Synthesis, photophysical and metal ion signalling behaviour of mono- and di-azacrown derivatives of 4-aminophthalimide

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Abstract. Synthesis, photophysical behaviour and metal ion signalling ability of 3-component systems, **I** and **II**, comprising a 4-aminophthalimido moiety as *fluorophore*, a dimethylene *spacer* and two different azacrown *receptors*, are reported. The fluorescence quantum yields and lifetimes of both the systems have been found to be significantly lower than that of the parent fluorophore indicating the occurrence of photoinduced electron transfer (PET) between the terminal moieties. PET is found to be more efficient in **II**, presumably due to the presence of more than one electron-donating centre in the receptor moiety. Fluorescence decay behaviour of the systems suggests a *through-space* nature of PET. The systems exhibit *off–on* fluorescence signalling in the aprotic media in the presence of several metal ions, some of which are well known for their fluorescence quenching abilities. Diazacrown derivative, **II**, appears to be a somewhat better signalling system than the monoazacrown derivative, **I**.

1. Introduction

In recent years, there has been a great deal of interest in molecular systems capable of performing light-induced logic operations.[1–3] A variety of molecular photonic devices, which have been developed in recent years, are essentially assemblies of suitably organized molecular components that perform logic functions characteristic of the assembly.[4–12] Of particular interest are the fluorosensors, molecular systems that are powered by light and whose response to the guest molecule or ion is based on fluorescence, for various metal ions of environmental and biological interest.

Fluorosensors are most often three-component systems consisting of a signalling moiety, called *fluorophore* and a guest-binding site, commonly referred to as *receptor*; the two are usually separated by a *spacer* group.[4] The components are chosen such that communication between the *receptor* and *fluorophore* results in 'switching off' of the fluorescence of the system. However, the fluorescence is 'switched on' in the presence of a guest, which turns off the communication between the *receptor* and *fluorophore*. Thus, the presence of a guest is indi-

cated by fluorescence enhancement (FE) of the system. Photoinduced electron transfer (PET) is the most commonly exploited mechanism of communication between the terminal moieties of a *fluorophore-spacer-receptor* system.[4] The design principle of the 'off-on' fluorescence signalling of a guest is schematically illustrated in scheme 1.
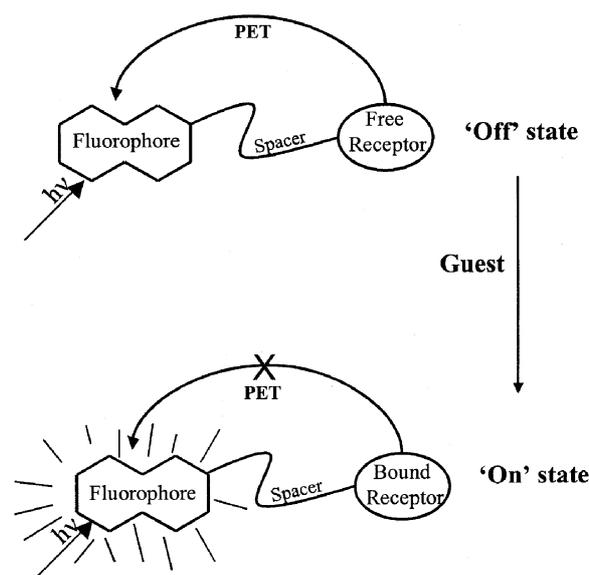
Scheme 1.

Sensing of the metal ions, particularly the transition and heavy metal ions, is of considerable interest for various reasons.[13–15] The crown compounds, because of the macrocyclic effect, expect to show stronger binding of the guests and to display selectivity in binding, depending on their cavity size.[3,16,17] Though the oxygen crowns bind the *s*-block metal ions, these are not good coordinating ligands for the transition metal ions. When the oxygen atom of the crown ether is replaced by nitrogen, one can expect stronger binding of the transition metal ions because of the enhanced binding ability of these metal ions with nitrogen.[18] Keeping this in mind and in continuation of our studies on systems capable of signalling metal ions through fluorescence enhancement,[19–26] we have developed *fluorophore-spacer-receptor* systems, **I** and **II** (chart 1). The fluorophore component used in these systems is 4-aminophthalimide (AP), whose photophysical behaviour is well understood.[27–29] Moreover, since AP is an electron-deficient molecule, it is ideally suited as the fluorophore component of the *fluorophore–spacer–receptor* sensor system.[19,22] In the present systems, two different azacrown moieties have been used as the receptor to examine the effect of the number of electron-donating centres on the signalling efficiencies. The synthetic procedure, photophysical properties and metal ion signalling behaviour of the two systems in tetrahydrofuran (THF) and acetonitrile (AN) are presented in this paper.

2. Experimental

2.1 *Materials*

Reagent grade reactants and solvents were obtained from commercial suppliers and used as received for synthesis. The solvents used for absorption and fluorescence studies were purified by standard proce-
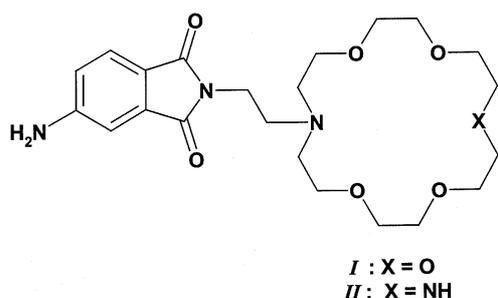
dures.[30] Hydrated perchlorate salts of the metals (Aldrich or Acros Organics Ltd.) were used throughout the investigation except in the case of mercury, whose chloride salt, mercuric chloride, was used. Starting materials required for the synthesis of **I** and **II** were prepared as described in the literature.[26,31,32]

2.1a *Synthesis of 5-amino-2-[2-(1,4,7,10,13-penta-oxa-16-aza-cyclooctadec-16-yl)-ethyl]-isoindole-1,3-dione (I):* 5-Amino-2-(2-bromoethyl)-isoindole-1,3-dione (0·5 g, 1·9 mmol) and the crown ether, 1,4,7,10,13-pentaoxa-16-aza-cyclooctadecane (2 g, 7·6 mmol) were stirred in acetonitrile at reflux temperature in the presence of potassium carbonate (1 g, 7·2 mmol) for 24 h. The reaction mixture was filtered, concentrated, washed with water and extracted using ethylacetate. The organic layer was dried using anhydrous sodium sulphate and reduced in volume. The crude solid obtained was purified using a neutral alumina column with 2% methanol in chloroform as the eluent. Yield: 0·4 g (47·63%). IR (neat, cm^{-1}): 3417, 2980, 2873, 1701, 1616, 1461, 1355, 1110, 952, 839, ^{1}H NMR (CDCl$_3$, 200 MHz): *d* 2·7 (*m*, 8H), 3·6 (*m*, 20H), 6·8 (*d*, 1H), 7·05 (*s*, 1H), 7·4 (*d*, 1H).

2.1b *Synthesis of 5-amino-2-[2-(1,4,10,13-tetra-oxa-7,16-diaza-cyclooctadec-7-yl)-ethyl]-isoindole-1,3-dione (II):* 5-Amino-2-(2-bromoethyl)-isoindole-1,3-dione (0·45 g, 1·7 mmol) and the diazacrown ether, 1,4,10,13-tetraoxa-7,16-diaza-cyclooctadecane (2 g, 7·6 mmol) were mixed in acetonitrile (25 mL) and stirred well in the presence of potassium carbonate (1 g, 7·2 mmol) under refluxing conditions. The reaction was continued for 24 h. The reaction mixture was filtered, concentrated, washed with water and extracted using ethylacetate. The organic layer was dried using anhydrous sodium sulphate and reduced in volume. The resulting solid was purified by column chromatography using a neutral alumina column and the required fraction was obtained with a 2% methanol in chloroform as eluent. Yield: 0·5 g (66·4%). Melting point: 142°C, IR (KBr, cm^{-1}): 3485, 2893, 2793, 1753, 1701, 1597, 1458, 1390, 1111, 987, ^{1}H NMR (CDCl$_3$, 200 MHz): *d* 2·7 (*m*, 12H), 3·5 (*m*, 16H), 6·8 (*d*, 1H), 7·05 (*s*, 1H), 7·4 (*d*, 1H), FAB-MS *m/z*: 451 [*M* + 1]$^+$.

Three-component systems, **I** and **II**, as stated above, were purified by column chromatography. Production of a single spot in TLC, which is an indicator of the purity of a sample, was checked prior to fluorescence measurements.

I : X = O
II : X = NH

Chart 1.

2.2 *Instrumentation and methods*

Steady state absorption and fluorescence spectra were recorded on a UV–Vis–NIR spectrophotometer (Shimadzu, UV-3101PC) and spectrofluorimeter (Spex, Fluoromax 3) respectively. NMR spectra were recorded on a Bruker ACF-200 spectrometer, the FAB mass spectra on a JEOL SX 102/DA-6000 mass spectrometer, and IR spectra on a Jasco FT-IR/5300 spectrometer. Fluorescence decay measurements were performed using a single-photon counting spectrofluorimeter (IBH, model 5000). The instrument was equipped with a thyratron-gated coaxial flash lamp filled with hydrogen gas at 0·5 atm pressure. The lamp frequency was maintained at 40 kHz and the FWHM of the lamp pulse under the operating condition was ~1·2 ns. The decay curves were analysed by a nonlinear least squares iteration procedure using IBH decay analysis software (version 6·1·36). The quality of the fit was judged by the c^2 values and plot of the residuals.

Fluorescence quantum yields of the systems were measured using 4-aminophthalimide as the reference compound ($f_f = 0.63$ in acetonitrile).[29] A solution of the systems in tetrahydrofuran/acetonitrile was prepared with absorbance (between 0·05 and 0·1) being the same as that of the reference compound at the exciting wavelength ($l = 360$ nm). Fluorescence spectra of the systems and the reference compound were measured under the same operating conditions and settings and the quantum yields were determined by comparing the areas beneath the fluorescence spectra.

Fluorescence measurements were carried out using ~10^{-5} M solutions of the compounds. The effect of the metal ions on the fluorescence intensity was examined by adding a few microlitres of the stock solution of the metal salts to a known volume of the solution of the sensor system (3 ml). The addition was limited to 100 *ml* such that the volume change was not significant.

3. Results and discussion

3.1 *Photophysical behaviour*

Both systems exhibit broad absorption bands (figure 1) typical of the intramolecular charge transfer (ICT) transition of the 4-aminophthalimide moiety[22,27,29] except that the spectral maxima for the crown derivatives are slightly red-shifted relative to that of

the parent system, AP (vide table 1) in any given solvent. The red-shift of the absorption maximum of the multi-component systems relative to that of the parent molecule is most likely due to the greater polar characteristic of the substituted fluorophore rather than due to any interaction between the terminal moieties of the molecules. As can be seen from the spectral data shown in table 1, the variation of l_{max}^{abs} of the two systems in any given medium is too small to comment upon. The l_{max}^{abs} values are marginally red-shifted in polar solvents. This behaviour is again consistent with that observed with the parent fluorophore, 4-aminophthalimide.

The crown compounds exhibit a broad structureless emission band (figure 1) characteristic of the ICT emission of AP with the l_{max}^{flu} Stokes-shifted relative to the parent molecule (table 1). Fluorescence spectral data show that the variation of l_{max}^{flu} among the different derivatives is quite small. However, unlike the absorption, the fluorescence maxima of the systems exhibit significant shift to longer wavelengths with increase in the polarity of
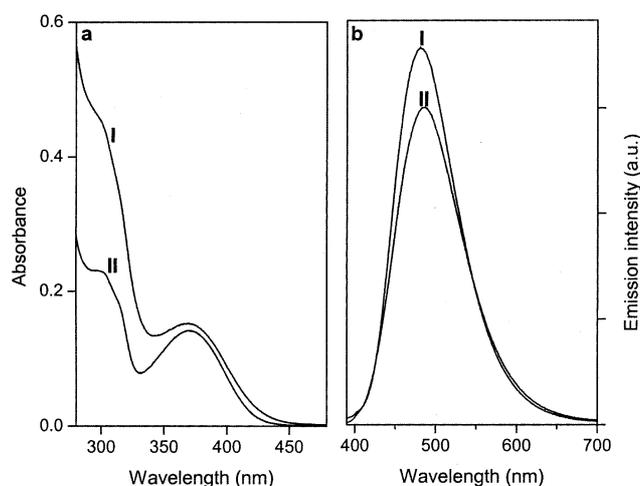

Figure 1. Absorption (**a**) and fluorescence (**b**) spectra of **I** and **II** in AN, $l_{exc} = 360$ nm.

Table 1. Wavelength (nm)[a] corresponding to the absorption and emission maxima[b] of the systems.

Compound	THF		AN	
	l_{abs}	l_{em}	l_{abs}	l_{em}
AP	358	452	359	462
I	369	468	370	480
II	367	483	370	484

[a]±1 nm; [b]$l_{exc} = 360$ nm

Table 2. Fluorescence quantum yield (f_f)[a] and decay parameters (t, in ns)[b] for the systems. The relative weightage of each decay component (in %) is given in brackets.

System	In THF			In AN		
	f_f	t_f	t_{av}	f_f	t_f	t_{av}
AP[c]	0·70	14·0	14·0	0·63	12·4	12·4
I	0·25	1·9 (35), 9·3 (16·4), 17·3 (48·6)	10·6	0·24	0·2 (78), 3·8 (8·9), 18·7 (13·1)	2·9
II	0·04	0·9 (71), 4·1 (24), 17·8 (5)	2·5	0·03	0·3 (89·7), 1·7 (8·7), 16·3 (1·6)	0·6

[a]±10%; [b]±10% for lifetimes more than 1 ns, t values lower than 1 ns may not be accurate because of the time resolution of the set up; [c]these values are taken from ref. [29]

the medium. This behaviour is consistent with the greater polar nature of the fluorescent state of AP and its derivatives.[29]

While the spectral behaviour of the crown compounds is very similar to that of AP, the fluorescence quantum yields (f_f) of these systems are found significantly lower than that of AP (table 2). AP is highly fluorescent in aprotic media with fluorescence quantum yield between 0·63 and 0·73.[29] The f_f values for **I** and **II** are ~0·24 and 0·04 respectively. The lower fluorescence quantum yield of crown derivatives is indicative of PET interaction between the terminal *fluorophore* and *receptor* moieties in these systems. The solvent effect on PET, as observable from the f_f values, is negligible.

The fluorescence decay parameters of the systems in THF and AN have been collected in table 2. Even though AP exhibits a single exponential decay with a long lifetime of 12.4–14 ns in aprotic media, both **I** and **II** exhibit tri-exponential decay behaviour with the average lifetime significantly shorter than that of AP. Among the three components, the major component is associated with short (sub-nanosecond) lifetime. The second component is characterized by long lifetime similar to that of the parent fluorophore. The third component has lifetime between that of the two other components. The lifetime values and the associated pre-exponential factors suggest that there exist at least three distinguishable conformations of each system. The short-component, which is the most dominant one, arises due to those molecules in which the orientation and distance between the interacting groups are most favourable for PET interaction. On the other hand, the component with the longest lifetime originates from those molecules in which the spatial disposition of the interacting groups is unfavourable for PET. This assignment and our earlier results[19–24] on systems with much simpler receptor moieties suggest that the PET interaction is mediated by *through-space* inter-

action between the fluorophore and the receptor moieties. The average fluorescence lifetime, which is one of the indicators of the extent of PET and is important from the point of view of fluorescence signalling, is relatively lower for the di-azacrown derivative, **II**. Interestingly, the lifetime values of the systems are relatively lower in polar solvent, AN.

3.2 *Effect of the metal ions*

Neither the extinction coefficient nor the wavelength of absorption changes significantly in the presence of the metal salts. A small red-shift of the absorption maximum (~5–7 nm) could be observed with a large majority of the metal salts. In most of the cases, no isosbestic point could be observed.

The effect of the metal ions is however much more pronounced on the fluorescence behaviour of the systems. Addition of the metal salts leads to larger Stokes shift of the fluorescence maximum (~30–40 nm) and is associated with an enhancement of the fluorescence intensity (figure 2). The maximum FE values observed for the systems are collected in table 3. As can be seen, the monoazacrown compound, **I**, exhibits very little FE in the presence of the metal ions. On the other hand, the diazacrown derivative, **II**, gives reasonably good enhancement in most of the cases. This behaviour is in agreement with our expectation based on the fluorescence lifetime of the individual compounds (table 2).

We have also examined the effect of the metal ions on the fluorescence decay behaviour of the systems. That the metal ions disrupt the PET communication between the terminal moieties of the systems is evident from the disappearance of the short component of the decay in the presence of the metal ions.

In summary, we have synthesised and fully characterised two new *fluorophore–spacer–receptor* systems consisting of two different azacrown moieties
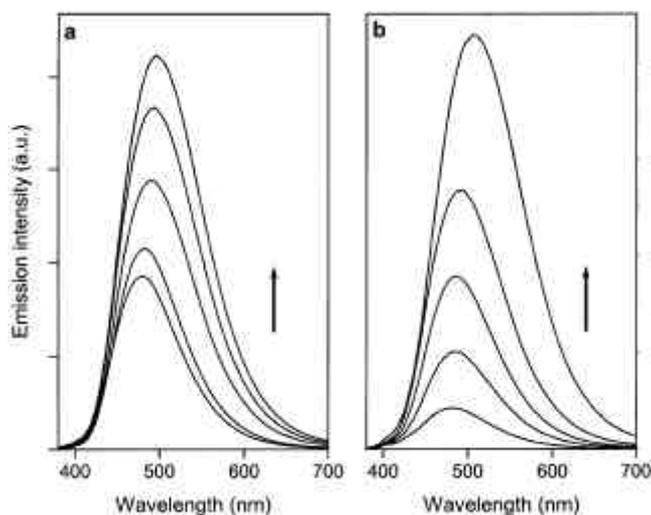
Figure 2. Effect of the addition of Cd^{2+} on the fluorescence behaviour of **I** (**a**) and **II** (**b**) in AN, $l_{exc} = 360$ nm; $[Cd^{2+}]$ (in mM) were: 0, 0·12, 0·28, 0·87 and 2·3 (in a) and 0, 0·036, 0·068, 0·28 and 0·7 (in b) respectively in the direction of the arrow.

Table 3. Maximum FE values[a] observed for the systems in the presence of the metal ions.

Metal ion	**I**		**II**	
	THF	AN	THF	AN
Cd^{2+}	2	3	17	12
Co^{2+}	2	2	5	17
Cu^{2+}	1·6	1·3	3	9
Fe^{3+}	1·6	1·4	5	8
Hg^{2+}	1·5	1·2	2	3
Mn^{2+}	2	2	10	4
Ni^{2+}	2	2	4	13
Pb^{2+}	2	2	5	5
Zn^{2+}	2	3	5	19

[a]±15%

as receptors and examined their photophysical and fluorescence signalling properties towards some metal ions of interest. The diazacrown derivative is found to show fairly good fluorescence enhancement even in the presence of quenching metal ions.

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