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A selective fluorescent probe for La^{3+} and Y^{3+} based on calix[6]arene

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Abstract—A new fluorescent probe based on calix[6]arene functionalized with three naphthoic acid groups was synthesized and showed selective fluorescence enhancement in the presence of La^{3+} and Y^{3+}. In addition, the fluorescence enhancement behaviors depended on the pH values of the solution.

There has been considerable interest in the use of organic chromophores for particular lanthanide ions (Eu^{3+}, Tb^{3+}, Gd^{3+}),[1] because the luminescence of lanthanide ion has its peculiar characteristics, for example, long life time and line-like emission bands in the visible region. Nevertheless, the determination of lanthanide ions such as Y^{3+} and La^{3+}, which are useful for radiotherapeutic applications,[2] catalysis,[3] or the synthesis of nanosized materials,[4] etc. has been less reported.[5]

Calixarenes have been extensively used as hosts for the complexation of lanthanide ions.[6] Recently, it was described that calixarene derivatives substituted with three carboxylic acid groups form neutral complexes with lanthanide ions.[1c,e,7] In an effort to design a useful fluorescent sensor for La^{3+} and other lanthanide ions, we incorporated three naphthoic acid groups to the C_{3v} symmetry compound **1** to make compound **3**. The three naphthoic acid groups in compound **3** can selectively sense Y^{3+} and La^{3+} as well as transduce the signal. Meanwhile, it is of interest that compound **3** exhibits pH-dependent recognition behaviors for Y^{3+} and La^{3+}.

Calixarenes are popular building blocks in supramolecular chemistry.[8] The fluorescent studies on the poor ability of compound **6** to recognize Y^{3+} and La^{3+} indicate that the calix[6]arene platform plays an important role in the recognition.

The target (compound **3**) was synthesized as shown in Scheme 1. Compound **1** was obtained in accordance with the literature.[9] Alkylation of **1** with methyl 3-(2′-bromo-ethoxy)-naphthalene-2-carboxylate gave **2** in 78% yield. Successive saponification of **2** by sodium hydroxide and then acidification provided **3** in 70% yield. Compound **6** could be obtained in 85% yield from the alkylated compound **5**, which was synthesized from 4-*tert*-butylphenol in 80% yield. The structures of **2**, **3**, **5**, and **6** were identified by IR, ^{1}H NMR, ^{13}C NMR, MALDI-TOF MS, and elemental analyses.[10] ^{1}H NMR data revealed that **2** and **3** have no preferred conformation and are flexible.

In the absorption spectra of **3**, maximum bands were observed at 327, 267, and 228 nm. Addition of La^{3+} and Y^{3+} resulted in a decrease of the absorption intensity at 228 nm and an increase of the intensity at 327 and 267 nm, with an isobestic point at 239 nm, which supports the complex formation.

All titration studies were carried out at pH 6.8 maintained with HEPES buffer (10 mM). The fluorescence emission is directly proportional to the concentration of compound **3** (1–10 μM). Therefore, **3** is not susceptible to self-quenching or aggregation, at least in the concentration range explored.

Keywords: Calix[6]arene; Fluorescent probe; Recognition; La^{3+}; Y^{3+}.

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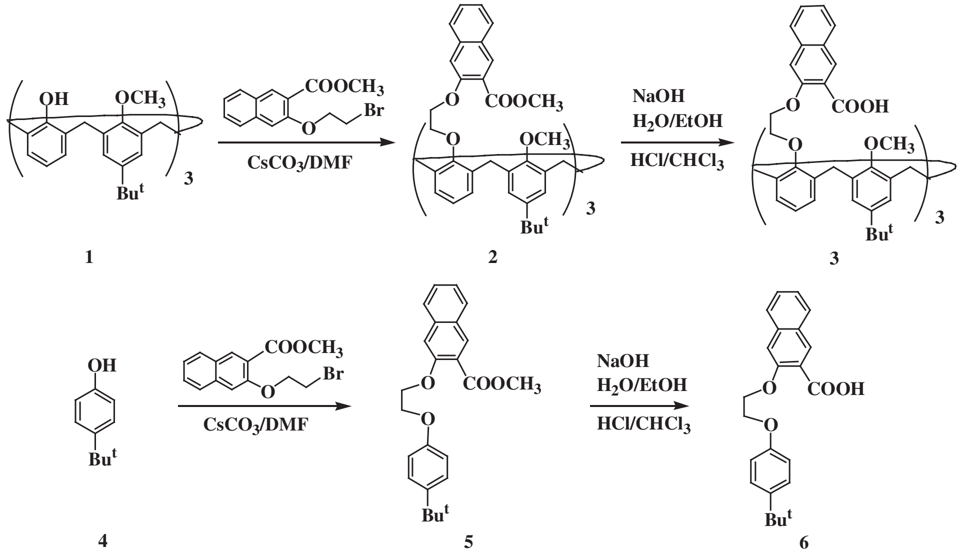

Scheme 1.

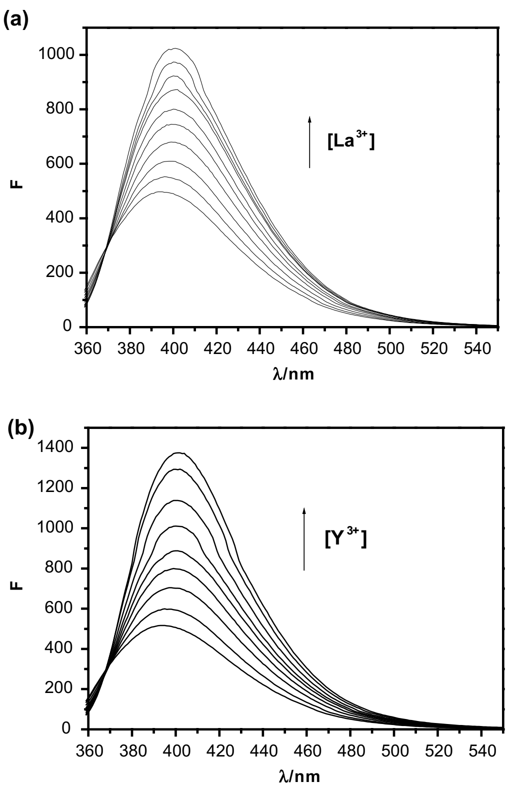

Figure 1. Fluorescence emission spectra of **3** (10 μM) in the presence of (a) La^{3+}; (b) Y^{3+} in $CH_3CN–H_2O$ (2:1 v/v) at pH 6.8 (HEPES 10 mM). Concentration of La^{3+}: 0, 5, 10, 15, 20, 25, 30, 35, 40, 45 μM. Concentration of Y^{3+}: 0, 5, 10, 15, 20, 25, 30, 35, 40 μM. $\lambda_{ex} = 340$ nm.

In the fluorescence spectra of **3**, maximum excitation and emission wavelengths were observed at 340 and 394 nm, respectively. Figure 1(a) shows the emission intensity of **3** (10 μM) in the presence of increasing amounts of La^{3+} (10–50 μM). The emission intensity of **3** increased and the emission maximum shifted to the red with an isoemissive point at 369 nm. Addition of Y^{3+} induced similar emission spectral changes, and the emission intensity significantly increased. Figure 1(b) shows the changes in the emission spectrum that occurred upon the addition of Y^{3+} (10–40 μM) to a $CH_3CN–H_2O$ (2:1 v/v) solution of **3** (10 μM). The stoichiometry of **3**–Ln^{3+} complexation was determined through Job plot by fluorescent spectroscopy and was found to be 1:1. From the fluorescent titrations, the binding constants for **3**–La^{3+} and **3**–Y^{3+} were calculated as 3.15×10^4 and 3.93×10^4 M^{-1}, respectively.

It is known that La^{3+} and Y^{3+} have no low-energy f–f states available for energy transfer, and that they do not significantly change the emission intensity of **3**.[1a] The mechanism of fluorescence increase may involve internal charge transfer (ICT). The 3-alkoxy-2-naphthoic acid that we choose as the fluorophore is an interesting π-electron system,[11] which has very different dipole moments in the ground and the lowest energy singlet excited states due to ICT.[12] It includes an electron-donating substitute (alkoxyl) conjugated to an electron-withdrawing substitute (carboxyl). When La^{3+} or Y^{3+} was bound by the electron-withdrawing terminal of the fluorophore, an increase of the electron-withdrawing ability in this system may induce fluorescence increase and red-shifts.

We also tested the fluorescent response of **3** (10 μM) to various Ln^{3+} (50 μM) under identical conditions. As summarized in Figure 2, the fluorescence of **3** at 394 nm was more or less quenched by the 4 equiv of lanthanide ions Tb^{3+}, Nd^{3+}, Sm^{3+}, Ce^{3+}, Gd^{3+}, and Eu^{3+}. This can be explained by an energy transfer (ET) between such lanthanide ions and the fluorophore, which can result in the quenching of the fluorescence of **3**, since such lanthanide ions have f–f transitions.[1a] On the other hand, Y^{3+} and La^{3+} enhanced the emission (2.66 and 1.86 times, respectively with 4 equiv each). These results implied that **3** could be a selective fluorescence probe for

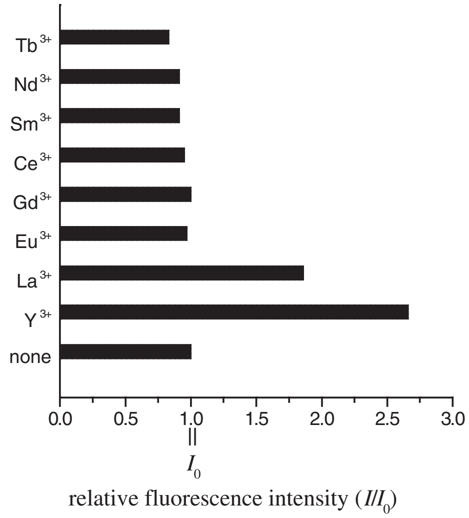

Figure 2. Relative fluorescence intensity of **3** (10 μM) responding to 4 equiv of lanthanide ions at pH 6.8 (10 mM HEPES) based on fluorescence intensity height at 405 nm (excitation at 340 nm).

Y^{3+} and La^{3+} at pH = 6.8 in CH_3CN–H_2O (2:1 v/v) solution.

To confirm the importance of the calixarene platform, studies of the fluorescent response of compound **6** to Y^{3+} and La^{3+} were carried out. It was expected that no noticeable spectral changes of **6** would be observed upon addition of Y^{3+} and La^{3+}.

Considering that chemosensor **3** is pH sensitive, its ability to recognize Y^{3+} and La^{3+} may depend on the pH of the solution. To investigate the influence of pH on fluorescence, we measured the variation in fluorescence intensity of **3**, **3**–La^{3+}, and **3**–Y^{3+} by adding different amounts of acid and base (Fig. 3). In this system, we chose 2 μM as the concentration of **3**, because the precipitation would appear in higher concentrated solution of **3** under acidic conditions. The free **3** exhibited a gradual enhancement in emission intensity upon addition of the acid. Such a phenomenon of increasing emission intensity was caused by the protonation of the carboxylate and carboxyl groups of the fluorophore, which facilitated charge transfer between the carboxylate and carboxyl groups and naphthyl ring. Under basic conditions, the emission intensity remained constant (Fig. 3 curve a).

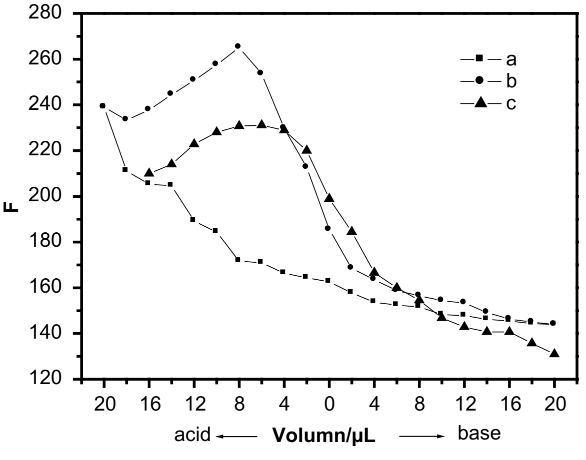

Figure 3. Fluorescence intensity of **3** (2 mL) upon the addition of acid or base (a) free **3**, (b) in the presence of 4 equiv of La^{3+}, (c) in the presence of 4 equiv of Y^{3+} ([**3**] = 2 μM), in CH_3CN–H_2O = 2:1 v/v; acid: aqueous $HClO_4$, 0.01 M; base: $(CH_3)_4NOH$, 0.01 M.

The pH-dependent fluorescence of **3**–La^{3+} and **3**–Y^{3+} solutions showed a feature quite different from that of free **3** (Fig. 3 curves b and c). The pronounced difference was observed in acidic conditions. Along with the addition of the acid, the emission intensity of **3**–La^{3+} and **3**–Y^{3+} appeared to have increased, and it achieved a maximum after addition of 7.5 and 4 μL $HClO_4$ solution (0.01 M), respectively. This phenomenon is understandable since lanthanide ions can easily form hydrates with H_2O and OH^-. Addition of the acid can induce the dissociation of the hydrates. Then the free Y^{3+} and La^{3+} would move to **3** and be bound by the carboxylate groups due to stronger complexation ability. When more acid (8–20 μL 0.01 M $HClO_4$ solution) was added, more carboxylate groups were protonated, and the complexes of **3**–La^{3+} and **3**–Y^{3+} were gradually dissociated. Under basic conditions, the emission intensity reached the same level as that of the free **3**, which indicated a complete dissociation. We deduced that La^{3+} and Y^{3+} can be displaced from the recognition sites and be bound by OH^- in solution on addition of $(CH_3)_4N^+OH^-$ (0.01 M).

In the experiments involving the addition of lanthanide ions to the CH_3CN–H_2O (2:1 v/v) solutions of **3**, no lanthanide luminescence was observed. This may have been caused by the existence of low-lying charge transfer states and the poor ability of the ligand unit to shield the bound metal ion from interacting with water molecules.[13]

In summary, we have developed a new fluorescent probe with three naphthoic acid groups based on calix[6]arene, of which the fluorescent intensity increased selectively in the presence of La^{3+} and Y^{3+}, and the increasing behavior was related to the pH value of the solution.

Acknowledgements

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10. **2**: Yield: 78%; mp: 125–126 °C; ^{1}H NMR: δ 8.23 (s, 3H, naph-*H*), 7.77 (d, $J = 8.0$ Hz, 3H, naph-*H*), 7.65 (d, $J = 8.2$ Hz, 3H, naph-*H*), 7.47 (t, $J = 6.9$ Hz, 3H, naph-*H*), 7.35 (t, $J = 6.9$ Hz, 3H, naph-*H*), 7.20 (s, 3H, naph-*H*), 7.14 (s, 6H, Ar*H*), 6.74–6.70 (m, 9H, Ar*H*), 4.40–4.38 (m, 6H, ArOCH_2), 4.20–4.10 (m, 6H, ArOCH$_2$CH_2), 4.00–3.96 (m, 9H, ArCH_2 Ar), 3.72–3.67 (m, 3H, ArCH_2Ar), 3.65 (s, 9H, ArCOOCH_3), 2.65 (s, 9H, ArOCH_3), 1.19 (s, 27H, C(CH_3)$_3$); ^{13}C NMR: δ 166.8, 154.7, 154.4, 154.1, 146.0, 135.9, 134.7, 133.5, 133.4, 132.6, 128.6, 128.2, 127.6, 127.1, 126.5, 124.4, 123.6, 122.4, 107.8, 70.8, 68.2, 59.8, 52.1, 34.1, 31.5, 30.6; IR (KBr): ν 2951, 1734, 1446 cm^{-1}; MALDI-TOF MS: *m/z* 1553 ([M+Na]$^+$), 1569 ([M+K]$^+$); Elemental analysis calcd for $C_{99}H_{102}O_{15}$: C, 77.62; H, 6.71. Found: C, 77.59; H, 6.89. **3**: Yield: 70%; mp: 156–157 °C; ^{1}H NMR: δ 8.59 (s, 3H, naph-*H*), 7.81 (d, $J = 8.0$ Hz, 3H, naph-*H*), 7.53–7.49 (m, 6H, naph-*H*), 7.44–7.39 (m, 3H, naph-*H*), 7.15 (s, 3H, naph-*H*), 7.06 (s, 6H, Ar*H*), 6.90–6.86 (m, 6H, Ar*H*), 6.65–6.61 (m, 3H, Ar*H*), 4.35–4.31 (m, 6H, ArOCH_2), 4.00–3.92 (m, 18H, ArOCH$_2$CH_2ArCH_2Ar), 2.97 (s, 9H, ArOCH_3), 1.13 (s, 27H, C(CH_3)$_3$); ^{13}C NMR: δ 165.6, 154.2, 154.0, 153.4, 146.3, 136.3, 135.8, 134.1, 133.2, 129.4, 129.3, 128.8, 128.3, 126.6, 126.5, 125.4, 124.0, 118.2, 108.6, 70.0, 69.2, 59.9, 34.1, 31.4, 31.0; IR (KBr): ν 2955, 1737, 1488 cm^{-1}; MALDI-TOF MS: *m/z* 1511 ([M+Na]$^+$), 1527 ([M+K]$^+$); Elemental analysis calcd for $C_{96}H_{96}O_{15}$: C, 77.40; H, 6.49. Found: C, 77.13; H, 6.76. **5**: Yield: 80%; mp: 107–108 °C; ^{1}H NMR: δ 8.30 (s, 1H, naph-*H*), 7.82 (d, $J = 8.1$ Hz, 1H, naph-*H*), 7.73 (d, $J = 8.3$, 1H, naph-*H*), 7.52 (t, $J = 6.8$ Hz, 1H, naph-*H*), 7.41 (t, $J = 6.9$ Hz, 3H, naph-*H*), 7.39 (s, 1H, naph-*H*), 7.32 (d, $J = 6.7$ Hz, 2H, Ar*H*), 6.92 (d, $J = 6.7$ Hz, 2H, Ar*H*); 4.51–4.48 (m, 2H, ArOCH_2), 4.44–4.40 (m, 2H, ArOCH$_2$CH_2), 3.91 (s, 3H, ArCOOCH_3), 1.30 (s, 9H, C(CH_3)$_3$); ^{13}C NMR: δ 166.8, 156.4, 154.8, 143.8, 136.0, 132.8, 128.7, 128.4, 127.9, 126.5, 126.3, 124.6, 122.4, 114.3, 108.7, 67.7, 66.4, 52.2, 34.1, 31.5; MS: *m/z* 378 (M$^+$); Elemental analysis calcd for $C_{24}H_{26}O_4$: C, 76.17; H, 6.92. Found: C, 76.27; H, 7.01. **6**: Yield: 85%; mp: 123–124 °C; ^{1}H NMR: δ 11.14 (s, 1H, ArCOO*H*), 8.82 (s, 1H, naph-*H*), 7.94 (d, $J = 8.2$ Hz, 1H, naph-*H*), 7.79 (d, $J = 8.3$ Hz, 1H, naph-*H*), 7.60 (t, $J = 6.9$ Hz, 1H, naph-*H*), 7.48 (t, $J = 6.9$ Hz, 1H, naph-*H*), 7.37 (s, 1H, naph-*H*), 7.34 (d, $J = 6.7$ Hz, 2H, Ar*H*), 6.92 (d, $J = 6.7$ Hz, 2H, Ar*H*), 4.67–4.70 (m, 2H, ArOCH_2), 4.47–4.44 (m, 2H, ArOCH$_2$CH_2), 1.31 (s, 9H, C(CH_3)$_3$); ^{13}C NMR: δ 165.3, 155.6, 153.4, 144.6, 136.4, 129.5, 129.4, 128.7, 126.6, 126.5, 126.4, 125.6, 118.4, 114.2, 108.7, 68.3, 65.4, 34.1, 31.5; MS: *m/z* 364 (M$^+$); Elemental analysis calcd for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64. Found: C, 75.64; H, 7.00.
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