Conformationally flexible calix[4]arene chromoionophores: optical transduction of soft metal ion complexation by cation–π interactions

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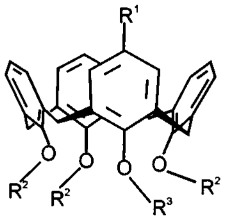
Soft metal ions like Pb^{2+}, Cd^{2+}, and Cu^{2+} form partial-cone complexes with a flexible calix[4]arene chromoionophore in which cation–π interactions cause a bathochromic shift of the UV/Vis absorption maximum.

Calix[4]arenes have been extensively used as selective ligands for a wide range of metal ions in selective transport,[1] potentiometric[2] and optical[3] sensors. Recently, they are also being used as building blocks for chromoionophores.[4] The conformation of the calix[4]arene moiety determines the size and geometry of the ligand and therefore has a significant influence on the selectivity.[5] In the partial-cone and 1,3-alternate conformations cation–π interactions between metal ion and the ligand's benzene rings play an important role.[6] Usually, the conformation of these ligands is *fixed* in the synthesis.[7] However, Bartsch *et al.* have shown that conformationally *flexible* calix[4]arene ionophores are selective for heavy metal ions like Pb^{2+} and Hg^{2+}.[8] We are currently studying the application of chromoionophores in integrated optical waveguide sensors selective for heavy metal ions. For this application it is desirable that the chromoionophores have a high selectivity for heavy metal ions over alkali metal ions and that complexation leads to a bathochromic shift of the absorption maximum. The calix[4]arene-based chromoionophores with substantial changes in their absorption spectra published thus far respond to alkali metal ions or Ca^{2+} and are based on the interaction of the complexed ion with a hard donor heteroatom of the chromophore.[9]

Here we report that conformationally flexible chromoionophore **1** is highly selective for Pb^{2+} over Na^+ and shows a *bathochromic* shift of λ_{max} upon complexation of *soft* metal ions. The bathochromic shift does *not* occur when alkali metal ions are complexed. Complexation of either Pb^{2+} or Na^+ by the conformationally fixed analogue **2** leads to a *hypsochromic* shift. Chromoionophores **1** and **2** were synthesized† from calix[4]arene **3**[10] by diazonium coupling with *p*-nitroaniline, followed by alkylation at the lower rim with MeI or PrI, respectively. Reference compound **4** was prepared in two steps from the parent calix[4]arene, *viz.* monomethylation at the lower rim followed by introduction of the (*N,N*-dimethylaminocarbonyl)methoxy functionalities on the three remaining hydroxy groups.



1 $R^1 = N_2C_6H_4NO_2$, $R^2 = OCH_2C(O)N(CH_3)_2$, $R^3 = OCH_3$
2 $R^1 = N_2C_6H_4NO_2$, $R^2 = OCH_2C(O)N(CH_3)_2$, $R^3 = OC_3H_7$
3 $R^1 = H$, $R^2 = OCH_2C(O)N(CH_3)_2$, $R^3 = OH$
4 $R^1 = H$, $R^2 = OCH_2C(O)N(CH_3)_2$, $R^3 = OCH_3$

It is well known that a methoxy substituent at the lower rim is not sufficiently bulky to fix the conformation of chromoionophore **1**, which can attain both the cone and the partial-cone conformation.[11] When a metal ion is complexed, the ligand will occupy the conformation optimal for the complexation of that particular metal ion. The UV/Vis absorption spectra in Fig. 1 show that complexation of Pb^{2+} ions by either **1** or **2** leads to shifts of λ_{max} in opposite directions. This is caused by the different conformations of the two complexes, involving two principally different modes of metal–chromophore interaction.

Compound **1** binds Pb^{2+} in the partial-cone conformation because in this geometry the metal ion interacts favorably with the π-surface of the chromophore,[12] leading to a 14 nm bathochromic shift of λ_{max} (Fig. 1). A Pb^{2+} ion complexed in chromoionophore **2**, fixed in the cone conformation, interacts with the methoxy oxygen atom lone-pair rather than with the chromophores' π-surface, resulting in a 22 nm hypsochromic shift. Na^+ prefers hard donor atoms, *i.e.* oxygen, and is therefore complexed by chromoionophore **1** in the cone conformation, causing a 4 nm hypsochromic shift of λ_{max}. This shift is small compared to the 22 nm hypsochromic shift of **2** upon Na^+ complexation, because **1** binds Na^+ only weakly.

^{13}C NMR spectroscopy proved that ionophore **4** complexes Na^+ and Pb^{2+} in different conformations.‡ These studies could

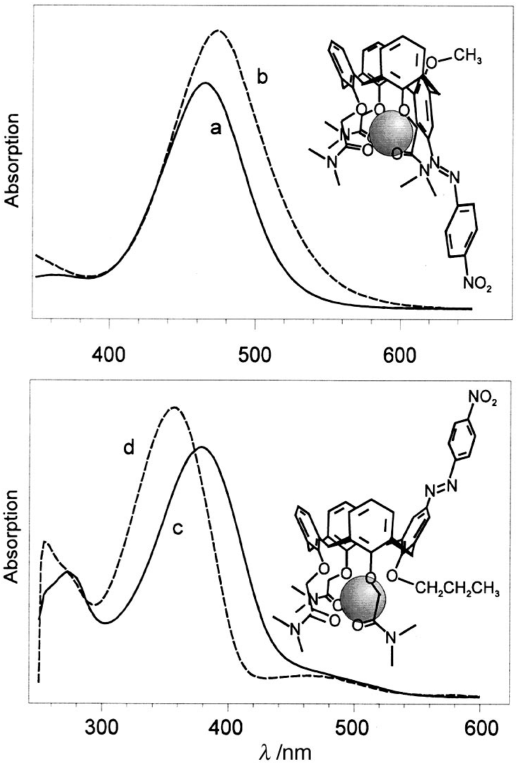


Fig. 1 UV/Vis absorption spectra of (a) **1**, (b) **1**·Pb^{2+}, (c) **2** and (d) **2**·Pb in CH_2Cl_2, with the proposed structures of the complexes.

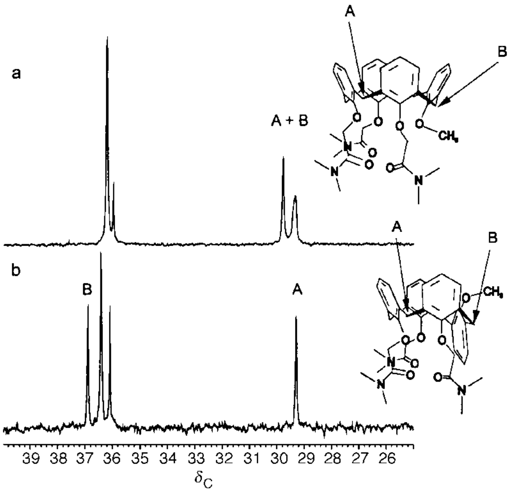


Fig. 2 ^{13}C NMR spectra (δ 40–25) of the complexes (a) **4**·Na$^+$ and (b) **4**·Pb^{2+}.

not be performed with **1** because of the low solubilities of its complexes. In the absence of metal ions, the NMR spectra of ionophore **4** show broad signals because of the equilibrium between cone and partial-cone conformation. When metal perchlorate salts are added, the signals sharpen into one set that can be attributed to a single conformation. For Na$^+$ this is the cone conformation, which can be determined from the ^{13}C NMR spectrum of the complex shown in Fig. 2: the methylene carbon atoms bridging the aromatic rings appear at δ 29.30 and 29.11, typical resonances for cone calix[4]arenes.[13] The Pb^{2+} complex has the partial-cone conformation, which can be determined from the two different chemical shifts of the bridging methylene carbon atoms at δ 36.90 and 29.31. The aromatic region of the ^{1}H NMR spectrum is consistent with a quasi-C_{4v} symmetry axis of the Na$^+$ complex, since all protons *para* with respect to the lower rim oxygen coincide, as do all *meta* protons. The more complex spectrum of the Pb^{2+} complex is typical for the partial-cone conformation.

The results of solution experiments in MeCN (Table 1) show that chromoionophore **1** exhibits bathochromic shifts upon complexation of different metal ions. Soft metal ions with high charges cause the largest shifts, with a maximum shift of 20 nm for Cu^{2+}. Under the same conditions, the alkali metal ions cause no, and alkaline-earth metal ions small, optical responses.

The complexation behavior of **1** shows that conformational flexibility can bias the selectivity of calix[4]arene chromoionophores towards soft heavy metal ions. Addition of 10 equiv. of Pb(ClO$_4$)$_2$ to a solution of **1** and a *thousand-fold excess* of NaClO$_4$ in MeCN leads to complete formation of the Pb^{2+} complex. This selectivity for Pb^{2+} over Na$^+$ should find its origin in the conformational flexibility, since ligating amides are generally used in Na$^+$-selective receptors. In fixed cone ligands, soft donating thioamide groups are necessary to obtain selectivity for Pb^{2+}.[14]

In conclusion, we have found a new type of optical transduction of soft metal ion complexation *via* a bathochromic shift of the absorption maximum due to side-on metal–chromophore interactions, unique to the partial-cone conformation of chromoionophore **1**. The selectivity for Pb^{2+} over Na$^+$ is due to the different preferential conformations of complexation by **1**. Our current research is aimed at improving the selectivity and sensitivity of flexible chromoionophores.

Table 1 Optical response of **1** (10^{-5} M) to different metal perchlorate salts (10^{-4} M) in MeCN. The samples were prepared by mixing equal volumes of stock solutions of **1** and the metal perchlorate salts. Reported values signify bathochromic shifts

Metal ion	$\Delta\lambda_{max}$/nm	Metal ion	$\Delta\lambda_{max}$/nm	Metal ion	$\Delta\lambda_{max}$/nm
Li$^+$	0	Ca^{2+}	8	Cd^{2+}	12
Na$^+$	0	Sr^{2+}	6	Pb^{2+}	14
Cs$^+$	0	Ba^{2+}	4	Ga^{3+}	2
Ag$^+$	0	Cu^{2+}	20	Ce^{3+}	16

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Notes and references

† All compounds reported were characterized by ^{1}H NMR analysis, melting point, elemental analysis and FAB mass spectrometry.

‡ *Selected data* for **3**·NaClO$_4$: δ_H(300 MHz, CD$_3$CN) 7.34–7.28 (m, 8H, ArH-*m*), 6.98–6.89 (m, 4H, ArH-*p*), 4.84 and 4.13 [AB q, 4H, *J* 14.4, OC*H*$_2$C(O)], 4.52 [s, 2H, OC*H*$_2$C(O)], 4.38 and 4.31 (AB q, 4H, *J* 12.0, ArC*H*$_2$Ar), 3.89 (s, 3H, OC*H*$_3$), 3.43 and 3.30 (AB q, 4H, *J* 12.0, ArC*H*$_2$Ar), 3.02 (s, 6H, NC*H*$_3$), 2.91 (s, 3H, NC*H*$_3$), 2.81 (s, 3H, NC*H*$_3$), 2.79 (s, 6H, NC*H*$_3$); δ_C 167.8, 167.4 (C=O), 154.2, 152.6, 151.6 (ArC–O), 135.3, 134.9, 134.7, 134.3 (ArC-*o*), 128.7, 128.6, 128.4 (ArC-*m*), 125.5, 125.3, 124.8 (ArC-*p*), 74.9, 74.5 (OCH$_2$), 64.2 (OCH$_3$), 35.1, 35.0, 34.7 (NCH$_3$), 29.3, 29.1 (ArCH$_2$Ar). For **3**·Pb(ClO$_4$)$_2$: δ_H 7.47 (d, 2H, *J* 7.8, ArH-*m*), 7.45 (d, 2H, *J* 7.8, ArH-*m*), 7.34 (t, 1H, *J* 7.8, ArH-*p*), 7.32 (d, 2H, *J* 7.8, ArH-*m*), 7.19 (d, 2H, *J* 7.8, ArH-*m*), 7.14 (t, 1H, *J* 7.8, ArH-*p*), 7.00 (t, 2H, *J* 7.8, ArH-*p*), 4.90 and 4.78 [AB q, 4H, *J* 14.7, OC*H*$_2$C(O)], 4.63 [s, 2H, OC*H*$_2$C(O)], 4.35 and 3.55 (AB q, 4H, *J* 12.6, ArC*H*$_2$Ar), 3.98 (s, 4H, ArC*H*$_2$Ar), 3.31 (s, 3H, OC*H*$_3$), 3.05 (s, 6H, NC*H*$_3$), 3.05 (s, 3H, NC*H*$_3$), 2.95 (s, 6H, NC*H*$_3$), 2.91 (s, 3H, NC*H*$_3$); δ_C 173.3, 171.3 (C=O), 159.7, 152.5, 151.4 (ArC–O), 137.8, 136.4, 136.1, 134.7 (ArC-*o*), 132.9, 130.5, 130.3, 130.3 (ArC-*m*), 127.5, 126.7, 125.7 (ArC-*p*), 74.5, 74.0, (OCH$_2$), 58.3 (OCH$_3$), 36.4, 36.1 (NCH$_3$), 36.9, 29.3 (ArCH$_2$Ar).

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