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Synthesis of a novel compound with indenoquinoxaline-pyrazole moieties and its colorimetric ion sensor properties

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A novel compound containing indenoquinoxaline and pyrazole units in quantitative yield, 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2*H*)-one (4) was synthesized and characterized using FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data and elemental analysis. The colorimetric sensor property of the title compound in aqueous acetonitrile solution for use in the detection of various metal cations such as Cu^{2+}, Hg^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+} and Fe^{2+} was investigated through changes in the absorption of the UV-vis spectrum. A well-defined discoloration that could be detected with the naked eye was also observed. Due to the presence of heteroatoms in the molecular structure and their conformations, it was observed that the title compound in aqueous acetonitrile solution showed receptor properties against the Cu^{2+}, Hg^{2+}, ions among these ions.

Keywords: Indenoquinoxaline; 4-Aminoantipyrine; Ion sensor; Naked eye; UV-Vis titration.

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1. Introduction

Recently, indenoquinoxaline derivatives constitute an important class of ben-zo-heterocyclic compounds which have attracted great attention due to both their biological activities and ion sensor applications [1–6]. These derivatives have gained importance as intermediates in organic synthesis due to the forming the main framework of anti-HIV activity [7], anticancer [8], antimicrobial [9,10], anti-inflammatory [11] antimalarial and antidiabetic drugs [12]. They are use as intermediates in cascade organic synthesis [13]. In addition, indenoquinoxaline derivatives are important functional groups in the synthesis of organic semiconductors because they are important classes of nitrogen-containing heterocycles [14]. Since indenoquinoxaline derivatives are compounds containing the C=N bonds attached to a heterocyclic moiety, they exhibit various chemical reactivity, and since they form solid subunits of macrocyclic receptors, they possess coordination activities with several metal ions. Moreover, pyrazolones as nitrogen-containing heterocyclic com-pounds are molecules with organic moieties used in the synthesis of biologically im-portant Schiff bases. 4-Aminoantipyrine (4-amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one), one of the important pyrazolone derivatives, can be used in the indirect determination of phenol [15], as well as various metal complexes can be formed with the numerous Schiff bases formed [16,17].

In this study, a new imine compound, 4-((11H-indeno[1,2-b]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (4), containing both indenoquinoxaline and pyrazole moieties was synthesized and characterized by spectroscopic methods. Pyrazolines and quinoxalines are nitrogen-containing heterocyclic compounds and are important ligands for coordination compounds. To investigate the colorimetric sensor property of the title compound, the sensing behavior of the receptor toward different metal ions such as Cu^{2+}, Hg^{2+}, Ni2+, Mn^{2+}, Zn^{2+} and Fe^{2+} in aqueous acetonitrile solution was monitored by changes in the absorption of the UV-vis spectrum. Among these ions, it was determined that it showed sensing behavior against Cu^{2+}, Hg^{2+} ions. Also, well-defined color changes that were practically detectable with the naked eye were observed.

2. Experimental

Materials and Methods

2.1. Reagents and techniques

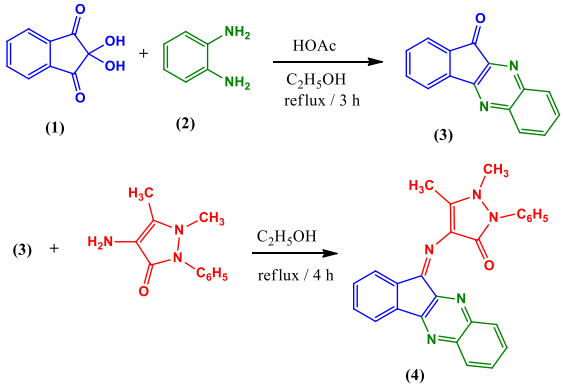
Melting point was measured with an Electro Thermal IA 9100 apparatus using a capillary tube. Infrared absorption spectra were obtained from a Perkin Elmer BX II spectrometer. A Perkin-Elmer Lambda-25 UV-vis spectrophotometer was used to record UV-visible spectra in solution. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECX- 400 NMR spectrometer operating at 400 and 100 MHz, respectively and using CDCl3 as solvent. The molecular weight of product was determined at Shimadzu LC-MS/MS 8040 Liquid Chromatograph Mass Spectrometer using an ESI. Ninhydrin, 1,2-phenlynediamine, 4-aminoantipyrine and all solvents were purchased from Aldrich. Unless otherwise specified, all reagents for synthesis were obtained commercially and were used without further purification. In the titration experiments, all the metal ions were added in the form of chloride salts (Cu^{2+}, Hg^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+} and Fe^{2+}) which were purchased from Argos, Sigma-Aldrich Chemical stored in a vacuum desiccator containing self-indicating silica, and fully dried before use.

2.2. Synthesis of the 11H-indeno[1,2-b]quinoxalin-11-one (**3**)

1,2-Phenylenediamine (0.540 g, 5 mmol) in ethanol (20 mL) was added dropwise to a solution of ninhydrin (0.890 g, 5 mmol) in ethanol (20 mL) and a dropped of conc. CH_3COOH in the mixture was refluxed by rapidly stirring. The progress of the reaction was monitored by thin layer chromatography (TLC) analysis. After the completion of the reaction, for 3 h, the obtained yellow solid was filtered and crude product was washed several times with methanol, as a bright yellow solid, mp. 214-215 °C, 0.998 g (86 %) yield. FT-IR, (cm^{-1}): 3067, 3040 ($C_{aromatic}$ -H), 1728 (C=O), 1604, 1568 (-C=N), 1183, 772 (C=C). ^{1}H-NMR (400 MHz; $CDCl_3$; δ ppm): 8.17 (1H, t), 8.14 (1H, d), 8.08 (1H, d), 8.06 (1H, d), 7.84 (1H, d), 7.72 (1H, m), 7.53 (1H, t), 7.46 (1H, t) (Figure S1- Figure S2).

2.3. Synthesis of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**)

11*H*-indeno[1,2-*b*]quinoxalin-11-one (**3**) (1.160 g, 5 mmol) was dissolved in chloroform (15 mL) then added to a solution of 4-aminoantipyrine (1.150 g, 5 mmol) in chloroform (10 mL) under permanent stirring. Then, reaction mixture, which turned red color was refluxed under stirring for 4 h.. The reaction was monitored by TLC (eluent: Methanol). After cooling, a blood red precipitate was formed which is filtered off, washed with ethyl acetate, dried. 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**): blood red powder, 87% yield, mp. 245 °C; FT-IR (ν cm^{-1}): 3093, 3060, 3047, 3029 (C-Haromatic), 2982, 2966 cm-1 ($C\text{-}H_{aliphatic}$), 1649 (N-N-C=O), 1573 (keto-imine group, C=N), 1042 (CO-N), 1308, 749 $(C=C)_{aromatic}$; ^{1}H-NMR (400 MHz, $CDCl_3$), δ ppm; 8.29 (d, 2H), 8.19 (d, 1H), 8.11 (d, 1H), 8.08 (t, 2H), 7.91 (d, 2H), 7.73 (t, 1H), 7.61 (t, 1H), 7.48 (t, 1H), 7.30 (t, 2H) ($C\text{-}H_{aromatic}$), 3.25 (s, 3H, CH_3), 3.25 (s, 3H, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): 158.7 (>C=N-), 158.1 (C=O), 146.8 (C-N), 133.8-122.2 ($C=C_{arom.}$), 122.2 (C=C), 36.9 (-CH_3), 29.5 (-CH_3); MS (ESI) m/z: calculated: 417.46, founded: 418.00.



Scheme 1. The synthesis of 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**).

3. Results

3.1. Spectral analysis

4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**) was synthesized by the reaction of **3** and 4-aminoantipyrine compounds in ethanol (Scheme 2). The formation of the title compound is supported by FT-IR, ^{1}H and ^{13}C-NMR spectroscopic methods as well as mass analysis. The FT-IR spectrum of the title compound has shown a prominent bant at 1649 cm^{-1} has been identified as the stretching vibration of carbonyl group (-C=O) in pyrazole moiety. The bands at 1574 and 1042 cm^{-1} belong to C=N (the keto-imine group) and CO—N (the keto-hydrazine group) of the pyrazole moiety in the title compound, respectively. The stretching and bending vibrations of C=C bonds are observed at 1198, 1183 cm^{-1} and 749, 728 cm^{-1}, respectively (Figure 1).

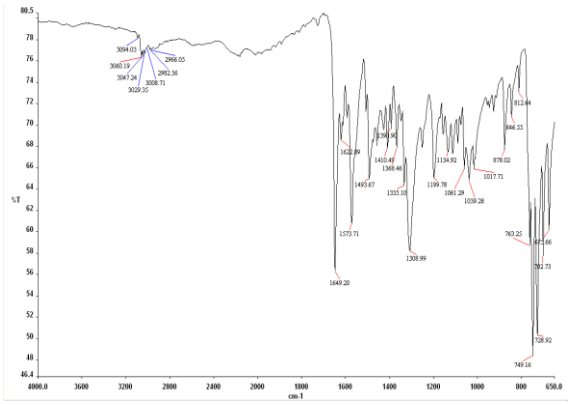


Figure 1. The FT-IR spectra of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**)

In the ^{1}H-NMR results of the title compound **4**, the presence of two different methyl protons is observed at 1.62 and 3.25 ppm, while aromatic protons are observed in the range of 7.28-8.30 ppm (Figure 2, Scheme 2-a).
In the ^{13}C NMR spectrum, the peaks at 158.75 and 158.13 ppm appear the presence of hydrazone carbonyl carbon and keto-imine carbon. The peak at 146.88 and 122.03 ppm confirms the presence of two different C-N carbons in the pyrazole unit. The peaks in the range of 133.89 – 123.24 ppm show aromatic carbons. (Figure 3, Scheme 2-b).

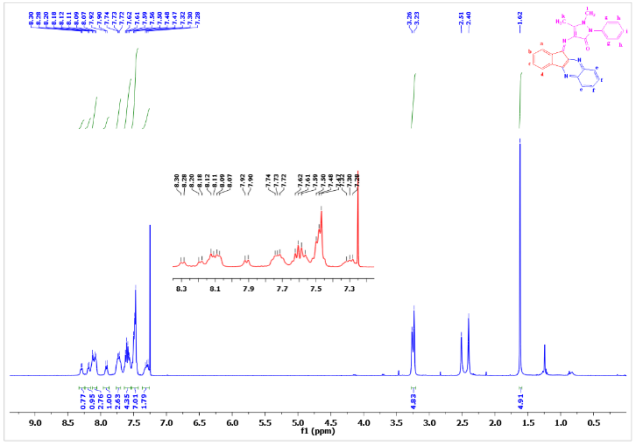


Figure 2. The ^{1}H-NMR spectra of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**) in $CDCl_3$.

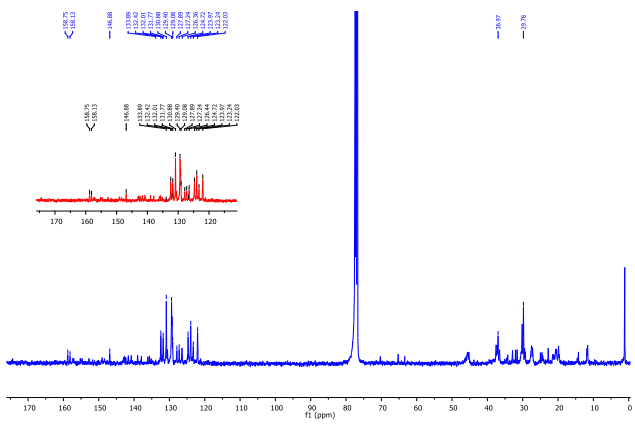
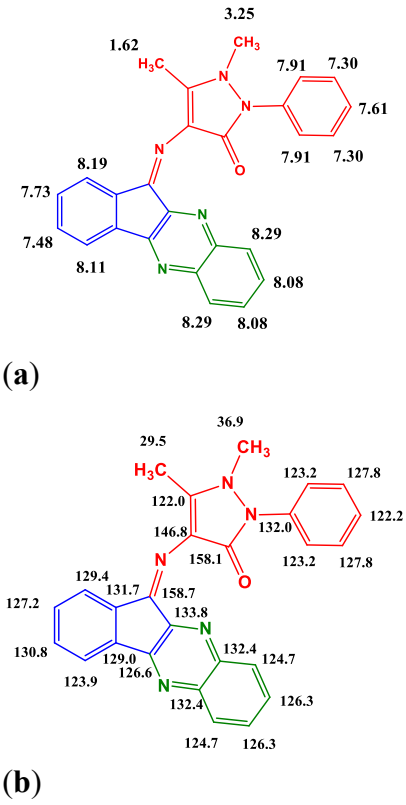


Figure 3. The ^{13}C-NMR spectra of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**) in $CDCl_3$.



Scheme 2. The ^{1}H-NMR and ^{13}C-NMR data for the title compound (**4**)

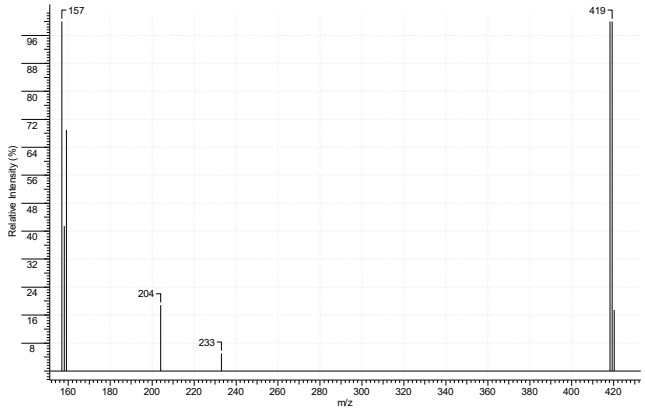


Figure 4. The mass spectrum of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**)

The UV-vis spectra of the title compound were studied in different solvent such as tetrahydrofuran, chloroform, methanol, acetonitrile and dimethyl sulfoxide. The title compound as a Schiff base exhibited absorptions in the range greater than 474, 477, 478, 485, 498 nm in nonpolar and polar solvents. [18,19].

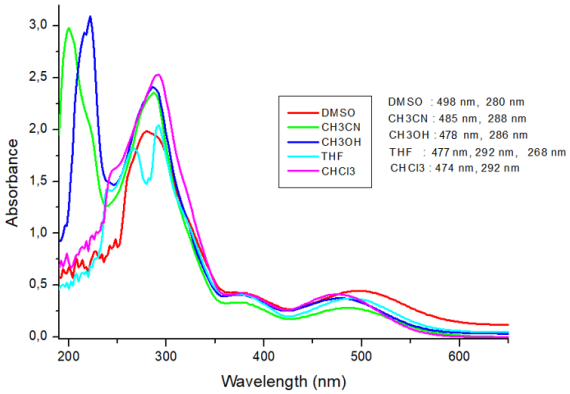


Figure 5. The UV-vis absorption spectrum of the 4-((11*H*-indeno[1,2-*b*]quinoxalin-11-ylidene)amino)-1,5-dimethyl-2-phenyl-1*H*-pyrazol-3(2*H*)-one (**4**) in different solvents.

3.2. Colorimetric ion sensing

In the absorbance spectrum of free compound as a receptor in the acetonitrile solution, three humps (at 485, 374 and 287 nm) appeared due to n-π*, π-π* transitions, respectively, as a results of the conjugation of indeno[1,2-*b*]-quinoxaline and pyrazole moieties (Figure S3). The sensing property of receptor (**4**) was first examined by mixing it with various metal ions solution as metal chloride salts in acetonitrile ($1x10^{-5}$ M). UV-vis spectra of the receptor in absence and the presence of different metal ions were recorded. Upon addition of 1 equivalent of various metal ions (Cu^{2+}, Hg^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+} and Fe^{2+}) to the acetonitrile solution of the receptor, the changes in absorbance were recorded. However, no significant change in the absorption spectra and color of the solution was exhibited, upon the Ni^{2+}, Mn^{2+}, Zn^{2+} and Fe^{2+} ion solutions (Figure 6-a). At the same time, it was observed that the color changes of receptor from reddish to yellow and lilac upon the addition of Cu^{2+} and Hg^{2+} solutions respectively (Figure S4 and Figure S5). It was also immediately observed in natural light and under a UV light at 365 nm, easily noticeable with the naked eye even at low concentration. (Figure 6-b, c).

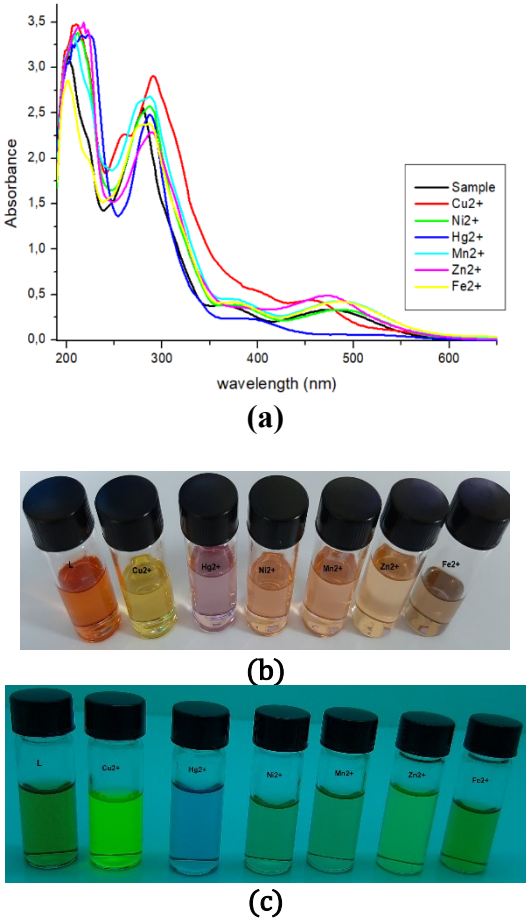


Figure 6. (a) UV-vis absorption spectra, (b) naked-eye color change observed under nat-ural light and (c) under a UV light 365 nm upon the addition of metal salts in CH3CN so-lution left to right Sample (L), Cu^{2+}, Hg^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+} and Fe^{2+}).

The stoichiometry of complexes was investigated via the titration method by using UV-vis spectrophotometry (Figure 7a, b) With the addition of Cu^{2+} and Hg^{2+} solutions ($1x10^{-5}$ M) to the title compound solution as receptor ($1x10^{-5}$ M), a decrease in the absorption band in-itially observed around 485 nm was detected. In the complexation titration, it gradually shifted to an absorption band approximately 460 nm for the addition Cu^{2+} solution, while it shifted to the absorption band range of 500 nm with the addition of Hg^{2+} solution (0-1 equiv). From the Job's plot data obtained, it

was determined that the complexation stoi-chiometry ([M^{n+} / L]) was 1:1 [20,21] (Figure 7c, d).

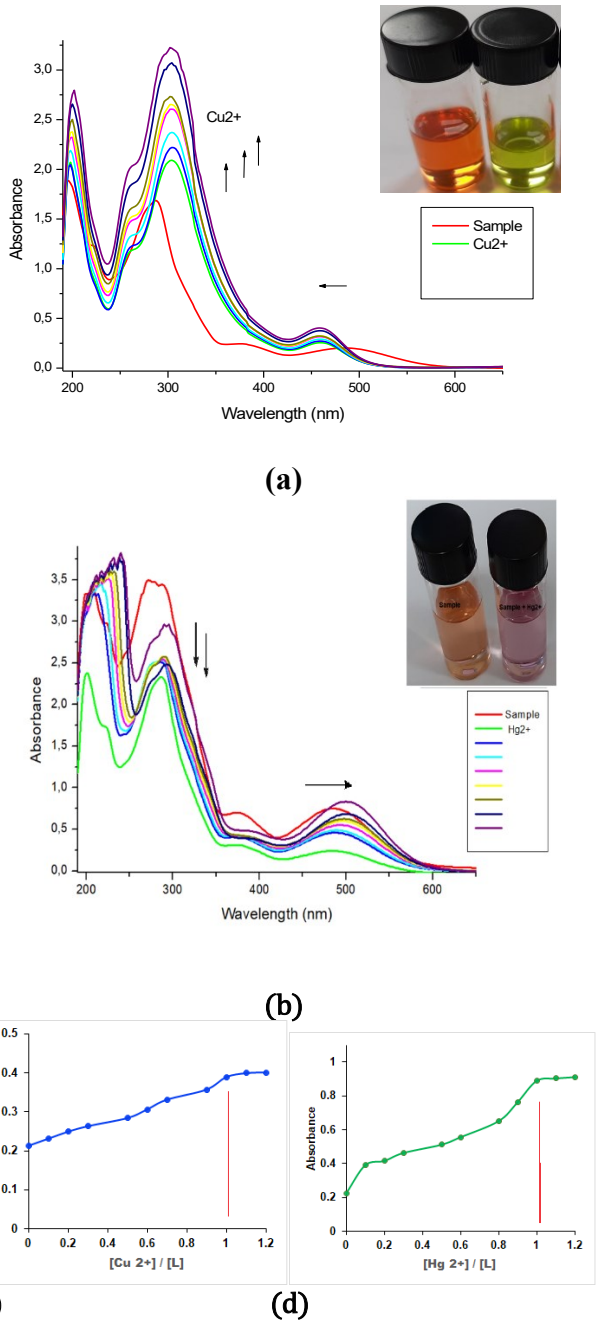


Figure 7. Change in UV-vis absorption spectra for acetonitrile solution of the title compound (1.0×10^{-5} M) with addition of different ions (0-1.2 equiv): (a) Cu^{2+}, (b) Hg^{2+}. The plots of absorbance changes in the title compound solution upon addition of Cu^{2+} and Hg^{2+} ions: (c) $0 \geq [Cu^{2+}]/[L] \leq 1.2$ at 460 nm, (d) $0 \geq [Hg^{2+}]/[L] \leq 1.2$) at 500 nm.

4. Conclusion

A new chemosensor including indeno[1,2-*b*]quinoxaline and pyrazol-3(2*H*)-one moieties has been synthesized as a Schiff base with good yield. Its structure was charactesized by spectroscopic methods. The colorimetric detection properties of different ions (Cu^{2+}, Hg^{2+}, Ni^{2+}, Mn^{2+} Zn^{2+} and Fe^{2+}) in acetonitrile solution by using the title compound were investigated both ultraviolet-visible (UV-Vis) spectroscopic method and the visibility with the naked-eye. In the detection of Cu^{2+} and Hg^{2+} ions among these ions, the change absorption values and the color from reddish to yellow and lilac, respectively, which is clearly to the naked-eye observed. The simple design of the title compound presented here may contribute to the development of more elaborate colorimetric ion chemosensors, as well as being used for the detection of Cu^{2+} and Hg^{2+} ions by test kits.

Acknowledgement

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