DALTON
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Polyaza and azaoxa macrocyclic receptors functionalised with fluorescent subunits; Hg^{2+} selective signalling

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A polyazacycloalkane containing naphthyl groups, 1,4,8,11-tetrakis(naphthylmethyl)-1,4,8,11-tetraazacyclotetradecane (L^1), and the azaoxa cycloalkane receptors containing anthracenyl groups, 7,13-bis(anthracenylmethyl)-1,4,10-trioxa-7,13-diazacyclopentadecane (L^2) and 10-anthracenylmethyl-1,4,7-trioxa-10-azacyclododecane (L^3), have been synthesized and their activity as fluorescent chemosensors studied towards the metal cations Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} in THF–water (70:30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1 and 1,4-dioxane–water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^2 and L^3. The crystal structure of the complex $[Cd(L^1)(Cl)][PF_6]$ has been determined by X-ray single crystal procedures. The co-ordination geometry about the cadmium atom is near square pyramidal with the ligand showing a conformation with the four naphthylmethyl groups pointing above the N_4 plane. Potentiometric experiments in THF–water for L^1 in the presence of Cu^{2+}, Hg^{2+} and Pb^{2+} and in 1,4-dioxane–water for L^2 in the presence of Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, and L^3 with Cd^{2+} and Pb^{2+} have also been carried out. All metals form stable complexes with L^1, L^2 and L^3 with stability constants for the formation of the $[M(L^1)]^{2+}$, $[M(L^2)]^{2+}$ and $[M(L^3)]^{2+}$ species in the sequence $Pb^{2+} < Hg^{2+} < Cu^{2+}$; $Zn^{2+} < Cd^{2+} < Pb^{2+} < Cu^{2+} \ll Hg^{2+}$ and $Cd^{2+} < Pb^{2+}$, respectively. The fluorescent behaviour of L^1, L^2 and L^3 in the presence of the Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} has been studied as a function of the pH: Cu^{2+} and Hg^{2+} selectively quench the fluorescence emission intensity of L^1 at neutral and acid pH. The emission intensity of L^2 is selectively enhanced in the presence of Hg^{2+} at basic pH. In contrast, the fluorescence intensity of the free receptor L^3 at a certain pH is not modified upon addition of any metal ion. The emission sensing behaviour of L^1, L^2 and L^3 towards metal ions is compared with the electrochemical sensing ability of analogous ferrocene-functionalised ligands.

Introduction

The design and synthesis of new systems that can be switched between different states have been used satisfactorily for the development of new chemical sensors.[1–9] Of interest are novel functionalised receptors that can change a measurable physical property upon co-ordination with target species. This allows transformation to the macroscopic level (the presence or not of a determined signal) of chemical information located at the molecular level (co-ordination or not of a determined guest). Chemical engineering in this field involves the selection of a suitable co-ordination site and its functionalisation with appropriate groups able to switch its state upon guest binding. A number of works have been devoted to the study of different molecular binding domains towards a large number of both cationic and anionic guests and in general the guest–receptor interaction is well understood. In contrast the non-covalent supramolecular interaction between a guest attached to the receptor part of the molecule and the signalling subunits is a field comparatively less studied. However control of the nature of the signalling subunit could determine not only the type of macroscopically observed signal but also affect the selectivity. These ideas are in line with the general interest of applying supramolecular concepts for the development of sensing systems. We have recently reported that a combination of suitable molecular architectures and redox groups could prove a good methodology strategically to design new molecules for the selective electrochemical recognition of target substrates.[10–15] For instance, the combination of azaoxa derivatives and ferrocenyl groups proved a good strategy electrochemically and selectively to sense heavy metal ions such as Hg^{2+}, Pb^{2+} or Cd^{2+} over other commonly water present transition metal ions.[16] Inspired by these recent advances, we have developed ligands analogous to those containing ferrocenyl but having fluorescent groups as signalling subunits. The work has been mainly to promote discrimination between heavy toxic metal ions using fluorescent techniques. The selective behaviour found with the fluorescent receptors here reported is compared with the selectivity found in the analogous ferrocene-functionalised molecules.

Experimental

Physical measurements

Potentiometric titrations were carried out in THF–water (70:30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1 and 1,4-dioxane–water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^2 and L^3, using a reaction vessel water-thermostatted at 25.0 ± 0.1 °C under nitrogen. The titrant was added by a Crison microburete 2031. The solvents of the titrants were THF–water (70:30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate) for L^1 and 1,4-dioxane–water (70:30 v/v, 0.1 mol dm^{-3} potassium nitrate) for L^2 and L^3. The potentiometric measurements were made using a Crison 2002 pH-meter and a combined glass electrode. A PC automatically controlled the titration system. The electrode was calibrated as a hydrogen concentration probe by titration of known amounts

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of HCl with CO_2-free KOH solution and determining the equivalence point by Gran's method[17] which gives the standard potential E'° and the ionic product of the solvent ($K'_w = [H^+][OH^-]$, log $K = -15.65$ for THF–water 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C and −16.20 for 1,4-dioxane–water (70:30 v/v), 0.1 mol dm^{-3} potassium nitrate, 25 °C). Metal ion salts were nitrate or perchlorate and the metal concentration was determined by standard methods. The computer program SUPERQUAD[18] was used to calculate the protonation and stability constants. The titration curves for each system (*ca.* 250 experimental points corresponding to at least three titration curves, pH = −log[H^+] range investigated 2.5–10, concentration of the ligand and cations *ca.* 1.2×10^{-3} mol dm^{-3}) were treated either as a single set or as separated entities without significant variations in the values of the stability constants. Fluorescence measurements were made on a Edinburgh Analytical Instrument using L^1, L^2 and L^3 with a concentration of 1.2×10^{-5} mol dm^{-3} in THF–water (70:30) v/v for L^1 and 1,4-dioxane–water (70:30) v/v for L^2 and L^3 in the presence of different metal ions (metal-to-ligand ratio = 1:1) as a function of the pH.

Synthesis of L^1

1,4,8,11-Tetraazacyclotetradecane (1.99 mmol) and 2-(bromomethyl)naphthalene (9.95 mmol) were refluxed in dichloromethane for 72 hours in the presence of 1 ml of triethylamine. The resulting solution was evaporated to dryness and basic water (20 mL) and dichloromethane (3 × 20 mL) added and transferred to a separatory funnel. The dichloromethane phase was treated with anhydrous magnesium sulfate, filtered and evaporated to dryness. The compound was then recrystallised from hot tetrahydrofuran, filtered and washed with chloroform. Yield 1200 mg, 79% (Found: C, 75.07; H, 6.70; N, 6.55. $C_{54}H_{56}N_4{\cdot}CHCl_3$ requires C, 75.04; H, 6.48; N, 6.36%). NMR ($CDCl_3$): ^1H, δ 1.94 (t, CH_2, 4 H), 2.60 (t, CH_2, 8 H), 2.70 (s, CH_2, 8 H), 3.57 (s, $CH_2C_{10}H_7$, 8 H), 7.33 (m, $C_{10}H_7$, 4 H), 7.41 (d, $C_{10}H_7$, 2 H) and 7.70 (d, $C_{10}H_7$, 2 H). Mass spectrum (FAB): *m*/*z* 762, (M + H^+, 100), 622 (5), 380 (15) and 227 (90%).

Synthesis of L^2 and L^3

The azaoxa macrocycle (1.39 mmol) and 9-(chloromethyl)-anthracene (2.78 mmol for L^2 and 1.39 mmol for L^3) were refluxed in dichloromethane for 24 hours in the presence of K_2CO_3. The solvent was then removed and the residue dissolved in dichloromethane and purified by column chromatography on alumina using CH_2Cl_2–CH_3OH (98:2) as eluent. A pale yellow oil was obtained. **L^2**: Yield 698 mg, 84% (Found: C, 72.13; H, 6.53; N, 3.57. $C_{40}H_{42}N_2O_3{\cdot}CH_2Cl_2$ requires C, 72.03; H, 6.44; N, 4.10%). NMR ($CDCl_3$): ^1H, δ 2.90 (s, CH_2N, 4 H), 3.50–3.70 (m, CH_2O, 12 H), 4.6 (s, $CH_2C_{14}H_9$, 2 H), 7.48 (m, $C_{14}H_9$, 4 H), 8.01 (d, $C_{14}H_9$, 2 H), 8.40 (s, $C_{14}H_9$, 1 H) and 8.60 (d, $C_{14}H_9$, 2 H). Mass spectrum (FAB): *m*/*z* 599 (M^+). **L^3**: Yield 395 mg, 78% (Found: C, 69.17; H, 7.13; N, 3.055. $C_{23}H_{27}NO_3{\cdot}0.25CH_2Cl_2 + H_2O$ requires C, 69.02; H, 7.29; N, 3.46%). NMR ($CDCl_3$): ^1H, δ 2.80 (t, CH_2N, 4 H), 2.95 (t, CH_2N, 4 H), 3.5–3.7 (m, CH_2O, 12 H), 4.60 (s, $CH_2C_{14}H_9$, 2 H), 7.50 (m, $C_{14}H_9$, 4 H), 8.01 (d, $C_{14}H_9$, 2 H), 8.40 (s, $C_{14}H_9$, 1 H) and 8.60 (d, $C_{14}H_9$, 2 H). Mass spectrum (FAB): *m*/*z* 366 (M^+).

Crystal data

$C_{55}H_{58}CdCl_3F_6N_4P$, $M = 1138.77$, triclinic, space group $P\bar{1}$, $a = 10.1175(11)$, $b = 12.9778(14)$, $c = 20.112(2)$ Å, $\alpha = 99.688(8)$, $\beta = 90.217(8)$, $\gamma = 91.558(9)$°, $Z = 2$, $U = 2602.1(5)$ Å^3, $D_c = 1.453$ g cm^{-3}, λ(Mo-Kα) = 0.71069 Å, $T = 293(2)$ K, μ(Mo-Kα) = 0.667 mm^{-1}. Crystal dimensions 0.30 × 0.37 × 0.38 mm. 9652 Reflections were measured of which 9098 were unique ($R_{int} = 0.0193$). Absorption (ψ scan) corrections were applied. The structure was solved by direct methods (SHELXTL)[20] and refined by full-matrix least-squares analysis on F^2. The refinement converged at *R*1 0.0544 ($F > 4\sigma(F)$) and *wR*2 0.1734 (all data)

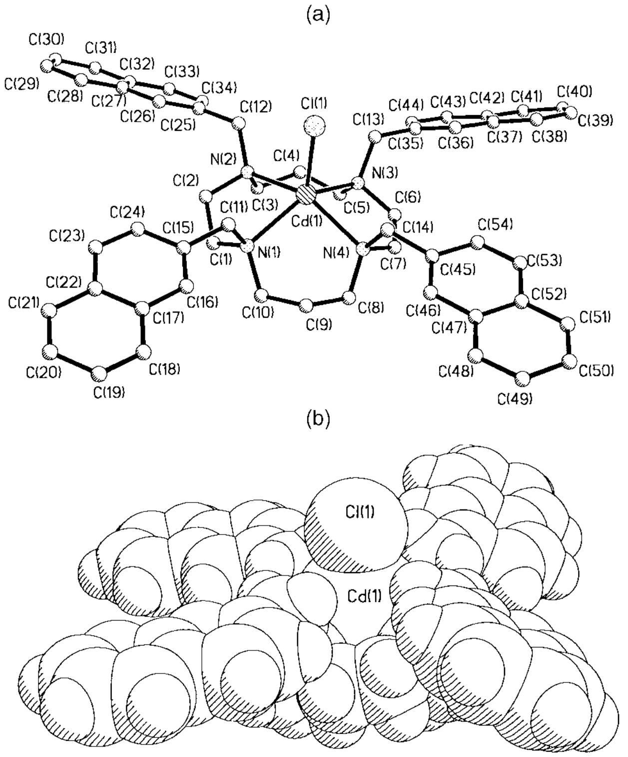


Fig. 1 (a) Molecular structure of the $[Cd(L^1)(Cl)]^+$ cation. (b) Space-filling representation of the $[Cd(L^1)(Cl)]^+$ cation emphasising the photoactive cavity.

CCDC reference number 186/1852.

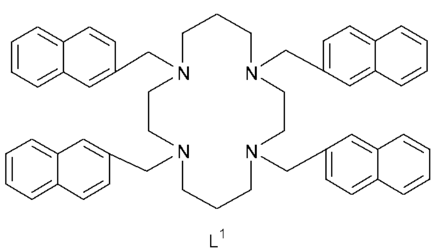
See http://www.rsc.org/suppdata/dt/a9/a908762a/ for crystallographic files in .cif format.

Results and discussion

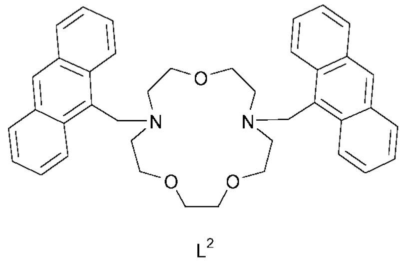
Reaction of 1,4,8,11-tetraazacyclotetradecane with 2-bromomethylnaphthalene and reaction of 1,4,10-trioxa-7,13-diazacyclopentadecane and 1,4,7-trioxa-10-azacyclododecane with 9-(chloromethyl)anthracene led to the isolation in a good yield of the compounds L^1, L^2 and L^3, respectively. These receptors are analogous to the ferrocene-functionalised molecules L^4, L^5 and L^6 (see references 10, 16 and 11, respectively). A similar receptor to L^1 has been described elsewhere.[19] Receptors L^1, L^2 and L^3 are a family of potential chemosensors where the number and nature of the binding atoms has been varied and whose response to transition metal ions will be studied. The following work has mainly been carried out to detect the ability of the fluorescent signalling subunit macroscopically to amplify potential selective complexation processes with transition metal ions.

Crystal structure of $[Cd(L^1)(Cl)][PF_6]{\cdot}CH_2Cl_2$

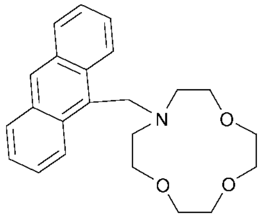
The reaction of cadmium chloride with L^1 at reflux and further addition of $[NH_4][PF_6]$ and water afforded a white solid that was crystallised from dichloromethane–hexane solutions and characterised as the salt $[Cd(L^1)(Cl)][PF_6]$. The mass spectrum of the solid shows a peak at *m*/*z* 909 corresponding to the $[Cd(L^1)(Cl)]^+$ cation. Fig. 1 shows a view of the $[Cd(L^1)(Cl)]^+$ unit with the atomic numbering scheme, whereas Table 1 gives some selected bond distances and angles. The crystal structure consists of $[Cd(L^1)(Cl)]^+$ cations linked by ionic interactions with hexafluorophosphate anions. One molecule of dichloromethane completes the molecular packing. The Cd–N distances range from 2.345(4) to 2.364(4) Å, whereas the Cd–Cl inter-



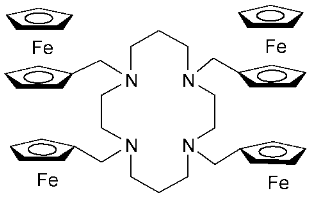
L1



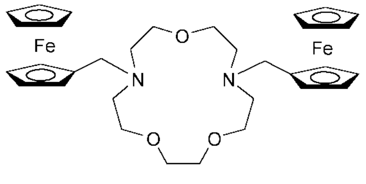
L2



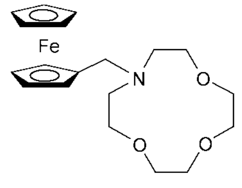
L3



L4



L5



L6

Table 1 Selected bond lengths (Å) and angles (°) for compound $[Cd(L^1)(Cl)][PF_6]\cdot CH_2Cl_2$

Cd(1)–N(1)	2.351(4)	Cd(1)–N(2)	2.364(4)
Cd(1)–N(3)	2.345(4)	Cd(1)–N(4)	2.355(5)
Cd(1)–Cl(1)	2.4611(13)	C(1)–C(2)	1.477(8)
C(2)–N(2)	1.532(7)	N(2)–C(3)	1.466(7)
C(3)–C(4)	1.535(9)	C(4)–C(5)	1.480(10)
C(5)–N(3)	1.458(9)	N(3)–C(6)	1.499(9)
C(6)–C(7)	1.265(11)	C(7)–N(4)	1.527(9)
N(4)–C(8)	1.463(9)	C(8)–C(9)	1.504(10)
C(9)–C(10)	1.492(9)	C(10)–N(1)	1.487(7)
N(1)–C(11)	1.513(7)	N(2)–C(12)	1.489(7)
N(3)–C(13)	1.495(7)	N(4)–C(14)	1.508(8)

N(3)–Cd(1)–N(1)	142.8(2)	N(3)–Cd(1)–N(4)	79.8(2)
N(1)–Cd(1)–N(4)	90.2(2)	N(3)–Cd(1)–N(2)	91.4(2)
N(1)–Cd(1)–N(2)	79.98(14)	N(4)–Cd(1)–N(2)	150.5(2)
N(3)–Cd(1)–Cl(1)	105.62(13)	N(1)–Cd(1)–Cl(1)	111.57(12)
N(4)–Cd(1)–Cl(1)	106.44(14)	N(2)–Cd(1)–Cl(1)	103.01(11)
C(1)–N(1)–C(11)	112.8(4)	C(1)–N(1)–C(10)	107.4(4)
C(10)–N(1)–C(11)	112.6(4)	C(1)–N(1)–Cd(1)	105.2(3)
C(10)–N(1)–Cd(1)	115.7(4)	C(11)–N(1)–Cd(1)	103.0(3)
C(3)–N(2)–C(12)	114.5(4)	C(3)–N(2)–C(2)	108.9(4)
C(12)–N(2)–C(2)	107.6(4)	C(3)–N(2)–Cd(1)	110.3(3)
C(12)–N(2)–Cd(1)	111.2(3)	C(2)–N(2)–Cd(1)	103.7(3)
C(5)–N(3)–C(13)	113.2(5)	C(5)–N(3)–C(6)	108.1(8)
C(13)–N(3)–C(6)	109.5(6)	C(5)–N(3)–Cd(1)	112.7(4)
C(13)–N(3)–Cd(1)	108.5(3)	C(6)–N(3)–Cd(1)	104.4(4)
C(8)–N(4)–C(14)	113.8(5)	C(8)–N(4)–C(7)	105.2(7)
C(14)–N(4)–C(7)	110.3(6)	C(8)–N(4)–Cd(1)	117.7(4)
C(14)–N(4)–Cd(1)	105.4(3)	C(7)–N(4)–Cd(1)	104.0(4)

action is of 2.4611(13) Å . The co-ordination number about the cadmium cations is five, with four non-coplanar nitrogen atoms from the macrocycle and a chloride anion, and co-ordination geometry closer to square pyramidal than to trigonal bipyramidal. In fact the τ value ($\tau = (\beta - \alpha)/60$ where α and β are the N(1)–Cd(1)–N(3) and N(2)–Cd(1)–N(4) bond angles) of 0.12 indicates that the complex could be described as being 12% distorted from a square pyramid ($\tau = 0$) towards a trigonal bipyramid ($\tau = 1$). The basal plane angles are N(1)–Cd(1)–N(2) 79.98(14), N(2)–Cd(1)–N(3) 91.4(2), N(3)–Cd(1)–N(4) 79.8(2) and N(4)–Cd(1)–N(1) 90.2(2)° and the axial Cl(1) atom giving angles of Cl(1)–Cd(1)–N(1) 111.57(12), Cl(1)–Cd(1)–N(2) 103.01(11), Cl(1)–Cd(1)–N(3) 105.62(13) and Cl(1)–Cd(1)–N(4) 106.44(14)°. Cyclic tetraamines such as cyclam can exist in different conformations when co-ordinated to metal ions. For instance, for R_4[14]aneN_4 containing five- and six-membered chelating rings a total of five combinations can be observed.[21] The cadmium complex shows L^1 with a conformation with the four naphthylmethyl groups pointing above the N_4 plane. A similar conformation has been found for instance in nickel(II) complexes containing 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane or 1,4,8,11-tetra(ferrocenylmethyl)-1,4,8,11-tetraazacyclotetradecane[22] as ligands. The compound L^1 is a host molecule containing a photoactive cavity built with four naphthylmethyl groups. Fig. 1(b) shows an alternative view of the $[Cd(L^1)(Cl)]^+$ cation emphasising the cadmium–guest(chloride) interaction surrounded by naphthylmethyl fluorescent subunits. These systems, with such a promising architecture, are good candidates as photoactive-catalytic systems capable of promoting photochemical reactions through the fluorescent groups on guest substrates activated by the metal ion.

Co-ordination behaviour

The protonation and co-ordination behaviour of L^1, L^2 and L^3 towards metal ions has been studied in THF–water (70 : 30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate) for L^1 and 1,4-dioxane–water (70 : 30 v/v, 25 °C, 0.1 mol dm^{-3} potassium nitrate) for L^2 and L^3 using potentiometric methods. Studies of L^1 in 1,4-dioxane–water were not carried out due to its insolubility in this solvent. Table 2 shows the protonation constants of L^1, L^2 and L^3. These display four, two and one protonation processes respectively with L^2 and L^3 showing basicity constants close to those found for the analogous non-functionalised receptors 4,10-diaza-15-crown-5 and 1-aza-12-crown-4 in water.[23,24] Comparison between protonation constants of 1,4,8,11-tetraazacyclotetradecane (cyclam) in water[25] with L^1 in THF–water shows that L^1 behaves as a stronger acid for the first two protonation processes but as a stronger base when the last two protonations are taken into account. Table 3 shows the stability constants for the formation of Cu^{2+}, Hg^{2+} and Pb^{2+} complexes with L^1. In THF–water (70 : 30 v/v) L^1 forms stable complexes with the metal ions studied with stability constants for the formation of the $[M(L^1)]^{2+}$ species in the sequence $Pb^{2+} < Hg^{2+} < Cu^{2+}$. The use of THF–water mixtures and the presence of naphthylmethyl groups significantly reduces the values of the stability constants. For instance, the formation constant of $[Cu(L^1)]^{2+}$ is around 10^{16} times smaller than that of cyclam (log $K = 27.2$)[26] in water. A reduction is also found when comparing the formation stability constants of the $[M(L^1)]^{2+}$ species for Hg^{2+} and Pb^{2+} (log $K = 11.26$ and 4.90, respectively) with those found with cyclam in water (log $K = 23$ and 11.3, respectively).[27] Fig. 2 shows the distribution diagram of the L^1–H^+–Cu^{2+} system. We have recently studied the interaction of Cu^{2+} with the ferrocenyl-functionalised receptor L^4 (see reference 12). Compound L^4 forms in THF–water the complex $[Cu(L^4)]^{2+}$ with a stability constant of log $K = 19.06$, which is around 10^7 times larger than that found for the formation of the $[Cu(L^1)]^{2+}$ complex. Bearing in mind that both L^1 and L^4 are tetrasubstituted cyclam derivatives, the results obtained suggest that the naphthylmethyl impose larger constraints than the ferrocenylmethyl groups making the formation constant of $[Cu(L^4)]^{2+}$ larger than that of $[Cu(L^1)]^{2+}$. In the L^1–H^+–Cu^{2+} system it was found that the logarithm of the first protonation of the $[CuL^1]^{2+}$ complex $\{[CuL^1]^{2+} + H^+ \rightleftharpoons [Cu(HL^1)]^{3+}$, log $K = 4.88\}$ is smaller than that of the third protonation of the free receptor, suggesting Cu–N cleavage upon protonation and that the number of nitrogens co-ordinated in $[CuL^1]^{2+}$ is four. This conclusion is similar to that found for receptor L^4 under similar conditions.[12]

Table 4 shows the stability constants of the Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} complexes of L^2 in 1,4-dioxane–water (70 : 30 v/v, 25 °C, 0.1 mol dm^{-3} potassium nitrate). All the metal ions form stable complexes with the receptor L^2 with the stability constants of the $[M(L^2)]^{2+}$ species in the sequence $Zn^{2+} < Cd^{2+} < Pb^{2+} < Cu^{2+} \ll Hg^{2+}$. The value of the stability constant of the formation of the $[Hg(L^2)]^{2+}$ complex ($Hg^{2+} + L^2 \rightleftharpoons [Hg(L^2)]^{2+}$) is *ca.* 10^4 times larger than that of $[Cu(L^2)]^{2+}$and about 10^7 times larger than those of Zn^{2+}, Cd^{2+} and Pb^{2+}. Compound L^2 forms the most stable complexes with mercury over other metal ions. In fact a method to determine the relative selectivity towards a couple of species is to plot ternary diagrams by means of the calculation of the overall percentages of each cation bound to the receptor over a determined pH range. The ternary L^2–Cu^{2+}–Hg^{2+} diagram shows a selective complexation of Hg^{2+} over Cu^{2+}. This larger stability constant found for Hg^{2+} was expected and attributed to the use of azaoxa cyclic receptors. Additionally the functionalisation of the azaoxa macrocycle with anthracenyl groups does not basically modify the co-ordination ability of the azaoxacycloalkane unit. For instance, the values of the logarithms of the stability constants for the formation of the $[M(L)]^{2+}$ complexes with the 1,4,10-trioxa-7,13-diazacyclopentadecane ligand and the metal ions Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} in water have been reported to range from 7.17 to 5.19 for Cu^{2+} and Zn^{2+}, respectively,[28] following the sequence $Zn^{2+} < Pb^{2+} < Cd^{2+} < Cu^{2+}$. Although different media have been used (1,4-dioxane–water and water, respectively), the stability constants found for the 1,4,10-trioxa-7,13-diazacyclopentadecane ligand are not very different to those for the anthracenyl-functionalised receptor L^2.

Table 2 Stepwise protonation constants in THF–water (70 : 30 v/v, 0.1 mol dm^{-3} tetrabutylammonium perchlorate, 25 °C) for L^1 and 1,4-dioxane–water (70 : 30 v/v, 0.1 mol dm^{-3} potassium nitrate, 25 °C) for L^2 and L^3

Reaction	log K L^1	L^2	L^3
$L + H^+ \rightleftharpoons [HL]^+$	8.64[a]	8.30(6)	7.80(2)
$L + 2H^+ \rightleftharpoons [H_2L]^{2+}$	14.48	13.87(6)	
$L + 3H^+ \rightleftharpoons [H_3L]^{3+}$	19.87		
$L + 4H^+ \rightleftharpoons [H_4L]^{4+}$	22.48		

[a] Values in parentheses are standard deviations on the last significant digit.

Table 3 Stability constants (log K) for the formation of Cu^{2+}, Hg^{2+}, Cd^{2+} and Pb^{2+}complexes of L^1 in THF–water (70 : 30 v/v) at 25 °C in 0.1 mol dm^{-3} of tetrabutylammonium perchlorate

Reaction	Cu^{2+}	Hg^{2+}	Pb^{2+}
$M^{2+} + L^1 + H^+ \rightleftharpoons [M(HL^1)]^{3+}$	16.55(4)[a]	16.82(2)	11.49(5)
$M^{2+} + L^1 \rightleftharpoons [M(L^1)]^{2+}$	11.67(7)	11.26(3)	4.90(3)
$M^{2+} + L^1 + H_2O \rightleftharpoons [M(L^1)(OH)]^+ + H^+$	6.70(5)	4.13(3)	−1.75(7)

[a] Values in parentheses are standard deviations on the last significant digit.

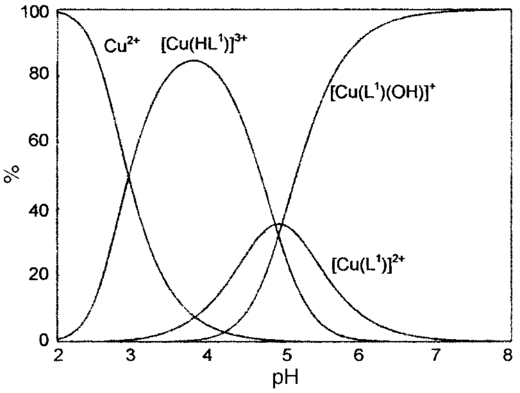


Fig. 2 Distribution diagram of the L^1–H^+–Cu^{2+} system as a function of the pH.

The solution behaviour of the receptor L^3 against metal ions has also been studied in 1,4-dioxane–water (70 : 30 v/v, 25 °C, 0.1 mol dm^{-3} potassium nitrate) using potentiometric methods. Table 5 shows the stability constants found in this medium for Cd^{2+} and Pb^{2+}. Stability constants with other metals such as Cu^{2+}, Zn^{2+} and Hg^{2+} were not determined due to the formation of an insoluble precipitate at pH > 5. This precipitate was not observed when a study of the fluorescence behaviour of L^3 in the presence of these metal ions was carried out. This is certainly due to the lower concentration used in the photophysical ($[L^3]$ *ca.* 1.2×10^{-5}) than in the potentiometric ($[L^3]$ *ca.* 2.4×10^{-3}) experiments.

The co-ordination behaviour of the receptor 1,4,7-trioxa-10-azacyclododecane has been reported in methanol–water with the metal cations Zn^{2+}, Cd^{2+} and Hg^{2+}, values of the logarithms for the formation of the $[M(L)]^{2+}$ complexes being 3.7, < 4.5 and > 11, respectively.[24] The logarithm of the stability constant for the formation of the $[Cd(L^3)]^{2+}$ complex ($L^3 + Cd^{2+} \rightleftharpoons$

Table 4 Stability constants (log K) for the formation of Cu^{2+}, Zn^{2+},Cd^{2+}, Pb^{2+} and Hg^{2+} complexes of L^2 in 1,4-dioxane–water (70 : 30 v/v) at 25 °C in 0.1 mol dm^{-3} KNO_3[a]

Reaction	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}
$M^{2+} + L^2 + H^+ \rightleftharpoons [M(HL^2)]^{3+}$	—	—	13.74(2)	—	16.33(3)
$M^{2+} + L^2 \rightleftharpoons [M(L^2)]^{2+}$	8.48(2)	5.21(6)	5.61(2)	5.96(2)	12.70(2)
$M^{2+} + L^2 + H_2O \rightleftharpoons [M(L^2)(OH)]^+ + H^+$	1.36(3)	−2.23(4)	−3.31(2)	−1.65(2)	6.60(2)

[a] Values in parentheses are standard deviations on the last significant digit.

Table 5 Stability constants (log *K*) for the formation of Cd^{2+}, Pb^{2+} complexes of L^3 in 1,4-dioxane–water (70:30 v/v) at 25 °C in 0.1 mol dm^{-3} KNO_3[a]

Reaction	Cd^{2+}	Pb^{2+}
$M^{2+} + L^3 \rightleftharpoons [M(L^3)]^{2+}$	3.63(4)	4.02(2)
$M^{2+} + L^3 + H_2O \rightleftharpoons [M(L^3)(OH)]^+ + H^+$	−4.76(2)	−2.50(1)

[a] Values in parentheses are standard deviations on the last significant digit.

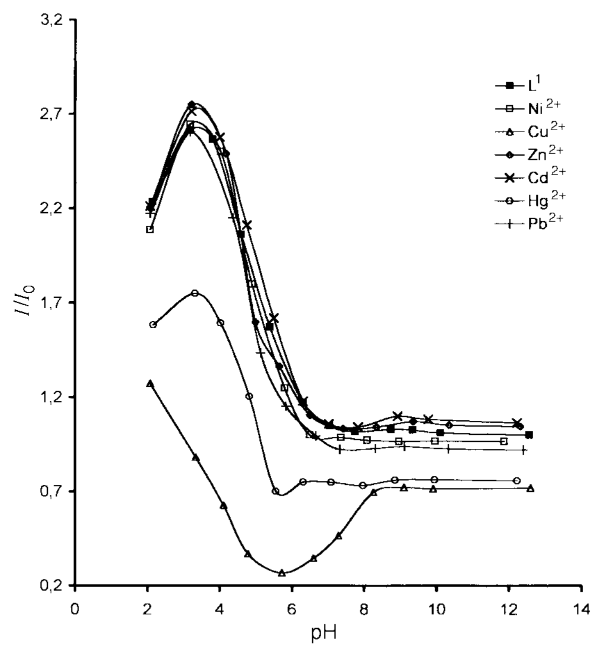


Fig. 3 Relative fluorescence intensity *versus* pH for the L^1–H^+–M^{2+} systems ($M^{2+} = Ni^{2+}$, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} or Pb^{2+}) ($\lambda_{ex} = 284$ nm, $\lambda_{em} = 336$ nm).

$[Cd(L^3)]^{2+}$) is 3.63(4), close to that of 4.5 found for the 1,4,7-triaza-10-azacyclododecane receptor in methanol–water. Although we have been unable to determine stability constants with Hg^{2+}, L^3 would also be expected to give selective complexation of mercury over other common metal ions.

From the potentiometric results it can be concluded that despite the N-functionalisation with bulky groups and the use of solvents different to water, the co-ordination behaviours of L^1, L^2 and L^3 are in line with the results described in water for the analogous non-functionalised molecules. For instance polyazacycloalkanes such as cyclam display larger formation stability constants with Cu^{2+} and Hg^{2+} than with other common transition metal ions.[26] For L^1 a similar trend appears to be observed. Additionally the presence of central oxygen donor atoms in macrocycles has been used to control the selectivity for larger metal ions over small ones,[29–31] as is in fact observed when comparing the co-ordination behaviour of L^2 and L^3 *versus* L^1. In general a similar behaviour, selective complexation towards Cu^{2+} with polyaza and Hg^{2+} with azaoxa derivatives, was found for the analogous ferrocene-functionalised ligands L^4, L^5 and L^6 (see references 12, 16 and 11).

Cation sensing investigations

The fluorescence behaviour of the receptors L^1, L^2 and L^3 towards metal ions as a function of the pH has been studied in the same medium where the potentiometric data were performed (THF–water 70:30 v/v for L^1 and 1,4-dioxane–water 70:30 v/v for L^2 and L^3). The following study was mainly carried out to detect the potential use of L^1, L^2 or L^3 as selective fluorescent chemosensors. The emitting behaviour of L^1, L^2 and L^3 in the pH range 2–9 was investigated by titration with KOH of a mixture containing acidified solutions of the receptor and the corresponding metal ions. Fluorophore L^1 shows a broad fluorescent band at 336 nm when excited at 284 nm in THF–water; L^2 and L^3 show a typical absorption and emission due to the presence of anthracenyl groups with a maximum in the absorption band at *ca.* 360 nm and a maximum in the emission fluorescent band at *ca.* 420 nm. The fluorescent behaviour of L^1, L^2 and L^3 is pH-dependent. This has also been observed in related naphthylmethyl and anthracenylmethyl functionalised polyamines[32,33] and attributed to a decrease of the reducing properties of the nitrogen atom upon protonation. Fig. 3 shows the relative emission intensity *versus* pH in the presence of transition metal ions for L^1 as a function of the pH. Receptor L^1 displays pH ranges of selective cation sensing. Whereas neither Cd^{2+}, Cd^{2+}, Ni^{2+} nor Zn^{2+} is able to modify the emission *versus* pH profiles of the free receptor, both Cu^{2+} and Hg^{2+} produce a significant quenching of the fluorescent band in the pH range 2–6. The quenching produced by Cu^{2+} is larger than that for Hg^{2+}. Some conclusions can be obtained when comparing the solution (see above) and the fluorescent behaviour. From potentiometric data, which allow determination of the nature of the complexes formed in solution, it can be observed that the quenching of the fluorescence intensity by Cu^{2+} is associated with the presence in solution of the $[CuL^1]^{2+}$ and $[Cu(HL^1)]^{3+}$ complexes, whereas the presence of hydroxo complexes does not appear substantially to modify the emission behaviour of the free receptor. For Hg^{2+}, also the existence of the protonated complex $[Hg(HL^1)]^{3+}$ at acid pH is mostly responsible for the quenching observed. It is also interesting that only Cu^{2+} and Hg^{2+}, which are the metal ions showing the largest formation stability constants with the cyclam core, are capable of inducing changes in the emission intensity of the fluorophore L^1. Also that the emission properties of a closely related compound to L^1, but containing four 1-naphthylmethyl substituents instead of 2-naphthylmethyl groups as L^1, has recently been studied in methanol and methanol–chloroform mixtures in the presence of alkali, alkaline-earth metal, ammonium and Zn^{2+} cations.[19] Under these conditions the related compound showed Zn^{2+} selectivity. In our case, Zn^{2+} does not produce significant emission changes at any pH for L^1. Those results show the importance of the medium and point towards the possibility of changing selectivity by modification of the solvent.

It is also interesting to compare the selective fluorescent sensing ability of L^1 with the electrochemical sensing behaviour of L^4.[12] Compound L^4 displays selective electrochemical sensing towards Cu^{2+}, Zn^{2+} and Cd^{2+} in a wide pH range with the largest electrochemical shift for Cu^{2+} at pH *ca.* 9. This behaviour contrasts with that observed for L^1 which shows selectivity towards Cu^{2+} and Hg^{2+} at acid pH. Thus, different sensing subunits present in L^1 and L^4 not only allow one to select the kind of signal observed at macroscopic level but also to modulate both pH ranges of selectivity and the metal ions to which the receptor is selective. Bearing in mind that both L^1 and L^4 receptors contain the same cyclam unit, the difference in selectivity has to concern the different non-covalent supramolecular interaction between the signalling subunits and the guest at a certain pH. Whereas the Cu^{2+}–ferrocenyl interaction is basically electrostatic, the nature of the interaction between the metal ion and the naphthyl group depends on the existence of photoelectron or energy transfer paths, the type of metal ions used, *etc.*

One of the goals of this paper is the development of potential fluorescent selective sensing receptors towards heavy metal ions such as Hg^{2+}. This ion is able significantly to quench the emission of L^1 at acid pH, however the response is not selective and also Cu^{2+} produces quenching at a similar pH range. Czarnick and co-workers[34] have recently reported the signalling of Hg^{2+} by using an anthracenyl-functionalised open-chain polyamine. However, as in our case, the sensing is not selective

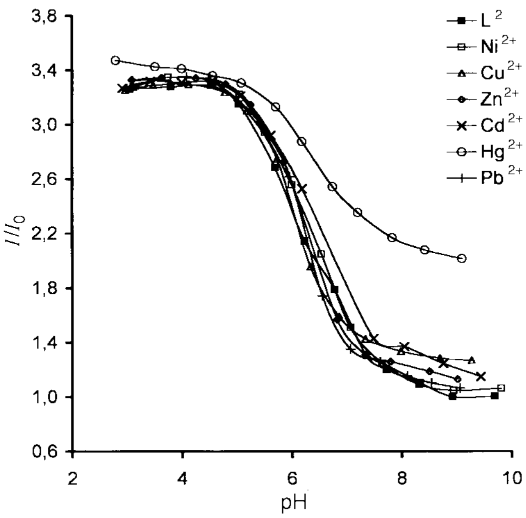


Fig. 4 Relative fluorescence intensity *versus* pH for the L^2–H^+–M^{2+} systems ($M^{2+} = Ni^{2+}$, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} or Pb^{2+}) ($\lambda_{ex} = 368$ nm, $\lambda_{em} = 420$ nm).

bearing in mind that also Cu^{2+} produces a change in the emission properties of the free fluorophore. Potentiometric results showed (see above) that receptors L^2 and L^3 have formation stability constants towards Hg^{2+} significantly larger than for other metal ions. Based on the fact that large stability constants could lead to a large selectivity, as found with L^1 and Cu^{2+}, Hg^{2+} *versus* other metal ions, the receptors L^2 and L^3 might be good candidates for the fluorescent signalling of the toxic metal cation Hg^{2+}. Although several papers have been published dealing with the fluorescent signalling of Hg^{2+},[34,35] to the best of our knowledge none of them concerns the use of azaoxa macrocycles as binding sites.

The signalling properties of L^2 and L^3 have been studied in 1,4-dioxane–water (70:30 v/v, 25 °C, 0.1 mol dm^{-3} potassium nitrate). Fig. 4 shows that, whereas the metal ions Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} are unable to modify the relative intensity *versus* pH profile of the free receptor, the presence of Hg^{2+} enhances the emission of L^2 in the pH 5–9 range. In contrast, the relative fluorescence intensity *vs.* pH ($\lambda_{ex} = 368$ nm, $\lambda_{em} = 420$ nm) in the presence of the metal ions Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+} and Pb^{2+} does not modify the emission of free L^3 at any pH range. This different behaviour towards Hg^{2+} of receptors L^2 and L^3 points out the importance of the binding domain in the recognition process. The different behaviour between L^2 and L^3 may be explained bearing in mind the larger ring cavity in L^2 than in L^3. For a ligand such as L^2 it is expected that cations with a large radius would better fit inside the cavity leading to a more effective co-ordination of the two nitrogen atoms that would produce a more effective reduction of the quenching properties of the lone pair involved in the co-ordination. Smaller ring sizes such as that of L^3 would produce a poorer interaction between the lone pair of the nitrogen and the metal cation and therefore a lower difference between the emission properties of the “free” ligand and its fluorescence upon cation binding would be expected.

Whereas only L^2 is able to signal Hg^{2+} (L^3 is not), both L^5 and L^6 showed electrochemical shifts upon addition of Hg^{2+}.[11,16] Again although both L^2 and L^5 are able selectively to sense Hg^{2+} there are some differences that deserve to be commented upon. Receptor L^5 electrochemically recognises other heavy metal ions such as Cd^{2+} and Pb^{2+} at pH *ca.* 7. In contrast L^2 only senses Hg^{2+}. Also receptors L^2 and L^5 contain the same binding domain, the difference between them being the presence of anthracenyl or ferrocenyl groups. The presence of one certain sensing subunit modulates the type of response (emission or electrochemical), the selectivity (Hg^{2+} or Hg^{2+}, Cd^{2+}, Pb^{2+}) and the pH range of signalling (neutral or basic).

For these receptors, containing a binding domain and signalling subunits, the macroscopic observed signal towards a target guest is controlled by two types of interactions. In a first step there is the connection between the guest and the binding sites. This is governed by well known covalent rules and selective co-ordination towards a certain metal ion is accessible by changing the topology and nature of the binding atoms. In a second step, there is a non-covalent interaction between the complex formed and the signalling subunits. This interaction is more subtle and might depend on parameters such as the nature of the signalling subunit, distance, energy levels, kind of complexes in solution, nature of the metal ion, *etc.* The control of both binding and signalling subunits is the basis strategically to design new potential receptors for selective sensing.

Conclusion

A family of polyaza and azaoxa derivatives functionalised with naphthyl or anthracenyl fluorescent signalling subunits have been characterised and their ability as chemosensors towards transition metal ions has been studied in water/organic solvent mixtures. Compound L^1 display selective co-ordination for Cu^{2+} and Hg^{2+}, whereas the inclusion of O-donor atoms in the macrocycle makes L^2 selectively co-ordinate Hg^{2+} over other transition metal ions. The fluorescent groups in L^1 and L^2 are able to transform the selective co-ordination observed in solution into a change in the emission behaviour of the free receptor. Metal ions Cu^{2+} and Hg^{2+} quench the emission intensity of L^1 at neutral and acid pH, whereas Hg^{2+} selectively enhances the emission fluorescence of L^2 at neutral and basic pH. A comparison between L^1, L^2 and L^3 containing fluorescent groups and L^4, L^5 and L^6 containing ferrocenyl groups shows that the nature of the signalling subunit plays an important role in the modulation of the selectivity and pH ranges of signalling.

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