

A new Hg²⁺-selective chromoionophore based on calix[4]arene diazacrown ether†

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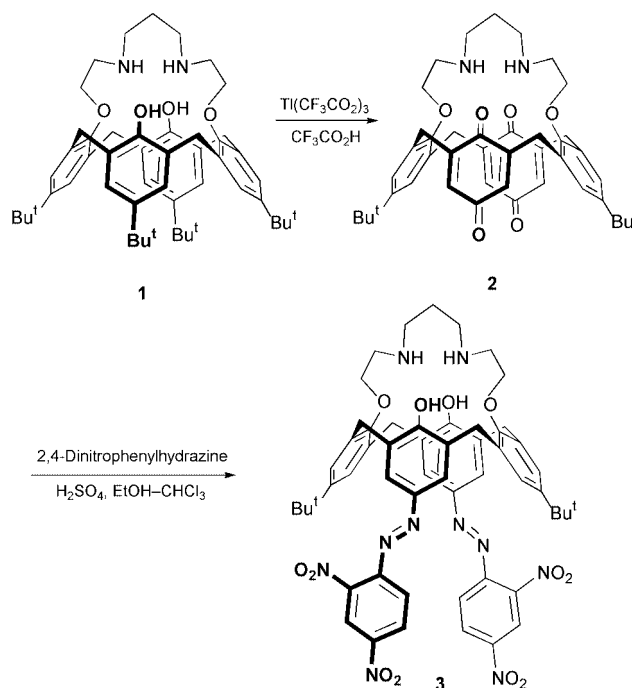
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A new azophenol type chromogenic ionophore based on the *p*-*tert*-butylcalix[4]arene diazacrown ether was prepared: the ionophore exhibited a pronouncedly selective chromogenic behaviour toward Hg²⁺ ions among the surveyed guests of alkali, alkaline earth, transition and heavy metal ions in liquid–liquid extraction experiments.

Selective signaling of heavy metal ions is a very important topic for the detection and treatment of the toxic metal ions in various chemical systems including living systems.^{1,2} There are, however, relatively few examples of designed sensors for the heavy metal ions in comparison with the variety of compounds developed for the alkali and alkaline earth metal ions.³ For the selective recognition of soft heavy metal ions, nitrogen binding sites might be a choice as is well exemplified with classical azacrown ethers.⁴ Obviously, a suitably designed calix[4]arene azacrown ether derivative might be a good candidate. This can be realized by combining the azacrown ether moiety as a binding site with the molecular framework of a calix[4]arene as a handle for the elaborate further functionalization to endow the signaling properties.⁵ Recently, sensitive ionophores having chromogenic and fluorogenic functions have begun to be devised for heavy metal ions.^{6–11} Azophenol groups are one of the most frequently employed functions as a signaling device for the design of chromogenic ionophores and a lot of derivatives based on the crown ethers and calixarenes showed unique chromogenic behaviours toward a variety of guest species.¹² Here, we report the synthesis of a new chromogenic ionophore having 2,4-dinitrophenylazophenol functions derived from the *p*-*tert*-butylcalix[4]arene diazacrown ether and its selective chromoionophoric behaviour toward Hg²⁺ ions in liquid–liquid extraction systems.

The azophenol derivative was prepared from diazacrown ether **1**,¹³ as shown in Scheme 1. Oxidation of the diazacrown ether **1** with Ti(CF₃CO₂)₃ in TFA gave the diquinone **2** (61%).[‡] Reaction of the resulting diquinone **2** with 2,4-dinitrophenylhydrazine (EtOH–CHCl₃, with trace H₂SO₄)¹⁴ afforded 2,4-dinitrophenylazophenol derivative **3** (44%). The resulting product was purified by column chromatography (silica gel, CH₂Cl₂–MeOH, 9:1) followed by recrystallization from CH₂Cl₂–MeOH.

The chromoionophoric properties of the azophenol **3** were investigated by the liquid–liquid extraction of metal ions from buffered aqueous solution into chloroform. The azophenol **3** itself showed a typical UV spectral behaviour of 2,4-dinitrophenylazophenol derivatives and revealed a distinct colour change from yellow ($\lambda_{\max} = 424$ nm) to blue ($\lambda_{\max} = 619$ nm) around pH 8.5 as the pH of the aqueous phase increases. The metal ion extraction experiments were performed at pH 6 buffered with morpholin-4-ylethanesulfonic acid (MES) to prevent the possible complications in chromogenic responses of **3**. The aqueous solution containing varying amounts of target metal ions (up to 0.05 mol dm⁻³) was extracted with the chloroform solution containing azophenol ionophore ([**3**] = 2 × 10⁻⁵ mol dm⁻³) at 25 °C. After extraction, the organic phase



Scheme 1

was separated and the UV spectra of the solution were measured. The guest ions surveyed were representative alkali (Li⁺, Na⁺, K⁺, Rb⁺), alkaline earth (Mg²⁺, Ca²⁺, Ba²⁺), transition metal (Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺) and heavy metal ions (Cd²⁺, Hg²⁺, Pb²⁺) in perchlorate.

The ionophore showed pronounced chromogenic responses to Hg²⁺ and Cd²⁺ ions among the tested metal ions (Fig. 1). Upon interaction with 100 equiv. of Hg²⁺ ions, the colour of the ionophore solution changed distinctly from yellow ($\lambda_{\max} = 424$ nm) to red ($\lambda_{\max} = 500$ nm). With Cd²⁺ ions, a more dramatic change in the UV spectrum was observed and the λ_{\max} of **3** was significantly red-shifted and transformed into two bands (from

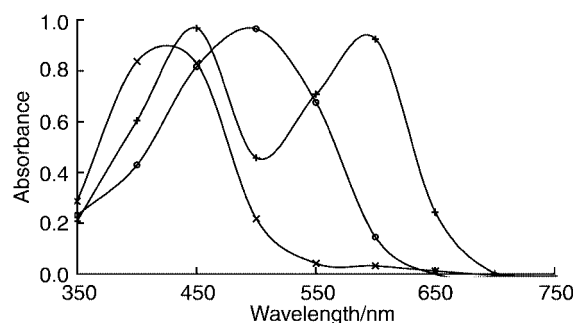


Fig. 1 Absorption spectra of **3** in CHCl₃ upon extraction with aqueous metal ion solution. [**3**] = 2 × 10⁻⁵ mol dm⁻³ in CHCl₃. [M²⁺] = 2 × 10⁻³ mol dm⁻³ in MES buffer at pH 6: (x) **3**, (+) **3** with Cd²⁺ and (o) **3** with Hg²⁺.

† Dedicated to Professor Iwhan Cho on the occasion of his 65th birthday.

Table 1 Spectral responses of **3** upon interaction with varying chemical stimuli

Initial form ^a	Reagent added ^b	Final form
3 -Hg ²⁺	Cd ²⁺	3 -Hg ²⁺
3 -Hg ²⁺	EDTA	3 ^c
3 -Cd ²⁺	Hg ²⁺	3 -Hg ²⁺
3 -Cd ²⁺	EDTA	3

^a Formed by the extraction with 50 equiv. of guest metal ions. [**3**] = 2×10^{-5} mol dm⁻³ in CHCl₃.^b Concentration of reagents added = 5×10^{-3} mol dm⁻³.^c Transforms relatively sluggishly compared with **3**-Cd²⁺-EDTA system.

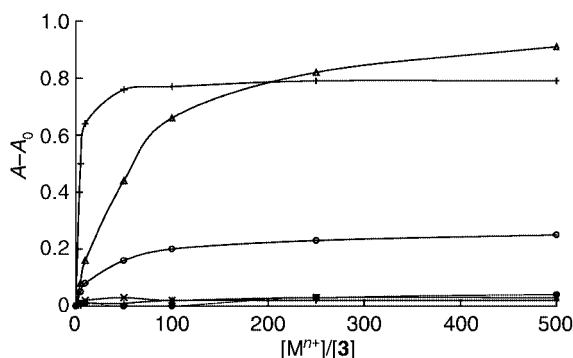


Fig. 2 Changes in absorbance of **3** induced by metal ions. Δ Abs at 500 nm with the addition of (\times) Na⁺, ($*$) Mg²⁺, (\bullet) Zn²⁺, (\circ) Cd²⁺ and ($+$) Hg²⁺ ions. (Δ) Δ Abs at 591 nm with Cd²⁺ ion addition. [**3**] = 2×10^{-5} mol dm⁻³. Δ Abs = (Abs of **3** in the presence of metal ion - Abs of **3**).

424 to 457 and 591 nm). Interestingly, the changes in spectral pattern induced by Cd²⁺ ions are quite different from Hg²⁺ ions, which suggests that the two metal ions can be discriminated, even visually, with the present chromogenic ionophore system. Other guest ions of alkali, alkaline earth, and transition metal ions revealed almost no changes in the chromogenic behaviour of **3** at the present extraction conditions of pH 6.

The selective chromogenic behaviour of **3** toward Hg²⁺ ions was further evidenced by the competitive extraction experiments. The ionophore **3** showed a pronounced Hg²⁺-selectivity even in the presence of a large excess of other metal ions. For example, the absorption spectrum of **3**-Hg²⁺ (obtained by the extraction of 2×10^{-5} mol dm⁻³ of **3** with 50 equiv. Hg²⁺ ions) in CHCl₃ was almost unaffected by the addition of 500 equiv. of alkali, alkaline earth, transition metal, and Pb²⁺ ions. Even with Cd²⁺ as competitive guest ion, the chromogenic behaviour of the **3**-Hg²⁺ system was retained up to 250 equiv. of Cd²⁺ ions (Table 1). In contrast to this, the spectral behaviour of **3**-Cd²⁺ was changed upon addition of 2 equiv. of Hg²⁺ ions, and the spectrum was progressively converted into almost that of **3**-Hg²⁺ system by treatment with 30 equiv. of Hg²⁺ ions. These observations clearly showed that the ionophore **3** has much higher affinity toward Hg²⁺ than Cd²⁺ ions, that is in good agreement with the transport results of parent calix[4]-arene diazacrown compound **1** reported earlier.¹³

To have more insight for the selectivity and sensitivity of the present ionophore system, the effects of metal ion concentration in aqueous phase on the absorption spectrum of **3** were investigated. Fig. 2 shows the changes in absorbance of **3** induced by the most responding ions among the surveyed alkali, alkaline earth, transition and heavy metal ions. The selectivity ratios for Hg²⁺ over other representative metal ions, estimated from the ratio of the metal ions required for the same Δ Abs value at 500 nm, were as follows: Na⁺, 830; Mg²⁺, 480; Zn²⁺, 250; Cd²⁺, 28. Upon interaction with as low as 4 equiv. of Hg²⁺ ions, visibly discernible changes in chromogenic behaviour

were observed for **3**. With Cd²⁺ ions, similar colour change from yellow to violet was observed with around 10 equiv. of guest ions, that can also be easily detected visually. From these measurements the detection limits of **3** for Hg²⁺ and Cd²⁺ ions were estimated to be 1×10^{-5} mol dm⁻³ (at 500 nm) and 8×10^{-5} mol dm⁻³ (at 591 nm), respectively. One more thing to note is the facile regeneration of the ionophore by simple treatment with EDTA solution, that suggests the reusability of the compound as a reversible sensor material. The ionophore solution **3**-Hg²⁺ and **3**-Cd²⁺ fully restored the spectrum of free **3** by the back extraction of extracted guest metal ions with 0.1 mol dm⁻³ EDTA solution at pH 6 (Table 1). In this case, however, the **3**-Hg²⁺-EDTA system restores the free **3** spectrum relatively sluggishly compared with the **3**-Cd²⁺-EDTA system, which also implies that Hg²⁺ interacts more strongly with **3** than Cd²⁺ ions.

In conclusion, we have developed a new azophenol type chromogenic ionophore having high selectivity toward Hg²⁺ and possibly Cd²⁺ ions via metal ion induced deprotonation of the azophenol moieties. Although ionophore **3** needs more optimization for the practical applications in terms of selectivity and sensitivity, we believe that this compound can be utilized, along with many intriguing systems developed up to now,^{15,16} for the detection of toxic Hg²⁺ and Cd²⁺ ions which are of general interest in the treatment of industrial waste streams.

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Notes and references

† Selected data for **2**: ¹H NMR (CDCl₃, 300 MHz) δ 6.92 (s, 4H, quinone-H), 6.69 (s, 4H, ArH), 4.01 (br t, 4H, OCH₂CH₂N), 3.91 and 3.29 (d, 4H each, $J = 13.5$ Hz, ArCH₂Ar), 3.03 (br t, 4H, OCH₂CH₂N), 2.96 (br t, 4H, NCH₂CH₂CH₂N), 1.72 (br m, 2H, NCH₂CH₂CH₂N), 1.12 (s, 18H, CMe₃); FAB MS (*m*-NBA), m/z 691 ($M + 1$)⁺. For **3**: ¹H NMR (CDCl₃, 300 MHz) δ 8.78 (s, 2H, ArH), 8.48 and 7.82 (d, 2H each, $J = 9$ Hz, ArH), 7.78 and 7.08 (s, 4H each, ArH), 4.37 and 3.57 (d, 4H each, $J = 13.2$ Hz, ArCH₂Ar), 4.28 (br t, 4H, OCH₂CH₂N), 3.33 (br t, 4H, OCH₂CH₂N), 3.13 (br t, 4H, NCH₂CH₂CH₂N), 2.08 (br m, 2H, NCH₂CH₂CH₂N), 1.11 (s, 18H, CMe₃); FAB MS (*m*-NBA), m/z 1051.5 ($M + 1$)⁺.

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