

Schiff Base Complexes and Their Importance

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ABSTRACT

Schiff base complexes are very useful. Schiff base ligands are easily synthesized and form complexes with almost all metal ions. Over the past few years, there have been many reports on their applications in biology including antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, antimalarial, antiviral activity and also as catalyst in several reactions such as polymerization reaction, reduction of thionyl chloride, oxidation of organic compounds, reduction reaction of ketones, aldol reaction, Henry reaction, epoxidation of alkenes, hydrosilylation of ketones, synthesis of bis(indolyl) methanes and Diels–Alder reaction.

Keywords: Schiff bases, Schiff base Complexes, Importance, Electronic and Vibrational Spectra.

INTRODUCTION

A Schiff base, named after Hugo Schiff, 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. Schiff bases in a broad sense have the general formula $R^1R^2C=N R^3$, where R is an organic side chain. In this definition, Schiff base is synonymous with azomethine. Some restrict the term to the secondary aldimines azomethines where the carbon is connected to a hydrogen atom), thus with the general formula $RCH=NR'$. Schiff bases can also be referred to as imines. The chain on the nitrogen makes the Schiff base a stable imine. A Schiff base derived from an aniline, where R³ is a phenyl or a substituted phenyl, can be called an anil.



General structure of an azomethine.



General structure of a Schiff base.

Schiff bases are usually formed by the condensation of a primary amine with an active carbonyl compound. The azomethine group of the Schiff bases can be aided further in forming a stable chelate by a second group suitably located on the organic ligand, such as –OH group can be present sufficiently near the azomethine group such as on the-ortho position on benzene so that a stable five or six member chelate ring can be formed upon reaction with a metal ion (Fig.1).

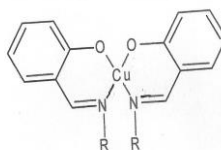


Fig.1

S. M. N. Azmi

Metal complexes of Schiff bases have occupied an important place in the development of co-ordination chemistry. Metal complexes derived from Schiff bases¹ have been known for over one hundred years. S.M Jørgensen, Werner and Ettling² in 1840 isolated a dark green isolated product from the reaction of cupric acetate, Salicylaldehyde and aqueous ammonia. This product was undoubtedly bis- (salicylaldiamino)- Cu(II). The corresponding aryl amine derivative was isolated in 1869 by Schiff³ who established the 1:2 metal ligand stoichiometries. In this work Schiff discovered the exceedingly important synthetic techniques of preparing salicylaldiamine complexes by reaction of the performed metal salicylaldehyde compound with a primary amine. Schiff⁴ prepared complexes obtained from the condensation of Urea and salicylaldehyde. Delpine⁵ in 1899 prepared complexes with R=Methyl and Benzyl in figure given above by reacting the metal acetate salicylaldehyde and primary amine in alcohol and demonstrated their 2:1 stoichiometry.

The complexes of β - keto-amine were prepared in 1889 by Combes⁶ who isolated the remarkable stable Cu(II) complex as shown below (Fig.2).

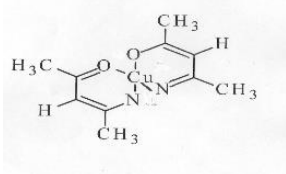


Fig. 2

At a later date Morgan and Mainsmith^{7,8} obtained a variety of complexes analogous to the above Cu(II) complexes. Schiff⁹ may be regarded as the first to have defined the composition of a metal complex with such a ligand by establishing the 1:2 metal-ligand ratios in Copper complexes derived from N-aryl-salicylaldimine. Pfeiffer and his co-workers¹⁰ are also responsible for the commencement of systematic study of Schiff base complexes in 1931. Dubskey and Sokoi¹¹ isolated N-N' bis-(salicylaldehyde) - ethylenediamine copper (II) and Ni (II), and correctly formulated their structures as shown in the figure given below (Fig.3).

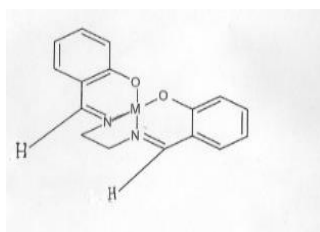


Fig. 3

In recent years Schiff base complexes have found much application in the study of Catalysis^{12,13} reaction inhibition and biological processes^{14,15,16,17(a),17(b),17(c),17(d),17(e),17(f)}

Schiff bases of several types can be synthesized some of them are discussed in outline hereunder: Several Schiff bases are prepared from salicylaldehyde and primary aryl amine (Fig.4).

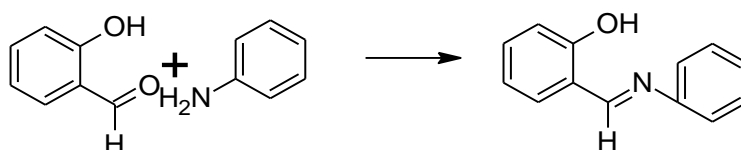


Fig. 4

Such Schiff bases are commonly known as anils. Many substituted anils are being studied for their co-ordination behavior¹⁸ they give stable complexes with many metals. They are bidentate and monobasic. Ketones instead of aldehydes are also used.

MATERIALS AND METHODS

The methodologies used are elemental analysis, uv and visible spectrophotometric measurement, magnetic susceptibilities infrared spectra nmr spectral studies, thermogravimetric analysis and information available in public domain.

RESULTS AND DISCUSSION

Spectroscopic Studies of Schiff Bases

UV–Visible spectroscopy is a very useful analytical tool for studying the spectral properties of Schiff bases generally obtained as mixture of geometrical isomers, their sensitivity to the solvent properties, effect of substitution, pH, ambient temperature, *etc.* Absorbance spectra are generally recorded in the range of 300–450 nm; and the spectra are strongly solvent dependent and the corresponding *E* or *Z* isomer. With isatin Schiff bases under consideration, *Z* (*cis*) isomer appeared at higher wavelengths, that is, of lower energy when compared with *E* (*Trans*) at lower wavelengths (higher energy); solvent-dependent electron density transfer was also observed, and the role of the position of substituent affected the appearance of frequency bands. Excited state was stabilized with a directional π -conjugative electron density shift in the molecule which might be a consequence of the long-range transmission of substituent effects, which supports the larger polarization of carbonyl group and thereby enhancing H-bonding capability of carbonyl oxygen and separation of electronic charges. Solvent affects are very complex phenomena, and the absorbance maxima altered inconsistently with respect to solvent and the position/type of the substituent(s) and geometrical features. In addition, other molecular properties like dipole moments, difference of electronegativity, partial charges, and chemical reactivity also significantly affected electronic spectra. In the IR spectra, C=N is most commonly reported in the 1690–1640 cm^{-1} region as a strong and a sharp band at somewhat lower frequencies than the bands of C=O groups and close to C=C stretching frequencies. Angle strain, steric repulsion, and other complicated local factors and solution concentration and nature of solvent, in neutral solvents, the stretching frequency of C=N is found to be at 1670 cm^{-1} , and the corresponding force constant, 10.6 dynes cm^{-1} , is in the harmonic oscillator approximation. The frequency is usually lowered in the absence of one or more groups in conjugation with the C=N. Generally, there is no difference between IR and Raman frequencies and between the spectra of pure liquids and solids and their solutions in common organic solvents CCl_4 or other not very associative solvents. Generally, water of crystallization appeared at 3300 cm^{-1} plus range.²²

Multinuclear (^1H and ^{13}C) and multidimensional (HSQC, HMBC, COSY, and NOESY) NMR spectral analyses are helpful to establish absolute configuration of isatin Schiff bases. For example, the chemical shifts were assigned by a combined use of 1-D (^1H and ^{13}C proton-decoupled and 2-D NMR experiments COSY, NOESY, HSQC, and HMBC). 2-D NOESY experiments were used assess solution conformation of Schiff bases; *E* (*trans*) stereochemistry was assigned as major isomer in DMSO-*d* 6 solutions. Signals of some protons considerably shifted upfield by approximately 1 ppm relative to the same signals in the parent isatin; in contrast, chemical shifts of the protons present in *Z* (*cis*) isomer showed no difference to those found in parent isatin. Similarly, the same analogy was applied to understand to the electronic influences of substituents like- NO_2 , and $-\text{OH}$ and $-\text{OCH}_3$ group showed only the presence of *E* (*trans*) isomer. In contrast, electron-donating

groups enhanced the stability of *Z (cis)* isomer; these factors affected the physicochemical properties and lead to the differences in biological behaviors because of varying isomeric compositions.

Generally, in physical sciences and especially in chemistry, hydrogen bonding is one of the very important concepts for the deciding properties of the new materials. Intramolecular hydrogen bonds in ortho-hydroxyaryl Schiff bases, in ortho-hydroxyaryl ketones and amides, and in proton sponges and related compounds could be considered as classical objects for the investigation. The geometric and spectroscopic characteristics of the H-bonds that are typical for H-bonds are of medium strength, that is, it is shortened XY contact, elongated XH, directionality trend, change in frequency, and shielding and de-shielding. One of the most prominent aspects is the possibility of delocalization of proton leading to tautomers; and the existence of tautomer's equilibrium depends on room temperature, nature of solvent, and substitution. Proton delocalization is also observed due to the formation of stronger intramolecular H-bonds with larger proton potentials and due to thermally fluctuating media; either of these phenomena cause influence on the geometry of H-bond. Tautomeric equilibria changed with the change in the intrinsic geometry and spectroscopic properties of contributing tautomers, which further complicated the analysis of the experimental data. Computational work often provides the necessary insight via adiabatic and nonadiabatic PES calculations; and lastly, stabilization is also achieved due to delocalization of electrons in the chelate systems which are defined as resonance-assisted hydrogen bonds (RAHB).

Anti-bacterial Activities

Schiff bases complexes containing of salicylaldehyde and 2-furaldehyde with *o*- and *p*-phenylenediamine of Platinum (II) were reported as antibacterial against *E. coli*, *Bacillus subtilis*, *P. aeruginosa*, and *Staphylococcus aureus*. The activity data show that the Platinum (II) complexes are more potent antimicrobials than the parent Schiff base ligands against one or more microorganisms.¹⁹

Anti-fungal activities of Schiff Base Complexes

Metal complexes Cu(II), Co(II), Ni(II) and Mn(II) are synthesized with Schiff bases derived from *o*-phthalaldehyde and amino acids viz., glycine l-alanine, l-phenylalanine, then tested against three fungi. It is clear that Cu(II) and Ni(II) complexes exhibit inhibition towards all the studied microorganisms. However, Co(II) and Mn(II) complexes exhibit less inhibition and VO(II) complexes have no activity towards the microorganisms²⁰. The metal complexes of Cu(II), Ni(II) and Co(II) with Schiff bases of 3-(2-hydroxy-3-ethoxybenzylideneamino)-5-methyl isoxazole and 3-(2-hydroxy-5-nitrobenzylidene amino)-5-methyl isoxazole which were obtained by the condensation of 3-amino-5-methyl isoxazole with substituted salicylaldehydes were screened against *Aspergillus niger* and *Rhizoctonia solani*. The ligands presented here and their transition metal complexes gave better results against the growth of fungi. It is found that the activity increases upon coordination. The increased activity of the metal chelates can be explained on the basis of chelation theory²¹. The orbital of each metal ion is made so as to overlap with the ligand orbital. Increased activity enhances the lipophilicity of complexes due to delocalization of pi-electrons in the chelate ring²². In some cases increased lipophilicity leads to breakdown of the permeability barrier of the cell^{23, 24}. The results of anti-fungal screening, indicate that Cu(II) complexes show more activity than the other complexes. These results may be due to higher stability constant of the Cu(II) complexes than the other complexes.

S. M. N. Azmi

A Schiff base ligand derived from 1,4-dicarbonyl-phenyl-dihydrazide and chromene-2,3-dione (2:2) formed complexes with Cr(III), Mn(III), and Fe(III) metal salt in methanolic medium, then tested for their antimicrobial activities to assess their inhibiting potential. The antifungal experimental results of the compounds were compared with the standard antifungal drug (Miconazole) at the same concentration. All the metal complexes exhibited greater antifungal activity against *Aspergillus* sp. However, they show slightly lesser activity against *Rhizoctonia* sp. than standard drug Miconazole. The Cr(III) and Fe(III) complexes are more effective against *Penicillium* sp. than the standard drug. From the data it has been also observed that the activity depends upon the type of metal ion and varies in the following order of the metal ion: Cr > Fe > Mn. The Gd(III), Dy(III) and Sm(III) complexes of Schiff base derived from acetoacetanilide and 1,3-diaminopropane, $[MX_3(LH_2)]$, where X = Cl⁻, NO₃⁻, NCS⁻, have been synthesized in alcohol and characterized by elemental analysis, electrical conductance in non-aqueous solvents, spectral as well as magnetic susceptibility measurements (Fig. 5). In these complexes, ligand LH₂ acts as a tetradentate ligand coordinating through the two azomethine nitrogen atoms and the two enolizable carbonyl group of acetoacetanilide moiety. The antifungal activity of the ligands LH₂ and some of their complexes were evaluated by agar diffusion method against the fungi *Candida albicans* and *Fusarium oxysporum* using Fluconazole as standard.

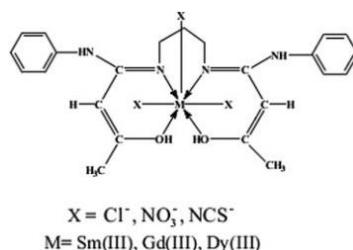


Fig. 5

Biological significance of Schiff Bases and their Metallic Derivatives

The progress of biological inorganic chemistry has seen a marked interest in Schiff base complexes, as many of these complexes may be considered as models for biologically important species. Co, Ni, Fe, Zn, and UO₂ Schiff base complexes of 2-thiophene displayed good antibacterial activity against *E. coli*, *P. aeruginosa*, and *S. pyogenes*; these complexes also inhibited the growth of Gram-positive bacterial strains *S. pyogenes* and *P. aeruginosa*. This unique property could be applied safely in the treatment of infections caused by any of these strains. Platinum complexes of salicylaldehyde and 2-furaldehyde Schiff base with o- and p-phenylenediamine were screened against *E. coli*, *B. subtilis*, *P. aeruginosa*, and *S. aureus*; the data proved the complexes were more potent than the parent Schiff bases. Complexes of Schiff bases derived from sulfametrole and varelaldehyde were screened against *E. coli* and *S. aureus*, and it was observed to have a significant effect on *E. coli*. Membrane of Gram-negative bacteria contains lipopolysaccharides; the reported Schiff bases and their metallic complexes could combine with these lipoic layers to enhance the membrane permeability of the Gram-negative bacteria. Lipophilicity is an important factor that controls the antibacterial activity as lipophilic cell membrane favored the passage of only lipid soluble materials; and this increase in lipophilic nature enhances the penetration of Schiff bases and their metallic complexes into the lipid membranes and seizing the growth of the organism.

CONCLUSION

It is considered that Schiff bases are very important class of organic compounds because of their ability to form complexes with transition metal ions and of their

pharmacological properties. Transition metal complexes containing Schiff bases have been of much interest over the last few years, largely because of its various applications in biological processes and potential applications in designing new therapeutic agents. But still there is need to explore the biological properties of these already synthesized transition metal complexes and to synthesize new complexes with more properties.

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