A pyrene-armed hexahomotrioxacalix[3]arene as a multi-sensor through synergistic effect and demetallation

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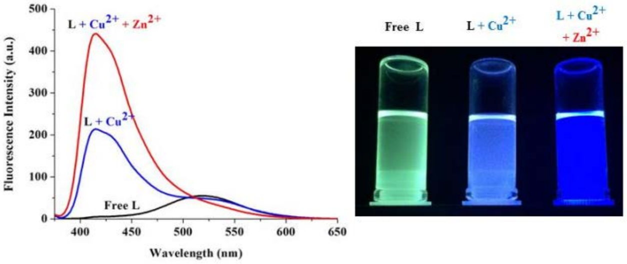
Supporting Information Placeholder

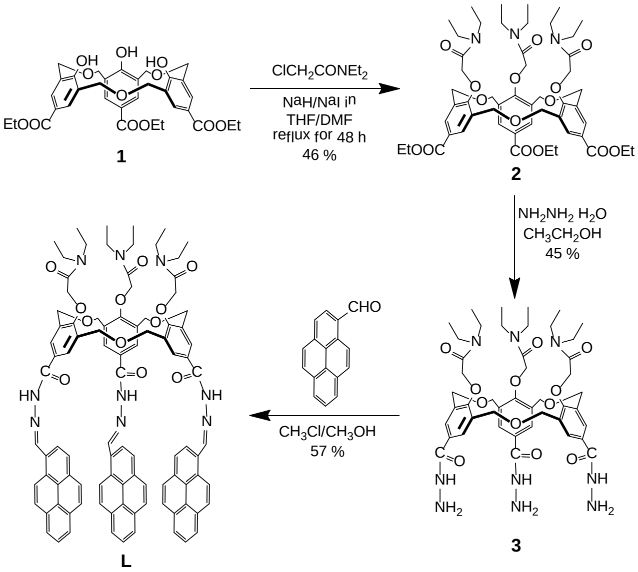


ABSTRACT: A new pyrene-armed hexahomotrioxacalix[3]arene **L** has been synthesized, which exhibits a pronounced fluorescence enhancement response toward Cu^{2+} ions via a Zn^{2+} or Cd^{2+} triggered synergistic effect. Additionally, the **L**•Cu^{2+} complex can subsequently serve as a sensor for F^- via anion-induced demetallation. The fluorescence responses by the input of Cu^{2+}, Zn^{2+}/Cd^{2+} and F^- can be constructed as combinational logic gate which mimics molecular trafic signals.

The development of fluorescent chemosensors for the sensing and recognition of environmentally and biologically important ionic species, is currently receiving considerable attention.[1] Calixarenes are well-known concave macrocyclic compounds that have been widely employed for the development of fluorescent chemosensors.[2] However, most of these fluorescence system have been reported utilizing the calix[4]arene scaffold,[3] whilst only a few papers have described the use of fluorescent homooxacalixarenes.[4] Indeed, homooxacalixarenes containing extra oxygen atoms in the macrocyclic ring, possess a flexible structure and exhibit characteristic affinities for metal cations,[5] ammonium cations,[6] and fullerene derivatives.[7] Therefore, the use of homooxacalixarenes as a platform has potential application in the development of novel fluorescence chemosensors.

As a part of our research into the construction of calixarene-derived chemosensors, we recently reported a ratiometric fluorescent sensor based on a triazole-modified homooxacalix[3]arene, which behaves as a potential molecular traffic signal with an R-S latch logic circuit upon chemical inputs via Zn^{2+} and $H_2PO_4^-$ ions.[8] Herein, we have synthesized a new sensor based on a pyrene-armed hexahomotrioxacalix[3]arene, which upon chemical inputs of Cu^{2+}, Zn^{2+}/Cd^{2+} and F^- in a sequential manner generates three kinds of outputs which mimics the function of molecular traffic signals. Such molecular traffic signals based on a hexahomotrioxacalix[3]arene are unprecedented.

The condensation of compound **3** with pyrene-1-carbaldehyde in chloroform-methanol furnished compound **L** in 57% yield (Scheme 1). The structure of compound **L** was confirmed by spectroscopic and analytical data. Conformation assignment for compound **L** is firmly established by the presence of AB quartets for the bridg



Scheme 1. Synthesis of the sensor **L**.

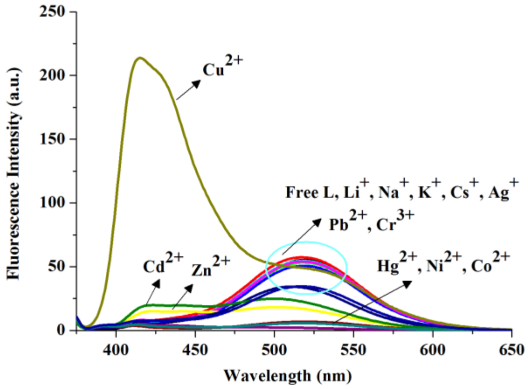


Figure 1. Fluorescence spectra of **L** (1.0 μM) upon addition of various metal cations (10 equiv.) in CH_3CN/CH_2Cl_2 (1000:1, v/v), λ_{ex} = 367 nm.

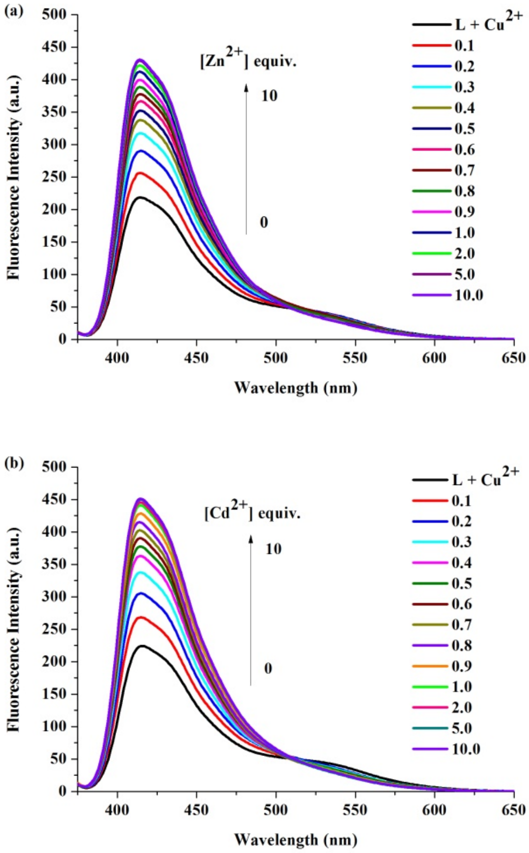
ing methylene protons with a $\Delta\delta$ separation between H_{ax} and H_{eq} of 0.42 ppm in the ^1H NMR spectrum. For calix[4]arenes, the $\Delta\delta_H$ values of the ArCH_2Ar protons have been correlated with the orientation of adjacent aromatic rings.[9] The same findings were observed for homotrioxacalix[3]arenes,[10] thus compound **L** has a flattened-cone conformation.

The chemosensor behavior of **L** with metal cations was investigated by fluorescence measurements in CH_3CN/CH_2Cl_2 (1000:1, v/v). As shown in Figure 1, the fluorescence spectra of **L** shows a comparatively strong excimer emission at 518 nm and a weak monomer emission at 415 nm, with an intensity ratio of monomer to excimer emission ($I_M/I_{Ex} \approx I_{415}/I_{518}$) = 0.09. The formation of an excimer band at 518 nm indicates strong face-to-face π–π stacking between the pyrene units. Upon the addition of Cu^{2+} ions to a solution of **L** leads to a significant increase in the monomer emission and a comparative decrease in the excimer emission to reveal a ratiometric change from 0.09 to 4.36, *ie* a 50-fold increase. By contrast, no significant spectral changes were observed upon the addition of the other metal cations employed herein, except for Zn^{2+} and Cd^{2+}, with an intensity ratio of monomer to excimer emission (I_M/I_{Ex}) = 0.79 and 0.80, respectively. Both monomer and excimer emission were strongly quenched by Hg^{2+}, Ni^{2+} and Co^{2+} due to the heavy metal ion effect.[11]

The fluorescence responses of **L** in the presence of an increasing concentration of Cu^{2+} ions are depicted in Figures S1–S3. The excimer emission of sensor **L** substantially decreased as the concentration of Cu^{2+} increased from 0 to 0.75 equiv. (Figure S1); the heavy metal effect of Cu^{2+} exists in this procedure, and generally quenches the emission of pyrene. Interestingly, the fluorescence intensity of both monomer and excimer emission gradually increased as the concentration of Cu^{2+} increased from 0.75 to 2.25 equiv. (Figure S2), and it is proposed that the coordination of Cu^{2+} with the Schiff base sites inhibits the PET effect. Moreover, the fluorescence intensity of the excimer emission of sensor **L** gradually decreased and was accompanied by an enhancement of the monomer emission as the concentration of Cu^{2+} increased from 2.25 to 7.0 equiv. (Figure S3). These spectral changes can be attributed to the cooperating effect of the geometrical structural changes and the reduced PET effect of sensor **L** on further binding of Cu^{2+} ions. Additionally, in supramolecular chemistry, isothermal titration calorimetry (ITC) is a useful method for monitoring the host–guest interactions. As shown in Figure S4, a representative titration curve can be obtained from an ITC experiment which reveals an abrupt transition point when the molar ratio of Cu^{2+} and **L** reaches 0.896, indicating the formation of a 1:1 complex of Cu^{2+} ions with receptor **L**. The binding constant was calculated to be (3.57 ± 0.1) × 10^5 M^{-1}.

To utilize **L** as an ion-selective fluorescent sensor for Cu^{2+}, competition experiments were carried out in the presence of Cu^{2+} (10 μM) mixed with 10 μM of other metal cations (Figure S5). No significant interference in the detection of Cu^{2+} was observed in the presence of many of the competitive metal ions, except for the cases involving the addition of Zn^{2+} or Cd^{2+} ions, which increased the monomer emission. The quenching effects of Hg^{2+}, Ni^{2+} and Co^{2+} decreased the fluorescence intensity to different degrees.

Inspired by the above results, we further investigated the fluorescent responsive behavior of the **L**•Cu^{2+} complex toward Zn^{2+} and Cd^{2+}. The fluorescence titrations of **L**•Cu^{2+} with Zn^{2+} and Cd^{2+} are presented in Figure 2. The initial emission intensity of **L**•Cu^{2+} enhances steadily on increasing the Zn^{2+} or Cd^{2+} concentration, it should be noted that just 1.0 equiv. of Zn^{2+} or Cd^{2+} led to a doubling of the emission enhancement. Meanwhile, the quantum yield of the **L**•Cu^{2+} complex increased from 0.05 to 0.19 upon addition of Zn^{2+} or Cd^{2+}. These interesting results suggest that the effects of Cu^{2+} and Zn^{2+} or Cd^{2+} ions are synergistic, because the presence of 10 μM Cu^{2+} alone does not induce such a large fluorescence enhancement in this recognition event. This may be due to the building blocks of **L** and Cu^{2+} being a good fit for the formation of the stable Zn^{2+}/Cd^{2+} complexes. On the other hand, Zn^{2+}/Cd^{2+} can still interact with another lone pair of electrons at the nitrogen atom of the C=N groups after it has coordinated with one lone



Figue 2. Fluorescence spectra of **L**•Cu^{2+} complex upon addition of increasing amounts of (a) Zn^{2+} and (b) Cd^{2+} in CH_3CN/CH_2Cl_2 (1000:1, v/v).

pair of electrons to Cu^{2+}, which can reduce the non-radiative decay of the excited state and thereby lead to the pronounced fluorescence enhancement observed.[12] The **L**•Cu^{2+} complex exhibits a high sensitive response to both Zn^{2+} and Cd^{2+}, which suggests that the **L**•Cu^{2+} complex could be utilized as a sensor for Zn^{2+} and Cd^{2+}. According to the fluorescence titration results, the detection limits were calculated to be 5.07×10^{-8} and 4.68×10^{-8} M for Zn^{2+} and Cd^{2+}, respectively (Figure S6, S7).

In an effort to gain more detailed information on the interactions between sensor **L** and Cu^{2+} and Zn^{2+}, ^1H NMR binding studies were carried out (Figure S8). Upon interaction with Cu^{2+}, the proton H_{NH} undergoes an up-field shift of δ 0.63 ppm from δ 12.17 to 11.54 ppm, and the proton $H_{CH=N}$ also demonstrated an up-field shift from δ 9.78 to 9.52 ppm. Similarly, in the presence of Zn^{2+}, the H_{NH} and $H_{CH=N}$ peaks exhibited up-field shifts of δ 0.71 and 0.33 ppm, respectively. Moreover, in order to clarify the fluorescence enhancement that occurs in the presence of both Zn^{2+} and Cu^{2+}, we also carried out a ^1H NMR spectroscopic experiment involving **L**•Cu^{2+} and Zn^{2+} (Figure S8-d). Upon the addition of Cu^{2+} and Zn^{2+}, the H_{NH} peak undergoes a large up-field shift of δ 0.96 ppm from δ 12.17 to 11.21 ppm, meanwhile the $H_{CH=N}$ peak also displayed a larger up-field shift of δ 0.54 ppm from δ 9.78 to 9.24 ppm. These spectral changes suggest that both Cu^{2+} and Zn^{2+} are bound by the nitrogen atom. The coordination of Cu^{2+} with receptor **L** leads to a decrease in the electron density on nitrogen which suppresses the electron transfer from the nitrogen to the photo-excited pyrene moieties, and hence allows for the monomer emission.[13] We tentatively propose that the presence of both Zn^{2+} and Cu^{2+} leads to the formation of a trimer complex, which could further decrease the electron density at nitrogen atom and lead to a further increase of the monomer emission of the pyrene moieties.

Given that F^- has a strong affinity toward Cu^{2+} forming the highly stable species CuF_2,[14] the **L**•Cu^{2+} complex was expected to act as a potential indirect sensor for F^- recognition via a Cu^{2+} displacement approach. To test this idea, the *in situ* generated **L**•Cu^{2+} complex was titrated with F^- anion. As shown in Figure 3, upon the incremental addition of F^- to a solution of **L**•Cu^{2+}, the fluorescence intensity of the monomer emission gradually decreased with a concomitant increase of the excimer emission. During this process, a visual fluorescent color change was also observed from blue to the original green color (Figure 3, inset). This F^- induced fluorescence recovery almost reverted to the initial state of the free sensor **L**, which suggests that the addition of F^- to the **L**•Cu^{2+} solution may lead to demetallation of the **L**•Cu^{2+} complex. Under the same conditions as used above for F^-, we also tested the fluorescence response of the **L**•Cu^{2+} complex to other halogen anions. As shown in Figure S9, a slight monomer emission decrease and excimer emission increase were also observed upon interaction with Cl^-, Br^- and I^-, but none were as obvious as the change observed with F^-. Furthermore, we also investigated the sensing properties of sensor **L** towards halogen ions (Figure S10), which caused either no or negligible effects on the fluorescence spectrum. These results indicate that the **L**•Cu^{2+} complex has potential application for F^- detection.

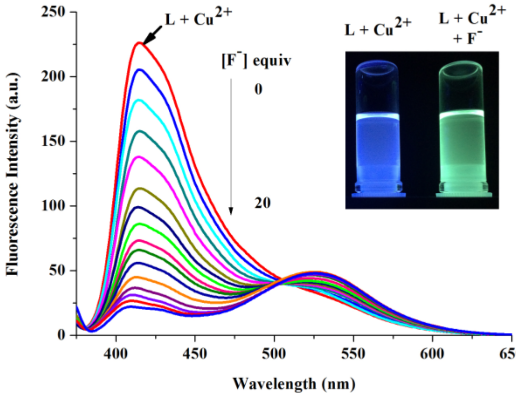


Figure 3. Fluorescence changes of **L**•Cu^{2+} complex upon addition of F^- in CH_3CN/CH_2Cl_2 (1000:1, v/v), λ_{ex} = 367 nm.

To ascertain the sensing ability of the **L**•Cu^{2+} complex towards F^-, ^1H NMR spectroscopic studies were also carried out (Figure S11). As mentioned above, upon interaction with Cu^{2+}, proton H_{NH} and proton $H_{CH=N}$ exhibited up-field shifts of δ 0.63 and 0.26 ppm, respectively. As anticipated, further addition of 1.0 equiv. of F^- to the **L**•Cu^{2+} complex, the $H_{CH=N}$ peak exhibited a down-field shift of δ 0.25 ppm, returning back to the initial position of free **L**; and the H_{NH} also exhibited a down-field shift of δ 0.44 from δ 11.54 to 11.98 ppm. On the other hand, upon the addition of F^- to sensor **L**, there was no obvious changes in the ^1H NMR spectrum (Figure S11-d), which indicated a lack of interactions between F^- and the sensor **L**. Based on the above results, the sensing mechanism of sensor **L** toward Cu^{2+} and F^- is a two-step process, namely 'complexation approach' and 'displacement approach'.

The addition of Zn^{2+}/Cd^{2+} to the solution of **L**•Cu^{2+} complex results in enhancement of the fluorescence intensity at 415 nm, on the other hand, the addition of F^- to the **L**•Cu^{2+} complex quenched the fluorescence emission. On the basis of above fluorescent behavior of sensor **L**, a combinational logic gate can be constructed based on INHIBIT and AND gates (Figure 4). The three chemical inputs of Cu^{2+}, Zn^{2+}/Cd^{2+} and F^- ions are designated as input 1, input 2 and input 3, respectively, and considered as "1" when they are present and "0" if they are absent. The output signal was measured as the fluorescence emission at 415 nm, which was defined as "1" in the case of fluorescence enhancement and "0" in the case of no change in fluorescence intensity (Table 1).

Tabel 1. Truth table for combinational logic gate.

Input 1 Cu^{2+}	Input 2 Zn^{2+}/Cd^{2+}	Input 3 F^-	Output	Fluorescence Emission
0	0	0	0	Low
0	0	1	0	Low
0	1	0	0	Low
0	1	1	0	Low
1	0	0	1	Medium
1	0	1	0	Low
1	1	0	1	Strong
1	1	1	0	Low

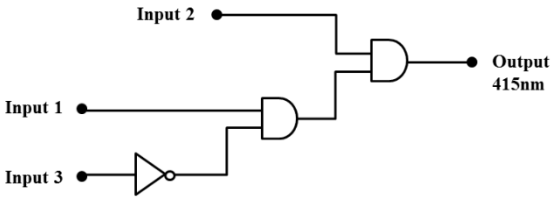


Figure 4. The combinational logic gate with Cu^{2+}, Zn^{2+}/Cd^{2+} and F^- as three chemical inputs.

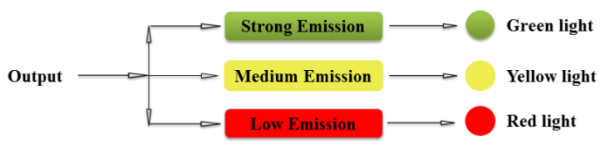


Figure 5. Assignment of output to different traffic signals.

The truth table values for output display different communication of input signals. Under the eight combinations of these inputs (Cu^{2+}, Zn^{2+}/Cd^{2+} and F^-), the conditions (100) and (110), exhibit enhancement in the fluorescence through exhibiting the output as "ON" with the readout signal as 1. However, the rest of the six combinations show no change in the fluorescence intensity of **L**, through exhibiting the output as "OFF" with the readout signal as 0. Particularly, it should be noted that the output exhibits strong, medium and low fluorescence emission. The different emission can be designated as green, yellow and red traffic lights, respectively (Figure 5). Thus, the combinational logic gate can mimic the function of a molecular trafic signals.

In summary, we have developed a new fluorescent sensor **L** based on a pyrene–armed hexahomotrioxacalix[3]arene with a C_3 symmetric structure. Sensor **L** exhibits a sequential recognition for Cu^{2+} and F^- via an anion-induced demetallation. Interestingly, the presence of Zn^{2+} or Cd^{2+} leads to a pronounced fluorescence enhancement of the **L**•Cu^{2+} complex through a synergistic effect, which allows for the **L**•Cu^{2+} complex to also serve as fluorescent sensor for Zn^{2+} and Cd^{2+}. With the triangular fluorescence outputs, a fluorescence based combinational logic gate can be used as potential candidate for a set of molecular traffic signals. The current result illustrates the successful modification of a hexahomotrioxacalix[3]arene to a multifunctional molecular device.

ASSOCIATED CONTENT

Supporting Information

Experimental section. Synthesis, NMR spectroscopy and titration data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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