Fluorescent and Chromogenic Receptor Bearing Amine and Hydroxyl Functionality for Iron (III) Detection in Aqueous Solution

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Abstract The noncyclic 2,2'-[ethane-1,2-diylbis (iminomethanediyl)]diphenol (4) fluorescent receptor bearing two amine and hydroxyl groups have been designed and investigated for their binding properties towards various cations. The fluorescent spectral measurements revealed that receptor 4 is a selective fluorescent sensor for Fe³⁺ ions but not for metal ions such as Cr^{3+} , Mn^{2+} , Co^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} , Pb^{2+} and Bi^{3+} . The binding ability was confirmed with spectroscopic methods and density functional theory calculation (DFT). This straightforward and cost effective receptor provides rapid detection of Fe³⁺ ions at concentrations as low as 2.5 µM and expected to be useful to design efficient chemically and biological sensor.

Keywords Fluorescence receptor \cdot Cation sensing \cdot Association constant \cdot DFT

Introduction

In recent year the development of fluorescent probe for the detection of heavy metal ions is the important research area in

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G. K. Chaitanya School of Chemical Sciences, Swami Ramanand Teerth Marathawada University, Nanded 431 606, MS, India the field of supramolecular chemistry [1–4]. Detection of heavy metal ions is important due to its involvement in many biological processes as well as toxic and known as environmental pollutants [5, 6]. Recently, many of cation receptors has been designed and synthesized. Many signals, such as redox potential changes [7], UV–Vis spectral changes [8], color changes [9, 10] and emission fluorescence changes [11, 12] have been developed in different methods. Among these methods, much effort has been made in colour changes and emission fluorescent changes because they can be easily observed by 'naked eye'.

Transition metal plays an important role in biology and chemistry. Among various transition metals, iron is the most abundant essential trace element in the human body which plays vital roles in many biological processes [13–15]. In well-cultivated people the total iron content is about 4 g. Iron is essential in living systems since it is the oxygen carrier in all tissues in the form of hemoglobin and assists to transport electrons as cytochromes. Deficiency of iron in primary stages can cause anemia [16–20], which can harm or even kill by depriving organs. Encouraged with this interesting report we have tried to propose a Fe³⁺ sensor using a distinctive reaction.

Herein, we report a convenient and efficient route for the preparation of noncyclic receptor i.e. 2,2'-[ethane-1,2-diylbis(iminomethanediyl)]diphenol (4) and its new application as a cation sensor. Synthesized receptor 4 provides two amine and two hydroxyl functional groups for cation binding.

Experimental Detail

Reagents and Apparatus

All commercial grade chemicals and solvents were used without further purification. ¹H NMR spectra were recorded on a Varian NMR mercury System 300 spectrometer operating at Scheme 1 Synthesis of 2,2'-[ethane-1,2-diylbis (iminomethanediyl)]diphenol (4); a CH₃OH, 30 min and b NaBH₄, THF/CH₃OH 70:30 v/v, 0–5 °C, and 90 min



300 MHz in CDCl₃ with Me₄Si (TMS) as an internal standard. The Fluorescence and UV-Visible spectra were recorded on Fluoromax-4 Spectrofluorometer and Shimadzu UV-24500 with 5 nm slit of fluorescence. The metal nitrate salts used for cations binding study. Ultrapure water with a Millipore Purification System (Milli-Q water) was used throughout the analytical experiments.

Sample Preparation

A stock solution of probe **4** ($c=1 \times 10^{-3}$ M) in CH₃OH/H₂O (60:40,v/v) solution was prepared (probe **4** is freely soluble in CH₃OH at 25 °C), and the corresponding working solutions($c=1 \times 10^{-4}$ M) were simply prepared by diluting with CH₃OH/H₂O (60:40,v/v). All stock and working solution were prepared in ultrapure water and spectroscopic grade methanol. Stock solution of all cations ($c=1 \times 10^{-2}$ M) were prepared

Fig. 1 Fluorescent intensity (λ_{ex} =272 nm) of probe 4 upon the addition of a particular metal salt in CH₃OH/H₂O (60:40, ν/ν) with CH₃OH/H₂O (60:40, ν/ν) solution and the corresponding working solutions ($c=1 \times 10^{-3}$ M) were simply prepared by diluting with CH₃OH/H₂O (60:40, ν/ν).

Fluorescence Study

The fluorescence titration experiments were carried out with a Fluoromax-4 spectrofluorometer in CH₃OH/H₂O solvent system at room temperatures (298 K) with the aim of determining the association constant (K) for receptor 4–cation in this solvent system. These titration experiments were accomplished through a stepwise addition of metal salt solutions (0.03 ml, 1×10^{-3} M, guest) to a solution of receptor 4 (2 ml, 1×10^{-4} M) in CH₃OH/H₂O (60:40, ν/ν) in the cell. The fluorescence intensity was recorded at $\lambda_{ex}/\lambda_{em}=272/307$ nm alongside a reagent blank. The excitation and emission slits were both set to 5 nm. This was followed by a 5 min interval



Fig. 2 a Fluorescence ratiometric response $(I-I_0/I_0)$ of probe 4 $(c=1 \times 10^{-4} \text{ M})$ upon the addition of a particular metal salt $(c=1 \times 10^{-3} \text{ M})$ in CH₃OH/H₂O (60:40, v/v). **b** Recognition of Fe³⁺ ion by receptor 4 in the presence of other metal ion



(in which the reaction cell was left under continuous stirring to ensure mixing). Then, the fluorescence data were collected and processed using the Hyper quad program to calculate the association constant (K) of the appropriate cation complexes.

Sysnthesis of Receptor 4

Compound 3 was synthesized by stirring one mole 1,2-diamine ethane (0.06 g, 1 mM) with two moles of 2-hydroxy

Fig. 3 Fluorescence spectrum of probe 4 ($c=1 \times 10^{-4}$ M) after the addition of Fe³⁺ salt of ($c=1 \times 10^{-3}$ M) in CH₃OH/H₂O (60:40, v/v)

benzaldehyde (0.24 g, 2 mM) in ethanol (50 mL) with stirring for 30 min [21]. Compound **3** was obtained with good yield and appears as a yellow crystalline powder with 88 % yield, mp >250 °C. Further receptor **4** was obtained from compound **3** by reduction under NaBH₄ in CH₃OH with good yield. 85 %, m.p. 124–126 °C, ¹H NMR (300 MHz, CDCl₃, ppm) : δ =2.83 (s, 4H, 2CH₂), 3.99 (s, 4H, 2Ar, CH₂), 6.76–6.84 (m, 4H, 2Ar-H), 6.96–6.98 (d, *J*=6.6 Hz, 2H, 2Ar-H),7.15–7.20 (m, 2H, 2ArH); IR (KBr): ν =620, 722, 760,795, 859, 964, 1,100,



Fig. 4 Normalized response of fluorescence signal to changing Fe^{3+} concentrations in the CH₃OH/H₂O (60:40, v/v) solution.(receptor 4, $c=1 \times 10^{-4}$ M and Fe^{3+} salt of $c=1 \times 10^{-3}$ M)



Fig. 5 1:1 Stoichiometry of the host guest relationship realised from the Job's plot between receptor 4 and Fe³⁺



Fig. 6 Benesi-Hildebrand Plot (adjusted equation: $1/F-F_0=-1.0E-10x+1E-06 1/[G],$ R=0.982) and the K value for Fe³⁺ at 10,000 M⁻¹



Fig. 7 Absorbance spectrum of probe 4 ($c=1 \times 10^{-4}$ M) upon the addition of Fe³⁺ metal ($c=1 \times 10^{-3}$ M) in CH₃OH/H₂O (60:40, v/v)



1,589, 1,615, 2,923, 3,275, 3,439 cm⁻¹; MS (M+H⁺): $C_{16}H_{20}N_2O_2$ requires 272.152 found 273.30.

Synthesis of 4.Fe³⁺ Complex

Fe³⁺ complex of receptor **4** was synthesized by reaction of one mole of receptor **4** (0.54 g, 2 mM) with one mole of FeCl₃ (0.32 g, 2 mM) in CH₃OH (50 mL) stirring for 3 h. The precipitation was collected at room temperature and dried in vacuum. Further it was washed with water then ethanol followed by petroleum ether. Yield- 88 %, IR (KBr, cm⁻¹) υ =662, 767, 846, 1,111, 1,598, 2,924, 3,163 cm⁻¹. MS (ESI): m/z requires C₁₆H₁₈FeN₂O₂: 326.17, found 327.30.

Result and Discussion

Synthesis of Receptor 4

Compound **3** was synthesized by reacting one mole of 1,2diamine ethane with two moles of 2-hydroxy benzaldehyde in methanol by stirring for 30 min. Ligand **3** was obtained with good yield and having yellow crystals. Receptor **4** was obtained from compound **3** by reduction with NaBH₄ with good yield (Scheme 1). The colorless compound **4** obtained was purified by recrystallization from methanol and characterized by IR, ¹H NMR and mass spectroscopy (S1-2, Supporting Information). The spectral data found to be consistent with its structure.



Fig. 8 The DFT optimized geometrical parameters of **4**.Fe³⁺ complex

Fluorescence Studies of Receptors 4

The responses of receptor 4 towards various cations were monitored in CH₃OH/H₂O (60:40, v/v) using fluorescence spectroscopic response. Figure 1 illustrates the change in fluorescence of 4 after addition of cation salts containing CH₃OH/H₂O (60:40, v/v). It exhibit emission with the emission maximum at 307 nm when they are excited at 272 nm. It is well understood from Fig. 1 that receptor are highly sensitive and selective towards Fe³⁺ ion by exhibiting different modes of emission. The fluorescence emission of receptor 4 was quenched effectively upon addition of 1 equiv. Fe^{3+} ions (Fig. 1). To account for such fluorescence quenching, the PET mechanism was exploited. As we all knew, the fluorescence of the cations PET chemosensor generally was 'switches off' rather than 'switch on' upon ion sensing unlike most PET sensors for anions. In the case of the receptor 4, the excited state of the fluorophore was not, or only to a small amount, quenched by electron transfer (ET) from the receptor 4 to the fluorophore prior to the sensor-cation interactions. However, upon interaction with cations, the reduction potential of the receptor 4 was increased and in other words, the electron transfer from the electron rich amine and hydroxyl moiety bonded with cation (Fe³⁺ ion) became more realistic. Upon further addition of Fe³⁺ ion, it appeared that the deprotonated species of receptor 4 (NH and OH functional group), being more electron rich compared to the coordination complex with Fe³⁺ ion, activated the PET process more efficiently and showed up a greater quenching.

Table 1 An optimized energy value calculated at B3LYP/6-31G(d)/ LanL2DZ level, bond lengths and bond angles related to noncovalent bonds between 4 and $4.Fe^{3+}$ ion based on optimized geometries

Bond angle/length	4 .Fe ³⁺
Fe-O1	1.881 Å
Fe-O2	1.954 Å
Fe-N1	1.978 Å
Fe-N2	1.979 Å

Fig. 9 The frontier molecular orbitals HOMO and LUMO of **4.Fe**³⁺



To study the influence of other metal ions on Fe^{3+} binding with receptor **4**, we performed competitive experiments with other metal ions in the presence of Fe^{3+} (Fig. 2a and b). The observed fluorescence enhancement for mixtures of Fe^{3+} with most metal ions was similar to that seen for Fe^{3+} alone. No other metal ions appeared to interfere with the fluorescence of the receptor **4** and Fe^{3+} . The interference studies have shown that the interference of other metal ions in Fe^{3+} detection was moderately low. Available data may be helpful for the researcher to develop the new applications of receptor **4** in separation science, biological and analytical chemistry.

Figure 3 shows the emission fluorescence spectra of receptor 4 on addition of Fe³⁺ ion on the various concentrations. When exciting at 272 nm the emission fluorescence intensity of probe 4 at 307 nm quench more than 7 fold for cation Fe³. A satisfactory linear relationship between concentrations was observed with the fluorescence intensity and correlation coefficient is high. Normalized response of fluorescence signal to changing concentrations cation in the CH₃OH/H₂O (60:40, v/v) solution shown in Fig. 4. Under optimal conditions, the limit of detection for Fe³⁺ ion is 2.5 μ M.

Stoichiometry and Binding Constant of Receptor 4

The binding stoichiometry between receptor 4 and Fe^{3+} ion was determined by the continuous variation method [22]. The results indicate the formation of a 1:1 adduct (Fig. 5). IR spectrum of free receptor 4 exhibits a broad band at $3,439 \text{ cm}^{-1}$ which can be assigned for OH group on the ring. On complexation two deprotonation of OH group took place and OH functional group was disappeared (Figure S3-4, SI). Similarly, furthermore, we have confirmed these trends by mass spectroscopic data. MALDI/TOF-MS data showed the formation 1:1 complex between two deprotonated ligand (receptor 4) and Fe^{3+} ion [(MS (ESI): m/z requires (Calculated)) C₁₆H₁₈FeN₂O₂: 326.17, found 327.30 (Figure S5, SI). All attempts was failed to grow the single crystal of receptor 4.Fe³⁺ ion complex. The association constant of Fe³⁺ ion was calculated from fluorescence titration experiments by Benesi– Hildebrand plot [23] and found as $10,000 \text{ M}^{-1}$ for Fe^{3+} (Fig. 6).

UV-Vis Absorption Spectral Studies

The absorption spectrum of receptor **4** with Fe^{3+} is shown in Fig. 7. Receptor **4** exhibit max peak at 240 and 272 nm in CH₃OH/H₂O (60:40, ν/ν) solution together with a swelling at 240 nm and a shoulder at 260 nm. The longer wavelength band at 272 nm and shoulder at 310 nm may be assigned to transitions associated with phenol ring. Figure 7 clearly show new peak appear at 335 nm after addition Fe³⁺.

Proposed Binding Mode and Mechanism of Sensing

The density functional theory (DFT) study was conducted by using Gaussian 09 program in an attempt to better understand the nature of receptor 4 and its interaction with Fe^{3+} ion. The hybrid level exchange correlation functional B3LYP was employed with 6-31G (d) basis set on main group elements and LanL2DZ for metal ions [24-26]. The optimized geometry has been further used for analytical frequencies to ensure that the optimized geometry is global minima on the potential energy surface. In order to reduce the stress from steric crowding, two arms held in different direction as are shown in Fig. 8 it was observed that the oxygen and nitrogen atoms of hydroxyl and amine groups constitute the pseudo cavity for metal ion coordination. On coordination of Fe^{3+} ion, there is increase in the stability of the whole system which was confirmed from geometry parameters depicted in Table 1. Further from the frontier molecular orbital pictures (Fig. 9) HOMO and LUMO it is found that the strong interaction between metal and ligand and LUMO is main contributor in electronic transition.

Conclusion

In conclusion, we have synthesized the selective and sensitive fluorescent chemical sensor i.e. 2,2'-[ethane-1,2-diylbis(iminomethanediyl)]diphenol (4) for the detection of Fe³⁺ in CH₃OH/H₂O (60:40, v/v) medium. The detection of Fe³⁺ gave rise to major colorimetric colour change, which can be easily detected by the naked eye. Furthermore, our sensor is not affected by the common interference of other ions like

 Cr^{3+} , Mn^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Cd^{2+} , Hg^{2+} , Pb^{2+} and Bi^{3+} . The 1:1 Stoichiometry of the host guest relationship was realized from the Job's plot and the binding constant value was obtained from Benesi-Hildebrand. Our methods are simple and allow the detection of Fe³⁺ with high selectivity in aqueous solution at a very low concentration (2.5 μ M).

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