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A direct fluorescence-on chemo-sensor for selective recognition of Zn(II) by a lower rim 1,3-di-derivative of calix[4]arene possessing bis-{*N*-(2-hydroxynaphthyl-1-methylimine)} pendants

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Abstract—The bis-{*N*-(2-hydroxynaphthyl-1-methylimine)} anchored 1,3-di-derivative of lower rim *p-tert*-butyl-calix[4]arene possessing a N_2O_2, N_2O_4 or N_2O_6 binding core was found to be selective for Zn(II) ions even at $\leqslant$60 ppb by eliciting fluorescence-on behaviour while the other ions, viz., Ti^{4+}, VO^{2+}, Cr^{3+}, Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Mg^{2+}, Cd^{2+} and Hg^{2+} caused no change in the fluorescence. The reaction between **1** and Zn^{2+} was found to be stoichiometric with the formation of a 1:1 complex; while H^+ quenched the fluorescence of the complex, OH^- restored it. The studies of the 1:1 isolated complexes of Zn^{2+}, Ni^{2+} and Cu^{2+} augmented the results.

Certain derivatives of calix[4]arene have recently been shown to be involved in the recognition of ions as well as neutral species and hence can act as sensors of various types.[1] Such derivatives require the synthesis of the molecules including reporter moieties. Therefore, calix[4]arene derivatives with appropriate binding cores and yet possessing a fluorescent probe are required for the sensitive fluorescence technique. Recent reports include calix[4]arene derivatives possessing a fluorescent probe sensitive to alkali[2–4] and alkaline earth[5] ions, and also to Eu^{3+}.[6] On the other hand, the calix[4]arene systems developed for transition metal ions[7] were rather limited and were not particularly specific to one metal ion. Calix[4]arene-based Zn(II) detection was reported through an energy transfer mechanism using a phenanthroline derivative[8] and also reported was trace detection of Cu(II) by another derivative.[9] An upper rim tetra-substituted azo-derivative was shown to be suitable for detecting mmolar Cr(III) by absorption spectroscopy.[10] Recognition of metal ion differs depending upon whether the chemical group or pendant is anchored to the lower rim or to the upper rim, though the reason for this is still not understood, for example, the recognition of metal ions by an anthryl-bound di-derivative of calix[4]arene flips from Fe^{2+} and Cu^{2+} to Co^{3+} and Cu^{2+} on going from a lower rim[11] to an upper rim[7b] derivative. Some non-calixarene based sensors for Zn^{2+} include those of the Rhodafluor, Zinspy and Zinpyr families,[12] as well as benzimidazole-based systems.[13] In our quest to find calixarene systems suitable for detecting one transition metal ion selectively over the others, we report here selective fluorescence detection of Zn^{2+} over all the other 3d-metal ions as well as Mg^{2+}, Cd^{2+} and Hg^{2+} directly by the bis-{*N*-(2-hydroxynaphthyl-1-methylimine)}-anchored 1,3-di-derivative of lower rim calix[4]arene.

The fluorescence-sensitive calix-di-imine derivative, **1** was synthesized by adapting a three-step procedure[14] and gave satisfactory analyses[15] and was used for all the fluorescence measurements.[16] ^1H and ^{13}C NMR data of **1** were consistent with the presence of a 1,3-di-derivative of calix[4]arene in its cone conformation. A metal ion binding core of the type N_2O_2, N_2O_4 or even N_2O_6 is present in **1** and this core is different from that observed with an anthryl derivative,[11] **2** (Fig. 1).

Free calix-di-imine, **1** exhibits two weak emissions centred at 355 and 440 nm where the first one corresponds

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Keywords: Bis-{*N*-(2-hydroxynaphthyl-1-methylimine)} anchored 1,3-di-derivative of *p-tert*-butyl-calix[4]arene; Fluorescence-on; Selective detection of Zn(II); Chemo-sensor; Fluorescence quenching; Fluorescence restoration.

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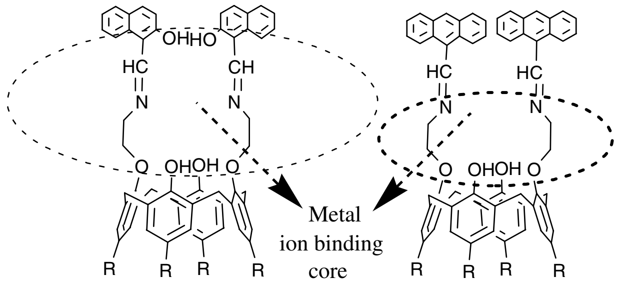


1 **2**

Figure 1. Comparison of the metal ion binding cores of calix[4]arene derivatives, **1** and **2**. R = *tert*-butyl.

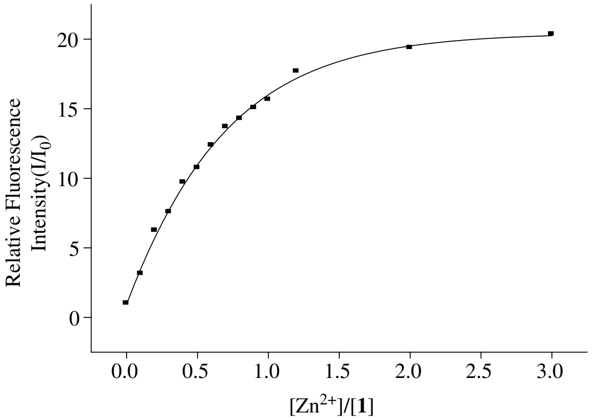


Figure 3. Plot of relative fluorescence intensity (I/I_0) versus $[Zn^{2+}]/[\mathbf{1}]$ mole ratio.

to that of naphthalene and the second one corresponds to a naphthalene in conjugation with an imine-moiety. The lone pair present on the nitrogen of –HC=N– results in the photo-induced electron transfer (PET) that quenches the fluorescence by several folds. This assignment has been further confirmed by comparing the emission spectra generated by a systematic study involving naphthalene itself and 2-hydroxy-1-naphthaldehyde, with that of **1**.

The effect of 3d-transition ions as well as Mg^{2+}, Cd^{2+} and Hg^{2+} on the fluorescence emission of calix-di-imine, **1** was studied. The fluorescence intensity of the 440 nm band of **1** increased gradually as a function of the addition of Zn^{2+} only (Fig. 2) indicating a fluorescence-on behaviour. No change was observed in fluorescence with any of the other metal ions studied. However, no significant change was observed in the fluorescence intensity of the 355 nm band with Zn^{2+} or other metal ions. A plot of relative fluorescence intensity (I/I_0) versus $[Zn^{2+}]/[\mathbf{1}]$ mole ratio clearly indicated a >20-fold increase when compared to unbound **1** and also revealed the formation of a 1:1 complex between **1** and Zn^{2+} (Fig. 3) and thereby refers to a stoichiometric reaction. The study thus indicated the role of the lone pair on the imine-N in quenching the fluorescence in the free ligand and the reversal of this quenching upon Zn^{2+} binding, which utilizes the lone pair.

Based on the Benesi–Hildebrand equation, the association constant of the complex formed between Zn^{2+} and **1** at a 1:1 ratio was found to be $2.3 \times 10^5\ M^{-1}$ and for **2** it is[11] $5.5 \times 10^4\ M^{-1}$. These association constants are much higher than those reported for a lower rim 1,2-di-imidazole-derivative of calix[4]arene towards Cu^{2+} and Zn^{2+}, viz., 9000 and 2500 M^{-1}, respectively.[7c] The 4-fold higher association constant observed with **1** versus **2** is attributable to additional possible chelation provided by the presence of two additional β-hydroxy groups present on the two naphthylidene moieties in **1** (Fig. 1). Based on the relative fluorescence intensities shown in Figure 4, it can be concluded that Zn^{2+} is selectively recognized by **1** among the 12 metal ions or species studied, viz., Ti^{4+}, VO^{2+}, Cr^{3+}, Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Mg^{2+}, Cd^{2+} and Hg^{2+}. A dilution experiment carried out whilst keeping the $[Zn^{2+}]/[\mathbf{1}]$ mole ratio at 1:1 clearly indicated that Zn^{2+} can be detected down to ⩽60 ppb where the fluorescence intensity increase was 200% (Fig. 5).

A preparative reaction between **1** and $Zn(OAc)_2$ yielded a product, **3** that analyzed as a 1:1 complex (Fig. 6), as

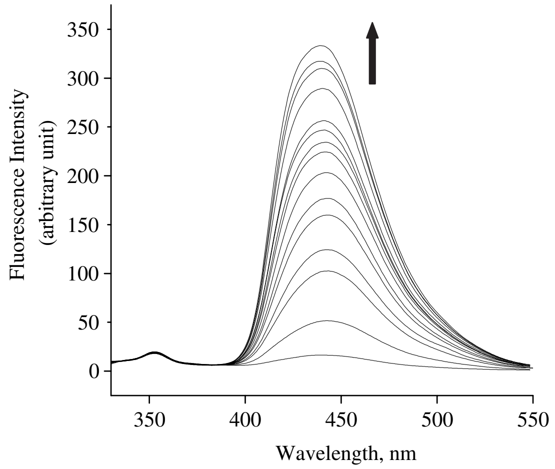


Figure 2. Fluorescence spectral traces of calix-imine, **1** as a function of added Zn^{2+} in order to produce $[Zn^{2+}]/[\mathbf{1}]$ mole ratios of 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.2, 1.6, 2.0 and 3.0. The arrow indicates the direction of increase in fluorescence intensity.

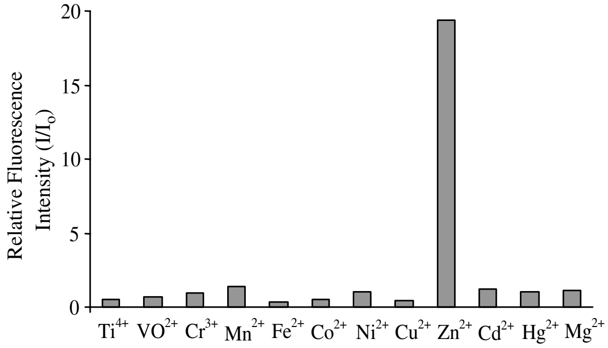


Figure 4. Relative fluorescence intensity at the metal ion to the ligand mole ratio of 2.0 (almost the same even at 1.0) in the titration of **1** with different metal ions or species.

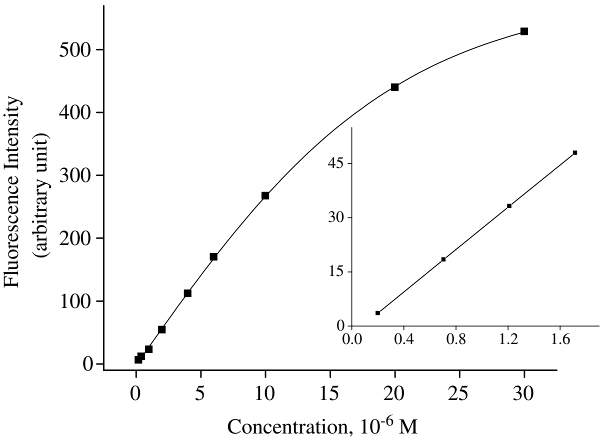
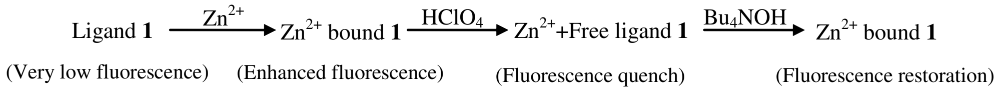


Figure 5. Plot of fluorescence intensity (*I*) versus [Zn^{2+}], keeping the [Zn^{2+}]/[**1**] mole ratio at 1:1. The inset is an expansion plot of the first four points.

established by FAB MS and ^1H NMR spectra.[17] The emission spectrum of a 10 μM solution of the isolated Zn^{2+} complex, **3** (Fig. 7) showed a relative fluorescence intensity of about 58-fold at 440 nm. On the other hand, isolated complexes[18,19] of Ni^{2+} **4** and Cu^{2+} **5** did not show any significant enhancement in the intensity, being consistent with the results obtained in solution titration studies.

The quantum yields of **1**, **1**+Zn^{2+} (1:1) and **3** were found to be 0.0134, 0.1322 and 0.0697, respectively, calculated using naphthalene as standard, with a value of 0.23 in hexane. Thus, when Zn^{2+} is bound to **1**, the quantum yield increases at least 10-fold and hence complex **1** provides a sensitive means to recognize Zn^{2+} by direct fluorescence measurement.

Addition of $HClO_4$ to the 1:1 complex formed between **1** and Zn^{2+}, or **3**, clearly indicated that one equivalent of this acid is sufficient to quench the fluorescence completely in both cases (Fig. 8a and b) as dissociation of the complex occurs upon protonation. However, when HCl was used instead of $HClO_4$, total quenching was only observed with more than 10 equiv. When a mixture of **1**, Zn^{2+}, $HClO_4$ in a 1:1:1 mole ratio was further titrated with Bu_4NOH, the fluorescence was completely restored (Fig. 8c) indicating a reversal and re-formation of the complex.



Similar observations have been reported in the literature for Cu^{2+} and Zn^{2+} complexes of calix[4]arene-imidazole derivatives.[7c]

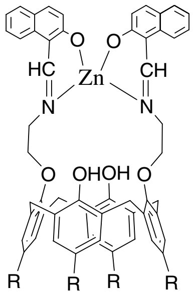


Figure 6. Schematic structure of the Zn^{2+} complex, **3**. R = *tert*-butyl.

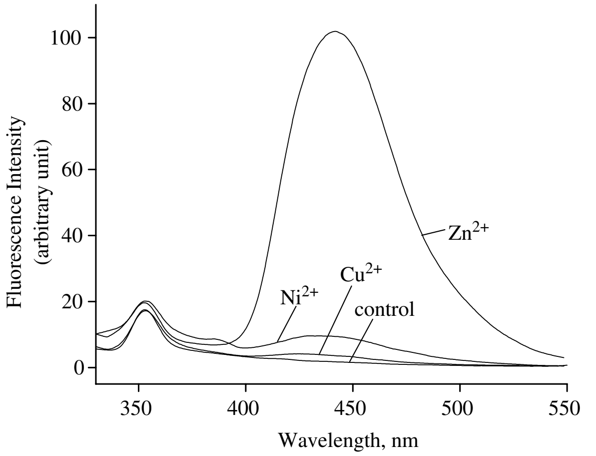


Figure 7. Emission spectral traces of isolated 1:1 complexes of Zn^{2+} **3**, Ni^{2+} **4** and Cu^{2+} **5** in methanol, which was also used for the metal ion titration. 'Control' refers to the solvent system.

While **1** selectively recognizes Zn^{2+} over other 3d-ions as well as Mg^{2+}, Cd^{2+} and Hg^{2+}, the anthryl-imine, **2** (Fig. 1) detects both Fe^{2+} and Cu^{2+} to the same extent but Zn^{2+} hardly at all. The difference between **1** and **2** (Fig. 1), besides the presence of naphthyl versus anthryl, is the presence of the β-hydroxy groups on the two naphthylidene moieties in the case of **1** providing additional chelation for the metal ion. This seems to suggest that the introduction of –OH *ortho* to an amine on an aromatic moiety provides selectivity towards metal ion recognition, in the present case, becoming selective for Zn^{2+}. The complex formed between **1** and Zn^{2+} can be quenched by H^+ and later restored by OH^-. Thus, **1** is a fluorescence-on chemosensor for Zn^{2+} owing to its selectivity as well as its high sensitivity in recognizing concentrations ⩽60 ppb. To our knowledge, this is the first calix[4]arene based Zn^{2+} chemosensor that depends directly on the emission behaviour of the ligand upon interaction with Zn^{2+}. Literature reports on Zn^{2+} recognition involve an energy transfer between bis-(8-oxyquinoline)calix[4]arene and batho-phenanthroline[8] from the medium that is precluded by the binding of Zn^{2+} to an 8-oxyquinoline moiety. The factors

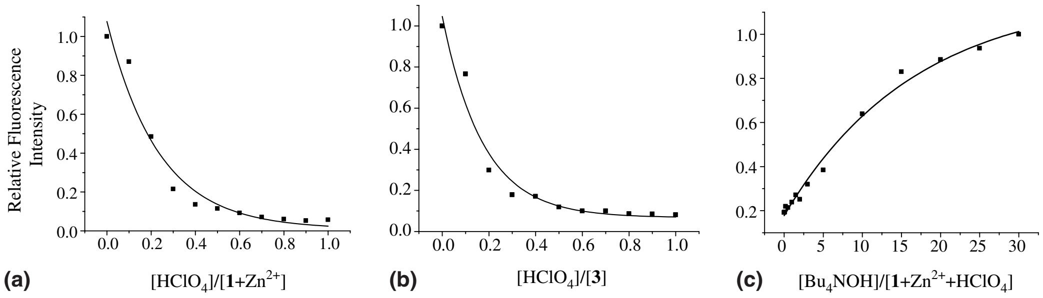


Figure 8. Fluorescence quenching in the titration of (a) [**1**+Zn^{2+}] (1:1) with $HClO_4$, and (b) **3** with $HClO_4$. (c) Restoration of the fluorescence in the titration of {**1**+Zn^{2+}+$HClO_4$ in 1:1:1} with Bu_4NOH.

that influence the selectivity of various binding cores on the calix[4]arene moiety towards different metal ions are still unexplored and our group is currently studying such aspects.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.09.079.

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15. Reaction of chloroacetonitrile with *p-tert*-butyl-calix[4]-arene results in calix-di-nitrile derivative, which upon reduction by $LiAlH_4$ results in the calix-di-amine derivative, and this upon condensation with 2-hydroxy-1-naphthaldehyde yields the fluorescence-sensitive calix-di-imine derivative, **1** in 67% yield. Selected data for **1**: δ_H ($CDCl_3$, 300 MHz) 0.87 (s, 18H, CMe_3), 1.27 (s, 18H, CMe_3), 3.3 (d, 4H, $J = 13.2$ Hz, Ar–C*H*$_2$–Ar), 3.9 (t, 4H, NC*H*$_2$), 4.10–4.25 (m, 8H, Ar–C*H*$_2$–Ar and OC*H*$_2$), 6.68 (s, 4H, calix–*Ar–H*), 6.88 (d, $J = 9.2$ Hz, 2H, naphthyl–*Ar–H*), 6.98 (s, 4H, calix–*Ar–H*), 7.24 (t, $J = 7.6$ Hz, 2H, naphthyl–*Ar–H*), 7.40 (t, $J = 7.0$ Hz, 2H, naphthyl–*Ar–H*), 7.56 (d, $J = 7.6$ Hz, 2H, naphthyl–*Ar–H*), 7.60 (d, $J = 9.2$ Hz, 2H, naphthyl–*Ar–H*), 8.00 (d, $J = 8.3$ Hz, 2H, naphthyl–*Ar–H*), 8.97 (s, 2H, *H*C=N), 14.6 (s, 2H, Ar–O*H*); δ_C ($CDCl_3$) 160.6 (*C*H=N), 173.5, 150.3, 149.6, 149.2, 141.6, 136.6, 133.7, 132.1, 129.1, 127.8, 127.7, 126.6, 125.7, 125.1, 123.6, 122.9, 119.0, 107.6 (*Ar–C*), 74.9 (O*C*H$_2$), 54.1 (*C*H$_2$N), 33.9, 33.9 (*C*Me$_3$), 31.8, 31.0 (C*Me*$_3$), 31.6 (Ar–*C*H$_2$–Ar); *m*/*z* (ES-MS) 1043 (M^+, 100%); Anal. (% found) C 80.20, H 7.27, N 2.31, $C_{70}H_{78}N_2O_6$ (% requires) C 80.58, H 7.54 N 2.68; FTIR (KBr, cm^{-1}) 3438 (ν_{OH}), 1631 ($\nu_{C=N}$).
16. Bulk solutions of **1** and the metal salts were prepared in $CHCl_3$ and MeOH, respectively, at 6×10^{-4} M. All the fluorescence titrations were carried out on a Perkin–Elmer LS55 at 320 nm excitation in 1 cm quartz cells by maintaining the final [**1**] at 10 μM in a total solution volume of 3 mL achieved by diluting with MeOH. Methanolic solutions of 6×10^{-4} M of $HClO_4$, HCl and Bu_4NOH were used in the corresponding titrations. Metal salts used were, $TiCl_2(acac)_2$, $VO(acac)_2$, $CrCl_3 \cdot 6H_2O$, $M(ClO_4)_2 \cdot 6H_2O$ {M = Mn, Fe, Co, Ni, Cu, Zn, Mg}, $Cd(CH_3CO_2)_2 \cdot 2H_2O$, $HgCl_2$; 'acac' is acetylacetonato. All the fluorescence experiments were repeated at least three times and the results were reproducible. The Zn^{2+} titration was repeated more than 10 times.
17. Zn^{2+} complex, **3**: To a solution of **1** (0.105 g, 0.1 mmol) in CH_2Cl_2 (5 mL), zinc(II) acetate (0.022 g, 0.1 mmol) in methanol was added dropwise. After stirring for one day, the volume was reduced to half by evaporation and the solid formed was filtered, washed with cold methanol (3 mL) and dried under vacuum to give **3** (70 mg, 64%). Selected data for **3**: δ_H ($CDCl_3$, 300 MHz) 0.82 (s, 18H,

C*Me*$_3$), 1.27 (s, 18H, C*Me*$_3$), 3.25 (d, 4H, $J = 13$ Hz, Ar–C*H*$_2$–Ar), 3.88 (br, 4H, NC*H*$_2$), 4.12 (d, $J = 13$ Hz, 4H, Ar–C*H*$_2$–Ar), 4.15 (br, 4H, OC*H*$_2$), 6.68 (s, 4H, calix–*Ar–H*), 6.88 (d, $J = 9.2$ Hz, 2H, naphthyl–*Ar–H*), 6.97 (s, 4H, calix–*Ar–H*), 7.22 (t, $J = 7.2$ Hz, 2H, naphthyl–*Ar–H*), 7.40 (t, $J = 7.6$ Hz, 2H, naphthyl–*Ar–H*), 7.55 (d, $J = 8.0$ Hz, 2H, naphthyl–*Ar–H*), 7.59 (d, $J = 9.2$ Hz, 2H, naphthyl–*Ar–H*), 8.00 (d, $J = 8.8$ Hz, 2H, naphthyl–*Ar–H*), 8.95 (s, 2H, *H*C=N); Anal. (% found) C 76.20, H 6.50, N 2.11, $C_{70}H_{76}N_2O_6Zn$ (% required) C 75.98, H 6.92, N 2.53; *m/z* (FAB-MS) 1106 (M·Zn$^+$, 24%); FTIR (KBr, cm^{-1}) 3439 (ν_{OH}), 1631 ($\nu_{C=N}$).

18. Ni^{2+} complex, **4**: This was synthesized in 66% yield by adapting the procedure used for **3** but using nickel(II) acetate. Anal. (% found) C 74.80, H 6.82, N 2.25, $C_{70}H_{76}N_2O_6Ni.CH_3OH$ (% required) C 74.74, H 7.12, N 2.48, *m/z* (FAB-MS) 1099(M·Ni$^+$, 35%), FTIR (KBr, cm^{-1}) 3439 (ν_{OH}), 1618 ($\nu_{C=N}$).
19. Cu^{2+} complex, **5**: This was synthesized in 62% yield by adapting the procedure used for **3** but using copper(II) acetate. Anal. (% found) C 75.40, H 6.71, N 2.28, $C_{70}H_{76}N_2O_6Cu.CH_3OH$ (% required) C 75.07, H 7.04, N 2.47; *m/z* (FAB-MS) 1105 (M·Cu$^+$, 50%); FTIR (KBr, cm^{-1}) 3442 (ν_{OH}), 1618 ($\nu_{C=N}$).