Multi-channel receptors based on thiopyrylium functionalised with macrocyclic receptors for the recognition of transition metal cations and anions

T. Ábalos,[a,b,c] D. Jiménez,[b] M. Moragues,[a,b,c] S. Royo,[a,b,c] R. Martínez-Máñez,*[a,b,c] F. Sancenón,[a,b,c] J. Soto,[a,b] A. M. Costero,*[a,d] M. Parra[a,d] and S. Gil[a,d]

Received 14th October 2009, Accepted 4th January 2010
First published as an Advance Article on the web 5th February 2010
DOI: 10.1039/b921486k

We report herein the synthesis and characterization of a family of ligands containing different cation binding sites covalently connected to a thiopyrylium signalling reporter. The receptors **L**^{1}–**L**^{6} are able to signal the presence of certain metal cations *via* three different channels; *i.e.* electrochemically, fluorogenically and chromogenically. An acetonitrile solution of **L**^{1}–**L**^{6} shows a bright blue colour due to a charge-transfer band in the 575–585 nm region. The colour variation in acetonitrile of **L**^{1}–**L**^{6} in the presence of the metal cations Ag^+, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} has been studied. A selective hypsochromic shift of the blue band was found for the systems **L**^{4}-Pb^{2+} and **L**^{5}-Hg^{2+}. Additionally, **L**^{1}–**L**^{6} are poorly fluorescent but coordination with certain metal cations induces an enhancement of the fluorescence at ca 500 nm. For instance, the presence of Cu^{2+} and Fe^{3+} induced a remarkable 42-fold and 45-fold enhancement in the emission intensity of **L**^{1} centred at 500 nm, respectively. Also remarkable was the 18-fold enhancement observed for **L**^{4} and **L**^{5} in the presence of Fe^{3+} and Cu^{2+}, respectively. The electrochemical behaviour of receptors **L**^{1}–**L**^{6} was studied in acetonitrile using platinum as a working electrode and $[Bu_4N][BF_4]$ as a supporting electrolyte. This family of receptors showed a one-electron reversible redox process at *ca.* -0.46 V *versus* sce attributed to the reduction of the thiopyrylium group. A moderate anodic shift in the presence of certain metal cations was observed. The effect in the UV-visible spectra of acetonitrile solutions of receptor **L**^{1}–**L**^{6} in the presence of anions was also studied. A remarkable bleaching was found in the presence of cyanide.

Introduction

One appealing research area within the field of supramolecular chemistry is the development of chemical sensors[1] that are generally composed of two subunits; namely the binding site and the signalling subunit.[2] The binding site carries out selective coordination with a certain target guest and is usually designed bearing in mind coordination and supramolecular chemistry principles in order to achieve a high degree of complementarity. The coordination event modulates the spectroscopic properties of the signalling unit, therefore transducing host–guest recognition into an easily measurable signal. Three main systems have been extensively employed as reporter units: fluorescent groups,[3] dyes,[4] and redox-active moieties[5] that transform the recognition event through changes in fluorescence emission, colour, and redox-potential shifts, respectively.

These two basic components, *i.e.* signalling and coordination subunits, could be spatially preorganised in different styles leading to several basic protocols for the development of chemosensors. The most commonly used is the so-called 'binding site-signalling subunit,[2,3] in which both subunits are connected through covalent bonds. A closely related approach relies on the formation of an ensemble between the binding site and the signalling subunit that is characterized by the absence of any covalent link between the two units.[6] In this case, the coordination platform incorporates an external indicator, and the overall signalling functions as a colorimetric displacement assay. Finally, the so-called 'chemodosimeter' approach made use of specific chemical reactions induced by the target species coupled with changes in certain physical properties.[7]

The coupling of these three main approaches with the three types of signalling subunits (fluorescence groups, organic dyes, and redox-active groups) has lead in recent years to a myriad of selective receptors for a number of chemical species including anions, cations and neutral guests. Additionally, the versatility of these protocols has resulted in the development of differential receptors that respond rather unspecifically, yet differently, to a group of similar guests.[8]

However, and despite the development of individual fluorogenic, chromogenic, and electrochemical molecular sensors, there are few examples of receptors capable of displaying two or more output signals upon guest binding. Moreover, in the past decade some groups have become increasingly interested in including more than one chemically addressable group in chemosensors.[9,10] These have been used as dual-responsive dyes, and also in the design

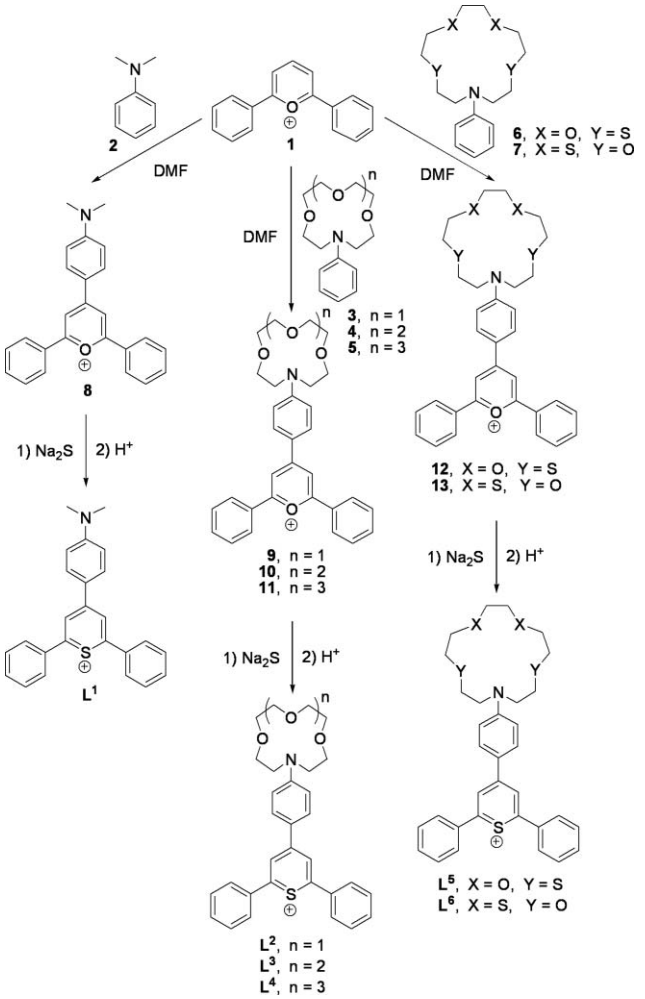
[a]*Instituto de Reconocimiento Molecular y Desarrollo Tecnológico, Centro Mixto Universidad Politécnica de Valencia-Universidad de Valencia, Valencia, Spain*
[b]*Departamento de Química, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022, Valencia, Spain. E-mail: rmaez@qim.upv.es*
[c]*CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN)*
[d]*Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad de Valencia, 46100, Burjassot, Valencia, Spain. E-mail: ana.costero@uv.es*

of molecular logic gates, ion-pair signalling, and cooperative recognition.

In relation to chemosensing, an easy mode for preparing multi-channel receptors is the functionalisation of certain binding sites with two different signalling subunits. Recent examples of this class of poly-functionalised ligands include the works of Delavaux-Nicot,[11] Beer,[12] Shimidzu and Lehn,[13] Martínez-Máñez,[14] Molina,[15-17] and Ghosh.[18]

The second class of multi-channel chemosensors are those that are functionalised with only one subunit capable of displaying two or more observable events upon addition of certain guests. Although examples showing both fluorescence and colour changes are not uncommon in intrinsic chemosensors,[19,20,21] paradigms displaying fluorescence or colour modulations and electrochemical responses are rare,[22] while chemosensors exhibiting three or more signalling channels are unusual.[23]

Because of our experience in the design of molecular probes[24] for various analytes and our background in functionalised chromophores we became interested in developing new multi-channel chemosensors able to detect the presence of metal cations *via* chromogenic, fluorogenic, and electrochemical signals. In this context we report herein the synthesis, characterisation, binding behaviour, and signalling properties of a new family of chemosensors containing different crown ether cation binding sites anchored to a 4-aminophenyl-2,6-diphenylthiopyrylium scaffolding. The 4-aminophenyl-2,6-diphenylthiopyrylium group is simultaneously a redox-active group, showing reduction processes at moderately modest potentials, and a chromo-fluorogenic signalling reporter. Additionally, the thiopyrylium moiety has been barely used as a signalling subunit in the development of chemical sensors–except for a recent example that used the pyrylium-to-thiopyrylium transformation for the development of a probe for sulfide anion detection in aqueous solution.[25] We have recently published a preliminary communication of part of this work.[26]



Scheme 1 Synthetic procedure and chemical structures of receptors $\mathbf{L^1}$–$\mathbf{L^6}$.

Results and discussion

Synthesis and characterization

Receptors $\mathbf{L^2}$–$\mathbf{L^6}$ contain macrocyclic binding sites (of different sizes and also containing different heteroatoms such as nitrogen, oxygen and sulfur) and a 4-aminophenyl-2,6-diphenylthiopyrylium salt as a signalling reporter (see Scheme 1). Receptor $\mathbf{L^1}$, containing an *N*,*N*-dimethylamino moiety, was selected as the model compound. $\mathbf{L^1}$ was prepared following literature procedures.[27] For the preparation of the ligands, firstly 2,6-dipheylpyrylium perchlorate (**1**) was synthesized[28] and the Richman-Atkins procedure was used to synthesise the phenyl-functionalised macrocyclic subunits **3-7**. The experimental details of the synthesis of these crowns and their spectroscopic characterization were published elsewhere.[22,29] Electrophilic aromatic substitution reaction between *N*,*N*-dimethylaniline (**2**) or the corresponding *N*-phenyl macrocycle (**3-7**) and 2,6-diphenylpyrylium perchlorate in dry DMF resulted in formation of the corresponding pyrylium derivatives **8-13**. Finally, multi-channel receptors $\mathbf{L^1}$–$\mathbf{L^6}$ were prepared by reaction of the pyrylium salts with an aqueous solution of sodium sulfide and subsequent treatment with perchloric acid (see Scheme 1).

The ^{1}H-NMR spectra of receptors $\mathbf{L^2}$–$\mathbf{L^4}$ showed the methylene protons of the macrocycle located near nitrogen and oxygen atoms in the 3.4–3.8 range whereas for receptors $\mathbf{L^5}$ and $\mathbf{L^6}$ the macrocycle protons appear split into two clearly defined zones: (i) methylene protons adjacent to the sulfur atoms at δ 2.6 to 2.9 ppm; and (ii) methylene protons located near nitrogen or oxygen atoms found in the 3.5–3.8 ppm range. The aromatic part of the spectrum was very similar for all the receptors synthesised showing a typical singlet centred at *ca.* 8.45 ppm from the aromatic 2,4,6-trisubstituted thiopyrylium ring. Also the presence of two doublets centred at *ca.* 6.90 and 8.15 was indicative of the presence of one *p*-disubstituted benzene derivative. The appended monosubstituted benzene rings show two broad multiplets centred at *ca.* 7.60 and 7.85 ppm. The ^{13}C-NMR showed the same well defined zones (see experimental section).

This family of receptors contains an extended π-conjugated system involving one donor anilino nitrogen atom and the acceptor thiopyrylium ring. The lowest-energy absorption bands for compounds $\mathbf{L^1}$–$\mathbf{L^6}$ are broad, structureless, and centred at *ca.* 580 nm in acetonitrile. This charge transfer band is responsible for the deep blue colour of the solutions.[30] $\mathbf{L^2}$–$\mathbf{L^6}$ are functionalised with macrocyclic subunits of different sizes and containing different types of heteroatoms that could coordinate with transition metal

Table 1 Abpsortion λ_{max} (nm) for receptors $\mathbf{L^1}$–$\mathbf{L^6}$ ($C = 1.0 \times 10^{-5}$ mol dm^{-3}) and their variation upon addition of metal cations in acetonitrile solutions

	λ_{max}	Cu^{2+}	Fe^{3+}	Hg^{2+}	Pb^{2+}
$\mathbf{L^1}$	585	560↓[a]	555↓[a]	585	585
$\mathbf{L^2}$	584	574↓[a]	554↓[a]	584↓[a]	584
$\mathbf{L^3}$	575	575	575↓[a]	575	575
$\mathbf{L^4}$	580	580	580↓[a]	580	560↓[a]/400↑[b]
$\mathbf{L^5}$	575	575↓[a]	555↓[a]	535↓[a]/405↑[b]	575
$\mathbf{L^6}$	582	560↓[a]	500↓[a]	550↓[a]	582

[a] The downward pointing arrows indicate a significant hypochromic change in the visible band with respect to that of the free ligand. [b] The upward pointing arrows indicate the appearance of a new visible band.

Table 2 Logarithm of constant stability for the formation $[M(\mathbf{L}^n)]^{m+}$ and $[M(\mathbf{L}^n)_2]^{m+}$ in acetonitrile solutions

M^{n+}	(L:M^{n+})	Fe^{3+}	Cu^{2+}	Hg^{2+}	Pb^{2+}
$\mathbf{L^1}$	(1 : 1)	3.69 ± 0.07	3.57 ± 0.03	—	—
$\mathbf{L^2}$	(1 : 1)	4.65 ± 0.02	3.1 ± 0.1	—	—
	(2 : 1)	9.94 ± 0.02	8.34 ± 0.05	—	—
$\mathbf{L^3}$	(1 : 1)	4.23 ± 0.01	—	—	—
$\mathbf{L^4}$	(1 : 1)	6.01 ± 0.08	—	—	4.01 ± 0.09
$\mathbf{L^5}$	(1 : 1)	—	—	6.98 ± 0.09	—
$\mathbf{L^6}$	(1 : 1)	4.8 ± 0.1	4.59 ± 0.07	4.72± 0.04	—

cations. Additionally, the presence of a positive charge in this thiopyrylium ring also determines its electronic properties and reactivity (vide infra).[31]

Spectroscopic studies involving metal cations

The chromogenic behaviour of receptors $\mathbf{L^1}$–$\mathbf{L^6}$ in the presence of the metal cations Ag^+, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} was studied in acetonitrile (see Table 1). Additionally, the logarithm of the stability constants for the formation of the corresponding complexes is summarised in Table 2. Firstly coordination studies with receptor $\mathbf{L^1}$, which lacks a macrocyclic subunit, in the presence of these metal cations were carried out. Acetonitrile solutions of receptor $\mathbf{L^1}$ show a visible band centred at 585 nm. Addition of up to 10 equivalents of Ag^+, Cd^{2+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} induced negligible changes in its visible spectra, suggesting very weak or no interaction with these metal cations. In contrast, upon the addition of Cu^{2+} and Fe^{3+} a colour change in the solution of $\mathbf{L^1}$ from blue to magenta was observed (see Fig. 1). In more detail, the presence of 10 equivalents of Cu^{2+} induced a moderate hypsochromic shift of 30 nm in the visible band together with a small hypochromic effect. The presence of defined isosbestic points at 540 nm and at 390 nm suggested the formation of a single 1 : 1 receptor–cation complex. The addition of 10 equivalents of Fe^{3+} to solutions of $\mathbf{L^1}$ resulted in a similar behaviour to that found for Cu^{2+}; *i.e.* a hypsochromic shift of 45 nm and a hypochromic effect. Again the presence of isosbestic points indicated the formation of the $[Fe(\mathbf{L^1})]^{3+}$ complex. These hypsochromic shifts observed upon addition of Cu^{2+} and Fe^{3+} are consistent with a binding of the cations with the aniline group, so weakening its donor character.

From the studied *N*-crowned receptors, $\mathbf{L^2}$ contains the smaller macrocycle. $\mathbf{L^2}$ shows a visible band centred at 584 nm. Addition of Ag^+, Cd^{2+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} metal cations (10 equivalents)

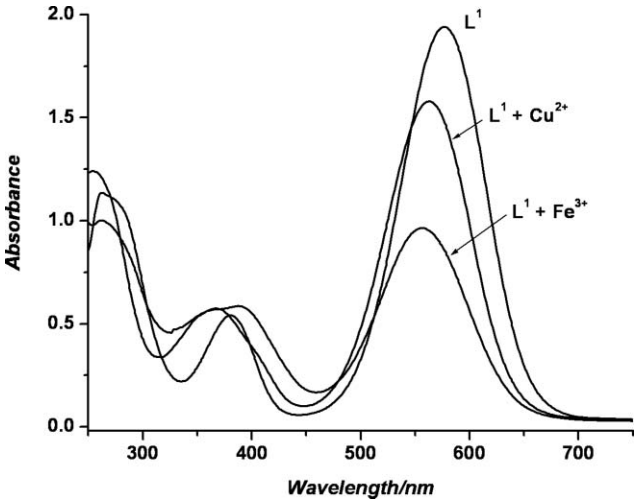


Fig. 1 UV-visible spectra of $\mathbf{L^1}$ in acetonitrile (1.0×10^{-5} mol dm^{-3}) and $\mathbf{L^1}$ in the presence of 10 equivalents of Fe^{3+} and Cu^{2+} cations.

to acetonitrile solutions of $\mathbf{L^2}$ induced negligible changes in the visible spectra. For Fe^{3+}, a strong hypochromic effect (10-fold intensity reduction) together with a moderate hypsochromic shift of 30 nm was found, whereas for Cu^{2+} a 1.5-fold decrease in intensity and a hypsochromic shift of 10 nm was measured. For $\mathbf{L^2}$, the absence of isosbestic points in the UV-visible titrations with Fe^{3+} and Cu^{2+} indicate the formation of 1 : 1 and 1 : 2 metal-to-ligand complexes. The formation of these species is most likely due to the large size of Fe^{3+} (64.5 pm) and Cu^{2+} (73.0 pm) that induced a poor fit on the macrocyclic cavity of $\mathbf{L^2}$; and resulted in the formation of 1 : 2 complexes in which the metal cation is most likely surrounded by two macrocycles in a sandwich-like structure.[32]

Receptor $\mathbf{L^3}$ is similar to $\mathbf{L^2}$ but contains one more oxygen atom and one more ethylene bridge. Acetonitrile solutions of receptor $\mathbf{L^3}$ show an absorption band at 575 nm. Of all the metal cations tested, only the addition of Fe^{3+} clearly induced changes, showing an intensity decrease of 1.7-fold without any remarkable shift in the wavelength.

Acetonitrile solutions of $\mathbf{L^4}$ showed an absorption band at 580 nm. $\mathbf{L^4}$ remains silent in the presence of the tested metal cations except for Fe^{3+} and especially Pb^{2+} (see Fig. 2). The response upon addition of Fe^{3+} induced a simple reduction in the extinction coefficient (3-fold). However, the most remarkable effect observed for receptor $\mathbf{L^4}$ was the selective response in the presence of the cation Pb^{2+}. Receptor $\mathbf{L^4}$ shows a large macrocyclic cavity ready to coordinate larger cations such as Pb^{2+} (119.0 pm of ionic radius). In fact, addition of equimolar quantities of Pb^{2+} induced the appearance of a new band centred at 400 nm; together with a 3-fold reduction of the intensity of the band at 580 nm. The existence of isosbestic points in the titration profiles indicates the formation of $[Pb(\mathbf{L^4})]^{2+}$ complex.

Interestingly, $\mathbf{L^5}$ also behaves very differently when compared with the other receptors. This different behaviour is governed by the presence in the macrocycle of two S atoms, near the aniline N atom, that strongly inhibit this site against complexation with non-thiophilic cations.[33d,33i] Therefore, $\mathbf{L^5}$ shows a remarkable selectivity for Hg^{2+} as can be seen in Fig. 3. In fact, it is well-known that Hg^{2+} coordination can be achieved by introducing

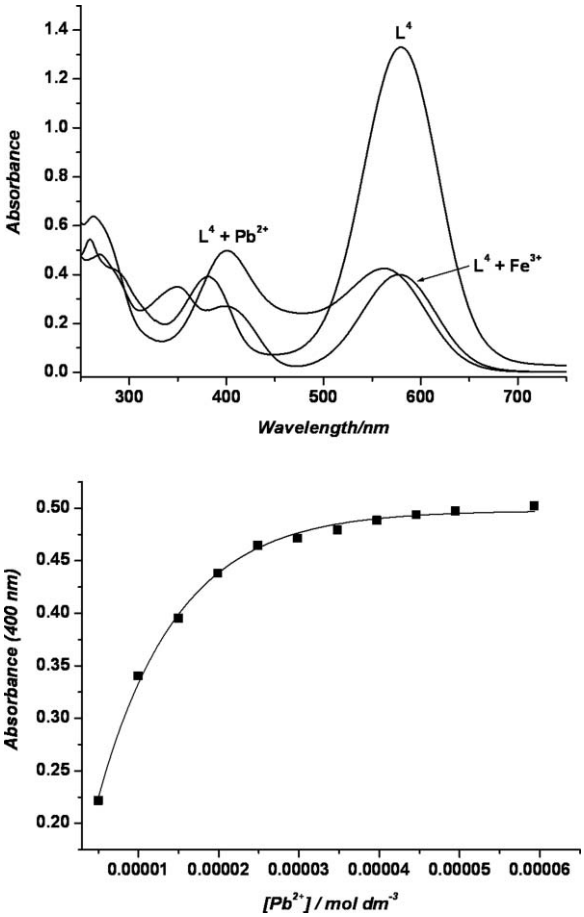


Fig. 2 (Top) UV-visible spectra of **L**^{4} in acetonitrile (2.0×10^{-5} mol dm^{-3}) and **L**^{4} in the presence of 10 equivalents of Fe^{3+} and Pb^{2+} cations. (Bottom) changes in the visible band centred at 400 nm for receptor **L**^{4} upon addition of increasing quantities of Pb^{2+} cation.

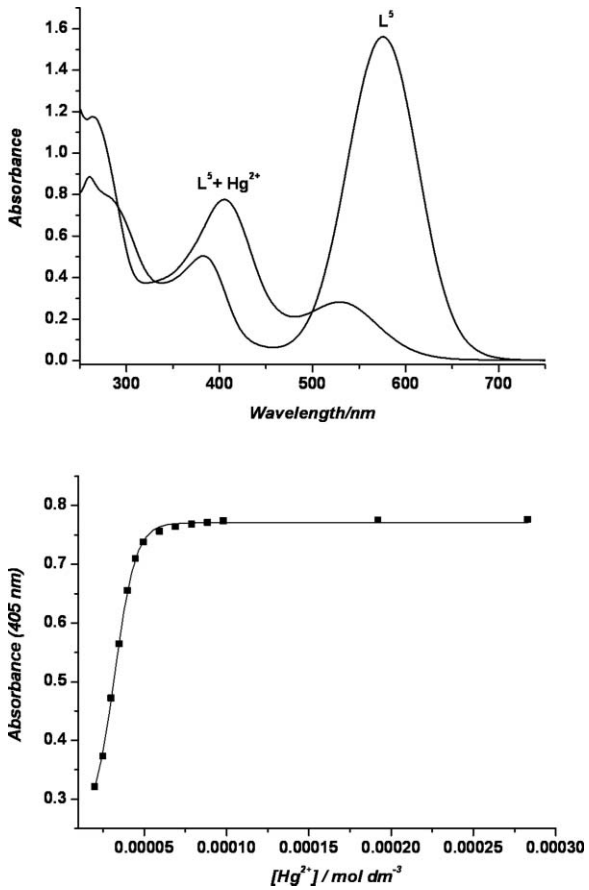


Fig. 3 (Top) UV-visible spectra of **L**^{5} in acetonitrile (1.0×10^{-5} mol dm^{-3}) and **L**^{5} in the presence of 10 equivalents of Hg^{2+} cation. (Bottom) changes in the visible band centred at 405 nm for receptor **L**^{5} upon addition of increasing quantities of Hg^{2+} cation.

sulfur atoms in the macrocyclic ring.[33] The addition of equimolar quantities of Hg^{2+} in acetonitrile solutions of **L**^{5} induced a 5-fold reduction in the extinction coefficient of the charge-transfer band centred at 575 nm together with a hypsochromic shift of 40 nm. At the same time, a new band centred at 405 nm grew in intensity. These changes in the visible zone of the spectrum were reflected in colour modulations; *i.e.* from bright blue for **L**^{5} to faint yellow upon the addition of Hg^{2+}.

The observed behaviour is consistent with a strong Hg^{2+} coordination with the macrocyclic subunit, and the engagement of the lone electron pair of the aniline N atom leading to a reduction of the push-pull character. The issue of selectivity was additionally confirmed by noting that the addition of other metal cations to acetonitrile solutions of **L**^{5} resulted in negligible changes in the position and in the intensity of the visible band.

On changing from **L**^{5} to **L**^{6}, in which the two sulfur atoms were located far from the nitrogen atom (separated by two oxygen atoms and two ethylene bridges), the selectivity towards Hg^{2+} cation was severely diminished. In fact, **L**^{6} shows a hypsochromic shift and a significant decrease of the intensity band at 582 nm in the presence of the metal cations Hg^{2+}, Cu^{2+} and Fe^{3+}.

In recent research we have prepared a family of *N*-crowned 4-(*p*-aminophenyl)-2,6-diphenylpyridines (MeNPys).[8e,8f] These compounds are similar to the **L**^{1}–**L**^{6} family but containing a pyridine ring instead of thiopyrylium. Although the coordination chemistry of the MeNPys derivatives is quite complex due to the presence of two coordination sites (*i.e.* the aniline and pyridine units) it is important to remark that MeNPy generally showed stability constants one order of magnitude greater than those found with the receptors **L**^{1}–**L**^{6}.[8e,8f] The lower stability constants observed for the thiopyrylium derivatives are most likely due to the positive charge located in the structure of the chromophoric system that leads to some degree of repulsion between the charged thiopyrylium ring and the metal cation.

Fluorescence studies involving metal cations

From the emission viewpoint the compounds 2,4,6-triphenylpyrylium (TPP) and 2,4,6-triphenylthiopyrylium (TPTP) are both emissive (quantum yields of 0.60 and 0.12, respectively in acetonitrile)[34] the former being extensively used as a photosensitizer in a wide range of photochemical reactions.[35] However, in contrast, acetonitrile solutions of receptors **L**^{1}–**L**^{6} are poorly fluorescent. This absence of any remarkable emission band may be ascribed to the presence of non-radiative deactivation pathways due to the existence of a nitrogen atom in the structure of the receptors directly attached to the TPTP chromophore.

In order to study the effect that coordination on the nitrogen has on the emission behaviour of the thiopyrylium derivatives,

the model compound **L**[1] was selected and its emission behaviour in acetonitrile studied in the presence of increasing quantities of protons (using acetonitrile solutions of perchloric acid). Whereas **L**[1] is not emissive, addition of protons resulted in the appearance of a broad intense emission band centred at 500 nm (λ_{ex} = 410 nm). This emission band reaches its highest intensity (305-fold enhancement) upon addition of 50 equivalents of protons, as can be seen in Fig. 4. This proton-induced switch-on response is most likely due to the inhibition of the non-radiative deactivation mechanism *via* nitrogen coordination that restores the emissive properties of the 2,4,6-triphenylthiopyrylium group.[36]

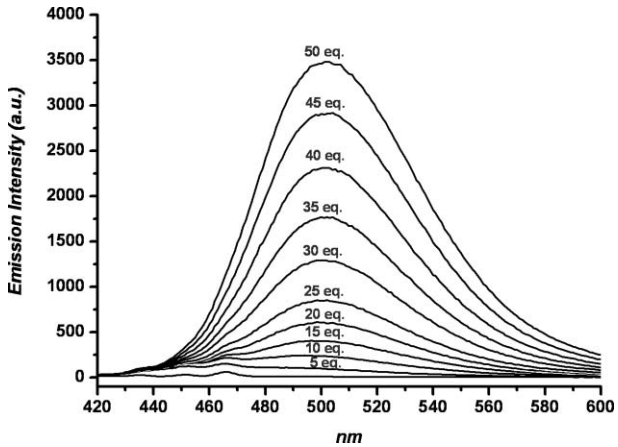


Fig. 4 Emission enhancement observed upon addition of 50 equivalents of protons to acetonitrile solutions of **L**[1] (1.0×10^{-5} mol dm^{-3}, λ_{exc} = 410 nm).

Intrigued by the high enhancement of the emission intensity observed in the presence of protons we carried out fluorescence studies with receptors **L**[1], **L**[4] and **L**[5] in the presence of target metal cations and using 410 nm as the excitation wavelength in all cases. The results are summarized in Table 3. The addition of 10 equivalents of Fe^{3+} to acetonitrile solutions of **L**[1] induced a remarkable 45-fold enhancement in the emission intensity centred at 500 nm. Nearly the same level of emission enhancement was observed in the presence of Cu^{2+} cation (41-fold, see Fig. 5). This large emission enhancement is remarkable bearing in mind that the usual behaviour with fluorogenic receptors in the presence of metal cations is an emission quenching upon complexation. Smaller enhancements in the emission intensity of 6- and 1.8-fold were measured for Hg^{2+} and Pb^{2+} cations respectively. It is also noteworthy that the enhancement observed with metal cations for **L**[1] is lower than that found in the presence of protons. This might be explained bearing in mind that the final observed

Table 3 Fluorescence emission intensity variation (as % of the receptor alone) obtained for **L**[1], **L**[4] and **L**[5] ($C = 1.0 \times 10^{-5}$ mol dm^{-3}) upon addition of 10 equivalents of metal cations in acetonitrile

	Cu^{2+}	Fe^{3+}	Hg^{2+}	Pb^{2+}
L[1][a]	4000↑	4400↑	500↑	80↑
L[4][a]	300↑	1660↑	300↑	11↑
L[5][a]	1660↑	220↑	520↑	5<

[a] Excitation wavelength 410 nm. [b] The upward pointing arrows indicate an increase in emission intensity.

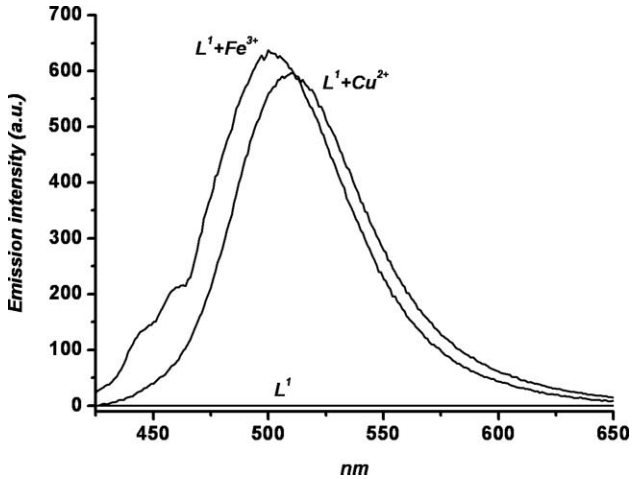


Fig. 5 Fluorescence enhancements observed upon addition of 10 equivalents of the corresponding metal cations to acetonitrile solutions of receptor **L**[1] (1.0×10^{-5} mol dm^{-3}, λ_{exc} = 410 nm).

behaviour for a certain cation is a sum of the contribution of the emission enhancement, due to the suppression of the non-radiative deactivation pathways upon metal coordination (and regeneration of the TPTP emission) and deactivation paths from the excited state due to the presence of a certain metal cation (for instance open-shell paramagnetic, or easily reducible metal cations).[37]

On changing to **L**[4], the highest enhancement in the emission intensity, upon excitation at 410 nm was observed upon addition of 10 equivalents of Fe^{3+} (17.6-fold). In general, the emission enhancements in this case are lesser than those observed with **L**[1] and the same cation. The addition of 10 equivalents of Hg^{2+} and Cu^{2+} induced a 4-fold enhancement in the emission intensity. Perhaps the most remarkable fact of the fluorescent behaviour of receptor **L**[4] was the absence of any significant response in the presence of Pb^{2+} (only a 1.1-fold enhancement) that greatly contrasts with the response obtained in UV-visible titration experiences (vide ante).[38] Whereas coordination of Pb^{2+} with the macrocycle in **L**[4] would induce the suppression of the non-radiative deactivation pathways thus leading to an increase in the emission intensity, the presence of a non-emissive decay pathway arising from a heavy atom effect would, in the opposite direction, deactivate the emission with the net effect of a very low fluorescence enhancement.

Upon excitation at 410 nm acetonitrile solutions of receptor **L**[5] showed a poor emission in the 430–600 nm range. However, the addition of increasing quantities of Hg^{2+} induced the development of an emission band centred at *ca.* 500 nm which reached a 6.2-fold enhancement upon addition of 10 equivalents of the cation.[39] The addition of the trivalent Fe^{3+} cation induced a 3.2-fold enhancement. However, the most remarkable emission change was obtained with Cu^{2+} that induced a 17.6-fold increase in the emission intensity (see Fig. 6). The fluorescent behaviour of **L**[5] in the presence of metal cations clearly contrasts with that observed in the UV-visible experiences (the most important shifts were obtained with Hg^{2+} cation). This fact may be related to a heavy atom effect that is more effective for Hg^{2+}. In the case of Cu^{2+} the strength of coordination with the macrocycle of **L**[5], when compared with Hg^{2+}, is less effective and leads to moderate changes in the visible band (only a slight hypochromic effect) whereas

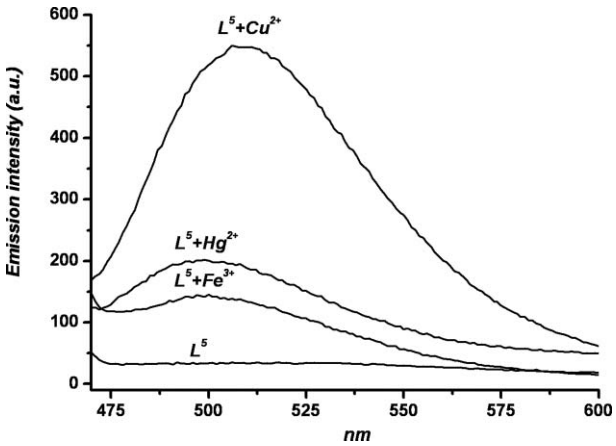


Fig. 6 Fluorescence enhancements observed upon addition of 10 equivalents of the corresponding metal cations to acetonitrile solutions of receptor **L**^{5} (1.0×10^{-5} mol dm^{-3}, $\lambda_{exc} = 410$ nm).

the emission of the 2,4,6-triphenylthiopyrylium moiety is restored more efficiently.

The selectivity trend observed in the fluorescence measurement for **L**^{5} was clearly different from that observed in the UV-titration experiences. Thus, **L**^{5} provides an example of sensing modulation by appropriate selection of the measurement technique; *i.e.* acetonitrile solutions of receptor **L**^{5} change colour selectively from blue to yellow in the presence of Hg^{2+} cation, whereas **L**^{5} shows in the presence of Cu^{2+} the greatest emission enhancement of the band centred at 500 nm.

The sensing features showed by these receptors, namely a remarkable enhancement of the emission intensity instead of quenching, led us to carry out prospective studies of the response in aqueous environments. From these studies it was observed that the addition of increasing amounts of water (up to 20%) to acetonitrile solutions of the $[Hg(\mathbf{L}^5)]^{3+}$ complex induced a reduction of only 2-fold in the emission. In contrast, addition of water to other metal complexes induced a severe decrease of the fluorescence intensity. The still high level of enhancement observed on adding Hg^{2+} to acetonitrile–water solutions of **L**^{5} opens the door for the use of this receptor as a selective fluorescent sensor for this highly toxic cation in aqueous environments.

Electrochemical studies involving metal cations

The electrochemical behaviour of thiopyrylium receptors **L**^{1}, **L**^{4} and **L**^{5} was studied in acetonitrile with platinum as the working electrode and $[Bu_4N][BF_4]$ as a supporting electrolyte. These receptors show a one-electron reversible reduction process in the –0.45, –0.49 V range *vs.* sce attributed to the reduction of the thiopyrylium ring (see Table 4).

Additionally, a detailed electrochemical study in the presence of metal cations was carried out with ligands **L**^{1}, **L**^{4} and **L**^{5} for which a remarkable chromo-fluorogenic behaviour was observed. In Table 5 the electrochemical responses regarding the difference between the reduction potential of the free ligand and the reduction potential in the presence of the corresponding metal cations is summarised. Only the presence of the metal cations Cu^{2+}, Fe^{3+}, Hg^{2+} and Pb^{2+} resulted in a significant electrochemical response, whereas the remaining cations gave no redox potential shifts ($\Delta E < 5$ mV).

Table 4 Electrochemical data for **L**^{1}, **L**^{4} and **L**^{5} complexes in acetonitrile solution (0.1 M $[Bu_4N][BF_4]$) at 298 K[a]

	Reduction $E_{1/2}$/mV[b]
L^1	–0.47
L^4	–0.45
L^5	–0.48

[a] Working electrode, platinum. [b] $E_{1/2} = (E_{pa} + E_{pc})/2$; E_{pa} and E_{pc} are peak anodic and peak cathodic potentials, respectively.

Table 5 Values of ΔE (mV) [a]for receptors **L**^{1}, **L**^{4} and **L**^{5} ($C = 1.0 \times 10^{-3}$ mol dm^{-3}) in the presence of metal cations

	$\Delta E(L^1)$[a]	$\Delta E(L^4)$[a]	$\Delta E(L^5)$[a]
Cu^{2+}	11	—	12
Fe^{3+}	18	25	28
Hg^{2+}	24	—	31
Pb^{2+}	—	24	—

[a] $\Delta E(L^n) = E(L^n + M^{n+}) - E(L^n)$ (ΔE in mV)

Electrochemical studies in the presence of certain metal cations show, in general, a moderate shift of the redox potential of the thiopyrylium derivatives with maximum anodic shifts of the redox wave of 31 mV for the **L**^{5}-Hg^{2+} system. This anodic shift is expected bearing in mind that the coordination of the ligand with the metal cations would result in highly positively charged species that should be prone to easier reduction. However, it is apparent that the transformation of the positively charged thiopyrylium scaffolding into the corresponding metal cations complexes does not result in a large decrease in the redox potential. This observation contrasts with other systems that we have recently reported where large redox shifts were observed in the presence of metal cations using similar coordination sites.[40]

Triple signalling

We have studied above the changes in colour, fluorescence emission, and redox potential for a family of thiopyrylium derivatives in the presence of certain metal cations in acetonitrile. An outcome of this study is that, for a given signalling channel, selectivity can be achieved *via* the use of different macrocyclic subunits. Thus for instance, the development of a new band at *ca.* 400 nm is observed selectively for Pb^{2+} and Hg^{2+} when using the receptors **L**^{4} and **L**^{5}, respectively. However, it is also noteworthy that for a certain ligand the response is somewhat different, depending on the transduction channel studied (electrochemical, chromogenic or fluorogenic). For instance, **L**^{4} shows a selective chromogenic response to Pb^{2+}, whereas it is the Fe^{3+} cation which gives a greater fluorescence enhancement and both cations induced a reduction wave shift greater than 20 mV. When using receptor **L**^{5}, the electrochemical response is of *ca.* 30 mV for Hg^{2+} and Fe^{3+}, whereas a very remarkable Cu^{2+} response is found in fluorescence and a selective response is observed in the chromogenic channel for Hg^{2+} (see Table 6).

In order to explain this effect, it has to be taken into account that the specific response observed in each channel strongly depends on the particularities of each coordination-transduction process.

Table 6 Different channel response of ligands **L**[1], **L**[4] and **L**[5] to metal cations[a]

	λ at 400 nm	*Emission enhancement > 1000%*	*ΔE > 20 mV*
L[1]	—	Cu^{2+}, Fe^{3+}	Hg^{2+}
L[4]	Pb^{2+}	Fe^{3+}	Fe^{3+}, Pb^{2+}
L[5]	Hg^{2+}	Cu^{2+}	Fe^{3+}, Hg^{2+}

[a] The ligand concentrations used for the UV-Vis, fluorescence and electrochemical experiments were 1×10^{-5}, 1×10^{-5} and 1×10^{-3} mol dm^{-3}, respectively.

Thus, for instance, the electrochemical response (changes in the redox wave of the redox-active groups) is usually governed by changes in the charge between the ligand and the complex; and by the existence of chemical (*i.e.* decomplexation) reactions before, or after, the electrochemical process. Chromogenic transduction (hypsochromic shift) will be expected when there is a strong enough interaction of a certain metal cation with the anilino nitrogen in the chromophore. Additionally, the strength in the coordination and the coordination mode of the metal cations with the different ligands can also modulate the final signal observed. Thus, it is expected that the interaction of a given cation with binding sites (such as the oxygen and sulfur atoms) in the macrocycle, but not directly with the nitrogen atom, may result in an electrochemical or flurogenic response, but not in changes in colour. Other variables such as the strength of the coordination bonding (more covalent or cation-dipole type), or the interaction with the photo-excited receptors with metal cations through energy or photo-electron transfer processes, can also influence the observed final response.

This differential response as a function of the channels selected has also been found in other multi-channel signalling receptors and we and other authors have suggested that this behaviour might open the possibility of using a unique receptor for different signalling applications and for the development of certain molecular logic gates.

Spectroscopic studies involving anions

The development of abiotic receptors for anions has been a subject of growing interest in recent years due to the crucial roles played by anions in biological and environmental processes.[41] In this section we were interested in studying the interaction of **L**[1]–**L**[6] with anions. For instance, it has been reported that the parent derivatives containing pyrylium rings suffer ring opening/closing processes in the presence of certain anionic species and this effect has been used in different signalling applications.[42]

The addition of 1 equivalent of Cl^-, Br^-, I^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, AcO^-, BzO^- and NCS^- to acetonitrile solutions of **L**[1] induced negligible changes in the UV-visible spectra or in the colour of the solutions. The most striking effect was observed upon the addition of 1 equivalent of cyanide anion because a complete bleaching of the colour of the solution was produced (see Fig. 7).[43] The same behaviour upon addition of anions was observed with the crown ether-functionalised **L**[2]–**L**[6] receptors, strongly suggesting that the presence of the macrocyclic subunits in **L**[2]–**L**[6] is not responsible for the observed selectivity. This, in turn, pointed to an interaction of cyanide anions with the 2,4,6-triphenylthiopyrylium moiety in a chemodosimeter fashion that is most likely related to a nucleophilic attack on the electron deficient thiopyrylium ring. In fact, similar behaviour was observed upon the addition of the anion OH^- (added as a tetrabutylammonium salt) with **L**[2]–**L**[6]; *i.e.* a complete bleaching.

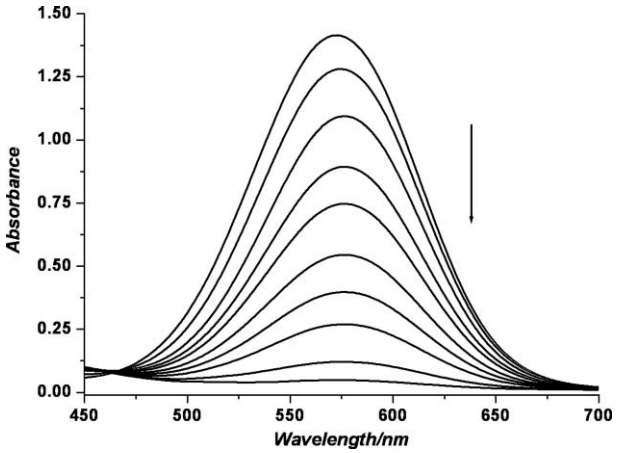


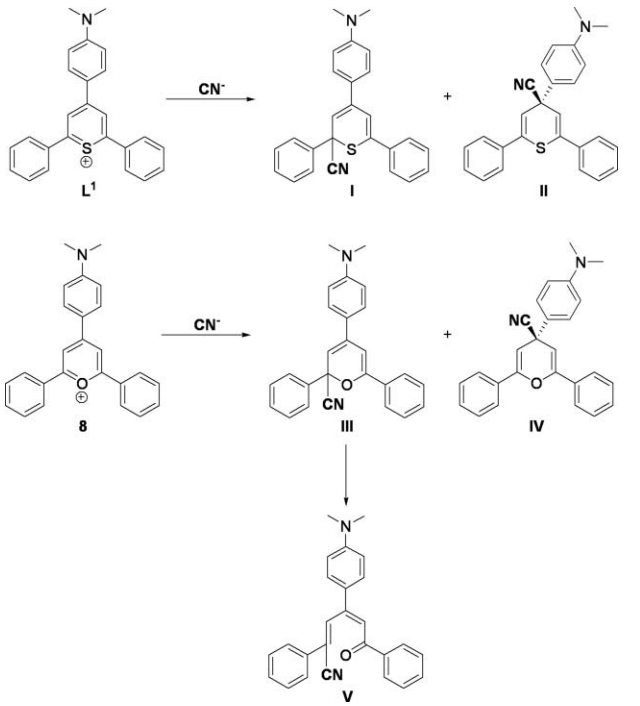
Fig. 7 Changes in the visible band of acetonitrile solutions of receptor **L**[1] (1.2×10^{-5} mol dm^{-3}) upon addition of increasing quantities of cyanide anion up to 1 equivalent.

Thiopyrylium, and the parent pyrylium heterocycles, contain in their structures one positively charged sulfur and oxygen atom respectively, that induce a certain electrophilic character in the carbons located in the heterocyclic rings.[28] In fact, quantum chemical calculations at semiempirical level[44] indicate that the charge density on atoms C2, C3, and C4 for 2,4,6-triphenylpyrylium are 0.233, –0.266 and 0.245, respectively. In the case of 2,4,6-triphenylthiopyrylium, similar calculations lead to values of –0.06, –0.191, and 0.206. These calculations suggest that the pyrylium and thiopyrylium rings are prone to suffer nucleophilic attack on C4 and C2 (see Scheme 2). These calculated charges, together with the fact that the C–O^+ and C–S^+ bonds in the ring are polarized by inductive effects, should account for the reactivity observed.

In order to confirm this possible attack, a detailed study was carried out with compound **L**[1] and cyanide. ^{1}H-NMR studies in acetonitrile-d_3 showed that two different compounds are clearly formed upon the addition of one equivalent of CN^-. The singlet at 8.63 ppm for **L**[1] turned into three new singlets at 5.96, 6.17, and 7.26, upon cyanide addition. The singlet at 6.17 ppm was assigned to the product obtained by cyanide attack on C4 (product **II**), whereas the other two signals corresponded to the product formed by cyanide addition on C2 (product **I**). From the area of the signals, a ratio of 75 : 25 for structures **I**·**II** was determined. Unfortunately, attempts to isolate the reaction products were unsuccessful and chromatographic techniques resulted in decomposition of the products.

These preliminary results pointed to the possible use of receptor **L**[1] for the colorimetric detection and quantification of cyanide anion. Unfortunately, it was also confirmed that the addition of small quantities of water (less than 5%) to acetonitrile solutions of receptor **1** inhibited bleaching in the presence of cyanide. We recently reported a more detailed study that included the signalling in cyanide with **L**[1] in water using micelles.[45]

Nearly the same chromogenic behaviour as that observed for thiopyrylium derivative **L**[1] was found for acetonitrile solutions of



Scheme 2 Proposed structures for the products of cyanide attack over thiopyrylium and pyrylium rings presented by receptors **L**[1] and **8**.

pyrylium salt **8** upon the addition of 1 equivalent of cyanide that induced the complete disappearance of the charge transfer band centred at 540 nm. ^{1}H-NMR studies in DMSO-d_6 (pyrylium salt **8** does not dissolve in acetonitrile-d_3) of **8** in the presence of cyanide resulted in a complex mixture of, at least, three compounds (**III**, **IV** and **V**). The major product was identified as coming from an attack of cyanide on the C4 (product **IV**) at the pyrylium moiety featuring a singlet at 5.14 ppm and the protons at the dimethylanilynium ring at 7.89 and 6.9 ppm. The mixture evolved over time producing a major product coming from the attack on C2 (product **III**) and the opening of the pyrylium ring (product **V**). In this final product, the dimethylanilynium protons are now at δ 6.26 and 6.71 (overlapped with the olephynic protons) and the phenyl protons are now deshielded.

Conclusions

A family of receptors based on functionalised thiopyrylium moieties have been synthesised and characterised and their interaction with metal cations studied *via* optical (colour and emission fluorescence) and electrochemical changes. The optical properties of the products reveal that the acceptor thiopyrylium group and the donor aniline moiety are strongly π-conjugated and produce intense CT bands at *ca.* 580 nm. The receptors show a rich chromogenic response to metal cations modulated by the nature of the coordination ring. A selective hypsochromic shift of the CT band was observed for the **L**[4]-Pb^{2+} and **L**[5]-Hg^{2+} systems. Receptors **L**[1]–**L**[6] are poorly fluorescent most likely because of the presence of non-radiative deactivation pathways due to the presence of a nitrogen atom directly linked to the chromophoric system. Moreover, coordination at the anilino moiety resulted in a very remarkable enhancement of the emission that is modulated by the nature of the metal cation and the coordination site. For instance, whereas **L**[1] is not emissive, protonation of the anilino group resulted in the appearance of a broad intense emission band centred at 500 nm (λ_{ex} = 410 nm). Additionally, the presence of Cu^{2+} and Fe^{3+} induced a remarkable 42-fold and 45-fold enhancement in the emission intensity band centred at 500 nm of receptor **L**[1]. Also remarkable was the 18-fold enhancement observed for **L**[4] and **L**[5] in the presence of Fe^{3+} and Cu^{2+}, respectively. This family of receptors showed a one-electron reversible redox process at *ca.* -0.46 V *versus* sce attributed to the reduction of the thiopyrylium group. A moderate anodic shift in the presence of certain metal cations was observed. Finally, the receptors **L**[1]–**L**[6] also show sensing features in the presence of cyanide, which is able to react with the electron-deficient pyrylium ring and results in a bleaching of the blue solution.

Experimental

General remarks

All commercially available reagents were used without further purification. Air/water-sensitive reactions were performed in flame-dried glassware under argon. Acetonitrile was dried with CaH_2 and distilled prior to use.

Physical measurements

Metal cations (Ag^+, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} as perchlorate or triflate salts) and anions (F^-, Cl^-, Br^-, I^-, NO_3^-, $H_2PO_4^-$, HSO_4^-, AcO^-, BzO^-, NCS^- and CN^- as tetrabutylammonium salts) were used to obtain acetonitrile solutions of concentration *ca.* 1.0×10^{-3} mol dm^{-3}. UV-visible studies were carried out with a Perkin Elmer Lambda 35 spectrometer. The concentrations of ligands used in the UV-visible measurements were *ca.* 5.0×10^{-5} mol dm^{-3} in acetonitrile. UV-visible spectra were recorded in the presence of equimolar quantities of the corresponding ligand and metal cation or anion. The fluorescence behaviour was studied with a FS900CDT Steady State T-Geometry Fluorimeter, Edinburgh Analytical Instruments. All solutions for photophysical studies were previously degassed. The concentrations of ligands were *ca.* 5.0×10^{-5} mol dm^{-3} in acetonitrile. Fluorescence emission spectra were recorded in the presence of equimolar quantities of ligand and the corresponding metal cation. Electrochemical data were carried out in dry acetonitrile solutions previously degassed, with a programmable function generator Tacussel IMT-1, connected to a Tacussel PJT 120-1 potentiostat. The concentration of ligands and metal ions were *ca.* 1.0×10^{-3} mol dm^{-3} in acetonitrile (the metal ions were perchlorate or triflate salts of Ag^+, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Pb^{2+} and Zn^{2+}). Electrochemical studies were carried out in the presence of equimolar quantities of ligand and the corresponding metal cation. The working electrode was platinum connected with a saturated calomel reference electrode separated from the test solution by a salt bridge containing the solvent and the supporting electrolyte (0.25 mol dm^{-3} [Bu_4N][BF_4]). The auxiliary electrode was a platinum wire. The ^{1}H and ^{13}C NMR spectra were recorded with a Varian Gemini spectrometer. Chemical shifts are reported in ppm downfield from TMS signal. Spectra taken in $CDCl_3$ were referenced to residual $CHCl_3$.

Synthetic procedures

The synthesis of macrocyclic subunits 10-phenyl-10-aza-1,4,7-trioxacyclododecane (**3**), 13-phenyl-13-aza-1,4,7,10-tetraoxacyclopentadecane (**4**), 16-phenyl-16-aza-1,4,7,10,13-pentaoxacycloheptadecane (**5**), 10-phenyl-10-aza-1,4-dioxa-7,13-dithiacyclopentadecane (**6**) and 4-phenyl-4-aza-1,7-dioxa-10,13-dithiacyclopentadecane (**7**) were previously published. The syntheses of pyrylium-based receptors (**8–13**) were also previously published.

General procedure for the synthesis of the thiopyrylium derivatives (L^1–L^6)

N,*N*-dimethylaniline (**2**, 2 mmol) or the corresponding *N*-phenyl macrocycle (**3–7**, 2 mmol) were reacted with 2,6-diphenylpyrylium perchlorate (**1**, 4 mmol) in dry DMF (20 mL) at 150° C for three hours. Pyrylium derivatives **8–13** (1 mmol, yield: 50%) were precipitated from the crude reaction as dark brown solids by addition of dimethyl ether (25 mL). These pyrylium derivatives (0.8 mmol) were then dissolved in acetone (50 mL), Na_2S (2 mL, 10% water solution) was added and the crude reaction was allowed to react for 20 min at room temperature. Finally, perchloric acid (2 mL, 20% water solution) was added and the crude reaction stirred for another 40 min at the same temperature. The final thiopyrylium derivatives were isolated as dark blue solids by vacuum filtration and successive washings with water and diethyl ether.

L^1: Yield: 50%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.16 (6H, s, N-(CH_3)$_2$), 6.89 (2H, d, C$_6H_4$), 7.60 (6H, m, C$_6H_5$), 7.88 (4H, m, C$_6H_5$), 8.19 (2H, d, C$_6H_4$), 8.49 (2H, s, C$_5H_2$S). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ = 40.5, 114.3, 122.2, 124.8, 127.7, 130.1, 132.6, 133.2, 134.5, 154.8, 156.6, 160.9. HRMS calc. for $C_{25}H_{22}NS$, 368.1473, found 368.1455.

L^2: Yield: 45%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.66 (8H, s, O–CH_2-O), 3.75 (4H, t, N–CH_2-O), 3.78 (4H, t, O–CH_2-O), 6.88 (2H, d, C$_6H_4$), 7.61 (6H, m, C$_6H_5$), 7.89 (4H, m, C$_6H_5$), 8.20 (2H, d, C$_6H_4$), 8.47 (2H, s, C$_5H_2$S). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ = 53.5, 70.0, 70.4, 71.3, 114.2, 122.2, 124.7, 127.9, 130.1, 132.4, 133.2, 134.6, 154.7, 156.6, 161.1. HRMS calc. for $C_{31}H_{32}NSO_3$, 498.2103, found 498.2095.

L^3: Yield: 48%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.62 (4H, s, O-(CH_2)$_2$-O), 3.67-3.78 (16H, m, O-(CH_2)$_2$-O, N-(CH_2)$_2$-O), 6.92 (2H, d, C$_6H_4$), 7.57 (6H, m, C$_6H_5$), 7.86 (4H, m, C$_6H_5$), 8.14 (2H, d, C$_6H_4$), 8.43 (2H, s, C$_5H_2$S). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ = 53.6, 68.2, 69.9, 70.4, 71.0, 114.5, 122.5, 125.1, 127.8, 130.2, 132.7, 133.2, 134.6, 154.7, 157.0, 161.3. HRMS calc. for $C_{33}H_{36}NSO_4$, 542.2365, found 542.2377.

L^4: Yield: 46%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 3.63-3.77 (24H, m, O-(CH_2)$_2$-O, N-(CH_2)$_2$-O), 6.95 (2H, d, C$_6H_4$), 7.56 (6H, m, C$_6H_5$), 7.87 (4H, m, C$_6H_5$), 8.14 (2H, d, C$_6H_4$), 8.39 (2H, s, C$_5H_2$S). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ = 51.9, 68.5, 70.6, 70.7, 114.3, 122.2, 124.8, 127.7, 130.1, 132.6, 133.2, 134.5, 154.9, 156.6, 160.9. HRMS calc. for $C_{35}H_{40}NSO_5$, 586.2627, found 586.2709.

L^5: Yield: 48%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 2.76 (4H, t, N-(CH_2)$_2$-S), 2.93 (4H, t, O-(CH_2)$_2$-S), 3.63 (4H, s, O-(CH_2)$_2$-O), 3.80 (8H, m, S-(CH_2)$_2$-N, O-(CH_2)$_2$-S), 6.92 (2H, d, C$_6H_4$), 7.57 (6H, m, C$_6H_5$), 7.86 (4H, m, C$_6H_5$), 8.14 (2H, d, C$_6H_4$), 8.43 (2H, s, C$_5H_2$S). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ = 30.1, 32.1, 52.7, 70.6, 73.6, 114.1, 122.5, 125.6, 127.9, 130.2, 132.8, 133.4, 134.6, 153.8, 157.5, 162.0. HRMS calc. for $C_{33}H_{36}NS_3O_2$, 574.1908, found 574.1867.

L^6: Yield: 40%, ^{1}H NMR (300 MHz, DMSO-D6): δ = 2.72 (4H, t, O-(CH_2)$_2$-S), 2.81 (4H, s, N-(CH_2)$_2$-S), 3.70 (4H, t, O-(CH_2)$_2$-O), 3.77 (4H, t, O-(CH_2)$_2$-S), 3.85 (4H, t, N-(CH_2)$_2$-S), 6.91 (2H, d, C$_6H_4$), 7.58 (6H, m, C$_6H_5$), 7.87 (4H, m, C$_6H_5$), 8.13 (2H, d, C$_6H_4$), 8.43 (2H, s, C$_5H_2$S). ^{13}C{^{1}H} NMR (75 MHz, CDCl3): δ = 31.93, 32.96, 51.73, 69.23, 72.16, 115.3, 123.5, 126.4, 128.3, 131.0, 131.6, 132.8, 133.7, 154.3, 158.6, 163.3. HRMS calc. for $C_{33}H_{36}NS_3O_2$, 574.1908, found 574.1987.

Acknowledgements

The authors wish to express their gratitude to the Spanish Government for financial support (projects CTQ2006-15456-C04-01, CTQ2006-15456-C04-02). T. A. is grateful to the Ministerio de Ciencia e Innovación for the fellowship awarded. The English revision of this paper was funded by the Universidad Politécnica de Valencia, Spain.

References

1 E. V. Anslyn, *J. Org. Chem.*, 2007, **72**, 687.
2 R. Martínez-Máñez and F. Sancenón, *Chem. Rev.*, 2003, **103**, 4419.
3 (*a*) R. Martínez-Máñez and F. Sancenón, *J. Fluoresc.*, 2005, **15**, 267; (*b*) T. Gunnlaugsson, H. D. P. Ali, M. Glynn, P. E. Kruger, G. M. Hussey, F. M. Pfeffer, C. M. G. dos Santos and J. Tierney, *J. Fluoresc.*, 2005, **15**, 287; (*c*) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, 1997, **97**, 1515; (*d*) S. K. Kim, D. H. Lee, J.–H. Hong and J. Yoon, *Acc. Chem. Res.*, 2009, **42**, 23.
4 (*a*) R. Martínez-Máñez and F. Sancenón, *Coord. Chem. Rev.*, 2006, **250**, 3081; (*b*) C. Suksai and T. Tuntulani, *Chem. Soc. Rev.*, 2003, **32**, 192; (*c*) V. Amendola, D. Esteban-Gómez, L. Fabbrizzi and M. Licchelli, *Acc. Chem. Res.*, 2006, **39**, 343.
5 See for instance: (*a*) P. D. Beer, *Chem. Commun.*, 1996, 689; (*b*) P. D. Beer, *Coord. Chem. Rev.*, 2000, **205**, 131; (*c*) P. D. Beer, J. Cadman, J. M. Lloris, R. Martínez-Máñez, J. Soto, T. Pardo and M. D. Marcos, *J. Chem. Soc., Dalton Trans.*, 2000, 1805; (*d*) J. M. Lloris, R. Martínez-Máñez, M. E. Padilla-Tosta, T. Pardo, J. Soto, P. D. Beer, J. Cadman and D. K. Smith, *J. Chem. Soc., Dalton Trans.*, 1999, 2359; (*e*) M. E. Padilla-Tosta, R. Martínez-Máñez, T. Pardo, J. Soto and M. J. López-Tendero, *Chem. Commun.*, 1997, 887.
6 S. L. Wiskur, H. Aït-Haddou, J. J. Lavigne and E. V. Anslyn, *Acc. Chem. Res.*, 2001, **34**, 963.
7 See for example: (*a*) V. Dujols, F. Ford and A. W. Czarnik, *J. Am. Chem. Soc.*, 1997, **119**, 7386; (*b*) O. Rusin, N. S. St Luce, R. A. Agbaria, J. O. Escobedo, S. Jiang, I. M. Warner, F. B. Dawan, K. Lian and R. M. Strongin, *J. Am. Chem. Soc.*, 2004, **126**, 438; (*c*) M. Tomasulo, S. Sortino, A. J. P. White and F. M. Raymo, *J. Org. Chem.*, 2006, **71**, 744; (*d*) Y.–K. Yang and J. Tae, *Org. Lett.*, 2006, **8**, 5721; (*e*) S. Y. Kim and J. I. Hong, *Org. Lett.*, 2007, **9**, 3109; (*f*) M. Comes, M. D. Marcos, R. Martínez-Máñez, M. C. Millán, J. V. Ros-Lis, F. Sancenón, J. Soto and L. A. Villaescusa, *Chem.–Eur. J.*, 2006, **12**, 2162; (*g*) S. Basurto, T. Torroba, M. Comes, R. Martínez-Máñez, F. Sancenón, L. A. Villaescusa and P. Amorós, *Org. Lett.*, 2005, **7**, 5469; (*h*) A. B. Descalzo, D. Jiménez, J. El Haskouri, D. Beltrán, P. Amorós, M. D. Marcos, R. Martínez-Máñez and J. Soto, *Chem. Commun.*, 2002, 562.
8 (*a*) S. L. Wiskur, P. N. Floriano, E. V. Anslyn and J. T. McDevitt, *Angew. Chem., Int. Ed.*, 2003, **42**, 2070; (*b*) J. J. Lavigne and E. V. Anslyn, *Angew. Chem., Int. Ed.*, 2001, **40**, 3118; (*c*) K. J. Albert, N. S. Lewis, C. L. Schauer, G. A. Sotzing, S. E. Stitzel, T. P. Vaid and D. R. Walt, *Chem. Rev.*, 2000, **100**, 2595; (*d*) R. Martínez-Máñez, J. Soto, E. García-Breijo, L. Gil, J. Ibáñez and E. Llobet, *Sens. Actuators, B*, 2005, **104**, 302; (*e*) B. García-Acosta, X. Albiach-Martí, E. García, L. Gil, R. Martínez-Máñez, K. Rurack, F. Sancenón and J. Soto, *Chem.*

Commun., 2004, 773; (*f*) B. García-Acosta, R. Martínez-Máñez, F. Sancenón, J. Soto, K. Rurak, M. Spieles, E. García-Breijo and L. Gil, *Inorg. Chem.*, 2007, **46**, 3123.
9 (*a*) A. P. de Silva, D. B. Fox, T. S. Moody and S. M. Weir, *Trends Biotechnol.*, 2001, **19**, 29; (*b*) A. P. de Silva and N. D. McClenaghan, *Chem.–Eur. J.*, 2004, **10**, 574; (*c*) A. P. de Silva, Y. Leydet, C. Lincheneau and N. D. McClenaghan, *J. Phys.: Condens. Matter*, 2006, **18**, S1847; (*d*) K. Rurack, A. Koval'chuck, J. L. Bricks and J. L. Slominskii, *J. Am. Chem. Soc.*, 2001, **123**, 6205; (*e*) A. P. de Silva and N. D. McClenaghan, *Chem. Eur. J.*, 2002, **8**, 4935.
10 (*a*) A. P. de Silva, H. Q. N. Gunaratne and C. P. McCoy, *J. Am. Chem. Soc.*, 1997, **119**, 7891; (*b*) H.–F. Ji, R. Dabestani and G. M. Brown, *J. Am. Chem. Soc.*, 2000, **122**, 9306; (*c*) S. A. de Silva, B. Amorelli, D. C. Isidor, K. C. Loo, K. E. Crooker and Y. E. Pena, *Chem. Commun.*, 2002, 1360; (*d*) A. P. de Silva, G. D. McClean and S. Pagliari, *Chem. Commun.*, 2003, 2010; (*e*) B. Bag and P. K. Bharadwaj, *Chem. Commun.*, 2005, 513; (*f*) A. M. Costero, J. Sanchis, S. Gil, V. Sanz and J. A. G. Williams, *J. Mater. Chem.*, 2005, **15**, 2848; (*g*) K. Kubo and A. Mori, *J. Mater. Chem.*, 2005, **15**, 2902; (*h*) M. D. Lankshear, A. R. Cowley and P. D. Beer, *Chem. Commun.*, 2006, 612; (*i*) D. C. Magri, G. J. Brown, G. D. McClean and A. P. de Silva, *J. Am. Chem. Soc.*, 2006, **128**, 4950; (*j*) M. de Sousa, B. de Castro, S. Abad, M. A. Miranda and U. Pischel, *Chem. Commun.*, 2006, 2051.
11 (*a*) J. Maynadie, B. Delavaux-Nicot, S. Fery-Forgues, D. Lavabre and R. Mathieu, *Inorg. Chem.*, 2002, **41**, 5002; (*b*) B. Delavaux- Nicot and S. Fery-Forgues, *Eur. J. Inorg. Chem.*, 1999, 1821.
12 (*a*) P. D. Beer, A. R. Graydon and L. R. Sutton, *Polyhedron*, 1996, **15**, 2457; (*b*) P. D. Beer and F. J. Szemes, *J. Chem. Soc., Chem. Commun.*, 1995, 2245; (*c*) P. D. Beer, A. R. Graydon, A. O. M. Johnson and D. K. Smith, *Inorg. Chem.*, 1997, **36**, 2112.
13 (*a*) T. Saika, T. Iyoda, K. Honda and T. Shimidzu, *J. Chem. Soc., Perkin Trans. 2*, 1993, 1181; (*b*) T. Iyoda, T. Saika, K. Honda and T. Shimidzu, *Tetrahedron Lett.*, 1989, **30**, 5429; (*c*) T. Shimidzu, T. Iyoda and K. Honda, *Pure Appl. Chem.*, 1988, **60**, 1025; (*d*) F. P. Funeriu, J. M. Lehn, K. M. Fromm and D. Fenske, *Chem.–Eur. J.*, 2000, **6**, 2103; (*e*) J. M. Lehn, *Chem.–Eur. J.*, 2000, **6**, 2097.
14 F. Sancenón, A. Benito, F. J. Hernández, J. M. Lloris, R. Martínez-Máñez, T. Pardo and J. Soto, *Eur. J. Inorg. Chem.*, 2002, 866.
15 (*a*) F. Otón, A. Tárraga, M. D. Velasco, A. Espinosa and P. Molina, *Chem. Commun.*, 2004, 1658; (*b*) F. Otón, A. Tárraga, A. Espinosa, M. D. Velasco and P. Molina, *J. Org. Chem.*, 2006, **71**, 4590.
16 F. Otón, A. Espinosa, A. Tárraga, C. Ramírez de Arellano and P. Molina, *Chem.–Eur. J.*, 2007, **13**, 5742.
17 F. Zapata, A. Caballero, A. Espinosa, A. Tárraga and P. Molina, *Org. Lett.*, 2008, **10**, 41.
18 T. Ghosh, B. G. Maiya and M. W. Wong, *J. Phys. Chem. A*, 2004, **108**, 11249.
19 M. Boiocchi, L. Fabbrizzi, M. Licchelli, D. Sacchi, M. Vázquez and C. Zampa, *Chem. Commun.*, 2003, 1812.
20 A. P. de Silva, H. Q. N. Gunaratne and M. Lynch, *J. Chem. Soc., Perkin Trans. 2*, 1995, 685.
21 (*a*) M. Yuan, Y. Li, J. Li, C. Li, X. Liu, J. Lv, J. Xu, H. Li, S. Wang and D. Zhu, *Org. Lett.*, 2007, **9**, 2313; (*b*) M. Zhu, M. Yuan, X. Liu, J. Xu, J. Lv, C. Huang, H. Liu, Y. Li, S. Wang and D. Zhu, *Org. Lett.*, 2008, **10**, 1481.
22 (*a*) D. Jiménez, R. Martínez-Máñez, F. Sancenón and J. Soto, *Tetrahedron Lett.*, 2004, **45**, 1257; (*b*) D. Jiménez, R. Martínez-Máñez, F. Sancenón, J. V. Ros-Lis, J. Soto, A. Benito and E. García-Breijo, *Eur. J. Inorg. Chem.*, 2005, 2393.
23 M. Schmittel and H.–W. Lin, *Angew. Chem., Int. Ed.*, 2007, **46**, 893.
24 See for instance: (*a*) E. Climent, P. Calero, M. D. Marcos, R. Martínez-Máñez, F. Sancenón and J. Soto, *Chem.–Eur. J.*, 2009, **15**, 1816; (*b*) M. Comes, M. D. Marcos, R. Martínez-Máñez, F. Sancenón, L. A. Villaescusa, A. Graefe and G. J. Mohr, *J. Mater. Chem.*, 2008, **18**, 5815; (*c*) E. Climent, R. Casasús, M. D. Marcos, R. Martínez-Máñez, F. Sancenón and J. Soto, *Chem. Commun.*, 2008, 6531; (*d*) J. V. Ros-Lis, R. Martínez-Máñez, F. Sancenón, J. Soto, M. Spieles and K. Rurack, *Chem.–Eur. J.*, 2008, **14**, 10101; (*e*) A. Costero, S. Gil, M. Parra, P. M. E. Mancini, R. Martínez-Máñez, F. Sancenón and S. Royo, *Chem. Commun.*, 2008, 6002.
25 D. Jiménez, R. Martínez-Máñez, F. Sancenón, J. V. Ros-Lis, A. Benito and J. Soto, *J. Am. Chem. Soc.*, 2003, **125**, 9000.
26 T. Ábalos, D. Jiménez, R. Martínez-Máñez, J. V. Ros-Lis, S. Royo, F. Sancenón, J. Soto, A. M. Costero, S. Gil and M. Parra, *Tetrahedron Lett.*, 2009, **50**, 3885.
27 R. Wizinger and P. Ulrich, *Helv. Chim. Acta*, 1956, **39**, 207.
28 D. Markovitsi, C. Jallabert, H. Strzelecka and M. Veber, *J. Chem. Soc., Faraday Trans.*, 1990, **86**, 2819.
29 (*a*) K. E. Krakowiak, J. S. Bradshaw and D. J. Zamecka-Krakowiak, *Chem. Rev.*, 1989, **89**, 929; (*b*) J. P. Dix and F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 857.
30 (*a*) B. Valeur and I. Leray, *Coord. Chem. Rev.*, 2000, **205**, 3; (*b*) K. Rurack, *Spectrochim. Acta, Part A*, 2001, **57**, 2161; (*c*) B. Unger, K. Rurack, R. Müller, H. Jancke and U. Resch-Genger, *J. Mater. Chem.*, 2005, **15**, 3069.
31 (*a*) A. T. Balaban and W. Silhau, *Tetrahedron*, 1970, **26**, 743; (*b*) C. Uncuta and A. T. Balaban, *J. Chem. Res.*, 2001, 170.
32 (*a*) R. M. Izatt, R. E. Terry, L. D. Hansen, A. G. Avondet, J. S. Bradshaw, N. K. Dalley, T. E. Jensen, J. J. Christensen and B. L. Haymore, *Inorg. Chim. Acta*, 1978, **30**, 1; (*b*) J. Massaux and J. F. Desreux, *J. Am. Chem. Soc.*, 1982, **104**, 2967.
33 For optical receptors for Hg^{2+} recognition functionalised with sulfur-containing systems see for example: (*a*) S. Yoon, E. W. Miller, Q. He, P. H. Do and C. J. Chang, *Angew. Chem., Int. Ed.*, 2007, **46**, 6658; (*b*) K. Rurack, U. Resch-Genger, J. L. Bricks and M. Spieles, *Chem. Commun.*, 2000, 2103; (*c*) P. Pallavicini, Y. A. Diaz-Fernandez, F. Foti, C. Mangano and S. Patroni, *Chem.–Eur. J.*, 2007, **13**, 178; (*d*) A. B. Descalzo, R. Martínez-Máñez, R. Radeglia, K. Rurack and J. Soto, *J. Am. Chem. Soc.*, 2003, **125**, 3418; (*e*) S. Yoon, A. E. Albers, A. P. Wong and C. J. Chang, *J. Am. Chem. Soc.*, 2005, **127**, 16030; (*f*) H. G. Lee, J.–E. Lee and K. S. Choi, *Inorg. Chem. Commun.*, 2006, **9**, 582; (*g*) S. H. Kim, K. C. Song, S. Ahn, Y. S. Kang and S.–K. Chang, *Tetrahedron Lett.*, 2006, **47**, 497; (*h*) J. V. Ros-Lis, M. D. Marcos, R. Martínez-Máñez, K. Rurack and J. Soto, *Angew. Chem., Int. Ed.*, 2005, **44**, 4405; (*i*) J. V. Ros-Lis, R. Martínez-Máñez, K. Rurack, F. Sancenón, J. Soto and M. Spieles, *Inorg. Chem.*, 2004, **43**, 5183; (*j*) M. Comes, E. Aznar, M. Moragues, M. D. Marcos, R. Martínez-Máñez, F. Sancenón, J. Soto, L. A. Villaescusa, L. Gil and P. Amorós, *Chem.–Eur. J.*, 2009, **15**, 9024.
34 R. Akaba, M. Kamata, A. Koike, K. Mogi, Y. Kuriyama and H. Sakuragi, *J. Phys. Org. Chem.*, 1997, **10**, 861.
35 M. A. Miranda and H. García, *Chem. Rev.*, 1994, **94**, 1063.
36 S. Parret, F. Morlet-Savary, J. P. Fouassier, K. Inomata, T. Matsumoto and F. Heisel, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 2791.
37 L. Fabbrizzi, M. Licchelli, P. Pallavicini, L. Parodi, A. Taglietti, in "*Transition metals in Supramolecular Chemistry*", Ed. J. P. Sauvage, 1999, p. 93-134, John Wiley & Sons Ltd.
38 For recent fluorescent Pb^{2+} sensing systems working in water see:(*a*) L. Marbella, B. Serli-Mitasev and P. Basu, *Angew. Chem., Int. Ed.*, 2009, **48**, 3996; (*b*) E. Roussakis, S. A. Pergantis and H. E. Katerinopoulos, *Chem. Commun.*, 2008, 6221.
39 For recent fluorescent Hg^{2+} sensing systems working in water see:(*a*) W. Shi and H. Ma, *Chem. Commun.*, 2008, 1856; (*b*) X.–Q. Zhan, Z.–H. Qian, H. Zheng, B.–Y. Su, Z. Lan and J.–G. Xu, *Chem. Commun.*, 2008, 1859; (*c*) M.–L. Ho, K.–Y. Chen, L.–C. Wu, J.–Y. Shen, G.–H. Lee, M.–J. Ko, C.–C. Wang, J.–F. Lee and P.–T. Chou, *Chem. Commun.*, 2008, 2438; (*d*) L.–J. Ma, Y. Li, J. Sun, C. Tian and Y. Wu, *Chem. Commun.*, 2008, 6345; (*e*) M. Tian and H. Ihmels, *Chem. Commun.*, 2009, 3175; (*f*) W. Jiang and W. Wang, *Chem. Commun.*, 2009, 3913; (*g*) B. Tang, B. Ding, K. Xu and L. Tong, *Chem.–Eur. J.*, 2009, **15**, 3147; (*h*) F. Song, S. Watanabe, P. E. Floreancig and K. Koide, *J. Am. Chem. Soc.*, 2008, **130**, 16460; (*i*) J. Huang, Y. Xu and X. Qian, *J. Org. Chem.*, 2009, **74**, 2167; (*j*) X. Chen, S.–W. Nam, M. J. Jou, Y. Kim, S.–J. Kim, S. Park and J. Yoon, *Org. Lett.*, 2008, **10**, 5235.
40 R. Martínez-Máñez, J. Soto, J. M. Lloris and T. Pardo, *Trends Inorg. Chem.*, 1998, **5**, 183.
41 (*a*) F. P. Schmidtchen and M. Berger,M., *Chem. Rev.*, 1997, **97**, 1609; (*b*) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; (*c*) See *Coord. Chem. Rev.*, 2006, **250**, special issue on anion receptors..
42 (*a*) M. Comes, M. D. Marcos, R. Martínez-Máñez, F. Sancenón, J. Soto, L. A. Villaescusa, P. Amorós and D. Beltran, *Adv. Mater.*, 2004, **16**, 1783; (*b*) B. García-Acosta, F. García, J. M. García, R. Martínez-Máñez, F. Sancenón, N. San-José and J. Soto, *Org. Lett.*, 2007, **9**, 2429; (*c*) F. Sancenón, A. B. Descalzo, M. A. Miranda and J. Soto, *Angew. Chem., Int. Ed.*, 2001, **40**, 2640; (*d*) F. Sancenón, R. Martínez-Máñez and J. Soto, *Chem. Commun.*, 2001, 2262; (*e*) F. Sancenón, R. Martínez-Máñez, M. A. Miranda, M.–J. Seguí and J. Soto, *Angew. Chem., Int. Ed.*, 2003, **42**, 647.
43 For recent cyanide sensing systems see:(*a*) X. Lou, L. Zhang, J. Qin and Z. Li, *Chem. Commun.*, 2008, 5848; (*b*) S.–J. Hong, J. Yoo, S.–H.

Kim, J. S. Kim, J. Yoon and C.–H. Lee, *Chem. Commun.*, 2009, 189; (*c*) C.–W. Chiu and F. P. Gabbaï, *Dalton Trans.*, 2008, 814; (*d*) P. Kaur, D. Sareen, S. Kaur and K. Singh, *Inorg. Chem. Commun.*, 2009, **12**, 272; (*e*) D.–G. Cho, J. H. Kim and J. L. Sessler, *J. Am. Chem. Soc.*, 2008, **130**, 12163; (*f*) H.–T. Niu, D. Su, X. Jiang, W. Yang, Z. Yin, J. He and J.–P. Cheng, *Org. Biomol. Chem.*, 2008, **6**, 3038; (*g*) Z. Ekmekci, M. D. Yilmaz and E. U. Akkaya, *Org. Lett.*, 2008, **10**, 461; (*h*) H.–T. Niu, X. Jiang, J. He and J.–P. Cheng, *Tetrahedron Lett.*, 2008, **49**, 6521; (*i*) Q. Zeng, P. Cai, Z. Li, J. Qin and B. Z. Tang, *Chem. Commun.*, 2008, 1094; (*j*) A. Touceda-Varela, E. I. Stevenson, J. A. Galve-Gasión, D. T. F. Dryden and J. C. Mareque-Rivas, *Chem. Commun.*, 2008, 1998; (*k*) S.–Y. Chung, S.–W. Nam, J. Lim, S. Park and J. Yoon, *Chem. Commun.*, 2009, 2866; (*l*) M. Jamkratoke, V. Ruangpornvisuti, G. Tumcharern, T. Tutulani and B. Tomapatanaget, *J. Org. Chem.*, 2009, **74**, 3919; (*m*) K.–S. Lee, H.–J. Kim, G.–H. Kim, I. Shin and J.–I. Hong, *Org. Lett.*, 2008, **10**, 49; (*n*) L. Peng, M. Wang, G. Zhang, D. Zhang and D. Zhu, *Org. Lett.*, 2009, **11**, 1943; (*o*) S. K. Kwon, S. Kou, H. N. Kim, X. Chen, H. Hwang, S.–W. Nam, S. H. Kim, K. M. K. Swamy, S. Park and J. Yoon, *Tetrahedron Lett.*, 2008, **49**, 4102; (*p*) J. Jo and D. Lee, *J. Am. Chem. Soc.*, 2009, **131**, 16283.

44 *HyperChem 6.03 Molecular Modeling System*, Hypercube Inc, Gainesville, Florida, USA, 2000.

45 T. Ábalos, S. Royo, R. Martínez-Máñez, F. Sancenón, J. Soto, A. M. Costero, S. Gil and M. Parra, *New J. Chem.*, 2009, **33**, 1641.