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Selective sensing of Zn(II) ion by a simple anthracene-based tripodal chemosensor

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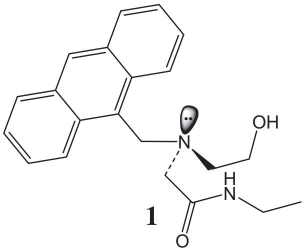
ABSTRACT

A new and an easy-to-make simple tripodal shaped chemosensor **1**, comprising an anthracene moiety as a fluorophore and amide, alcohol functionalities as ligating groups has been designed and synthesized for Zn(II). In CH_3CN containing 0.1% DMSO, upon excitation at 370 nm, the chemosensor **1** exhibited an emission at 412 nm, which increased to a large extent upon complexation of Zn(II). Among the other metal ions examined in the study, Cd^{2+} moderately perturbed the emission of **1** under similar conditions.

The development of fluorescent molecular sensors for metal ions is of considerable importance in supramolecular chemistry due to the important role of metal ions in biological and environmental systems.[1] Of the different metal ions, zinc ion is an abundant component in the human body and plays an important role in various fundamental biological processes, such as gene transcription, regulation of metalloenzymes, mammalian reproduction, and neural signal transmission.[2] It is recognized as one of the most important cations in catalytic centers and structural cofactors of many Zn^{2+}-containing enzymes and DNA binding proteins (e.g., transcriptions factor). Besides these, free zinc pools exist in brain, intestine, retina, etc. Therefore, detection of zinc ion is very important. Due to d^{10} electronic configuration, Zn^{2+} is spectroscopically silent for its detection and thus fluorescent receptors have been developed as useful tools to sense Zn^{2+}. Various fluorescent chemosensors for Zn^{2+} are known in the literature.[3] Although significant progress has been made in relation to the detection of Zn^{2+} ion, there is still a demand for a fluororeceptor of new architecture with improved properties, especially in fluorescence. Careful scrutiny of the literature reveals that di-2-picolylamine (DPA) is the most popular chelator of Zn^{2+} and thus its installation onto the different chromophores has been found to be the basic strategy for the construction of a series of chemosensors for Zn^{2+} ion.[3d,4]

We herein report an easy-to-make tripodal shaped simple chemosensor **1**, comprising an anthracene moiety as a fluorophore and amine, amide, alcohol functionalities as ligating groups for metal ions. The chemosensor **1** selectively recognizes Zn^{2+} ion in CH_3CN by exhibiting a drastic increase in emission of anthracene. In the study of other metal ions considered, except Cd^{2+} no other metal ion showed significant interaction. In order to understand the role of the alcoholic and amide functional groups in **1** in the binding of metal ions, a model compound **2** was synthesized.



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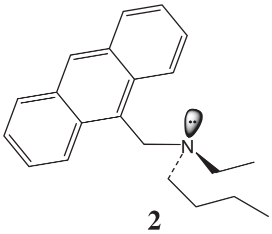

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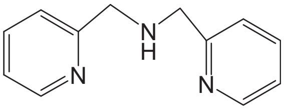

DPA

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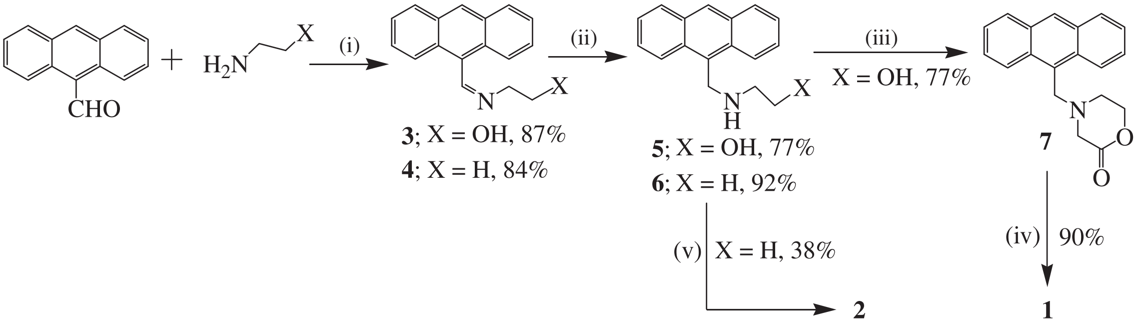

Scheme 1. Reagents and conditions: (i) dry MeOH, reflux, 9 h; (ii) $NaBH_4$, dry MeOH, reflux, 3 h; (iii) ethyl 2-chloroethanoate, K_2CO_3, dry Me_2CO, reflux, 7 h; (iv) ethylamine, THF, stirring, 4 h; (v) *n*-butyl bromide, K_2CO_3, CH_3CN, reflux 5 h.

Scheme 1 describes the synthesis of both **1** and **2**. Condensation of 9-anthraldehyde with ethanolamine yielded Schiff base **3**, which was reduced *in situ* to the amine **5** using $NaBH_4$ in MeOH. Reaction of **5** with ethyl 2-chloroethanoate in the presence of K_2CO_3 in dry acetone under refluxing condition afforded the 4-substituted morpholin-2-one **7** in 77% yield. We achieved the synthesis of this 4-substituted morpholin-2-one in a simple way although other methods, in this context, are known in the literature.[5] Most of them were not straightforward and required more steps. However, in the present case, the intermediate 4-substituted morpholin-2-one **7** was next reacted with ethylamine in THF to give the compound **1** in 90% yield. Similarly, compound **2** was obtained from 9-anthraldehyde after performing a series of reactions such as Schiff base formation with ethylamine, reduction of Schiff base by $NaBH_{4,}$ and then alkylation on the nitrogen center using *n*-butylbromide. All the compounds were characterized by ^1H NMR, ^{13}C, FTIR, and mass analysis (Supplementary data).

Compound **1** exhibits a weak fluorescence emission at 412 nm in CH_3CN containing 0.1% DMSO (DMSO was used for homogeneity of the solution) upon excitation at 370 nm. Upon titration with different metal ions, the emission of **1** changed to different extents. Figure 1 shows a comparative view when different metal ions were added in 4 equiv amounts to the solution of **1** in CH_3CN containing 0.1% DMSO.

While the emission at 412 nm increased dramatically in the presence of Zn^{2+}, it was moderately perturbed in the presence of Cd^{2+}. Among the other cations, Mg^{2+} and Hg^{2+} perturbed the emission weakly. Figure 2 displays the change in emission spectra of **1** in CH_3CN containing 0.1% DMSO upon gradual addition of zinc perchlorate. During the titration, the emission intensity at 412 nm progressively increased with red shift ($\Delta\lambda = 4$ nm). Such a significant change in emission of **1** in the presence of Zn^{2+} is attributed to the better coordination of Zn^{2+} by amine nitrogen and amide, alcohol functionalities in the open cavity due to which rigidification of the molecule results, and the photo-induced electron transfer (PET) from the binding sites to the excited state of anthracene is inhibited. As Zn^{2+} has closed-shell d-orbitals, energy or charge transfer processes cannot take place.

The stoichiometry of the Zn-complex was found to be little complex in the excited state. Initially receptor **1** forms 1:1 complex and thereafter attains higher order stoichiometry (2:1/3:1 guest to host) in the presence of excess concentration of Zn^{2+}. The break of the titration curve (Fig. 3) and the fluorescence Job plot[6] (Fig. 4) clearly represent these binding features. On the other hand, the sensor **1** attains 1:1 stoichiometry with Cd^{2+} and Mg^{2+} as evidenced from the break of the titration curves (Fig. 3) and Job plots (Supplementary data). The linear change in emission upon complexion of Hg^{2+} in Figure 3 is an indication of a weak interaction involving 1:1 stoichiometry. Moreover, the increase in emission of **1** up to the addition of 1 equiv of Cu^{2+} and then gradual decrease in emission upon addition of excess Cu^{2+} is an interesting feature of Cu^{2+} ion sensing in the present study (Supplementary data) although the change in emission is less compared to Zn^{2+} and Cd^{2+}.

However, we determined the fluorescence enhancement factor[7] of **1** at emission 412 nm in the presence of 4.0 equiv amounts of each metal ion in CH_3CN containing 0.1% DMSO. The emission in-

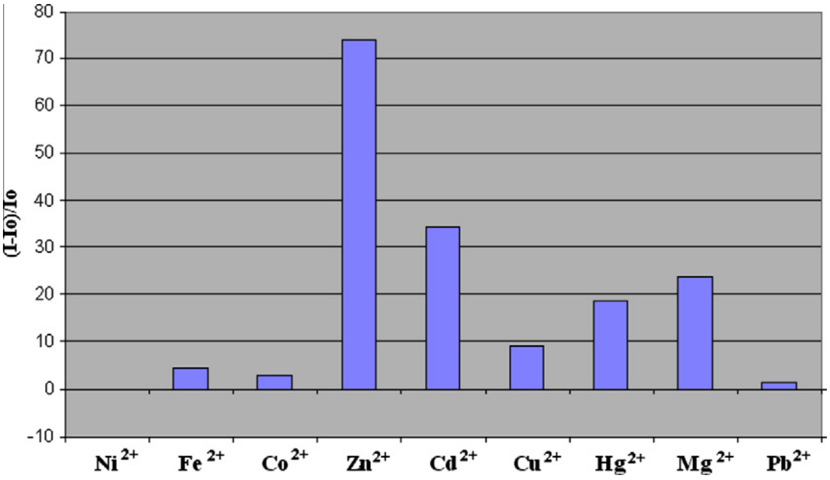

Figure 1. Fluorescence ratio $(I - I_0)/I_0$ of receptor **1**($c = 3.95 \times 10^{-5}$ M) at 412 nm upon addition of 4.0 equiv of a particular cation ($c = 1.50 \times 10^{-3}$ M, as perchlorate salt) in CH_3CN containing 0.1% DMSO ($\lambda_{ex} = 370$ nm).

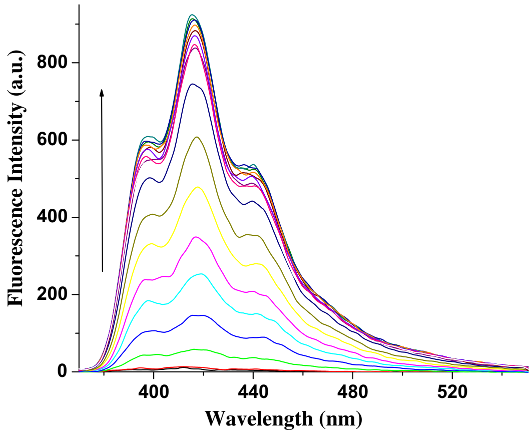

Figure 2. Change in emission spectra of **1** ($c = 3.95 \times 10^{-5}$ M) upon addition of Zn^{2+} ($c = 1.50 \times 10^{-3}$ M, as perchlorate salt) in CH_3CN containing 0.1% DMSO ($\lambda_{ex} = 370$ nm).

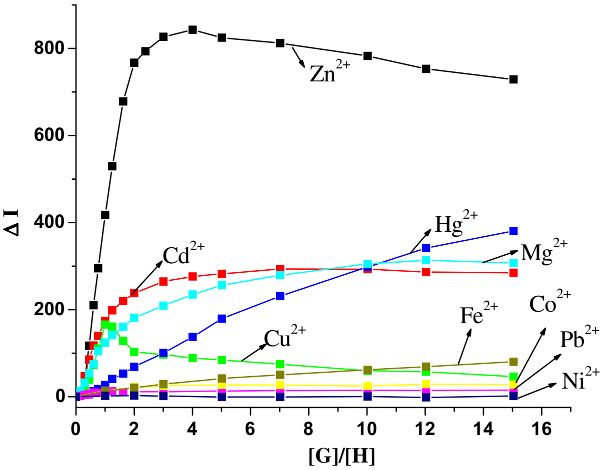

Figure 3. Fluorescence titration curves ([Guest]/[Host] versus change in emission) of **1** ($c = 3.95 \times 10^{-5}$ M) measured at 412 nm in CH_3CN containing 0.1% DMSO ($\lambda_{ex} = 370$ nm).

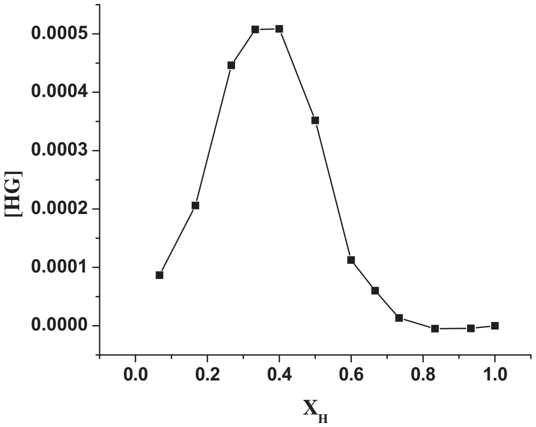

Figure 4. Fluorescence Job plot of receptor **1** ($c = 4.67 \times 10^{-5}$ M) for Zn^{2+} at 412 nm ($\lambda_{ex} = 370$ nm).

crease is a relative indicator of binding strength. Figure 5, in this regard, shows the plot of fluorescence enhancement factor (Z) in the presence of the different cations. From the plot it is clearly understood that the response of the simple sensor **1** toward Zn^{2+} is significant and also selective over Cd^{2+} and Mg^{2+}. Such selectivity in the binding process is attributed to the coordination behavior of the alcoholic and amide functional groups along with the trivalent amine nitrogen in **1**. To substantiate this, we studied the emission change of model compound **2** in the presence of the same metal ions under similar experimental conditions. Figure 6, in this regard, displays the fluorescence enhancement factor after the addition of 3 equiv amounts of each metal ion. Here also the increase in emission is due to the complexation-induced inhibition of PET process occurring in between the aliphatic nitrogen center and the excited state of anthracene. But it is evident from Figure 6 that compound **2** is incompetent in reporting the selectivity in the binding process. This experimental result underlines the fact that the metal coordinating suitable functional groups are necessary around the trivalent nitrogen center in **2** for accommodating metal ions with different affinities. Thus, the dimension of the open cavity as well as the different coordination abilities of the anchoring groups introduces **1** as a good host for Zn^{2+} and as a moderate one for Cd^{2+}.

To understand the selective sensing of Zn^{2+} by **1**, we recorded the emission spectra of the receptor upon adding 10 equiv amounts of Zn^{2+} in the presence of 5 equiv amounts of other metal ions examined in the present study. Figure 7 displays the comparative view on the change in emission of **1** in the presence of Zn^{2+} when the other metal ions (excluding Cu^{2+}) are absent and present in the receptor solution. The greater increase in emission upon addition of Zn^{2+} to the solution of **1** containing other metal ions (Fig. 7) corroborates the selectivity in the binding process. The paramagnetic effect of Cu^{2+} ion[8] and its closeness in size with Zn^{2+} presumably interfere in the binding strongly so that Zn^{2+}-induced change in emission was found to be almost nil (Supplementary data). In addition, we also investigated the interaction of **1** with the metal ions in aqueous CH_3CN (CH_3CN/H_2O = 3:1 v/v) and no characteristic change in emission was observed.

The UV–vis study of **1** in the presence of the same metal ions under similar conditions showed minor change in absorbance (Supplementary data), which indicated that the chemosensor **1** behaves as an ideal PET system as interpreted by de Silva et al.[1b] For example, Figure 8 shows the change in absorbance upon the gradual addition of Zn^{2+}. During interaction a small red shift of the absorption peak for anthracene occurred. This was true for Ni^{2+}, Pb^{2+}, Co^{2+} ions also (Supplementary data). Decrease in absorption for anthracene (centered at 365 nm) with a significant red shift was noticed during the titration of **1** with Cu^{2+}. This is presumably due to cation–π interaction that possibly interplays when the metal ion resides in the tripodal cavity of **1** under the guidance of alcohol and amide functional groups. In the ground state interaction, the stoichiometry of the Zn-complex was found to be 1:1 as determined by UV Job plot[6] (Supplementary data). Similar composition (host/guest = 1:1) of the complexes of **1** with Cd^{2+}, Cu^{2+}, Mg^{2+}, and Hg^{2+} was observed in the ground state and thus a binding mode in Figure 9 can be assumed. To establish the binding mode we recorded the ^{1}H NMR of **1** in the absence and presence of Zn^{2+} in $CDCl_3$. During interaction the signals for amide ($\Delta\delta = 0.1$ ppm) and other protons of type a, b, c, and, d became broad and underwent downfield shifts ($\Delta\delta$ for a, b, c, and, d are 0.05, 0.03, 0.01, and, 0.08 ppm, respectively; see Fig. 9 for labeling of the proton types). The signal for –OH was difficult to detect due to broadening. The anthracyl protons (type e and f) close to the metal coordination center suffered a little downfield chemical shift ($\Delta\delta$ for e and f are 0.02 and 0.04 ppm, respectively). This is possible only when the indicated interactions in Figure 9 exist. The relevance of the proposed mode was further substantiated by optimization of the complex using DFT theory where Zn^{2+} is held comfortably in the cavity involving the possible interactions of amide, alcohol, and, aliphatic tertiary amine nitrogen (Fig. 10). For DFT calculation we used 6-31G* basis set and the popular b3LYP functional.[9]

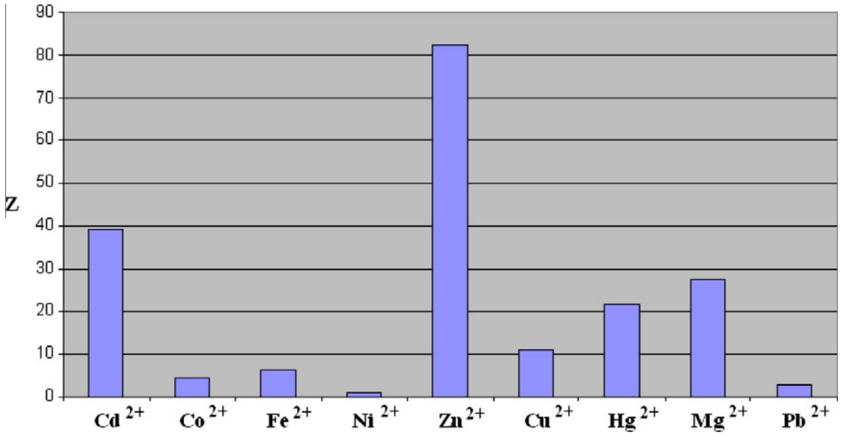

Figure 5. Fluorescence enhancement factor of receptor **1** ($c = 3.95 \times 10^{-5}$ M) upon addition of 4 equiv various metal ions ($c = 1.50 \times 10^{-3}$ M) as their perchlorate salts ($\lambda_{ex} = 370$ nm).

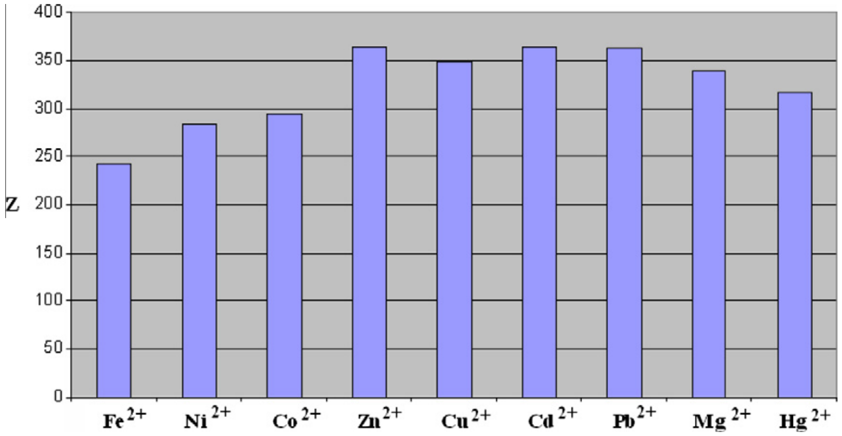

Figure 6. Fluorescence enhancement factor of receptor **2** ($c = 3.16 \times 10^{-5}$ M) upon addition of 3 equiv various metal ions ($c = 1.50 \times 10^{-3}$ M) as their perchlorate salts ($\lambda_{ex} = 370$ nm).

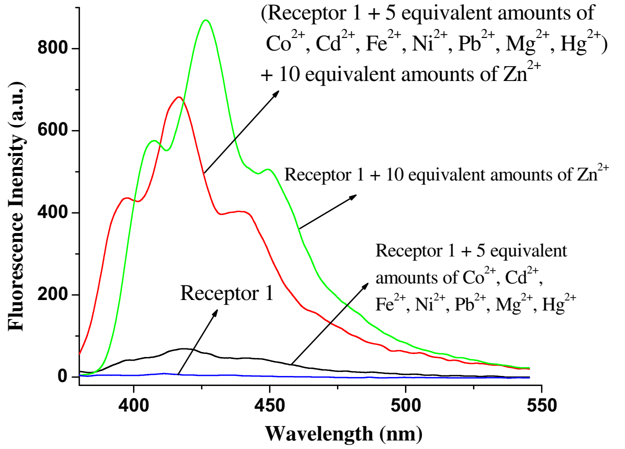

Figure 7. Change in emission of receptor **1** ($c = 4.38 \times 10^{-5}$ M) upon addition of Zn^{2+} ($c = 1.50 \times 10^{-3}$ M, as perchlorate salt) in the presence and absence of other metal ions (excluding Cu^{2+}).

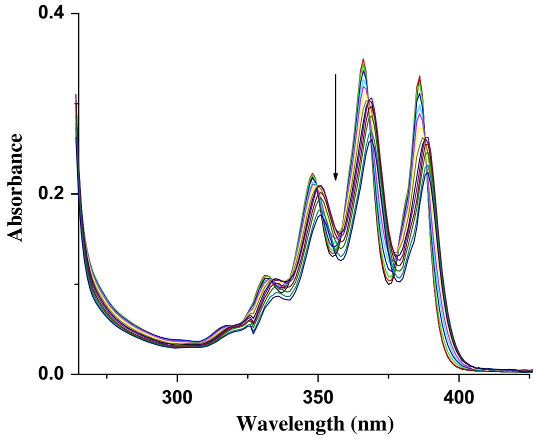

Figure 8. Change in absorbance spectra of **1** ($c = 3.95 \times 10^{-5}$ M) upon addition of Zn^{2+} ($c = 1.50 \times 10^{-3}$ M, as perchlorate salt) in CH_3CN containing 0.1% DMSO.

The relative change in emission intensity of **1** at 412 nm was considered for determining the binding constant values.[10] Due to complex stoichiometry of the Zn-complex in the excited state we considered the emission data up to the addition of 1 equiv amount of Zn^{2+} ion for determining the binding constant value and it was found to be ($\log K = 13.94$) higher than the values determined for Cd^{2+} ($\log K = 7.99$), Mg^{2+} ($\log K = 5.73$) and, Hg^{2+} ($\log K = 6.38$). We did not evaluate the binding constant values for other metal ions due to a minor change in emission.

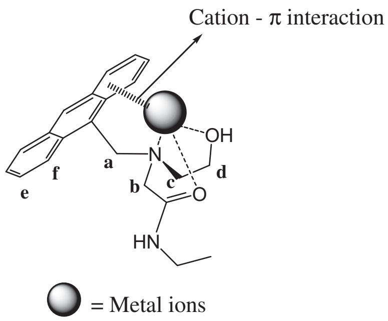

Figure 9. Proposed binding mode of **1** for the metal ions.

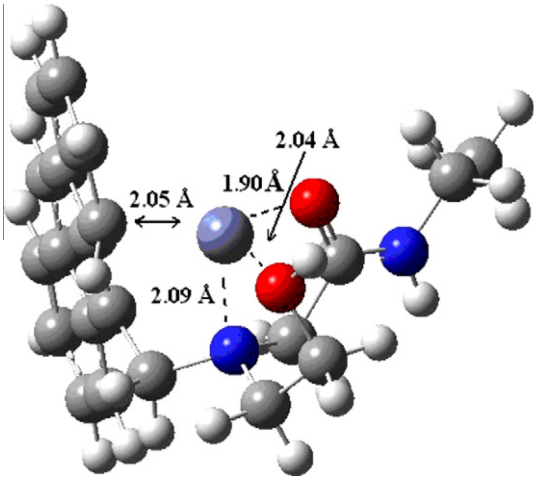

Figure 10. DFT optimized structure of Zn-complex.

In conclusion, we have thus described an easy-to-make simple fluorescent chemosensor **1**, which selectively recognizes Zn^{2+} in CH_3CN containing 0.1% DMSO. The chemosensor **1** also shows a measurable sensitivity toward Cd^{2+}. Selectivity is attained due to the participation of tertiary amine, amide, and alcoholic functional groups in the binding process. Although the chemosensor **1** is nonfunctional in aqueous CH_3CN, it undoubtedly holds good for effective sensing of Zn^{2+} and moderate for Cd^{2+} in organic solvent. This simple architecture can be considered as an alternative of di-2-picolylamine (DPA) for Zn^{2+} ion and can beneficially be attached to any support in the form of amide using anthracene-labeled morpholin-2-one **7**. Further exploration along this direction is in progress in our laboratory.

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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.2010.07.070.

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