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Selective metal detection in an unsymmetrical 1,3-alternate calix[4]biscrown chemosensor

Ju Han Bok,[a] Hyun Jung Kim,[a] Jeong Won Lee,[a] Sung Kuk Kim,[a] Jung Kyu Choi,[a] Jacques Vicens[b,*] and Jong Seung Kim[a,*]

[a]*Department of Chemistry, Dankook University, Seoul 140-714, Republic of Korea*
[b]*Laboratoire de Conception Moléculaire, UMR 7512, ECPM-ULP, Strasbourg, France*

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Abstract—Calix[4]crown-based chemosensors **1**, **2**, and reference **3** have been synthesized. The weak fluorescence intensity of 1,5-naphthalene of **1** suggests that the benzene rings of the calix[4]arene as well as the oxygen atoms of the crown-5 ring take part in PET. The complexation of two K^+ ions by both crown-5 and 1,5-naphthalene-crown-6 loops of **1** caused fluorescence enhancement of the naphthalene unit by CHEF. Pb^{2+} acted as a quenching metal ion.

In a recent *Tetrahedron* report,[1] Callan et al. showed the important development of luminescent sensors in the early 21st century with in perspectives the constant need for molecular devices with selective complexing properties toward a chosen substrate. Selective signaling of metal ions is an important topic for the detection and treatment of the toxic metal ions in chemical systems including living systems.[1] The design of efficient chemosensors for the detection of ionic guest is one of the most attractive topics in supramolecular chemistry.[2] A chemosensor is a molecule capable of transforming chemical information, such as the presence of a particular metal ion, into an analytically useful signal. A metal-ion chemosensor comprises a metal recognition site and a signaling unit that is activated upon ion binding. For instance, metal chelation may result in fluorescence enhancement.[2] Sensors operating according to this mechanism are known as chelation-enhanced fluorescence (CHEF)-type sensors. The selectivity in metal ion assays is achieved by choosing ion-selective binding moieties.[2] Calixarenes have been paid much attention as basic molecules for constructing chemosensors due to their selectivity in cation complexation.[3] Among them, calix[4]crown-ethers and more particularly 1,3-calix[4]biscrowns[4] have been used because of their unique binding modes: they afford two metal-binding cavities on each side of the calixarene, in the 1,3-alternate conformation, composed of two phenolic oxygen donor atoms and two aromatic moieties.[5]

In this letter, we report recent results on the fluorescence behavior of **1**–**3** (see below) in the presence of K^+ and Pb^{2+}. Compound **1** is an unsymmetrical 1,3-calix[4]biscrown having one crown-5 and one crown-6 containing a 1,5-naphthylene unit in the middle. Compounds **2** and **3** were investigated as helpful tools for comparison with **1**.

The synthesis[6] of **1** and **2** was achieved according to procedures well-known for preparing 1,3-calix[4]biscrowns.[7] *cone*-Calix[4]monocrown-5[8] and 1,3-dipropoxy *cone*-calix[4]arene[9] were reacted with 1,5-naphthalene glycolic ditosylate derivative[10] **4** in basic conditions to afford **1** and **2** in 67% and 44% yields, respectively.[6] The 1,3-*alternate* conformation was deduced from their ^1H NMR spectra in $CDCl_3$ exhibiting singlets at 3.59 and 3.68 ppm, respectively for the $ArCH_2Ar$ of the calix[4] moiety of **1** and **2**. Reaction of ditosylate **4** with phenol in similar conditions gave 1,5-naphthalene tetraethylene glycol diphenyl ether **3** in 66% yield.[6]

We investigated fluorescence changes of **1**–**3** in CH_3CN upon addition of metal (K^+, Cs^+, Pb^{2+}, and Al^{3+}) as perchlorates. The results depicted in Figure 1 indicated to us that the cation complexation can be monitored

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* Corresponding authors. Tel.: +82 2 799 1351; fax: +82 2 797 3277 (J.S.K.); e-mail addresses: vicens@chimie.u-strasbg.fr; jongskim@dankook.ac.kr

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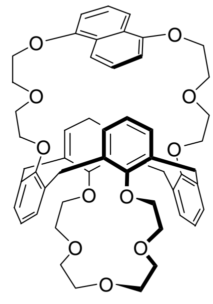
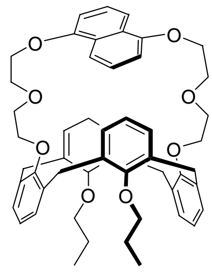


1



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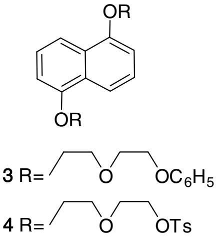

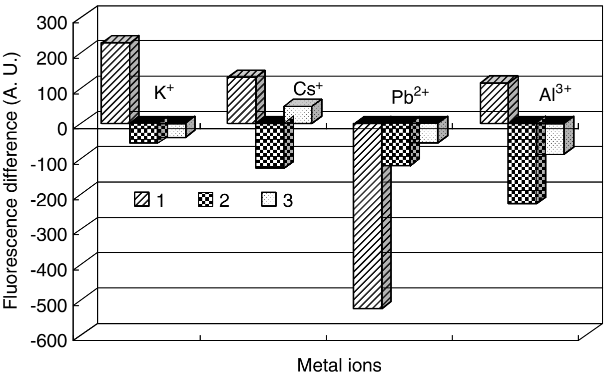

Figure 1. Bar profiles of fluorescence changes ($I - I_0$) of 3.0 μM solutions of **1**–**3** in CH_3CN upon addition of 500 equiv of various metal ions. Excitation at 304 nm; I_0: fluorescence emission intensity of free **1**–**3**. I: fluorescence emission intensity of metal complexes of **1**–**3**. (+) and (−) denote fluorescence increase and decrease, respectively.

by fluorometric technique. And, we chose K^+ and Pb^{2+} for further investigations.

With an excitation at 304 nm (maximum absorption), the fluorescence intensity of **1** increased as a function of added K^+ (Fig. 2a) while that of monocrown **2** (Fig. 2b) remained almost unchanged. This showed that the crown-5 plays a key role in K^+ complexation. It is known that the crown-5 loop(s) of 1,3-calix[4]biscrowns preferentially complex K^+.[4a,b] The fluorescence mechanism is rationalized as follows: the weak fluorescence intensity of 1,5-naphthalene of **1** suggests that the benzene rings of the calix[4]arene as well as the oxygen atoms of the crown take part in PET (photo-induced electron transfer). When K^+ is bound to the donor oxygen atoms of the crown-5, with probable π-metal interactions with the aryl groups of the calix[4] unit, one observes an uprising fluorescence intensity of **1** in emission by CHEF.

We carried out Job's plot experiment by varying the concentration of both **1** and K^+ (see Fig. 3a). The maximum point at the mole fraction of 0.7 is a little higher than that of the typical ligand mole fraction (0.66) for 1:2 (ligand:metal) complexes.[11] This implies that a first K^+ is entrapped by the crown-5 and then a second K^+ is subsequently complexed by the 1,5-naphthalene-crown-6 causing decreased fluorescence emission. In order to prove that the complexation is related to fluorescence increment, we investigated **3** having no crown-5 loop. No changes of the fluorescence intensity were observed, suggesting the need of a crown-5 cavity to adapt metal ions.

In contrast, complexation of Pb^{2+}, known as a quenching metal ion[5j,k] induced a quenched fluorescence emission of **1** whereas that of **2** was weakly quenched as shown in Figure 4a and b, respectively.

No changes of **3** with an excess amount of Pb^{2+} were observed. K_a value[12] of **1** for Pb^{2+} was estimated to be 6.0×10^4 M^{-1} (approximately 260 times larger than that

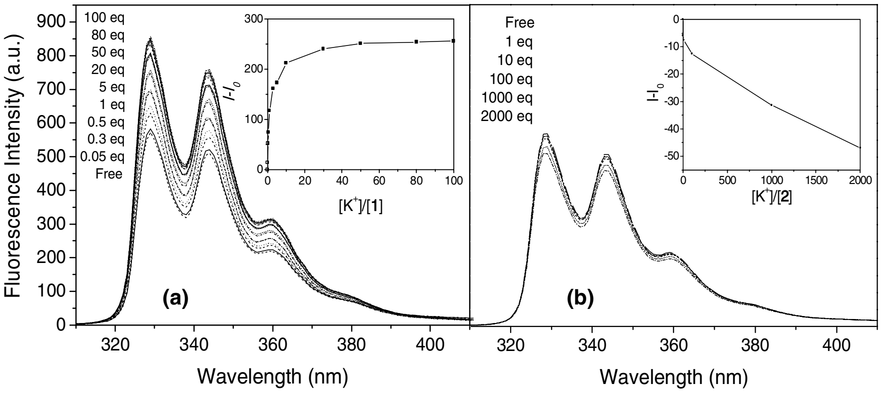

Figure 2. Fluorescence change of (a) **1** (3.0 μM) and (b) **2** (3.0 μM) with increasing K^+ concentrations in CH_3CN. The excitation wavelength is 304 nm.

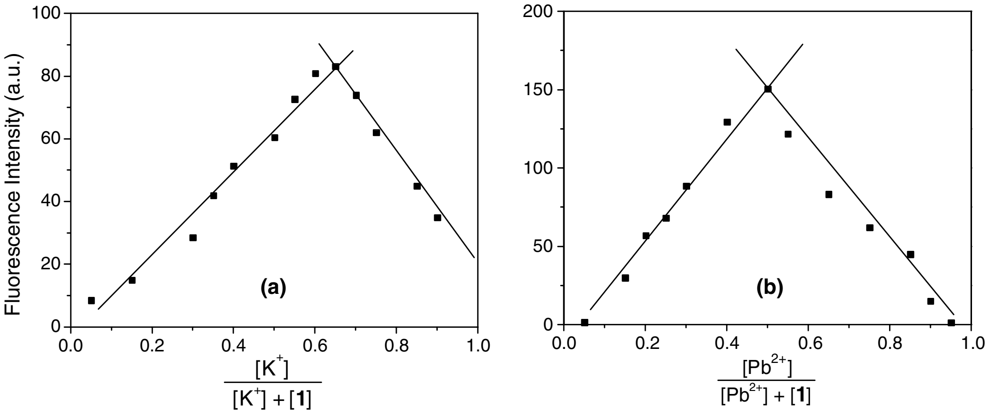

Figure 3. Job plots for (a) **1**·K^+ and (b) **1**·Pb^{2+}. *Y* axis is fluorescence changes of **1** for (a) increase (b) decrease.

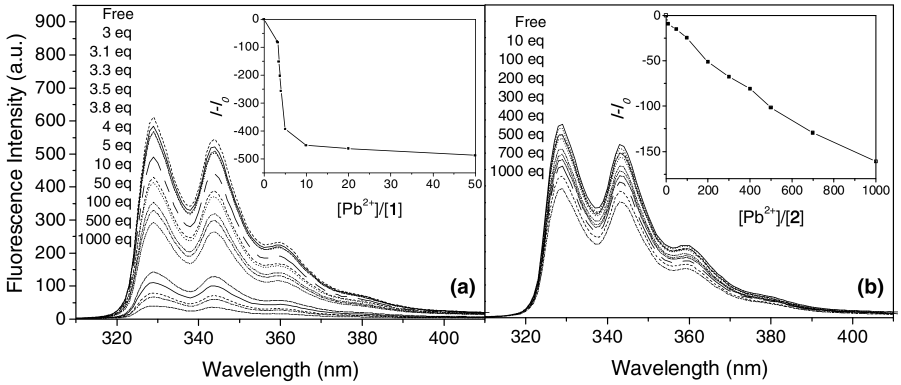

Figure 4. Fluorescence change of (a) **1** (3.0 μM) and (b) **2** (3.0 μM) with increasing Pb^{2+} concentrations in CH_3CN. The excitation wavelength is 304 nm.

of **2**) was also in agreement of the important role played by the crown-5 in the complexation selectivity of **1** toward Pb^{2+} as well. This behavior was believed to come from a fair complementarity between the radius of Pb^{2+} and the crown-5 loop. Job's plot analysis exhibited a maximum at 0.52 mol fraction of Pb^{2+} indicating the formation of a 1:1 complex (Fig. 3b). Therefore, one can assert that the quenching effect is a major contribution factor in fluorescence changes of **1** with Pb^{2+}, but the CHEF is to be second.

In summary, a novel calixarene-based fluorescent chemosensor **1** having two different crown loops showed large fluorescence changes upon the addition of metals by CHEF effect and quenching metal effect. In agreement with previous studies,[4] between conventional crown-5 and 1,5-naphthalene-crown-6 in 1,3-calix[4]biscrowns, the former behaves as a better partner for metal ion complexation than the later.

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6. *General*: Uncorrected melting points (Mps), Buchi 500. ^{1}H NMR and ^{13}C NMR, Varian (δ in ppm from TMS, J in hertz). FAB MS mass spectra, JEOL-JMS-HX 110A/110A High Resolution Tendem Mass Spectrometry in Korea Basic Science Institute (Korea). All the reactions were 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 a RF-5301PC spectrofluorophotometer. Stock solutions of **1**–**3** (3.0 μM) were prepared in CH_3CN. For all measurements, excitation was at 304 nm with excitation and emission slit widths at 3 nm. Fluorescence titration experiments were performed using 3.0 μM solutions of **1**–**3** in CH_3CN and various concentrations of metal perchlorate in CH_3CN. After calculating the concentrations of the free ligands and complexed forms of **1**–**3** from the fluorescence titration experiments, the association constants were obtained using the computer program ENZFITTER.[12] *Preparation of* **1**. *cone*-Calix[4]monocrown-5 (1.00 g, 1.72 mmol), **4** (1.22 g, 1.89 mmol), Cs_2CO_3 (1.68 g, 5.16 mmol), and CH_3CN (50 mL) were refluxed for 24 h. After removal of the solvent, the resulting solid was dissolved in CH_2Cl_2 and water. The organic layer was dried over anhydrous $MgSO_4$. After filtration, solvents were evaporated to give a solid which was submitted to column chromatography on silica gel using ethylacetate/hexane (1:5) as an eluent to give pure **1** (1.02 g, 67% yield) as a white solid. Mp: 243–245 °C. ^{1}H NMR (200 MHz, $CDCl_3$): 7.75 (d, 2H, $J = 8.4$ Hz, naphthyl-H_2 and -H_6), 7.26 (t, 2H, $J = 8.4$ Hz, naphthyl-H_3 and -H_7), 7.15 (d, 8H, $J = 6.6$ Hz, Ar_{calix}–H_m, Ar'_{calix}–H_m), 6.93 (t, 2H, $J = 6.6$ Hz, Ar_{calix}–H_p), 6.88 (t, 2H, $J = 6.6$ Hz, Ar'_{calix}–H_p), 6.60 (d, 2H, $J = 8.4$ Hz, naphthyl-H_4 and -H_8), 4.30–3.84 (m, 8H, –OCH_2CH_2O-naphthyl-crown-6), 3.66–3.45 (m, 12H, –OCH_2CH_2O– of the crown-5 and naphthyl-crown-6), 3.59 (s, 4H, Ar_{calix}–CH_2–Ar'_{calix}), 3.42 (t, 4H, $J = 2.8$ Hz, Ar'_{calix}–CH_2CH_2O– of the crown-5), 3.15 (t, 4H, $J = 2.8$ Hz, $Ar_{calix}OCH_2CH_2O$– of the naphthyl-crown-6), 3.12 (t, 4H, $J = 2.8$ Hz, $Ar'_{calix}OCH_2CH_2O$– of the crown-5). ^{13}C NMR ($CDCl_3$): 177.9, 156.4, 154.2, 134.1, 129.4, 126.7, 122.8, 114.5, 105.4, 76.4, 68.9, 67.5, 38.1, 28.8 ppm. FAB MS m/z (M^+): calcd, 883.03. Found: 882.90. Anal. Calcd for $C_{54}H_{58}N_2O_{11}$: C, 73.45; H, 6.62. Found: C, 73.91; H, 6.94. *Preparation of* **2**. Same procedure as for **1**: 1,3-dipropoxy *cone*-calix[4]arene (1.00 g, 1.97 mmol), **4** (1.39 g, 2.16 mmol) and Cs_2CO_3 (1.92 g, 5.89 mmol), CH_3CN (50 mL), reflux 24 h, chromatography on silica gel using ethylacetate/hexane (1:5), **4** (0.7 g, 44% yield), yellowish solid. Mp: 252–255 °C. ^{1}H NMR (200 MHz, $CDCl_3$): 7.90 (d, 2H, $J = 6.2$ Hz, naphthyl-H_2 and -H_6), 7.28 (t, 2H, $J = 6.2$ Hz, naphthyl-H_3 and -H_7), 7.26 (d, 4H, $J = 6.4$ Hz, Ar_{calix}–H_m), 7.03–6.95 (t, $J = 6.2$ Hz, 2H, naphthyl-H_4 and -H_8), 7.01 (d, 4H, $J = 6.4$ Hz, Ar'_{calix}–H_m), 6.75 (t, 2H, $J = 6.4$ Hz, Ar_{calix}–H_p), 6.68 (t, 2H, $J = 6.4$ Hz, Ar'_{calix}–H_p), 4.38–4.01 (m, 4H, naphthyl-OCH_2CH_2O–), 3.87–3.47 (m, 16H, $Ar_{calix}OCH_2CH_2O$–, $Ar_{calix}OCH_2CH_2CH_3$), 3.68 (s, 4H, $Ar_{calix}CH_2Ar'_{calix}$), 1.54 (sextuplet, 4H, $J = 7.1$ Hz, –$CH_2CH_2CH_3$), 0.87 (t, 6H, $J = 7.1$ Hz, –$CH_2CH_2CH_3$). ^{13}C NMR ($CDCl_3$): 178.6, 134.3, 130.4, 128.8, 125.7, 115.3, 106.4, 70.4, 68.5, 36.7, 29.4, 11.1 ppm; FAB MS m/z (M^+): calcd, 809.00. Found: 808.72; Anal. Calcd for $C_{52}H_{56}O_8$: C, 76.98; H, 7.15. Found: C, 77.21; H, 6.94. *Preparation of* **3**. Same procedure as for **1**: phenol (0.36 g, 3.88 mmol), **4** (1.00 g, 1.55 mmol), K_2CO_3 (1.07 g, 7.75 mmol), CH_3CN (50 mL), reflux 24 h, chromatography on silica gel using ethylacetate/hexane (1:5), **3** (0.5 g, 66% yield), yellowish solid. Mp: 213–216 °C. ^{1}H NMR (200 MHz, $CDCl_3$): 7.86 (d, 2H, $J = 4.2$ Hz, naphthyl-H_2 and -H_6), 7.30 (t, 2H, $J = 4.2$ Hz, naphthyl-H_3 and -H_7), 7.32–7.25 (m, 6H, phenyl-H), 6.94–6.92 (m, 4H, phenyl-H), 6.84 (d, 2H, $J = 4.2$ Hz, naphthyl-H_4 and -H_8), 4.32 (t, 4H, $J = 2.2$ Hz, naphthyl-OCH_2CH_2O–), 4.17 (t, 4H, $J = 2.2$ Hz, phenyl-OCH_2-CH_2O–), 4.06 (t, 4H, $J = 2.2$ Hz, naphthyl-OCH_2CH_2O–), 4.00 (t, 4H, $J = 2.2$ Hz, phenyl-OCH_2CH_2O–). ^{13}C NMR ($CDCl_3$): 178.2, 170.0, 149.4, 140.3, 134.5, 133.0, 132.7, 132.6, 131.8, 128.5, 76.7, 47.9, 31.9, 25.4. FAB MS m/z (M^+): calcd, 488.57. Found: 488.21. Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 74.21; H, 6.74.
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