

# **Part I**

## **Synthesis and Characterization**

### **Chapter 1**

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## CHAPTER I

### INTRODUCTION AND REVIEW

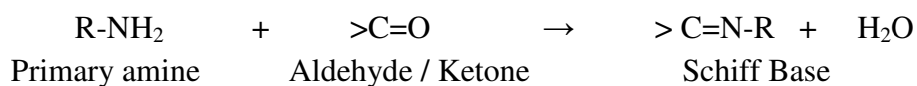
Coordination chemistry has always been a challenging and fascinating field to inorganic chemists. Metal complexes derived from carbonyl and amino compounds have found multidimensional applications apart from being instrumental in the tremendous development of coordination chemistry. The real impetus towards the progress in coordination chemistry of these potential chelating species was probably provided by the remarkable biological activity observed for some of these derivatives. These findings have led recently to an increased interest in the chemistry of transition metal chelates of Schiff bases and related ligands. There is wide scope for extensive studies regarding the coordination compounds of transition metals with Schiff bases derived from heterocyclic carbonyl compounds.

#### **Schiff bases**

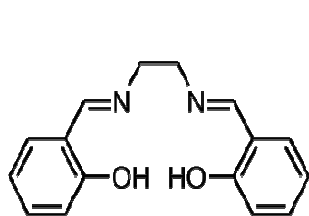
Schiff bases are common ligands in coordination chemistry. They are a class of compounds which have profound use as ligands as well as in the form of complexes. These are named after Hugo Joseph Schiff who is one of the founders of modern chemistry. Schiff bases have an influencing role in the development of coordination chemistry. A Schiff base is a compound with a functional group that contains a carbon-nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group<sup>1</sup>. They have the general formula  $R^1R^2C=NR^3$ , where R is an organic side chain. A Schiff base is synonymous with azomethine and is also called as imines.

Schiff bases can be synthesized from aliphatic/aromatic amines and carbonyl compounds (aldehydes or ketones) by nucleophilic addition forming an

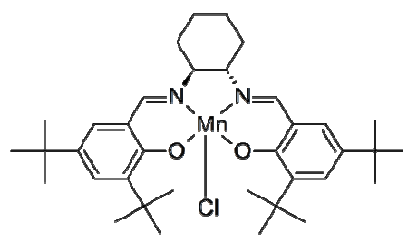
unstable hemiaminal, followed by acid or base catalyzed dehydration to generate an imine. The dehydration of the carbinolamine is the rate-determining step of Schiff base formation. If the amine is protonated, it becomes non-nucleophilic and the equilibrium is shifted to the left and the hemiaminal formation cannot occur. Therefore, many Schiff base synthesis are best carried out at mildly acidic pH. The imine nitrogen is basic and exhibits pi-acceptor properties. Schiff base ligands are typically derived from primary amines and carbonyl compounds<sup>2</sup>.



Schiff bases are used as precursors of countless organic processes, for the production of intermediates or products. It can be summarised into four different types of organic reactions in which Schiff bases are widely used: (1) addition of organometallic reagents or hydride to C=N bond (2) hetero Diels-Alder reaction to furnish six membered nitrogen containing heterocyclic compounds (3) skeletons for the building-up scaffolds; for eg, the famous salen scaffold which is used as 'privileged ligand' for the formation of the corresponding chiral salen metal complexes (4) Staudinger reaction with ketene to furnish biologically important  $\beta$ -lactam ring. The figure given below represents one of the common Schiff base ligand, Salen and its complex.



(a)



(b)

(a) Salen : a common tetradentate ligand and (b) Jacobsen's catalyst : derived from chiral salen ligand.

Schiff bases are useful chelators because of their ease of preparation and structural varieties<sup>3-6</sup>. Its variable denticities and subtle steric and electronic control on their framework make these molecules excellent ligands. Recently a great deal of interest have developed in the synthesis and characterization of transition metal complexes containing Schiff bases as ligands due to their applications as catalysts for many asymmetric reactions. In 1968 Ryoji Noyori developed a copper-Schiff base complex for the metal-carbenoid cyclopropanation of styrene and was awarded a share of the Nobel Prize in Chemistry in the year 2001.

Schiff bases are important intermediates in bio-processes like transamination reaction (from amino-acid to ketoacid and vice versa). It is interesting to study the use of Schiff bases which have wide application in pharmaceutical or biological fields and also in analytical tools. Some Schiff bases including radioactive nuclide complexes show anticancer, antibacterial, antifungal and antiviral agents<sup>7-11</sup>. Moreover, Schiff bases are present in various natural, semi-synthetic, and synthetic compounds and have been demonstrated to be essential because of their biological activities<sup>12, 13</sup>.

Another outstanding application of Schiff bases is their use as an effective corrosion inhibitor, which is based on their ability to get adsorbed spontaneously to form a monolayer on the surface to be protected. A large number of different Schiff base ligands have been used as cation carriers in potentiometric sensors as they have shown excellent selectivity, sensitivity and stability for specific metal ions<sup>14-19</sup>.

A number of Schiff base chelating agents, used for the detection of metal ions, can also be applied for their quantitative determination. Photometric methods are there which are based on the colour formation resulting from the reaction between Schiff base

and the metal ion. Tantarú et. al.<sup>20</sup> have prepared Salen-type Schiff base, 1-ethyl-salicylidene-bis-ethylene diamine by condensing ethyl-o-hydroxyphenyl ketone with ethylene diamine. These Schiff's bases possess very good capacity of complexation with Mn(II) ions, resulting brown complexes. The Schiff base forms a brown complex with Mn(II) cation, with maximum absorbance at 460 nm. The complex showed a maximum stability at pH 6.0. Spectrophotometric determination of Mn(II) using this Schiff base as reagent were successfully applied to pharmaceutical products containing Mn(II) cation. A Schiff base namely bis-(3-methoxysalicylaldehyde)-1,6-diaminohexane was used by Mashhadizadeh et. al.<sup>21</sup> for the extraction of copper. Holzbecher<sup>22</sup> proposed that Schiff bases prepared from salicylaldehyde and aniline can be used for titration of acids with bases and the compound O-[N-(O-hydroxyphenyl)formimidoyl]phenol can be used for the quantitative determination of aluminium. Further, the use of Schiff bases as sensors and solid phase extraction sorbents are increasing in analytical chemistry techniques.

Now a days many Schiff bases are utilized as synthons in the preparation of a number of industrial and biologically active compounds like formazans, 4-thiazolidinines and benzoxazines. The fact that the Schiff base derivatives employed in various processes are environmental-friendly, encourage the researchers for designing of novel heterocyclic and aryl Schiff bases.

### **Transition metal complexes of Schiff bases – a review**

The versatile use of Schiff bases as ligands is due to its ability to coordinate to the metal ions via the azomethine nitrogen. Literature survey reveals that Schiff bases and their complexes are extensively studied and used in many fields. Multidentate Schiff base ligands and their coordination with metals attract much attention because of their

biological relevance. The geometry, oxidation state and redox characteristics of these complexes make them an interesting and challenging class of compounds for the researchers.

A large number of copper complexes have remarkable biological catalytic properties and are used in dyes and polymers, as plant growth regulators and in pharmaceutical fields. N. Raman et. al.<sup>23</sup> prepared complexes of Cu(II), Ni(II), Co(II), and Zn(II) metals with Schiff base derived from benzil-2,4-dinitrophenylhydrazone and aniline. <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, UV-Vis, EPR and CV studies were carried out to propose the structure of these complexes. Mixed ligands complexes of Cr(III), Co(III), Ni(II) and Cu(II) were synthesized by R. K. Upadhyay et. al.<sup>24</sup> with 2-imino-3-(2-hydroxyphenyl)-1-thiazolidin-4-one and they were characterized by elemental analysis, infrared and UV-Visible spectroscopy. The Cu(II) complex had square planar geometry and the others, Cr(III), Co(III) and Ni(II) complexes exhibited octahedral geometry.

Zahid H. Chohan et. al.<sup>25</sup> reported that substituted pyridine Schiff base complexes of copper(II), zinc(II), nickel(II) and cobalt(II) were synthesized and characterized by physical, analytical and spectral data. The ligands were deprotonated on complexation with Co(II), Ni(II) and Zn(II) and showed tridentate nature. The complexes had the general formula  $[M(L)_2]$  with octahedral geometry. The antibacterial activity of the Schiff bases and their complexes were analysed on bacterial strains such as *E. coli*, *P. aeruginosa* and *S. aureus*. It was also reported that on chelation, the Schiff bases become more antibacterial as compared to uncomplexed Schiff bases.

Emad Yousif and co-workers<sup>26</sup> succeeded in synthesizing five new complexes of 2N-salicylidene-5-(*p*-nitro phenyl)-1,3,4-thiadiazole. The VO(II), Co(II), Rh(III), Pd(II)

and Au(III) complexes were monomeric and four-coordinated. Micro elemental analysis, mass spectroscopy, FTIR spectroscopy, UV-Vis spectroscopy,  $^1\text{H}$  and  $^{13}\text{C}$  NMR, conductivity and magnetic susceptibility measurements were conducted to ascertain the structure. VO(II) and Co(II) complexes existed as square pyramidal and tetrahedral respectively while all others had square planar geometry. The *in vitro* antibacterial activity studies established the enhanced activity of the complexes than the ligands.

A novel multidentate and macrocyclic Schiff base (10,21-bis-iminomethyl-3,6,14,17-tricyclo[1,1,3,17]tetracos-1(23),2,6,8,10,12(24),13,17,19,21-decaene-23,24-disodium) and its copper(II), Zinc(II), Manganese(II) and Cobalt(II) complexes were obtained by Riyadh M. Ahmed et. al.<sup>27</sup> in 2013. The ligand consisting of two submacrocyclic units, formed tetranuclear macrocyclic-based complexes by the condensation reaction between sodium 2,4,6-triformyl phenolate and ethylenediamine in 2: 3 mole ratio. Physicochemical and spectroscopic studies suggested that Mn(II), Co(II) and Zn(II) complexes had tetrahedral structure and square planar geometry for Ni(II) and Cu(II) complexes. Antibacterial studies on gram positive and gram negative bacteria proved the inhibitive action of the complexes which was more prominent than the ligand.

Copper(II), nickel(II), zinc(II) and Cobalt(II) complexes were prepared in situ by Aurora Reiss and team mates<sup>28</sup> by the condensation of salicylaldehyde with cefotaxime in the presence of divalent metal salts. The complexes having the general formula  $\text{ML}_2(\text{H}_2\text{O})_2$  were of non-electrolyte type as evident from the molar conductance measurements. Tetragonal geometry was proposed for the Cu(II) complex and octahedral geometry for all others. The authors reported that programs based on quantum molecular studies and chemical modeling were employed to formulate the structure of the ligand

and the complexes. They conducted antibacterial studies on *E. coli*, *P. aeruginosa*, *K. pneumoniae*, *B. subtilis* and *S. aureus* and concluded that all the complexes have excellent activity against the bacterial stain.

A bidentate Schiff base ligand was obtained from 2-hydroxy-3-formylquinoline and substituted p-iodoaniline by M. Mustapha et. al.<sup>29</sup> in 2011. They succeeded in synthesizing Cu(II), Ni(II) and Zn(II) complexes of square planar geometry. Another Schiff base was derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and o-phenylenediamine by N. Raman<sup>30</sup> and he was able to prepare a series of complexes with cobalt(II), manganese(II), copper(II), zinc(II) and mercury(II) ions. Usual characterization techniques like IR, UV-Vis, <sup>1</sup>H NMR, ESR, mass spectra, magnetic susceptibility, molar conductance etc. were performed on the newly synthesized compounds to decide the structures of complexes as ML type. The VO(IV) complex was assigned square-pyramidal geometry and all others square-planar geometry. Cyclic voltammetry was applied to analyse the redox behaviour of copper and vanadyl complexes. In this case also the antibacterial activity was checked and proved that on chelation the inhibitory activity is enhanced. It is reported that only Ni, Co and Cu complexes could cleave the DNA through redox chemistry.

Muna. A. Hadi<sup>31</sup> was able to synthesize a nitrogen and oxygen donor Schiff base by reacting 2-amino benzoic acid and 4-(N,N-dimethyl amino) benzaldehyde which was a monobasic bidentate ligand. This ligand formed chelates with Cu(II), Zn(II) and Cd(II) ions in 1:2 metal-ligand stoichiometry. Conductivity measurements of the complexes gave results which were consistent with those expected.



Recently manganese and cobalt complexes of unsymmetrical Schiff bases were synthesized and characterized by Fatima T. Esmadi<sup>32</sup>. The ligand was the product of reaction between o-phenylenediamine derivatives and 1-hydroxy-2-acetonaphthone and then followed by reaction with the salicylaldehyde, 2-pyridinecarboxaldehyde, 2-hydroxynaphthaldehyde and 2-quinolinecarboxaldehyde. The unsymmetrical tetradentate ligands were then converted into monocentric complexes and characterized by IR and UV-visible spectroscopy, elemental analysis, magnetic susceptibility and electrical conductivity studies. Gram-positive and gram-negative pathogens were taken for the evaluation of the antibacterial activity of the complexes. The manganese complexes showed significant activity against *S. aureus*. Some manganese and cobalt complexes exhibited genotoxic activity in cultured human blood lymphocytes with 8-hydroxy-2-deoxy guanosine (8-OHdG) assay in the concentration range 0.1–10 µg/mL. The exhibition of mutagenicity by some complexes leaves a scope for further research.

Condensation of dehydroacetic acid, 3-nitrobenzaldehyde and 6-methyl- 1,3,5-triazine-2,4-diamine (L) in alcohol medium gave a Schiff base and neutral tetradentate zinc(II), chromium(III), cobalt(II), Ferric(III) and copper(II) complexes were obtained by V. L. Borde et. al.<sup>33</sup> <sup>1</sup>H NMR, UV- visible, X-ray diffraction, microanalytical data, molar conductance, magnetic susceptibility and thermogravimetric analysis were also conducted. Antibacterial studies on *S. aureus*, *E. coli* and *B. subtilis* (gram positive), *K. pneumoniae* (gram negative) were conducted which gave good results.

Synthesis of a ligand from 2-hydroxy-5-methylacetophenone and glycine and its complexation with UO<sub>2</sub>(VI), manganese(II), cobalt(II), iron(II), nickel(II), cadmium(II), zinc(II) and copper(II) ions were reported by V.B. Badwaik et. al.<sup>34</sup> They were

characterized by IR, ESR and electronic spectra, magnetic susceptibility measurements, electrical conductance, and thermogravimetric analysis. The complexes were found to be semiconducting in solid state DC electrical conductivity measurements in the range 313–398 K. The ligand was a monobasic bidentate (OO) donor in Zn complex whereas a dibasic tridentate (ONO) donor in other complexes. Antibacterial activities against many gram positive and gram negative bacterial strains were studied both for ligand and complexes.

A uni-negative tridentate ligand was invented by Suraj B. Ade<sup>35</sup> et. al. from 2-amino-4-chlorobenzoic acid and isatin. Chloride salts of Ti(IV), Zr(IV) and Cd(II) were used to convert into complexes in alcoholic medium. Characterization methods and spectral studies suggested six and four coordinated geometry for those complexes and the presence of coordinated water molecule. Tertiary nitrogen, ketonic carbonyl and carboxylic group were the donor sites in the ligand.

Achut S. Munde<sup>36</sup> studied the Schiff base formed from dehydroacetic acid, 4-methyl-o-phenylenediamine and salicylaldehyde and its complexes. The ligand acted as a dibasic tetradentate with ONNO donor atoms towards Cu(II), Ni(II), Co(II), Mn(II) and Fe(III) ions with 1:1 metal ligand stoichiometry. The physico-chemical studies suggested octahedral geometry for the Co(II), Mn(II) and Fe(III) complexes and square planar geometry for Ni(II) and Cu(II) complexes. TGA and DTA studies of the complexes were conducted and Horowitz–Metzger and Coats–Redfern methods were employed to determine the kinetic parameters. The powder X-ray diffraction data suggested a monoclinic crystal system for the Co(II), Mn(II) and Fe(III) complexes. Anti-fungicidal

activity against *A. niger* and *T. viride* and antibacterial activity against *S. aureus* and *E. coli* were analysed using the ligand and their metal complexes.

Badma Priya et. al.<sup>37</sup> reported that a Schiff base, from L-tryptophan and 2-hydroxyacetophenone and its zinc(II), copper(II), cobalt(II), cadmium(II) and nickel(II) complexes were synthesized. The ternary ligand and complexes were characterized by spectroscopic methods. The complexes were found to have potential antimicrobial activity against *K. pneumonia*, *S. enterica* and *E. coli* and antifungal activity against *R. nigricans*, *A. flavus* and *P. notatum*.

A bidentate ligand and its complexes with Cu(II), Ni(II), Co(II) and Zn(II) ions were isolated by Sudhir S. Sawant<sup>38</sup> from 4-methyl-7-hydroxy-8-formylcoumarin and N-methylaminopropylenediamine. The bidentate ligand, upon complexation gave octahedral geometry. Here, the ligand and complexes were exhibiting antibacterial and antifungal activity; particularly the complexes were superior.

### **Complexes of Schiff bases derived from thiophene-2-carbaldehyde - a review**

Literature survey reveals that a number of Schiff bases were derived from heterocyclic carbonyl compounds. The presence of hetero atoms in such ligands gives them excellent characteristics. Many researchers have reported the synthesis and characterization of Schiff bases derived from thiophene-2-carbaldehyde. A few of them are mentioned here.

Gehad Geindy Mohamed et. al.<sup>39</sup> synthesized a Schiff base ligand from 2-thiophenecarboxaldehyde and 2-aminothiophenol and characterized it. They reported that the ligand was tridentate on coordination to the metal ions like Co(II), Ni(II) and Cu(II) with SNS donor sites of azomethine-N, thiophene-S and thiol-S. These complexes were

assigned octahedral and tetrahedral geometries based on the magnetic and solid reflectance spectral data. On thermal decomposition these hydrated chelates lost water of hydration initially and followed by decomposition of the anions and ligand molecules. Coats-Redfern method was employed to calculate the thermodynamic parameters like  $\Delta H$ ,  $E$ ,  $\Delta S$  and  $\Delta G$  from the thermogravimetric curves. The antibacterial activities of these complexes were screened on fungi and bacterial species like *P. aeruginosa*, *E. coli* and *S. Pyogones*. Here also, the complexes were proved to be potential inhibitors than the ligands.

Thiophene-2-carbaldehyde was condensed with 2-aminothiophenol and propane-1,2-diamine to prepare Schiff bases by Mohammad Nasir Uddin<sup>40</sup> and coworkers. Cadmium(II), zinc(II), nickel(II) and copper(II) complexes were prepared and characterized by elemental analysis, magnetic and spectroscopic measurements. The coordination of the ligand through nitrogen of the azomethine (-HC=N-) group and the sulfur atom of the thiophene ring was established by IR and NMR spectra. Magnetic susceptibility and conductance measurements suggested octahedral geometry and non-electrolytic nature of the complexes. *In vitro* antibacterial screening against four human pathogenic bacteria showed that some of metal chelates had high antibacterial activity and the ligands showed only moderate activity.

Microwave irradiation method was adopted for the condensation of 2-amino-1,3,4-thiadiazole with thiophene-2-carbaldehyde, furfuraldehyde and pyrrole-2-carboxaldehyde to prepare Schiff base ligands by K. P. Srivastava et. al.<sup>41</sup>. The process was carried out using acid catalyst in a water suspension medium and excellent yield is reported. The ligands were tridentate with two nitrogen and one oxygen atom as donor

atoms. Then copper(II), nickel(II), zinc(II) and cobalt(II) complexes were synthesized and spectrometrically and analytically studied. The antibacterial activity against four gram negative and two gram positive bacterial strains were evaluated by agar-well diffusion method and the conclusion was that upon complexation the inhibitory action was considerably increased for all compounds.

Schiff base derived from furan-2-carbaldehyde and 2-aminobenzoic acid and its complexes with Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) were reported by M. M. Omar et. al<sup>42</sup>. Characterizations of these compounds were based on different spectroscopic, magnetic, electrical and elemental analysis. Thermal behaviour of these chelates was studied and the thermodynamic parameters were calculated using Coats-Redfern method. The ligand and its metal complexes showed biological activity against some bacterial species.

### **Scope of present investigation**

A thorough literature survey on Schiff base compounds reveals that much systematic investigation has already been done on metal complexes of Schiff bases derived from heterocyclic carbonyl compounds. The presence of hetero atom in such Schiff bases gave them special characteristics<sup>43-45</sup>. It will be worthwhile to study the characteristics of Schiff bases derived from thiophene-2-carbaldehyde, furan-2-carbaldehyde and their derivatives. The synthesis, characterization and investigations on the applications of some novel Schiff bases are the prime focus of present work.

Different Schiff base ligands can be prepared from thiophene-2-carbaldehyde and furan -2-carbaldehyde with different amino compounds. Also the aryl derivatives of these heterocyclic carbonyl compounds can be converted into Schiff bases. The chelating

ability of these ligands will be evaluated by complexation with transition metal ions. Physicochemical methods such as spectroscopic, electrical, magnetic and elemental analysis can be utilized for the proper formulation of the structures of Schiff bases and their metal complexes. The thermogravimetric analysis will be useful to evaluate the thermal stabilities and the decomposition patterns of these complexes. The inhibition ability of these Schiff bases against mild steel corrosion in different acid media can be investigated by conventional weight loss method, electrochemical methods like electrochemical impedance spectroscopy (EIS) and potentiodynamic polarization studies. Also it is proposed to evaluate the antitumour activities of the copper(II) complexes of these Schiff base ligands.