

Chapter I

Multidentate Ligand Systems and Their Applications

Abstract

The importance of various multidentate ligands has been outlined in this chapter with a special emphasis on ion sensing and the applications of their metal complexes as catalysts. The scope and objectives of the present research work have been delineated.

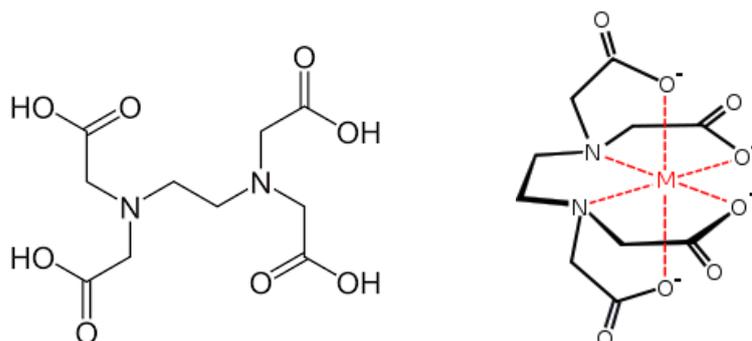
I.1. Introduction

Design and synthesis of customized ligand systems is often considered as a great challenge in synthetic chemistry. Combination of metals and suitable ligand systems have shepherded the discovery of novel organometallics, efficient catalytic systems, useful sensing platforms for the detection of (bio) molecules or ions, molecular AND logic gates etc [1]. According to conventional coordination chemistry, co-ordination of a ligand to a metal centre involves the donation of unshared pair of electrons from the ligand to metal. The metal ions are treated as Lewis acids, as they accept the unshared pair of electrons from ligands. The coordinating ligands, which donate their unshared pair of electrons, are considered as Lewis bases. Multidentate ligands may also coordinate to anions depending on their charge density and anionic radii, where the unshared pair of electrons can interact with the anions. In such a case, they may be considered as a 'receptor' rather than a conventional ligand. The binding phenomenon of ligands or more precisely the receptors with various species is termed as '*molecular recognition*', a process which involves *selection* and *binding* with a substrate. The chemistry of the artificial receptor molecules may be considered as generalized coordination chemistry, where the receptors coordinate with various types of species: cations, anions, neutral organic species, inorganic and biological molecules. As the multidentate ligand systems have more than one receptor sites, they can provide higher order of recognition [2]. The multidentate ligands have widely been used by the nature because of their high recognition power. Multidentate ligands are also attractive due to their strong binding ability to stabilize metal ions in their different oxidation states through complex formation. Macrocyclic ligands constitute another group of multidentate ligands where the donor atoms are incorporated in a cyclic backbone. The macrocyclic ligands with conjugation provide a rigid structure around the metal ion, whereas the saturated or non conjugated macrocyclic ligands are flexible in nature. The multidentate receptors for ions have led the researchers to establish suitable protocols for the detection of various ions important in biological, industrial and pharmaceutical fields. In this chapter we would focus on the application of multidentate receptors as chemosensors for cations and anions, followed by the catalytic activity of first row transition metal complexes of multidentate ligands.

I. 2. Application of multidentate ligand systems

Multidentate ligands have attracted wide importance due to various reasons such as (i) significant enhancement in stability constant of receptor-substrate association; (ii) efficiency in differentiating between closely related metal ions; (iii) capability to offer different structural features depending on the environmental conditions and (iv) the ability to mimic the structure and also selective metal ion coordinating property of biological relevant ligands. Jean- Marie Lehn, in his Nobel Lecture had significantly described the concept of supramolecular chemistry including cation and anion recognition, catalysis, transport and storage of ions and molecular devices offered by various multidentate cyclic ligands like cryptands [2].

The synthetic hexadentate ligand ethylenediaminetetraacetic acid (H_4EDTA) is a classic example of multidentate ligand. This ligand was first synthesized by Ferdinand Münz from the reaction of ethylenediamine and chloroacetic acid in the year 1935 [3]. EDTA can bind with almost all metal ions present in the periodic table, which makes the basis of detection method for various metal ions in alloys.



Scheme I.1. Ethylenediaminetetraacetic acid and its coordination pattern.

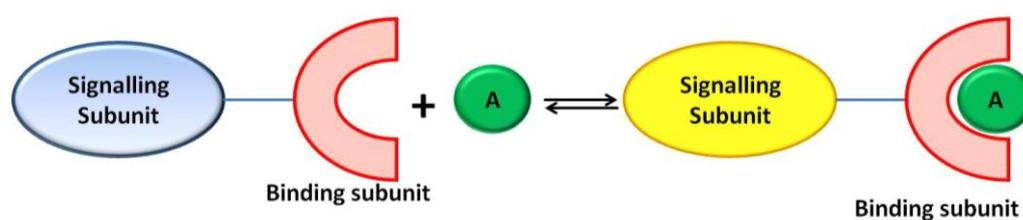
EDTA also has wide range of applications in industrial field, medicinal field and pharmaceutical fields. The disodium monocalcium salt of EDTA ($Na_2CaEDTA$) is used to treat lead poisoning by forming $Na_2PbEDTA$ salt. This complex is also used for the treatment of zinc and radioactive strontium contamination. The monocalcium salt of H_2EDTA^{2-} (CaH_2EDTA) is also employed to remove stone from urinary tract [4]

Based on few more literature survey we present a brief account on the application of multidentate ligands in various fields.

I.2.1. Multidentate ligand systems as chemosensors

Chemosensor is a term associated with a molecular phenomenon in host guest chemistry. The characteristics of sensor molecules undergo detectable changes in

presence of guest molecules [5]. The most widely employed methods to establish a molecule as a chemosensor are electronic absorption spectroscopy, fluorescence emission spectroscopy and potentiometry. The presence of cations and anions in appropriate proportion *in vivo* is essential to sustain various biological processes. On the other hand, deviation from the required proportion can lead to severe malfunction in living organisms. Therefore the design and synthesis of sensor molecules for the detection and quantification of these ions have been a very important and widely studied area in chemical, biochemical, medicinal and industrial research. Numerous efforts are being focussed on finding inexpensive, reliable and simple ways of ion detection in solution.



Scheme 1.2. Schematic representation showing binding of an analyte or guest molecule to a receptor or host molecule which is capable of signalling changes in state.

An efficient molecular sensor device is designed by the combination of three basic parts;

- i) A binding subunit; which reversibly or irreversibly binds with the guest or the analyte.
- ii) A signalling subunit; which converts the binding phenomenon into an observable and measurable physical as well as chemical change.
- iii) An easy and suitable method through which one can measure the changes in the molecule observed as a consequence of binding.

The binding site and the signalling subunit are attached to each other via a covalent linkage [6]. The binding of an analyte with the receptor site induces changes in the electronic properties of the signalling subunit, which is referred to as sensing of the targeted analyte or guest. Depending on the type of signals generated by the binding phenomenon, the sensor molecules can be classified into two categories: (i) optical sensors, which show changes in optical properties (absorbance, fluorescence emission, refractive indices etc.) of the molecule after coordinating with the guest or analyte and (ii) electronic sensors, produce changes in electronic property.

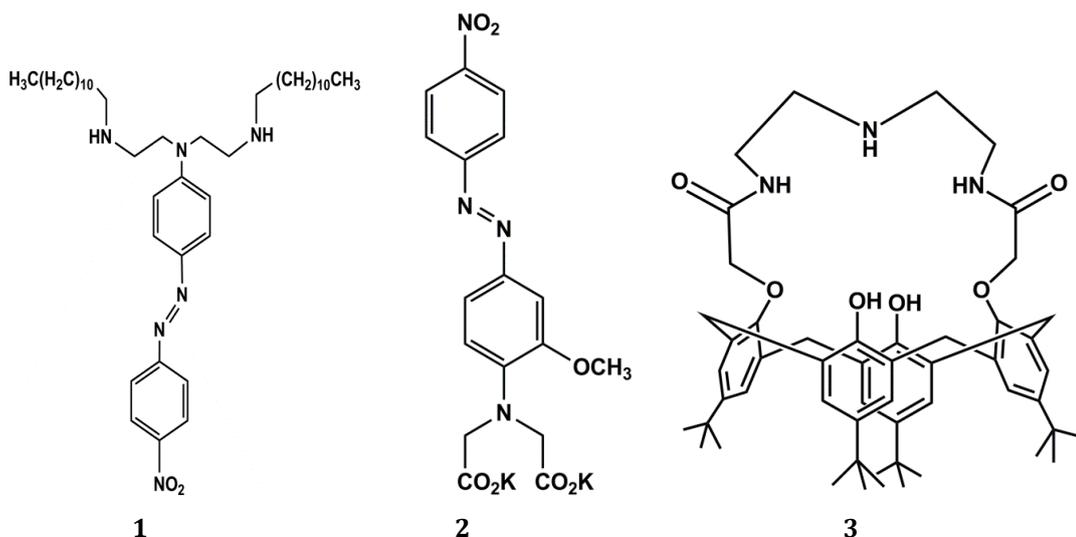
The optical sensors are further classified into two categories:

(i) Chromogenic sensors, which show visible colour changes upon binding of an analyte with the receptor site. The chromogenic or colorimetric chemosensors are very interesting as the guest detection can be performed very easily even without the engagement of sophisticated instruments and the other one is (ii) fluorogenic sensors, which show changes in fluorescence emission property of the signalling subunit. Fluorescence emission spectroscopy is very sensitive and offers sub micromolar detection of the analytes. Hence, the application of fluorogenic sensors is more advantageous than that of chromogenic sensors.

Based on the nature of the analytes the sensors can be grouped into i) cation sensors, which senses cations in mixture; ii) anion sensors, which signals the presence of anions in a mixture and iii) neutral molecular sensors, which offer their molecular cavity as the receptor or binding site.

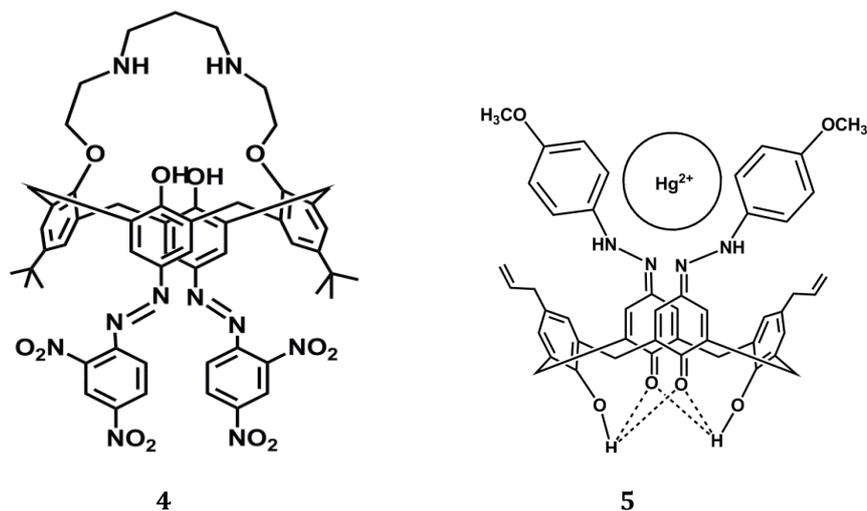
I.2.1.1. Selective cation sensors

As the chemical properties of cations are precisely known, examples of sensor molecules for cations are prevalent in literature. The binding of a cation with multidentate ligands has an important contribution in molecular recognition chemistry. Based on the background of crown ether chemistry, many efficient and selective cation sensors have been reported in literature in past few decades. Receptor **1** shows visible colour change when binds with Cu^{2+} ion in solution [7].

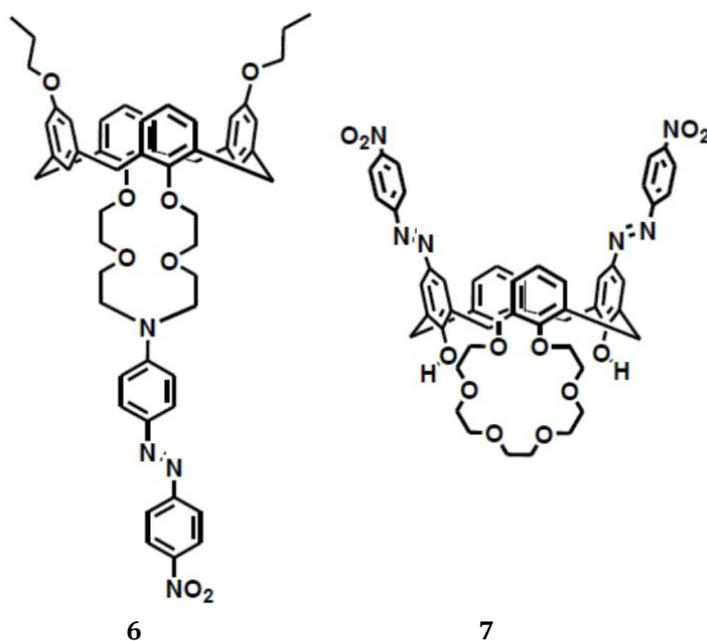


Azo 8-hydroxyquinoline benzoate **2** shows visible colour change in the presence of $\text{Hg}(\text{II})$ in CH_3CN , which enables the visual detection of $\text{Hg}(\text{II})$ [8]. A lower rim substituted calix[4]arene derivative **3** shows selective chromogenic detection

property in presence of Hg^{2+} ion in solution by exhibiting blue shift of 38 nm in UV-visible absorption spectra. The detection is selective over other metal ions in solution [9]. The ligands based on calix[4]arene framework **4**, **5**, **6** show visual optical colour changes when Hg^{2+} ion is added to their solutions.



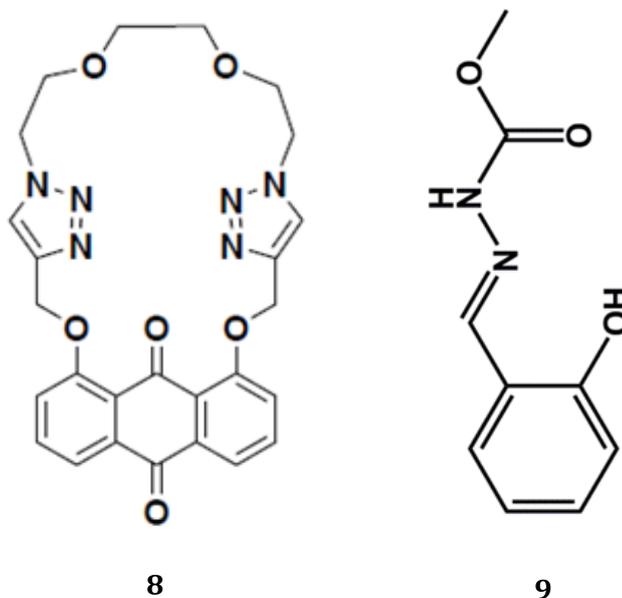
Kim *et al.* have reported an azo coupled calix[4]arene derivative **6**, where the azo group is introduced as a chromogenic group [10].



This receptor shows selectivity for K^+ due to the size compatibility between the K^+ ion and the azacrown-5 cavity as well as a significant $\text{K}^+\cdots\pi$ (cation- π) interaction between the two aromatic rings and the K^+ ion. The receptor **7** shows visual colour change in solution after entrapping alkali earth metal ions like Ca^{2+} and Mg^{2+} in its crown based receptor site [11].

Apart from chromogenic sensors numerous luminescent cation sensors have been developed. They sense target ions via photo induced electron transfer (PET), photo induced charge transfer (PCT), Fröster resonance energy transfer (FRET) mechanisms [12-14]. The application of luminescent sensors is advantageous over chromogenic sensors due to high responsive ability and selectivity [12, 13]. The luminescent sensor molecule is conventionally prepared by the insertion of an ion binding site with a suitable luminophore.

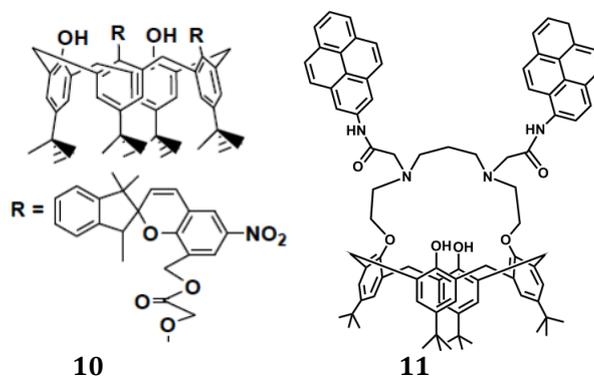
A 1,2,3-triazole based selective chemosensor for Al^{3+} , **8** was synthesized and its optical and electrochemical properties were studied [15]. A significant enhancement in fluorescence emission intensity was observed at 556 nm, after the addition of Al^{3+} . The selective Al^{3+} ion sensing through emission enhancement was attributed to the combined effect of internal charge transfer (ICT) and chelation enhanced fluorescence effect (CHEF) caused by 1, 2, 3-triazole ring, which acts as the fluorophore and carbonyl groups acting as the binding site via 2:1 binding ratio.



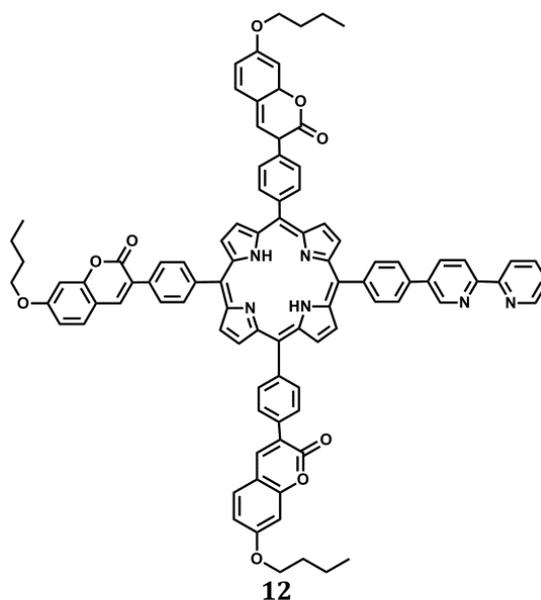
Sensor **9** shows fluorescence turn on upon the addition of $\text{Al}(\text{NO}_3)_3$ solution. In the UV-visible absorption spectra of **9** in presence of Al^{3+} ion, the absorption peak undergoes bathochromic shift from 317 nm to 358 nm in acetonitrile and in the fluorescence emission spectra the emission peak at 453 nm is blue shifted to 447 nm [16, 17].

The calix[4]arene derivative **10** containing two spirobenzopyran fragments were reported [18] as lanthanide ions sensor. In presence of lanthanide ions significant

changes in UV–visible spectra and the emission spectra were observed. For this sensor molecule changes in solution colour was also observed with naked eye over other cations such as Na^+ , K^+ , Mg^{2+} , Ca^{2+} , Fe^{3+} , Cu^{2+} and Zn^{2+} .



A calix[4]arene derivative (**11**) appended with a pyridinylacetamide functional group selectively detects Hg^{2+} ion over other competing heavy metal ions like Pb^{2+} , Cd^{2+} , Cu^{2+} and other metal ions by showing fluorescence emission quenching with an association constant as high as $4.5 \times 10^4 \text{ M}^{-1}$ [19] in methanol.

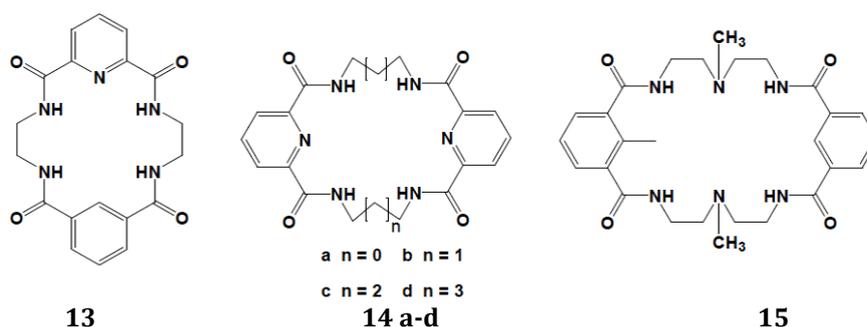


A small-molecule FRET sensor **12** for Co^{2+} ion has been derived from coumarin conjugated porphyrins [20]. A series of these sensors were designed in such a way that in absence of Co^{2+} ion the excitation energy is sufficiently transferred to the porphyrin receptor. After the addition of Co^{2+} ion the FRET efficiency is decreased considerably. Beside the ratiometric sensing of Co^{2+} ion the sensor shows colorimetric sensing for Co^{2+} ion. The free receptor shows red colour which upon addition of Co^{2+} is changed to blue.

1.2.1.2. Selective anion sensor

Multidentate ligands having N-atom at their donor site provide wide range of receptors for anion sensing. The free base multidentate anion sensors are designed on the basis of H-bonding or electrostatic attraction between the receptor and the anion. We will describe a few anion sensors developed on the basis of amide, [21 (a-b)] pyrrole, [22(a-b)] urea/thiourea, [23(a-e)], naphthalene/naphthalimide units, [24 (a-b)], porphyrin units containing neutral hosts [25]. All of the neutral or positively charged receptors have polarized N-H fragments which behave as H-bond donors towards anions. The metal ion sensing can be studied in both protic and aprotic solvents, but the anion sensing studies are preferably carried out in aprotic solvents to rule out competition for the anion by the H-bonding solvent.

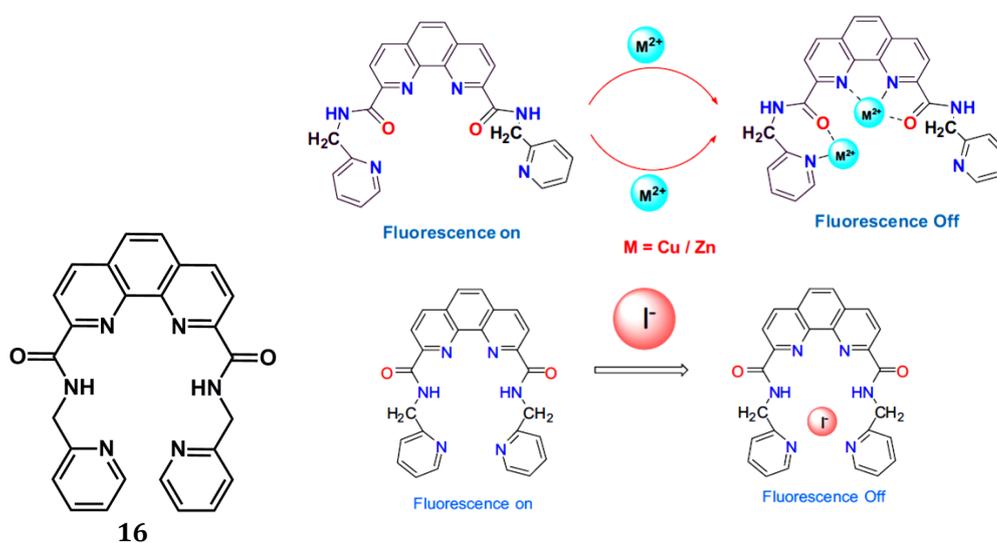
The amide -NH group has widely been employed as receptors for anion recognition. An acetate ion selective macrocyclic receptor **13** with two Pyridine moieties linked via two di-amide arms was reported by Szumna *et al.* The receptor shows a 1:1 binding with CH_3COO^- ion in solution and a 2:1 binding in solid state [26].



In the selective sensing of anion by **14a-d**, the receptor core size has been reported to play a vital role in the efficiency and selectivity of these ligands. The association constant of chloride ion with these receptors increases with increase in the core size. Good size compatibility between chloride and **14b** was observed as compared to **14d**. Receptor **14d** showed strong binding affinity towards anions with large ionic radii, such as phosphate, sulfate or carboxylate anions [27]. An acid based amide receptor, **15** shows selectivity for sulfate and phosphate anions [28]. Both the amide and bridging amine sites are capable of showing anion recognition property. Complementarities between the receptor sizes along with deprotonation of the amine groups of receptor play important role in the binding.

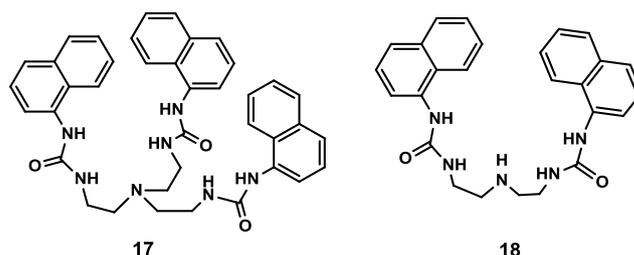
Recently, a new multi-ion responsive fluorophore **16** having an amide functionality combined with 1, 10-phenanthroline backbone has been reported for Cu^{2+} , Zn^{2+} and

I⁻ ion sensing by Alreja *et al.* [29]. The multi-ion responsive sensor was so designed that the -NH groups provided by two dangling amide chains and the N atoms of the 9, 10-phenanthroline unit provide an efficient coordination site for Cu²⁺ and Zn²⁺ ion binding in 1:2 stoichiometry. On the same time the pyridinyl amine and amide N-atoms provide selective I⁻ ion binding pseudocavity, through which the anion binds with the ligand in 1:1 stoichiometry (Scheme I.3.).

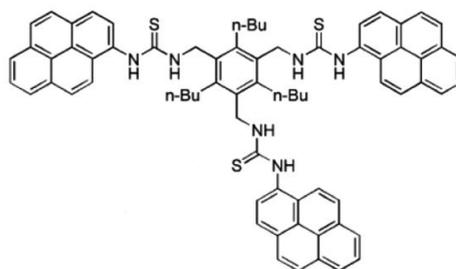


Scheme I.3. The proposed coordination pattern of **16** with metal ions, M²⁺ (M²⁺: Cu²⁺/Zn²⁺) and I⁻ ions (adopted from ref: [29] *J. Lumin.* 2015, **168**, 186).

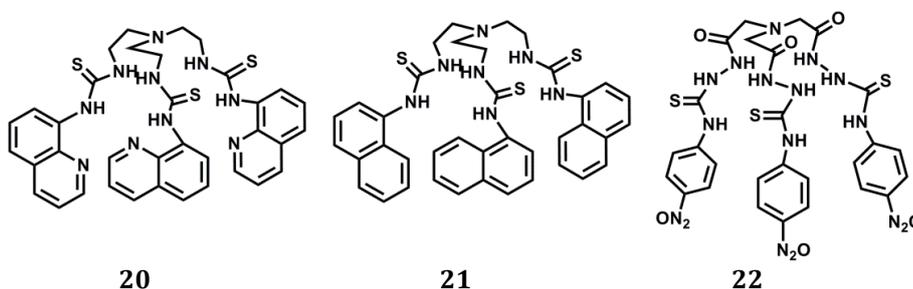
Urea and thiourea based receptors are particularly efficient hydrogen bond donors and are excellent sensors for anions providing the formation of two hydrogen bonds. A tripodal host **17** and a bipodal receptor **18** with naphthylurea groups had been reported by Wu *et al.* [30] which show high selectivity for H₂PO₄⁻ ion in DMF.



The selective sensing is observed by decrease in the fluorescence emission intensity of the naphthalene fragments present in the receptors after addition of H₂PO₄⁻ ion via photo electron transfer (PET) process.

**19**

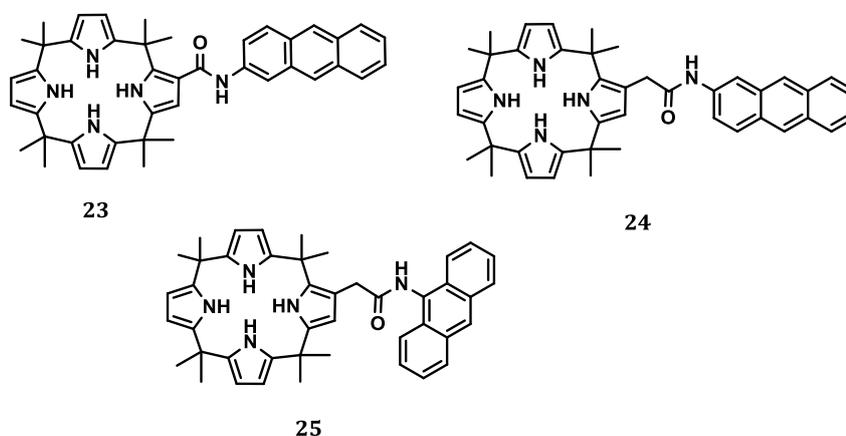
Receptor **19** with a preorganized cavity comprised by three thiourea fragments and three pyrene fragments as fluorescence signaling subunit for selective H_2PO_4^- ion sensing has been reported [31]. The core size effect of the tripodal receptor increased the selectivity toward the tetrahedral H_2PO_4^- anion over planer anions.

**20****21****22**

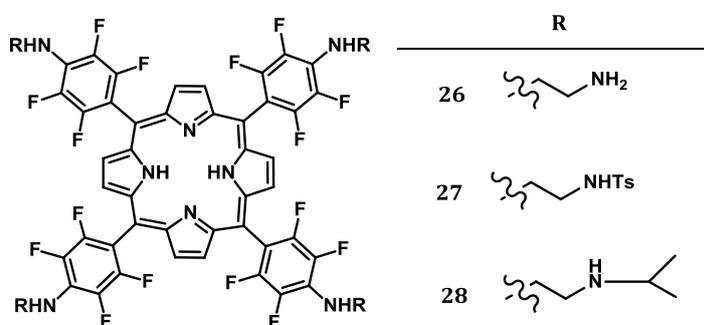
Naphthyl thiourea receptors (**20** and **21**) were derived from a tripodal amine compound TREN (1,1,1-trisaminoethyl amine) with spherical pseudocavities suitable for anion sensing. The quinoline-based tripodal receptor **20** exclusively encapsulates F^- and H_2PO_4^- anion in 1:1 stoichiometry among the other anions in DMSO medium [32(a, b)]. The binding of anions with this receptor in DMSO is furnished by the formation of strong hydrogen bonding. The naphthalene based tripodal receptor **21** forms 1:1 host-guest complexes with H_2PO_4^- and HSO_4^- respectively in DMSO. The recognition of these anions were monitored by measuring a concomitant decrease in the absorption band at 294 nm and appearance of a new absorbance band at ~340 nm after the addition of these anions [33 (a-b)]. A tripodal colorimetric sensor **22** with thiourea unit, and a 4-nitrobenzene unit as chromophore was introduced by Wei *et al.* for selective detection of CH_3COO^- and F^- anions in DMSO through multiple hydrogen bonding formation [34].

In amine based multidentate receptors for selective anion sensing, the amine functional group is often coupled with some conjugated aromatic rings which are also very good colorimetric and fluorimetric signaling units. These neutral amine based receptors recognize anions via H-bond formation, $\text{CH}\cdots\pi$, anion $\cdots\pi$ type of

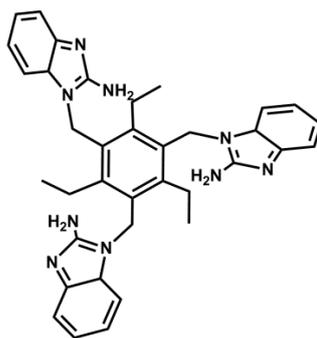
non-covalent interactions. Calix[4] pyrroles constitute one of the most efficient sensor groups, which offers strong H-bond formation and high association constant with anions. Some calix[4]pyrrole based chromogenic and fluorescent anion sensors (**23-25**) appended with anthracene as the signalling unit was reported by Sessler, Gale and Král [35 (a-e)]. These receptors display selective F⁻ ion sensing in organic solvents, but remain unresponsive in water. In dichloromethane or acetonitrile solutions these receptors undergo fluorescence quenching upon addition of F⁻ ion. Also the addition of dihydrogen phosphate and chloride ions resulted in partial fluorescence quenching, but the extent of sensing was very low in comparison to that of fluoride ion.



Tomé and his co-workers reported the anion binding property a series of novel porphyrin-based anion receptors (**26-28**) detectable with UV-visible absorption spectroscopy. These receptors were prepared from *meso*-tetrakis(pentafluorophenyl)porphyrin (TPPF₂₀) and diamine derivatives in neutral and protonated porphyrins [36].

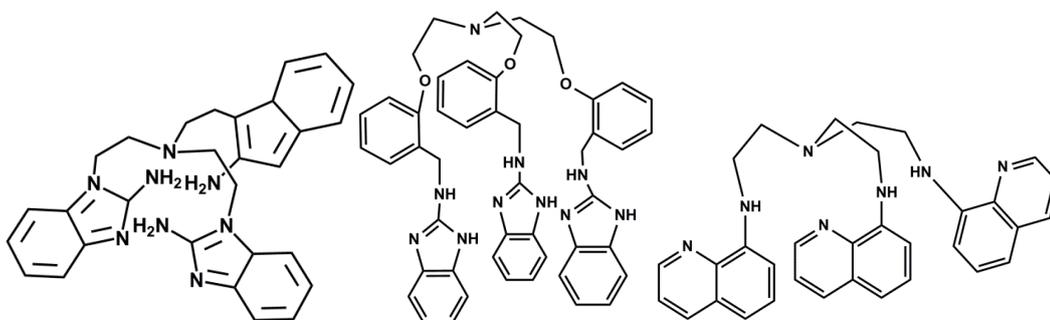


The UV-visible spectra of these receptors show decrease in the Soret band after the addition of tetrabutylammonium salt of dihydrogen phosphate anion (H₂PO₄⁻).



29

The receptor **29** was designed by Lee *et al.*, with a bulky aromatic platform furnished by three benzimidazole fragments. This receptor shows 1:1 host-guest binding stoichiometry with iodide anion in CH₃CN/H₂O medium [37].



30

31

32

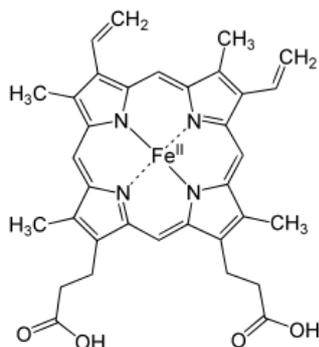
The tripodal fluorescent receptor **30** with benzimidazole motifs as signaling unit was described as chromogenic and fluorescence sensor for I⁻ ion in CH₃CN/H₂O (99:1, v/v, HEPES buffer pH = 7.91) medium [38]. In presence of I⁻ ion the emission intensity of **30** at 260 nm and 315 nm is quenched. A benzimidazole based tripodal fluorescent receptor **31** was reported for I⁻ ion sensing with a compatible pseudocavity. The fluorescence emission signal of **31** at 495 nm ($\lambda_{\text{excitation}} = 346$ nm) is quenched after binding with I⁻ ion in CH₃CN/H₂O (9:1, v/v) at neutral pH (HEPES buffer) [39]. The so formed host-guest complex has a 1:1 stoichiometry and the recognition took place through the formation of multiple hydrogen bonds. A quinoline based tripodal receptor **32** selectively senses PO₄³⁻ anion. The sensor **32** has emission signal at 310 nm corresponding to a monomeric form and at 475 nm appeared due excimer formation when excited at 270 nm in THF medium [40]. When a solution of sodium salt of PO₄³⁻ is added to a solution of **32**, the emission intensity

of the excimer band is decreased. But addition of protonated phosphate (H_3PO_4) resulted in the quenching of both the monomer and excimer emission.

I. 2. 2. Metal complexes with multidentate ligand systems in biological science

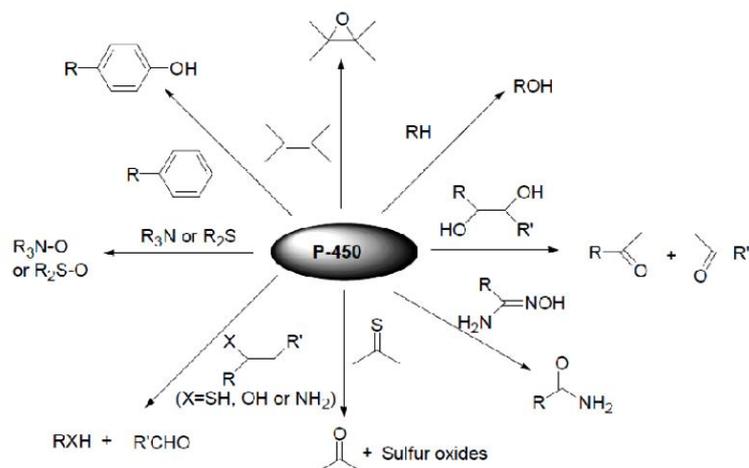
The multidentate ligands have a unique property to bind and stabilize metal ions in their different oxidation states. Multidentate ligands find their application as the coordinating backbone in various metalloenzymes due to their flexibility and ability to coordinate metal ion in either neutral or anionic form [41]. Herein, the discussion is in no way exhaustive but is limited to important members only.

Metal complexes with tetradentate heme ligands as well as non-heme ligands have wide range of applications in various biological activities. The heme group in hemoglobin (Hb) and myoglobin (Mb) are one of the most important examples among the various metal complexes of heme ligands.



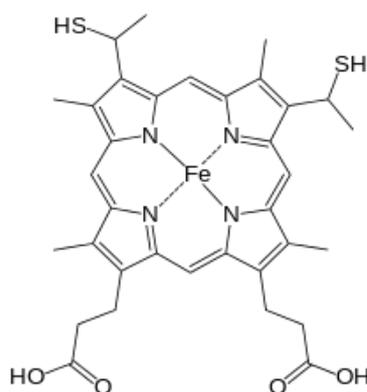
Scheme I.4. Structure of the heme group in hemoglobin (Hb) and myoglobin (Mb).

These proteins are responsible for the transportation and storage of oxygen in blood cells of higher mammals. The active site of the heme group in Hb and Mb contains an iron (II) centre coordinated to four pyrrole subunits of a porphyrin ring (Scheme I.4). The cytochrome P450 (Cyt P450) is another widely investigated system belonging to the family of heme protein. The active site of Cyt P450 possesses a macrocyclic tetradentate N₄ coordination site offered by a porphyrin ring to an iron (II) metal centre [42]. This metalloenzyme is capable of catalyzing various types of reactions such as epoxidation of alkenes, N-alkylation, S-oxidation, hydrocarbon oxidation (scheme I.5) and metabolize potentially toxic compounds, including drugs and products of endogenous metabolism such as bilirubin, principally in the liver [43(a-c)-45].



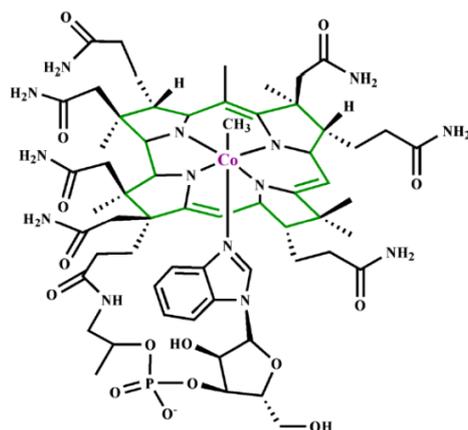
Scheme I.5. Various oxidation reactions catalyzed by Cyt P450.

Another important group of iron heme proteins that act as electron carriers in different biological systems are cytochromes. On the basis of their electronic spectral properties they are classified as a, b, c, d, etc. Among them Cytochrome c is the best known for its significant role in evolution process.



Scheme I.6. Structure of the heme group in cytochrome c.

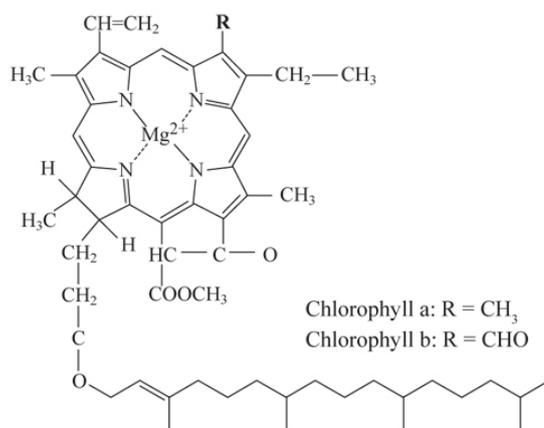
Apart from porphyrin ring in heme enzymes, corrin ring of vitamin B12 is another example of macrocyclic tetrapyrrolic ligand (Scheme I.7), coordinated to a cobalt (II) centre.



Scheme I.7. Structure of corrin, the tetrapyrrolic ligand of the B12 cofactor.

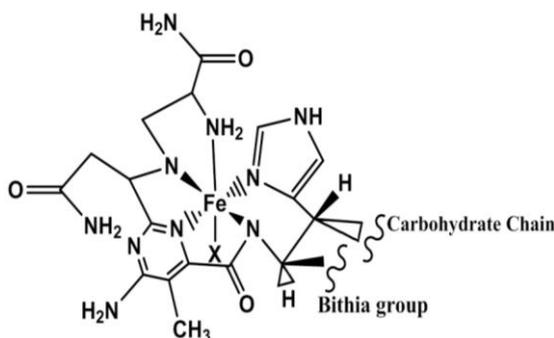
The corrin ligand is a close structural analogue of porphyrin framework with just one *meso* carbon atom short from the porphyrin ring [46].

The molecular structure of chlorophyll (a and b) has a chlorin ring, which is also very close to the porphyrin ring structure. The four nitrogen atoms of chlorine are coordinated to a central magnesium (II) ion (Scheme I.8).



Scheme I.8. Molecular structure of chlorophyll.

Among the various non-heme ligands, Bleomycin (BLM) is worthy to mention. *In vivo*, the iron complex of BLM is well known to exhibit anti tumor activity [47] (Scheme I.9). In medicinal field BLM has an important contribution as a drug to treat testicular cancer, ovarian cancer, and less commonly non-Hodgkin's disease [48].



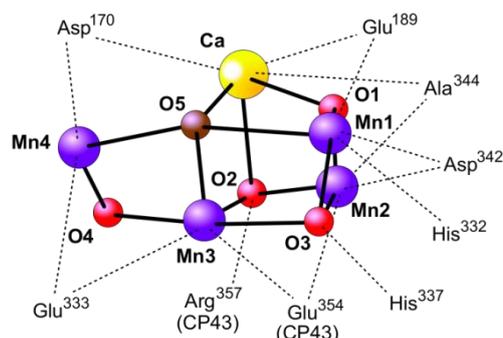
Scheme I.9. Schematic representation iron bleomycin complex.

It has been proposed that iron centre of $\text{Fe}^{\text{II}}\text{BLM}$ is surrounded by the pentadentate ligand BLM in square pyramidal geometry and the vacant axial position *trans* to the anionic N-atom is either occupied by a solvent molecule or a carbohydrate chain [47, 49]. The Fe^{III} center of Fe-BLM binds with dioxygen to generate a $\text{Fe}^{\text{III}}\text{-OOH}$ intermediate, which has been identified as the catalytically active intermediate formed during its catalytic cycle [47].

Over the last few decades, significant research efforts have been devoted to mimic the functional models of these enzymes [50 (a-i)].

I.2.2.1. Manganese complexes with multidentate ligands used in oxygenation reactions

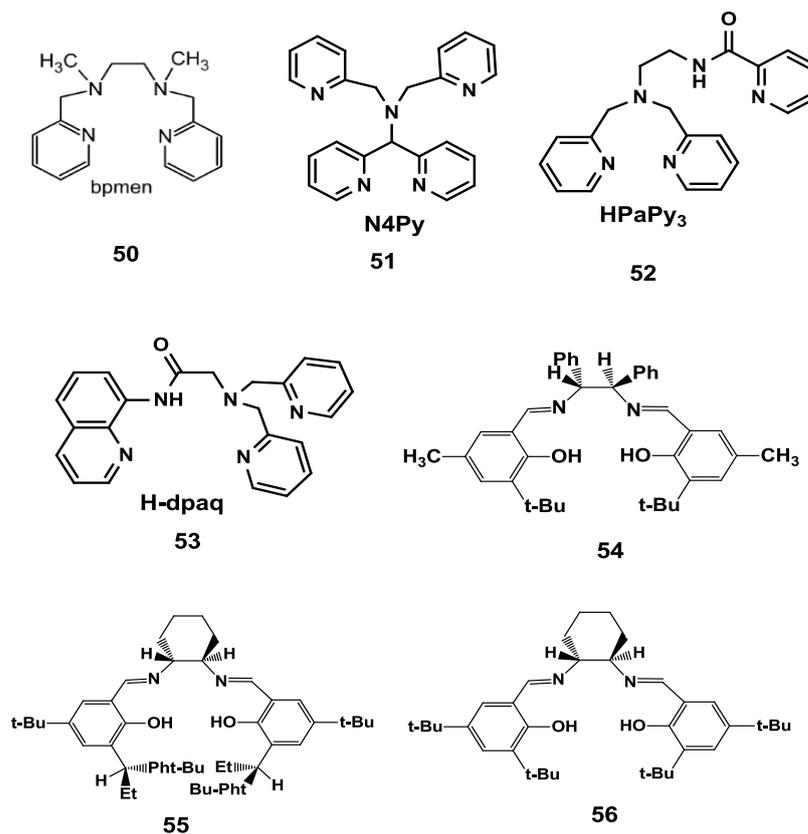
Several naturally occurring metalloenzymes are known which have manganese ions at their active center. Manganese is recognized as a versatile redox element due to its widely accessible oxidation states (0 to VII). The manganese containing metalloenzymes includes oxidoreductases, transferases, hydrolases, lysases, isomerases, ligases [51] etc. Some of the widely studied manganese containing metalloenzymes are Superoxide dismutase (MnSOD) [52], Mn catechol dioxygenase [53], Mn catalase (catalyze dihydrogen peroxide decomposition) [54], oxygen evolving complex (which converts water to dioxygen) [55], Mn lipoxygenase (catalyzes polyunsaturated fatty acid oxidation) [56]. The oxygen evolving complex (OEC) in photosystem II (PS II) and manganese catalase have been most widely investigated systems among various manganese containing enzymes. The OEC in PS II is a composition of Mn_4CaO_5 core (Scheme I.7).



Scheme I.10. Active site of oxygen evolving complex (OEC), Mn₄CaO₅-cluster (Mn-cluster) (Figure adopted from ref. 73).

The OEC releases molecular oxygen by catalyzing photoinduced oxidation of water. This process involves an oxo-atom transfer to manganese centre formed by a four electron oxidation of water. The cubane like Mn₃CaO₄ cluster which is attached with the fourth Mn atom supplies the electrons in this transformation [57]. A tetrameric Mn^{III}Mn₃^{IV} unit has been assigned as the active centre in this regard although a Mn₃^{III}Mn^{IV} unit has also been proposed alternatively [58]. Though the exact function of Ca²⁺ ion is not known precisely, it has been proposed to act as an essential cofactor for the photoinduced water splitting in presence of a Mn^V=O center [59]. Although there is much debate regarding the exact function of manganese center, it is believed that nucleophilic attack of water on an electrophilic Mn^{IV}-oxyl species is the pivotal step in O-O bond formation in PS II [60].

A wide range of multidentate ligands have been designed and synthesized with a purpose to model the active site of manganese containing metalloenzymes which show catalytic activity. The catalytic oxygenation of hydrocarbons by manganese (III)-porphyrin complexes with various terminal oxidants, Mn^V-O species frequently encountered as the active intermediate [61(a-c)]. A remarkable breakthrough was made by Grove *et al.* in characterizing the manganese (V)-oxo porphyrin in aqueous solution and subsequent olefin epoxidations in 1997 [62]. Manganese complexes of non-porphyrinic ligands attracted a wide attention when Jacobsen and Katsuki reported manganese (III) complexes with salen group of ligands as highly efficient epoxidation catalysts (ligands **54**- **56**, Scheme I.11) [63 (a, b)].



Scheme I.11. Various ligands used for synthesis of manganese complexes.

De Vos and Bein reported a series of manganese complexes with tridentate macrocyclic amine based ligands substituted 1,4,7-triazacyclononanes (Me_3TACN , **57**). These complexes were employed for epoxidation of several olefins with H_2O_2 and showed high turnover number up to 1000 with satisfactory selectivity (71–99 %) [64]. Therein a dimanganese(IV)- μ -oxo species ($[(\text{Me}_3\text{TACN})_2\text{Mn}^{\text{IV}}_2(\mu\text{-O})_3](\text{PF}_6)_2$) was established (**58** and **59**) by ESI mass characterization (Fig.I.1).

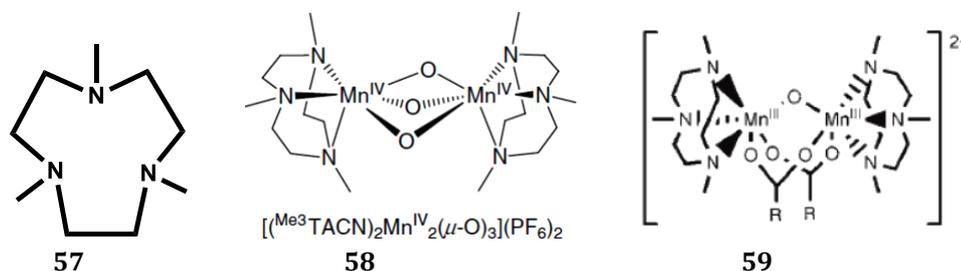


Fig.I.1. Structure of Me_3TACN (**57**), $[(\text{Me}_3\text{TACN})_2\text{Mn}^{\text{IV}}_2(\mu\text{-O})_3](\text{PF}_6)_2$ (**58**) and $[\text{Mn}^{\text{III}}_2(\mu\text{-O})(\mu\text{-RCO}_2)_2(\text{tmtacn})_2]^{2+}$ (**59**).

Later on several manganese complexes of this type of ligand were synthesized and their reactivity was studied [65]. Alternatively, generation of a manganese(IV)oxo-hydroperoxo intermediate, $\{[(\text{Me}_2\text{EBC})\text{Mn}^{\text{IV}}=\text{O}(\text{OOH})]^+\}$ was proposed by Busch and coworkers from the catalytic system $(\text{Me}_2\text{EBC})\text{Mn}^{\text{II}}/\text{H}_2\text{O}_2$ on the basis of ^{18}O -

labelling studies (Fig.I.3). Me₂EBC is a macrocyclic tetradentate amine ligand with an ethyl bridge between two alternate N-atoms [60 in Fig.I.2].

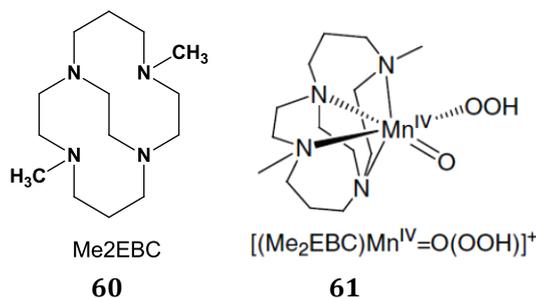
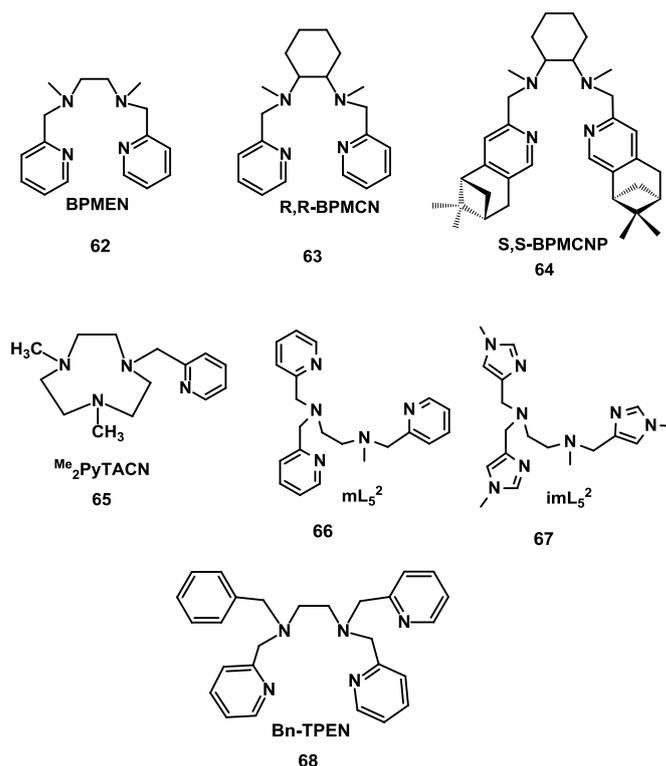


Fig.I.2. Structure of Me₂EBC and [(Me₂EBC)Mn^{IV}=O(OOH)]⁺.

They proposed that the coordinated -OOH group directly transfers an O-atom to the olefin during the formation of epoxide [66]. They reported several Mn^{IV}-oxo complexes bearing EBC and Me₂EBC ligand frameworks [67 (a-c)]. In the year 2003, Stack *et al.* reported manganese (II) complexes of two tetradentate tetraamine non-macrocyclic ligands BPMEN and R,R-BPMCNC (62 and 63 in scheme I.12 respectively).



Scheme I.12. Some polydentate ligands used for complexation with manganese (II).

The manganese (II) complexes of these ligands were catalytically active for epoxidation of alkenes with commercial peracetic acid [68]. As the asymmetric epoxidation by the manganese (II) complexes of these ligands were not successful, Costas and his group modified the ligand backbone by appending a pinene ring at the

4th and 5th position of the two pyridine rings (**64** in the above scheme) [69a]. They also showed that the Mn^{II} complexes of BPMEN and R, R-BPMCN along with **63** and Me₂PyTACN (**65**) also catalyze epoxidation reaction with H₂O₂ in presence of CH₃COOH [69b]. A peroxo-manganese (III) complex of a pentadentate neutral N5 ligand N4Py (*N,N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine) (**51** in Scheme I.11) was reported by Jackson and his group. This peroxo-manganese complex of N4Py closely resembles the peroxo-manganese (III) complexes of two other pentadentate neutral ligands mL₅² (*N*-methyl-*N,N',N''*,-tris(2-pyridylmethyl)ethane-1,2-diamine) and imL₅² (*N*-methyl-*N,N',N''*,-tris((1-methyl-4-imidazolyl)methyl)ethane-1,2-diamine) (**66** and **67** in Scheme I.12) [70 a, b].

Leto *et al.* characterized the oxo-manganese (IV) complex of N4Py spectroscopically and described the complex as reactive towards the activation of alkanes with weak C-H bonds like 9, 10-dihydroanthracene [70]. The reactivity of this complex was shown to be influenced by the presence of redox inactive metal ion, Sc³⁺ [71a]. Among the various oxo-manganese (IV) complexes, the Mn^{IV}(O) complex of Bn-TPEN (**68**) was reported as an extremely reactive species for C-H abstraction reaction of deactivated alkanes [72]. Till date the manganese (III) salen group complexes reported by Jacobsen are the most successful epoxidation catalysts among various manganese (III) complexes.

I. 3. Scope and objective of the present study

The objective of our present study encompasses the following aspects:

1. The design and synthesis of novel multidentate ligands with N- donor atoms with an aim to investigate their photophysical properties to evaluate their anion/cation/pH sensing abilities.
2. Endeavour to develop first-row transition metal complexes with suitable multidentate ligands to generate high-valent oxo-metal species and their reactivity towards Hydrogen Atom Transfer (HAT) and Oxygen Atom Transfer (OAT) reactions.

A brief outline of the scope and work plan is given below.

1. The tripodal amine based receptors have been widely used as chemosensors [30-34, 73] and remain as attractive backbone for ion sensing molecules. The

pseudocavity created by the tripodal arms provides suitable binding sites for anions through formation of hydrogen bonding with the anion or through anion- π interaction between the π -cloud of the fluorophore and negative charge density on anions. To achieve the objective, efforts would be made to design novel tripodal N3-receptors.

(1) To design an efficient fluorescent anion sensing receptor/sensor, 1-oxophenylene group (PLY) as a substituent at the three pods of a tripodal N3-ligand has been chosen. PLY is an odd alternant hydrocarbon and some of its 9-substituted derivatives are known to exist in three different oxidation states: positive, neutral and negative [74]. PLY derivatives in radical or complexed form with elements like Fe, Zn, B, Si have been widely utilised in the areas of semiconductors [75-78], molecular conductors [79] organic light emitting diodes (OLEDs) [80] and fuel cell. The use of PLY in neutral form is sparse and their uses as fluorophore particularly as chemosensors are non-existent in literature [81]. The 1-oxophenalenone is known to exhibit very weak luminescence property as the non bonding electrons on the oxygen atom of carbonyl function do not take part in extended conjugation. These non-bonding electron pairs on the oxygen atom of carbonyl function deactivate the fluorescence property by inter-combinational conversions [82]. However, the introduction of alkyl amine group (-NHR or -NR₂) in the conjugated π system of PLY fragment has been found to be effectively enhance the fluorescence signals better than alkoxy substituents [83]. The lone pair of electrons on N-atom takes part in the conjugation and lowers the $\pi - \pi^*$ excitation energy below n- π^* excitation energy, consequently minimises the possibility of inter-combinational conversions.

Our endeavour would be focussed on the design of a novel tripodal N4-receptor, based on PLY framework. The PLY based tripodal N3-receptor is expected to be suitable for anion sensing. The response of the receptor in presence of various anions particularly halides would be studied by UV-visible and fluorescence spectroscopy, which would lay a platform for the development of novel chemosensor system.

(2) Apart from ion sensing under ambient condition, development of chemosensors for pH detection remains an attractive area in single molecule chemosensor research. A small change in environmental pH widely affects the biological processes. Thus, the

pH monitoring of samples collected from various sources is considered important from environmental viewpoint.

The conventional pH detection is done by potentiometric method using Glass electrodes. In spite of their high sensitivity and stability to environmental conditions, they suffer from the limitations towards potential drift arising from high activity of H^+ ion and 'alkali error' at highly alkaline conditions [84]. The development of reversible optical pH sensors may help to overcome the limitations of glass electrode. Several fluorescent molecules either with phenol or amine groups as substituents to conventional fluorophores such as 1, 8-naphthalimide derivatives [85], rhodamines [86], carbazole derivatives [87] as pH sensors are well known in the literature. Both phenol and ammine functions of these molecules act as efficient photo induced electron transfer (PET) groups [88]. The presence of phenol as PET group is expected to quench the emission intensity of the probe with increase in pH. Furthermore, the phenol substituted pH sensors show visible colour change. Another group of phenol substituted aza-boron dipyrromethene (aza-BODIPY) compounds are also attractive fluorescent pH sensors due to their strong emission property [89].

In this context, we wish to design novel small molecules derived from 9-amino-1-oxopentalene with substituted phenol group. The study of the UV-visible absorption and fluorescence emission properties of these compounds at different pH ranges would give us a scope to develop novel pH sensors. Furthermore, 1H NMR spectroscopic experiments and computational studies on the molecular orbital energy levels of these sensors at various pH ranges will be undertaken. This would provide a clear insight into the PET mechanism operative in the pH sensing phenomenon.

(3) Wide range of biological reactions is catalyzed by metalloenzymes, which are of immense importance in chemical research. Nature has adopted predominantly first transition metal ions in metalloenzymes through evolutionary process. Extensive investigations have been focussed on the reactivities of first transition metal ions due to their biological relevance and easy availability.

Manganese enjoys a unique position among the members of first transition series and often recognized as the most versatile redox element due to its widest array of oxidation states (0 to VII). Manganese is well known to contribute as redox catalysts in both chemical and biological sciences.

The most significant role played by manganese in living organism is catalytic water oxidation in oxygen-evolving complex (OEC) of photosystem II. High-valent oxomanganese species has been invoked as key intermediate during water oxidation by OEC. [90].

Another important group of manganese containing enzymes is manganese superoxide dismutase (Mn-SOD), which catalyzes the dismutation of superoxide (O_2^-) (generated from one electron reduction of dioxygen) to oxygen (O_2) and hydrogen peroxide (H_2O_2) in the living organisms. The importance of high valent oxo-manganese species in the oxidized state of manganese-superoxide dismutase (Mn-SOD) have been revealed by spectroscopic and computational studies [91]. The structure and reactivity of the manganese containing metalloenzymes have inspired the development of suitable model catalytic systems for oxygenation of hydrocarbons under ambient reaction condition.

Multidentate N-donor ligands are used to provide desired backbone for the synthesis of manganese containing catalysts for hydrocarbon oxygenation reactions [92]. The non-conjugated macrocyclic ligands are important because of their structural flexibility. The redox innocent multidentate saturated macrocyclic ligand Cyclam (1,4,8,11-tetraazacyclotetradecane) appears to be a promising candidate for this purpose. The structural flexibility of cyclam enables the metal center to adopt the desired stereochemistry for effective binding of substrate.

The catalytic oxygenation of hydrocarbons by manganese-cyclam complexes remains elusive till to date. In this background, the study of catalytic efficacy of the manganese (III) complex of cyclam towards hydrocarbon oxidation has been envisaged. In the present work, we wish to explore the oxygenation of hydrocarbons catalyzed by manganese (III) cyclam complex under ambient conditions with several terminal oxidants.

(4) High-valent manganese-oxygen adducts play important biological role in metalloenzymes, such as in manganese containing superoxide dismutases (Mn-SOD) and in the oxygen evolving center in photosystem II. So far, several polydentate ligands have been employed to stabilize the high-valent manganese species [93]. In general, electron-rich ligand scaffolds appear promising in this regard [94]. The ligand framework of 2-[bis(pyridin-2-ylmethyl)]amino-N-quinolin-8-yl-acetamide (H-dpaq) (**53** in Scheme I.11) has been chosen. The anionic carboxamido unit of H-dpaq is expected to bind the metal ion *trans* to the potential oxo site, which consequently weakens the metal-oxo bond leading to the formation of reactive oxomanganese transients. Moreover, the quinoline moiety is expected to provide some protective shields around the metal-oxo bond.

The role of proton coupled electron transfer (PCET) in the formation of the oxomanganese transient is to be studied. The reactivity of the oxo-manganese species towards hydrogen atom abstraction (HAT) from hydrocarbons and oxygen atom transfer (OAT) reactions with various thioanisoles is to be evaluated in non-aqueous solution. The formation of Mn^{IV} species and its spin state would be studied by electron paramagnetic resonance (EPR) spectroscopy. The TD-DFT studies on the probable structure of the Mn^{IV}-oxo intermediate would also be undertaken.

Furthermore, attempts would be made to generate high-valent oxo-manganese intermediate in aqueous solution with a strong one electron oxidant. The reactivity of the high valent oxo-manganese species for the HAT reactions from hydrocarbons and OAT reactions with thioanisoles would be studied in aqueous solution.

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