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A sensitive recognition of cyanide through supramolecularly complexed new calix[4]arenes

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Two new calix[4]arene based fluorescence sensors (**L1** and **L2**) have been synthesized and characterized. **L1** was found to selectively quench fluorescence intensity on addition of Cu^{2+} ions through host guest complexation and display “off-off” behavior while **L2** was not that efficient. The in-situ generated **L1**. Cu^{2+} complex could further recognize CN^- from the anionic broth with a distinct “off-on” behavior in the fluorescence titrations.

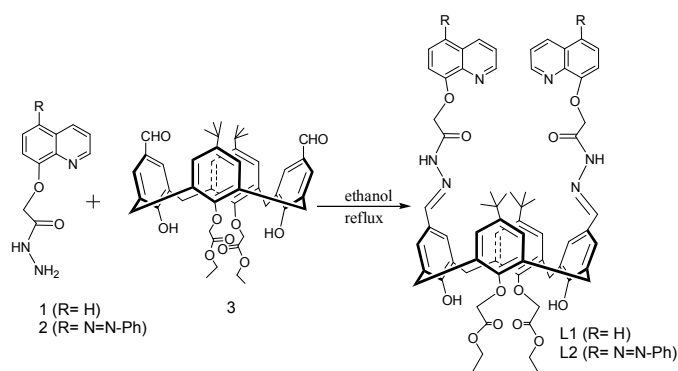
A strategy that involves the formation of a host guest type complex with a specific metal ion and its utilization for selective interaction with a target anion is highly desirable for potential application in multi ion detection systems.^{1,2,3} The positive charge on designed metallo-supramolecular complex is usually balanced by large counter ions like perchlorate and picrate. The quenched metallo-supramolecular entity in situ can in principle be further used for anionic recognition through anion displacement.^{4,5} The latter studies would require more nucleophilic anionic species than often encountered counter ions.⁶ Since the counter ions usually deployed in ionic recognition are not found in real systems, evaluation of such strategies would entail further research in the area.

Considerable efforts have been expended to design sensor molecules for both copper and cyanide ions due to their widespread use in chemical, manufacturing and biological processes despite their toxicity.^{7,8} Since cyanide is a very good nucleophile and can form strong back- π bonding with Cu^{2+} , we have attempted to test the hypothesis for copper and cyanide ion recognition. To achieve this, we first designed and synthesized calixarene based receptors **L1** and **L2** for copper ions through the hybrid structure of quinoline and calix[4]arene and then examined the complex entity formed for detection of CN^- in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ (7:3, v/v). The choice of calixarene skeleton was based upon our previous work on such systems and the efficacy of calixarene cavity for recognition of copper ions through fluorescence spectroscopy.

Accordingly, the ion binding properties of **L1** and **L2** have been examined by fluorescence spectroscopy. It was determined that **L1** showed a significant change in its fluorescence spectrum while changes induced by **L2** were only

marginal. Repeat evaluations established that all fragments present in the designed receptors are important for fluorescence changes upon interaction with **L1** to encourage detailed studies on its utility.

The required starting materials 2-(quinolin-8-yloxy) acetoacetylhydrazide (**1**)⁹, 5-substituted azo derivative (**2**)¹⁰ and formyl derivative of calix[4]arene (**3**)¹¹ were synthesized by using methods available in the literature. **L1** and **L2** were synthesized in moderate yields by separately reacting **1** and **2** with bisformylcalix[4]arene derivative in ethanol as shown in scheme 1.



Scheme 1. Synthesis of receptors **L1** and **L2**

The structure of **L1** and **L2** was confirmed by ^1H and ^{13}C NMR as well as IR spectroscopy and mass spectrometric analysis.

L1 exhibited an absorption maximum at 315 nm with strong emission at 405 nm in the fluorescence spectrum. No change was noticed when different cations (Zn^{2+} , Pb^{2+} , Co^{2+} , Ni^{2+} , Na^+ , Li^+ , Fe^{2+} , Hg^{2+} , Cd^{2+} , K^+ , Mn^{2+} and Ag^+ perchlorate salts) were added to the solution of **L1** (20 μM , in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$; 7:3, v/v). It was only on addition of varying concentration of Cu^{2+} ion to the solution of **L1**, that the intensity of the emission band at 405 nm gradually decreased. Addition of 2 equiv. of Cu^{2+} to the solution of **L1** afforded 90% quenching of fluorescence

intensity (Figure 1). Receptor **L2** absorbed at 370 nm with an emission maximum at 480 nm. In contrast to **L1**, receptor **L2** showed only 8% quenching upon addition of the same concentration of Cu^{2+} ions as added for **L1**, possibly due to the presence of an electron withdrawing azo group (SI, Figure S6) present in **L2**.

Under identical conditions, addition of the same concentration of other metal perchlorates produced a marginal change in the fluorescence spectra of **L1** (SI, Figure S7). A comparative study on the selectivity profile of **L1** in metal/ Cu^{2+} coexisting systems indicated that the other metal ions pose little impact on the fluorescence intensity of Cu^{2+} .**L1** complex (SI, Figure S8). These results clearly indicate that **L1** bears a high sensitivity for Cu^{2+} in the presence of other competitive ions.

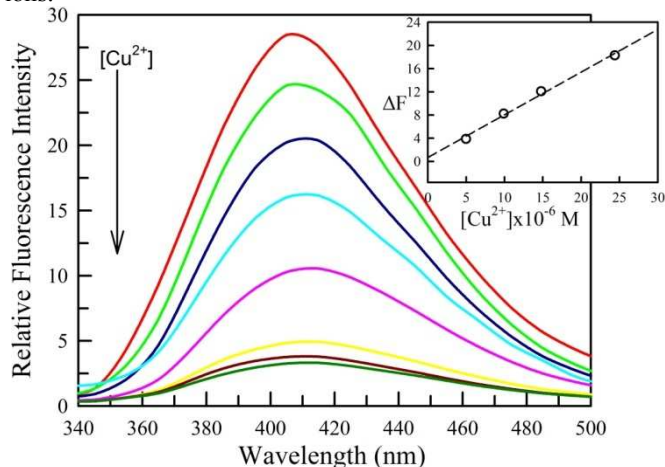


Fig. 1 Quenching of fluorescence intensity of **L1** in presence of Cu^{2+} (2 equiv.) in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (7:3, v/v) [**L1** = 20 μM , $\lambda_{\text{excitation}} = 315$ nm]. Inset shows change in the fluorescence intensity of **L1** with varying concentration of Cu^{2+}

High resolution mass spectrum of **L1**. Cu^{2+} complex revealed a molecular ion peak at m/z 1225.4413 indicating it to be in a 1:1 stoichiometry (SI, Figure S9). It is known that Stern-Volmer quenching constant for 1:1 stoichiometry represents the efficiency of the fluorescence quenching and the higher the K_{sv} value, the less is the quencher needed to quench the fluorescence. In the present case the value of Stern-Volmer constant was obtained by using the values of slope and the y -intercept in the F_0/F vs. $[\text{Cu}^{2+}]$ plot as $1.472 \times 10^5 \text{ M}^{-1}$.

The detection limit of **L1** for the determination of Cu^{2+} was estimated to be 0.4 μM . Complete quenching of fluorescence intensity revealed that **L1** could serve as a fluorescence “ON-OFF” (quenching of fluorescence) sensor for copper ions with a high sensitivity and selectivity.

The quenched **L1**. Cu^{2+} complex was further examined for its interaction with simple anions. It was determined that addition of several anions (F^- , Cl^- , Br^- , I^- , S^{2-} , OAc^- , CO_3^{2-} , HSO_4^- , H_2PO_4^-) to the **L1**. Cu^{2+} complex gave a very little or poor response (Figure 3) except when cyanide ion was added.

The fluorescence titration of **L1**. Cu^{2+} with CN^- revealed that (Figure 2) incremental addition of CN^- led to gradual increase in fluorescence intensity till it got restored. It was found that addition of 10 equiv. of CN^- ions to the solution of **L1**. Cu^{2+} complex led to slight broadening of spectrum with the appearance of a shoulder at ca. 450 nm. This could be ascribed to the formation of an adduct between **L1**. Cu^{2+} and CN^- . This inference was confirmed by analyzing the spectra at full width at half height. The two curves of **L1** and **L1**. Cu^{2+} + CN^- were

plotted on the same graph and same axis and scale by normalizing their fluorescence intensities (ESI, Figure S10). It was observed that Fwhm is 78 nm and 82 nm respectively for **L1** (Figure 1) and **L1**. Cu^{2+} + CN^- (Figure 2) at λ_{max} .

These results clearly indicated that the **L1**. Cu^{2+} has an excellent selectivity for CN^- over other competing anions. It was significant to note that addition of CN^- to a solution of **L1** alone did not give any enhancement of fluorescence intensity. The complexation of CN^- with receptor **L1** could proceed only when a Cu^{2+} ion is present in the calixarene scaffold.

The competitive experiments were performed by adding cyanide and other anions (F^- , Cl^- , Br^- , I^- , S^{2-} , OAc^- , HSO_4^- and H_2PO_4^-) to **L1**. Cu^{2+} in equimolar concentrations. It was observed that different coexisting anions have almost no influence on the fluorescence intensity and detection of CN^- was very specific (SI, Figure S11).

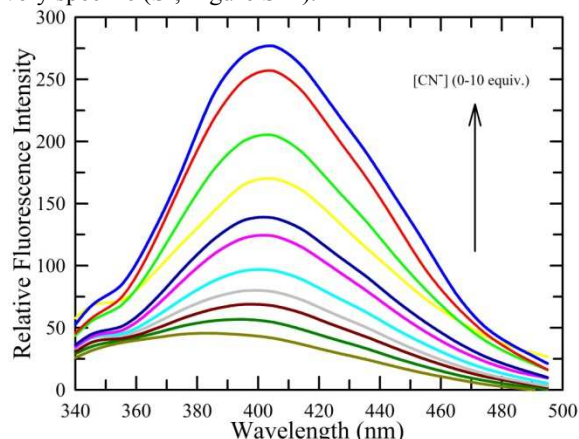


Fig. 2 Enhancement of fluorescence intensity of **L1**. Cu^{2+} (10 μM) in the presence of CN^- in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (7:3, v/v) [**L1**. Cu^{2+}] = 10 μM , $\lambda_{\text{excitation}} = 315$ nm]

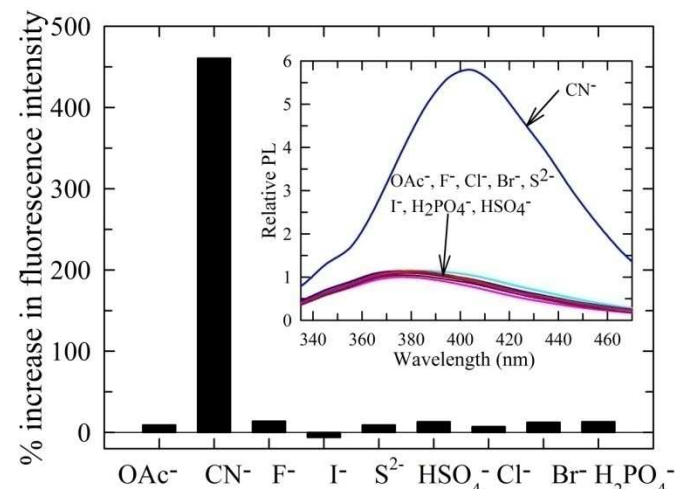


Fig. 3 Relative change in the fluorescence intensity of **L1**. Cu^{2+} complex in the presence of various anions (8 equiv.). Inset shows change in the fluorescence intensity of **L1**. Cu^{2+} complex in the presence of cyanide anion (10 equiv.).

The limit of detection of CN^- by **L1**. Cu^{2+} was calculated to be 1.26 μM by using the literature method.¹² This value is found to be lower than the limit set by US EPA for detection of CN^- in water (1.9 μM)¹³.

The effect of pH on the fluorescence spectrum of **L1**. Cu^{2+} in the presence and absence of CN^- was studied by measuring the

fluorescence intensity at different pH values (SI, Figure S12). It was observed that the interaction of **L1** with copper was most effective between pH 6-8. Consequently interaction of the metallo-supramolecular complex with cyanide was examined in this pH range. Lesser reactivity of the **L1** at lower pH could be attributed to protonation of the quinoline nitrogen while higher pHs may entail lesser availability of copper ions for interaction with **L1** respectively.

ESI-MS spectrum of **L1**.Cu²⁺ complex in the presence of CN⁻ was recorded which revealed a peak at *m/z* 1185 corresponding to (**L1**+Na)⁺. These observations indicate that the cyanide interaction with the Cu.**L1** complex eventually leads to the formation of **L1**. Since copper and cyanide have strong affinity, the observations can be explained by assuming efficient and selective decomplexation of the Cu.**L1** complex by cyanide ion. That this explanation is too simplistic was proved by the fact that **L1** forms a host guest type of complex involving weak interaction and also because the concentrations used for cyanide interaction in the present experiments were too small. The commonly deployed concentrations for decomplexation processes by CN⁻, are often more than 2-3 times the concentration used in the present case.

Though further studies are in progress, we believe the operative mechanism involves gradual disruption of weak binding forces between **L1** and Cu²⁺ leading to eventual decomplexation of copper from **L1**.

In summary, we submit that the synthesized molecular receptor, **L1** can be used for selective recognition of both Cu²⁺ and CN⁻ ions through "on-off-on" fluorescence response.

Experimental

Synthesis of compound L1

To a solution of bis(formyl) calixarene **3**¹¹ (100 mg, 0.13 mmol) in EtOH, **1** (56 mg, 2 mmol) and few drops of glacial acetic acid were added. The reaction mixture was heated to reflux for 24h. After completion of the reaction, solvent was evaporated to dryness under reduced pressure and product was filtered and recrystallized from CHCl₃/MeOH.

White solid. Yield: 56%, mp 205°C (decomposed). IR (KBr pellet, cm⁻¹): 3376, 1752, 1682, 1602, 1479. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 11.93 (s, 2H, NH, D₂O exchangeable), 8.85 (s, 2H), 8.39 (s, 2H, OH, D₂O exchangeable), 8.10 (m, 2H), 7.88 (dd, 2H), 7.52 (s, 4H), 7.43 (m, 8H), 6.84 (s, 4H), 4.96 (s, 4H), 4.72 (s, 4H), 4.47 (d, 4H), 4.37 (q, 4H), 3.47 (d, 4H), 1.37 (t, 6H), 0.90 (s, 18H). ¹³C NMR (75 MHz, CDCl₃, δ in ppm): 184.5, 161.2, 150.6, 141.7, 133.9, 128.3, 127.2, 114.9, 33.8, 31.2, 29.8. ESI-MS *m/z*: calcd. 1163.5124, found 1163.5152 [M+H]⁺.

Synthesis of compound L2

This compound was prepared from bis(formyl) calixarene **3** (100 mg, 0.13 mmol) and **2**¹⁰ (84 mg, 2 mmol) as an orange red solid by adopting the same reaction protocol as that described for **L1**.

Orange-red solid. Yield: 68%, mp 223°C (decomposed). IR (KBr pellet, cm⁻¹): 3408, 2957, 1742, 1686, 1504, 1479. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 11.60 (s, 2H, NH, D₂O exchangeable), 9.40 (d, 2H), 9.06 (s, 2H), 8.26 (s, 2H, OH, D₂O exchangeable), 8.02 (m, 8H), 7.67 (m, 10H), 7.36 (m, 4H), 6.82 (s, 4H), 5.03 (s, 4H), 4.68 (s, 4H), 4.42 (m, 8H), 3.46 (d, 4H), 1.33 (t, 6H), 0.95 (s, 18H). ¹³C NMR (75 MHz, DMSO-d₆,

δ in ppm): 168.4, 157.8, 151.2, 1315, 129.8, 127.8, 126.4, 123.4, 113.9, 109.7, 72.1, 61.3, 39.2, 34.4, 31.4. ESI-MS *m/z*: calcd. 1371.5873, found 1371.5866 [M+H]⁺.

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