# Novel fluorogenic calix[4]arene-bis(crown-6-ether) for selective recognition of thallium(I)†

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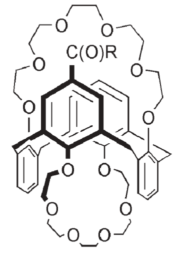
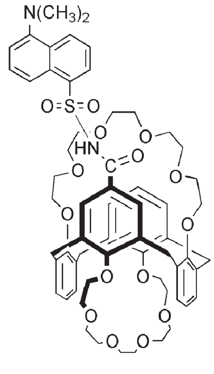
**A new fluorogenic, dansyl group-containing derivative of *1,3-alternate* calix[4]arene-bis(crown-6-ether) provides optical recognition of Tl$^+$ with selectivity over many other metal cations, including Na$^+$, K$^+$, Ca$^{2+}$, Ag$^+$, Hg$^{2+}$ and Pb$^{2+}$, and embodies the first example of a calixarene-based fluorescent Tl$^+$-chemosensor.**

The necessity for monitoring concentrations of hazardous metal ions that are brought into the environment in elevated amounts as a result of human activities dictates the need for the development of new detection methods and reagents. During the last decade, numerous specific optical chemosensors for metal ions have been obtained *via* covalent attachment of fluorophore moieties to macrocyclic receptors or by incorporation of an optical probe into the macrocycle.[1] Thus, promising results for optical detection of various hazardous metal cations were obtained with employment of fluorogenic derivatives of calixarenes.[2] For example, proton-ionizable calix[4]arenes containing dansyl groups on the lower rim behaved as selective sensors for heavy metal ions Hg$^{2+}$ [3a] and Pb$^{2+}$;[3b] coumarin-, anthracene- and other fluorophore-derivatized *1,3-alternate* calix[4]arene-crown-6 and -bis(crown-6) ethers allowed for efficient detection of Cs$^+$.[4] However, no fluorogenic calixarene- or calixcrown-based ligands for recognition of Tl$^+$ have been reported, to the best of our knowledge.[5] The aim of the present research was design of a fluorescent chemosensor for this toxic heavy metal ion.

It was envisioned that for Tl$^+$, which is a soft electron acceptor known for π-coordination with a calix[4]arene aromatic framework[6] and, on the other side, for forming stable complexes with crown ethers (in particular, with 18-crown-6 derivatives),[7] calix[4]arene-crown-6 in *1,3-alternate* conformation would be an appropriate ligand scaffold. Ionophores of this type, designed originally for selective separation of Cs$^+$, favor cation–π interactions and discriminate metal ions by size. The ionic radius of Tl$^+$ (which is almost equal to that of Rb$^+$, the principal competing species for Cs$^+$ in complexation with the *1,3-alternate* calixcrown-6 framework),[8] is expected to be a good geometric fit for the cavity of such a macrocyclic ligand. Earlier, we prepared a series of mono-ionizable *1,3-alternate* calix[4]arene-bis(crown-6) derivatives (structure **1**) for efficient and selective extraction of Cs$^+$.[8] Herein, introduction of a dansyl moiety into the pendant proton-ionizable group of the ligand **1** scaffold gave rise to a novel fluoroionophore **2**, which we now report as the first example of a calixarene-based fluorescent chemosensor for Tl$^+$.



**1**: R = NHSO$_2$X
X = CF$_3$, CH$_3$, Ph,
4-NO$_2$C$_6$H$_4$



**2**

Fluorogenic calix-biscrown **2** was obtained by reaction of *1,3-alternate* 5-chlorocarbonylcalix[4]arene-bis(crown-6) **3**[8] with dansyl amide in the presence of NaH in THF.‡

The acidic nature of the sulfonylamide NH-group in **2** results in proton dissociation of this ligand in solution and, therefore, suggests that complex formation of **2** may proceed *via* proton displacement by a metal cation. Due to this, the effect of acid-dissociation of **2** on its fluorescence spectrum§ in H$_2$O–CH$_3$CN (1 : 1 v/v) mixture was evaluated prior to the metal complexation studies in the same solvent. Evolution of the emission spectrum of **2** at varied pH is shown in Fig. 1a. In agreement with the data reported earlier for other dansyl-containing calixarene-based ionophores,[3b] the emission band of **2**, which was observed at $\lambda_{em}$ = 541 nm (with excitation at 330 nm) in acidic solutions (dil. HNO$_3$), exhibited a gradual hypsochromic shift $\Delta\lambda_{em}$ of up to 46 nm accompanied by enhancement of the fluorescence intensity *I* as the pH increased from 1.0 to 8.0. For further metal recognition studies of **2** in H$_2$O–CH$_3$CN (1 : 1 v/v), a working pH of 3.5 was chosen. At this pH, the fluorogenic ligand exists predominantly in undissociated form HL, as evident from the dependence of $\Delta\lambda_{em}$ *vs.* pH (Fig. 1b).

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† Electronic supplementary information (ESI) available: $^1$H NMR spectra of **2** and complex Tl$^+$(**2**)$^-$. See DOI: 10.1039/b510348g

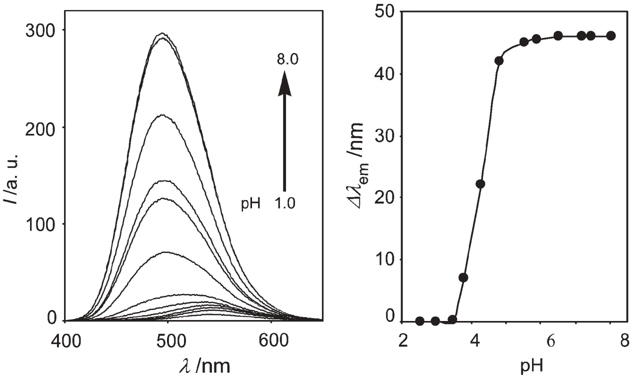

**Fig. 1** (a) Evolution of the fluorescence emission spectrum of **2** ($7.5 \times 10^{-6}$ M, excitation at 330 nm) in $H_2O$–$CH_3CN$ (1 : 1, v/v) with increasing pH and (b) the plot of the emission band shift as a function of pH.

Addition of $Tl^+$ (as $TlNO_3$)¶ to the solution of **2** in $H_2O$–$CH_3CN$ (1 : 1 v/v, pH 3.5) in the range of metal-to-ligand molar ratio $C_{Tl}/C_2$ from 0 to 200 produced a gradual decrease of the ligand fluorescence intensity along with hypsochromic shift of the emission band (Fig. 2a). Such a trend is distinctive from the earlier observed effects for complexation of dansyl-containing calix[4]-arenes with soft $Hg^{2+}$ (*i.e.*, significant fluorescence quenching at unchanged emission wavelength, rationalized in terms of photo-induced electron transfer, PET)‖ as well as for harder $Pb^{2+}$ (which was analogous to the *vide supra* effect from the pH variation, rationalized in terms of NH-proton displacement by the metal ion).[3b] It may be assumed that interaction of soft cation of Tl(I) with the dansyl-calixbiscrown **2** engages both of the above mechanisms. The observed moderate reduction of the emission intensity of **2** is a combined effect from at least two divergent factors: fluorescence quenching *via* PET involving $Tl^+$ and fluorescence enhancement associated with dansyl NH-group ionization. With an excess of **2** over the analytical concentration of $Tl^+$ in solution ($C_{Tl}/C_2$ 0 ÷ 1), only slight deviation of $\lambda_{em}$ from 541 nm (HL) is observed, and the emission intensity $I$ at this wavelength declines linearly with increasing $C_{Tl}$ (Fig. 2b). This plot was used as a calibration curve for determination of microconcentrations of $Tl^+$, with the detection limit under given experimental conditions of $7.0 \times 10^{-8}$ M, or 14 μg $L^{-1}$. Further studies of $Tl^+$ complexation with **2** and its non-fluorogenic analogs are in progress.

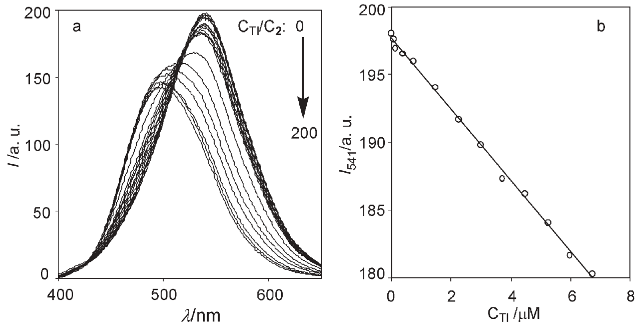

**Fig. 2** (a) Changes in the fluorescence emission spectrum of **2** ($7.5 \times 10^{-6}$ M, excitation at 330 nm) in $H_2O$–$CH_3CN$ (1 : 1, v/v) at pH 3.5 upon addition of increasing concentrations of $Tl^+$ and (b) the plot of the emission intensity at 541 nm as a function of analytical concentration of $Tl^+$.

Addition under otherwise identical conditions of $Na^+$, $K^+$, $Ag^+$, $Ca^{2+}$, $Pb^{2+}$, $Hg^{2+}$ and some of the transition metal ions to the solution of **2** did not produce any evident effect on the fluorescence spectrum of this ionophore. The only noteworthy exception was $Cs^+$, whose interaction with the dansyl-calixbiscrown **2** was accompanied by spectral changes different from those observed at $Tl^+$ complexation and typical for the dansyl NH-group ionization.**

Structural studies of $Tl^+(\mathbf{2})^-$ complex were performed by $^1H$ NMR††. Preliminary results showed that binding of $Tl^+$ produces significant changes in the spectrum of **2**, in particular, in chemical shifts of a singlet from the aromatic protons in the *o*-positions to the site of attachment of the proton-ionizable side arm and a doublet from the corresponding protons on the opposite aryl moiety. Such a behavior suggests participation of the *1,3-alternate* calixarene framework in $Tl^+$ coordination. Detailed analysis of the NMR spectra for the complexes of **2** with $Tl^+$ and other metal ions is in progress and will be reported elsewhere.

In summary, our results demonstrate that *1,3-alternate* calix[4]-arene-crown-6 is a promising scaffold for design of ligands for selective recognition of Tl(I).

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## Notes and references

‡ Preparation of **2**. To a mixture of dansyl amide (0.31 g, 1.22 mmol) and NaH (0.08 g, 3.27 mmol) in THF (25 mL), a solution of **3** (0.72 g, 0.82 mmol) in THF (25 mL) was added. The mixture was stirred under nitrogen at rt for 18 h, then 1 mL of water was added. The THF was evaporated *in vacuo*, and $CH_2Cl_2$ (50 mL) was added to the residue. The organic phase was washed with aqueous $Na_2CO_3$, dried ($Na_2SO_4$) and evaporated *in vacuo*. Column chromatography of the residue on silica gel with $CH_2Cl_2$–MeOH (95 : 5) as an eluent gave a yellow substance which was dissolved in $CH_2Cl_2$, washed with 10% aqueous HCl, evaporated and dried *in vacuo*. Compound **2** is a bright greenish-yellow solid. Yield 0.64 g (71%), mp 203–205 °C; $^1H$ NMR (400.13 MHz, $CDCl_3$, 298 K): 2.87 (s, 6 H), 3.24–3.53 (m, 16 H), 3.55–3.92 (m) + 3.69 (s) (32 H), 6.87 (t, $J$ = 7.4 Hz, 2 H), 6.90 (t, $J$ = 7.4 Hz, 1 H), 7.05–7.18 (m) + 7.11 (d, $J$ = 7.4 Hz) (7 H), 7.39 (s, 2 H), 7.56–7.62 (m, 2 H), 8.48 (d, $J$ = 8.5 Hz, 1 H), 8.53–8.59 (m, 2 H), 10.87 (br s, 1 H); HRMS (ESI): found 1103.4576 $[M - H]^-$ (calcd. for $C_{61}H_{71}N_2O_{15}S$ 1103.4575), found 1127.4552 $[M + Na]^+$ (calcd. for $C_{61}H_{72}N_2O_{15}SNa$ 1127.4551). Anal calcd. for $C_{61}H_{72}N_2O_{15}S \times H_2O$: C 65.16, H 6.59, N 2.49. Found: C 65.28, H 6.51, N 2.18.

§ Corrected fluorescence spectra were recorded with a Shimadzu RF-5301PC spectrofluorophotometer.

¶ CAUTION! Compounds of Tl(I) are highly toxic and may cause severe health effects if swallowed, inhaled or adsorbed through skin.

‖ Observed for complexation of $Hg^{2+}$ with di(dansyl)-calix[4]arene originally in solvent extraction system $H_2O$–$CHCl_3$ (ref. 3*a*) and later in a $H_2O$–$CH_3CN$ mixture (ref. 3*b*).

** Studies of $Cs^+$ recognition with **2** are in progress and will be published elsewhere.

†† $Tl^+(\mathbf{2})^-$ was prepared by interaction of **2** in $CDCl_3$ with an excess of solid $Tl_2CO_3$, analogous to the procedure given in ref. 8. $^1H$ NMR (299.94 MHz, $CDCl_3$, 298 K): 2.83 (s, 6 H), 3.34 (br s, 2 H), 3.50 (br s, 2 H), 3.57–4.03 (m, 38 H), 4.07–4.18 (m, 2 H), 4.18–4.30 (m, 2 H), 4.35–4.47 (m, 2 H), 6.83–7.25 (m, 10 H), 7.40 (dd, $J$ = 8.5 Hz, 7.6, 1 H), 7.49 (dd, $J$ = 8.4 Hz, 7.2, 1 H), 7.63 (d, $J$ = 8.5 Hz, 2 H), 8.34 (d, $J$ = 8.4 Hz, 1H), 8.45 (dd, $J$ = 7.2 Hz, 1.2, 1 H), 8.86 (d, $J$ = 8.6 Hz, 1 H).

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