Translocation of copper within the cavity of cryptands: reversible fluorescence signaling†

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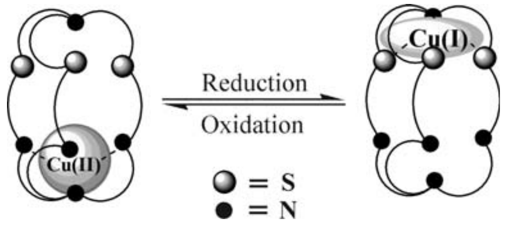
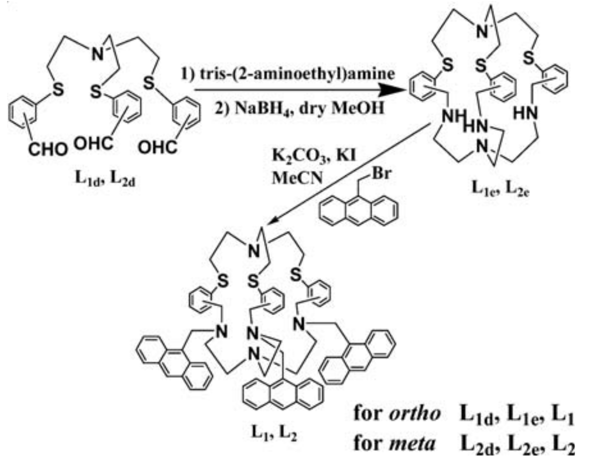
The movement of a copper ion inside the cavity of cryptands having two distinct metal binding sites at each end is linked to a fluorescence ON–OFF process in a reversible manner, providing a new way of fluorescence switching.

Transition metal ions used for signal transduction in fluorescence signaling systems are attractive due to the availability of various redox states for the metal ion. We have been using aza cryptands[1] as receptors in the configuration "fluorophore–spacer–receptor" for emission enhancement by transition/heavy metal ions. Herein, we describe two new cryptand receptors with NS$_3$ and N$_4$ donor sets at each end of the cavity, segregated by aromatic spacers. Our design is based on the fact that Cu(I) has a preference to bind soft S donors, whereas Cu(II) prefers N donors. Thus, a copper ion, depending upon its oxidation state, can translocate between the ends of the cryptand receptor, leading to fluorescence switchability (Scheme 1). This appears to be the first example of the translocation of a metal ion inside a cryptand cavity. Translocation and fluorescence modulation[2,3] by metal ions in cyclic and acyclic systems has been achieved through a change of pH[2d] and redox state of the metal ion. Besides this, the use of a triple-stranded helical complex as molecular redox switch,[3a] a calixarene as a molecular syringe[3b] for metal ions and metal tunneling[3c] are some of the other important results in this field.

Syntheses of the cryptands were achieved in several steps, as illustrated in Scheme 2. The key intermediate in each case is a tripodal trialdehyde, incorporating thioether groups, which undergoes Schiff base condensation with *tris*-(2-aminoethyl) amine to afford the desired cryptand.



Scheme 1 A schematic view of the translocation of a redox-active metal ion within a cryptand cavity.



Scheme 2 The synthetic route to investigated compounds $\mathbf{L_1}$ and $\mathbf{L_2}$.

Freshly purified THF was used as the solvent in all UV-vis spectral measurements. The unsubstituted cryptands $\mathbf{L_{1e}}$ and $\mathbf{L_{2e}}$ exhibited a strong absorption band at around 290 nm, attributable to a combination of transitions involving amines[4] and aromatic thioether[5] moieties. Upon addition of a metal ion, such as Cu(II), Co(II) or Zn(II), no noticeable change in the UV region was observed. This indicates that these metal ions occupy the N$_4$ end of the cavity, because thioether S → M(II) ligand to metal charge transfer (LMCT) transitions usually appear[6] around 360 nm. The N → M(II) LMCT band for secondary amines usually appears[7] around 280 nm, merging with the band at 290 nm in the present cases. The ligand field transitions for Cu(II) in our two cases appear as broad low-intensity bands centered around ~790 nm. For the anthryl derivatives $\mathbf{L_1}$ and $\mathbf{L_2}$, three strong bands characteristic[8] of 9-alkyl-substituted anthracene appear at 389, 369 and 349 nm, in addition to the 290 nm band. Both $\mathbf{L_1}$ and $\mathbf{L_2}$ show a small (~2 nm) bathochromic shift of the anthryl bands upon addition of a metal ion, such as a first row transition metal, Cd(II) or Ag(I), with no significant change in molar absorptivity. Upon addition of Hg(II) or Pb(II), or upon protonation, no change in band positions could be observed.

All emission measurements were undertaken using 10^{-5} M solutions of freshly purified THF. The parent cryptands $\mathbf{L_{1e}}$ and $\mathbf{L_{2e}}$ were non-emissive in nature. However, cation-free $\mathbf{L_1}$ and $\mathbf{L_2}$ in THF exhibited an emission that consisted of a well-resolved anthracene monomer emission, corresponding[1a] to a locally excited (LE) (π–π*) state, along with a red-shifted, broad, structureless emission centered at 525 nm.† This structureless emission, visible at high concentration, is due to

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† Electronic supplementary information (ESI) available: Characterization and synthesis of the ligands $\mathbf{L_1}$ and $\mathbf{L_2}$: FAB-MS, ^{13}C-NMR, ^{1}H-NMR, UV-vis and fluorescence spectral data. See DOI: 10.1039/b806426a

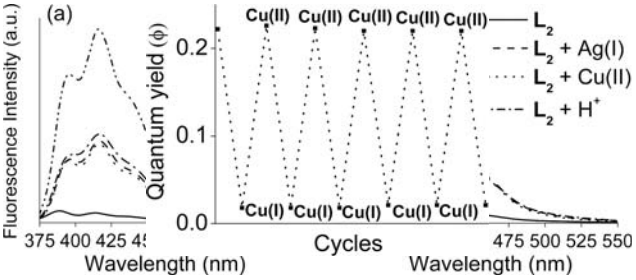


Fig. 1 (a) Emission spectra of $\mathbf{L_1}$, $\mathbf{L_1}$ + Cu(II), $\mathbf{L_1}$ + Ag(I), $\mathbf{L_1}$ + Zn(II), $\mathbf{L_1}$ + H^+ (concentration of $\mathbf{L_1}$ = 1.1×10^{-6} M) in THF. (b) Emission spectra of $\mathbf{L_2}$, $\mathbf{L_2}$ + Cu(II), $\mathbf{L_2}$ + Ag(I), $\mathbf{L_2}$ + H^+ (concentration of $\mathbf{L_2}$ = 1.0×10^{-6} M) in THF.

exciplex formation, as observed earlier both by us[1a] and by others,[9] and is formed between the N lone pair and the anthryl moiety. In case of metal-free $\mathbf{L_1}$ and $\mathbf{L_2}$, observed ϕ_{FT} ($\phi_{FT} = \phi_{FM} + \phi_{FE}$, where ϕ_{FT} is the total quantum yield, ϕ_{FM} is the quantum yield of the monomer emission and ϕ_{FE} is the quantum yield of the exciplex emission) values are very low due to efficient photoinduced electron transfer (PET) from the HOMO of the donor N-atom to the excited anthracene fluorophore.

Upon addition of a metal ion as input to either $\mathbf{L_1}$ or $\mathbf{L_2}$, ϕ_{FE} vanished as expected, while ϕ_{FM} increased greatly (Fig. 1) due to the N lone pairs at the N_4 end being coordinated to the metal ion, blocking PET. The extent of enhancement depended on the nature of the metal ion, as well as on the receptor (Table 1). Noticeable enhancements could be observed in presence of protons in both systems.

Table 1 Fluorescence quantum yields of $\mathbf{L_1}$ in THF with different ionic inputs[a]

	Quantum yield ϕ (enhancement factor) (λ_{ex} = 370 nm)					
	$\mathbf{L_1}$			$\mathbf{L_2}$		
Input	ϕ_{FM}	ϕ_{FE}	ϕ_{FT}	ϕ_{FM}	ϕ_{FE}	ϕ_{FT}
None	0.001	0.001	0.002	0.001	0.001	0.002
Mn(II)	0.109	—	0.109 (55)	0.194	—	0.194 (97)
Co(II)	0.063	—	0.063 (34)	0.038	—	0.038 (19)
Ni(II)	0.112	—	0.112 (56)	0.015	—	0.015 (7)
Cu(I)[b]	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Cu(II)	0.222	—	0.222 (111)	0.218	—	0.218 (109)
Zn(II)	0.113	—	0.113 (57)	0.240	—	0.240 (120)
Cd(II)	0.134	—	0.134 (67)	0.243	—	0.243 (122)
Ag(I)	0.121	—	0.121 (62)	0.226	—	0.226 (113)
Tl(I)	0.082	—	0.082 (41)	0.220	—	0.220 (110)
Pb(II)	0.009	—	0.009 (5)	0.008	—	0.008 (4)
Hg(II)	0.012	—	0.012 (6)	0.012	—	0.012 (6)
H^+	0.155	—	0.155 (73)	0.204	—	0.204 (102)

[a] Experimental conditions: medium = THF, concentration of both $\mathbf{L_1}$ and $\mathbf{L_2}$ = 1.1×10^{-6} M in THF and concentration of ionic input = 10^{-5} M. Excitation at 350 nm with an excitation band-pass = 5 nm, emission band-pass = 5 nm and temperature = 298 K. ϕ calculated by comparison of the corrected spectrum with that of anthracene (ϕ = 0.297), taking the area under the total emission. The error in ϕ is within 10% in each case, except for the free ligands, where the error in ϕ is within 15%. [b] n.d. = not determined.

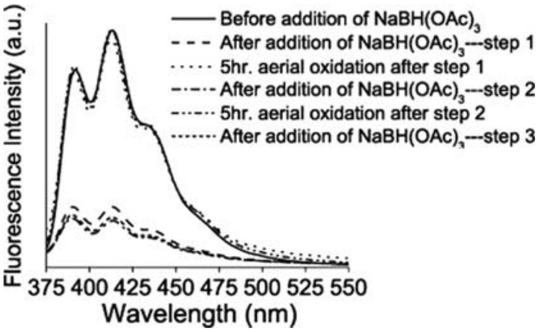


Fig. 2 Emission spectra of $\mathbf{L_1 \subset Cu(II)}$ under different conditions.

Hydrated metal perchlorate and nitrate salts can generate protons in organic solvents. To verify that the fluorescence enhancement was due to the metal ion and not to protonation, several controlled experiments were carried out.[1a,e] We also recorded emission with Cu(II) as an input in the presence of 2,6-di-tertbutylpyridine (10^{-2} M), which is a poorly coordinating base. No change in emission enhancement was observed.

Fluorescence titrations of $\mathbf{L_1}$ and $\mathbf{L_2}$ were carried out using metal ions and protons as titrants. The plot† of fluorescence quantum yield as a function of cation concentration indicates 1 : 1 complex formation with metals and 1 : 2 complex formation with protons. The complex stability constants (K_s) were determined from linear regression plots obtained from the changes in fluorescence quantum yield by following a reported procedure.[10] The values obtained were found to be consistent with those available in the literature,[11] with good correlation coefficients (≥ 0.98). K_s was found to be in the order of $\sim 10^6$ M^{-1} for Cu(II) and Zn(II) with either $\mathbf{L_1}$ or $\mathbf{L_2}$.

Since Cu(I) prefers soft thioether S rather than hard amino N centres, it was decided to utilize site preference for the two oxidation states of the metal ion, with the ultimate goal of having reversible fluorescence signaling. The green Cu(II) inclusion complexes of both $\mathbf{L_1}$ and $\mathbf{L_2}$ dissolved in freshly purified THF, giving emission spectra very similar to those obtained by adding $Cu(BF_4)_2 \cdot xH_2O$ to either $\mathbf{L_1}$ or $\mathbf{L_2}$, with comparable quantum yields. Upon addition of one equivalent of $NaBH(OAc)_3$ to the THF solution of the $\mathbf{L_1 \subset Cu(II)}$ complex, the metal ion was reduced to Cu(I) instantaneously, accompanied by a quenching of the fluorescence (Fig. 2) as the Cu(I) ion moved away from the 'N_4' end, making PET operational once again. Upon exposure to air, Cu(I) was oxidized to Cu(II) and moved to the 'N_4' end. This blocked PET, and fluorescence was recovered to the original ϕ_{FM} value in 12 h. Cu(II) could then be reduced again to Cu(I), and so the

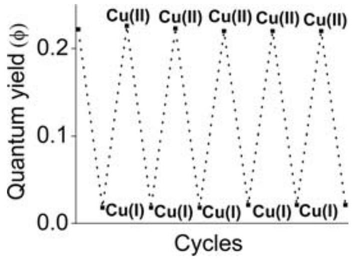
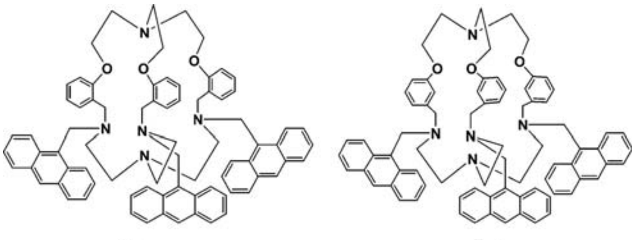


Fig. 3 Quantum yield plot of the $\mathbf{L_1 \subset Cu(II)}$ complex after reduction by $NaBH(OAc)_3$ and subsequent aerial oxidation.



Scheme 3 Aza-oxa cryptand-based fluorescence signaling systems.

cycle continued. The receptor in $\mathbf{L_2}$ is more rigid,[12] and this helped in the movement of the metal ion from one end to the other (Fig. 3). Accordingly, in $\mathbf{L_2}$, the complete recovery of fluorescence upon exposure of the Cu(I) complex to air took 5 h. There is a possibility that the metal ion actually went outside of the cavity when it was reduced to Cu(I) and then came back in again upon re-oxidation. To investigate this, we probed two aza-oxa cryptands[1a] ($\mathbf{L_3}$ and $\mathbf{L_4}$, Scheme 3) as receptors. Both $\mathbf{L_3 \subset Cu(II)}$ and $\mathbf{L_4 \subset Cu(II)}$ complexes showed high fluorescence enhancement in THF. Upon addition of one equivalent of $NaBH(OAc)_3$ to THF solutions of the $\mathbf{L_3 \subset Cu(II)}$ or $\mathbf{L_4 \subset Cu(II)}$ complexes, the fluorescence was quenched. However, upon exposure to air, no fluorescence recovery could be observed. It is believed that in these two cases, the metal ion came out of the cavity because it did not prefer the NO_3 binding site. When the metal ion came out of the cavity and went into the bulk medium, it did not return to cavity upon oxidation.

Upon undertaking a mass spectral investigation, it was found that both $\mathbf{L_1 \subset Cu(II)}$ and $\mathbf{L_2 \subset Cu(II)}$ showed ~40% peak intensity.† Upon reduction of $\mathbf{L_1}$ and $\mathbf{L_2}$ with one equivalent of $NaBH(OAc)_3$, the corresponding species showed a 100% peak intensity due to $\mathbf{L_1 \subset Cu(I)}$ and $\mathbf{L_2 \subset Cu(I)}$, respectively, showing that the metal was still inside the cavity. The possibility of the binding of Cu(I) in the N_4 region was overruled from the fluorescence spectra, as no enhancement was observed when Cu(I) was generated (Fig. 2). Therefore, the only possible binding site of Cu(I) was the NS_3 region, whereas Cu(II) was in the N_4 region, blocking PET. The different binding zones for Cu(I) and Cu(II) supports the movement of the ion within the cavity. Cyclic voltamograms for the $\mathbf{L_1 \subset Cu(II)}$ and $\mathbf{L_2 \subset Cu(II)}$ complexes† show well-defined cyclic responses for the Cu(II)/Cu(I) couple, although ΔE_p (the difference of the oxidation and reduction peak potentials) is more than 60 mV. Thus, it can be concluded that this couple is chemically reversible but electrochemically quasi-reversible. In comparison, with receptors $\mathbf{L_3}$ and $\mathbf{L_4}$, the ESI mass spectra of the Cu(II) inclusion complexes gave a 50% peak, both for $\mathbf{L_3 \subset Cu(II)}$ and $\mathbf{L_4 \subset Cu(II)}$. However, on reduction with one equivalent of $NaBH(OAc)_3$, the ESI mass spectra gave a 100% peak for the metal-free $\mathbf{L_3}$ and $\mathbf{L_4}$; no peak due to $\mathbf{L_3 \subset Cu(I)}$ or $\mathbf{L_4 \subset Cu(I)}$ was observed. This shows that upon reduction, the metal ion came out of the cavity in $\mathbf{L_3}$ and $\mathbf{L_4}$ but did not in $\mathbf{L_1}$ and $\mathbf{L_2}$.

In conclusion, we have shown for the first time that a copper ion can translocate inside the cavity of thio-aza cryptands, depending upon its oxidation state. This property of the metal ion is utilized here to have a reversible ON–OFF fluorescence, which represents the first of a new generation of fluorescence signaling systems. We are currently working on enhancing the rate of translocation with different cryptand receptors.

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