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Pyrene-Linked Triazole-Modified Homooxacalix[3]arene: A Unique C_3 Symmetry Ratiometric Fluorescent Chemosensor for Pb^{2+}

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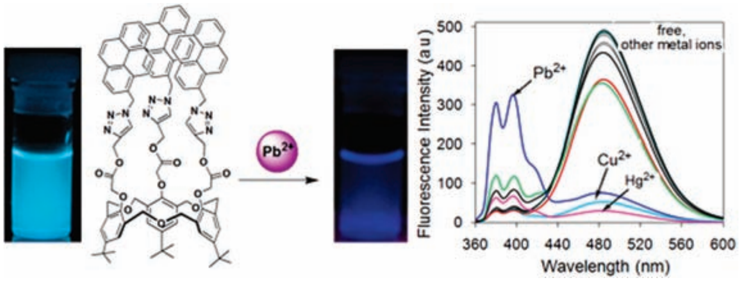
ABSTRACT



A new type of fluorescent chemosensor based on homooxacalix[3]arene was synthesized. The fluorescent sensor was highly selective for Pb^{2+} in comparison with other metal ions tested by enhancement of the monomer emission of pyrene. The C_3 symmetric structure of homooxacalix[3]arene has potential application in the development of a new ratiometric fluorescent chemosensor for heavy metal ions.

The Pb^{2+} ion is one of the most toxic heavy metal ions and is responsible for a range of adverse environmental and health problems. A variety of symptoms have been attributed to lead poisoning, including memory loss, anemia, muscle paralysis, and, particularly, mental retardation of children.[1] Consequently, the selective signaling of Pb^{2+} is a very important topic in relation to the detection and treatment of this toxic metal ion in chemical and biological systems.[2] Among these detection approaches for the Pb^{2+} ion, fluorescence spectroscopy is widely used because of its high sensitivity, simple application, and low cost. Calixarenes are ideal scaffolds or building blocks for the development of fluorescent receptors for molecular recognition via the incorporation of an appropriate sensory group. Therefore, many fluorescent chemosensors based on calixarenes, which show highly selective recognition of alkaline and alkaline-earth cations, have been synthesized.[3] However, fluorescent sensors for heavy metal ions, particularly ratiometric receptors for lead,[4] have remained rare up to now because these metal ions are known to quench fluorescence emission via enhanced spin−orbital coupling,[5] energy, or electron transfer.[6] Fluorescence quenching is not only disadvantageous for

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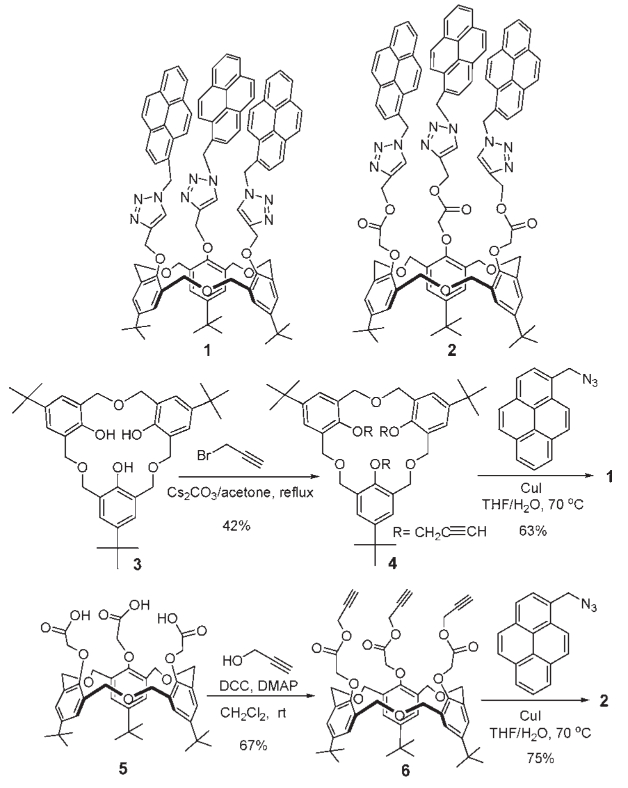
a high signal output during detection but is also undesirable for analytical purposes.[7] Thus, it is important that the recognition of Pb^{2+} by the chemosensor does not quench the fluorescence. On the other hand, homooxacalix[3]-arene, which has a basic C_3-symmetric cavity and is related to both calixarenes and crown ethers, has attracted supramolecular chemists to make receptors for metal cations,[8] ammonium cations,[9] and fullerene derivatives.[10]

Additionally, click chemistry has attracted considerable attention recently and has been applied in a wide range of fields[11] for its efficiency, regioselectivity, and compatibility with reaction conditions. For example, Chung and Kim et al. have incorporated triazole rings onto tailored calix[4]arene scaffolds as receptors and fluorescent sensors for metal ions.[12] Furthermore, it is well-known in coordination chemistry that the complexation of lead with a ligand containing at least three nitrogen donor atoms is favored by the activation of the inert pair on the Pb^{2+} ion, leading to a shortening of the Pb−N bond length and a much stronger covalent bonding.[13] Therefore, we hypothesized that suitably arranged functionalized ligand moieties containing nitrogen atoms attached to homooxacalix[3]arene should be a good receptor candidate for lead ions. Therefore, with this in mind, we have synthesized compounds **1** and **2** and studied their cation-binding affinity.

Scheme 1



The synthetic routes for fluorescent sensors **1** and **2** are described in Scheme 1. We first synthesized **4** with a 42% yield by the reaction of **3** and propargyl bromide in the presence Cs_2CO_3 in dry acetone solution. The ^1H NMR results suggested that compound **4** adopts a partial-cone structure (Figure S23). Previously, Shinkai et al. established that interconversion between conformers of **3**, which occurs by oxygen-through-the-annulus rotation, can be sterically allowed for methyl, ethyl, and propyl groups whereas it is inhibited for the butyl group.[14] However, the selective introduction of a propargyl group onto phenolic groups has not yet been accomplished. Thus, we first carried out the ^1H NMR titration experiment of **4** with n-$BuNH_3ClO_4$ in $CDCl_3/CD_3CN$ (10:1 v/v). The results indicated that the interconversion between the cone and partial-cone conformation also takes place with a propargyl moiety on compound **4** (Figure S1).

Most interestingly, the X-ray crystal structure of **4** (Figure 1) clearly revealed that there are two different conformations in the unit cell and that one exhibits a classical partial-cone structure (Figure 1a) while the other exhibits an intermediate from the partial-cone to cone structure (Figure 1b). Accordingly, fluorescent sensor **1** can be obtained from the reaction of **4** with 1-azidomethylpyrene under standard conditions for click chemistry with

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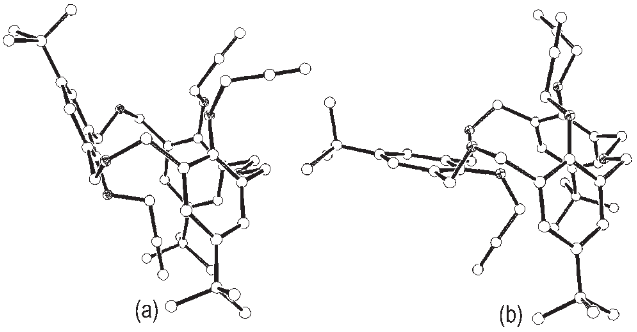

Figure 1. X-ray structure of **4** with two different conformations in the unit cell; hydrogen atoms are omitted for clarity.

a 63% yield of the cone conformation (Figure S25). A similar procedure was employed in the synthesis of chemosensor **2** from compound **5** in 75% yield (Figure S29).

Dilution experiments at different concentrations of **1** and **2** indicated that the excimer emission resulted from the intramolecular excimer, rather than the intermolecular excimer (Figure S3). Use of an organic solvent was unavoidable due to limited solubility of **1** and **2** in water. So, the fluorescent spectra properties of **1** and **2** were evaluated in organic solvent systems and their aqueous solutions (Figure S4). In order to obtain more optimal conditions for the realization of the peak selectivity for the targeting cations, the effects on the fluorescence of **1** and **2** with various metal ions in the absence and presence of water were systematically investigated (Figures S5−S13). On the basis of these observations, the fluorescent behaviors of **1** and **2** toward metal ions were studied in an organic aqueous solution ($CH_3CN/H_2O/DMSO$, 1000:50:1, v/v).

Figure 2 shows the fluorescence intensity changes of the monomer emission for receptors **1** and **2** in the presence of various metal ions. As can be seen, among the metal ions tested, no significant spectral changes were observed upon addition of alkali metal ions; a much weaker response was given compared to Pb^{2+} at the same concentration for Ag^{+}, Co^{2+}, Ni^{2+}, Hg^{2+}, Zn^{2+}, and Cd^{2+}, apart from Cu^{2+} where quenching was observed. The larger different fluorescence intensities caused by Pb^{2+} for receptors **1** and **2**, relative to their monomer ratios, suggest that receptor **2** has a much higher affinity and selectivity toward the Pb^{2+} ion. This may be attributed to the greater flexibility of triazole moieties on receptor **2** enabling them to adopt the appropriate geometry for the binding of the Pb^{2+} ion.

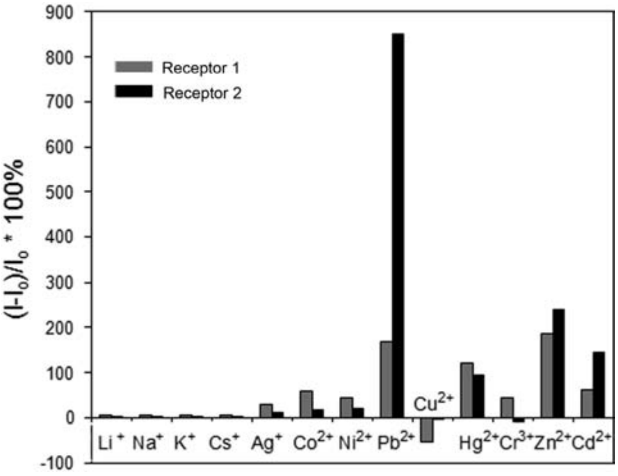

Figure 2. Fluorescence intensity changes ($(I - I_o)/I_o \times 100\%$) of receptors **1** and **2** (each of 1.0 μM) in $CH_3CN/H_2O/DMSO$ (1000:50:1, v/v) at 298 K upon addition of various metal perchlorates (30 equiv). I_o is fluorescence emission intensity at 396 nm for free host **1** and **2**, and I is the fluorescent intensity after adding metal ions. λ_{ex} = 343 nm.

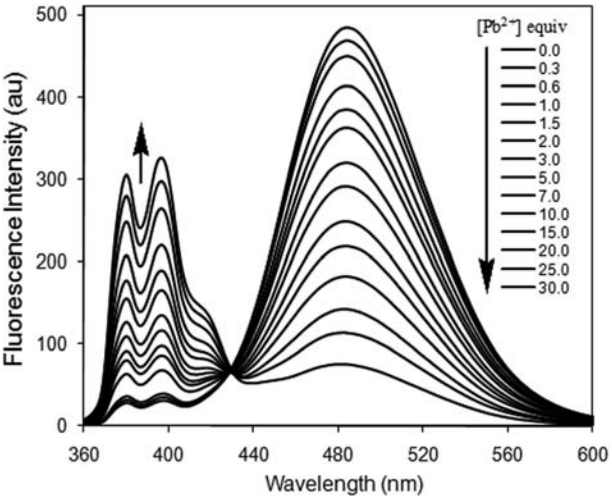

Figure 3. Fluorescence spectra of receptor **2** (1.0 μM) upon addition of increasing concentrations of $Pb(ClO_4)_2$ in $CH_3CN/H_2O/DMSO$ (1000:50:1, v/v). λ_{ex} = 343 nm.

The fluorescence sensing mechanisms of receptors **1** and **2** are attributed to pyrene moieties which form the fluorophore. These are appended to the calixarene scaffold by triazole groups to form a strong excimer. This results in a characteristic decrease of the excimer emission intensity and a concomitant increase of monomer emission intensity when the triazole rings selectively bind to cations.[12c,15] Figure 3 shows the fluorescence spectra of receptor **2** by the addition of increasing concentrations of Pb^{2+}.The fluorescence intensity of the excimer emission of receptor **2** markedly decreased while the monomer emission intensity significantly increased and reached a plateau after addition of ~30 equiv of Pb^{2+}. Meanwhile, a discernible isoemissive point was observed at 429 nm. The 1:1 complex of $\mathbf{2}{\bullet}Pb^{2+}$ was confirmed by a Job plot[16] (Figure S16). The association constant (K_a)[17] was determined to be 2.60×10^5 M^{-1} (error < 10%). Similar fluorescence titration experiments were

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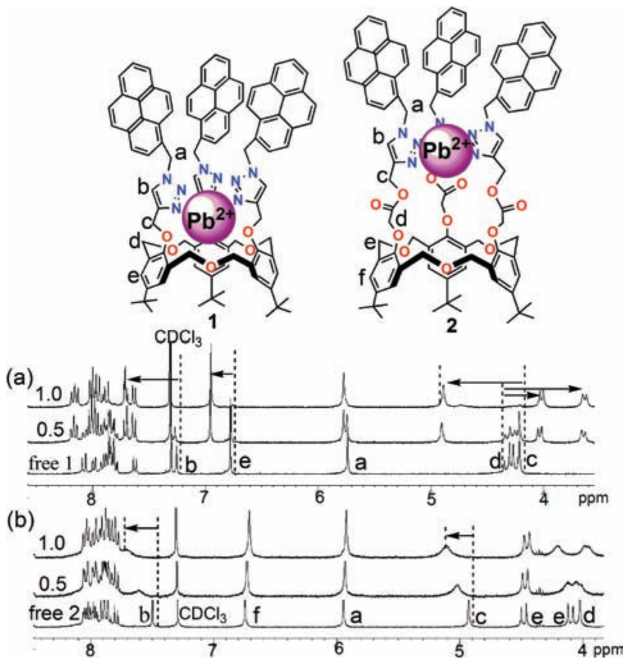

Figure 4. Plausible complexation of **1** and **2** for Pb^{2+} ion, and partial ^{1}H NMR spectra of **1** (a) and **2** (b) in CDCl$_3$/CD$_3$CN (10:1,v/v) upon addition of Pb^{2+} at 298 K.

carried out for **1**•Pb^{2+}, **1**•Zn^{2+}, **1**•Hg^{2+}, **1**•Cu^{2+}, **2**•Hg^{2+}, **2**•Cu^{2+}, **2**•Cr^{3+} **2**•Zn^{2+}, and **2**•Cd^{2+} (Figures S7−S18), and related association constants were determined (Figure S19), respectively.

To further investigate the selectivity for lead ions over other metal ions, interferences to the selective response of receptor **2** to Pb^{2+} by coexisting ions were evaluated (Figure S20); no significant interference in detection of Pb^{2+} was observed in the presence of other competitive cations. These results suggested that **2** can be used as a potential chemosensor for the Pb^{2+} ion.

To protect the fluorescence of an ionophore from being quenched by heavy atoms, several potential approaches are available:[18] (i) insulating the fluorophore from the metal by a particular molecular spacer; (ii) separating the metal from the fluorophore by placing the latter some distance from the metal binding site; and (iii) isolating the metal from the fluorophore by introducing sufficient ionophore. It is believed that the fluorescence of ionophore with two triazole moieties incorporated onto a tailored calixarene scaffold can be strongly quenched by Pb^{2+}.[12] However, for receptors **1** and **2**, which depend on the C_3 symmetry of homooxacalix[3]arene, the three nitrogen-rich triazole ligands serve as an adequate electronic effect to isolate the lead ion from the pyrene moiety and maintain the fluorescence.

To seek further more detailed information on the binding properties of receptors **1** and **2** with metal ions, ^{1}H NMR titration experiments were carried out in a mixture of CDCl$_3$/CD$_3$CN (10:1, v/v). As shown in Figure 4a, upon gradual addition of Pb^{2+} salt (0.5 equiv) to a solution of **1**, the resonances corresponding to the protons on receptor **1** were split into two sets of signals. In the presence of 1 equiv of Pb^{2+}, the original proton signal disappeared (Figure 4a). This result may be attributed to the complexed and uncomplexed forms of receptor **1** with Pb^{2+} being slower than the NMR time scale; therefore, free receptor **1** and complex **1**•Pb^{2+} are individually observed. Moreover, the significant ^{1}H NMR shifted signal for protons b, c, d, and e indicated that the Pb^{2+} ion is recognized by the nitrogen atoms of the triazole ring and oxygen atoms in the macrocycle of receptor **1**.[8e] However, in the case of the titration experiments for complex **2**•Pb^{2+}, no significant chemical shift changes of the protons were observed, except for the triazole ring proton H$_b$ and OCH_2-triazole linker H$_c$ of receptor **2** (Figure 4b). These observations suggested that only the nitrogen atoms in triazole moieties of receptor **2** participated to complex with Pb^{2+}.[19]

In summary, we have prepared a new type of fluorescent chemosensor based on homooxacalix[3]arene that incorporates a sufficient ionophore to avoid fluorescence quenching by Pb^{2+}. It possesses a high affinity and selectivity for lead ions relative to most other competitive metal ions by enhancement of the monomer fluorescence emission of pyrene in organic aqueous solution. We expect that the present design strategy and the remarkable photophysical properties of this sensor will help to extend applications of fluorescent sensors for heavy metal ions.

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Supporting Information Available. Detailed synthetic procedures and characterization of compounds **1**, **2**, **4**, and **6**, including crystallograhic data for **4** and additional spectrascopic details, are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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