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Ratiometry of monomer/excimer emissions of dipyrenyl thiacalix[4]arene for Cu^{2+} detection: a potential Cu^{2+} and K^+ switched INHIBIT logic gate with NOT and YES logic functions

Abhimanew Dhir, Vandana Bhalla *, Manoj Kumar *

Department of Chemistry, Guru Nanak Dev University, Amritsar 143 005, Punjab, India

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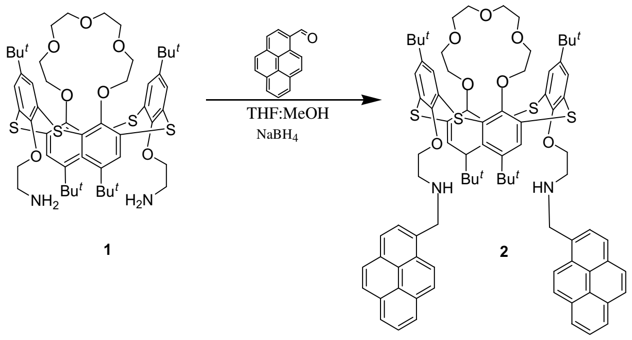
ABSTRACT

A new thiacalix[4]arene derivative **2** of 1,3-*alternate* conformation possessing two pyrene groups has been synthesized and examined for its cation recognition abilities towards different cations such as lithium, sodium, potassium, nickel, zinc, cadmium, silver, mercury, lead and copper by fluorescence spectroscopy. In CH_3CN/CH_2Cl_2 (1:1), the presence of Cu(II) induces the formation of a 1:2 ligand/metal complex, which exhibits increasing monomer emission at 376 nm at the expense of the fluorescent excimer emission of **2** centered at 476 nm. In the presence of K^+, the intensity of the excimer emission increases along with the formation of a new blue shifted band at 435 nm which corresponds to a static dimer. The compound behaves as a fluorescent molecular switch upon chemical input of Cu^{2+} and K^+.

The selective signalling of copper[1] ions is a very important topic for the detection and treatment of these ions in various chemical systems including living systems. Copper plays an important role in fundamental physiological processes in organisms ranging from bacteria to mammals.[1] However, copper can be toxic if the level exceeds cellular needs. It is also capable of displacing other metals which act as co-factors in enzyme-catalyzed reactions.[1b] Thus, designing sensors for copper has recently drawn worldwide attention. In most of the fluorescent sensors reported for copper, so far, the binding of copper with an ionophore results in nonspecific fluorescence quenching[2] via photo-induced electron transfer or fluorescence enhancement.[3] However, to increase the selectivity and sensitivity, ratiometric sensing has also been utilized. Ratiometric fluorescent probes have the important feature of permitting signal rationing, and thus increase the dynamic range and provide built-in correction for environmental effects.[4] Thus, a few ratiometric sensors for Cu^{2+} have been reported in the literature recently.[5] Our research work involves the design, synthesis, and evaluation of calix[4]arene and thiacalix[4]arene based receptors, which are selective for soft metal ions[6] and anions.[7] We reported recently a ratiometric[8] fluorescent sensor for copper based on a thiacalix[4]arene of *cone* conformation possessing dansyl moieties which exhibited an increased emission at 433 nm at the expense of the fluorescent emission centered at 504 nm, but which did not exhibit any logic functions. Now, we have prepared a new ratiometric fluorescent sensor for copper based on a thiacalix[4]arene of 1,3-*alternate* conformation possessing two pyrene moieties and amine groups. The compound behaves as an INHIBIT logic gate with NOT and YES logic functions in the presence of Cu^{2+} and K^+ as chemical inputs. To the best of our knowledge, this is the first report where a thiacalix[4]arene moiety has been used as a receptor for molecular switching with multiple outputs.

Condensation of diamine[9] **1** with 2.0 mol equiv of 1-pyrene carboxaldehyde in a mixture of tetrahydrofuran and methanol (1:1) and in situ reduction of the Schiff base formed with $NaBH_4$ gave target compound **2**[10] in 75% yield (Scheme 1). The cation binding properties of compound **2** were investigated by fluorescence spectroscopy. The titration experiments were carried out in CH_3CN/CH_2Cl_2 (1:1) by adding aliquots of different metal ions. In the fluorescence spectrum, compound **2** exhibited a typical excimer emission band of the pyrene group centered at 476 nm (Fig. 1) and a very weak monomer emission at 376 nm. The formation of only



Scheme 1.

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* Corresponding authors. Tel.: +91 183 2258802/9x3205; fax: +91 183 2258820.
E-mail address: mksharmaa@yahoo.co.in (M. Kumar).

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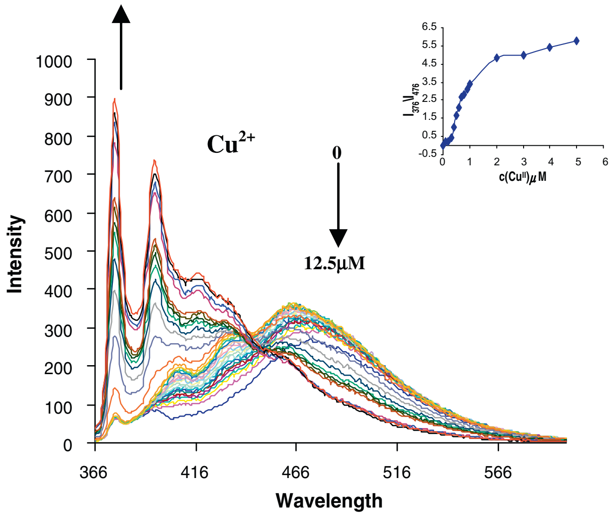

Figure 1. Fluorescent emission spectra of **2** in the presence of different concentrations of Cu^{2+} (0–12.5 μM) CH_3CN/CH_2Cl_2 (1:1, v/v). Excitation wavelength was 343 nm and emission was at 376 and 476 nm.The concentration of **2** was 2.5 μM. Inset: Ratiometric calibration curve I_{376}/I_{476} as a function of Cu^{2+}concentration.

an excimer band indicates that compound **2** exists in a stacked or folded conformation with the two pyrene units very close to each other. Upon addition of small amounts of Cu^{2+} (0–12.5 μM) to the solution of compound **2**, a decrease in the 476 nm emission band was observed with a significant increase in the monomer emission band centered at 376 nm. The isoemission point was observed at 456 nm (Fig. 1). This ratiometric behavior is due to the coordination of Cu^{2+} with receptor **2** which leads to a decrease in the electron density on nitrogen which suppresses the electron transfer from the nitrogen to the photoexcited pyrene moiety,[11] and hence allows the monomer emission. The inset in Figure 1 shows the dependence of the intensity ratio of emission at 376 nm to that at 476 nm (I_{376}/I_{476}) on Cu^{2+}, which indicates the formation of a complex between **2** and Cu^{2+}. Under the same conditions as used above for Cu^{2+}, we also tested the fluorescence response of **2** towards other metal ions such as Li^+, Na^+, K^+, Ni^+, Zn^{2+}, Cd^{2+}, Ag^+, Hg^{2+}, and Pb^{2+} and as shown in Figure 2, no significant ratiometric change of **2** occurred in the presence of these metal ions.

However, in the presence of K^+ ions, a new blue shifted band was observed at 435 nm (vide infra). Fitting the changes in the fluorescence spectra of compound **2** with copper ions, using the nonlinear regression analysis program SPECFIT[12] gave a good fit and demonstrated that 1:2 stoichiometry (host/guest) was the most stable species in the solution with a binding constant log $\beta_{12} = 13.46$.

The method of continuous variation (Job's plot) was also used to prove the1:2 stoichiometry (host/guest). To test the practical applicability of compound **2** as a Cu^{2+} selective fluorescent sensor, competitive experiments were carried out in the presence of Cu^{2+} at 12.5 μM mixed with Li^+, Na^+, K^+, Ni^+, Zn^{2+}, Cd^{2+}, Ag^+, Hg^{2+}, and Pb^{2+} at 12.5 μM. As shown in Figure 3, no significant variation in the intensity ratio (I_{376}/I_{476}) was found by comparison with and without the other metal ions. This indicates that compound **2** has a high selectivity for Cu^{2+} ions. The detection limit[13] of **2** as a fluorescent sensor for the analysis of Cu^{2+} was found to be 2.1×10^{-6} mol L^{-1}, which is sufficiently low for the detection of submillimolar concentrations of Cu^{2+} ions as found in many chemical systems.

Recently, there has been significant activity in the development of supramolecular systems behaving as a molecular logic gate.[14,15] In particular, a system consisting of chemically encoded information as input and a fluorescent signal as output has attracted interest. Thus, various molecular systems showing AND, OR, NOR, INHIBIT, XOR, YES, NOT, and XNOR logic gates have been reported.[14,15] Most of the reported molecules contain only one output mode. Recent interest is focused on integrated systems involving multiple fluorescent output modes[16] as with multiple output modes, molecular systems forming basic logic gates can be programmed into single molecular switches. These molecular switches can be used in complex circuits in the design and development of molecular electronic and photonic devices for information, processing, sensing, and computation. However, there are only a few reports of such logic circuits. Since there has not been any report in which thiacalix[4]arene was used as a molecular logic gate and copper and potassium being used as inputs, we examined our system as an INHIBIT logic gate with NOT and YES logic functions. Addition of Cu^{2+} to a solution of receptor **2** resulted in quenching of excimer and enhancement of monomer emission (Fig. 1). When K^+ ions were added to receptor **2**, the intensity of the excimer band was enhanced at 476 nm and a new blue shifted band appeared at 435 nm (Fig. 4). The reason for the increase in the intensity of the excimer band at 476 nm is due to the fact that the K^+ ions bind to the polyether chain and as a result of which, the photoinduced electron transfer to the photoexcited pyrene dimer is suppressed.

The formation of the new blue shifted band at 435 nm can be ascribed to the pyrene dimer formed in the ground state, a so called 'static dimer'.[17–19] This type of 'static dimer' formation has been reported previously by Kim[18] in the presence of fluoride ions, whereas, Yang[19] et al. reported the same type of 'static dimer' formation in the presence of Cu^{2+} ions. Addition of Cu^{2+} to the **2**. K^+ complex, completely quenched the excimer emission with enhancement of the monomer bands, which indicates that the

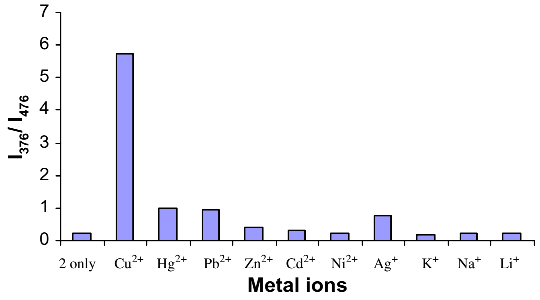

Figure 2. Ratiometric (I_{376}/I_{476}) selectivity of **2** (2.5 μM) upon addition of different cations (12.5 μM).

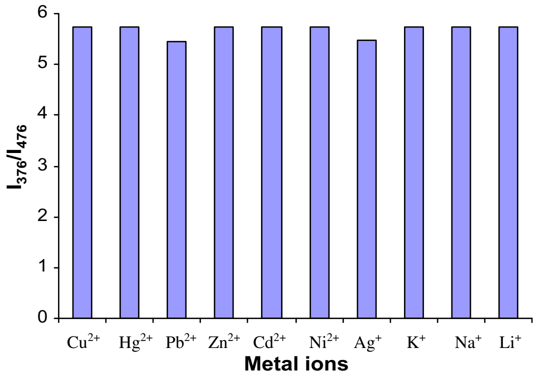

Figure 3. Ratiometric fluorescent response of sensor **2** (2.5 μM) to Cu^{2+}(12.5 μM) over other selected metal ions (12.5 μM).

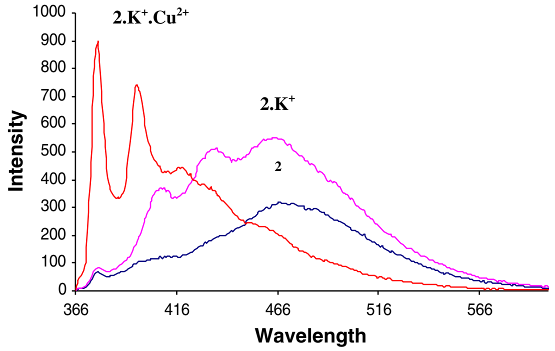

Figure 4. Fluorescent emission changes of **2** at a concentration of 2.5 μM upon addition of K^+ (2500 μM) and further addition of Cu^{2+} in CH_3CN/CH_2Cl_2 (1:1, v/v).

Table 1

Truth table for a two-input, three-output molecular switch

Entry	Input 1 K^+	Input 2 Cu^{2+}	Output 1 Dynamic excimer emission $\lambda = 476$ nm	Output 2 Static excimer emission $\lambda = 435$ nm	Output 3 Monomer emission $\lambda = 376$ nm
1	0	0	1	0	0
2	1	0	1	1	0
3	0	1	0	0	1
4	1	1	0	0	1

equilibrium shifts towards the more strong Cu^{2+} complex (Fig. 4). Thus, from the above fluorescent behavior of receptor **2** following a truth table (Table 1)[20] and logic circuit (Fig. 5)[16,20] can be constructed.

In the absence of any chemical input, the receptor **2** shows excimer emission at 476 nm, that is, output 1 due to the formation of a dynamic excimer. Operation by K^+ as (Input 1) to receptor **2**, the output 1 remains '1' but the new output 2 due to static dimer formation becomes '1'. Operation by Cu^{2+} as (Input 2) the ouput 1 becomes '0', while ouput 3 becomes '1', which was '0' initially (Fig. 1). In the simultaneous presence of both the chemical inputs (1 and 2), the ouput 1 and output 2 become '0' and output 3 becomes '1' due to the formation of a more stable Cu^{2+}complex (Fig. 4). The truth table values for output 2 (at $\lambda = 435$ nm) give an INHIBIT[16,20–23] logic gate, which is a combination of an AND[23b,24,25] gate with a NOT[20,24] logic function at one of its inputs (Cu^{2+} in this case). A YES[20,25]logic function at the Cu^{2+} terminal explains the truth table values for output 3 ($\lambda = 376$ nm). The YES logic function is a single input device which delivers the same output signal given by the input. Similarly, an output generated by a NOT logic function at Cu^{2+} terminal justifies the truth table values for output 1 at ($\lambda = 476$ nm). A NOT logic function is a single input device which reverts the input signal. The combination of these intrinsic properties with selectivity of actions by different chemical inputs allows its implementation in the design of a complex molecular switch as shown in Figure 5.

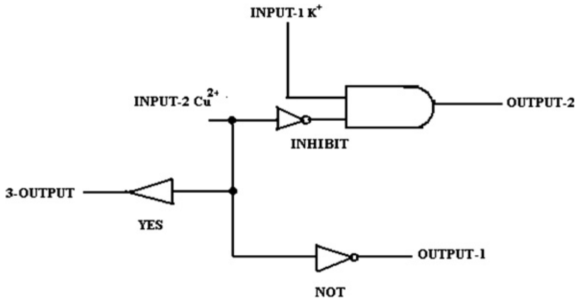

Figure 5. Combinatorial logic circuit for a two input, three output molecular switch.

Thus, we have synthesized a novel pyrene appended thiacalixarene based receptor which behaves as a ratiometric fluorescent Cu^{2+} sensor. In addition, a fluorescent molecular switch is designed in which the system is operated by Cu^{2+} and K^+ as inputs and multiple outputs are generated. The concept presented here also controls the monomer and excimer emission which may contribute to the construction of miniaturized and integrated molecular level devices with multiple functions.

Acknowledgments

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10. *Synthesis of* **2**: To a solution of **1** (100 mg, 0.10 mmol) in dry tetrahydrofuran/dry methanol (1:1) was added 1-pyrenecarboxyaldehyde (48 mg, 0.20 mmol). $NaBH_4$ (90 mg, 2.38 mmol) was added after 5 h. The resulting mixture was stirred at room temperature for 24 h. The solvent was then removed under vaccum. Water (15 ml) was added to the residue and the pH of the solution was maintained at 9 with aqueous ammonia. The solution was then extracted with chloroform and the organic layer was dried over anhydrous sodium sulfate and distilled under reduced pressure to give a crude product which was recrystallized from $CHCl_3/MeOH$ (1:1) to give a light yellow solid compound. Yield (0.11 g, 75%); mp 280 °C, IR ν_{max} (KBr Pellet, cm^{-1}) 3425; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.13 [s, 18H $C(CH_3)_3 \times 2$], 1.38 [s, 18H, $C(CH_3)_3 \times 2$], 2.45 [t, $J = 6.3$ Hz, 4H, $NCH_2 \times 2$], 3.01 [t, $J = 7.8$ Hz, 4H, $OCH_2 \times 2$], 3.40 [br, 4H, $OCH_2 \times 2$], 3.63 [br, 4H, $OCH_2 \times 2$], 3.92 [t, $J = 8$ Hz, 4H, $OCH_2 \times 2$], 4.13 [t,$J = 6.5$ Hz, 4H, $OCH_2 \times 2$], 4.41 [s, 4H, $NCH_2 \times 2$], 7.33 [s, 4H, ArH × 4], 7.42 [s, 4H, ArH × 4], 7.82–8.31 [m, 18H Pyrene]; ^{13}C NMR (300 MHz, $CDCl_3$): δ 31.3 [$(CH_3)_3$], 31.4 [$(CH_3)_3$], 34.2 [C], 34.35 [C], 48.43 [NCH_2], 51.52 [NCH_2], 65.4 [OCH_2], 67.6 [OCH_2], 70.19 [OCH_2], 71.4 [OCH_2], 73.5 [OCH_2], 110.65 [ArC], 124.9 [ArC], 125.73 [ArC],126.63 [ArC], 126.95 [ArC], 127.39 [ArC], 127.57 [ArC], 127.96 [ArC], 129.04 [ArC], 130.51 [ArC], 130.70 [ArC], 131.18 [ArC], 133.66 [ArC], 146.31 [ArCO], 156.17 [ArCO]; FAB MS *m/z* 1394 $(M+H)^+$; Anal. Calcd for $C_{86}H_{92}N_2O_7S_4$: C, 74.13%; H, 6.60%; N, 2.01%. Found: C, 73.92%; H, 6.45%; N, 2.00%.
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