A new phthalimide based chemosensor for selective spectrophotometric detection of Cu(II) from aqueous medium

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ABSTRACT

A new phthalimide based chemosensor 2-(Pyridin-2-yl-(pyridine-2-ylimino)methyl)isoindoline-1,3-dione (PP3) was synthesized and characterized by IR, LCMS and NMR spectroscopic methods. The metal ions sensing ability of PP3 was examined by naked-eye and UV–Vis absorption techniques. The colorless solution of PP3 turned to yellow upon addition of Cu^2 and a new absorption band appeared at 434 nm. The Job's plot and HR-MS data confirms the formation of a new complex species between PP3 and Cu^2 in 1:1 binding stoichiometry. The sensor PP3 allowed the detection of Cu^2 down to 1.65 μM without any remarkable interference from the other tested metal cations.

1. Introduction

The development of optically active receptors for the qualitative and quantitative detection of transition metal ions has gained significant interest due to their crucial roles in various biological, engineering and ecological processes [1–3]. Copper is the third most abundant metal in the human body after zinc and iron, and well known for important roles in biological processes like biosynthesis of hemoglobin, developments of bones and protein enhancement [4–7]. The different metalloenzymes like tyrosinase, copper zinc superoxide dismutase (SOD), cytochrome *c* oxidase and lysyl oxidase in breathing organisms, copper has a vital role in them [8–10]. However, the redox-active properties of copper generate some reactive species which cause several troubles in the metabolism [8,9]. Nevertheless, over-accumulation of copper in an individual led to a range of disease counting neurodegenerative diseases such as Menkes disease, Alzheimer's disease, gastrointestinal disorders, Wilson's disease, prion disease, amyotrophic sclerosis, inflammatory disorders, kidney damage and lipid metabolism [11–14]. Further, copper has wider applications also in industrial and pharmaceutical sectors for the manufacture of wires, alloys, batteries, machine parts, drugs and fertilizers [15]. It may be noted here that in drinking water the permissible limit of copper is 2 ppm (30 μM)

according to World Health Organization (WHO) whereas, in the blood, the concentration of copper should not go beyond 100–150 μg/dL [16,17]. But extensive utilization of copper all over the world in industry and agricultural sectors amplified the risk associated with the Cu^2 pollution. Therefore, there is a need to develop novel, highly selective and cost-effective approaches to monitor and detect Cu^2 from various biological, industrial and environmental samples.

With the advancement of chemosensing field, the detection of Cu^2 down to micro/submicromolar levels by naked-eye and spectrophotometric recognition technique has raised an enormous significance due of its simplicity and cost-effectiveness [18,19]. Phthalimide and N-substituted phthalimides are important class of compounds because they possess a variety of applications including in the field of sensors development due to their fascinating photophysical properties [20–22]. Herein, as a part of our ongoing research [23–27], we have introduced a new receptor 2-[Pyridin-2-yl-(pyridine-2-ylimino)methyl] isoindoline-1,3-dione (PP3) for the discriminatory recognition of Cu^2 from the aqueous medium. The phthalimide based chemosensor PP3 developed in this communication becomes ultimate host molecule due to the presence of two pyridine rings joined by amidines linkage with two carbonyl groups of phthalimide moiety creating ideal environment for complexation with metal cations. Also, receptor PP3 is advantageous because it has uncomplicated structure, optical and thermodynamic stability and easy synthetic method. Receptor PP3 shows a perceptible color alteration from monotonous to bright yellow

and a hyperchromic shift in the absorption spectra selectively upon addition of Cu^2 among the other experienced metal cations.

2. Experimental

2.1. Materials and instrumentations

The chemicals, reagents, and solvents employed for performing various experimentation were obtained from Sigma Aldrich or Spectrochem depending on their accessibility and were utilized without any further purification. The progress of reactions as well as the purity of the compounds was analyzed by thin layer chromatography (TLC).

The IR spectra were recorded on Perkin-Elmer Spectrum One FT-IR spectrometer using KBr pellets and nujol mulls and the IR bands are expressed in frequency (cm^{-1}). The 'Bruker Avance II' Spectrometer, operating at 500 MHz was used to record ^1H and ^{13}C NMR spectra in $CDCl_3$ using TMS as an internal standard and the chemical shifts are given in ppm. U-3900 spectrophotometer (Perkin Elmer Co., USA) was used for UV–Visible absorption study. LC-MS spectra were recorded on Agilent's LCMS.

2.2. Synthesis of 2-(pyridin-2-yl(pyridine-2-ylimino)methyl) isoindoline-1,3-dione(PP3)

The intermediate compound N-(pyridine-2-yl) picolinimidamide was synthesized according to our known reported method [28].

In 100 mL dry round bottom flask, phthalic anhydride (1.48 g, 0.01 mol) and N-(pyridine-2-yl) picolinimidamide (1.98 g, 0.01 mol) were refluxed in acetic acid (50 mL) for 4 h. The reaction mixture was filtered-off when hot and the solvent was evaporated. The solid separated was filtered and recrystallized from ethanol.

IR (KBr pellet, cm^{-1}): 1728 ($\nu_{C=O}$), 1615 ($\nu_{C=C}$ Ar), 1465–1375 (for pyridine $\nu_{C=C}$); Mass: Expt. (ESI Ve): 329 (M 1), 330 (M 2), Cacl. 328.09; ^1H NMR (500 MHz, $CDCl_3$, δ ppm): 7.08 (dd, $J = 5.5$ Hz and $J = 1.3$ Hz, 1H), 7.38 (ddd, $J = 7.5$ Hz and $J = 4.5$ Hz and $J = 2.7$ Hz, 1H), 7.50 (ddd, $J = 7.5$ Hz and $J = 4.8$ Hz and $J = 2.7$ Hz, 1H), 7.76 (ddd, $J = 6.2$ Hz and $J = 4.7$ Hz and $J = 2.7$ Hz, 1H), 7.79 (ddd, $J = 5.3$ Hz and $J = 4.8$ Hz and $J = 2.7$ Hz, 1H), 7.85 (dd, $J = 5.5$ Hz and $J = 2.7$ Hz, 2H), 7.89 (dd, $J = 7.5$ Hz and $J = 2.7$ Hz, 2H), 8.38 (d, $J = 4.1$ Hz, 1H), 8.43 (d, $J = 8.2$ Hz, 1H), 8.65 (d, $J = 4.8$ Hz, 1H). ^{13}C NMR (500 MHz, $CDCl_3$, δ ppm): 168.1, 162.5, 151.0, 149.2, 148.2, 148.1, 138.3, 137.5, 134.2, 132.6, 126.7, 123.5, 122.3, 119.8, 113.9.

2.3. Spectroscopic study

The solution of PP3 (1.0×10^{-3} M) was prepared in ethanol: H_2O (20:80, v/v) and used as stock solution. All cations solutions (1.0×10^{-2} M) were made in water. For the UV–Vis absorption titration, the requisite quantity of the diluted receptor PP3 solution (2 mL, 1×10^{-5} M) was poured into the cuvette. The Cu^2 ions (0–500 μL, 1.0×10^{-3} M, in H_2O) were added with help of micropipette and after each consecutive addition, the spectra were recorded.

3. Results and discussion

The synthesis of receptor PP3 was shown in Scheme 1. The structure of PP3 was well characterized by various spectral (NMR, IR and LCMS) data (Figs. S1–S4). Then, the recognition properties of PP3 were studied experimentally towards different metal cations by naked-eye and UV–Vis absorption techniques.

In naked-eye experiment (Fig. 1), the colorless solution of PP3 (2 mL, $1x 10^{-3}$ M) in ethanol:H_2O (20:80, v/v) becomes yellow in presence of Cu^2 (1 mL, 1×10^{-2} M, in H_2O) among the other tested metal cations (Ag, Al^3, Ba^2, Ca^2, Cd^2, Co^2, Cr^3, Cs, Fe^2, Fe^3, Hg^2, K, Li, Mg^2, Mn^2, Na, Ni^2, Pb^2, Sr^2 and Zn^2). These obtained results evidently pointed out the selective colorimetric response of PP3 towards Cu^2. Further, the quantitative Cu^2 ions recognition ability of PP3 was examined in details with the help of spectrophotometric method.

The variations in the absorption spectrum of PP3 in EtOH:H_2O (20:80, v/v) (2 mL, 1.0×10^{-5} M) in presence of different metal ions (40 μL, 1.0×10^{-2} M in H_2O) are shown in Fig. 2. The $\pi \rightarrow \pi^*$ transitions in receptor PP3 are responsible for generation of two intense absorption bands at 288 nm and 352 nm. The addition of Cu^2 ions considerably and specifically affects the absorption bands of PP3. The absorption band of PP3 at 288 nm was shifted to 277 nm whereas the absorbance of the band at 352 nm was diminished and concurrently a new band appeared at 434 nm. The appearance of a new band in the visible region is responsible for the generation of the distinct yellow color for the new complex species formed in the solution. On the other hand, no perceptible spectral transformation was observed with the other tested metal ions.

3.1. Sensitivity study of PP3

To attain a clearer perception of the cation recognition ability of PP3, the absorption titration of PP3 was performed with Cu^2 ions. As shown in Fig. 3, upon successive incremental addition of Cu^2 ions (0–500 μL, 1.0×10^{-3} M, in H_2O) to the PP3 solution (2 mL, 1×10^{-5} M) in EtOH:
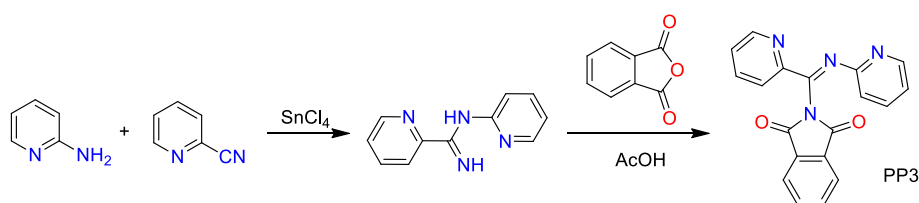
Scheme 1. Synthesis of sensor PP3.

Fig. 1. Naked-eye recognition of Cu^2: the vials containing PP3 (2 mL, 1.0×10^{-3} M) in EtOH:H_2O (20:80, v/v) upon addition of various metal ions (1 mL, 1.0×10^{-2} M, in H_2O).
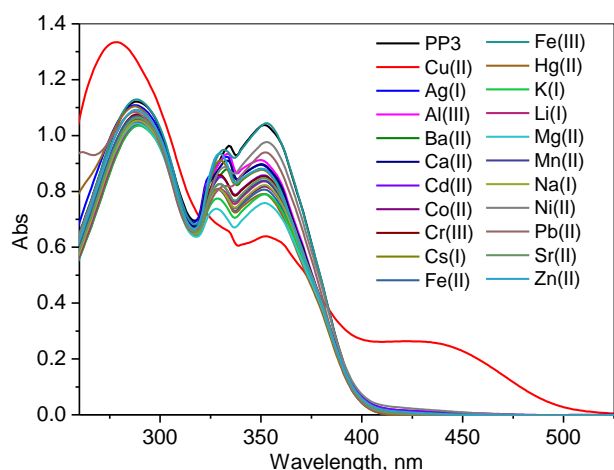
Fig. 2. Absorption spectra of PP3 (2 mL, 1.0×10^{-5} M) in EtOH:H$_2$O (20:80, v/v) on addition of different metal ions (40 L, 1.0×10^{-2} M, in H$_2$O).

H$_2$O(20:80, v/v), the absorption band centered at 288 nm was blue-shifted whereas the band at 352 nm was drenched and concomitantly a new red-shifted band appeared to 434 nm with the formation of an isosbestic point at 384 nm. The emergence of a new band at 434 nm and formation of an isosbestic point indicates the development of a new complex species in solution upon interaction of Cu^2 with PP3.

Using the titration data, the absorbance at 434 nm was plotted against the concentration of Cu^2 added (Fig. S5) and then the slope of the calibration curve was determined. According to the IUPAC definition, the limit of detection (LOD) and limit of quantification (LOQ) can be calculated by using the relationship LOD = (3.3 x standard deviation)/slope and LOQ = (10 x standard deviation)/slope, where the standard deviation was obtained by recording the absorption of ten blank samples. The estimated LOD and LOQ of PP3 for Cu^2 was found to be 1.65 μM and 5.00 μM, respectively. The obtained LOD is far lower than the maximum permissible limit of Cu^2 concentration approved in drinking water. Also, the analytical parameters of PP3 are superior/comparable with the reported Cu^2 selective colorimetric sensors (Table S1).
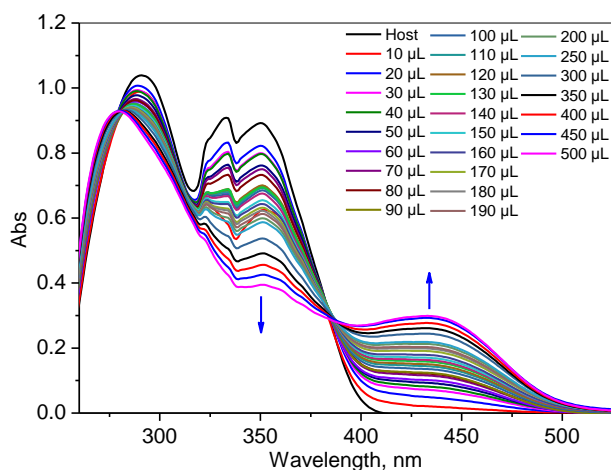
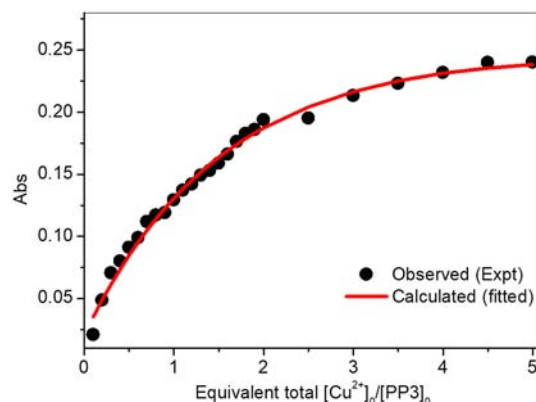### 3.2. Binding stoichiometry study of PP3

The binding stoichiometry of PP3 with Cu^2 was first analyzed by Job's Method [29]. The complex formation between PP3 and Cu^2 in a 1:1 binding stoichiometry was supported by Job's plot (Fig. S6). In addition to this, direct confirmation for the formation of a 1:1 complex was achieved from the HR-MS spectra of PP3 in the presence of Cu^2 ions (Fig. S7). When 1.0 equivalents of Cu^2 was added to PP3 solution, a new peak appeared at $m/z = 547.0$ corresponds to the complex [(PP3) Cu^2 ClO$_4^-$ H$_2$O K].

The association constant (K$_a$) of the complex species formed in solution upon interaction of PP3 with Cu^2 was estimated from the absorption titration data by applying the non-linear curve fitting approach proposed by Thordarson [30] and the online analysis tool bindfit available freely on the link 'http://app.supramolecular.org/'. The fitted titration data at 434 nm gave best fit for the 1:1 model with the estimated K$_a$ of $11,616.96 \pm 3.5$ M^{-1} (Fig. 4). Analyzing the titration data also gave the species distribution curve of PP3 and the PP3-Cu^2 complex at different intervals during the titration is shown in Fig. S8.

Considering the experimental evidence, the optimized molecular geometry of PP3 and its PP3-Cu^2 complex was predicted by using B3LYP functional level and 6-31G basis set with the computer program Gaussian 09 W [31] (Fig. S9). The adopted DFT method gave satisfactory results in predicting the electronic properties of the host-guest complex [32,33]. Analyzing the electronic properties of PP3 and its complex with Cu^2, it is observed that the energy of both highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) reduces in PP3 to PP3-Cu^2 system, and resulting an overall decrease of the gap from 3.7068 eV to 0.9821 eV (Fig. 5). The figure also exposes that the charge density at HOMO of PP3 is gathered over pyridine fragment and phthalic anhydride moiety and upon complexation with copper ion the charge density is shifted towards terminal pyridine moiety. The driving force for decreasing the energy from PP3 to PP3-Cu^2 is probably due to the higher stabilization of PP3-Cu^2.

3.3. Interference study of PP3

The UV–Vis absorption response of receptor PP3 towards Cu^2 ions in the presence of probable interfering metal cations was examined. In this experiment, 16 μL of Cu^2 ions (2 equivalents, 1.0×10^{-2} M, in H$_2$O) were added to the solution containing PP3 (1.0×10^{-5} M) in EtOH:H$_2$O (20:80 v/v) and two equivalents of the other competitive metal ions (16 μL, 1×10^{-2} M, in H$_2$O) and then their absorption spectra were recorded. The bar representation of the spectral changes observed during interference study indicates that the Cu^2 selectivity of PP3 was not interfered by the existence of the additionally tested metal cations (Fig. 6).

Fig. 3. Change in absorption spectrum of PP3 (2 mL, 1×10^{-5} M) in EtOH:H$_2$O (20:80, v/v) with the incremental addition of 0–5 equivalents of Cu^2 ions (1×10^{-3} M, in H$_2$O).

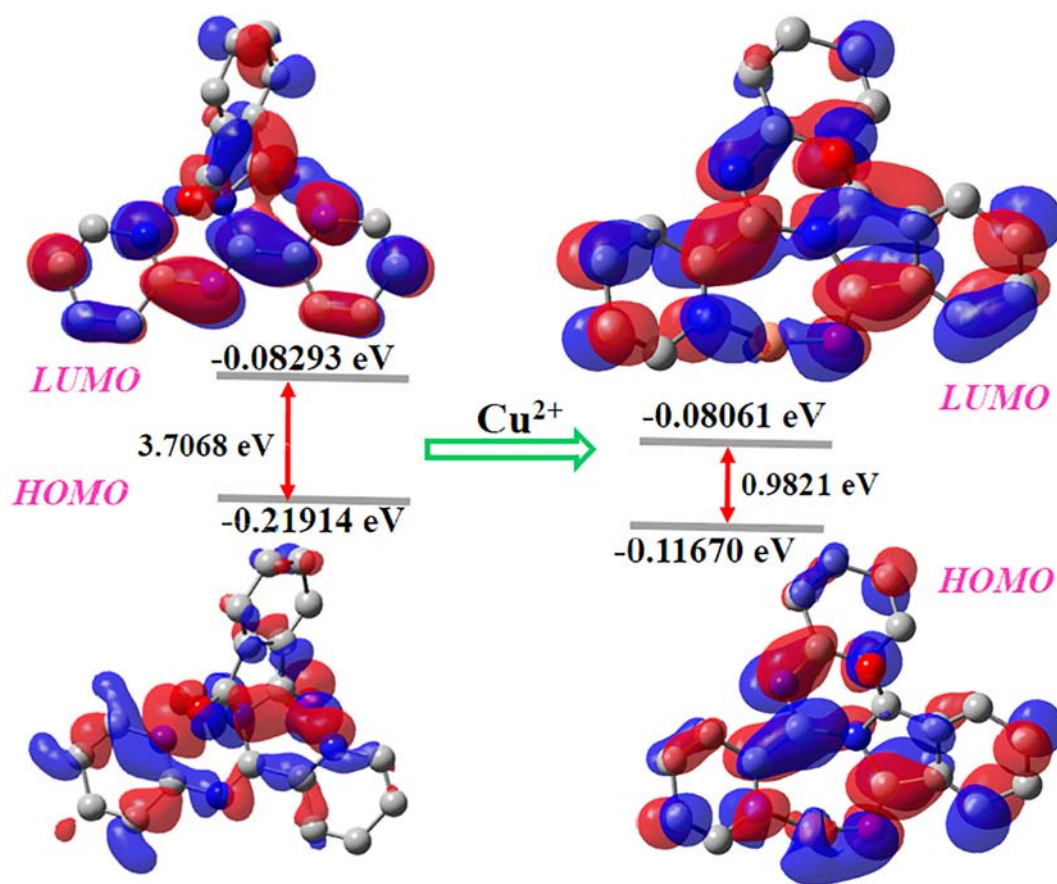**Fig. 4.** The binding fitting curve for receptor PP3 with Cu^2.

Fig. 5. HOMO-LUMO energy gaps in PP3 and PP3-Cu^2 complex.

3.4. Practical applications of PP3 based on test strips and solid supported techniques

To inspect the practical utilization of receptor PP3 to sense Cu^2 ions from an aqueous atmosphere, test strips loaded with sensor PP3 were prepared. The tiny strips of cellulose paper (Whatman No. 42) were prepared by soaking in the solution of PP3 (1×10^{-3} M) in methanol and then desiccated in the air. The monotonous strips piercingly turned to dark yellow color when the strip was wet into an aqueous solution of Cu^2 (1×10^{-2} M) (Fig. 7a). The speedy alteration of the color of the test strip in solution undoubtedly deduces the practical application of PP3. Then, the solid support method was employed to examine the detection of Cu^2 by sensor PP3. The 5.0 g of colorless silica (60–120 mesh) was dripping wet in PP3 (in MeOH, 5 mL, 1×10^{-3} M) and then the solvent

was removed. Due to the adsorption of the sensor PP3 on the surface, the color of the silica gel becomes visible as very faint off-white. When an aqueous solution of Cu^2 (10 mL, 1×10^{-2} M) was added into it, the colorless solution rapidly twisted to an orange-yellow colored (Fig. 7b). The instant color transform of the solid silica gel in solution evidently figure out the practical application of PP3for the qualitative recognition of Cu^2 in aqueous media.

4. Conclusions

In summary, the selective recognition of Cu^2 ions from the aqueous environment by simple to prepare phthalimide based chemosensor PP3 was introduced. The generation of a absorption band at 434 nm is the result of complex formed between sensor PP3 with Cu^2 in 1:1 binding stoichiometry. The spectral changes occurred at 434 nm can be
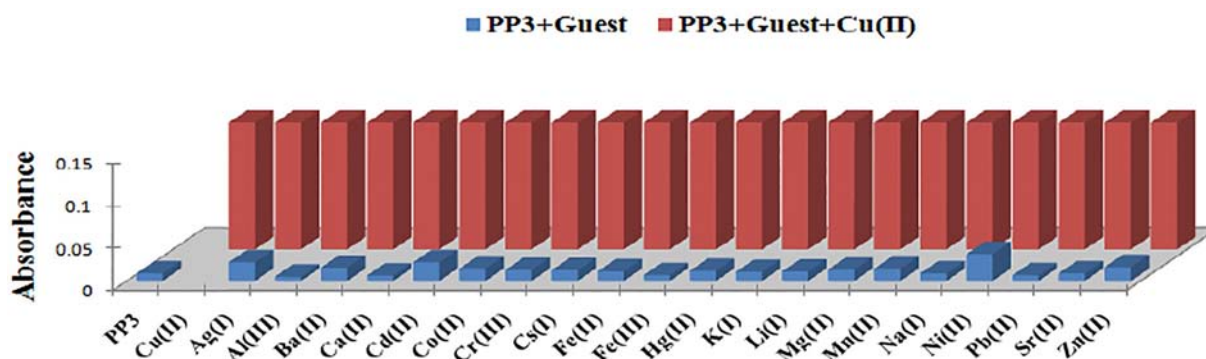

Fig. 6. Competitive responses of PP3 in the presence of Cu^2 and other intrusive metal cations.

Fig. 7. Practical application of PP3 to detect Cu^2 by: (a) test strip and (b) Solid support techniques.

calibrated with the added concentration of Cu^2 to the PP3 solution and the detection of Cu^2 can be made possible down to 1.65 μM, which is a lot improved than the permissible concentration limit of Cu^2 in drinking water. Without any noticeably interference effect, sensor PP3 can be useful for the colorimetric recognition of Cu^2 ions in an aqueous medium by naked-eye by means of test trip and silica support method.

Acknowledgement

Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data includes experimental details, spectral characterization data, job's plot, DFT computed structure, mass data of complex, calibration curve. Supplementary data to this article can be found online at doi:https://doi.org/10.1016/j.saa.2019.05.034.

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