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Dansyl-containing fluorogenic calixarenes as optical chemosensors of hazardous metal ions: a mini-review

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Dansyl-containing fluorogenic calixarenes as optical chemosensors of hazardous metal ions: a mini-review[†]

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Fluorescent chemosensors serve as an efficient tool for selective detection of toxic metal ions (Hg^{2+}, Cd^{2+}, Pb^{2+}, etc.) in the environment. This review is focused on optical metal ion recognition with employment of calixarene-based sensors containing one or more dansyl fluorophore groups. The effect of structural variations, including the mode of dansyl unit attachment, calixarene scaffold type and conformation, as well as the identity and pattern of upper- and lower-rim substituents on the selectivity and sensitivity of these fluoroionophores towards hazardous metal ions is discussed.

Keywords: fluorogenic calixarenes; dansyl; chemosensors; optical recognition; heavy metal ions

Introduction

Presence of elevated amounts of hazardous metal ions, mercury(II), lead(II), cadmium(II), thallium(I), caesium(I) and others in the environment produces severe effects on human health. This necessitated the US Environmental Protection Agency (EPA) and World Health Organization (WHO) to impose strict limits on the allowable levels of these pollutants in water (*1*, *2*). In particular, the EPA regulates the maximum contaminant level in drinking water at 2 μg/l (or ppb) for Hg(II) and Tl(I), 5 μg/l for Cd(II), 15 μg/l for Pb(II) and 1.3 mg/l for Cu(II) (*1*). Therefore, the development of new reagents and techniques for selective and efficient detection of hazardous metal ions has been continuously attaining efforts of scientists. In these terms, analytical procedures involving complexation-based fluorescent sensors are expected to provide a simpler and more affordable alternative to such commonly used instrumental methods as inductively coupled plasma mass spectrometry, cold vapour atomic absorption spectroscopy, cold vapour atomic fluorescence spectroscopy, etc. A typical design of an optical chemosensor consists of a metal receptor with covalently attached fluorophore responsive to complexation-induced changes in the electron environment (*3*). During the last decade, fluorogenic calixarene derivatives have received significant attention as promising reagents for selective metal ion recognition (see (*4–6*) for the recent reviews). Among these fluoroionophores, a populated group of ligands incorporating dansyl probes occupy an important place due to their general propensities for cations of heavy and transition metals. This mini-review focuses on the progress in the development of dansyl-containing calixarenes as selective chemosensors of hazardous metal ions.

Dansyl (5-dimethylaminonaphthalene-1-sulphonyl) group is a convenient environment-sensitive optical probe with a large Stokes shift which has been widely used in biochemical research (e.g. see (*7–11*)). Dansyl fluorophore has found numerous applications in the design of optical sensors for neutral analytes (e.g. dansyl-appended cyclodextrins (*12–15*)) as well as for metal ions on the basis of open-chain (*16–20*) and macrocyclic chelators (*21–26*), fluorescent peptides and proteins (*27–29*) and modified materials (film-coated glass (*30*), silica nano-particles (*31*, *32*), silicon nano-wires (*33*), dendrimers (*34*), microgels (*35*), etc.). In the late 1990s, first dansyl group-containing thiacalix[4]arene (*36*) and calix[4]arene (*37*) were reported as selective chemosensors of Cd^{2+} and Hg^{2+}, respectively. At present, publications describing hazardous metal ion recognition with the employment of more than 40 different calixarene-based ligands (including calix[4]arenes, calix[4]-crowns and thiacalix[4]arenes) with conjugated dansyl fluorophores are available in the literature. One may also find the reports of dansyl-appended calixarenes responsive to neutral molecules, such as alkaloids (*38*), and inorganic (*39*) and amino acid anions (*40*). However, such sensors are outside of the scope of this review.

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[†] This paper is dedicated to the memory of our dear friend and colleague, Prof. Dmitry M. Rudkevich.

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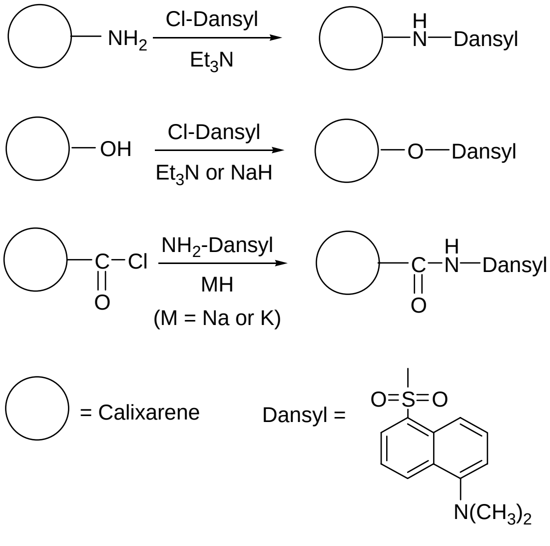
General characteristics of dansyl-containing calixarene-based fluoroionophores

Known metal-sensing dansyl-containing fluorogenic calixarenes (as well as thiacalixarenes) vary in the fashion of the fluorophore attachment to the receptor moiety as *HN*-dansyl (*37*, *41–54*) and *O*-dansyl ligands (*36*, *55–57*) (for the structural formulae, see Figures 1–4). In the former type, the anchor NH-group usually is a part of carbamoyl or aminoalkyl linker, or it may be bound directly to the aromatic ring of the calixarene; while in the latter type, the dansyl moiety is a substituent on the calixarene lower-rim phenolic oxygen. Typically, conjugation of dansyl unit is achieved by the reaction of dansyl chloride with phenolic or amino groups of calixarene derivatives, except for *N*-dansylcarboxamides which are obtained by the treatment of the appropriate calixarene acid chlorides with dansylamide in the presence of a metal hydride (Scheme 1).

Fluorescence spectral characteristics of both types of dansyl-containing calixarenes, similarly to any other compounds containing this optical probe, are sensitive to the environment. In particular, their emission wavelength and intensity vary with polarity and hydrophobicity of the solvent. At the same time, *HN*-dansyl calixarene derivatives have a distinctive feature: in contrast to *O*-dansyl, the *HN*-dansyl group is capable of proton dissociation, and its acidity depends on the electron-withdrawing capacity of the adjacent part of the ligand molecule. Ionisation of the neighbouring NH-group increases the electron density on the 5-dimethylaminonaphthalene moiety which results in a hypsochromic (blue) shift and intensity enhancement of its fluorescence emission band relative to that in the spectrum of non-ionised compound. This makes fluorescence wavelength and intensity of *HN*-dansyl calixarenes responsive to factors that may cause ionisation, i.e. pH and metal ion coordination.



Scheme 1. Conjugation of dansyl units to calixarenes.

Photoinduced electron transfer (PET) (*4*, *6*) is the most common photophysical mechanism behind sensing of redox-active transition metal ions, including soft heavy metal cations, e.g. Hg^{2+}, Cd^{2+} and Tl^{+}, by calixarenes with dansyl fluorophores. In these systems, the complex formation produces strong quenching of the ligand fluorescence intensity explained in terms of electron transfer from the excited dansyl fluorophore to the coordinated redox-active metal ion (the so-called reverse PET). At the same time, the proton-ionisable nature of *HN*-dansyl group makes complexation behaviour of such ionofluorophores distinctive and enables their sensing of metal ions in an alternative fashion. Binding of a metal cation may proceed via the NH-proton displacement. Accordingly, the spectral response of the dansyl fluorophore to the ion recognition event consists of an increase in the fluorescence intensity accompanied by hypsochromic shift of the emission band, consistent with the enhancement of electron density on the 5-dimethylaminonaphthalene ring caused by ionisation of the adjacent NH-group. In particular, this allowed to use a ratiometric approach in monitoring the concentrations of such hazardous metal ions as Pb^{2+}(*43*, *44*) and Cs^{+} (*58*) with the employment of *HN*-dansyl-containing calixarenes.

Metal coordination properties of *HN*-dansyl and *O*-dansyl groups have peculiarities as well. The former behaves as a softer donor of electrons, in part, due to the possibility of negative charge delocalisation upon the NH-proton dissociation. Accordingly, *HN*-dansyl-appended calixarenes are especially attractive for soft heavy metal ions (in particular, Hg^{2+}(*37*, *41*, *42*, *50–53*)). By contrast, a somewhat harder electron donor, *O*-dansyl group shows greater tendency for coordination of intermediate in softness transition metal ions such as Cu^{2+} (*56*).

Optical sensing of hazardous metal ions by dansyl-containing fluoroionophores

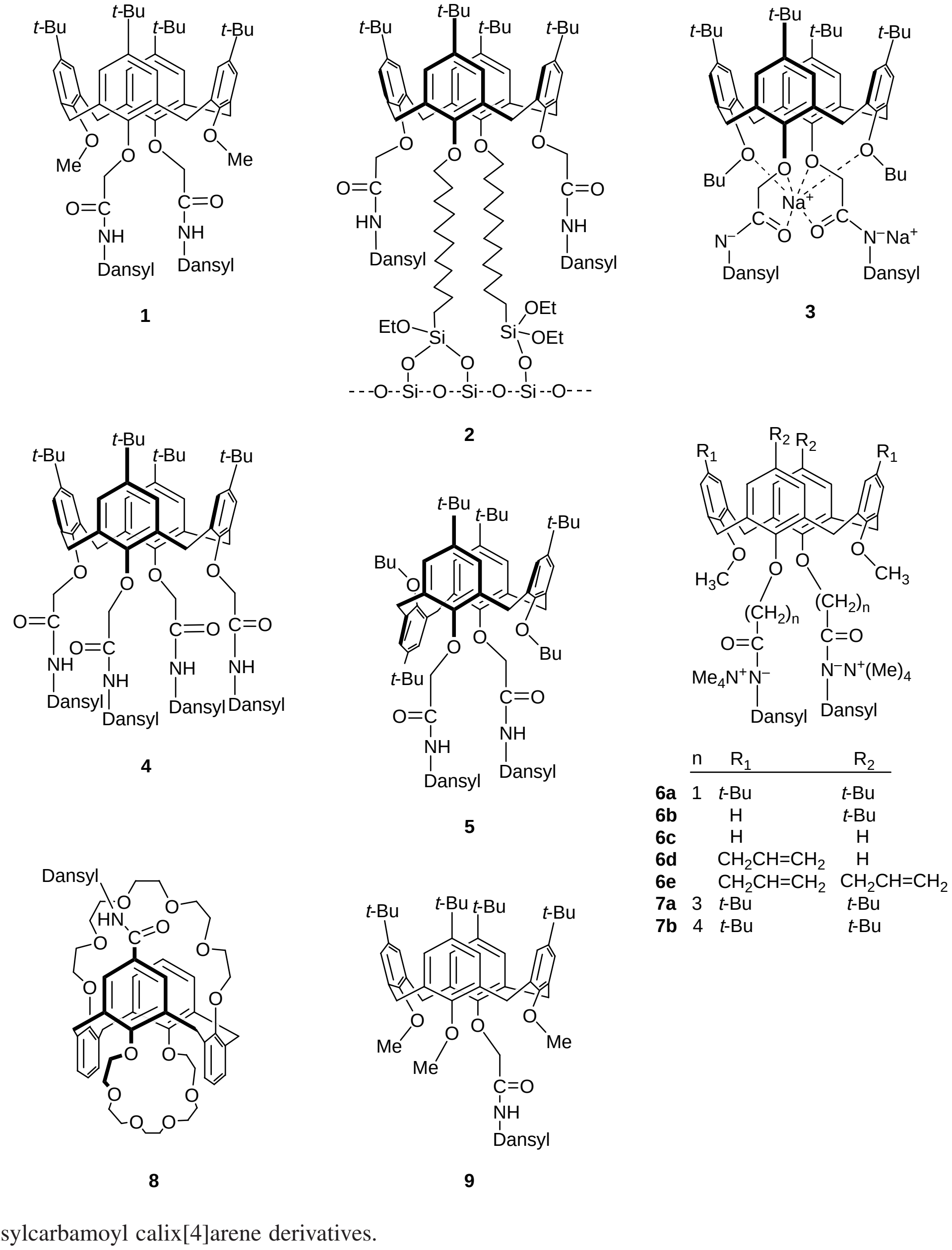
It should be mentioned that despite general similarities in fluorescence behaviour of calix[4]arene and thiacalix[4]arene dansyl derivatives, thiacalixarenes as metal ion receptors possess unique features that are responsible for their divergent selectivities from their methylene-bridged calixarene analogues (*59*). Due to this, in the following discussion of metal ion sensing by dansyl-containing fluoroionophores, calix[4]arene-based ligands and thiacalix[4]arenes will be considered separately. Furthermore, the former group will be subdivided into *HN*-dansyl and *O*-dansyl calixarenes. The readers will find the structural formulae of the ligands organised by the type in Figures 1–4. Quantitative characteristics of metal ion recognition by the fluoroionophores, such as detection limits (for one of the commonly used analytical methods, see (*60*)) and complex formation constants (*61*), if available, are presented in Tables 1–3 along with other pertinent information.

HN-dansyl-appended calix[4]arene and calix[4]-crown sensors

N-Dansylcarboxamides

We begin the discussion of hazardous metal ion sensing by dansyl-containing calixarenes with *N*-dansylcarboxamides which is the most represented group of the fluoroionophores under consideration. These ligands possess appreciable acidity of *HN*-dansyl group and hence, metal ion complexation typically involves their ionisation due to the proton displacement.

Ligands with two and four N-dansylcarbamoyl groups. The earliest representative of dansyl-containing calix[4]arenes, conformationally mobile ligand **1** (Figure 1) with two pendent *N*-dansylcarbamoyl groups on the lower rim was reported in 1999 by Bartsch and co-workers (*37*). At the time of publication, it was the first calixarene-based chemosensor for selective optical recognition of mercury(II). In solvent extraction of increasing concentrations of Hg^{2+} from acidic aqueous solutions (pH 2.5, dil. HNO_3) into $CHCl_3$, **1** exhibited gradual decrease in its fluorescence emission at essentially constant wavelength,



	n	R1	R2
6a	1	t-Bu	t-Bu
6b		H	t-Bu
6c		H	H
6d		$CH_2CH{=}CH_2$	H
6e		$CH_2CH{=}CH_2$	$CH_2CH{=}CH_2$
7a	3	t-Bu	t-Bu
7b	4	t-Bu	t-Bu

Figure 1. *N*-dansylcarbamoyl calix[4]arene derivatives.

λ_{em}, of 520 nm (with excitation at 330 nm). This spectral response of the dansyl-containing ligand to mercury(II) coordination was attributed to PET from the excited fluorophore to Hg^{2+} ion. Under the indicated experimental conditions, with the analytical concentration of the ligand in the organic phase $C_1 = 5.0 \times 10^{-2}$ M, the detection limit for mercury(II) in the aqueous phase of 5.0×10^{-6} M was achieved (Table 1). Selectivity of **1** for mercury(II) was probed in the competitive extractions of aqueous $Hg(NO_3)_2$ (pH 2.5, dil. HNO_3) from binary mixtures with 100-fold excess of alkali, alkaline earth metal cations as well as Ag(I), Tl(I), Cd(II), Co(II), Cu(II), Ni(II), Pb(II), Pd(II), Zn(II) and Fe(III) nitrates. The experiments showed no significant interferences from the competing metal ions (the fluorescence intensity variation under ±3%) with Hg^{2+} recognition by **1**. This early work demonstrated the promise of dansyl-containing calixarenes as fluorescent chemosensors of hazardous metal ions.

For practical applications, sensitivity towards the analyte is a crucial characteristic of any detection method, and it may be improved by variation of the reagent and/or optimisation of the experimental conditions (solvent, reagent concentration, pH, etc.). The latter was demonstrated by Leray et al. (*62*) who employed **1** in optical recognition of Hg^{2+} in aqueous acetonitrile ($MeCN-H_2O$ 60:40 v/v) (Table 1) and achieved the detection limit of 3×10^{-7} M, i.e. nearly 17 times lower than that in (*37*), with the selectivity of mercury determination remaining very high. Compound **1** was found to bind Hg^{2+} as 1:1 complex with formation constant, K_f^{app}, of 1.5×10^7 l/mol.

It is interesting that although the complexation of Hg^{2+} by the proton-ionisable **1** is expected to proceed via the NH-proton displacement, no noticeable blue shift of the ligand fluorescence maximum was observed in the presence of increasing concentrations of mercuric ion both in solvent extraction system (*37*) and homogeneous solution (*62*). A possible reason for this phenomenon consists of a substantially covalent nature of Hg–N bond (e.g. see (*63*)).

Investigation of the effect of calixarene scaffold structure on the efficiency and selectivity of the *N*-dansylcarboxamide fluoroionophores for hazardous metal ions has been receiving continuous effort of scientists. As it follows from the analysis of the literature data, work in this direction has been focused on such structural aspects as calixarene conformation, number of pendent fluorophore groups, identity of the upper-rim substituents and the length of the spacers connecting *N*-dansylcarbamoyl groups with the calixarene unit.

Thus, it is known that during complexation with a metal ion, a conformationally mobile calixarene tends to adopt the shape which is the most appropriate for accommodation of this particular guest (for sample publications, see (*64*, *65*)). Preorganisation via synthesis of the calixarene moiety in the favourable conformation is expected to yield the reagent with improved sensorial properties towards the targeted metal cation. The preferred geometry in solution may be determined by NMR spectroscopy applied to the metal complex of the flexible ligand. In particular, in complexes with Hg^{2+}, mobile calix[4]arene *N*-dansylcarboxamide **1** was found to prefer the *cone* (*62*) and, under different experimental conditions, *1,3-alternate* conformation (*44*).

With the aim to develop an optical sensor for efficient and selective practical determination of Hg^{2+} in water, Leray and co-workers (*41*) grafted calix[4]arene di(*N*-dansylcarboxamide) moiety fixed in the *cone* conformation on mesoporous silica (**2**, Figure 1). This fluoroionophore-modified material used as a suspension in water allowed for the reversible detection of mercury(II) at the level of 3.3×10^{-7} M (Table 1). The stability of **2**-Hg^{2+} complex in H_2O as well as selectivity of the *cone* **2** towards Hg^{2+} over other relevant metal ions were found to be somewhat smaller than those for the mobile prototype **1** in $MeCN-H_2O$ solution (see above). This decrease was explained by the effect of the changed solvent system and possible lack of the ligand flexibility due to its immobilisation on the silica surface. Another probable reason might consist of hindered access of Hg^{2+} to the lower-rim cavity formed by pendent *N*-dansylcarbamoyl groups in **2**.

Very recently, a rigid analogue **3** of mobile fluoroionophore **1** preorganised in the *cone* conformation for improved Hg^{2+} sensing has been reported by our research group (*42*). During the synthesis, the ligand was found to possess strong affinity for Na^+ and due to this, it was isolated, characterised and further used in metal ion recognition studies as a disodium salt of the di-ionised calixarene di(*N*-dansylcarboxamide) (Figure 1). Nevertheless, the metal complexation study of **3** revealed even higher propensity of this reagent for binding Hg^{2+}. In solvent extraction ($CHCl_3$) of mercuric ion from aqueous solutions with high sodium content (pH 5.0, 0.1 M Na-acetate buffer), a strong quenching of fluorescence intensity of **3** at λ_{em} of 468 nm (emission wavelength of the ionised *N*-dansylcarbamoyl fluorophore; λ_{ex} 340 nm) was observed which allowed for determination of Hg^{2+} in water with the detection limit of 8.0×10^{-7} M (Table 1). Compound **3** was found to extract Hg^{2+} as a 1:1 complex via sodium displacement by the mercuric ion. (It should be mentioned at this point that the ability to detect hazardous metal ions in the presence of excess Na^+, the most abundant metal ion in natural water, is a crucial property of any chemosensor.) Preorganisation of the calixarene framework in the favourable *cone* conformation resulted in significant enhancement of both sensitivity of Hg^{2+} detection by **3** relative to the flexible prototype **1** and its selectivity in competitive extractions from aqueous binary mixtures with other metal ions (Pb^{2+}, Cd^{2+}, Fe^{3+}, Cu^{2+}, Zn^{2+}, Ca^{2+}, etc.). To further investigate the influence of

Table 1. Metal ion recognition by *HN*-dansyl-appended calix[4]arene-based ligands.

Ligand	Conformation	Metal ion	Solvent/conditions	λ_{em} (λ_{ex}), (nm)	Detection limit	Complex formation constant (log β)	Complex stoichiometry (M:L)	Reference
N-dansylcarboxamides								
1	Mobile	Hg^{2+}	Extraction H_2O–$CHCl_3$; pH 2.5 (HNO_3); $C_L = 5.0 \times 10^{-2}$ M	520 (340)	5.0×10^{-6} M[a]	–	1:1	(*37*)
		Hg^{2+}	MeCN–H_2O (6:4 v/v); pH 4.0 ($HClO_4$); $C_L = 1.6 \times 10^{-5}$ M	575 (350)	60 µg/l or 3.0×10^{-7} M[a]	7.18 ± 0.28	1:1	(*62*)
		Pb^{2+}			–	4.02 ± 0.10	1:1	
		Na^{+}			–	4.49 ± 0.05	1:1	
		Cu^{2+}			–	4.64 ± 0.05	1:1	
2	*Cone*	Hg^{2+}	Suspension in H_2O (0.25 mg/2.5 ml H_2O); pH 4.0 ($HClO_4$); $C_L = 3.5 \times 10^{-6}$ M	540 (350)	66 µg/l or 3.3×10^{-7} M[a]	5.47 ± 0.02	1:1	(*41*)
		Pb^{2+}			–	3.10 ± 0.10	1:1	
		Cu^{2+}			–	3.16 ± 0.05	1:1	
		Na^{+}			–	3.90 ± 0.15	1:1	
3	*Cone*	Hg^{2+}	Extraction H_2O–$CHCl_3$; pH 5.0 (Na-acetate buffer); $C_L = 1.0 \times 10^{-5}$ M	468 (340)	8.0×10^{-7} M[b]	4.41[c,d]	1:1	(*42*)
4	*Cone*	Pb^{2+}	MeCN–H_2O (6:4 v/v); pH 5.2 (lutidine buffer); $C_L = 3.6 \times 10^{-6}$ M	515/565 (350)	4 µg/l or 2.0×10^{-8} M[a]	33.5 ± 1.5	2:3	(*43*, *62*)
						10.0 ± 0.5	1:1	
		Hg^{2+}			–	5.89 ± 0.07	1:1	
		Cd^{2+}			–	7.30 ± 0.08	1:1	
		Cu^{2+}			–	4.80 ± 0.09	1:1	
		Ca^{2+}			–	7.23 ± 0.28	1:1	
		K^{+}			–	3.69 ± 0.05	1:1	
		Na^{+}			–	4.68 ± 0.04	1:1	
5	*Partial cone*	Pb^{2+}	MeCN–H_2O (1:1 v/v); pH 4.0 (HNO_3); $C_L = 1.25 \times 10^{-5}$ M	496/544 (330)	2.5 µg/l or 1.2×10^{-8} M[a]	6.53	1:1	(*44*)
6a	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	473 (328)	–	3.84 ± 0.02	1:1	(*45*)
		Pb^{2+}				4.43 ± 0.02	1:1	
		Fe^{3+}				4.06 ± 0.03	1:1	
6b	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	471 (326)	–	4.83 ± 0.03	1:1	(*45*)
		Pb^{2+}				4.26 ± 0.03	1:1	
		Fe^{3+}				4.74 ± 0.04	1:1	
6c	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	471 (326)	–	4.53 ± 0.03	1:1	(*45*)
		Pb^{2+}				4.76 ± 0.04	1:1	
		Fe^{3+}				3.94 ± 0.02	1:1	
6d	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	470 (326)	–	5.16 ± 0.03	1:2	(*46*)
		Pb^{2+}				3.10 ± 0.03	1:1	
		Fe^{3+}				5.34 ± 0.01	1:2	
6e	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	471 (326)	–	4.91 ± 0.02	1:1	(*46*)
		Pb^{2+}				3.27 ± 0.05	1:1	
		Fe^{3+}				5.40 ± 0.03	1:2	

Table 1 – *continued*.

Ligand	Conformation	Metal ion	Solvent/conditions	λ_{em} (λ_{ex}), (nm)	Detection limit	Complex formation constant (log β)	Complex stoichiometry (M:L)	Reference
7a	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	470 (328)	–	5.99 ± 0.04	1:2	(*47*)
		Pb^{2+}				5.24 ± 0.02	1:1	
		Fe^{3+}				5.96 ± 0.03	1:2	
7b	Mobile	Hg^{2+}	MeCN; $C_L = 2.58 \times 10^{-5}$ M	472 (328)	–	5.64 ± 0.03	1:1	(*47*)
		Pb^{2+}				5.67 ± 0.01	1:1	
		Fe^{3+}				5.40 ± 0.05	1:1	
8	*1,3-Alternate*	Tl^{+}	MeCN–H_2O (1:1 v/v); pH 3.5 (HNO_3); $C_L = 7.5 \times 10^{-6}$ M	541 (330)	14 μg/l or 7.0×10^{-8} M[a]	–	1:1	(*48*)
			MeCN–H_2O (1:1 v/v); pH 5.5 (Na-acetate buffer); $C_L = 3.8 \times 10^{-6}$ M	495 (330)	10 μg/l or 5.0×10^{-8} M[a]	5.20[d]	1:1	(*58*)
		Cs^{+}	MeCN–H_2O (1:1 v/v); pH 3.5 (HNO_3); $C_L = 7.5 \times 10^{-6}$ M	495/541 (330)	53 μg/l or 4.0×10^{-7} M[a]	3.36[d]	1:1	(*58*)
9	Mobile	Tl^{+}	Extraction H_2O–$CHCl_3$; pH 7.7 (borax buffer); $C_L = 1.0 \times 10^{-5}$ M	462/505 (340)	–	5.59[c]	1:1	(*49*)
Other HN-dansyl fluoroionophores								
11	*Cone*	Hg^{2+}	MeCN–H_2O (4:1 v/v); $C_L = 1.0 \times 10^{-5}$ M	520 (338)	4.1×10^{-6} M[b]	5.12[d]	1:1	(*51*)
		Cu^{2+}			–	3.38[d]	1:1	
		Cd^{2+}			–	3.18[d]	1:1	
		Ni^{2+}			–	3.17[d]	1:1	
		Mn^{2+}			–	3.14[d]	1:1	
		Ag^{+}			–	3.13[d]	1:1	
		Mg^{2+}			–	3.05[d]	1:1	
		Na^{+}			–	2.94[d]	1:1	
		Li^{+}			–	2.98[d]	1:1	
12	*Partial cone*	Hg^{2+}	THF–H_2O (9/1 v/v); pH 7.0 (HEPES); $C_L = 1.0 \times 10^{-6}$ M	435/502 (338)	1×10^{-7} M[b]	5.94	1:1	(*52*)
		Cu^{2+}		502 (338)	$\sim 8 \times 10^{-6}$ M	–		
13a	*Cone*	Hg^{2+}	MeCN–H_2O (1:1 v/v); $C_L = 1.0 \times 10^{-5}$ M	531 (340)	–	2.91[d]	1:1	(*53*)
13b	*Cone*	Hg^{2+}	MeCN–H_2O (1:1 v/v); $C_L = 1.0 \times 10^{-5}$ M	531 (340)	–	3.69[d]	1:1	(*53*)
13c	*Cone*	Hg^{2+}	MeCN–H_2O (1:1 v/v); $C_L = 1.0 \times 10^{-5}$ M	531 (340)	3.41×10^{-6} M	5.47[d]	1:1	(*53*)
		Pb^{2+}			–	3.94[d]	1:1	
		Cu^{2+}			–	3.83[d]	1:1	
		Zn^{2+}			–	3.77[d]	1:1	

[a] Determined as three times the signal-to-signal noise ratio or three times the standard deviation of the background noise.

[b] Determined as three times the ratio of standard deviation for the blank sample to the slope of the calibration plot (3 s/m) (*60*).

[c] Extraction constant, log K_{ex}^{app}.

[d] Calculated from the originally reported equilibrium constant value.

calixarene geometry on mercury(II) sensing characteristics, a new di(*N*-dansylcarboxamide) analogue fixed in *1,3-alternate* conformation (found to be another preferred conformation in the complexes of **1** with Hg^{2+} (*44*)) has been obtained and the study of its metal recognition ability is currently in progress.

It is noteworthy that by increasing the number of pendent lower-rim *N*-dansylcarbamoyl groups to four on the calix[4]arene moiety fixed in the *cone* conformation, Leray et al. (*43*, *62*) obtained a fluorogenic reagent **4** which demonstrated highly efficient and selective sensing of Pb^{2+} (Table 1). In the presence of increasing concentrations of lead(II) in aqueous acetonitrile solutions, a gradual increase in the ligand fluorescence with the concomitant 50-nm blue shift of the emission maximum (from 565 to 515 nm) was observed. In contrast to the effect from soft Hg^{2+} binding with calixarene *N*-dansylcarboxamides (see above), such spectral response to coordination of medium-soft Pb^{2+} is justified in terms of the complexation-induced ligand ionisation. This enabled ratiometric optical determination of lead(II) with the detection limit of 4 ppb (2.0×10^{-8} M), which is fully compatible with the regulations of the US EPA and WHO on the limiting content of this hazardous pollutant in drinking water. The study showed **4** to bind lead(II) as 1:1 and 2:3 complexes (values of the corresponding complex formation constants are presented in Table 1). Appreciable selectivity of **4** for lead(II) was verified by competitive complexation studies involving equimolar concentrations of Pb^{2+} and other relevant metal ions (Na^+, K^+, Ca^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}). Recently, fluoroionophore **4** has been employed in the development of microfabricated device for selective optical recognition of lead(II) in H_2O (*66*). The microchip-based sensor allows for determination of Pb^{2+} with a detection limit of 5 ppb.

The approach based on preorganisation of the calix[4]arene moiety in the favourable conformation was used in the design of another highly efficient and selective ratiometric chemosensor of lead(II) (**5**) which contained two *N*-dansylcarbamoyl groups on the lower rim of the ligand fixed in the *partial cone* conformation (*44*). This geometry of the calixarene moiety was chosen based on the prior ^{1}H NMR study of conformations adopted by the flexible dansyl-containing prototype **1** upon its complexation with lead ion. In acidic MeCN–H_2O (1:1 v/v) solutions, the *partial cone* fluoroionophore allowed for the detection of Pb^{2+} at the level as low as 2.5 ppb (Table 1) meeting the EPA and WHO regulations. To the best of our knowledge, the only fluorescent reagent with comparable sensitivity for lead(II) is the *cone* tetra(*N*-dansylcarboxamide) **4** (*43*, *62*) described above. Complexation of **5** with Pb^{2+} involved the NH-proton displacement which resulted in a gradual blue shift of the dansyl fluorescence emission band of up to 48 nm from the λ_{em} of 544 nm for non-ionised **5** (λ_{ex} 330 nm), accompanied by the enhancement of the fluorescence intensity. The formation constant for 1:1 Pb^{2+}–**5** complex may be found in Table 1. In the competitive metal recognition experiments, no significant interference with Pb^{2+} sensing by **5** was encountered from other relevant metal cations, Na^+, K^+, Mg^{2+}, Ca^{2+}, Cd^{2+}, Cu^{2+}, etc. Fluorescence recognition of Pb^{2+} was not affected by varying concentrations of background Hg^{2+} as well, unless the latter was present in a large excess, at millimolar levels (hardly applicable to real-life drinking water). Therefore, fluoroionophore **5** was found to be a highly selective reagent for the determination of submicro concentrations of lead(II).

Therefore, choosing the proper calix[4]arene framework conformation is important, but it is not the only aspect to be considered in the design of an efficient and selective metal sensor. Thus, Bartsch and co-workers (*45–47*) focused their attention on investigation of the effect of other structural features of calix[4]arene di(*N*-dansylcarboxamides) on the optical sensing of metal ions. In particular, the influence of the upper-rim substituent variation on the complexation ability of the fluoroionophores was explored (*45*, *46*). The study carried out in acetonitrile solutions involved di(tetramethylammonium) salts of di-ionised **1** (compound **6a**, Figure 1) with four *t*-Bu groups in the *p*-positions of the phenol rings and its analogues with two *t*-Bu and two H (**6b**), four H *p*-substituents (**6c**) (*45*), as well as two or four upper-rim allyl groups (**6d** and **6e**, respectively) (*46*). In the presence of different alkali, alkaline earth and transition metal ions, including Cd^{2+}, Hg^{2+}, Pb^{2+}, Zn^{2+}, Co^{2+}, Fe^{2+}, Mn^{2+} and Fe^{3+}, all of the calixarene ion pairs **6a**–**6e** demonstrated bathochromic (red) shifts of the fluorescence emission bands, accompanied by a decrease in the fluorescence intensity, obviously, due to the cation exchange. For many of the studied metals, the observed red shift magnitude was found to change inversely to the ionic size. Hg^{2+}, Pb^{2+} and Fe^{3+} produced the strongest, comparable fluorescence quenching attributed to the heavy metal effect. The corresponding complex formation constants for **6a**–**6e** are presented in Table 1. The data obtained for di-ionised compounds **6a**–**6c** did not allow the authors to discern the effect of upper-rim *t*-Bu groups (*45*). Introduction of allyl substituents on the calixarene upper rim (*46*) enabled the binding of two ligand ions with each Fe^{3+} (for **6d** and **6e**) and Hg^{2+} (for **6d**), while no such complex stoichiometry change was observed in the case of Pb^{2+} (Table 1). A second ligand in the 1:2 complexes was suggested to coordinate with the metal ion via its allyl groups. Unfortunately, the influence of number of allyl substituents on the efficiency of optical recognition of Hg^{2+}, Pb^{2+} and Fe^{3+} is hard to judge from the available data, since allowable comparison of stability constants is limited to complexes with the same metal-to-ligand stoichiometry.

The same group of scientists (*47*) investigated the effect of the length of linker connecting *N*-dansylcarbamoyl groups with the calixarene framework on metal ion recognition by di(tetramethylammonium) salts **6a**, **7a** and **7b** in acetonitrile. This structural variation on the calixarene lower rim had greater influence on the complexation properties of the di-ionised fluoroionophores than the upper-rim changes discussed above. **6a**, **7a** and **7b** in general exhibited preference for binding transition and heavy metal ions, all of which produced quenching of the ligand fluorescence along with red shift of the emission band. Hg^{2+}, Pb^{2+} and Fe^{3+} caused the strongest quenching effect. For these three metal ions, complex formation constants (Table 1) increase on going from **6a** with the shortest linker to **7b** with the longest one, and this effect is the most significant in the case of Hg^{2+}. Interestingly, in contrast to **6a** and **7b**, **7a** with intermediate linker forms equally strong 1:2 metal-to-ligand stoichiometry complexes with Fe^{3+} and Hg^{2+}, while all three of the calixarenes bind Pb^{2+} as 1:1 complexes.

Before proceeding to the next chapter of this review, we would like to point out that knowing the coordination mode of heavy metal ions with dansyl-appended calixarenes would be advantageous to directed design of chemosensors selective towards specific analytes. Unfortunately, the pertinent solid-state structural information available in the literature to date is limited to the X-ray crystal structure of Pb^{2+}-complex with a calix[4]arene with one pendent *N*-dansylcarbamoyl and one carboxyl group (*44*) (the structural formula is not shown, since the ligand was not employed in metal ion sensing studies). As it was obvious from that structure, surprisingly, nitrogen atom of deprotonated dansylcarboxamide is not involved in lead(II) ion coordination. Instead, the bonding takes place via carbamoyl oxygen atoms, as well as oxygens of carboxylate and phenolic groups. As far as Hg^{2+} complexes of dansyl-calixarenes are concerned, no crystallographic data have been reported for such compounds, to the best of our knowledge.

Ligands with one N-dansylcarbamoyl group. Two fluoroionophores of this type have been reported, a *1,3-alternate* calix[4]arene-bis(crown-6-ether) **8** (Figure 1) (*48*) and a conformationally mobile calix[4]arene **9** (*49*). Both of these mono(*N*-dansylcarboxamides) demonstrated high selectivity towards Tl^+ and both of them behaved as multi-purpose chemosensors that, in contrasting modes, allowed for the detection of two different heavy metal ions.

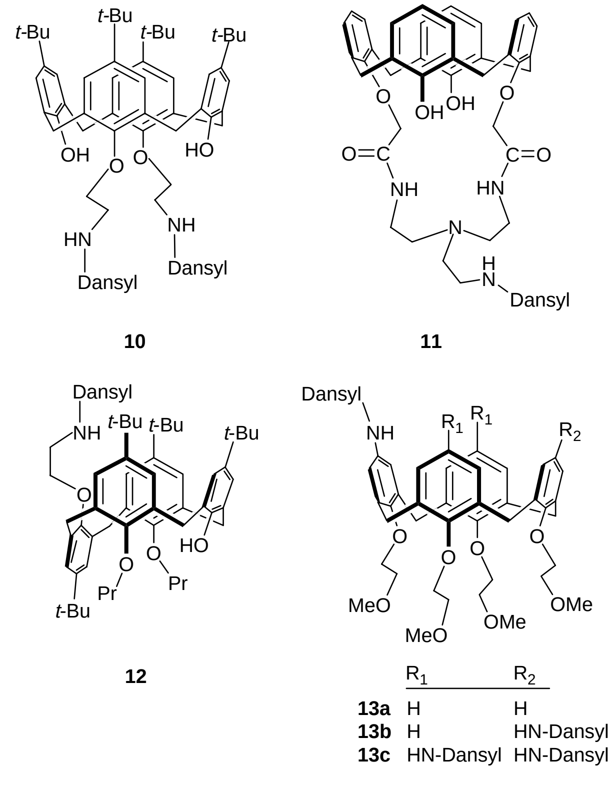
Fluoroionophore **8** reported by our research group (*48*) comprised of a calix[4]arene-bis(crown-6-ether) scaffold preorganised in the *1,3-alternate* conformation (utilised originally for selective separation of Cs^+ (*67*, *68*) with attached proton-ionisable *N*-dansylcarbamoyl side arm. At the time of publication, **8** exemplified the first calixarene-based fluorogenic reagent for selective optical sensing of Tl^+. No surprise that under otherwise different conditions of pH, in a contrasting fashion, **8** was found capable of recognising Cs^+ as well (*58*). Favouring of both of these metal ions by the ligand was explained in part by their tendency for cation–π interactions offered by the calix[4]arene framework in *1,3-alternate* conformation. In the presence of Tl^+ in aqueous acetonitrile (1:1 v/v) solutions with high content of Na^+ at pH 5.5 (Na-acetate buffer), the dansyl-calixcrown demonstrated a strong PET-associated quenching of the fluorescence intensity at wavelength of 495 nm (emission of deprotonated ligand, L^-; $\lambda_{ex} = 330$ nm) which was not affected by 100-fold excess of background hard and soft metal ions, such as K^+, Ca^{2+}, Pb^{2+}, Hg^{2+}, Cd^{2+}, Ag^+, Cu^{2+} and Fe^{3+}. Under these conditions, **8** allowed for Tl^+ detection as low as 10 ppb (Table 1). In the same solvent system at pH 3.5 (HNO_3), the addition of increasing concentrations of Cs^+ produced a blue shift of the ligand fluorescence emission band from 541 (λ_{em} of non-ionised **8**;$\lambda_{ex} = 330$ nm) to 495 nm (deprotonated **8**) accompanied by an increase in the fluorescence intensity, consistent with the NH-proton displacement by the metal ion. The magnitude of this spectral response of **8** to Cs^+ coordination remained essentially invariant in the presence of 100-fold excess of the relevant competing metal ions, in particular, Na^+, K^+, Mg^{2+}, Ca^{2+} and Al^{3+}. In Cs^+ sensing by **8**, the detection limit of 53 ppb was achieved. Both Tl^+ and Cs^+ were bound by **8** as 1:1 complexes with the complex formation constants of 1.6×10^5 and 2.3×10^3 l/mol, respectively (Table 1).

A mono(*N*-dansylcarbamoyl)-containing calixarene **9** obtained in our group afterwards (*49*) was probed for sensing of hazardous metal ions in solvent extraction from aqueous solutions into $CHCl_3$. It was discovered that with the aqueous-phase pH adjusted at 7.7 (borax buffer), in the presence of nearly 0.1 M Na^+, **9** provided selective recognition of microconcentrations of soft Tl^+. Extraction of thallium ion by **9** resulted in a gradual blue shift of the emission band (from 505 to 462 nm with excitation at 340 nm), along with the fluorescence enhancement associated with the ligand ionisation. Solution ^1H NMR study revealed that in the complex with Tl^+, flexible calixarene **9** adopts predominantly the *partial cone* conformation with inverted phenol ring bearing *N*-dansylcarbamoyl group. Evidently, a soft electron acceptor Tl^+ shapes the ligand in a geometry that allows for its π-coordination with the calixarene aromatic cavity and simultaneous interaction with the ionised *N*-dansylcarbamoyl group. The formation constant for this 1:1 complex is listed in Table 1. On the other hand, under the conditions of higher aqueous phase pH (pH 8.6, borax buffer) in the presence of excess Na^+, ionised **9** was found capable of sensing Hg^{2+} in a contrasting fashion. Uptake of mercury by the ligand produced its fluorescence quenching (justified by PET) with concomitant red shift of the emission band from 480 to 513 nm. This phenomenon may be explained in terms of a substantially covalent character of Hg–N bond (*63*) in the complex formed.

Other HN-dansyl appended calix[4]arene derivatives

Fluorogenic calix[4]arene **10** (Figure 2) obtained by Brown et al. (*50*) in solution adopted the *cone* conformation evidently stabilised by the intramolecular H-bonding involving the lower-rim phenol and neighbouring O-CH_2 groups. (Such behaviour is typical of phenol OH-containing calix[4]arenes (*69*).) Upon the extraction of Hg^{2+} by 1.2×10^{-6} M **10** from acidic aqueous solutions (pH 4, dil. HNO_3) into 1,2-dichloroethane, strong quenching (up to 85%) of the ligand fluorescence intensity in the organic phase was observed at constant wavelength of 502 nm (with excitation at 340 nm). The spectral response of **10** to mercury binding, similar to that of the analogous *N*-dansylcarboxamide **1**, was justified by PET. No fluorescence quenching of **10** was observed upon extraction of alkali metal cations, Sr^{2+}, Cu^{2+} and Pb^{2+}. (Unfortunately, the quantitative characteristics of Hg^{2+} sensing by **10** are not available.)

Unlike for the *HN*-dansyl calixarene derivative **10**, fluorescence of *N*-dansyl-substituted calix[4]arene-azacrown (*50*) was reported to be insensitive to metal ion coordination (existence of the latter was established by other independent method.) In contrast, a dansylamide-armed lariat calix[4]-azacrown **11** obtained by the Chen group (*51*) demonstrated an efficient fluorescence sensing of Hg^{2+} in aqueous acetonitrile (Table 1), with the detection limit of 4.1×10^{-6} M and formation constant of the 1:1 Hg^{2+}–**11** complex of 1.31×10^5 l/mol. In the competitive complexation experiments, mercury-induced quenching of the ligand emission intensity at 520 nm (excitation at 338 nm) was essentially unaffected by many other metal ions, except for Pb^{2+}, Cu^{2+}, Cd^{2+} and Zn^{2+} (for the complex formation constants of **11** with some of the metals, see Table 1).



10

11

12

	R_1	R_2
13a	H	H
13b	H	HN-Dansyl
13c	HN-Dansyl	HN-Dansyl

Figure 2. *HN*-dansyl-appended calix[4]arene-based ligands.

Quite unusual spectral behaviour in the presence of mercury(II) was observed by Kumar et al. (*52*) for compound **12** which comprises the calix[4]arene moiety in the *partial cone* conformation containing single pendent *HN*-dansyl group oriented towards the upper rim. Increasing concentrations of Hg^{2+} in buffered neutral aqueous THF solutions (1:9 v/v; pH 7.0) produced gradual quenching of the ligand fluorescence at 502 nm, ($\lambda_{ex} = 338$ nm) accompanied by the evolution of new emission bands at 435 and 412 nm. Appearance of these blue-shifted bands was explained by protonation of the dansyl's dimethylamino group due to the transfer of proton from the phenolic hydroxyl triggered by mercury(II) complexation. With the use of ratiometric approach, the detection limit of Hg^{2+} sensing at 1×10^{-7} M was achieved (Table 1). No significant changes in the fluorescence of **12** were observed in the presence of other relevant metal ions, but Cu^{2+} produced emission quenching at wavelength 502 nm (weaker than that from Hg^{2+}) with no new bands emerging. Based on different modes of Hg^{2+} and Cu^{2+} sensing by **12**, the authors suggested the design of a dual output molecular switch for a system operated by inputs of these two metal ions.

Compounds **13** (**a–c**) (Figure 2) obtained by Huang and co-workers (*53*) thus far are the only representatives of fluorogenic ligands with *HN*-dansyl groups attached directly to the aromatic rings of the calixarene scaffold. This structural feature must be conducive to the NH-proton dissociation due to the presence of an extensive system for the negative charge delocalisation. Indeed, complexation of **13c** containing four HN-dansyl groups with mercury(II) perchlorate in aqueous acetonitrile (1:1 v/v) produced significant quenching of the ligand fluorescence intensity (in agreement with PET mechanism) with concomitant 32-nm blue shift of the emission band from the original λ_{em} of 531 nm (excitation at 340 nm) rationalised by the fluorophore ionisation. (For **13a** with one and **13b** with two H*N*-dansyl groups, only weak fluorescence decrease and no emission band shift was observed under the same conditions.) **13c** was found to bind Hg^{2+} as 1:1 complex with the complex formation constant of $(2.93 \pm 0.01) \times 10^5$ l/mol and it allowed for Hg^{2+}

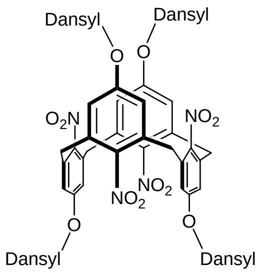
detection at the level of 3.41×10^{-6} M. Most of other relevant metal ions (alkali, alkaline earth and transition metal cations, including Cd^{2+}, Pb^{2+}, Cu^{2+} and Zn^{2+}) produced only insignificant spectral response of **13c**. (The corresponding complex formation constants are listed in Table 1.)

O-dansyl-appended calix[4]arenes

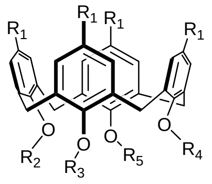
In contrast to *O*-dansyl-appended thiacalixarenes that have been known since 1998 (*36*), their metacyclophane analogues, calix[4]arenes with dansyl groups attached directly to the lower-rim phenolic oxygens (Figure 3) are the most recent type of fluoroionophores under consideration which was introduced in 2009 by two research groups (*55*, *56*). As it will be obvious from the discussion below, introduction of a harder *O*-dansyl electron donor shifts coordination preferences of these ligands from soft metal cations (such as Hg^{2+}), which is typical for the *HN*-dansyl fluoroionophores, to intermediate in softness transition metal ions. From the practical point of view, it should be mentioned that although fluorescence of *O*-dansyl calixarenes is environment-sensitive (as for any other compound with this fluorophore), it is not as pH-dependent as that of the *HN*-dansyl type ligands.

Chawla et al. (*55*) reported synthesis and photophysical studies of six *O*-dansyl calixarenes varying in the conformation, number of *O*-dansyl fluorophores and identity of upper- and lower-rim substituents. Hg^{2+} complexation studies conducted for these reagents in MeCN revealed that only fluoroionophore **14** (Figure 3) containing four *O*-dansyl and four NO_2 groups on the calixarene moiety fixed in *1,3-alternate* conformation was an efficient optical sensor of this hazardous metal ion, while other five ligands (all found to exist in the *cone* conformation) demonstrated no or weak spectral response to the presence of mercury. Hg^{2+} recognition by **14** produced sharp decrease in fluorescence emission intensity at essentially constant wavelength, similarly to most of *HN*-dansyl-containing mercury-selective calixarenes described *vide supra*. For the complexation of this fluoroionophore with Hg^{2+}, 1:2 metal-to-ligand stoichiometry was determined with the complex formation constant as large as $(5.2 \pm 0.8) \times 10^{10}\,l^2/mol^2$ (Table 2). The reagent allowed for the optical detection of mercury(II) at the level of approximately 1×10^{-7} M. The authors proposed the difference in the calixarene conformation of **14** and other ligands in the series (*1,3-alternate* and *cone*, respectively) as the rationale behind the observed striking disparity in their mercury sensing abilities.

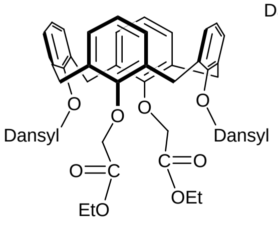
Another large pool of *O*-dansyl calix[4]arenes with varying structures (**15**–**18**, Figure 3) was developed by Weber and co-workers (*56*). In addition to ligands differing in the identity and pattern of the substituents on the lower and upper rim, this set included also two conformational isomers of calixarene **16**, the *cone* **16a** and *partial cone* **16b**. Studies of optical metal ion recognition by **15**–**18** conducted in acetonitrile demonstrated notable preference of all of these fluoroionophores but **18** for binding Cu^{2+}(**18** favoured Hg^{2+} with a moderate selectivity over other metal ions). Presence of $Cu(ClO_4)_2$ resulted in strong quenching



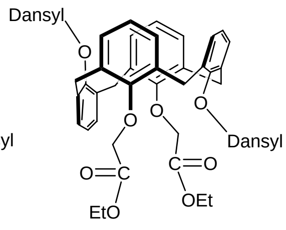
14



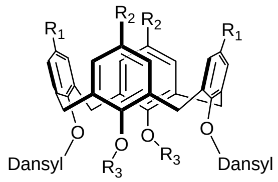
	R₁	R₂	R₃	R₄	R₅
15a	*t*-Bu	$CH_2CH{=}CH_2$	Dansyl	$CH_2CH{=}CH_2$	Dansyl
15b	*t*-Bu	Pr	Dansyl	Pr	Dansyl
15c	*t*-Bu	Pr	Dansyl	Dansyl	Pr



16a



16b



	R₁	R₂	R₃
17	$CO(CH_2)_4CH_3$	$CO(CH_2)_4CH_3$	Pr
18	NO_2	H	CH_2CO_2Et

Figure 3. *O*-dansyl-appended calix[4]arenes.

Table 2. Metal ion recognition by *O*-dansyl-appended calix[4]arenes.

Ligand	Conformation	Metal ion	Solvent/conditions	λ_{em} (λ_{ex}), (nm)	Detection limit[a]	Complex formation constant (log β)	Complex stoichiometry (M:L)	Reference
14	*1,3-Alternate*	Hg^{2+}	MeCN; $C_L = 1 \times 10^{-5}$ M	est. 455[b] (351)	~20 ppb or $\sim 1 \times 10^{-7}$ M	10.72[c]	1:2	(*55*)
15a	*Cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	550 (368)	4.4×10^{-6} M	5.64 ± 0.04	1:1	(*56*)
15b	*Cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	549 (364)	4.0×10^{-6} M	4.19 ± 0.02	1:2	(*56*)
15c	*Cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	546 (359)	7.2×10^{-6} M	4.36 ± 0.05	1:1	(*56*)
16a	*Cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	549 (364)	1.37×10^{-5} M	3.76 ± 0.04	1:2	(*56*)
		Hg^{2+}			–	5.17 ± 0.07	1:2	
16b	*Partial cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	537 (362)	1.52×10^{-5} M	4.86 ± 0.03	1:2	(*56*)
17	*Cone*	Cu^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	552 (368)	1.84×10^{-5} M	3.87 ± 0.03	1:1	(*56*)
18	*Cone*	Hg^{2+}	MeCN; $C_L = 3.5 \times 10^{-5}$ M	462 (379)	1.48×10^{-5} M	4.03 ± 0.04	1:2	(*56*)

[a] Determined as three times the ratio of standard deviation for the blank sample to the slope of the calibration plot (3 s/m) (*60*).

[b] λ_{em} not reported; estimated from the spectral picture.

[c] Calculated from the originally reported equilibrium constant value.

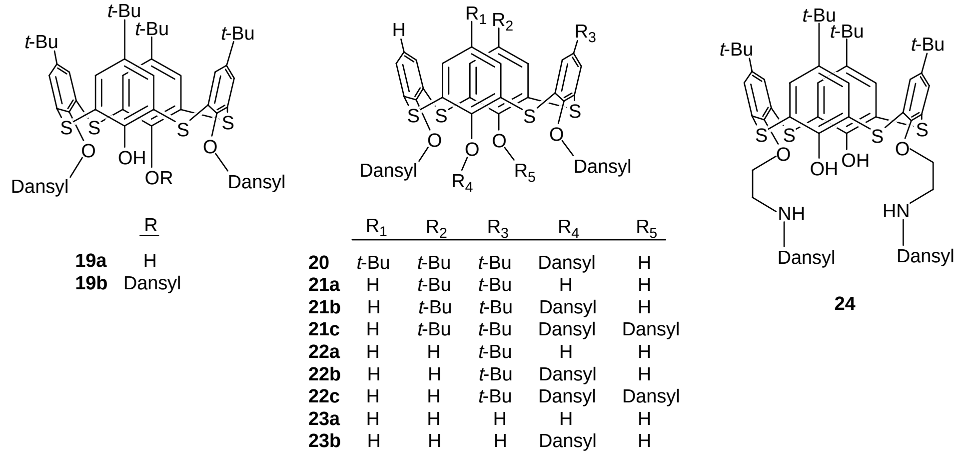
of the ligand fluorescence which was explained by energy transfer to the coordinated metal ion. At the same time, spectral response to increasing concentration of Cu^{2+} of the *cone* **16a** (unlike for its *partial cone* relative **16b**) had a peculiarity: along with gradual decrease in the emission intensity at a wavelength of 547 nm (excitation at 369 nm), evolution of two new, blue-shifted bands at 416 and 442 nm was observed, the origin of which is not obvious. (Interestingly, appearance of such new emission bands, but no quenching of fluorescence at λ_{em} of 547 nm, was noticed for **16a** in the presence of $LiClO_4$ as well.) Calixarenes **15a**, **15b** and **15c** with *t*-Bu groups on the upper rim, all in the *cone* conformation, possessed the largest sensitivity for copper(II) (for the detection limits, see Table 2). For **15b**, **16a** and **16b**, 1:2 Cu^{2+}-to-ligand complex stoichiometry was established, while with other reagents in the series, 1:1 complexes were formed. **16a** and **18** also produced 1:2 complexes with Hg^{2+}. The corresponding complex formation constants are listed in Table 2. Competitive complexation experiments for Cu^{2+} and other metal ions, including alkali metal cations, Ba^{2+}, Hg^{2+}, Pb^{2+}, Co^{2+} and Ni^{2+}, confirmed especially high copper selectivity for **15b** and **16a**. Apart from copper(II) ion, fluorescence quenching of significantly smaller magnitude was observed for all of the studied *O*-dansyl calixarenes upon addition of Hg^{2+} (Table 2). The authors of the work attributed this phenomenon to the heavy atom effect.

Dansyl-containing thiacalix[4]arenes

Dansyl-appended thiacalix[4]arenes is the longest known, yet the least populated group of calixarene-type metal sensors with this fluorescent probe. The first representatives of these fluoroionophores, thiacalix[4]arenes **19a** and **19b** (Figure 4) were reported by Kumagai et al. (*36*). Initial metal ion recognition studies of **19a** and **19b** carried out in 10% aqueous DMF with pH 7.41 maintained with Sörsnen buffer (a Na-containing phosphate buffer) demonstrated preference of both of these ligands for cadmium(II). Presence of Cd^{2+} produced the largest increase in these reagents' fluorescence emission intensity at λ_{em} of 489 nm among the tested metal ions. (The detection limits for Cd^{2+} or complex formation constants were not reported). Metal-induced fluorescence enhancement of **19a** and **19b** was explained by the dansyl groups moving from the aqueous exterior environment towards the hydrophobic interior of the thiacalixarene cavity following the complexed metal cation. The next best-recognised metal cation after Cd^{2+} was Al^{3+}. Complex formation constants for aluminium ion with **19a** and **19b** are listed in Table 3. In general, the sensing ability of ligand **19a** featuring two lower-rim *O*-dansyl groups was much higher than that of **19b** with three fluorophores.

Afterwards (*57*), metal ion complexation of these two ligands as well as a large series of their analogues varying in the number of upper-rim *t*-Bu groups and lower-rim *O*-dansyl fluorophores (**20**–**23**, Figure 4) was studied in unbuffered 10% aqueous DMF. Interestingly, in the absence of buffer (in particular, Na^{+}), the addition of metal ions produced quenching of fluorescence for all of the 11 studied thiacalixarenes. Ligands **19**–**23** favoured transition metal cations, Co^{2+}, Ni^{2+}, Zn^{2+} and Cd^{2+}, over the alkali metal cations. (Complex formation constants for 1:1 complexes of these thiacalixarenes with Cd^{2+}, Co^{2+} and K^{+} are presented in Table 3.) Upper-rim *t*-Bu groups were found to decrease the sensing ability of the reagents. Compound **23a** exhibited an outstanding selectivity for Cd^{2+} over Zn^{2+} which was hardly recognised by this thiacalixarene.

More recently, an *HN*-dansyl-appended thiacalix[4]arene **24** has been obtained by Bhalla et al. (*54*). The ligand was found to exist in solutions in the *cone* conformation, evidently, due to hydrogen bond formation on the lower rim. Metal sensing ability of **24** was investigated in



	R
19a	H
19b	Dansyl

	R_1	R_2	R_3	R_4	R_5
20	*t*-Bu	*t*-Bu	*t*-Bu	Dansyl	H
21a	H	*t*-Bu	*t*-Bu	H	H
21b	H	*t*-Bu	*t*-Bu	Dansyl	H
21c	H	*t*-Bu	*t*-Bu	Dansyl	Dansyl
22a	H	H	*t*-Bu	H	H
22b	H	H	*t*-Bu	Dansyl	H
22c	H	H	*t*-Bu	Dansyl	Dansyl
23a	H	H	H	H	H
23b	H	H	H	Dansyl	H

Figure 4. Dansyl-containing thiacalixarenes.

Table 3. Metal ion recognition by dansyl-containing thiacalix[4]arenes.

Ligand	Metal ion	Solvent/conditions	λ_{em} (λ_{ex}), (nm)	Detection limit	Complex formation constant, K (l/mol)	Complex stoichiometry (M:L)	Refererence
19a	Al^{3+}	DMF–H_2O (1:9); pH 7.41 (Sörensen phosphate buffer); $C_L = 1 \times 10^{-6}$ M	489 (350)	–	$(3.50 \pm 0.60) \times 10^3$	1:1	(*36*)
	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(6.90 \pm 0.90) \times 10^2$	1:1	(*57*)
	Co^{2+}			–	$(5.20 \pm 0.70) \times 10^2$	1:1	
	K^+			–	$(1.10 \pm 0.60) \times 10^2$	1:1	
19b	Al^{3+}	DMF–H_2O (1:9); pH 7.41 (Sörensen phosphate buffer); $C_L = 1 \times 10^{-6}$ M	489 (350)	–	$(1.20 \pm 0.17) \times 10^3$	1:1	(*36*)
	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(2.50 \pm 0.40) \times 10^2$	1:1	(*57*)
	Co^{2+}			–	$(1.30 \pm 0.70) \times 10^2$	1:1	
	K^+			–	$(8.90 \pm 1.40) \times 10^2$	1:1	
20	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(1.30 \pm 0.29) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(9.80 \pm 2.20) \times 10^2$	1:1	
	K^+			–	$(5.40 \pm 0.80) \times 10^2$	1:1	
21a	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(1.95 \pm 0.26) \times 10^3$	1:1	(*57*)
	Co^{2+}				$(1.72 \pm 0.13) \times 10^3$	1:1	
	K^+				$(3.98 \pm 0.23) \times 10^3$	1:1	
21b	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(1.98 \pm 0.30) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(1.39 \pm 0.27) \times 10^3$	1:1	
	K^+			–	$(4.30 \pm 0.70) \times 10^2$	1:1	
21c	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(1.95 \pm 0.26) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(1.72 \pm 0.13) \times 10^3$	1:1	
	K^+			–	$(3.10 \pm 0.29) \times 10^3$	1:1	
22a	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(2.55 \pm 0.41) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(2.26 \pm 0.23) \times 10^3$	1:1	
	K^+			–	$(2.05 \pm 0.15) \times 10^3$	1:1	
22b	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(1.51 \pm 0.08) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(2.38 \pm 0.01) \times 10^3$	1:1	
	K^+			–	$(6.20 \pm 0.50) \times 10^2$	1:1	
22c	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(3.80 \pm 0.50) \times 10^2$	1:1	(*57*)
	Co^{2+}			–	$(7.30 \pm 1.60) \times 10^2$	1:1	
	K^+			–	$(2.30 \pm 0.10) \times 10^2$	1:1	
23a	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(3.42 \pm 0.14) \times 10^3$	1:1	(*57*)
	Co^{2+}			–	$(2.04 \pm 0.17) \times 10^3$	1:1	
	K^+			–	$(2.88 \pm 0.12) \times 10^3$	1:1	
23b	Cd^{2+}	DMF–H_2O (1:9); $C_L = 1 \times 10^{-6}$ M	520 (350)	–	$(8.90 \pm 1.00) \times 10^2$	1:1	(*57*)
	Co^{2+}			–	$(9.10 \pm 0.80) \times 10^2$	1:1	
	K^+			–	$(1.25 \pm 0.07) \times 10^3$	1:1	
24	Cu^{2+}	MeCN–CH_2Cl_2 (1:1 v/v); $C_L = 1 \times 10^{-5}$ M	433/504 (338)	2×10^{-7} M[a]	6.77×10^3	1:1	(*54*)
	Pb^{2+}			–	8×10^2	1:1	

[a] Determined as three times the ratio of standard deviation for the blank sample to the slope of the calibration plot (3 s/m) (*60*).

acetonitrile–methylene chloride (1:1). The reagent revealed strong affinity for Cu^{2+}. The addition of copper(II) to the solution of **24** produced a decrease in the dansyl fluorescence intensity at wavelength of 504 nm (excitation at 338 nm) and the emergence of a blue-shifted emission band at 433 nm. This allowed for ratiometric determination of Cu^{2+} with the detection limit of 2×10^{-7} M as a 1:1 complex with complex formation constant of 6.77×10^3 l/mol (Table 3). In competitive metal sensing experiments, fluorescence intensity of Cu^{2+}–**24** complex was not affected in the presence of equimolar amounts of alkali and transition metal ions; however, a strong interference was observed from 5-fold excess of Pb^{2+} as well as 10-fold excess of Zn^{2+} and Cd^{2+}. The formation constant for Pb^{2+}–**24** complex is found in Table 3. Interestingly, fluorescence of **24** was also found to be sensitive towards F^- anion.

Concluding remarks

The above-presented analysis of the available information allows to conclude that calixarene-based fluoroionophores with appended dansyl probes are promising optical chemosensors of hazardous metal ions, e.g. Hg^{2+}, Pb^{2+}, Cd^{2+}, Cu^{2+}, Tl^+ and Cs^+. Most of these ligands offer highly selective recognition of targeted metals and some of them are capable of detecting the analytes (in particular, Pb^{2+}) at sub-microlevels that meet or approach the EPA and WHO regulations on drinking water quality. At the same time, further development of new methods and reagents with improved sensitivity towards Hg^{2+}, Cd^{2+} and other heavy metal ions in aqueous solutions is strongly desirable. We envision that provided in this review discussion of the influence of structural factors on the sensorial characteristics of dansyl-containing calixarenes and their derivatives may be useful in future design of efficient metal-selective fluoroionophores.

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