CHAPTER - 1

GENERAL INTRODUCTION

1.1. Schiff base: Definition and concepts

Compounds containing an azomethine (-CH=N-) group are known as Schiff bases. They are usually formed by condensation of primary amine with a carbonyl compound according to the following scheme.

\[ \text{Carbonyl compound} + \text{Primary amine} \rightarrow \text{Schiff base} + \text{H}_2\text{O} \]

where \( R_1, R_2 \) and \( R_3 \) may be an alkyl or aryl groups. Hugo Schiff described for the first time the condensation between an aldehyde and an amine leading to a Schiff base in the year 1864 [1] and hence the compounds are named after him. Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerize [2-3] while those of aromatic aldehydes having an effective conjugation system, are more stable [4-5]. Schiff bases
obtained from aromatic amines are known as anils. The mechanism of Schiff base formation is an acid catalysed nucleophilic addition of an amine to a carbonyl compound forming a hemiaminal, followed by dehydration to generate an imine.

Condensation of amines with aldehydes and ketones find numerous applications that include preparative use, identification, detection and determination of aldehydes and ketones, purification of carbonyl compounds or amines or protection of these groups during complex or sensitive reactions. In chemistry, Schiff bases find versatile use [6-8]; some serve as basic units in certain dyes, some exhibit liquid crystalinity whereas some are fluorescent. Schiff bases that have solvent dependent UV/VIS spectra (solvatochromicity) are suitable for NLO (non linear optical) active materials [9]. These
are also useful materials in solid phase extraction [10] and synthesis of ion selective electrodes for determination of anions in analytical samples [11-14]. They are also useful in enantioselective [15-16] and regioselective [17] ring opening of epoxides, enentioselective epoxidation of alkenes [18] and asymmetric oxidation of methyl phenyl sulphide [19].

1.2. Biological importance of Schiff bases

Schiff bases play an important role in many biological processes involving amino acids and keto acids, including trans-amination, decarboxylation, condensation, β-elimination, and racimization, which may involve Schiff base intermediates [20]. A large number of enzymatic reactions are known that involve Schiff base intermediates. One of the most prevalent types of catalytic mechanism in biochemical processes involves condensation of primary amine in an enzyme, usually that of a lysine residue, with a carbonyl group of the substrate to form an imine or Schiff base. Schiff bases derived from pyridoxal (the active form of vitamin B₆) and amino acids are considered as very important ligands from biological point of view. Transition metal complexes of such ligands are important enzyme models. Many biologically important Schiff bases have been reported in literature possessing antibacterial [21, 22], antifungal [23-25] antimicrobial [26-29], anticonvulsant [30], anti-HIV [31], anti-inflammatory [32] and antitumor [33] activities. Certain polymeric Schiff bases are also reported to possess antitumor or activity [34]. The biosynthesis of porphyrin, for which glycine is a precursor, is another important pathway that involves the intermediate formation of Schiff base between keto group of one molecule of δ-amino levulinic acid and ε-amino group of lysine residue of an enzyme. Another important role of Schiff base is in transamination [35]. Transamination reactions are catalysed by a class enzyme called transaminases or aminotransferases. Transaminases are found in mitochondria and cytosal of eukaryotic
cells. All the transaminases appear to have same prosthetic group, i.e. pyridoxal phosphate, which is covalently attached to them via an imine or Schiff base linkage. Schiff bases formation is also involved in chemistry of vision, where the reaction occurs between the aldehyde function of 11-cis retinal and amino group of the protein (opsin) [36].

1.3. Schiff base transition metal complexes

Schiff bases are generally bi, tri or polydentate ligands capable of forming very stable mononuclear, binuclear and polynuclear complexes with transition metals. Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde. Modern chemists still prepare Schiff bases, and nowadays active and well-designed Schiff base ligands are considered “privileged ligands”. In fact, Schiff bases are able to stabilize many different metals in various oxidation states, controlling the performance of metals in a large variety of useful catalytic transformations. Metal complexes of Schiff base have occupied a central place in development of coordination chemistry after the work of Jorgensen and Werner [37]. Schiff prepared complexes of metal salicyldehyde with primary amines [38]. Subsequently he prepared complexes from the condensates of urea and salicyldehyde [39]. Delepine prepared complexes by reacting metal acetates, salicyldehydes and a primary amine in alcohol and showed a 2:1 stoichiometry [40]. However, there was no comprehensive and systematic study until the preparative work of Pfeiffer and associates [41]. Pfeiffer and his co-workers prepared a series of complexes derived from Schiff bases of salicyldehyde and its substitution products [42]. The activity of trace metals in biological system is attained through the formation of complexes with different bio-ligands and the thermodynamic or kinetic properties of the complexes govern the mode of biological action. It is worthwhile to mention that the antitumor
activity of some Schiff bases has been attributed to their ability to chelate with trace transition metals [43, 44]. The coordination chemistry of Schiff bases as multidentate ligands gained importance because of their use as models in biological systems, in catalysis and in material chemistry. The presence of both nitrogen and oxygen donor atoms permits coordination with a wide range of transition and non-transition metals yielding stable and intensely coloured metal complexes, some of which have interesting physico-chemical [45, 46] and potentially beneficial chemotherapeutic properties [47-52]. In the past two decades synthesis, structure and properties of Schiff base complexes have stimulated much interest for their noteworthy contributions in the field of photoluminescence, magnetism, molecular architecture, material science, corrosion inhibitors, sensor design and catalysis of many reactions like carbonylation, hydroformylation, reduction, oxidation, epoxidation and hydrolysis etc. [53-58]. The flexibility of disposition of different donor sites is the secret behind their successful performances in mimicking peculiar geometries around the metal centres, leading to very interesting spectroscopic properties with varied magnetic activities [59].

1.4. Coordination chemistry of iron-Schiff base complexes

The common oxidation states of iron are +2 and +3. The relative stability of the two oxidation states in aqueous solution is defined by the standard electrode potential of +0.77 V for the Fe³⁺/Fe²⁺ couple. The chemistry of iron, including its importance in biology is closely associated with the ready interconversion of these two oxidation states and with the dependence of redox potential on the ligand environment. The versatility of the chemistry of iron is reflected by the variety of roles it plays in biological system where it is frequently found at the active centers involved in processes such as oxygen and electron transport in nitrogenase, many oxidases and in metalloenzymes such as hydrogenases and reductases.
The Fe^{III} ion has a d^5 electron configuration showing a high spin (S=5/2) in most of its complexes. However, there is a possibility of stabilization of low spin (S=1/2) ground states in strong octahedral field such as generated by CN ion and many bi or polydentate ligands containing unsaturated nitrogen. In addition, intermediate spin (S=3/2) states may also be produced in fields of lower symmetry. The commonest coordination number of iron is six but a range of other coordination numbers three, four, five, seven and eight are also established.

Condensation reactions between carbonyl compounds and primary amines have provided one of the most important and widely studied class of chelating ligand which vary in denticity, flexibility, nature of the donor atoms and in electronic properties. A wide diversity in coordination geometries and magnetic behaviour has also been found.

The bidentate [N, O] donor schiff bases like N-substituted salicylaldimines (1) form complexes of stoichiometry [Fe(L)Cl_2X] (2) where X=Cl or Br and L=ligand which have a high spin (S=5/2) monomeric five coordinated structures [60]. An X-ray investigation of the compound indicated a stereochemistry intermediate between trigonal bipyramidal and square pyramidal [61].

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\[ \text{The [ONO] donor tridentate dianionic ligand (L) of the type (3) form a five coordinated dimeric complexes of stoichiometry [Fe(L)Cl}_2\text{] (4). The iron atom of the dimer are bridged by the alkoxide oxygens to form a four membered ring with the Fe-O distances of 1.983 and 1.934 Å and angles 75.9 and 104.1° at iron-oxygen, respectively. The geometry of the complex is distorted square pyramidal, the basal plane being made up} \]
of the donors of tridentate ligand and the bridging alkoxide oxygen with the chlorine atom in apical position. The magnetic behaviour of the complex accords with the occurrence of antiferromagnetic super exchange interaction mediated by the dialkoxy bridge. The $\mu_{\text{eff}}$ having a reduced value of 4.52 B.M. at room temperature and falling further to 2.37 B.M. at liquid nitrogen temperature.

Condensations of two equivalent of salicyldehyde with a diprimary amine, commonly 1,2-diaminoethane (en), provide a convenient route to $[\text{N}_2\text{O}_2]$ donor tetradentate Schiff base ligands of the type (5). Complexation with iron(III) yields monomeric form (6) and dimeric form (7) depending upon the methods of preparation or isolation [62].

The monomeric form is obtained from recrystallisation of the dimeric form from nitromethane, containing a molecule of solvent in the lattice and has a square pyramidal geometry with the metal atom sitting about 0.46 Å above the plane defined by the $\text{N}_2\text{O}_2$ donor set of the tetradentate ligand, in the direction of the apical chlorine atom [63]. In the dimer, isolated from acetone solution, two molecules of monomer each share one
oxygen atom from each ligand to give an overall octahedral environment for each metal atom [64].

The monomers have magnetic moments at room temperature close to the spin only value of 5.92 B.M. and obey the Curie-Weiss law with small Weiss constant. The dimers, on the other hand, have subnormal room temperature moments which reduced further on lowering the temperature, thereby describing the antiferromagnetic superexchange interaction between the pair of iron atoms.

Spin-crossover phenomenon has also been encountered in several examples of iron(III) complexes with tridentate and hexadentate Schiff base ligands.

\[
\text{Fe}^{III}(t_{2g}^5) \rightleftharpoons \text{Fe}^{III}(t_{2g}^3e_g^2)
\]

These complexes may be high spin or low spin depending on nature and position of substituents, counterions, lattice solvents and even geometrical isomerism.

Iron(III) complexes of tetradentate macrocyclic Schiff base ligands having N₄ donor set are generally five coordinated or six coordinated having square pyramidal or nearly octahedral geometry. These complexes may be high spin (S=5/2), intermediate spin (S=3/2) or low spin (S=1/2) depending upon nature of the macrocyclic ligand i.e. size and degree of unsaturation and on the number of the axial ligands.

Mixed ligand Fe(II)-bis-Schiff base complexes (10 and 11) of tetradentate ligand bis(o-vanillin)-o-phenylenediimine (8) or bis(o-vanillin)-2,3-naphthalenediimine (9) and pyrazine are reported with their crystal structures and magnetic property. Compound 10 shows a two-step spin cross over behavior while 11 shows high spin at all the temperature range measured [65].

The macrocyclic complexes of the type, [FeLCl₂]Cl [13] have been prepared by reacting iron(III) chloride with a novel Schiff base tetraimine macrocyclic ligand, (L): 5,6,11,12-
dibenzophenone-2,3,8,9-tetraphenyl-1,4,7,10-tetraazacyclo-dodeca-1,3,7,9-tetraene (12). The ligand was obtained from [2+2] condensation between 3, 4-diamino benzophenone and benzil.
1.5. Coordination chemistry of vanadium-Schiff base complexes

Vanadium may exhibit formal oxidation states from $-3$ to $+5$ with the exception of $-2$.
Under ordinary conditions, the most stable states are $+4$ and $+5$. The coordination chemistry of vanadium is strongly influenced by the oxidizing/reducing properties of the metallic center, and the chemistry of vanadium ions in aqueous solution is limited to oxidation states $+2$, $+3$, $+4$ and $+5$.

Vanadium easily switches between the oxidation states $V$ and $IV$, which along with $III$ are the oxidation states of naturally occurring vanadium compounds. The redox potential at pH 7, for the couple $H_2V0_4^-$ + $4H^+$ + e $\rightarrow$ $VO^{2+}$ + $3H_2O$ amounts to -0.341V and so, it is the range where vanadyl($VO^{2+}$) is oxidized to vanadate under aerobic conditions, and vanadate is reduced to vanadyl by cellular components such as cysteine containing peptides (glutathione) and proteins, ascorbate, NADH and phenolic compounds [66]. The main species present under physiological aerobic conditions is the acid–base pair $H_2V0_4^-$ $\rightarrow$ $HVO_4^{2-}$ + $H^+$ (pKa 8.1) [67]. Cationic $V^V$ species such as $VO^{3+}$ or $VO_2^{+}$ are stable in solution around pH 7 only when coordinated to sufficiently strong ligands, which prevent precipitation of hydroxides.

The $+4$ oxidation state is the most stable under ordinary conditions and the majority of the vanadium(IV) compounds contain $VO^{2+}$ unit (Vanadyl ion). It forms stable anionic, cationic, and neutral complexes with all type of ligands and has one coordination position occupied by the vanadyl oxygen.

The complexes are typically square pyramidal (14) or bipyramidal (15) with the vanadyl oxygen apical and the vanadium atom lying above the plane defined by the equatorial ligands. Trigonal bipyramidal complexes (16) are also known. Many vanadium(V) compounds are known to exist as oxo complexes containing the $VO^{3+}$ or
the VO$^{2+}$ entity and the cis geometry in dioxo complexes has been confirmed by structure determinations.

The V=O stretching frequency is an important characteristics of oxovanadium(IV) complexes, generally observed at 985±50 cm$^{-1}$. Ligands that increase the electron density reduce V-O multiple bond character and hence the stretching frequency. For complexes $\text{VOL}_4^{ne}$, $\nu(\text{V=O})$ falls in the order $\text{L}=\text{H}_2\text{O} > \text{NCS}^->\text{CN}^->\text{F}^-$. Reduction in V=O frequency from 950-1000 to 800-850 cm$^{-1}$ indicate polymerization or VO---VO---VO interactions.

Oxovanadium(IV) complexes with [N, O] donor bidentate Schiff bases derived from diamines and salicyldehydes (17) or β-diketones (18) normally have a monomeric structure with 1:1 stoichiometry having magnetic moment of 1.78 B.M. at 295 K and it obeys Curie-Weiss law over the range 95-295 K.

With various types of tridentate Schiff bases having [N, O, O] donor set (19-22) the complexes are very often found to be dimeric. It is presumed that the dibasic character of the ligands forces the VO$^{2+}$ ion to dimerize (23-24) leading to anomalous magnetic
properties. The subnormal magnetic moment of the complexes decrease considerably as the temperature is lowered and this phenomenon is the characteristics of intramolecular antiferromagnetic exchange [68].

The complex 23 on treatment with a strong chelating agent such as phen, the dimer is broken with the formation of a mononuclear mixed ligand complex \([\text{VO(SB)(phen)}]\) [69]. The dimeric structure is also broken on treatment of the complex with pyridine; a monopyridine adduct forms which obeys the Curie-Weiss law with \(\theta=2K\) and \(\mu_{\text{eff}}=1.75\) B.M [70].

Schiff bases derived from 2-hydroxynapthaldehyde and o-aminophenol and some substituted derivative also formed a subnormal dimeric \(\text{VO}^{2+}\) complexes (24). Like 23,
treatment of the complex 24 with phen, the dimmer is broken and a mixed ligand complex is obtained.

Several VO$^{2+}$ complexes were prepared with the ligand 20 and 21. High melting or decomposition temperature and insolubility in common noncoordinating solvents suggest a dimeric or polymeric nature. $v_{\text{V=O}}$ occurs at 910-985 cm$^{-1}$ for complexes of 20 and at 900-910 cm$^{-1}$ for those of 21; this argues against the presence of a V=O· · · V=O polymeric chain structure. The $\mu_{\text{eff}}$ values of the complexes were shown to be remarkably less than the spin only values and the magnetic moments decrease significantly as the temperature is lowered, suggesting antiferromagnetic exchange interaction of neighbouring VO$^{2+}$ ions.

Oxovanadium(IV) complexes with Schiff bases 25 and 26 derived from alkyl aminoalcohols and salicylaldehyde or o-hydroxyacetophenone (and substituted derivative) respectively, have been prepared by adding an alcoholic solution of Schiff base to alcoholic solution of vanadyl acetate. The compounds obtained have been formulated as [VOL]$_2$ with structure 27. This structural feature is supported by IR spectra and magnetic properties. They have subnormal $\mu_{\text{eff}}$ and the dependence of $\chi_M^{\text{corr}}$ on temperature is characteristics of antiferromagnetic exchange.

The electronic spectra of such complexes with tridentate Schiff bases of the type (25-26) generally exhibit three ligand field bands: (i) ca. 715-770, (ii) ca. 625 and (iii) ca. 500-550 nm, assigned to d-d transitions according to the Vanquickenborne and Gray
McGlynn MO scheme [71]. Some of these bands are not well developed and this gave rise to ambiguity in their assignment. No band characteristics of VO$^{2+}$-VO$^{2+}$ interaction has been observed in complexes with these Schiff bases.

Several VO$^{2+}$ complexes were prepared with Schiff bases 28 and 29 derived from dibenzoyl methane or pyrol-2-carboxaldehyde and several amines (taurine, anthranilic acids, β-alanine). These Schiff bases also behave as tridentate ligands and the complexes were formulated as [VO(SB)(H$_2$O)$_2$] [72]. The monomeric structure was confirmed on the basis of μ$_{\text{eff}}$ and ebulliometric measurements in dioxane.

Oxovanadium(IV) complexes with tetradeionate Schiff bases (30) obtained from the reaction of two moles of benzoyl hydrazide with acetylacetone was monomeric square pyramidal (31) with v(V=O) at 995 cm$^{-1}$ and μ$_{\text{eff}}$ of 1.7 B.M [73].

Mixed-ligand oxovanadium(IV) and oxovanadium(V) complexes with a tridentate dinegative ONO donor Schiff base ligand derived from acetylacetone and benzoyl hydrazine [viz., 4-(1-hydroxybenzylidenehydrazono)-2-penten-2-ol (H$_2$L)] and bidentate NN [viz., 2,2'-bipyridine (bipy) and 1,10-phenanthroline (phen): complexes (32) and
(33), respectively] or OO) [viz., ethylene glycol (H2gol), salicylaldehyde (Hsal) and vanillin (Hvan): complexes (34-36), respectively] donor ligands have been prepared and characterized. The complexes with NN donor ligands are one electron paramagnetic, displaying axial EPR spectra and exhibiting two ligand-field transitions in the visible region, whereas the complexes with OO donor ligands are diamagnetic and display only LMCT bands. The pentavalent complexes (35) and (36) exist in two isomeric forms [74].

Reaction of VOSO₄ with the tridentate ONO donor ligand derived from the condensation of acetylhydrazide with either 2-hydroxybenzaldehyde (H₂L¹) or 2-hydroxyacetophenone (H₂L²) in an equimolar ratio in the presence of two equivalents of sodium acetate in aqueous-methanolic medium in air produces yellow dioxovanadium(V) complexes of the type, [V⁵O₂(H⁺-L)], (37) and (38) in good yield [75].
Vanadyl complexes of N$_2$O$_2$ donor tetradentate Schiff base ligands, derived from aromatic aldehydes and aliphatic diamine (2, 2'-Dimethylpropanediamine) assumes a square pyramidal structure (39). The compound showed excellent selectivity for epoxidation of cyclooctene and good selectivity for styrene [76].

1.6. **Goal**

Set in this backdrop and also based on review of literature (Chapter 2) pertaining to the chosen area of research it was thought worthwhile to undertake investigation on synthesis, physicochemical characterization, reactivity and antimicrobial activity of some Schiff base ligands of different denticity and their complexes of iron (II, III) and vanadyl (IV).

Specifically the objectives of the present Ph.D. research are detailed as follows.

(i) To synthesize low molecular mass mesogenic Schiff bases from simple amines and to study the effects of complexation on mesogenicity.
(ii) To design newer multidentate Schiff base ligands and to devise appropriate synthetic strategy to access mononuclear and binuclear VO(IV) and Fe(III) complexes.

(iii) To synthesize and characterize mixed ligand Fe(III) complexes of Schiff bases.

(iv) To synthesize and characterize macrocyclic Schiff bases derived from benzil and diamines and their complexes with iron(III) and oxovanadium(IV).

(v) To carry out ligand exchange reactions of the solvated complexes with neutral or anionic donor ligands to afford newer mixed ligand complexes.

(vi) To investigate mesogenic, magnetic, electrochemical and thermal behaviour of the complexes.

(vii) To explore antimicrobial activities of the selected synthesized compounds against various microbial strains.

(viii) DFT studies on selected compounds to ascertain optimised geometry, single point energy and vibrational frequencies using GAUSSIAN 03 program.