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Synthesis of an optically switchable salicylaldimine substituted naphthopyran for selective and reversible Cu^{2+} recognition in aqueous solution

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A light controlled reversible switch for copper ion was synthesized by substituting photochromic naphthopyran with a salicylaldimine moiety. The naphthopyran based photoreversible receptor was characterized using IR, NMR, HRMS and single crystal X-ray crystallographic techniques. The photochromic properties of receptor under light irradiation were investigated using UV-Visible spectroscopy. Affinities towards transition metal ions in both closed and the open form were determined. The open form of the receptor displayed increased affinity towards copper ions. A 3.25×10^4 fold difference in binding affinity for copper ions between the closed and the open form in aqueous methanol solution suggested that the receptor can act as a selective photoswitch for copper ions. Theoretical investigations at molecular level supported the experimental observations.

Introduction

The design and synthesis of photochromic ligands that are able to complex paramagnetic transition metal ions such as Cu^{2+} to produce complexes controlled by light, constitute a largely unexplored subject in the interdisciplinary area of supramolecular chemistry. Recently, the copper ions based switchable molecular magnets are discovered as promising systems, which are strongly dependent on the coordination geometry of Cu^{2+} ions.[1] The switchable magnetic properties requires spin crossover compound (SCO) consisting of transition metal ions and organic ligands with switching ability between two different spin states induced through external stimuli such as light, temperature etc.[1, 2] The presence of small amount of copper ions is also essential for biological processes such as gene expression and enzymatic reaction.[3] However, copper ions in excess are also believed to be responsible for a number of disorders.[4, 5] The deposition of surplus copper causes dreaded Menkes and Wilson disease,[6] amyotrophic lateral sclerosis [7] and Alzheimer disease,[8] which pose a key challenge to the researchers to devise sensors in a highly judicious manner. Chemical complexation or chemical therapy with judicious selection of synthetic receptor can be helpful to counter Cu^{2+} accumulation in the cells and the environment. The utility of the synthetic receptor can be enhanced if the receptors are regenerated. The synthetic receptors reported in the literature for detection of transition metal ions at low concentration are usually difficult to regenerate. Reversible light controlled receptors, which can be conveniently regenerated using light are worth being explored as no other additives are required. If the release of encapsulated metal ion is controlled by light, the time and the location of release is dependent on when and where light of suitable wavelength is applied. Therefore, there is a need to develop reversible complex systems using photochromic compounds to complex transition metal ions like copper.

Photochromic molecules are extensively investigated for potential applications in digital electronics, optical senors, data recording devices, spintronics, logic gate, optical lenses, quantum computing and environmental monitoring to prevent toxic effect of metal ion pollution.[9-15] Photoreversible frameworks like chromene,[16] spirooxazine,[17] spiropyran,[18-22] spiroindoline and others[23, 24] show enhanced affinity towards heavy metal coordination on incorporation of heteroatoms.[25] Photochromism is an interesting phenomenon,[26] where the structural alternation takes place between two different forms having different absorption bands in a reversible manner. Light stimulation alters the structural arrangement of photochromic molecules into two different forms, namely the closed form and the open form. The polar open form attract and coordinate the polar species such as metal ions.[17] The polar open form having a suitably positioned hetero atom (ortho to the phenolic oxygen atom) is expected to enhance the coordination of metal ion. Therefore, in this paper, a host naphthopyran receptor was designed by incorporating a salicylaldimine unit at a suitable position for improved metal ion coordination. The receptor is expected to swiftly respond to the UV-light irradiation and display good fatigue resistance

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owing to the presence of naphthopyran unit. The presence of suitably positioned functional group Schiff's base (-CH=N) and -OH in the parent molecule adjacent to the phenolic oxygen atom may force the vulnerable C-O single bond to break in the presence of metal ion and lead to an open form complex with visible color change. In a first-of-its-kind, we have designed a naphthopyran chelator, with excellent switching ability. To our knowledge, rarely articles based on photoreversible naphthopyran are reported for Cu^{2+} detection. For example, a recent report based on detection of trivalent metal ions and Cu^{2+} ions appeared in literature.[27] However, the sensor was not selective. Couple of reports are also available in the literature for Ca^{2+} and Pb^{2+} ions.[28, 29]

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz *Joel NMR* ECX 400 NMR spectrometer. IR spectra were recorded on a Perkin Elmer IR spectrometer. Chemical shifts are reported in parts per million relative to residual solvent signal or TMS. UV–visible spectra were recorded on an Ocean optics USB4000 UV–visible spectrometer.

The compound **4** was prepared as per the procedure given in the literature (Scheme S1).

Synthesis of naphthopyran 1:

A solution of **4**[29] (1.0 g, 2.86 mmol) in ethyl acetate (20 mL) was taken in a 100 mL round bottom flask equipped with a magnetic stirrer bar. Then salicylaldehyde (0.30 mL, 2.85 mmol) in methanol (30 mL) was transferred to the above reaction flask. The resulting mixture was allowed to stir for 2 hours. The solution was concentrated under reduced pressure and the residue was precipitated out using methanol to afford orange colored compound **1** in (0.61 g) 47 % yield (m.pt. 196-198 ^{o}C.) which was characterized by ^{1}H and ^{13}C-NMR, FT-IR and MALDI-MS. ^{1}H-NMR (400MHz, DMSO-d_6): δ =13.93 (*s*, 1H, OH), 9.20 (*s*, 1H, N=CH-), 8.11 (*d*, 1H, *J* = 8Hz, ArH), 7.93 (*s*, 1H, ArH), 7.84 (*d*, 1H, *J* = 8 Hz, ArH), 7.71 (*d*, 1H, *J* = 7.6 Hz) 7.57-7.38 (m, 8H, ArH), 7.34 (*t*, 4H, J = 7.2 ArH), 7.22 (*t*, 2H, *J*= 14.8, ArH & ArC=CH), 7.02 (t, 2H, *J* = 7.6 Hz) 6.73 (*d*, 1H, *J* = 10Hz, ArC=CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7 (N=CH), 157.0, 150.9, 143.0, 141.7, 141.4, 140.6, 140.1, 139.2, 139.1, 136.3, 135.7, 135.2, 134.4, 131.8, 130.7, 130.1, 126.3, 122.9, 117.5, 85.3 (C_{spiro}-O). Elemental analysis: calculated for ($C_{32}H_{23}NO_2$) C: 84.74, H: 5.11, N: 3.09, found C: 84.48, H: 4.96, N: 3.09. HR-MS (MALDI-MS): $C_{32}H_{23}NO_2$, *m/z* = calculated 453.1729 M^+ found 453.1585.

Computation: For all calculations, the program Gaussian 09 with Gaussview were used.[30] The initial geometry of the receptor **1** was constructed using Gaussview 05 and optimized with AM1 method using Gaussian 09. The receptor **1** was then subjected to geometry optimization using different methods which include B3LYP, PBEPBE and hybrid density functional models (mPW1PW91) using 6-31G(d) basis set. PCM model for solvation was employed for optimization in solvents.[31] The frequency calculations were used to confirm the presence of transition state or local minima for the optimized structure. The resulting geometries were used to obtain single point energy. The ring opening process was defined by scanning C_{spiro}-O bond length, while the *cis-trans* isomerization of the open form was investigated through respective dihedral angle scan. The energy maximum obtained through the potential energy scan was used as initial geometry for further optimization using "opt = TS" command, followed by procedure as reported earlier in the literature.[32, 33] The open form of the parent naphthopyran unit may exist as four stereoisomers (Scheme S2) with two out of the three bonds connecting the aromatic benzene rings may be cissoids ("c") or transoid ("t").

Similarly, closed and open form (TC) geometries complexed to copper ions were also optimized using MPW1PW91/6-31G(d)/LanL2dz and B3LYP/6-31G(d)/Lanl2dz methods.

Procedure for UV-visible spectra of open and closed forms of 1 with different metal ions:

A 1.1 mL solution of chelator **1** (5.0×10^{-5} M) was prepared in a quartz cuvette and 1.1 mL of different metal ions (5.0×10^{-5} M) were mixed well and the UV-visible spectrum was recorded on an Ocean Optics USB4000 UV-Visible spectrometer.

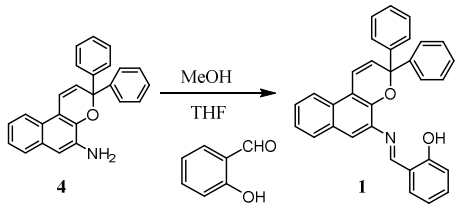
Procedure for determination of first order rate constant for thermal bleaching: A 2.2 mL solution of **1** (1.4×10^{-5} M) was prepared in a cuvette, maintained at 25 ^{o}C. The absorbance was recorded every second using the Ocean Optics software. The solution was irradiated, stirred while monitoring the change in absorbance till no further change in absorbance was detected in the visible region. Similar procedures were followed for determination of rate of thermal decay in different solvents and corresponding rate constants (k_T, s^{-1}) were calculated.

Fatigue study procedures:

A 2 mL solution of **1** (3.6×10^{-5} M) was prepared in a cuvette maintained at 25 ^{o}C. The solution was irradiated with a Mercury vapor 125 W lamp. The absorbance was recorded every second using the Ocean Optics software. The lamp was closed and the sample was left in the dark until the spectrum resembles that of the original solution. This process was repeated five times.

Results and Discussion

The target naphthopyran receptor **1** was synthesized using amine substituted naphthopyran **4** in four steps (Scheme 1 and S1). The naphthopyran derivative **4** was synthesized starting from 3-amino-2-naphthol, which was treated with di-*tert*-butyl dicarbonate in THF to yield an intermediate **2**. The intermediate **2** was refluxed with 1,1-diphenyl-2-propyn-1-ol in ethylene dichloride to obtain **3**, which on acidic hydrolysis provided intermediate **4** in good yield. The intermediate **4** was treated with salicylaldehyde in methanol:ethyl acetate (1:1) solvent in presence of catalytic amount of HCl to produce yellow crystals of naphthopyran receptor **1** in 47 % yield. The receptor was characterized by ^{1}H and ^{13}C NMR spectroscopy, MALDI-MS and FT-IR spectroscopy (Figure S1-S3, ESI).



Scheme 1. Synthesis of the naphthopyran receptor **1**.

Suitable crystals of naphthopyran receptor **1** for single crystal X-ray diffraction were obtained through the slow evaporation method using ethyl acetate as the solvent. The receptor **1** crystallized as monoclinic crystal with $p2_1/n$ space group (Figure 1). The asymmetric unit of the receptor **1** revealed the presence of short intramolecular hydrogen bond contact between O_4 and N_2 [2.562(3) Å]. The aromatic ring of salicylaldimine moiety and the naphthopyran unit displayed a torsion angle (C_{26}-C_3-C_8-C_{17}) of 77.6(2)°. The aromatic benzene rings attained a perfect orthogonal shape with respect to the naphthopyran unit. The bond lengths and bond angle observed in the crystal structure are listed in Tables S3 and S4. The crystal packing diagram of the receptor **1** revealed several intermolecular short contacts (Figure S4, Table S2, ESI) particularly between O_4-H_{32}, O_4-H_{19}, C_{22}-H_{25} and H_{34}-C_{25}, C_3, C_{20}. The high stability or rigidity of the crystal structure can be ascribed to the presence of short intermolecular contacts. The two phenyl groups held each other to the spiro carbon atom in two different planes and are present away from the substituted phenol unit to provide chance to hetero atoms for effective interaction. Intermolecular π···π stacking interactions with centroid (C_3-C_{20}-C_{12}-C_{26}-C_{27}-C_{25}) to centroid (C_6-C_{16}-C_7-C_{19}-C_{17}-C_{14}) distance 3.676(2) Å (Figure S5, ESI) and intermolecular edge to face interactions with a distance of 2.551(2) Å (Figure S6, ESI) were also observed between the aromatic rings of naphthopyran.

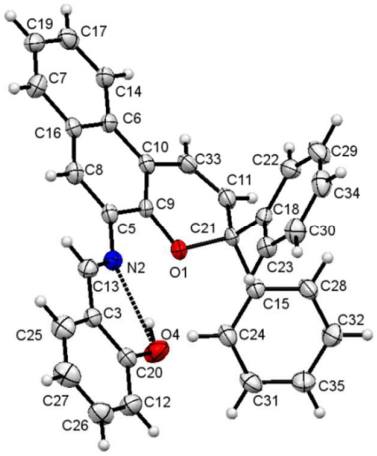


Figure 1. ORTEP[34] view of receptor **1** with displacement ellipsoids at the 50% probability level. An intramolecular H-bonding of 2.562(3) Å (shown by dotted line) between O_4-N_2 (CCDC 1422523).

Normally, the photoswitching behavior of a photochromic molecule is largely dependent on C_{spiro}-O bond length and probably considered as one of the most important parameter in the conversion of the closed form to the open form. The crystal structure of the receptor **1** provided a value of 1.462 Å for C_{spiro}-O bond length, which indicated that the receptor **1** is a reasonably good photochrome. The absorption spectra of the receptor **1** was recorded in different solvents and observed an absorption band in 280-390 nm region. The UV light irradiation of a solution of the receptor **1** in different solvents resulted in an absorption band in 390-530 nm range (Figure 2). The thermal decay of the open form to the closed spiro form was monitored with time. The thermal decay of the open form followed first order reaction kinetics (equation 1). The experimental data obtained was fitted to the first order reaction kinetic equation to obtain the rate constant values in different solvents (Table 1, Figures S8 and S9), where A_t, A_{eq} and A_0 are absorbance of the open form at time t, infinity and zero after UV light irradiation.[29] The thermal bleaching data was also interpolated to mono-exponential (equation 2) and bi-exponential functions (equation 3). The slow decaying component of the open form was negligible leading to better fit with monoexponential function (Figure S10).[35-39]

$$\ln\left(\frac{A_t - A_{eq}}{A_0 - A_{eq}}\right) = -k_{dec}t \quad \text{------ equation 1}$$

$$A = A_1\exp(-k_{dec}t) + R \quad \text{------ equation 2}$$

$$A = A_1\exp(-k_{1dec}t) + A_2\exp(-k_{2dec}t) + R \quad \text{------ equation 3}$$

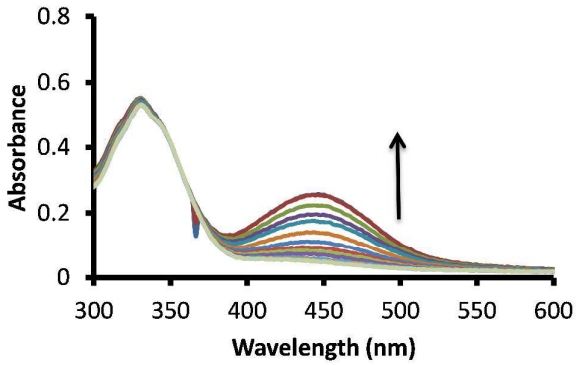


Figure 2. UV-Visible spectra of ring opening of naphthopyran receptor **1** ([**1**]=2.5×10^{-5} M) in methanol:water (1:1, pH=7.6, 1.0 mM HEPES) at 25 °C.

Table 1. Thermal bleaching Rate constants (k_T/s^{-1}) in different solvents ([**1**] = 1.4 ×10^{-5} M) at 25 °C.

Solvent	EA	THF	DCM	i-PrOH	Acetone	MeCN	MeOH	DMSO
k_T/s^{-1} at 25 °C	0.030	0.032	0.033	0.019	0.051	0.031	0.070	0.063
ε	2.38	6.02	7.85	8.93	17.9	20.7	37.5	32.7

The rate constant data obtained was correlated with the dielectric constant values, which suggested that the receptor **1** exhibit solvent independent photochromism (Table 1).

The fatigue resistance properties of the receptor **1** were investigated in methanol (Figure S11) and methanol:water solvent system (1:1, pH 7.6, 1.0 mM HEPES). A solution of the receptor **1** in methanol or methanol:water (1:1, pH 7.6, 1.0 mM HEPES) was treated five times with UV light followed by ring closure under dark conditions. The absorption maxima at 445 nm *versus* time was plotted with light in, switch on and switch off manner, which suggested remarkable fatigue resistance (Figure 3).

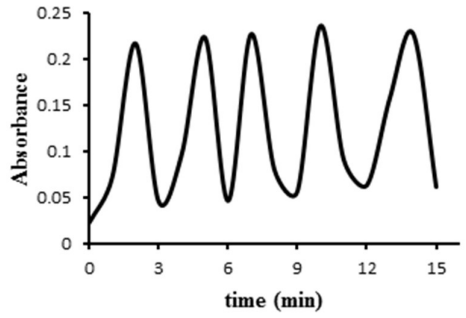


Figure 3. Five cycles of UV irradiation of **1** ([**1**] = 3.6 × 10^{-5} M) at 25 °C followed by visible light irradiation (absorbance at 445 nm) in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

The advantage of receptor **1** is the presence of salicylaldimine moiety at a unique position, which can be exploited for selective binding of metal ions. Therefore, receptor **1** was evaluated for affinity towards transition metal ions through naked eye detection. A pale yellow color visible to the naked eye was observed in the presence of one equivalent copper ions in aqueous buffered methanol solution (1:1, pH 7.6, 1.0 mM HEPES) (Figure 4). A more intense color was observed in pure methanol solution (Figure S12). No change in color was observed in the presence of other metal ions.

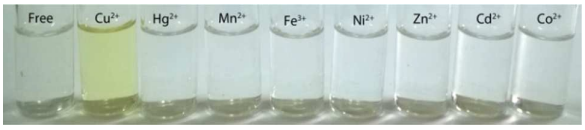


Figure 4. Color change on addition of one equivalent of acetate salt of various cations into a solution of receptor **1** in MeOH:water (1:1, pH 7.6, 1.0 mM HEPES). [**1**]=[Cu^{2+}]=[Hg^{2+}]=[Zn^{2+}]=[Ni^{2+}]=[Co^{2+}]=[Mn^{2+}]=[Fe^{3+}]=[Cd^{2+}]=2.5×10^{-5} M.

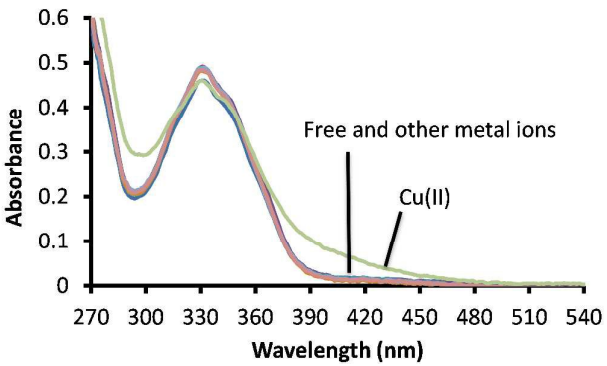


Figure 5. Spectral change upon addition of one equivalent of acetate salt of various cations into a solution of receptor **1** in MeOH:water (1:1, pH 7.6, 1.0 mM HEPES). [**1**]=[Cu^{2+}]=[Hg^{2+}]=[Zn^{2+}]=[Ni^{2+}]=[Co^{2+}]=[Mn^{2+}]=[Fe^{3+}]=[Cd^{2+}]=2.5×10^{-5} M.

The selective complex formation between the copper ions and the receptor **1** was further investigated using UV-Visible spectroscopy. A spectral shift to 400 nm was observed in the absorption spectra of receptor **1** on addition of one equivalent copper ions (Figure 5, S13), while no spectral change was observed on addition of other metal ions.

In order to assign the observed spectral shift in the presence of copper ions to the open form complex or to the closed form complex in methanol:water solvent system (1:1, pH 7.6, HEPES), a UV-Visible spectrum of the receptor **1** in the presence of one equivalent triethylamine was recorded. The shift in the UV-Visible spectra of the receptor **1** (Figure S14) to 400 nm was observed. This shift in the spectra of receptor **1** suggested that the spectral shift observed in a solution of copper ions and receptor **1** was due to the formation of a complex between the closed form of the receptor **1** with copper ions.

In order to obtain the affinity of the closed form of the receptor **1** towards the copper ions in the dark, titration experiments were performed and data obtained was used for calculation of the association constant using HypSpec software (Figure 6).[40] Different binding models were considered to fit the experimental data to observe best fit model (Scheme 2). When 1:1 binding model was considered between copper ions and receptor **1**, a best fit model was attained between the observed and the calculated data (Figure 7). The association constant logβ value of 2.036 ± 0.004 ($K_{association}$ = 1.08 × 10^2 M^{-1}) suggested that the closed form of the receptor **1** has an affinity for copper ions. The 1:1 complex stoichiometry between copper ions and receptor **1** was further confirmed by Job's plot (Figure 8).

$$\mathbf{1} + Cu^{2+} \overset{K_{11}}{\rightleftharpoons} \mathbf{1}\text{-}Cu^{2+}$$

$$\mathbf{1} + Cu^{2+} + \mathbf{1} \overset{K_{21}}{\rightleftharpoons} \mathbf{1}_2\text{-}Cu^{2+}$$

$$\mathbf{1}\text{-}Cu^{2+} + Cu^{2+} \overset{K_{12}}{\rightleftharpoons} \mathbf{1}\text{-}(Cu^{2+})_2$$

Scheme 2. The binding model used in the determination of the association constant.

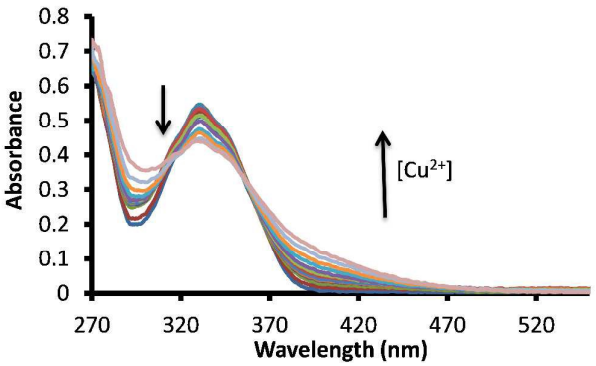


Figure 6. UV-Visible spectra of **1** upon addition of a solution of copper ions in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

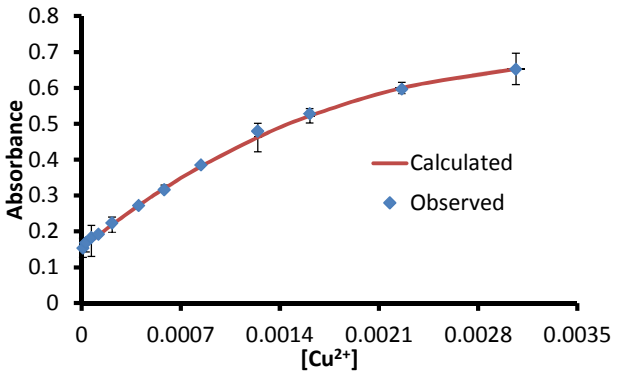


Figure 7 Observed and calculated absorbance of receptor **1** at 374 nm upon addition of copper ions in 1.0 mM HEPES:methanol (1:1) at pH 7.6), [**1**] = 2.5 × 10^{-5} M and [Cu^{2+}] = 0-3.9 mM).

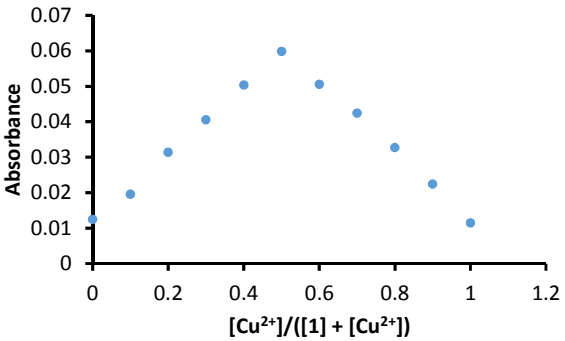


Figure 8. Job's plot for determination of stoichiometry of complex formed between receptor **1** and copper ions in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

In addition, the copper ion induced change in the UV-visible spectra of the receptor **1** was not significantly affected by the presence of other divalent of trivalent cations (Figure 9).

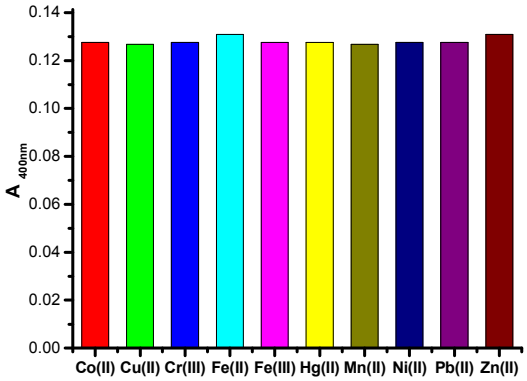


Figure 9. The copper ion induced absorbance change (**1**+Cu^{2+}) in the UV-visible spectra of the receptor **1** in the presence of divalent or trivalent cations in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

To check the practical utility of the receptor **1** for the recognition of copper ions, filter paper strips were prepared. The test strips were immersed in solutions of different metal ions. A change in color visible to the naked eye was observed in the presence of copper ions (Figure 10).

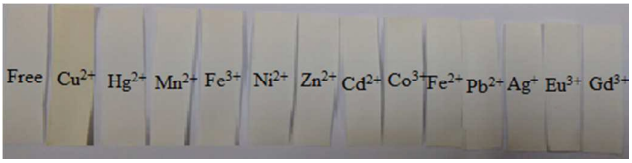


Figure 10. Photographs of the test strips of the receptor **1** prepared for the detection of Cu^{2+} ions.

In order to investigate whether the stereoisomers of the open form also interact with metal ions. Solutions of receptor **1** in methanol:water (1:1, pH 7.6, 1.0 mM HEPES) were photoirradiated in the presence of different concentration of metal ions. The rate of thermal decay of the open form to the closed form were determined in the presence of different concentrations of metal ions. The thermal decay data were plotted as a function of time and fit to the first order reaction kinetics to obtain the rate constant data (Table 2, Figures S15 and S16). The rate constant data suggested a decrease in the rate constant value of receptor **1** in the presence of increasing concentration of copper ions. Such a decrease in the thermal bleaching rate constant value of receptor **1** was not observed in the presence of other metal ions. The results indicated the formation of a complex between the open form isomer and the copper ions.

Table 2. The rate constant of thermal bleaching calculated for receptor **1** in the presence of different concentration of metal ions in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

[M^{n+}]/ M	9.9 × 10^{-7}	1.4 × 10^{-6}	2.4 × 10^{-6}	4.7 × 10^{-6}	2.0 × 10^{-5}	3.3 × 10^{-5}
Cu^{2+}	0.0728	0.0691	0.0631	0.0611	0.0574	0.0551
Zn^{2+}	0.0678	0.0690	0.0689	0.0695	0.0751	0.0758
Mn^{2+}	0.0695	0.0683	0.0682	0.0705	0.0676	0.0726
Ni^{2+}	0.0695	0.0611	0.0688	0.0699	0.0638	0.0645
Fe^{3+}	0.0615	0.0587	0.0641	0.0695	0.0717	0.0708
Fe^{2+}	0.0534	0.0595	0.0644	0.0693	0.0691	0.0712
Co^{2+}	0.0601	0.0767	-	0.0695	0.0626	0.0657
Cd^{2+}	0.0678	0.0690	0.0689	0.0694	0.0664	0.0676
Hg^{2+}	0.0666	0.0642	0.0665	0.0682	0.0680	0.0652
Ag^{+}	0.0685	0.0615	0.0683	0.0696	0.0621	0.0716
Eu^{3+}	0.0806	0.0700	0.0721	0.0682	0.0701	0.0716
Gd^{3+}	0.0610	0.0625	0.0534	0.0695	0.0625	0.0718
Pb^{2+}	0.0683	0.0707	0.0690	0.0702	0.0683	0.0722

Absorption spectra of the open form of the receptor **1** in the presence of one equivalent metal ions were analysed. The analysis revealed a small bathochromic shift in the absorption spectra of receptor **1** in the presence of copper ions (Figure 11), while no bathochromic shift was observed in the presence

of other metal ions (Figure S17). The small bathochromic shift in the presence of copper ions indicated the interaction between phenolic oxygen of naphthopyran unit and the copper ions. Similar interactions between phenolic oxygen and metal ions were also reported in the literature.[29] The interaction between phenolic oxygen of the naphthopyran unit and copper ions also indicated more polar nature of the excited state.[29] However, since the bathochromic shift is small, difference in polarity between the open form and closed form is small. This interaction seems to stabilize the open form of the naphthopyan receptor or may lead to different open form stereoisomer distribution, which may be responsible for reduction in rate constant values.[29] The maximum absorbance value obtained for the receptor **1** on exposure to UV light in the presence of copper ions was plotted against the concentration of the copper ions. A slight increase was observed indicating the stabilization of the open form by copper ions (Figure S18).

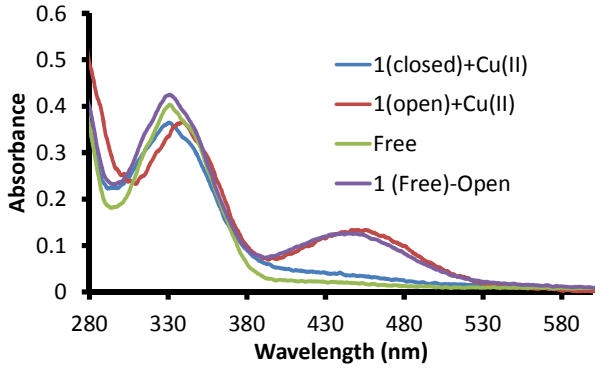


Figure 11. Normalized UV-Visible spectra of receptor **1** on irradiation with light of 265 nm in the presence and the absence of one equivalent copper ions in methanol:water (1:1, pH 7.6, 1.0 mM HEPES).

In the absence of a stable open form isomer, it is difficult to calculate the association constant directly. Therefore, a binding model based on rate constant of thermal decay of the open form in the absence and presence of metal ions was used to calculate the association constant, as reported in the literature[29] (Figure S19). The rate constant was plotted against the reciprocal of the concentration of copper ions to observe a straight line (Figure 12). A value of 3.51×10^{6} M^{-1} was obtained. A ratio of 3.25×10^{4} was obtained between the open and closed forms of the receptor **1**, which indicated that the receptor **1** can act as a photoswitch for copper ions.

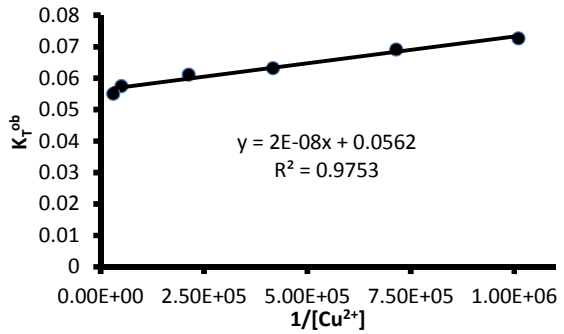


Figure 12. A plot of observed variation in the fading rate constant as a function of reciprocal of Cu^{2+} ions. [**1**] = 1.70×10^{-5} M in methanol:water (1:1, 1.0 mM HEPES, pH 7.6 at 25 °C).

To further check the utility of the receptor **1**, fluoroscence spectra were recorded in the presence of different metal ions. Howeve, no fluorescence change was detected in the floroscence spectrum in the presence of one equivalent metal ions (Figure S20).

The detailed knowledge of reactants, products, intermediate and transition state at the molecular level can help understand the photochemistry and the mechanism of the complex formation. Therefore, DFT calculations were also employed to investigate the photochemistry and the process of copper ion binding to the receptor **1**. The C_{spiro}-O bond length has a direct influence on the ring opening process in photochromic molecules. A photochromic system with C_{spiro}-O bond length greater than 1.46 Å generally display good photochromic properties.[41] Therefore, calculations were carried out using different DFT methods to obtain a geometry, which provide a C_{spiro}-O bond length close to the experimentally observed value. The C_{spiro}-O bond length obtained from single crystal X-ray data and equilibrium geometry calculated using different DFT methods were correlated to assess suitable method to predict the photochemistry of the naphthopyran receptor **1**. The PBEPBE/6-31G(d) and B3LYP/6-31G(d) were observed to be most accurate method among three DFT methods [B3LYP/6-31G(d), PBEPBE/6-31G(d) and MPW1PW91/6-31G(d)] utilized in this study (Table S5). PBEPBE/6-31G(d) was the fasted method among the three methods used in the study. Several ground state geometries of the closed form of the receptor **1** were optimized, the geometry obtained through the single crystal X-ray data was predicted as the most stable geometry by all the three DFT methods. The crystal structure of the receptor **1** indicated the presence of an intramolecular hydrogen bond. The intramolecular H-bond must be broken to achieve complex with copper ions. Therefore, it is important to estimate the strength of this hydrogen bond. In order to estimate the strength of the H-bond, the structure of the receptor **1** was optimized in such a manner that hydrogen atom attached to the oxygen atom of the salicylaldimine moiety could not make H-bond with the nitrogen atom, an increase in energy of the receptor **1** by 14.41 kcal/mol [B3LYP/6-31G(d)] was observed (Figure S21a). In another study, the lowest energy optimized structure of the closed form of the receptor **1** was selected. The hydrogen atom attached to the oxygen atom of the salicylaldimine moiety was dihydrally rotated by 180° such that it is not in a position to make hydrogen bond with the nitrogen atom. The resultant geometry was not optimized further (Figure S21b) and the single point energy was calculated, an increase in energy of the receptor **1** by 17.56 kcal/mol was observed. The two theoretical observations provided an estimate of the hydrogen bond strength in the receptor **1**.

The ring opening process, which involve cleavage of C_{spiro}-O bond, was investigated by performing energy calculations as a function of C_{spiro}-O distance ranging from 1.6 to 2.8 Å in gas

phase using Gaussian 09 software.[30] The intermediate structure at each point was optimized using DFT/B3LYP/6-31G(d) method. A plot shown in figure 13 was obtained which indicated an energy maxima at R = 2.1. The structure corresponding to energy maxima at R = 2.1 was used to obtain the transition state of the ring opening process (Figure 13, S22).[32] Frequency calculations were performed to confirm the transition state through the presence of single negative frequency. The energy of activation for the ring opening process of naphthopyran derivative **1** was calculated (Figure 14) by three different DFT methods to provide an average value of 18.31 kcal/mol. The high value of the activation energy suggested inaccessibility of the ring opening process at room temperature. The C_{spiro}-O distance was observed to be 3.19 Å at TS1, which indicated that the bond is considerably broken (Figure 14).

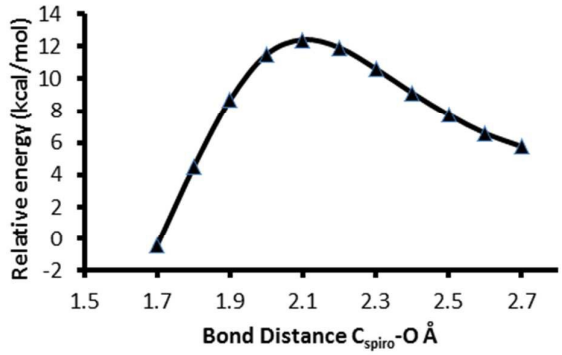


Figure 13. Relative energy (kcal/mol) values along C_{spiro}-O closed form to open form (CC) path calculated using B3LYP/6-31G(d).

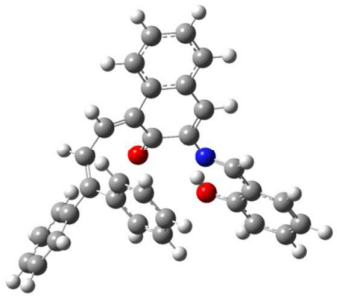


Figure 14. Calculated structure of the transition state of the receptor **1** using DFT/B3LYP/6-31G(d) method.

The stereoisomer (CC) of the open form of the receptor **1** can lead to other stereoisomers through *cis-trans* rearrangement of two of the three bonds that link the two aromatic units. The photochromic properties of the receptor **1** can be understood better, if the isomerization process is explored in detail. Therefore, it is important to understand the relative stability and activation energy required for isomerization process. The figure 15 shows the entire photoisomerization potential energy pathway calculated using B3LYP/6-31G(d) method involved in the conversion of the closed form of the receptor **1** to the various open form stereoisomers. The process initiates with the breaking of C_{spiro}-O bond to yield CC isomer *via* transition state TS1. The CC stereoisomer in turn gets converted into more stable TC stereoisomer through *cis-trans* isomerization passing through TS2 transition state. The conversion of CC isomer to TC requires significantly lower activation energy in comparison to the ring opening process (Table 3). The conversion of TC to TT require 15.81 kcal/mol activation energy, while the difference in stability between the TC and TT isomers is of the order 2.79 kcal/mol. Therefore, it is reasonable to conclude that the conversion of TC to TT is inaccessible at room temperature. The process of conversion of ring closed structure to ring open stereisomer CT passes through high activation energy in comparison to CC isomer. Therefore, it may be concluded that the ring closed structure provide CC isomer preferentially. The energy of various isomers of the closed and the open form were calculated using different quantum chemical methods and relative energy is reported in the table 3 (Table S6 list the total energy). The energy, calculated using B3LYP and PBEPBE methods was observed to be almost similar, while MPW1PW91 method provided significantly different energy.

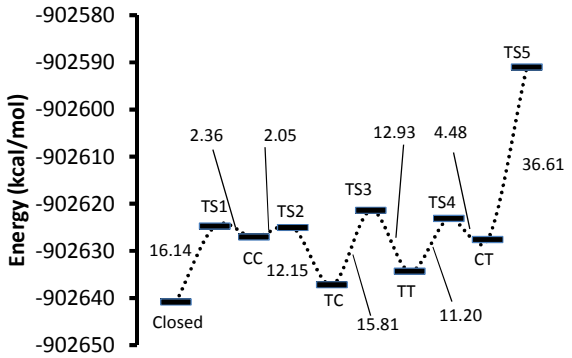


Figure 15. Potential energy diagram of ring opening/closing process in receptor **1** calculated using DFT/B3LYP/6-31G(d).

Table 3. The relative energy (kcal/mol)[a] of the conformer calculated using different quantum chemical methods.

Conformer	B3LYP/6-31G(d)	MPW1PW91/6-31G(d)	PBEPBE/6-31Gd)
Closed	0	0	0
TC	3.67258	8.38715	3.74273
TT	6.54806	11.2287	6.72525
CT	13.2705	17.3813	12.9602
CC	13.7826	18.4306	13.4280

[a] Energy of most stable isomer is listed in the table.

Figure 2 shows the changes in the absorption spectra of the receptor **1** on exposure to UV light (365 nm). To explore and understand the changes in the absorption spectra further, time dependent density functional theory calculations were performed using three different methods [B3LYP/6-31G(d), PBEPBE/6-31G(d) and MPW1PW91/6-31G(d)]. The calculations were performed on the most stable stereoisomer (TC) of the open form. It was observed that B3LYP/6-31G(d) provided a value (450 nm) in agreement with the experimentally observed value. The MPW1PW91/6-31G(d) method provided 432 nm value for λ_{max} while PBEPBE/6-31G(d) calculated value (535.95 nm) was observed to be in disagreement with the experimentally observed value.

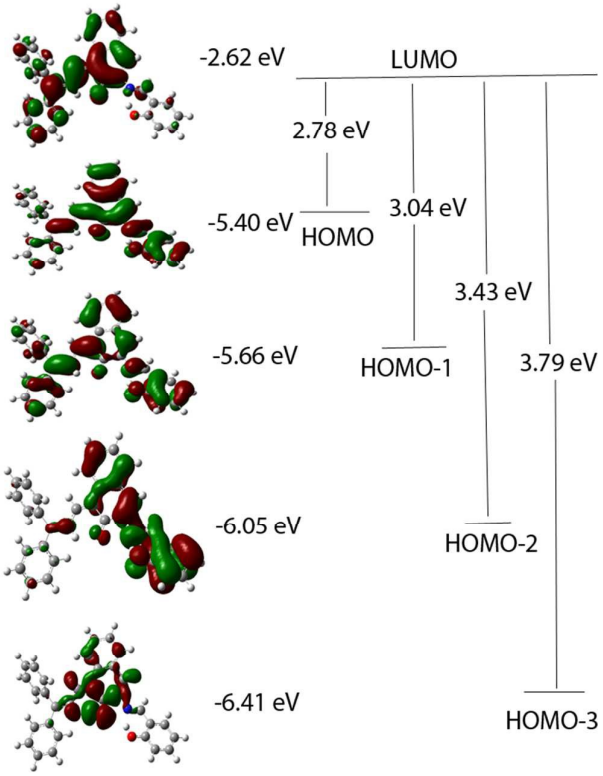


Figure 16. Energy diagram of the main orbitals of naphthopyran receptor **1** calculated using DFT/B3LYP/6-31G(d) method.

A close examination of the data obtained using B3LYP/6-31G(d) (Figure 16) revealed that the singlet excitation wavelength were mainly contributed by the HOMO to LUMO (S_o to S_1), and HOMO-1 to LUMO (S_o to S_3) orbitals. The energy of HOMO-1 to LUMO transition (2.75 ev, 451 nm) is close to the experimentally observed value (445 nm) of absorption maxima (Table 4).

Table 4. Electronic excitation parameters for receptor **1** obtained using TD-DFT/6-31G(d).

	S_o to S_1	S_o to S_2	S_o to S_3	S_o to S_4
CIC	H to L	H-3 to L	H-1 to L	H-2 to L
	(0..62)	(0.54)	(0.51)	(0.62)
E(eV) [λ	2.37	2.71	2.75 (251)	2.98 (416)
(nm)	(523.72)	(456.96)		
μ_x	4.51	-1.06	-6.26	1.26
μ_y	-0.04	-1.51	-3.44	1.00
μ_z	0.24	0.10	-0.19	0.10
μ_{total}	8.03	1.34	20.07	1.02
ƒ	0.1834	0.0352	0.5318	0.0293

Similarly, various geometries of closed and open form (TC) of the receptor **1** complexed to copper ions were also optimized using MPW1PW91/6-31G(d)/LanL2DZ and B3LYP/6-31G(d)/Lanl2DZ methods. Since the TC isomer was observed as the most stable and accessible isomer at room temperature (Table 5). Therefore, the open form geometries of the complex with copper ions were optimized using TC stereoisomer. The process of complex formation may or may not involve the abstraction of a proton from the phenolic OH group. Therefore, both the processes were considered. The most stable geometries are shown in figure 17. The energy calculation suggested that the open form of receptor **1** has a high affinity for the copper ion in comparison to the closed form, verifying the experimental observations.

Table 5. The energy (kcal/mol) calculated using B3LYP and MPW1PW91 methods.

	B3LYP/6-31G(d)	MPW1PW91/6-31G(d)	B3LYP/6-31G(d)	MPW1PW91/6-31G(d)
	Total Energy		Relative energy	
1-Closed-Cu	-1025401	-1025209	0	0
1-Closed-H-Cu	-1025224	-1025033	0	0
TC-Cu	-1025407	-1025207	-5.594981[a]	2.01191[a]
TC-H-Cu	-1025236	-1025039	-11.05559[b]	-5.398521[b]

[a] Relative E=**1**-closed-Cu – TC-Cu. [b]. Relative E= **1**-Closed-H-Cu – TC-H-Cu

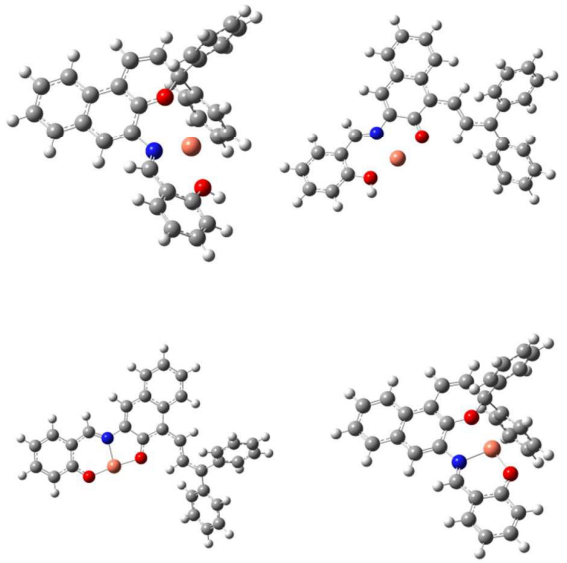


Figure 17. The most stable geometries obtained using DFT/B3LYP-LanL2DZ/6-31G(d) method for the copper ion complex of receptor **1**.

Conclusions

In summary, we have designed a simple naphthopyran photoswitch for Cu^{2+} ion detection. The molecule exhibited high selectivity towards Cu^{2+} ions in comparison to other heavy metal ions. The open form of the isomers was proved to possess significantly high affinity for copper ions in comparison to the closed form. The theoretical studies confirmed the experimental observation by indicating the high affinity of the open form towards copper ions. A 3.25×10^4 fold difference in binding affinity towards copper ions between the closed and the open form of the receptor **1** was observed in aqueous methanol solution. Therefore, the experimental observations unambiguously confirmed that the receptor **1** can act as a photoswitch for copper ions. The study may pave the way for mimicking heavy metal recognition for future generation.

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