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Selective separation of heavy metal ions able to cause adverse environmental and health problems have been much attention to chemists. In particular, Pb²⁺ ion can affect almost every organ and system in 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. In this point of view, development of Pb²⁺ ion-selective fluorescent chemosensor would be helpful to clarify the cellular role of the lead ions in vivo as well as to measure the amount of Pb²⁺ ion in the sources contaminated with lead ion including human body. In fact, although a variety of effective fluorescent chemosensors for alkali, alkaline earth metal ions, Hg²⁺, and Zn²⁺ have been already developed, so far few for Pb²⁺ ion have been reported.

Most fluorescent chemosensors for cations consist of a cation recognition unit (ionophore) along with a fluorogenic unit (fluorophore) and are thus called a fluoroionophore. The best effective fluorescence chemosensor must convert the event of cation recognition by the ionophore into light signals over the fluorophore with a high sensitivity and ease to monitor. In designing sensors, therefore, the recognition moiety linked to the fluorophore should be preliminarily considered because they are responsible for the selectivity and the binding efficiency of the whole chemosensor.

As such recognition moieties, thiacalixarenes having proper functional groups would be good candidates for cation probes because of their high selectivity toward specific cations. Since the convenient synthetic methods for thiacalixarenes were reported in 1997 by Kumagai et al., they have been paid much attention as alternatives to the conventional calixarenes by providing sites for functionalization not only on the aromatic rings but also on the bridging sulfide. Thiacalix[4]arene is composed of four benzene rings, linked to each other via sulfide bridges, through which, unlike the conventional calix[4]arene, it can form complex with metal ions. Thus far, synthesis and complexation studies with thiacalix[4]arene framework are rarely known while many other calixarene-based fluorescent chemosensors have been developed.

Scheme 1. Synthetic route for fluorescence chemosensor 1.

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calix[4]arene. In this system, the amide oxygen atoms not only participate in the binding with Pb\(^{2+}\) ion but also behave as a PET acceptor from the pyrene units.

Scheme 1 shows the synthetic route for the 1-(methylpyrenyl) amide-bearing tert-butylthiacalix[4]crown-6 (1). tert-Butylthiacalix[4]monocrown-6 (2) was prepared from the reaction of tert-butylthiacalix[4]arene and pentaethyleneglycol ditosylates in the presence of 1 equiv. of K\(_2\)CO\(_3\) in acetone. The reaction of 2 with 2 equiv. of N-(1-pyrenylmethyl)chloroacetamide (3)\(^{18}\) using K\(_2\)CO\(_3\) as a base in acetonitrile with a catalytic amount of sodium iodide provided the fluorogenic chemosensor 1 in 34% yield. The \(^1\)H NMR spectrum of 1 shows two singlets at 7.01 and 7.13 ppm attributable to the meta-protons of the thiacalixarene framework, suggesting that 1 is in the cone conformation. The cone conformation of 1 is also evidenced by the fact that there is a monomer emission band at around 400 nm without an excimer emission. This is because the crown-6 ring blocks excimer formation between the facing pyrene groups. For this regard, we have reported that in the 1,3-alternate conformation two facing pyrene amides incorporated with the calix[4]crown exhibit strong excimer fluorescence around 470 nm, whereas pyrene groups of the cone calix[4]crowns display a monomer emission only.\(^{19}\)

To obtain insight into the ability of 1 to selectively sense metal ions we first investigated fluorescence changes of 1 upon the addition of various metal ions such as Li\(^+\), Na\(^+\), K\(^+\), Rb\(^+\), Cs\(^+\), Ag\(^+\), Ca\(^{2+}\), Mg\(^{2+}\), Zn\(^{2+}\), and Pb\(^{2+}\). The results show that Pb\(^{2+}\) ions cause a significant change in fluorescence spectra of 1, whereas upon the addition of Cs\(^+\), Ag\(^+\), and Ca\(^{2+}\), minor emission changes are observed (Figure 1). The remarkable fluorescence quenching induced by Pb\(^{2+}\) is ascribed not only to reverse PET from pyrene units to the carbonyl oxygen atoms of which the electron density is diminished by metal ion complexation, but also to heavy metal effect.\(^{5b,17}\) For 1, the high selectivity toward Pb\(^{2+}\) is probably achieved by the assistance of the crown ring. In contrast, the N-methylpyrene amide-appended calix[4]arene derivative having two propyl groups instead of a crown ring exhibited no selectivity for specific metal ions,\(^{20}\) suggesting that the crown part of the 1 plays an important role in its selective encapsulation of Pb\(^{2+}\).

Figure 2 shows the fluorescence changes of 1 with Pb\(^{2+}\) ion concentration. The fluorescence intensity was gradually decreased by the addition of the Pb\(^{2+}\) ion up to 500 equiv. and then saturated. From this titration experiment, we could obtain the association constant of 1 (2.57 \times 10^5 M\(^{-1}\)) for Pb\(^{2+}\) ion complexation in acetonitrile/chloroform (1:1, v/v). The excitation wavelength was 344 nm.

In conclusion, a new tert-butylthiacalix[4]arene-framed fluorescent chemosensor bearing two facing amide groups and a crown-6 ring as cation recognition sites was synthesized in the cone conformation and its binding properties were investigated via fluorescence changes upon metal ion complexation. The free ligand 1 displayed strong emission at around 400 nm by excitation at 344 nm. The fluorescence changes upon the addition of metal ions showed that compound 1 has a high selectivity for Pb\(^{2+}\) over other metal ions tested. When Pb\(^{2+}\) ions were added to compound 1, the fluorescence intensity markedly decreased because of the reverse PET from the pyrene unit to the electron-deficient...
amide oxygen atom caused by Pb$^{2+}$ ion binding as well as the heavy metal effect.

**Experimental Section**

Synthesis. Compound 3 was prepared following procedures reported in literature.18

5,11,17,23-Tetra-tert-butyl-26,28-dihydroxy-2,8,14,20-tetraethiacalix[4]-25,27-monocrown-6, Cone (2). Under nitrogen, tert-butylthiacalix[4]arene (5.00 g, 6.93 mmol), pentaethyleneglycol ditosylates (5.69 g, 10.4 mmol) and K$_2$CO$_3$ (0.96 g, 6.93 mmol) in 100 mL of acetone were heated to reflux temperature. After refluxed for 24 hours, acetone was removed in vacuo. To the resulting white solid, 5% aqueous HCl solution (100 mL) and CH$_2$Cl$_2$ (50 mL) were added and the organic layer was separated and washed three times with 50 mL of water. The organic layer was dried over anhydrous MgSO$_4$ and the solvent was evaporated in vacuo to give a white solid. Column chromatography on silica gel using a mixture of ethyl acetate/hexane (1/3) as an eluent gave 0.433 mmol) of (0.22 mmol) of (1-pyrenylmethyl)chloroacetamide oxygen atom caused by Pb$^{2+}$ ion binding as well as the heavy metal effect.

**References**


21. (a) Association constants were obtained using the computer program ENZFITTER, available from Elsevier-BIOSOFT, 68 Hills Road, Cambridge CB2 1LA, United Kingdom. (b) Connors, K. A. Binding Constants; Wiley: New York, 1987.