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A new metallo-supramolecular sensor for recognition of sulfide ions

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ABSTRACT

Article history: Received 18 October 2014 Revised 9 December 2014 Accepted 10 December 2014 Available online 16 December 2014 A hydroxynaphthyl hydrazine linked calix[4]arene derivative (**4**) has been designed, synthesized and evaluated for multi ion recognition. **4** not only recognizes copper ions selectively through a change in color, UV–Vis and fluorescence spectrum but the resultant metallo-supramolecular complex (**4**·Cu²⁺) emulates specific recognition of S²⁻ ions as well. © 2014 Elsevier Ltd. All rights reserved.

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During recent years, there has been an upsurge in research activity in the design, synthesis and evaluation of molecular receptors for anions.¹ This is partly due to the academic challenges involved and the utility of anion recognition in numerous biological, chemical and environmental processes.² Simple anions like fluoride, cyanide, sulfide, arsenate, phosphate, nitrate, chloride, sulfate, chlorate, and chromate are often considered as critical anions due to their importance in drinking water and consequent onset of diseases when they are present in higher concentrations.³ The studies are also very useful for effluent treatments and in ensuring a green environment. Besides mentioned inorganic anions, molecular receptors are also being investigated for the recognition of organic anions like citrate, tartrate and aliphatic and aromatic carboxylates.⁴

Major difficulties encountered in the design of molecular receptors for anions⁵ are due to their larger size and charge spread in comparison to those in cations. Their shape (which may vary from linear to octahedral), smaller window for manipulation of pH of the medium as well as stiff competition from electron donor solvents further complicate investigations on receptors for anions. The approaches used for the design of target molecular receptors have been based upon complementarity of charge, shape, size or through the electron deficient nature of the functional group appendages. In this connection, the use of metal ions with expandable valence shells (e.g., use of ferrocene, boron trifluoride residues attached to the organic molecular scaffolds)⁶ have proven useful for recognition of anions. Recently secondary supramolecular forces have been deployed for anion recognition.^{7,8,19}

Molecular scaffolds generally employed for the target purpose are hydrophobic cavity containing organic macrocycles or pseudo molecular macrocycles such as calixarenes,¹⁰ resorcinarenes,¹¹ cyclodextrins,¹² steroids,¹³ molecular tweezers,¹⁴ and clefts¹⁵ which provide templates for assembling efficient platforms for anion recognition.

In the family of active anions, sulfide is known to strongly interfere in numerous biological processes. Continuous exposure to sulfide can cause gradual and cumulative damage that include loss of consciousness, irritation of mucous membranes, and suffocation.^{16,17} Once protonated, sulfide ions become more toxic and caustic. Some of the strategies evolved for recognition of S^{2–} at low concentrations include spectroscopic and electrochemical titrations,¹⁸ metal anion affinity,^{7–9,19} ion chromatography,²⁰ and chemo luminescence measurements.²¹ In this Letter we have focused our attention to the design of reversible sensors for sulfide ions by using its known affinity for copper ions to make a stable copper sulfide complex.

The synthesis and evaluation of a molecular Schiff base molecular probe **4** reveals that it is not only capable of detecting copper ion but the formed supramolecular metalloreceptor **4**·**Cu**²⁺ could be further used for selective and specific detection of sulfide ions from among various related anions via colorimetric and fluorescence protocols.

Calix[4]arene with a naphthalene moiety attached at the lower rim was synthesized by adopting a reaction sequence given in Scheme 1.^{22,23} Bis(4-formylphenylpropyloxy)-*p*-tert-butylcalix[4] arene (**3**) was prepared by the method reported earlier.²⁴ It was





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Scheme 1. Synthesis of molecular receptor 4.

refluxed with 2-hydroxy-1-naphthaldehyde hydrazone in the presence of glacial acetic acid in ethanol to yield a product which when washed with methanol gave a novel calixarene derivative **4** in good yield (83%). The identity of all the intermediates and the target molecular receptor **4** was established by IR, ¹H and ¹³C NMR as well as by ESI-MS analysis (ESI, Fig. S1). The synthesized molecular receptor **4** showed a \geq C=N- signal at 1603 cm⁻¹ and a sharp pair of doublets at a δ 3.36 and δ 4.29 for axial and equatorial protons, respectively, in the ¹H NMR spectrum. A distinct signal at δ 31.02 for the methylene carbons in its ¹³C NMR spectrum revealed its symmetric cone conformation for the calix[4]arene scaffold. It was further confirmed by observing D₂O exchangeable singlets at δ 13.03 which could be assigned to the –OH protons. Non deuterable singlets at δ 9.69 and 8.29 for the azo-methine proton (-N=CH) confirmed the depicted structure for **4** (Scheme 1).

The sensing ability of naphthalene based molecular receptor $\mathbf{4}$ for cations was examined in CH₃CN by naked eye color change, UV–Vis absorption and fluorescence spectroscopy.

On gradual addition of metal cations such as Li⁺, Na⁺, K⁺, Cs⁺, Ag⁺, Ca²⁺, Mn²⁺, Co²⁺, Cd²⁺, Pb²⁺, Fe²⁺, Ni²⁺, Zn²⁺, and Cu²⁺ as their perchlorate salts in CH₃CN, a color change from light yellow to dark yellow was observed only in the presence of copper ions. ESI-MS of the **4** showed a molecular–ion peak [M+Na]⁺ at m/z 1331.5334 and at m/z 1371.7741 (ESI, Fig. S5) due to the presence of [**4**+Cu²⁺]. Other metal ions did not produce any noticeable change in color even on adding higher concentrations.

Following our observations based on color change, cation sensing ability of receptor **4** in CH₃CN was further monitored by UV–Vis absorption spectroscopy. UV–Vis spectra of **4** was characterized by two peaks (337 nm and 405 nm) with $\varepsilon = 6.4 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$. Addition of different cations as perchlorates, led to no change in the absorption spectra of **4** except copper perchlorate.

On addition of Cu²⁺ ions, there was considerable change in the absorption spectra of synthesized calixarene derivative. To further

comprehend the Cu²⁺ binding nature of **4**, quantitative UV–Vis titration of **4** (20 μ M) was carried out with increasing equivalents of Cu²⁺ ions (0–1.45 equiv). It was determined that gradual addition of Cu²⁺ ions to the receptor **4** led to a decrease and a shift in absorbance at 405 nm to 430 nm (Fig. 1) accompanied by a color change of the solution of receptor.

Fluorescence emission spectra of 4 (20 µm) in CH₃CN was recorded after excitation at 337 nm. It was determined that on addition of Cu²⁺ ions a prompt change in the intensity of fluorescence emission of **4** was observed to yield more than 90% guenching of the emission maxima at 505 nm. To learn more about the properties of **4**–Cu²⁺ complex formation, a titration of the receptor was performed with increasing concentration of Cu²⁺ ions. The fluorescence intensity of a 20 μ M solution of **4** decreased with an increase in the concentration of copper perchlorate to reach saturation levels after addition of 1.5 equiv of Cu²⁺ ions (Fig. 2). Though analysis of the vibronic spectrum is outside the scope of this study. it appears that the fluorophore gets excited to its S₁ state in the absence of metal ions to result in higher intensity emission band due to $S_1 \rightarrow S_0$ state. However in the presence of copper ions, specific complexation leads to intersystem cross over from S₁ to T₁ state to usher a much decreased intensity of fluorescence and deactivation by bimolecular non radiative processes. Analysis of the infrared spectrum of the compound and its complex with Cu^{2+} reveals that a significant shift (26 cm⁻¹) in v(OH) of the



Figure 1. Change in the UV–Vis spectra of **4** (20 μ M) upon addition of Cu²⁺ (0–28 μ M) in CH₃CN; inset: color change upon addition of Cu²⁺ to the solution of molecular receptor **4**.



Figure 2. Quenching in the fluorescence intensity of $4~(20~\mu M)$ in CH_3CN in the presence of Cu^{2+} (0–29 $\mu M).$

naphthalene moiety (3436–3410 cm⁻¹), may be due to its interaction with copper ions which weakens the OH bonds. These conclusions are in consonance with literature precedents.

The influence of other metal ions on the fluorescence signal of the molecular probe was evaluated. It was observed that the addition of other metal ions did not elicit any change in the fluorescence intensity of the molecular receptor, thereby revealing its high selectivity for Cu^{2+} ion (ESI, Fig. S2). In addition, presence of various competing metal ions hardly had any effect in the detection of copper ions (Fig. 3). All these observations suggest that it is a useful probe for recognition of Cu^{2+} ions with high selectivity.

Job's plot revealed the stoichiometry between **4** and Cu²⁺ ions as 1:1 (ESI, Fig. S3). Based on 1:1 binding mode, the binding constant²⁵ was calculated to be $5 \times 10^5 \text{ M}^{-1}$ from the UV–Vis titration data.

The optical properties of the supramolecular complex, $4-Cu^{2+}$ were further explored to determine possible selective detection of anions. It was observed that from among different anions such as F⁻, Cl⁻, Br⁻, I⁻, S²⁻, H₂PO₄⁻, HSO₄⁻ and AcO⁻ (added as their tetrabutylammonium salts) only addition of S²⁻ to the solution containing $4-Cu^{2+}$ complex gave a discernible spectral change (Fig. 4). Moreover, the original color of **4** was also restored only on addition of S²⁻.

Fluorescence titration experiments on $4-Cu^{2+}$ complex with different amounts of S^{2-} was performed (Fig. 5) to reveal that the $4-Cu^{2+}$ displayed a stepwise fluorescence enhancement on



Figure 3. Comparative study of molecular receptor 4 in CH_3CN in presence of 3.5 equiv of various metal ions.



Figure 4. Relative change in the fluorescence intensity upon addition of various anions to the solution of $4-Cu^{2+}$ (48 μ M) in CH₃CN.



Figure 5. Changes in fluorescence spectrum of $4\text{-}Cu^{2*}$ solution (48 $\mu M)$ upon addition of S^{2-} (0–145 $\mu M).$

addition of 145 μ M of sulfide ions. Both intensity and shape of the initial emission spectrum of compound **4** could be restored probably due to S²⁻ induced Cu²⁺ sequestering. These results showed that **4**-Cu²⁺ has a good sensing property for S²⁻. No difference in the fluorescence intensity was observed in our experiments when other anions were added.

The competitive experiments were performed by adding sulfide and equimolar concentrations of other anions (F⁻, Cl⁻, Br⁻, I⁻, AcO⁻, HSO₄⁻ and H₂PO₄⁻) to **4**·Cu²⁺. It was observed that different coexisting anions have almost no influence on the fluorescence intensity and detection of S²⁻ was very specific (Fig. 6).

The mass spectrum of the $4-Cu^{2+}$ system was studied in the presence of S^{2–}gave a peak at m/z 1347.8261. This could be attributed to free $4 [M+K]^+$ thereby establishing that sulfide anion is sensed through copper extraction from the $4 \cdot Cu^{2+}$ complex.

It was also observed that the fluorescence intensity at 505 nm has an excellent linear relationship with the concentration of S^{2–} ion up to 67 μ M. The LOD for sulfide ions could be calculated as 1.58 μ M (ESI, Fig. S4) by using LOD_[S^{2–}] = 3 × s_o/m where s_o represents the standard deviation and *m* represents the slope of relative fluorescence intensity versus [S^{2–}] in the aforementioned range.²⁶

These results reveal that $4-Cu^{2+}$ complex may be used as the platform for selective sensing of S²⁻. It appears that stability of Cu²⁺ ion inside the $4-Cu^{2+}$ complex can in principle be maintained in such a way that the disruption of the supramolecular complex



Figure 6. Selectivity of 4-Cu²⁺ for S²⁻ over other anions.

takes place selectively and exclusively in the presence of sulfide ions.

In summary we have achieved a copper ion responsive molecular probe that can be deployed for sensitive and selective recognition of sulfide ions through absorption spectral and fluorescence measurements.

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Supplementary data

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- 22. Procedure for the synthesis of 4: To a solution of calix[4]arene derivative (3) in ethanol was added 2-hydroxy napthaldehyde hydrazone and a catalytic amount of acetic acid. The reaction mixture was refluxed for 24 h. After completion of the reaction (TLC), the precipitate was filtered and washed with water. The structure of 4 was confirmed by ¹H NMR and ¹³C NMR spectra as well as ESI-MS analysis.
- 23. Analytical data for **4**: Light yellow solid; Melting point: 324 °C (decomposed); UV (λ_{max} , ACN): 337 nm. IR (KBr pellet, cm⁻¹): 3436, 1678, 1603, 752; ¹H NMR (300 MHz, CDCl₃ δ in ppm): 13.03 (s, 2H, D₂O exchangeable, OH),9.69 (s, 2H, C<u>H</u>=N), 8.29 (s, 2H, N = CH), 8.20 (d, 2H, ArH_{nap}), 7.91 (d, 2H, ArH_{nap}), 7.82 (d, 2H, ArH_{nap}), 7.73 (t, 2H, ArH_{nap}), 7.42 (t, 2H, ArH_{nap}), 7.62 (d, 4H, ArH), 6.87 (d, 4H, ArH), 7.08 (s, 2H, ArH), 6.91 (d+s, 6H, ArH), 4.31 (t, 4H, $-OCH_2-CH_2-CH_2$), 4.24 (d, 4H, ArCH₂Ar), 4.13 (t, 4H, $-OCH_2-CH_2-CH_2-CH_2$), 2.36 (qu, 4H, $-OCH_2-CH_2-CH_2$), 1.27 (s, 18H, $-C(CH_3)_3$), 1.04 (s, 18H, $-C(CH_3)_3$); ¹³C NMR (75 MHz, DMSO- d_6 , δ in ppm): 161.06, 160.80, 150.69, 149.42, 147.18, 141.67, 137.86, 135.07, 132.80, 130.43, 128.25, 127.71, 125.68, 12.88, 120.03, 119.16, 72.92, 64.86, 34.02, 33.83, 31.05; HRMS (ESI-MS) *m/z*: calcd 1331.5384, found 1331.5334 (M+Na⁺).
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