Lower rim amide (1,3) functionalised calix[4]arene amido-thiourea derivatives as dimetallic Zn(II) coordination complexes for anion recognition/sensing

Stefano De Solis\textsuperscript{a,b}, Fausto Elisei\textsuperscript{b} and Thorfinnur Gunnlaugsson\textsuperscript{a}\textsuperscript{*}

\textsuperscript{a}School of Chemistry and Trinity Biomedical Sciences Institute (TBSI), Trinity College Dublin, University of Dublin, Dublin 2, Ireland;
\textsuperscript{b}Department of Chemistry, Biology and Biotechnology & Centro di Eccellenza sui Materiali Innovativi Nanostrutturati (CEMIN), University of Perugia, Perugia, Italy

(Received 27 April 2015; accepted 29 July 2015)

The synthesis of two amido-thiourea based receptors/sensors 1 and 2, formed by functionalisation of the lower rim of a calix[4]arene, and the photophysical analysis of these with Zn(II) and various anions is described. The two structures, differing by the substituent on the thiourea moiety, were found to bind Zn(II) effectively in ethanol (EtOH); the recognition giving rise to significant changes in the UV-vis absorption spectra, which was red-shifted for both chemosensors. The changes in the absorption spectra were further analysed using nonlinear regression analysis programme (using the global analysis software ReactLab\textsuperscript{\textregtext} Equilibria), which revealed high binding constants for both systems. The resulting dimetallic complexes (1,2)–Zn\textsubscript{2} were (pre-formed and) then used to coordinate anionic species such as AcO\textsuperscript{2−}, H\textsubscript{2}PO\textsubscript{4}\textsuperscript{−} and Br\textsuperscript{−} through electrostatic interactions, showing high affinity towards these anions. In all cases, nonlinear regression analysis showed both 1:1 or 1:2 sensor:anion depending on the anion used. Although the 2-Zn\textsubscript{2} complex showed high affinity for acetate, phosphate and bromide, the 1-Zn\textsubscript{2} complex showed selectivity towards the recognition of phosphate in EtOH.

Keywords: sensors; Zn(II); anions; calix[4]arenes; colorimetric

Introduction

The recognition and sensing of ions has been receiving much attention in the last few decades owing to their large applications in either biological or environmental areas (1). Although substituted thioureas are mainly known as anion receptors (2), they have also been developed for the binding of metal ions (3) and recently, it was demonstrated that the interaction, or the formation of complexes, between thiourea moieties and metal ions such as zinc can facilitate serum albumin bioactivity (4). Consequently, there currently exist an interest in the development of sensors for the ratiometric fluorescent sensing of Zn(II) using a substituted amido-thiourea moiety (5), that could be used to interact with serum albumin (6). It is well known that calix[4]arenes are largely used as molecular frameworks to ‘build’ supramolecular architectures, which allow for molecular recognition and sensing of anions (7), cations (8), aminoacids (9), etc. In particular, the 1,3-functionaldervatives are of great interest for ion complexation and many examples of such molecular hosts have been reported to date, using either luminescent or UV-vis absorption spectroscopy output (10). Bearing this in mind, we set out to develop two new molecular sensors based on the amido-thiourea motif that would be appended to the calix[4]arene structure in a 1,3-conformation, giving 1 and 2, respectively (Figure 1). The only difference between these two sensors being the nature of the para-substituted aryl moiety attached to the thiourea-derived pendant arms. We foresaw that this double-armed amido-thiourea structure would enable us to complex zinc, through a synergetic action of the two sulphur atoms of the thiourea moieties and the carbonyl amide function, allowing the resulting complex to form ternary complexes with anions. Alternatively, at higher ion concentration, the formation of higher order complexes, i.e. the 2:1 (metal to ligand) could be formed. For both ligands 1 and 2 the zinc and anion recognitions gave rise to significant changes in the UV-Vis absorption spectra that were analysed using nonliner regression analysis; the latter demonstrating that indeed two zinc ions could be complexed within these structures. Moreover, owing to the electrostatic nature of the interactions between the complexes (1,2)–Zn\textsubscript{2} and anions, it was possible to work in a polar and H-bond donor solvent such as ethanol, giving rise the formation of complexes with high stability constants. Herein, we present our results from these experiments which demonstrate that the 1,3-alternative calix[4]arene scaffold is an excellent candidate for use in such sensing.

\textsuperscript{*}Corresponding author. Email: gunnlaut@tcd.ie

© 2015 Taylor & Francis
Results and discussion

Synthesis of 1 and 2

The synthesis of 1 and 2 is shown in Scheme 1. Both sensors were synthesised starting from the same bis-ester derivative 25,27-Bis[(ethoxycarbonyl)methoxy]-26,28-dihydroxycalix[4]arene, 3, which was formed using established protocols (12). The di-ester of 3 was then converted to the corresponding di-hydrazide derivative 4 in one-step upon reaction of 3 with hydrazine monohydrate using microwave assisted synthesis. After removing excess of hydrazine, the resulting solid residue was triturated with water and then washed with methanol to give 4 in 73% yield. Finally, 4 was converted to 1 and 2 upon reaction with 4-(trifluoromethyl)phenyl isothiocyanate and 4-nitrophenyl isothiocyanate, respectively. For both the yellow precipitate obtained was filtered and washed with water and methanol to give the desired products in 61% and 63% yield, respectively. Both sensors were characterised using conventional methods (see Experimental), which included the use of both 1D and 2D NMR (see Supporting Information).

Absorption properties and complexation study with Zn(II)

Having synthesised and characterised both 1 and 2, we next investigated their photophysical properties in ethanol solution. The UV-vis absorption spectra of 1 and 2 in ethanol are shown in Figure 2; in both cases, the presence of the para substituted-phenylthiourea moieties gives rise to an internal charge transfer (ICT) band (11, 12). The UV-vis spectrum of 1 shows a maximum at 277 nm with a slight shoulder above 300 nm. In contrast, sensor 2 shows a band centred around 280 nm and a broad band, which was red-shifted compared to that of the p-CF3 derivative, centred at ca. 370 nm. This red-shift to longer wavelength in 2 is due to the presence of the p-NO2 substituents that increases the electronic delocalisation in such structures giving rise to stronger ICT character (13). These structures were not shown to be strongly luminescent, and because of that, only the changes in the absorption spectra were monitored upon recognition of either zinc or various anions.

The changes in the UV-vis absorption spectra are shown in Figure 3 for the titration of 1 with Zn(II) (as Zn (ClO4)2.6H2O). As can be seen, then upon the addition of zinc, significant changes were observed in the ICT band of the sensor. Here, a significant increase in absorbance,
resulting in a new red-shifted band centred at 307 nm, while concomitantly the higher energy transition was reduced in absorbance. By analysing these absorption changes as a function of added zinc equivalents, it was clear that significant changes occurred between 0–1 equivalents; however, further significant changes occurred up to the addition of 2 equivalents of the metal ion (c.f. Figure 1, inset for the long wavelength absorption), suggesting the formation of the aforementioned 1:2 (host: guest) complex, as beyond the addition of 2 equivalents saturation occurred. Moreover, an isosbestic point was initially formed to occur at 290 nm that disappeared after addition of ca. 1 equivalent of divalent zinc, clearly indicating that structural reorganisation in the ligand upon complexation of the second zinc equivalent. The experimental data were next analysed by using the global analysis software ReactLab™ Equilibria, to further assess the stoichiometry of the complex and to determine the binding constant for the interactions of zinc with 1. The best fit was obtained using both the 1:1 and the 1:2 H:G stoichiometry, with binding constants of log $K_{1:1}$ 6.39 ± 0.24 and log $K_{1:2}$ 7.23 ± 0.17 (see also Table 1) being determined for these stoichiometries. The speciation distribution diagram is shown in Figure 3b, demonstrating that the end product is indeed the formation of the 2:1 complex, and that during the titration process the formation of the 1:2 H:G complex does not exceed the formation of ca. 15%. Scheme 2 demonstrates the possible 1:1 and 1:2 binding stoichiometries in a schematic manner; the former being based on crystallographic evidence obtained in our laboratory for Zn(II) complexes obtained using structurally similar thiosemicarbazides binding motives (3), to that used herein. The latter binding would without doubt involve solvent coordinating molecules and possibly weak counter-ion integrations (omitted).

It is worth noting that, in this case unlike that seen in the literature, the value of the second binding constant is an order of magnitude higher than that seen for the first one. It is also clear, from the speciation distribution diagram, that the most abundant species is the 1:2 H:G, even at low concentration of the guest; which clearly shows that the ligand design favours the formation of the higher order 2:1 complex. The complex stoichiometry was further confirmed using the continuous variation method (14) (Job’s plot analysis); the results showing good agreement with the experimental data fitting using nonlinear regression analysis (Figure 4), the plot showing a maximum at 0.33 mole fraction ([H]/([H] + [G])) confirming the 1:2 H:G stoichiometry as the main species. Thus, this suggested that no cooperation between the two arms occurs during the binding event, and that each of the zinc ions is complexed by each of the pendant arms, respectively.

In a similar manner, ligand 2 was titrated with zinc. As above, a hyperchromic effect was observed for the band centred at 370 nm, along with an initial small shift towards longer wavelength (of ca. 3–4 nm). However, upon further addition of zinc, a shift to a shorter wavelength was observed (Figure 5). Also in this case, a plateau is reached after the addition of 2 equivalents of zinc; however, unlike that seen the spectral shape showed a small variation at high concentration of the guest.

Unlike that seen for 1, the best fit was obtained by analysing the changes using 1:1, 1:2 and 1:3 H:G species (Table 1), which is probably due to the binding event between the nitro groups of the aryl rings and a zinc ion,

| Ligand (L) | Metal (M) | Log $K_{L:M}$ 1:1 | Log $K_{L:M}$ 1:2 | Log $K_{L:M}$ 1:3 |
|------------|-----------|------------------|------------------|------------------|
| 1          | Zn$^2+$   | 6.39 ± 0.24      | 7.23 ± 0.17      | -                |
| 2          | Zn$^2+$   | 9.11 ± 0.31      | 7.95 ± 0.29      | 3.88 ± 0.77      |

Figure 3. (a) The changes observed in the absorption spectrum of 1 (8 × 10^{-6} M) upon addition of Zn(ClO$_4$)$_2$·6H$_2$O (0 → 2.9 × 10^{-5} M) in EtOH. Inset: titration profile at 307 nm. (b) The speciation distribution diagram of 1 (L) with Zn(II) in EtOH as obtained after fitting the changes using nonlinear regression analysis programme ReactLab™ Equilibria.
similar observations have been observed by us and others previously (15–17). Nevertheless, considering the speciation distribution diagram (Figure 5b), the 1:3 complex was only formed in low concentration and only upon addition of elevated equivalents of zinc (18). From Figure 5b, it is also clear that the 1:1 species is initially formed as expected, being formed in ca. 60% yield at the early stages of the titration. However, the 1:2 H:G formation is also an abundant species, becoming the dominant species in solution at 10 μM. Moreover, the association constants obtained for the binding of 2 to zinc are higher than those seen for 1 (Table 1). This might be due to the higher polarisation of the N–H bond (because of the electron-withdrawing effect of the nitro groups) that can cause a deprotonation to occur, which can give rise to stronger binding to the metal ion through resonance stabilisation (19). The association constants of the two substrates are however in good agreement with those reported in the literature (20, 21).

**Anions coordination through dimetallic complexes**

Since the receptor molecules 1 and 2 detect Zn²⁺, the in situ prepared LZn₂ complexes were used for anion recognition studies. The complexes were prepared taking into account the speciation distribution diagrams for the titrations of both ligands with divalent zinc. The amount of zinc was evaluated in order to have almost entirely the L-Zn₂ complex in solution. Both oxy anions such as acetate and phosphate as well as halides such as bromide were used.

The anion titrations were carried out in ethanol solution, which is a competitive hydrogen bonding media for ion recognition (22). Upon titrating 1–Zn₂ with the above anions, the most significant changes observed in the UV-vis absorption spectra of 1–Zn₂ were seen for H₂PO₄⁻ (Figure 6a). The titration of both Br⁻ and AcO⁻ unfortunately gave rise to only minor changes. In fact, the changes for AcO⁻ only allowed for the determination of a 1:1 species in solution which could indicate that both to the amido-thiourea are binding of a single acetate in a concerted manner or that the second binding event, the formation of the 1:2 species is not strong enough to give rise to large spectral changes. However, in the case of H₂PO₄⁻, the changes in the absorption band centred at 307 nm reduced in absorbance while the higher energy band centred at 270 nm was restored. These changes were accommodated with a clear isosbestic point at 285 nm. The overall changes seen in the absorption spectra upon recognition of the Zn(II) centres are most likely due to a weakening of the 1–Zn(II) bonds upon coordination of the zinc ion with the phosphate anion; giving rise to a blue shift. While a de-complexation could also be taking place in this system then we believe that this unlikely to happen.
based on previous work by Akkaya and co-workers \((23, 24)\). Analysis of the changes observed using nonlinear regression analysis gave both good fit and demonstrated that two equilibrium, occurred; the anion interacting with both zinc centres with \(\log K_{1:1} = 4.84 \pm 0.02\) and \(\log K_{1:2} = 2.68 \pm 0.10\), respectively (Table 2).

In a similar manner the \(2^-\text{Zn}_2\) complex was formed and the anion titrations carried out using the same anions as discussed above. Addition of these anions to \(2^-\text{Zn}_2\) resulted in a significant UV-vis changes on all occasions, showing that \(2^-\text{Zn}_2\) displayed a high affinity towards all the anions tested. The changes observed in the absorption spectra of \(2^-\text{Zn}_2\) upon titrating with phosphate is shown in Figure 7a. The results demonstrate that the long wavelength absorption was significantly affected, being accommodated with a small red-shift. Moreover, as was the case for \(1^-\text{Zn}_2\), the interaction with \(\text{H}_2\text{PO}_4^-\) was quite strong for \(2^-\text{Zn}_2\) and the best fit was obtained using both 1:1 and 1:2 H:G stoichiometries (summarised in Table 2), where the latter represented the dominant species in solution at high anion concentration (Figure 7b).

Similar spectral changes were seen upon titration of \(2^-\text{Zn}_2\) with \(\text{Br}^-\) as demonstrated in Figure 8a; here the changes were most prominent for the long wavelength addition, which showed that after the addition of two equivalents the absorption of the 370 nm band had reduced significantly in absorbance, while smaller changes were observed at higher energy. Analysis of these changes (Figure 8b) showed that each of the Zn(II) centres was coordinating to the halide, though an accurate binding constant for the second, 2:1 stoichiometry could not be determined with great accuracy (Table 2). It is however important to point out that the overall changes for the titration of \(\text{Br}^-\) are very different to that seen above for \(\text{H}_2\text{PO}_4^-\), indicating that the absorption spectra can be used to distinguish between both the nature of the binding event, i.e. halide vs. phosphate, and as such function as a ‘fingerprint’ for the recognition of these two types of anions. Unfortunately, we were not able to determine the stepwise equilibrium constants for the recognition of

![Figure 5](image1.png)

*Figure 5.* (a) The changes in the absorption spectrum of \(2\) \((5 \times 10^{-6} \text{ M})\) upon addition of \(\text{Zn(ClO}_4)_2\cdot6\text{H}_2\text{O} (0 \rightarrow 1.9 \times 10^{-5} \text{ M})\) in EtOH. *Inset:* the titration profile at 370 nm. (b) The speciation distribution diagram obtained by fitting the absorption data using nonlinear regression analysis.

![Figure 6](image2.png)

*Figure 6.* Left: changes in the UV-vis spectrum of \(1^-\text{Zn}_2\) \((\text{ca. } 8 \times 10^{-6} \text{ M})\) upon addition of TBAH_2PO_4 \((0 \rightarrow 1.55 \times 10^{-4} \text{ M})\) in EtOH. *Inset:* titration profile at 307 nm. Left: speciation distribution diagram.
Br\(^-\) as the 1:2 (L:H), and only the 1:1 binding constant could be determined (c.f. discussion below and Table 2).

We next assessed the binding of 2–Zn\(^{2+}\) with AcO\(^-\). Here, the formation of 1:2 complex was anticipated given the nature of the linear binding of acetate with metal-ion complexes of this nature (i.e. mono-dentate (25)). The changes in the absorption spectra of 1–Zn\(^{2+}\) upon titration with AcO\(^-\) is shown in Figure 9a. While the changes are significantly ‘smaller’ than that seen for H\(_2\)PO\(_4\), then once again, these results demonstrate that the overall spectral changes are very different to that seen above for Br\(^-\) and H\(_2\)PO\(_4\); potentially allowing for assigning of each of the anion recognition event based purely on the spectral change at the titration end point. In the case of acetate, only minor changes were observed in both the ICT and the high-energy transitions; these being accompanied by both an isosbestic point as well as a minor red-shift (Figure 9a).

For both Br\(^-\) and AcO\(^-\), analysis of the changes in the absorption spectra using nonlinear regression analysis showed that the best fit was obtained with 1:1 stoichiometry, resulting in very similar association constants of log K 5.70 ± 0.02 and 5.72 ± 0.07 for AcO\(^-\) and Br\(^-\), respectively (see Table 2). In fact, these results show that a direct discrimination is not possible based on the binding constant analysis alone, and that spectral analysis, i.e. shape and absorption intensity needs to be taken in to the account. From the fitting of these spectral changes, no evidence of the 1:2 stoichiometry was observed within the concentration range investigated for these two latter anions, this would possibly indicate that synergetic or cooperation binding of these anions takes place between the two zinc ions and the anion. While we do not have direct experimental proof for this (except by fitting the data), the results demonstrate that such 1,3-diconjugates calix[4]arene structures have great potential for use in both cation and anion recognition and sensing applications. This we are currently further exploring.

**Conclusion**

In this work, the calix[4]arene 1,3-diconjugates 1 and 2 were synthesised in high yield and characterised by UV-vis absorption spectroscopy in EtOH. Both compounds were found to be good ligands for divalent zinc in H-bond donor solvent, by changing their absorption properties due to the perturbation of the ICT band. Moreover, this was pointed out by the high association constants, which also showed higher affinity of the para-NO\(_2\) derivative towards Zn(II); both showing the formation of the 1:1 and 1:2 stoichiometries in solution. Furthermore, this study highlighted the versatility of the thiourea moiety that is able to bind either anionic or cationic species. However, the two pendants did not bind cooperatively the Zn(II). We also analysed the binding affinity of these structures for anions; the presence of the amido-thiourea moieties providing an excellent platform for such binding. Unless in the cases of 1 with AcO\(^-\) and Br\(^-\), anion addition to the in situ prepared (1,2)–Zn\(^{2+}\) complexes showed strong UV-vis changes. The high association constants, due to electrostatic interactions, showed high affinity towards anions. While in the case of H\(_2\)PO\(_4\), the binding event was found to occur with 1:2 H:G stoichiometry with both ligands, AcO\(^-\) and Br\(^-\) were bound in a cooperative fashion by the thiourea receptors of 2, leading to a high log K\(_{ass}\) value within both cases. We are in the process of

| Complex (C) | Anion (A) | Log K\(_{C:A}\) 1:1 | Log K\(_{C:A}\) 1:2 |
|-------------|-----------|-------------------|-------------------|
| 1–Zn\(^{2+}\) | AcO\(^-\) | 4.84 ± 0.01       | –                 |
|             | Br\(^-\)  | 2.68 ± 0.10       | –                 |
| 2–Zn\(^{2+}\) | H\(_2\)PO\(_4\) | 5.73 ± 0.08       | 4.90 ± 0.02       |
|             | Br\(^-\)  | 5.72 ± 0.07       | –                 |

Table 2. Association constants of the complexes-anions in EtOH obtained by ReactLab™ Equilibria.

![Figure 7](image-url) (a) The changes in the UV-vis absorption spectrum of 2–Zn\(^{2+}\) (ca. 5 × 10\(^{-6}\) M) upon addition of TBAH\(_2\)PO\(_4\) (0 → 3.4 × 10\(^{-4}\) M) in EtOH. Inset: titration profile at 370 nm. (b) The speciation distribution diagram.
exploring the applications of such pre-organised structures in greater detail.

**Experimental**

**General**

**Methods and materials**

All chemicals were purchased from commercial sources and, unless specified, used without further purification. Melting points were determined using an Electrothermal IA9000 digital melting point apparatus. Elemental analysis was carried out at the Microanalytical Laboratory, School of Chemistry and Chemical Biology, University College Dublin using an Exeter Analytical CE 440 elemental analyser. Infrared spectra were recorded on a Perkin–Elmer Spectrum One FT-IR Spectrometer fitted with a universal ATR sampling accessory. Absorption spectra were recorded with a Perkin–Elmer Lambda 800 spectrophotometer. NMR spectra were recorded using a Bruker DPX-400 Avance spectrometer or Agilent DD2/LH spectrometer, operating at 400.13 MHz for $^1$H-NMR, 100.6 MHz for $^{13}$C-NMR (see both in SI). All spectra were recorded using commercially available deuterated solvents, and were referenced to solvent residual proton signals. All $^1$H–$^1$H coupling constants, J, are quoted with an accuracy of ±0.3 Hz. Electro-spray mass spectra were measured on a Micromass LCT spectrometer calibrated using a leucine enkephalin standard. MALDI Q-Tof mass spectra were carried out on a MALDI Q-Tof Premier (Waters Corporation, Micromass MS Technologies, Manchester, UK) and high-resolution mass spectrometry was performed using Glu-Fib as an internal reference (peak at m/z 1570.677). All microwave reactions were carried out in Biotage Microwave Vials in a Biotage Initiator Eight EXP microwave reactor.

**Synthesis**

25,27-Bis[(hydrazidocarbonylmethyl)oxy]calix[4]arene (4)

25,27-Bis[(ethoxycarbonylmethoxy)-26,28-dihydroxy calix[4]arene (1 g, 1.69 mol) was dissolved in MeOH (17 ml) and hydrazine monohydrate (1.5 ml, large excess) was added. The reaction was carried out in the microwave for 1 hour at 100°C. The solvent and the excess of hydrazine were then removed under reduced pressure and...
the solid residue was triturated with water and then washed with methanol to yield a white solid (0.795 g, 1.4 mmol) with 73% yield.  

1H NMR (400 MHz, DMSO-d$_6$, $\delta_{H}$): 9.54 (s, 2H, Ar-OH), 8.32 (s, 2H, NH), 7.17 (d, 4H, Ar-H), 7.07 (d, 4H, Ar-H), 6.82 (t, 2H, Ar-H), 6.61 (t, 2H, Ar-H), 4.71 (s,4H, -NH$_2$), 4.53 (s, 4H, Ar-O-CH$_2$-CO$_2$), 4.20 (d, 4H, Ar-CH$_2$-Ar), 3.48 (d, 4H, Ar-CH$_2$-Ar).

Acknowledgements

We thank Dr Emma Veale and Dr Chris Hawes for their assistance during the writing of this manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

We thank University of Dublin for financial support. This research was also supported by Science Foundation Ireland (SFI) through the PRTLI and PI programmes and by Higher Education Authority (HEA) through PRTLI Cycle 5 funding. We also thank Ministero per l’Universita’ e Ricerca Scientifica e Tecnologica (Rome, Italy) and the University of Perugia under the PRIN 2010–2011 [grant number 2010FM738P].

References

(1) a) Bazzicalupi, C.; Bianchi, A.; García-Españo, E.; Delgado-Pinar, E. Inorg. Chem. Acta. 2014, 417, 3. b) Gunnlaugsson, T.; Parkesh, R.; Veale, E.B.; Kitchen, J.A. Luminescent Sensing. In Luminous Sensing to Nanomaterials in Supramolecular Chemistry: from Molecules, pp 2611–2642, 2012, Steed J.W., Gale P.A. Eds.; John Wiley: Chichester, 2012. c) Veale E.B.; Gunnlaugsson, T. Annu. Rep. Prog. Chem., Sect. B: Org. Chem. 2010, 106, 376. d) de Silva, A.P.; Moody T.S.; Wright, G.D. Analyst 2009, 134, 2385. e) Callan, J.F.; de Silva, A.P.; Magri, D.C. Tetrahedron 2005, 61, 8551. f) de Silva, A.P.; Gunaratne, H.Q.N.; Gunnlaugsson, T.; Huxley, A.J.M.; McCoy, C.P.; Rademacher J.T.; Rice, T.E. Chem. Rev. 1997, 97, 1515.

(2) a) Gale, P.A.; Gunnlaugsson, T. Chem. Soc. Rev. 2010, 39, 3595. b) Duke, R.M.; Veale, E.B.; Pfeffer, F.M.; Kruger, P.E.; Gunnlaugsson, T. Chem. Soc. Rev. 2010, 39, 3936. c) Veale, E.B.; Gunnlaugsson, T. Annu. Rep. Prog. Chem. Sect. B: Org. Chem. 2010, 106, 376–406. d) Amendola, V.; Fabbrizi, L.; Mosca, L. Chem. Soc. Rev. 2010, 39, 3889. e) Carroll, C.N.; Naleway, J.J.; Haley M.M.; Johnson, D.W.; Chem. Soc. Rev. 2010, 39, 3875. f) Wenzel, M.; Hiscock, J. R.; Gale, P.A. Chem. Soc. Rev. 2012, 41, 4080.

(3) a) Chen, H.-L.; Guo, Z.-F.; Lu, Z.-I. Org. Lett. 2012, 19, 5070. b) Pandurangan, K.; Kitchen, J.A.; McCabe, T.; Gunnlaugsson, T. Cryst. Eng. Comm. 2013, 15, 1421. c) Burrows, A.D.; Menzer, S.; Michael, D.; Mingos, P.; White, A.J.P.; Williams, D.J. J. Chem. Soc. Dalton Trans., 1997, 4237. d) Burrows, A.D.; Harrington, R.W.; Mahon, M.F.; Teat, S.J. Eur. J. Inorg. Chem. 2003, 766. e) Delgado-Pinar, E. Inorg. Chem. Acta. 2014, 417, 3.

25,27-Bis[(4-trifluoromethyl)phenyl]thioureidocarboxamoyl methoxyl calix[4]arene (1)

25,27-Bis[(4-nitrophenyl)thioureidocarboxamoyl methoxyl calix[4]arene (2)

25,27-Bis[(4-nitrophenyl)thioureidocarboxamoyl methoxyl calix[4]arene (2)
A.D.; Harrington, R.W.; Mahon, M.F.; Teat, S.J. Cryst. Eng. Comm. 2002, 4, 8.
(4) Rauf, M.K.; Imtiaz-ud-Din, A.; Badshah, M.; Gielen, M.; Ebihara, M.; de Vos, D.; Ahmed, S. Inorg. Biochem. 2009, 103, 1135–1144.
(5) Ji, Z.-J.; Wu, Y.-M.; Wu, F.-Y. Chem. Lett. 2006, 35 (8), 950–951.
(6) Wu, F.-Y.; Zhang, L.-N.; Ji, Z.-J.; Wan, X.-F. J. Lumin. 2010, 130, 1280–1284.
(7) a) Quinlan, E.; Matthews, S.E.; Gunnlaugsson, T. J. Org. Chem. 2007, 72, 7497. b) Sun, X.H.; Li, W.; Xia, P.F.; Luo, H.-B.; Wei, Y.; Wong, M.S.; Cheng, Y.-K.; Shuang, S. J. Org. Chem. 2007, 72, 2419.
(8) a) Lincheneau, C.; Quinlan, E.; Kitchen, J. A.; McCabe, T.; Matthews, S.E.; Gunnlaugsson, T. Supramol. Chem. 2013, 25, 896. b) Leray I.; Valeur, B. Eur. J. Inorg. Chem., 2009, 3525.
(9) Muthiac, L.; Lee, J.H.; Kim, J.S.; Vicens, J. Chem. Soc. Rev. 2011, 40, 2777.
(10) Joseph, R.; Rao, C.P. Chem. Rev. 2011, 111, 4658–4702.
(11) Giacco, T.; Carlotti, B.; De Solis, S.; Barbafina, A.; Elisei, F. Phys. Chem. Chem. Phys. 2010, 12, 8062.
(12) Quinlan, E.; Matthews, S.E.; Gunnlaugsson, T. Tetrahedron Lett. 2006, 47, 9333–9338.
(13) a) Boyle, E.M.; Comby, S.; Molloy, J.K.; Gunnlaugsson, T. J. Org. Chem. 2013, 78, 8312. b) Duke, R.M.; O’Brien, J.E.; McCabe, T.; Gunnlaugsson, T. Org. Biomol. Chem. 2008, 6, 4089. (b) Wei, L.-H.; He, Y.-B.; Wu, J.-L.; Meng, L.-Z.; Yang, X. Supramol. Chem. 2004, 16, 561. c) Duke, R.M.; McCabe, T.; Schmitt, W.; Gunnlaugsson, T. J. Org. Chem. 2012, 77, 3115.
(14) Hirose, K. J. Incl. Phenom. Macro cycl. Chem. 2001, 39 (3/4), 193–209.
(15) Pandurangan, K.; Kitchen, J.A.; Gunnlaugsson, T. Tetrahedron Lett. 2013, 54, 2770–2775.
(16) a) Li, A.-F.; Wang, J.-H.; Wang, F.; Jiang, Y.-B. Chem. Soc. Rev. 2012, 39, 3729. b) Wang, S.-H.; Wang, S.-F.; Xuan, W.; Zeng, Z.-H.; Jin, J.-Y.; Mad, J.; Tian, G.R. Bioorg. Med. Chem. 2008, 16, 3596. c) Pfeffer, F.M.; Lim, K.F.; Sedgwick, K.J. Org. Biomol. Chem. 2007, 5, 1795. d) Yang, R.; Liu, W.-X.; Shen, H.; Huang, H.-H.; Jiang, Y.-B. J. Phys. Chem. B 2008, 112, 5105. e) Veale, E.B.; Gunnlaugsson, T. J. Org. Chem. 2008, 73, 8073.
(17) Perez-Casas, C.; Yatsimirsky, A.K. J. Org. Chem. 2008, 73, 2275–2284.
(18) It is important to emphasize that the 1:3 stoichiometry only needed to be included to obtain the best fit to the titration data shown in Figure 5a, as omitting it gave rise to unacceptable error in the fitting of the data. Moreover, the speciation distribution diagram in Figure 5b shows that this species is only formed when all the 1:1 species has been omitted.
(19) a) Shen, X.; Shi, X.; Kang, B.; Liu, Y.; Tong, Y.; Jiang H.; Chen, K. Polyhedron. 1998, 17, 4049. b) Martinez-Calvo, M.; Romero, M.J.; Pedrido, R.; Gonzalez-Noya, A.M.; Zaragoza, G.; Bermejo, M.R. Dalton Trans. 2012, 41, 13395.
(20) a) Jiang, P.; Guo, Z. Coord. Chem. Rev. 2004, 248, 205. b) Boens, N.; Leen, V.; Dehaen W. Chem. Soc. Rev. 2012, 41, 1130. c) Tamanini, E.; Flavin, K.; Motevalli, M.; Piperno, S.; Gheber, L.A.; Todd, M.H.; Watkinson, M. Inorg. Chem. 2010, 49, 3789. d) Gunnlaugsson, T.; Lee, C.T.; Parkesh, R. Org. Biomol. Chem. 2003, 1, 3265. e) Pope, S.J.A.; Laye, R.H. Dalton Trans. 2006, 3108. (b) Andrews, M.; Jones, J.E.; Harding, L.P.; Pope, S.J.A. Chem. Commun. 2011, 47, 206. (c) Ye, Z.; Wang, G.; Chen, J.; Zhang, W.; Yuan, J. Biosens. Bioelectron. 2010, 26, 1043.
(21) Comby, S.; Tuck, S.A.; Truman, L.K.; Kotova, O.; Gunnlaugsson, T. Inorg. Chem. 2012, 51, 10158–10168.
(22) a) Caffrey, D.F.; Gunnlaugsson, T. Dalton Trans. 2014, 43, 17964. b) Kitchen, J.A.; Boyle, E.M.; Gunnlaugsson, T. Inorg. Chem. Acta 2012, 381, 236. c) dos Santos, C.M.G.; Gunnlaugsson, T. Supramol. Chem. 2009, 21, 173. d) Leonard, J.P.; dos Santos, C.M.G.; Plush, S.E.; McCabe, T.; Gunnlaugsson, T. Chem. Commun. 2007, 129. e) Gunnlaugsson, T.; Bichell, B.; Nolan, C. Tetrahedron 2004, 60, 5799. f) Gunnlaugsson, T.; Bichell, B.; Nolan, C. Tetrahedron Lett. 2002, 43, 4989. g) Gunnlaugsson, T.; Nieuwenhuizen, M.; Richard, L.; Thoss, V. Tetrahedron Lett. 2001, 42, 4725.
(23) Coskun, A.; Baytekin, B.T.; Akkaya, E.U. Tetrahedron Lett. 2003, 44, 5649–5651.
(24) Even though de-complexation is possible we believe that the changes occurring with other anions demonstrate that since each of the anions gives rise to different absorption profile the final product of each of these has to be different, i.e. not the free ligand. This we have seen previously in Ali, H.D.P.; Kruger, P.E.; Gunnlaugsson, T. New J. Chem. 2008, 32, 1153.
(25) Kitchen, J.A.; Martinho, P.N.; Morgan, G.G.; Gunnlaugsson, T. Dalton Trans. 2014, 43, 6468–6479.