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A Simple but Effective Dual Redox and Fluorescent Ion Pair Receptor Based on a Ferrocene−Imidazopyrene Dyad

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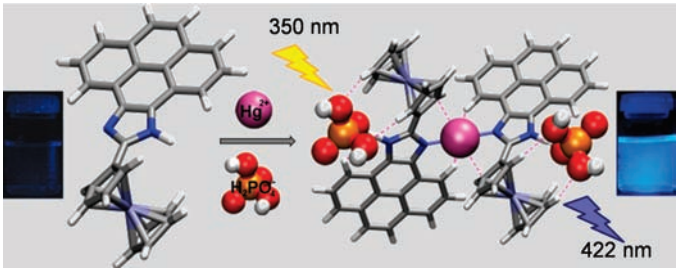

The ferrocene−imidazopyrene dyad, bearing the imidazole ring as the only receptor site, acts as a redox and optical molecular sensor for ion pairs, exhibiting an easily detectable signal change in the redox potential of the ferrocene/ferrocinium redox couple and in the emission spectrum. Perturbation of the emission spectrum follows the order $Pb^{2+} > Hg^{2+} > Zn^{2+}$ for cations and $H_2PO_4^- > AcO^-$ for anions.

The design of ion pair receptors that contain two quite different binding sites for the simultaneous complexation of cationic and anionic guest species is a new emerging and topical field of supramolecular chemistry. These multisite receptors are able to bind a single heteroditopic guest or simultaneously bind to nonidentical guests. The development of convergent ion pair hosts is a challenging problem in molecular design because the binding sites have to be incorporated into a suitably preorganized scaffold that holds them in close proximity, but not so close that species can interact.[1] However, despite their potential applications in various fields, such as salt solubilization, extraction, and membrane transport,[2] the number of well-characterized ion pair receptors remains limited.[3] In these systems crown ethers and π-electron donors, such as functionalized calixarenes, have been frequently utilized as cation binding units, while the anion is coordinated using Lewis acidic, electrostatic, or hydrogen bonding interactions.

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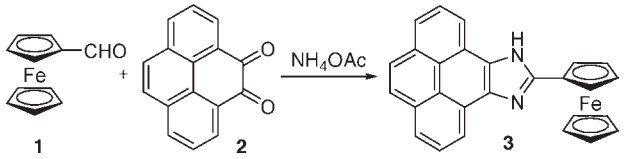
Nevertheless, it is worth mentioning that only one example for the detection of an ion pair by fluorescence enhancement has been reported.[4]

Here, we describe the synthesis and binding properties of one ion pair receptor **3** which, acting in a sequential fashion, exhibits remarkable enhancement of the fluorescence in the presence of anions when divalent metal cations are bounded to the cation binding-site. To this end, we have combined in a highly preorganized system the redox activity of the ferrocene group with the fluorogenic behavior of pyrene and the binding ability of the imidazole ring, which is embedded into the framework of the imidazopyrene ring system. The multiresponsive character of the receptor **3** and the ability of the previously unreported imidazopyrene ring system to act not only as a fluorescent antenna but also as favorable binding for cations and anions in the recognition event are most noteworthy.

Receptor **3** was prepared in excellent yield by condensation of pyrene-4,5-dione, available by oxidation of pyrene with the system ruthenium(III) chloride and sodium periodate in CH_3CN at room temperature,[5] with formylferrocene in the presence of NH_4OAc following an improved modification[6] of the previously reported method for related compounds[7] (Scheme 1).

Scheme 1. Preparation of Dyad **3**



The chemosensor behavior of **3** toward a variety of cations (Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Hg^{2+}, and Pb^{2+}) and anions (F^-, Cl^-, Br^-, AcO^-, NO_3^-, HSO_4^-, $H_2PO_4^-$, and $HP_2O_7^{3-}$) was investigated by cyclic (CV) and Osteryoung square-wave (OSWV)[8] voltammetries as well as through spectrophotometric and ^1H NMR techniques. The titration experiments were further analyzed using the computer program Specfit.[9]

The free receptor exhibited a reversible one-electron redox wave typical of a ferrocene derivative, at the halfwave potential value of $E_{1/2}$ = 608 mV, calculated versus the decamethylferrocene (DMFc) redox couple. The results obtained on stepwise addition of the above-mentioned metal ions show that addition of Zn^{2+}, Hg^{2+}, and Pb^{2+} metal cations causes significant changes in the redox potential of receptor **3**, with a difference found between the $E_{1/2}$ for receptor−metal system and $E_{1/2}$ for the free receptor ($\Delta E_{1/2}$) ranging from 279 mV for Hg^{2+} to 245 mV for Pb^{2+} (see the Supporting Information). However, addition of Cu^{2+} induces the oxidation of the ferrocene moiety (see the Supporting Information). Titration studies with the addition of the above-mentioned set of anions, as their tetrabutylammonium salts (TBA^+), to an electrochemical solution of receptor **3** ($c = 10^{-3}$ M) in CH_3CN, containing 0.1 M [n-Bu_4N]PF_6 as a supporting electrolyte, have also been carried out. Interestingly, the stepwise addition of $H_2PO_4^-$ and AcO^- induced the progressive appearance of new oxidation waves cathodically shifted by $\Delta E_{1/2}$ = −95 mV and $\Delta E_{1/2}$ = −212 mV, respectively which are associated with a recognition process. The addition of Cl^-, Br^-, NO_3^-, and HSO_4^- anionic species had no effect on their CV and OSWV, even when present in a large excess, whereas F^- and $HP_2O_7^{3-}$ induced deprotonation (see the Supporting Information)

Interestingly, upon addition of the $H_2PO_4^-$ anion to the electrochemical solution of the $[\mathbf{3}\cdot Zn]^{2+}$ complex ($E_{1/2}$ = 873 mV) a cathodically shifted oxidation peak appears at $E_{1/2}$ = 550 mV. As this value is intermediate between those found for the cationic $[\mathbf{3}\cdot Zn]^{2+}$ and the anionic $[\mathbf{3}\cdot H_2PO_4]^-$ complexes ($E_{1/2}$ = 513 mV), the oxidation wave is ascribed to the $[\mathbf{3}\cdot Zn(H_2PO_4)_2]$ complex. However, such addition on the $[\mathbf{3}\cdot Pb]^{2+}$ species promotes the appearance of the redox peak ascribed to the free receptor **3** (see Supporting Information). This result clearly shows the ability of the electrochemical DPV technique for detecting the formation of the ion pair $[\mathbf{3}\cdot Zn(H_2PO_4)_2]$ complex

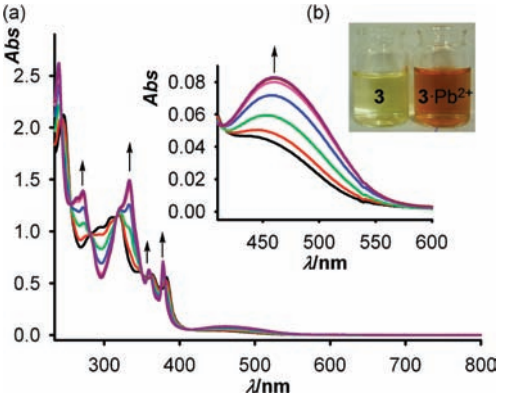


Figure 1. (a) Changes in the absorption spectra of **3** (black) (5×10^{-5} M) in CH_3CN upon addition of increasing amounts of $Pb(ClO_4)_2$, until 1 equiv (purple). (b) Visual features observed by passing from **3** to the complex $\mathbf{3}\cdot Pb^{2+}$.

Ion recognition properties of the receptor **3** toward metal cations and anions have also been studied by using absorption and emission techniques. The UV−vis spectrum of receptor **3** in CH_3CN ($c = 5 \times 10^{-5}$ M) exhibits two bands at λ = 364 nm (ε = 610 M^{-1} cm^{-1}) and 383 nm (ε = 578 M^{-1} cm^{-1}).

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(9) Specfit/32 Global Analysis System, 1999−2004; Spectrum Software Associates: Singapore, 1999−2004; http:www.bio-logic.info/spectfits-up/index.html.

The addition of Zn^{2+}, Hg^{2+}, and Pb^{2+} cations to a solution of receptor **3** elicited the same optical response. In all cases, the addition of such divalent cations caused the progressive appearance of a new LE band located at $\lambda = 461$ nm, as well as a blue-shift by $\Delta\lambda = 5$ nm of the original two absorption bands. Three well-defined isosbestic points at 375, 380, and 415 nm indicated that neat interconversion between the uncomplexed and complexed species occurs. The new LE band is responsible for the change of color, from yellow to orange which can be used for a "naked eye" detection of these metals (Figure 1). Binding assays using the method of continuous variations (Job's plot) suggest a 2:1 (receptor/cation) binding model, the global association constants being $\beta = 1.68 \times 10^{10}$ M^{-2} for Pb^{2+}, $\beta = 7.28 \times 10^{10}$ M^{-2} for Hg^{2+}, and $\beta = 8.71 \times 10^{10}$ M^{-2} for Zn^{2+}.

Titration studies of receptor **3** toward the same set of anions revealed that only $H_2PO_4^-$ and AcO^- induced detectable changes. The most prominent feature observed upon addition of successive substoichiometric amounts of these anions is an increase in the intensity of the absorption bands. In these cases, 1:1 binding models were observed and the corresponding binding constants were determined by the analysis of the spectral titration data, $K_a = 8.22 \times 10^5$ M^{-1} for AcO^- and 1.54×10^5 M^{-1} for $H_2PO_4^-$.

Assessments of the ion affinities also came from observing the extent to which the fluorescence intensity of receptor **3** was affected in the presence of anions and cations. As expected, receptor **3** showed a weak fluorescence in CH_3CN ($c = 10^{-5}$ M) revealing that the excitation spectrum at $\lambda_{exc} = 350$ nm is an ideal excitation wavelength. The emission spectrum displays two well-defined emission bands at 382 and 402 nm, ascribed to the monomeric emission, with a rather low quantum yield ($\Phi = 8 \times 10^{-3}$). Upon addition of Zn^{2+}, Hg^{2+}, and Pb^{2+} cations a remarkable increase of the emission bands at 382 and 402 nm was observed along with a red-shifted structureless maximum at 502 nm probably due to excimer fluorescence (Figure 2).

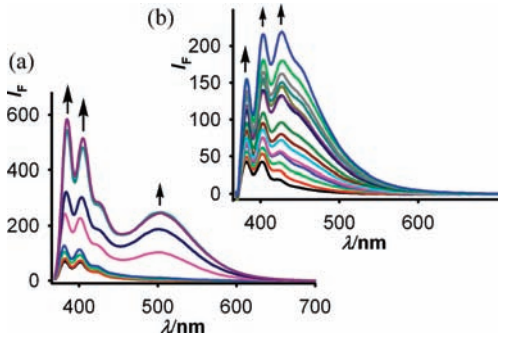

Figure 2. Changes in the fluorescence emission spectra of **3** (black) ($c = 1 \times 10^{-5}$ M in CH_3CN) upon addition of increasing amounts of (a) $Pb(ClO_4)_2$ until 0.5 equiv (purple) and (b) $[(n\text{-}Bu)_4N]H_2PO_4$ until 2 equiv (blue).

The ratio of the fluorescence intensity $\lambda_{402}/\lambda_{502}$ was 1.80 for Zn^{2+}, 1.60 for Hg^{2+}, and 1.83 for Pb^{2+}, and the quantum yields ($\Phi = 9.2 \times 10^{-2}$ for Zn^{2+}, 8.9×10^{-2} for Hg^{2+}, and 1.02×10^{-1} for Pb^{2+}) resulted in about a 13-fold increase compared to that of receptor **3**.

The stoichiometries of the complexes were determined by the changes in the fluorogenic response of **3** in the presence of varying concentrations of these metal cations, and the obtained result also indicates the formation of 2:1 complexes with global association constants: $\beta = 4.40 \times 10^{10}$ M^{-2} for Zn^{2+}, 5.78×10^{10} M^{-2} for Hg^{2+}, and 7.78×10^{10} M^{-2} for Pb^{2+}. Interestingly, the addition of 1 equiv of AcO^- and $H_2PO_4^-$ anions also produced an intensity increase of the monomeric emission band at 382 and 402 nm, albeit lower than than that originated by the above-mentioned metal cations. An additional strong emission band was also observed at 430 nm (Figure 2b). Fluorogenic titrations indicate the formation of 1:1 complexes giving association constants K_a of 6.62×10^5 M^{-1} for AcO^- and 1.21×10^5 M^{-1} for $H_2PO_4^-$, and the quantum yields ($\Phi = 8.3 \times 10^{-2}$ for AcO^-, 4.6×10^{-2} for $H_2PO_4^-$) resulted from an 8- to 14-fold increase compared to that of receptor **3**.

Next, titrations with cations were carried out in the presence of anions. The addition of 0.5 equiv of cations to a solution containing the preformed complex $[\mathbf{3}\cdot H_2PO_4]^-$ results in the appearance of a red-shifted broad emission band at 422 nm, whose intensity is higher for Pb^{2+} ($\lambda_{422}/\lambda_{402} = 2.02$) and Hg^{2+} ($\lambda_{422}/\lambda_{402} = 1.89$) than for Zn^{2+} ($\lambda_{422}/\lambda_{402} = 0.89$).[10] Identical results were obtained by changing the addition sequence: addition of 2 equiv of anions to a solution of the preformed $[\mathbf{3}_2\cdot M]^{2+}$ complex (M: Zn, Hg, Pb). So we believe this emission band at 422 nm is due to the formation of the $[\mathbf{3}_2\cdot M\cdot(H_2PO_4)_2]$ ion pair complex (Figure 3). When the titrations were carried out on the preformed $[\mathbf{3}\cdot AcO]^-$ complex, the changes were much lower.

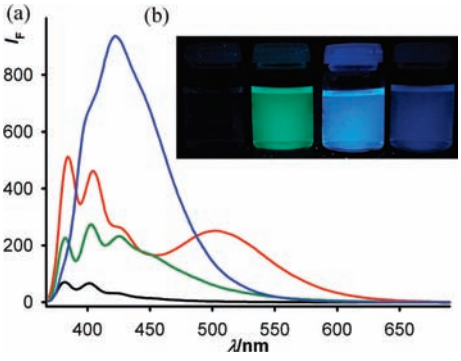

Figure 3. (a) Changes in the fluorescence emission spectra of **3** (black) ($c = 1 \times 10^{-5}$ M in CH_3CN) in the presence of 0.5 equiv of $Pb(ClO_4)_2$ (red); 2 equiv of $[(n\text{-}Bu_4N)]H_2PO_4$ (green); and 0.5 equiv of $Pb(ClO_4)_2$ plus 2 equiv of $[(n\text{-}Bu_4N)]H_2PO_4$ simultaneously (blue). (b) Visual features observed; from left to right: **3**, **3** + Pb^{2+}, **3** + Pb^{2+} + $H_2PO_4^-$, **3** + $H_2PO_4^-$.

To seek more detailed information on the binding properties of receptor **3** with cations and anions, ^1H NMR titration

(10) From the titration data, the β values were found to be of the same order as those found in the titration of the free receptor.

experiments were carried out in DMSO-d_6. Upon gradual addition of Hg^{2+} cations (0.5 equiv) to a solution of **3** the pyrene protons are downshifted by 0.1−0.2 ppm, whereas the monosubstituted cyclopentadienyl protons are shifted by 0.20−030 ppm. Likewise, addition of the $H_2PO_4^-$ anion (1 equiv) induced only an appreciable downshift by 0.15 ppm of the H1 and H8 pyrene protons adjacent to the imidazole ring, whereas the α-ferrocenyl protons are downshifted by 0.21 ppm and the β-protons are upshifted by 0.10 ppm (Figure 4). Shifts of the ferrocene CH protons have already been observed before in some electrochemical sensors for anions.[11] Solubility problems do not allow a study with anions and cations simultaneously.

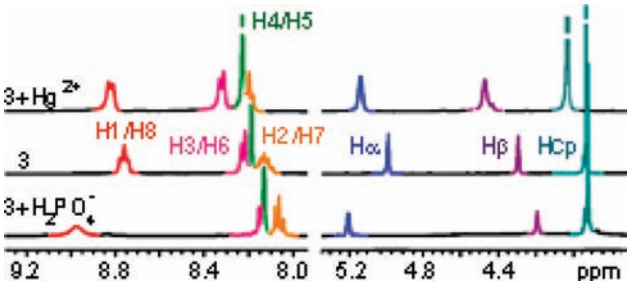

Figure 4. Evolution of ^{1}H NMR spectra of **3** (middle), in DMSO-d_6, upon addition of 0.5 equiv of $Hg(OTf)_2$ (up) and upon addition of 1 equiv of $[(n\text{-}Bu_4N)]H_2PO_4$ (down).

Further insight into the binding mode of the reported ion pair complexes was provided by DFT calculations and analyzed utilizing AIM (atoms-in-molecules) methodology.[12] In the case of mercury, the most stable C_2-symmetric complex shows a well-defined receptor-separated ion pair structure (Figure 5),[13] sketched as $[(H_2PO_4)\cdot\mathbf{3}\cdot Hg\cdot\mathbf{3}\cdot(H_2PO_4)]$, in which binding of every ion cooperatively enhances binding of the others. Thus, the moderately basic $H_2PO_4^-$ anions partially deprotonate the imidazole NH group ($d_{O\cdots HN}$ = 1.340 Å, $WBI_{O\cdots HN}$ = 0.245, $\rho(\mathbf{r_C})_{O\cdots HN} = 11.51 \times 10^{-2}$ e/a_0^3; d_{N-H} = 1.174 Å, WBI_{N-H} = 0.506, $\rho(\mathbf{r_C})_{N-H} = 22.27 \times 10^{-2}$ e/a_0^3) therefore strengthening the ligand−metal bond (d_{N-Hg} = 2.092 Å, WBI_{N-Hg} = 0.449, $\rho(\mathbf{r_C})_{N-Hg} = 11.69 \times 10^{-2}$ e/a_0^3). The essentially linear dicoordination around the

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(13) Figure 5 was generated with AMD: Humphrey, W.; Dalke, A.; Schulten, K. *J. Molec. Graphics* **1996**, *14*, 33–38 (http://www.ks.uiuc.edu/Research/vmd/).

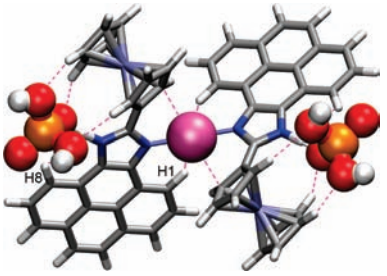

Figure 5. Calculated structure for the $[\mathbf{3}_2\cdot Hg\cdot(H_2PO_4)_2]$ complex.

Hg^{2+} cation is complemented by two cation-π type interactions with adjacent ferrocenyl C atoms ($d_{C\cdots Hg}$ = 3.046 Å, $WBI_{C\cdots Hg}$ = 0.035, $\rho(\mathbf{r_C})_{C\cdots Hg} = 1.71 \times 10^{-2}$ e/a_0^3) as unambiguously evidenced by the presence of the corresponding bond critical point (BCP) featuring a relatively high ellipticity (ε = 1.133). Moreover, the rigid imidazopyrene frameworks locate two H1 ring protons pointing toward the central Hg^{2+} cation (C−H···Hg angle 133.0°) allowing the formation of complementary anagostic[14] bonds ($d_{H\cdots Hg}$ = 2.662 Å, $WBI_{H\cdots Hg}$ = 0.017, $\rho(\mathbf{r_C})_{H\cdots Hg} = 1.40 \times 10^{-2}$ e/a_0^3). A set of secondary contacts (with pyrene H8 and ferrocene H atoms) also reinforces the binding to every peripheral $H_2PO_4^-$ anion (ΣWBI = 0.010, $\Sigma\rho(\mathbf{r_C})$ = 3.08 × 10^{-2} e/a_0^3).

In conclusion, the ferrocene−imidazopyrene dyad **3** behaves as a host-separated ion pair receptor. A salient feature of this simple receptor is the presence of only one receptor site, the imidazole ring, which is able simultaneously to recognize an anion and a cation through variation of the oxidation potential of the ferrocene/ferrocinium redox couple and a remarkable perturbation of the emission spectrum.

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Supporting Information Available. General experimental comments. Titration spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

(14) Anagostic M−H−C bonds are best described as a "hydrogen bond" involving a 3-center-4-electron orbital interaction with an electrostatic contribution in which the metal serves as a hydrogen bond acceptor. They are characterized by relatively long M···H distances (~2.3−3.2 Å) and large M−H−C angles (~110−170°).