

Structurally Simple Ferrocene Derivatives for Selective Cadmium Sensing

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Received: 30 December 2013 / Accepted: 20 March 2014 / Published online: 6 April 2014
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Abstract Three new ferrocene based Schiff bases 4- $\{[(E)$ -ferrocenylmethylidene] amino $\}$ benzenethiol (**1b**), 3- $\{[(E)$ -ferrocenylmethylidene]amino $\}$ benzenethiol (**1c**), 2- $\{[(E)$ -ferrocenylmethylidene]amino $\}$ benzenethiol (**1d**) have been synthesized to study their sensor property to various metal ions. It has been observed that **1b** is highly fluorescent and its fluorescence changes in presence of metal ions. It was further observed that compound **1b** is highly selective towards Cd^{2+} ion in solution.

Keywords Ferrocene · Sensor · Cadmium · Fluorescence

Introduction

In recent years sensing of metal ion attracted the interest of many research groups due to its various ill effects on environment [1–3]. Of all the toxic metal ions, cadmium gets special attention due to its high toxicity [4–8]. It represents one of the highly toxic metals whose contamination occurs from variety of geological and man made sources [9–11]. Bioaccumulation of cadmium in living organism can be extremely toxic even at low concentration [12–14]. Cadmium poisoning can lead to kidney damage, high blood pressure, hypertension, bone marrow disorder and cancer [15–19]. Classically cadmium sensing include sophisticated techniques such

as atomic adsorption spectroscopy [20, 21], ICP (inductively coupled plasma) atomic emission spectroscopy [22] and graphite furnace atomic absorption spectrometry (GFAAS) [23]. Although they are accurate for trace amount detection of the metal ion, they have disadvantages such as high cost and complexity of operation. Thus there is need for analytical method for the detection of cadmium.

Recently, fluorescent chemosensors have received considerable interest due to their distinct advantages such as operational simplicity and high sensitivity [24–31]. However, till date, only a few literature are available for ferrocene sensors for cadmium [32–42]. In the design and development of cadmium selective sensor, presence of zinc in the sample often creates problem. Cadmium and zinc being in the same group of the periodic table have similar properties. Therefore they very often cause similar spectral changes while coordinated with fluorescent sensor [43, 44]. Thus it is desirable to prepare fluorescence sensors which can distinguish cadmium from zinc with high selectivity and sensitivity.

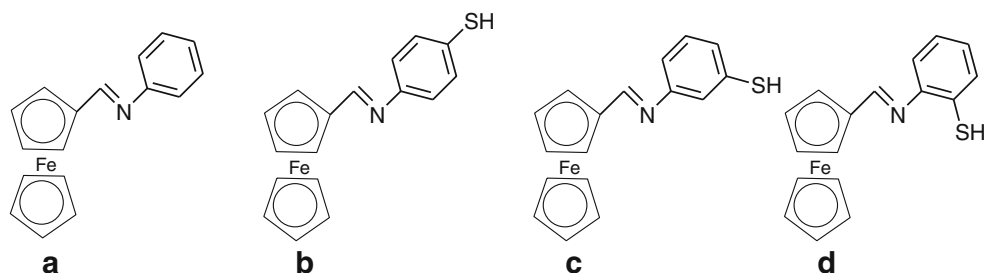
Ferrocene based chemosensors found wide applicability in the field of sensor for various ions. When the signaling unit is ferrocene, redox potential is the method of choice due to its low analyte detection limit. In this regard cyclic voltammetry is often applied to measure the change of redox potentials, which can be correlated to the binding strengths of target analyte [45–49]. However, the fluorescent activity of ferrocene based molecules for the ion sensor have not been studied explicitly [50–54]. To the best of our knowledge there is not any reference of ferrocene based fluorescent sensor for cadmium till date.

Bearing that in mind we have synthesized a series of ferrocenyl Schiff bases (**1**) which show fluorescent property (Fig. 1). In this paper we report the selective sensing of cadmium over a wide variety of competing ion including zinc by compound **1b** using ferrocene spectroscopy.

Electronic supplementary material The online version of this article (doi:10.1007/s10895-014-1382-3) contains supplementary material, which is available to authorized users.

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Fig. 1 Molecular structures of **1a**, **1b**, **1c** and **1d**



Experimental

Synthesis

The compound **1b**, **1c** and **1d** were synthesized by usual procedure of Schiff base synthesis. To a solution of ferrocenecarboxaldehyde (1 mmol) in dry methanol, 4-aminothiophenol (1 mmol) was added and the reaction mixture was stirred for 1 h. The red precipitate was filtered and recrystallize from DCM/Hexane mixture to afford pure ferrocenyl imine as dark red solid. Compound **1a** was synthesized according to literature procedure [55]. Ferrocenecarboxaldehyde (0.22 g, 1.0 mmol) and benzylamine (0.21 g, 2.0 mmol) in presence of catalytic amount of K_2CO_3 were dissolved in toluene (10 ml) and reflux under Dean-Stark for 24 h. Then 4 Å molecular sieves were added to the hot reaction mixture and stirring was continued for another 48 h at room temperature. Then the reaction mixture was filtered and the filtrate was evaporated to dryness. The solid residue was washed with hexane and dried in vacuo.

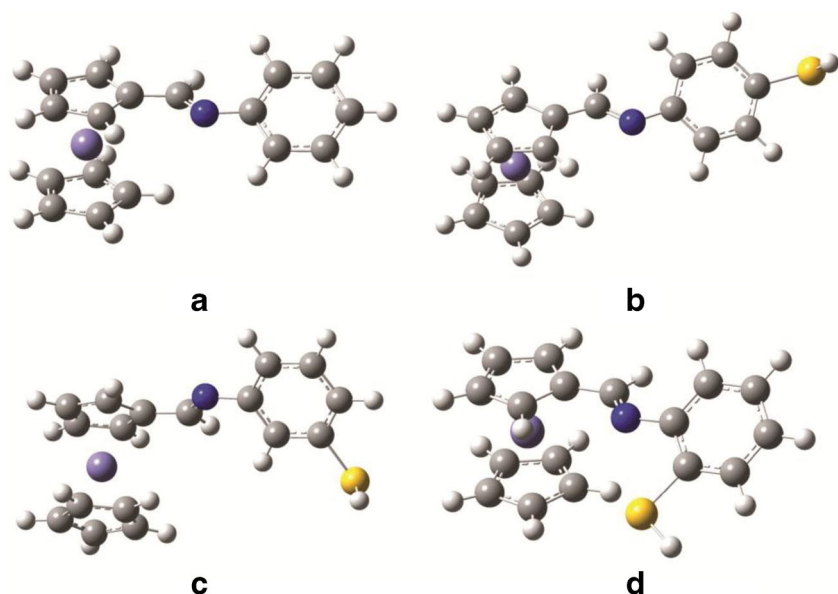
N-[(E)-ferrocenylmethylidene]aniline (1a): Dark red solid. Yield 77 %. Mp: 105–106 °C. IR (KBr, cm^{-1}): ν 1430,

1691, 3022. 1H NMR (300 MHz, $CDCl_3$, TMS): δ 4.29 (s, 5H), 4.53 (s, 2H), 4.86 (s, 2H), 6.65–6.92 (m, 2H), 7.15–7.35 (m, 3H), 7.37–7.55 (m, 1H) 8.38 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 68.9, 69.1, 71.2, 80.1, 120.47, 125.1, 129.0, 152.6, 161.3.

4-[(E)-ferrocenylmethylidene]amino}benzenethiol (1b): Red Solid. Yield 80 %. Mp: 160–161 °C. IR (KBr, cm^{-1}): ν 1442, 1690, 2587, 3071. 1H NMR (300 MHz, $CDCl_3$, TMS): δ 1.71 (s, 1H), 4.25 (s, 5H), 4.51 (s, 2H), 4.80 (s, 2H), 7.10 (d, $J=9$ Hz, 2H), 7.52 (d, $J=9$ Hz, 2H), 8.33 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 69.1, 69.3, 71.5, 80.1, 131.4, 130.1, 133.4, 152.4, 161.8. LC-MS (m/z %): 321 [M^+] (18), 279 (15), 215 (32), 157 (55), 65 (100).

3-[(E)-ferrocenylmethylidene]amino}benzenethiol (1c): Red solid. Yield: 78 %. Mp: 130–133 °C. IR (KBr, cm^{-1}): ν 1452, 1655, 1569, 3078. 1H NMR (300 MHz, $CDCl_3$, TMS): δ 1.83 (s, 1H), 4.16 (s, 5H), 4.51 (s, 2H), 5.01 (s, 2H), 7.30–7.54 (m, 3H), 7.80–8.05 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 68.6, 70.4, 70.7, 80.1, 121.3, 122.2, 124.3, 126.0, 134.7, 153.9, 169.7. LC-MS (m/z %): 322 [M^+H] (20), 320 (100), 301 (9), 287 (12).

Fig. 2 Computer generated optimized structures of (a) N-[(E)-ferrocenylmethylidene]aniline (**1a**), (b) 4-[(E)-ferrocenylmethylidene]amino}benzenethiol (**1b**), (c) 3-[(E)-ferrocenylmethylidene]amino}benzenethiol (**1c**), (d) 2-[(E)-ferrocenylmethylidene]amino}benzenethiol (**1d**)



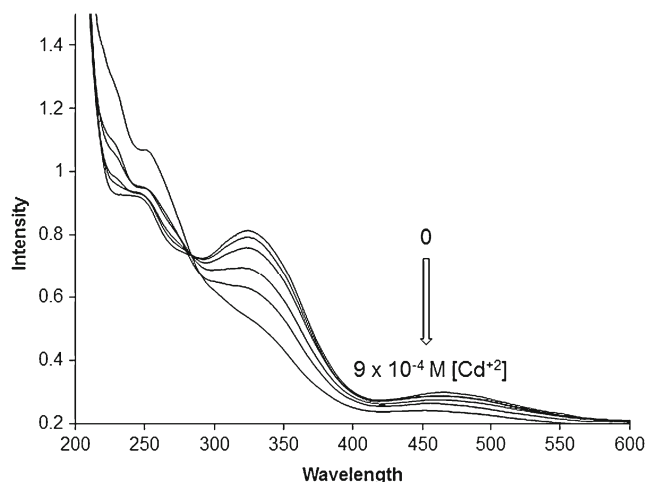


Fig. 3 Absorption spectra of compound **1b** at different amount of Cd^{2+} ion (0 – 9×10^{-4} M) in MeOH and H_2O mixture (1:1)

2-[(E)-ferrocenylmethylidene]amino}benzenethiol (1d): Red Solid. Yield: 70 %. Mp: 119–120 °C. IR (KBr, cm^{-1}): ν 1498, 1677, 2569, 3033. ^1H NMR (300 MHz, CDCl_3 , TMS): δ 1.76 (s, 1H), 4.22 (s, 5H), 4.50 (s, 2H), 4.78 (s, 2H), 6.40–7.51 (m, 4H), 8.26 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3 , TMS): δ 69.29, 69.6, 71.47, 80.0, 117.3, 118.9, 119.9, 123.8, 129.7, 137.7, 162.2. LC-MS (m/z %): 322 [M+H] (38), 321 [M $^+$] (37), 320 (100).

Results and Discussion

The structures of the compounds were determined using Gaussian03/DFT. To optimize the structure, density functional calculations were carried out with the Gaussian03/DFT series of programs [56]. The B3LYP formulation [57, 58] of density functional theory was used employing the LANL2DZ basis set. No symmetry constraints were imposed on the molecules.

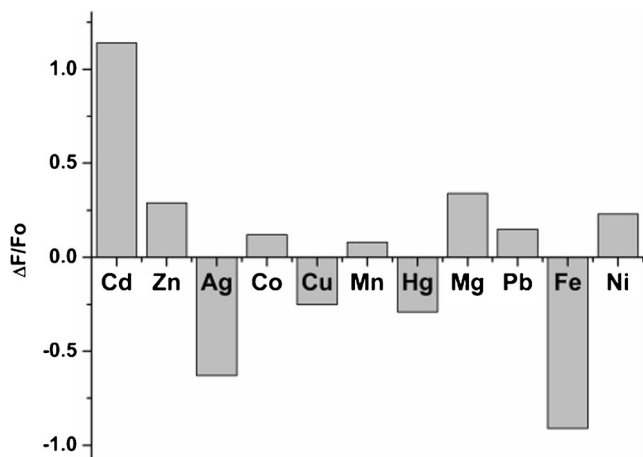


Fig. 4 Fluorescence change ($\Delta F/F_0$) of compound **1b** at 290 nm in the presence of different metal ions in MeOH– H_2O (1:1) mixture ([compound **1b**]=0.001 M, $[\text{M}^{n+}]$ = 2.0×10^{-4} M, λ_{ex} =280 nm)

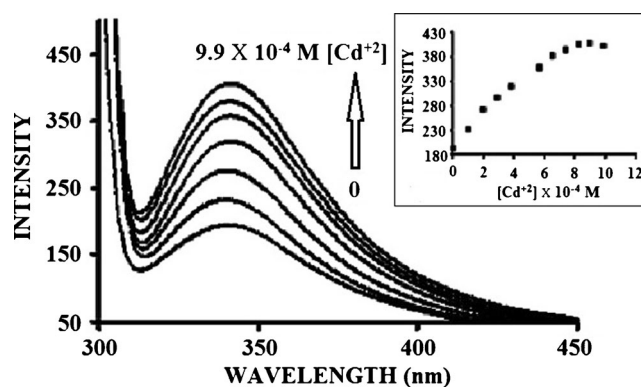


Fig. 5 Fluorescence spectra of compound **1b** in presence of different amount of Cd^{2+} ion (0 – 9.9×10^{-4} M) in a mixed solution of MeOH and H_2O (1:1). Inset: Fluorescence intensity as a function of Cd^{2+} concentration

No solvent modeling was employed. Eclipsed conformation of the two cyclopentadienyl ring for compound **1a**, **1c** and **1d** was observed on optimization. However the ferrocene moiety **1b** takes a staggered conformation (Fig. 2).

In the first set of experiment we investigated the complexation of compound **1b** and Cd^{2+} in detail. UV–vis spectra of compound **1b** were recorded at different added concentration of Cd^{2+} . In a solution of MeOH: H_2O (1:1) compound **1b** shows two peaks in UV–vis spectrum at 325 nm (prominent) and 240 nm. In the presence of increasing amount of Cd^{2+} ion the absorption at $\lambda_{\text{max}}=325$ nm constantly decreases whereas that at $\lambda_{\text{max}}=240$ nm increases. Moreover, on gradual addition of Cd^{2+} a new peak appears at 230 nm. The spectra show only one isobestic point at 285 nm probably due to the equilibrium between compound **1b** and compound **1b**+ Cd^{2+} (Fig. 3).

The fluorescence sensing property of compound **1b** towards Cd^{2+} was carried out in a mixed solution of MeOH and H_2O (1:1). Free compound **1b** shows weak fluorescence

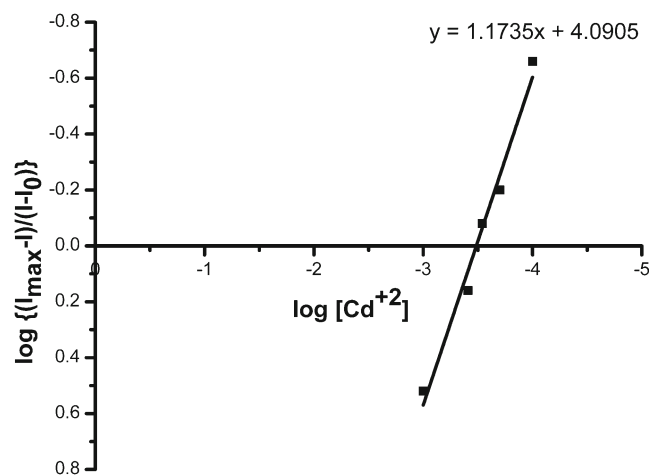
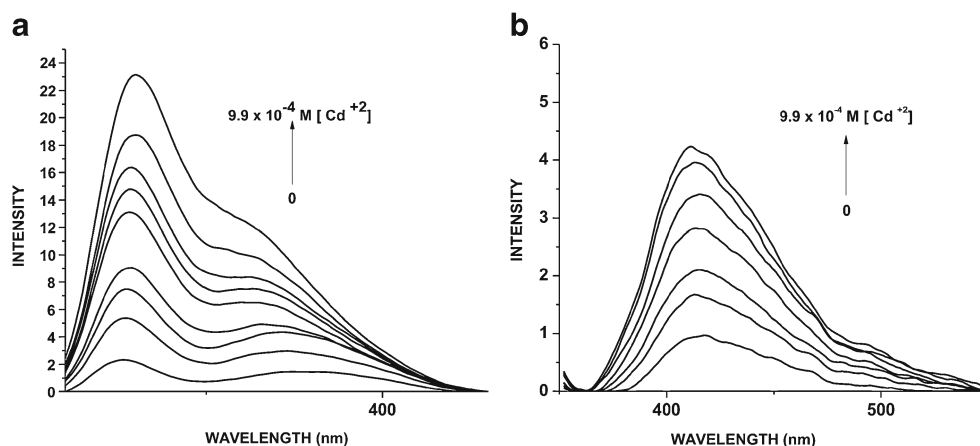


Fig. 6 Hill plot for the complexation of compound **1b** with Cd^{2+} ion from fluorescence. I_0 , I and I_{max} are fluorescence intensity of compound **1b** at zero, at an intermediate and at the infinite concentration of Cd^{2+} ion respectively

Fig. 7 Fluorescence spectra of (a) compound **1a** and (b) compound **1c** in presence of different amount of Cd^{2+} ion



emission at 290 nm upon excitation at isobestic point of 280 nm. However, when Cd^{2+} ion was added to the above solution, we observed a significant increase in the fluorescence emission at 290 nm. To inspect the specificity towards Cd^{2+} , next we examined the fluorescence response of compound **1b** in presence of various metal ions. This can be observed by plotting $\Delta F/F_0$ versus various metal ions (where F_0 is the fluorescence of **1b** in absence of metal ion and $\Delta F = F_m - F_0$ (F_m = fluorescence of **1b** in presence of metal ion)). As seen in the Fig. 4, the $\Delta F/F_0$ value of **1b** is 1.14 in presence of Cd^{2+} , while Zn^{2+} shows a low $\Delta F/F_0$ value of 0.29 under the same condition. In addition, Co, Mn, Pb and Ni show very little fluorescence increase under our experimental condition. In contrast, compound **1b** displays a fluorescence quenching effect with Cu, Hg, Fe and Ag.

To scan the signal response towards Cd^{2+} , the fluorescence emission of compound **1b** were tested in different concentration of the metal ion (Fig. 5). On stepwise addition of Cd^{2+} ion, the fluorescence intensity of compound **1b** at 290 nm was gradually increased. The fluorescence intensity of compound **1b** increased linearly with Cd^{2+} upto 1:1 mole ratio and then remains constant with increasing Cd^{2+} ion, indicating that compound **1b** and Cd^{2+} undergoes 1:1 complex formation.

The fact that 1:1 complexation occurs between ligand and the metal is further supported by Hill plot of the fluorescence data as shown in the Fig. 6. The plot of $\log\{I_{\text{max}} - I\}/(I - I_0)$ Vs $\log[\text{Cd}^{2+}]$ is linear with a slope of 1.1735 and intercept 4.0905 indicating binding of one Cd^{2+} ion per ligand with $\log \beta = 4.09$.

For a deeper insight into the relationship between selectivity and structure of **1b**, compound **1a**, **1c** and **1d** are prepared. The fluorescence activities of all these compounds in presence of different metal ion were investigated. All the compounds have different response to the metal ions.

Compound **1a** and **1c** do respond to the presence of different metal ion in their respective fluorescence, but its selectivity is very low (Figs. 7 and 8). The metal sensing property of **1a** (Figs. 7a and 8a) indicates that -SH is not a binding site for the metal ion, however, its presence and position greatly influence the selectivity of the ligands.

To examine the binding mode of cadmium with **1d**, ^1H NMR spectra was measured in MeOD: D_2O (1:1) solution (Figure S1). Upon interaction with Cd^{2+} the iminium proton experienced approximately 0.08 ppm of downfield shift to 8.51 ppm. A similar trend was also observed for the aromatic protons. This shift of the signal can be attributed to deshielding effect of the metal ion on the protons of its proximity. It is possible only when cadmium ions bind to the

Fig. 8 Fluorescence change ($\Delta F/F_0$) of (a) compound **1a** and (b) compound **1c** in presence of different metal ion

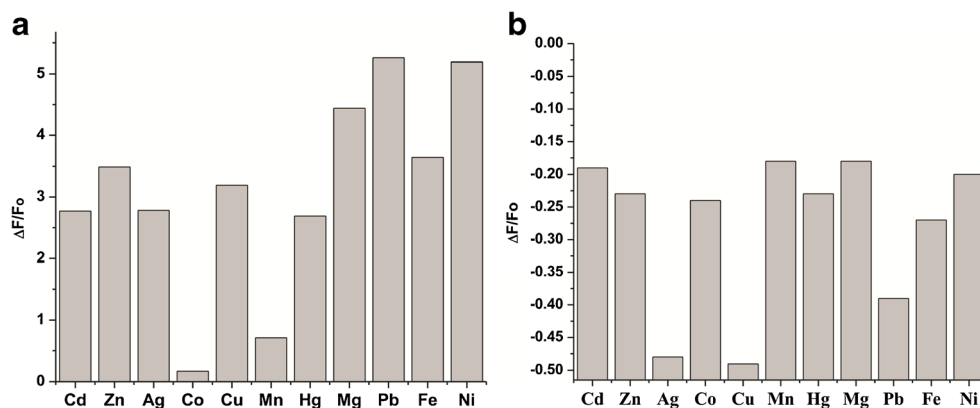
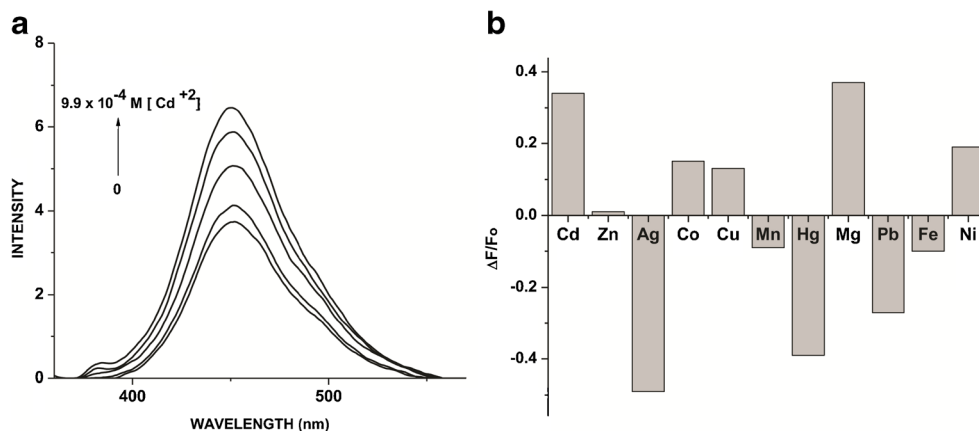


Fig. 9 Fluorescence change of compound **1d** (a) In presence of different amount of Cd^{2+} ion; (b) in presence of different metal ion



nitrogen atom. From this study we have confirmed that nitrogen atom of the molecule coordinate with Cd^{2+} ion to form **1d**/ Cd^{2+} complex.

Interestingly, the performance of compound **1d** (Fig. 9), towards selective sensing of Cd^{2+} in presence of Zn^{2+} is better than that of compound **1b**. However, the fluorescence of **1d** is very low makes it unsuitable to use as sensor.

The fluorescence enhancement of compound **1b** in presence of Cd^{2+} can be explained on the basis of PET process. In absence of Cd^{2+} ion there is a flow of electron density from nitrogen atom to the fluorophore part, which quenches the fluorescence of compound **1b**. The Cd^{2+} is likely to bind through N atom of compound **1b**. As a result the energy of the HOMO of the receptor part of compound **1b** lowered and consequently the oxidation potential of receptor unit increases which effectively stops the PET process and accordingly fluorescence intensity increases.

The driving force for the electron transfer from the receptor unit to the fluorophore unit in the PET process can be expressed by modified Weller equation as follows.

$$\Delta G_{\text{et}} = -E_{\text{s}} - E_{\text{red, fluo}} + E_{\text{ox, receptor}}$$

Where E_{s} , $E_{\text{red, fluo}}$ and $E_{\text{ox, receptor}}$ represent the singlet energy, reduction potential of the fluorophore and the oxidation potential of the receptor unit respectively. If the binding of

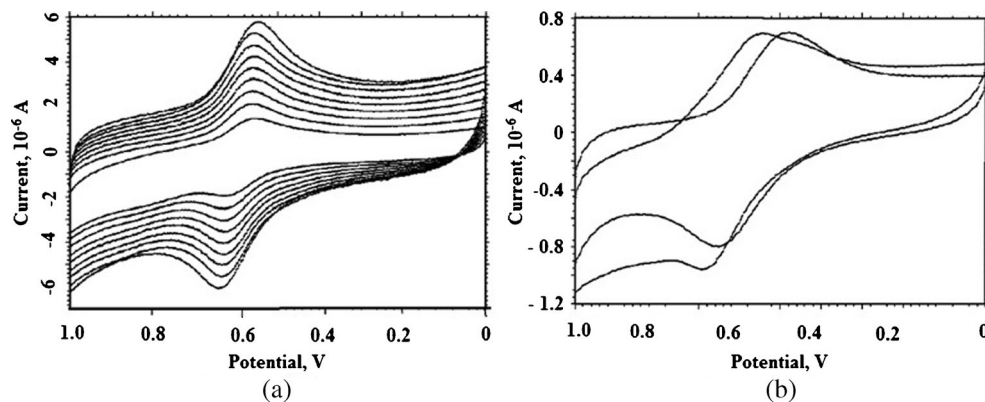
the cation increases the oxidation potential of the receptor unit than this process will increase the ΔG_{et} , which will decrease the PET process and consequently it allows the excited chromospheres to relax by fluorescence.

Cyclic voltammogram of compound **1b** was recorded in MeOH in absence and presence of equivalent amount of Cd^{2+} ions using GC as working electrode and Ag-AgCl as reference (Fig. 10). Both the oxidation as well as reduction potential changes in the positive direction. The oxidation potential changes from 0.6 to 0.7 V while the reduction potential increases from 0.52 to 0.58 V. Therefore from the Weller equation it is clear that the binding of Cd^{2+} ion increases the ΔG_{et} value and consequently fluorescence intensity increases.

Conclusion

In summary we have developed a structurally simple ferrocene derivative as a sensitive fluorescent probe for selective detection of Cd^{2+} . It is excited at 280 and emit at 290 nm and displays a significant fluorescent enhancement after complexation with Cd^{2+} . Presence of -SH group in *para*-position of the aromatic ring greatly enhances the fluorescence intensity and selectivity for Cd^{2+} over other competitive metal ion including Zn^{2+} .

Fig. 10 Cyclic voltammetry of (a) **1b** at different scan rate (10–500 mV/sec) (b) shift of CV peaks of **1b** in presence of Cd^{2+}



Acknowledgments Financial Support from DST, India (Grant No. SR/S1/RFP-C-07/2006) India is gratefully acknowledged. BK thanks CSIR for Senior Research Fellowship.

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