

An Imidazole based probe for relay recognition of Cu^{2+} and OH^- ions leading to AND logic gate

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Abstract. 2-(2-methoxyphenyl)-4,5-diphenyl-1H-imidazole **1**, an imidazole-based compound, was found to sense Cu^{2+} ions via fluorescence and absorption spectroscopy over a number of other metal ions. During Cu^{2+} sensing, the chemosensor **1** followed a “switch-off” mechanism. Job’s plot supported 1:1 stoichiometry of **1**- Cu^{2+} complex. The **1**- Cu^{2+} complex formed *in situ* underwent different absorption changes with OH^- ions. These differential absorption changes observed with the addition of Cu^{2+} and OH^- ions were used to mimic AND logic gate using $A_{274\text{nm}}$ as output.

Keywords. Imidazole; Chemosensor; Cu^{2+} sensing; quenching; logic gate

1. Introduction

Imidazoles are common scaffolds in highly significant bio molecules, including biotin, histidine, histamine and many alkaloids, which have been shown to exhibit antimicrobial, anticryptococcal, cytotoxic and other biological activities.¹ Biological activity of imidazole derivatives is the main motive for their wide use in medicine, agriculture and pharmaceutical industry.² Moreover, they also have a great potential in the area of optical and chemical sensors,³ fuel cell membranes,⁴ luminescent materials,⁶ ion-conducting electrolytes⁷ and photovoltaic materials for solar cell applications.⁸ The presence of a donor pyridine like nitrogen atom within the imidazole ring makes it a good metal ion sensor. In this sense, the binding properties of the imidazole core may be modulated by linear or angular annulations to aza-heterocycles leading to expanded imidazole derivatives bearing several binding sites.⁹ Moreover, the appreciable changes observed in the fluorescence upon metal binding makes imidazole derivatives more attractive as chelators. Therefore, imidazole derivatives have been used to construct highly sensitive fluorescent chemosensors for sensing and imaging of metal ions as well as making organic light emitting diodes.¹⁰ Amongst different metal ions, Cu^{2+} ions play significant roles in various biological processes such as hemopoiesis, metabolism, growth, and immune system.¹¹ However exposure to high level of

copper can cause gastrointestinal disturbance and also liver or kidney damage upon long term exposure.¹² Therefore, detection of Cu^{2+} is of great importance for elucidating its complex physiological and pathological roles. A number of recent literature reports show quenching of fluorescence intensity with addition of Cu^{2+} ions in non-aqueous medium.¹³

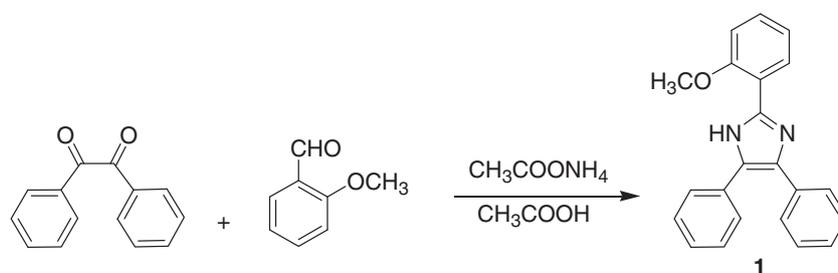
Also, the ability of chemosensors to produce different optical signals lead to the construction of photonic driven systems and network that functions as molecular logic gates,¹⁴ molecular keypad lock devices,¹⁴ lab-on-molecule type devices,^{14b,16} and ion-pair receptors.¹⁷ These systems use physical or chemical inputs to generate outputs based on a set of logical operators and mimic the function of logic gates by applying the laws of Boolean algebra.

Herein, we report an imidazole possessing chemosensor (**1**) which can function as a molecular AND type binary logic gate with two inputs viz. Cu^{2+} and OH^- ions. The output is the increased absorbance in the presence of both the inputs. The literature survey for efficient synthesis of **1** reveals several methods with¹⁸ and without catalyst.¹⁹ Imidazole derivatives similar to **1** possess antinociceptive, anti-inflammatory²⁰ and analgesic activity^{19b} and have been recently reported to exhibit α -glucosidase inhibition to treat diabetes.²¹

2. Experimental

The chemosensor **1** was synthesized according to scheme 1.

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Scheme 1. Synthesis of chemosensor **1**.

Benzil (1 g, 4.75 mmol) and ammonium acetate (10.56 g, 137 mmol) were dissolved in 10 mL of hot glacial acetic acid. While the mixture was stirred, a solution 2-methoxy benzaldehyde (0.646 g, 4.75 mmol) in 10 mL of glacial acetic acid was added drop wise to the mixture. The mixture was heated at 90°C for 3 h and was then poured in 200 mL of water. The solution was neutralized with ammonia to pH 7 and the contents were filtered to yield crude precipitates which were washed with large portions of water.²² Recrystallization of crude product from mixture of methanol and chloroform resulted in formation of pure chemosensor **1** (figure S1–S4). Pale white solid, 80% Yield, M.p: 190–194°C; IR peaks (KBr, cm⁻¹): 3063 ($\nu_{\text{N-H}}$), 2978 ($\nu_{\text{Aromatic C-H}}$), 1584 ($\nu_{\text{C=N}}$); ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 3.96 (s, 3H, -OCH₃), 6.95 (d, $J = 8.28$ Hz, 1H, Ar-H), 7.04 (t, 1H, Ar-H), 7.30 - 7.18 (m, 7H, Ar-H), 7.51 (s, 4H, Ar-H), 8.43 (dd, $J_A = 7.76$ Hz, $J_B = 1.68$ Hz, 1H, Ar-H), 10.52 (s, 1H, NH); ¹³C NMR (CDCl₃, 75 MHz, ppm) δ : 55.92, 111.21, 118.06, 121.73, 127.27, 127.82, 128.61, 128.71, 129.60, 144.03, 155.75. LC-MS: $m/z = 327$ ($M^+ + 1$).

3. Results and Discussion

3.1 Spectral Characteristics of **1** towards metal ions

The metal binding ability of chemosensor **1** was initially evaluated by UV-vis spectral analysis using different metal perchlorates. In the absence of metal ions, the maximum absorption of **1** in CH₃CN was at about 315 nm. On addition of Cu²⁺ (10 equiv.) to the solution of chemosensor **1** (10 μ M), decrease in absorbance at 315 nm was observed. The addition of other metal ions did not show any significant change in absorption spectra even with large excess of metal ions *viz.* Na⁺, K⁺, Mg²⁺, Al³⁺, Mn²⁺, Fe²⁺, Co²⁺, Ni²⁺, Cu²⁺, Cd²⁺ and Hg²⁺. However, addition of 100 equiv. of Zn²⁺ results in 40% decrease in absorbance as compared to 67% decrease in absorbance observed with 10

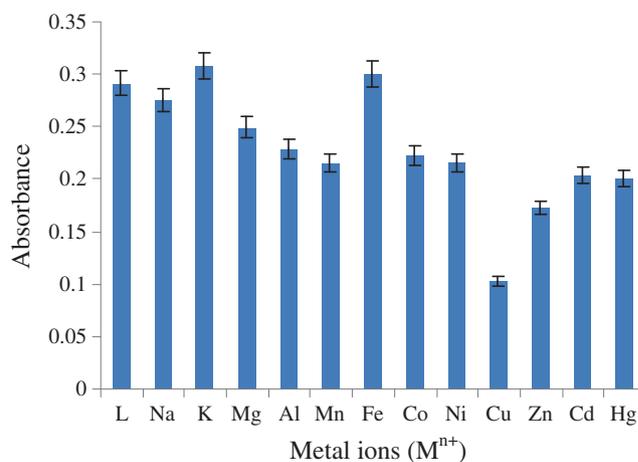


Figure 1. UV-vis. absorption responses of **1** (10 μ M) to various metal ions (1000 μ M) in CH₃CN. Bars represent the intensity of absorption at 315 nm.

equiv. of Cu²⁺ ions (figure 1). Therefore, chemosensor **1** showed selective detection of Cu²⁺ ions in the presence of other metal ions such as alkali, alkaline earth and transition metal ions. This Cu²⁺ selectivity could be attributed to the highest Lewis acid character of Cu²⁺ amongst divopositive cations in parallel with Irving-Williams series of stability of divopositive metal ion complexes.²²

The selectivity of **1** was also investigated by measuring the fluorescence emission spectra against different metal ions in CH₃CN. Figure 2 shows clearly that very little change in fluorescence intensity resulted by the addition of different metal ions except in case of Cu²⁺. This data explicitly showed the selectivity of **1** towards Cu²⁺ ions. The quenching caused by Cu²⁺ transition metal ion can be attributed to its paramagnetic nature by which it can easily participate in energy transfer or electron transfer processes with organic fluorophores via non-radiative deactivation channel and thus, resulting in quenching effect.²⁴

To determine the quantitative sensitivity range for binding of **1** with Cu²⁺, spectrophotometric titration experiments were performed in the presence of Cu²⁺

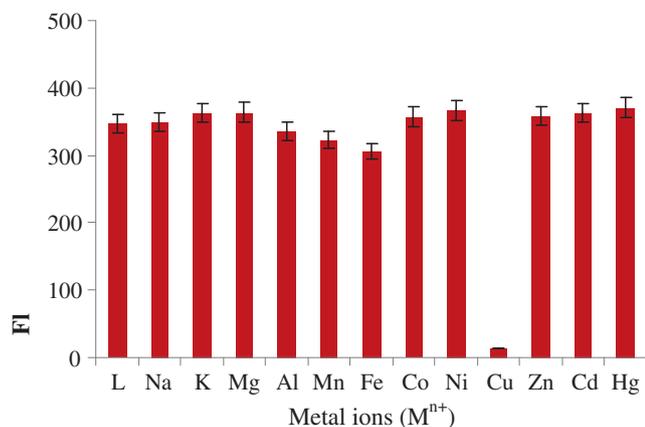


Figure 2. Fluorescence responses of **1** ($0.5 \mu\text{M}$) to various metal ions ($50 \mu\text{M}$) in CH_3CN . Bars represent the fluorescence intensity at 382 nm.

ions. The UV-vis titration data suggested that the intensity of the absorbance at λ_{max} 315 nm decreased gradually with the increase in concentration of Cu^{2+} to solution of chemosensor **1** ($10 \mu\text{M}$) in CH_3CN , upto $30 \mu\text{M}$ and then a plateau was achieved (figure 3). The chemosensor **1** ($0.5 \mu\text{M}$) showed emission maximum at 382 nm in CH_3CN when excited at 315 nm.

Figure 4 shows the gradual change in fluorescence intensity of **1** upon progressive addition of Cu^{2+} in various concentration ranges. Addition of 3 equiv. of Cu^{2+} showed quenching close to 100% with negligible spectral shift. This data probably suggested photoinduced electron transfer (PET). PET sensors usually exhibit little or no spectral shift with increase or decrease in emission intensity.²⁵

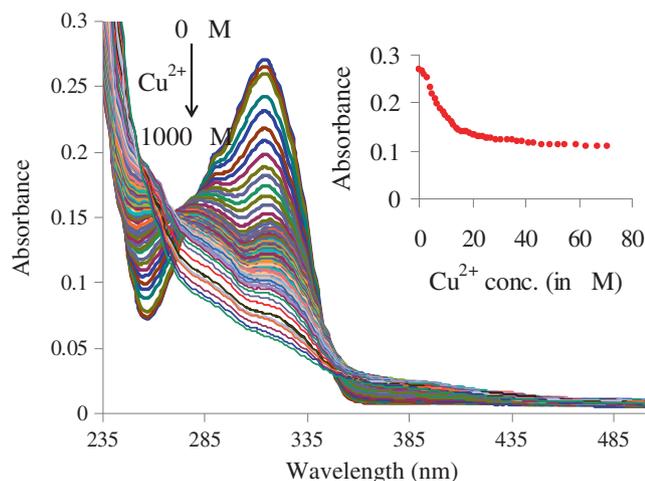


Figure 3. Family of UV-vis spectra taken in the course of the titration of **1** ($10 \mu\text{M}$ in CH_3CN) with Cu^{2+} ions. Inset: Change in the absorbance of **1** as a function of Cu^{2+} ion concentration.

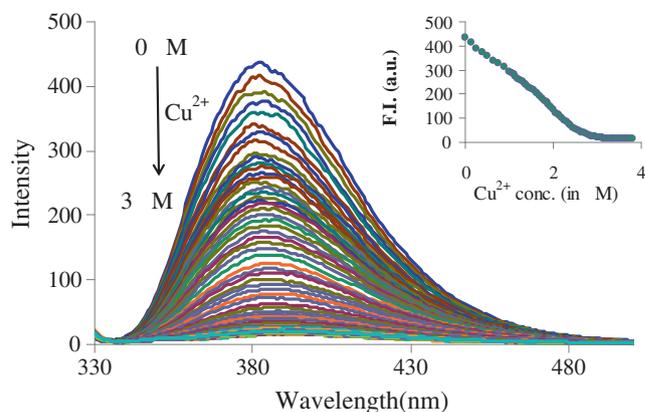


Figure 4. Fluorescence response of chemosensor **1** ($0.5 \mu\text{M}$) on addition of Cu^{2+} ions in CH_3CN ; λ_{ex} 315 nm. Inset: Change in the fluorescence intensity of **1** as a function of Cu^{2+} ion concentration.

The limit of detection (LOD) and limit of quantification (LOQ) are calculated from UV-vis titrations. Linear regression graph of titrations was used to calculate standard deviation and slope of linear response.

$$\text{LOD} = 3\sigma s^{-1}$$

$$\text{LOQ} = 10\sigma s^{-1}$$

where σ = standard deviation of response and s = slope of the calibration curve. The detection limit and limit of quantification for Cu^{2+} ions has been reasonably estimated²⁶ to be $1.24 \mu\text{M}$ and $4.12 \mu\text{M}$.

3.2 Calculation of binding constant

Figure 5 supports the 1:1 stoichiometry of **1**- Cu^{2+} complex.

The binding constant of the chemosensor **1** with Cu^{2+} was $1.77 \times 10^5 \text{ M}^{-1}$ as calculated using Benesi-Hildebrand equation.²⁷

$$\frac{1}{A - A_0} = \frac{1}{A_{\text{max}} - A_0} + \frac{1}{[A_{\text{max}} - A_0] K [C]}$$

Here, A_0 , A , and A_{max} is the absorbance of free **1**, measured with Cu^{2+} and measured with excess amount of Cu^{2+} at 315 nm, respectively and K is the association constant and $[C]$ is the concentration of Cu^{2+} ion added. Plotting of $1/(A-A_0)$ versus $1/[\text{Cu}^{2+}]$ showed a linear relationship (figure 6), which also indicated that **1** is associated with Cu^{2+} in a 1:1 stoichiometry. Although Job's plot clearly indicated 1:1 stoichiometry of the complex, it was observed in the UV-vis titration that nearly three times $[\text{Cu}^{2+}]$ was required to achieve the plateau. This might be due to the reversibility of the reaction. Addition of large excess of Cu^{2+} concentration made the complex equilibrium to be shifted towards complex formation.²⁸

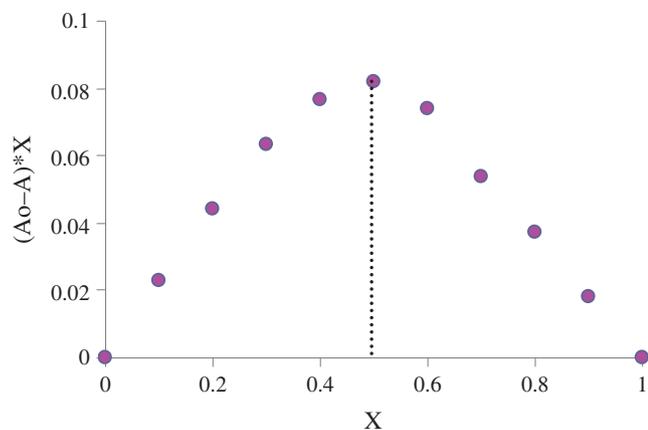


Figure 5. Job's plot for the determination of the stoichiometry of **1**.Cu²⁺ in CH₃CN.

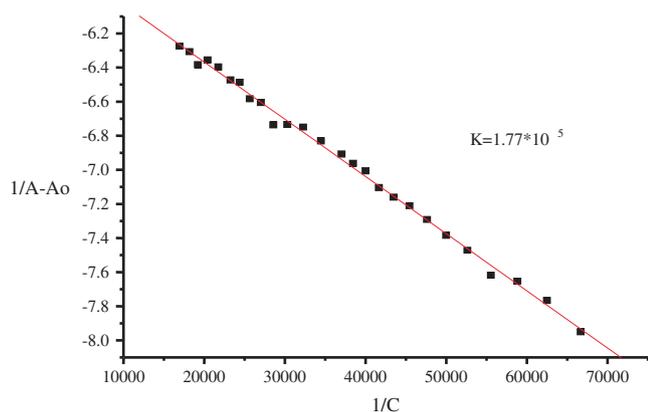


Figure 6. Plot of $1/(A-A_0)$ versus $1/[Cu^{2+}]$ showing a linear relationship.

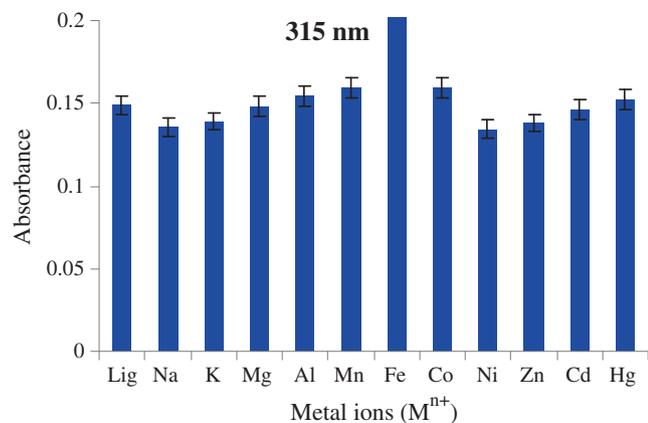


Figure 7. UV-vis absorption response of **1** (10 μ M) containing 50 μ M Cu²⁺ (Lig.) to the selected metal ions (1000 μ M).

To establish the selectivity of **1** toward Cu²⁺ over a range of various metal ions (Na⁺, K⁺, Mg²⁺, Al³⁺, Mn²⁺, Fe²⁺, Co²⁺, Ni²⁺, Cu²⁺, Zn²⁺, Cd²⁺ and Hg²⁺), we carried out the competitive recognition studies

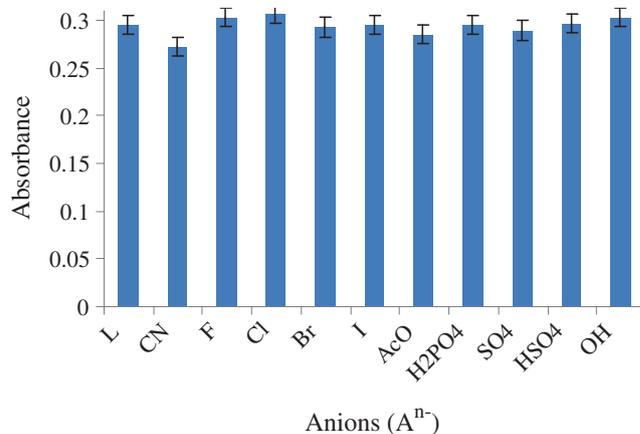


Figure 8. UV-vis. absorption responses of **1** (10 μ M) to various anions (1000 μ M) in CH₃CN. Bars represent the intensity of absorption at 315 nm.

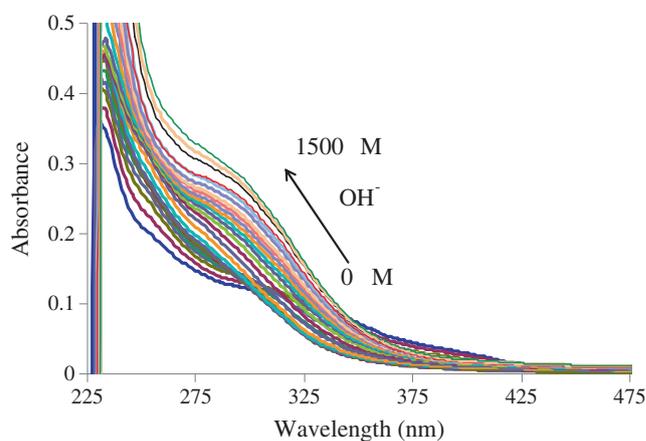


Figure 9. UV-vis. absorption responses of **1**-Cu²⁺ (10 μ M) on addition of OH⁻ ions in CH₃CN.

where the other cations were used in higher concentration (figure 7). From the bar diagram, one could easily understand that the effects on absorbance of **1** upon the addition of higher concentrations of various cations were almost negligible. These results showed excellent selectivity for Cu²⁺ over a wide range of cations.

3.3 Spectral Characteristics of **1** towards anions

As the chemosensor **1** possesses imidazole NH that can bind with anions, so the binding ability of **1** towards different anions was also monitored. Figure 8 shows the absorption changes of chemosensor **1** (10 μ M) towards 1000 μ M of various anions *viz.* CN⁻, F⁻, Cl⁻, Br⁻, I⁻, AcO⁻, H₂PO₄⁻, SO₄²⁻, HSO₄⁻ and OH⁻. This bar diagram points towards negligible interaction of chemosensor **1** with various anions.

However, **1**+Cu²⁺ complex is expected to act as a chemosensing ensemble for anion recognition especially

for more basic OH^- ion. For this, the probe **1** + Cu^{2+} was prepared *in situ* by addition of 5 equiv. of Cu^{2+} to **1** solution ($10\ \mu\text{M}$). The addition of OH^- ions ($0\text{--}1500\ \mu\text{M}$) to the solution of *in situ* generated **1** + Cu^{2+} complex results in a new hypsochromically shifted absorption in the region $270\text{--}290\ \text{nm}$ (figure 9). The intensity of this new band gradually increased with increasing concentration of OH^- ion.

3.4 Sensing mechanism

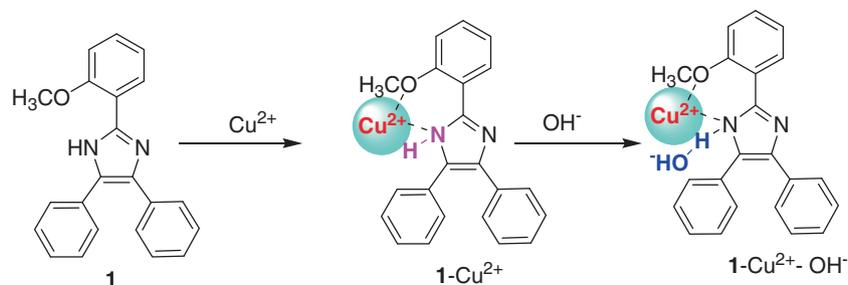
The possible binding model of chemosensor **1** is shown in scheme 2. The Cu^{2+} ions are expected to bind through imidazole nitrogen and methoxy oxygen to make **1**- Cu^{2+} complex. Binding of Cu^{2+} with imidazole N makes imidazole NH more acidic, increasing its binding ability towards more basic OH^- ion.

3.5 Logic gate

Logic gate devices are used to perform basic logic operations whose output (high or low) depends on input

conditions. The conventional computer, based on silicon-circuitry, uses electrical signal as input and output. Following laws of Boolean algebra, the tailor-made chemosensors can be viewed as computational devices that use physical or chemical inputs to generate outputs based on a set of logical operators.

The first example of a molecular logic gate is described by de Silva in 1993 that mimicked an AND function.²⁸ The AND gate is the principal logic gate and gives logical multiplication output. Here, the UV-vis absorbance behaviour of chemosensor **1** in the presence of Cu^{2+} and OH^- can satisfactorily mimic an AND logic gate function with Cu^{2+} and OH^- as inputs and $A_{274\ \text{nm}}$ as output. Free **1** showed low absorbance at $\lambda_{\text{max}}\ 274\ \text{nm}$, corresponding to a “0” state. Upon the individual presence of Cu^{2+} or OH^- , the absorbance at $274\ \text{nm}$ was still low (“0” state). However, the simultaneous presence of Cu^{2+} and OH^- could give high absorbance at $274\ \text{nm}$, corresponding to “1” state. The absorption changes at $274\ \text{nm}$ in the presence of Cu^{2+} and OH^- ions and the corresponding truth table with logic circuit for AND function are given in figure 10.



Scheme 2. The possible binding model of chemosensor **1**.

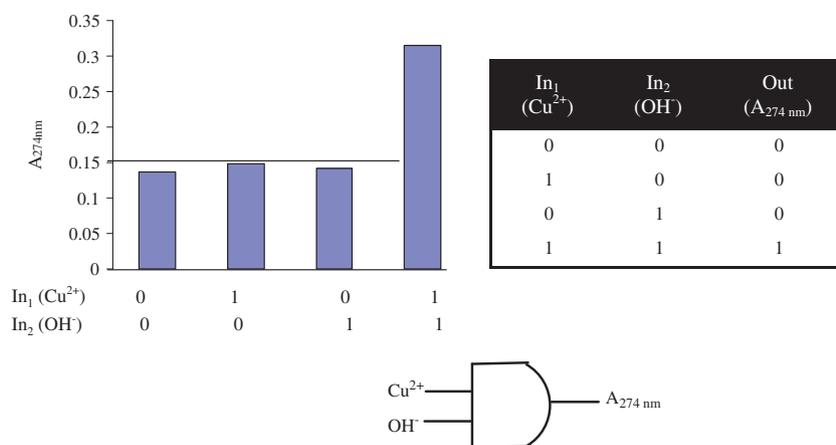


Figure 10. $A_{274\ \text{nm}}$ responses of **1** ($10\ \mu\text{M}$) in CH_3CN in the presence of Cu^{2+} , OH^- and $\text{Cu}^{2+} + \text{OH}^-$. **1** mimic an AND logic gate function with Cu^{2+} and OH^- as inputs and $A_{274\ \text{nm}}$ as output.

4. Conclusions

In conclusion, an imidazole based chemosensor **1** has been established as the molecular AND logic gate for relay recognition of Cu^{2+} and OH^- ions. The Cu^{2+} sensing by **1** followed “switch-off” mechanism. The sensing selectivity and sensitivity of this chemosensor toward Cu^{2+} ions were established by both UV-vis and fluorescence spectroscopy.

Supplementary Information

Supplementary Information is available at www.ias.ac.in/chemsci.

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