

A Prototype for the Chemosensing of Ba²⁺ Based on Self-Assembling Fluorescence Enhancement

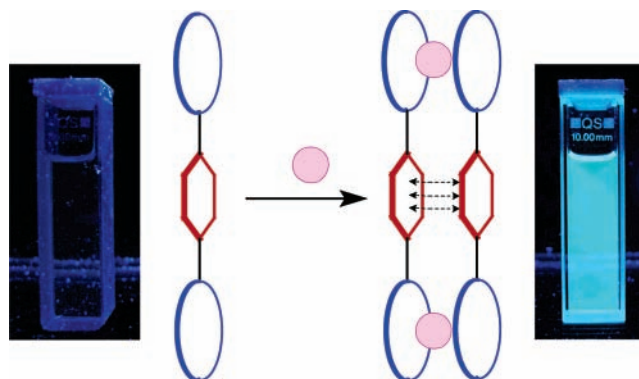
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ABSTRACT



Barium ion can be revealed at the micromolar concentration level by the blue-green fluorescence which arises upon the self-assembling process involving the metal ion and a novel bis-15-crown-5-naphthalenediimide derivative.

The design of fluorescent chemosensors for the detection of specific analytes has attracted a growing interest during the last two decades.¹ Considerable attention has been devoted to the development of selective sensors for alkali and alkali-earth cations since the in situ detection of such analytes is needed in different research areas (e.g., environmental and life sciences). For example, selective fluorescent sensors for cesium were studied aimed at the detection of ¹³⁷Cs⁺ in nuclear reactor wastes.^{2,3} The detection of intracellular Ca²⁺

is performed worldwide by employing the fluorescent chemosensors developed by Tsien.⁴

On the other hand, only a few examples of selective fluorescent chemosensors for Ba²⁺ have been reported,⁵ although the problems related to its toxicity⁶ should encourage the development of new detection systems for this analyte. Therefore, the design of novel and specific chemosensors for barium seems to be particularly desirable.

Owing to the well-known ability of crown ethers to host s-block metals,⁷ many fluorescent chemosensors designed in recent years for alkali and alkali earth ions contain at least one crown ether moiety (or a related derivative) which

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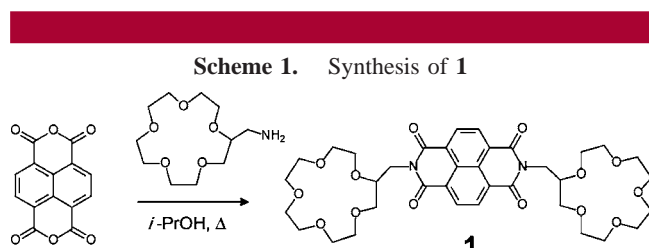
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behaves as a “recognition subunit” connected to one or more fluorophores.^{1a,8} In these systems, the output signal following the crown/cation interaction involves a change in the emission properties of the fluorophore(s) and is often related to a PET (photoinduced electron transfer) process.⁹ Other examples involving different mechanisms, e.g., photoinduced energy transfer,¹⁰ excimer or exciplex formation,¹¹ conformational change,¹² and proton transfer,¹³ have also been reported.

Recently, the fluorescence enhancement observed in the selective sensing of K^+ and Cs^+ by bis-15-crown-5 and bis-18-crown-6 systems, respectively, has been described as self-assembling fluorescence enhancement (SAFE) since this effect is closely related to the formation of “sandwich” structures in solution.^{2,14}

In this paper, we report the behavior of the bis-15-crown-5-naphthalenediimide **1**, which displays a strong fluorescence enhancement upon interaction with Ba^{2+} . This selective enhancement is ascribed to a specific self-assembling process, i.e., the formation of [2 + 2] species in which an intramolecular excimer is allowed to form.

The bis-crown derivative **1** was prepared by a direct reaction involving aminomethyl-15-crown-5 and 1,8:4,5-naphthalene dianhydride in isopropyl alcohol (Scheme 1),



according to a synthetic route previously reported for other functionalized naphthalenediimides.¹⁵

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In acetonitrile solution, system **1** shows the typical absorption and emission spectra expected for naphthalenediimide derivatives (relative absorption maxima at 235, 357, and 377 nm, $\epsilon = 30\,470$, $19\,280$, and $23\,000\text{ cm}^{-1}\text{ M}^{-1}$, respectively; fluorescence maxima at 386 and 407 nm, $\Phi = 2.2 \times 10^{-3}$). The presence of the cyclic polyether moieties does not seem to induce any noticeable variation in both the absorption and the emission properties if compared to those reported for other N,N' -dialkyl-naphthalenediimides.¹⁶ On addition of $Ba(ClO_4)_2$, the absorption bands undergo a red-shift (by about 4 nm), an intensity decrease, and a general broadening. Titration experiments performed on MeCN solutions of the bis-crown derivative **1** with Ba^{2+} suggest the formation of an adduct according to a formal 1:1 stoichiometry (Figure 1).

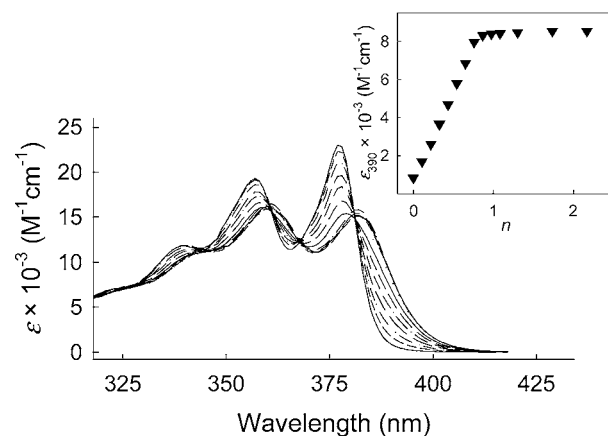


Figure 1. Absorption spectra recorded during the titration of **1** ($5 \times 10^{-4}\text{ M}$ in MeCN) with $Ba(ClO_4)_2$ in MeCN. Titration profile is reported in the inset ($n = \text{equiv of } Ba^{2+}/\text{equiv of } \mathbf{1}$).

The addition of the metal ion strongly affects the emission properties of the naphthalenediimide derivative: in the presence of Ba^{2+} , a MeCN solution of the very poorly emissive **1** displays a light blue fluorescence when exposed to a UV lamp or even to sunlight. A spectrofluorimetric titration experiment performed on a solution of **1** (10^{-6} M in MeCN) with $Ba(ClO_4)_2$ shows the development of a broad band centered at 440 nm which should be responsible for the light blue fluorescence (Figure 2). An enhancement factor of 35 is observed after the addition of an equimolar amount of Ba^{2+} . The corresponding titration curve (ratio of fluorescence intensities, I_f/I_0 , vs number of equivalents, n) confirms

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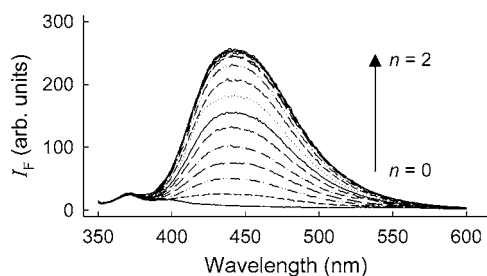


Figure 2. Emission spectra recorded during the titration of **1** (10^{-6} M in MeCN) with $\text{Ba}(\text{ClO}_4)_2$ in MeCN; $\lambda_{\text{exc}} = 335$ nm. (I_{F} = fluorescence intensity; n = equiv of Ba^{2+} /equiv of **1**).

that an apparent 1:1 stoichiometry governs the bis-crown/barium interaction (Figure 3). Similar titration profiles have

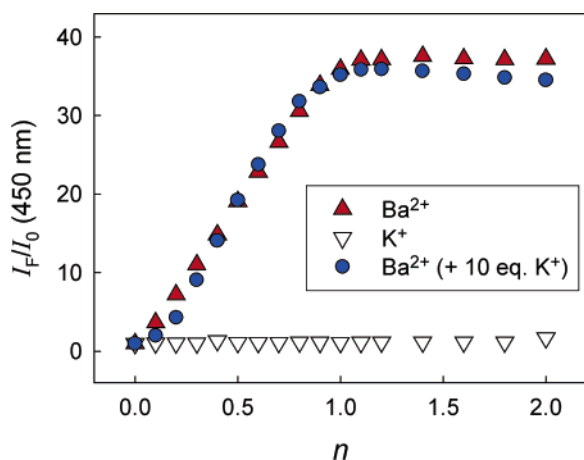


Figure 3. Spectrofluorimetric titration plots of **1** (10^{-6} M in MeCN, $\lambda_{\text{exc}} = 335$ nm) with Ba^{2+} , K^+ , and Ba^{2+} in the presence of excess K^+ (10 equiv).

also been obtained at higher concentration values (10^{-6} – 10^{-4} M) of **1**. A completely comparable behavior is also observed if BaCl_2 is used instead of BaClO_4 , suggesting that no significant counterion effect is active.

On the basis of the known ability of 15-crown-5 to interact with Ba^{2+} according to a sandwich-like mode,¹⁷ the results obtained from both spectrophotometric and spectrofluorimetric titration experiments can be explained by the formation of a [2 + 2] adduct, in which each Ba^{2+} ion coordinates to two 15-crown-5 subunits belonging to different molecules of **1**, even if the formation of other oligonuclear species (e.g., [3 + 3] or [4 + 4] adducts) in principle cannot be ruled out.

ESI-MS experiments were performed in order to assess more clearly the identity of the complex species formed in solution by the bis-crown compound and Ba^{2+} . The ESI-

MS spectrum of an acetonitrile solution containing equimolar amounts of $\text{Ba}(\text{ClO}_4)_2$ and **1** (10^{-4} M) shows a base peak at m/z 434.2 (corresponding to $\{[\text{Ba}_2(\mathbf{1})_2]\}^{4+}$) and two peaks of lower intensity, respectively, at 611.8 ($\{[\text{Ba}_2(\mathbf{1})_2]\text{ClO}_4\}^{3+}$) and at 967.1 ($\{[\text{Ba}_2(\mathbf{1})_2](\text{ClO}_4)_2\}^{2+}$), confirming the [2 + 2] nature of the adduct (Figure 4). The peak corre-

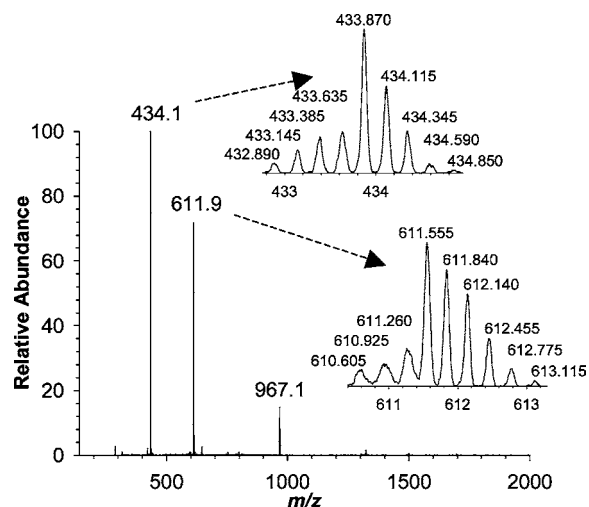


Figure 4. ESI-MS spectrum of an equimolar mixture of **1** and $\text{Ba}(\text{ClO}_4)_2$ in acetonitrile (10^{-4} M). The high-resolution spectra corresponding to the peaks at 434.1 and 611.9, reported in the insets, show typical peak separations (about 0.25 and 0.33, respectively) which are expected for the tri- and tetrapositive ions, $\{[\text{Ba}_2(\mathbf{1})_2]\text{ClO}_4\}^{3+}$ and $[\text{Ba}_2(\mathbf{1})_2]^{4+}$, respectively.

sponding to the $\{[\text{Ba}_2(\mathbf{1})_2](\text{ClO}_4)_3\}^+$ species, expected at $m/z = 2034.55$, cannot be detected since this value exceeds the limit of the ESI-MS apparatus ($m/z = 2000$).

The strong emission band which is observed in the spectrum of **1** in the presence of barium can be ascribed to an excimeric species which originates from the interaction between the two naphthalenediimide moieties facing each other in the [2 + 2] adduct. The formation of intramolecular excimers in self-assembled species involving naphthalenediimide derivatives has been previously reported.^{15a}

The changes (bathochromic shift and hypochromic effect) observed in the electronic spectrum of **1** after the addition of barium might suggest that a ground-state interaction occurs.¹⁸ However, further investigations are needed in order to assess the real nature of the excimer, whether “static” or “dynamic”.¹⁹

The fluorescence lifetime (τ_{f}), measured by the time-correlated single-photon counting technique, has a distinctly higher value (3.24 ± 0.02 ns, monitored at 500 nm) than that of the locally excited species (<1.0 ns, monitored at 375 nm), which is normally observed upon excitation of **1** (or other related naphthalenediimide compounds)¹⁶ and is consistent with the hypothesized excimeric nature of the broad emission band displayed by the $[\text{Ba}_2(\mathbf{1})_2]^{4+}$ adduct.

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The emissive behavior of **1** was also studied in the presence of other *s*-block metal ions in order to check possible interferences in the self-assembling (and sensing) process. Spectrofluorimetric titration experiments performed on MeCN solutions of the bis-crown compound **1** (10^{-6} M) with different cations (Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Mg^{2+} , Ca^{2+} , Sr^{2+}) showed that they induce only slight or even undetectable changes on the emission properties exhibited by **1**. In particular, no variation in the region of the excimeric emission was observed under these experimental conditions, as shown, in the case of potassium, by the titration plot reported in Figure 3. Furthermore, the response of system **1** toward Ba^{2+} is scarcely affected even in the presence of an excess of other alkali cations. Figure 3 shows that the titration profiles obtained by titrating system **1** with Ba^{2+} in the presence and in the absence of K^+ (10 equiv) are practically superimposable.

Particular attention was devoted to the behavior of **1** in the presence of potassium which is expected to form [2 + 2] adducts, analogously to barium. In fact, K^+ and Ba^{2+} have similar atomic radii and are both known to form sandwich-like complexes with 15-crown-5 derivatives.^{17,20} At any rate, the absence of an “excimer” band in the emission spectrum taken in the presence of equimolecular amounts of **1** and potassium (10^{-6} M) could be explained as follows: the [2 + 2] species formed by K^+ should be reasonably less stable than that formed by Ba^{2+} , owing to the different positive charges of the cations.²¹ As a consequence of its lower stability, the $[\text{K}_2(\mathbf{1})_2]^{4+}$ complex could form in solution but not in a detectable amount at a low concentration level (10^{-6} M) of the bis-crown derivative. Such a hypothesis is confirmed by a spectrofluorimetric titration experiment performed by adding KPF_6 to a more concentrated (5×10^{-4} M) solution of **1** in MeCN: in this case, the broad band at 440 nm is observed, accounting for the formation of the [2 + 2] adduct and the corresponding intramolecular excimer.

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(21) Preliminary spectrophotometric studies for the determination of the stability constants values of the [2 + 2] adducts gave the following results: $\log \beta = 12.55 \pm 0.59$ (for Ba^{2+}) and $\log \beta = 10.14 \pm 0.07$ (for K^+).

In summary, the novel bis-crown compound **1** is able to reveal the presence of barium in solution at low concentration values ($\leq 10^{-6}$ M) owing to a self-assembling fluorescence enhancement (SAFE) process. In fact, the interaction of the poorly fluorescent **1** with Ba^{2+} affords a [2 + 2] self-assembled system in which the formation of an emissive intramolecular excimer (broad emission band at 440 nm) is allowed by the favorable spatial arrangement of the two naphthalenediimide subunits. The self-assembling process is not affected by other alkali or alkali-earth cations at low concentration of the bis-crown ($\sim 10^{-6}$ M), even if an interference by potassium could be expected at a higher concentration of **1** ($\geq 10^{-4}$ M).

Therefore, the naphthalenediimide derivative **1** can be considered a very interesting prototype of fluorescent chemosensor for Ba^{2+} . Although a direct application for the detection of barium in organic solvents (e.g., MeCN) is not needed at the moment, this work represents a first step in the design of molecular sensors (based on the SAFE process) aiming to detect Ba^{2+} in different media (for example in water/organic solvent mixtures and/or aqueous micellar solutions⁵). At any rate, a fluorescent sensor developed from the prototype **1** could offer some advantages such as: (i) its coordinating behavior should not be affected by pH variations since it does not contain basic or acidic groups (e.g., amino nitrogens); (ii) the SAFE mechanism is operative only in the presence of the target analyte and the fluorescence cannot be switched on by other species in solution, such as, for instance, H^+ which influences the behavior of several PET-based fluorosensors.

Finally, the SAFE approach could be applied to the design of a variety of chemosensors by properly changing the fluorophore or ligand subunit. Further work in this direction is in progress.

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Supporting Information Available: Synthesis of **1**; experimental details for spectrophotometric, spectrofluorimetric, and ESI-MS determinations. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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