

A dipyrenyl calixazacrown as a selective sensor for Pb²⁺

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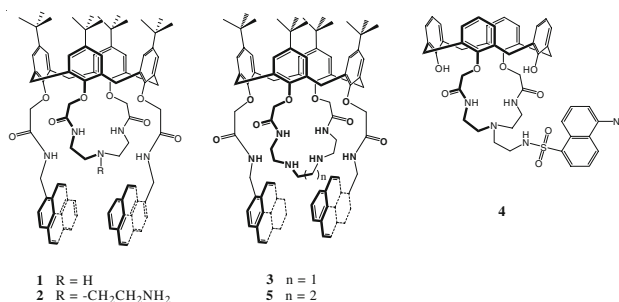
Abstract New fluorogenic calixazacrown (**5**) bearing two pyrene amide pendent groups has been synthesized. Based on ratiometric changes of monomer and excimer emissions, **5** has been found to act as a selective sensor for Pb²⁺ ion due to conformational change upon chelation of Pb²⁺ within 1:1 complex.

Keywords Calixarenes · Fluorescence · Detection · Complexation · Excimer · Lead

Introduction

Since the preliminary account on fluoroionophores by Löhr and Vögtle [1], much attention has been paid during the last decade to molecular sensors able to detect and signal the presence of specific substrates [2–18]. Molecular sensors combine the properties of supramolecular receptors, as they specifically recognize a proper guest among various

ones, with the ability to produce a measurable signal. Optical signals based on changes of fluorescence are the most frequently used because of simple application. The combination of molecular recognition with a fluorescent reporter permits the presence of the guest to be observed and quantified. The term supramolecular analytical chemistry has recently been coined to describe the application of molecular sensors to analytical chemistry [19]. Pb²⁺ ion can affect almost every organ and system in the human body, causing various symptoms such as anemia, kidney damage, a disorder of the blood, memory loss, muscle paralysis, and mental retardation by lead poisoning [3, 25].



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In precedent papers, we have described the synthesis and fluorescent properties of fluorogenic dipyrenyl calix[4]azacrowns chemosensors **1-3** [20–22]. Compounds **1-3** are composed of a *p*-*tert*-butylcalix[4]arene unit in the cone conformation, an azacrown unit bridging two opposite *o*-positions of the calix, and two amido pyrene groups on the remaining *o*-positions. The azacrown unit acts as a metal chelating part while the pyrenes act as signalling elements.

The binding properties of **1-3** were investigated by fluorescence toward metal ions (Li⁺, Na⁺, K⁺, Cs⁺, Pb²⁺, Co²⁺, Ag⁺, Mg²⁺, Ca²⁺, Zn²⁺) in acetonitrile.

Calix[4]triazacrown-5 (**1**) revealed an excimer emission at 448 nm when excited at 343 nm. Pb^{2+} and Co^{2+} , known as quenching metal ions, quenched the fluorescence of **1** both in monomer and particularly in the excimer bands [20]. This was attributed to a combination of heavy metal ion effect, reverse-PET and conformational changes. $^1\text{H-NMR}$ showed that Pb^{2+} is located in the triazacrown-5 with the turning of the amido carbonyl groups inside the azacrown loop to bind the metal [20]. Calix[4]arene (**2**), corresponding to **1** with a pendent ethylene amine $-\text{CH}_2\text{CH}_2\text{NH}_2$ attached on the central nitrogen atom of the triazacrown-5 displayed a relative weak emission due to a PET process between the NH_2 function and the pyrenes [21]. Addition of metal ions reduced the PET due to interactions of NH_2 with the included metal ions. In contrast, both monomer and excimer emissions were observed to increase due to a CHEF effect and unchanged conformation with the other cations. As for **1**, Pb^{2+} was shown to be encapsulated in the azacrown loop of **2** with the carbonyl functions pointing inside the cavity and with the participation of the $-\text{CH}_2\text{CH}_2\text{NH}_2$ arm [21]. In a further paper we investigated calix[4]tetraazacrown-6 (**3**) having a larger crown loop due to the presence of an additional $-\text{CH}_2\text{CH}_2\text{NH}-$ unit and showing a selectivity for Mg^{2+} [22]. The pyrene monomer emission increased while the excimer emission declined in a ratiometric manner. $^1\text{H-NMR}$ showed a ratiometric change due to the conformational changes of the pyrenes during the chelation of Mg^{2+} by the amide functions. In all cases **1-3** were shown to form 1:1 complexes. As to compare with **2** the corresponding calix[4]azacrown (**4**) without amido pyrenes (replaced by OH) and functionalized by $-\text{CH}_2\text{CH}_2\text{NH-dansyl}$ showed selectivity for Hg^{2+} in acetonitrile–water (4:1, v/v) [23]. The formation of a 1:1 complex was described as a four-coordinate mode in which three amide nitrogens and one amine nitrogen constructed nearly a tetrahedron, whose center is occupied by Hg^{2+} [23].

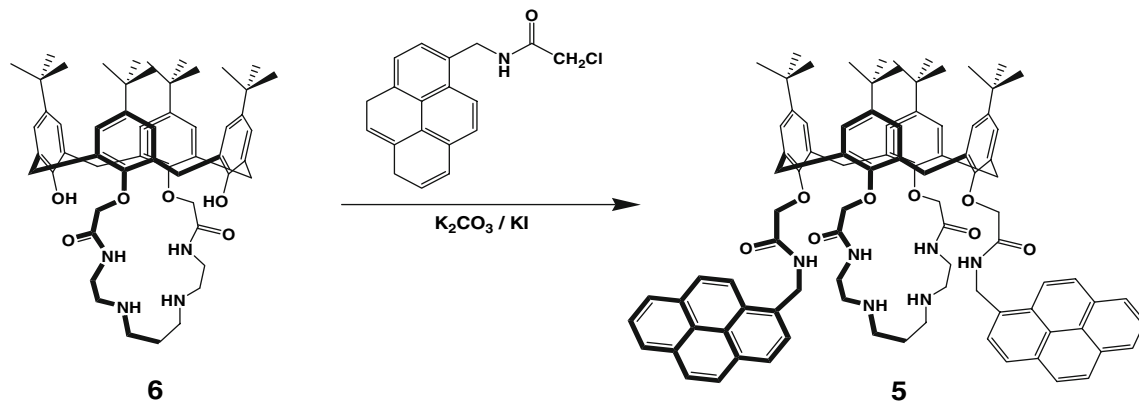
In order to learn more in detail on factors involved in the selective detection (ion-crown size-complementarity and/

or quenching of fluorescence by the metal ion) we decided to investigate dipyranyl calix[4]tetraazacrown-7 (**5**) corresponding to dipyranyl calix[4]tetraazacrown-6 (**3**) in which the central ethylene $-\text{HNCH}_2\text{CH}_2\text{NH}-$ unit is replaced by a propylene $-\text{HNCH}_2\text{CH}_2\text{CH}_2\text{NH}-$.

Experimental procedure

Uncorrected melting points (Mps), Büchi 500. ^1H NMR spectrum, Varian 300 MHz (δ in ppm from TMS, J in Hz). FAB MS mass spectrum, JEOL-JMS-HX 110A/110A High Resolution Tandem Mass Spectrometry in Seoul National University (Korea). The reaction was run under a nitrogen atmosphere. SiO_2 (Geduran 1.11567) was used for column chromatography. All reagents and solvents were commercial and used without further purification. Fluorescence spectra were recorded with an RF-5301PC spectrophotometer. Stock solutions (1.00 mM) of the metal perchlorate salts were prepared in CH_3CN . Stock solutions of **5** (0.05 mM) were prepared in CH_3CN . For all measurements, excitation was at 340 nm with excitation and emission slit widths at 3.0 nm. Fluorescence titration experiments were performed using 5.0 μM solutions of **5** in CH_3CN and various concentrations of metal perchlorate CH_3CN .

Synthesis of **5** is similar to the synthesis of **3** (Scheme 1) [22]. Thus, *p-tert*-Butylcalix[4]tetraazacrown-7 (**6**) [24] was reacted with 2.5 equiv of *N*-(1-pyrenemethyl)chloroacetamide [25] and 1 equiv of K_2CO_3 as base and an excess of KI as catalyst with a 24 h-reflux in CH_3CN . After the work-up, elution of the residue on silica gel using 95:5 $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ as eluent gave dipyranyl calix[4]tetraazacrown-7 (**5**) (38% yield). Calixarene **5** was fully characterized by $^1\text{H-NMR}$, MALDI-TOF mass spectrometry, and elemental analysis. The conservation of the fixed cone conformation of *p-tert*-butyl calix[4]tetraazacrown-7 (**6**) was confirmed by the presence of doublets of ArCH_2Ar



Scheme 1 Synthesis of dipyranyl calix[4]tetraazacrown-7 (**5**)

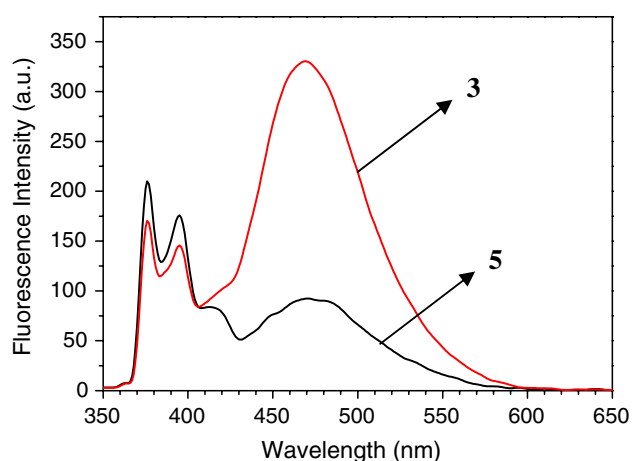


Fig. 1 Fluorescence spectra of **3** and **5** (5.0 μM) in CH_3CN . The excitation wavelength is 340 nm

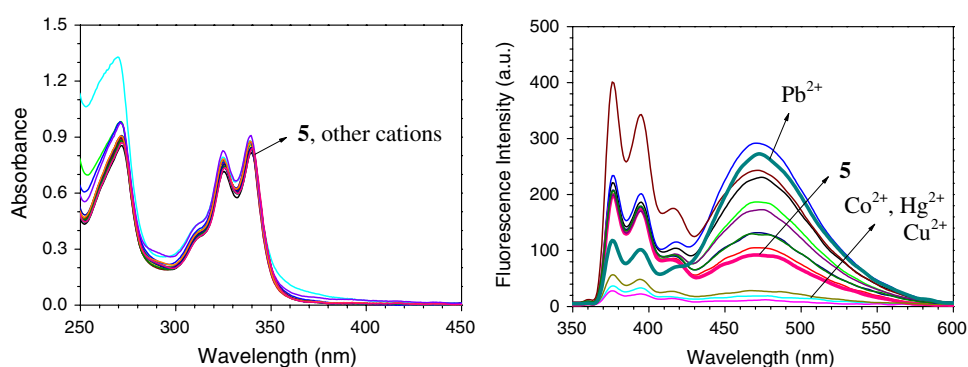
protons at ~ 3 and 4 ppm. The presence of amido functions was deduced from the distinct triplet at 7.05 ppm and a broad singlet at 6.19 ppm.

All fluorescence experiments were performed in CH_3CN . On excitation at 340 nm, the maximum absorption wavelength of the pyrene of **5** displays both monomer and excimer emission at 375 and 468 nm respectively. Notably, compared with **3**, pyrenes of **5** show weak excimer emission. It is proposed that unlike in **3**, the formation of the excimer emission in **5** induced by intramolecular π - π^* interaction between two facing pyrene groups is rather difficult mainly due to the steric bulkiness of the propylene unit (Fig. 1).

Results and discussion

The binding property of **5** toward metal ions was investigated by monitoring the absorption and fluorescence changes upon addition of the perchlorate salt of a wide range of cations including Li^+ , Na^+ , K^+ , Ag^+ , Mg^{2+} , Ca^{2+} , Co^{2+} , Ba^{2+} , Sr^{2+} , Cu^{2+} , Hg^{2+} and Pb^{2+} in CH_3CN .

Fig. 2 UV/Vis and Fluorescence spectra of **5** upon addition of ClO_4^- salt of Li^+ , Na^+ , K^+ , Ag^+ , Mg^{2+} , Ca^{2+} , Co^{2+} , Ba^{2+} , Sr^{2+} , Cu^{2+} , Hg^{2+} and Pb^{2+} (50 equiv) in CH_3CN (UV: 20 μM , Fluorescence: 5.0 μM)



The UV and fluorescence changes are depicted in Fig. 2. Compound **5** shows two characteristic absorption bands centred at 326 and 340 nm corresponding to the pyrene units. No considerable band shift was observed upon addition of other metal cations (50 equiv).

Addition of Pb^{2+} ion to the CH_3CN solution of **5** induced a marked ratiometric change where the monomer emission declines while its excimer emission increases. It is supposed that the ratiometric change of **5** is due to conformational changes of the two pyrenyl moieties during Pb^{2+} complexation [26]. In addition, we observed that when other heavy metal ions such as Hg^{2+} , Co^{2+} and Cu^{2+} were added to the solution of **5**, both monomer and excimer emissions were quenched because of the heavy metal ion effects.

Figure 3 shows the titration profile of **5** (5.0 μM) upon the addition of Pb^{2+} ion. When the concentration of Pb^{2+} is increased up to 20 μM , intensities of the monomer and excimer emissions decrease and increase by 2-fold, respectively at the same time. The association constant (K_a) of **5** was thus determined to be $1.39 \times 10^5 \text{ M}^{-1}$ for the Pb^{2+} ion.

To further prove the complexation of **5** with Pb^{2+} , MALDI-TOF spectroscopy was taken. It was observed the relevant peaks at $m/z = 1431.9678$ and $m/z = 1637.9333$ corresponding to the free ligand **5** and the 1:1 complex 5-Pb^{2+} , respectively (Fig. 4).

To test a selectivity of **5** as a Pb^{2+} -selective fluorescence chemosensor, competition experiments were carried out. Compound **5** (5.0 μM) was treated with 50 equiv Pb^{2+} in the presence of other metal ions (50 equiv). As shown in Fig. 5, no interference in detection of Pb^{2+} was observed in the presence of Li^+ , Na^+ , K^+ , Ag^+ , Mg^{2+} , Ca^{2+} , Ba^{2+} and Sr^{2+} ions. However, the ratiometry of **5** is quite a bit interfered by the addition of Co^{2+} , Hg^{2+} , Cu^{2+} ions because of their heavy metal ion effects. Thus, it is notable that **5** can be at least used as a Pb^{2+} selective ratiometric fluorescent sensor in the presence of most of the alkali metal and alkaline earth metal cations, respectively (Fig. 5).

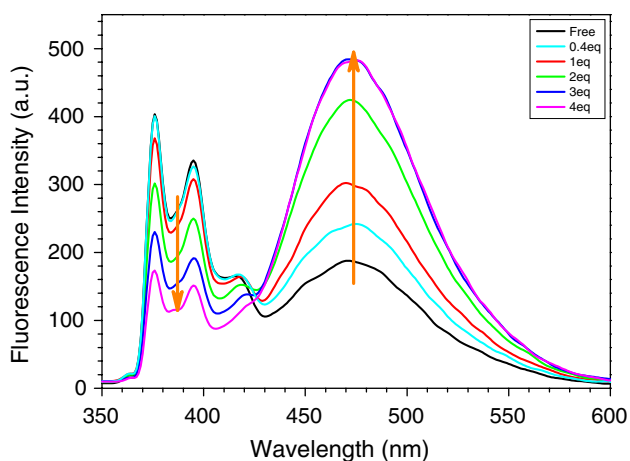


Fig. 3 Fluorescence spectra of **5** (5.0 μM) in CH_3CN upon addition of increasing concentrations of $\text{Pb}(\text{ClO}_4)_2$ (0, 0.4, 1.0, 2.0, 3.0, 4.0 equiv) with an excitation at 340 nm

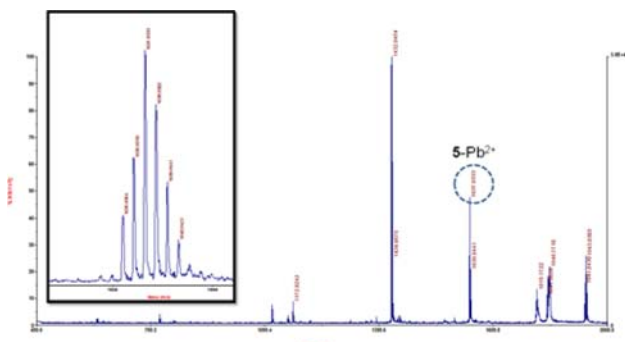


Fig. 4 MALDI TOF spectrum of **4-Pb**²⁺ in CD_3CN

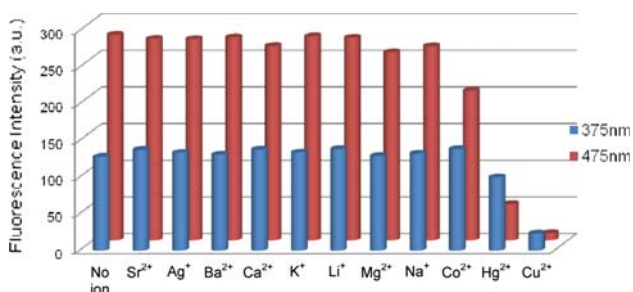


Fig. 5 Fluorescent intensity of **5** (5.0 μM) upon addition of 50 equiv Pb^{2+} in the presence of 50 equiv of other metal ions in CH_3CN at 375 nm (blue bar) and 475 nm (red bar)

Conclusions

New fluorogenic calixazacrown (**5**) bearing two pyrene amido groups has been synthesized and shows a selective for Pb^{2+} . When Pb^{2+} is bound to **5**, the pyrene monomer emission declined while the excimer emission increased in a ratiometric manner. This ratiometric change is attributable

to the conformational changes of the pyrenes during the chelation of Pb^{2+} to form a 1:1 complex. If one compares the selectivities data offered by chemosensors **1-5** one can see that the selectivity of the sensors is not defined by the molecular recognition of the receptor but is rather depending on the signal feed-back. This maybe due on the type of metals that is in action (quenching effect) and on the fluorescent state of the free receptor before complexation. Work is continuing in this direction by studying related receptors with various azacrown elements to determine which effect has to be taken into account.

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