Pergamon

Tetrahedron Letters 43 (2002) 9209–9212

TETRAHEDRON
LETTERS

A new fluorescent chemosensor for Fe^{3+} and Cu^{2+} based on calix[4]arene

Jun-Min Liu, Qi-Yu Zheng,* Jun-Ling Yang, Chuan-Feng Chen and Zhi-Tang Huang*

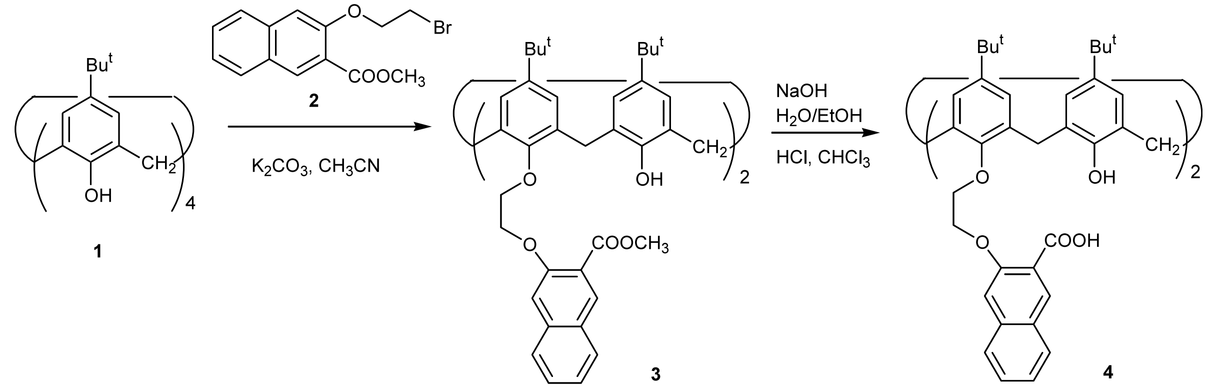
Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China

Received 10 June 2002; revised 23 September 2002; accepted 4 October 2002

Abstract—A novel fluorescent compound derived from calixarene which possesses two 3-alkoxy-2-naphthoic acid moieties has been synthesized in moderate yield. In H_2O/CH_3OH (1:1), its fluorescent intensity was quenched sharply in the presence of Cu^{2+} or Fe^{3+}, and the degree of quenching was related to the pH of the solution. Other metal ions, such as Co^{2+}, Ni^{2+}, Zn^{2+}, Mn^{2+}, Mg^{2+} and Ba^{2+} did not affect its fluorescent spectra. This research may provide a new fluorescent probe for Cu^{2+} and Fe^{3+}.

Molecular recognition is a crucial process in biological systems such as enzymes, antibodies or genes, and also is fundamental to supramolecular chemistry.[1] Chemical sensing, which combines a recognition element with an optical or electronic transduction element, has received much attention as an efficient analytical technique for the detection of particular species.[2] Among chemosensory systems, the fluorescent method is very important due to its simpler instrumentation, high selectivity, and direct visual perception even in very dilute solutions.[3] In addition on/off fluorescence switching based on molecular recognition has potential for information processing.[4]

Calixarenes, which possess a versatile three-dimensional cavity, are ideal frameworks or building blocks for the development of fluorescent receptors for molecular recognition via the incorporation of an appropriate sensory group into the calixarene having a preorganized substrate binding site. Several fluorescent chemosensors based on calixarenes have been synthesized and show highly selective recognition, especially towards alkali metal cations.[5] A few transition metal cations, e.g. Cu^{2+}, Ni^{2+} etc. have also been investigated.[6] However, the generation of fluorescent sensors for transition metals is of increasing importance for biological and environmental applications. Unlike alkali and alkaline



Scheme 1.

Keywords: calix[4]arene; chemosensor; fluorescent spectra; iron; copper.

* Corresponding authors. Tel.: +86-10-62544082; fax: +86-10-62559373; e-mail: huangzt@public.bta.net.cn

PII: S0040-4039(02)02265-7

earth metals, transition metals do not differ too much in size, but they can establish coordinative interactions of very different energies, which can be used for discriminative purposes, especially for fluorescent sensing.[7]

3-Hydroxy-2-naphthoic acid (HNA) is an interesting fluorescent transduction system, which can be phototautomerised involving intermolecular hydrogen bonding with the solvent in the ground state.[8] Although the use of acyclic polyether dicarboxylic acids derived from HNA in competitive solvent extraction of alkaline-earth cations has been investigated,[9] there is no report on the fluorescent chemosensory properties of calixarenes with HNA as the fluorescent moiety. Here, we report a new fluorescent chemosensor for Fe^{3+} and Cu^{2+} based on the calix[4]arene framework and transduction of HNA.

The synthesis of chemosensor **4** is very convenient. Alkylation of calix[4]arene **1** with methyl 3-(2-bromoethoxy)-naphthalene-2-carboxylate **2**, which can be obtained from methyl 3-hydroxynaphthalene-2-carboxylate,[10] was carried out to give *1,3-distal* substituted calixarene **3** in 42% yield. After hydrolysis of **3** in the presence of NaOH, and acidification with $HCl–H_2O/CHCl_3$, the fluorescent ligand **4** could be obtained in almost quantitative yield (Scheme 1). The spectroscopic and elemental analyses of **3** and **4** confirmed their structures and also indicated that the calixarene moiety of these compounds adopts the cone conformation.[11]

The UV absorption spectrum of **4** upon the addition of cations in a mixed solvent of $CH_3OH–H_2O$ (1/1, v/v) at different pHs shows no obvious change, apart from the addition of the absorbance of the substrate. However their fluorescent spectra show different behavior. The emission spectra ($\lambda_{ex} = 238$ nm) of compound **4** (0.92 μM) at pH 6.9 in the presence of various concentrations of $Cu(ClO_4)_2$ are shown in Fig. 1 from which it can be seen that the fluorescence intensity ($\lambda_{em} = 387$ nm) of **4** is decreased continually upon addition of Cu^{2+} with no significant change in the position of the emission maxima. When the concentration of Cu^{2+} is 4 times that of the ligand, the intensity decreased 12-fold. So, **4** is a sensitive Cu(II) fluorescent probe. Since under these conditions, $Cu(ClO_4)_2$ had very little absorption at the excitation wavelength of 238 nm, the decrease in the fluorescence intensity of **4** was not due to the absorption of $Cu(ClO_4)_2$.

A Stern–Volmer plot is shown in Fig. 2, which demonstrates that chelation between **4** and Cu^{2+} enhanced the fluorescence quenching. In addition, from Fig. 2 we deduced that this plot fits the 1:1 stoichiometry of the complex at the low $[Cu^{2+}]$ concentration ($[Cu^{2+}]/[\mathbf{4}] \leq 1$). On increasing the concentration of $[Cu^{2+}]$, other complexes with different stoichiometries were present in the solution.

Similar measurements for several soft metal ions, such as Fe^{3+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Mn^{2+}, Mg^{2+} and Ba^{2+} were examined. However, except for Fe^{3+}, the changes in the fluorescence spectra could scarcely be detected when these cations were added to the solutions of **4** under the same conditions. So it can also be concluded that the calixarene **4** has higher selectivity for recognition of Cu^{2+} and Fe^{3+}.

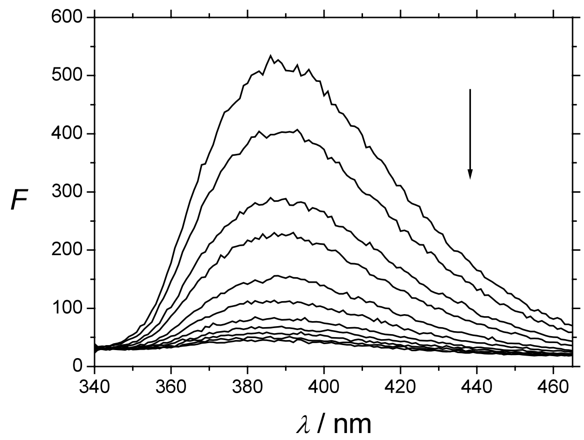


Figure 1. Fluorescence of calixarene **4** (9.2×10^{-7} M) quenched by $Cu(ClO_4)_2$ ($\lambda_{ex} = 238$ nm) in $CH_3OH–H_2O$ (1/1, pH 6.9). The concentration of $Cu(ClO_4)_2$ (9.2×10^{-7} M): 0, 0.4, 0.8, 1.2, 1.6, 2, 2.4, 2.8, 3.2, 3.6, 4. Spectral resolution of the instrument: 1 nm.

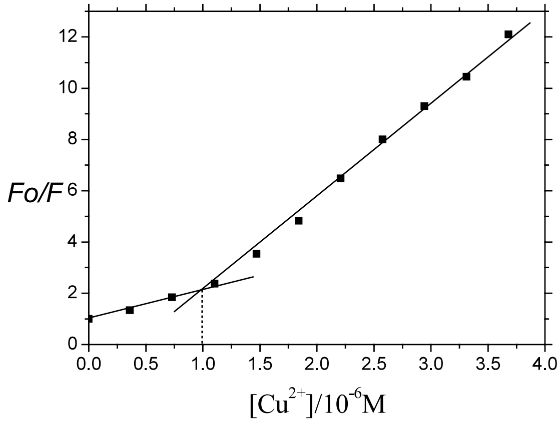


Figure 2. Relative fluorescence intensity for a mixture of **4** and $Cu(ClO_4)_2$ plots against $[Cu(ClO_4)_2]$. ($\lambda_{ex} = 238$ nm, $CH_3OH–H_2O$ (1/1, pH 6.9), $[\mathbf{4}] = 9.2\times10^{-7}$ M).

It is interesting that the degree of quenching in the presence of Cu^{2+} and Fe^{3+} was associated with the pH of the solution (adjusted with H_2SO_4 or KOH), and the trend is shown in Fig. 3. At a pH<4.5, the two naphthalene acids are not deprotonated and **4** displays the most fluorescent intensity. On increasing the pH, the fluorescent intensity decreased, and reaching a minimum at pH 5.6 for Fe^{3+}, and pH 6.9 for Cu^{2+}, respectively. This can be explained by deprotonation of **4** and the formation of complexes. The electron-rich carboxylate groups (in particular, their deprotonated oxygen atoms) can act as electron donors and quench, through an eT mechanism, the nearby photoexcited fluorophores. However, we are not very clear as to why the fluorescent intensity is increasing along with the increasing pH after reaching the lowest point. Maybe on increasing the pH of the solution, the two phenol groups of the calixarene will be deprotonated, and Fe^{3+} or Cu^{2+}

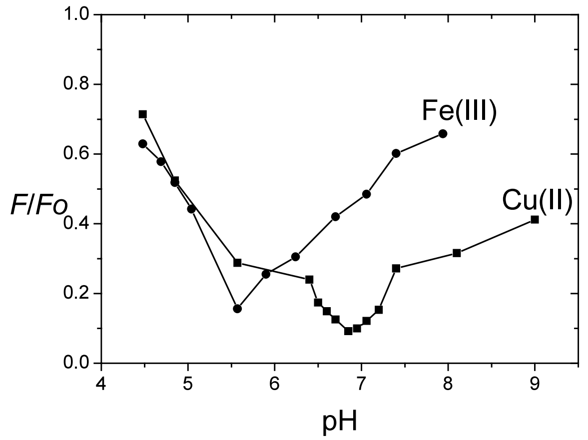


Figure 3. pH–Fluorescence profiles of **4**: ● in the presence of 4 molar equivalents of Fe^{3+}, ■ in the presence of 4 molar equivalents of Cu^{2+} (CH_3OH:H_2O = 1:1 v/v).

moves into the cavity formed by the skeleton of the calixarene due to the stronger complexation ability of the phenolic oxygen (Fig. 4).

In this system, the fluorescent sensors could be denoted as switches. On–off fluorescent switching is activated by ionic substrates and on–off–on fluorescent switching is activated by H^+ in the presence of Fe^{3+} or Cu^{2+}. We have changed the pH value by adding acid or base to the same solution containing both **4** and Fe^{3+} or Cu^{2+}, and the fluorescent intensity changes reversibly according to Fig. 3.

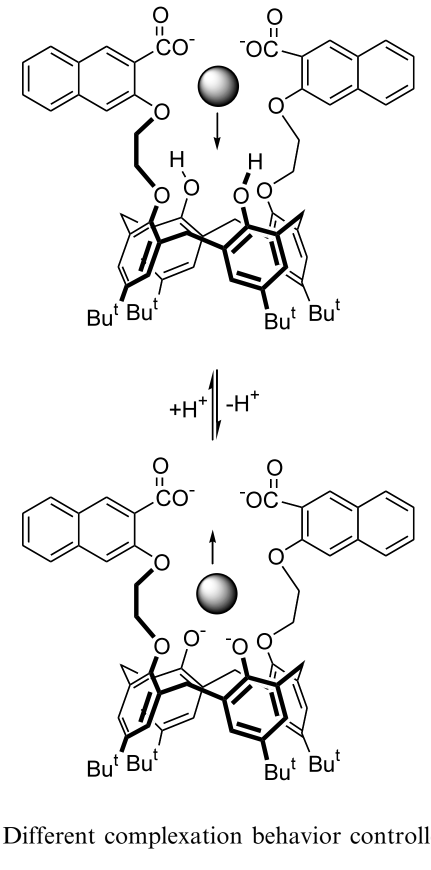


Figure 4. Different complexation behavior controlled by pH.

In summary, we have synthesized a new fluorescent ligand based on calix[4]arene of which the fluorescent intensity was quenched selectively in the presence of Cu^{2+} or Fe^{3+}, and the quenching behavior was related to the pH value of the solution.

Acknowledgements

We thank the National Natural Science Foundation of China, the Major State Basic Research Development Program of China (Grant No. G2000078100) and the Chinese Academy of Sciences for financial support.

References

1. (a) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*; John Wiley and Sons Ltd: Chichester, 2000; (b) Schneider, H.-J.; Yatsimirsky, A. *Principles and Methods in Supramolecular Chemistry*; John Wiley and Sons Ltd: Chichester, 2000; (c) Lehn, J.-M.; Atwood, J. L.; Davies, J. E. D.; MacNicol, D. D.; Vögtle, F. Eds, *Comprehensive Supramolecular Chemistry*; Pergamon: New York, 1996; (d) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinhheim, 1995.
2. Desvergne, J.-P.; Czarnik, A. W. *Chemosensors of Ion and Molecule Recognition*, *NATO ASI series*; Kluwer Academic: Dordrecht, 1997.
3. *Fluorescent Chemosensors for Ion and Molecule Recognition*, ACS Symposium Series No. 538; Czarnik, A. W., Ed.; American Chemical Society: Washington, DC, 1992.
4. De Silva, A. P.; Gunaratne, H. Q. N.; McCoy, C. P. *Nature* **1993**, *364*, 42.
5. Matsumoto, H.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 77.
6. Bodenant, B; Weil, T.; Businelli-Pourcel, M.; Fages, F.; Barbe, B.; Pianet, I.; Laguerre, M. *J. Org. Chem.* **1999**, *64*, 7034.
7. Fabbrizzi, L.; Licchelli, M.; Pallavicini, P.; Parodi, L.; Taglietti, A. In *Transition Metals in Supramolecuar Chemistry*; Sauvage, J. P., Ed. Fluorescent sensors for and with transition metals; John Wiley & Sons Ltd: Chichester, 1999.
8. (a) Ware, W. R.; Shukla, P. R.; Sullivan, P. J.; Bremphis, R. V. *J. Chem. Phys.* **1971**, *55*, 4048; (b) Kovi, P. J.; Schulman, S. G. *Anal. Chem.* **1973**, *45*, 989.
9. Kang, S. I.; Czech, A.; Czech, B. P.; Stewart, L. E.; Bartsch, R. A. *Anal. Chem.* **1985**, *57*, 1713.
10. Reina, J. A.; Serra, A.; Cádiz, V. *Macromol. Chem. Phys.* **1996**, *197*, 3001.
11. **3**: Yield: 42%; mp: 254–255°C; ^1H NMR: δ 8.24 (s, 2H, naph-H), 7.85 (s, 2H, naph-H), 7.75 (t, J = 8.1 Hz, 4H, naph-H), 7.51 (t, J = 7.4 Hz, 2H, naph-H), 7.35 (t, J = 7.5 Hz, 2H, naph-H), 7.07 (s, 2H, OH), 6.98 (s, 4H, ArH), 6.91 (s, 4H, ArH), 4.33 (AB, J = 13.0 Hz, 4H, $ArCH_2Ar$), 4.22 (m, 8H, OCH_2CH_2O), 3.52 (s, 6H, OCH_3), 3.30 (AB, J = 12.9 Hz, 4H, $ArCH_2Ar$), 1.22 (s, 18H, $C(CH_3)_3$), 1.07 (s, 18H, $C(CH_3)_3$); ^{13}C NMR: δ 166.7 (CO_2), 154.5, 150.5, 149.9, 146.9, 141.3, 135.8, 132.9, 132.5, 128.6, 128.3, 127.7, 127.6, 126.5, 125.7, 125.2, 124.5, 122.6, 107.8 (ArC), 73.5, 67.6 (OCH_2), 52.0 (OCH_3), 34.0, 33.8

(C(CH$_3$)$_3$), 32.0 (ArCH$_2$Ar), 31.6, 31.2 (C(CH$_3$)$_3$); IR (KBr) ν 3457, 2956, 1733, 1631, 1478 cm^{-1}; MALDI-TOF MS: *m*/*z* 1127 [(M+Na)$^+$]; anal. calcd for $C_{72}H_{80}O_{10}$: C, 78.23; H, 7.30; found C, 78.22; H, 7.28%. **4**: Yield: 97%; mp: 270–271°C; ^{1}H NMR: δ 8.49 (s, 2H, naph-H), 7.75 (t, *J*=7.9 Hz, 4H, naph-H), 7.69 (s, 2H, naph-H), 7.51 (t, *J*=7.4 Hz, 2H, naph-H), 7.39 (t, *J*=7.5 Hz, 2H, naph-H), 7.32 (s, 2H, OH), 7.01 (s, 4H, ArH), 6.87 (s, 4H, ArH), 4.63 (m, 4H, OCH$_2$CH$_2$O), 4.51 (m, 4H, OCH$_2$CH$_2$O), 4.33 (AB, *J*=13.0 Hz, 4H, ArCH$_2$Ar), 3.32 (AB, *J*=12.9 Hz, 4H, ArCH$_2$Ar), 1.24 (s, 18H, C(CH$_3$)$_3$), 1.00 (s, 18H, C(CH$_3$)$_3$); ^{13}C NMR: δ 167.7 (CO$_2$), 154.0, 150.2, 149.6, 147.9, 142.3, 136.6, 135.6, 133.1, 129.5, 129.3, 128.6, 128.2, 126.9, 126.3, 125.5, 125.5, 120.7, 108.8 (ArC), 73.9, 68.6 (OCH$_2$), 34.4, 34.2 (C(CH$_3$)$_3$), 32.0 (ArCH$_2$Ar), 32.0, 31.4 (C(CH$_3$)$_3$); IR (KBr) ν 3457, 2956, 1733, 1631, 1478 cm^{-1}; MALDI-TOF MS: *m*/*z* 1099 [(M+Na)$^+$]; IR (KBr) ν 3464, 2959, 1728, 1632, 1479 cm^{-1}; anal. calcd for $C_{70}H_{76}O_{10}$: C, 78.04; H, 7.11. Found C, 77.59; H, 7.21%.