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Hg^{2+} and Cu^{2+} selective detection using a dual channel receptor based on thiopyrylium scaffoldings

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ABSTRACT

2,4,6-Triphenylthiopyrylium functionalized with an aza-oxa-thia macrocycle is able to selectively recognize Hg^{2+} cation by a color change and Cu^{2+} cation by a remarkable significant emission enhancement.

One of the more promising fields within supramolecular chemistry deals with the preparation of optical probes for target guest.[1] The chemosensors are generally formed by two moieties, namely a binding site and a signaling subunit connected through a covalent bond. The binding site is responsible for the interaction with the host and is designed bearing in mind supramolecular chemistry principles in order to achieve a high degree of complementarity between both components. In the probes, this interaction between the binding site and the host is transformed in an easy-to-observe output by the signaling subunit. Three main groups have been extensively employed as reporter subunits: fluorescent groups,[2] organic dyes,[3] and redox-active moieties.[4]

The coupling of several binding sites, generally of macrocyclic nature, and certain optical signaling subunits has led to the development of a number of receptors for the selective recognition and for sensing of metal cations.[5] In spite of this work it is noticeable that there are relatively few examples of receptors capable of displaying two or more output signals (different signaling channels) upon cation binding. This could be achieved by the use of two or more signaling subunits attached near the binding site[6] or by the use of one unique signaling group capable of displaying two or more observable events (usually fluorescence, color changes, or electrochemical modulations).[7] Additionally, it is remarkable that receptors that are able to display sensing abilities to different cations when using different signaling channels are very rare. However, these systems can be of interest for designing future probes that are able to signal, not just one, but multiple analytes.

In this Letter, we show the synthesis, metal coordination ability, and dual sensing features of a 2,4,6-triphenylthiopyrylium derivative functionalized with a macrocycle containing nitrogen, oxygen, and sulfur atoms. Thiopyrylium salts have been extensively used as photosensitizers in a great range of photochemical transformations.[8] However, as far as we know, the thiopyrylium moiety has never been used as signaling subunit for the development of optical chemosensors and only recently our research group used the pyrylium-to-thiopyrylium transformation for the development of a novel chromogenic chemodosimeter for sulfide anion that displayed sensing features in aqueous environments.[9]

The synthesis of receptor $\mathbf{L^1}$ was achieved following a four-step procedure from *N*-phenyldiethanolamine (**1**) (see Scheme 1). The first step consists of the mesylation of **1** with mesyl chloride in dichloromethane and triethylamine. The obtained dimesylated derivative (**2**) was reacted with 3,6-dioxaoctane-1,8-dithiol (**3**) to give the macrocycle 10-phenyl-10-aza-1,4-dioxa-7,13-dithiacyclopentadecane (**4**) in 40% yield.[7c] Electrophilic aromatic substitution reaction between **4** and 2,6-diphenylpyrylium perchlorate (**5**) yields the pyrylium salt derivative **6** in a 40% yield. Finally receptor $\mathbf{L^1}$ was obtained upon reaction of compound **6** with Na_2S in acetone and subsequent acidification.[10]

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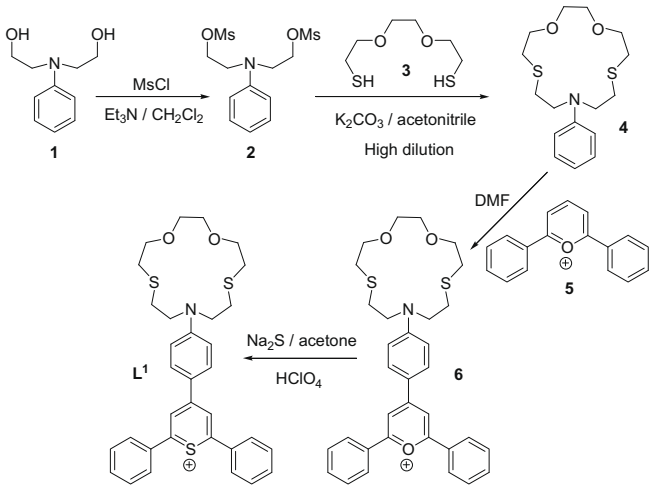

Scheme 1. Reagents and conditions for the synthesis of receptor $\mathbf{L^1}$.

Acetonitrile solutions of $\mathbf{L^1}$ showed a blue coloration due to the presence of a broad structureless intense band in the visible zone centered at 575 nm. The optical behavior can be tentatively attributed to allowed internal charge transfer (ICT) transitions due to the presence of an electron donor aniline group and an electron acceptor thiopyrylium moiety in the molecular skeleton.[11] Also a relatively less intense band in the near-UV zone centered at ca. 400 nm was observed.

In a first step the chromogenic behavior of acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}) was tested in the presence (10 equiv) metal cations (Ag^+, Al^{3+}, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+}). Since the cation binding unit is in the donor side of the molecule, it would be expected that coordination of cations would reduce the donor character and produce a hypsochromic shift through a modulation of the energetic positions of the HOMO and LUMO orbitals. The presence of Ag^+, Cd^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+} resulted in negligible changes in the visible spectra of $\mathbf{L^1}$ indicating no coordination, whereas Al^{3+}, Cu^{2+}, and Fe^{3+} gave a small hypochromic effects of the charge transfer band that does not induce any remarkable change in the color of the solutions. Moreover, the most remarkable outcome was the selective chromogenic response observed in the presence of Hg^{2+} cation; a large hypochromic effect on the band centered at 575 nm together with a hypsochromic shift of 40 nm was observed, resulting in a color modulation from blue to faint yellow (see Fig. 1). The response is fully consistent with coordination of Hg^{2+} to the macrocycle.

Addition of increasing quantities of Hg^{2+} to acetonitrile solutions of $\mathbf{L^1}$ allowed us to measure, through a least square treatment of the titration profile, the logarithm of the stability constant for the formation of $[Hg(\mathbf{L^5})]^{2+}$ complex that amounts to 6.98 ± 0.09. This value for the complex formation constant is of the same order as that found for other chromo- and fluorogenic receptors reported in the literature containing the same aza-oxa-thia macrocyclic subunit.[7c,12] As conclusion of this part, receptor $\mathbf{L^1}$ shows a high selective response toward Hg^{2+} when the UV–visible channel is measured.

Analogous spectroscopic studies were also carried out upon protonation, resulting in a similar behavior found for Hg^{2+}, that is the proton attacks the aniline nitrogen, reducing its donor strength and leading to the hypochromic effect and hypsochromic shift of the charge transfer band. This engagement of the lone pair of the aniline nitrogen is also reflected in the hyperchromic effect and bathocromic shift of the band at 390 nm that is tentatively attributed to the 2,4,6-triphenylthiopyrylium chromophore.

Fluorescence measurements of $\mathbf{L^1}$ in the presence of protons support the UV/vis-spectroscopic observations. $\mathbf{L^1}$ is poorly fluorescent and excitation of acetonitrile solutions of receptor $\mathbf{L^1}$ at the bands of 575 or 400 nm resulted in no significant emission in the range of 460–600 nm due to the existence of a very effective non-radiative deactivation of the excited state most likely due to the presence of the anilinium group. However, in the presence of protons there is appearance of a new emission at 500 nm attributed to the protonated $\mathbf{L^1}$. The intensity of this emission band reaches the highest intensity upon addition of 50 equiv of protons as could be seen in Fig. 2. This emission, and also the absorption band at 400 nm, correspond well with the optical properties of the parent 2,4,6-triphenylthiopyrylium neat dye that lacks any donor in the 4-position ($\lambda_{ab} = 400$ nm and $\lambda_{em} = 502$ nm in acetonitrile).[13]

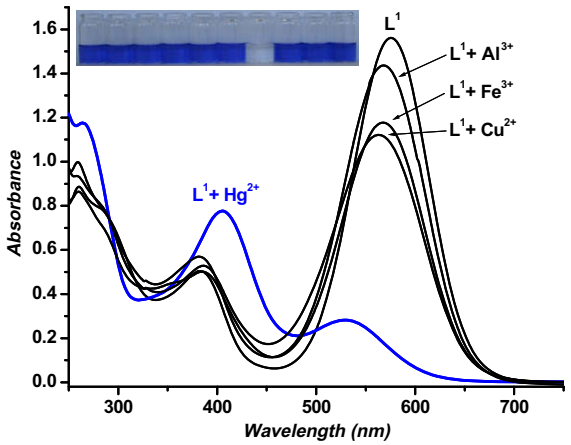

Figure 1. UV–visible spectra of receptor $\mathbf{L^1}$ in acetonitrile (1.0×10^{-5} mol dm^{-3}) and $\mathbf{L^1}$ in the presence of 10 equiv of Hg^{2+}, Al^{3+}, Fe^{3+}, and Cu^{2+}. The inset shows the color changes observed for acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}) in the presence of 10 equiv of the corresponding metal cations. From left to right: receptor alone, Ag^+, Al^{3+}, Cd^{2+}, Cu^{2+}, Fe^{3+}, Hg^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+}.

Protonation studies suggest that the engagement of aniline nitrogen lead to a partial suppression of the non-radiative deactivation path resulting in a restoration of the 2,4,6-triphenylthiopyrylium emission. Therefore, further fluorescence studies involving metal cations and $\mathbf{L^1}$ were carried out. The addition of up to 10 equiv of Cd^{2+}, Ni^{2+}, Pb^{2+}, and Zn^{2+} did not induce the appearance of any significative emission band in the range of 460–600 ($\lambda_{ex} = 400$ nm). In contrast, the addition of Al^{3+} and Fe^{3+} to $\mathbf{L^1}$ induced a 3.2- and 4.6-fold emission enhancement of the band centered at 500 nm, respectively. At the same time addition

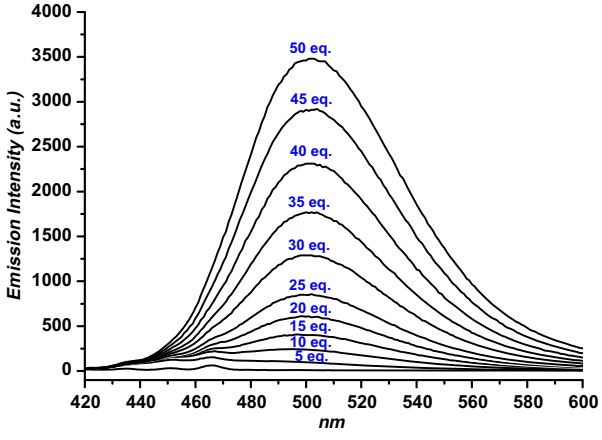

Figure 2. Emission enhancement observed upon addition of increasing quantities of protons to acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}, $\lambda_{exc} = 400$ nm).

of 10 equiv of Hg^{2+} induced a higher 6.2-fold enhancement of the emission band (see Fig. 3). Figure 4 shows the emission intensity enhancement observed upon addition of increasing quantities of Hg^{2+} cation to acetonitrile solutions of $\mathbf{L^1}$.

However the most remarkable behavior was that of Cu^{2+}, which was able to induce a remarkable 17.6-fold enhancement of the emission band of $\mathbf{L^1}$ (see again Fig. 3). Also the spectroscopic behavior of $\mathbf{L^1}$ as a function of increasing Cu^{2+} concentration is shown in Figure 5. This selective emission revival in the presence of Cu^{2+} contrasts with the selective colorimetric response to Hg^{2+} of receptor $\mathbf{L^1}$. We believe that this might be related to a heavy atom effect that is more effective for Hg^{2+}. Thus, although coordination of Hg^{2+} to the lone pair of the nitrogen atom of the aniline group would restore the emission of the 2,4,6-triphenylthiopyrylium chromophore, at the same time Hg^{2+} induced a partial quenching of the emission intensity. In the case of Cu^{2+} the strength of coordination with the macrocycle of $\mathbf{L^1}$, when compared with Hg^{2+}, is less effective leading to moderate changes in the visible band (only a slight hypochromic effect) whereas the emission of the 2,4,6-triphenylthiopyrylium moiety is restored more efficiently. Thus the selectivity shown by $\mathbf{L^1}$ toward metal cations is easily selected by an appropriate choice of the output channel, that is detection of Hg^{2+} via the color channel (from blue to pale yellow) and signaling of Cu^{2+} via a remarkable enhancement of the emission intensity.

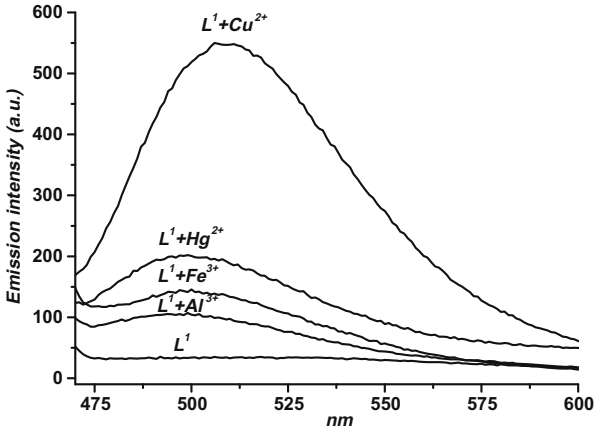

Figure 3. Fluorescence enhancements observed upon addition of 10 equiv of the corresponding metal cations to acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}, λ_{exc} = 400 nm).

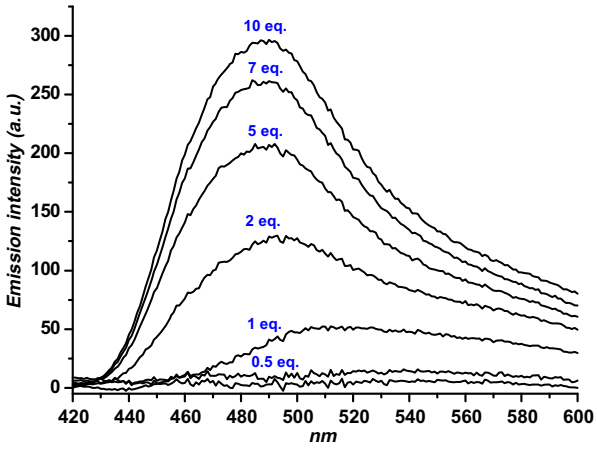

Figure 4. Emission enhancement observed upon addition of increasing quantities of Hg^{2+} to acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}, λ_{exc} = 400 nm).

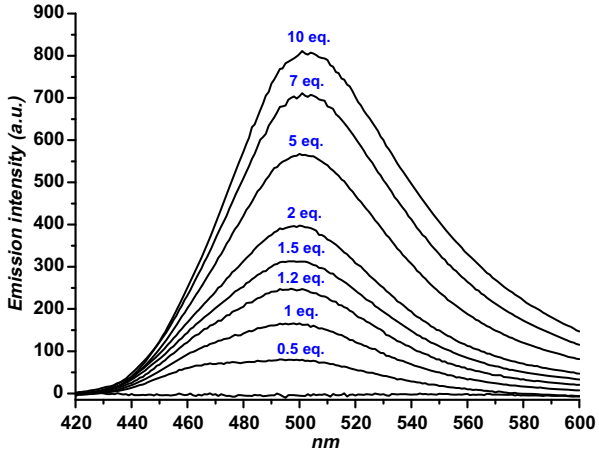

Figure 5. Emission enhancement observed upon addition of increasing quantities of Cu^{2+} to acetonitrile solutions of receptor $\mathbf{L^1}$ (1.0×10^{-5} mol dm^{-3}, λ_{exc} = 400 nm).

Signaling of metal cations through changes in color or in emission intensity in organic solvents is not as appealing as signaling events in water or in mixed organic solvent-water mixtures. For this reason we studied the color and the emission intensity changes of receptor $\mathbf{L^1}$, in the presence of Hg^{2+} and Cu^{2+} cations, in acetonitrile-water mixtures with water contents ranging from 5% to 20%. Unfortunately the presence of water, in a content as low as 5%, inhibited the colorimetric and the fluorimetric responses of $\mathbf{L^1}$ toward Hg^{2+} and Cu^{2+} cations.

In summary, for the first time we have used the 2,4,6-triphenylthiopyrylium moiety for the design of intrinsic chemosensors. In particular, we have prepared $\mathbf{L^1}$ that is a chromo-fluorogenic probe based on the thiopyrylium scaffolding functionalized with an aza-oxa-thia macrocycle. This new receptor has the ability to selectively recognize Hg^{2+} through a change in color whereas this is able to give strong emission enhancements in the presence of Cu^{2+} cation. This dual signaling is of significance because, as stated above, there are few examples in the literature of optical receptors showing a modulation of the selectivity by the choice of the output signal. We believe that the design of multi-channel probes could be a suitable mode to enhance recognition features in single chemosensors via signaling of multiple guests but using a unique molecular entity.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.04.060.

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10. *Synthesis of* $\boldsymbol{L^1}$: *N*-phenyl macrocycle (**4**, 2 mmol) was reacted with 2,6-diphenylpyrylium perchlorate (**5**, 4 mmol) in dry DMF (20 mL) at 150 °C for 3 h. Pyrylium derivative **6** (1 mmol, yield 50%) was precipitated from the crude reaction by addition of dimethyl ether (25 mL). Then, compound **6** was dissolved in acetone (50 mL), Na_2S (2 mL, 20% 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 mixture was stirred for 40 another minutes at the same temperature. The final thiopyrylium derivative $\mathbf{L^1}$ (0.48 mmol, 48% yield) was isolated by vacuum filtration and successive washings with water and diethyl ether as dark blue solid. ^{1}H NMR (300 MHz, DMSO-d_6): 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_2S). ^{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 calcd. for $C_{33}H_{36}NS_3O_2$, 574.1908, found: 574.1867.
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