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Selective Fluorescence Sensing of Li^+ in an Aqueous Environment by a Ferrocene–Anthracene-Linked Dyad

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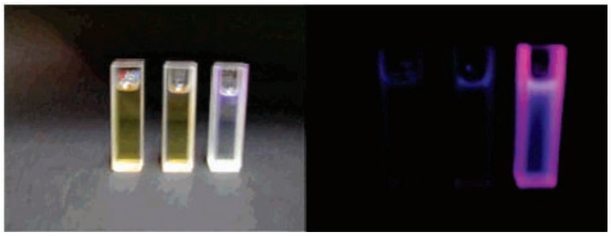
ABSTRACT



A new 1-(9-anthryl)-4-ferrocenyl-2-aza-1,3-butadiene showing selective fluorescence enhancement upon binding to lithium cations over other alkaline cations in aqueous environment has been conveniently synthesized and characterized.

The design of new ligands with the ability to bind metal ions, and capable of recognizing the presence of these ions in solution, is of great interest in a wide variety of chemical fields, in particular the detection of metal ions involved in biological processes (e.g., sodium, potassium, calcium, magnesium), clinical diagnostics (e.g., lithium, potassium, aluminum), or pollution (e.g., lead, mercury, cadmium). Among the various kinds of chemosensors described, fluorescent sensors for metal ions have received special attention.[1]

Lithium is one target of this research; the interest in this ion is due to its significant role not only in industrial applications but also in medicinal and biological chemistry.[2] Although several lithium sensors are known,[3] a few reports on the development of fluorescent chemosensors for selective recognition of lithium in organic solvents have recently appeared.[4]

We have been interested in the combination of ferrocene with active molecules to design new ferrocene-containing

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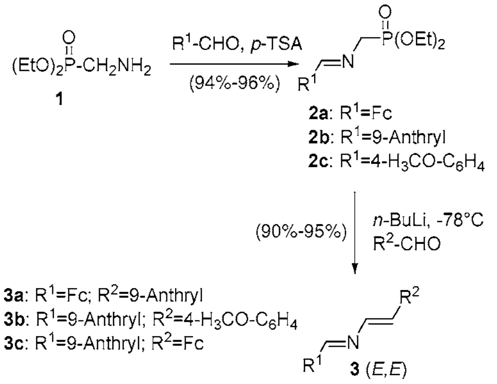
luminescent molecules. This may seem something of a contradiction in that ferrocene has been widely used as an emission quencher in intramolecular processes taking place in solution. However, it is also established that incorporating a ferrocenyl derivative into a luminescent system does not necessarily extinguish the luminescence.[5] Recently, ferrocene has been advantageously used as a redox center to provide multiresponsive photo- and electrochemically active compounds.[6] On the basis of this body of work, we decided to combine in an open-shell system the redox activity of the ferrocene group with the photoactive behavior of the anthracene ring and the cation binding ability of the unsaturated nitrogen atom.[7] The combined effects of these structural features suggest that this kind of compounds might experience an electron-cloud perturbation upon coordination or/and protonation, thus functioning as chemosensors for metal ions or protons.

Compounds **3** were prepared from the readily available diethyl aminomethylphosphonate **1**,[8] which was condensed with the appropriate aromatic or organometallic aldehyde, to give the corresponding N-substituted diethyl aminomethylphosphonate **2** in excellent yields (94−96%). Generation of the metalloenamine by reaction with *n*-BuLi at −78 °C and subsequent reaction with 1 equiv of the adequate aldehyde provided the 1,4-disubstituted 2-aza-1,3-butadienes **3** in yields ranging from 90 to 95% (Scheme 1).

Scheme 1. Preparation of 2-Aza-1,3-butadiene Derivatives



All the synthesized dyads displayed UV−vis absorption spectra that extended into the UV−vis region, with diagnostically important bands at wavelengths longer than 300 nm. In acetonitrile or acetonitrile−water as solvents, the typical structured pattern of the parent anthracene, characteristic of its lowest energy transition, was absent. However, upon acidification of the solutions of compound **3a** the anthracene-like spectrum was clearly observable. This was not the case for compound **3c**, under the same acidic conditions, where the shape and position of the bands were also strongly modified.

In view of the influence of protonation on the UV−vis absorption properties, the fluorescence spectra were recorded for solutions of the different compounds, after addition of acid or base in variable amounts. The emission spectra obtained showed a weak intensity and low quantum yield values ($\phi = 0.042-0.008$). However, an important observation was made during our initial experiments: the presence of water was critical to achieve the desired fluorescence enhancement. Thus, upon addition of 1 equiv of HBF_4 to a solution of **3c** in acetonitrile, a modest enhancement of the emission intensity was observed (2-fold), whereas in the presence of water this effect was more remarkable (10-fold). So, the acetonitrile/water (70:30) mixture was the solvent of choice. These results are shown in Table 1.

Table 1. Effect of pH on the Relative Fluorescence Intensity of **3** in the Presence of Li^+ Cation[a]

	pH = 7		pH = 5		pH = 3	
compound[b]	I_H/I_0	I_{Li^+}/I_H	I_H/I_0	I_{Li^+}/I_H	I_H/I_0	I_{Li^+}/I_H
3a	1	1	1	1	3.5	1
3b	1	1	1.4	1	nd	1
3c	1	1	1.5	7.3	11	1

[a] Added as its perchlorate salt. [b] Concentration of **3a**−**c** and Li^+: 2.5×10^{-5} M.

Following the general trend, the emission intensities increased with decreasing pH.[6a] This effect was already observable at moderate acidities, reaching its maximum at pH ca. 3. The shapes of the fluorescence spectra did not change significantly within the employed pH range except in the case of **3b**, which underwent hydrolysis during the measurements. This process was easily detectable through the appearance of a broad and structureless band, shifted to the red (λ_{max} ca. 520 nm), characteristic of anthraldehyde.

It is worth mentioning that the structurally related compound 1-(9-anthryl)-4-ferrocenyl-2-aza-1-butene **4**, prepared by condensation of 9-anthraldehyde with β-ferrocenylethylamine,[9] exhibited the same behavior as **3b** when it was treated under the above-mentioned acidic conditions.

As stated above, the main goal of the present work was to explore the possibility of developing fluorescent sensors capable of achieving a selective recognition of Li^+ cations under an aqueous environment. As shown in Table 1, the presence of this cation produced a remarkable fluorescence enhancement (I_{Li+}/I_{H+}) for compound **3c** at pH = 5 (Figure

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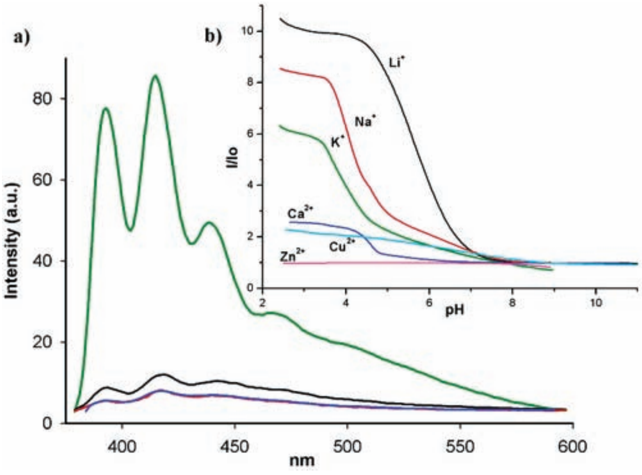

Figure 1. (a) Fluorescence spectra of **3c** (2.5×10^{-5} M, in CH_3CN/H_2O, 70/30) at: (i) pH = 7 (red), (ii) pH = 5 (black), (iii) pH = 7 in the presence of Li^+ (blue), and (iv) pH = 5 in the presence of Li^+ (green). (b) Changes in the relative intensities of the fluorescence spectra of **3c** (excitation wavelength 370 nm) with the pH, upon addition of Li^+, Na^+, K^+, Ca^{2+}, Cu^{2+}, and Zn^{2+} cations (2.5×10^{-5} M) as perchlorate salts.

1a). Interestingly the response was much higher for Li^+ than for other alkaline cations such as Na^+ or K^+ (Figure 1b). The difference was even more clear when the comparison was done with divalent cations including Ca^{2+}, Cu^{2+}, or Zn^{2+} (Figure 1b). When Figure 1b is examined, it becomes evident that the best opportunities for selective Li^+ sensing by means of compound **3c** have to be developed in a narrow pH window, centered at pH = 5.

Since the fluorescence emission of **3c** at pH = 5 is highly dependent on the Li^+ concentration and no other significant spectral changes were seen in the emission spectra, e.g., no changes were seen in the λ_{max} and no excimer emission was observed at longer wavelengths, one can thus conclude that **3c** is behaving like an ideal sensor. Interestingly, it is well stablished that nitrogen functionalities show fluorescence quenching because of the interaction between the lone-pair electron of nitrogen and the fluorophore π-system, which disappears upon protonation or coordination of the receptor molecule.[1d,10] However, it is rather remarkable that there have been no reports on this special effect in the case of 2-azadiene bridges.

From the fluorescence titration experiments, the association constant was calculated as $K_{as} = 11.757\ (\pm 0.019)\ M^{-1}$, and the titration profile obtained by plotting the fluorescence intensity values (excitation wavelength 370 nm) versus the ratio $[Li^+]/[\mathbf{3c}]$ indicates the formation of an adduct with an apparent 1:1 stoichiometry (Figure 1, Supporting Information).

Information about the interaction of **3c** with Li^+ has also been obtained by performing UV−vis and ^1H NMR measurements on solutions of **3c** at pH = 5 and in the presence of increasing amounts of Li^+.

The UV−vis spectrum of **3c** at pH = 5 was found to be identical to that of the free ligand; however, it was substantially affected by the Li^+ recognition. Thus, after addition of 1 equiv of Li^+, the low-energy (LE) absorption band at 414 nm ($\epsilon = 6173\ M^{-1}\ cm^{-1}$), produced by a metal-to-ligand charge transfer (MLCT) process, was blue-shifted to 383 nm ($\epsilon = 3255\ M^{-1}\ cm^{-1}$) and the absorption intensity decreased significantly. In addition to this fact, the high-energy (HE) absorption band at 317 nm ($\epsilon = 5602\ M^{-1}\ cm^{-1}$), assigned to a localized $\pi-\pi^*$ excitation due to the presence of the azadiene bridge, disappeared (Figure 2, Supporting Information).

From a ^1H NMR spectroscopic analysis it was possible to obtain additional information about the coordination of the Li^+ by ligand **3c** at pH = 5. The ^1H NMR spectra were recorded in CD_3CN/D_2O (70/30) (see Supporting Information). The spectrum of free ligand **3c** shows the typical pattern of signals corresponding to the monosubstituted ferrocene and anthracene units as well as those corresponding to the (*E*,*E*)-2-aza-1,3-butadiene bridge. While the pattern due to the monosubstituted ferrocene unit does not change upon addition of H^+ (HBF_4) to the CD_3CN/D_2O (70/30) solution until pH = 5, the following significant changes are evidenced in the other regions of the spectrum: (i) the iminic proton (9.50 ppm) moves to downfield (11.43 ppm); (ii) the N−C*H*═CH moves from $\delta = 6.87$ (doublet) to the multiplet arising at 7.53−7.59 ppm, which also includes 4 H of the aromatic ring; (iii) the CH═C*H*−Fc moves from 7.50 (doublet) to 7.69 ppm; (iv) in general, all signals corresponding to the 9-anthryl unit are also slightly displaced ($\Delta\delta = 0.1-0.2$ ppm) to downfield. From the magnitude of these observed shifts, it can be surmised that the protonation exerts a more powerful deshielding effect on the 2-aza-1,3-butadiene bridge than on the anthracene or ferrocene units (Figure 3, Supporting Information).

Interestingly, addition of $LiClO_4$ to the previously protonated ligand $\mathbf{3c}\cdot H^+$ (pH = 5) gives rise to a new species that only shows a significant change in the pattern of the ferrocene unit, with respect to that of the protonated ligand $\mathbf{3c}\cdot H^+$. Indeed, a close inspection of the Cp protons in the ferrocene spectral region showed the existence of a multiplet at $\delta = 3.93-4.33$ ppm, slightly upfield shifted, which includes the 9H present in the ferrocene subunit. In contrast, signals attributable both to the bridge and to the 9-anthryl unit do not change their chemical shift upon addition of Li^+ (Figure 3, Supporting Information). The most likely explanation for the above-mentioned upfield shift is that the tilt angle between the Cp rings of the ferrocene subunit should increase upon complexation with the Li^+ cation. Additionally, it is worth underlying that addition of Na_2CO_3 to the $\mathbf{3c}\cdot H^+\cdot Li^+$ complex gives rise to the same ^1H NMR spectrum as that obtained for the free ligand **3c**.

It is also important to underline that when these experiments were carried out in $CDCl_3$ or CD_3CN but in the absence of added water, the addition of Li^+ to the ligand

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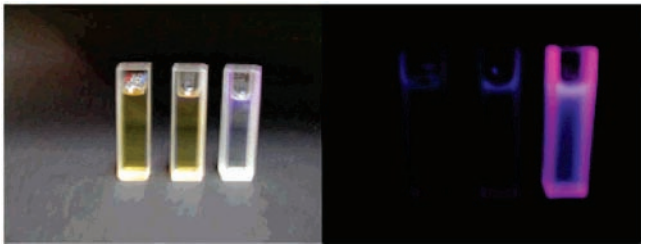

Figure 2. Visual features observed in the acetonitrile/water (70/30) solutions of **3c**. Left, absorption; right, emission (at pH = 7, at pH = 5, and at pH = 5 in the presence of Li^+).

did not promote any change in the ^1H NMR spectrum of the protonated ligand.

The above results clearly show that the fluorescence enhancement observed in the presence of Li^+ (Figure 2) must be associated with a synergic participation of protons, water, the 2-aza-1,3-butadiene bridge, and the ferrocene unit.

We believe that protonation takes place on the N atom of the bridge, whereas lithium complexation occurs through the ferrocene moiety; the resulting complex is stabilized by water molecules via hydrogen bonds. Indeed, our preliminary ab initio DFT calculations[11] showed an absolute minimum corresponding to the above proposed structural features (Figure 3) with the lithium cation directly bonded to the ferrocenyl Fe atom[12] (2.46 Å) and solvated by a water molecule ($d_{Li\cdots O}$ = 1.76 Å, $angle_{Fe-Li\cdots O}$ = 172.7°). The latter is bonded to a second water molecule ($d_{OH\cdots O}$ = 1.60 Å, $angle_{O-H\cdots O}$ = 171.8°) through a hydrogen bond, which in turn interacts both with the azadiene protonated N atom ($d_{NH+\cdots O}$ = 1.84 Å, $angle_{O-H\cdots O}$ = 167.2°) and, more weakly, with C1 at the anthryl ring ($d_{OH\cdots C}$ = 2.25 Å, $angle_{O-H\cdots C}$ = 127.1°). In fact, there are literature precedents for M−Fe bonds in several complexes of transition metal ions in which a ferrocenyl group acts as a donor in the coordination sphere of the metal ion.[13] In this context, it has been reported that ferrocene behaves as a moderately strong base toward the Li^+ cation to form complexes.[14] Recently, a [1.1]diborataferrocenophane·Li^+ has been isolated and characterized:[15] the Li^+ cation is located inside the ferrocenophane cavity and a contribution from bonding Fe····Li interactions to the stability of the complex is considered.

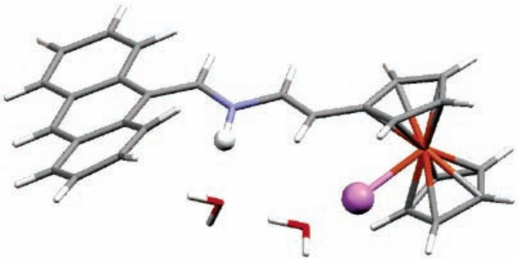

Figure 3. Calculated (B3LYP/3-21G*) structure of **3c**·H^+·Li^+·$2H_2O$.

We have demonstrated that by using a structurally simple motif, whereby an anthracene ring and a ferrocene moiety are linked by a 2-aza-1,3-butadiene bridge, highly selective Li^+ sensing can be achieved in aqueous acetonitrile.

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Supporting Information Available: Experimental procedures and full characterization for compounds **2**−**4**, comparison of the UV−vis data for the neutral and protonated compounds, and figures showing the changes in the fluorescence emission spectra, UV−vis spectra, and ^1H NMR spectra of **3c**, at pH = 5, upon addition of increasing amounts of Li^+. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Calculations were performed with the Spartan'02 package [*Spartan'02* (build 119); Wavefunction, Inc.: Irving, CA] at the standard B3LYP/3-21G* level.

(12) We assume that this relatively rigid structure is stable and maintained in aqueous phase due to the bridging role of the two water molecules system. Indeed, only one water molecule was found not to be enough for such stabilization and when calculations were run without water molecules (gas phase) at the same level, a related structure was obtained with the lithium atom more strongly Fe-bonded (2.40 Å) and in a *transoid* conformation relative to the azadienyl substituent. Nevertheless, the absolute minimum (ca. 13.7 kcal/mol below in the potential energy surface) was found to be the isomer with the lithium cation η^5-coordinated by the ferrocenyl unsubstituted Cp ring (1.91 Å from the ring centroid), in agreement with previous calculations reported for the lithium basicity of the parent ferrocene [ref 12b].

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