigation. Thus, sets of spectrophotometric titrations were made for which the mol fraction of Cu$^+$ was progressively increased but kept <0.3, with the total concentration of **NIM** being held constant at various values throughout the range $10 < [NIM] < 80$ μmol dm^{-3}; the solvent was deoxygenated CH$_3$CN containing 0.1 mol dm^{-3} NBu$^n_4$PF$_6$. Global analysis of the titration data,[11,12] collected for 28 different [Cu$^+$], each made at 8 different [**NIM**], using 50 separate

wavelengths, allowed stability constants for the mononuclear species and for the simplest binuclear complex to be established:

$$Cu^+ + NIM \rightleftharpoons [Cu(NIM)]^+ \qquad \log \beta_1 = 5.0 \pm 0.6$$

$$Cu^+ + 2\,NIM \rightleftharpoons [Cu(NIM)_2]^+ \qquad \log \beta_2 = 10.7 \pm 0.9$$

$$Cu^+ + 3\,NIM \rightleftharpoons [Cu(NIM)_3]^+ \qquad \log \beta_3 = 13.9 \pm 1.6$$

$$2\,Cu^+ + 3\,NIM \rightleftharpoons [Cu_2(NIM)_3]^{2+} \qquad \log \beta_4 = 19.8 \pm 1.4$$

This analysis indicates $[Cu(NIM)_3]^+$ to be relatively unstable, except at early stages of the titration where a large excess of **NIM** abounds. Increasing the mol fraction of Cu$^+$ shifts the equilibrium towards $[Cu(NIM)]^+$ while higher ligand concentrations facilitate formation of the binuclear species. It is interesting to note the change in coordination around the metal center that must accompany equilibration of these species. While $[Cu(NIM)]^+$ is bound to two ancillary CH$_3$CN molecules, both $[Cu(NIM)_2]^+$ and $[Cu_2(NIM)_3]^{2+}$ are set to form tetrahedral geometries but $[Cu(NIM)_3]^+$ seems more
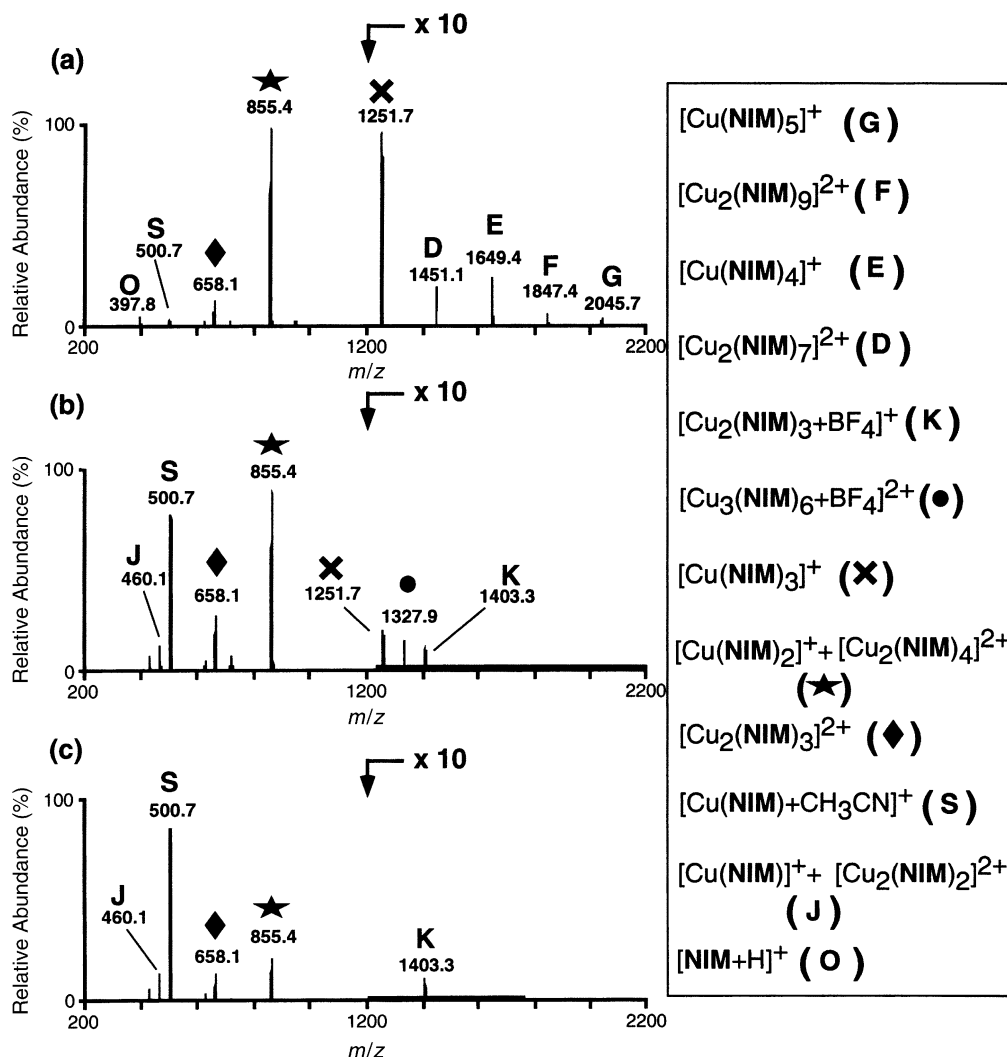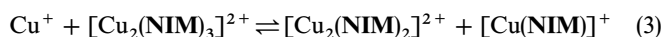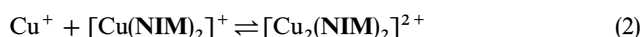
Fig. 3 ES-MS of three titration solutions, in acetonitrile, containing **NIM** (0.1 mmol dm^{-3}) and (a) 0.1 equiv., (b) 0.5 equiv. and (c) 1 equiv. of [Cu(CH$_3$CN)$_4$](BF$_4$). Calcd m/z as for Fig. 2; [Cu(NIM)$_2$]$^+$ 2045.8; [Cu$_2$(NIM)$_9$]$^{2+}$ 1847.5; [Cu(NIM)$_4$]$^+$ 1649.3; [Cu$_2$(NIM)$_7$]$^{2+}$ 1451.1; [NIM + H]$^+$ 397.5.

likely to favour a penta- or octahedral structure around the cation. It is also apparent that there is only a modest thermodynamic driving force {$\Delta G_D = -RT \ln[\beta_4/(\beta_2 \beta_1)] = -23 \pm 15$ kJ mol^{-1}} for formation of the binuclear species.

Continuing the titration to include mol fractions of Cu$^+$ of <0.95, and with the total concentration of **NIM** being held within the range $10 <$ [**NIM**] < 40 μmol dm^{-3}, allowed determination of the overall stability constant for the metallo-helicate:

$$2 \text{ Cu}^+ + 2 \text{ NIM} \rightleftharpoons [\text{Cu}_2(\text{NIM})_2]^{2+} \quad \log \beta_5 = 15.2 \pm 1.6$$

Allowing for the ES-MS results, and in particular the absence of species such as [Cu$_2$(NIM)]$^+$, we can suppose that helicate formation must involve at least one of the following reactions:

$$2[\text{Cu(NIM)}]^+ \rightleftharpoons [\text{Cu}_2(\text{NIM})_2]^{2+} \tag{1}$$

$$\text{Cu}^+ + [\text{Cu(NIM)}_2]^+ \rightleftharpoons [\text{Cu}_2(\text{NIM})_2]^{2+} \tag{2}$$

$$\text{Cu}^+ + [\text{Cu}_2(\text{NIM})_3]^{2+} \rightleftharpoons [\text{Cu}_2(\text{NIM})_2]^{2+} + [\text{Cu(NIM)}]^+ \tag{3}$$

In trying to resolve the most likely assembly processes we note that replacement of two acetonitrile molecules bound to Cu$^+$ with one molecule of **NIM** involves a total binding energy of *ca.* 28 kJ mol^{-1} (*i.e.* log $\beta = 5.0$). This holds true for formation of one {*i.e.* [Cu(NIM)]$^+$}, two {*i.e.* [Cu(NIM)$_2$]$^+$}, or four {*i.e.* [Cu$_2$(NIM)$_3$]$^{2+}$} coordination sites and implies that the overall stability constant for the metallo-helicate should be 20 rather than 15.2. The disparity corresponds to a

destabilization energy ($\Delta E = 25$ kJ mol^{-1}) for the helicate arising from electrostatic and/or structural effects.

On the basis of these stability constants it is to be expected that the helicate undergoes partial dissociation in solution, as indicated by the ES-MS results. A key observation concerns the fact that addition of low concentrations of neocuproine (**Neo**) results in formation of [Cu(Neo)]$^+$, and this species can arise only by coordination to free Cu$^+$. Higher concentrations of **Neo** favour formation of the mixed complex [Cu(NIM)(Neo)]$^+$ (log $\beta = 13.6$) before the equilibrium is driven in favour of [Cu(Neo)$_2$]$^+$ (log $\beta = 14.2$).[13] These observations indicate that an important route for helicate dissociation involves ejection of a Cu$^+$ cation (reaction 2) but unwinding (reaction 1) also contributes to the overall instability of the helicate. Both dissociative reactions depend on total concentration and combine to ensure 92 and 25% dissociation at initial helicate concentrations of 10 and 1000 μmol dm^{-3}, respectively. The relative stability of the helicate at high concentration explains why it crystallises from the mixture. Alternately, helicate formation can be driven by high [Cu$^+$] (reaction 2) at modest [**NIM**]. With the two disssociative reactions running in parallel it is not surprising that a multitude of species exists in solution.

Metallo-helicate formation is a consequence of high concentrations and does not depend on cooperative associations. In the present case, electrostatic repulsion between closely spaced cations and the rigidity of the central naphthyridine nucleus might contribute towards helicate instability. In fact, the

importance of structural factors can be seen by comparing stability constants for the helicate (log $\beta_5 = 15.2$) and $[Cu_2(\mathbf{NIM})_3]^{2+}$ (log $\beta_4 = 19.8$), since the two complexes are likely to contain comparable binding sites and be subject to similar electrostatic energies.

Notes and references

1 M. Munakata, L. P. Wu and T. Kuroda–Sowa, *Adv. Inorg. Chem.*, 1999, **46**, 173.
2 A. Pfeil and J.-M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1992, 838.
3 R. Ziessel, A. Harriman, J. Suffert, M.-T. Youinou, A. De Cian and J. Fischer, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2509.
4 A. El-ghayoury, A. Harriman, A. De Cian, J. Fischer and R. Ziessel, *J. Am. Chem. Soc.*, 1998, **120**, 9973.
5 G. Baum, E. C. Constable, D. Fenske, C. E. Housecroft and T. Kulke, *Chem. Commun.*, 1999, 195.
6 All new compounds were authenticated by NMR, FT-IR, MS and elemental analyses.
7 *Crystal data* for $Cu_2C_{48}H_{40}N_8O_4 \cdot 2BF_4 \cdot CH_3CN$: $M = 1134.65$, monoclinic, $P2_1/n$, $a = 14.13(1)$, $b = 28.39(1)$, $c = 13.816(5)$ Å, $\beta = 116.82(5)^\circ$, $U = 4946(4)$ Å^3, $Z = 4$, $\mu = 9.476$ cm^{-1}, $F(000) = 2312$. Data were collected on an automatic diffractometer CAD4 Enraf-Nonius with graphite Mo-Kα radiation (0.710 73 Å) at 294 K. Data collection [$2\theta_{max} = 50^\circ$, scan $\omega/2\theta = 1$, $\tau_{max} = 60$ s, *hkl* range: 0.15; 0.31; -15.15; intensity controls without appreciable decay (0.3%)] gave 6877 reflections of which 3055 were independent with $I > 1.5\sigma(I)$. The structure was solved using the Nonius OpenMoleN packages and refined by full matrix least-squares with anisotropic thermal parameters for all non-hydrogen atoms except for solvent molecules and counteranions (the latter are disordered). Final results: $R(F) = 0.111$, $wR(F) = 0.105$ and $Sw = 5.18$ (residual $\Delta\rho \leqslant 0.96$ eÅ^{-3}). Some disorder of the counterions has been found. CCDC reference number 440/206. See http://www.rsc.org/suppdata/nj/b0/b003342l/ for crystallographic files in .cif format.
8 OpenMoleN, Enraf-Nonius Molecular Structure Determination Package, Nonius B. V., Delft, The Netherlands, 1990.
9 M. Munakata, M. Maekawa, S. Kitagawa, M. Adachi and H. Masuda, *Inorg. Chim. Acta*, 1990, **167**, 181.
10 C. He and S. J. Lippard, *J. Am. Chem. Soc.*, 2000, **122**, 184.
11 H. Gampp, M. Maeder, C. J. Meyer and A. D. Zuberbühler, *Talanta*, 1985, **32**, 95.
12 H. Gampp, M. Maeder, C. J. Meyer and A. D. Zuberbühler, *Talanta*, 1985, **32**, 257.
13 U. M. Frei and G. Geier, *Inorg. Chem.*, 1992, **31**, 3132.