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# A new $Hg^{2+}$-selective fluorescent sensor based on a dansyl amide-armed calix[4]-aza-crown

Qi-Yin Chen[a,b] and Chuan-Feng Chen[a,*]

[a] *Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China*
[b] *Graduate School of Chinese Academy of Sciences, Chinese Academy of Sciences, Beijing 100080, China*

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**Abstract**—A new fluorescent chemosensor for $Hg^{2+}$ based on a dansyl amide-armed calix[4]-aza-crown was reported. It exhibits high sensitivity and selectivity toward $Hg^{2+}$ over a wide range of metal ions in MeCN–$H_2O$ (4:1, v/v). The association constant of the 1:1 complex formation for **2**-$Hg^{2+}$ was calculated to be $1.31 \times 10^5\,M^{-1}$, and the detection limit for $Hg^{2+}$ was found to be $4.1 \times 10^{-6}\,mol\,L^{-1}$.

Recognition and sensing of heavy and transition metal ions via artificial receptors are of current interest in supramolecular chemistry because of their significant importance in chemical, biological, and environmental assays.[1] Of particular interest in this regard are fluorescent sensors, because they have both high sensitivity and ease of signal transduction.[2] A practical fluorescent sensor for targeting ions of specific importance should at least have the following properties: simplicity, high selectivity, strong signal output, wide conditions of coordination and recognition in aqueous environments.[2a]

In recent years, considerable effort has been devoted to the selective and efficient detection of $Hg^{2+}$ ion, as mercury and its salts have high toxicity, and they are widely used in industry and widespread in environment.[3] Some examples of fluorescent chemosensors for $Hg^{2+}$ have been reported,[4] however, many of these systems displayed short-comings in practical use, such as the lack of aqueous solubility, cross-sensitivities toward other metal ions, short emission wavelength and weak fluorescence intensity. As a result, developing new and practical sensor systems for $Hg^{2+}$ is still a challenge. More recently, Nolan and Lippard[5] reported a water-soluble fluorescein-based sensor for $Hg^{2+}$, and Qian and co-workers[6] reported a simple and water-soluble PET chemosensor for $Hg^{2+}$.

Calixarenes are an important class of macrocyclic compounds and also an ideal platform for the development of complexing agents for heavy and transition metal ions.[7] Although optical sensors based on calixarene derivatives for selective $Hg^{2+}$ recognition have received ever-increasing attention,[8] only a few calix[4]arene-based fluorescent sensors for $Hg^{2+}$ have been reported.[4g] On the other hand, dansyl group is one of the most attractive fluorophores[9] due to its strong fluorescence, relatively long emission wavelength and easy derivation. In this letter, we report a new fluorescent **2** for $Hg^{2+}$ based on a dansyl amide-armed calix[4]-aza-crown.[10b] Strong signal output in neutral aqueous environments of recognition, high selectivity, and sensitivity made **2** to be a potential powerful candidate as a practical fluorescent sensor for $Hg^{2+}$.

The calix[4]-aza-crown **1** was synthesized according to the literature.[10] Compound **1** was reacted with dansyl chloride in $CH_2Cl_2$ in the presence of triethylamine to give the fluorescent receptor **2** in 90% yield (Scheme 1). The structure of **2** was identified by $^1H$ NMR, $^{13}C$ NMR, MALDI-TOF MS, and elemental analysis, which indicated that the calix[4]arene backbone adopted the cone conformation.[11]

All of the fluorescence titration experiments were performed in MeCN–$H_2O$ (4:1, v/v) and the maximum excitation wavelength was selected at 338 nm. As shown in

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* Corresponding author. Tel.: +86 10 62588936; fax: +86 10 62554449; e-mail: cchen@iccas.ac.cn

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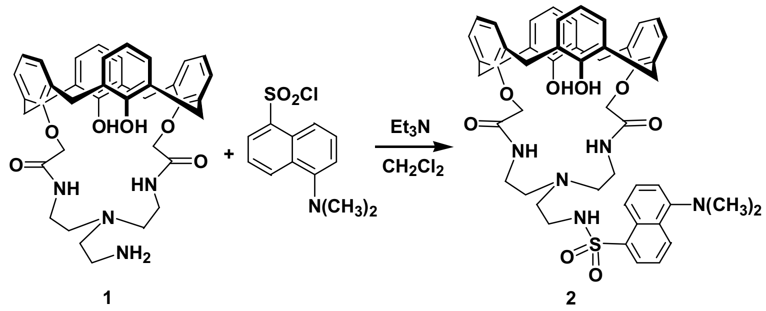


**Scheme 1.** Synthesis of compound **2**.

Scheme 1, compound **2** showed a typical emission band of the dansyl group around 520 nm, which was considerably quenched in the presence of $Hg^{2+}$. This phenomenon may occur by electron transfer from the exited dansyl moiety to the proximate mercuric ion.[8b] When the concentration of $Hg^{2+}$ ions was increased up to $3.5 \times 10^{-5}$ mol $L^{-1}$ (3.5 equiv), more than 80% quenching of the initial fluorescence of **2** was observed (Fig. 1). From the fluorescence titration experiments, the association constant ($K_a$) of the 1:1 complex formation for **2**-$Hg^{2+}$ was calculated to be $(1.31 \pm 0.02) \times 10^5 M^{-1}$ by Stern–Volmer equation.[12] Furthermore, the detection limit[13] of **2** as a fluorescent sensor for the analysis of $Hg^{2+}$ was also determined from the plot of the fluorescence intensity as a function of the concentration of added metal ions. It was found that **2** has a detection limit of $4.1 \times 10^{-6}$ mol $L^{-1}$ for $Hg^{2+}$ ions, which is sufficiently low for the detection of the submillimolar concentration range of $Hg^{2+}$ ions found in many chemical and biological systems.

In order to determine the stoichiometry of the **2**-$Hg^{2+}$ complex, the method of continuous variations (Job's method) was also used (Fig. 2). As expected, the result obtained from the Job plot unambiguously indicates the formation of a 1:1 complex between **2** and $Hg^{2+}$. Thus, a four-coordinate mode[4e] of **2**-$Hg^{2+}$ complex could be proposed, in which three amide nitrogens and one amine nitrogen constructed nearly a tetrahedron, whose center was occupied by $Hg^{2+}$ ion (Scheme 2).

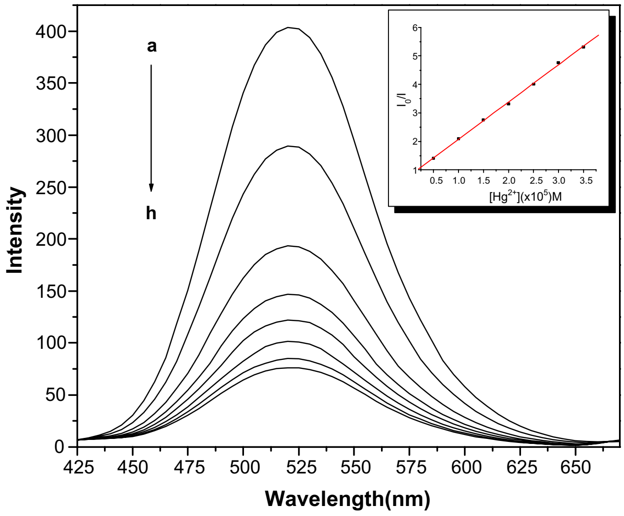


**Figure 1.** Fluorescent titration of **2** with $Hg^{2+}$ in MeCN–$H_2O$ (4:1, v/v), $[\mathbf{2}] = 1 \times 10^{-5}$ mol $L^{-1}$, $[Hg^{2+}] = 2 \times 10^{-3}$ mol $L^{-1}$, $\lambda_{ex} = 338$ nm. From a–h: 0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5 equiv. Inset: the plot of $I_0/I$ versus $[Hg^{2+}]$.

Under the same conditions as above, we also tested the fluorescent response of **2** to other metal ions besides $Hg^{2+}$. As shown in Figure 3, although the fluorescence of **2** at 520 nm was strongly quenched by $Hg^{2+}$, no significant spectral changes of **2** occurred in the presence of 3.5 equiv $Li^+$, $Na^+$, $K^+$, $Mg^{2+}$, $Ca^{2+}$, $Ba^{2+}$, $Mn^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, $Zn^{2+}$, $Ag^+$, $Cd^{2+}$, and $Pb^{2+}$, respec-

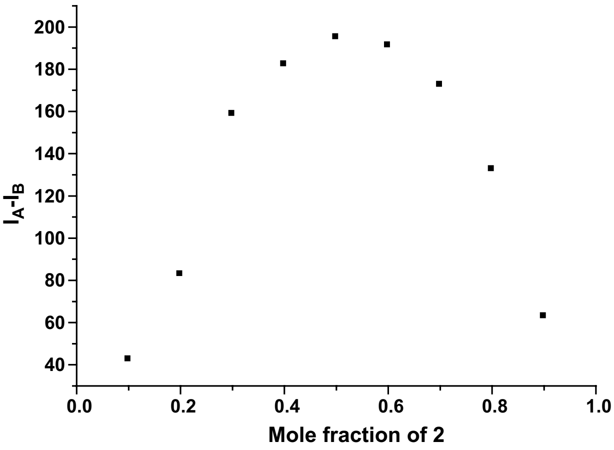
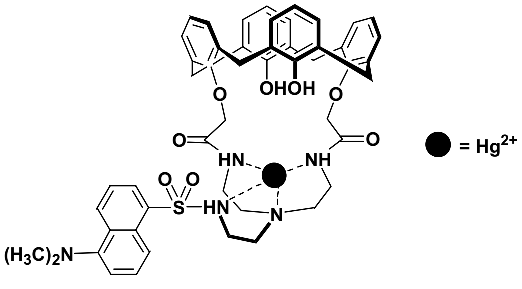


**Figure 2.** Job plot for **2** and $Hg^{2+}$: $[\mathbf{2}] + [Hg^{2+}] = 2.0 \times 10^{-5}$ mol $L^{-1}$ in MeCN–$H_2O$ (4:1, v/v), $\lambda_{ex} = 338$ nm.



**Scheme 2.** Proposed binding mode of **2** with $Hg^{2+}$.

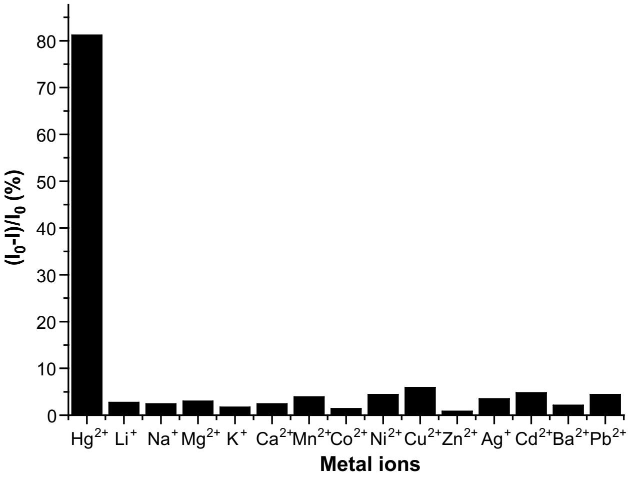


**Figure 3.** Quench ratio ($(I_0 - I)/I_0$) of fluorescent intensity of **2** ($1 \times 10^{-5}$ mol L$^{-1}$) upon the addition of 3.5 equiv metal ions in MeCN–$H_2O$ (4:1, v/v).

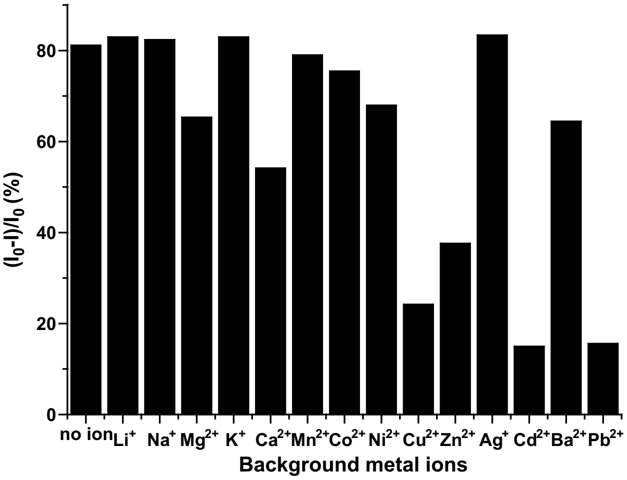


**Figure 4.** Quench ratio ($(I_0 - I)/I_0$) of fluorescent intensity of **2** upon the addition of 3.5 equiv $Hg^{2+}$ in the presence of 10 equiv background metal ions in MeCN–$H_2O$ (4:1, v/v).

tively, in MeCN–$H_2O$ (4:1, v/v). Furthermore, the $K_a$ values (errors $\leqslant \pm 0.08 \times 10^3$ M$^{-1}$) of 1:1 complexes **2**-$M^{n+}$ for other metal ions were calculated from the fluorescence titration experiments, and summarized in Table 1. The selectivity[9b] toward $Hg^{2+}$ with respect to other metal ions (expressed as the ratio of the stability constants) was found about 55-fold or more. These results implied that **2** showed high selectivity towards $Hg^{2+}$ over other metal ions tested in a neutral aqueous solution.

To test practical applicability of **2** as a $Hg^{2+}$-selective fluorescence chemosensor, competition experiments were carried on. Thus, **2** ($1 \times 10^{-5}$ mol L$^{-1}$) was treated with 3.5 equiv $Hg^{2+}$ in the presence of background metal ions ($10 \times 10^{-5}$ mol L$^{-1}$), respectively, which resulted in diverse fluorescence behaviors. As shown in Figure 4, except for $Pb^{2+}$, $Cu^{2+}$, $Cd^{2+}$, and $Zn^{2+}$ ions,[14] other background metal ions had small or no obvious interference with the detection of $Hg^{2+}$ ions. These results suggested that compound **2** could be used as a potential $Hg^{2+}$-selective fluorescent chemosensor.

In summary, we have presented a new fluorescent sensor **2** based on a dansyl amide-armed calix[4]-aza-crown, which showed high sensitivity and selectivity toward $Hg^{2+}$ ions over a wide range of metal ions in MeCN–$H_2O$ (4:1, v/v). The detection limit for $Hg^{2+}$ was found to be $4.1 \times 10^{-6}$ mol L$^{-1}$. Thus, **2** may be considered as a potentially practical $Hg^{2+}$-selective fluorescent chemosensor.

## Acknowledgements

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**Table 1.** The $K_a$ values ($\times 10^3$ M$^{-1}$) of 1:1 complexes **2**-$M^{n+}$

| $M^{n+}$ | $Li^+$ | $Na^+$ | $K^+$ | $Mg^{2+}$ | $Ca^{2+}$ | $Ba^{2+}$ | $Mn^{2+}$ | $Co^{2+}$ | $Ni^{2+}$ | $Cu^{2+}$ | $Zn^{2+}$ | $Ag^+$ | $Cd^{2+}$ | $Pb^{2+}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $K_a$ | 0.95 | 0.88 | —[a] | 1.13 | —[a] | —[a] | 1.37 | —[a] | 1.47 | 2.39 | —[a] | 1.36 | 1.50 | —[b] |

[a] Not available because of the minor spectral change.

[b] The stoichiometry between **2** and $Pb^{2+}$ was not determined.

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11. To the mixture of compound **1** (1.2 g, 1.85 mmol) and $Et_3N$ (1.1 mL) in $CH_2Cl_2$ (100 mL) was added dropwise dansyl chloride (0.5 g, 1.85 mmol) in $CH_2Cl_2$ (50 mL) over a period of one hour at 0 °C. After being stirred for 3 h at room temperature, the reaction mixture was washed with water (50 mL) three times, dried over anhydrous $Na_2SO_4$ and filtered. The solvent was evaporated under reduced pressure and then the resulting residue was separated by column chromatography using dichloromethane/ethyl acetate as eluent to give **2** as a yellow power solid (1.47 g, 90% yield): mp 233–234 °C; $^1$H NMR ($CDCl_3$, 300 MHz): 8.95 (t, $J = 5.34$ Hz, 2H, CON**H**), 8.48 (d, $J = 8.56$ Hz, 1H), 8.47 (d, $J = 8.39$ Hz, 1H), 8.21 (d, $J = 7.19$ Hz, 1H), 7.96 (s, 2H, OH), 7.48–7.52 (m, 2H), 7.14 (d, $J = 7.58$ Hz, 4H), 7.11 (d, $J = 8.30$ Hz, 1H), 6.93 (d, $J = 7.55$ Hz, 4H), 6.75–6.81 (m, 4H), 6.50 (t, $J = 4.27$ Hz, 1H, N**H**$SO_2$), 4.69 (s, 4H, OC**H**$_2$), 4.24 (d, $J = 13.42$ Hz, 4H, ArC**H**$_2$Ar), 3.52 (t, $J = 5.34$ Hz, 4H, C**H**$_2$NHCO), 3.49 (d, $J = 13.42$ Hz, 4H, ArC**H**$_2$Ar), 3.13 (t, $J = 5.44$ Hz, 2H, C**H**$_2$NH$O_2$S), 2.84 (s, 6H, $CH_3$), 2.80 (t, $J = 5.34$ Hz, 4H, NC**H**$_2$), 2.62 (t, $J = 5.44$ Hz, 2H, NC**H**$_2$); $^{13}$C NMR ($CDCl_3$, 75 MHz): 169.5, 152.1, 151.7, 151.1, 136.6, 132.6, 129.9, 129.8, 129.7, 129.1, 128.4, 128.0, 127.7, 126.6, 123.2, 120.7, 119.7, 115.0, 75.1, 54.5, 52.3, 45.4, 40.9, 39.9, 31.6; MALDI-TOF MS: $m/z = 884.7$ $(M+H)^+$. Anal. Calcd for $C_{50}H_{53}N_5O_8S{\cdot}H_2O$: C, 66.57; H, 6.15; N, 7.76; S, 3.55. Found: C, 66.39; H, 6.25; N, 7.42; S, 3.57.
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14. Similar phenomena, see Refs. 4b and 5.