

Applications of 2-Aminophenol derived Schiff Base Transition Metal Complexes. A Review

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Abstract: The literature survey showed that the chelating Schiff base ligands derived from 2-aminophenol compounds encompass a highly remarkable class of compounds having a wide range of applications in clinical, biochemical and physiological activities. The involvement of metal complex formation in normal life processes has led to reviews from medical chemistry research, Inorganic chemistry research and several field of chemistry research. The literature survey showed that the chelating Schiff base ligands derived from 2-aminophenol compounds encompass a highly remarkable class of compounds having a wide range of applications in clinical, biochemical and physiological activities. Many Schiff base complexes with transition metals have drawn wide attention because of their diverse biological and pharmaceutical activities. The aim of this review is to draw the attention of coordination chemist to focus research on application of schiff base transition metal complexes derived from 2-amino phenol for it has several important application in biological system.

Keywords: physiological, 2-aminophenol, Schiff base, Metal chelates

I. Introduction

Coordination chemistry employs Schiff bases which have achieved prime importance in this era. The extensive studies have been conducted on complexation of Schiff bases with metals due to the attractive physicochemical properties of metal complexes and broad range of utilization in various areas of science. Such types of complexes have paved the way for exploration and findings of a variety of metal complexes in recent years.

Transition metal complexes of 2-aminophenol based Schiff bases have been the subject of extensive investigation because of their wide use in various fields. These Schiff base complexes have wide applications in biological field, as antidepressants, antimicrobial, antitumor, antiphlogogistic, nematocide, and other medicinal agents have been reported based on these compounds. Furthermore these complexes have good catalytic role in many reactions. The data available for 2-aminophenol based Schiff bases in literature embraces very wide and diversified subjects, comprising vast areas of organo-metallic compounds and multiple aspects of bioinorganic chemistry.

Abdallah et al [1] prepared a new Schiff base (H₂L) ligand is via condensation of o-phthaldehyde and 2-aminophenol. The metal complexes of Cr(III), Mn(II), Fe(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) with the ligand are prepared in good yield from the reaction of the ligand with the corresponding metal salts. Then they have screened their parent Schiff base and its eight metal complexes against two fungal and two bacterial species. With respect to antifungal activity, the parent Schiff base and four metal complexes inhibited the growth of the tested fungi at different rates. Ni(II) complex is the most inhibitory metal complex, followed by Cr(III) complex, parent Schiff base then Co(II) complex. With regard to bacteria, only two of the tested metal complexes (Mn(II) and Fe(II)) weakly inhibit the growth of the two tested bacteria.

Omima M.I. Adly[2] synthesized metal complexes of Ni(II), Co(II), Cd(II), VO(IV) and UO₂(VI) as well as several Cu(II) salts with a tridentate O₂N donor Schiff base ligand (H₂L), by condensation of 5-acetyl-4-hydroxy-2H-1,3-thiazine-2,6(3H)-dione with 2-aminophenol.

The antimicrobial activities of the synthesized compounds were tested *in vitro* against the sensitive organisms *Staphylococcus aureus* as Gram positive bacteria, *Proteus vulgaris* as Gram negative bacteria and *Candida albicans* as fungus strain, and the results are discussed. The investigation of antibacterial and antifungal screening data revealed that most of the synthesized complexes were found to possess various antimicrobial activities toward all microorganisms, while the ligand did not show any activity toward all types of microorganism, suggesting greater lipophilic nature of the complexes than the free ligand.

Ayman A. Abdel Aziz et al [3] worked on the reactions of acetate salts of M(II) (M = Mn, Co, Ni, Cu and Zn) with N-salicylidene-o-aminophenol (saphH₂) in ethyl alcohol afforded new four coordinated complexes. The new complexes have been tested for their abilities to catalyze aerial oxidation of benzaldehyde to benzoic acid. The *in vitro* antimicrobial activities of the new complexes were studied against the bacteria: *S. aureus* (gram +ve) and *E. coli* (gram -ve) and fungi: *A. flavus* and *C. albicans*. The data has shown that Mn(II)

complex show the higher antibacterial and antifungal activity, while other complexes showed no to moderate activity. The results have been compared with some known antibiotics.

Mixed ligand complexes derived from 2,6-pyridinedicarboxaldehydebis(*o*-hydroxyphenylimine), 6-pyridinedicarboxaldehydebis(*p* hydroxyphenylimine) (1ry ligands) and 2-aminopyridine 2ry ligand). IR spectra show that the Schiff bases are coordinated to the metal ions in a terdentate manner with NNN donor sites of the pyridine-*N* and two azomethine-*N*. While 2-aminopyridine coordinated to the metal ions via its pyridine-*N*. Magnetic and solid reflectance spectra are used to infer the coordinating capacity of the ligand and the geometrical structure of these complexes are found to be octahedral. The biological activity of the two Schiff base ligands (L1 and L2), their mixed ligand complexes and chloroamphenicol (as a standard compound) were tested against bacteria because bacteria can achieve resistance to antibiotics through biochemical and morphological modifications. The organisms used in the present investigations included *Staphylococcus aureus* and *Bacillus subtilis* (as gram positive bacteria) and *Pseudomonas aeruginosa* and *Escherichia coli* (as gram negative bacteria). The diffusion agar technique was used to evaluate the antibacterial activity of the synthesized mixed ligand complexes. The activity of the two Schiff base ligands and their mixed ligand complexes increases as the concentration increases because it is a well-known fact that concentration plays a vital role in increasing the degree of inhibition [4].

Radhika Pallikkavil et al [5] prepared terephthalaldehyde on reaction with 2-aminophenol and 2-aminothiophenol and it yielded a new series of polydentate Schiff's base ligands (H2La and H2Lb). Dibasic tetradentate coordination of the compounds in their [M2L2] complexes [M = Ni(II), Cu(II) and Zn(II)] has been established on the basis of analytical and spectral data.

Bibhesh K. Singh et al [6] developed a new Schiff base 2-aminophenol-pyrrole-2-carboxaldehyde and its Zn(II), Cd(II), Sn(II) and Pb(II) complexes. The bio-efficacy of the ligand and their complexes has been examined against the growth of bacteria *in vitro* to evaluate their antimicrobial potential. The ligand and complexes exhibited high activity against *E. coli* (100 ppm) and others show very effective against *S. aureus* (100 ppm) bacteria. The zinc complex showed better activity than other metal complexes for both microorganisms.

Amr A. Ibrahim et al [7] derived metal complexes of novel Schiff base (HL) ligand, prepared via condensation of 4-aminoantipyrine and 2-aminophenol. The synthesized ligand, in comparison to its metal complexes is screened for its antibacterial activity against bacterial species, *Escherichia coli*, *Pseudomonas putida*, *Exiguobacterium acetylicum* and *Bacillus simplex*. The activity data show that the metal complexes to be more potent/antibacterial than the parent Schiff base ligand against one or more bacterial species.

Ru(III) Schiff base complexes of the type [RuX(EPh₃)L] (X = Cl/Br; E = P/As; L = dianion of the Schiff bases were derived by the condensation of 1,4-diformylbenzene with *o*-aminobenzoic acid/*o*-aminophenol/ *o*-aminothiophenol in the 1:2 stoichiometric ratio) from the reactions of [RuX₃(EPh₃)₃] with appropriate Schiff base ligands in benzene in the 2:1 stoichiometric ratio [8].

Three pathogenic microbials were used to test the biological potential of the Schiff bases and their ruthenium(III) complexes. They were (i) *Escherichia coli*, (ii) *Aeromonas hydrophilla* and (iii) *Salmonella typhi*. The antibacterial activity of the compound was determined by disc diffusion method. The results showed that the ruthenium chelates are more toxic compared to their parent ligands against the same microorganisms under identical conditions. The toxicity of ruthenium chelates increases on increasing the concentration. The increase in the antibacterial activity of metal chelates may be due to the effect of the metal ion on the normal cell process. Though the complexes possess some significant activity, it could not reach the effectiveness of the standard drug *Streptomycin*.

VD Bhatt et al [9], dinuclear complexes from salicylaldehyde and 2-aminophenol with Cu (II), Ni (II) & Co (II) were obtained by new synthetic route and characterized. The presence of two coordinated water molecules was detected both from elemental analysis and thermo gravimetric analysis. The molecular ion peaks in the mass spectra also supported the formation of dinuclear complexes. The magnetic studies of the complexes revealed ferromagnetic and antiferromagnetic coupling in the complexes under present investigation. Finally, the molecular mechanical method used for energy minimization corroborated the proposed structure of the complexes. This first report on the synthesis of dinuclear complexes via novel route is capable of opening a new era in the preparation of complexes with lot more variations.

Masoud Salavati-Niasari et al [10], new square-planar Mn(II), Cu(II), Ni(II) and Co(II) complexes of a tetradentate Schiff-base ligand "bis(2-hydroxyanil)benzil, H₂[habenzil]; have been prepared. The results suggest that the symmetrical Schiff-base is a bivalent anion with tetradentate N₂O₂ donors derived from the phenolic oxygen and azomethine nitrogen. The formulae was found to be [M(habenzil)] for the 1:1 non-electrolytic complexes. Alumina-supported metal complexes (ASMC; [M(habenzil)/Al₂O₃]) catalyze the oxidation of cyclohexene with *tert*-butylhydroperoxide (TBHP) and H₂O₂. Oxidation of cyclohexene with TBHP gave 2-cyclohexene-1-one, 2-cyclohexene-1-ol and 1-(*tert*-butylperoxy)-2-cyclohexene whereas, oxidation with H₂O₂

resulted in the formation of cyclohexene oxide and cyclohexene-1,2-diol. Manganese(II) complex supported on alumina "[Mn(habenzil)]/Al₂O₃" shows significantly higher catalytic activity than other catalysts.

Krishnankutty et al[11] derived Phenylazo- and thiazolylazo-2,4-pentanediones on reaction with 2-aminophenol and 2-aminothiophenol yielded a new series of polydentate Schiff's base ligands. Four new polydentate Schiff base ligands have been prepared by the condensation of 3-(phenylazo)- and 3-(2-thiazolylazo)-2,4-pentanediones with 2 aminophenol and 2-aminothiophenol.

Analytical, IR, ¹H-NMR and mass spectral data revealed a 1:2 product (H₂tap) with 3-(2-thiazolylazo)-2,4-pentanedione and 2-aminophenol in which both carbonyl groups of the dione are involved in the Schiff base formation. In all other cases, 1:1 condensation products (H₂pap, H₂pat and H₂tat) are formed. The analytical, physical and spectral data of the [ML] complexes of Ni(II), Cu(II) and Zn(II) showed dibasic tetradentate N₂O₂ coordination involving the azomethine nitrogens and the phenolic oxygens of H₂tap. All the other ligands functioned as dibasic tridentates where the imine and hydrazone nitrogens and the O–H/S–H groups are coordinated in their 1:1 metal chelates.

Sayudevi et al[12] prepared two new Schiff bases containing olefinic linkages have been synthesized by condensing *ortho*-substituted aromatic amines with dicinnamoylmethane under specified conditions. The existence of these compounds predominantly in the intramolecularly hydrogen bonded keto-enamine form has been well demonstrated from their IR, ¹H NMR and mass spectral data. Details on the formation of their complexes with Ni(II), Cu(II) and Zn(II) and their nature of bonding are discussed on the basis of analytical and spectral data.

Anita Sharma et al[13] have synthesized transition metal complexes which is derived from 2-((3-(4-fluorophenyl)-1-phenyl-1H-pyrazol-4-yl) methylene amino) phenol. The most probable stereochemistry of the synthesized Cu(II), Ni(II) and Co(II) complexes was given by its magnetic moment. The effective magnetic moments of Cu (II), Co (II) and Ni (II) complex were measured in DMF solution at room temperature. Thermogram of Cu- complex indicated the total weight loss of 79.9% up to 1000°C. Thermogram of Co complex indicated the total 92.5% up to 1000°C. The thermo gravimetric analysis (TGA) provides authentic information regarding the presence of water molecules in the coordination sphere of the all complexes.

Akila et al[14] prepared a new binuclear Schiff base metal complexes of Cu(II), Ni(II) and Co(II) with a new hexadentate N₄O₂ ligand derived from *p*-phenylenediamine, glyoxal/ biacetyl and 2-aminophenol. Biological activity of the ligand and a series of its metal complexes [Cu(II), Ni(II) and Co(II) complexes] were screened for antibacterial activity against *Staphylococcus aureus* (G +ve), *Escherichia coli* (G -ve) and *Klebsilla pneumoniae* (G-ve) by disc diffusion method. It is known that the chelation tends to make the ligand acts as more powerful and potent bacterial agent. On chelation, the ligand with the N and O donor system might have inhibited enzyme production, since enzyme which requires a free –OH group for their activity appear to be especially susceptible to deactivation by the ions of the complexes. The chelation also reduces the polarity of central metal ion because of partial sharing its +ve charge with the donor group and possible π electron delocalization within the whole chelate ring. This increases the nature of central metal ion which favors its permeation through lipid layers of the cell membrane. This increased lipophilicity enhances the penetration of complexes into the lipid membrane and blocks the metal binding sites in enzymes of microorganisms. These Cu(II), Ni(II) and Co(II) complexes also disturb the respiration process and thus block the synthesis of proteins, which restrict further growth of the organisms.

Some new transition metal complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with Schiff base ligand (HL) derived from condensation of vanillin with 2-aminophenol was synthesized in alcoholic medium[15].

The antimicrobial results revealed that the ligand showed moderate activity against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Bacillus subtilis* with maximum zone of inhibition of 25mm against *Escherichia coli*. Mn(II) show considerable activity at all concentrations against *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis* with maximum zone of inhibition of 30mm at 300mg/ml against *Salmonella typhi*. Co (II) showed very low activities against *Klebsilla pneumoniae*, *Streptococcus pyogenes* and *Bacillus subtilis* with zone of inhibition range within 07- 08, 08-12 and 07-10 respectively. Ni (II) complex was found to be reasonably active against *Escherichia coli*, *salmonella typhi*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Bacillus subtilis* with highest zone of inhibition of 36mm against *Salmonella typhi*. Cu(II) complex exhibited only moderate inhibitory activity range between 07-18 mm against *Salmonella typhi*, *Klebsella pneumonia*, *Streptococcus pyogenes* and *Bacillus subtilis*. It is evidenced from the result that Zn(II) complex did not produce any inhibitory zones against all the Gram-negative bacteria used, but it was found to be effective at all concentrations, against all the Gram-positive bacteria.

II. Conclusion

In this review, an overview of the effects of 2-aminophenol and its derivatives which have shown promising results had been discussed. Schiff bases have been widely explored for biological applications. However, the biological activity of this class of compounds deserves further investigation. A number of reports disclosing the effects of the 2-aminophenol Schiff bases on the clinical interest have recently been increasing. This kind of Schiff base compounds have been shown to be promising leads for the design of more efficient antimicrobial agents.

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