

Design and Development of Arylether Based Receptors for Electroanalytical Applications

A
Thesis submitted in partial
fulfillment of the requirement for the degree of

Doctor of Philosophy

Submitted by

**Rashmi
(901309001)**

Under the supervision of

Dr. Susheel Mittal
Senior Professor

Dr. Manmohan Chhibber
Associate Professor



School of Chemistry & Biochemistry

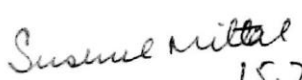
Thapar University
Patiala-147004, India

July, 2016

Certificate

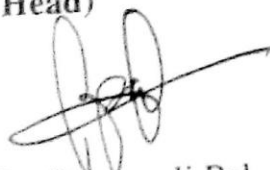
Certified that the thesis entitled "**Design and Development of Arylether Based Receptors for Electroanalytical Applications**" which is submitted by Ms. Rashmi in partial fulfillment of the requirement for the award of the Degree of Doctor of Philosophy in the School of Chemistry and Biochemistry, Thapar University, Patiala, is a record of candidate's own independent and original research work carried out by her under our supervision and guidance. The material embodied in this thesis has not been submitted in part or full to any other University or Institute for the award of any degree.

(Supervisors)


15.7.2016
Dr. Susheel Mittal
Senior Professor
School of Chemistry and Biochemistry
Thapar University, Patiala-147004


15/7/2016
Dr. Manmohan Chhibber
Associate Professor
School of Chemistry and Biochemistry
Thapar University, Patiala-147004

(Head)


Dr. Bonamali Pal
Professor
School of Chemistry and Biochemistry
Thapar University, Patiala-147004, Punjab (INDIA)

Candidate's Declaration

I, hereby declare that the work presented in the thesis entitled "**Design and Development of Arylether Based Receptors for Electroanalytical Applications**" in partial fulfillment of the requirements for the award of the degree of Doctor of Philosophy, School of Chemistry and Biochemistry, Thapar University, Patiala, is an authentic record of my own work carried out under the joint supervision of Dr. Susheel Mittal, Senior Professor and Dr. Manmohan Chhibber, Associate Professor, School of Chemistry & Biochemistry, Thapar University, Patiala, India. The matter embodied in this thesis has not been submitted in part or full to any other university or institute for the award of any degree in India or Abroad.

Place: Patiala

Date: 15.07.16



Rashmi

901309001

Acknowledgements

Apart from the efforts of oneself, the success of any project depends largely on the encouragement and guidelines of many others. In my journey to the completion of Ph.D. thesis there are many who walked along and beside me to help support and motivate me all these years.

I take this opportunity to gratefully acknowledge the enthusiastic supervision of Dr. Susheel Mittal, Senior Professor, School of Chemistry & Biochemistry, Thapar University, Patiala and Dr. Manmohan Chhibber, Associate Professor, School of Chemistry & Biochemistry, Thapar University, Patiala, for having faith in me and entrusting me with this opportunity to work under their guidance and supervision, providing all kinds of support and inspiration, wise counsel, constant encouragement, valuable suggestions and comments, expertise and fruitful advice throughout this exploration and preparation of the thesis. It's a great privilege to experience a sustained enthusiastic, involved interest, constructive criticism, tremendous enthusiasm and careful supervision from their side throughout the period of my work.

I express my gratitude to Director, Thapar University, Patiala and Dr. Bonamali Pal, Head, School of Chemistry and Biochemistry, for all the facilities which have been immensely helpful for the completion of my work.

I express my regards to Dr. Raj Kumar Gupta and Dr. Vijay Luxami (PhD committee member- Subject expert) for suggestions and taking interest in the progress of work along with laboratory facilities.

I extend my thanks to all the faculty members of School of Chemistry and Biochemistry, Thapar University, Patiala for providing necessary guidance during my research work. I am thankful to Mr. Chandar Thakur and other non-teaching staff, School of Chemistry and Biochemistry for the constant official help and cooperation.

I owe a debt of gratitude and heartfelt thanks to my seniors - Dr. Jasinder Singh and Dr. Karamjeet Kaur, Dr. Komal Matharu, Dr. Ramandeep Kaur, my best companions throughout Ms. Manisha Pabbi, Ms. Sonia, Mrs. Rupinder Kaur, Ms. Ritika Chhabra, Ms Ramandeep Kaur, Mr. Sanjeev Kumar, Mr. Akul Sen Gupta, Mr. Yuvraj Garg and Mr. Anirudh Sharma for their kind concern, critical observations in designing and planning experiments and above all their support, which always helped me endure hard times and to accomplish all my goals.

I owe a word of thanks to all research scholars at the School of Chemistry and Biochemistry for providing constant support, encouragement and a good working atmosphere.

I am thankful to all the students who worked with me and people, who taught me various lessons of life and helped me in polishing my skills of both personal and professional arena.

I feel deeply indebted and sense of gratitude for my parents (Mr. Naresh Kumar and Mrs. Neena Rani), who despite of all the difficulties, made me what I am today, my siblings (Rahul Sharma, Shivam Sharma), my grandparents (Lt. Nand Kishore and Sheela Wanti), for their blessings and belief in me, who have always showered unconditional love on me, encouraged and supported me in every aspect. They formed a part of my vision and taught me the good things that really matter in life.

Above all, I'm grateful to Almighty God for blessing me to complete this work successfully.


Rashmi

List of Contents

S.No	Contents	Page No.
	Abstract	ix-xi
	Chapter 1 Introduction	1-14
1.1	Chemical sensing	1-1
1.2	Methods of chemical sensing	1-8
1.2a)	Receptor unit based classification of chemical sensors	
1.2b)	Transducer unit based classification of chemical sensors	
1.3	Techniques used	8-12
1.3.1	Spectrophotometry	
1.3.2	Spectrofluorimetry	
1.3.3	Voltammetry	
1.3.1a)	Cyclic voltammetry	
1.3.1b)	Differential pulse voltammetry	
1.4	References	13-14
	Chapter 2 Review of Literature	15-31
2.1	Cation sensing	15-15
2.1.1	Alkaline and transition metal ions	15-19
a)	Spectrophotometric methods	
b)	Electrochemical methods	
2.1.2	Rare earth metal ions	19-21
a)	Spectrophotometric methods	
b)	Electrochemical methods	
2.2	Anion sensing	21-26
2.2.1	Spectrophotometric methods	
2.2.2	Electrochemical methods	
2.3	References	27-31
	Chapter 3 Materials and Methods	32-42
3.1	Chemicals	32-32
3.2	Instrumental techniques	

3.2.1 Spectrophotometry	
3.2.2 Spectrofluorimetry	
3.2.3 Voltammetry	
3.2.4 Computational studies	
3.3 Experimental section	34-41
3.3.1 Synthesis of Diphenyl ether based receptors	
3.3.2 Synthesis of Triphenyl ether based receptors	
3.3.3 Experimental set-up for voltammetric study	
3.3.4 Stock solution for cation/anion/lanthanide interaction	
3.4 References	42-42
Chapter 4 DIPHENYLETHER BASED RECEPTORS	43-77
4.1 Synthesis and characterization	43-45
4.2 Ion- recognition studies	
4.2.1 Ion-recognition studies of SMR-1 & SMR-2	46-60
Electrochemical behaviour of SMR-1 and SMR-2	
Computational studies	
Real life sample analysis	
Conclusions	
4.2.2 Ion-recognition studies of SMR-3 & SMR-4	61-76
Spectrophotometric measurements	
Electrochemical measurements	
¹ H NMR Studies	
Computational studies	
Conclusions	
4.3 References	77-77
Chapter 5 TRIPHENYLETHER BASED RECEPTORS	78-127
5.1 Synthesis and characterization	78-80
5.2 Ion- recognition studies	
5.2.1 Ion-recognition studies of SMR-15	80-97
Design of receptor SMR-15	
Spectrophotometric studies	
Spectrofluorimetric studies	
Electrochemical studies	
Computational studies	
Analytical application (<i>Dip strip test</i>)	
Conclusions	97-97
5.2.2 Lanthanide interaction studies with SMR-15	97-109

Spectrophotometric studies	
Electrochemical studies	
Computational studies	
Conclusions	109-109
5.2.3 Ion-recognition studies of SMR-16	109-127
Spectrophotometric studies	
Spectrofluorimetric studies	
Electrochemical studies	
Computational studies	
Conclusions	127-127
5.3 References	127-127
Chapter 6 OTHER VOLTAMMETRIC SENSORS DEVELOPED	128-154
6.1 Voltammetry of nanoparticle coupled imine linkage based receptors for sensing of Al(III) and Co(II) ions	128-142
Electrochemical behavior of SNR-4, SNR-5 and SNR-6	
Real life sample analysis	
Conclusions	142-142
6.2 Electrochemical detection of fluoroquinolone drug: Levofloxacin	143-152
Ion-pair formation	
Electrochemical determination of ion pair	
Computational studies	
Analytical applications	
Conclusions	152-152
6.3 References	153-154
6.4 List of publications	155-156

Different derivatives of di- and triphenylether molecules were synthesized by aromatic nucleophilic substitution reactions. Molecules named **SMR-1** to **SMR-16** were synthesized using various organic tools, which were then analyzed for their ion-recognition studies using spectrophotometric and voltammetric techniques. All the molecules were studied for their analytical applications as chemical sensors for target ions without interference from other ions. Complexation or interaction studies were also supported by theoretical studies using DFT calculations on Gaussian 03W software.

4-(2,4-dinitrophenoxy)-3-methoxybenzaldehyde (**SMR-1**) and (4-(2,4-dinitrophenoxy)-3-methoxyphenyl)methanol (**SMR-2**) were investigated for their complexation behaviors with various cationic species (Na(I), K(I), Mg(II), Cu(II), Ba(II), Cr(III), Fe(III), Co(II), Ni(II), Zn(II), Cd(II) and Pb(II)) in HEPES buffered CH₃CN:H₂O system. Both receptors showed high degree of selectivity for Fe(III) over other cations. Electrochemically, **SMR-1** facilitated reduction of nitro group due to the presence of electron withdrawing (carbonyl) group and peak potentials of the cathodic two curves (for **SMR-1**) appeared at -1.16 V (E_{pc1}) and -1.39 V (E_{pc2}) respectively. In **SMR-2**, due to electron donating character of the methanolic group made reduction of the nitro group a little difficult due to which peak potentials occur at higher potential as compared to **SMR-1** i.e. at -1.30 V (E_{pc1}) and -1.43 V (E_{pc2}), respectively. **SMR-1** and **SMR-2** can be projected as Fe(III) chemosensors with no interference from any other metal ion.

SMR-3 and **SMR-4** were studied for their binding ability with some selected anions like fluoride, cyanide, acetate, bisulphate, etc. by spectrophotometric and voltammetric methods, supported by theoretical studies. Results of the study showed that **SMR-3** has high selectivity for fluoride ions over other anions in the acetonitrile medium. More importantly, **SMR-3** displays naked-eye detection of fluoride ions at room temperature with a linear response in the range 0.1 to 20 μ M.

SMR-15 molecule with ether-imine functional groups was analyzed for its interaction with different cations, anions and lanthanides. **SMR-15** showed instant visual color change on addition of fluoride, cyanide and cobalt ions, which led to the study of interaction of **SMR-15** with Co(II), F⁻ and CN⁻. A sharp color change from light yellow to colorless was observed for CN⁻ through a nucleophilic addition mechanism, while F⁻ was detected through H-bonding mechanism with a distinct color change from light yellow to dark yellow. Co(II) was detected

by formation of complex in pseudocavity in **SMR-15** causing color change from yellow to blue. Paper strips of **SMR-15** receptor were also prepared to detect the presence of Co(II), F⁻ and CN⁻.

SMR-15 was also studied for its interaction with various lanthanides and has been developed as a new sensitive and selective chemosensor for the determination of cerium ions. The proposed receptor works as an excellent receptor by spectrophotometry and voltammetric methods in CH₃CN:H₂O (95:5, v:v) solvent medium. Detection limit obtained by this sensor is 5×10^{-7} M without any interference in CH₃CN:H₂O medium, which makes it a potent sensor for cerium detection.

SMR-16 with unique ether-imine combination was also analyzed for its binding behavior with various cationic species (Na(I), K(I), Ag(I), Cu(II), Ni(II), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Hg(II), Fe(II), Al(III)) in CH₃CN:H₂O system. Observable color change from dark yellow to colourless was the first signalling system for the interaction of **SMR-16** with Cu(II) ions. Binding constant calculated from UV-visible spectrophotometric studies was 2.0×10^5 M⁻¹ and the detection limit obtained was 50 nM. Highlight of the work is ratiometric sensing of water content by **SMR-16**-Cu(II) complex in pure acetonitrile medium. Detection limit for the detection of water content in a medium was determined as low as 0.06 ppb. Electrochemically, **SMR-16** showed a major anodic peak at 1.05 V and a cathodic peak at 0.95 V along with small peaks at 1.35 V (anodic peak) and 0.5 V (cathodic peak). The anodic and cathodic peaks were found shifted in presence of copper ions only. Chemosensor showed 1:1 complexation with Cu(II) ions by sandwiching two copper ions between two **SMR-16** molecules as observed by theoretical studies as well. The optimized electrochemical method was successfully used for the detection of copper (II) ions from real samples.

In addition to aryether molecules, zinc oxide nanoparticle coupled imine linkage based receptors (**SNR-4**, **SNR-5** and **SNR-6**) were also studied for their electrochemical characteristics. **SNR-4** and **SNR-5** having electron withdrawing and electron donating substituents at meta-position of the imine linkage showed prominent cathodic (reduction of imine group) peaks at -0.930 V and -1.850 V, respectively, while **SNR-6** (without any substituent) showed a cathodic peak at -1.220 V. Voltammograms of the receptors indicated that **SNR-4** and **SNR-5** responded quantitatively for aluminium ions, while **SNR-6** responded for cobalt ions. All the three receptors exhibited a linear dynamic range between 0.1 μ M to

0.42 μ M with regression coefficients ≥ 0.98 . The proposed analytical method has been validated with complexometric method for metal detection in real time samples.

Further, Levofloxacin (LFX), an antimicrobial agent has also been determined by using picric acid (PA) as an anionic reagent in aqueous medium using voltammetric method. On mixing the reactants in distilled water, yellow colored product was separated within two minutes as an ion-association complex (LFX-PA) of both the reactants. Voltammetric studies were carried out to explain the interaction between levofloxacin and picric acid. In voltammetric experiments, a shift of 70 mV from that of LFX was noticed in an anodic peak of LFX-PA (1.64V) accompanied with a large decrease in peak current. In addition, a number of new peaks appeared in voltammogram of LFX-PA. A calibration curve was drawn using the peak current values of the LFX. The linear increase in peak current with increasing LFX concentration was obtained in the concentration range 1.5×10^{-3} M – 6.0×10^{-3} M with $R^2 = 0.994$. A study on the solvent effect by voltammetric methods for LFX suggested that water is the best medium for the study. Stability of the complex was also determined by computational methods using DFT/B3LYP/6-31G basis sets. Further, analysis of LFX in commercially available drug tablets proved that the proposed method is valid in real life sample analysis.

INTRODUCTION

1.1 Chemical sensing

According to IUPAC definition “a chemical sensor is a device that transforms chemical information like composition, presence of a particular element or ion, concentration or chemical activity into an analytically useful signal.” The chemical information may originate from a chemical reaction of an analyte or from a physical property of the system under investigation [1]. This whole procedure leads to chemical sensing. Chemical sensing can be carried out by using different mechanisms based on Potentiometry, Voltammetry, Optical devices etc. depending on the type of transducer used. Receptor and transducer parts are two basic units of chemical sensors which are connected in series. In the majority of chemical sensors, the receptor interacts with analyte molecules. Consequently, a characteristic physical/chemical parameter varies and this variation is reported by means of an integrated transducer that generates the output signal. The receptor part transforms the chemical information into a form of energy which may be measured by the transducer which further transforms the information into a useful analytical signal. Important parameters for any sensor to be effective include selectivity, sensitivity, reversibility, resolution, durability and specificity. Selectivity defines the degree to which one chemical form can be distinguished from another by a sensor. Sensitivity is a measure of output produced by the change of concentration of any chemical form. Reversibility refers to the recovery of the device to its original state [2]. Resolution is a measure of minimum detectable change of the input quantity by a sensor. Specificity defines the number of chemicals a sensor can detect or distinguish in between.

1.2 Methods of chemical sensing

The development of instrumentation and techniques make it possible to design sensors which utilise most of the known chemical, physical and biological principles for effective chemical sensing based on two categories as follows:

- a) Receptor unit based
- b) Transducer unit based

1.2a) Receptor unit based classification of chemical sensors

In theory, the principle of sensing materials is based upon the fact that a receptor molecule can recognize guest molecules in a very selective way using weak and generally reversible non-covalent bonds [3]. Receptor is an organic building block that can hold a guest which is a cation, anion or a neutral molecule. One or more receptor molecules orient themselves in such a way that an enclosed cavity is formed to entrap any cation or anion inside it. Among the cations, sodium, potassium, magnesium and calcium are ubiquitous in biological systems. Some transition metal ions such as Cu(I or II), Co(II), Zn(I) and Mn(II) play important roles in metalloenzymes and other proteins [4]. Further, other metals such as Hg(II), Cd(II), and most radioactive species are very toxic. Thus, the facile detection and, in some cases, extraction of these cations are very important. A number of receptors, including crown ethers [5], cryptands, calixrenes [6-7], benzimidazoles [8], triazoles [9], Schiff base derivatives [10-11], anthrones [12] and ferrocene based derivatives [13-14] have been studied as cation complexants and their selectivity is highly dependent on structure.

Coming from the literature of supramolecular, co-ordination or host-guest chemistry, receptors mainly include crown ethers, podands, cryptands and spherands as shown in Fig. 1.1.

- (a) **Crown Ethers:** Crown Ethers (Fig. 1.1a) are cyclic polyethers i.e. the repeating unit being ethyleneoxy, i.e., $-\text{CH}_2\text{CH}_2\text{O}-$ discovered by Pederson in 1967 [15]. The characteristic chemistry of crown ethers involves complexation of the ether oxygens with various ionic species. This is termed "host-guest" chemistry, with the ether as host and the ionic species as guest.
- (b) **Podands:** Podands (Fig. 1.1b) are open-chained analogues of crown ether compounds. Podands now exist in various structural variations from single-chained basic compounds to multi-armed dendrimers. Podands are also called as multidendate organic ligands or multi-donor host compounds [16].
- (c) **Cryptands:** Cryptands (Fig. 1.1c) are three-dimensional analogues of crown ethers and are more selective and strong as complexes for the guest ion. Cryptands are a family of synthetic bi- and polycyclic multidentate ligands for a variety of cations [17].

(d) **Spherands:** Spherands (Fig. 1.1d) are the most preorganized and rigid of the macrocyclic receptors. Unlike the crown ethers and even cryptands, the binding activation energy of spherands is extremely high due to their rigid structure.

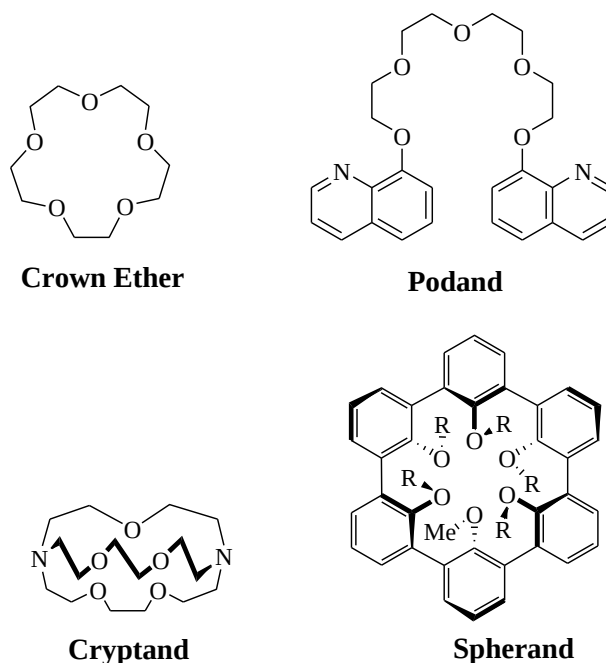


Figure 1.1 Classifications and topology of receptors

Complexation properties and host behaviour of receptors

The behaviour of the podands to act as multi-donor ligand was assessed with a variety of metallic and organic compounds. However, due to acyclic nature of podands as compared to macrocyclic crown ethers there is also difference in the behaviour of two compound types.

To begin with, dimethoxyethane or all glymes and simple polyethylene glycols were found to form complexes with alkali metal cations of increasing stability with increasing chain length of the podands [18-20]. However, when making a comparison between crown ethers and open chained podands, the macrocyclic podands generally exhibit higher degree of stability of complexes due to “macrocyclic effect” and can be explained by enthalpic and entropic effects unfavourable in case of podands [21]. Nevertheless, the podands profit from the well-known “chelate effect”, which relates to the observation that metal complexes of bidentate or oligodentate ligands are more stable than unidentate ligands [21]. In addition to this, affinity for metal cations is also regulated by the donor atoms present in the framework of the podand [18-20]. All oxygen containing podands may favour the formation of complexes with alkali

and alkaline earth metals due to hard nature of oxygen donor atoms. Incorporation of nitrogen or sulphur as donor atom into the podand framework increases the chances of complexation with transition metal cations such as Cd, Hg, Ni, Co, Ag [21]. Another typical feature of podands is that the stability constants of their complexes are largely independent of the metal cation radius resulting in relatively small discrimination factors as compared to more preorganized crown ethers and cryptands [22]. This is a consequence of flexible nature of open podand chain which can readily adapt to the metal ions. However, in one important aspect podands are undoubtedly superior than the cyclic analogues, which is the kinetics of complexation and decomplexation of cation [22]. It is a general phenomenon that more preorganized a host is for cation binding, the slower is the kinetics of the process. Thus, both the forward and reverse complexation rates of podands are high, while the rates of cyclic analogues are slower. In comparison to the complexation with cations, complexation between anions and podands is also a recent development [23]. Anions complexing with the podands range from inorganic halide ions to biological phosphate or carboxylate ions. Considering the properties of the podands, we prefer to use podands as receptor for the sensing of ions for the design of sensor which is better in selectivity and sensitivity as well.

Owing to the flexible structure of podands, these have been widely used in chemical sensing. Amido analogues of this compound type (Fig. 1.2a) show clear preference for alkaline earth metals such as Ca(II), Sr(II), rare earth metals such as Yb(III), La(III), while certain aza and thia derivatives of glymes (Fig. 1.2b) show good carrier property for Cu(II), Ag(I), Hg(II) and Au(II). On the other hand, podands have also been used as carriers in membrane transport, which is another technique to accumulate and separate chemical species such as metal cations e.g. Fig. 1.2c is selective for Ag(I) ions [24].

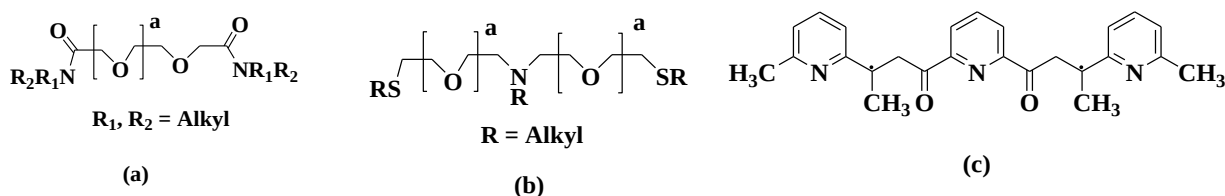


Figure 1.2 Structures of podands

Diphenylether molecule as a receptor unit

Aryl rings have proved to be common substituent in crown ethers among macrocyclic compounds. Dibenzocrown compound is an isomer of the Pedersen compound that incorporates a diphenyl ether unit. Though large number of macrocycles containing aryl rings along with hetero atoms (O, N, and S) has been reported in literature [25], only a few groups have reported the synthesis and utilization of the complexing properties involving diaryl ethers. The selectivity and behaviour of the ligands can be modified by steric and electronic variation in the region of the donor atom [26].

As seen in open chained podands, hetero atoms are separated by a carbon containing unit of two or more atoms. Keeping in view the chemical and practical considerations, ethyleneoxy units (OCH_2CH_2) are preferred in aliphatic crown ethers. Repeating ethyleneoxy units are readily available by polymerization of ethylene oxide. Use of (OCH_2CH_2) unit also means that every third atom is a donor, so the macrocycle's interior void is electron rich. Of course, a higher concentration of donors would be possible if methyleneoxy (OCH_2) chains were used, but the acetal (OCH_2O) linkage is hydrolytically unstable. Fewer donors would be available in the same size of macrocyclic ring if propyleneoxy ($\text{OCH}_2\text{CH}_2\text{CH}_2$) units were used for construction of the macrocycle. But it would create unfavourable conformational interactions. Rotation about ethylene linkage is facile when oxygen occupies the 1, 2 positions (i.e. $\text{OCH}_2\text{CH}_2\text{O}$). The corresponding $\text{OCH}_2\text{CH}_2\text{CH}_2$ interaction is energetically less favourable.

The two carbon units that separate hetero atoms may be part of an aromatic system (benzene, naphthalene and pyridine) e.g. the first crown isolated by Pederson was dibenzo -18-crown-6. Three isomers of this compound are possible, e.g. compound shown in Fig. 1.3(a) is a Pseudo-ortho isomer of the Pederson's compound that incorporates a diphenylether unit. Even the conformational interactions observed in case of three or more carbon units can be avoided by incorporating aryl rings in the macrocyclic structure, e.g. compound shown in Fig. 1.3(b), has benzene which is a conformationally inflexible part of the spacer chain. An aryl ring may also be present as a subcyclic unit that contributes no heteroatom to the macro-cycle but does not otherwise alter the essential (O-C-C) n crown ether framework. Compound in Fig. 1.3(c) for example, has an 18-membered macro-ring, but a benzene ring occupies two sites that would be heteroatoms if the structures were 18-crown-6. This has three obvious effects on the structure. First, replacement of $\text{OCH}_2\text{-CH}_2\text{OCH}_2\text{CH}_2\text{O}$ by $\text{OCH}_2\text{-C-CH-CCH}_2\text{O}$ rigidifies the macrocycle.

Second, each replacement results in the loss of a donor group relative to diethyleneoxy. Third, CH is larger than O and intrudes into the binding cavity. Thus aryl substituents impart rigidity and selectivity to the macro-cyclic structure.

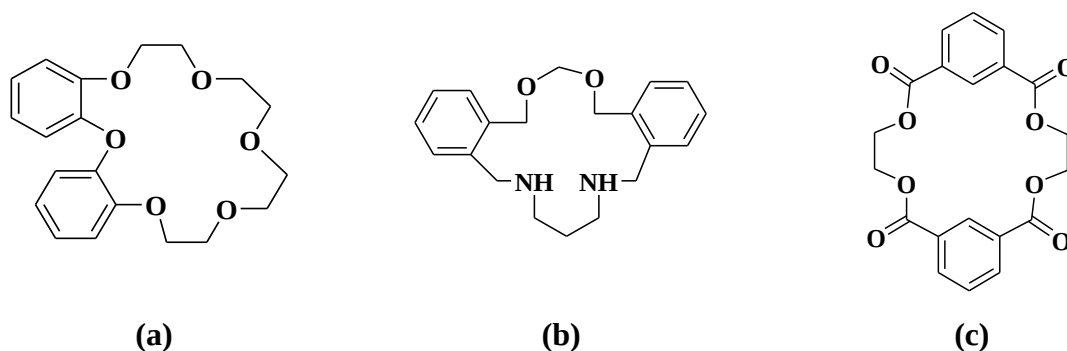


Figure 1.3 Structures of aromatic receptors

The cavity can be manipulated for the increased or decreased charge density by varying the substituents on the phenyl rings to accommodate different cations and anions. Diphenylether structures provide a right combination of flexibility and rigidity to the molecule to accommodate.

Rapid development in the synthesis of neutral macrocyclic ligands capable of complexing with cations and anions has stimulated research efforts in many fields of chemistry. The pioneering work of Pederson on macrocyclic polyethers or crown ethers [25-27] was chiefly concerned with oxygen-containing ring systems and produced a series of powerful receptors for alkali and alkaline earth metal cations. Nitrogen is often incorporated into these structures and may predominate when binding to transition metals is the objective. Likewise receptors containing sulphur atoms in the donor array favour transition metals over alkali metal ions.

Not much work has been done on the receptors containing aryl ethers motifs. Considering properties of aryl containing macrocyclic compounds like introducing reasonable rigidity due to aromatic ring, replacement of one of the heteroatoms of the cyclic ring with a larger aromatic CH group which might help in creation of flexibility in the cavity size. Thus, aryl substituents are likely to impart flexible cavity size and better ion selectivity to the macrocyclic structure. Due to such properties design of aryether based molecules is proposed in this research work to develop different di and triphenylether based molecules to project them as electroanalytical probes for various cations or anions. Further, these molecules can also be

modified by increasing the number of hetero atoms which help in entrapment of metal ions or modification in terms of incorporation of imine linkages on both open ended arms of aryether moiety to enhance the flexibility of the receptor.

1.2b Transducer unit based classification of chemical sensors

Signals are processed almost exclusively by means of electrical instrumentation with the help of transducer. Development of instrumentation and techniques has made possible to design sensors which utilize most of the known physical, chemical and biological principles that are being used in chemistry. According to the operating principle of transducer, chemical sensors may be classified into following types:

1. **Optical** devices transform changes of optical phenomena, which are the result of an interaction of the analyte with the receptor part. This group may be further subdivided according to the type of optical properties which have been applied in chemical sensors:

- a) absorbance, measured in a transparent medium, caused by the absorptivity of the analyte itself or by a reaction with some suitable indicator.
- b) reflectance, measured in non-transparent media, usually using an immobilized indicator.
- c) luminescence, based on the measurement of the intensity of light emitted by a chemical reaction in the receptor system.
- d) fluorescence, measured as the positive emission effect caused by irradiation. Also, selective quenching of fluorescence may be the basis of such devices.
- e) refractive index, measured as the result of a change in solution composition. This may include also a surface plasmon resonance effect.
- f) optothermal effect, based on a measurement of the thermal effect caused by light absorption.
- g) light scattering, based on effects caused by particles of definite size present in the sample.

2. **Electrochemical** devices transform the effect of the electrochemical interaction analyte – electrode into a useful signal. Such effects may be stimulated electrically or may result in a spontaneous interaction at the zero-current condition.

The following subgroups may be distinguished:

- a) voltammetric sensors, in which current is measured in the d.c. or a.c. mode.
- b) potentiometric sensors, in which the potential of the indicator electrode (ion-selective electrode, redox electrode) is measured against a reference electrode.

c) chemically sensitized field effect transistor (CHEMFET) in which the effect of the interaction between the analyte and the active coating is transformed into a change of the source-drain current.

d) potentiometric solid electrolyte gas sensors, they work in high temperature solid electrolytes and are usually applied for gas sensing measurements.

3. Electrical devices based on measurements, where no electrochemical processes take place, but the signal arises from the change of electrical properties caused by the interaction of the analyte.

a) metal oxide semiconductor sensors used principally as gas phase detectors, based on reversible redox processes of analyte gas components.

b) organic semiconductor sensors, based on the formation of charge transfer complexes, which modify the charge carrier density.

c) electrolytic conductivity sensors.

d) electric permittivity sensors.

4. Mass sensitive devices transform the mass change at a specially modified surface into a change of a property of the support material. The mass change is caused by accumulation of the analyte. a) piezoelectric devices b) surface acoustic wave devices

5. Magnetic devices based on the change of paramagnetic properties of a gas being analysed. These are represented by certain types of oxygen monitors.

6. Thermometric devices based on the measurement of the heat effects of a specific chemical reaction or adsorption which involve the analyte. In this group the heat effects may be measured in various ways, for example in the so called catalytic sensors the heat of a combustion reaction or an enzymatic reaction is measured by use of a thermistor. The devices based on measuring optothermal effects can alternatively be included in this group.

Among all the above transducers, our work is focussed on the use of electrochemical transducer to get the electrical signal in the form of voltammetric information acquired through the chemical reaction occurring on the surface of working electrode. Techniques which were used for the chemical sensing include cyclic voltammetry and differential pulse voltammetry, discussed in detail below:

1.3 Techniques used for chemical sensing

1.3.1 Spectrophotometry

Spectrophotometry is a quantitative measurement of how much a chemical substance absorbs light by measuring the intensity of light as a beam of light passes through sample solution. The basic principle is that each compound absorbs or transmits light over a certain range of wavelength. This measurement can also be used to measure the amount of a known chemical substance. Spectrophotometry is one of the most useful methods of quantitative analysis in various fields such as chemistry, physics, biochemistry, material and chemical engineering and clinical applications.

1.3.2 Spectrofluorimetry

Spectrofluorimetry is a type of electromagnetic spectroscopy that analyzes fluorescence from a sample. It involves using a beam of light, usually ultraviolet light, that excites the electrons in molecules of certain compounds and causes them to emit light; typically, but not necessarily, visible light. In fluorescence, the species is first excited, by absorbing a photon, from its ground electronic state to one of the various vibrational states in the excited electronic state. Collisions with other molecules cause the excited molecule to lose vibrational energy until it reaches the lowest vibrational state of the excited electronic state. This process is often visualized with a Jablonski diagram.

1.3.3 Voltammetry

Voltammetry is application of a constant or varying potential at the surface of an electrode and measurement of the resulting current using a three electrode system. It reveals the oxidation/reduction potential of an analyte and gives us the information of its electrochemical reactivity. Voltammetry is mainly used by analytical, physical, inorganic and biological chemists for fundamental studies. The analytical advantages of voltammetric techniques include rapid location of redox potentials of the electroactive species, quantitative and qualitative determination of organic and inorganic compounds in aqueous/non-aqueous solutions, determination of number of electrons involved in each step of the chemical process, adsorption processes occurring on surfaces, rapid analysis time, simultaneous determination of various analytes, ability to determine mechanistic and kinetic parameters,

(Kounaves, 1997) [28]. To study the electrochemical properties of supramolecular systems capable of sensing cations or anions as guests and reporting their complexation by an electrochemical response [29-30] is an area of keen interest [31] for the last two decades. Voltammetry is divided into four categories: linear sweep voltammetry (LSW), differential pulse voltammetry (DPV), square wave voltammetry (SWV) and cyclic voltammetry (CV). Since CV and DPV were the techniques used for study, they are discussed in detail.

1.3.3a Cyclic voltammetry

Cyclic voltammetry is the most widely used technique to study qualitative information about electrochemical reactions. It offers a rapid location of redox potentials of the electroactive species and evaluation of the effect of medium on the redox process. In typical cyclic voltammetry, potential of a stationary working electrode is scanned linearly by using a triangular potential waveform. During the potential sweep, current resulting from the applied potential is measured by the potentiostat. Thus obtained current–potential plot is termed a cyclic voltammogram. In typical cyclic voltammetry, analyte solution is electrolyzed by placing the solution in contact with an electrode surface and then making the surface of electrode highly positive or negative in voltage in order to enable it to force electron transfer. The potential is first varied linearly in one direction and then direction is reversed to initial starting potential value. The rate at which the potential is swept between initial and final potential window is called scan rate i.e., V/sec or mV/sec. Important parameters of a cyclic voltammogram are anodic peak potential (E_{pa}), cathodic peak potential (E_{pc}), anodic peak current (I_{pa}) and cathodic peak current (I_{pc}) as developed by Nicholson and Shain [32] for analyzing any electrochemical response.

Reversible systems

For any reversible electrochemical reaction, voltammogram recorded has certain well defined characteristics [33].

i) The separation between the peak potential for a reversible redox couple is given by

$$\Delta E = E_p^a - E_p^c = (59/n) \text{ mV} \quad (1.1)$$

ii) The positions of peak potentials do not change with scan rate

iii) The anodic to cathodic peak currents ratio is equal to one

$$\left| \frac{i_p^a}{i_p^c} \right| = 1 \quad (1.2)$$

iv) The peak currents are directly proportional to the concentration and increase with square root of scan rate

In a reversible system at 25°C, peak current (A) for the redox couple is given by the Randles-Sevcik equation:

$$i_p = (2.69 \times 10^5) A C D^{1/2} n^{3/2} v^{1/2} \quad (1.3)$$

where n is the number of electrons, A is *electrode area* (cm²), D is diffusion coefficient (cm²/s) and C is bulk concentration of the electroactive species (mol/cm³) and v is the potential scan rate (V/s).

Irreversible and quasi-reversible systems

For irreversible processes (sluggish electron exchange), the peaks are reduced in size [34]. Totally irreversible electrochemical response is characterized by shift of peak potential with change in scan rate:

$$E_p = E^\circ - \frac{RT}{\alpha n F} \left[0.78 - \ln \left(\frac{k^\circ}{D^{1/2}} \right) + \ln \left(\frac{\alpha n F}{RT} \right)^{1/2} \right] \quad (1.4)$$

α is the transfer coefficient and n represents the number of electrons involved in the charge-transfer step. Thus, E_p occurs at potentials higher than E° , with the overpotential related to k° and α . Independent of the value k° , such peak displacement can be compensated by an appropriate change of the scan rate. The peak potential and the half-peak potential (at 25°C) will differ by $48/\alpha n$ mV. Hence, the voltammogram becomes more drawn-out as αn decreases. Peak current in case of irreversible systems is given by equation 1.5

$$i_p = (2.99 \times 10^5) n (\alpha n')^{1/2} A C D^{1/2} v^{1/2} \quad (1.5)$$

Where, n' denotes the number of electrons transferred in the rate determining reaction step, whereas n is the number of electrons, A is *active electrode surface area* (cm²), D is diffusion coefficient (cm²/s) and C is bulk concentration of the electroactive species (mol/cm³) and v is the potential scan rate (V/s), α is transfer coefficient.

For quasi-reversible systems, current is controlled by charge transfer and mass transport as well. The shape of the voltammogram is a function of $k^\circ/\sqrt{v\pi aD}$ (where $a=nFv/RT$). In case of

quasi-reversible case, peaks are more drawn out and exhibit a large separation in peak potentials as compared to reversible systems.

1.3.3b Differential pulse voltammetry

The importance of DPV over CV lies in the superior elimination of the capacitive/background current. Background current is eliminated by sampling the current twice i.e. once before pulse application and then at the end of the pulse. Then, output from the potentiostat is equal to the difference in the two current values. In differential pulse voltammetry, voltammograms are peak-shaped due to double sampling. The width of the peak (at half height) is related to the electron stoichiometry [32].

$$W_{1/2} = \frac{3.52RT}{nF} \quad (1.6)$$

Where, R is gas constant, T (K) is temperature, n is number of electrons transferred and F is faraday's constant.

1.4 References

1. A. Hulanicki, S. Glab and F. Ingman, "Chemical sensors: definitions and classification." *Pure and Applied Chemistry*, **1991**, 63, 1247-1250.
2. H. Wohltjen, D. Ballantine, R. White, S. Martin, A. Ricco, E. Zellers and G. Frye, "Acoustic Wave Sensors: Theory, Design, & Physico-Chemical Applications" Academic press, New York, **1996**.
3. K. Ariga and T. Kunitake, *Supramolecular chemistry-fundamentals and applications: advanced textbook*, Springer Science & Business Media, **2006**.
4. D. W. Christianson and J. D. Cox, *Annu. Rev. Biochem.*, **1999**, 68, 33-57.
5. P. Wei, X. Yan and F. Huang, *Chem. Soc. Rev.*, **2015**, 44, 815-832.
6. H. M. Chawla, S. N. Sahu, R. Shrivastava and S. Kumar, *Tetrahedron Lett.*, **2012**, 53, 2244-2247.
7. Z. Yan, Y. Lu, H. Wang, S. Wu and B. Zhao, *J. Mol. Liq.*, **2013**, 183, 72-78.
8. J. Liu, Y.-Q. Xie, Q. Lin, B.-B. Shi, P. Zhang, Y.-M. Zhang and T.-B. Wei, *Sensor Actuat. B – Chem.*, **2013**, 186, 657-665.
9. P. Kumar and H. K. Sharma, *Electrochim. Acta*, **2013**, 87, 925-929.
10. A. Afkhami, F. Soltani-Felehgari, T. Madrakian, H. Ghaedi and M. Rezaeivala, *Anal. Chim. Acta*, **2013**, 771, 21-30.
11. S. K. Shoorra, A. K. Jain and V. K. Gupta, *Sensor Actuat. B – Chem.*, **2015**, 216, 86-104.
12. K. Kaur, S. K. Mittal, A. Kumar and S. Kumar, *Anal. Methods*, **2013**, 5, 5565-5571.
13. M. Alfonso, A. Tarraga and P. Molina, *Org. Lett.*, **2011**, 13, 6432-6435.
14. A. Kamal, K. Kumar, V. Kumar and R. K. Mahajan, *Electrochim. Acta*, **2014**, 145, 307-313.
15. A. J. Pedersen, *J. Am. Chem. Soc.*, **1967**, 89, 7017-7036.
16. E. Weber and H.-P. Josel, *J. Inclusion Phenom.*, **1983**, 1, 79-85.
17. A. Von Zelewsky, *Stereochemistry of coordination compounds*, John Wiley & Sons, 3, **1996**.
18. F. Vogtle and E. Weber, *Angew. Chem. Int. Ed.*, **1979**, 18, 753-776.
19. H. B. Melkburg, F. Vögtle and W. Jaworek, *Angew. Chem. Int. Ed.*, **1992**, 31, 1571-1576.

20. D. S. C. Black and A. Hartshorn, *Coord. Chem. Rev.*, **1973**, 9, 219-274.
21. H. J. Schneider and A. K. Yatsimirsky, *Principles and Methods in Supramolecular Chemistry*, J. Wiley, **2000**.
22. F. Vogtle and E. Weber, *Ethers, Crown Ethers, Hydroxyl Groups and their Sulphur Analogues*: **1989**, 1, 59-156.
23. J. W. Steed and J. L. Atwood, *Supramolecular chemistry*, John Wiley & Sons, **2013**.
24. J. E. D. Davies and J. L. Atwood, *Comprehensive supramolecular chemistry. 8. Physical methods in supramolecular chemistry*, Pergamon Press, **1996**.
25. G. W. Gokel, W. M. Leevy and M. E. Weber, *Chem. Rev.*, **2004**, 104, 2723-2750.
26. E. Otazo-Sanchez, L. Perez-Marn, O. Estevez-Hernandez, S. Rojas-Lima and J. Alonso-Chamarro, *J. Chem. Soc., Perkin Trans.* **2001**, 2, 2211-2218.
27. D. Meshcheryakov, F. Arnaud-Neu, V. Böhmer, M. Bolte, V. Hubscher-Bruder, E. Jobin, I. Thondorf and S. Werner, *Org. Biomol. Chem.*, **2008**, 6, 1004-1014.
28. F. A. Settle, *Handbook of instrumental techniques for analytical chemistry*, Prentice Hall PTR, **1997**.
29. A. Lorenzo, E. Aller and P. Molina, *Tetrahedron*, **2009**, 65, 1397-1401.
30. V. K. Gupta, A. K. Singh and N. Gupta, *Sensor Actuat. B- Chem.*, **2014**, 204, 125-135.
31. P. D. Beer, *Adv. Inorg. Chem*, **1992**, 39, 79.
32. R. S. Nicholson, *Analytic. Chem.*, **1965**, 37, 1351-1355.
33. F. Scholz, *Electroanalytical Methods*, Springer, **2010**.
34. J. Wang, *Analytical Electrochemistry*, John Wiley & Sons, **2006**.

REVIEW OF LITERATURE

Analytical chemistry has a long history of development of various analytical techniques used for the detection of analyte by using receptor molecules. These techniques mainly include spectrophotometric and electrochemical characteristics for the determination of optical and electrical changes of the receptor solution when introduced with any analyte. In order to ascertain the current state of knowledge, recent publications from technical journal articles are included in this chapter.

2.1 Cation sensing

Cation sensing has been of keen interest to the analytical scientists because of their harmful effects, if present in excessive concentration. Most commonly used techniques for cation sensing are spectrophotometry, spectrofluorimetry, potentiometry, inductively coupled plasma mass spectroscopy (ICP-MS), atomic absorption spectroscopy (AAS) etc. Another technique used for cation sensing is voltammetry, which is based on redox properties of the molecules or the changes observed with the addition of analyte which are not provided by any other technique.

A huge literature is available on cation sensing whether transition metals or rare earth metals by using spectrophotometric and electrochemical techniques in which various kinds of receptor molecules are used and are detailed below:

2.1.1 Alkaline and transition metal ions

(a) Spectrophotometric methods

Optical properties of various receptor molecules like schiff bases, calixarenes, thiourea, fluorescein, flavonol, thiophosphonated rhodol, benzimidazole etc. are well developed for sensing of various metal ions. Devaraj *et al* (2009) [1], reported two thiourea based receptors for the spectrophotometric detection of copper ions, which showed a visual change on

addition of Cu(II). Abebe *et al* (2011) [2], developed a fluorescein based molecular receptor for the fluorescent and colorimetric detection of copper ions in aqueous medium.

Calixarenes as spectrophotometric receptors

Calixarenes, due to their molecular design and CH- π or π - π interactions, are used commonly for metal binding studies. Chawla *et al* (2012) [3], developed a calix[4]arene based ditopic receptor for the detection of Co(II) ions. A bathochromic shift in the UV-visible spectrum with a profound colour change enables this receptor to engineer novel applications. Chawla *et al* in the same year (2012) [4] again developed a calix[4]arene based receptor for the detection of Zn(II) by quenching fluorescence intensity of receptor molecule without interference from any of other transition metal ions. Chawla *et al* 2013 [5a] and [5b] developed a chemosensor for Ag(I) and Cu(II) ions by using calix[4]arene and calixarene based molecules with fluorescein appendages based receptor, respectively. A profound color change from colorless to yellow in acetonitrile medium and colorless to purple in fully aqueous medium indicates copper ion recognition due to selective ring opening of fluorescein spirolactam ring.

Benzimidazoles as spectrophotometric receptors

Benzimidazole due to the presence of nitrogens as hetero atom is widely used in sensing field. Liu *et al* (2013) [6] developed a benzimidazole based dipodal fluorescent chemosensor for the selective detection of Fe(III). The sensor displayed high selectivity and sensitivity for Fe(III) ions in H₂O/DMSO (4:6, v/v) solutions, which served as an on-off type chemosensor. Wang *et al* (2013) [7] also developed a benzimidazole based fluorescent chemosensor for the selective detection of Cr(III) and Fe(III) ions in aqueous solution. Gupta *et al* (2014) [8], designed two flavonol derivatives for the detection of Zn(II) ions using UV-Visible and fluorescence technique. Also, these derivatives served as highly selective chemodosimeter for Zn(II) ions at neutral pH with naked-eye detection. Gyu Im *et al* (2014) [9], developed a diphosphonated rhodol derivative by the dual signalling of Hg(II) ions; thiophosphinated rhodol showed prominent chromogenic and fluorogenic signaling for the Hg(II) ions.

Schiff base molecules as spectrophotometric receptors

Schiff bases are used very commonly among chemosensors due to the presence of imine linkage which provide rigidity to the molecules for the selective entrapment of metal ions. There are numerous reports on the Schiff based chemosensors. Wei *et al* (2012) [10], developed a fluorescent chemosensor for Zn(II) ions, Receptor exhibited an ‘off–on-type’ mode with high selectivity in presence of Zinc ion. The selectivity for Zn(II) was the consequence of combined effect of chelation-enhanced fluorescence (CHEF), C=N isomerization, and inhibition of photoinduced electron transfer (PET). Chang *et al* (2013) [11], developed an imine based turn-on and reversible receptor for aluminium ions. The receptor displayed dramatically enhanced fluorescence intensity selectively for Al(III) over other ions in EtOH–H₂O (95: 5 v/v) solution. The addition of EDTA quenched the fluorescence of the complex indicating that receptor was a reversible chemosensor. Afkhami *et al* (2013) [12], developed a newly synthesized schiff base for simultaneous determination of Cd(II), Cu(II) and Hg(II) ions in water and some foodstuff samples. Shoorra *et al* (2015) [13], developed two Schiff based molecules for the spectrophotometric detection of Al(III) ions. Both the receptors showed huge fluorescence enhancement on the addition of Al(III) ions which was recognized by calorimetry.

(b) Electrochemical methods

Redox-active receptors for cation sensing can be either oxidizable (ferrocene) or reducible e.g. quinone, anthraquinone and calixarenes, nitroaromatic, lariat ethers and crown ethers containing moieties.

Calixraenes as electrochemical receptors

Lyskawa *et al* (2010) [14], reported a sodium selective calixarene having substitution of four redox active tetrathiafulvalene (TTF) moieties by utilizing the redox active property and high π donating efficiency of TTF along with the binding capability of calixarene for electrochemical sensing of metal ion. Bingol *et al* (2011) [15], designed a novel Cr(II) selective azacalix[4]arene derivative and used it as electrochemical sensor for Cr(II) ion detection with no interference from any other metal ions. Yan *et al* (2013) [16], synthesized a calixarene based neutral ionophore and explored it as an ionophore for polymeric membrane Ag⁺-selective electrode. Gupta *et al* (2013) [17], developed a Hg(III) selective potentiometric

sensor based on low rim functionalized thiacalix [4]arene as a cationic receptor with a lower detection range of 1×10^{-8} M. Maity *et al* (2014) [18], synthesized a calix[4]arene by incorporating dithiocarbamate unit functionalized gold nanoparticles for the electrochemical sensing of Co(II) ions in organic as well as aqueous medium.

Triazoles as electrochemical receptors

Triazoles are also used widely in electrochemical sensing due to presence of three nitrogens bearing lone pair of electrons which makes triazole a redox active moiety. Kim *et al* (2009) [19], developed a novel electrochemical selective 1, 2, 3-Triazole ring-appended chemosensor for the Al(II) ion. Kumar *et al* (2013) [20], developed a solid state Cr(III) selective sensor by using newly synthesized triazole derivative as an ionophore in PVC matrix. They also used this sensor for the determination of Cr(III) activity in the waste from electroplating and lather tanning industry. Tomas *et al* (2013) [21], developed a series of mono-substituted and di-substituted triazoles for the sensing of Hg(II) and anions as well. Receptors undergo clear shifts of the oxidation peak of the ferrocene/ferrocenium redox couple in the presence of F^- , AcO^- , $H_2PO_4^-$, and $HP_2O_7^{3-}$ anions, whereas two receptors behave as dual redox and optically selective sensors for Hg(II) cations.

Rhodamines as electrochemical receptors

Rhodamine moiety based receptors are also used for electrochemical sensing of ions. Kamal *et al* (2014) [22], developed a voltammetric and potentiometric sensor for the determination of Fe(III) ions by using rhodamine dimer as an electroactive material. Further, the potentiometric response of proposed PVC based solid contact coated graphite electrode was linear for Fe(III) ions. Kamal *et al* (2014) [23], again developed a rhodamine-dimethyliminocinnamyl based electrochemical sensors for selective detection of Fe(II). Yuan *et al* (2015) [24], developed a rhodamine-ferrocene conjugate chemosensor for selective sensing of copper ions. Free receptor displayed a reversible one-electron oxidation process at 0.508 V in the cyclic voltammogram which corresponds to the ferrocene/ferrocenium redox couple. Upon stepwise addition of Cu(II), the original peak gradually evolved to 0.495 V ($\Delta E_{1/2} = 140$ mV), associated with the formation of the complexed species of receptor with Cu(II).

Ferrocenes as electrochemical receptors

Ferrocene based molecules are also used widely as electrochemically active receptors as they show electroactivity on its inclusion and respond to various metals by changing the oxidation potential of it. Shi *et al* (2011) [25], synthesized Hg(II) selective voltammetric sensor based on 8-hydroxyquinoline ferrocenoate. Alfonso *et al* (2011) [26], synthesized an electroactive ferrocene-imidazopyrene based molecule for sensing cations and anions in order $\text{Pb}^{2+} > \text{Hg}^{2+} > \text{Zn}^{2+}$ and $\text{H}_2\text{PO}_4^- > \text{AcO}^-$, respectively. Thakur *et al* (2012) [27], developed an efficient ferrocene derivative for electrochemical recognition of Hg(II) ions in aqueous solutions. He claimed that this ferrocene-based ligand is the rare example of a dual electrochemical-optical Ni(II) ion sensor in which the Fc/Fc^+ redox couple was significantly shifted ($\Delta E_{1/2} = 187$ mV) on complexation, with a concomitant change in color from yellow to blue, that allows its potential use for “naked eye” detection. Juan *et al* (2013) [28], synthesized a series of ferrocene based dipeptide receptors for selective sensing of Zn(II), Cd(II) and Hg(II) ions. Receptors showed a well-defined stable redox waves in the potential range 0.00-1.0V on GC electrode attributed to Fc/Fc^+ redox couple. Kamal *et al* (2014) [29], also developed an electrochemical and chromogenic sensor based on ferrocene appended chalcone for selective quantification of copper (II) ions. The proposed mechanism involved the interaction of copper ion with the π -electron of chromophore and d-electrons of ferrocenyl moiety.

Likewise, a huge literature is available on receptor molecules containing moieties like urea, thiourea, tetrathiafulvalenes, quinones, imine linkages etc., reported as electrochemical sensors or probes for cation sensing.

2.1.2 Rare earth metals ions

(a) Spectrophotometric methods

Like transition metal ions, a lot of receptors based on carbothioamides, 18-Crown-6, carbazides, dansyl moiety etc., are reported which can sense different lanthanides by using spectrophotometric techniques. Xia *et al* (2000) [30], reported a fluorescent chemosensor for the detection of lanthanides. They observed that on addition of various lanthanides luminescent properties of chromophore are quenched by lanthanide (Ln(III)) ions with larger ionic radii and existing f-f transitions (Ce(III) , Pr(III) and Nd(III)). Alkali, alkaline earth ions and lanthanides with smaller radii (Ge(III) , Tb(III) , Dy(III) , and Yb(III)) do not affect the

emission. Ganjali *et al* (2009) [31], developed a Tb (III) selective fluorescent chemosensor having phenylhydrazinecarbothioamide as a moiety. This fluorescent probe exhibited high selectivity over other common metal ions (mono-, di-, and trivalent cations) indicating good selectivity for Tb (III) ions over a large number of interfering rare earth metals.

Maji *et al* (2009) [32], reported a fluorescent sensor for the determination of uranium in the presence of all rare earth metals. The receptor molecule has also been useful for sensitizing the fluorescence of Tb(III) and Eu(III) and demonstrated as a method for the simultaneous determination of UO₂(II), Tb(III) and Eu(III) also. Hosseini *et al* (2010) [33], developed terbium ions in phosphate rocks by using a dansyl derivative as a neutral ionophore. Ganjali *et al* (2012) [34], designed a dysprosium (III) selective fluorimetric bulk optode having sulfonohydrazide moiety. Response of the optode is based on the fluorescence quenching of optode by Dy(III) ions.

Ganjali *et al* (2013) [35], developed a novel europium-sensitive fluorescent nano-chemosensor based on new functionalized magnetic core-shell Fe₃O₄@SiO₂ nanoparticles. The enhancement in fluorescence intensity of nano- chemosensor is because of the strong covalent binding of Eu(III) ion to CD-Fe₃O₄@SiO₂ NPs with a large binding constant value of $1.7 \times 10^5 \text{ mol L}^{-1}$. Faridbod *et al* (2015) [36], developed a turn on fluorescent chemosensor for lutetium ions in ethanol-water solutions. Likewise a lot of literature is available on different receptors detecting different lanthanides spectrophotometrically.

(b) Electrochemical methods

A lot of electroactive receptor molecules are used for the detection of rare earth metals by using electrochemical techniques, which respond by changing the electrical properties of receptor solution on addition of an analyte. Ganjali *et al* (2006) [37], reported a novel Er(III) electrochemical sensor based on hydrazone moiety. The proposed electrode shows excellent discrimination toward Er(III) ions with regard to most common metal ions and especially, all lanthanide ions. Ma *et al* (2010) [38], developed a highly sensitive and selective chemosensor based on sodium dodecyl sulphonate for the determination of Eu(III) ions. Good linear relationship between DPV peak current and the concentration of Eu(III) is obtained in the range of 0.0–0.10 μM with a LOD of 6.0 nM. Rounaghi *et al* (2011) [39], developed a novel ion-selective electrode which displayed a rapid response time of 10 s, improved selectivity

towards Ce(III) cations in the presence of alkali, alkaline earth, transition and heavy metal cations. Upadhyay *et al* (2011) [40], developed two hydrazone based electrochemical sensors by fabricating the receptors on graphite electrodes. The receptors responded selectively to Eu(III) over a large number of cations.

Gupta *et al* (2013) [41], reported a gadolinium(III) selective electrode from poly vinyl chloride (PVC) matrix membrane which is based on synthesized neutral carrier 2-(2-aminothiazol-4-yl)phenol and 2-(4-phenyl-1,3-thiazol-2-yliminomethyl)phenol as ionophores. Membrane sensor was also used as an indicator electrode for determination of end point in potentiometric titration of Gd (III) ion with EDTA. Bandi *et al* (2013) [42], designed two Schiff based molecules for the determination of Nd(III) ions by using potentiometric method.

Cruickshank *et al* (2015) [43], first time reported the electrochemical detection of europium ions using cyclic voltammetry at gold electrodes modified with 2-pyridinol-1-oxide. the peak current increased linearly with europium concentration over the range from 1 to 80 μM with detection limit 0.3 μM . Alizadeh *et al* (2016) [44], developed a voltammetric sensor for the ultra trace level determination of cerium ions. They modified the carbon paste electrode with a Ce(III)-imprinted polymer (Ce-IP) and used for voltammetric determination of Ce(III) ions in real water samples.

2.2 Anion sensing

Design of anion receptors is particularly challenging because of their larger size than isoelectronic cations [45] and hence lower charge to radius ratio. In spite of these facts, there are a lot of recent advances in recognition of anionic substrates. With the aim of advancing chemical sensor technology, considerable attention has been focused on the design of artificial receptors that have the capability to selectively bind and sense the anion recognition event through optical or electrochemical response. There are a lot of reports on anionic chemical sensors which sense or recognise the different anions by different mechanisms.

2.2.1 Spectrophotometric methods

The high sensitivity of optical or fluorescent techniques for sensing target anionic species has stimulated an enormous amount of interest in the covalent attachment of organic and inorganic chromophores or luminophores in close proximity to charged guest-recognition

sites [46]. Shao *et al* (2009) [47], synthesized a novel azo derivative for the dual chromogenic and fluorimetric detection of H_2PO_4^- ions. The receptor color changes from yellow to orange and fluorescent intensity gets turned on addition of H_2PO_4^- . Recognition process was based on the occurrence of tautomeric equilibrium. Yu *et al* (2010) [48], synthesized a novel trifluoroacetamide based receptor having anthracene moiety for cyanide sensing. In this receptor, anthracene moiety acted as a fluorophore and trifluoroacetyl group as cyanide acceptor. Compared with other reported trifluoroacetamide derivative-based cyanide chemosensors, N-2-anthracenyl trifluoroacetamide exhibited a better cyanide response with higher sensitivity. Li *et al* (2010) [49], synthesized a phenylhydrazone based chemosensor and applied it to acetate anion recognition. The receptor solution changes its colors on addition of acetate ions and that make the naked-eye recognition in DMSO and even in DMSO/ H_2O come true. The fluorescence enhancement was also observed after the host is coordinated with the AcO^- anion and excited at 280 nm.

Anthraquinones as spectrophotometric receptors

For the recognition of certain anions (e.g., fluoride and cyanide), anthraquinone derivatives have also been reported as suitable systems for colorimetric sensing since they are an example of electron acceptor groups that can be electronically connected with recognition units (Jung *et al* (2009) [50], Cammetti *et al* (2009) [51], Saha *et al* (2010) [52], Wang *et al* (2010) [53], Kumari *et al* (2011) [54], Ren *et al* (2011) [55], Xu *et al* (2012) [56], Li *et al* (2012) [57]. Batista *et al* (2013) [58], also synthesized two novel anthraquinone based receptors and presented these as F^- , CN^- and OH^- selective receptors in organic system by using colorimetric and fluorimetric techniques. While in organic-aqueous mixture solvent system, it was found that selectivity for CN^- was achieved for both the receptors, with an easily detectable colour change from yellow to orange. Batista *et al* (2014) [59], again developed another imidazo- anthraquinone based receptors with combination of containing thiazole, (benzo)furan, thiophene and imidazole heterocycles. All anthraquinone derivatives exhibited great selectivity for cyanide anion only over all other anions in acetonitrile/water (9:1) solution showing a distinct colour change from yellow to orange and the fluorescence emission was switched “off”.

Azides as spectrophotometric receptors

Lee *et al* (2014) [60], developed an azide sensitive sensor by deprotection of dichlorofluorescein. The detection limit for the determination of azide ions by the chloroacetate of 2', 7'-dichlorofluorescein in 10% aqueous acetonitrile was found to be 17 ppb. They also analyzed the signaling of azide ions in real samples by using tapwater and simulated wastewater.

Phenylhydrazones as spectrophotometric receptors

Phenyl-hydrazine containing chromophoric group like nitro and bearing hydrogen donor capability are also used widely as good anion receptor (Thiagarajan *et al* (2005) [61], Pei *et al* (2012) [62]. Gupta *et al* (2014) [63], developed a biologically active 2,4 dinitro phenyl hydrazones as colorimetric sensors for the selective detection of acetate ions via H-bonding and proton transfer with acetate ion. In the same year Gupta *et al* (2014) [64], again developed two biologically active phenylhydrazones for the detection of cyanide and acetate ions. The hydrazones showed selective colorimetric changes with cyanide and acetate ions i.e., change in the color of ionophore solution, dark yellow color and dark orange color to violet color over the other anions.

Hence, from the literature survey we can observe that a lot of spectrophotometric receptors containing amides, phenylhydrazones, anthraquinones, urea/thiourea, pyrroles etc. have been reported till now.

2.2.2 Electrochemical methods

Anion sensing using electrochemical techniques by artificial receptors is an expanding research area at the interface of electrochemical and supramolecular chemistry due to their important roles in our daily life (Snowden *et al* (1999) [65], Reynes *et al* (2001) [66]. Anzenbecher *et al* (2005) [67], developed a series of receptors containing a chromophore capable of undergoing an intensive change in color and a redox-active quinone moiety to generate strong electrochemical signals. Anion binding by sensors was investigated by cyclic (CV) and square-wave voltammetry (SWV). Both methods confirmed that the selective binding of H_2PO_4^- is accompanied by an anion specific change in redox potential as well as by decrease in current, a behavior attributed to the formation of the sensor anion complex with a

lower diffusion coefficient. Beer *et al* (2005) [68], gave a chemical review on metal based receptors used for the anion sensing. He reviewed the literature on the basis of organometallic anion receptors, complexes of transition metals and mixed metal receptors. Issac *et al* (2006) [69], developed a voltammetric sensor for sulfite detection in food and beverages. Cyclic voltammograms detailed the oxidation of increasing sulfite concentration (66–320 μ M, pH 7) at a glassy carbon electrode which corresponded to irreversible $2e^-$ conversion to sulfate.

Ferrocenes as electrochemical receptors

Miyaji *et al* (2008) [70], recognised the acetate ion by the ferrocene-based hetero-ditopic receptor. The cyclic voltammetric study showed that receptor induced a positive shift in the ferrocene oxidation potential upon binding to a potassium cation, whereas it induced a negative shift upon binding an acetate anion, both of which can be reversed by ion-pairing process. In the same year Lorenzo *et al* (2009) [71], reported bisferrocenyl-substituted urea and thiourea and trisferrocenyl-substituted guanidine. All these derivatives showed electrochemical selectivity towards $H_2PO_4^-$ with a cathodic shift of 100-170 mV. Ma *et al* (2009) [72], also reported ferrocene-based compounds for electrochemical sensing of anions. Both the receptor molecules showed selective recognition toward $H_2PO_4^-$.

Li *et al* (2008) [73], also developed a ferrocene for the detection of anions by voltammetric method. They observed that the addition of the same concentrations of F^- , AcO^- and $H_2PO_4^-$ caused a significant electrochemical response that the oxidation wave moves to more negative potentials, whereas F^- showed the best response among the three with the $\Delta E_{pa} = 157$ mV. Carlos *et al* (2016) [74], synthesized and compared two dendrimers containing two biferrocene units. He reported the voltammetric sensing of hydrogen phosphate anions with both the dendrimers and of hydrogen sulfate with tetra-ferrocenyl dendrimer. He observed that sensing takes place in a relatively polar solvent (DMSO), where hydrogen-bonding interactions between the amide functional groups and the anion are usually weakened by competing solvent molecules.

Sathyaraj *et al* (2012) [75], developed two chemosensors having imidazolyl and phenol moieties as linkers and ferrocene moiety as redox active unit. Spectrophotometric as well as electrochemical studies were conducted for sensing of anions as well as cations. Garcia *et al*

(2013) [76], synthesized a fluoride selective receptor based on pyrrole-quinone units for anion recognition. They synthesized the receptor from natural product perezone by two step process. Hassan *et al* (2013) [77], developed a potentiometric sensor for the determination of nitrite ion in waste water and meat products. In the same year, Luo *et al* (2013) [78], developed a voltammetric sensor for nitrate determination at an in-situ copper modified glassy carbon electrode. They reported that nitrates could be quantitatively determined in the range 10 to 300 μM ; without being interfered from other common anions in the water samples except nitrite ions. Kaur *et al* (2013) [79], developed two voltammetric sensors for cyanide detection based on anthrone moiety. The proposed electrochemical sensors were found to be selective for CN^- , OAc^- and F^- based on binding constants which were much larger than for anions like Cl^- , Br^- , I^- and HSO_4^- .

Karagollu *et al* (2014) [80], reported a novel phosphate ion sensors based on triazole connected with ferrocene moieties. Sensors responded to the addition of H_2PO_4^- and $\text{HP}_2\text{O}_7^{3-}$ anions in by shifting their redox potentials cathodically. Satheshkumar *et al* (2014) [81], developed electrochemical receptors with redox active ferrocene and quinine centers bridged by imidazole moiety. Addition of incremental amounts of F^- and CN^- ions, to these two receptors, shifted the $E_{1/2}$ of the quinone redox couple to less negative potentials. Sariguney *et al* (2014) [82], synthesized a thiazole derivative as an electrochemical sensor for fluoride ion. He reported that there was a weak potential shift for receptor with other anions except fluoride, while the obvious peak potential shifts were obtained for the first peak as well as dramatic decrease for current values of the second oxidation peak for receptor on addition of fluoride. Lim *et al* (2015) [83], reported halogen bonding enhanced electrochemical halide anion sensing by redox-active ferrocene receptors. They reported that halogen bonding was found to significantly amplify the magnitude of the receptor's metallocene redox-couple's voltammetric responses for halide sensing compared to their hydrogen bonding analogues in both acetonitrile and aqueous-acetonitrile solvent media. Manivannan *et al* (2015) [84], synthesized six indole based receptors for fluoride detection. They reported that upon the addition of incremental amounts of F^- ions to the receptor solutions, both the reduction peaks shift towards more negative potential with a concomitant decrease in their peak currents i.e. the electroreduction of the quinone moiety becomes increasingly difficult.

From the above literature survey, we can observe that there are unlimited numbers of reports on cation/anion sensing by using different-different motifs like urea/thiourea, amides, ferrocene, crown ethers, calixrenes, triazole, quinines, pyrroles etc. but hardly any report on aryether motifs which can provide a revolutionary change in sensing field. Arylethers can easily replace crown ethers due to their similar structural behaviour irrespective of aryl rings. Aryl rings in aryether molecules provide rigidity to the whole molecule for selective entrapment of ions.

2.3 References

1. S. Devaraj, D. Saravanakumar and M. Kandaswamy, *Sensor Actuat. B - Chem.*, **2009**, 136, 13-19.
2. F. A. Abenncbe and E. Sinn, *Tetrahedron Lett.*, **2011**, 52, 5234-5237.
3. H. M. Chawla, S. N. Sahu, R. Shrivastava and S. Kumar, *Tetrahedron Lett.*, **2012**, 53, 2244-2247.
4. H. M. Chawla, R. Shukla and S. Pandey, *Tetrahedron Lett.*, **2012**, 53, 2996-2999.
5. (a) H. M. Chawla and T. Gupta, *Tetrahedron Lett.*, **2013**, 54, 1794-1797. (b) H. M. Chawla, R. Shukla and S. Pandey, *Tetrahedron Lett.*, **2013**, 54, 2063-2066.
6. J. Liu, Y. Q. Xie, Q. Lin, B. B. Shi, P. Zhang, Y. M. Zhang and T. B. Wei, *Sensor Actuat. B- Chem.*, **2013**, 186, 657-665.
7. M. Wang, J. Wang, W. Xue and A. Wu, *Dyes Pigments*, **2013**, 97, 475-480.
8. V. K. Gupta, N. Mergu and A. K. Singh, *Sensor Actuat. B - Chem.*, **2014**, 202, 674-682.
9. H. G. Im, H. Y. Kim and S. K. Chang, *Sensor Actuat. B - Chem.*, **2014**, 191, 854-859.
10. W. H. Hsieh, C. F. Wan, D. J. Liao and A. T. Wu, *Tetrahedron Lett.*, **2012**, 53, 5848-5851.
11. C. H. Chen, D. J. Liao, C. F. Wan and A. T. Wu, *Analyst*, **2013**, 138, 2527-2530.
12. A. Afkhami, F. S. Felehgari, T. Madrakian, H. Ghaedi and M. Rezaeiava, *Anal. Chim. Acta*, **2013**, 771, 21-30.
13. S. K. Shoora, A. K. Jain and V. K. Gupta, *Sensor Actuat. B - Chem.*, **2015**, 216, 86-104.
14. J. Lyskawa, D. Canevet, M. Allain and M. Salle, *Tetrahedron Lett.*, **2010**, 51, 5868-5872.
15. H. Bingol, E. Kocabas, E. Zor and A. Coskun, *Electrochim. Acta*, **2011**, 56, 2057-2061.
16. Z. Yan, Y. Lu, H. Wang, S. Wu and B. Zhao, *J. Mol. Liq.*, **2013**, 183, 72-78.
17. V. K. Gupta, B. Sethi, R. Sharma, S. Agarwal and A. Bharti, *J. Mol. Liq.*, **2013**, 177, 114-118.
18. D. Maity, R. Gupta, R. Gunupuru, D. N. Srivastava and P. Paul, *Sensor Actuat. B - Chem.*, **2014**, 191, 757-764.

19. S. H. Kim, H. S. Choi, J. Kim, S. J. Lee, D. T. Quang and J. S. Kim, *Org. Lett.*, **2009**, 12, 560-563.
20. P. Kumar and H. K. Sharma, *Electrochim. Acta*, **2013**, 87, 925-929.
21. T. Romero, R. A. Orenes, A. Tarraga and P. Molina, *Organometallics*, **2013**, 32, 5740-5753.
22. A. Kamal, N. Sharma, V. Bhalla, M. Kumar and R. K. Mahajan, *Talanta*, **2014**, 128, 422-427.
23. A. Kamal, N. Kumar, V. Bhalla, M. Kumar and R. K. Mahajan, *Sensor Actuat. B - Chem.*, **2014**, 190, 127-133.
24. Y. Fang, Y. Zhou, Q. Rui and C. Yao, *Organometallics*, **2015**, 34, 2962-2970.
25. L. Shi, W. Song, Y. Li, D. W. Li, K. N. Swanick, Z. Ding and Y.-T. Long, *Talanta*, **2011**, 84, 900-904.
26. M. Alfonso, A. Tarraga and P. Molina, *Org. Lett.*, **2011**, 13, 6432-6435.
27. A. Thakur and S. Ghosh, *Organometallics*, **2012**, 31, 819-826.
28. J. Zheng, K. L. Wu, T. H. Shi and Y. Xu, *Appl. Organomet. Chem.*, **2013**, 27, 698-703.
29. A. Kamal, K. Kumar, V. Kumar and R. K. Mahajan, *Electrochim. Acta*, **2014**, 145, 307-313.
30. W. S. Xia, R. H. Schmehl and C. J. Li, *Tetrahedron*, **2000**, 56, 7045-7049.
31. M. Ganjali, B. Veismohammadi, M. Hosseini and P. Norouzi, *Spectrochim. Acta Part A*, **2009**, 74, 575-578.
32. S. Maji and K. Viswanathan, *J. Lumin.*, **2009**, 129, 1242-1248.
33. M. Hosseini, M. R. Ganjali, B. Veismohammadi, F. Faridbod, P. Norouzi and S. D. Abkenar, *Sensor Actuat. B - Chem.*, **2010**, 147, 23-30.
34. M. R. Ganjali, V. K. Gupta, M. Hosseini, M. Hariri, F. Faridbod and P. Norouzi, *Sensor Actuat. B - Chem.*, **2012**, 171, 644-651.
35. M. R. Ganjali, M. Hosseini, M. Khobi, S. Farahani, M. Shaban, F. Faridbod, A. Shafiee and P. Norouzi, *Talanta*, **2013**, 115, 271-276.
36. F. Faridbod, M. Sedaghat, M. e. Hosseini, M. Ganjali, M. Khoobi, A. Shafiee and P. Norouzi, *Spectrochim. Acta Part A*, **2015**, 137, 1231-1234.
37. M. R. Ganjali, F. Faridbod, P. Norouzi and M. Adib, *Sensor Actuat. B - Chem.*, **2006**, 120, 119-124.

38. X. Ma, Z. Xu, H. Yuan, Y. He, D. Xiao and M. M. Choi, *Sensor Actuat. B - Chem.*, **2010**, 147, 152-158.
39. G. Rounaghi, R. M. Z. Kakhki and H. Sadeghian, *Electrochim. Acta*, **2011**, 56, 9756-9761.
40. A. Upadhyay, A. K. Singh, K. R. Bandi and A. Jain, *Talanta*, **2013**, 115, 569-576.
41. V. K. Gupta, A. K. Singh and L. K. Kumawat, *Electrochim. Acta*, **2013**, 95, 132-138.
42. K. R. Bandi, A. K. Singh and A. Upadhyay, *Electrochim. Acta*, **2013**, 105, 654-664.
43. L. Cruickshank, S. Officer, P. Pollard, R. Prabhu, M. Stutter and C. Fernandez, *Analytical Sciences*, **2015**, 31, 623-627.
44. T. Alizadeh, M. R. Ganjali, M. Akhoundian and P. Norouzi, *Microchim. Acta*, **2016**, 183, 1123-1133.
45. R. Shannon, *Acta Crystallogr. Sect. A: Cryst. Phys., Diffraction, Theor. Gen. Crystallogr.*, **1976**, 32, 751-767.
46. A. P. De Silva, H. N. Gunaratne, T. Gunnlaugsson, A. J. Huxley, C. P. McCoy, J. T. Rademacher and T. E. Rice, *Chem. Rev.*, **1997**, 97, 1515-1566.
47. J. Shao, H. Lin and H. Lin, *Dyes Pigments*, **2009**, 80, 259-263.
48. H. Yu, Q. Zhao, Z. Jiang, J. Qin and Z. Li, *Sensor Actuat. B - Chem.*, **2010**, 148, 110-116.
49. Y. Li, J. Li, H. Lin, J. Shao, Z. S. Cai and H. Lin, *J. Lumin.*, **2010**, 130, 466-472.
50. H. S. Jung, H. J. Kim, J. Vicens and J. S. Kim, *Tetrahedron Lett.*, **2009**, 50, 983-987.
51. M. Cametti and K. Rissanen, *Chem. Commun.*, **2009**, 2809-2829.
52. S. Saha, A. Ghosh, P. Mahato, S. Mishra, S. K. Mishra, E. Suresh, S. Das and A. Das, *Org. Lett.*, **2010**, 12, 3406-3409.
53. Q. Wang, Y. Xie, Y. Ding, X. Li and W. Zhu, *Chem. Commun.*, **2010**, 46, 3669-3671.
54. N. Kumari, S. Jha and S. Bhattacharya, *J. Org. Chem.*, **2011**, 76, 8215-8222.
55. J. Ren, Z. Wu, Y. Zhou, Y. Li and Z. Xu, *Dyes Pigments*, **2011**, 91, 442-445.
56. L. Xu, Y. Li, Y. Yu, T. Liu, S. Cheng, H. Liu and Y. Li, *Org. Biomol. Chem.*, **2012**, 10, 4375-4380.
57. Q. Li, Y. Yue, Y. Guo and S. Shao, *Sensor Actuat. B - Chem.*, **2012**, 173, 797-801.
58. R. M. Batista, S. P. Costa and M. M. M. Raposo, *J. Photochem. Photobiol. A*, **2013**, 259, 33-40.

59. R. M. Batista, S. P. Costa and M. M. M. Raposo, *Sensor Actuat. B - Chem.*, **2014**, 191, 791-799.
60. J. W. Lee, H. W. Kim, H. G. Im, H. Y. Kim and S. K. Chang, *Sensor Actuat. B - Chem.*, **2014**, 192, 9-14.
61. V. Thiagarajan, P. Ramamurthy, D. Thirumalai and V. T. Ramakrishnan, *Org. Lett.*, **2005**, 7, 657-660.
62. L. M. Pei, Q. T. Lin, H. Chao and L. N. Ji, *Inorg. Chem. Commun.*, **2012**, 22, 90-92.
63. V. K. Gupta, A. K. Singh, S. Bhardwaj and K. R. Bandi, *Sensor Actuat. B - Chem.*, **2014**, 197, 264-273.
64. V. K. Gupta, A. K. Singh and N. Gupta, *Sensor Actuat. B - Chem.*, **2014**, 204, 125-135.
65. T. S. Snowden and E. V. Anslyn, *Curr. Opin. Chem. Biol.*, **1999**, 3, 740-746.
66. O. Reynes, F. Maillard, J. C. Moutet, G. Royal, E. Saint-Aman, G. Stanciu, J. P. Dutasta, I. Gosse and J. C. Mulatier, *J. Organomet. Chem.*, **2001**, 637, 356-363.
67. P. Anzenbacher, M. A. Palacios, K. Jursikova and M. Marquez, *Org. Lett.*, **2005**, 7, 5027-5030.
68. P. D. Beer and S. R. Bayly, "Anion sensing by metal-based receptors." *Anion Sensing. Springer Berlin Heidelberg*, **2005**. 125-162.
69. A. Isaac, J. Davis, C. Livingstone, A. J. Wain and R. G. Compton, *TrAC Trends Anal. Chem.*, **2006**, 25, 589-598.
70. H. Miyaji, D. S. Kim, B. Y. Chang, S. M. Park and K. H. Ahn, *Bull. Korean Chem. Soc.*, **2008**, 29, 2355.
71. A. Lorenzo, E. Aller and P. Molina, *Tetrahedron*, **2009**, 65, 1397-1401.
72. L. Ma, L. Wang, Q. Tan, H. Yu, J. Huo, Z. Ma, H. Hu and Z. Chen, *Electrochim. Acta*, **2009**, 54, 5413-5420.
73. J. Li, H. Lin, P. Jiang and H. Lin, *J. Inclusion Phenom. Macrocyclic Chem.*, **2008**, 62, 209-213.
74. C. Villena, J. Losada, P. Garcia-Armada, C. M. Casado and B. Alonso, *Organometallics*, **2012**, 31, 3284-3291.
75. G. Sathyaraj, D. Muthamilselvan, M. Kiruthika, T. Weyhermuller and B. U. Nair, *J. Organomet. Chem.*, **2012**, 716, 150-158.
76. L. Chacon-Garcia, M. Valle-Sanchez and C. A. Contreras-Celedon, *Lett. Org. Chem.*, **2013**, 10, 632.

77. S. S. Hassan, S. A. Marzouk and H. E. Sayour, *Talanta*, **2003**, 59, 1237-1244.
78. X. Luo, J. Wu and Y. Ying, *Ionics*, **2013**, 19, 1171-1177.
79. K. Kaur, S. K. Mittal, A. Kumar and S. Kumar, *Anal. Methods*, **2013**, 5, 5565-5571.
80. O. Karagollu, M. Gorur, F. Gode, B. Sennik and F. Yilmaz, *Sensor Actuat. B - Chem.*, **2014**, 193, 788-798.
81. A. Satheshkumar, R. Manivannan and K. P. Elango, *J. Organomet. Chem.*, **2014**, 750, 98-106.
82. A. B. Sarigüney, A. O. Saf and A. Coskun, *Spectrochim. Acta Part A*, **2014**, 128, 575-582.
83. J. Y. Lim, M. J. Cunningham, J. J. Davis and P. D. Beer, *Chem. Commun.*, **2015**, 51, 14640-14643.
84. R. Manivannan, A. Satheshkumar, E.-S. H. El-Mossalamy, L. M. Al-Harbi, S. A. Kosa and K. P. Elango, *New J. Chem.*, **2015**, 39, 3936-3947.

MATERIALS AND METHODS

This chapter reports the materials and methods used to synthesize di/triphenylether based molecules and further their ion recognition studies by using spectroscopic and voltammetric techniques. Theoretical studies further support the mode of interaction of cation/anion with the receptor molecule. Nuclear Magnetic Resonance Spectroscopy was carried out to confirm the synthesis of designed molecules. Techniques used throughout to carry out the ion-recognition studies include spectrophotometry, spectrofluorimetry, cyclic voltammetry and differential pulse voltammetry. Experimental details of the methods and techniques are mentioned in this chapter in detail.

3.1 Chemicals

All chemicals were purchased from Sigma Aldrich for analysis studies and from Spectrochem for synthesis and used without further purification. Column chromatography was performed on silica gel (120-200 mesh). Solvents used in the spectrophotometric and electrochemical experiments were of HPLC grade (Sd Fine, India) and used as received. For cation interaction investigation, perchlorate salts (Sigma Aldrich) of the metal were used while for anion interaction studies all the Tetrabutylammonium salts were used. For lanthanide interaction studies, nitrate salts of all the lanthanide (Analytical Reagent grade CDH, India) were used as obtained. Tetrabutylammonium hexafluorophosphate (Sigma Aldrich) was used as a supporting electrolyte in all the voltammetric experiments. HPLC grade solvents like acetonitrile, dimethyl sulphoxide (DMSO), N,N' dimethylformamide (DMF), tetrahydrofuran (THF), dichloromethane (DCM), methanol, ether and ethyl acetate were obtained from Merck and used as received. Potassium chloride (KCl) and silver nitrate (AgNO_3) of analytical reagent (AR) grade were obtained from Loba Chemie, India. HEPES buffer used to maintain pH was of AR grade obtained from Loba Chemie, India. Stock solutions of compounds and salts were prepared by using above mentioned solvents as per the requirements. All the glassware were cleaned with HNO_3 and rinsed thoroughly with distilled

water before use. Nitrogen purging was carried out for 5 minutes in the test solution to carry out all the voltammetric experiments.

3.2 Instrumental techniques

^1H NMR spectra were recorded using JEOL A1 spectrometer operating at 400 MHz. ^{13}C NMR spectra were recorded at 100 MHz. UV-visible studies were recorded on Analytic Jena Specord PC 205 spectrophotometer using slit width of 1.0 cm and matched quartz cells. Spectrofluorimetric studies were carried out on Perkin Elmer LS-55 fluorescence spectrometer. Electrochemical measurements were performed on Gamry Potentiostat / Galvanostat / ZRA Interface 1000. For voltammetric experiments, 3-electrode cell configuration was used. Glassy carbon (GC) electrode (CH Instruments, USA, 3mm diameter) was used as working electrode, platinum as counter electrode and Ag/Ag^+ as reference electrode for all the voltammetric experiments. The Ag/Ag^+ electrode contained an internal solution of 0.01M AgNO_3 and 0.1M TBAP in solvents as same as of test solutions like acetonitrile (ACN), dimethyl formamide (DMF), dimethylsulfoxide (DMSO) and dichloromethane (DCM). In case of aqueous system, all the potentials were recorded against Ag/AgCl reference electrode which contained 1 M KCl as inner filling solution. To carry out voltammetric experiments, working GC electrode was polished with alumina followed by washing with water and solvent before each experiment. All the electrochemical measurements were carried out at a temperature of $25.0 \pm 0.1^\circ\text{C}$.

For ion-recognition studies of synthesized receptor molecules, preliminary studies were carried out using spectrophotometric techniques followed by voltammetric methods. A detailed account of the voltammetric method applied is discussed in following paragraphs.

3.2.1 Spectrophotometry

Spectrophotometry is a quantitative measurement of how much a chemical substance absorbs light by measuring the intensity of light as a beam of light passes through sample solution. The basic principle is that each compound absorbs or transmits light over a certain range of wavelength. This measurement can also be used to measure the amount of a known chemical substance. Spectrophotometry is one of the most useful methods of quantitative analysis in

various fields such as chemistry, physics, biochemistry, material and chemical engineering and clinical applications.

3.2.2 Spectrofluorimetry

Spectrofluorimetry is a type of electromagnetic spectroscopy that analyzes fluorescence from a sample. It involves using a beam of light, usually ultraviolet light, that excites the electrons in molecules of certain compounds and causes them to emit light; typically, but not necessarily, visible light. In fluorescence, the species is first excited, by absorbing a photon, from its ground electronic state to one of the various vibrational states in the excited electronic state. Collisions with other molecules cause the excited molecule to lose vibrational energy until it reaches the lowest vibrational state of the excited electronic state. This process is often visualized with a Jablonski diagram.

3.2.3 Voltammetry

Voltammetry is one of the categories of electroanalytical method used in analytical chemistry. In voltammetry, information about an analyte is obtained by measuring current as a function of applied potential [1, 2]. Voltammetric studies impart us the knowledge of oxidation – reduction process occurring at the electrode surface, adsorption process occurring on the surface, electron transfer mechanisms taking place at chemically modified electrode surfaces. Voltammetry is divided into four major categories: (i) linear sweep voltammetry (LSW), (ii) differential pulse voltammetry (DPV), (iii) square wave voltammetry (SWV) and (iv) cyclic voltammetry (CV). We have conducted experiments on CV and DPV only, so they are discussed in detail as below.

Cyclic voltammetry

Cyclic voltammetry is a type of potentiodynamic electrochemical measurement in which the working electrode potential is ramped linearly versus time. In a CV experiment, the working electrode's potential is ramped in the opposite direction to return to the initial potential in order to obtain a voltammogram. The rate at which the potential is varied between the applied potential ranges is called scan rate. Important parameters of CV are anodic/cathodic peak potential ($E_{pa/c}$) and anodic/cathodic peak current ($I_{pa/c}$). Cyclic voltammograms obtained may be having reversible or non-reversible couples [3].

Differential pulse voltammetry

The importance of DPV in chemical analysis lies in minimizing the effect of charging current and hence increases its sensitivity. Effect of the charging current can be minimized by sampling the current just before the potential is changed and the current difference is plotted as a function of potential. The important parameters for pulse techniques are as follows:

1. **Pulse amplitude:** height of the potential pulse.
2. **Pulse width:** duration of the potential pulse.
3. **Sample period:** time at the end of the pulse during which the current is measured.
4. **Pulse period:** time required for one potential cycle.

3.2.4 Computational studies

Theoretical studies of the molecules were done using DFT (density functional theory) [4-6], calculations using B3LYP/6-31+G** basis sets with GAUSSIAN 03W software. Optimization of structures was carried out at ground state and further metal complexation studies were carried out at LANL2DZ method while anion complexation was carried out using B3LYP/6-31G basis sets. HOMO–LUMO orbitals of the optimized structure of molecules and their complexed forms were located to find the electron density in their molecular structures.

3.3 EXPERIMENTAL SECTION

Di/Tri-phenyl ether based receptors were synthesized by nucleophilic aromatic substitution reactions and their further manipulation. A total of sixteen receptors (**SMR 1-16**) were synthesized and the detailed synthetic methodology has been presented below. Electroanalytical probes based on the receptors are also developed for cations and anions as target ions.

3.3.1 Synthesis of diphenyl ether based receptors

SMR-1: 4-(2,4-dinitrophenoxy)-3-methoxybenzaldehyde [7]

Receptor **SMR-1** has been synthesized by using 2, 4- dinitrofluorobenzene (1 mmol) and vanillin (1.1 mmol) in the presence of mild base, K₂CO₃, catalytic amount of 18-crown-6 and

aprotic solvent (DMF) at room temperature by overnight stirring. Progress of the reaction was monitored by TLC and after completion of reaction crude product was purified by column chromatography using petroleum ether and ethyl acetate (75:25, v/v) as the solvent system. Purified compound was characterized by ^1H and ^{13}C NMR spectroscopy and the structure was consistent with the proposed compound (**SMR-1**). Yield obtained was 80%. **Melting Point:** 130-131°C. **^1H NMR (400 MHz, CDCl_3):** δ 3.8 (s, 3H), 6.9 (d, J = 6.9 Hz, 2H), 7.4 (m, 1H), 7.6 (m, 2H), 8.3 (dd, J = 2.8 Hz, 1H), 8.9 (d, J = 2.4 Hz, 1H), 10.0 (s, 1H). **^{13}C NMR (CDCl_3):** δ 56.3, 111.9, 117.9, 122.1, 122.6, 125.2, 128.6, 135.8, 139.0, 141.9, 146.6, 151.7, 155.3, 190.4.

SMR-2: (4-(2,4-dinitrophenoxy)-3-methoxyphenyl)methanol [7]

Receptor **SMR-2** was synthesized by reduction of compound **SMR-1** (1 mmol) using NaBH_4 (2.5 mmol) as a reducing agent in methanol (20 ml). Color of the reaction changes from yellow to violet with gradual addition of NaBH_4 . Progress of the reaction was monitored by TLC and after completion of reaction crude product was purified by column chromatography using petroleum ether and ethyl acetate (70:30, v/v) as the solvent system. The isolated compound from column chromatography was analysed and confirmed by ^1H and ^{13}C NMR spectroscopy to be compound **SMR-2**. Yield obtained was 62%. **Melting Point:** 108-109°C. **^1H NMR (400 MHz, CDCl_3):** δ 3.8 (s, 3H), 4.7 (s, 2H), 6.9 (d, J = 9.3 Hz, 1H), 7.0–7.3 (m, 3H), 8.3 (m, 1H), 8.9 (m, 1H), 10.9 (br s, 1H). **^{13}C NMR (CDCl_3):** δ 56.0, 64.7, 111.7, 117.3, 119.7, 122.1, 122.4, 128.7, 138.5, 140.5, 141.0, 146.0, 151.0, 156.5.

SMR-3: 3-(2,4-dinitrophenoxy)phenol

To a solution of 1-fluoro-2,4-dinitrobenzene (20.9 mmol) in DMF (25 mL) were added K_2CO_3 (83.9 mmol), resorcinol (26.3 mmol) and 18-crown-6 (0.2 mmol). The mixture was stirred at room temperature for 12 h. After completion of reaction (Thin layer chromatography monitoring), the reaction mixture was diluted with CH_2Cl_2 (100 mL), washed with water (50 mL), 1 N NaOH (3×10 mL), water (until neutral to litmus paper), brine and dried over Na_2SO_4 . Evaporation of the organic solvent gave yellow solid which was purified using SiO_2 column chromatography and solvent (Pet. ether/ethyl acetate = 75:25) to afford product **SMR-3** in 63% yield. **Melting point:** 90-93°C. **^1H NMR (400 MHz, CDCl_3):** δ 5.0 (brs, 1H), 6.6 (t, J = 2.3 Hz, 1H), 6.7 (dd, J = 10.5, 2.7 Hz, 1H), 6.8 (dd, J = 10.5, 2.3 Hz, 1H), 7.1 (d, J = 9.2 Hz, 1H), 7.3 (t, J = 8.2 Hz, 1H), 8.3 (dd, J = 11.9, 2.7 Hz, 1H), 8.8 (d, J = 2.8

Hz, 1H). ¹³C NMR (CDCl₃): δ 108.0, 112.5, 113.6, 118.6, 122.0, 128.7, 131.3, 139.4, 141.4, 154.5, 155.9, 157.5.

SMR-4: 3-(2-nitrophenoxy)phenol

Using procedure detailed for compound **SMR-3**, compound **SMR-4** was obtained using 1-fluoro-2, nitrobenzene (20.9 mmol) instead of 1-fluoro-2,4-dinitrobenzene. Purification was done using SiO₂ column chromatography and solvent (toluene) to afford pale yellow sticky oil in **51%** yield. **Melting point:** 80-81°C. ¹H NMR (400 MHz, CDCl₃): δ 5.3 (br s, 1H), 6.5 (m, 2H), 6.6 (m, 1H), 7.0 (dd, *J* = 9.6, 1.1 Hz, 1H), 7.1-7.2 (m, 2H), 7.4-7.5 (m, 1H), 7.9 (dd, *J* = 9.6, 1.6 Hz, 1H). ¹³C NMR (CDCl₃): δ 106.5, 110.8, 111.7, 120.6, 123.2, 125.5, 130.5, 134.4, 140.7, 150.3, 156.5, 157.0.

SMR-5: 2-(2-methoxyphenoxy)benzaldehyde

To a solution of 2- methoxyphenol (20.9 mmol) in DMF (25 mL) were added K₂CO₃ (883.9 mmol), 2- bromo benzaldehyde (26.3 mmol) and 18-crown-6 (0.2 mmol). The mixture was stirred at room temperature for 10 h. After the reaction is complete (TLC monitoring), the reaction mixture was diluted with CH₂Cl₂ (100 mL), washed with water (50 mL), 1 N NaOH (3×10 mL), water (until neutral to litmus paper), brine and dried over Na₂SO₄. Evaporation of the organic solvent gave yellow solid which was purified using SiO₂ column chromatography and solvent (Pet. ether/ethyl acetate = 80:20) to afford a product in **75%** yield. **Melting point:** 85-86°C. ¹H NMR (400 MHz, CDCl₃): δ 3.8 (s, 3H), 6.7 (d, *J* = 9.16 Hz, 1H), 7.0 (m, 4H), 7.2 (m, 1H), 7.4 (m, 1H), 7.9 (m, 1H), 10.6 (s, 1H). ¹³C NMR (CDCl₃): δ 55.8, 112.9, 116.3, 121.2, 121.9, 122.3, 125.5, 125.9, 128.0, 135.5, 143.8, 151.5, 160.8, 189.6.

SMR-6: 1-methoxy-2-(2-nitrophenoxy)benzene

To a solution of 2- methoxyphenol (20.9 mmol) in DMF (25 mL) were added K₂CO₃ (883.9 mmol), 1-fluoro-2- nitrobenzene (26.3 mmol) and 18-crown-6 (0.2 mmol). The mixture was stirred at room temperature for 10 h . After the reaction is complete (TLC monitoring), the reaction mixture was diluted with CH₂Cl₂ (100 mL), washed with water (50 mL), 1 N NaOH (3×10 mL), water (until neutral to litmus paper), brine and dried over Na₂SO₄. Evaporation of the organic solvent gave yellow solid which was purified using SiO₂ column chromatography and solvent (Pet. ether/ethyl acetate = 70:30) to afford a product in **82.5%** yield. **Melting point:** 92-93°C. ¹H NMR (400 MHz, CDCl₃): δ 3.79 (s, 3H), 6.85 (dd, *J* = 1.36, 9.64 Hz, 1H),

6.9 (m, 2H), 7.1 (m, 2H), 7.2 (m, 1H), 7.4 (m, 1H), 7.9 (m, 1H). ^{13}C NMR (CDCl_3): δ 55.7, 112.9, 117.8, 121.1, 121.6, 121.8, 125.4, 126.2, 133.9, 139.7, 143.0, 151.1, 151.5.

SMR-7: 2-(2-methoxyphenoxy)benzenamine

SMR-6 (4.1 mmol) was dissolved in 100 ml of dried methanol and catalytic amount of Pd/C (10 mg) was added. The solution was stirred at room temperature for 2 hours in the presence of H_2 gas. The yellow color slowly disappeared that indicates the reduction of nitro group. Finally Pd/C was filtered off from reaction mixture. The solvent was evaporated using rotavapor and product was obtained. Yield: 85%. **Melting point:** 80-81°C. ^1H NMR (400 MHz, CDCl_3): δ 3.8 (s, 3H), 3.87 (brs, 2H), 6.6 (m, 1H), 6.8 (m, 2H), 6.87 (d, $J = 3.8\text{ Hz}$, 2H), 6.9 (m, 1H), 6.99 (d, $J = 7.6\text{ Hz}$, 1H), 7.0 (m, 1H). ^{13}C NMR (CDCl_3): δ 55.8, 112.4, 116.1, 118.4, 118.5, 118.6, 120.9, 123.7, 124.1, 138.0, 143.9, 145.7, 150.3.

3.3.2 Synthesis of triphenyl ether based receptors

General procedure for the synthesis of compounds **SMR-8**, **SMR-9** and **SMR-10**

Reaction of triclosan (1.1 mmol) with fluorobenzene (1.0 mmole) under the conditions as described for compound **SMR-1** gave corresponding crude triphenylether that purified by column chromatography using Pet. ether and ethyl acetate as solvent. All purified products were characterized by ^1H , ^{13}C NMR techniques.

SMR-8: 4-chloro-1-(2,4-dichlorophenoxy)-2-(2,4-dinitrophenoxy)benzene

Melting point: 85-86°C. ^1H NMR (400 MHz, CDCl_3): δ 6.86 (d, $J = 8.72\text{ Hz}$, 1H), 6.9 (d, $J = 8.72\text{ Hz}$, 1H), 7.1 (d, $J = 11.48\text{ Hz}$, 1H), 7.15 (dd, $J = 2.32, 16.96\text{ Hz}$, 1H), 7.25 (dd, $J = 2.32, 11.0\text{ Hz}$, 1H), 7.31 (d, $J = 11.9, 2.28\text{ Hz}$, 1H), 7.32 (d, $J = 4.12\text{ Hz}$, 1H), 8.3 (dd, $J = 2.76, 12.36\text{ Hz}$, 1H), 8.7 (d, $J = 2.76\text{ Hz}$, 1H). ^{13}C NMR (CDCl_3): δ 117.9, 120.2, 120.7, 122.1, 123.6, 125.8, 127.9, 128.4, 128.8, 130.0, 130.5, 130.6, 138.6, 141.8, 143.0, 146.1, 149.5, 154.9.

SMR-9: 4-chloro-1-(2,4-dichlorophenoxy)-2-(2-nitrophenoxy)benzene

Melting point: 90-91°C. ^1H NMR (400 MHz, CDCl_3): δ 6.82 (d, $J = 8.72\text{ Hz}$, 1H), 6.9 (d, $J = 8.68\text{ Hz}$, 1H), 7.0 (d, $J = 8.48\text{ Hz}$, 1H), 7.1 (d, $J = 2.32\text{ Hz}$, 1H), 7.15 (m, 2H), 7.2 (m, 1H), 7.3 (d, $J = 2.28\text{ Hz}$, 1H), 7.5 (m, 1H), 7.9 (dd, $J = 1.36, 9.6\text{ Hz}$, 1H). ^{13}C NMR (CDCl_3): δ

119.0, 149.7, 146.1, 145.4, 140.4, 134.5, 134.1, 129.9, 128.6, 127.3, 126.0, 125.8, 123.2, 122.2, 121.0, 120.3, 119.3, 119.0.

SMR-10: 4-chloro-1-(2,4-dichlorophenoxy)-2-(4-nitrophenoxy)benzene

Melting point: 95-96°C. ¹H NMR (400 MHz, CDCl₃): δ 6.8 (d, *J* = 8.72 Hz, 1H), 6.89 (d, *J* = 8.68 Hz, 1H), 6.9 (s, 1H), 6.94 (s, 1H), 7.1 (dd, *J* = 2.76, 11.48 Hz, 1H), 7.18 (d, *J* = 2.76 Hz, 1H), 7.2 (t, *J* = 2.8 Hz, 1H), 7.3 (d, *J* = 2.28 Hz, 1H), 8.14 (d, *J* = 2.28 Hz, 2H). ¹³C NMR (CDCl₃): δ 116.5, 120.2, 120.8, 123.7, 125.9, 126.9, 128.2, 129.8, 129.9, 130.5, 143.1, 144.7, 146.6, 150.3, 162.2.

General procedure for the synthesis of compounds SMR-15 & SMR-16

Both the compounds were synthesized by a three step procedure.

Step-1: Synthesis of compounds SMR-11 & SMR-12

Following protocol used for compound SMR-3 and using 1-fluoro-2-nitrobenzene and 1-fluoro-4-nitrobenzene compounds SMR-11, SMR-12 were isolated and purified by SiO₂ column chromatography using solvent (Pet. ether: ethyl acetate).

SMR-11: 1,3-bis(2-nitrophenoxy)benzene

Melting point: 105-106°C. ¹H NMR (400 MHz, CDCl₃): δ 6.73 (t, *J* = 2.3 Hz, 1H), 6.8 (dd, *J* = 10.5, 2.7 Hz, 2H), 7.2 (m, 2H), 7.3 (t, *J* = 9.2 Hz, 1H), 7.5 (m, 2H), 7.9 (dd, *J* = 11.9, 2.7 Hz, 2H). ¹³C NMR (CDCl₃): δ 109.5, 114.4, 121.2, 123.9, 125.8, 131.0, 134.4, 149.7, 157.3.

SMR-12: 1,3-bis(4-nitrophenoxy)benzene

Melting point: 95-96°C. ¹H NMR (400 MHz, CDCl₃): δ 8.2 (m, 4H), 7.4 (t, *J* = 8.2 Hz, 1H), 7.0 (m, 4H), 6.9 (dd, *J* = 2.28 Hz, 2H), 6.8 (t, *J* = 2.28 Hz, 1H). ¹³C NMR (CDCl₃): δ 162.4, 156.5, 143.2, 131.6, 126.1, 11.7, 116.8, 112.5.

Step-2: Synthesis of compounds SMR-13 & SMR-14

Compounds SMR-11/12 (4.1 mmol) was dissolved in 100 ml of dried methanol and catalytic amount of Pd/C (10 mg) was added. The solution was stirred at room temperature for 2 hours in the presence of H₂ gas. The yellow color was slowly disappeared that indicates the

reduction of nitro group. Finally Pd/C was filtered off from reaction mixture. The solvent was evaporated using rota-vapor and product was obtained. Yield: 80%.

SMR-13: 2-(3-(2-aminophenoxy)phenoxy)benzenamine

Melting point: 110-112 °C. ¹H NMR (400 MHz, CDCl₃): δ 3.65 (bs, 4H), 6.5 (dd, J = Hz, 2H), 6.6 (s, 1H), 6.7 (m, 2H), 6.8 (dd, J = 1.36Hz, 2H), 6.89 (t, J = 7.76Hz, 2H), 6.9 (m, 2H), 7.1 (t, J = 8.28Hz, 1H). ¹³C NMR (CDCl₃): δ 158.8, 142.4, 138.6, 130.2, 125.1, 120.5, 118.7, 116.5, 110.6, 106.1.

SMR-14: 4-(3-(4-aminophenoxy)phenoxy)benzenamine

Melting point: 90-92 °C. ¹H NMR (400 MHz, CDCl₃): δ 3.65 (bs, 4H), 7.1 (t, J = 7.8Hz, 1H), 6.8 (m, 4H), 6.6 (m, 4H), 6.56 (m, 2H), 6.5 (d, J = 2.28Hz, 1H). ¹³C NMR (CDCl₃): δ 160.1, 147.9, 142.7, 129.8, 121.2, 116.1, 110.5, 106.4.

Step-3: Imine formation using compounds SMR-13 & SMR-14

2-hydroxy naphthaldehyde (2.2 mmol) was dissolved in ethanol (30 ml) and stirred at room temperature. To this solution, **SMR-13/14** (1 mmol) was added drop-wise dissolved in ethanol (5mL) under stirring. The resultant reaction mixture was refluxed for 2-3 h and brought to room temperature. The product precipitated out and was filtered. Washing was done with ethanol and water, then dried under vacuum. Yield: 85%.

SMR-15: 1-((E)-(2-(3-(2-((E)-(2-hydroxynaphthalen-1-yl)methyleneamino)phenoxy)phenoxy)phenylimino)methyl)naphthalen-2-ol

Melting Point: 150-151 °C. ¹H NMR (400 MHz, CDCl₃): δ 15.4 (s, 1H), 9.3 (s, 2H), 8.1 (d, J = 8.2 Hz, 2H), 7.8 (d, J = 9.1Hz, 2H), 7.74 (d, J = 8.2Hz, 2H), 7.5 (m, 2H), 7.36 (m, 7H), 7.13 (m, 6H) 6.78 (m, 3H). ¹³C NMR (CDCl₃): δ 168.2, 158.8, 155.2, 155.0, 141.7, 136.2, 132.9, 130.6, 129.3, 128.0, 127.3, 123.5, 121.8, 121.6, 120.2, 118.8, 113.3, 109.3, 108.5.

SMR-16: 1-((E)-(4-(3-(4-((E)-(2-hydroxynaphthalen-1-yl)methyleneamino)phenoxy)phenoxy)phenylimino)methyl)naphthalen-2-ol

Melting Point: 155-157 °C. ¹H NMR (400 MHz, CDCl₃): δ 9.3 (s, 2H), 8.1 (d, J = 8.2 Hz, 2H), 7.8 (d, J = 9.1Hz, 2H), 7.7 (d, J = 8.2Hz, 2H), 7.5 (m, 2H), 7.38 (m, 4H), 7.34 (m, 3H), 7.1 (m, 6H) 6.7 (m, 3H). ¹³C NMR (CDCl₃): δ 168.0, 158.5, 155.6, 155.0, 141.6, 136.2, 133.0, 130.5, 129.3, 128.0, 127.3, 123.5, 121.8, 121.6, 120.2, 118.8, 113.3, 109.2, 109.0.

3.3.3 Experimental conditions for cyclic voltammetric study

Stock solutions of the receptor compounds (5×10^{-3} M) were prepared in acetonitrile. Applied potential window for molecules was first optimized in between -2.0 to +2.0V potential range to get the best resolved peaks. Scan rate was varied from 20 mV/sec to 200 mV/sec to study the nature of material transport. All solutions of different concentration of the compounds were made from the stock solutions (5×10^{-3} M), in different solvents to carry the further studies.

3.3.4 Experimental conditions for differential pulse voltammetric study

All the differential pulse voltammetric studies were done at pulse amplitude of 50 mV and scan rate was varied from 20 mV/sec to 200 mV/sec. Potential window was adjusted as per the cyclic voltammogram results of the molecule.

3.3.5 Stock solutions for cation/anion/lanthanide interaction studies

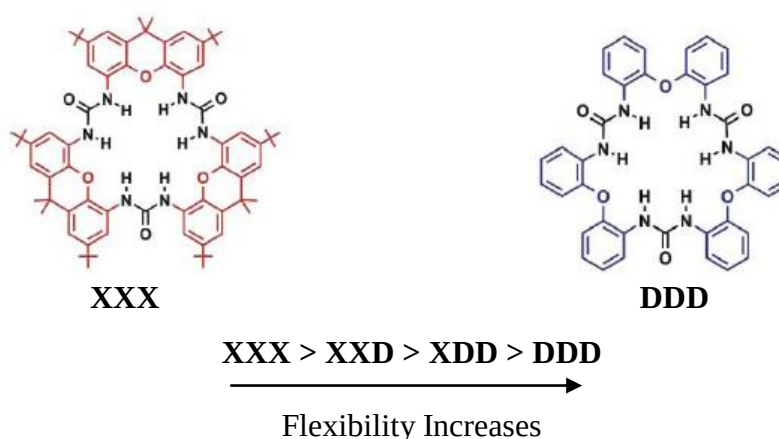
For cation interaction studies, perchlorate salts of different metals (Na(I), K(I), Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Ba(II), Hg(II), Cd(II) and Pb(II)) were used by preparing separate stock solutions of concentration 10^{-2} M in acetonitrile and in water. Similarly, separate stock solutions were prepared for tetrabutylammonium salts of anions like CN^- , Cl^- , Br^- , AcO^- , I^- , HSO_4^- , OH^- , H_2PO_4^- and ClO_4^- in acetonitrile and in water. For lanthanide interaction studies, nitrate salts of Dy(III), Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Ce(III) were used for the preparation of stock solution of concentration 10^{-2} M in acetonitrile and in water separately.

3.5 References

1. W. R. Heineman and P. T. Kissinger, "Large-amplitude controlled-potential techniques." *Laboratory Techniques in Electroanalytical Chemistry*, PT Kissinger and WR Heineman, Eds., Marcel Dekker, New York, **1996**, 51-125.
2. C. G. Zoski, Ed. *Handbook of Electrochemistry*, Elsevier, **2006**.
3. F. Scholz, *Electroanalytical Methods*, Vol. 1. Berlin-Heidelberg: Springer, **2010**.
4. A. D. Becke, *J. Chemical Phys.*, **1993**, 98, 5648-5652.
5. C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, **1988**, 37, 785.
6. P. J. Hay and W. R. Wadt, *J. Chemical Phys.*, **1985**, 82, 270-283.
7. M. Chhibber, G. Kumar, P. Parasuraman, T. Ramya, N. Surolia and A. Surolia, *Bioorg. Med. Chem.*, **2006**, 14, 8086-8098.

DIPHENYLETHER BASED RECEPTORS

Receptor properties of a host molecule are determined by the donor atom and cavity size. Diphenylethers can be impeccable receptors for the ions because besides above requirements they offer right blend of “rigidity” and “flexibility.” The phenyl ring provides sufficient rigidity to the cavity and the rotation around ether linkage propose ample flexibility. Meshcheryakov *et al* [1] have shown the comparison between xanthenes and diphenyl ether units to show the available flexibility in case of later. In case of cyclic triureas the replacement of rigid xanthenes (X) unit in XXX by more flexible diphenyl ether (D) unit influenced the conformation of host molecules and hence complexation with different ions as shown below.

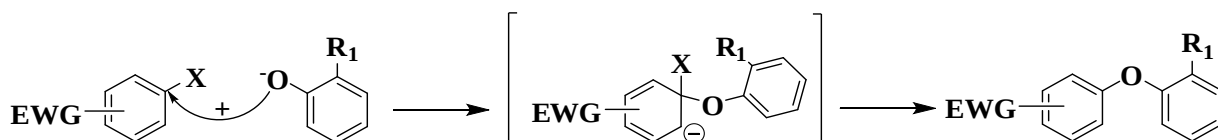


Urea based diphenylethers as Receptors

Besides that diphenyl ether units offer another advantage of substitution on the phenyl ring that can influence the electron density in cavity and hence their binding with variable ions. This chapter describes synthesis of various diphenyl ethers and their ability to sense different ions by spectroscopic and voltammetric methods.

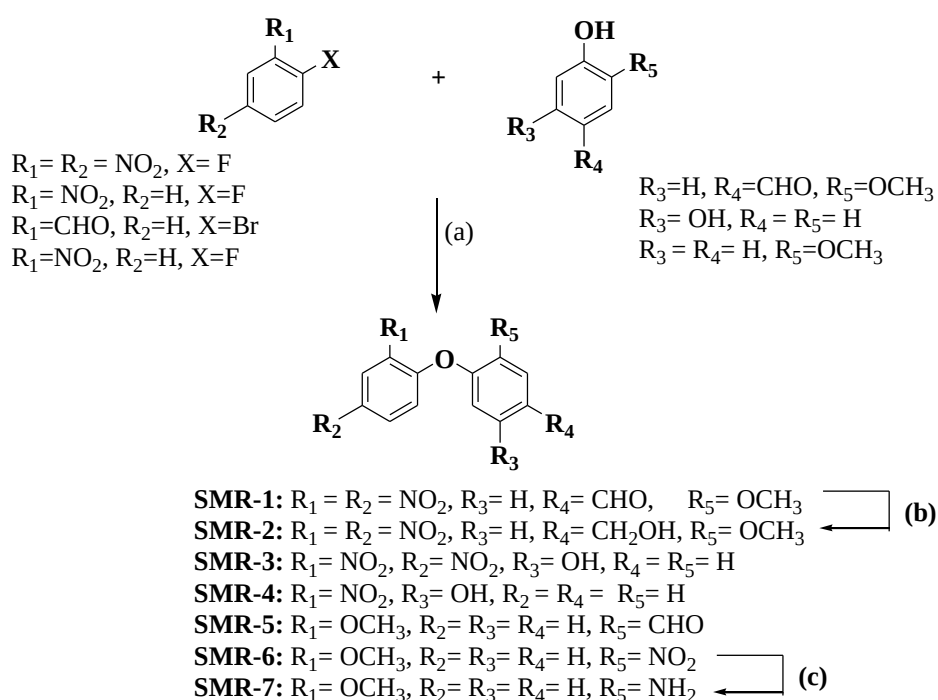
4.1 Synthesis and characterization

Initial step in the synthesis of all diphenyl ethers was nucleophilic aromatic substitution of halogen in the electron deficient benzene ring by phenolate ion as shown in **Scheme 4.1**.



Scheme 4.1 Mechanism for synthesis of diphenylether

Thus, all the reactions were carried out in the presence of mild base K_2CO_3 , catalytic amount of 18-crown-6 and aprotic solvent (DMF) along with halobenzene and corresponding phenol at room temperature. Overnight stirring followed by usual work up afforded compounds **SMR-1** and **SMR-3** to **SMR-6**. Purification was done by column chromatography in all the cases and confirmation of the structure was done by ^1H and ^{13}C NMR spectroscopy. In case of compound **SMR-1** six aromatic protons (6.9 ppm to 8.9 ppm), a sharp singlet due to $-OCH_3$ (3.8 ppm) and due to aldehyde (10.0 ppm) were obtained. Similarly compounds **SMR-3** and **SMR-4** were characterized by seven (6.6 ppm to 8.8 ppm) and eight (6.5 ppm to 7.9 ppm) aromatic protons respectively along with broad singlet (at 5.0 ppm and 5.3 ppm respectively) due to $-OH$ group. In case of compounds **SMR-5** and **SMR-6**, both of which have methoxy group, corresponding signals were obtained at 3.8 ppm and 3.79 ppm respectively. The aldehyde group in case of **SMR-5** gave sharp singlet at 10.6 ppm. In case of **SMR-6** the methoxy group previously reported appeared along with eight aromatic protons (6.85 ppm to 7.9 ppm).

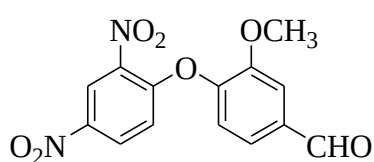


Scheme 4.2 (a) K_2CO_3 , DMF, 18-Crown-6 (b) $NaBH_4$, MeOH, (c) $H_2/Pd/C$, Dry MeOH.

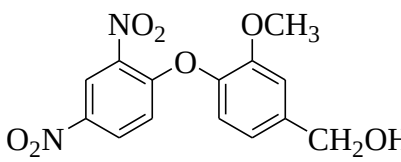
Further, reduction step in case of **SMR-2** and **SMR-7** was carried out by using NaBH₄ and H₂/Pd/C as reducing agents respectively. NaBH₄, being the mild reducing agent, was used for the reduction of aldehyde in **SMR-1** to corresponding alcohol (**SMR-2**). This was confirmed by the presence of a singlet due to 2 aliphatic protons at 4.7 ppm. The reduction of aromatic nitro groups, in **SMR-6**, to corresponding amines in **SMR-7** was done using H₂/Pd/C as reducing agent. NaBH₄ being mild reducing agent cannot be employed for this reduction. Confirmation of the reduction reaction was done by the presence of a broad peak at 3.79 ppm due to 2 amine protons.

4.2 Ion- recognition studies of diphenylether based receptors

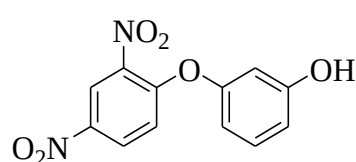
STRUCTURES OF DIPHENYL ETHER BASED SYNTHESIZED RECEPTORS



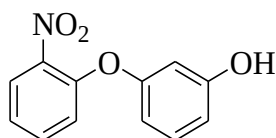
SMR-1



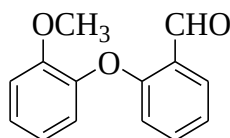
SMR-2



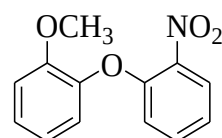
SMR-3



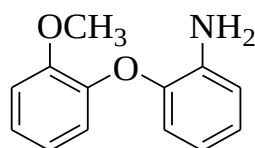
SMR-4



SMR-5



SMR-6



SMR-7

Among various synthesized diphenylethers (**SMR-1 - SMR-7**) as shown above, **SMR-1, 2, 3 & 4** were investigated for their interaction with various cations and anions to project these as cation/anion based chemical sensors. Receptor-metal interaction studies were carried out using spectrophotometric and electrochemical techniques. Further, the mode of interaction of

cation or anion with the respective molecule was supported by theoretical calculations using Gaussian 03W software.

4.2.1 Ion-recognition studies of SMR-1 & SMR-2

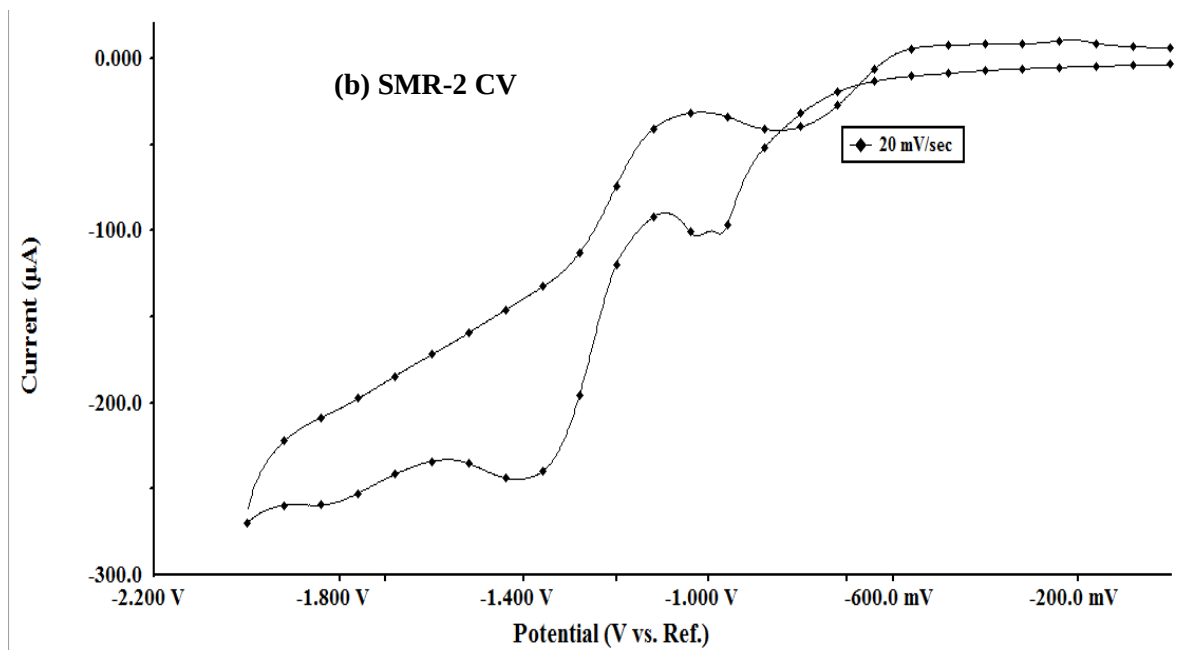
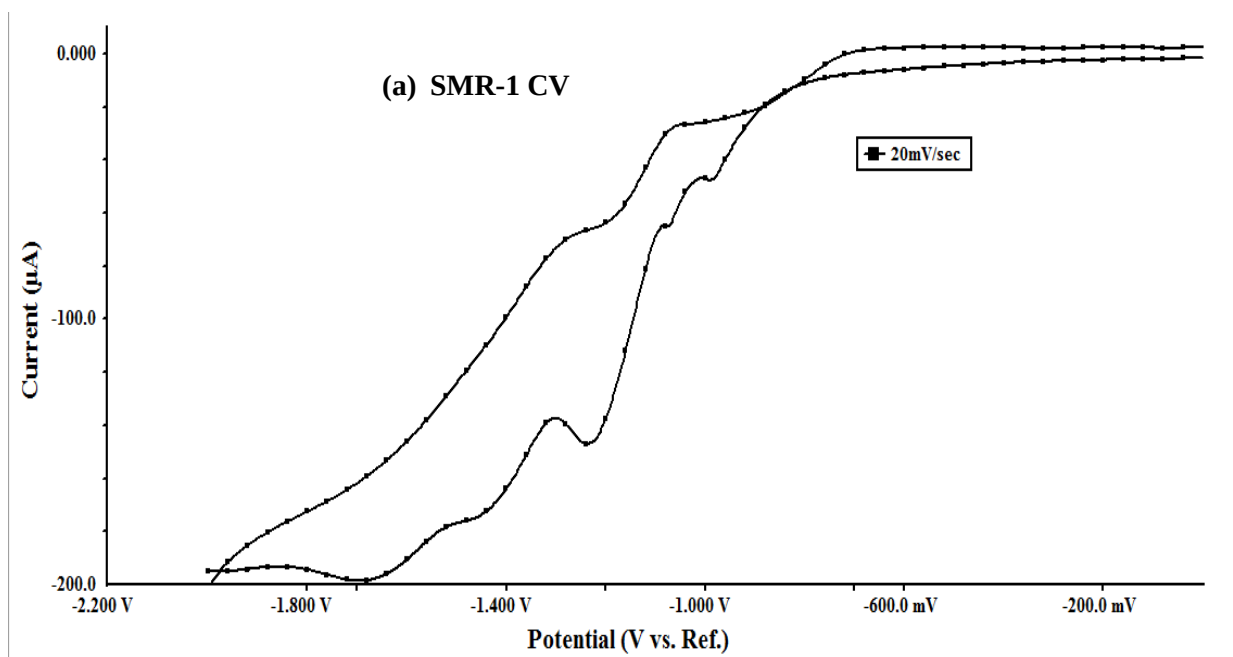
SMR-1 (4-(2,4-dinitro phenoxy)-3-methoxybenzaldehyde) and **SMR-2** (4-(2,4-dinitro phenoxy)-3-methoxyphenyl)methanol) were synthesized by nucleophilic aromatic substitution reaction as shown in Scheme 4.2. The binding ability of **SMR-1** and **SMR-2** with different metal ions viz., Na(I), K(I), Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Ba(II), Hg(II), Cd(II) and Pb(II) was studied using voltammetric experiments. **SMR-1** and **SMR-2** were taken in CH₃CN:H₂O (9:1) medium.

Electrochemical Studies

Electrochemical properties of **SMR-1** and **SMR-2** were investigated by cyclic voltammetry and differential pulse voltammetry. Cyclic voltammograms for **SMR-1** and **SMR-2** in CH₃CN:H₂O (9:1, v/v) medium containing 0.1 M TBAPF₆ as the supporting electrolyte are shown in Figures 4.1a and 4.1b.

Electrochemical behaviour of SMR-1 and SMR-2

Synthesis of **SMR-1** and **SMR-2** containing electron donating and electron withdrawing substituents, respectively was done to check their remote substituent effect on the electronic environment around the ethereal oxygen of the diphenylether group. These compounds are identified as **SMR-1** (containing –CHO group meta to methoxy group on benzene ring) and **SMR-2** (containing –CH₂OH group meta to methoxy group on benzene ring). It is hypothesized that the aldehydic group should facilitate reduction of nitro group on benzene ring of the molecule, while methanolic group, due to its electron donating character, should make the reduction of nitro group, a little difficult. Peak potentials of the two curves obtained for **SMR-1** appeared at -1.16 V (E_{pc1}) and -1.39 V (E_{pc2}), respectively, whereas corresponding peaks for **SMR-2** are observed at -1.30 V (E_{pc1}) and -1.43 V (E_{pc2}), respectively (Figures 4.1a and 4.1b) thereby supporting the proposed hypothesis. Corresponding peak currents for the respective peak potentials are shown in Table 4.1.



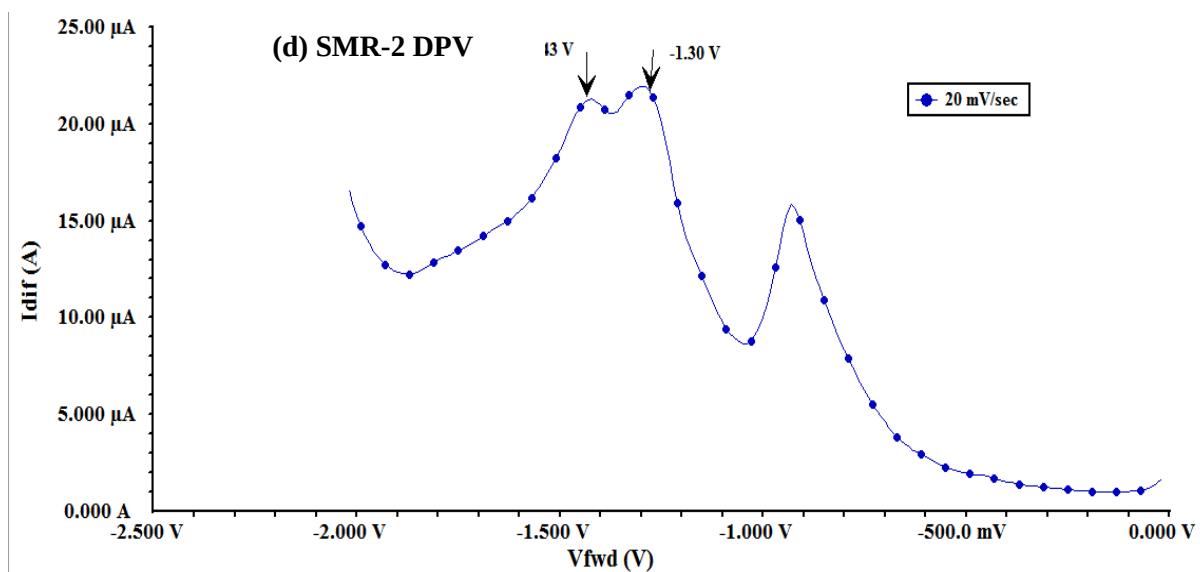
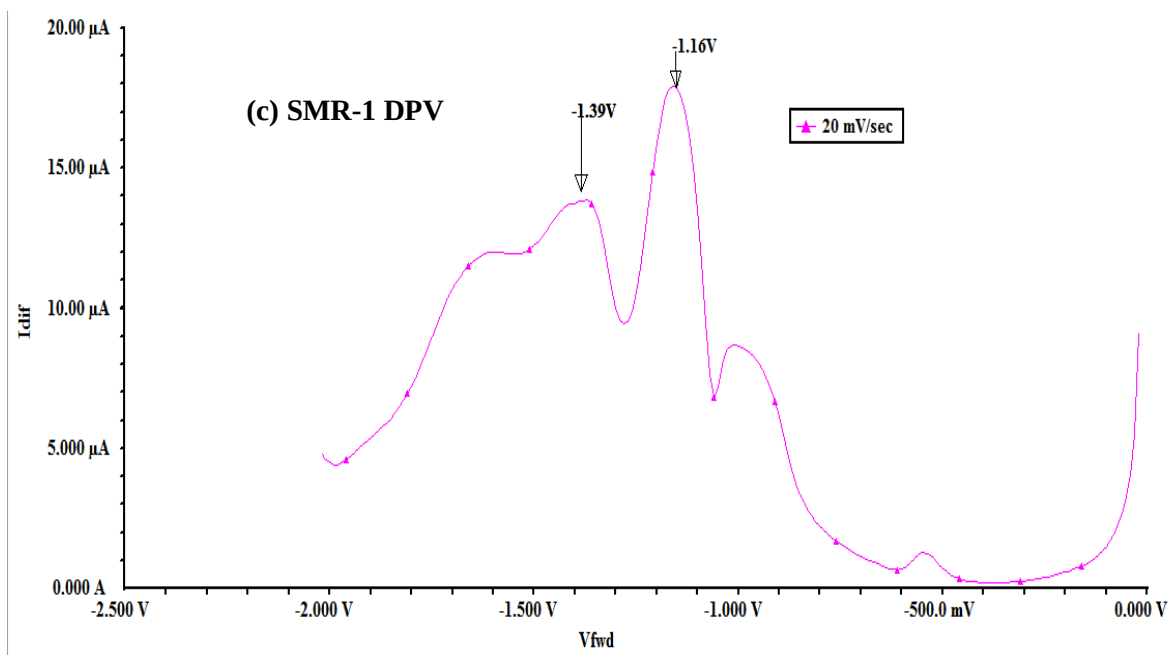


Figure 4.1 Cyclic and differential pulse voltammograms of (a, c) **SMR-1** (b, d) **SMR-2** ($5 \times 10^{-4} M$) at $pH 7.0 \pm 0.1$ (10 mM HEPES in $CH_3CN:H_2O$ 9:1, v:v) using 0.1M $TBAPF_6$ as supporting electrolyte, scan rate 20 mV s^{-1} and GC as working electrode. Modulation amplitude for DPV: 50 mV sec^{-1}

Table 4.1 Peak potential (V) and peak current (μA) values for **SMR-1** and **SMR-2** ($5 \times 10^{-4}\text{M}$), scan rate 100 mV/sec

Compound	Peak potentials (V)		Cathodic peak currents (μA)	
	E_{pc1}	E_{pc2}	i_{pc1}	i_{pc2}
SMR-1	-1.16	-1.39	-45.7	-37.4
SMR-2	-1.30	-1.43	-62.6	-76.5

Effect of scan rate

In order to understand nature of the electrode processes taking place for **SMR-1** and **SMR-2**, peak currents of cathodic waves were plotted against square root of scan rate (Figure 4.2). A linear relation between peak current and square root of scan rate shows that Fick's law of diffusion is obeyed and the charge transport is diffusion based process.

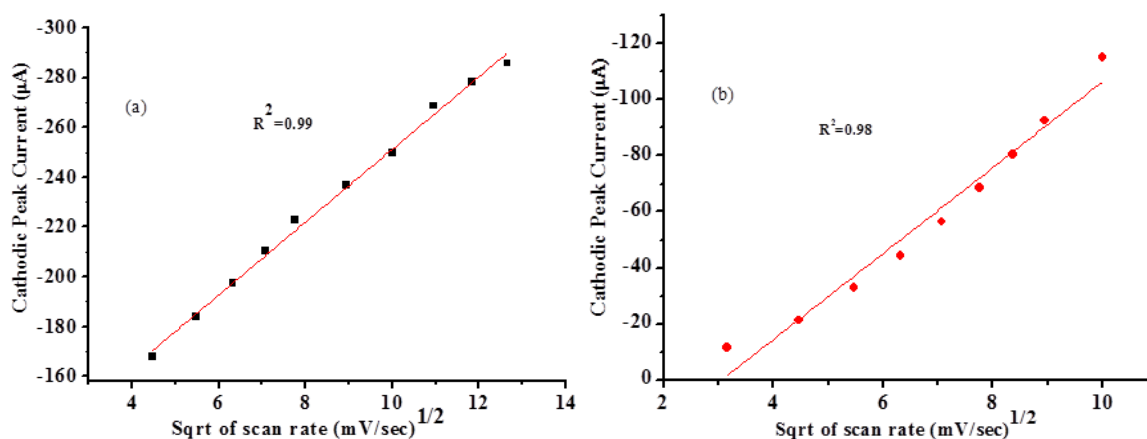


Figure 4.2 Plots of peak current and square root of scan rate for (a) **SMR-1** and (b) **SMR-2**

For **SMR-2** with increase in scan rate from 20 mV s^{-1} to 100 mV s^{-1} , two separate reduction peaks at -1.30 V and -1.43 V merge to form a single broad reduction peak. It indicated that at higher scan rates the two different reduction processes were observed as a single step, while for **SMR-1** both the reduction steps were observed as separate peaks even at 200 mV s^{-1} or higher scan rates. This observation is also supported by the DPV curves.

Effect of concentration of the electroactive compound

Electrochemical study of the compounds **SMR-1** and **SMR-2** was done to know the effect of different concentrations on their respective CV behaviours. With increase in concentration of each of **SMR-1** and **SMR-2**, a corresponding increase in the respective peak currents was observed along with a cathodic shift in the peak potential. This is due to the reason that increase in concentration of redox substances makes the velocity of mass diffusion rapid and

hence the electrode processes become more controlled by the electrode reactions. Calibrations for concentration of analyte species and cathodic peak currents were plotted and observed coefficients of regression varied within range 0.98-0.99, as shown in Figure 4.3.

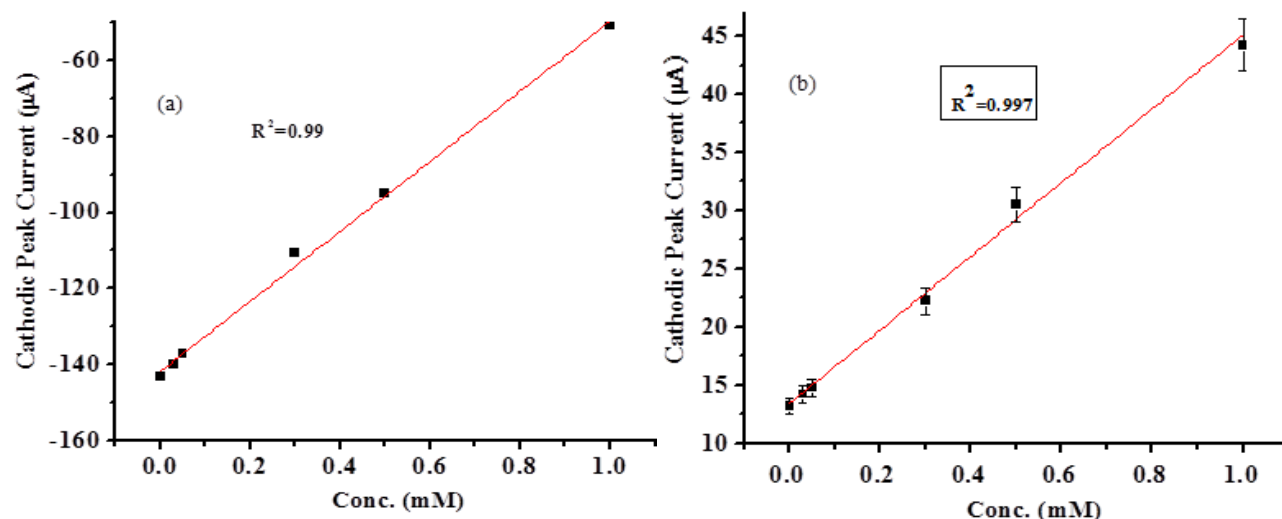


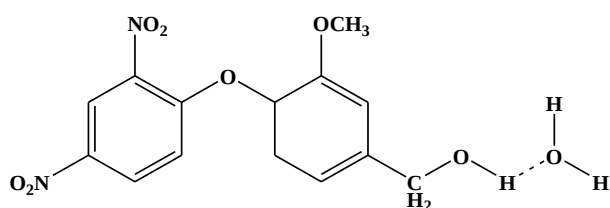
Figure 4.3 Calibration curves between concentrations of receptors and peak current for (a) **SMR-1** and (b) **SMR-2**

Effect of solvent

Receptors **SMR-1** and **SMR-2** were studied for their voltammetry in different solvent systems like dichloromethane (DCM), acetonitrile (ACN) and N, N-dimethylformamide (DMF). In addition, mixed solvent systems of ACN:H₂O (9:1, v/v) and DMF:H₂O (9:1, v/v) were also taken for the study anticipating some interactions of water with substituents –CHO in **SMR-1** and –CH₂OH in **SMR-2**. DPV peaks for both the compounds in all solvent systems are represented in Table 4.2. It is interesting to note that **SMR-1** shows only one reduction peak while **SMR-2** shows three reduction peaks in ACN solvent system. These can be explained as below:

In receptor **SMR-1** there are three prominent functional groups like –CHO, –OCH₃ and –NO₂ which can be responsible for the cathodic current peaks. Amongst these three groups, because of its electron withdrawing inductive effect nitro is the most probable candidate for reduction and hence shows a peak at lowest value of applied potential i.e. -1.36 V. The absence of cathodic peaks in cyclic voltammograms of **SMR-1** (-1.68 V) as compared to that of **SMR-2** (-1.85 V) is due to replacement of carbonyl bearing functional group –CHO in **SMR-1** with –CH₂OH in **SMR-2**. This change in functional group in fact results in decrease in electronic density on ethereal oxygen para to –CHO group, thereby resulting in, the disappearance of

cathodic peak at -1.68 V. The cathodic peak at -1.68 V in **SMR-2** is probably due to the methoxy group. The cathodic peak at -1.85 V in **SMR-2** disappears with change in solvent system from ACN to ACN:H₂O (9:1, v/v) system due to interaction of -OCH₃ group indicating its involvement with H₂O through hydrogen bonding. Moreover, the absence of corresponding peak (-1.85 V) in **SMR-2** in both ACN and its mixture with water can also be justified due to poor reduction potential of -CHO (in **SMR-1**) as compared to -CH₂OH (in **SMR-2**). The absence of E_{pc3} in ACN:H₂O solvent system is clear indication of hydrogen bonding of CH₂OH group with water as shown below:



Hydrogen bonding of -CH₂OH group of **SMR-2** with water molecule

In solvent media like DCM, the main observation as compared with ACN solvent system is with regard to shift in all peaks of **SMR-1** and **SMR-2** to lower potential values. These important shifts are due to low dipole moment of DCM (1.60 D) as compared to ACN (3.92 D) and DMF (3.86 D). Hence, polarity of the solvent does influence reduction potentials of target molecules. It is further noticed that the reduction potentials of **SMR-1** and **SMR-2** are almost similar due to similar dipole moments of ACN and DMF solvents.

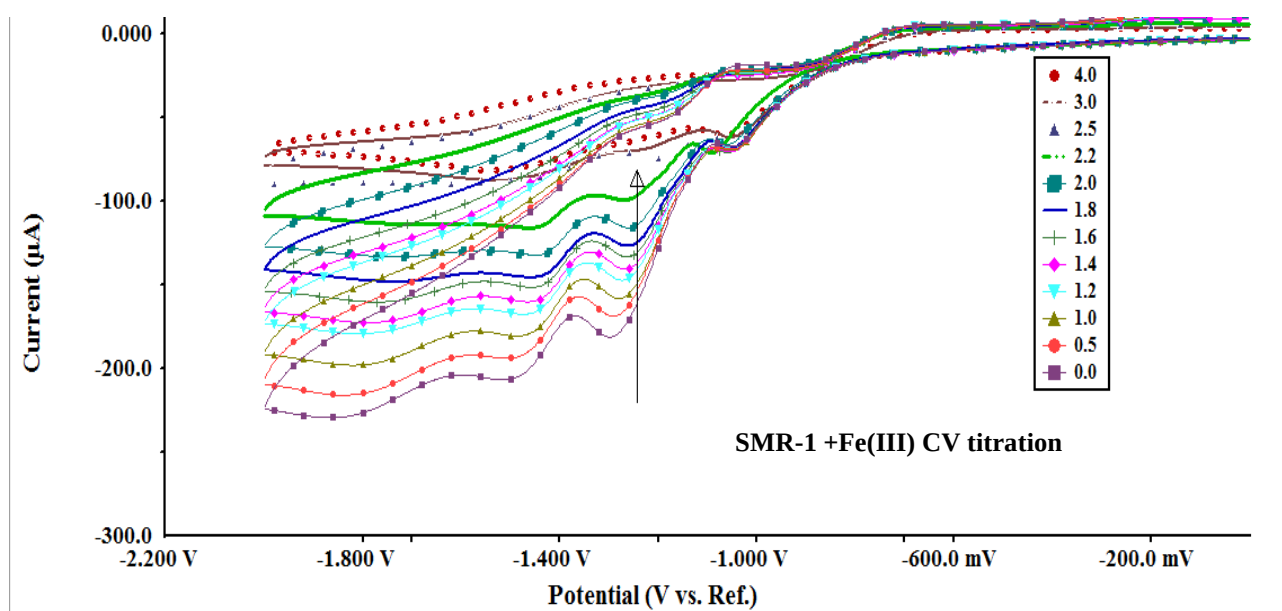
Table 4.2 Peak potentials for **SMR-1** (5×10^{-4} M) and **SMR-2** (5×10^{-4} M) in different solvent systems

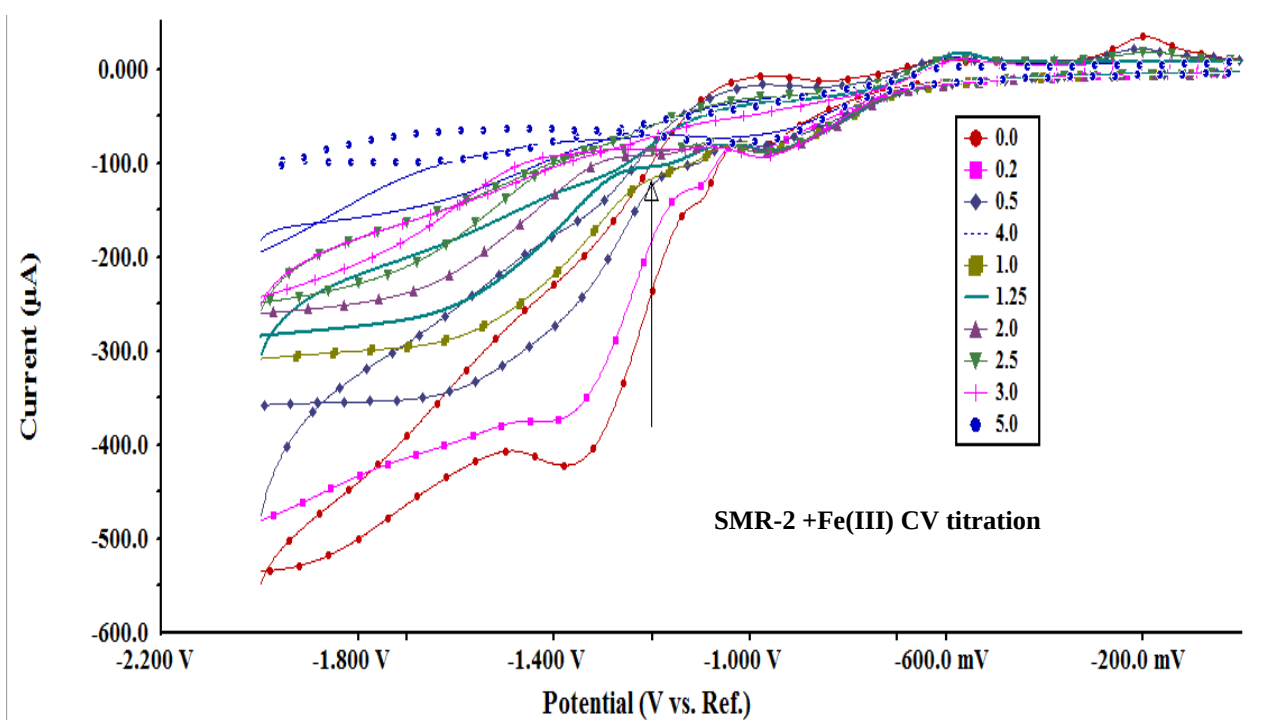
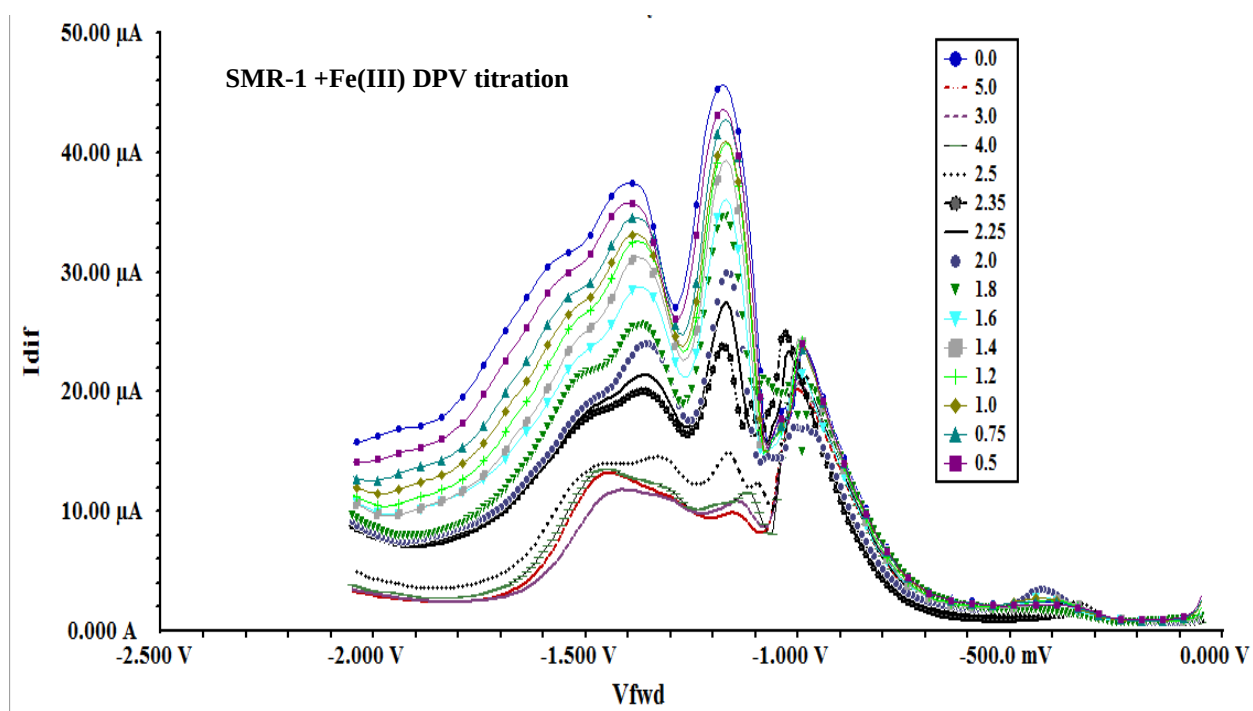
Solvent (Dipole moment)	SMR-1			SMR-2		
	E _{pc1} (V)	E _{pc2} (V)	E _{pc3} (V)	E _{pc1} (V)	E _{pc2} (V)	E _{pc3} (V)
ACN (3.92D)	-1.36	-----	----	-1.32	-1.68	-1.85
DMF (3.86D)	-1.25	-1.48	-1.87	-1.348	-1.70	-1.89
DCM (1.60D)	-1.23	-1.47	-1.750	-1.290	-1.62	-1.82
ACN:H ₂ O	-1.16	-1.39	----	-1.30	-1.43	----

Metal-Ligand complexation studies of SMR-1 and SMR-2

Voltammetric studies of the synthesized diphenylether based compounds **SMR-1** and **SMR-2** were performed to see their tendency to complex with transition metal ions, so that these can be projected as ionophores suitable for heavy metal detection by simple voltammetric methods. Voltammograms were drawn for both **SMR-1** and **SMR-2** with and without Fe(III) ions. Significant decrease in current magnitude of E_{p1} and E_{p2} from 45.7 μA to 9.7 μA and 37.4 μA to 11.0 μA respectively, for **SMR-1** prompted us to study complexation on a quantitative way as shown in Figure 4.4.

Incremental amounts of Fe(III) were added to 2.5 μmoles of **SMR-1** and the resulting current magnitudes are given in Table 4.3. Similar experiments were carried out on **SMR-2** compound. It can be seen from Table 4.3 that with addition of increasing concentration of Fe(III), a linear fall in cathodic peak current is observed till metal ion ratio with the ligand is reached 1:1 (Figure 4.5). Further addition of the metal ions did not bring any further change in current magnitude. Exactly similar trend in current magnitude was observed for **SMR-2**. Hence, **SMR-1** and **SMR-2** can be projected as ionophores for Fe(III) metal detection. Calibration curves for the detection of Fe(III) using **SMR-1** and **SMR-2** are shown in Figure 4.5. The proposed method is valid for the detection of Fe(III) species in the concentration range 0-2.5 μmoles . Presence of other metal ions (Na(I), K(I), Cr(III), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Ba(II), Hg(II), Cd(II) and Pb(II)) have also been studied and results indicate selectivity for Fe(III) ions only.





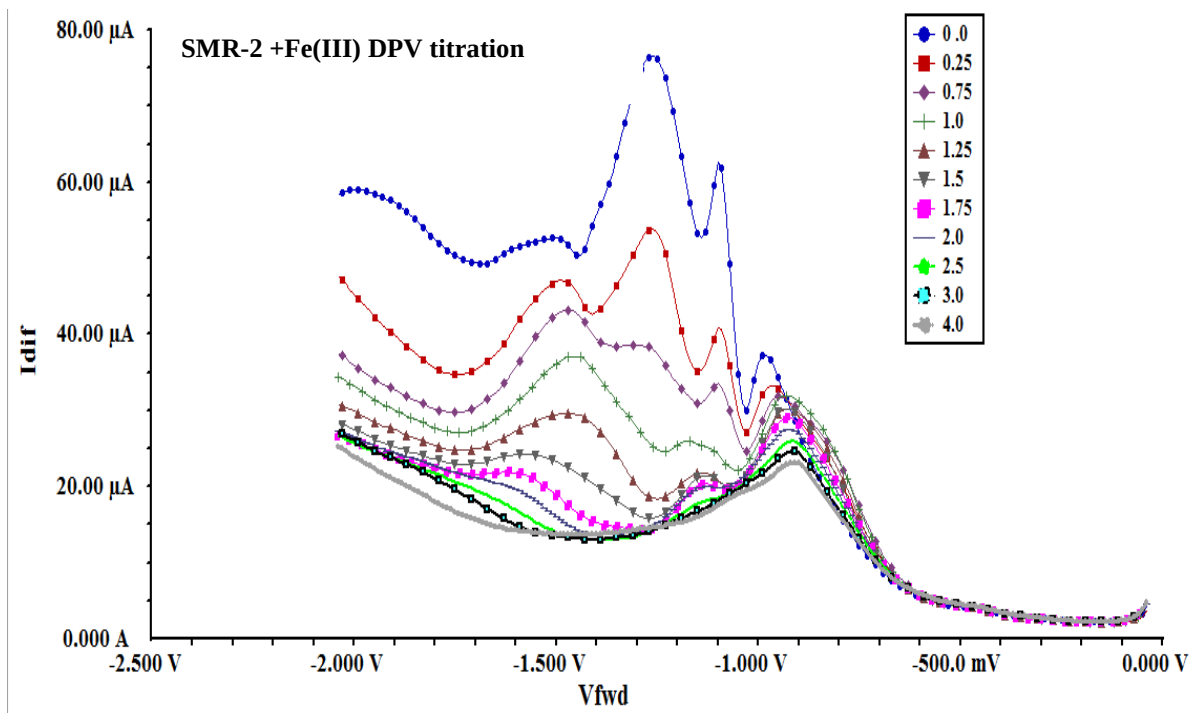


Figure 4.4 Cyclic and differential pulse voltamograms of Ligands (**SMR-1** and **SMR-2**) upon increment addition of metal (μM Fe(III)) at pH 7.0 ± 0.1 (10 mM HEPES in $CH_3CN:H_2O$ 9:1, v:v), 0.1M $TBAPF_6$

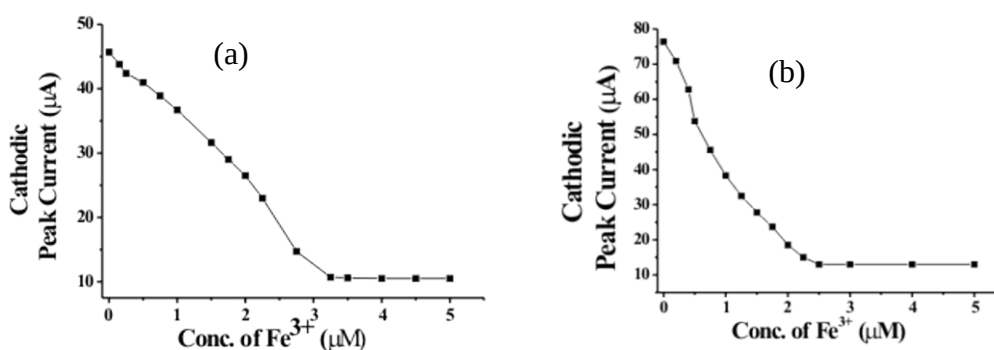


Figure 4.5 Calibration curves showing response of metal (Fe(III)) addition to ligands (a) **SMR-1** and (b) **SMR-2**

Interference studies

Selectivity of **SMR-1** and **SMR-2** was confirmed further by interference studies with various interfering metal ions added in excess to the target metal ion. Voltammetric experiments were carried out to study the effect of presence of interfering ions on the response of **SMR-1** and **SMR-2** for Fe(III) ions. Both the derivatives responded selectively to Fe(III) ions even in the presence of 10^{-5} M concentration of the interfering ions (Table 4.4) as indicated from quenching of the electroactive nature of ligands (**SMR-1** and **SMR-2**) i.e., large decrease in peak currents 29.41% and 25.40% for **SMR-1** and **SMR-2** at -1.39 V and -1.30 V,

respectively. On complexation with Fe(III) ions, the receptor molecules do not remain electroactive due to non-availability of lone pair of electrons on the heteroatoms, which are now coordinating with the central metal ion.

Table 4.3 Peak current values for **SMR-1** and **SMR-2** with and without Fe(III) ion

Ligand 'L' (SMR-1 /SMR-2)	SMR-1				SMR-2			
	i_{p2} (-1.39V) μA	i_{p1} (-1.16V) μA	Δi_{p2}^* (-1.39V) μA	Δi_{p1}^* (-1.16V) μA	i_{p2} (-1.43V) μA	i_{p1} (-1.30V) μA	Δi_{p2}^* (-1.43V) μA	Δi_{p1}^* (-1.30V) μA
Without metal (2.5 μ moles)	-37.43	-45.67	---	---	-76.51	-62.59	---	---
L + Fe ³⁺ (0.5 μ moles)	-32.64	-40.79	-4.79	-4.88	-53.79	-40.82	-22.72	-21.77
L + Fe ³⁺ (1.0 μ moles)	-24.08	-30.01	-13.35	-15.66	-38.29	-33.56	-38.22	-29.03
L + Fe ³⁺ (1.5 μ moles)	-20.05	-23.75	-17.38	-21.92	-27.77	-24.61	-48.74	-37.98
L + Fe ³⁺ (2.5 μ moles)	-14.56	-14.85	-22.87	-31.07	-13.03	-15.99	-63.48	-46.60
L + Fe ³⁺ (2.8 μ moles)	-11.01	-10.71	-26.42	-34.96	-13.02	-15.90	-63.49	-46.69
L + Fe ³⁺ (3.5 μ moles)	-11.01	-9.73	-26.42	-35.94	-13.02	-15.90	-63.49	-46.69

* Change in Δi_p ($M_L - M_{xi}$) $x_i = 0.5 \mu$ moles, 1.0 μ moles, 1.5 μ moles, 2.5 μ moles, 2.8 μ moles, 3.5 μ moles.

Table 4.4 Anodic Peak potential (V) values for **SMR-1** and **SMR-2** with different metal ions

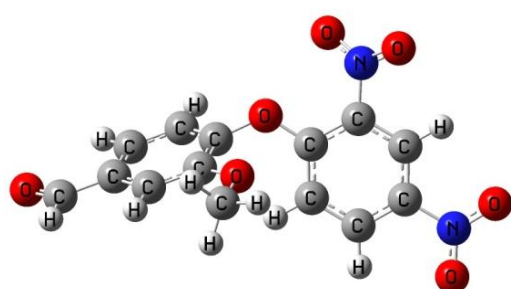
Metal studied	Peak Potential Values (V)			
	SMR-1		SMR-2	
	E_{pa1} (V)	E_{pa2} (V)	E_{pa1} (V)	E_{pa2} (V)
Ligand	-1.16	-1.39	-1.30	-1.43
Na(I)	-1.20	-1.36	-1.31	-1.45
K(I)	-1.14	-1.38	-1.23	-1.41
Mg(II)	-1.15	-1.39	-1.27	-1.41
Cr(III)	-1.01	-1.22	-1.21	-1.42
Fe(III)	--	--	--	--
Co(II)	-1.14	-1.36	-1.30	-1.42
Cu(II)	-1.16	-1.36	-1.28	-1.42
Zn(II)	-1.10	-1.35	-1.32	-1.44
Ba(II)	-1.16	-1.39	-1.29	-1.38

Computational studies

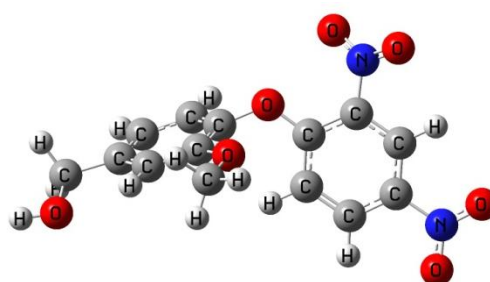
Energy minimization studies were carried out on the new compounds by using Density Functional Theory (DFT) in an attempt to better understand nature of the receptors and their interaction with metal ions. B3LYP function was employed for calculations with 6-31G basis set on Gaussian 03W programme except for Fe(III), for which LanL2DZ was used [2-4]. As per the DFT results on these molecules the receptors **SMR-1** and **SMR-2** have three dimensional structure forming a pseudo cavity between ethereal oxygen, nitrogen of nitro group and oxygen of methoxy group and B3LYP/6-31G basis set was employed for optimization of the receptors and their complexes with metal ions (Figure 4.6a and 4.6 b). However, **SMR-1- Fe(III)** and **SMR-2- Fe(III)** were optimized by using B3LYP/6-31G and LanL2DZ basis set for Fe(III) (Figure 4.6c and 4.6d).

Optimized structures revealed the possible mode of complexation in which ether group, due to its flexible nature gets rotated and forms best fit metal-ligand coordination sites between Fe(III) and the receptors. On coordination with Fe(III), there is an increase in the stability of the whole system which was confirmed from the value of energy optimization (Table 4.5). The gap between HOMO-LUMO is less for **SMR-1- Fe(III)** and **SMR-2- Fe(III)** as compared to receptor **SMR-1** and **SMR-2** alone, as depicted in Figure 4.7. Further, the HOMO-LUMO of the **SMR-1+ Fe(III)** and **SMR-2+ Fe(III)** showed that LUMO is main contributor in electronic transition [2-4].

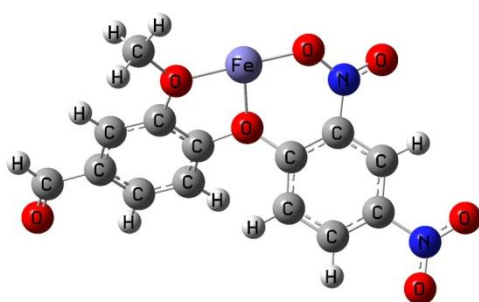
Binding energies obtained from the theoretical studies indicate that energy values of **SMR** molecules decrease with the addition of Fe(III). Energy for **SMR-1** decreases from -1175 a.u to -1298 a.u while for **SMR-2** the energy decreased from -1177 a.u to -1299 a.u., hence leading to the formation of stable complexes. Energy decrease in case of **SMR-2** is slightly more than that of **SMR-1** suggesting that **SMR-2** is a little more stable than **SMR-1** when it complexes with Fe(III).



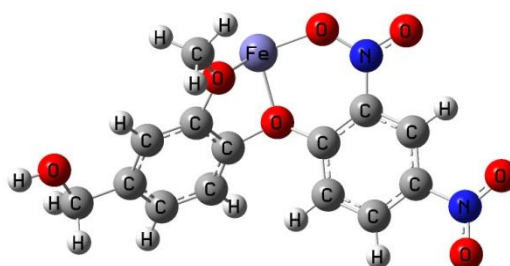
(a) SMR-1



(b) SMR-2



(c) SMR-1+ Fe(III)



(d) SMR-2+ Fe(III)

Figure 4.6 DFT optimized structures of receptors **SMR-1** and **SMR-2** and their complexes with Fe(III) calculated at the B3LYP/6-31G/LanL2DZ level respectively. The red, blue, gray, and purple spheres refer to O, N, C, and Fe, respectively

Table 4.5 Energy values (in a.u) of HOMO, LUMO and LUMO+1 for **SMR-1** and **SMR-2** and their complexes with Fe(III) using DFT calculations

Receptor/ Receptor- Fe(III)	Energy in a.u				
	E_{HOMO}	E_{LUMO}	$E_{\text{LUMO}+1}$	E_{gap1}	E_{gap2}
SMR-1	0.256	0.113	0.107	0.143	0.149
SMR-1+ Fe(III)	0.487	0.468	0.435	0.019	0.052
SMR-2	0.236	0.093	0.087	0.143	0.149
SMR-2+ Fe(III)	0.488	0.467	0.453	0.021	0.035

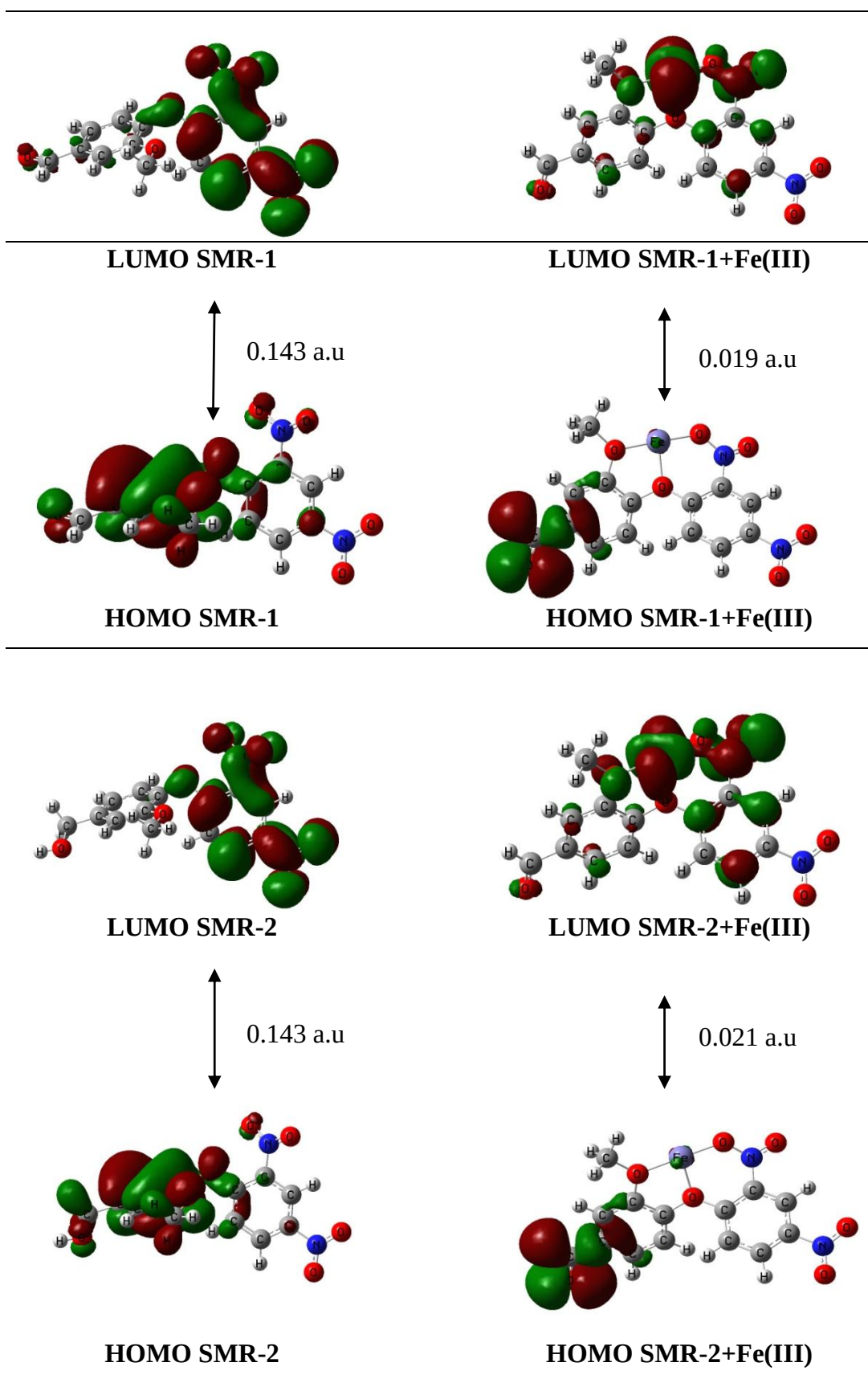


Figure 4.7 The HOMO-LUMO gap of: receptors **SMR-1** and **SMR-2** and their **Fe(III)** complexes calculated at the B3LYP/6-31G/LANL2DZ level respectively

Real life sample analysis

In order to test applicability of the proposed voltammetric method in analytical chemistry, the proposed methods were used for the determination of iron in pharmaceutical samples (Feriron) and water samples (tap water and mineral water) and some synthetic samples. Pharmaceutical samples were prepared by dissolving tablets of Feriron (a commercially available tablet containing Fe(III) as a mineral supplement) in 10 mL HCl and heated to near dryness (in closed fuming hood). The sample was then dissolved in 10 mL distilled water, filtered and transferred to a 25 mL volumetric flask and this volume was completed with distilled water to prepare synthetic samples of Fe(III) solutions. Each synthetic sample so prepared was spiked with 1 mL of 10^{-2} M standard solution of Fe(III) ions, keeping total volume of the sample equal to 100 mL. Voltammetric experiments were conducted on the sample solutions maintained at pH 3.5 using glassy carbon electrode, scan rate 20 mV/sec and TBAPF₆ as supporting electrolyte. The solution was purged with nitrogen gas for 5-6 minutes to remove dissolved oxygen. Complexometric method was also used for the determination of iron contents in these samples. Results of the **SMR-1** and **SMR-2** based voltammetric sensors are presented in Table 4.6. Results are also compared with those obtained by complexometric titration method using EDTA. The voltammetric sensor based methods are found to be in satisfactory agreement with those obtained from the complexometric method. These observations and results confirmed that the proposed chemosensors can be used for practical analysis of Fe(III) ions in aqueous media.

Table 4.6 Determination of Fe(III) in real samples using **SMR-1** and **SMR-2** based voltammetric method and complexometric method

Sample Name	Total Iron Found ($\mu\text{g}\cdot\text{mL}^{-1}$ or $\text{g}\cdot\text{kg}^{-1}$)			
	Chemosensor (SMR-1)	Complexometric method	Chemosensor (SMR-2)	Complexometric method
Feriron	10.7 ± 0.02	11.1 ± 0.03	12.5 ± 0.02	12.2 ± 0.01
Tap Water	6.1 ± 0.08	6.4 ± 0.06	6.6 ± 0.07	7.1 ± 0.02
Mineral Water	5.3 ± 0.01	5.1 ± 0.01	4.9 ± 0.06	4.9 ± 0.02
RS-1	11.5 ± 0.03	11.4 ± 0.03	12.8 ± 0.05	12.7 ± 0.01
RS-2	15.4 ± 0.02	15.5 ± 0.04	16.9 ± 0.05	16.9 ± 0.04

± Shows the standard deviation (n=3).

Conclusions

Receptors form 1:1 complexes with Fe(III). **SMR-1** showed fluorescence quenching on complexation with Fe(III) ion at 350 nm due to PET (photon induced transfer) mechanism between Fe(III) and the large π electron conjugate system of ligand, while **SMR-2** displayed emission band at 314 nm which underwent fluorescence quenching selectively on gradual addition of Fe(III) at 314nm and simultaneously a new band at 424 nm emerged with isobestic point at 355 nm indicating a transition state; which increases with increase in Fe(III) conc. Electrochemically, **SMR-1** facilitates reduction of nitro group due to presence of electron withdrawing (aldehydic group) hence, peak potentials of the two curves obtained for **SMR-1** appear at -1.16 V (E_{pc1}) and -1.39 V (E_{pc2}) respectively, while in **SMR-2** the methanolic group due to its electron donating character makes the reduction of nitro group a little difficult due to which peak potentials occur at higher potential as compared to **SMR-1** i.e. at -1.30 V (E_{pc1}) and -1.43 V (E_{pc2}) respectively. **SMR-1** and **SMR-2** can be projected as Fe(III) chemosensors with no interference from any other metal ion. Both receptors showed high degree of selectivity for Fe(III) over other cations.

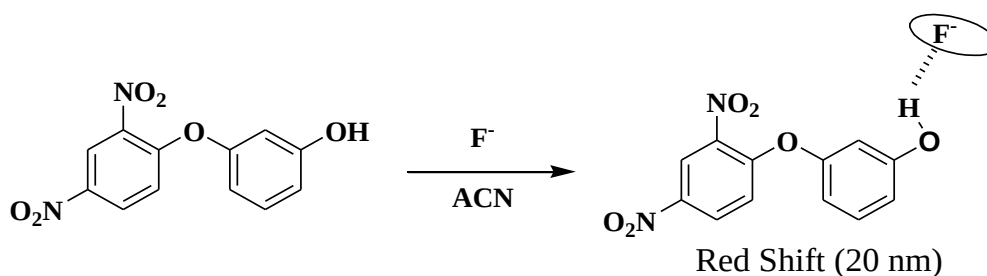
4.2.2 Ion-recognition studies of SMR-3 & SMR-4

Two compounds **SMR-3** and **SMR-4** were synthesised (as explained in Scheme: 4.2) and used as receptors for anions. **SMR-3** has two nitro groups at ortho and para positions to the ether group of the receptor while **SMR-4** has only one nitro group at ortho position. Nitro groups were placed at different locations on the benzene ring of **SMR-3** and **SMR-4** by design so as to tune acidic character of the hydroxyl group, remotely. To understand the role of nitro groups in tuning the acidic character of -OH group of the ligands, voltammetric studies were conducted on both the compounds **SMR-3** and **SMR-4**. The results show that two nitro groups enhance acidity of the phenolic group more than a single nitro group, thereby enhancing its deprotonation behaviour. Complexation behaviour of the newly synthesized 3-(2,4-dinitrophenoxy)phenol (**SMR-3**) and 3-(2-nitrophenoxy)phenol (**SMR-4**) was investigated with different anions like CN^- , F^- , Cl^- , Br^- , AcO^- , I^- , HSO_4^- , OH^- , $H_2PO_4^-$, ClO_4^- to find the most suitable species that form complex/interaction with either of the two **SMR-3** and **SMR-4**. The voltammetric studies exhibited significant change in anodic peak potentials only with fluoride ions.

Colorimetric experiments

In an attempt to achieve fluoride sensing which can be observed with naked eyes, receptor molecules **SMR-3** and **SMR-4** were tested. **SMR-3** showed amazing selective response towards the target anion in the form of distinct change in colour from colourless to dark yellow immediately on bringing in contact the two species. The intensity of colour was found to increase with concentration of the fluoride ions. For quantitative application of the sensing phenomenon, experiments were designed to study the reproducibility and workable concentration range and are discussed below. To check the change in color of the receptor solution, 10 volumetric flasks having same concentration of **SMR-3** solution were prepared. Each of the volumetric flasks was having 10^{-4} M receptor solution (**SMR-3**) in CH_3CN . First flask was having only receptor solution, while in rest 9 volumetric flasks 1 equivalent of anion was added in separate volumetric flasks and color change was observed (Figure 4.8a). Addition of 1 equivalent of fluoride ion solution induced an instant colour change from colourless to dark-yellow in the second volumetric flask which gets dark on increasing the concentration of fluoride ions in the receptor solution as shown in Figure 4.8a. Similarly, 1 equivalent of each of the several anions were added in separate sets of 10 volumetric flasks each containing 10^{-4} M receptor solution in acetonitrile. There was no colour change in other volumetric flasks containing different anions (CN^- , Cl^- , Br^- , AcO^- , I^- , HSO_4^- , OH^- , H_2PO_4^- , ClO_4^-). The inactivity of all selected anions except F^- to develop any colour with receptor **SMR-3** can be due to their weak basicity and the strong intramolecular hydrogen bonds of **SMR-3** which hindered the binding of these anions with proton of the phenolic $-\text{OH}$ group. No change in colour was observed on addition of F^- and any of the other anionic solutions in flasks containing **SMR-4** (having one electron withdrawing group, $-\text{NO}_2$).

This sharp change in colour on addition of F^- ions to **SMR-3** may be attributed to high affinity of the fluoride ions to abstract proton from hydroxyl group of the receptor **SMR-3**, which has two electron withdrawing groups ($-\text{NO}_2$) on the same aromatic ring, hence responsible for the hard-acid character of the receptor as shown in Scheme 4.2. It was further observed that on standing, the colour intensity increased with time and changed from yellow to violet after about 2 hours (Figure 4.8b). Fluoride can be detected colorimetrically up to a concentration of 10^{-5} M as shown in Figure 4.8c. Each experiment was repeated at least 3 times to confirm reproducibility of the observations.



Scheme 4.3 Probable interaction between receptor (**SMR-3**) and anion

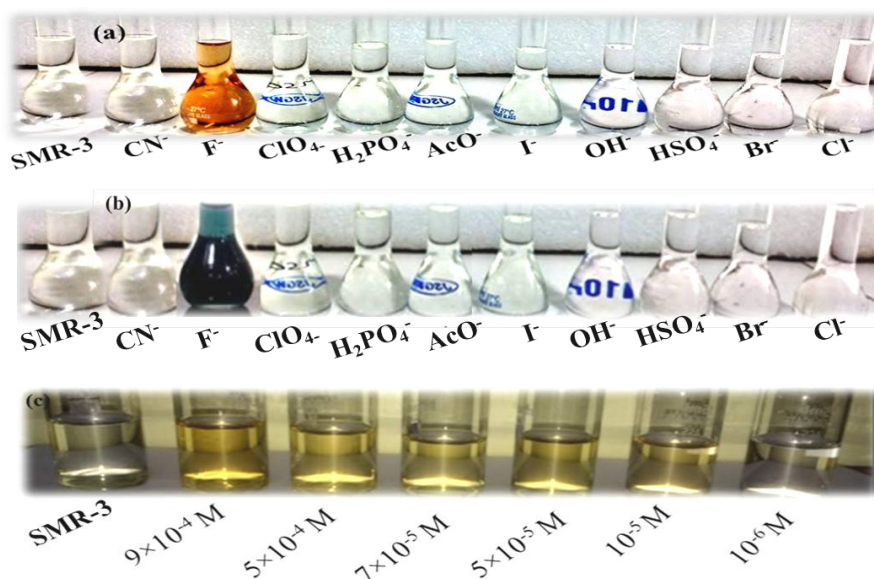


Figure 4.8 Colorimetric response upon addition of one equivalent tetrabutylammonium salts of each anion into receptor solution **SMR-3** (10^{-4} M) (a) Just after addition of anions. (b) After 2 hours (c) Colour variation with decreasing concentration of fluoride ion (from left to right in mol l^{-1} : free (**Ligand**), 9×10^{-4} , 5×10^{-4} , 7×10^{-5} , 5×10^{-5} , 10^{-5} and 10^{-6})

Spectrophotometric measurements

Interaction of the receptor (**SMR-3**) (20 μM) with different anions was investigated through UV-visible spectra and all the studies were carried out in CH_3CN solution (Figure 4.8a). In the absence of anions, the maximum absorption wavelength of receptor (**SMR-3**) was observed at 290 nm. As shown in Figure 4.8b, when successive additions of TBAF (Tetra -n-butylammonium fluoride) were added upto 10 equivalents to the solution of receptor **SMR-3** (20 μM), the peak (λ_{max}) at 290 nm was red shifted respectively by 20 nm to 310 nm and a new peak appeared at 250 nm due to deprotonation of **SMR-3** by fluoride ion. Under same conditions, no significant changes were observed when 10 equivalents of other anions were added, as shown in Figure 4.9a. The results suggest that receptor (**SMR-3**) has a high

selectivity for fluoride ion over other common anions with binding constant $2.8 \times 10^4 \text{ M}^{-1}$. Selectivity for the fluoride ion can be rationalized on the basis of Lewis acid-base interactions between hydroxyl group of ligands and the guest anions. The deprotonation of $-\text{OH}$ group occurred only on the addition of fluoride ions and no other ion could abstract proton from the $-\text{OH}$ group of **SMR-3/4**. This is due to highly electronegative character of fluoride ions and higher basicity of fluoride ion over other anions like CN^- , Cl^- , Br^- , AcO^- , I^- , HSO_4^- , OH^- , H_2PO_4^- , ClO_4^- , hence leading to the selectivity. This Lewis basic behaviour of fluoride is applicable only in non-aqueous medium like acetonitrile.

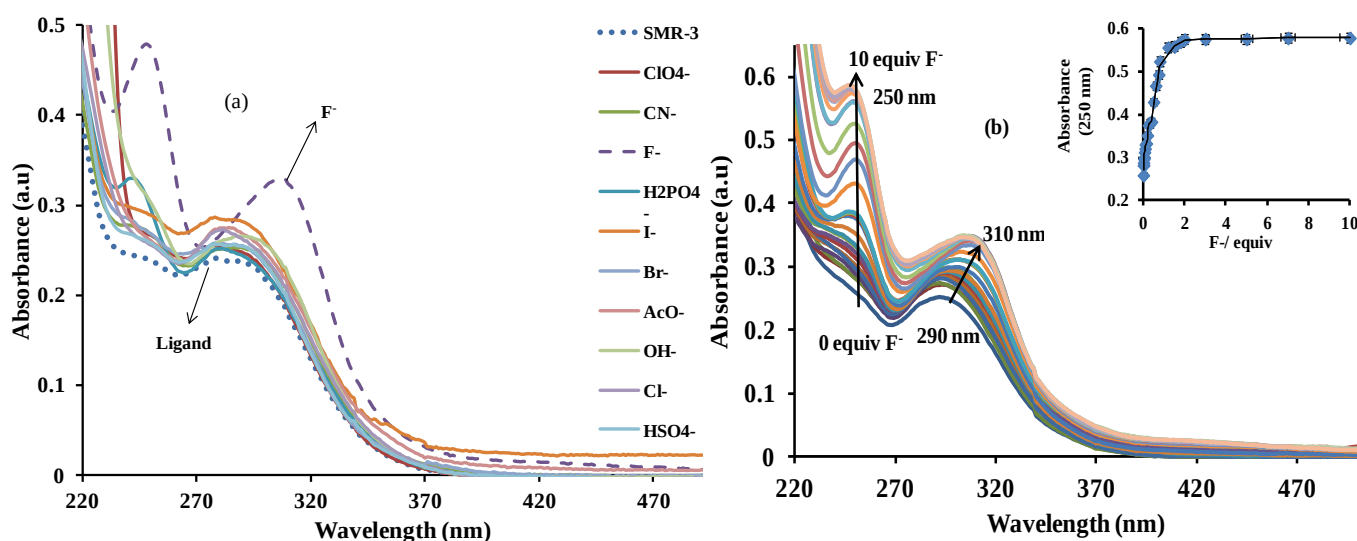


Figure 4.9 UV-visible absorption spectra of receptor (**SMR-3**) ($20 \mu\text{M}$), (a) upon addition of various anions (10 equivalents) and (b) incremental addition of F^- (0–10 equivalents) in acetonitrile; Inset shows UV-visible absorption intensity at 250 nm vs. concentration of F^-

Inset of Figure 4.9b shows that there was a good linearity between absorbance and concentrations of F^- in the range from 0.1 to $20 \mu\text{M}$ at 250 nm, indicating that receptor (**SMR-3**) can detect quantitatively the concentrations of F^- . The change in the absorption spectra was significant up to the addition of 1 equivalent of F^- (inset, Figure 4.9b) only, indicating that the binding of F^- with receptor takes place in a 1:1 ratio. Similarly, **SMR-4** having one nitro group on phenyl ring has a maximum absorption band at 320 nm ($200 \mu\text{M}$) which gets red shifted by 15 nm on the deprotonation of phenolic $-\text{OH}$ group. To determine the practical applicability of receptors (**SMR-3** and **SMR-4**), competitive experiments were carried out in the presence of 1 equivalent of fluoride ion mixed with 2 equivalents of different anions. No significant variations in the absorption spectra were found when comparing the results with or without other anions.

Job's plot analysis

Job's method of continuous variation was carried out to know the binding ratio of ligands and anion. The Job's function A_{Job} is calculated according to the equation $A_{\text{Job}} = (1 - X) A_0 - A$ [5]. Separate plots of absorbance versus mole fraction were drawn for each ligands. Each plot displays two parts in which, first the absorbance increases to a maximum and then decreases down. Figure 4.10 shows the intersection point of these two parts at mole fraction 0.5, which shows 1:1 stoichiometry for each ligand. The probable mechanism for 1:1 stoichiometry is shown in Scheme 4.3.

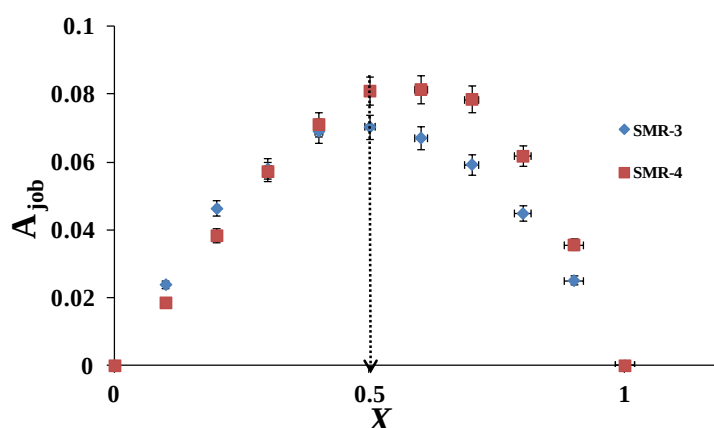
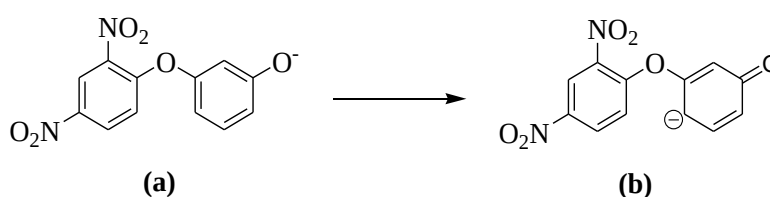


Figure 4.10 Job's plot for determining the binding stoichiometry in acetonitrile solution, showing a 1:1 stoichiometry between **SMR-3**/**SMR-4** and F^- . The variation of Job's function (F_{Job}) at 290 nm (**SMR-3**) and at 320 nm (**SMR-4**) was measured as a function of the mole ratio X ($[\text{F}^-]/([\text{F}^-] + [\text{chemosensor}])$), respectively

Time dependent studies

UV- visible spectroscopic studies were carried out separately on species **SMR-3** and **SMR-3'** (after deprotonation of $-\text{OH}$ group of **SMR-3** by fluoride ions (10^{-3} M)). A large red shift was observed from 290 nm to 315 nm and then to 625 nm (visible region) after 2 hours of contact with F^- ions. The absorbance at 625 nm is due to **SMR-3'** species stabilized on keeping in contact with solvent for long time. We propose that with time structure **a** changes to **b** as shown below and lead to the appearance of new band at 625 nm due to charge transfer taking place within the ring system after deprotonation.



Absorbance measurements were made on solutions of **SMR-3** and **SMR-3'** (**SMR-3** + Fluoride) after keeping their solutions for extended hours till 4 days to see if any new species are developed with time. It was observed that no new peak or shifts in peaks were observed indicating that there was no further change in chemical species (Figure 4.11a). However, there was decrease in intensities of peaks at 290 nm, 315 nm and increase in intensity at 625 nm in the spectrum of **SMR-3'** (Figure 4.11b). No change in intensity of peaks for **SMR-3** without fluoride interaction was observed even after 4 days.

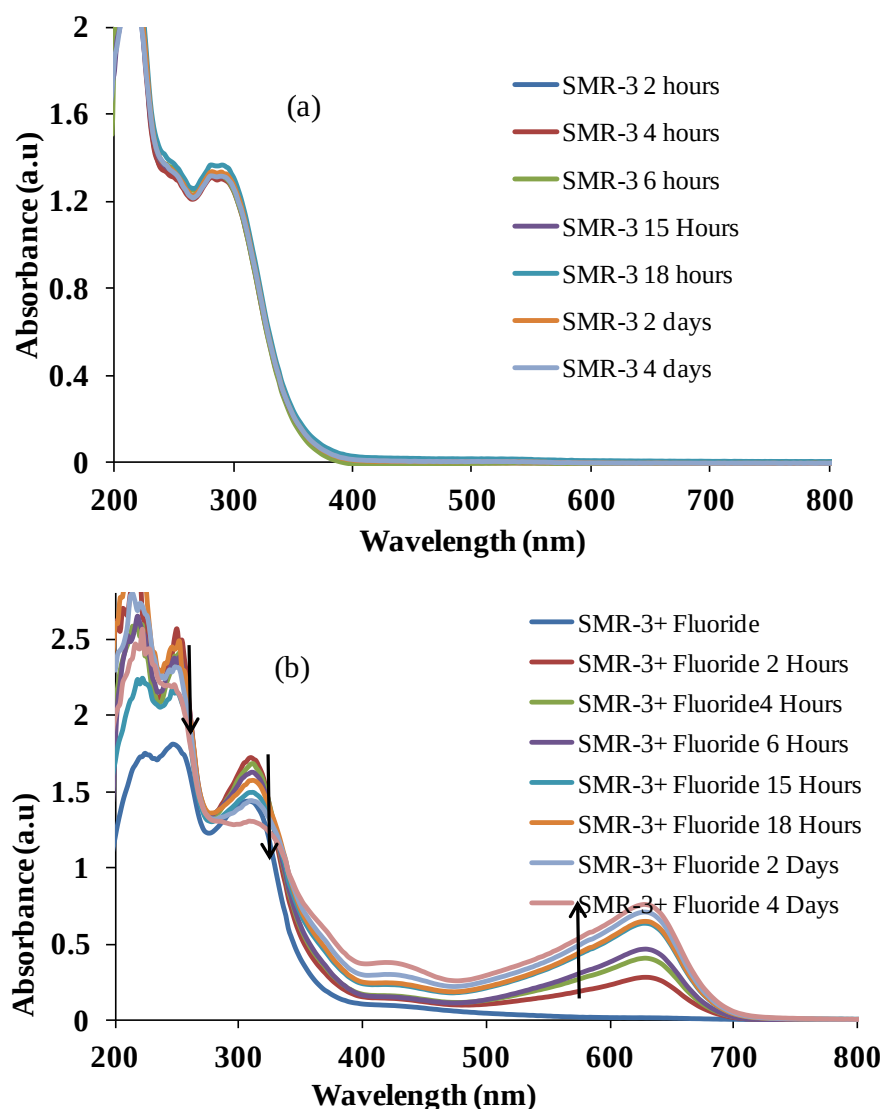


Figure 4.11 UV-visible spectra of **SMR-3** and **SMR-3+F⁻** (10^{-3} M) in acetonitrile with different time durations

UV- visible spectrum in mixed solvent system (CH₃CN:H₂O)

It is hypothesized that F⁻ ions interact with –OH group of the **SMR-3** and is responsible for major red shift of 20 nm from 290 nm to 310 nm in the UV-visible spectrum. It was

supported by another study on UV-visible spectrum of **SMR-3** taken in presence of a mixed solvent of acetonitrile and water. Experiments were carried out in successive increase in water ratio in mixed solvent media to check the interaction of fluoride ions with **SMR-3** in presence of water. Water ratio was increased from 1% to 10% successively in the solvent medium. As expected, hydroxyl group of **SMR-3** preferably formed H-bonding with water molecules (present in mixed solvent) in preference to fluoride ions. Therefore, on addition of 1% water to the acetonitrile medium, **SMR-3-F⁻** complex broke down and **SMR-3-H₂O** complex was formed, as indicated from the decrease in intensity of a band at 310 nm. With increase in proportion of H₂O in the medium, the band intensity at 310 nm decreased (Figure 4.12) with each successive increase in H₂O:CH₃CN ratio till 10% of water, when total intensity was quenched.

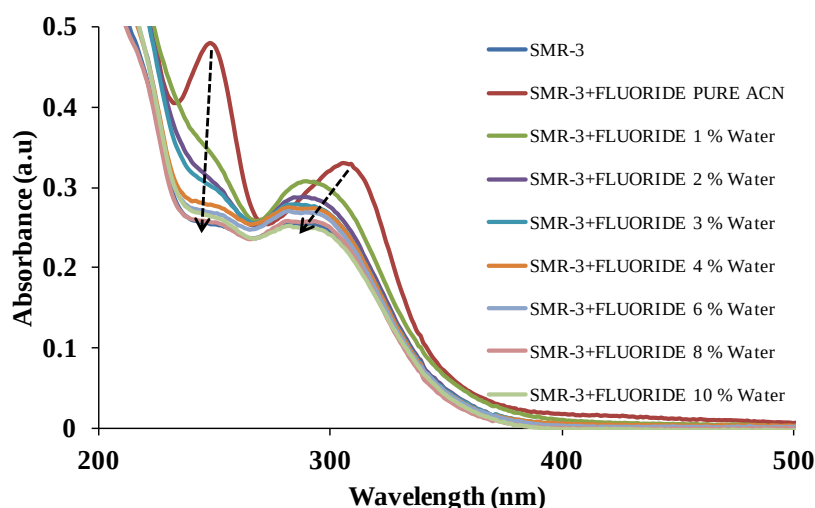


Figure 4.12 UV- visible spectrum of **SMR-3+F⁻** (20 μ M) in different acetonitrile:H₂O ratios

Electrochemical measurements

To investigate electrochemical properties of the receptors, voltammetric studies were carried out by using three-electrode cell in acetonitrile medium. Receptors **SMR-3** and **SMR-4** showed anodic peaks at 1.16V and 1.34V, respectively, due to oxidation of phenolic hydroxyl group on both the ligands (Figure 4.13a). In case of cathodic cycle of DPV, two peaks were observed for **SMR-3** (-1.63V and -1.72V) and only one peak (-1.64V) for **SMR-4** (Figure 4.13b). Values of peak currents for **SMR-3** and **SMR-4** are shown in Table 4.7. Cathodic peaks observed for both the ligands (**SMR-3** and **SMR-4**) are due to the reduction of nitro group [6]. The reduction of nitro group takes place in two steps. In the first step -NO₂ gets reduced to -NHOH by a slow step followed by further reduction to nitroso group (-NO)

through a fast step. This two step mechanism for the reduction of nitro to nitroso group could be captured only at slow scan rate i.e., 20 mV/sec. The two peaks get merged at scan rate ≥ 30 mV/sec (Figure 4.13c) and a single peak is observed at -1.74V. The two step mechanism was not observed for **SMR-4** where only one cathodic peak was observed (Figure 4.13c) at -1.64V. This might be due to faster kinetics of reduction in case of **SMR-4** ligand with one nitro substituent (Figure 4.13d).

Table 4.7 Peak potentials (V) and corresponding differential peak current (μA) values for receptors **SMR-3** and **SMR-4** (scan rate 20mV/sec)

Receptor	Peak potentials (V)			Differential Peak current (μA)		
	$E_{\text{pa}1}$	$E_{\text{pc}1}$	$E_{\text{pc}2}$	$\Delta i_{\text{pa}1}$	$\Delta i_{\text{pc}1}$	$\Delta i_{\text{pc}2}$
SMR-3	1.16	-1.63	-1.72	5.75	6.57	6.55
SMR-4	1.34	-1.64	--	5.05	4.72	--

E_{pa} : anodic peak potential, E_{pc} : cathodic peak potential
 i_{pa} : anodic peak current, i_{pc} : cathodic peak current

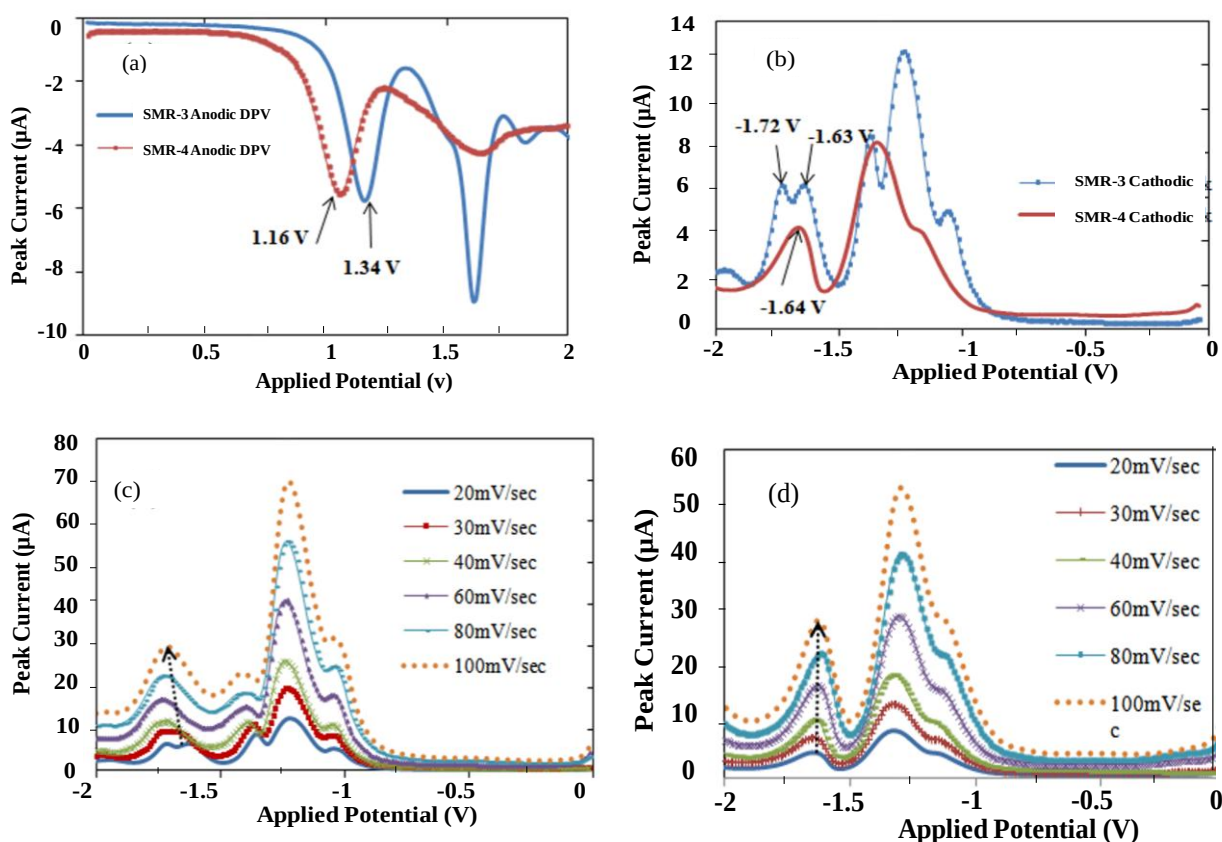


Figure 4.13 (a) Anodic Differential Pulse Voltammograms of **SMR-3** and **SMR-4** (10^{-3} M) (b) Cathodic Differential Pulse Voltammograms of **SMR-3** and **SMR-4** (10^{-3} M) in using 0.1 M TBAPF₆ (tetrabutylammonium hexafluoro-phosphate) as supporting electrolyte, scan rate 20 mV s⁻¹ and GC as working electrode,

Modulation amplitude: 50 mV/sec (c) Cathodic Differential Pulse Voltammograms of SMR-3 (10^{-3} M) showing peaks at -1.63 V and -1.72 V merged with increasing scan rate (d) Cathodic Differential Pulse Voltammograms of SMR-4 (10^{-3} M) showing only one peak at all scan rates

Scan rate study

Voltammograms were drawn at different scan rates for both the receptors to know whether the mass transport occurring on the electrode surface was diffusion based or kinetically controlled. Scan rate was varied from 20mVs^{-1} to 100mVs^{-1} . Peak currents of anodic and cathodic waves were plotted against square root of scan rates for both the receptors as shown in Figure 4.14. A linear relation between peak current and square root of the scan rate indicated a diffusion based process. The peak potential shifted linearly with scan rate for both the receptors.

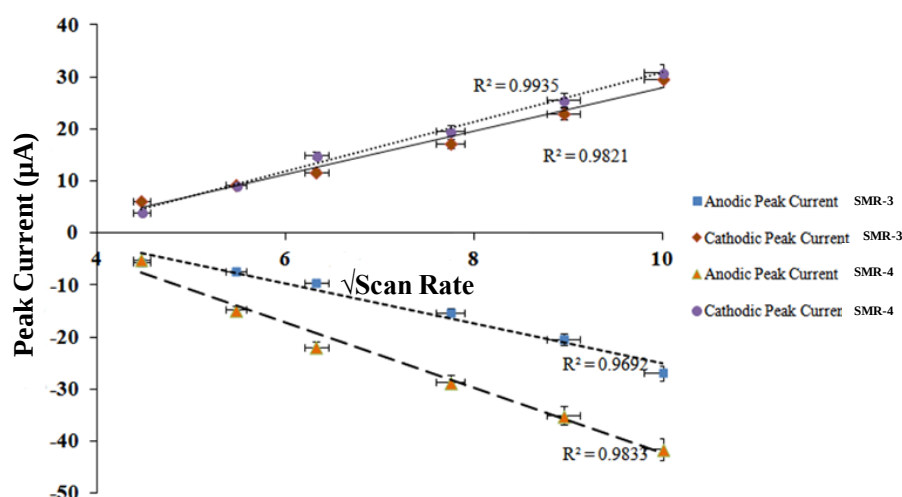


Figure 4.14 Plot showing the variation of peak current with square root of scan rate

Concentration study

Calibration plots of peak current versus concentration of receptor solutions were drawn to know the working range of concentration of both the receptors **SMR-3** and **SMR-4**, as shown in Figure 4.15. Both the receptors showed linear variations in the concentration range 10^{-6} M to 10^{-3} M. Hence, these receptors can be used as electroanalytical probes till 10^{-6} M concentration.

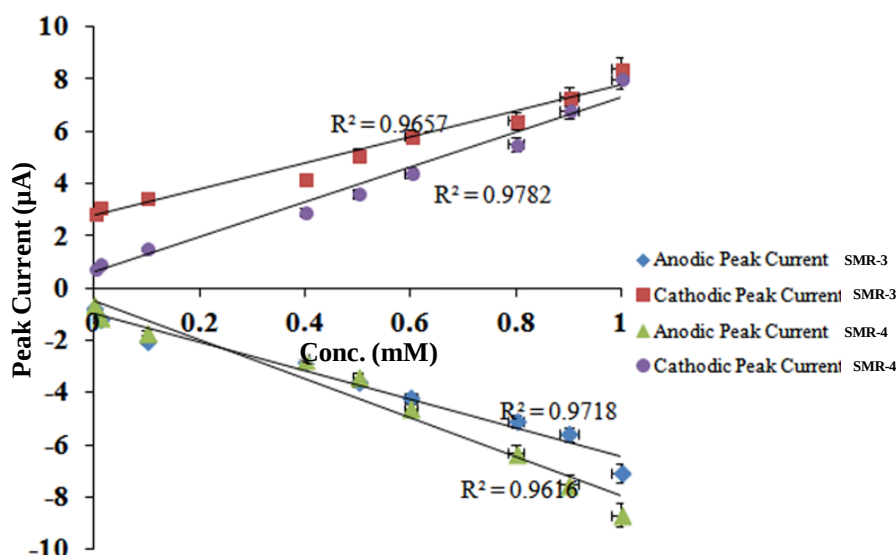


Figure 4.15 Calibration curves between concentrations of receptors and peak current for **SMR-3** and **SMR-4**

Solvent study

To know the voltammetric behaviour of the ligands in different solvents, studies were carried out in acetonitrile, dimethyl sulfoxide, dichloromethane and methanol. When methanol (polar protic solvent) was used as solvent, the lone pair electrons on oxygen of ether group do not give anodic peak due to hydrogen bonding between the solvent (methanol) and the ligands **SMR-3** and **SMR-4**. Interestingly, on changing the solvent to methanol in **SMR-3** anodic peak appears at its usual position (1.14V), whereas it is still missing in case of **SMR-4**, which may be due to insufficient electron withdrawing intensity of the single nitro group to cause oxidation.

On changing the solvent medium from acetonitrile (3.92 D) to dimethyl sulfoxide (3.96 D) the anodic peak for **SMR-3** was observed again at 1.16 V. This anodic peak appeared in the form of a flat plateau and sustained the current over a large applied potential range up to 2.0 V. The flat plateau suggests that some continuous source of electrons was available in the DMSO medium. This voltammetric behaviour of **SMR-3** in dimethyl sulfoxide can be explained by considering much better lewis basicity of lone pairs on oxygen of dimethyl sulfoxide as compared to that of nitrogen (with only one lone pair) in acetonitrile. Because of large excess of dimethyl sulfoxide the anodic current after solvation of **SMR-3** with dimethyl sulfoxide is possible. Voltammograms showed a significant shift in anodic peak for **SMR-4** on changing the solvent medium from acetonitrile to dimethyl sulfoxide. The anodic peak at 1.34 V in acetonitrile appeared at 0.72 V in dimethyl sulfoxide indicating much facilitated oxidation due to absence of nitro group (electron withdrawing) at para position of ring B

which is more prominent in presence of dimethyl sulfoxide. However, the cathodic peak does not move on changing the solvent from acetonitrile to dimethyl sulfoxide.

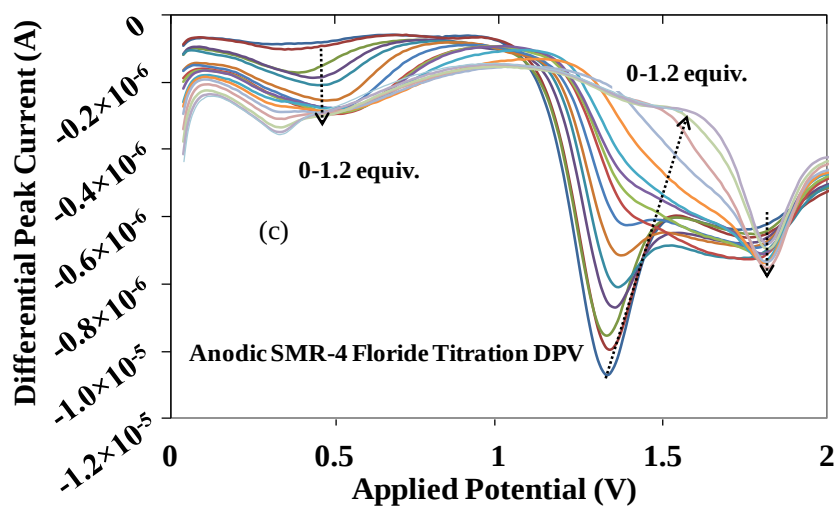
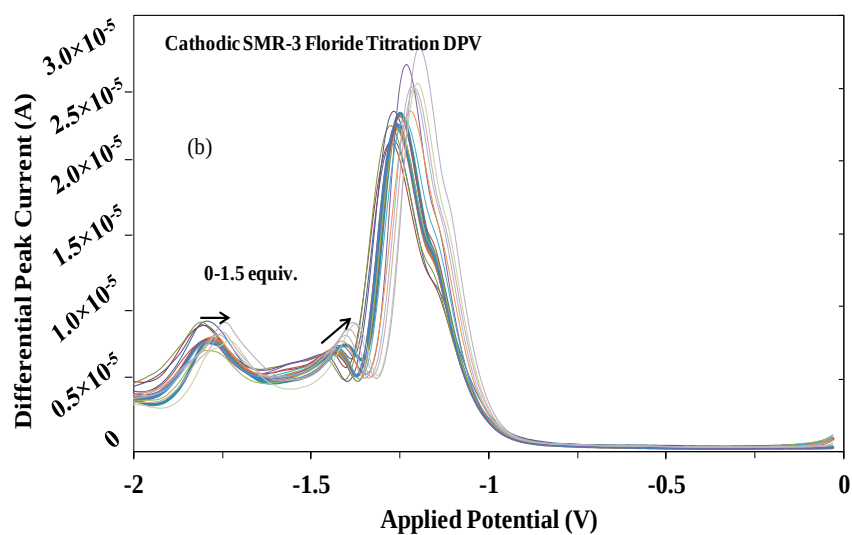
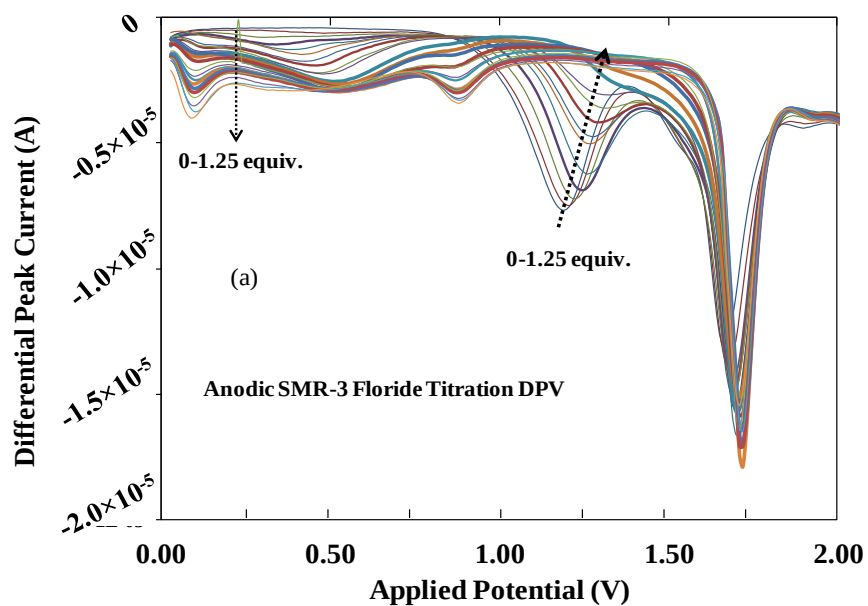
Further, on changing the solvent medium from acetonitrile (3.92 D) to dichloromethane (1.60 D) which is far less polar than acetonitrile and dimethyl sulfoxide, the anodic peak appears almost at same position for **SMR-3**. While for **SMR-4**, it was observed at a potential little lower than in acetonitrile. The greater effect of change of solvent in case of **SMR-4** shows that the oxidation is more sensitive to change in polarity than in **SMR-3**; as observed from peak potential values mentioned in Table 4.8. Similar sensitivity was observed for cathodic peak as well.

Table 4.8 Peak potentials (V) for **SMR-3** and **SMR-4** (10^{-3} M) in different solvent systems

Solvent	Dipole moment (D)	SMR-3			SMR-4	
		E_{pa} (V)	E_{pc1} (V)	E_{pc2} (V)	E_{pa} (V)	E_{pc} (V)
Acetonitrile	3.92	1.16	-1.63	-1.72	1.34	-1.64
Dimethyl Sulfoxide	3.96	>1.16	-1.38	-1.56	0.72	-1.70
Dichloromethane	1.60	1.19	-1.69	-1.79	1.27	-1.34
Methanol	1.69	1.14	-1.52	---	---	-1.13

Anion selectivity

Electroanalytical study of both compounds **SMR-3** and **SMR-4** was done to check their selectivity for anions. Both **SMR-3** and **SMR-4** showed relative selectivity for fluoride ions. Anodic peak gets completely quenched in the presence of 1 equivalent of fluoride ions while cathodic peaks get shifted to lower cathodic peak potentials as shown in Figure 4.16. Fluoride addition caused the abstraction of proton from phenolic –OH leaving behind O^- species because of which oxidation peaks at 1.16 V for **SMR-3** and 1.34 V for **SMR-4** get diminished completely with incremental addition of fluoride ions upto 1 equivalent establishing 1:1 complexation. This complexation takes place by following EC mechanism i.e., electron transfer through a sequence of electrochemical (E) processes (e.g. redox process of **SMR-3**) followed by a chemical (C) process i.e., electrochemically inactive but chemically active complexation of **SMR-3** with the anion. The same mechanism was observed in case of **SMR-4**. Interestingly, no such change was observed in the presence of other anions confirming rare selective behaviour of **SMR-3** and **SMR-4** for fluoride ions.



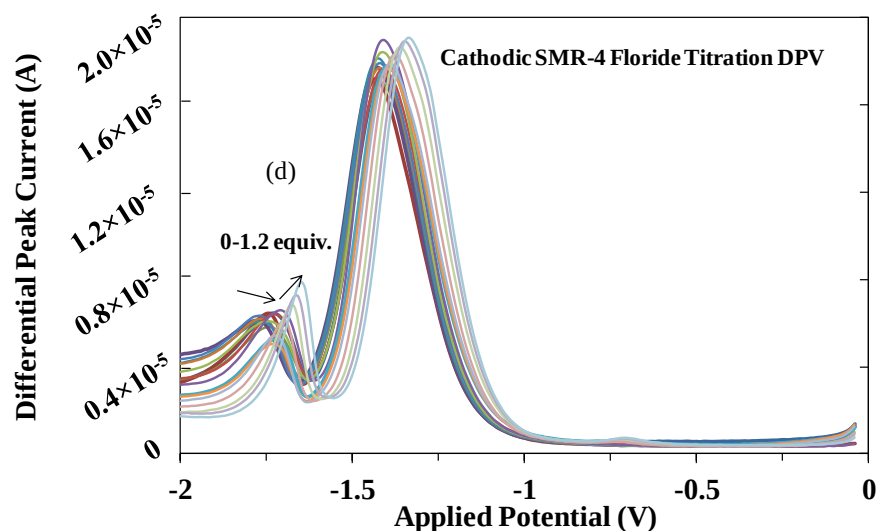


Figure 4.16 Differential Pulse Voltammograms of (a) Anodic **SMR-3** (b) Cathodic **SMR-3** and (c) Anodic **SMR-4** (d) Cathodic **SMR-4** (10^{-3} M) with incremental addition of fluoride ion; using 0.1M TBAPF₆ (tetrabutylammonium hexafluorophosphate) as supporting electrolyte, scan rate 20 mVs⁻¹ and GC as working electrode

Binding constants were calculated for both **SMR-3** and **SMR-4** by using the equation:

$$E_{1/2}^{\text{complex}} - E_{1/2}^{\text{free ionophore}} = (RT/nF) \ln(K)$$

Binding constants for both compounds **SMR-3** and **SMR-4** were found to be infinity (∞) as oxidation peaks get completely quenched on complexation with anion.

Calibration curve for fluoride ion

Experiments were conducted for the measurement of current at peak potential values (from DPV studies for receptors **SMR-3** and **SMR-4**) for different concentrations of fluoride ions added to the solutions of **SMR-3** and **SMR-4** and plots were drawn between fluoride concentrations and the current values. The calibration studies were repeated at least three times to see reproducibility of the proposed method. The calibration curve (Figure 4.17a and 4.17b) shows straight line with lower detection limit of 2.9×10^{-4} ($\pm 2\%$) M as indicated on the interpolation of two straight line portions of the curve [7]. A linear decrease in anodic peak current with increase in concentration of the fluoride ion was observed. It was because of the progressive decrease of the availability of phenolic -OH of receptors to undergo electrochemical oxidation at the electrode. A calibration curve was plotted with a slope of -2.2×10^4 $\mu\text{A}/\text{M}$ and an intercept of 7.5 μA with a relative standard deviation of 2% as mentioned in insets in Figure 4.17a and 4.17b.

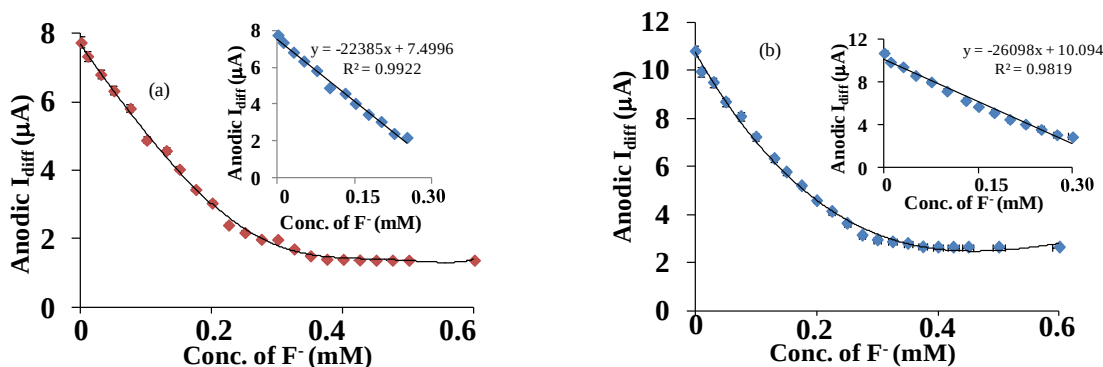


Figure 4.17 Calibration plots between concentration of fluoride and anodic current for (a) **SMR-3** and (b) **SMR-4** in acetonitrile medium using 0.1M TBAP as supporting electrolyte (GC working electrode, scan rate 20 mVs⁻¹ E vs Ag/Ag⁺)

Interference of ions

Interference studies were carried out by adding 2 equivalents of different anions like CH₃COO⁻, CN⁻, Cl⁻, Br⁻, I⁻ and HSO₄⁻ as interfering ions in 1 equivalent concentration of F⁻ ion as primary ion. Voltammograms for compounds **SMR-3** and **SMR-4** in presence of fluoride did not show any change in quenching of anodic peak, indicating that there is no interference from these anions to the detection of fluoride with **SMR-3** and **SMR-4**. It can be concluded that receptors respond with exceptional selectivity towards fluoride ion in the presence of many other commonly available anions.

¹H NMR studies

In order to study the interactions of receptors with fluoride ions, ¹H NMR studies were carried out on **SMR-3/SMR-4** by addition of F⁻ ions as its TBA salt in CDCl₃ at room temperature. The changes in ¹H NMR spectra of **SMR-3** after the addition of F⁻ are shown in Figure 4.18. The signal for -OH proton at 5.0 ppm disappeared completely after the addition of F⁻. This is due to the transformation of the strong hydrogen bonding interaction of fluoride with phenolic H (-O-H...F⁻ to -O...H-F, Scheme 4.3). Simultaneously, a new peak appears at 7.6 ppm due to proton of HF formed. Besides this, it was observed that addition of F⁻ affects mainly protons of the ring B. Native ¹H NMR of **SMR-3** gave signals for ring A at 8.8, 8.3 and 7.1 ppm (H1 to H3) and at 7.3, 6.8, 6.7, and 6.6 ppm (H4-H7) for ring B. Figure 4.18 shows that on addition of F⁻ ions the position of protons for ring A remain unchanged while for ring B protons at 7.3 ppm changes to 7.1 ppm and at 6.7 ppm changes to 6.3 ppm.

Both represent protons ortho to phenolic group (H4 and H7) as observed from COSY spectra. Up field shift of protons is due to shielding by increased charge density on phenolic oxygen.

There is marginal change in the position of other two protons (H5 and H6) of ring B. Similar observations were found in case of **SMR-4** in which –OH signal completely diminished on addition of 0.5 equivalent fluorides.

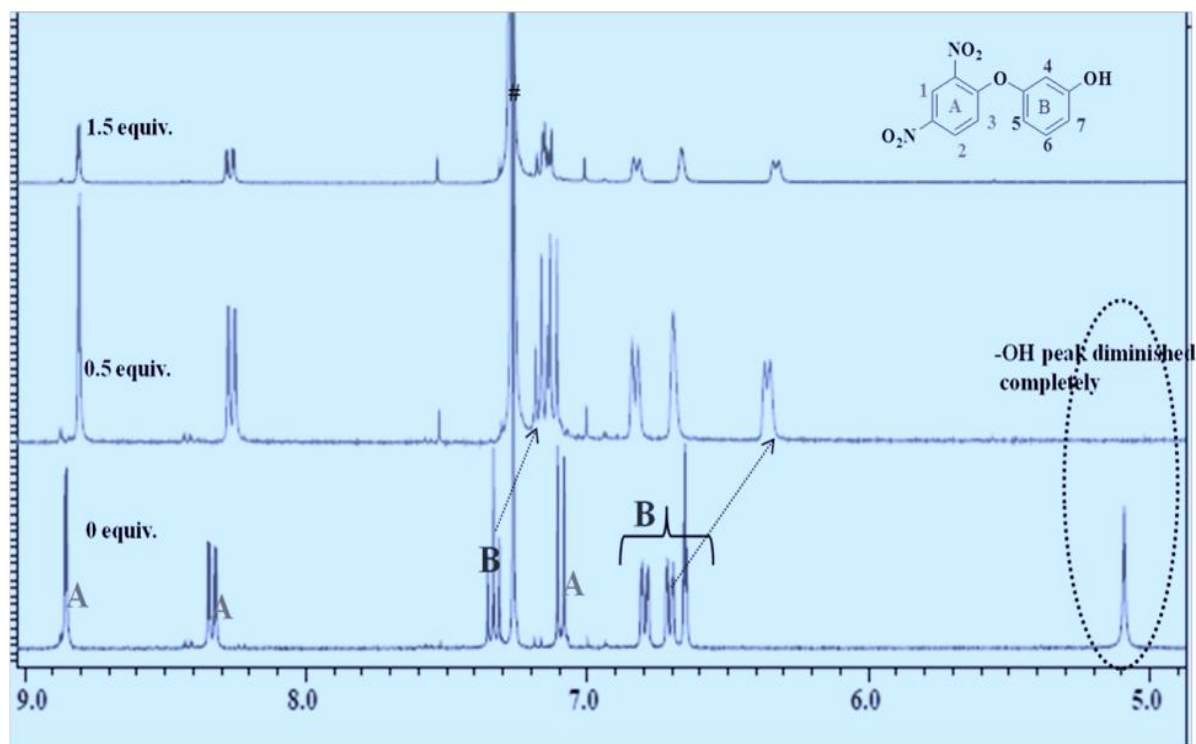


Figure 4.18 Partial ^1H NMR titration of **SMR-3** in CDCl_3 (a) in the absence; and in the presence of (b) 0.5 equivalents; (c) 1.5 equivalents of F^- (# CDCl_3)

Computational studies

In order to understand whether recognition process is mediated by H-bonding interaction between **SMR-3/SMR-4** and F^- or alternately by proton abstraction from phenolic O-H of receptors to F^- , the receptors **SMR-3/SMR-4** and their deprotonated species were examined by using the DFT/B3LYP functional in combination with 6-311G level for **SMR-3/SMR-4** and its F^- complexes. These structures were optimized by using Gaussian 03W software.

In the anion free receptors the bond lengths of O-H is 0.971 Å for **SMR-3** and **SMR-4** at B3LYP/6-311G level. When fluoride anion is involved, the O-H bond is elongated to 1.39 Å for **SMR-3** and 1.63 Å for **SMR-4** indicating that O-H bond is broken and a new H-F bond is formed. New H-F bond is formed after deprotonation having bond lengths 2.43 Å and 2.58 Å for **SMR-3** and **SMR-4**, respectively (Table 4.9). These z matrix coordinates prove that the presence of fluoride ions caused the deprotonation of phenolic O-H and formed the keto-tautomer in the gaseous state as shown in Figure 4.19. This implies that the basicity of F^- is

stronger than those of the arylether anions in the gas phase. Therefore, the H(O) atom is fully abstracted from receptors by fluoride anion as shown in optimized structure formed after deprotonation by fluoride anion.

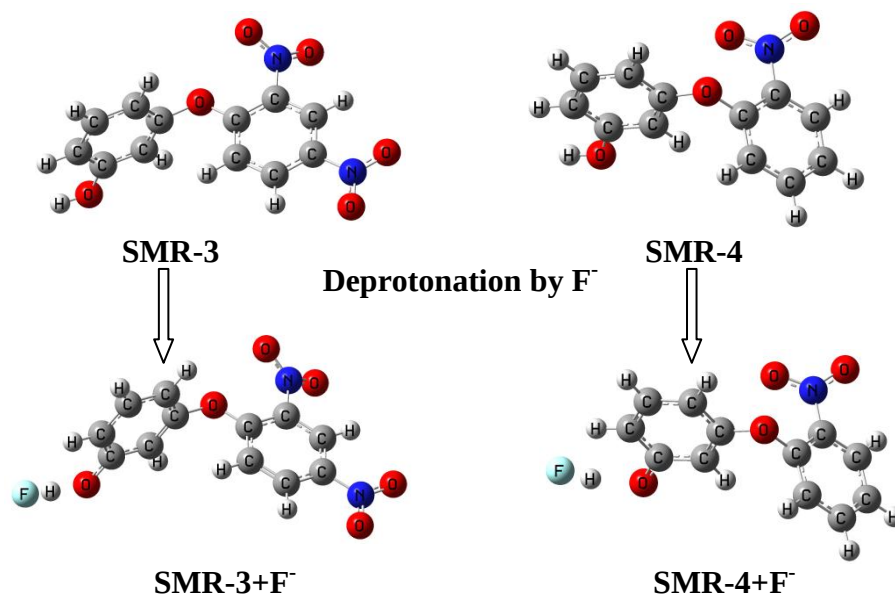


Figure 4.19 The DFT optimized structures of receptors **SMR-3** and **SMR-4** and their deprotonated species calculated at the B3LYP/6-311G level. The red, blue, gray, and sky blue spheres refer to O, N, C, and F respectively

Further, molecular frontier orbitals were calculated which showed the intramolecular charge transfer in the receptors from one aromatic ring to the ring containing nitro groups. ICT phenomenon is occurring after deprotonation by fluoride ion. After deprotonation, energy gap between HOMO-LUMO energy levels decreases drastically, indicating the increased stability of species formed.

Table 4.9 Theoretically calculated structural parameters^a of the receptors- fluoride ion systems

System	d (O-H)	d (H--F)	α (OHF)
SMR-3	0.971 Å	---	---
SMR-3+F⁻	1.39 Å	2.43 Å	110.57°
SMR-4	0.971 Å	---	---
SMR-4+F⁻	1.63 Å	2.58 Å	108.19 °

^aBond lengths (d) are in angstroms and angles (α) are in degrees

Conclusions

Synthesis and structural characterization of compounds (**SMR-3** and **SMR-4**) are described and their binding ability with some selected anions like fluoride, cyanide, acetate, bisulphate, etc. were determined by spectrophotometric and voltammetric methods, supported by theoretical studies. Results of the study showed that **SMR-3** has high selectivity for fluoride ions over other anions in the acetonitrile medium. More importantly, **SMR-3** displays naked-eye detection of fluoride ions at room temperature with a linear response in the range 0.1 to 20 μM . A bathochromic shift of 20 nm for **SMR-3** is observed in the presence of fluoride ion while shift is hypsochromic for **SMR-4** in its absorption spectra. In voltammetric studies, both the molecules showed one oxidation peak (corresponding to phenolic –OH group) and one/two reduction peaks (number depending on the number of nitro groups present in the ligand) with clear quenching of anodic peaks in presence of stoichiometric amounts of fluoride ions. Interactions of the ligands with different anions, observed in voltammetric experiments were supported by ^1H NMR titrations.

4.3 References

1. D. Meshcheryakov, F. A. Neu, V. Bohmer, M. Bolte, V. Hubscher-Bruder, E. Jobin, I. Thondorf and S. Werner, *Org. Biomol. Chem.*, **2008**, 6, 1004-1014.
2. A. D. Becke, *J. Chem. Phys.*, **1993**, 98, 5648-5652.
3. C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, **1988**, 37, 785.
4. P. J. Hay and W. R. Wadt, *J. Chem. Phys.*, **1985**, 82, 270-283.
5. D. Schaming, C. Costa-Coquelard, I. Lampre, S. Sorgues, M. Erard, X. Liu, J. Liu, L. Sun, J. Canny and R. Thouvenot, *Inorg. Chim. Acta*, **2010**, 363, 2185-2192.
6. J. M. Zen, J. J. Jou and A. S. Kumar, *Anal. Chim. Acta*, **1999**, 396, 39-44.
7. K. Kaur, S. K. Mittal, A. Kumar and S. Kumar, *Anal. Methods*, **2013**, 5, 5565-5571.

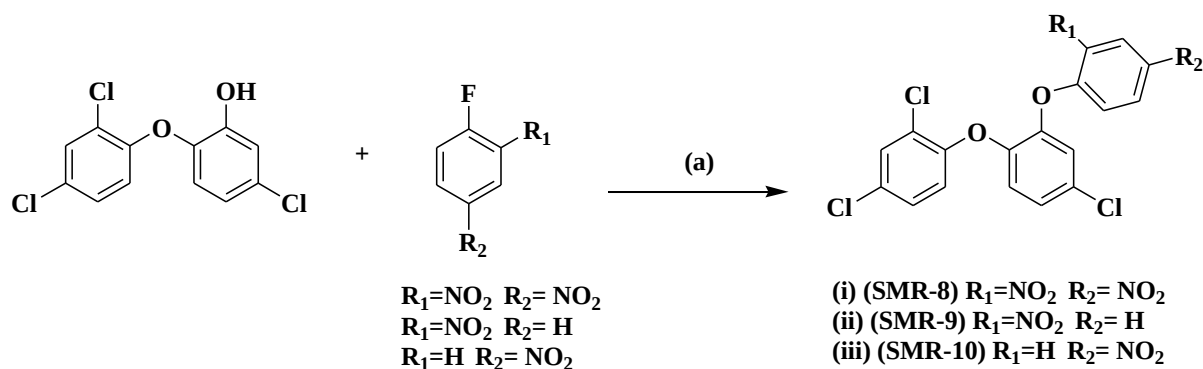
TRIPHENYLETHER BASED RECEPTORS

Phenyl ether moiety imparts both rigidity and flexibility to the receptor molecule. The rigidity is due to planer phenyl rings and flexibility is due to ether linkages. Previous chapter deals with the synthesis of diphenyl ether molecules. Here we envisaged to synthesize various triphenylether molecules that will increase the cavity size to further strengthen the host-guest complexation.

5.1 Synthesis and characterization

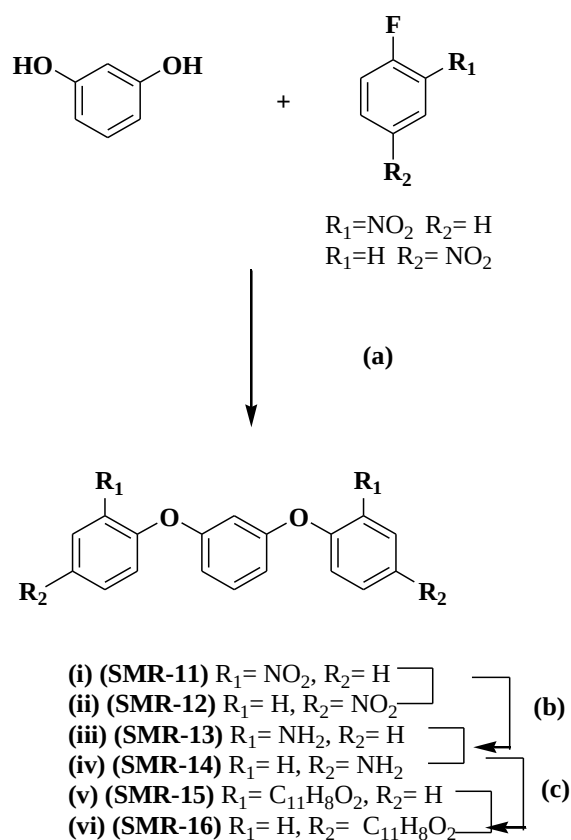
Synthesized triphenyl ether molecules have been characterized into two broad categories. Category-1 has ortho substituted central phenyl ring (**Scheme: 5.1**) and category-2 has meta substituted central phenyl ring (**Scheme: 5.2**).

For category-1, various fluorobenzenes (2, 4-dinitrofluorobenzene, 2-nitrofluorobenzene, 4-nitrofluorobenzene) were substituted with hydroxyl group of a commercially available diphenyl ether, triclosan (**Scheme: 5.1**). The conditions used for the reaction were similar to that used for the synthesis of diphenyl ethers. Generation of nucleophile required mild base as potassium carbonate and an aprotic solvent, DMF, in the presence of phase transfer catalyst, 18-crown-6. Thus, compounds **SMR-8**, **9** and **10** after purification showed in their ^1H NMR spectra presence of nine, ten and ten aromatic protons respectively.



Scheme: 5.1 K_2CO_3 , DMF, 18-Crown-6.

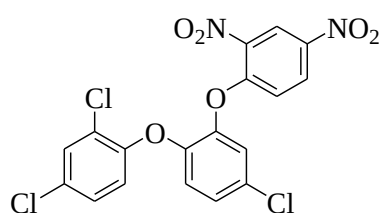
Category-2 included synthesis of resorcinol based triphenyl ether molecules (**Scheme: 5.2**). Basic skeleton was synthesized by reacting two equivalents of 2-nitrofluorobenzene and 4-nitrofluorobenzene with one equivalent of resorcinol under mild basic conditions to give compounds **SMR-11** and **SMR-12** respectively. Presence of 12 aromatic protons in their ^1H NMR spectra confirmed the synthesis of precursors. Nitro group on both the synthesized compounds were reduced to corresponding amino groups using palladium-carbon catalyzed reaction in the presence of hydrogen gas to give **SMR-13** and **SMR-14**. Reduction was confirmed by ^1H NMR spectra. Presence of broad singlets due to NH_2 groups corresponding to 4 protons appeared at 3.65 ppm and at 3.65 ppm for **SMR-13** and **SMR-14** respectively. Further condensation of compounds **SMR-13** and **SMR-14** with commercially available 2-hydroxy naphthaldehyde in presence of ethanol gave imines **SMR-15** and **SMR-16** respectively. Sharp singlet at 9.3 ppm and at 9.3 ppm due to imine protons ($-\text{CH}=\text{N}$) along with required number of aromatic protons and peaks at 168.2 ppm and 168.0 ppm in ^{13}C NMR spectra confirmed the formation of final compounds **SMR-15** and **SMR-16** that were further used for ion recognition studies.



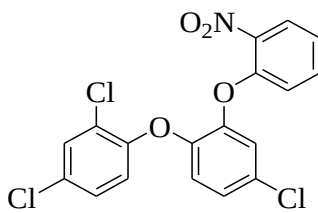
Scheme: 5.2 (a) K_2CO_3 , DMF, 18-Crown-6, (b) **SMR-11/12**, $\text{H}_2/\text{Pd/C}$, Dry MeOH, (c) **SMR13/14**, $\text{C}_{11}\text{H}_8\text{O}_2$, EtOH.

5.2 Ion- recognition studies of triphenylether based receptors

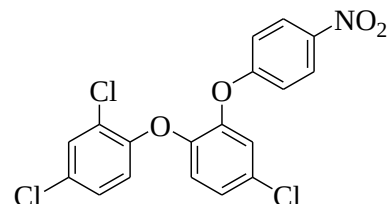
STRUCTURES OF TRIPHENYL ETHER BASED SYNTHESIZED RECEPTORS



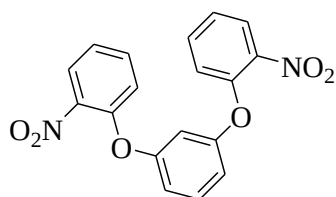
SMR-8



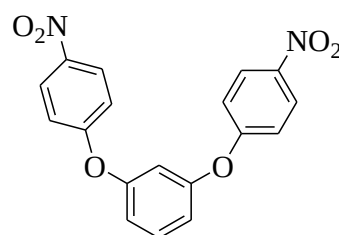
SMR-9



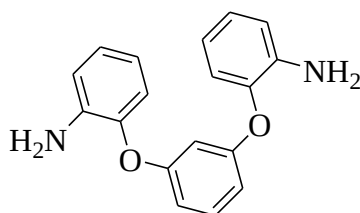
SMR-10



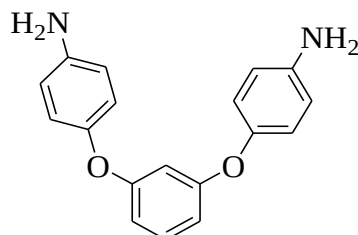
SMR-11



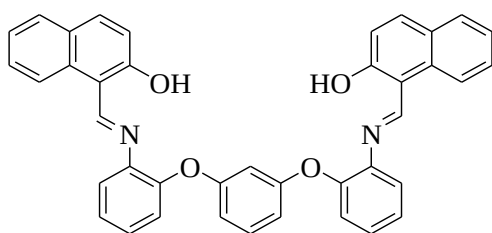
SMR-12



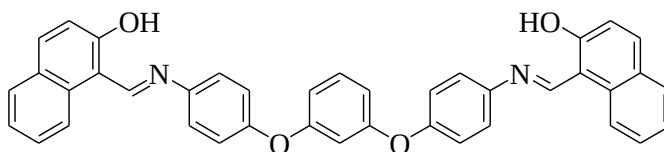
SMR-13



SMR-14



SMR-15



SMR-16

Among various synthesized triphenylethers (**SMR 8-16**), all the molecules were studied preliminary for their interaction with various cations/ anions/lanthanides. But only **SMR-15** and **SMR-16** responded to detection of cations/ anions/lanthanides as detailed below 5.2.1-5.2.3 and hence only **SMR-15** and **SMR-16** were investigated for their interaction with various cations, anions and lanthanides to project them as cation/anion/lanthanide based chemical

sensors. Interaction studies were carried out using spectrophotometric and electrochemical techniques. Further, the mode of interaction of cation or anion with the respective molecule was supported by theoretical calculation using Gaussian 03W software.

5.2.1 Ion-recognition studies of SMR-15

Design of receptor SMR-15

It is very well known that the ionophores undergo host-guest type of interactions with a number of species, primarily the heavy metal ions. The ionophores are designed in such a way to create a cavity in the molecule where the target metal ion can enter. In order to facilitate entry of the metal ion in the cavity some hetero atoms must be present which would hold the target ion through electrostatic binding while acting as Lewis bases.

Keeping in mind the requirements of Host-Guest Chemistry, a new molecule was designed where two nitrogen atoms and two oxygen atoms would form an electronic environment in the pseudocavity conducive to acid-base (in Lewis sense) interaction with the guest species (Heavy metal ion sensing as electron deficient species). Another novelty introduced in the design of the molecule is the use of triphenyl ether motif. **SMR-15** motif is an ideal 'reproducible' component in the new molecule owing to its property of limited flexibility and rigidity of structure. The idea of keeping -OH groups ortho to the imine linkage was to seek complexation of the **SMR-15** with anions as well. Since the anionic guests interact with the host molecule through H-bonding, -OH groups are likely to facilitate interaction with the anionic species as well.

Synthesized receptor **SMR-15** was studied for its interaction with different cations and anions. As per our hypothesis, the ionophores showed sharp changes of its optical properties of the **SMR-15**, when allowed to interact with the target species. Experiments revealed that there was sudden change in absorbance in presence of cobalt, fluoride and cyanide ions from 325 nm to 300 nm for cobalt ions, from 385 nm to 435 nm for fluoride ions and complete disappearance of absorption bands at 325 nm, 385 nm and 435 nm for cyanide ions. These changes were detectable with naked eye on addition of cobalt/fluoride/cyanide ions in **SMR-15** solution. Based on these visual changes, binding properties of the receptor **SMR-15** were interpreted by using spectrophotometric, spectrofluorimetric and voltammetric techniques supported by DFT calculations.

Colorimetric experiments

Experiments were conducted to observe changes in absorbances on the interactions of the receptor **SMR-15** with different cations and anions. These experiments were done in pure acetonitrile and acetonitrile- water in various combinations and pure water. Best response was noticed in the mixture of acetonitrile and water in the ratio 95:5; v/v. All the further experiments were carried out in this medium. The absorption response of various cations/anions in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) showed visual change of color of solution from yellow to blue in the presence of cobalt, yellow to dark yellow in the presence of fluoride and yellow to colorless in the presence of cyanide ions, while no such color change was observed in the presence of any other ion (Figure 5.1). The UV-visible spectra of **SMR-15** receptor also showed changes in the presence of cobalt, fluoride and cyanide ions consistent with the change of color as seen visually and are shown in Figure 5.2a and 5.2b. In case of anion also, sharp changes in absorbances were noticed with fluoride and cyanide ions while with all other ions, no noticeable changes were seen. Mechanisms could possibly be explained by hydrogen bonding ability of the heteroatoms and nucleophilic addition of the anions. Hydrogen bonding tendency of the anions is in the order $\text{F}^- > \text{AcO}^- > \text{H}_2\text{PO}_4^- > \text{N}_3^-$, CN^- , based on their electronegativity. Therefore, fluoride ions could easily form hydrogen bonds with **SMR-15** even in aqueous solution, which eventually caused the naphtholic protons of **SMR-15** to deprotonate, thus showing a bathochromic shift in UV-visible spectra. In case of interaction of **SMR-15** with CN^- , the decolorization of **SMR-15** might be due to the nucleophilic addition of CN^- onto **SMR-15**, forming the colorless leuconitrile species [1].

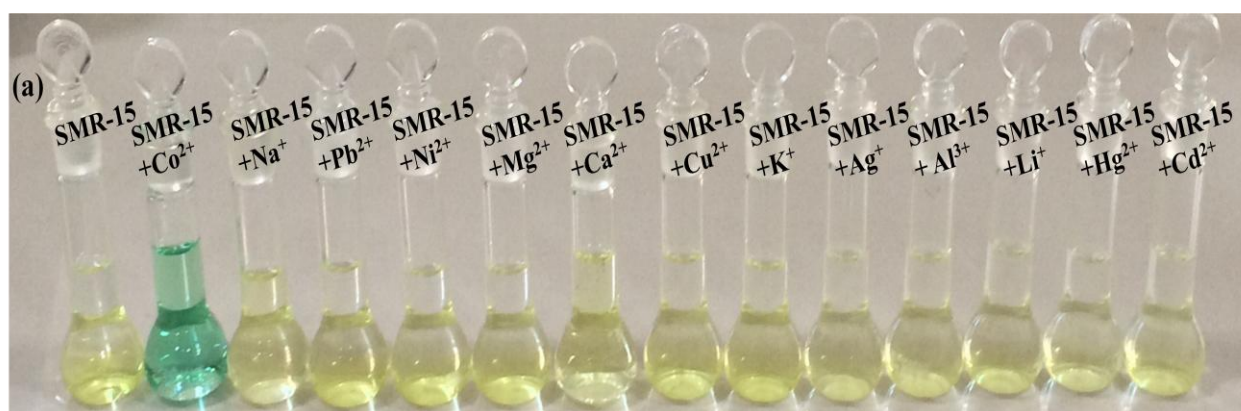




Figure 5.1 Visual changes in color of **SMR-15** receptor alone (20 μM) and upon addition of (a) various cations (50 equivalents) and (b) various anions (50 equivalents) in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) HEPES buffered solvent system

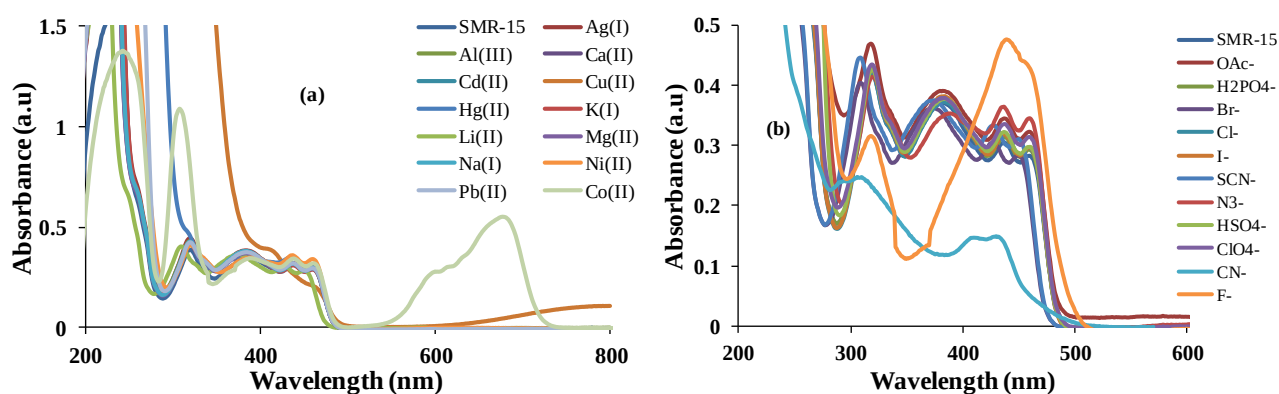


Figure 5.2 UV-visible spectral changes of **SMR-15** receptor alone (20 μM) and upon addition of (a) various cations (50 equivalents) and (b) various anions (50 equivalents) in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) HEPES buffered solvent system

Spectrophotometric studies

Determination of Cobalt Ions: Binding properties of **SMR-15** with cobalt ions were studied by UV-visible titration experiment (Figure 5.3). The absorption band at 325 nm shifted by 25 nm to appear at 300 nm accompanied with appearance of a new absorption peak at 675 nm, which increased steadily with increasing amount of cobalt ions. The increase in absorbance on addition of cobalt ions was linear due to the formation of **SMR-15-Co(II)** complex. Calibration plots drawn between concentration of cobalt ions and absorbance were linear in the range 0-70 μM of cobalt ions with $R^2 = 0.99$ and are shown in Figure 5.3. Job's plot measurements were done to find the metal-ligand binding ratio. The parabolic curve with maxima at 50 μM concentration of the ligand proved that the complexation between cobalt and **SMR-15** was in 1:1 ratio (Figure 5.4a). To study interference from a large number of metal ions in the **SMR-**

15-Co(II) complexes experiments were carried out in presence of a number of metal ions like Al(III), Cd(II), Hg(II), Li(II), Na(I), Pb(II), Ag(I), Ca(II), Cu(II), K(I), Mg(II) and Ni(II), as shown in Figure 5.4b. Since no change in absorbance values were noticed due to presence of interfering ions no interference was found with any of other metal ions, which established the selectivity of **SMR-15** for cobalt ions only. The binding constant value of **SMR-15** with Co(II) was found as $4.2 \times 10^5 \text{ M}^{-1}$ and the detection limit was calculated as 2 μM .

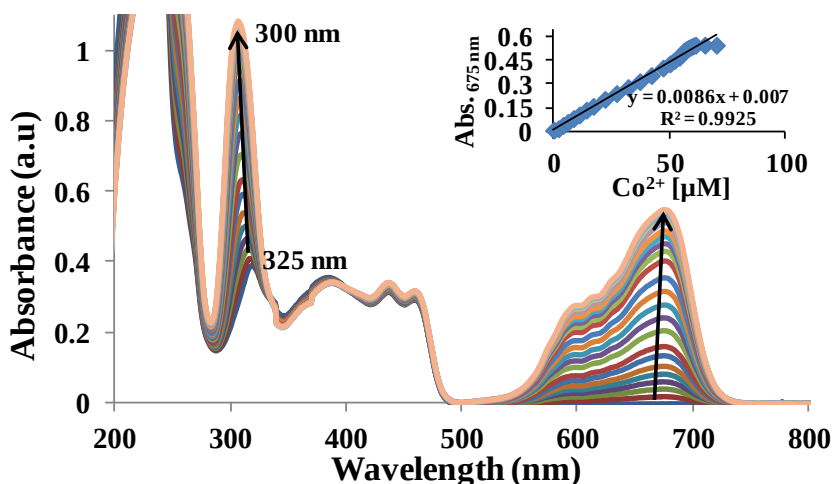


Figure 5.3 Absorption spectral changes **SMR-15** in the presence of different concentrations of Co(II) at room temperature

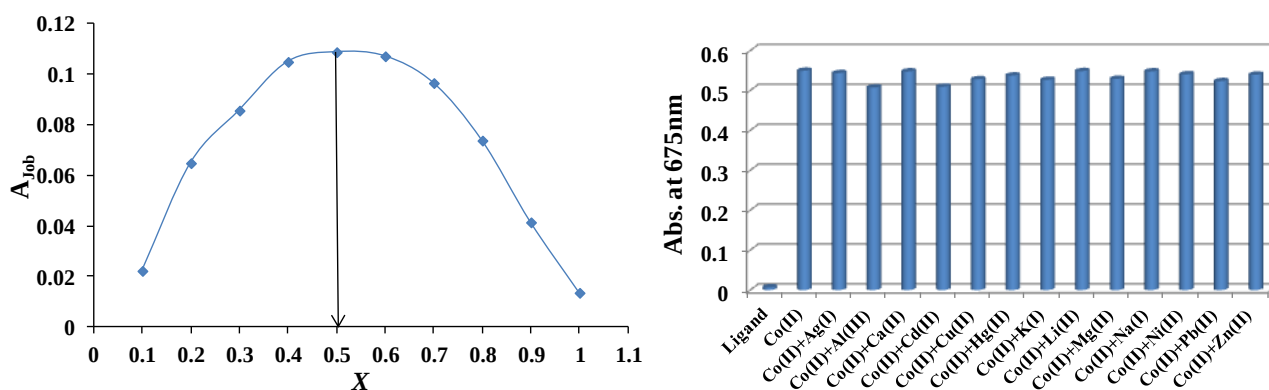


Figure 5.4 (a) Job's plot analysis of **SMR-15** and Co(II) ions showing 1:1 stoichiometry (b) Absorption changes of **SMR-15** upon addition of different interfering metal ions at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v: v)

Determination of Fluoride Ions: In presence of fluoride ions, the band at 385 nm in the absorption spectrum of **SMR-15** disappeared while intensity of the band at 435 nm increased with addition of fluoride ions. An isobestic point observed at 400 nm, suggested the formation of only one UV–visible active species (Figure 5.5). A bathochromic shift of the absorption band from 385 nm to 435 nm led us to propose the change of intramolecular charge transfer

(ICT) band through the deprotonation of **SMR-15** by fluoride ions. The negative charge of **SMR-15**²⁻ generated from the deprotonation of the naphtholic protons of **SMR-15** by F⁻ would lead to the red shift from 385 nm to 435 nm, resulting in the increased intensity of the yellow color of **SMR-15**. Job's plot [2] indicated to a 1:1 stoichiometry between **SMR-15** and F⁻ (Figure 5.9). The binding constant (K) for **SMR-15** with F⁻ ($2.6 \times 10^5 \text{ M}^{-1}$) was estimated by using Benesi–Hildebrand equation based on the UV–visible titration [3]. From the calibration curve, detection limit for F⁻ ions was determined as $0.15(\pm 0.02) \text{ }\mu\text{M}$. To explore the ability of **SMR-15** as a colorimetric chemosensor for F⁻ ions, competition experiments were conducted in the presence of F⁻ mixed with various competing anions. Spectrophotometric titration of **SMR-15** was done against fluoride ion solution in the presence of interfering ions, taken in different concentrations ranging from 1 to 50 equivalents. At least 5 titrations were done with different equivalents of each interfering ion. When **SMR-15** was treated with 50 equivalents of F⁻ in the presence of an equal concentration of other competing anions, no change in absorbance was observed. Hence, there was no interference in the determination of F⁻ in the presence of Cl⁻, Br⁻, I⁻, OAc⁻, H₂PO₄⁻, N₃⁻, SCN⁻, HSO₄⁻ and ClO₄⁻. Only CN⁻ ions interfered with the determination of F⁻ as shown in Figure 5.6. These results indicated that **SMR-15** could be a selective colorimetric sensor for F⁻ in the presence of various competing anions except CN⁻.

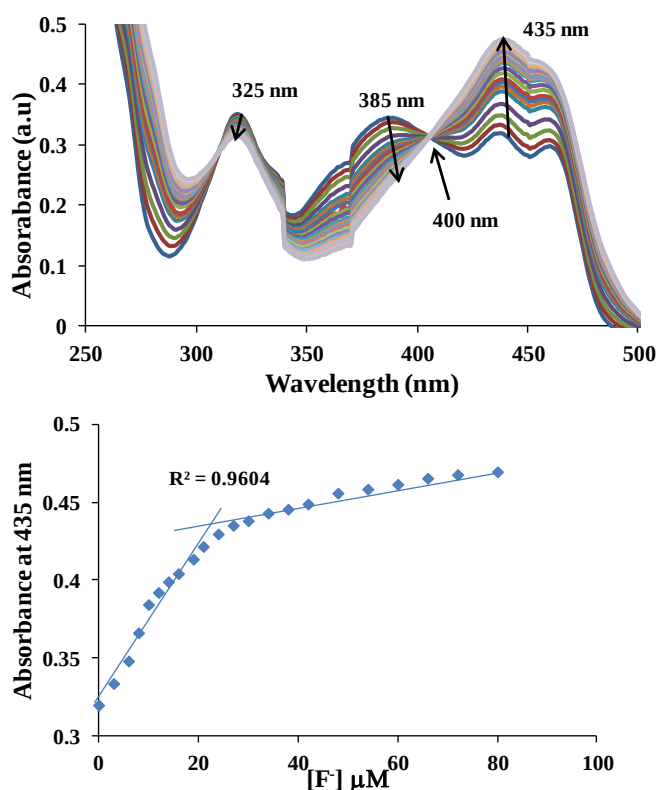


Figure 5.5 Absorption spectra of **SMR-15** in the presence of different concentrations of F⁻ at room temperature



Figure 5.6 The color changes of **SMR-15** upon addition of F^- and then various interfering anions in $CH_3CN:H_2O$ (95:5; v/v) HEPES buffered solvent system

Determination of Cyanide Ions: High selectivity of **SMR-15** was noticed for cyanide ions which may be due to the deprotonation of **SMR-15** by CN^- followed by the subsequent nucleophilic addition of cyanide into the imine moiety of **SMR-15** in a solvent mixture of $CH_3CN:H_2O$ (95:5; v/v). Cyanide ions do not have any tendency to form hydrogen bonding with water molecules. The property of cyanide as a strong base is responsible for deprotonation of naphtholic proton of **SMR-15** instead of forming the hydrogen bonding with water molecules. Subsequently, the resulting naphtholate ions $SMR-15^{-2}$ might form hydrogen bonding with water molecules. In presence of cyanide ions, these would add on the imine group of **SMR-15** to produce the nucleophilic addition product [4, 5]. Importantly, the addition of $HCN/NaCN$ on the imine group, the absorbance at 435 nm (responsible for yellow color of the **SMR-15** solution) goes off giving a clear colorless solution. Solution of **SMR-15** in presence of CN^- showed the color change from yellow to colorless against various anions (Figure 5.1). In consistency with the color change as seen in Figure 5.1, **SMR-15**- CN^- showed sharp decrease of absorption band at 325 nm, 385 nm and 435 nm (Figure 5.7) which could be only due to nucleophilic addition product, ruling out the possibility of ICT process [6]. An isobestic point was observed at 300 nm which also supported the formation of $SMR-15 + CN^- - H^+$ adduct. The Job's plot for the binding between **SMR-15** and CN^- exhibited a 1:2 stoichiometry (Figure 5.9). From the Benesi–Hildebrand equation, the association constant for the **SMR-15**- CN^- complex was found to be $6.0 \times 10^3 M^{-1}$ and detection limit of cyanide ions was found to be 0.1 μM . To check the possible interference of other anions on cyanide complexation with the receptor **SMR-15**, competition experiments were performed in the presence of CN^- mixed with various anions (Figure 5.8). All of these competing anions such as F^- , Cl^- , Br^- , I^- , OAc^- , $H_2PO_4^-$, N_3^- , SCN^- , HSO_4^- and ClO_4^- did not interfere with naked-eye detection of CN^- by **SMR-15**, which means that the receptor **SMR-15** displays a good

selectivity for CN^- over other competing anions. These results clearly showed that the receptor **SMR-15** can act as a specific chromogenic chemosensor for cyanide.

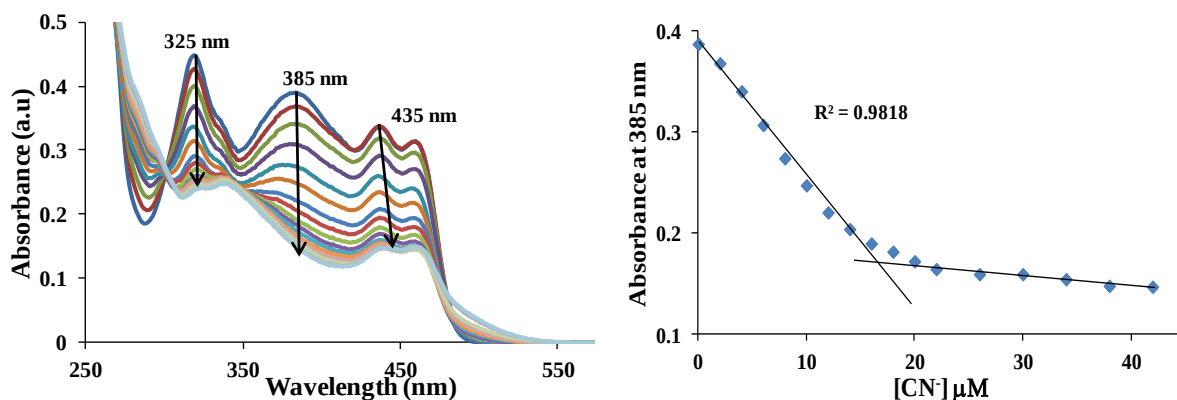


Figure 5.7 Absorption spectra of **SMR-15** in presence of different concentrations of CN^- at room temperature in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) HEPES buffered solvent system



Figure 5.8 The color changes of **SMR-15** upon addition of CN^- and various interfering anions in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) HEPES buffered solvent system

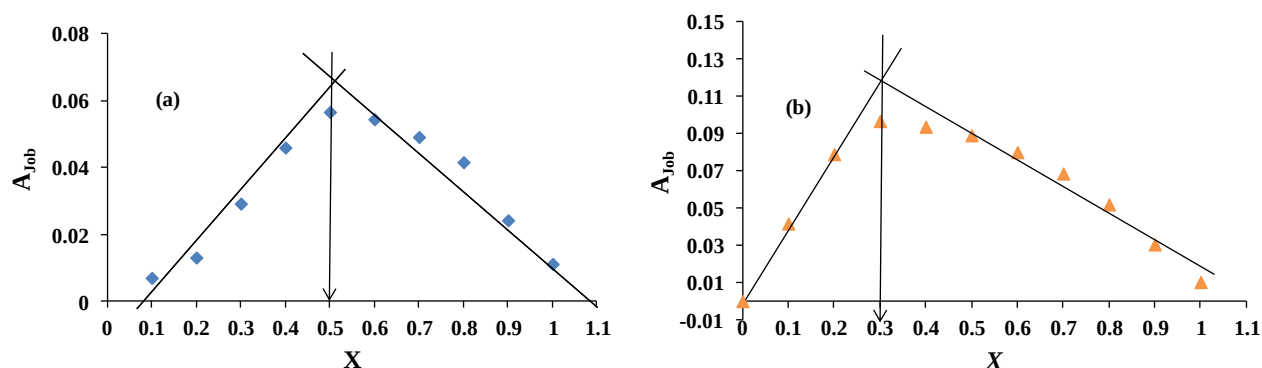


Figure 5.9 Job's plot analysis of **SMR-15** (a) with varying mole ratio of CN^- and (b) with varying mole ratio of F^-

Spectrofluorimetric studies

Fluorescence monitoring studies of **SMR-15** were carried out with different cations as well as anions to check its fluorescence properties. Receptor **SMR-15** alone displayed no fluorescence emission when excited at 390 nm. With the addition of different cations and anions, no significant change was observed except with cyanide (Figure 5.10a). On the addition of CN^- into **SMR-15**, there was an instant enhancement (52-fold) of the emission intensity at 450 nm which demonstrated that the ICT process in **SMR-15** was inhibited upon the addition of CN^- , as was also observed in spectrophotometric studies. Therefore, the weak fluorescence intensity of **SMR-15** could be attributable to ICT from the naphthol group to the ethereal group. The nucleophilic addition of cyanide to the imine group of **SMR-15** prevented ICT resulting in an enhanced fluorescence emission [7].

For a detailed study of fluorescent sensing behaviour of **SMR-15**, fluorescence titration experiments were performed (Figure 5.10b). When the receptor **SMR-15** (10 μM) was titrated with CN^- solution, fluorescence intensity remained almost unchanged upto 0.8 μM of CN^- probably due to stoichiometric reasons and then increased on further addition of CN^- from 0.8-20 μM . There was no further change on addition of the titrate beyond 20 μM . Calibration graph can also be looked as a 2-step process taking place for cyanide ion measurement. The two parts of the calibration curve have different slopes but linear in shape. Presence of two step change in slope of calibration curve for CN^- ions is due to two step reaction of CN^- with **SMR-15**. In the first step, CN^- deprotonates naphthol moiety and in the second step the HCN so formed adds on to the imine double bond. Since these steps take place in sequence hence result in calibration curves independent of each other [7].

According to the World Health Organization (WHO), cyanide concentrations lower than 1.9 μM is acceptable in drinking water [8]. The detection limit for CN^- complex was determined as 0.01 μM which is far below the WHO guidelines of drinking water. Hence, the receptor **SMR-15** could be used as a powerful tool for the determination of cyanide in water samples.

To check further the practical applicability of **SMR-15** as a CN^- selective fluorescence sensor, competition experiments (Figure 5.11) were carried out. When **SMR-15** was treated with 50 equivalents of CN^- in the presence of other anions with equal concentration, there was no fall in fluorescence intensity in presence of F^- , Cl^- , Br^- , I^- , OAc^- , H_2PO_4^- , N_3^- , SCN^- , HSO_4^- and ClO_4^- as interfering ions.

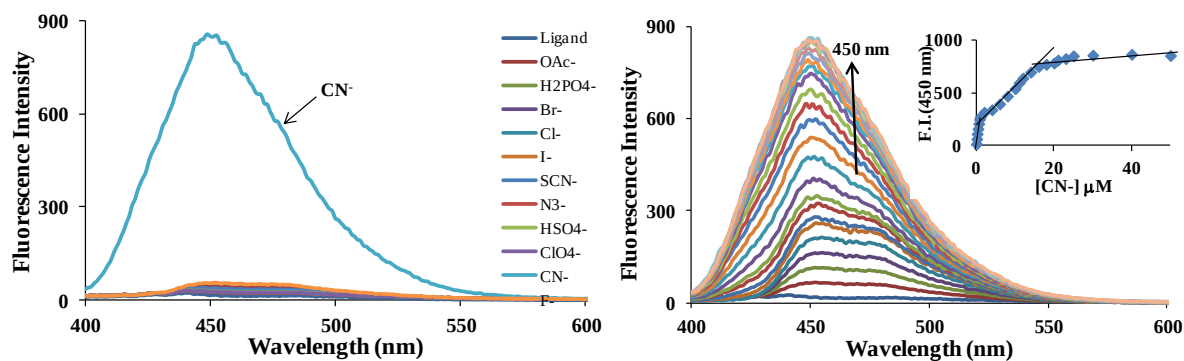


Figure 5.10 Fluorescence spectral response of (a) **SMR-15** (10 μM) upon addition of various anions (50 equivalents) (b) Fluorescence spectral change of **SMR-15** in the presence of different concentrations of CN^- at room temperature in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5; v/v) HEPES buffered solvent system

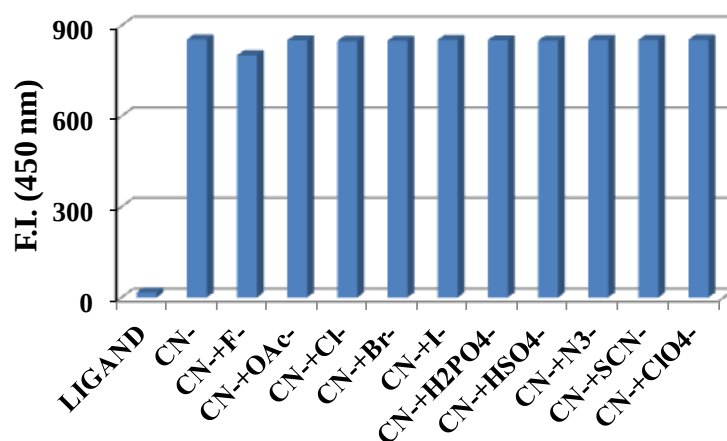
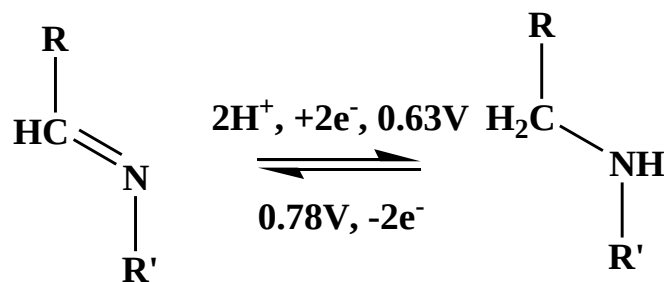


Figure 5.11 Competitive experiments in the presence of 50 equivalents of interfering anions and 50 equivalent of CN^-

These results indicated that receptor **SMR-15** showed an excellent selectivity for cyanide in the presence of other anions, making it very useful in practical applications.

Electrochemical studies

Electrochemical detection of cobalt/fluoride/cyanide using **SMR-15** receptor was carried out by cyclic and differential pulse voltammetric techniques in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5, v/v) solution containing 0.1 M TBAPF_6 as a supporting electrolyte. Voltammograms for **SMR-15** receptor showed anodic peaks at 0.55 V and 0.78 V and a minor cathodic peak at 0.63 V. The cathodic peak at 0.63 V represented reduction of imine moiety. Anodic peaks at 0.55 V and 0.78 V represented oxidation of ether group and reoxidation process of the reduced imine group, respectively [9], as explained in Scheme 5.3.



Scheme 5.3 Electrochemistry of the imine moiety

Voltammograms of **SMR-15** were drawn with a number of cations and anions to know selectivity of the receptor. Cobalt, fluoride and cyanide showed the major shifts in peak potentials on their respective additions in **SMR-15** receptor solution.

Cobalt sensing: Addition of cobalt ions in **SMR-15** receptor solution in CH₃CN:H₂O (95:5, v/v) caused the diminishing of peak currents at 0.55 V and 0.78 V accompanied with anodic shifts and emergence of a new peak at 0.98 V which rises in peak current abruptly from 0.93 A (value at 0 concentration of Co(II)) to 40 μA approximately, as shown in Figure 5.12a and b.

Fluoride sensing: On addition of fluoride ions, there was a complete quenching of anodic peaks at 0.55 V and 0.78 V (Figure 5.13a and b), due to the deprotonation of naphtholic protons, which caused the whole molecule to come into resonance. Hence, the lone pairs of electrons on ether group and nitrogen of imine group became unavailable for oxidation at the electrode, as proved spectrophotometrically in this chapter under paragraph Spectrofluorimetric studies.

Cyanide sensing: Addition of cyanide led to an increase in peak current of anodic peak at 0.68 V, which later merges with the new peak at 1.0 V till the current magnitude reaches 36 μA. Anodic peak at 0.55 V decreased in current only after merging of the peaks at 0.68 V and 1.0 V. Simultaneously, a new peak at 0.2 V is seen which increased its peak current till 12 μA, as shown in Figure 5.14a and b. These observations too supported a two step mechanism in case of cyanide detection, as discussed earlier.

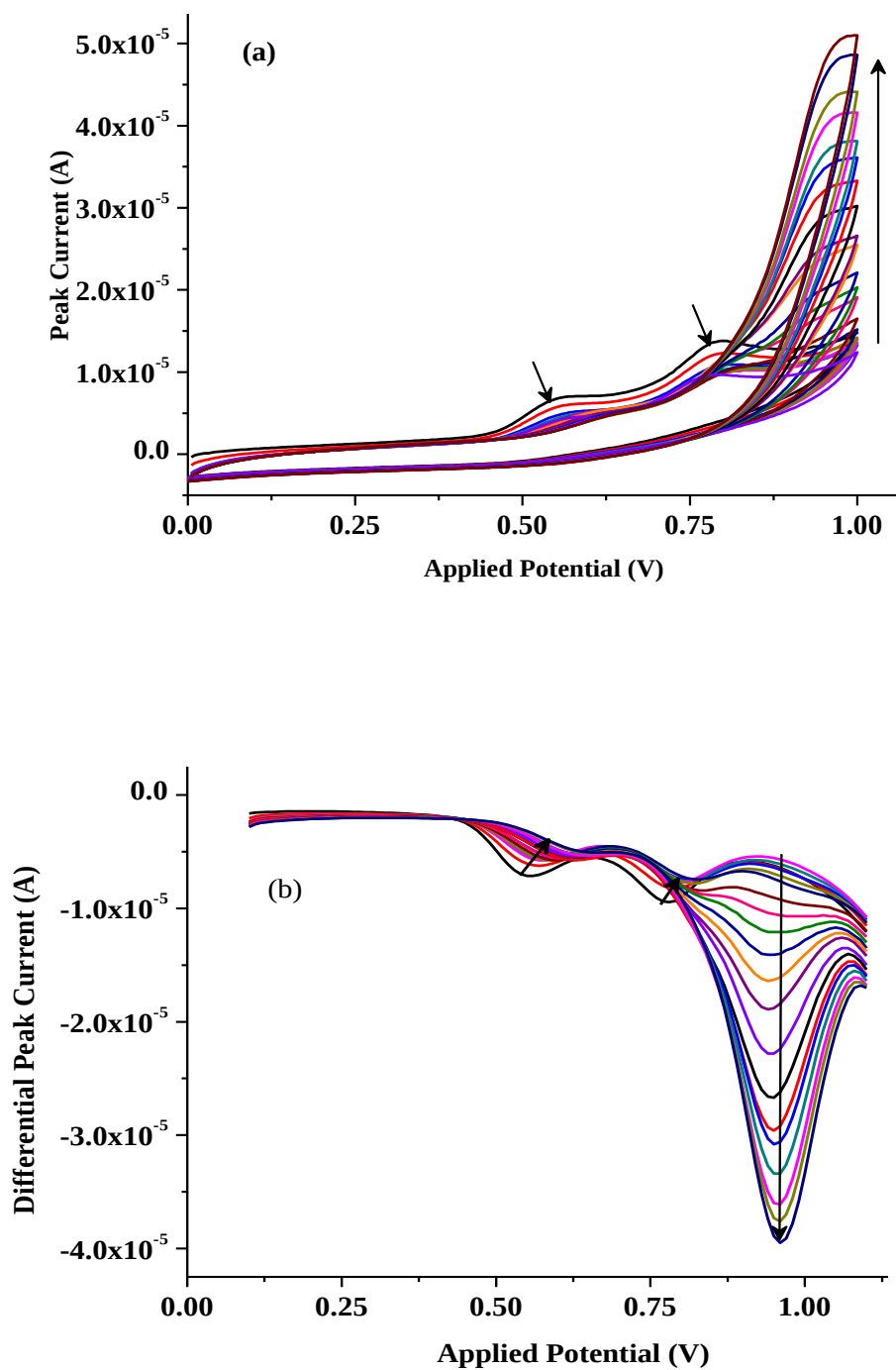


Figure 5.12 (a) Cyclic and **(b)** Differential Pulse Voltammograms of **SMR-15** solution (10^{-5} M) with incremental additions of Co(II) ions (0-12 μ M), at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v), 0.1M TBAPF₆, scan rate: 50mV/sec, working electrode: GC

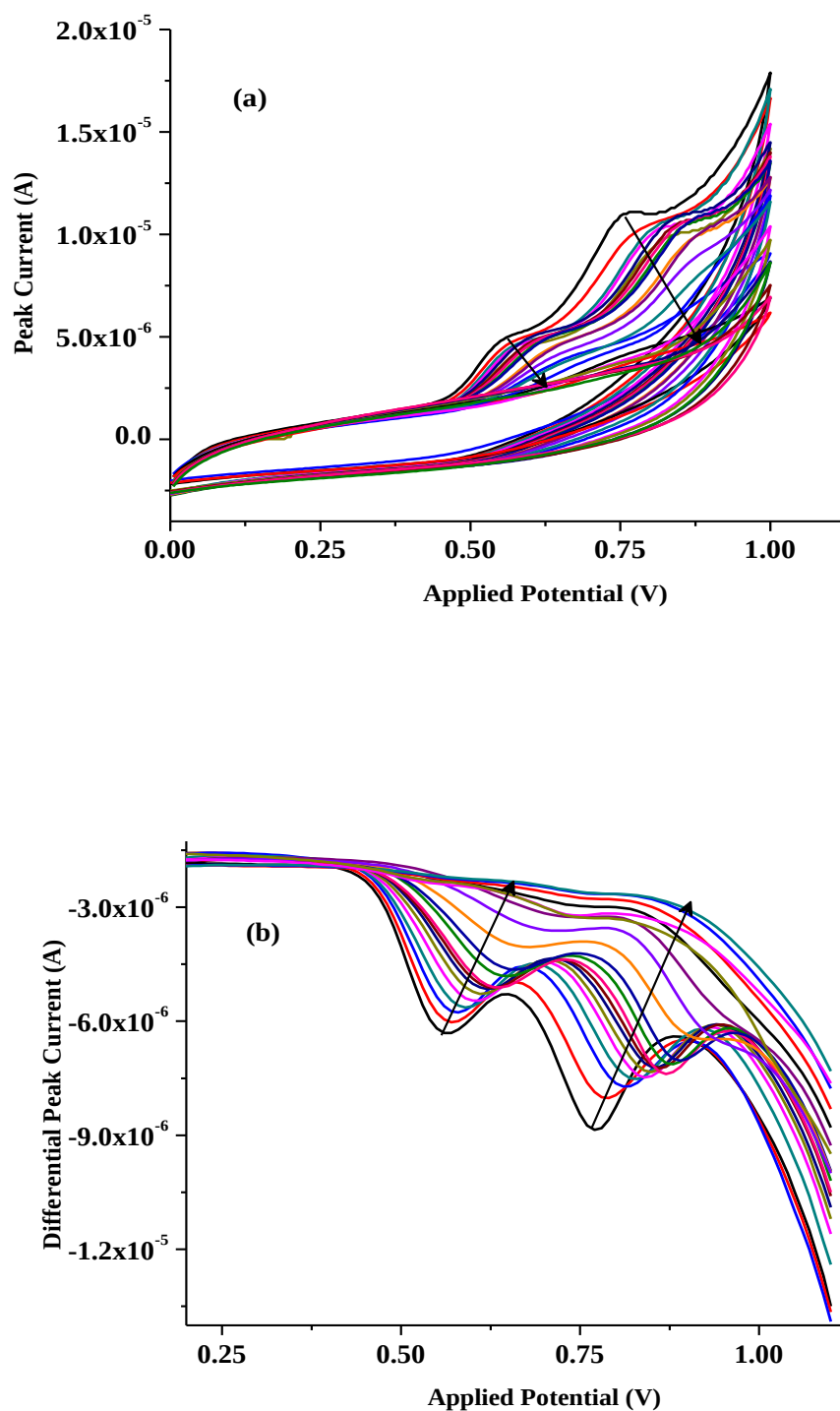


Figure 5.13 (a) Cyclic and **(b)** Differential Pulse Voltammograms of **SMR-15** solution (10^{-5} M) with incremental additions of F^- ions (0 - $10 \mu\text{M}$), at $\text{pH } 7.0 \pm 0.1$ (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ $95:5$, v:v), 0.1M TBAPF₆, scan rate: 50mV/sec , working electrode: GC

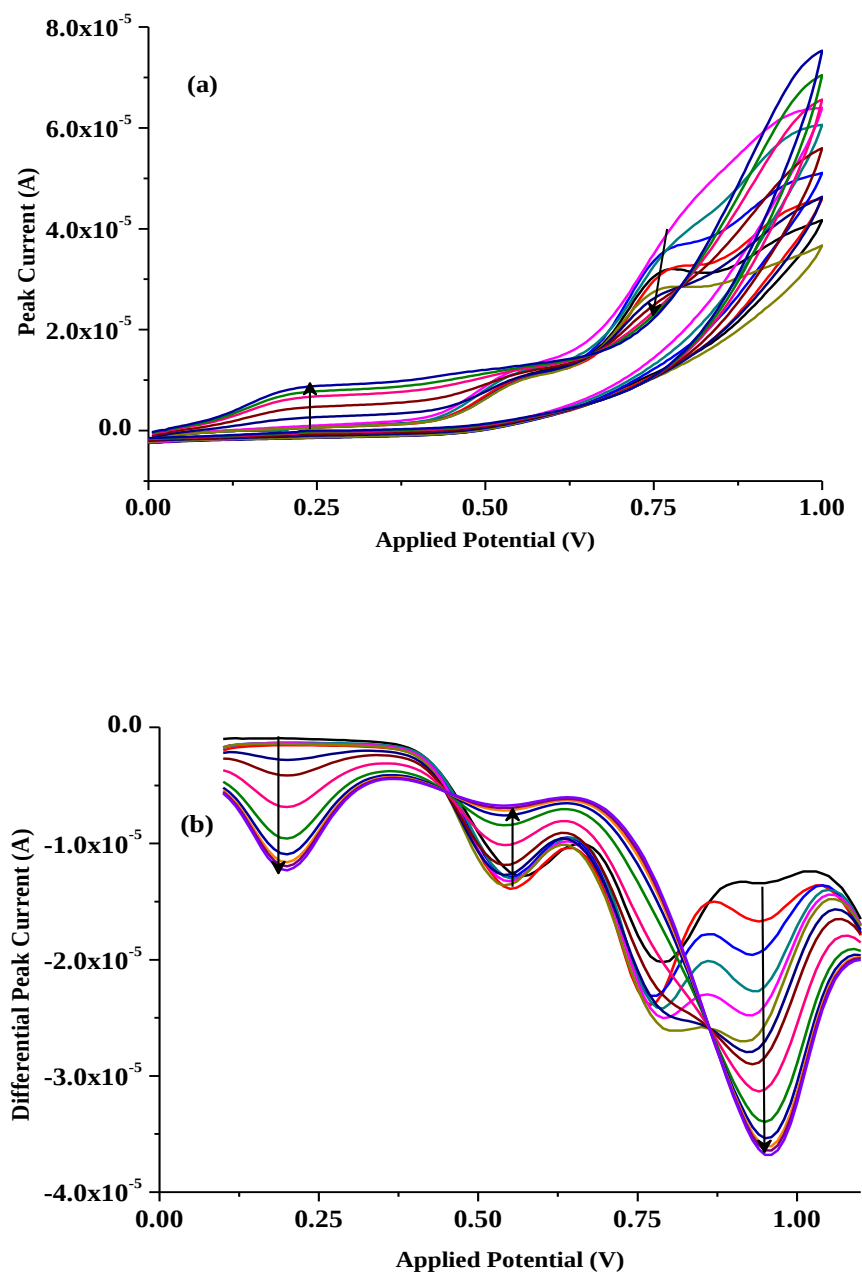
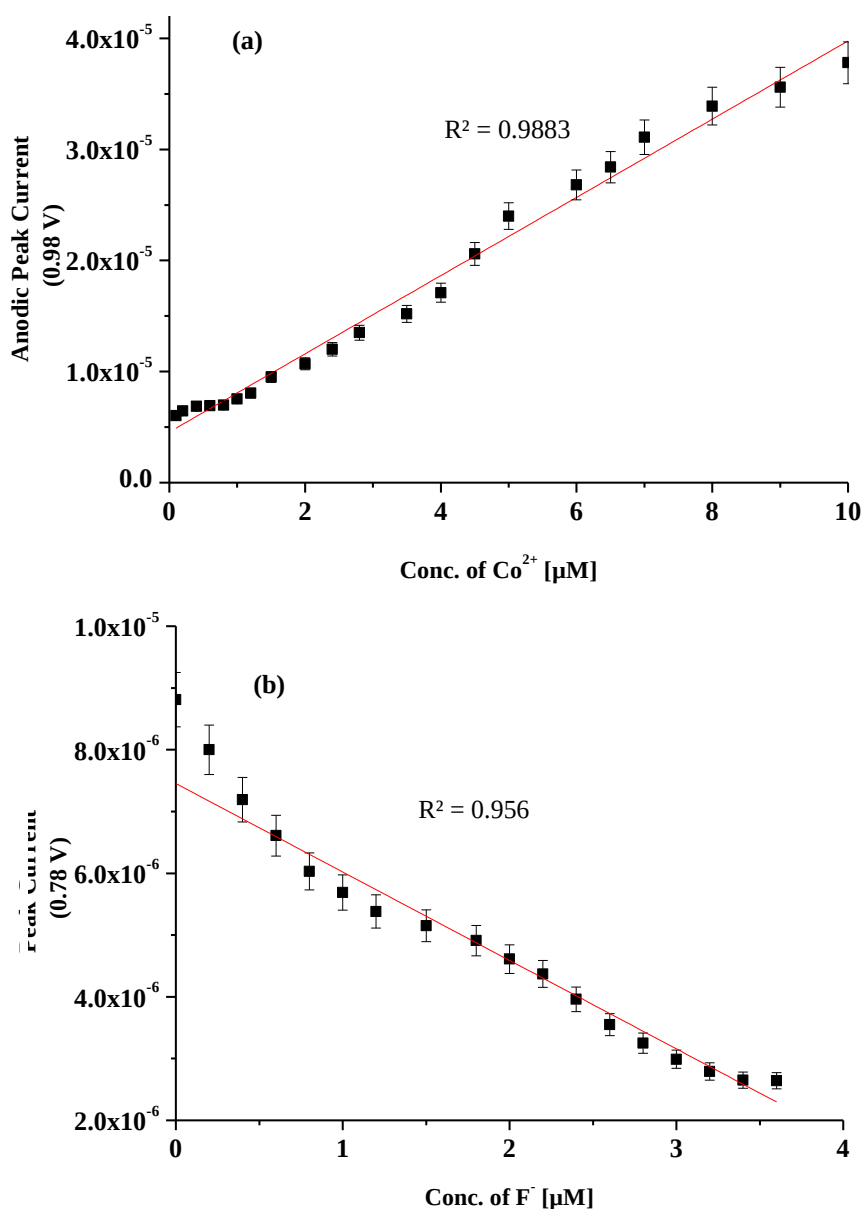


Figure 5.14 (a) Cyclic and (b) Differential Pulse Voltammograms of **SMR-15** receptor solution (10^{-5} M) with incremental addition of CN^- ions (0 – $23 \mu\text{M}$), at $\text{pH } 7.0 \pm 0.1$ (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v), 0.1M TBAPF_6 , scan rate: 50mV/sec, working electrode: GC

Sensitivity (LOD and LOQ)

Sensitivity of **SMR-15** was determined from the limit of detection (LOD) and limit of quantification (LOQ) values. The LOD is calculated by the equation $\text{LOD}=3(\text{SD}/b)$, where SD is the standard deviation of the intercept and b is the average slope of the regression line. The LOQ is examined by the equation $\text{LOQ}=10(\text{SD}/b)$. Peak current (μA) versus concentration (μM) was plotted which resulted in a straight line (Figure 5.15 a, b and c). The experiment was repeated 3 times and the representative curve from the 3 sets of data was used for further calculations of LOD and LOQ. By using 3-sigma method [10] the limit of detection was found to be $0.03 \mu\text{M}$, $0.04 \mu\text{M}$, $0.07 \mu\text{M}$ for cobalt, cyanide and fluoride, respectively. Limit of quantification values come out to be $0.12 \mu\text{M}$, $0.13 \mu\text{M}$, $0.25 \mu\text{M}$ for cobalt, cyanide and fluoride, respectively.



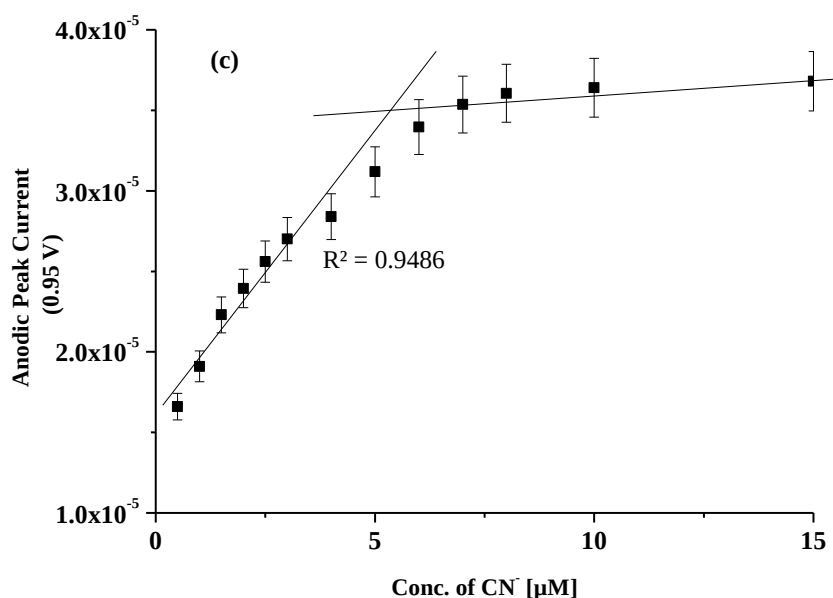


Figure 5.15 Calibration plot of peak current w.r.t (a) conc. of Co(II) ions (b) conc. of F⁻ ions (c) conc. of CN⁻ ions

Interference investigation

Selectivity of **SMR-15** was confirmed further by interference studies with various interfering cations/anions added in excess to the target ion. Voltammetry was done to study the effect of the presence of other ions on the response of **SMR-15** for Co(II) and F⁻/CN⁻ ions. **SMR-15** responded selectively to Co(II) ions even in the presence of other interfering metal ions. In case of anions, the interaction of **SMR-15** with cyanide was found selective in the presence of all the competing anions, while in case of fluoride ions no ion other than cyanide ions did interference. Hence, **SMR-15** receptor can be used as a cyanide selective chemosensor without any interference of all the other anions, as shown in Figure 5.16.

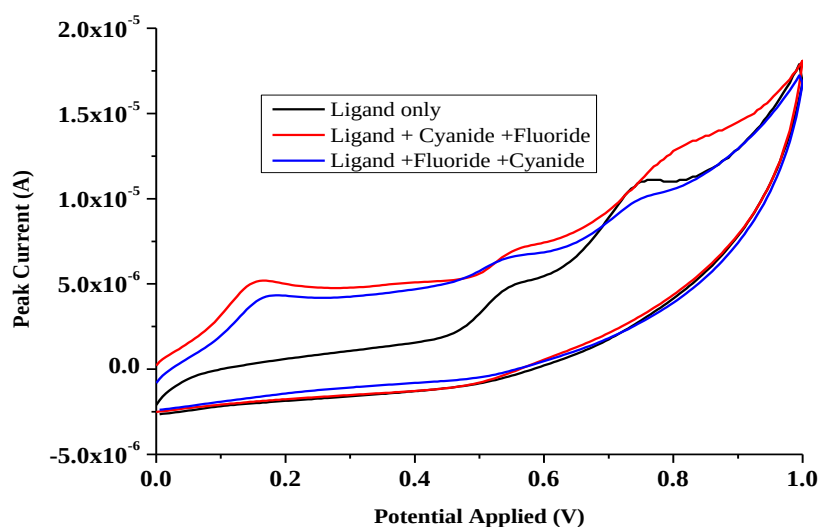


Figure 5.16 Voltammograms showing interference of CN⁻ in detection of F⁻ and selectivity of CN⁻ over F⁻ when added in equal concentrations into **SMR-15** solution

Computational studies

Density Functional Theory (DFT) calculations were used to understand the behaviour of **SMR-15** with the F^- , CN^- and $Co(II)$ ions. Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) for **SMR-15** and their complexes have been generated from the optimized structures of the **SMR-15** and their respective cation/anion complexes (Figure 5.17). The structural optimization and the computational calculations were carried out using Gaussian03W software. In the present scenario, DFT/B3LYP/6-31G method was implemented for the **SMR-15** under gas phase condition, while LANL2DZ method was used for optimization with cobalt ion.

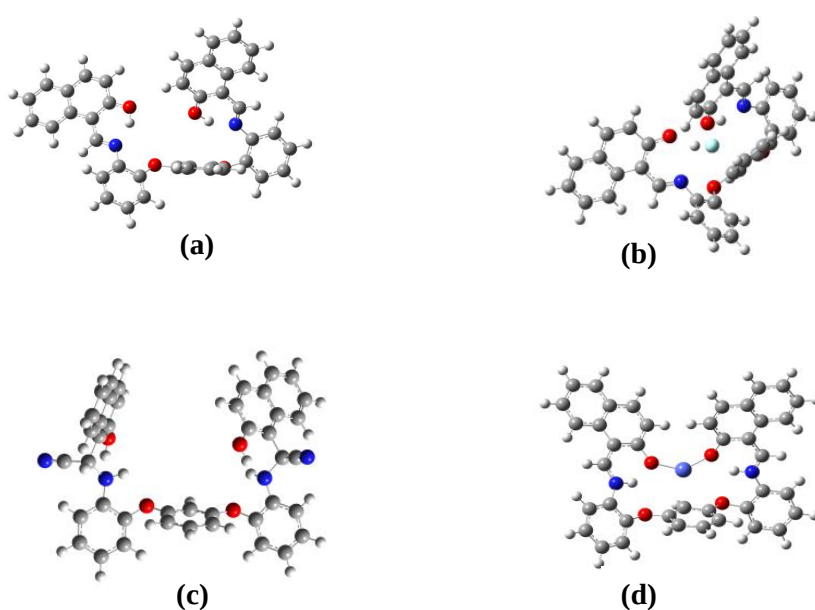


Figure 5.17 Optimized geometries of (a) **SMR-15**, (b) **SMR-15**+ F^- , (c) **SMR-15**+ CN^- , (d) **SMR-15**+ $Co(II)$

Analytical application (*Dip strip test*)

To check the practical applicability of the proposed sensor, dip strip test was performed. Ligand strips were prepared by dipping the cut filter paper into a solution of **SMR-15** receptor which gets absorbed on the filter paper and then drying the strips into the air oven maintained at $50 \pm 0.1^\circ C$. Then, these ligand strips which turned light yellow in colour were dipped into the test solutions of F^- , CN^- and $Co(II)$ to check the visual change of these strips for the selective ions. Instantaneous color change from light yellow to dark yellow was observed for F^- , light yellow to colorless for CN^- and light yellow to blue for $Co(II)$ ions, as shown in Figure 5.18. It also explained colorimetric sensing of **SMR-15** with different ions.

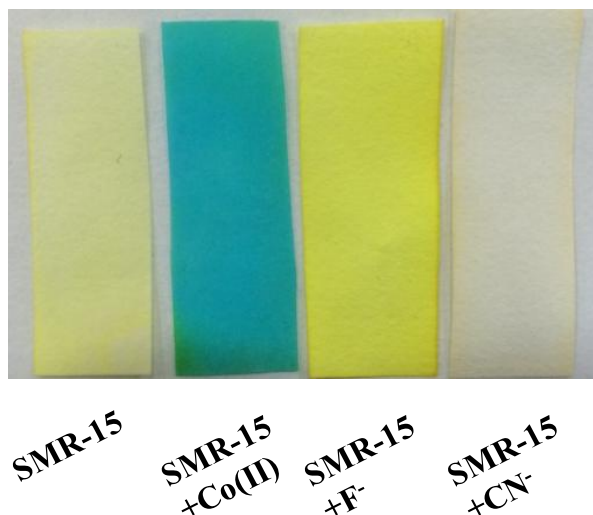


Figure 5.18 Dip strip test showing the applicability of **SMR-15** receptor in real life samples

Conclusions

In the present report, a single sensor has been developed which can be used for the detection of multiple analytes (F^- , CN^- and $Co(II)$) through different approaches. Colorimetric sensing makes the proposed receptor unique in its use as a strip sensor in various matrices.

5.2.2 Lanthanide interaction studies with SMR-15

SMR-15, a novel compound was further investigated for its interaction with various lanthanides viz. $Ce(III)$, $Dy(III)$, $Ho(III)$, $La(III)$, $Sm(III)$, $Eu(III)$, $Gd(III)$, $Tb(III)$, $Er(III)$, $Yb(III)$, $Tm(III)$, $Pr(III)$ and $Nd(III)$ by using spectrophotometric and voltammetric techniques like cyclic voltammetry and differential pulse voltammetry.

Spectrophotometric studies

UV-visible studies of **SMR-15** ($10\ \mu M$) were carried out in CH_3CN solvent system, which showed absorption bands at 320 nm, 380 nm, 440 nm and 460 nm. A broad band at 320 nm band is attributed to $n-\pi^*$ transition of ether group while 380 nm corresponds to $\pi-\pi^*$ transition. Bands at higher wavelength i.e., 440 nm and 460 nm correspond to open and closed forms of two conformations of the imine group [11]. In order to check its interaction with various lanthanides, preliminary studies were carried out with $Ce(III)$, $Dy(III)$, $Ho(III)$, $La(III)$, $Sm(III)$, $Eu(III)$, $Gd(III)$, $Tb(III)$, $Er(III)$, $Yb(III)$, $Tm(III)$, $Pr(III)$ and $Nd(III)$. It was observed that in case of $Ce(III)$ and $Dy(III)$ the absorption intensity at 320 nm band rises abruptly as shown in Figure 5.19a, while no change was observed with other lanthanide ions. In case of

pure CH₃CN solvent system, interference was also observed by Dy(III) ions but no such interference was observed in the presence of Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Nd(III) when added as interfering ion.

Selectivity

Selectivity is one of the most important features for a ligand responding to a metal ion target. So, different solvent systems with different ratios of water and acetonitrile were tried. A solvent system CH₃CN:H₂O (95:5, v/v) gave the best results and are discussed in further discussion. An acetonitrile and 5% water system was tried to obtain selectivity for a particular lanthanide ion. Various lanthanide ions were checked in a solution of **SMR-15** under identical conditions, including Ce(III), Dy(III), Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Nd(III). As observed in absorption studies (Figure 5.19 b), the enhancement of spectral intensity at 310 nm due to Ce(III) was expected over other lanthanide ions. This suggested that the novel compound **SMR-15** is an example of a Ce(III) selective probe. Sharp increase in intensity of absorption band at 320 nm, due to the interaction of Ce(III) ions with etheral group was observed. This observation was further supported by voltammetric studies as well.

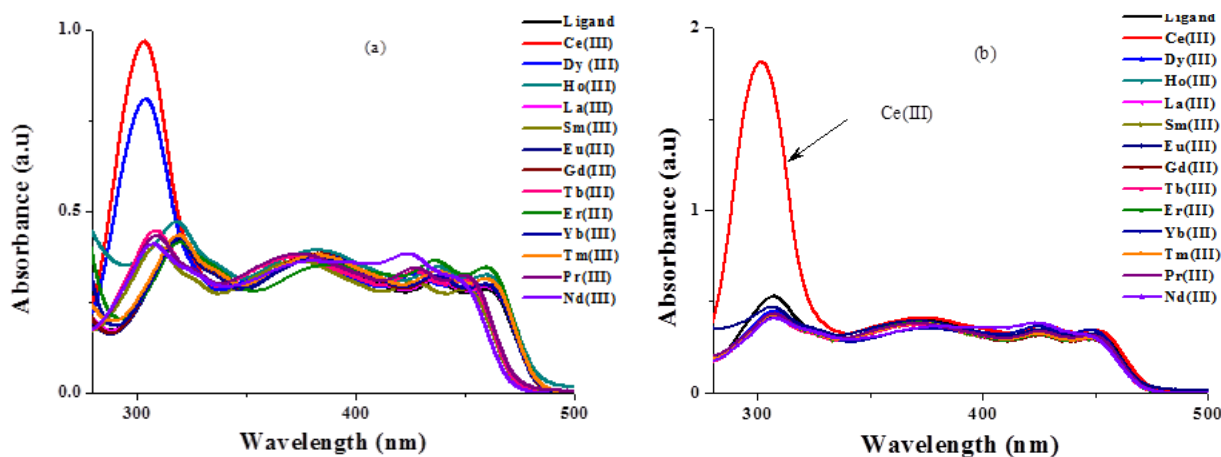


Figure 5.19 (a) Absorption spectra of **SMR-15** (10 μ M) in pure CH₃CN and (b) **SMR-15** (10 μ M) in HEPES buffered CH₃CN:H₂O (95:5, v/v) at pH 7.0 $\pm$ 0.1 in the presence of various lanthanides at GC electrode with scan rate 50 mV/sec

In order to evaluate the complete structural binding information, incremental additions of Ce(III) ions (0-40 μ M) was carried out in HEPES buffered **SMR-15** (10 μ M) using CH₃CN:H₂O (95:5, v/v) solvent system. It was observed that with increase in concentration of Ce(III) ions, there was a gradual increase in absorption intensity at the band of 300 nm with blue shift of 10 nm (Figure 5.20a) until 1:1 complexation, as observed from the calibration

graph (Figure 5.20b). Further, Job's plot analysis also confirmed 1:1 stoichiometry (Figure 5.20c). Binding constant ($5 \times 10^5 \text{ M}^{-1}$) was obtained by using Benesi- Hildebrand equation and the lower detection limit obtained was $0.05 \text{ } \mu\text{M}$. To study practical applicability of **SMR-15**, competitive experiments were carried out in the presence of 1 equivalent of Ce(III) ions mixed with 2 equivalents of each of the different lanthanide ions. No significant variations in the absorption spectra were observed in the presence of a number of interfering ions like Dy(III), Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Nd(III), as shown in Figure 5.20d.

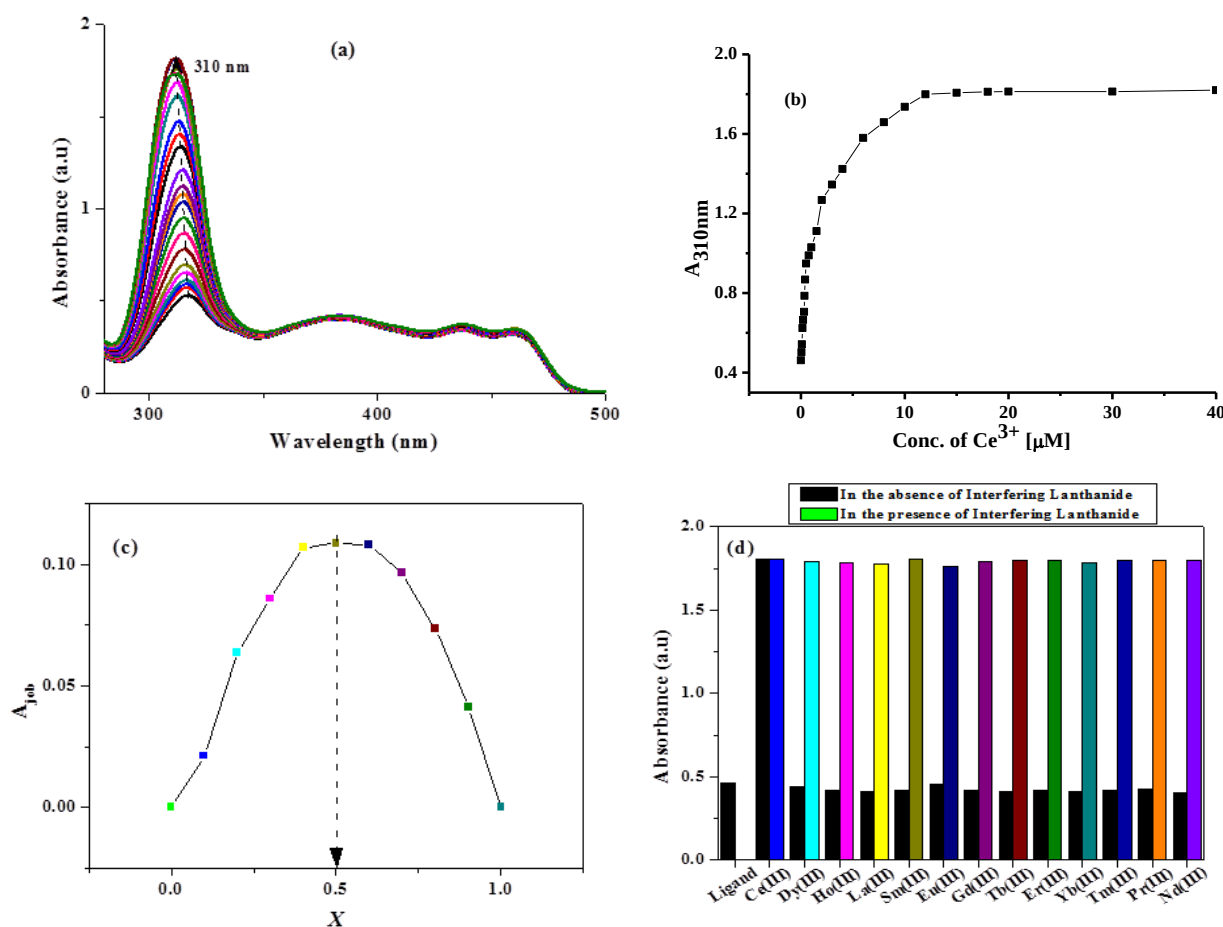


Figure 5.20 (a) Absorption spectra of (a) **SMR-15** (10 μM) in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (b) Ratiometric response of different concentrations of Ce(III) ions on **SMR-15** and at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v), (c) Job's plot analysis showing 1:1 stoichiometry, (d) Competitive studies of **SMR-15** in the presence of different lanthanides

Electrochemical studies

Electrochemical properties of **SMR-15** ligand was investigated by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) studies. The cyclic voltammograms and differential

pulse voltammograms for **SMR-15** in CH₃CN:H₂O (95:5, v/v) solution containing 0.1 M TBAPF₆ as the supporting electrolyte are shown in Figure 5.21 a-c with their respective peak currents as mentioned in Table 5.1.

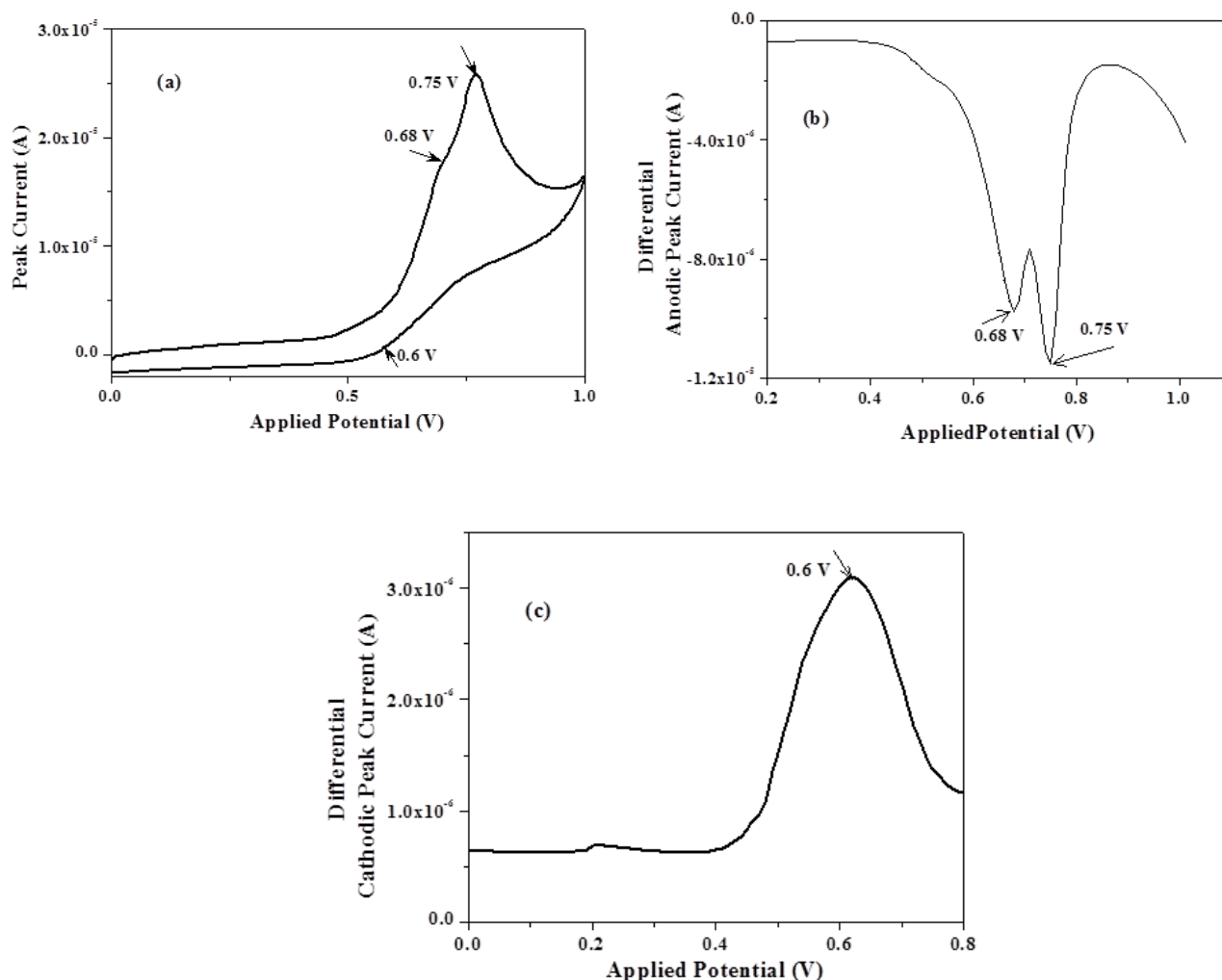


Figure 5.21 (a) Cyclic Voltammogram (b) Anodic Differential Pulse Voltammogram (c) Cathodic Differential Pulse Voltammogram of **SMR-15** (5×10^{-4} M) at pH 7.0 ± 0.1 (10 mM HEPES in CH₃CN:H₂O 95:5, v:v) using 0.1M TBAPF₆ as supporting electrolyte, scan rate 60 mV s^{-1} and GC as working electrode. Modulation amplitude for DPV: 50 mV sec^{-1}

Electrochemical response

Cyclic voltammograms obtained for **SMR-15** showed a major anodic peak at 0.75 V with a minor hump at 0.68 V, which was clearly visible in differential pulse voltammetry as shown in Figure 5.21b. **SMR-15** molecule has two functional groups (-O- & -CH=N) responsible for redox processes to take place. Cathodic peak at 0.6 V takes place due to reduction of imine group, while the anodic peak at 0.68 V might be responsible for the first step of oxidation at ether group to, which gets completely oxidized in the second step at 0.75 V. At 0.75 V, the

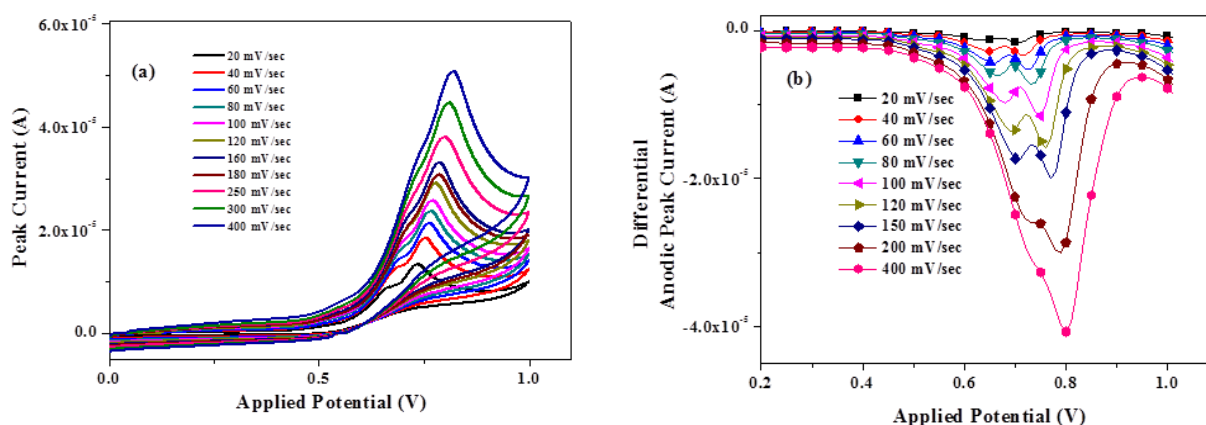
current rises so sharp that it can involve two processes simultaneously at this particular peak potential. One process involves reoxidation of the reduced imine and complete oxidation of ether group which gets partially oxidized at 0.68 V. These observations are well verified with cyclic as well differential pulse voltammetric techniques.

Table 5.1 Peak potential (V) and peak current (μA) values for **SMR-15** (5×10^{-4} M), scan rate 60mV/sec

Compound	Peak potentials (V)			Differential peak currents (A)		
	E_{pa1}	E_{pa2}	E_{pc1}	i_{pa1}	i_{pa2}	i_{pc1}
SMR-15	0.68	0.75	0.6	9.74×10^{-6}	1.14×10^{-5}	3.0×10^{-6}

Fick's law of diffusion

The effect of scan rate on peak current of **SMR-15** was studied by differential pulse voltammetry as well as cyclic voltammetry. Figure 5.22a-c shows voltammograms of **SMR-15** at glassy carbon electrode for 0.1 mM **SMR-15** and scan rate was varied from 20 to 400 mV/sec. As per Randles–Sevcik's equation, the square root of scan rate must be directly proportional to the peak current. The graph of anodic (I_{pa}) and cathodic peak current (I_{pc}) versus square root of scan rate ($v^{1/2}$) was plotted in the range from square roots of 20 to 400 mV/sec. A good linearity of the anodic/cathodic peak currents with respect to $v^{1/2}$ was obtained with correlation coefficient 0.9875 and 0.9457, respectively, as shown in Figure 5.22d. It indicated that the electrode transfer reaction was diffusion-controlled process on the electrode surface and obeyed Fick's law of diffusion.



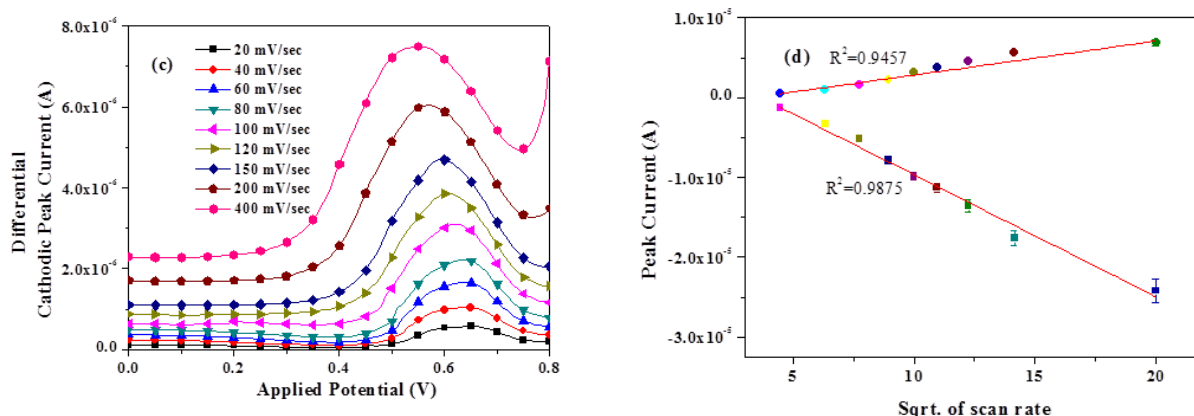


Figure 5.22 (a) Cyclic Voltammogram (b) Anodic Differential Pulse Voltammogram (c) Cathodic Differential Pulse Voltammogram of **SMR-15** (5×10^{-4} M) with scan rates 20- 400 mV/sec (d) Plot of square root of scan rate vs peak currents at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v) using 0.1M TBAPF_6 as supporting electrolyte, and GC as working electrode

Effect of concentration of electroactive species

To know electroactive nature of the compound, studies on concentration profiles were carried out by using CV and DPV techniques. Fig. 5.23a-c represents voltammograms for **SMR-15** in a wide concentration range of 1 mM to 10^{-4} mM. Increase in the peak currents was observed with increase in the concentration of the electroactive species. This is due to the reason that increase in concentration of electroactive substances makes the velocity of mass diffusion rapid and hence the redox processes occurring at electrode surface become more controlled by the electrode reactions. As seen in the plots of peak currents (anodic as well as cathodic in Figure 5.23d) there is a linear relationship of current with concentration of **SMR-15** which entitles it for a quantitative method. The calibration curves so obtained were reproducible with the RSD of 3%. The medium used for the study was $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (95:5, v/v) buffered at pH 7 with HEPES in the presence of sufficient amount of the supporting electrolyte. Presence of water in the solvent medium improved solubility of the compound.

Solvent study

To optimise the amount of H_2O in the organic solvent, cyclic voltammograms were run by selecting two aprotic solvents (dichloromethane and acetonitrile) and two protic solvents (Dimethyl formamide and Dimethyl sulfoxide) as media for preparing the solution of **SMR-15**. There were no regular trends observed by change of solvent polarity, as evidenced from peak potential values (Table 5.2 & Figure 5.24 a-c). Hence, polarity of the solvent did not cast any visible influence on the peak potentials.

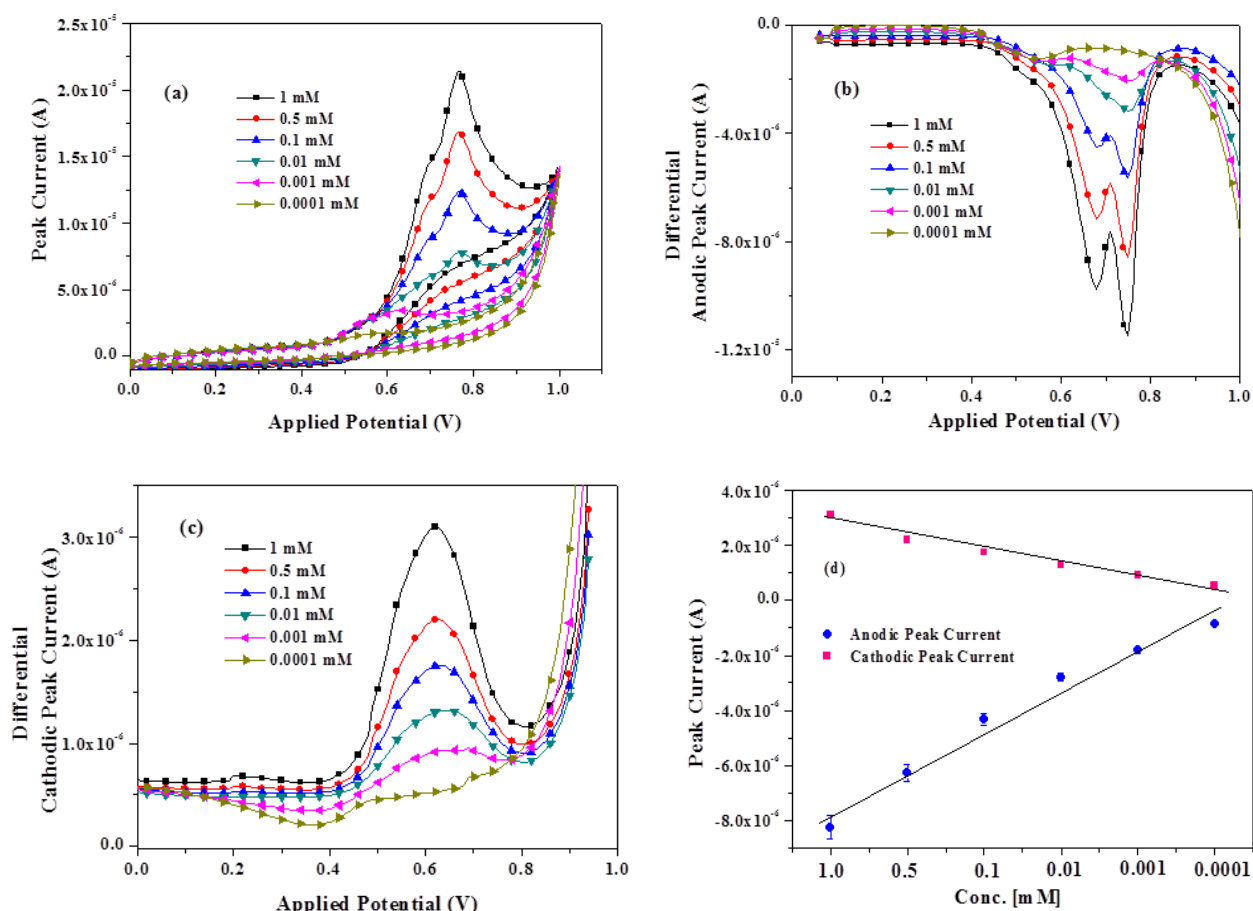
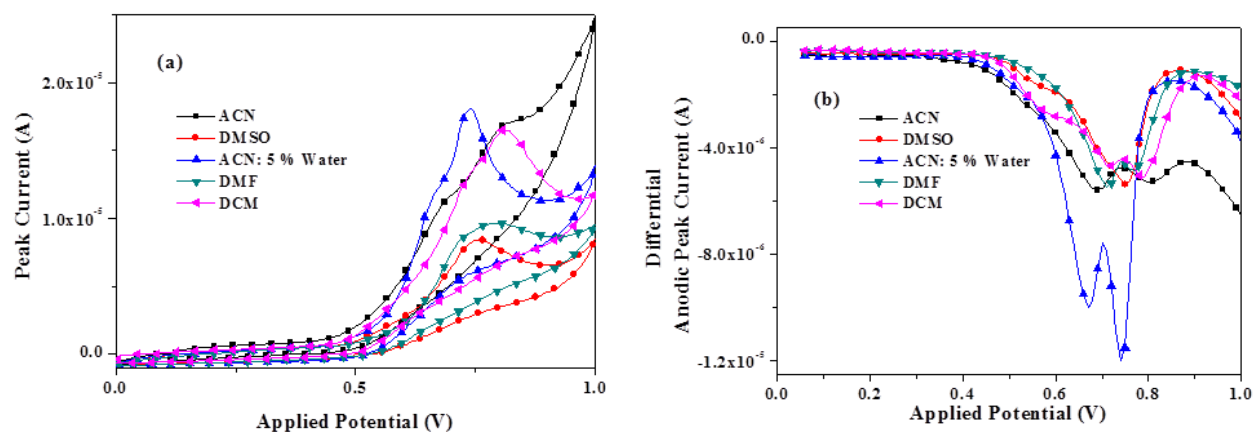


Figure 5.23 (a) Cyclic Voltammogram (b) Anodic Differential Pulse Voltammogram (c) Cathodic Differential Pulse Voltammogram of **SMR-15** at varying concentrations. (d) Plot of concentration of **SMR-15** vs peak currents at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v) using 0.1M TBAPF_6 as supporting electrolyte, and GC as working electrode. (RSD = $\pm 3\%$)



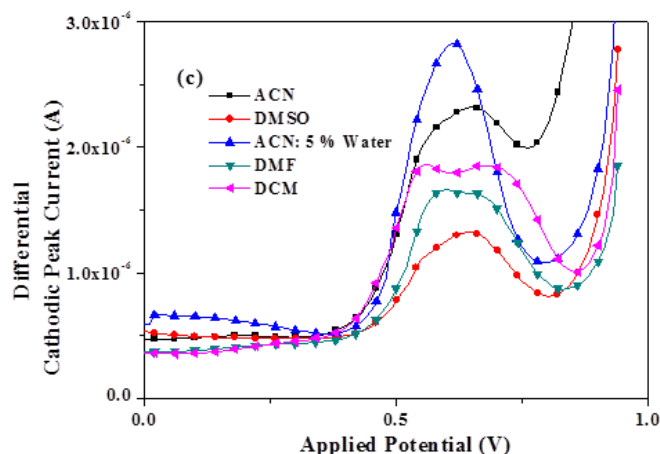


Figure 5.24 (a) Cyclic Voltammogram (b) Anodic Differential Pulse Voltammogram (c) Cathodic Differential Pulse Voltammogram of **SMR-15** in different solvent systems using 0.1M TBAPF₆ as supporting electrolyte, and GC as working electrode

Table 5.2 Peak potentials (V) for **SMR-15** in different solvent systems

Solvent Used	Dipole moment (D)	E _{pa1} (V)	E _{pa2} (V)	E _{pc1} (V)	E _{pc2} (V)
Dimethylformamide (DMF)	3.86	0.71	0.76	0.58	0.67
Dimethyl Sulfoxide (DMSO)	3.96	0.74	---	0.63	---
Dichloromethane (DCM)	1.60	0.72	0.78	0.55	0.70
Acetonitrile (CH ₃ CN)	3.92	0.69	0.81	0.63	---
Acetonitrile:Water (95:5, v:v)	--	0.68	0.75	0.60	---

Voltammetric detection of lanthanides

Voltammetric studies were performed on **SMR-15** to evaluate its tendency to complex with lanthanide ions so that it could be projected as an ionophore suitable for rare earth elements determination by simple voltammetric methods. Based on the studies of **SMR-15** in presence of lanthanides, each taken separately, it showed reproducible and stable complexation behaviour with Ce(III) ions. So, the detailed investigations were carried out with cerium ions. Cyclic and differential pulse voltammograms were drawn for **SMR-15** with and without Ce(III) ions (Figure 5.25a-c). With incremental addition of Ce(III) ions, anodic peak at 0.68 V due to lone pair of electrons on the ethereal oxygen gets completely diminished. Another

anodic peak at 0.75 V which was due to complete oxidation of ether group and re-oxidation of reduced imine group; gets reduced in current.

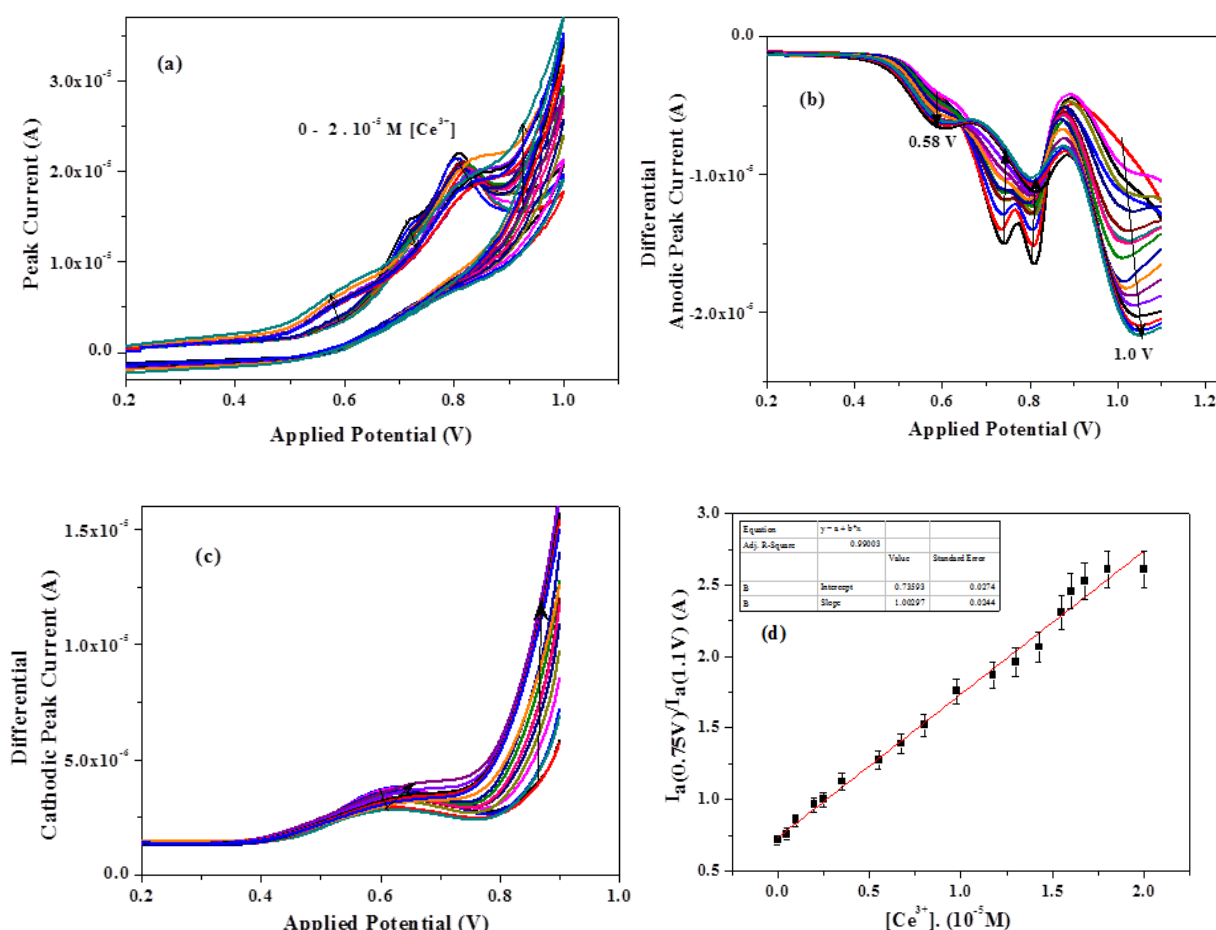


Figure 5.25 (a) Cyclic Voltammogram (b) Anodic Differential Pulse Voltammogram (c) Cathodic Differential Pulse Voltammogram of **SMR-15** with incremental addition of Ce(III) ions. (d) Calibration plot of peak currents vs. Ce(III) concentration at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v) using 0.1M TBAPF_6 as supporting electrolyte, and GC as working electrode

These observations prove that oxygen atoms of ether group are playing an important role in complexation with Ce(III) ions as electron donating group and were no longer available for oxidation of **SMR-15** as seen by quenching of anodic peak at 0.75 V in presence of Ce(III) ions. In case of cathodic peak (due to reduction of imine group) at 0.6 V, there was hardly any decrease in current leading to the confirmation that there was no involvement of imine group in binding in the complex. With Ce(III) complexation, new anodic peaks at 0.58 V and 1.0 V were observed which increased with increase in concentration of cerium ions till 1 equivalent, as shown in cyclic and differential pulse voltammograms (Figure 5.25 a and b). These peaks might be due to complexation of cerium with **SMR-15**.

Experimental studies for **SMR-15** were conducted for the measurement of currents at the peak potential values for different concentrations of cerium ions added to the receptor solution (2×10^{-5} M) and plots were drawn between cerium concentrations and the current values, as shown in Figure 5.25d. The calibration studies were repeated at least three times to see reproducibility of the proposed method. The lowest detection limit obtained from calibration curve is 5×10^{-7} M ($\pm 2\%$) with $R^2 = 0.99$ and corresponding slope and intercept shown in Figure 5.25d.

Cerium ion selectivity

Complexation of the ionophore **SMR-15** with metal ions can be understood from the concept of host-guest chemistry. Holding of metal ion in the pseudocavity created from the suitable orientation of the ionophore is influenced by two important factors: steric factor (cavity size) and electronic factor (availability of heteroatoms for electron sharing with the guest metal ion). An ideal combination of these two factors would enhance selectivity of the receptor for a given metal ion as a “Guest”. From the experimental results of voltammetric studies of **SMR-15** in presence of different lanthanide ions, an exceptionally good response of **SMR-15** was observed with cerium ions in comparison to all other lanthanide ions. The additional anodic peak observed for **SMR-15** in presence of Ce(III) (Fig. 5.26) at 0.58 V and 1.0 V are exclusive to Ce(III) ions and not observed for any other lanthanide ion. This special feature of **SMR-15** makes it selective for Ce(III) ions in presence of all other lanthanides taken in twice the concentration to that of the primary ion i.e. cerium. The probable reason for selectivity of **SMR-15** for cerium ions might be the size of cavity to just suitable for accommodating Ce(III) ions (ionic radius $1.03 \text{ \AA}$) while it might be too large for all other lanthanide ions which have much smaller ionic radii and would form too loosely held complexes. The other possible reason of electronic nature can be ruled out easily as all the lanthanides carry more or less same electronic charge over them. Presence of other lanthanides (Dy(III), Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Nd(III)) have also been studied and results indicate selectivity for Ce(III) ions only. Interference studies carried out by using 2 equivalents of interfering ions individually mixed with 1 equivalent of cerium also showed no interference as seen in Table 5.3. Voltammogram was run by adding the 1 equivalent of all the interfering lanthanides (Dy(III), Ho(III), La(III), Sm(III), Eu(III), Gd(III), Tb(III), Er(III), Yb(III), Tm(III), Pr(III) and Nd(III)), simultaneously and then adding 1 equivalent of cerium ion.

Table 5.3 Peak potential (V) values for **SMR-15** alone and with different lanthanides in differential pulse voltammograms

Lanthanide studied	E _{pa1} (V)	E _{pa2} (V)	E _{pa3} (V)	E _{pa4} (V)	E _{pc} (V)
SMR-15	0.68	0.75 (16 μ A)	--	--	0.60
Ce(III)	--	9 μ A	0.58	1.0	Flattens
Dy(III)	0.67	0.73	--	--	0.58
Ho(III)	0.64	0.72	--	--	0.59
La(III)	0.67	0.74	--	--	0.61
Sm(III)	0.66	0.75	--	--	0.60
Eu(III)	0.68	0.71	--	--	0.61
Gd(III)	0.65	0.72	--	--	0.59
Tb(III)	0.69	0.77	--	--	0.60
Er(III)	0.68	0.76	--	--	0.61
Yb(III)	0.66	0.75	--	--	0.59
Tm(III)	0.68	0.74	--	--	0.58
Nd(III))	0.69	0.75	--	--	0.59
Pr(III)	0.67	0.77	--	--	0.60

As observed from Figure 5.26, no interference was caused by all the lanthanides and the receptor responds selectively to cerium ions only, which makes **SMR-15** as a potential sensor for cerium ions only even in the presence of all other rare earth metals.

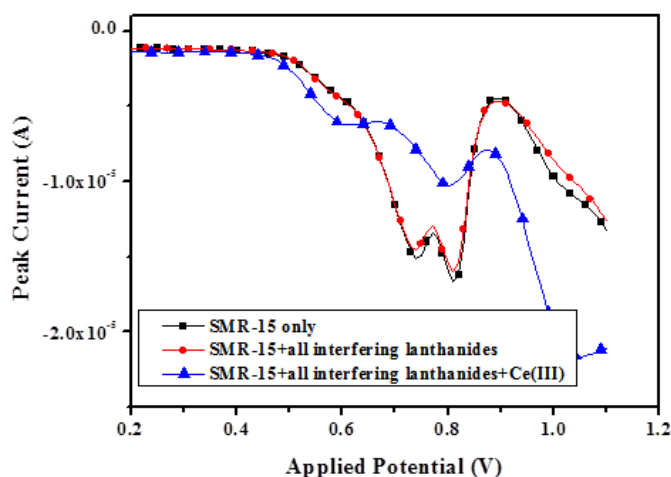


Figure 5.26 Anodic Differential Pulse Voltammograms of **SMR-15** showing selectivity for cerium ion only at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 95:5, v:v) using 0.1M TBAPF_6 as supporting electrolyte, and GC as working electrode

Computational studies

Geometry of the receptor **SMR-15** was fully optimized by using Gaussian 03W software. Basis sets B3LYP-6-31G were used and optimization was done in gaseous phase. Receptor **SMR-15**

exhibits a property of proton exchange due to the presence of hetero atoms in its domain. So, **SMR-15** has KETO and ENOL configurations which are shown in Figure 5.27.

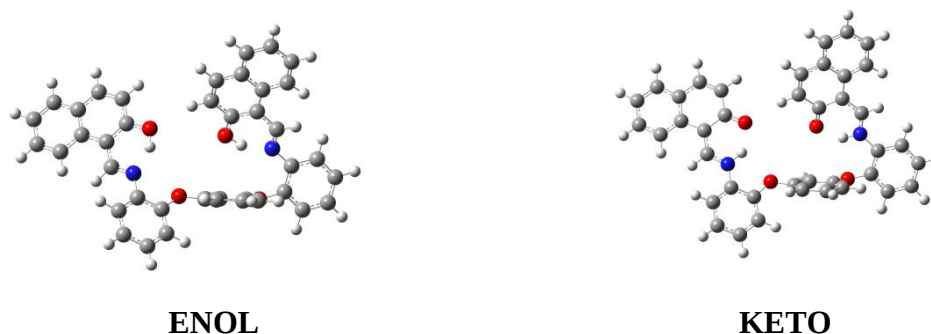


Figure 5.27 Optimized geometries of different conformations of **SMR-15** by using DFT/B3LYP/6-31G method

Molecular orbital diagrams of KETO-ENOL conformers show the intramolecular charge transfer in the molecule as shown in Figure 5.28. Both the configurations have equal probability of binding of any lanthanide ion being studied. As observed from the spectrophotometric and voltammetric studies, involvement of only ethereal group is taking place in the bonding. Imine linkages are providing reasonable rigidity to the molecule to hold the guest metal ion.

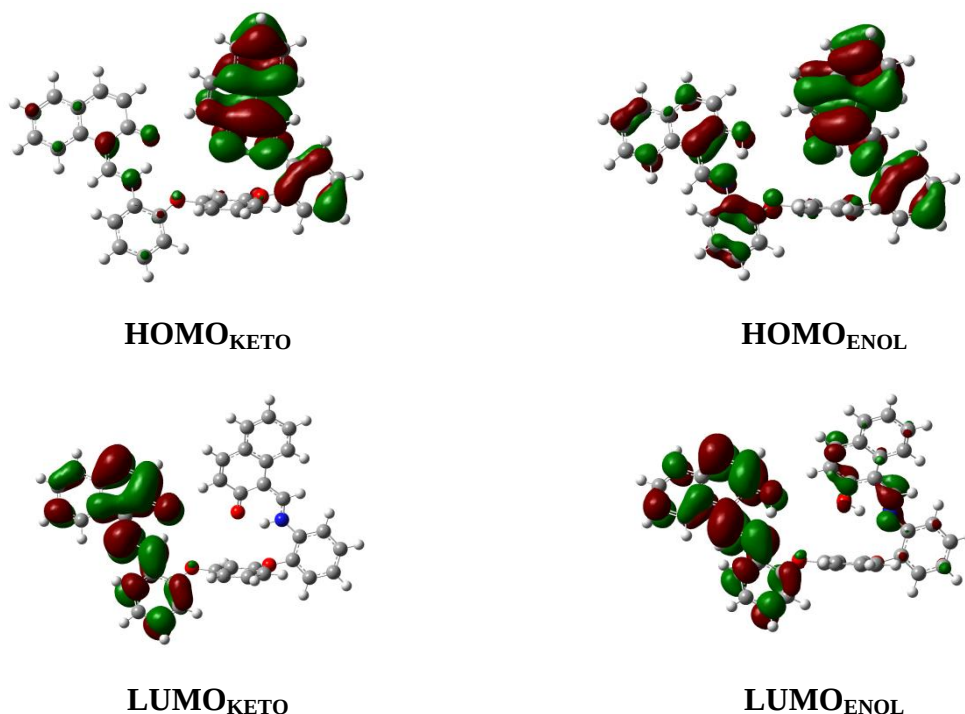


Figure 5.28 Molecular orbital diagrams of KETO-ENOL conformations of **SMR-15** receptor

In spite of the modern computational techniques like QM/MM methods as well as fast computers which have resulted in immense progresses in the field of computational studies, calculations of lanthanide complexes are still at the limit of computational feasibility. Theoretical studies of d-transition metal elements is well established for understanding structures and mechanisms in organic chemistry and in organometallic chemistry [12-14], the theoretical studies of 4f elements have been considered difficult due to the presence of open shell 4f electrons. Another difficulty in the computational study of lanthanides complexes is related to their high coordination number.

For this reason, it is of great interest to develop a calculation level which allows computational studies of large size systems for the entire lanthanide family. So, due to limitations of the software package, studies of the complexed molecule could not be achieved in solvent phase by Gaussian 03W software.

Conclusions

A new sensitive and selective chemosensor has been developed for the determination of cerium ions. The proposed sensor works well spectrophotometrically and is electroactive as well. Hence, it has been used as an electrochemical sensor too. Detection limit obtained by this sensor is 5×10^{-7} M without any interference which makes it a potent sensor for cerium detection.

5.2.3 Ion-recognition studies of SMR-16

A novel compound **SMR-16** owns dual-function groups (ether and imine), it is a potential sensor for some transition metal ions through selective complexation using hetero atoms (oxygen of ether and nitrogen of imine linkages). Spectrophotometric and voltammetric studies of **SMR-16** are as discussed below:

Spectrophotometric studies

SMR-16 exists in two conformations I and II depending upon the type of solvent used. A polar solvent would facilitate intramolecular H-bonding and conformation I results while for non-polar solvent conformation II is likely to exist. Absorption spectra of **SMR-16** were recorded in different solvents and are displayed in Figure 5.29. **SMR-16** exhibits two main absorption bands. A broad band at ≈ 380 nm with a shoulder at ≈ 440 nm.

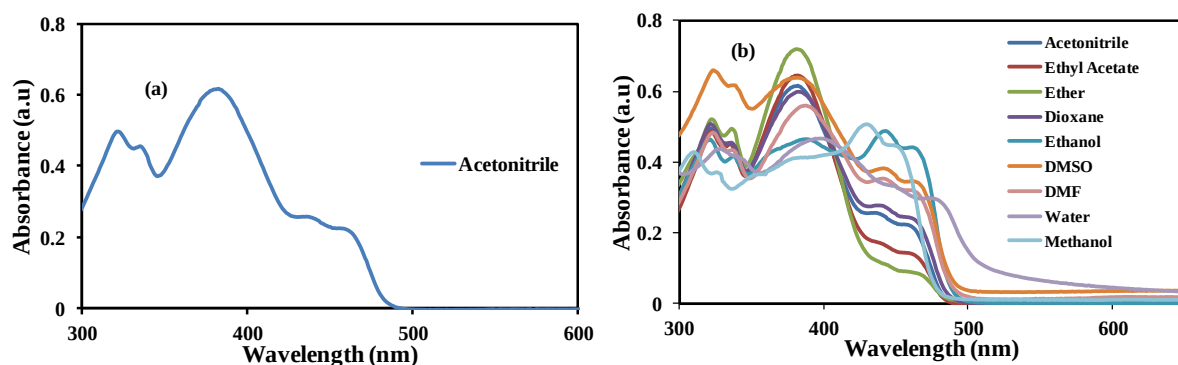
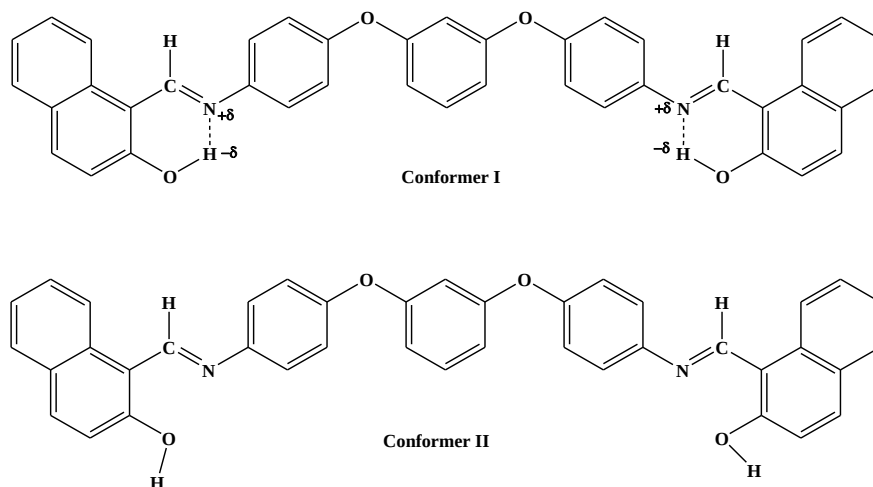


Figure 5.29 Effect of solvent polarity on the UV-visible absorption spectra of chemosensor **SMR-16**, showing solvatochromism phenomena

In parallelism to the spectral features of the parent molecule 1-hydroxy 2-naphthaldehyde (HNAP) [15] and other similar reported systems [16–18], the ≈ 440 nm absorption band is assigned to the intramolecularly hydrogen bonded lowest energy ground state conformer, i.e. conformer **I** (Scheme 5.3). The higher energy band (≈ 380 nm) may be due to the open conformer (conformer **II** in Scheme 5.3). Conformer **I** absorbing in the lower energy region is an affirmation of the extra degree of stabilization due to intramolecularly hydrogen bonded interaction. Additionally, it is notable at this stage that the absorption band for the conformer **I** ($\lambda_{\text{abs}} \approx 440$ nm) gains a greater intensity compared to that for the open form (i.e. conformer **II** in Scheme 5.3; $\lambda_{\text{abs}} \approx 380$ nm) in polar solvents, while the reverse pattern is noted in nonpolar solvent (Figure 5.29). This is not surprising since the partially charged species (Conformer I) is expected to be more stabilized and hence more populated in polar solvents than in nonpolar solvents.



Scheme 5.3 Schematic of different conformers of **SMR-16**.

Transition metal ion-induced modulation of absorption properties of SMR-16

Absorption spectrum of the ligand indicates a λ_{max} at 380 nm besides a smaller band at 320 nm in acetonitrile medium. On addition of 50 equivalents of each metal ion (Al(III), Na(I), Cu(II), Ni(II), Ag(I), K(I), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Hg(II), Fe(II)) the λ_{max} absorbance intensity decreases to some extent. The decreases in absorbance being different to different metals indicated that the metals are forming complex with the ligand to different extents. Changes in absorbance on addition of Hg(II) and Fe(II) were irregular owing to their precipitation. Very little changes in absorbances were noticed in case of Ca(II) indicating a small extent of formation of the complex. However, the decrease in absorbance at 380 nm λ_{max} of ligand does indicate removal of small amount of ligand as complex and hence decrease in absorbance. On addition of 50 equivalents of metals like Cu(II), the λ_{max} at 380 nm of the ligand is quenched and simultaneously resulting in a new peak at 420 nm due to complexed ligand as shown in Figure 5.30a.

In order to evaluate the complete structural behaviour of **SMR-16** towards Cu(II), titration of **SMR-16** was performed with different concentrations of the metal ion. On the addition of increasing concentration of Cu(II) (0-74 μM) the band at 380 nm gets completely quenched and simultaneously a new band at 420 nm increases in intensity with isobestic point at 400 nm (Figure 5.30b). The absorption ratio at 420 nm and 380 nm varied from 0.464 to 1.533, indicating a 3.30 fold change in absorption ratio for **SMR-16**.

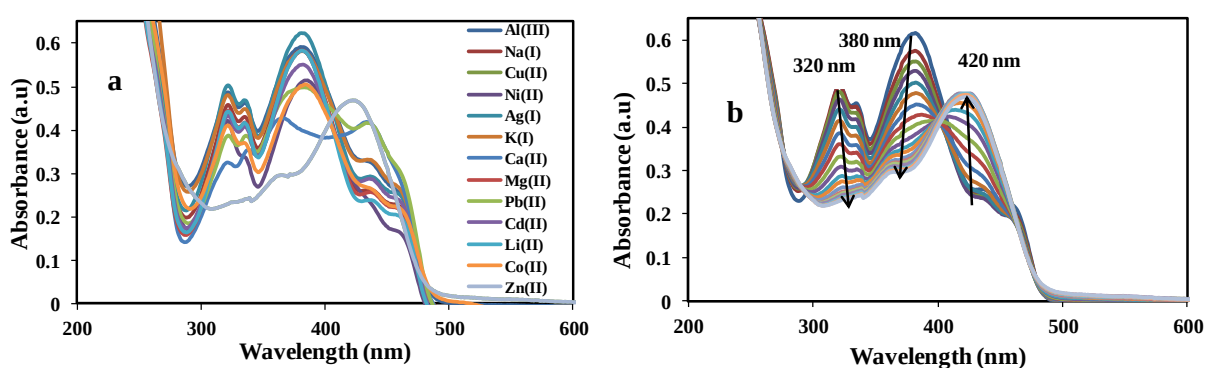


Figure 5.30 (a) Absorption spectra of **SMR-16** in CH_3CN in the presence of different metal ions (50 equivalents) (b) Absorption spectra of **SMR-16** upon addition of increasing amounts of Cu(II) in CH_3CN solution

Further, to get the practical applicability of the receptor **SMR-16**, all studies were performed in HEPES buffered $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (1:1, v/v) maintained at $\text{pH}=7.0\pm0.1$ at 25°C . **SMR-16** showed a

visual color change from dark-yellow to colorless on addition of stoichiometric molar ratio of Cu(II).

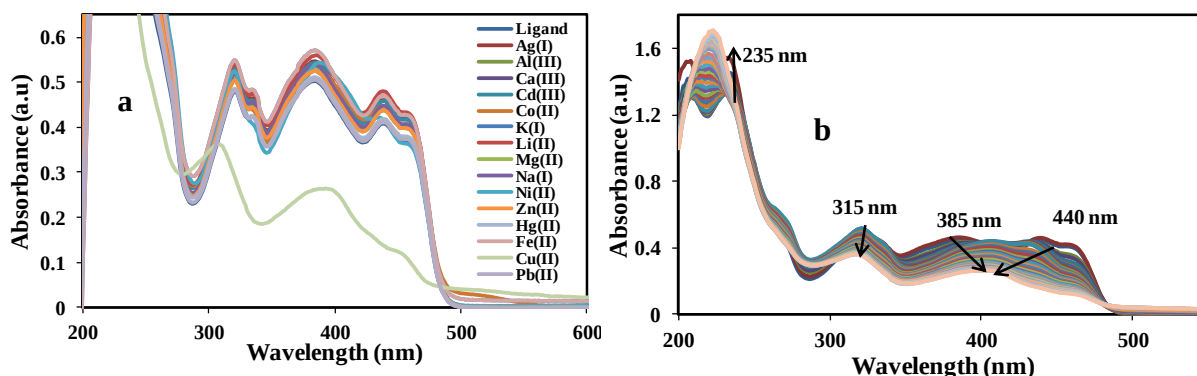


Figure 5.31 (a) Absorption spectra of **SMR-16** in HEPES buffered CH₃CN:H₂O (1:1, v/v) in the presence of different metal ions (50 equivalents) (b) Absorption spectra of **SMR-16** upon addition of increasing amounts of Cu(II) in HEPES buffered CH₃CN:H₂O (1:1, v/v)

Receptor showed absorption bands at 235 nm, 315 nm, 385 nm and 440 nm (Figure 5.31a). Upon gradual addition of Cu(II) ions in increasing concentration (0–25 equivalents), a band of **SMR-16** at 235 nm showed a significant increase in the initial absorption intensity, while there was a gradual decrease in intensity at 315 nm. The absorption band at 385 nm gets red shifted by 15 nm and the band at 440 nm gets blue shifted by 40 nm to be merged at 400 nm with lower absorbance intensity (Figure 5.31b). Further, the decrease in absorbance at 400 nm shows linear relationship with Cu(II) concentration ($R^2=0.9668$) and a very low detection limit of 50 nM. Using the Benesi-Hildebrand [19] methodology, calculation of association constant (K) was done.

$$\frac{1}{(A - A_0)} = \frac{1}{(A_\infty - A_0)K[Cu^{2+}]} + \frac{1}{(A_\infty - A_0)}$$

Where,

A_0 = Absorbance of free receptor

A = Absorbance of receptor during titration with metal ion

A_∞ = Absorbance of receptor after titration.

K = Association constant

From Benesi-Hildebrand equation, computed association constant (K) from UV data is $K = 2.0 \times 10^5 \text{ M}^{-1}$. Interestingly, the addition of other metal cations like Al(III), Na(I), Ni(II), Ag(I), K(I), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Hg(II), and Fe(II) did not alter the initial absorption spectra of the receptor significantly. From these UV-visible studies, it is

clear that receptor shows a very high selective binding affinity in the ground state for Cu(II) ions only even in the presence of other metal ions (Figure 5.32a). Ligand-metal binding analysis using Job's plots suggested that a 1:1 stoichiometry is the most likely binding mode between **SMR-16** and Cu(II) (Figure 5.32b). To achieve this 1:1 stoichiometry, carbonyl O and imino N atoms of the compound are the most likely binding sites for Cu(II).

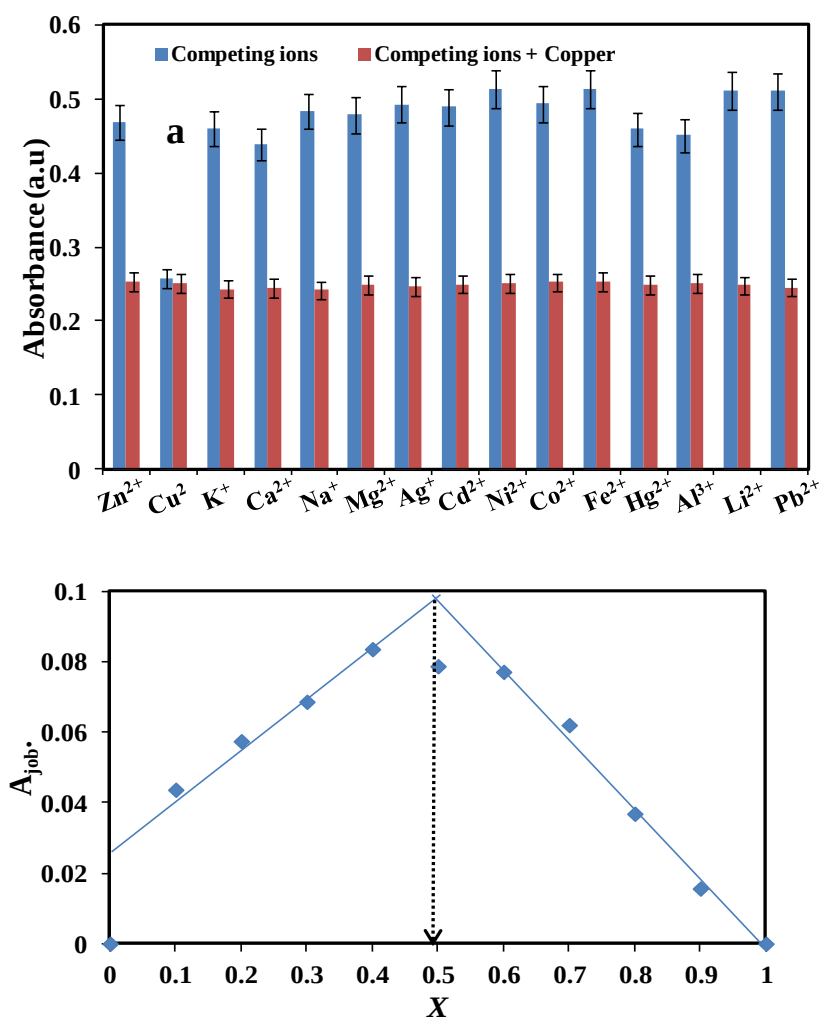


Figure 5.32 (a) Interference studies of **SMR-16** in HEPES buffered CH₃CN:H₂O (1:1, v/v) in the presence of different metal ions (50 equivalents) **(b)** Job's plot analysis of **SMR-16**

Detection of water content in solvent system

Determination of traces of water in organic solvents has always attracted attention of researchers, as its presence may influence the course of reaction in organic solvent media. Preference of solubility of the **SMR-16**-Cu(II) complex in aqueous medium can be used to track traces of water in acetonitrile medium.

Water titration i.e. titration of **SMR-16**-Cu(II) complex dissolved in pure acetonitrile was carried out with water as titrant. Small aliquots of water were added in the complex and absorbance was recorded at 440 nm to determine the effect of water content on the complex formed in pure acetonitrile. Gradual decrease in absorbance of the $\lambda_{\text{max}} = 440$ nm of complex was observed, as shown in Fig. 5.33a, with the color intensity diminishing from dark yellow to light yellow and ultimately changing of colorless solution. Although the decrease in absorbance was not linear but the trend could be divided in two parts; initial sharp linear fall in absorbance on addition of 0.0 to 0.2 μL followed by relatively slower change in absorbance on the addition of 0.5-1.5 μL of water to **SMR-16**- Cu(II) solution in 3 mL of acetonitrile medium. The observed change in absorbance could be due to greater solubility of the complex in aqueous medium as compared to that in acetonitrile medium. Addition of a very small amount of water, as little as 0.05 μL in 3 mL of the acetonitrile complex resulted in measurable change in absorbance of 1.095 unit. Ratiometric sensing of water content in acetonitrile media proves the detection limit of water content in medium as low as 0.06 ppb (Figure 5.33b). Hence, this sensor can be used as an indicator for the water content determination in non-aqueous media.

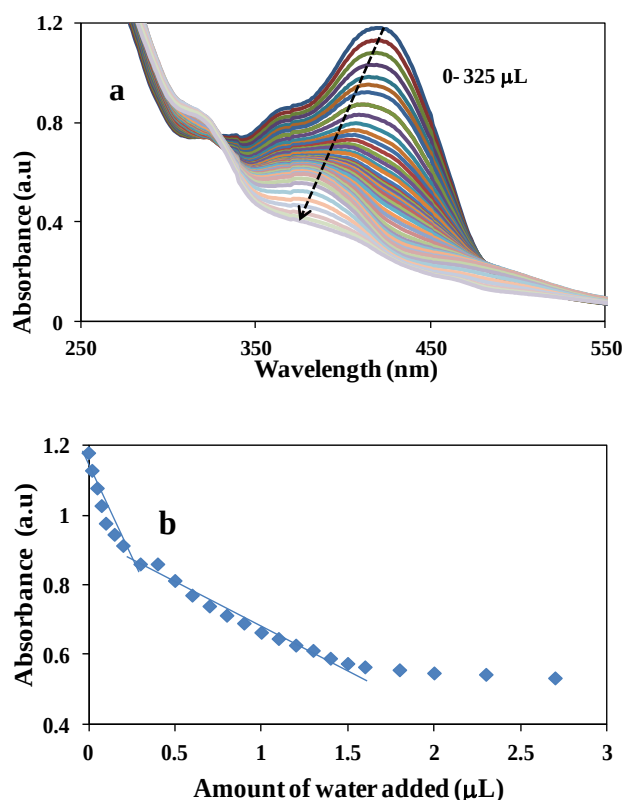


Figure 5.33 (a) Absorption spectra of **SMR-16**- Cu(II) in CH₃CN (b) Ratiometric response of different amount of water (0-3 μL) on **SMR-16**-Cu(II) (60 μM) in acetonitrile medium

Reversibility of water titration

The reversibility of Cu(II) binding to **SMR-16** in aqueous solution system is a very crucial parameter for applications. Hence, the interaction between **SMR-16** and Cu(II) was investigated by introducing EDTA into the aqueous solution containing **SMR-16**-Cu(II) complex (generated in-situ by taking ligand and metal ion in 1:1 ratio) (Figure 5.34). Absorbance of **SMR-16** restored back to its original value immediately on addition of 1 equivalent of EDTA to **SMR-16**- Cu(II) complex. Further additions of Cu(II) in the solution, returned back the absorbance of **SMR-16**- Cu(II) complex at 440 nm with appearance of yellow color in the solution, as the additional Cu(II) solution would form complex with EDTA (being more stable) restoring back the **SMR-16**-Cu(II) complex. These results confirmed that Cu(II) and EDTA recognition processes were reversible and sensor **SMR-16** is recyclable and reusable; simply through treatment with a proper reagent, such as EDTA in our experiment. The principle of sensor regeneration is based on the competitive complex equilibria. Apparently, EDTA is a stronger competitor for Cu(II) than **SMR-16**. Therefore, the presented chemosensor carrier will conveniently have a promising potential for practical applications in the environmental protection field.

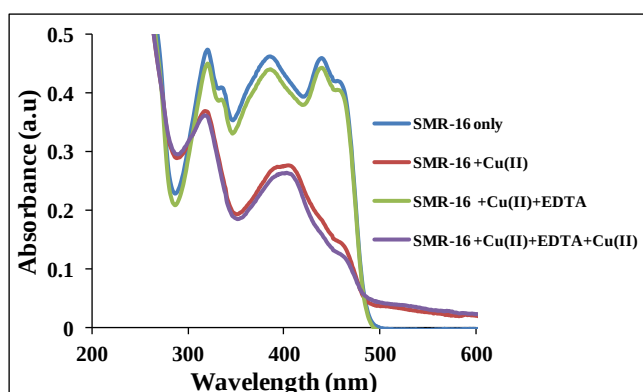


Figure 5.34 Reversibility of **SMR-16** (20 μ M) binding with Cu(II) in aqueous solution while adding Cu(II) (1 equivalent to **SMR-16**) and EDTA (1 equivalent to Cu(II)) to the **SMR-16** solution

Spectrofluorimetric studies

To obtain an insight into the fluorescent properties, the receptor was excited at 300 nm which resulted in broad emission band centered at 490 nm, which is attributed to the ESIPT process belonging to the hydroxyl naphthyl units. Emission spectra of **SMR-16** were recorded in different solvents and studied the solvatofluorism phenomena (Figure 5.35). Chemosensor shows an emission in the range 487-500 nm in non-polar solvents as well as polar aprotic

solvents viz., Dioxane, Ethyl Acetate, CH₃CN, Diethyl Ether, DMSO, DMF which is due to the ESIPT mechanism, while in case of polar protic solvents (such as H₂O, Ethanol and Methanol), the ESIPT band is inhibited and replaced by a normal emission at around 420 nm.

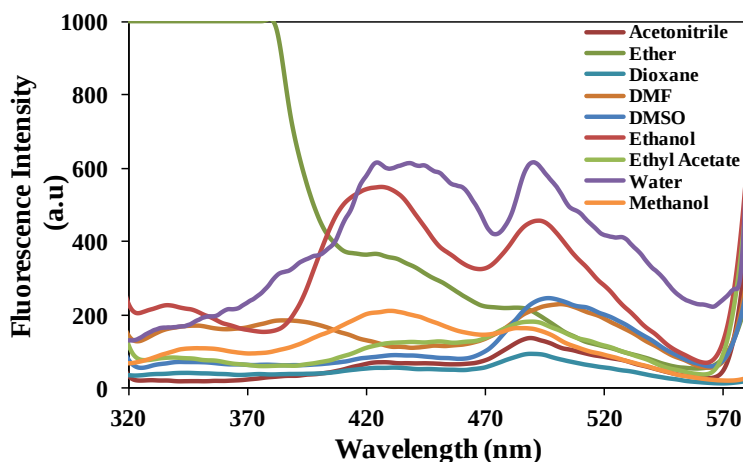


Figure 5.35 Effect of solvent polarity on the fluorescence intensity of chemosensor **SMR-16**, showing solvatofluorism phenomenon

The cation recognition behavior of **SMR-16** was evaluated from the changes in fluorescence intensity of receptor upon addition of a particular metal salt. On addition of 50 μ M solution of Cu(II) to the 10 μ M solution of **SMR-16**, the band at 490 nm got quenched and a new band emerged at $\lambda_{\text{max}}=450$ nm with isobestic point at 470 nm. Under the same conditions (as used for Cu(II)), the fluorescence response of **SMR-16** was tested for other metal ions such as Na(I), Ag(I), K(I), Ni(II), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Al(III). No significant change in fluorescence of **SMR-16** occurred in the presence of any of these tested metal ions. In the titration of **SMR-16** with Cu(II), the emission band at 490 nm was quenched at 1 equivalent of Cu(II) ions and on further addition of Cu(II) ions, a new blue-shifted emission band at 450 nm was observed. Intensity of the band at 450 nm increased only upto 2 times on addition of 10.0 equivalents of the concentration of Cu(II) ions (Figure 5.36a &b).

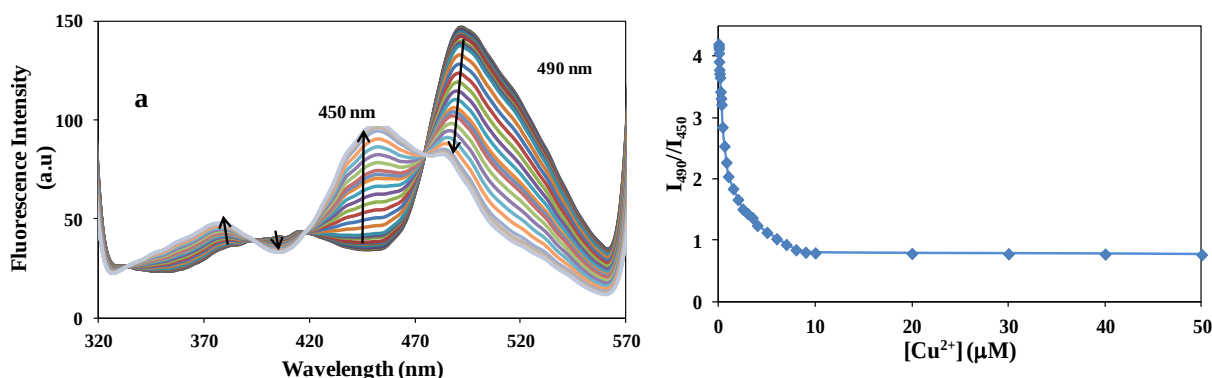


Figure 5.36 (a) Fluorescence spectra of **SMR-16** on addition of Cu(II) ions, λ_{ex} 300 nm, Slit

width (Ex/Em = 10 nm) **(b)** Ratiometric response of different concentrations of Cu(II) ions on **SMR-16** in HEPES buffered CH₃CN:H₂O (1:1, v/v)

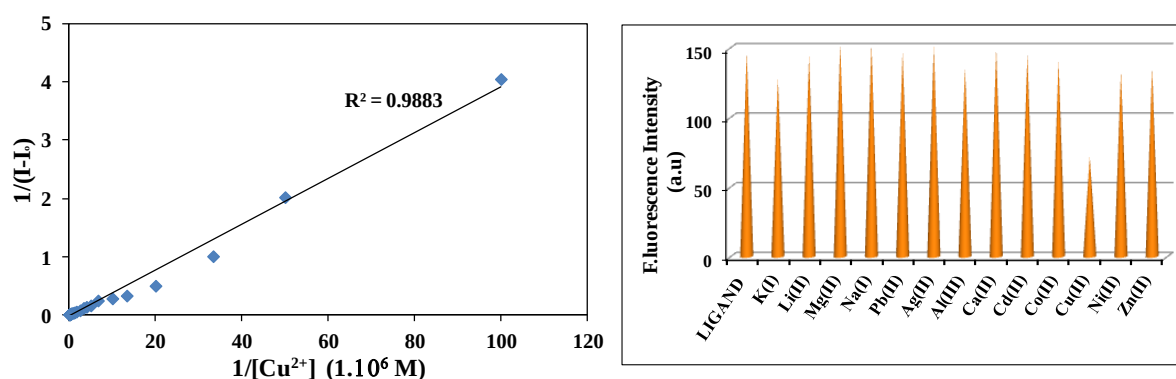


Figure 5.37 (a) Benesi–Hildebrand plot (fluorescent intensity at 450 nm) of **SMR-16** assuming 1:1 binding stoichiometry with Cu(II) **(b)** Interference studies in the presence of 50 equivalents of interfering ion and equal concentration of copper ions

Linear fitting of the fluorescence titration profiles using Benesi–Hildebrand plot, based on a 1:1 binding mode was also examined. Plotting of $1/(I - I_0)$ versus $1/[Cu(II)]$ showed a linear relationship (correlation coefficient is 0.9883) (Figure 5.37a), which also strongly supported the 1:1 binding stoichiometry of **SMR-16** and Cu(II). Interference studies supported the selectivity of **SMR-16** for copper ions only as shown in Figure 5.37b.

Electrochemical studies

Voltammograms of **SMR-16** were recorded at $25 \pm 0.2^\circ C$ in HEPES buffered CH₃CN:H₂O (1:1, v/v) medium with ionic strength was maintained at 0.1 mol. L⁻¹ and using n-Bu₄NClO₄ as supporting electrolyte. The differential pulse voltammograms are given in Figure 5.38. Voltammetric study of **SMR-16** from 0 to 1.5 V showed a major anodic peak at 1.05 V and a cathodic peak at 0.95 V along with small peaks at 1.35 V (anodic peak) and 0.5 V (cathodic peak) due to intermediate stage. The cathodic peak at 0.95 V corresponds to the reduction of the imine moiety, which gets reoxidized at 1.05 V in the next sweep, the second peak is attributed to the reduction of the imine moiety. Peaks at 0.5 V and 1.35 V may be corresponding to the intermediates probably being formed during the redox cycle of imine-amine formation and then back to imine after re-oxidation process.

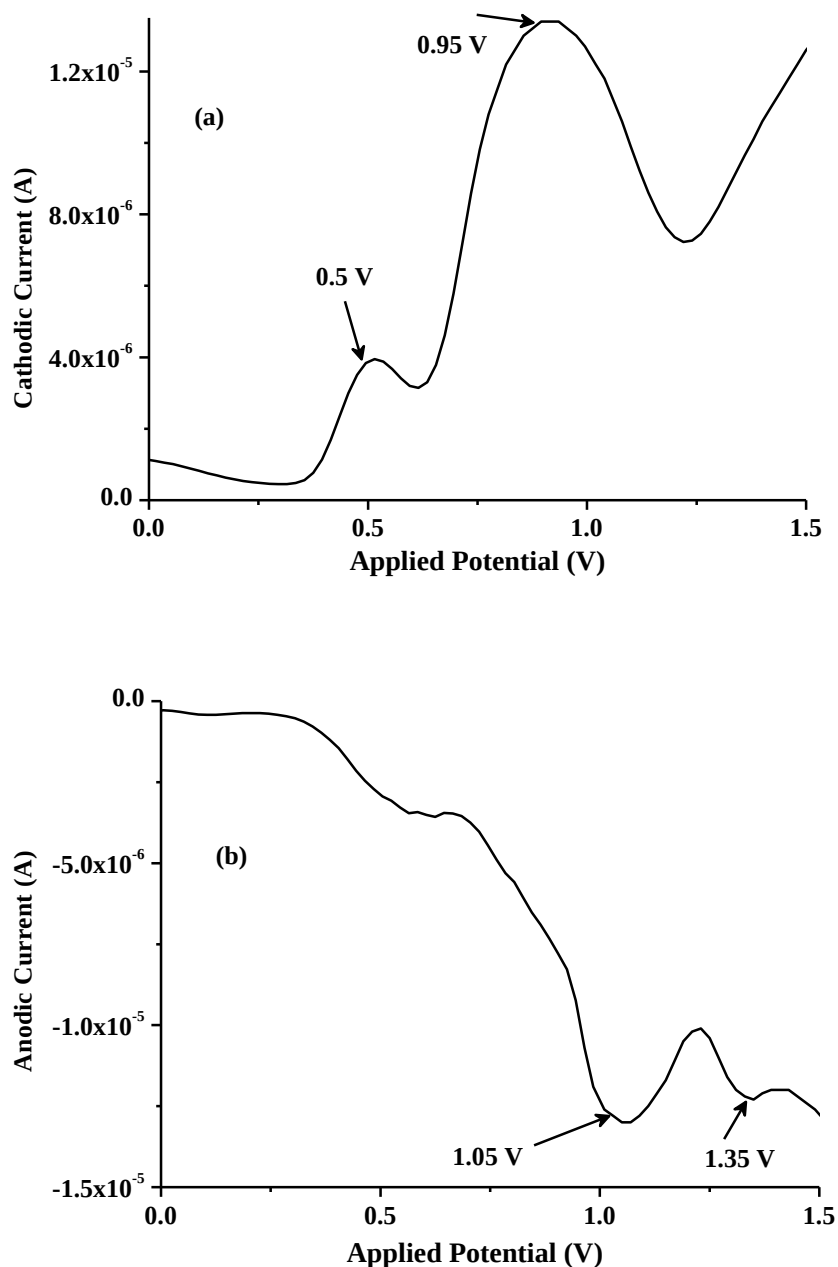


Figure 5.38 (a) Cathodic and (b) Anodic differential pulse voltammogram of **SMR-16** (5×10^{-4} M) at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 1:1, v:v) using 0.1M TBAPF_6 as supporting electrolyte, scan rate 20 mV s^{-1} and GC as working electrode

Effect of scan rate

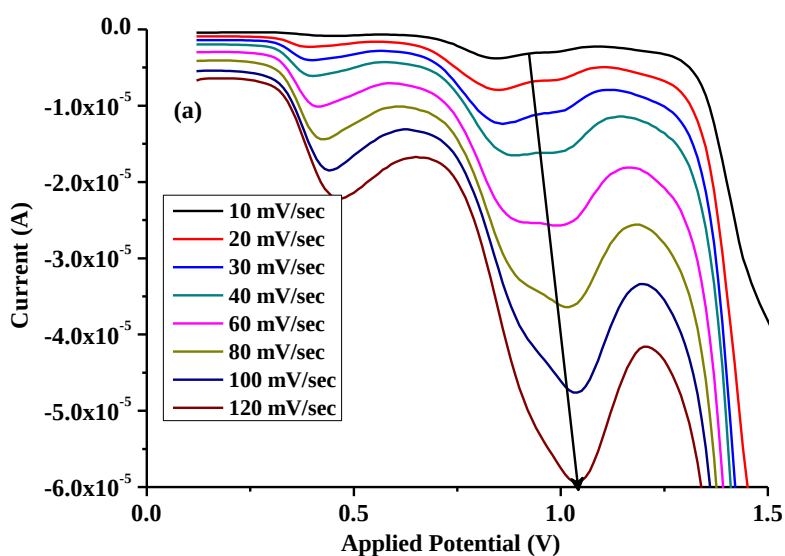
According to Randles–Sevcik’s equation, the scan rate was directly proportional to peak current. Figure 5.39a & b reveal the DPVs of **SMR-16** at glassy carbon electrode for 10^{-4} M **SMR-16** at scan rates from 20 to 120 mV/sec and pH maintained at 7.0 ± 0.1 . The effect of scan rate on the peak current of **SMR-16** was studied by differential pulse voltammetry showing an increase in the peak current ($I_{\text{pa/pc}}$) with increase in scan rate. The anodic (I_{pa}) and cathodic

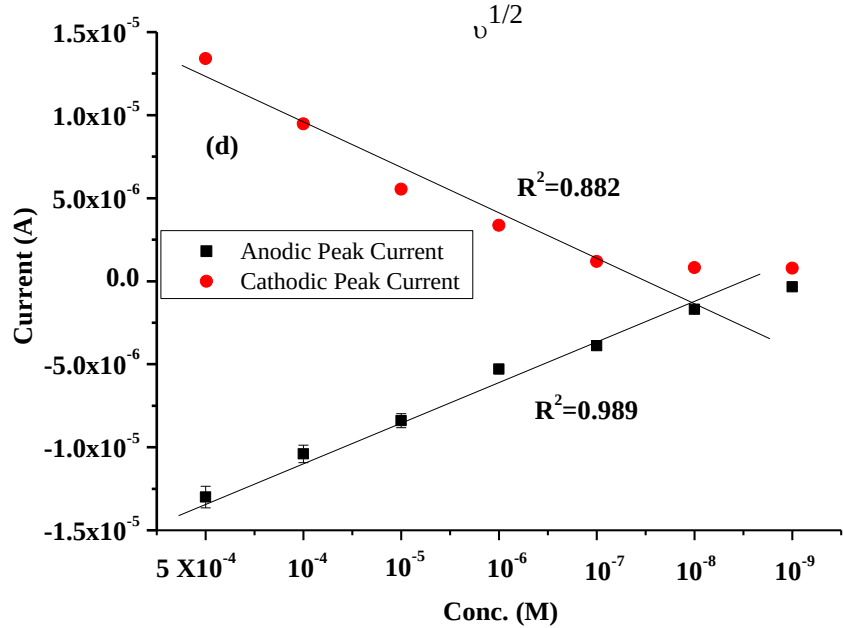
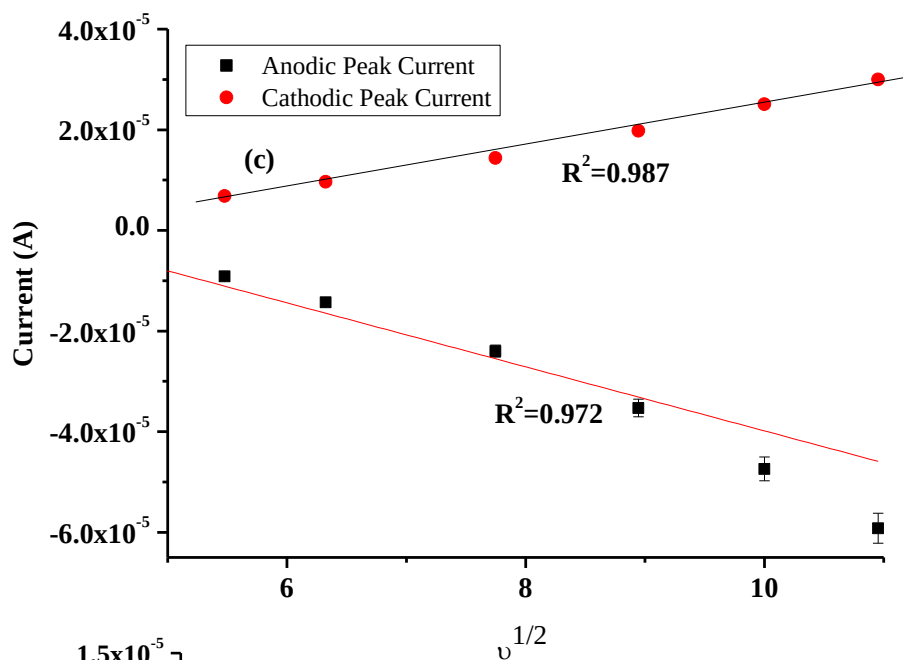
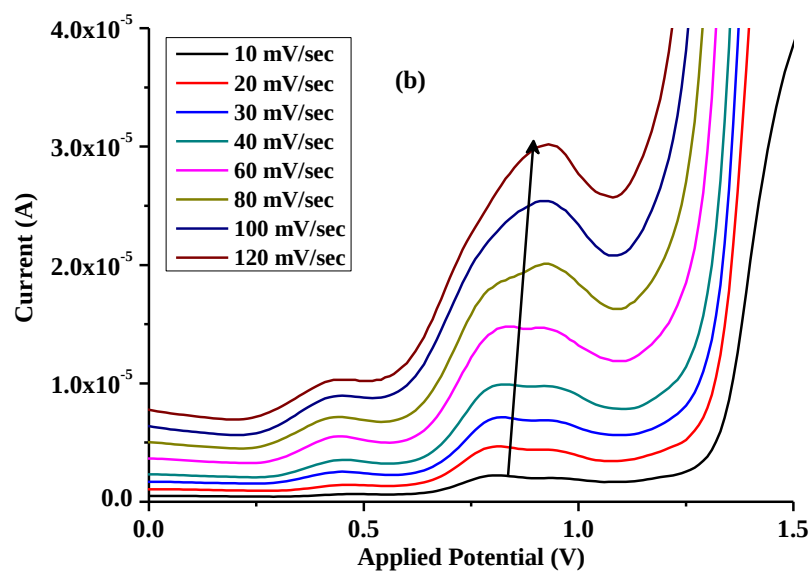
peak currents (I_{pc}) were plotted against square root of scan rate ($v^{1/2}$). A good linearity of the anodic/cathodic peak currents was proportional to the $v^{1/2}$ with correlation coefficient 0.9716 and 0.9871, respectively as shown in Figure 5.39c. It indicated that the electrode transfer reaction was diffusion-controlled process on the electrode surface. For a reversible wave, the potential was independent of scan rate and I_{pa} or I_{pc} (as well as the current at any other point on the wave) was proportional to $v^{1/2}$. The property of the electrode indicated a diffusion-controlled process which depended on “ n ” and the constant could be used to estimate “ n ” by using Eq. (2), and recorded in Table 5.4 from the range of 20 to 120 mV/sec [20].

$$E_p - E_{p/2} = \frac{56.5}{n} \text{ mV at } 25^\circ\text{C}$$

Table 5.4 Number of electrons transferred for different scan rate in the range 20 to 120 mV/sec

Scan Rate (mV/sec)	E_p (mV)	$E_{p/2}$ (mV)	n
10	850.2	800.2	2.26
20	860.2	835.2	2.26
30	880.2	850.2	1.88
40	890.2	860.2	1.91
60	990.2	935.2	2.0
80	1040	980.1	1.89
100	1040	980.1	1.89
120	1040	981.8	1.94





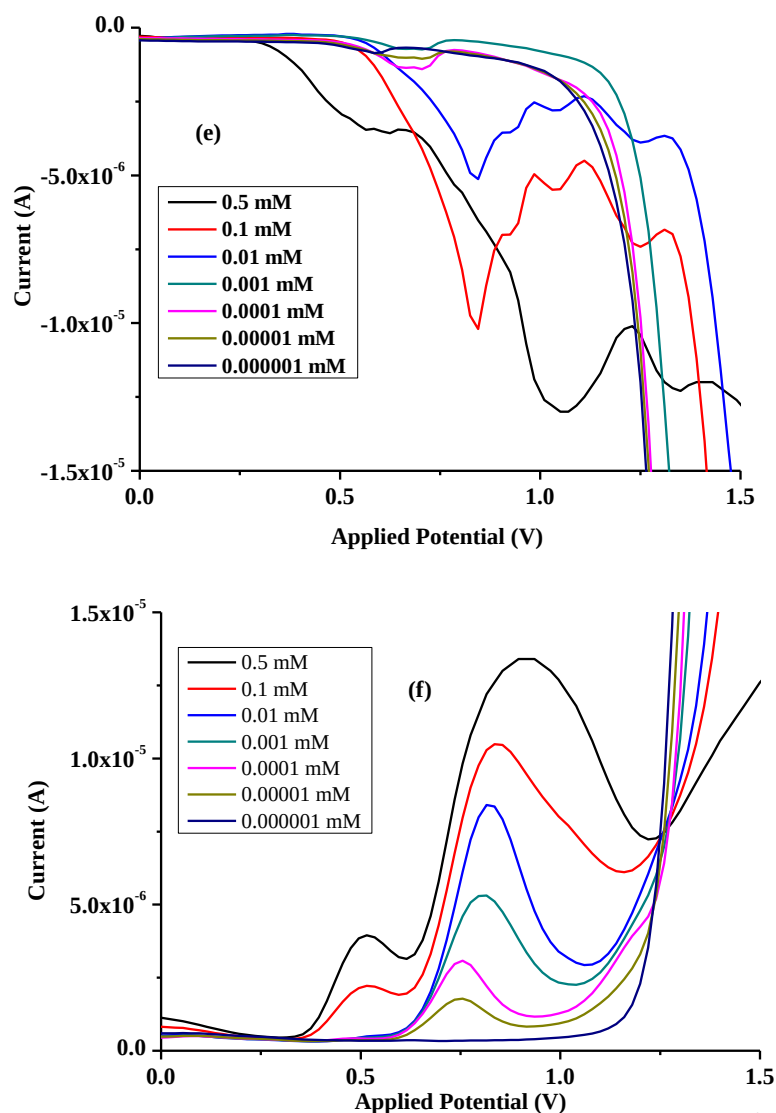


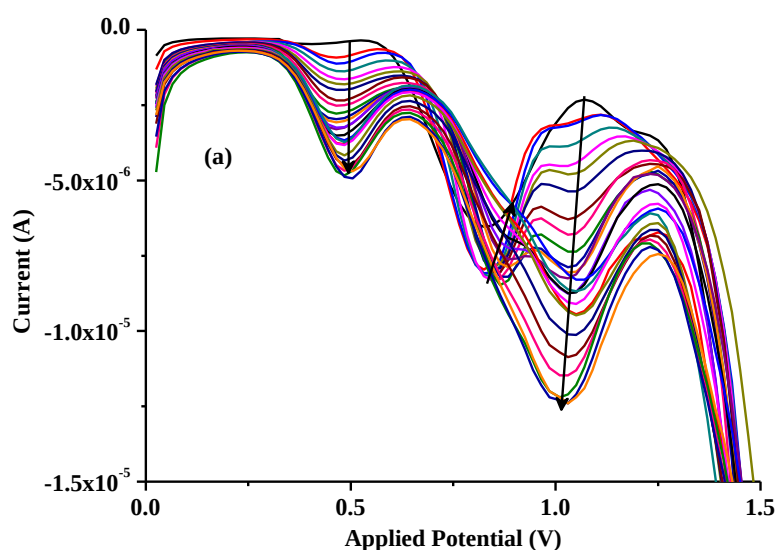
Figure 5.39 (a) Anodic (b) Cathodic Differential Pulse Voltammograms of 10^{-4} mol/L **SMR-16** with different scan rates (c) Graph of the redox peak currents versus the square root of the scan rate for **SMR-16** (d) Graph of the redox peak currents versus the concentration of **SMR-16** (e) Anodic (f) Cathodic Differential Pulse Voltammograms of **SMR-16** with varying concentrations at scan rate 40 mV/sec

Concentration studies

Differential pulse voltammetric plots were recorded at different concentrations of **SMR-16** in the range from 5×10^{-4} to 10^{-9} M (Figure 5.39e and f). There was a dramatic enhancement in the peak current with increase in the concentration of electroactive species. This is due to the reason that increase in concentration of redox substances makes the velocity of mass diffusion rapid and hence the electrode processes become more controlled by the electrode reactions. Calibrations for concentration of analyte species were plotted against cathodic and anodic peak currents. The observed coefficients of regression varied within range 0.8823 and 0.9896, respectively as shown in Figure 5.39d.

Metal complexation study

Voltammetric studies were carried out on **SMR-16** to know its tendency to complex with transition metal ions so that it could be projected as an ionophore suitable for heavy metal detection by simple voltammetric methods. Based on the better response of **SMR-16** for copper ions amongst a series of transition metal ions, voltammetric studies were carried out with copper. Voltammograms were drawn for **SMR-16** receptor in the presence and absence of Cu(II) ions. On addition of Cu(II) ions, the anodic peak current at 0.865 V gets reduced with a little shift to higher potential with appearance of a new anodic peak at 1.05 V, which goes on increasing in peak current with addition of copper ions. Current magnitude of the new anodic peak at 1.05 V rises upto 12 μA as shown in Figure 5.40a. Simultaneously, another anodic peak appears at 0.505 V which also increases current upto 5 μA , whereas, the cathodic peak at 0.795 V gets shifted to higher potential with an increase in peak current on the addition of copper ions. The anodic peak at 0.505 V appeared on the addition of copper ions with current magnitude 2.28 μA (Figure 5.40b). Experiments were conducted for the measurement of currents at the peak potential values (from DPV studies of **SMR-16** receptor) for different concentrations of copper ions added to the receptor solution (5×10^{-5} M) and plot was drawn between copper concentrations and the current values as shown in Figure 5.40c. Calibration studies were repeated at least three times to see reproducibility of the proposed method. Lower detection limit obtained from calibration curve is $0.01 \mu\text{M} \approx 10 \text{ nM}$ ($\pm 2\%$) with corresponding slope and intercept shown in the respective Figure 5.40c. Presence of other metal ions (Al(III), Na(I), Ni(II), Ag(I), K(I), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Hg(II), Fe(II)) on the voltammetric behaviour of **SMR-16** was also studied and results indicated selectivity for Cu(II) ions only.



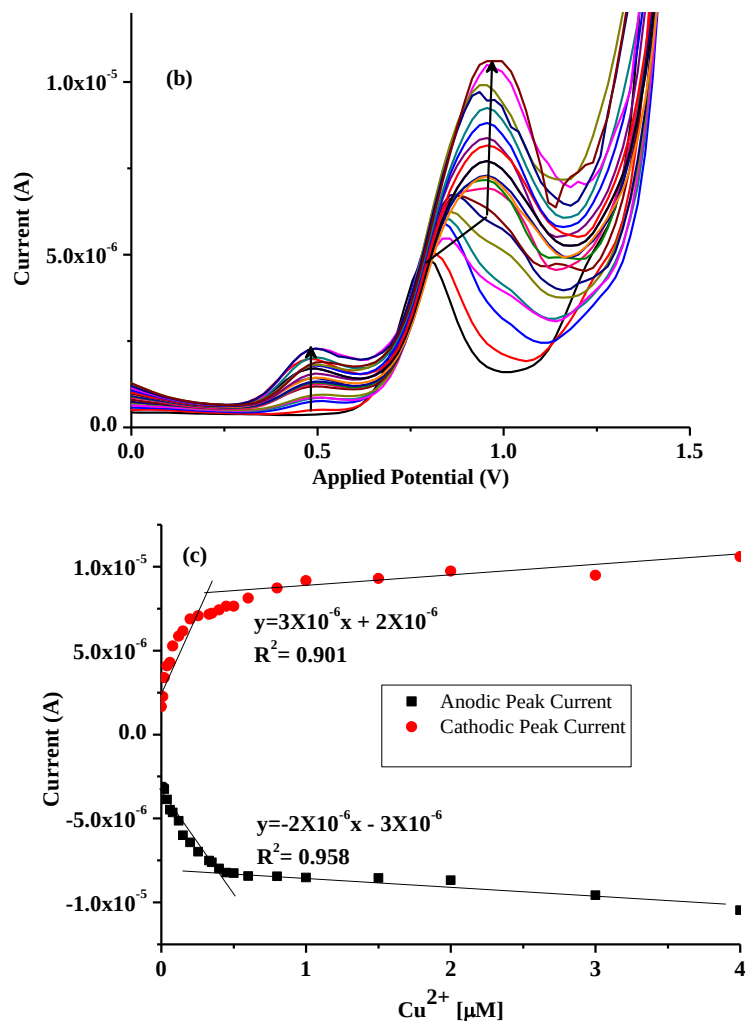


Figure 5.40 (a) Anodic (b) Cathodic Differential Pulse Voltammograms of 5×10^{-5} mol/L **SMR-16** with increasing concentration of Cu(II) ions (c) Calibration plots between concentration of Cu(II) and current for **SMR-16** receptor at pH 7.0 ± 0.1 (10 mM HEPES in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ 1:1, v:v) using 0.1M TBAPF_6 as supporting electrolyte, scan rate 20 mV s^{-1} and GC as working electrode

Interference studies

Studies on interference of metal ions to the **SMR-16**-Cu(II) complex measurements by voltammetry were carried out by adding 2 equivalents of various cations like Al(III), Na(I), Ni(II), Ag(I), K(I), Ca(II), Mg(II), Pb(II), Cd(II), Li(II), Co(II), Zn(II), Hg(II), Fe(II) as interfering ions in 1 equivalent concentration of Cu(II) ion as primary ion. Voltammograms for compound **SMR-16** in presence of interfering ion did not show any change in redox activity of the complex formed with copper, indicating that there is no interference from these cations to the detection of copper with **SMR-16**. It can be concluded that the receptor responds with exceptional selectively towards copper ion in the presence of many other commonly available cations.

Computational studies

To elucidate the structure of the Cu(II)– **SMR-16** complexes, density functional theory (DFT) calculations were used using the Gaussian 03W software package. **SMR-16** and Cu(II)– **SMR-16** complexes were subjected to energy optimization using B3LYP/6-31G and B3LYP/LANL2DZ, respectively.

The two possible conformations of **SMR-16** were optimized using the B3LYP (6-31G) basis set. The energy of conformations ‘ENOL’ and conformation ‘KETO’ forms were found to be of almost same level. Thus, there is a dynamic equilibrium between these two conformations, and the molecule can attain either of the two conformations. **SMR-16** is under keto-enol tautomerism with equilibrium having equal abundance of both forms as also expected from DFT results by having approximately equal energy for enol (-1951.58 a. u.) and keto (-1951.57 a. u.) form.

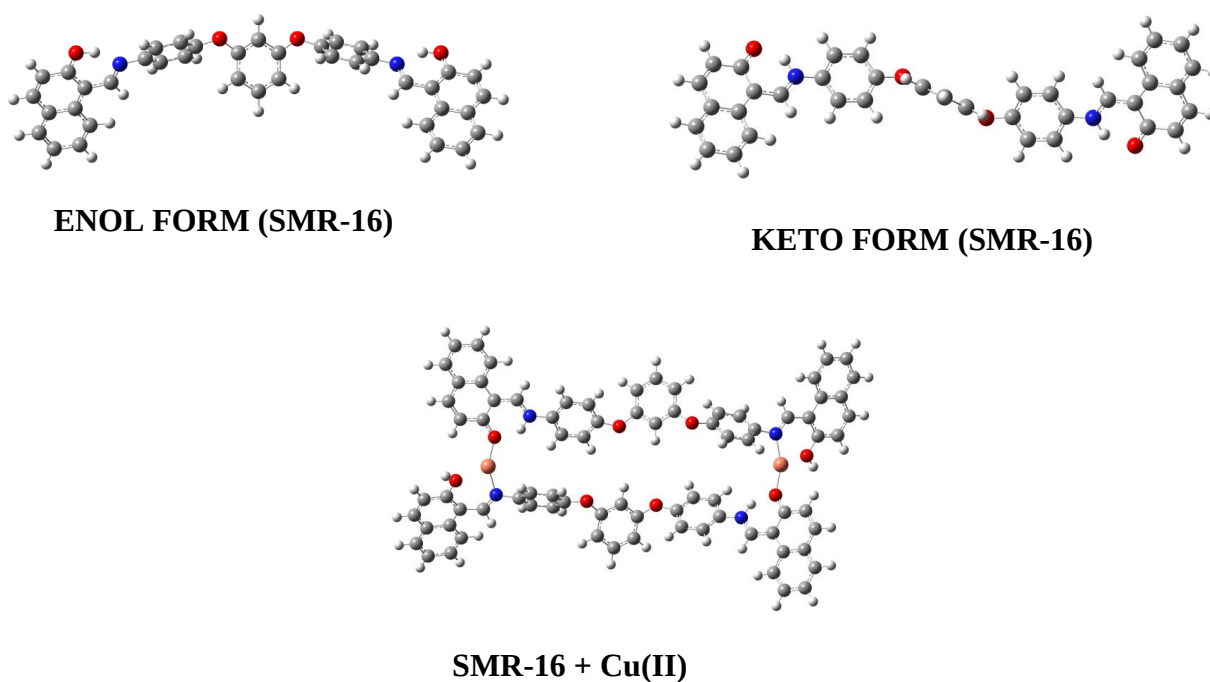
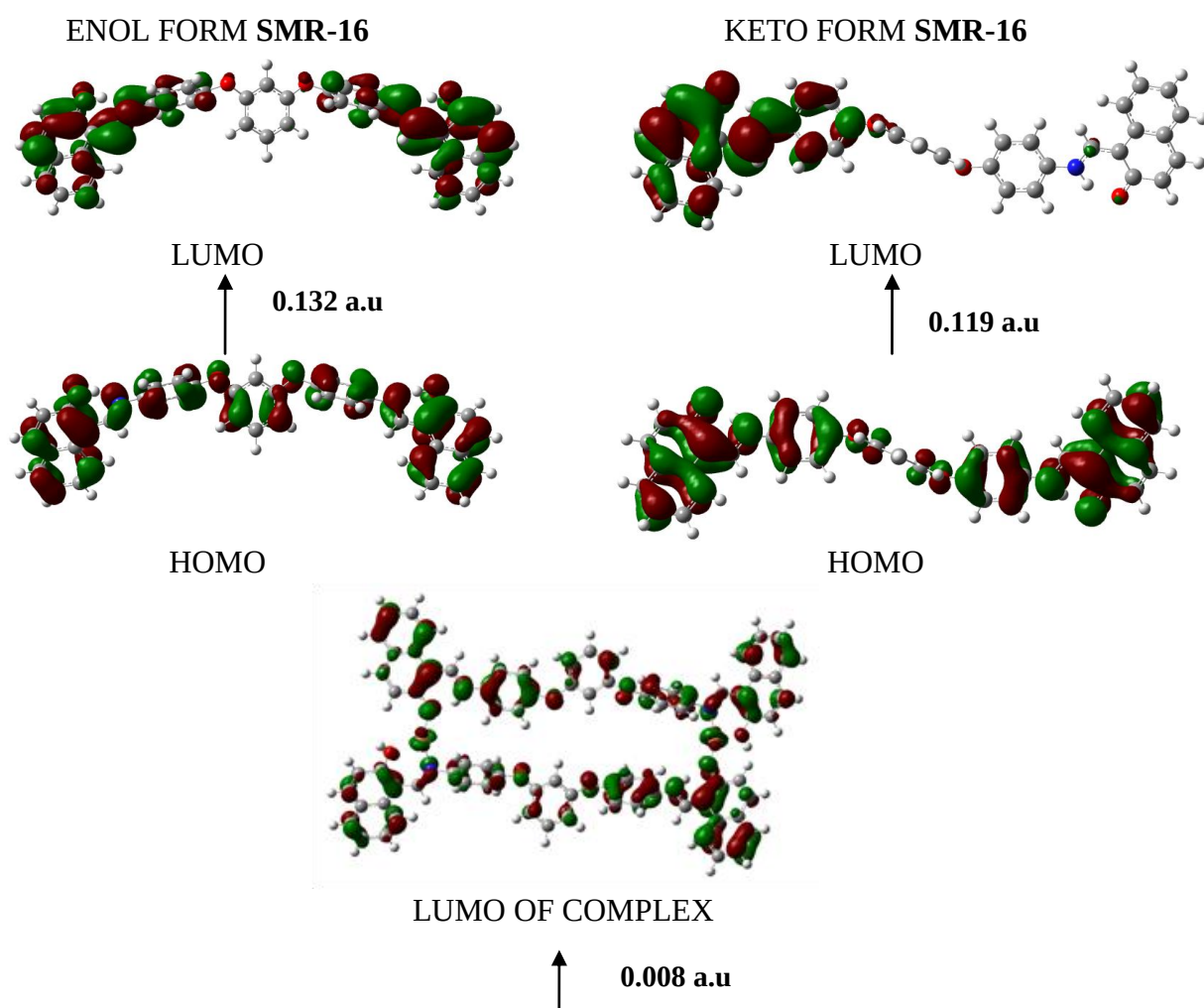


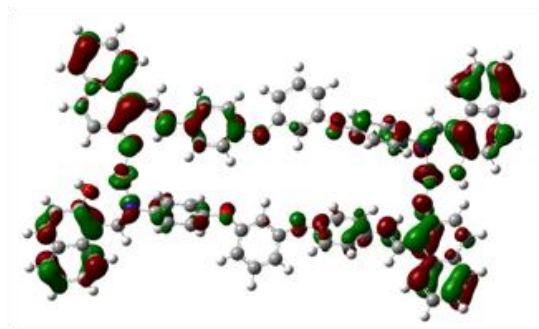
Figure 5.41 Optimized geometries of different conformations of **SMR-16** and **SMR-16**- Cu(II) by using DFT/B3LYP/6-31G method

Optimized geometry of enol form shows that molecule is fully symmetrical and both the edges are involved in ESIPT mechanism while in keto form of **SMR-16**, both the edges of molecule are in opposite direction but are involved in ESIPT mechanism as well as evident from optimized structures shown in Figure 5.41. Thus, both the conformations are involved in binding with Cu(II) ions. The molecular orbital diagrams (Figure 5.42) illustrate that keto form

of receptor has lesser energy gap (0.1185 a.u.) between HOMO-LUMO as compared to enol form (0.1400 a.u.). Further, complexation of **SMR-16** with Cu(II) leads to greater fall in energy gap between HOMO-LUMO. Hence, forming the stable complexes.

Optimized geometries of **SMR-16** with copper shows the sandwich type bimolecular complex formed, in which two copper ions get sand-witched between two **SMR-16** molecules. Half part of the **SMR-16** undergoes proton transfer and assumes keto conformation to complex the copper ion and metal binds with oxygen of keto form of first **SMR-16** molecule and nitrogen of imine bond of second **SMR-16** molecule. Likewise, on the second end of the moiety, oxygen of keto form of second **SMR-16** molecule and nitrogen of imine bond of first **SMR-16** molecule complexes the copper ion. Hence, two **SMR-16** molecules trap two copper ions on both ends to form a cage like structure. This is first ever report on such type of complexation in which two molecules of a receptor traps two metal ions by using half keto- half enol conformation; ratiometrically leading to 1:1 complexation.





HOMO OF COMPLEX

Figure 5.42 Molecular energy level diagrams of **SMR-16** and **SMR-16+Cu(II)** complex

Conclusions

The ethereal-imine containing compound has been used for detection of Cu(II) by naked eye in semi aqueous medium (pH 7). The probe express fast, selective and sensitive signal towards Cu(II) with low detection limit (50 nM) without any interference. The studies revealed the binding mode between chemosensor **SMR-16** and the Cu(II) 1:1, which was further supported by DFT calculations. Electrochemical properties were used to explore the interaction between chemosensor **SMR-16** and the Cu(II). The probe was practically applied for detection of water content in non-aqueous media and analysis of Cu(II) with water sample and multivitamins capsule containing copper content.

5.3 References

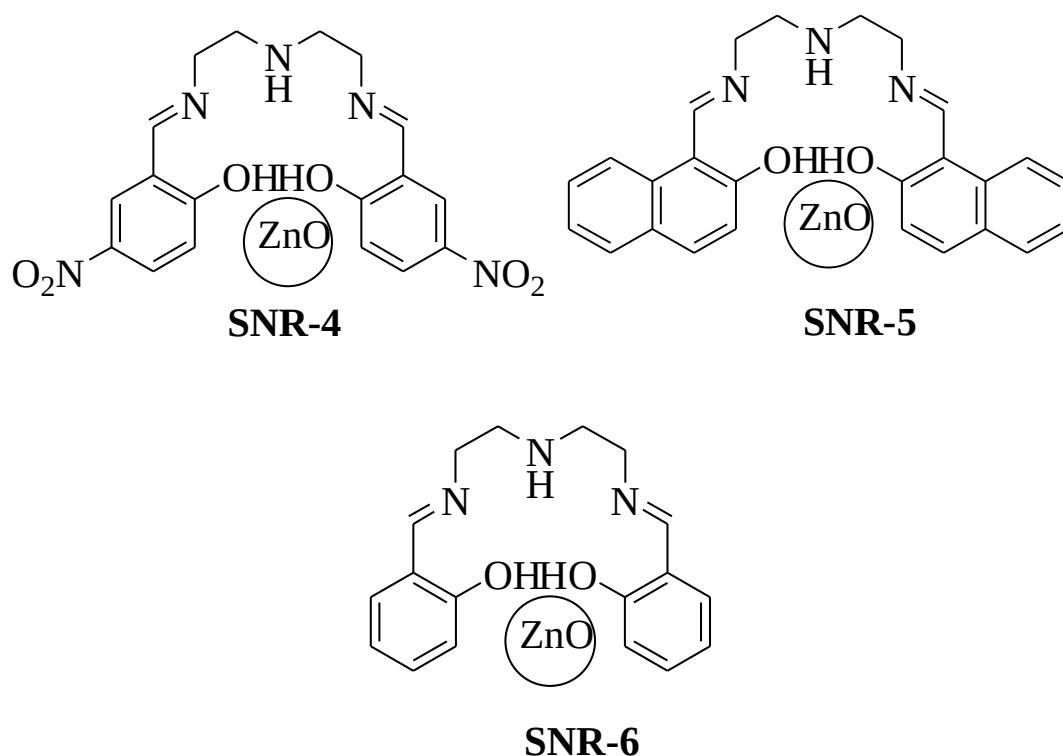
1. J. J. Lee, G. J. Park, Y. W. Choi, G. R. You, Y. S. Kim, S. Y. Lee and C. Kim, *Sensor Actuat. B: Chem.*, **2015**, 207, 123-132.
2. P. Job, *Ann. Chim.*, **1928**.
3. H. A. Benesi and J. Hildebrand, *J. Am. Chem. Soc.*, **1949**, 71, 2703-2707.
4. J. Y. Noh, I. H. Hwang, H. Kim, E. J. Song, K. B. Kim and C. Kim, *Bull. Korean Chem. Soc*, **2013**, 34, 1985-1992.
5. J. Kang, E. J. Song, H. Kim, Y.-H. Kim, Y. Kim, S.-J. Kim and C. Kim, *Tetrahedron Lett.*, **2013**, 54, 1015-1019.
6. (a) S.-Y. Na, J.-Y. Kim and H.-J. Kim, *Sensor Actuat. B: Chem.*, **2013**, 188, 1043-1047. (b) S. Park and H.-J. Kim, *Sensor Actuat. B: Chem.*, **2012**, 161, 317-321. (c) S. Park and H.-J. Kim, *Sensor Actuat. B: Chem.*, **2012**, 168, 376-380.
7. C. H. Lee, H. J. Yoon, J. S. Shim and W. D. Jang, *Chem. Euro. J.*, **2012**, 18, 4513-4516.
8. W. H. Organization, Guidelines for the programmatic management of drug-resistant tuberculosis-2011 update, *Geneva, Switzerland*, **2011**.
9. Y. Li and S. M. Chen, *Int. J. Electrochem. Sci.*, **2012**, 7, 2175-2187.
10. V. Thomsen, D. Schatzlein and D. Mercurio, *Spectroscopy*, **2003**, 18, 112-114.
11. R. B. Singh, S. Mahanta, S. Kar, N. Guchhait, *J. Chem. Phys.*, **2007**, 331, 373-384.
12. F. Maseras, A. Lledós, E. Clot, O. Eisenstein, *Chem. Rev.*, **2000**, 100, 601-636.
13. S. Niu, M.B. Hall, *Chem. Rev.*, **2000**, 100, 353-406.
14. M. Torrent, M. Sola, G. Frenking, *Chem. Rev.*, **2000**, 100, 439-494.
15. R. B. Singh, S. Mahanta, S. Kar, N. Guchhait, *J. Chem. Phys.*, **2007**, 331, 373-378.
16. S. R. Vazquez, M. Rodriguez, M. Mosquera, F. Rodriguez-Prieto, *The journal of physical chemistry. A*, **2007**, 111, 1814-1824.
17. C. Rodriguez-Rodriguez, N. Sanchez de Groot, A. Rimola, A. Alvarez-Larena, V. Lloveras, J. Vidal-Gancedo, S. Ventura, J. Vendrell, M. Sodupe, P. Gonzalez-Duarte, *J. Am. Chem. Soc.*, **2009**, 131, 1436-1442.
18. W. H. Chen, Y. Pang, *Tetrahedron Lett.*, **2010**, 51, 1914-1923.
19. H. A. Benesi, J. Hildebrand, *J. Am. Chem. Soc.*, **1949**, 71, 2703-2717.
20. A. J. Bard, L. R. Faulkner, "Fundamentals and Applications" *Electrochemical Methods*, 2nd ed.; Wiley: New York, **2001**.

OTHER VOLTAMMETRIC SENSORS DEVELOPED

In continuation to developing arylether based receptors as chemical sensors for the detection of cations and anions; some other voltammetric sensors have also been developed. This chapter comprises of the details of all other chemical sensors developed during the course of study, which includes nanoparticles incorporated imine linked molecules for Al(III) and Co(II) determination, voltammetric method for the determination of an antimicrobial drug using picric acid as an anionic reagent.

6.1 Voltammetry of nanoparticle coupled imine linkage based receptors for sensing of Al(III) and Co(II) ions

Studies on electrochemical reduction of imine linkage [1-3] has always been important for analytical chemists as the charge distribution over the imine bond can be influenced easily by substitutions at position – meta to the imine linkage. This redistribution of electron density results in shift of cathodic peaks by significant potentials which forms the basis of sharp chemical sensing using receptors based on imine linkages. Further doping with ZnO nanoparticles is found to affect grain boundaries [4, 5] and hence influence redox characteristics of the parent compound [6]. The imine-linked receptor is expected to adsorb on the surface of ZnO, and this strategy has a second advantage as the imine linkages of the resultant sensor (ZnO coated with an imine-linked receptor) may offer additional binding sites for the recognition of metal ions. In this research work, ZnO coated imine linkage based chemosensors have been used for the determination of aluminium and cobalt ions. Till now, there is no report on imine based voltammetric chemosensor for the detection of metal ions. So, voltammetric sensors based on imine linkages are reported for the detection of aluminium and cobalt ions. **SNR-4**, **SNR-5** and **SNR-6** have been synthesized by using the literature method [7, 8] and used for the determination of aluminium and cobalt ions by voltammetric methods. Structures of the molecules studied for voltammetric detection of aluminium and cobalt ions are as shown below; named as **SNR-4**, **SNR-5** and **SNR-6**:



Electrochemical behavior of SNR-4, SNR-5 and SNR-6

Cyclic voltammograms of **SNR-4** and **SNR-5** showed two reduction peaks each at -0.930 V, -1.199 V and -0.996 V, -1.850 V, respectively, while **SNR-6** showed one reduction peak (-1.220 V) as shown in Table 6.1. These observations are also supported by the DPV curves of the molecules (inset (a), (b) and (c) in Figure 6.1). It can be seen in Table 6.1 that the cathodic peak potential of **SNR-6** due to reduction of imine group is affected by substitution at ortho (**SNR-5**) with phenyl group and meta (**SNR-4**) with nitro group attached to the imine bond. The cathodic peak potential of **SNR-6** at -1.22 V is shifted to higher potential at -1.850 V in **SNR-4** due to presence of electron donating phenyl group. Substitution on benzene ring with nitro group at meta position moves the cathodic peak in **SNR-6** (at -1.22 V) to a little lower potential (at -1.199 V).

Table 6.1 Peak potentials (V) and peak currents (μA) values for **SNR-4**, **SNR-5** and **SNR-6**

Compound	Peak potentials (V)		Peak current (A)	
	E_{pc1}	E_{pc2}	i_{pc1}	i_{pc2}
SNR-4	-0.930	-1.199	1.05×10^{-5}	1.63×10^{-5}
SNR-5	-0.996	-1.850	1.56×10^{-5}	1.16×10^{-5}
SNR-6	---	-1.220	---	5.23×10^{-6}

E_{pc} : Cathodic peak potential

i_{pc} : Cathodic peak current

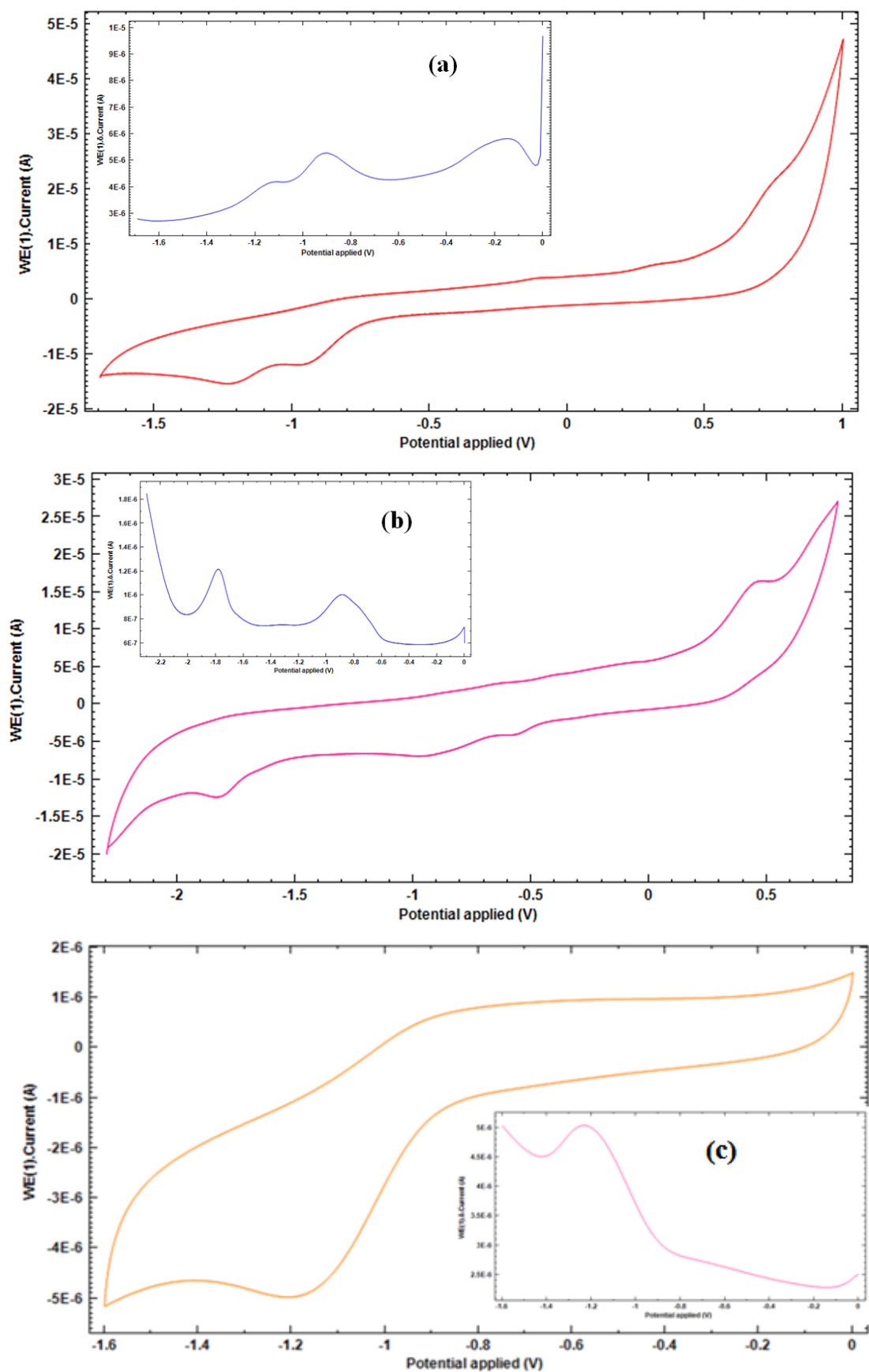
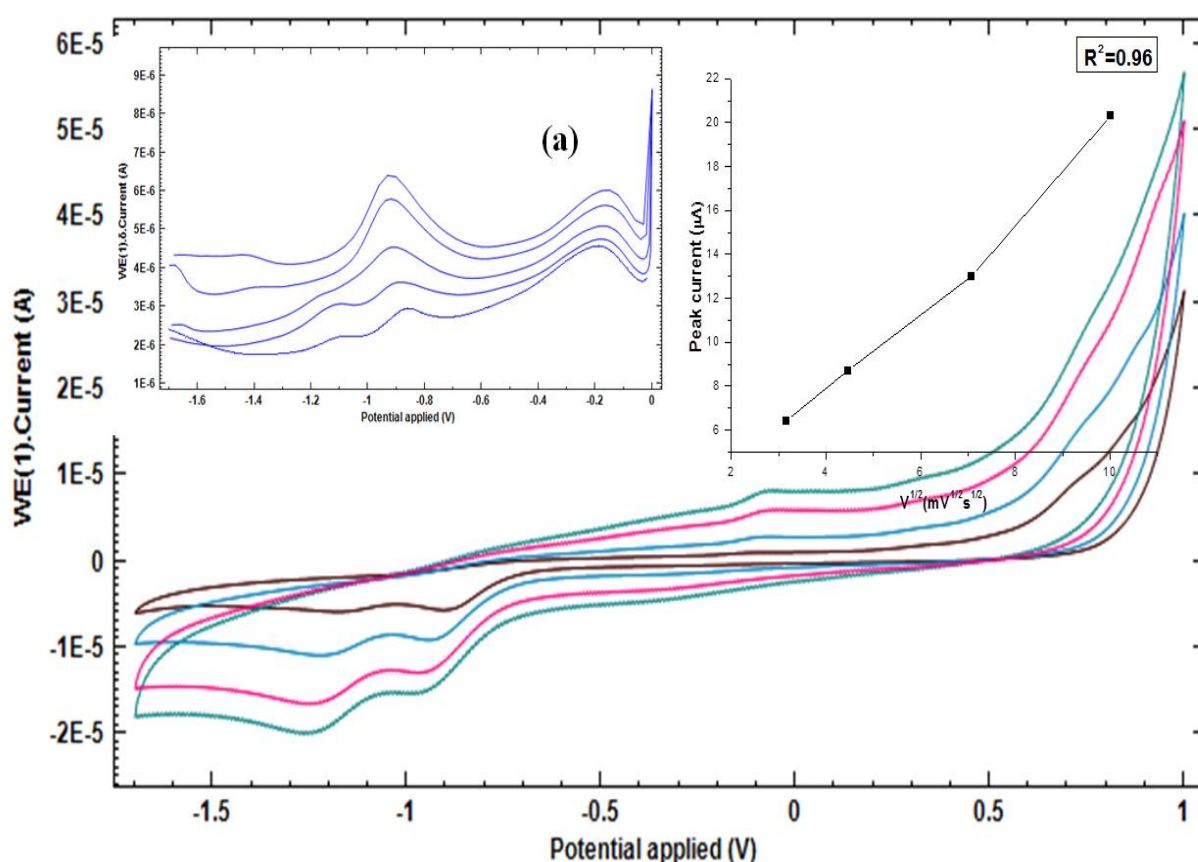


Figure 6.1 Cyclic voltammograms of (a) SNR-4 (b) SNR-5 and (c) SNR-6 (5×10^{-4} M) in DMSO:H₂O (8:2, v/v) using 0.1 M TBAP as supporting electrolyte, scan rate 20

mV s^{-1} and GC as working electrode. Inset: DPV for (a) **SNR-4** (b) **SNR-5** and (c) **SNR-6** ($5 \times 10^{-4} \text{M}$) Modulation amplitude 50mVsec^{-1}

Influence of scan rate

With increase in scan rate from 5 mV s^{-1} to 50 mV s^{-1} , the cathodic peak at -1.199 V slowly disappears in **SNR-4**, probably an indication of two separate reduction reactions, out of which one reaction is very slow and cannot be recorded at a scan rate 50 mV s^{-1} or more. One of the two cathodic peaks for **SNR-4**, the one at -0.930 V was selected for quantitative studies on the basis of its reproducible behavior. Unlike **SNR-4**, the corresponding peak in **SNR-5** sustains fast scan but shifts to -1.85 V due to the remote effect of substituent (NO_2 to Phenyl group) on the meta position to the electroactive centre (imine group) in the molecule (as explained in previous paragraphs also). Peak currents of cathodic waves for **SNR-4**, **SNR-5** and **SNR-6** were plotted against square root of the scan rates, separately for each curve. A linear relation between peak current and the square root of scan rate indicated a diffusion based process (Figure 6.2).



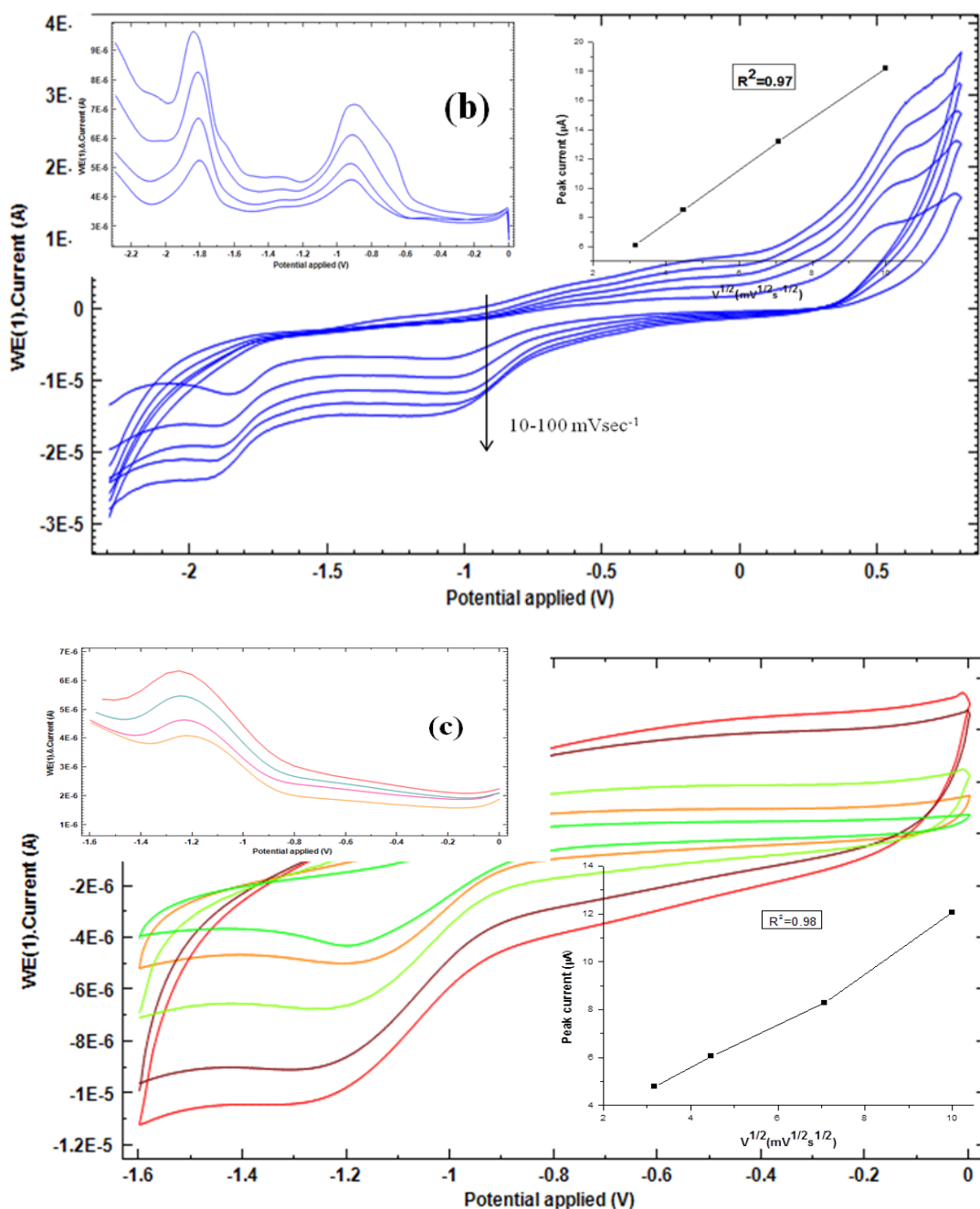
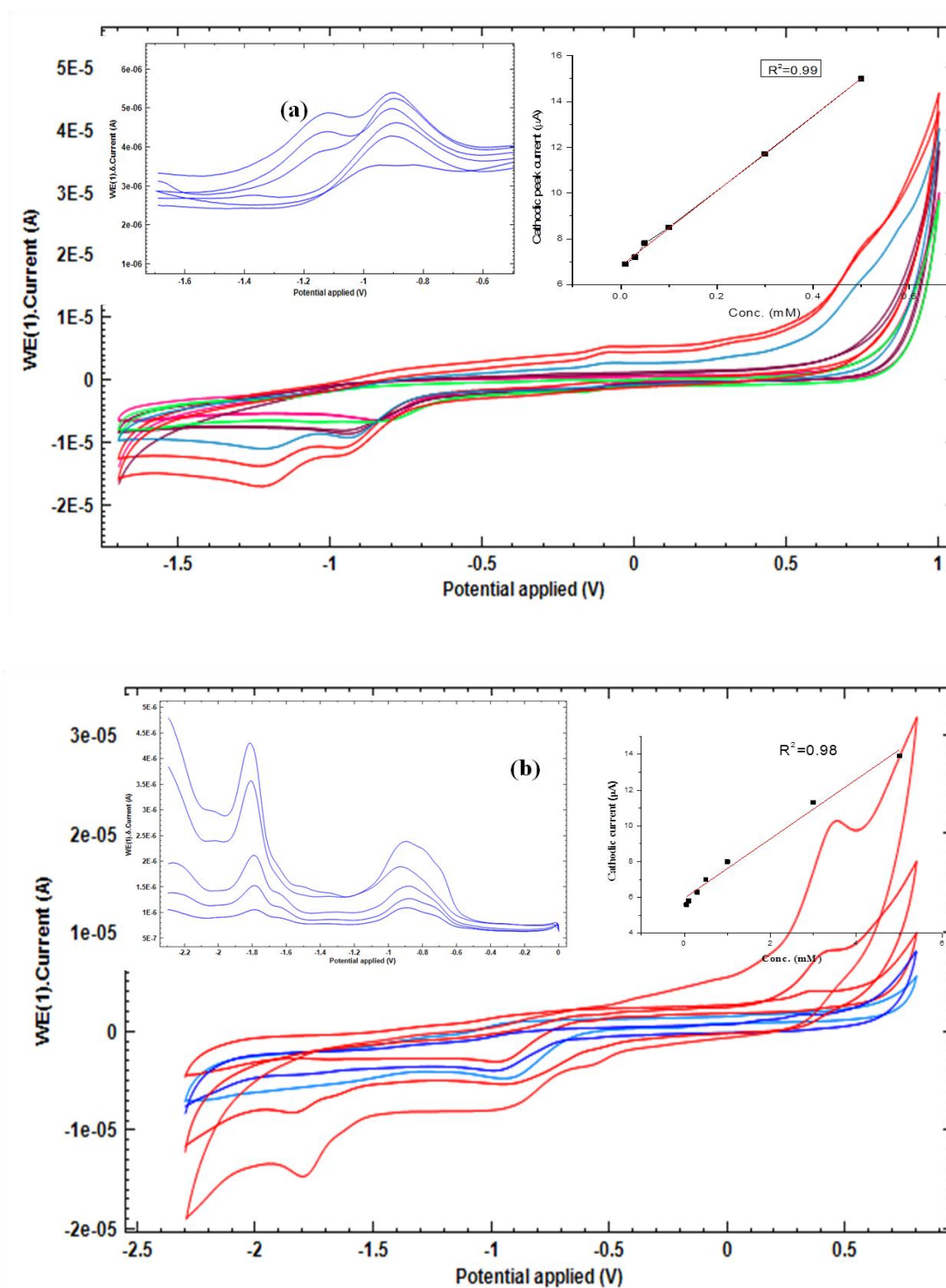


Figure 6.2 Cyclic voltammograms of (a) **SNR-4** (b) **SNR-5** and (c) **SNR-6** (5×10^{-4} M) showing the effect of scan rate in DMSO:H₂O (8:2, v/v). From inner to outer the scan rates are (10, 30, 50, 70, 100 mVsec⁻¹), 0.1M TBAP, GC as working electrode. Inset: DPV for (a) **SNR-4** (b) **SNR-5** and (c) **SNR-6** (5×10^{-4} M) Modulation amplitude 50mVsec⁻¹

Effect of concentration of **SNR-4**, **SNR-5** and **SNR-6**

Electrochemical study of the compounds was done to know the effect of different concentrations on their respective DPV behaviors. The results are shown in Figure 6.3. With increase in concentration of each of **SNR-4**, **SNR-5** and **SNR-6**, increase in the respective peak currents was observed along with a cathodic shift in the peak potential.

1. This is due to the reason that increase in concentration makes the velocity of mass diffusion rapid and hence the electrode processes are more controlled by the electrode kinetics. Calibrations for concentration of analyte species and cathodic peak currents were plotted and the coefficient of regression varied within a range 0.98-0.99 as shown in Figure 6.3.



i.

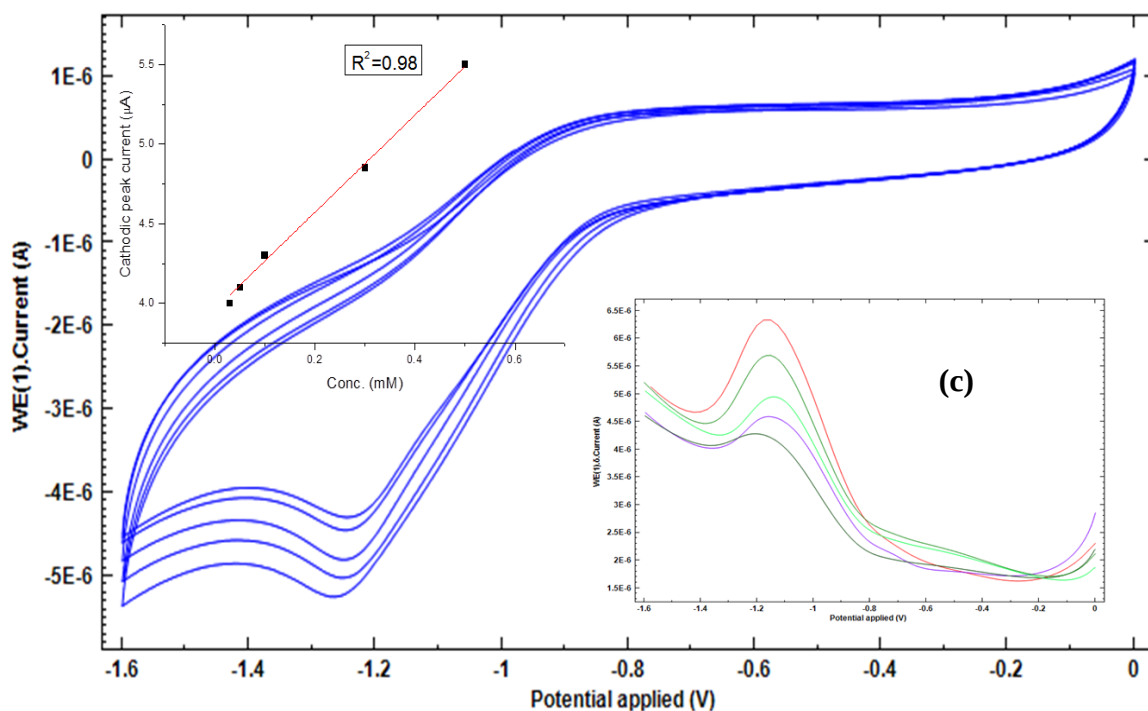


Figure 6.3 Cyclic voltammograms of (a) **SNR-4** (b) **SNR-5** and (c) **SNR-6** (5×10^{-4} M) at different concentrations (0.5 mM to 0.01 mM, from outer to inner), using 0.1 M TBAP as supporting electrolyte (scan rate 20 mV s^{-1} and GC as working electrode) Inset: DPV for (a) **SNR-4** (b) **SNR-5** and (c) **SNR-6** (5×10^{-4} M), Modulation amplitude 50 mV sec^{-1}

Effect of solvent

Voltammetric scans of **SNR-4** were studied in different solvent systems like CH_3CN , DMSO and DCM (Figure 6.4). Solvents were selected in such a way that their electron donating tendencies (Lewis basicity) were significantly different. As expected, CH_3CN influenced reduction of imine bond in **SNR-4** molecule more than DMSO because of more basic character of lone pair on nitrogen atom of CH_3CN resulting in increase in electron density of imine bond in **SNR-4** as compared to that of oxygen in DMSO. This is indicated from greater peak potential (-1.212 V) in CH_3CN as compared to peak potential (-0.998 V) in DMSO as a solvent, while DCM did not give good curves.

Experiments were also conducted in solvent: H_2O mixtures taken in 8:2 ratios (Figure 6.5). Presence of H_2O in DMSO resulted in significant shift (0.214 V) in cathodic peak potential from -0.998 V to -1.212 V . This is because H_2O being more basic in character as compared to

DMSO further strengthened electron cloud over imine bond resulting in a significant positive shift in cathodic peak potential.

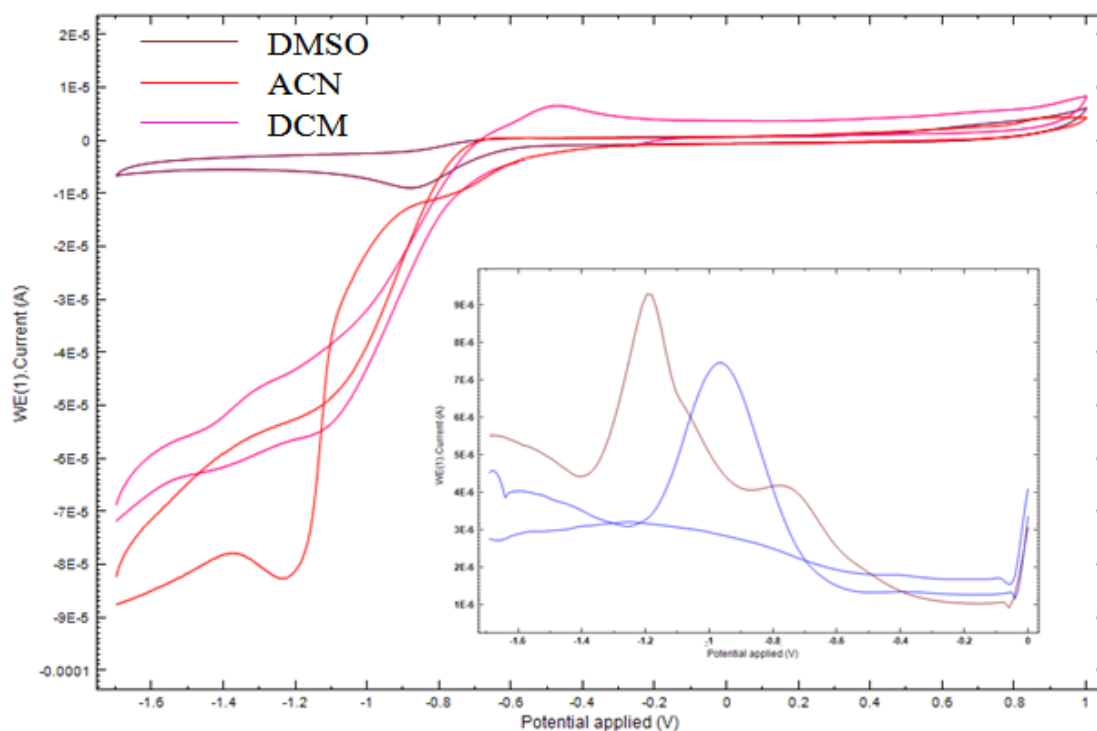


Figure 6.4 Cyclic voltammograms of **SNR-4** (5×10^{-4} M) in different solvents using 0.1 M TBAP as supporting electrolyte (GC working electrode scan rate 20 mVs^{-1} E vs Ag/Ag^+); Inset: DPV of **SNR-4** (5×10^{-4} M) in different solvents, Modulation amplitude: 50 mVsec^{-1}

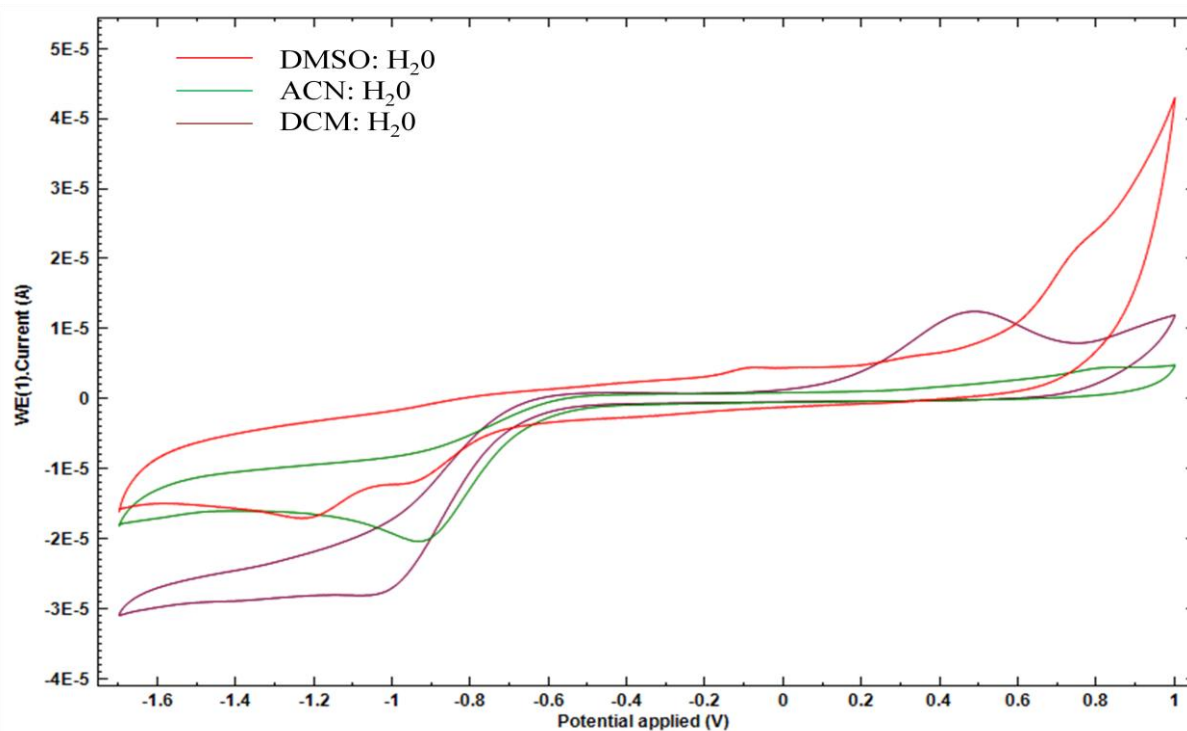


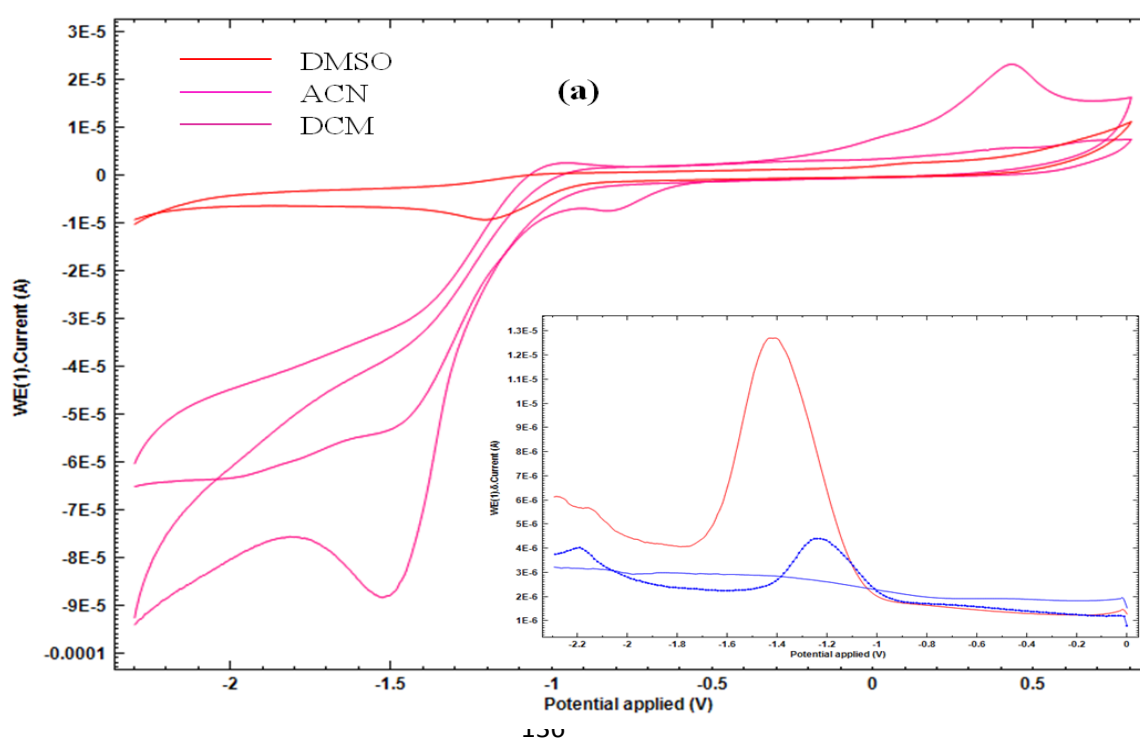
Figure 6.5 Cyclic voltammograms of **SNR-4** (5×10^{-4} M) in different solvents: H_2O using 0.1M TBAP as supporting electrolyte (GC working electrode scan rate 20 mVs^{-1} E vs Ag/Ag^+)

In case of $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ mixture, trend in shift is reversed as basicity of H_2O is much lower than that of CH_3CN . So, replacement of 20% of CH_3CN with H_2O molecules results in significant shift of cathodic peak potential from -1.212 V to -0.910 V . Because of immiscibility of DCM in aqueous medium, it did not give discrete bands or peaks. These results have also been observed in differential pulse voltammetry as well. For all the three molecules, trends of voltammograms were the same as the electroactive site in all of these is an imine bond. Studies of solvent effect on voltammograms of molecules **SNR-5** and **SNR-6** indicated that trends of peak potentials were same as for **SNR-4** molecule. Voltammograms are given in Figure 6.6. A complete record of peak potentials and shifts for all the molecules **SNR-4**, **SNR-5** and **SNR-6** are given in Table 6.2.

Table 6.2 Peak potentials of cathodic peak of **SNR-4**, **SNR-5** and **SNR-6** in different solvents

Solvent	Dipole moment (D)	E_{pc} (V)		
		SNR-4	SNR-5	SNR-6
CH_3CN	3.92	-1.212	-1.404	-1.454
DMSO	3.96	-0.998	-1.211	-1.261
DCM	1.60	---	---	---

E_{pc} : cathodic peak potential



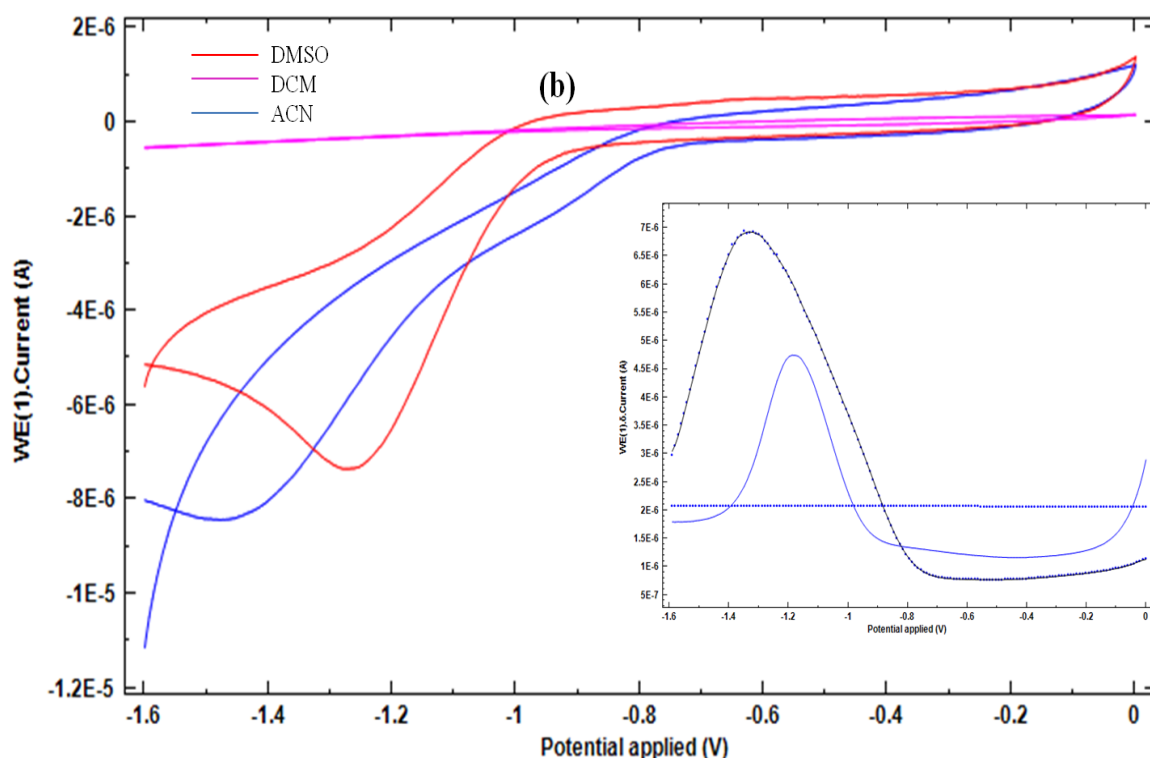


Figure 6.6 Cyclic voltammograms of (a) **SNR-5** ($5 \times 10^{-4} \text{M}$), (b) **SNR-6** ($5 \times 10^{-4} \text{M}$) in different solvents using 0.1M TBAP as supporting electrolyte (GC working electrode scan rate 20 mVs^{-1} E vs Ag/Ag^+); Inset: DPV for (a) **SNR-5** ($5 \times 10^{-4} \text{M}$), (b) **SNR-6** ($5 \times 10^{-4} \text{M}$) in different solvents, Modulation amplitude: 50 mVsec^{-1}

Electrochemical recognition of metal ions by **SNR-4**, **SNR-5** and **SNR-6**

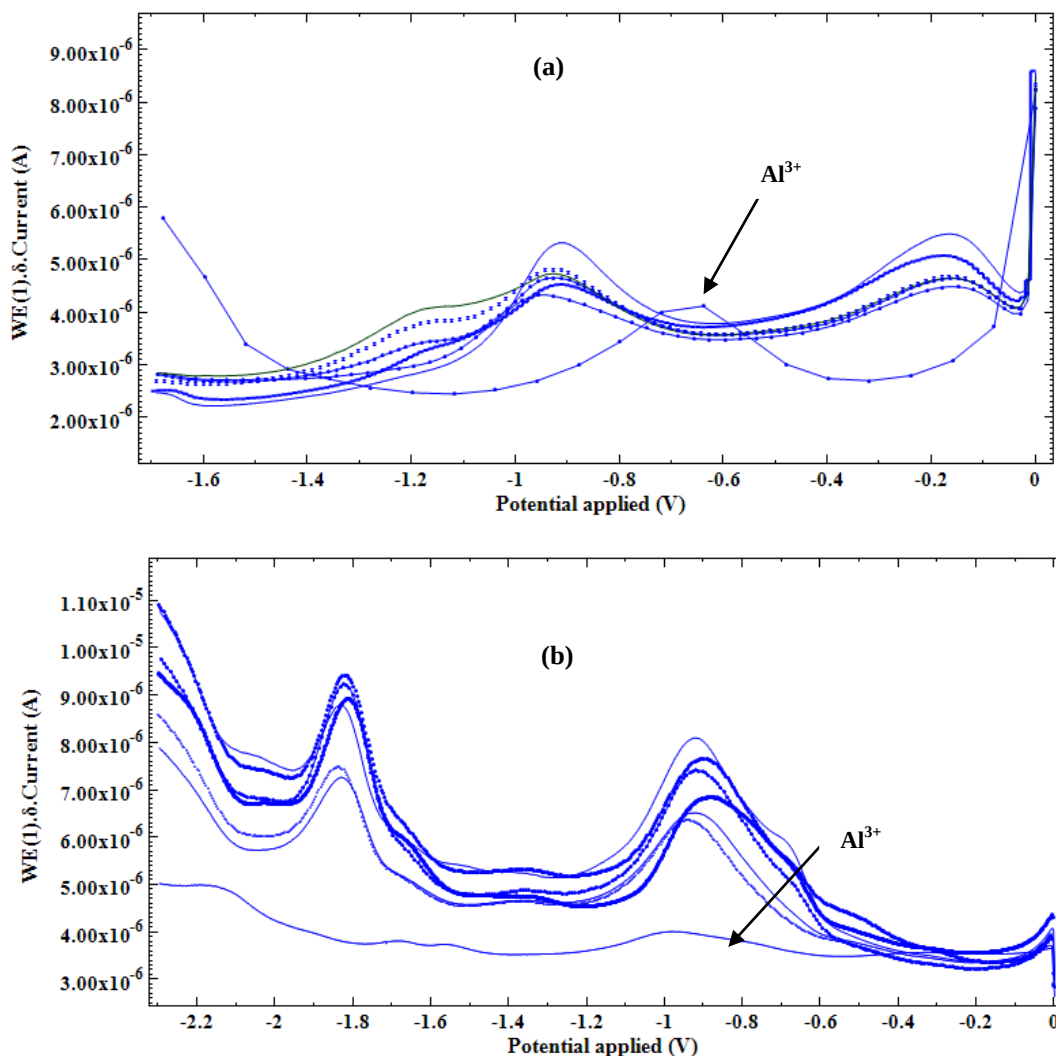
Experiments were conducted with different metal ions like Co(II) , Mg(II) , Ca(II) , Na(I) , K(I) and Al(III) in $\text{DMSO}:\text{H}_2\text{O}$ (8:2, v/v) at a scan rate of 20 mV s^{-1} to understand complexation behaviour of **SNR-4**, **SNR-5** and **SNR-6** with metal ions. In the presence of Al(III) ions, shapes of voltammograms of **SNR-4** and **SNR-5** were different from those of **SNR-6** (Figure 6.7) which shows a decrease in peak current at peak potential -1.205 V in presence of Co(II) ions. Voltammogram for Al(III)-SNR-4 complex showed an additional peak at -0.648 V , as shown in Figure 6.7a. A detailed study was done with different concentrations of metal ions ranging from $0.0 \mu\text{M}$ to $0.42 \mu\text{M}$ of the **SNR-4**, **SNR-5** and **SNR-6**.

Voltammograms of **SNR-4**

In voltammogram of **SNR-4** (Figure 6.8), intensity of the cathodic peak at -1.160 V ($1.72 \times 10^{-5} \text{ A}$ for $0.30 \mu\text{M}$) decreased with increase in concentration of Al^{3+} ions and got diminished at $0.10 \mu\text{M}$ of the metal ion. With further increase in concentration of the metal ion from $0.10 \mu\text{M}$ to $0.42 \mu\text{M}$, a new cathodic peak emerges at -0.648 V , due to the formation of metal-

ligand complex. Before this concentration the new peak was not visible probably due to instability of the complex. An almost linear change in cathodic peak current was observed (for peak at -0.648 V) for different concentrations indicating a quantitative response of **SNR-4** for Al(III) ions (Figure 6.8).

On gradual addition of Al(III) ions, the current magnitude increased because of the electroactive nature of the complex. On complexation with Al(III) ions, a cathodic shift of about 0.254 V in the cathodic peak potential of **SNR-4** was observed while in presence of other metal ions a shift of 0.002-0.013 V was recorded and their peak currents remained almost same even at high concentrations of different metal ions. This indifference in peak currents in the presence of metal ions other than Al(III), indicated that **SNR-4** is more selective towards Al(III) ions.



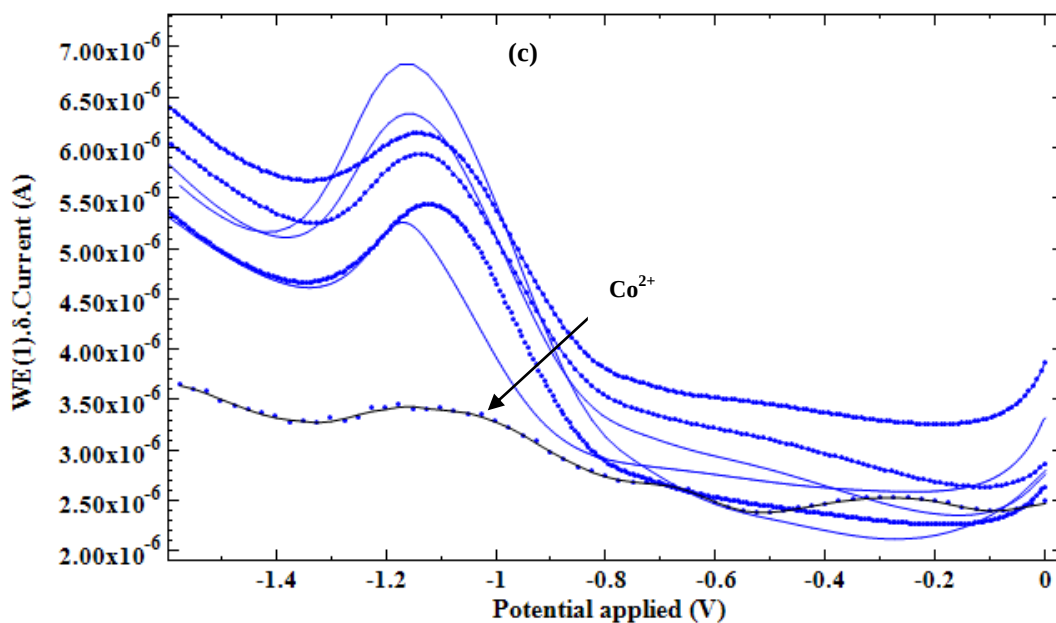
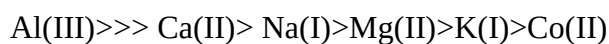


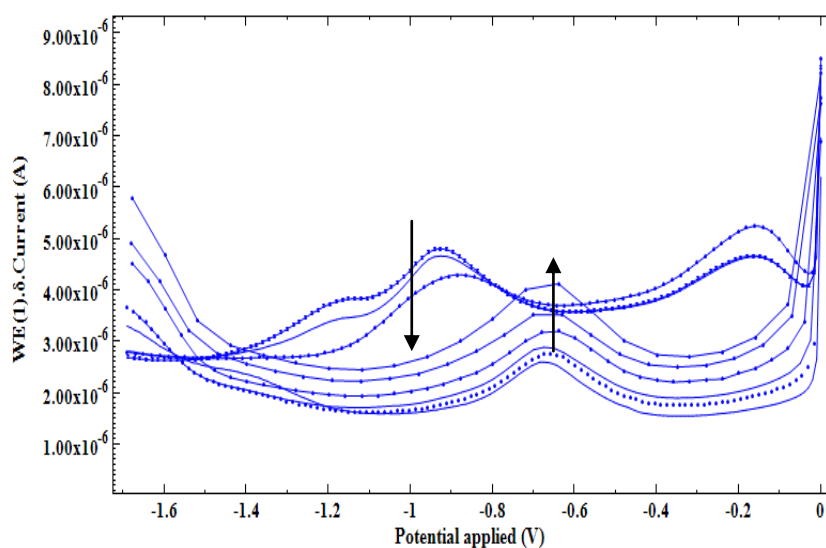
Figure 6.7 Differential Pulse Voltammograms of (a) **SNR-4**, (b) **SNR-5** and (c) **SNR-6** with 0.10 μM of different metal ions (Na(I), K(I), Ca(II), Co(II), Mg(II), Al(II)) in HEPES buffered DMSO:H₂O (8:2, v/v) using 0.1 M TBAP as supporting electrolyte (GC working electrode, scan rate 20 mVsec⁻¹ E vs Ag/Ag⁺)

A tentative selectivity order for metal ions in case of **SNR-4** based on shift in peak potential at -0.902 V can be written as:-



Voltammograms of SNR-5

In voltammogram of **SNR-5** (Figure 6.9), intensity of the cathodic peaks at -1.810 V and -0.967 V decreased with increase in concentration of Al(III) ions and got fully diminished at 0.42 μM .



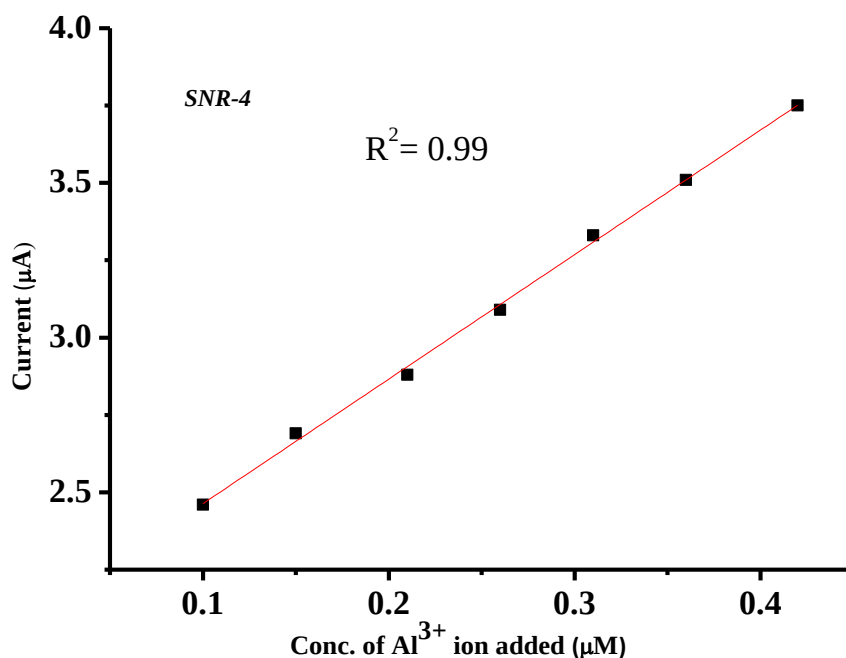
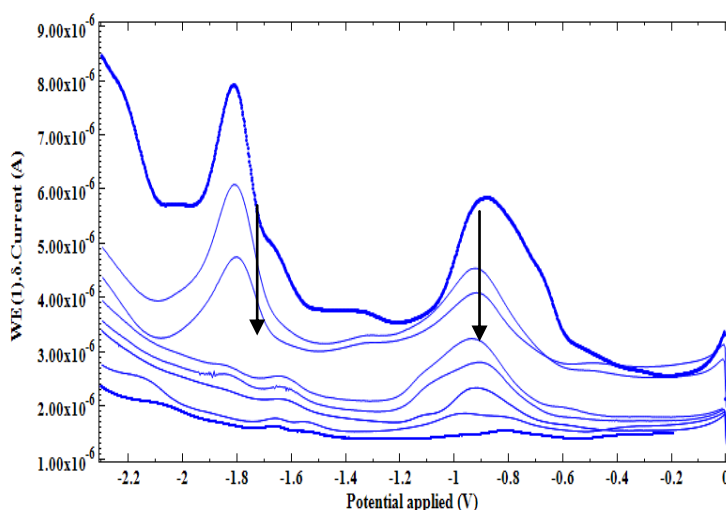
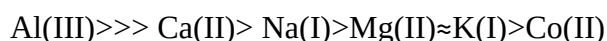


Figure 6.8 Differential Pulse Voltammogram and calibration plot of **SNR-4** (0.30 μM) with 0-0.42 μM of Al(III); in HEPES buffered DMSO:H₂O (8:2, v/v) using 0.1 M TBAP as supporting electrolyte (GC working electrode, scan rate 20 mVsec⁻¹ E vs Ag/Ag⁺)

An almost linear change in cathodic peak current was observed for different concentrations indicating a quantitative response of **SNR-5** for Al(III) ions (Figure 6.9). In presence of other metal ions a shift of 0.001-0.028 V was recorded and their peak currents remained almost same even at high concentration. This indifference of peak current in the presence of metal ions other than Al(III) indicated that **SNR-5** is more selective towards Al(III) ions.

Based on shifts in peak potentials in presence of different metal ions, a tentative selectivity order for metal ions can be written as:-



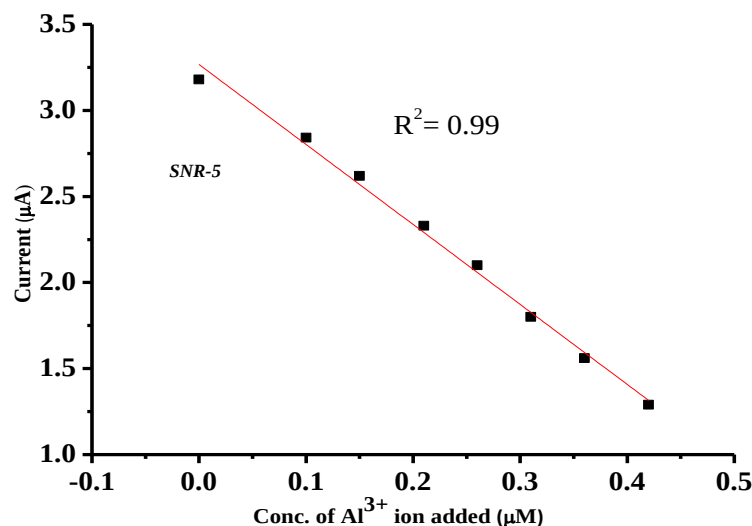
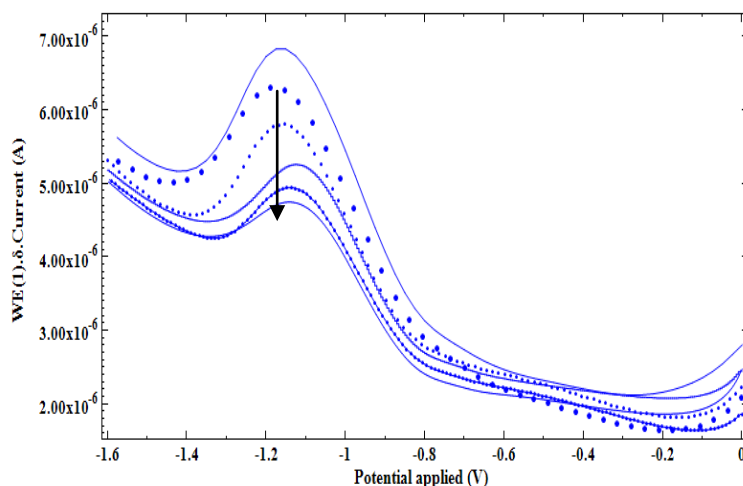
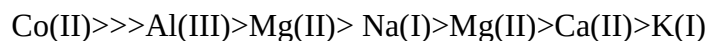


Figure 6.9 Differential Pulse Voltammogram and calibration plot of **SNR-5** (0.30 μM) with 0-0.42 μM of Al(III); in HEPES buffered DMSO:H₂O (8:2, v/v) using 0.1 M TBAP as supporting electrolyte (GC working electrode, scan rate 20 mVsec⁻¹ E vs Ag/Ag⁺)

Voltammograms of SNR-6

In voltammogram of **SNR-6** (Figure 6.10), intensity of the cathodic peak at -1.205 V decreased with increase in concentration of Co(II) ions and got diminished at 0.42 μM of the metal ion. A change in cathodic peak current was observed for different concentrations indicating a quantitative response of **SNR-6** for Co(II) ions (Figure 6.10). In presence of other metal ions, a shift of 0.001-0.009 V was recorded and their peak currents remained almost same even at higher concentrations of metal ions. This indifference of peak current in the presence of metal ions other than Co(II) indicated that **SNR-6** is more selective towards Co(II) ions.

Based on shifts in peak potentials of **SNR-6**, a tentative selectivity order for metal ions can be written as:-



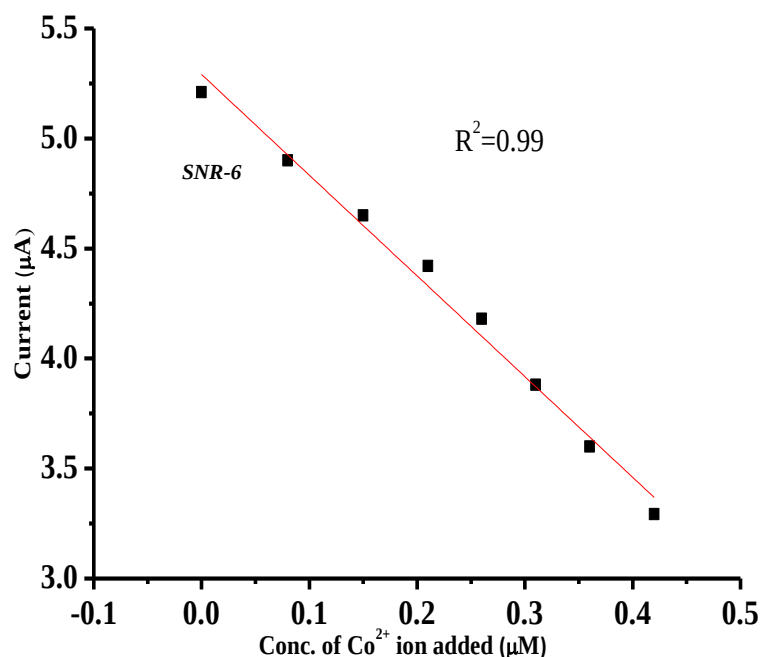


Figure 6.10 Differential Pulse Voltammogram and calibration plot of **SNR-6** (0.30 μM) with 0-0.42 μM of Co(II) ; in HEPES buffered $\text{DMSO:H}_2\text{O}$ (8:2, v/v) using 0.1 M TBAP as supporting electrolyte (GC working electrode, scan rate 20 mVsec^{-1} E vs Ag/Ag^+)

Real life sample analysis

SNR-4, **SNR-5** and **SNR-6** based chemosensors were tested for the analysis of real time samples taken from the laboratory waste water drain. Each sample was spiked with the addition of 1 mL of 10^{-2} M standard metal ion solution, keeping the total volume of the sample equal to 100 mL. The results obtained were verified by using complexometric method as a reference method for the determination of heavy metal ions. Table 6.3 shows that the results obtained by the chemosensors are in complete agreement with the results obtained with complexometric method.

Conclusions

Imine bridged receptors coupled with ZnO nanoparticles (**SNR-4**, **SNR-5** and **SNR-6**) formulate a cavity just suitable to hold reversibly metal ions like Al(III) and Co(II) . Behaviour of these molecules was studied both by voltammetric and potentiometric methods. Different substituents on the phenyl ring resulted in changing electronic environment in the cavity, experienced in the form of selectivity for the target metal ions. Interestingly, the observations are supported sufficiently with energy minimized conformations of the complexed receptors with target metal ions. Response characteristics of the proposed

molecules were supported by theoretical studies as well. While **SNR-4** and **SNR-5** responded selectively for aluminium ions in partially aqueous medium, **SNR-6** responded equally well for cobalt ions as evident from the linear regression coefficients in the range 0.99 to 0.98 over a reasonably wide concentration range upto 0.42 μM of the metal ions.

Table 6.3 Real time sample analysis of laboratory drain waste water samples and its verification with complexometric method (n=3)

Sample Name	Al(III) Conc. (10^7)		Al(III) Conc. (10^7)		Co(II) Conc. (10^7)	
	SNR-4	Complexo-metric method	SNR-5	Complexo-metric method	SNR-6	Complexo-metric method
SM-1	12.57 $\pm$ 0.02	12.6 $\pm$ 0.1	12.59 $\pm$ 0.02	12.5 $\pm$ 0.5	13.29 $\pm$ 0.03	13.3 $\pm$ 0.1
SM-2	21.71 $\pm$ 0.09	21.7 $\pm$ 0.1	22.59 $\pm$ 0.07	22.6 $\pm$ 0.2	17.59 $\pm$ 0.09	17.6 $\pm$ 0.3
SM-3	20.19 $\pm$ 0.01	20.1 $\pm$ 0.2	19.89 $\pm$ 0.06	19.9 $\pm$ 0.2	18.59 $\pm$.01	18.6 $\pm$ 0.4
SM-4	21.59 $\pm$ 0.07	21.5 $\pm$ 0.1	20.79 $\pm$ 0.05	20.7 $\pm$ 0.2	20.19 $\pm$.04	20.2 $\pm$ 0.2
SM-5	15.69 $\pm$ 0.09	15.5 $\pm$ 0.3	14.89 $\pm$ 0.05	14.9 $\pm$ 0.1	14.61 $\pm$ 0.03	14.5 $\pm$ 0.2

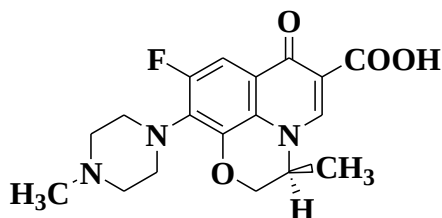
$\pm$ Shows the standard deviation (n=3).

Presence of interfering metal ions like Na(I), K(I), Mg(II), Ca(II), Co(II) (in case of **SNR-4** and **SNR-5**) and Al(III) (in case of **SNR-6**) did not show any effect on the peak potential and high selectivity can be assigned to their respective complexing metal ions (Al(III) for **SNR-4** and **SNR-5**, Co(II) for **SNR-6**). Differential pulse voltammetric studies on all the three complexing systems supported observations from cyclic voltammetric data. The proposed analytical method has been validated with complexometric method for heavy metal detection in real time samples.

6.2 Electrochemical detection of fluoroquinolone drug: Levofloxacin

Fluoroquinolones are a group of compounds which contain fluorine at 6 position of basic quinolone core structure. These are used for treatment of bacterial infection, pneumonia, urinary tract infection, joint and bone infection, skin infections, typhoid fever and several other infection conditions [9]. Fluoroquinolones include Ciprofloxacin, Levofloxacin, Norfloxacin, Gatifloxacin and Ofloxacin. Levofloxacin, (–) -(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-ethyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid hemihydrate, is one of the fluoroquinolone having activity twice that of racemate

mixture of ofloxacin. It is an antimicrobial agent and used in the treatment of different kinds of infections and are available commercially. Levofloxacin (LFX) shows good bactericidal activity against gram-positive and gram-negative bacteria [10,11].



Structure of Levofloxacin

A number of reports are available for the spectrophotometric determination of levofloxacin using different anionic dyes at acidic pH [12-16]. Different techniques have been reported for the determination of levofloxacin in Spectrophotometry [17-19], High Performance Liquid Chromatography [20], Capillary Zone Electrophoresis [21], Ligand Exchange Chromatography [22] and Nuclear Magnetic Resonance Spectroscopy [23]. From the literature survey, it was revealed that levofloxacin (LFX) has been determined in only acidic medium. No attempt has been made to study the voltammetric determination of levofloxacin without optimization of pH.

In this research work, we have used picric acid as an anionic reagent for the voltammetric determination of levofloxacin and no optimization of pH is required because of picric acid, which due to presence of three nitro groups enables the easy removal of H^+ ions, resulting in ion-pair interaction between levofloxacin and picric acid. This work for the first time proposes the electrochemical detection of levofloxacin using picric acid as a reagent. Stability of the ion association was further supported with the DFT calculations. The proposed method was found to be reliable, sensitive and reproducible.

Results and discussion

As discussed above, a lot of attempts have been made for the direct determination of levofloxacin by using various analytical techniques. Ion-pair formation method for the determination of levofloxacin has an advantage of extraction of the drug in real life samples also. On addition of picric acid into the sample containing levofloxacin, development of ion-pair in the form of solid helps in easy removal of excessive drug presence in various real life samples which is not possible in case of direct determination of levofloxacin. Moreover, this

system works well in fully aqueous medium which is the best green solvent when compared with other organic solvents which have to be used in case of extraction procedures used till now in the literature. Keeping in mind the above benefits of ion-pair formation, determination of levofloxacin was carried out using picric acid for the formation of ion-pair without optimizing pH.

Ion-pair formation

In a 25 mL separatory funnel, 3mL each of LFX [10^{-3} M] and PA [10^{-3} M] were added in 1:1 stoichiometric ratio. Shook the mixture well for 5-10 minutes. On keeping the liquid for few minutes a bright yellow colored solid separated out from the reaction which was filtered through filter paper, washed several times with distilled water and dried overnight in oven at 60-70 °C.

Electrochemical determination of ion pair

Electrochemical behavior of LFX and PA

Cyclic voltammograms of LFX showed one major anodic peak at 1.71V with two minor anodic peaks at 0.61 V and 1.15 V. The cathodic peaks were observed at 1.65V (major) and 1.13 V (minor). The redox cycle near 1.71 V corresponds to quasi reversible process probably occurring at the piperazine moiety as observed from the peak current values [24]. Differential pulse voltammetry also supported the observed peak potentials as shown in Figure 6.11b and c.

In case of PA, a redox cycle at 1.31 V, cathodic peaks appeared at 1.35 V, -0.51 V, -0.84 V, -1.62 V and -1.92 V which might be due to the reduction processes occurring at the nitro groups of PA. Likewise, two oxidation peaks at 1.63 V and 1.82 V were observed in the anodic cycle which corresponded a two step oxidation of phenolic hydroxyl group (Figure 6.11a). Similar results were obtained in differential pulse voltammograms as shown in Figure 6.11b and c.

Ion-pair determination voltammetrically

Ion-pair formed from the interaction of drug LFX and PA was studied for its peak potentials by cyclic and differential pulse voltammograms. As observed from the voltammograms (Figure 6.11a, b and c), anodic peak of LFX-PA (1.64 V) got shifted by 70 mV when

compared with peak potential of LFX (1.71 V) with large decrease in peak current from 25.4 μA to 9.2 μA . In case of LFX-PA, new peaks appeared at 0.90 V, 1.12 V, 1.45 V, 1.64 V and 1.88 V. Similarly, in case of cathodic cycle, peaks at 1.63 V, -0.80 V, -1.62 V and -1.92 V appeared which proved the interaction of the PA and LFX. Deviation in the peak potentials of LFX-PA from that of PA and large difference in peak current values might be due to the interaction of PA with the drug LFX.

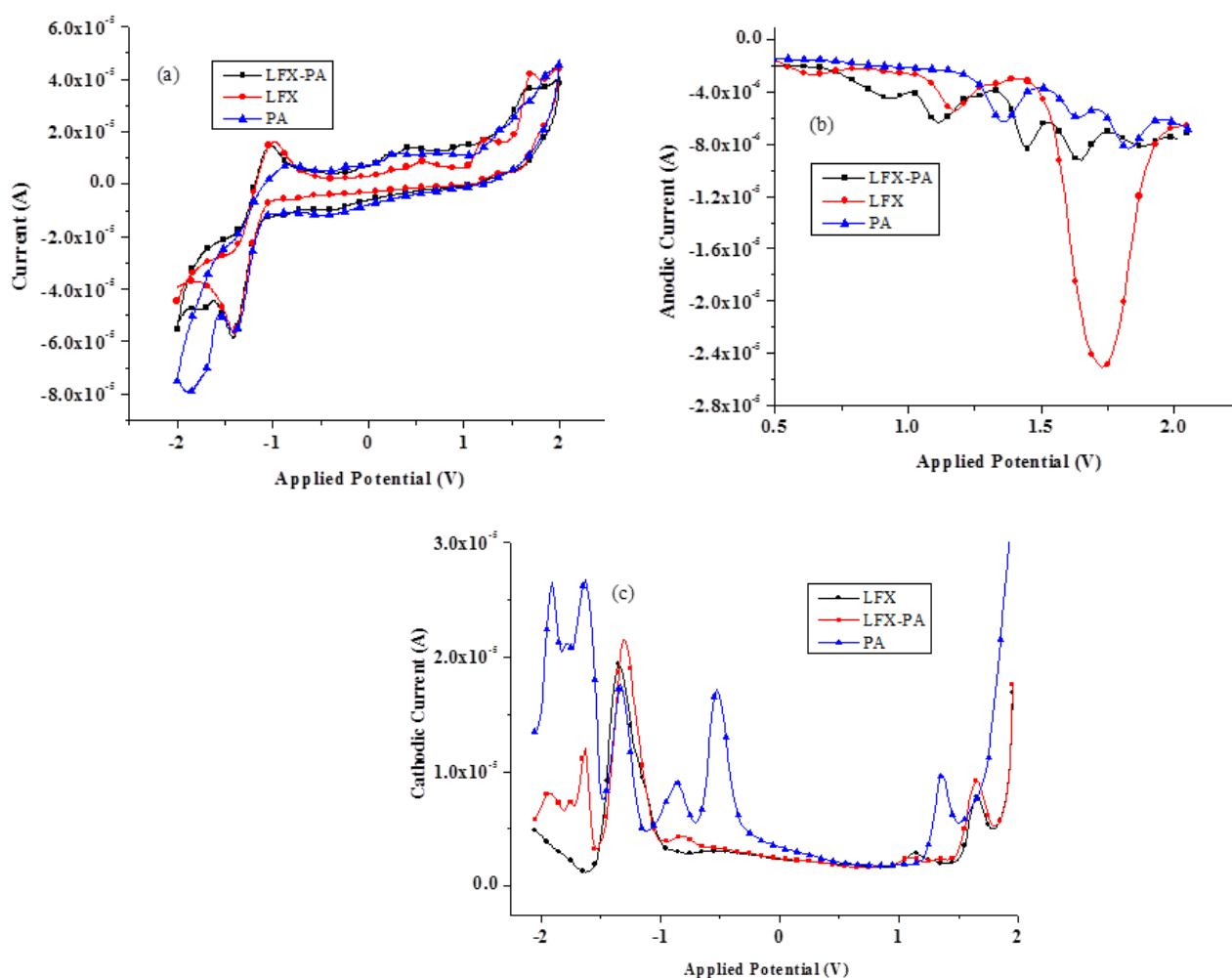
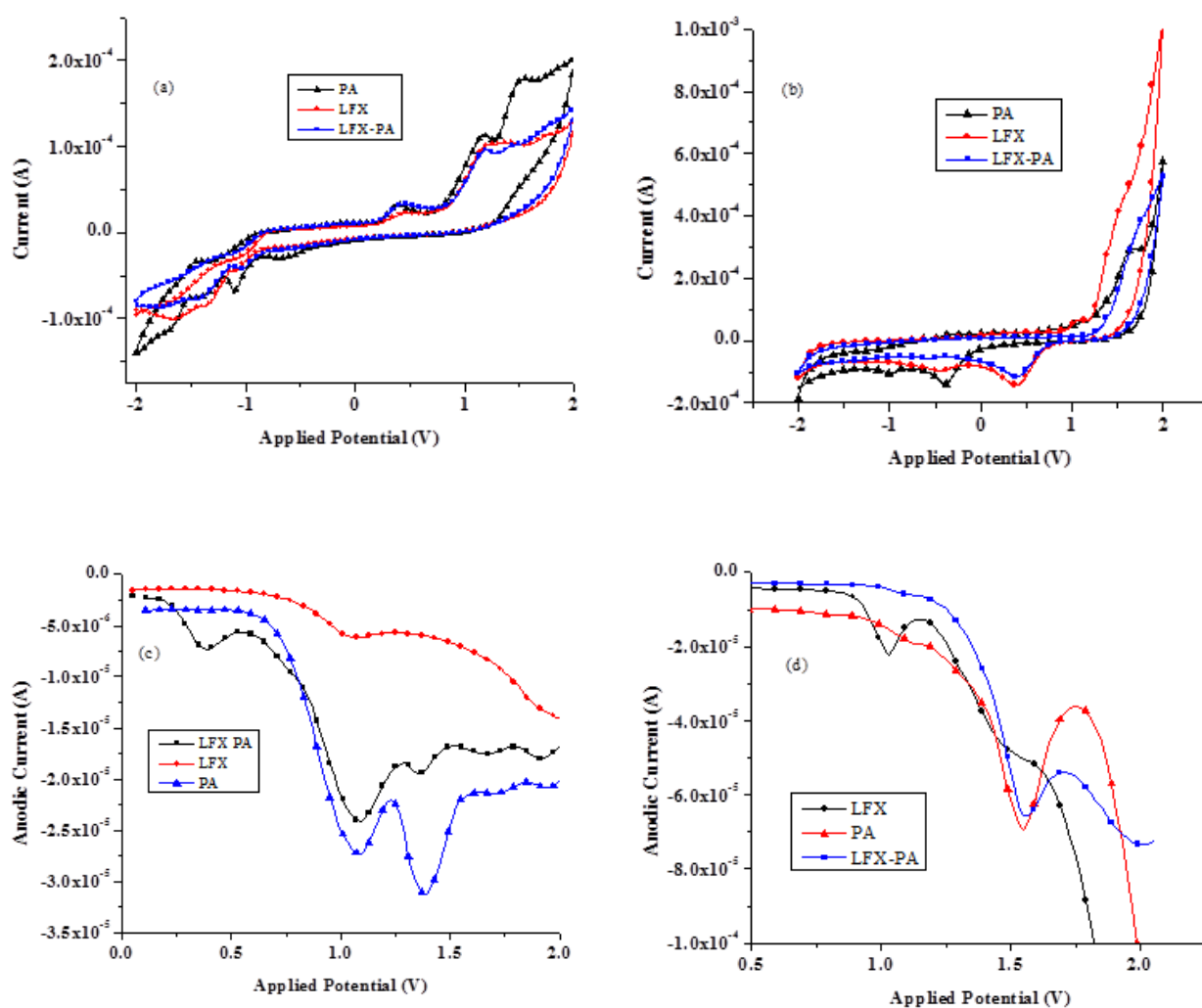


Figure 6.11 (a) Cyclic Voltammograms of LFX, PA and LFX-PA (b) Anodic Differential Pulse Voltammograms of LFX, PA and LFX-PA (c) Cathodic Differential Pulse Voltammograms of LFX, PA and LFX-PA in CH_3CN containing 0.1M TBAPF_6 as supporting electrolyte at scan rate 50mV/sec

Effect of solvent

Voltammetric determination of LFX-PA was also carried out in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (9:1; v/v) and H_2O as solvent systems (Figure 6.12). It was observed that in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (9:1; v/v) there was a large increase in cathodic and anodic peak currents with small shift in their peak potentials from 9 μA to approximately 24 μA for anodic peak and 11.8 μA to 20.3 μA for

cathodic peak. While in case of aqueous medium, oxidation occurs with only single peak potential (1.56 V) with a huge increase in the peak current i.e. 9 μA to 65.9 μA from. The results demonstrated the use of H_2O as a perfect solvent because complete oxidation takes place at a single peak potential i.e., 1.56 V having sufficiently high peak current as included in Table 6.4. Water being a highly polar solvent further increases the chance of oxidation occurring at the piperazine moiety and hence high peak current was observed as compared to CH_3CN and $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (9:1; v/v) as solvent media. In case of cathodic cycle of LFX-PA, it was observed that with increasing water content in solvent medium, cathodic peak potentials got shifted to lower values. These observations prove that oxidation of piperazine moiety and reduction of nitro groups can be easily carried out if we move from pure CH_3CN to $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ mixture media increasing water ratio in solvent medium. Similar results were also observed in pure LFX and PA.



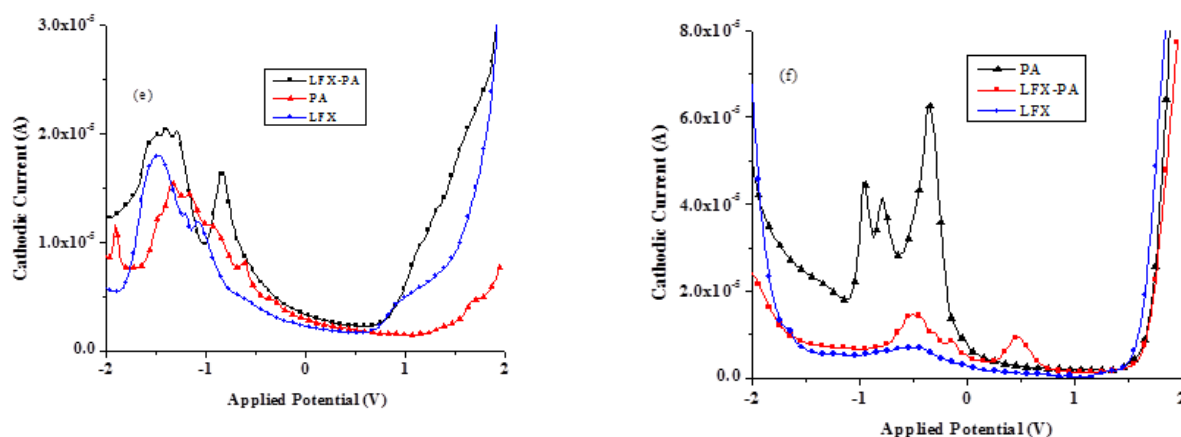
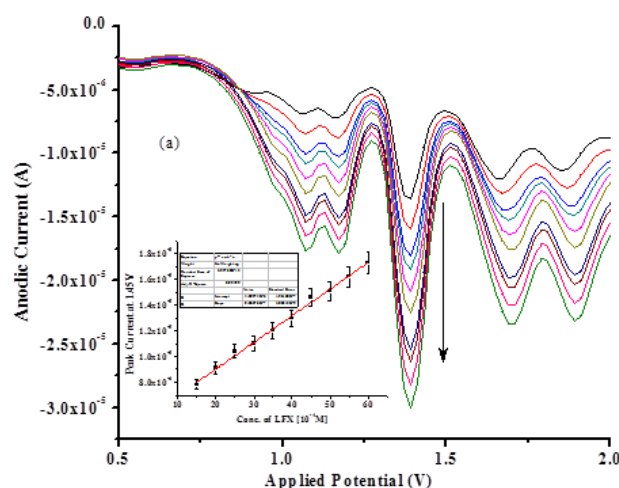


Figure 6.12 Voltammograms of LFX, PA and LFX-PA (a), (c) and (e), in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$. (b), (d) and (f), in H_2O . (a) and (b), cyclic voltammograms. (c) and (d), anodic differential pulse voltammograms. (e) and (f), cathodic differential pulse voltammograms containing 0.1 M TBAPF_6 as supporting electrolyte at scan rate 50 mV/sec

Quantitative study

Voltammetric measurements of Levofloxacin (LFX) are quantitatively valid. Differential pulse voltammograms were drawn with different concentrations of LFX taken separately in all the three solvent media i.e. pure acetonitrile, a mixture of acetonitrile and water in 95:5 ratio and pure water. Voltammograms for different solvents are shown in Figure 6.13. Figure 6.13 shows the dependence of voltammetric peak current on levofloxacin concentration value. It can be seen that peak current at 1.45V increases linearly with increasing LFX concentration from $15 \times 10^{-4} \text{ M}$ – $60 \times 10^{-4} \text{ M}$ with $R^2 = 0.994$ with relative standard deviation 5% in CH_3CN as solvent medium. Likewise, calibration graphs were plotted in $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ and H_2O (Figure 6.13 b and c). From these calibration graphs, we can conclude that PA can be used as an anionic reagent for the determination of LFX in different solvent systems.



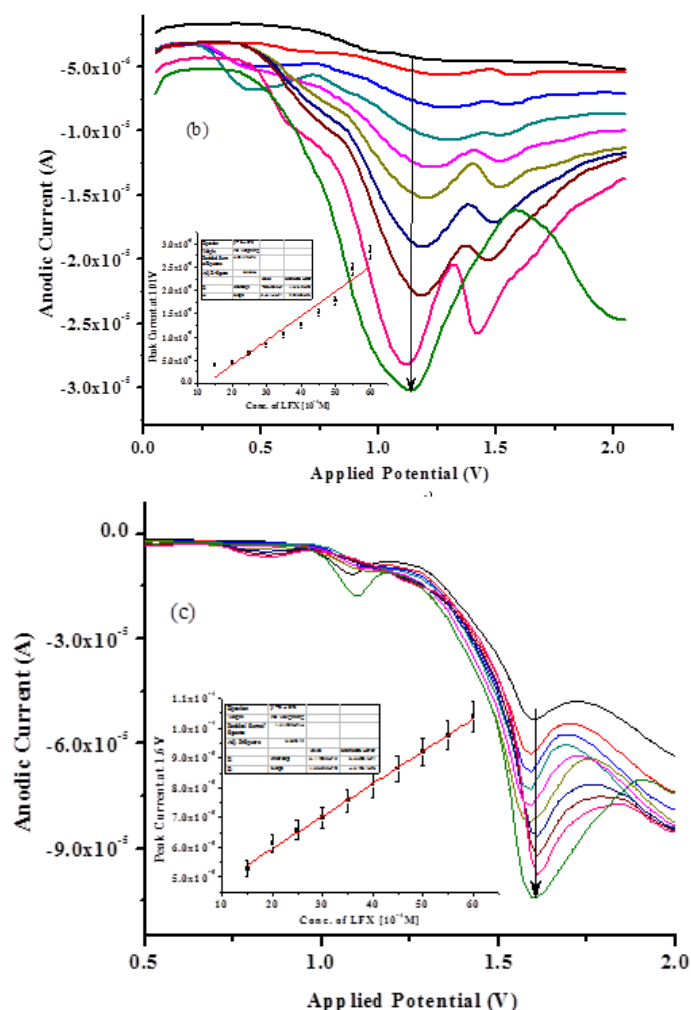


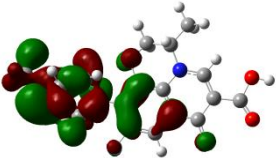
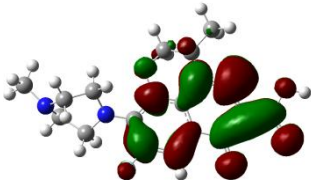
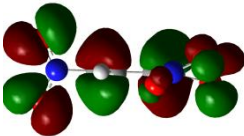
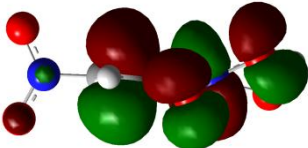
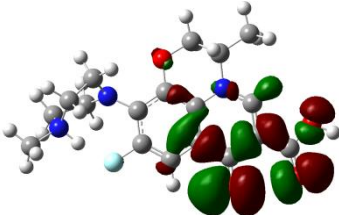
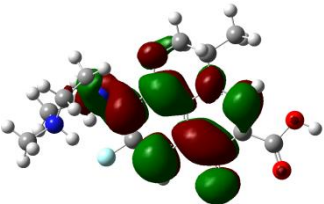
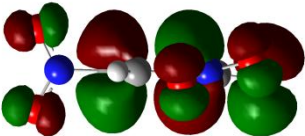
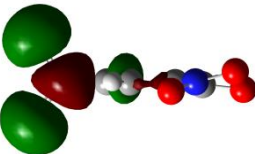
Figure 6.13 Differential Pulse Voltammograms of LFX-PA at different concentrations of LFX ($15 \times 10^{-4} \text{ M}$ - $60 \times 10^{-4} \text{ M}$) in (a) CH_3CN (b) $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (c) H_2O ; Insets representing the calibration plots of their respective peak currents w.r.t. concentrations

Computational studies

Computational study of LFX, PA, LFXH^+ , PA^- , LFX-PA^- and $\text{LFXH}^+-\text{PA}^-$ was carried out on Gaussian 03W software. All the structures were optimized for minimum energy by using DFT calculations. Basis sets used for optimization of structures and complexes were B3LYP/6-31G in gaseous state. The complex ($\text{LFXH}^+-\text{PA}^-$) was assigned net zero charge and all the optimizations were carried out in ground state. The DFT calculations of ionized and unionized complexes indicate the energy of HOMO, LUMO, energy gap and gas phase energy of LFX, PA, LFXH^+ , PA^- , LFX-PA^- and $\text{LFXH}^+-\text{PA}^-$ as shown in Table 6.4. Surfaces of HOMOs and LUMOs of LFX, PA, LFXH^+ , PA^- , LFX-PA^- and $\text{LFXH}^+-\text{PA}^-$ appear in Figure 6.14. Energy gap of $\text{LFXH}^+-\text{PA}^-$ gets reduced after ion-ion association complex and leads to the stability of the interaction.

Table 6.4 Energy of HOMO, LUMO, gas phase energy and energy gap of various compounds and complexes

Compounds	Gas Phase Energy (eV)	HOMO (eV)	LUMO (eV)	Energy Gap (eV)
LFX	-34355	-5.3	-1.4	-3.9
PA	-25050	-8.6	-4.0	-4.5
LFXH ⁺	-34366	-8.59	-4.1	-4.4
PA ⁻	-25037	-2.9	-0.1	-2.7
LFX-PA ⁻	-59407	-6.2	-3.0	-3.2
LFXH ⁺ -PA ⁻	-59393	-2.7	-0.3	-2.4

Compound	HOMO	LUMO
LFX		
PA		
LFXH ⁺		
PA ⁻		

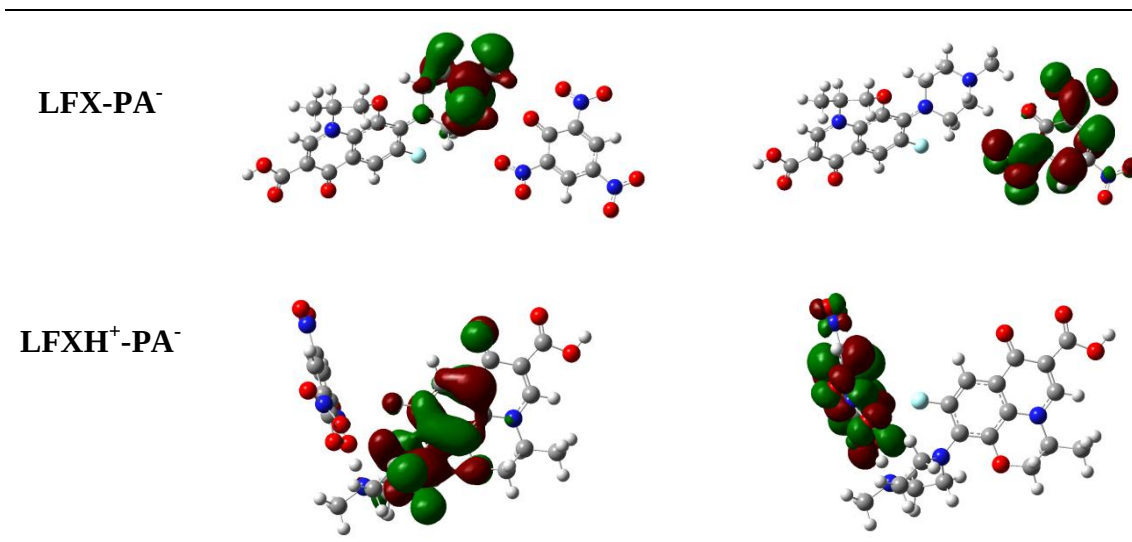


Figure 6.14 HOMO-LUMO surfaces of various compounds and complexes

The DFT calculations show that in case of LFXH⁺-PA⁻, picric acid lies perpendicular to the plane of LFX and appears as a V-shaped structure as shown in Figure 6.15. Hydrogen ion of picric acid gets ionized and interacts with nitrogen of piperazine moiety of LFX. Bond distance between terminal nitrogen of piperazine moiety and ionized hydrogen is 1.06 Å, while bond distance between phenolate oxygen of PA and ionized hydrogen gets elongated and is 1.62 Å as measured from optimized geometry of the complex.

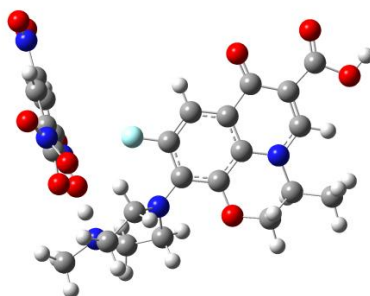


Figure 6.15 Interaction diagram of optimized structures of PA and LFX using DFT/B3LYP/6-31G method. Red balls represent oxygen, blue balls represent nitrogen and grey balls represent carbon atoms

Analytical applications

The proposed method was successfully applied for the determination of levofloxacin content in commercial drug tablets. Commonly used additives in the manufacturing of tablets were not found to interfere in the analysis. To establish validity of this proposed method, recovery test was performed by using standard addition technique. Recovery is calculated as:

$$\% \text{ recovery} = (\text{measured levofloxacin} \times 100) / \text{added levofloxacin}$$

Concentration values obtained by this method for different series of tablets were compared with results done with spectrophotometric method are shown in Table 6.5. The regression equation of standard addition curve was found for levofloxacin at 1.64V. Results given in Table 6.5 reveal that recoveries obtained were in the range 94.6% to 100% proving the validity of the proposed method.

Table 6.5 Recovery studies using standard addition method

Pharmaceutical Preparations	Proposed method					
	Spectrophotometric method			Voltammetric method		
	Taken (µg/mL)	Found (µg/mL)	Recovery (%)*	Taken (µg/mL)	Found (µg/mL)	Recovery (%)*
Levomac tablets ^a (Levofloxacin, 500 mg/tablet)	20.0	18.9	94.6	20.0	19.3	96.7
	40.0	39.2	98.0	40.0	40.0	100
	60.0	59.4	99.0	60.0	59.7	99.5
	100.0	98.6	98.5	100.0	99.9	99.9
Levac tablets ^b (Levofloxacin, 750 mg/tablet)	20.0	19.9	99.9	20.0	19.9	99.3
	40.0	39.5	98.8	40.0	39.9	99.9
	80.0	79.4	99.3	80.0	79.9	99.9
	100.0	99.3	99.3	100.0	99.3	99.3
Levomac tablets ^c (Levofloxacin, 250 mg/tablet)	20.0	19.7	98.8	20.0	19.9	99.7
	40.0	39.5	98.9	40.0	39.6	99.2
	60.0	58.9	98.3	60.0	59.9	99.9
	100.0	99.6	99.6	100.0	99.4	99.4

* Average of at least 3 determinations.

^a MACLOEDS PHARMACEUTICAL LTD., MUMBAI. (Batch No. KLB502A).

^b Franklin Laboratories Pvt. Ltd. Roorkee. (Batch No. LYC75-14).

^c MACLOEDS PHARMACEUTICAL LTD., MUMBAI. (Batch No. ALC401C).

Conclusions

Voltammetric methods were developed for the determination for levofloxacin at µg level. Picric acid having three nitro groups facilitates the removal of H⁺ ion from phenolic hydroxyl group, which eventually forms the ion association at the nitrogen center of piperazine moiety of levofloxacin. The method described herein has many advantages; easy synthesis of ion pair complex, stability of the complex, less time consuming, sensitive and electrochemically active.

6.3 References

1. R. A. Olowu, P. M. Ndangili, A. A. Baleg, C. O. Ikpo, N. Njomo, P. Baker and E. Iwuoha, *Int. J. Electrochem. Sci*, **2011**, 6, 1686-1708.
2. N.-N. Bui, J.-T. Hong, S.-i. Mho and H.-Y. Jang, *Notes*, **2008**, 29, 1395.
3. O. B. Sutcliffe, A. Chesney and M. R. Bryce, *J. Organomet. Chem.*, **2001**, 637, 134-138.
4. B. B. Straumal, A. Myatiev, P. Straumal, A. Mazilkin, S. Protasova, E. Goering and B. Baretzky, *JETP Lett.*, **2010**, 92, 396-400.
5. B. B. Straumal, S. Protasova, A. Mazilkin, G. Schütz, E. Goering, B. Baretzky and P. Straumal, *JETP Lett.*, **2013**, 97, 367-377.
6. H. Sharma, N. Kaur, T. Pandiyan and N. Singh, *Sensor Actuat. B: Chem.*, **2012**, 166, 467-472.
7. H. Karimi-Maleh, F. Tahernejad-Javazmi, M. Daryanavard, H. Hadadzadeh, A. A. Ensafi and M. Abbasghorbani, *Electroanal.*, **2014**, 26, 962-970.
8. H. Sharma, A. Singh, N. Kaur and N. Singh, *ACS Sustainable Chem. Eng.*, **2013**, 1, 1600-1608.
9. P. S. G. Britain, "Martindale: The Complete Drug Reference Pharmaceutical Press," London (UK) 33, **1941**.
10. M. Tanaka, T. Kurata, C. Fujisawa, Y. Ohshima, H. Aoki, O. Okazaki and H. Hokusui, *Antimicrob. Agents Chemother.*, **1993**, 37, 2173-2178.
11. D. Ross and C. Riley, *Intl. J. Pharm.*, **1990**, 63, 237-240.
12. A. W. Qassim, *Int. J. Adv. Sci. Tech. Res.*, 3, **2015**, 135-146.
13. S. Ashour, M. F. Chehna and R. Bayram, *Int. J. Biomed. Sci.*, **2006**, 2, 273-289.
14. W. Sun, J. Han, Q. Li and K. Jiao, *S. Afr. J. Chem.*, **2015**, 60, 42-46.
15. A. M. El-Brashy, M. E.-S. Metwally and F. A. El-Sepai, *Farmaco*, **2004**, 59, 809-817.
16. Z. Shoaibi and A. Gouda, *J. Young Pharm.*, **2012**, 4, 42-48.
17. C. Sastry, K. R. Rao and D. S. Prasad, *Talanta*, **1995**, 42, 311-316.
18. H. Salem, *Am. J. Appl. Sci.*, **2005**, 2, 719-729.
19. A. M. El-Brashy, M. E.-S. Metwally and F. A. El-Sepai, *Bull. Korean Chem. Soc.*, **2004**, 25, 365-372.
20. A. Nadukuru and T. S. Kumar, *Int. J. Food Drug Anal.*, 1, **2013**, 37-48.

21. K. L. See, A. A. Elbashir, B. Saad, A. S. M. Ali and H. Y. Aboul-Enein, *Biomed. Chrom.*, **2009**, 23, 1283-1290.
22. H. Yan and K. H. Row, *Anal. Chim. Acta*, **2007**, 584, 160-165.
23. A. Salem, H. Mossa and B. Barsoum, *Spectrochim. Acta Mol. Biomol. Spectrosc.*, **2005**, 62, 466-472.
24. A. Radi and Z. El-Sherif, *Talanta*, **2002**, 58, 319-324.

LIST OF PUBLICATIONS

1. **Rashmi Sharma**, Manmohan Chhibber, Susheel K Mittal*, A new ionophore for chemical sensing of F^- , CN^- and Co^{2+} using voltammetric, colorimetric and spectrofluorimetric techniques, *RSC Advances* (2016) 6: 51153-51160. **(IF:3.289)**
2. **Rashmi Sharma**, Manmohan Chhibber*, Susheel K Mittal, Diphenylether based derivatives as Fe (III) chemosensors: Spectrofluorimetry, Electrochemical and Theoretical studies, *RSC Advances* (2015) 5: 21831-21842. **(IF: 3.289)**
3. **Rashmi Sharma**, Susheel K Mittal*, Manmohan Chhibber, Voltammetric Sensor for Fluoride Ions Using Diphenylether Derivatives Supported by NMR and Theoretical Studies, *Journal of Electrochemical Society* (2015) 162: B248-B255 **(IF:3.266)**
4. Susheel K Mittal*, **Rashmi Sharma**, Manisha Sharma, Narinder Singh, Jasinder Singh, Navneet Kaur and Manmohan Chhibber, Imine linked chemosensors coupled with ZnO for the detection of Al^{3+} by voltammetric method, *Journal of Applied Electrochemistry* (2014) 44: 1239-1251. **(I.F.: 2.409)**
5. **Rashmi Sharma**, Manmohan Chhibber, Susheel K Mittal*, Etheral-Imine based multiresponsive colorimetric and reversible dipodal receptor for nanomolar detection of copper ions. (Under revision)
6. Susheel K Mittal*, **Rashmi Sharma**, Palak Narang, A green electroanalytical method for the determination of Levofloxacin by Ion-Pair formation with Picric acid. (Communicated)

Patent Filing

1. Susheel K Mittal, Manmohan Chhibber, **Rashmi Sharma**, Novel aryether receptor as an ion specific probe for cerium (III). (Applied for filing)

Papers/ Posters in Conferences

1. **Poster Presentation** in National Conference on Innovative Molecules for Sustainable Future (NCIMSF-2013) held on February 24-26, 2013 at Thapar University, Patiala.
2. **Oral Presentation** in 3rd National Conference on Advances in Metreology [Admet 2014] held on February 19-21, 2014 at Thapar University, Patiala.

3. **Poster Presentation** in 17th CRSI National Symposium in Chemistry held on February 06-08, 2015 at CSIR-NCL, Pune.
4. **Poster Presentation** in 7th National Seminar entitled "Synergistic Aspects of Chemical and Other Sciences-2015 (SACOS-2015)" held on February 19-20, 2015 at Punjabi University, Patiala.
5. **Poster Presentation** in Professor R.C. Paul National Symposium on "INNOVATIONS IN CHEMICAL SCIENCES" held on 20-21 March, 2015, Punjab University, Chandigarh.
6. **Attended Short Term Course** on "Advance materials and Characterization Techniques" from 01-07 June, 2015 at NIT Jalandhar.
7. **Poster Presentation** in 18th CRSI National Symposium in Chemistry held on February 05-07, 2015 at Punjab University, Chandigarh.