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A two-channel molecular dosimeter for the optical detection of copper(II)†

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A cyclam-like macrocycle with an integrated push-pull chromophore selectively detects Cu^{2+} inclusion through both orange-to-yellow colour change and quenching of the green fluorescence.

There exists compelling interest in the design of receptors capable of recognising cations and anions, and of communicating recognition through a visual signal. In the case of metal ions, a convenient procedure involves the incorporation of a push–pull chromophore into a multidentate ligand: coordinative interaction with a given metal may alter the intensity of the dipole of the chromophore, thus modifying the energy of the charge transfer transition and ultimately changing the colour. Such a topic has been especially exploited for the colorimetric detection of s block metal ions, by equipping crown ether receptors with a variety of chromophores.[1] On the other hand, much less interest has been devoted to colorimetric sensors for transition metals based on push–pull chromophores.

We describe here the design of two tetramine macrocycles containing an incorporated push–pull chromophore, suitable for interaction with 3d metal ions. In system **1**, the classical (4-nitrophenyl)amine fragment (yellow colour) is a part of the cyclam ring, while in system **2** the macrocycle contains the 7-nitrobenzo[1,2,5]oxadiazol-4-ylamine chromophore, which maintains the skeleton of 4-nitrophenylamine, but also possesses a condensed furazan ring (orange-red colour).

Metal inclusion was investigated by titrating an aqueous solution of **1**, adjusted to pH = 4.75 with acetate buffer, with an aqueous standard solution of the metal salt and looking at colour changes and modifications of the absorption spectrum. Interesting results were observed in the case of Cu^{2+}, whose gradual addition induced (i) decolorisation of the yellow solution and (ii) a decrease of the band at 386 nm and development of a new band at 266 nm (see Fig. 1). Very significantly, the absorbance at 386 nm stopped decreasing after the addition of 1 equiv. of Cu^{2+} (see inset of Fig. 1), thus indicating the formation of a Cu^{2+}/**1** adduct of 1 : 1 stoichiometry. On concentration of the colourless solution, a violet solid precipitated, whose elemental analysis corresponded to the formula $[Cu^{2+}(\mathbf{1})](ClO_4)_2$. Recrystallisation of the complex salt from MeCN gave violet crystals, which were investigated through X-ray diffraction studies.‡

The ORTEP diagram of the $[Cu^{2+}(\mathbf{1})](ClO_4)_2$ complex is shown in Fig. 2. The Cu^{2+} ion is fully encircled by the tetra-aza subunit of **1** according to a square geometry. More interestingly, the Cu^{II}–N(aniline) bond, 2.07 Å, is only slightly longer than the three Cu^{2+}–N(amine) bonds (average value: 2.00 ± 0.01 Å), indicating the existence of a regular metal–ligand interaction. Noticeably, the macrocycle adopts an unusual configuration for metal complexes of cyclam and its derivatives. In particular, a diastereoisomer of type *trans-I* is observed (with the substituents on the nitrogen atoms, hydrogens and 4-nitrophenyl all above the N_4 plane; nitrogen configuration *R,S,R,S*; notice that the Cu^{II} centre stays on the same side, at 0.03 Å over the N_4 plane). Such a configuration has been previously observed only in the case of complexes of *N,N′,N″,N‴*-tetra-substituted cyclams, *e.g.* $[Cu^{2+}(Me_4cyclam)Br]Br$.[5] Usually, diastereoisomers of type *trans-III* (*R,S,S,R*) are observed.[6]

On the basis of the structural evidence, it is possible to account for the spectral features of the titration of **1** with Cu^{2+}, as illustrated in Fig. 1. On titration, the Cu^{2+} ion is fully chelated by the tetra-aza ring of **1**. Hence, the interaction of the metal with the lone pair of the aniline nitrogen modifies the intensity of the dipole of the chromophore, raising the energy of the

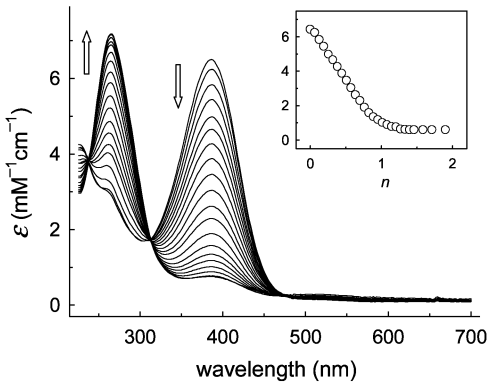


Fig. 1 Titration of an aqueous solution 10^{-4} M in **1**, buffered at pH = 4.75, with a standard solution of Cu^{2+}. Inset: absorbance at 386 nm *vs*. equivalents of Cu^{2+} (*n*).

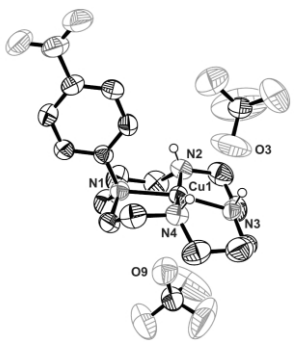
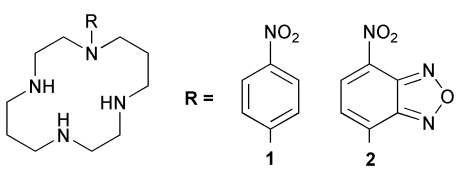


Fig. 2 ORTEP diagram of the $[Cu^{2+}(\mathbf{1})](ClO_4)_2$ complex. Thermal ellipsoids are at 50% probability. Selected bond lengths (Å) and angles (°): Cu1–N1 2.067(5), Cu1–N2 2.006(6), Cu1–N3 1.996(5), Cu1–N4 2.005(6), N1–Cu1–N2 94.1(2), N1–Cu1–N3 167.4(2), N1–Cu1–N4 87.2(2), N2–Cu1–N3 87.1(3), N2–Cu1–N4 170.7(2), N3–Cu1–N4 93.7(3).



† Electronic supplementary information (ESI) available: additional figure and synthesis of ligands **1** and **2**. See http://www.rsc.org/suppdata/cc/b3/b305456j/

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charge transfer from the dialkylamine fragment to the nitro group, with a consequent shift of the pertinent absorption band from 386 to 266 nm (which makes colour disappear). Afterward, analogous titration experiments were carried out with a variety of metal ions, which included Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Zn^{2+} and Pb^{2+}: in all cases, neither a colour change nor a modification of the spectral features of **1** were observed, indicating that the metal does not interact with the aniline group of the chromophore and, presumably, with the tetra-aza macrocycle. Lack of interaction may be due to thermodynamic reasons. In particular, the presence of the aniline nitrogen atom in the donor set reduces the donating tendencies of the macrocycle, which is able to form a stable complex only with the metal highest in the Irving–Williams series, *i.e.* Cu^{2+}.

Lack of interference by the above mentioned metals was further demonstrated by titrating with a standard Cu^{2+} solution an aqueous solution containing **1** plus 10 equiv. of the interfering metal: in all cases, the family of spectra and the titration profile shown in Fig. 1 were not altered. Thus, **1** is able to detect Cu^{2+} through the perceptible disappearance of its yellow colour and through a distinct change of the spectrum. In particular, the amount of Cu^{2+} in solution can be estimated from the absorbance of the band at 266 nm, whose limiting value is 7185 mol^{-1} L cm^{-1}. It has to be noted that the inclusion of the Cu^{2+} ion within the macrocycle is not reversible.

For instance, Cu^{2+} is not removed from the poly-aza ring of **1**, even after the addition of a large excess of strong acid, a feature typically observed for the especially inert transition metal cyclam complexes. Thus, **1** cannot be defined as a molecular *sensor*, a feature which requires quick reversibility and potential re-utilisation. It should be rather defined as a *dosimeter*, *i.e.* an irreversible device, which progressively accumulates the dose, each time adding up the signal, and which, after extended use, has to be discarded.[7]

System **2** contains a more versatile chromogenic fragment in which the increased π-delocalisation over all the unsaturated molecular framework ensures (i) the occurrence of a charge transfer transition of lower energy (orange-red colour), and (ii) provides emissive behaviour (green fluorescence). In particular, system **2**, in an aqueous solution adjusted to pH = 4.75 with CH_3COO^-/CH_3COOH buffer, shows its low-energy band at 473 nm, with ε = 28700 mol^{-1} L cm^{-1} and the solution exhibits an orange-red colour. On addition of Cu^{2+}, the solution turns yellow, while the absorption spectrum is substantially modified. In particular, the band at 473 nm decreases and disappears, while bands at 323 nm and at 268 nm strengthen (spectrum not shown; see ESI†). Also in the present case, the spectrophotometric titration profile, *e.g.* absorbance at 323 nm *vs.* equiv. of Cu^{2+}, indicates 1 : 1 stoichiometry and formation of the $[Cu^{2+}(\mathbf{2})]^{2+}$ tetra-aza-macrocyclic complex. As previously observed for system **1**, addition of the same series of transition metal ions causes neither colour change nor spectral modification. Thus, the functionalised macrocycle **2** behaves as an exclusive optical dosimeter for Cu^{2+}, whose detection is now visually signalled by a sharp orange-to-yellow colour change.

On the emission side, we observed that system **2**, when irradiated at either 470 nm or 356 nm (iso-absorbing point), gives rise to a green fluorescence. The emission band of an aqueous solution of **2** adjusted to pH = 4.75 is centred at 523 nm and results from the radiative decay of the charge transfer excited state. On titration with Cu^{2+}, the intensity of the emission band progressively decreases, to be quenched after the addition of 1 equiv. of metal. (see spectra in Fig. 3). Again, the I_F *vs.* equiv. plot indicates 1 : 1 stoichiometry (see inset of Fig. 3). Fluorescence quenching has to be ascribed to the occurrence of either an electron transfer or an electronic energy transfer involving the transition metal and the nearby excited fluorophore. On the other hand, titration with other transition metal ions does not affect emission, indicating no interference.

Thus, system **2** is a novel and unique dosimeter for copper(II), which operates through two different channels: (i) the orange-to-yellow colour change and (ii) the quenching of the green fluorescence. A sensor operating through both absorption and emission has been reported by de Silva.[8] Visual features of systems **1** (colour) and **2** (colour and fluorescence) before and after the addition of Cu^{2+} and selected metal ions are shown in Fig. 4.

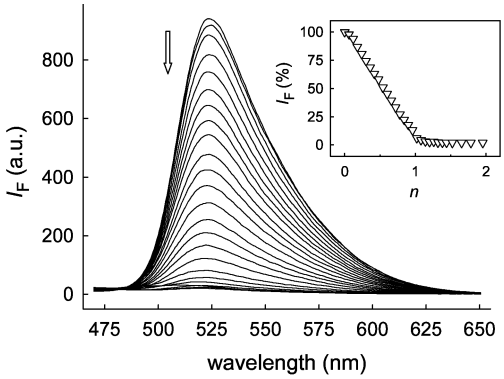

Fig. 3 Spectrofluorimetric titration of an aqueous solution 2×10^{-5} M in **2**, buffered to pH = 4.75, with a standard solution of Cu^{2+}. On metal addition, the emission band at 523 nm decreases and the green fluorescence is quenched. Inset: fluorescence intensity at 523 nm *vs.* equivalents of Cu^{2+} (*n*).

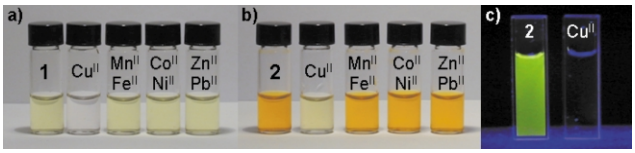

Fig. 4 Visual features of the interactions of metal ions with **1** (a, colour) and **2** (b, colour; c, fluorescence) in aqueous solution at pH = 4.75.

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Notes and references

‡ Crystal structure analysis. X-Ray diffraction data were collected from a violet prismatic crystal (~0.9 × 0.4 × 0.3 mm) by means of an Enraf Nonius Cad4 diffractometer. Crystal data of $C_{16}H_{27}Cu_1N_5O_2(ClO_4)_2$: M = 583.87, T = 273 K, monoclinic $P2_1/c$ (no. 14), a = 8.688(12), b = 13.153(5), c = 21.497(22) Å, β = 108.05(6)°, V = 2336(4) Å^3, Z = 4, ρ_{calc} = 1.660 g cm^{-3}, μ = 1.226 mm^{-1}, psi-scan empirical absorption correction applied,[2] 0.617 and 0.707 min and max transmission factors, λ = 0.7107 Å, omega scans, $2\theta_{max}$ = 52°, 6348 measured reflections, 4573 independent reflections (R_{int} = 0.0419), 3197 independent reflections with $I_O > 2\sigma(I_O)$, 336 parameters refined, GOF 1.040, R_1 = 0.0747 ($I_O > 2\sigma(I_O)$) and 0.1075 (all data), R_{2w} = 0.1936 ($I_O > 2\sigma(I_O)$) and 0.2154 (all data), largest difference peak and hole 0.80 and −0.50 e Å^{-3}. Crystal structure was solved by direct methods (SIR 97)[3] and refined by full-matrix least-squares procedures on F^2 using all reflections (SHELXL 97).[4] CCDC 203828. See http://www.rsc.org/suppdata/cc/b3/b305456j/ for crystallographic files in CIF or other electronic format.

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