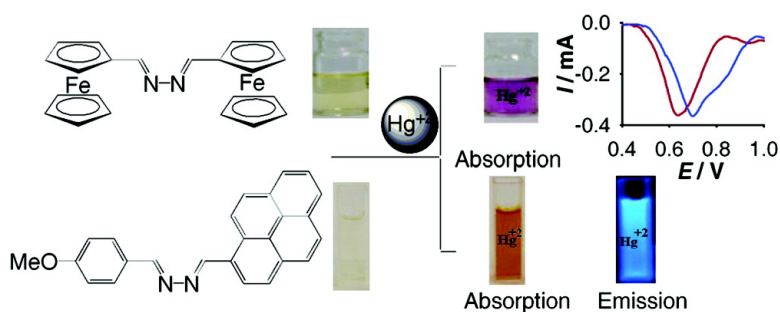Communication

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Highly Selective Chromogenic and Redox or Fluorescent Sensors of Hg^{2+} in Aqueous Environment Based on 1,4-Disubstituted Azines

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Mercury contamination occurs through a variety of natural and anthropogenic sources,[1] and it causes serious environmental and health problems because marine aquatic organisms convert inorganic mercury into neurotoxic methylmercury which bioaccumulates through the food chain.[2] A number of selective Hg^{2+} sensors have been devised using redox,[3] chromogenic,[4] or fluorogenic[5] changes. However, most of these molecules display shortcomings in practical use, such as cross-sensitivities toward other metal ions, delayed response to mercury ions, and/or low water solubility. Despite the development of individual single-signaling sensors, there are no multichannel signaling receptors on Hg^{2+} binding. As a result, developing new and practical multi-signaling sensors for Hg^{2+} in aqueous media is still a challenge.[6]

For the selective recognition of soft heavy metal ions, nitrogen binding sites might be a choice as it is well exemplified with classical azacrown ethers.[7] Previous studies on complexation of ferrocene with binding ligands have shown that not only the characteristic band between 400 and 500 nm, ascribed to the lowest energy metal-to-ligand transition, is perturbed by complexation but also a positive shift of the Fe^{II}/Fe^{III} redox couple is observed.[8] Pyrene has often been used as an effective fluorescence probe because of its high detection sensitivity.[9] Formation of a complex results in a change in the fluorescence emission intensities of pyrene excimer and monomer.[10] Two informative parameters associated with the pyrene excimer are the intensity ratio of the excimer to the monomer emission (I_E/I_M) and the wavelength corresponding to the maximum of the excimer emission (λ_E). While the I_E/I_M parameters are sensitive to the structure of the pyrene systems, the emission λ_E is less variable and locates at 475−485 nm. On the basis of such precedents, suitable designed aza-substituted ferrocene and pyrene derivatives might be good candidates as dual signaling sensors. This can be realized by combining the 2,3-diazabutadiene ligand[11] (azine) with the redox activity of the ferrocene and the photoactivity of the pyrene.

Herein we report the synthesis, characterization, and metal recognition properties of 1,4-disubstituted 2,3-diaza-1,3-butadienes bearing two redox ferrocene groups, **1**, and one photoactive pyrene and a *p*-methoxyphenyl group, **2**. These structural motifs would thus yield a combined optical and redox, or fluorescent-based sensors, in a single molecule. Symmetrical azine **1** (70% yield) was prepared by known procedures,[12] while the unsymmetrical azine **2** was obtained by a modification of the Zwierzak's method.[13] The X-ray structure of **1** reveals that the bridge is in the *E,E* form, and that the dihedral angles between the bridged Cp ring of both Fe and the C−C−N plane are −5.5 and 5.5°, bearing a good electronic conjugation along the bridge (see Supporting Information)
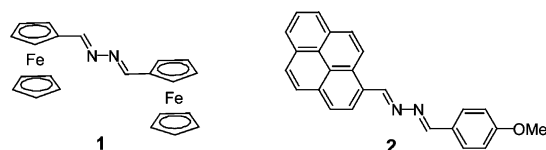
The metal recognition properties of **1** were evaluated by electrochemical and optical analysis. The cyclic voltammetric (CV) and differential pulse voltammetric (DPV) analyses in acetonitrile show two almost-overlapped one-electron oxidation processes for **1**, whereas in acetonitrile/water (7:3), only one oxidation peak around 0.65 V is observed, versus decamethylferrocene. Whereas no perturbation of the DPV voltammogram of **1** was observed upon addition of Mg^{2+}, Ca^{2+}, Ni^{2+}, Zn^{2+}, and Cd^{2+} metal ions,[14] a significant modification was observed upon addition of Hg^{2+}. In acetonitrile, the two oxidation peaks were converted into one and anodically shifted. Most remarkably is the fact that the selective response toward Hg^{2+} is preserved in the presence of water. Thus, the peak was also anodically shifted upon complexation in acetonitrile/water (7:3) ($\Delta E_{1/2} = 60$ mV) (Figure 1a). The UV/visible spectra of compound **1** are almost identical in dichloromethane, acetonitrile, and acetonitrile/water (7:3). These spectra are characterized by two maximum at 309 and 476 nm, which are assigned to a localized $\pi-\pi*$ excitation within the diaza-bridge and a metal-to-ligand charge transfer, respectively.[15]

The addition of increasing amounts of Hg(ClO$_4$)$_2$ to a solution of **1** in acetonitrile/water (7:3) caused the appearance of a new band at $\lambda = 521$ nm and the disappearance of the initial band at 476 nm (Figure 1b). The three well-defined isosbestic points indicate that a neat interconversion between the uncomplexed and complexed species occurs. The new band is red-shifted by 45 nm and is responsible for the change of color from yellow (neutral azine **1**) to deep purple (complexed azine). This color change can be used for a "naked-eye" detection of Hg^{2+} ions in an aqueous environment (Figure 1c), with a detection limit of 5.2×10^{-5} M. The absorption spectral data indicate a 1:1 binding model and an association constant of 4.35
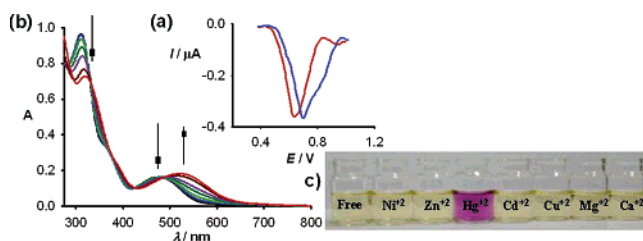

Figure 1. (a) DPV of free ligand **1** (red) and after formation of **1**·Hg^{2+} (blue) in CH$_3$CN/H$_2$O 7/3 with [(*n*-Bu)$_4$N] ClO$_4$ as supporting electrolyte. (b) Absorption spectra of **1** in CH$_3$CN/H$_2$O (7:3) upon addition of increasing amounts of Hg(ClO$_4$)$_2$. (c) Color change due to binding of **1** in CH$_3$CN/H$_2$O (7:3) ($c = 1 \times 10^{-4}$ M) with Hg^{2+} in comparison with other metal cations.

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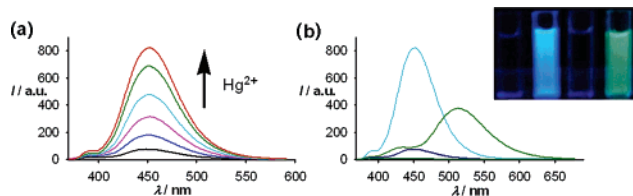‡ Institut de Ciència dels Materials de Barcelona.
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Figure 2. (a) Fluorescence emission spectra of **2** (excitation at 350 nm) in CH$_3$CN/H$_2$O (7:3) upon titration with Hg(ClO$_4$)$_2$. The final spectrum (red) corresponds to the complexed form **2·Hg^{2+}** after addition of 1 equiv of Hg^{2+}. (b) Fluorescence spectra after the addition of 1 equiv of Hg(ClO$_4$)$_2$ to **2** in CH$_3$CN/H$_2$O (7:3) (blue) and in CH$_3$CN (green). Spectra for the free ligand **2** in CH$_3$CN/H$_2$O (7:3) (deep blue) and CH$_3$CN (deep green). (Inset) From left to right: **2** in CH$_3$CN/H$_2$O (7:3) and adding 1 equiv of Hg(ClO$_4$)$_2$, and **2** in CH$_3$CN and adding 1 equiv of Hg(ClO$_4$)$_2$.

$\times$ 10^5 M^{-1} in acetonitrile (see Supporting Information). This result has also been confirmed by MALDI-TOF/MS, where a peak corresponding to the 1:1 complex is observed (see Supporting Information).

The ability of the azine bridge to complex Hg^{2+} selectively was checked with compound **2**, which has a fluorogenic instead of a redox signaling unit as **1**. The absorption spectra of ligand **2** in acetonitrile or acetonitrile/water (7:3) show the typical pyrene absorption bands[16] at 238, 285, and 313 nm, along with a low-energy band centered at 383 nm, attributed to the charge transfer between the donor and acceptor units of the molecule, which is responsible of its pale-yellow color. When Hg^{2+} metal ions are added, the low-energy band suffers a bathochromic shift (51 nm). Four well-defined isosbestic points indicated that a neat interconversion between the uncomplexed and complexed species occurs. The red-shift of the low-energy band is responsible for the change of color of the solution from pale-yellow to deep-orange. The resulting titration was fitted to a 1:1 binding model, and the association constant was 9.79 $\times$ 10^7 M^{-1} in acetonitrile (see Supporting Information). It is noticeable that only Hg^{2+} from Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Ni^{2+}, Sm^{3+}, Eu^{3+}, Yb^{3+}, and Lu^{3+} metal ions is able to produce a bathochromic shift of this band, indicating that the color variation is highly specific for Hg^{2+} ions. The spectrum of the free ligand **2** in acetonitrile shows weak fluorescence with typical emission bands at 387 and 435 nm (λ_{exc} = 350 nm), which are attributed to the pyrene monomeric emission,[17] with rather low quantum yield (Φ_o = 0.0006).[18] However, in acetonitrile/water (7:3), it also shows weak fluorescence with one emission band at 390 nm (monomer emission) but also a red-shifted structureless maximum at 450 nm, typical of pyrene excimer fluorescence,[9] with low quantum yield (Φ_o = 0.005). The low quantum yield of the unbounded ligand **2** results from the quenching of the pyrene emission by the lone pair of the nitrogen atoms[19] in the free state. So, it could be expected that, upon complexation with a metal cation, the lone pairs no longer participate in the quenching process, causing the recovery of the fluorescence.

To evaluate the sensing behavior of **2**, we measured its fluorescence in acetonitrile as function of the Hg^{2+} concentration. Addition of only small amounts of Hg^{2+} to the solution dramatically increased the excimer emission band at 510 nm.

This band increased until addition of 1 equiv of Hg^{2+} was completed. The result obtained indicates the formation of a 1:1 complex. The final fluorescence enhancement factor (FEF) was 157, the ratio $I_{E(510)}/I_{M(387)}$) = 17, and the quantum yield was 67-fold (Φ = 0.04). Upon addition of 1 molar equiv of Hg^{2+} ions to a solution of **2** in acetonitrile/water (7/3), a remarkable FEF = 11 of the excimer emission band at 450 nm was also clearly observed. A blue-shift upon increasing solvent polarity can visually and readily be discernible by the change of the blue fluorescence in acetonitrile/water to green fluorescence in acetonitrile (Figure 2b). Analysis of

emission spectral data indicates a 1:1 binding model and an association constant of 1.65 $\times$ 10^6 M^{-1} in acetonitrile (see Supporting Information). Compound **2** was found to have high selectivity toward Hg^{2+} ions and a detection limit[20] of 4.6 $\times$ 10^{-6} M, which is sufficiently low to allow the fluorogenic detection of submillimolar concentrations of Hg^{2+}. The fluorescence quantum yield was 10-fold (Φ = 0.04), and the ratio $I_{E(450)}/I_{M(390)}$ = 13. Fluorescence spectra of **2** recorded in the presence of Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Ni^{2+}, Sm^{3+}, Eu^{3+}, Yb^{3+}, and Lu^{3+} metal ions did not alter the shape or the intensity of the fluorescence spectra, indicating no interference.

In summary, we have reported for the first time two new sensors which operate through two different channels (**1**: optic/redox, and **2**: optic/fluorescent) exhibiting higher sensitivity and selectivity for Hg^{2+} in aqueous environment than other previously reported sensors, although they cannot operate in pure water as it does in the seminal example of Lippard et al.[6] Remarkable is sensor **2** since its optical change in sensing can be used for a naked-eye detection of Hg^{2+} ions, whereas its fluorescent response can be modulated by varying the solvent polarity.

Supporting Information Available: Crystallographic and electrochemical data of **1**, synthesis, optical, fluorescence, selectivity, and detection limit data of **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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