

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

Umesh Fegade · Shivaji Tayade · G. Krishna Chaitanya · Sanjay Attarde · Anil Kuwar

Received: 18 October 2013 / Accepted: 28 January 2014 / Published online: 13 February 2014  
© Springer Science+Business Media New York 2014

**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  $\text{Fe}^{3+}$  ions but not for metal ions such as  $\text{Cr}^{3+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Pb}^{2+}$  and  $\text{Bi}^{3+}$ . The binding ability was confirmed with spectroscopic methods and density functional theory calculation (DFT). This straightforward and cost effective receptor provides rapid detection of  $\text{Fe}^{3+}$  ions at concentrations as low as 2.5  $\mu\text{M}$  and expected to be useful to design efficient chemically and biological sensor.

**Keywords** Fluorescence receptor · Cation sensing · Association constant · DFT

## Introduction

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

**Electronic supplementary material** The online version of this article (doi:10.1007/s10895-014-1358-3) contains supplementary material, which is available to authorized users.

U. Fegade · S. Tayade · A. Kuwar (✉)  
School of Chemical Sciences, North Maharashtra University,  
Jalgaon 425001, MS, India  
e-mail: kuwaras@gmail.com

U. Fegade · S. Attarde  
School of Environmental & Earth Sciences, North Maharashtra  
University, Jalgaon 425001, MS, India

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  $\text{Fe}^{3+}$  sensor using a distinctive reaction.

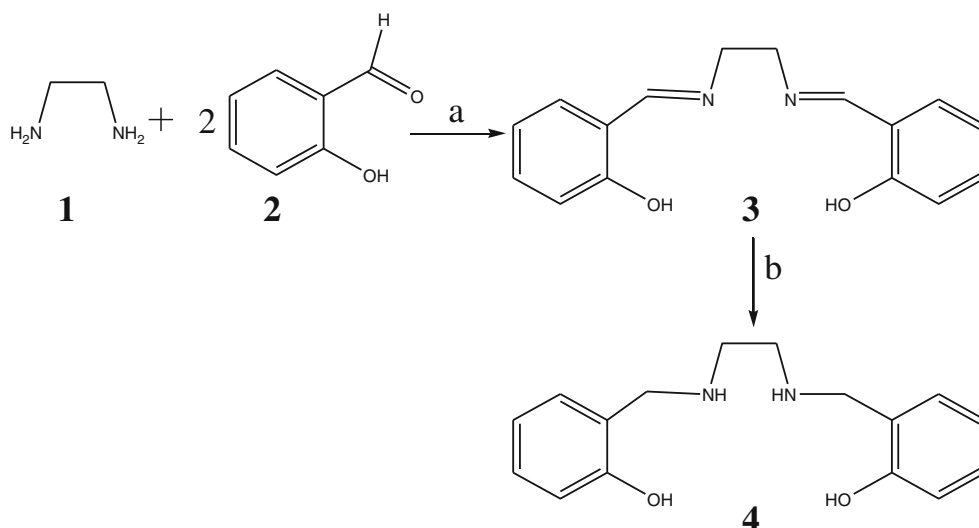
Herein, we report a convenient and efficient route for the preparation of noncyclic receptor i.e. 2,2'-[ethane-1,2-diylbis(iminomethanediyl)]diphenol (**4**) and its new application as a cation sensor. Synthesized receptor **4** provides two amine and two hydroxyl functional groups for cation binding.

## Experimental Detail

### Reagents and Apparatus

All commercial grade chemicals and solvents were used without further purification.  $^1\text{H}$  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** CH<sub>3</sub>OH, 30 min and **b** NaBH<sub>4</sub>, THF/CH<sub>3</sub>OH 70:30 v/v, 0–5 °C, and 90 min



300 MHz in CDCl<sub>3</sub> with Me<sub>4</sub>Si (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

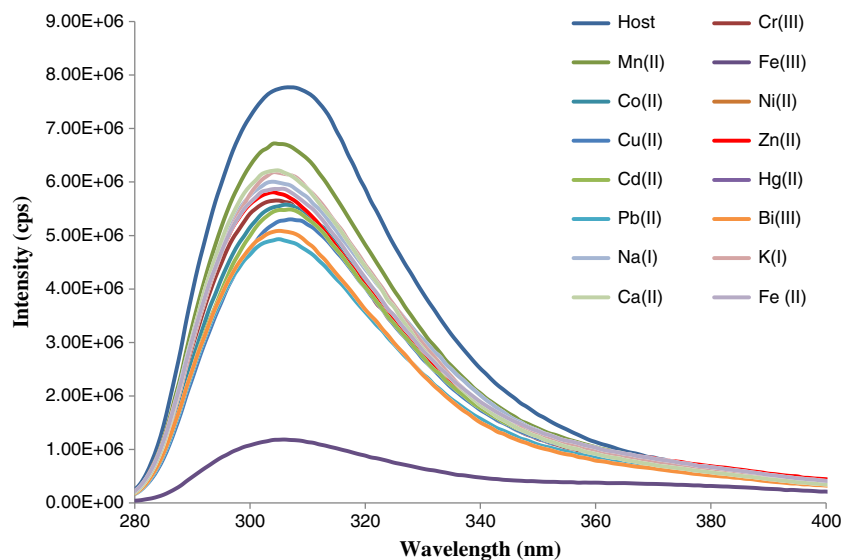
A stock solution of probe **4** ( $c=1 \times 10^{-3}$  M) in CH<sub>3</sub>OH/H<sub>2</sub>O (60:40, v/v) solution was prepared (probe **4** is freely soluble in CH<sub>3</sub>OH at 25 °C), and the corresponding working solutions ( $c=1 \times 10^{-4}$  M) were simply prepared by diluting with CH<sub>3</sub>OH/H<sub>2</sub>O (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

with CH<sub>3</sub>OH/H<sub>2</sub>O (60:40, v/v) solution and the corresponding working solutions ( $c=1 \times 10^{-3}$  M) were simply prepared by diluting with CH<sub>3</sub>OH/H<sub>2</sub>O (60:40, v/v).

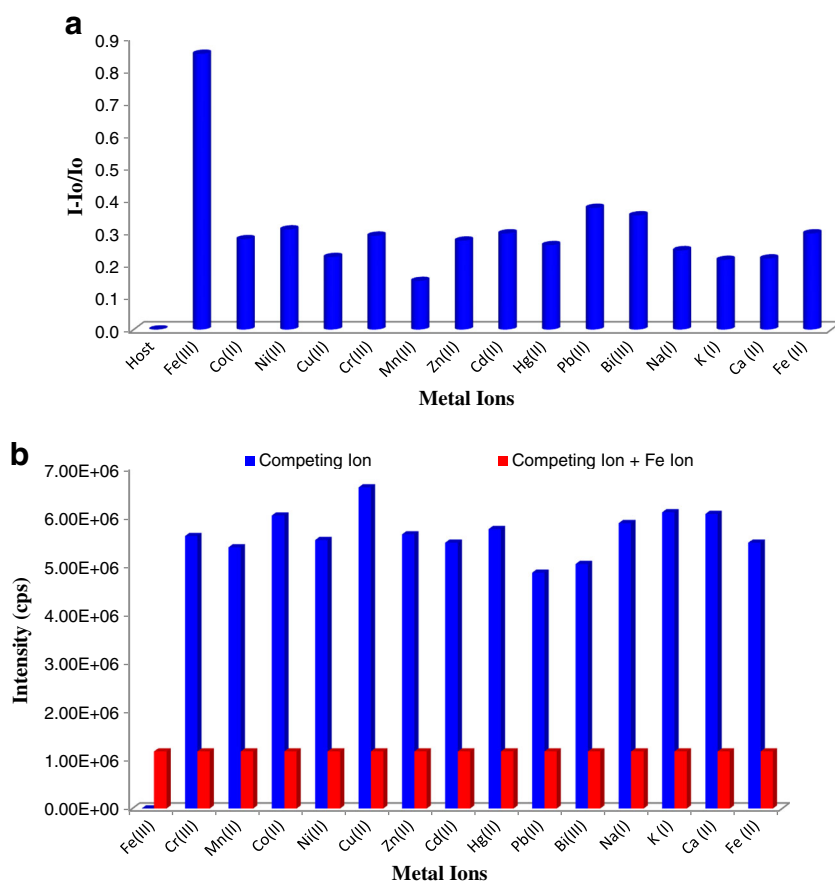
#### Fluorescence Study

The fluorescence titration experiments were carried out with a Fluoromax-4 spectrofluorometer in CH<sub>3</sub>OH/H<sub>2</sub>O 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,  $1 \times 10^{-3}$  M, guest) to a solution of receptor **4** (2 ml,  $1 \times 10^{-4}$  M) in CH<sub>3</sub>OH/H<sub>2</sub>O (60:40, v/v) in the cell. The fluorescence intensity was recorded at  $\lambda_{\text{ex}}/\lambda_{\text{em}}=272/307$  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. 1** Fluorescent intensity ( $\lambda_{\text{ex}}=272$  nm) of probe **4** upon the addition of a particular metal salt in CH<sub>3</sub>OH/H<sub>2</sub>O (60:40, v/v)



**Fig. 2** **a** Fluorescence ratiometric response ( $I-I_0/I_0$ ) of probe **4** ( $c=1 \times 10^{-4}$  M) upon the addition of a particular metal salt ( $c=1 \times 10^{-3}$  M) in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v). **b** Recognition of  $\text{Fe}^{3+}$  ion by receptor **4** in the presence of other metal ion



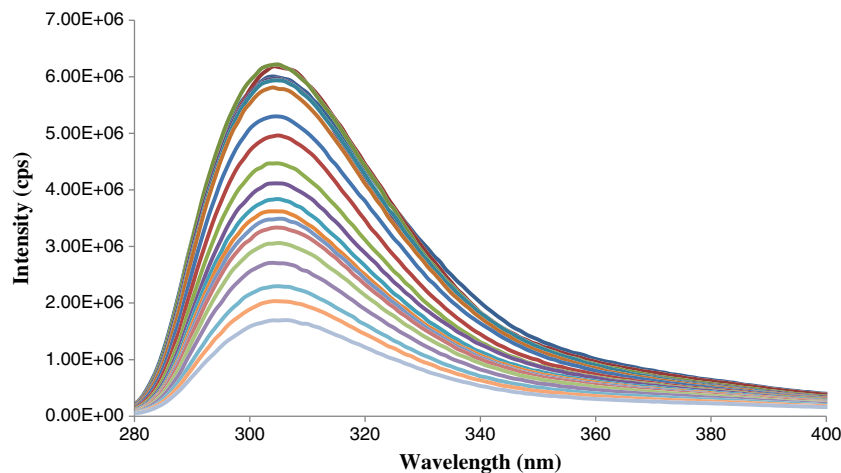
(in which the reaction cell was left under continuous stirring to ensure mixing). Then, the fluorescence data were collected and processed using the Hyper quad program to calculate the association constant ( $K$ ) of the appropriate cation complexes.

#### Synthesis of Receptor 4

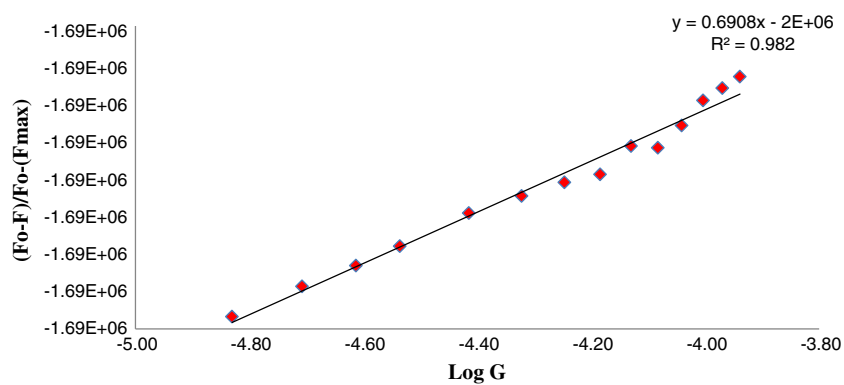
Compound **3** was synthesized by stirring one mole 1,2-diamine ethane (0.06 g, 1 mM) with two moles of 2-hydroxy

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  $\text{NaBH}_4$  in  $\text{CH}_3\text{OH}$  with good yield. 85 %, m.p. 124–126 °C,  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , ppm) :  $\delta=2.83$  (s, 4H, 2 $\text{CH}_2$ ), 3.99 (s, 4H, 2Ar,  $\text{CH}_2$ ), 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, 2Ar-H); IR (KBr):  $\nu=620, 722, 760, 795, 859, 964, 1,100,$

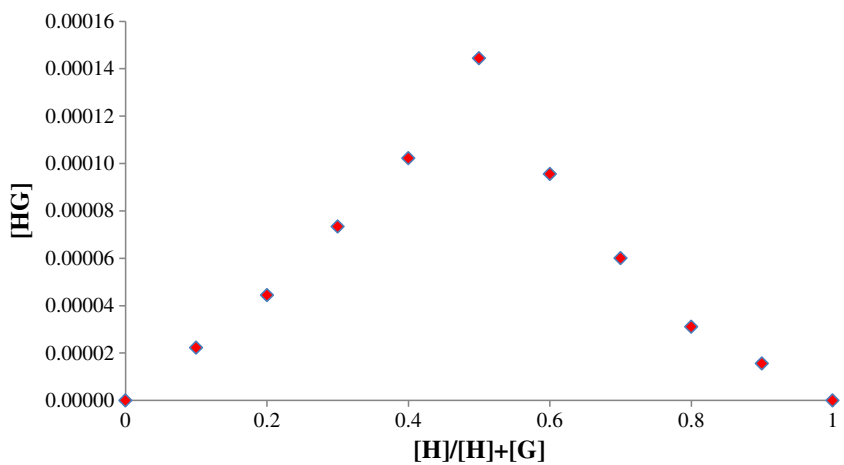
**Fig. 3** Fluorescence spectrum of probe **4** ( $c=1 \times 10^{-4}$  M) after the addition of  $\text{Fe}^{3+}$  salt of ( $c=1 \times 10^{-3}$  M) in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v)



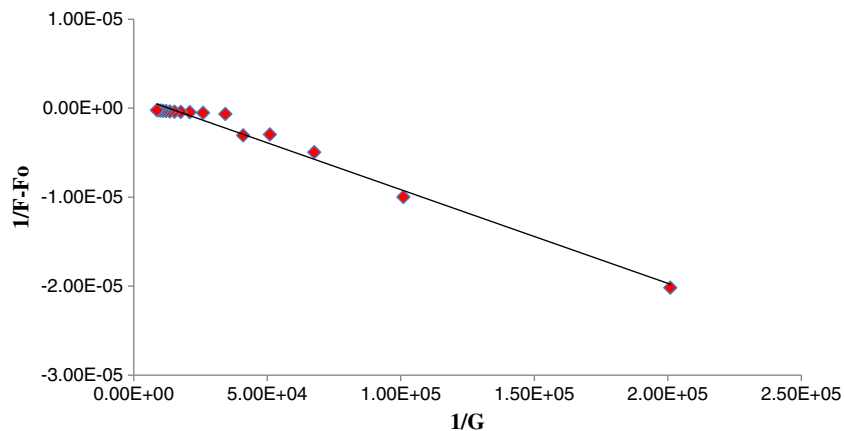
**Fig. 4** Normalized response of fluorescence signal to changing  $\text{Fe}^{3+}$  concentrations in the  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v) solution. (receptor **4**,  $c=1 \times 10^{-4}$  M and  $\text{Fe}^{3+}$  salt of  $c=1 \times 10^{-3}$  M)



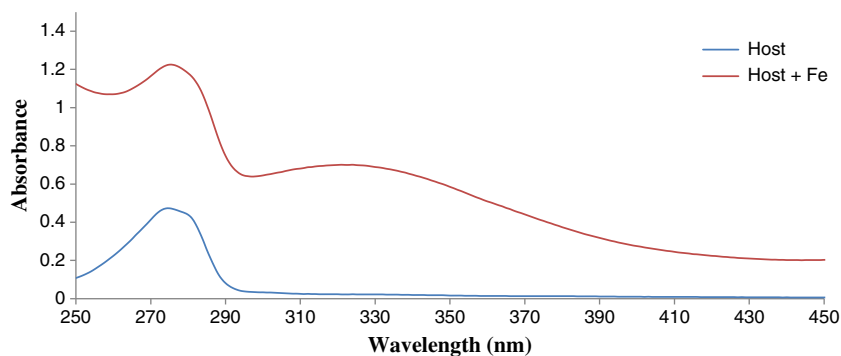
**Fig. 5** 1:1 Stoichiometry of the host guest relationship realised from the Job's plot between receptor **4** and  $\text{Fe}^{3+}$



**Fig. 6** Benesi-Hildebrand Plot (adjusted equation:  $1/F-F_0=-1.0\text{E}-10x+1\text{E}-06$   $1/[\text{G}]$ ,  $R=0.982$ ) and the K value for  $\text{Fe}^{3+}$  at  $10,000 \text{ M}^{-1}$



**Fig. 7** Absorbance spectrum of probe **4** ( $c=1 \times 10^{-4}$  M) upon the addition of  $\text{Fe}^{3+}$  metal ( $c=1 \times 10^{-3}$  M) in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v)



1,589, 1,615, 2,923, 3,275, 3,439  $\text{cm}^{-1}$ ; MS ( $\text{M}+\text{H}^+$ ):  $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$  requires 272.152 found 273.30.

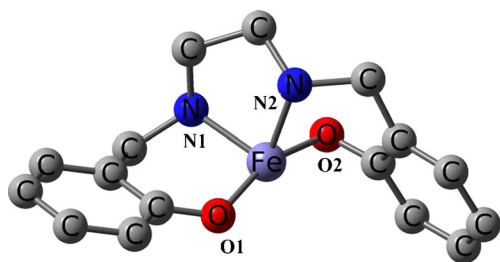
### Synthesis of $4\cdot\text{Fe}^{3+}$ Complex

$\text{Fe}^{3+}$  complex of receptor **4** was synthesized by reaction of one mole of receptor **4** (0.54 g, 2 mM) with one mole of  $\text{FeCl}_3$  (0.32 g, 2 mM) in  $\text{CH}_3\text{OH}$  (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,  $\text{cm}^{-1}$ )  $\nu = 662, 767, 846, 1,111, 1,598, 2,924, 3,163 \text{ cm}^{-1}$ . MS (ESI):  $m/z$  requires  $\text{C}_{16}\text{H}_{18}\text{FeN}_2\text{O}_2$ : 326.17, found 327.30.

## Result and Discussion

### Synthesis of Receptor **4**

Compound **3** was synthesized by reacting one mole of 1,2-diamine 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  $\text{NaBH}_4$  with good yield (Scheme 1). The colorless compound **4** obtained was purified by recrystallization from methanol and characterized by IR,  $^1\text{H}$  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  $4\cdot\text{Fe}^{3+}$  complex

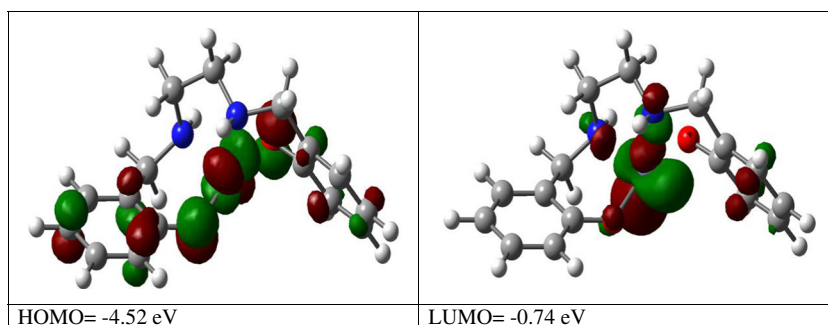
### Fluorescence Studies of Receptors **4**

The responses of receptor **4** towards various cations were monitored in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v) using fluorescence spectroscopic response. Figure 1 illustrates the change in fluorescence of **4** after addition of cation salts containing  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (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  $\text{Fe}^{3+}$  ion by exhibiting different modes of emission. The fluorescence emission of receptor **4** was quenched effectively upon addition of 1 equiv.  $\text{Fe}^{3+}$  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 ( $\text{Fe}^{3+}$  ion) became more realistic. Upon further addition of  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$  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  $4\cdot\text{Fe}^{3+}$  ion based on optimized geometries

Bond angle/length	$4\cdot\text{Fe}^{3+}$
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  $4\text{Fe}^{3+}$



To study the influence of other metal ions on  $\text{Fe}^{3+}$  binding with receptor **4**, we performed competitive experiments with other metal ions in the presence of  $\text{Fe}^{3+}$  (Fig. 2a and b). The observed fluorescence enhancement for mixtures of  $\text{Fe}^{3+}$  with most metal ions was similar to that seen for  $\text{Fe}^{3+}$  alone. No other metal ions appeared to interfere with the fluorescence of the receptor **4** and  $\text{Fe}^{3+}$ . The interference studies have shown that the interference of other metal ions in  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$ . 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  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v) solution shown in Fig. 4. Under optimal conditions, the limit of detection for  $\text{Fe}^{3+}$  ion is 2.5  $\mu\text{M}$ .

#### Stoichiometry and Binding Constant of Receptor **4**

The binding stoichiometry between receptor **4** and  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$  ion [(MS (ESI): m/z requires (Calculated)  $\text{C}_{16}\text{H}_{18}\text{FeN}_2\text{O}_2$ : 326.17, found 327.30 (Figure S5, SI). All attempts was failed to grow the single crystal of receptor **4**. $\text{Fe}^{3+}$  ion complex. The association constant of  $\text{Fe}^{3+}$  ion was calculated from fluorescence titration experiments by Benesi–Hildebrand plot [23] and found as  $10,000\text{ M}^{-1}$  for  $\text{Fe}^{3+}$  (Fig. 6).

#### UV-Vis Absorption Spectral Studies

The absorption spectrum of receptor **4** with  $\text{Fe}^{3+}$  is shown in Fig. 7. Receptor **4** exhibit max peak at 240 and 272 nm in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v) 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  $\text{Fe}^{3+}$ .

#### 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  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$  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  $\text{Fe}^{3+}$  in  $\text{CH}_3\text{OH}/\text{H}_2\text{O}$  (60:40, v/v) medium. The detection of  $\text{Fe}^{3+}$  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

$\text{Cr}^{3+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Pb}^{2+}$  and  $\text{Bi}^{3+}$ . 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  $\text{Fe}^{3+}$  with high selectivity in aqueous solution at a very low concentration (2.5  $\mu\text{M}$ ).

## References

- Aragoni MC, Arca M, Bencini A, Blake AJ, Caltagirone C, Decortes A, Demartin F, Devillanova FA, Faggi E, Dolci LS, Garau A, Isaia F, Lippolis V, Prodi L, Wilson C, Valtancoli B, Zaccheroni N (2005) Coordination chemistry of N-aminopropyl pendant arm derivatives of mixed N/S-, and N/S/O-donor macrocycles, and construction of selective fluorimetric chemosensors for heavy metal ions. *Dalton Trans* 21:2994–3004
- Prodi L (2005) Luminescent chemosensors: from molecules to nanoparticles. *New J Chem* 29:20–31
- Fernandez YD, Gramatges AP, Amendola V, Foti F, Mangano C, Pallavicini P, Patroni S (2004) Using micelles for a new approach to fluorescent sensors for metal cations. *Chem Commun* 14:1650–1651
- Beer PD, Gale PA (2001) Anion Recognition and Sensing: The State of the Art and Future Perspectives, *Angew. Chem Int Ed* 40:486–516
- Quang DT, Kim JS (2010) Fluoro- and Chromogenic Chemodosimeters for Heavy Metal Ion Detection in Solution and Biospecimens. *Chem Rev* 110:6280–6301
- Zheng YJ, Orbulescu J, Ji XJ, Andreopoulos FM, Pham SM, Leblanc RM (2003) Development of fluorescent film sensors for the detection of divalent copper. *J Am Chem Soc* 125:2680–2686
- Schumacher AL, Hill JP, Ariga K, D'Souza F (2007) Highly effective electrochemical anion sensing based on oxoporphyrinogen. *Electrochem Commun* 9:2751–2754
- Jose DA, Kumar DK, Kar P, Verma S, Ghosh A, Ganguly B, Ghosh HN, Das A (2007) Highly effective electrochemical anion sensing based on oxoporphyrinogen. *Tetrahedron* 63:12007–12014
- Moon KS, Singh N, Lee GW, Jang DO (2007) Highly effective electrochemical anion sensing based on oxoporphyrinogen. *Tetrahedron* 63:9106–9111
- Gale PA (2011) Anion receptor chemistry. *Chem Commun* 47:82–86
- Joo TY, Singh N, Lee GW, Jang DO (2007) Benzimidazole-based ratiometric fluorescent receptor for selective recognition of acetate. *Tetrahedron Lett* 48:8846–8850
- Linder MC, Hazegh-Azam M (1996) Copper biochemistry and molecular biology. *Am J Clin Nutr* 63:797S–811S
- Uauy R, Olivares M, Gonzalez M (1998) Essentiality of copper in humans. *Am J Clin Nutr* 67:952S–959S
- Lee JD (2008) Concise of inorganic chemistry. Wiley, India
- Lippard SJ, Berg JM (1994) Principles of bioorganic chemistry. University Science, Mill Valley
- Kaim W, Schwederski B (1995) Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life, John Wiley & Sons Ltd
- Jacobs A (1977) Low molecular weight intracellular iron transport compounds. *Blood* 50:433–439
- Fegade U, Attarde S, Kuwar A (2013) Fluorescent recognition of  $\text{Fe}^{3+}$  ion with photo induced electron transfer (PET) sensor. *Chem Phys Lett* 584:165–171
- Fegade U, Sharma H, Attarde S, Singh N, Kuwar A (2013) Urea Based Dipodal Fluorescence Receptor for Sensing of  $\text{Fe}^{3+}$  Ion in Semi-Aqueous Medium. *J Fluoresc*. doi:10.1007/s10895-013-1297-4
- Fegade U, Marek J, Patil R, Attarde S, Kuwar A (2014) A selective fluorescent receptor for the determination of nickel (II) in semi-aqueous media. *J Lumin* 146:234–238
- Fegade U, Singh A, Chaitanya GK, Singh N, Attarde S, Kuwar A (2014) Highly selective and sensitive receptor for  $\text{Fe}^{3+}$  probing, *Spectrochim Acta A Mol Biomol Spectrosc* 121:569–574
- Job P (1928) Formation and stability of inorganic complexes in solution. *Ann Chim* 9:113–203
- Benesi HA, Hildebrand JH (1949) A Spectrophotometric Investigation on the Interaction of Iodine with Aromatic Hydrocarbons. *J Am Chem Soc* 71:2703–2707
- Becke AD (1993) Density functional thermo chemistry. III. The role of exact exchange. *J Chem Phys* 98:5648–5652
- Lee C, Yang W, Parr RG (1988) Development of the Colle–Salvetti correlation of energy formula into a functional of the electron Density. *Phys Rev B* 37:785–789
- Gaussian 09, Revision C.01, Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA, Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Keith T, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam JM, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas O, Foresman J B, Ortiz JV, Cioslowski J, Fox DJ, Gaussian, Inc. (2010) Wallingford CT