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Review Article

A review on versatile applications of transition metal complexes incorporating Schiff bases

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ABSTRACT

Schiff bases and their complexes are versatile compounds synthesized from the condensation of an amino compound with carbonyl compounds and widely used for industrial purposes and also exhibit a broad range of biological activities including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic properties. Many Schiff base complexes show excellent catalytic activity in various reactions and in the presence of moisture. Over the past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis. The high thermal and moisture stabilities of many Schiff base complexes were useful attributes for their application as catalysts in reactions involving at high temperatures. The activity is usually increased by complexation therefore to understand the properties of both ligands and metal can lead to the synthesis of highly active compounds. The influence of certain metals on the biological activity of these compounds and their intrinsic chemical interest as multidentate ligands has prompted a considerable increase in the study of their coordination behaviour. Development of a new chemotherapeutic Schiff bases and their metal complexes is now attracting the attention of medicinal chemists. This review compiles examples of the most promising applied Schiff bases and their complexes in different areas.

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1. Introduction

Schiff bases are formed when any primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the

carbonyl group (CO) has been replaced by an imine or azomethine group (Fig. 1).

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

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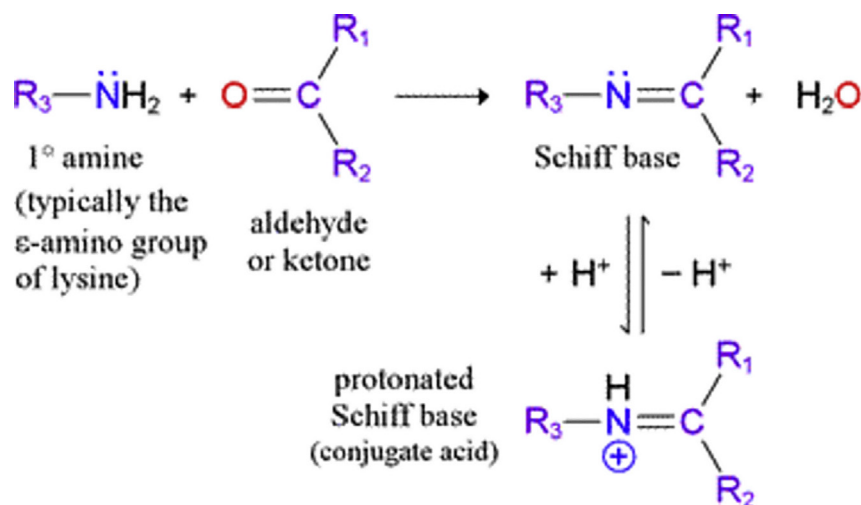


Fig. 1 – General scheme for formation of Schiff bases.

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, hence the need for a review article highlighting the uses of Schiff base ligands and their complexes.

2. Biological importance of Schiff base complexes

The development in the field of bio-inorganic chemistry has increased the interest in Schiff base complexes, since it has been recognized that many of these complexes may serve as models for biologically important species. Thus, we report them in the following:

2.1. Anti-bacterial activity of Schiff base complexes

Metal complexes of Schiff base derived from 2-thiophene carboxaldehyde and 2-aminobenzoic acid (HL) and Fe(III) or Co(II) or Ni(II) or UO₂(II) showed a good antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus pyogenes*. Fe(III), Cu(II), Zn(II) and UO₂(II) complexes caused inhibition for *E. coli*. The importance of this lies in the fact that these complexes could be applied fairly in the treatment of some common diseases caused by *E. coli*. However, Fe(III), Co(II), Cu(II), Zn(II) and UO₂(II) complexes were specialized in inhibiting Gram-positive bacterial strains (*Staphylococcus pyogenes* and *P. aeruginosa*). The importance of this unique property of the investigated Schiff base complexes lies in the fact that, it could be applied safely in the treatment of infections caused by any of these particular strains (Mohamed et al., 2005).

Four Platinum(II) Schiff bases complexes containing of salicylaldehyde and 2-furaldehyde with o- and p-phenylenediamine were reported as antibacterial against *E. coli*, *Bacillus subtilis*, *P. aeruginosa*, *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 (Gaballa et al., 2007).

Metal complexes of a novel Schiff base derived from condensation of sulphametrole and varelaldehyde were screened against bacterial species (*E. coli* and *S. aureus*). The newly prepared Schiff base and its metal complexes showed a higher effect on *E. coli* (Gram-negative bacteria) and *S. aureus* (Gram-positive bacteria) (Mohamed et al., 2010). It is known that the membrane of Gram-negative bacteria is surrounded by an outer membrane containing lipopolysaccharides. The synthesized Schiff base and its metal complexes seem to be able to combine with the lipophilic layer in order to enhance the membrane permeability of the Gram-negative bacteria. The lipid membrane surrounding the cell favours the passage of only lipid soluble materials; thus the lipophilicity is an important factor that controls the antimicrobial activity. Also the increase in lipophilicity enhances the penetration of Schiff base and its metal complexes into the lipid membranes and thus restricts further growth of the organism (Tumer et al., 1999; Imran et al., 2007; Raman et al., 2009). The Schiff base and its metal complexes are more toxic on *S. aureus* than on *E. coli*, probably due to the sulphonic OH, OCH₃, S and CH₃CH₂CH groups, which might interact with the double membrane (Mohamed et al., 2010). This activity is related to the nature and structure of the complexes (Fig. 2).

2-Aminomethylthiophenyl-4-bromosalicylaldehyde Schiff base and its metal complexes have been screened for their antimicrobial activities using the disc diffusion method against bacteria, the results of antimicrobial activity show that the metal complexes exhibit antimicrobial properties and they show enhanced inhibitory activity compared to the parent ligand under experimental conditions. The antibacterial activity has been explained on the basis of chelation theory. Also, the results indicated that tested complexes were more active against Gram-positive than Gram-negative bacteria. It may be concluded that antibacterial activity of the compounds is related to cell wall structure of the bacteria. It is possible because the cell wall is essential to the survival of

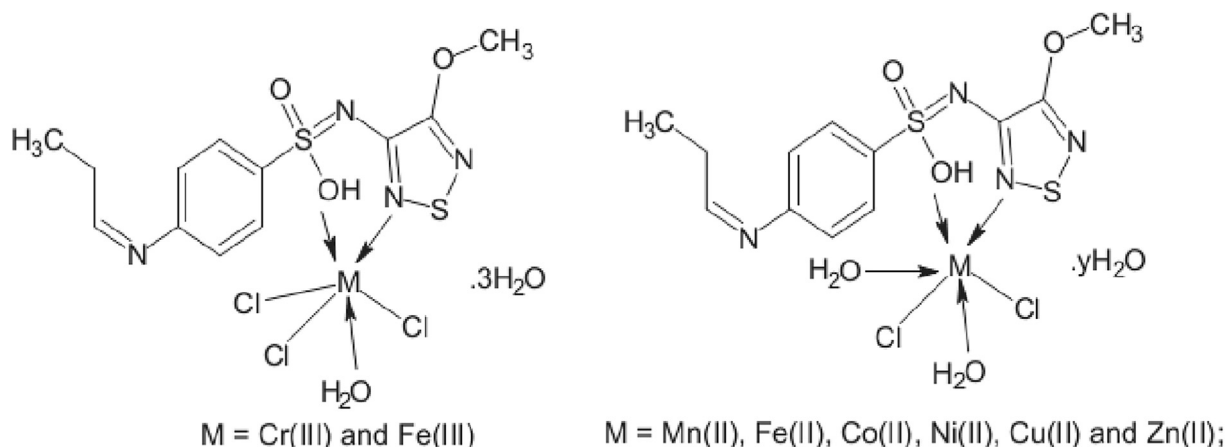


Fig. 2 – The proposed structural formulae of metal complexes.

many bacteria and some antibiotics are able to kill bacteria by inhibiting a step in the synthesis of peptidoglycan (El-Sherif and Eldebss, 2011) (Fig. 3).

Schiff base complexes of Co(II), Ni(II), Cu(II) and Zn(II) incorporating indole-3-carboxaldehyde and m-aminobenzoic acid were screened by disc diffusion method. The activity order of the synthesized compounds is as follows: Cu(II) > Co(II) > Ni(II) > Zn(II) > Ligand. The higher activity of the metal complexes may be owing to the effect of metal ions on the normal cell membrane. Metal chelates bear polar and nonpolar properties together; this makes them suitable for permeation to the cells and tissues. In addition, chelation may enhance or suppress the biochemical potential of bioactive organic species (Nair et al., 2012).

A series of new Iron(II) Schiff base amino acid complexes derived from the condensation of amino acid and sodium 2-

hydroxybenzaldehyde-5-sulfonate have been synthesized. The complexes were characterized by elemental, electronic, IR spectral analyses and conductance measurements. The stability and solubility of the prepared complexes were determined. The antibacterial activity of the prepared complexes has been tested against *Bacillus cereus*, *P. aeruginosa* and *Micrococcus bacteria* (Shaker et al., 2013).

Also a series of new iron(II) complexes based on Schiff bases amino acids ligands have been designed and synthesized from condensation of 5-bromosalicylaldehyde (bs) and α -amino acids (L-alanine (ala), L-phenylalanine (phala), L-aspartic acid (aspa), L-histidine (his) and L-arginine (arg)). The structure of the investigated iron(II) complexes was elucidated using elemental analyses, infrared, ultraviolet–visible, thermogravimetric analysis, as well as conductivity and magnetic susceptibility measurements. The structure of the complexes was validated

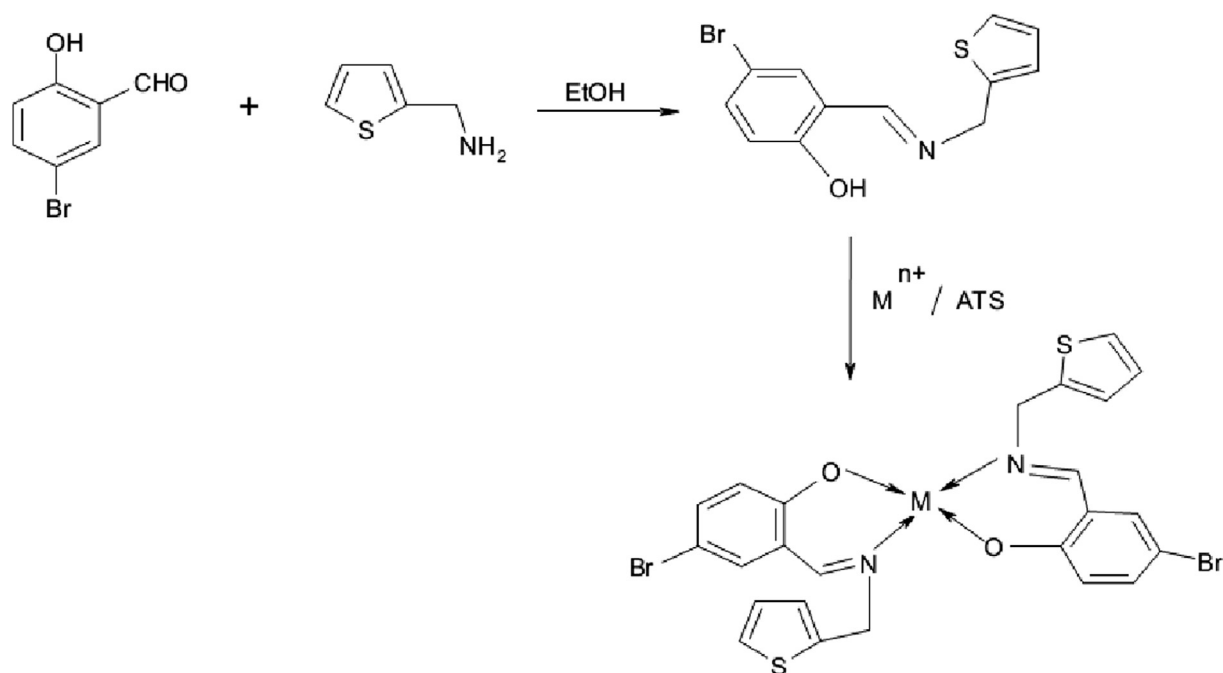


Fig. 3 – Suggested structure of Schiff base ligand and its metal(II) complexes where M = Cu(II), Ni(II) and Zn (II).

using quantum mechanics calculations based on accurate DFT methods. Geometry optimization of the Fe-Schiff base amino acid complexes showed that all complexes had octahedral coordination. Moreover, the prepared compounds are screened for their *in vitro* antibacterial activity against three types of bacteria, *E. coli*, *P. aeruginosa* and *B. cereus* using disk diffusion method. The results of these studies indicated that the metal complexes exhibit a stronger antibacterial and antifungal efficiency than their corresponding Schiff base amino acid ligands (Abdel-Rahman et al., 2013, 2014). Further more, the DNA interaction of these complexes with was tested at pH = 7.2, by using electronic absorption spectra and viscosity measurements. The experimental results indicated that the investigated complexes could bind to DNA via intercalative mode and showed a different DNA binding according to the sequence: bsari > bshi > bsali > bsasi > bsphali (Abdel-Rahman et al., 2013, 2014) (Fig. 4).

Also, five novel Cu(II) complexes derived from the condensation between 5-bromosalicylaldehyde (bs) and α -amino acids (L-alanine, L-phenylalanine, L-aspartic acid, L-histidine and L-arginine) were synthesized and characterized by their elemental analyses, thermogravimetric analysis, IR, mass and electronic spectra, conductance and magnetic measurements. Moreover, the stoichiometry and the stability constants of the prepared complexes have been determined spectrophotometrically using continuous variation and molar ratio methods. The obtained results indicated that the Schiff bases of the amino acids: L-alanine, L-phenylalanine, L-histidine and L-arginine behave as tridentate ligands. The ligands are coordinating with the Cu(II) via azomethine nitrogen, deprotonated carboxylate oxygen and phenolic oxygen. While in the case of L-aspartic, the ligand acts as tetradentate due to the coordination of the second carboxylate group. Based on the studies of magnetic moments and electronic spectra, a square planar geometry has been proposed for all Cu(II) complexes except bromosalicylaldehyde aspartate complex which has a distorted tetrahedral structure. The representative Schiff bases and their Cu(II) complexes were tested *in vitro* for their antibacterial activity against two Gram-Positive bacteria (*Micrococcus luteus* and *B. cereus*) and one Gram-negative bacteria (*P. aeruginosa*). All the complexes showed

activity against the organisms more than the free Schiff base ligands and the activity increases with the increase in concentration of test solution containing the new complexes. The activity data show that the metal complexes have a promising biological activity comparable with the parent Schiff base ligand against bacterial species (Abu-Dief and Nassr, 2015).

2.2. Anti-fungal activity 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 microorganisms (Neelakantan et al., 2008).

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 theory (Raman et al., 2001; Prashanthi et al., 2008). 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 ring (Srivastava, 1981). In some cases increased lipophilicity leads to breakdown of the permeability barrier of the cell (Gupta et al., 1997; Cukurovali et al., 2002). 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.

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

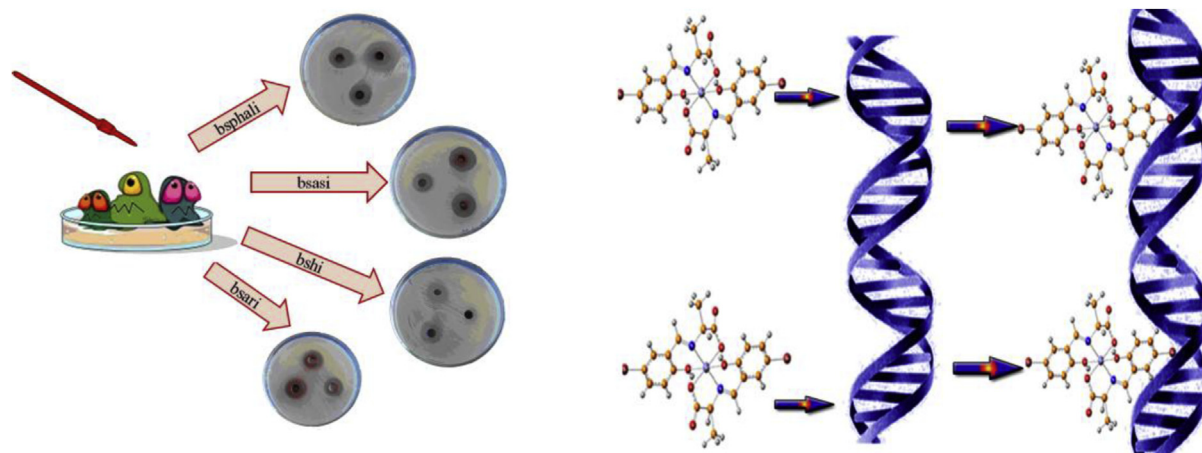


Fig. 4 – Schematic diagram for antibacterial activity and DNA interaction of the investigated complexes.

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: $\text{Cr} > \text{Fe} > \text{Mn}$ (Kumar et al., 2012).

The Gd(III), Dy(III) and Sm(III) complexes of Schiff base derived from acetoacetanilide and 1,3-diaminopropane, $[\text{MX}_3(\text{LH}_2)]$, where $\text{X} = \text{Cl}^-$, NO_3^- , NCS^- , have been synthesized in alcohol and characterized by elemental analysis, electrical conductance in non-aqueous solvents, spectral as well as magnetic susceptibility measurements. In these complexes, ligand LH_2 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 LH_2 and some of their complexes were evaluated by agar diffusion method against the fungi *Candida albicans* and *Fusarium oxysporum* using Fluconazole as standard (Santhi and Radhakrishnan Namboori, 2013) (Fig. 5).

2.3. Anti-cancer activity of Schiff base complexes

Cancer or malignant neoplasm is a class of diseases in which a group of cells display uncontrolled growth, invasion and even sometimes metastasis (De Vita et al., 2005; Thomas and Vinay, 2007). It continues as a serious public health problem throughout the world as the most feared diagnosis. It is the second leading cause of human death after cardiovascular diseases in developing as well as in developed countries (Babasaheb et al., 2010). Currently, the treatment for cancer primarily includes surgery and chemotherapy, but the curative effects of the existing chemotherapeutic drugs are not good enough and they have plentiful side effects. The development of more effective

drugs for treating patients with cancer has been a main attempt over the past 50 years. In recent years, various Schiff bases derivatives have been found to be associated with anticancer properties.

Five ternary complexes of the rare earth ions with o-phenanthroline and Schiff base salicylaldehyde L-phenylalanine were tested as anti-cancer. Methyl thiazolyl tetrazolium colorimetry and flow cytometry were used to test the anti-cancer effect of the complexes with K562 tumour cell. The research showed that the complexes could inhibit K562 tumour cell's growth, generation, and induce apoptosis. The inhibition ratio was accelerated by increasing the dosage, and it had significant positive correlation with the medication dosage. The anticancer activities testing showed that all these complexes exhibited excellent anticancer ability against K562 tumour cell (Dongfang et al., 2008).

Three transition metal coordination complexes $\text{Cu}(\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2)_2 \cdot 2\text{CH}_3\text{OH}$ (1), $\text{Zn}(\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2)_2 \cdot 2\text{CH}_3\text{CH}_2\text{OH}$ (2) and $\text{Cd}(\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2)_2 \cdot 2\text{CH}_3\text{OH}$ (3), derived from the same ligand of 2-acetylpyridine and L-tryptophan ($\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2$) are prepared, then the anticancer activities of these three complexes on MDA-MB-231 breast cancer cells were also investigated. The results indicate that all of the three complexes can inhibit the cellular proliferation. Furthermore, $\text{Cd}(\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2)_2 \cdot 2\text{CH}_3\text{OH}$ (3) has the highest anti-proliferative activity among the three complexes. In addition, complex (3) can inhibit proteasomal chymotrypsin like activity and also can induce apoptosis on human breast cancer MDA-MB-231 cells. Complex (3) has potential to be used as a proteasome inhibitor and anticancer agent (Zhang et al., 2012).

A series of water-soluble platinum(II) complexes of reduced amino acid Schiff bases as potential anticancer agents and characterized them by ^1H NMR, EA, MS, IR, and molar conductivity. These compounds were tested for their DNA interaction with salmon sperm DNA, and their *in vitro* anticancer activities have been validated against HL-60, KB, BGC-823, and Bel-7402 cell lines by the MTT assay. The cytotoxicity of one complex (5g) is better than that of cisplatin against BGC-823 and HL-60 cell lines, and show close cytotoxic effect against Bel-7402 cell line (Li et al., 2013) (Fig. 6)

Antiproliferative effect of a copper (II) complex on HT-29 colon cancer cells has been examined (Hajrezaie et al., 2014). The $\text{Cu}(\text{BrHAP})_2$ Schiff base compound demonstrated a potent antiproliferative effect in HT-29 cells, with an IC_{50} value of $2.87 \mu\text{g/ml}$ after 72 h of treatment. HT-29 cells treated with Cu (II) complexes underwent apoptosis death, as exhibited by a progressive elevation in the proportion of the G1 cell population. At a concentration of $6.25 \mu\text{g/ml}$, the $\text{Cu}(\text{BrHAP})_2$ compound caused significant elevation in ROS production following perturbation of mitochondrial membrane potential and cytochrome c release, as assessed by the measurement of fluorescence intensity in stained cells. Furthermore, the activation of caspases 3/7 and 9 was part of the Cu (II) complex-induced apoptosis, which confirmed the involvement of mitochondrial-mediated apoptosis. Meanwhile, there was no significant activation of caspase-8. Taken together, these results imply that the $\text{Cu}(\text{BrHAP})_2$ compound is a potential candidate for further *in vivo* and clinical colon cancer studies to develop novel chemotherapeutic agents derived from metal-based agents.

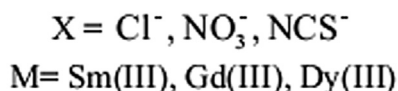
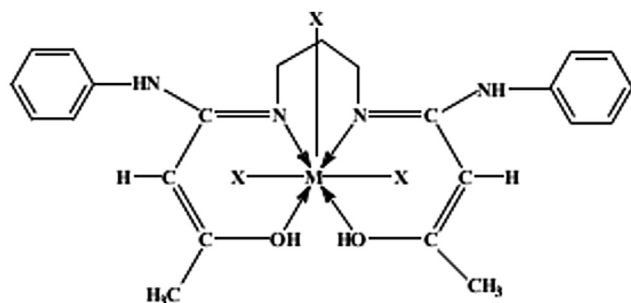


Fig. 5 – Proposed structure for the complexes.

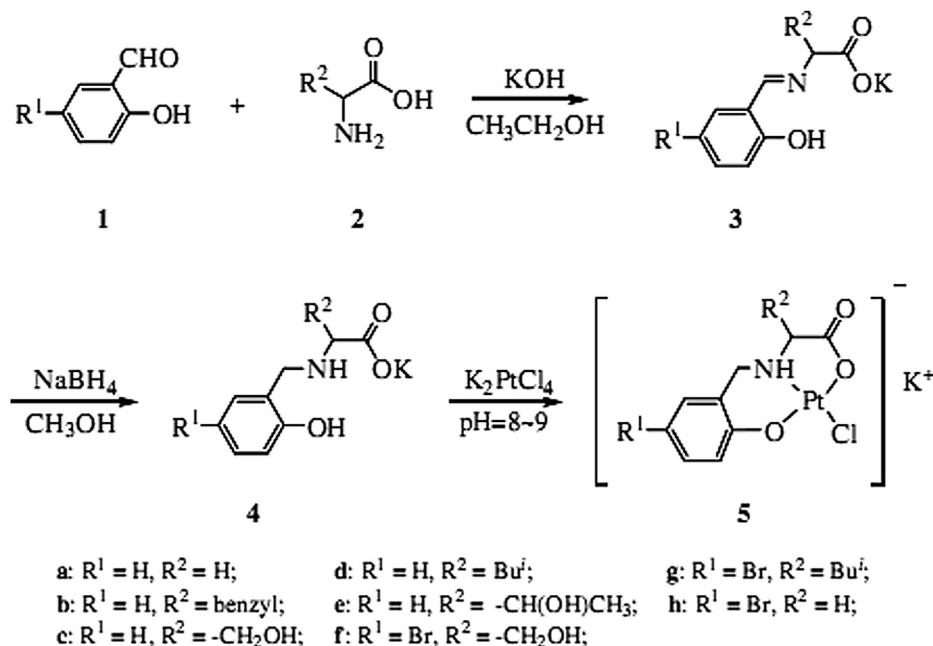


Fig. 6 – Pt(II) complexes of reduced amino acid Schiff bases.

2.4. Antioxidant activity of Schiff bases

The search for metal-derived antioxidants has received much attention and effort in order to identify the compounds having high capacity in scavenging free radicals related to various disorders and diseases associated with oxidative damage, caused by reactive oxygen species (ROS). Presently, synthetic antioxidants are widely used because they are effective and cheaper than natural antioxidants. Currently a number of Schiff-base metal complexes have been investigated as effective scavengers of ROS, acting as antioxidants.

Five kinds of Schiff bases of chitosan and carboxymethyl chitosan (CMCTS) prepared and the antioxidant activity was studied using an established system, such as superoxide and hydroxyl radical scavenging. Obvious differences between the Schiff bases of chitosan and CMCTS were observed, which might be related to contents of the active hydroxyl and amino groups in the molecular chains. The scavenging effect increases with increases the concentration of the Schiff bases (Guo et al., 2005).

Glutamic acid–salicylaldehyde Schiff-base metal complexes are bound into bovine serum albumin (BSA), which afforded BSA binding Schiff-base metal complexes (BSA-Sal-GluM, M = Cu, Co, Ni, Zn). It showed that the protein structures of BSA kept after coordinating amino acid Schiff-bases metal complexes. The effect of the antioxidant activity was investigated. The results indicate that the antioxidant capacity of BSA increased more than 10 times after binding Schiff-base metal complexes (Wang et al., 2007).

The antioxidant capacities of ferrocenyl Schiff bases including o-(1-ferrocenylethylideneamino)phenol (OFP), m-(1-ferrocenylethylideneamino)phenol (MFP), and p-(1-ferrocenylethylideneamino)phenol (PFP) were evaluated in 2,2'-azobis(2-amidinopropane hydrochloride) (AAPH), $\text{Cu}^{2+}/$

glutathione (GSH), and hydroxyl radical (OH^\cdot) induced oxidation of DNA, and in trapping 2,2'-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonate)cationic radical ($\text{ABTS}^{+\cdot}$), respectively. OFP, MFP and PFP possessed similar activities to trap DPPH and $\text{ABTS}^{+\cdot}$. All the ferrocenyl Schiff bases employed herein behaved as prooxidants in $\text{Cu}^{2+}/\text{GSH}^-$ and OH^\cdot induced oxidation of DNA except that OFP exhibited weak antioxidant activity in OH^\cdot induced oxidation of DNA. PFP, OFP and MFP can terminate about 15.2, 11.3, and 9.4 radical-chain-propagations in AAPH-induced oxidation of DNA. Especially, the introduction of ferrocenyl group to Schiff base increased the antioxidant effectiveness more remarkably than benzene-related Schiff bases (Li and Liu, 2011).

The developing of more efficient, less toxic, target specific metal drugs and evaluate their anticancer properties in terms of oxidation state and co-ligand sphere, a sequence of Ru(II), Ru(III) complexes bearing 4-hydroxy-pyridine-2,6-dicarboxylic acid and $\text{PPh}_3/\text{AsPh}_3$ were synthesized and structurally characterized (Kamatchi et al., 2012). Biological studies such as DNA binding, antioxidant assays and cytotoxic activity were carried out and their anticancer activities were evaluated. Interactions of the complexes with calf thymus DNA revealed that the triphenylphosphine complexes could bind more strongly than the triphenylarsine complexes. The free radical scavenging ability, assessed by a series of *in vitro* antioxidant assays involving DPPH $^\cdot$ radical, hydroxyl radical, nitric oxide radical, superoxide anion radical, hydrogen peroxide and metal chelating assay, showed that the Ru(III) complexes possess excellent radical scavenging properties compared to those of Ru(II). Cytotoxicity studies using three cancer lines viz. HeLa, HepG2, HEP-2 and a normal cell line NIH/3T3 showed that Ru(II) complexes exhibited substantial cytotoxic specificity towards cancer cells.

2.5. Anti-inflammatory activity of Schiff bases

Schiff base of functionalised 5-nitroisoquinolines was synthesized and the *in vitro* activity of these compounds against an ACC Niger chloroquine resistant *P. falciparum* strain investigated (Rathelot et al., 1995). The Schiff base: N-[(1E)-(5-nitro-1-naphthyl)methylene]-1-[2-(trifluoromethyl)phenyl]methanamine was the most effective antimalarial agent among the synthesized 5-nitroisoquinoline derivatives. The concentration of this Schiff base necessary to inhibit *P. falciparum* growth by 50% (IC50) was 0.7 µg/mL.

A new series of complexes of the type [Cu (dien) (2a-2tzn) Y₂] and [Cu (dienXXY₂) (2a-5mt)] and of the type [Cu (dptaS) Cl₂] and [Cu (dptaS) Br₂] (dptaS ¼ 1,3-propanediamine) or Schiff mono-base of dipropylene-triamine with 2-thiophene-carboxaldehyde, has been tested for anti-inflammatory and antioxidant activity. The tested compounds inhibit the carrageenin-induced rat paw oedema (52.0–82.6%) and present important scavenging activity. Compound 6 is the most potent (82.6%) in the *in vivo* experiment. Lipophilicity-as RM values – has been determined. The results support that in general, adducts of the type [Cu (dienXXY₂) (2a-5mt)] exhibit increased activity compared to the starting material of type [Cu (dienXXY₂)]. An attempt to correlate the biological results with their structural characteristics and physicochemical parameters has been made (Pontiki et al., 2008).

A series of novel 3-(4-(benzylideneamino) phenylimino) 4-fluoroindolin-2-one derivatives were synthesized and characterized by spectral (I.R, ¹H NMR, mass). The title compounds (N₁–N₁₀) were evaluated for analgesic, anti-inflammatory, and ulcerogenic index activities. Results displayed that compound N₃ exhibited significant analgesic activity. Among the title compounds studied, N₂, N₃, and N₈ exhibited significant anti-inflammatory activity comparable to reference standard diclofenac sodium. Interestingly, the test compounds showed only mild ulcerogenic side effect when compared to aspirin (Nirmal et al., 2010).

Schiff base derived from 4-aminoantipyrine (4-amino-1,5-dimethyl-2-phenylpyrazole-3-one) and benzaldehyde derivative was tested for its anti-inflammatory. The results showed promising anti-inflammatory activity which could be beneficial for use in the treatment of inflammatory diseases. The results of this study may lead to the development of a new therapeutic agent useful in fighting diseases caused by oxidative stress and inflammation (Alam et al., 2012).

A series of Schiff base derivatives of 4-aminophenazone (4APZ-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one) with different aldehydes were synthesized. The synthetic compounds were screened for their anti-inflammatory, analgesic and antipyretic activities. Carrageen an-induced paw oedema (CIPO) and histamine induced paw oedema (HIPO) methods were used to determine the anti-inflammatory activity of commercial sample of 4APZ and its synthesized Schiff bases in mice. The anti-inflammatory activity was in the order of 4APZAB > 4APZBB > 4APZCB > 4APZVn and all the test compounds exhibited considerable dose dependent inhibition of the paw oedema. The effect of the compounds on

membrane stabilization was also determined which showed that compounds 4APZ (120 and 240 mg/kg doses), 4APZAB (160 mg/kg) and 4APZVn (600 mg/kg) produced highly significant inhibition (*P* < 0.001) of hypotonicity-induced haemolysis. Further, it was also observed that 4APZ (120 and 240 mg/kg doses), 4APZBB (500 mg/kg) and APZCB (150, 300 and 600 mg/kg dose) produced highly significant inhibition (*P* < 0.001) of albumin denaturation; a consistent dose dependent anti-inflammatory effect of test compounds as compared to the standard drug. Analgesic activity of the compounds was investigated by formalin-induced paw licking (FIPL) and acetic acid-induced writhing (AIW) methods in mice. It was observed that 4APZ (240 mg/kg), 4APZAB (160 mg/kg), 4APZBB (500 mg/kg), 4APZCB (600 mg/kg) and 4APZVn (600 mg/kg) showed analgesic effect with highly significant (*P* < 0.001) reduction of paw licking and writhing activity in the treated mice. The order of analgesic effect of the compounds was 4APZAB > 4APZBB > 4APZVn > 4APZCB. Moreover, phenobarbitone-induced sleeping time (PIST) in mice was also studied but only 600 mg/kg of 4APZVn significantly increased the duration of induced sleep which also suggested its sedative property. Brewer's yeast was used to induce fever in rabbits and analyzed the compounds for their antipyretic activity. Different doses of 4APZ for different time durations (240 mg/kg-after 1 h, 120 and 240 mg/kg doses-after 2 h) produced highly significant (*P* < 0.001) inhibition of hyperpyrexia. Other compounds showed good antipyretic activity after 2, 3 and 4 h (Murtaza et al., in press).

2.6. Antiviral activity of Schiff bases

Although there are many therapeutic options for viral infections, currently available antiviral agents are not yet fully effective, probably due to the high rate of virus mutation. They may also present any of a number of side effects. Salicylaldehyde Schiff bases of 1-amino-3-hydroxy-guanidine tosylate are a good platform for the design of new antiviral agents (Sriram et al., 2006). In fact, from a set of different 1-amino-3-hydroxyguanidine tosylate-derived Schiff bases, 2-(3-allyl-2-hydroxybenzylidene)-N-hydroxyhydrazinecarboximidamide derivative was shown to be very effective against mouse hepatitis virus (MHV), inhibiting its growth by 50% when employed at concentrations as low as 3.2 µM (Sriram et al., 2006).

A new series of 3-(benzylideneamino)-2-phenylquinazoline-4(3H)-ones were prepared through Schiff base formation of 3-amino-2-phenyl quinazoline-4(3H)-one with various substituted carbonyl compounds. Their chemical structures were elucidated by spectral studies. Cytotoxicity and antiviral activity were evaluated against herpes simplex virus-1 (KOS), herpes simplex virus-2 (G), vaccinia virus, vesicular stomatitis virus, herpes simplex virus-1 TK-KOS ACVr, para influenza-3 virus, reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus, feline corona virus (FIPV), feline herpes virus, respiratory syncytial virus, influenza A H1N1 subtype, influenza A H3N2 subtype, and influenza B virus. Compound 2a showed better antiviral activity against the entire tested virus (Kumar et al., 2010).

3. The oxygen affinity of Schiff base complexes

Oxygen absorption properties of cobalt(II) complexes of N,N'-bis (salicylidene)-2,2'-dimethyl-1,3-propanediimine ligand derivatives, termed CoSaldmpr, were reported (Park et al., 1998). The complexes gave significant results in 1-methyl-2-pyrrolidinone (NMP) solution. The complexes with 2-cyanopyridine (2 M) as axial base, loading of Co(3-methoxy-Saldmpr), measured in (g O₂/g solution) remains about 35% higher than Co(3-methoxy-Salen) for at least four absorption/desorption cycles.

Oxygen absorption-desorption processes for square planar Mn(II), Co(II) and Ni(II) complexes of tetradentate Schiff base ligands derived from condensation reaction of ethylenediamine with salicylaldehyde, o-hydroxyacetophenone or acetyl acetone in DMF and chloroform solvents were investigated. The sorption processes were undertaken in the presence and absence of (pyridine) axial-base in 1:1 M ratio of (pyridine:metal(II) complexes). Complexes in DMF indicate significant oxygen affinity than in chloroform solvent. Cobalt(II) complexes showed significant sorption processes compared to Mn(II) and Ni(II) complexes. The presence of pyridine axial base clearly increases oxygen affinity. This kind of material can be used as a catalyst in oxidative addition reactions in the organic chemistry and petrochemicals, which is reproducible and is considered environmentally friendly (Emara et al., 2014).

4. Schiff base complexes as catalysts

Many Schiff base complexes of metal ions show high catalytic activity and played a significant role in various reactions to enhance their yield and product selectivity. The convenient route of synthesis and thermal stability of Schiff base ligands have contributed significantly for their possible applications in catalysis as metal complexes (Gupta and Sutar, 2008).

Schiff base complexes of transition metal ions are efficient catalysts both in homogeneous and heterogeneous reactions and the activity of these complexes varied with the type of ligands, coordination sites and metal ions. Chiral Schiff base complexes are more selective in various reactions such as oxidation, hydroxylation, aldol condensation and epoxidation. The catalytic activity of metal complexes has been reported in various reactions as given below:

4.1. For polymerization reaction

The polymerization reactions are catalyzed with various catalysts and based on experimental observations; the following conditions apply to the efficient use of catalysts in the polymerization of different monomers (Gupta and Sutar, 2008):

- Catalyst must have high olefin-insertion ability.
- Catalyst must have two available cis-located sites for polymerization.
- Catalyst must be stable enough under the usual polymerization conditions.

Iron(III) and cobalt(II) complexes with pyridine bis(imine) ligands showed significant activity in the polymerization of ethylene. These complexes were also used successfully for copolymerization of ethylene with 1-hexene (Souane et al., 2002). The iron(III) Schiff base complexes showed higher yield and activity than the cobalt(II) complexes (Souane et al., 2002).

The salen complexes also showed activity in ring opening oligomerization or polymerization of epoxides (Mason and Perkins, 2000).

Catalytic oxidative polymerization of 2,2'-dihydroxybiphenyl (DHBp) was performed by using both the Schiff base monomer-Cu(II) complex and Schiff base polymer-Cu(II) complex compounds as catalysts and hydrogen peroxide as oxidant, respectively. The dependence of monomer conversion and molecular weight distribution on various reaction parameters, including time, temperature, solvent as well as the amount of catalyst and oxidant were investigated. The structure of the poly-2,2'-dihydroxybiphenyl (PDHBp) was confirmed by UV-vis, IR, ¹H and ¹³C NMR spectroscopy techniques. The electrochemical and thermal properties of PDHBp were also studied. DSC data revealed that PDHBp was amorphous (Bilici et al., 2009).

4.2. For reduction of thionyl chloride

The catalytic effects of some Co(II), Cu(II), and Ni(II) Schiff base complexes derived from 1,2-bis (naphthylidene-imino) ethane, 1,3-bis(naphthylidene-imino)propane, 1,2-bis(naphthylideneimino) butane and 1,2-bis(naphthylidene-imino) pentane on the reduction of thionyl chloride on a glassy carbon electrode were studied and the kinetic parameters with cyclic voltammetry determined. The charge transfer process during the reduction of thionyl chloride is affected by the concentration of catalysts. Thermodynamic and kinetic parameters of the reduction process are affected by the chelate ring size of the ligands (Choi et al., 2000).

A symmetric tetradentate Schiff base ligand bis(3-methoxysalicylidene)-o-phenylenediamine (H₂L) was prepared. A series of transition metal complexes with this Schiff base ligand have been synthesized and structurally characterized by IR and elemental analysis. The catalysis for reduction of thionyl chloride was studied by means of constant resistance discharge. The result shows that [Mn(III)Cl(H₂O)] CH₃OH and [Co(II)HLCl(H₂O)] have a good catalytic activity for the reduction of thionyl chloride, which improves the cell voltage, the rate of discharge, and the lifetime of Li/SOCl₂ batteries (Lin Che et al., 2008).

4.3. Oxidation of organic compounds

The reaction between ONS donor ligands (H₂L) (derived from salicylaldehyde or its derivatives or 2-hydroxy-1-naphthaldehyde and o-aminothiophenol) and [RuHCl(CO)(PPh₃)₃] afforded new ruthenium(II) complexes of composition [Ru(L)(CO)(PPh₃)₂] (L = dianionic ONS donor Schiff base ligand). These complexes are found to be effective catalysts for the oxidation of alcohols at room temperature using N-Methylmorpholine-N-Oxide (NMO) as oxidant. This provides a general and simple method for the oxidation of different kind

of alcohols under mild conditions. Benzylic primary and secondary alcohols are oxidized in good to excellent yields, and aliphatic and cyclic alcohols give carbonyl compounds in moderate yields (Tamizh et al., 2012).

Three complexes RuLCl (L derived from salicylaldehyde or 2-hydroxyacetophenone or 3,5-dibromosalicylaldehyde and ethylenediamine) were used as catalysts in the oxidation of cyclo-octene and tetraline in the presence of molecular dioxygen associated with benzoic anhydride. The efficiency of this oxidation reaction was tested in the presence of two apical bases: 1- or 2-methylimidazole. All complexes exhibit a quasireversible redox system. The electrolysis experiments were carried out at controlled potential for each complex, using different substrates such as cyclo-octene and tetraline. The oxidized products are cyclo-octene oxide (turnover 6.7), a mixture of 1-tetralol and 1-tetralone (turnover 7.6) respectively. For the oxidation of hydrocarbon compound such as tetraline, higher yield and selectivity were observed in the presence of 1-methylimidazole instead of its isomer 2-methylimidazole (Ourari et al., 2012).

Two mononuclear copper (II) complexes have been prepared by the reaction of two ONNO type Schiff base ligands, ([bis(2-hydroxy-propionophenone)2,2'-dimethyl-propanediamine] (H_2L_1) and [bis(5-bromosalicylaldehyde)2,2'-dimethyl-propanediamine] (H_2L_2)) with $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ in 1:1 M ratios. The catalytic performance of the prepared Cu(II) complexes for the oxidation of styrene and cyclooctene with *tert*-butyl hydroperoxide has been evaluated. The selective oxidation of styrene to benzaldehyde was carried out with Schiff base complex as catalyst using *tert*-butylhydroperoxide 100% conversion was obtained. Production of benzaldehyde in the oxidation of styrene may be due to the further oxidation of the epoxide formed with the *tert*-butylhydroperoxide (Maurya et al., 2007; Heshmatpour et al., 2012). The styrene conversion was found to be strongly dependent on the solvent nature and maximum conversion was obtained in the chloroform. Oxidation of cyclooctene with *tert*-butyl hydro-peroxide gave cyclooctene oxide as the sole product (Heshmatpour et al., 2012).

Two Mo(VI) tetradentate Schiff base complexes derived from 2, 2'-dimethylpropylenediamine and aromatic aldehydes prepared, and catalytic performance of the prepared molybdenum complexes for oxidation of different olefins with *tert*-butylhydroperoxide was evaluated. These complexes were found to be an efficient and selective catalyst for the homogeneous oxidation of various olefins. $\text{MoO}_2\{\text{sal-nptn}(3\text{-OMe})_2\}$ with a methoxy groups on the salicylidene ring of the ligand promote the effectiveness (Rayati et al., 2012).

Kraft pulp has to be bleached to eliminate the chromophoric structures, which cause a darkening of the pulp. In Nature, an equivalent role is assumed by ligninolytic enzymes such as lignin peroxidases, manganese peroxidases and laccases. The development of low molecular weight manganese peroxidase mimics may achieve environmentally-safe bleaching catalysts for the industry. Herein we report the synthesis and characterization of six manganese(III) complexes 1–6, incorporating dianionic hexadentate Schiff base ligands ($\text{H}_2\text{L}^1\text{--H}_2\text{L}^4$) and different anions. Complex 4, $\text{Mn}_2\text{L}_{22}(\text{H}_2\text{O})_2(\text{DCA})_2$ was crystallographically characterized. Complexes 1–4 behave as more efficient mimics of peroxidase

in contrast to 5–6. We have studied the use of these complexes as catalysts for the degradation of the lignin model compound veratryl alcohol. The biomimetic catalysts were used in conjunction with chlorine-free inexpensive co-oxidants as dioxygen or hydrogen peroxide. Yields up to 30% of veratryl alcohol conversion to veratraldehyde have been achieved at room temperature in presence of air flow using 0.5% of catalyst (González-Riopiedre et al., 2013) (Fig. 7).

4.4. For reduction reaction of ketones

The asymmetric reduction of dialkyl ketones to alcohols (Fehring and Selke, 1998) is a difficult process but Schiff base complexes of transition metals are efficient catalysts in carrying out these reductions (Nishibayashi et al., 1999; Langer et al., 1996). Although the presence of formic acid has favoured asymmetric reduction of ketones (Petra et al., 2000), the aqueous phase reduction is of great significance (Himeda et al., 2003) from an environmental point of view.

The reduction of ketones using iridium and ruthenium analogous was also performed (Faller and Lavoie, 2001; Cross et al., 2001). The reduction rate was affected by central metals and decreased in order $\text{Rh} \geq \text{Ir} \gg \text{Ru}$. The reduction of ketones was also carried using chiral complexes in place of bipyridine complexes. The reduction of ketones (Faller and Lavoie, 2001; Cross et al., 2001) was better when carried out in the presence of chiral Schiff base, which produced (S)-1-phenylethanol 99% yield. A variety of ketones were examined from which, it was observed that enantioselectivity was influenced by the position and electronic properties of ring substituents in aryl ketones. The ortho substituted acetophenones were more enantioselective than meta- and para-substituted ketones.

A silica supported chitosan-Schiff base Pd(II) catalyst was prepared in a simple way and characterized by XRD, FT-IR, SEM-EDS, XPS and TG, and the ability of this complex to catalyze hydrogenolysis of 1-tetralone into 1,2,3,4-tetrahydronaphthalene was also investigated in the presence of hydrogen. It has been revealed that the catalyst had high catalytic activity for hydrogenolysis of 1-tetralone at

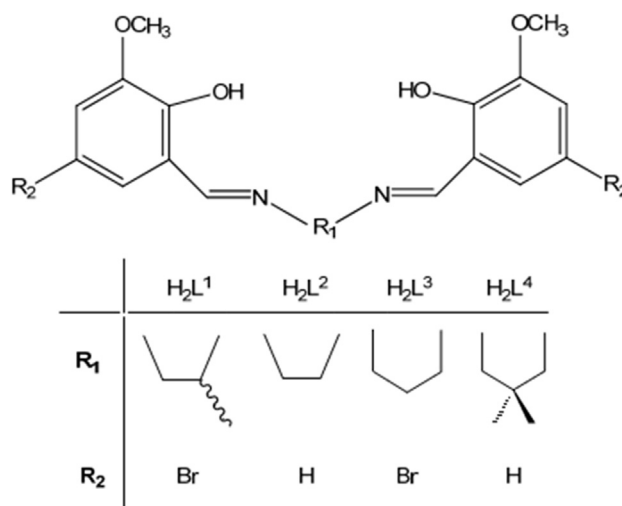


Fig. 7 – Structure of the Schiff base ligands $\text{H}_2\text{L}^1\text{--H}_2\text{L}^4$.

ambient temperature and normal pressure of hydrogen. Especially, the hydrogenolysis of 1-tetralone in ethanol solvent gave excellent results and the 100% conversion of 1-tetralone and the 100% selectivity for 1,2,3,4-tetrahydronaphthalene were obtained under optimized reaction conditions. The influences of reaction temperature, reaction time and solvent on the hydrogenolysis of 1-tetralone were also investigated. It has been also revealed that the catalyst was efficient and eco-friendly for the hydrogenolysis of carbonyl that connected with a benzene ring to give corresponding aromatic hydrocarbons (Gu et al., 2013).

4.5. For aldol reaction

Al(III) Schiff base complexes were used as catalyst for reaction between 5-methoxyoxazoles and benzaldehydes to produce optically active cis-oxazoline adducts (Evans et al., 2001).

Moreover, highly selective Aldol reaction of 1,3-dibenzoylmethanes with formaldehyde catalyzed by tetradentate hydroxycobalt(III) Schiff base complexes under neutral condition (Maruyama et al., 1995).

Catalytic asymmetric synthesis of unnatural amino acids with vicinal tetrasubstituted chiral carbon stereocenters is described. In the first part, direct catalytic asymmetric aldol reaction of simple non-activated ketone electrophiles with α -substituted α -isothiocyanato ester donors was realized. A Mg/Schiff base catalyst promoted the aldol reaction, and α -amino- β -hydroxy esters were obtained in up to 98% ee and 98:2 d.r. In the second part, the Mg/Schiff base catalyst and a Sr/Schiff base catalyst were utilized for stereodivergent direct asymmetric Mannich-type reaction of ketimines. The Mg/Schiff base catalyst gave *syn*- α,β -diamino esters, while the Sr/Schiff base catalyst produced *anti*- α,β -diamino esters in good to high enantioselectivity, up to 97% (Matsunaga and Yoshino, 2011).

4.6. For Henry reaction

A series of Schiff bases derived from cinchona alkaloids were developed as chiral ligands for the copper(II)-catalyzed asymmetric Henry reaction. The optimized catalyst can promote the Henry reaction of both aromatic and aliphatic aldehydes with nitromethane or nitroethane. Those reactions can afford the chiral β -nitro alcohol adducts with high enantioselectivities (Wei et al., 2011). Solvent always plays an important role in various catalytic processes. A series of reaction solvents, such as THF, toluene, diethyl ether, hexane, methanol, ethanol, isopropanol, acetonitrile, acetone, dichloromethane, DMF, and dioxane were tested in the catalytic enantioselective Henry reaction between benzaldehyde and nitromethane. THF was clearly the best choice for this reaction in terms of yield and enantioselectivity (Wei et al., 2011).

A series of novel Schiff bases bearing triazole structure complexed with Mn(OAc)₂, then tested to catalyze Henry reaction of nitroalkanes with aldehydes to produce the corresponding products of β -nitro alcohols. Mn(II) Schiff base complex was an effective catalyst for the Henry reaction and produced β -hydroxy nitroalkanes in high yield. The procedure with above-mentioned catalyst has several merits including

simplicity of operation, mild reaction condition and easy isolation (Zhou et al., 2012).

4.7. For epoxidation of alkenes

Cis-cyclooctene is often used as a diagnostic substrate whenever a new catalytic system is synthesized. First, the high stability of cis-cyclooctenoxide, its main oxidation product, enables easy evaluation of the catalyst efficiency. Besides, epoxides are very useful intermediates in the chemical industry, since they are the starting point for the preparation of a wide variety of products.

A series of Schiff-base complexes has been synthesized by the condensation of 1,2-diaminocyclohexane with salicylaldehyde, 2-pyridinecarboxaldehyde, and 2-hydroxy-1-naphthaldehyde, followed by the metallation with manganese (1, 2, 3a), cobalt (3b), copper (3c) and iron (3d) salts. Mn complex (3a) resulting from N,N'-bis (2-hydroxy-1-naphthalidene) cyclohexanediamine (L₃) ligand was considerably active for the catalytic epoxidation of styrene under mild conditions, in which the highest yield of styrene oxide reached 91.2 mol%, notably higher than those achieved from simple salt catalysts Mn(Ac)₂·4H₂O and MnSO₄·H₂O. However, another two salen-Mn complexes 1 and 2 derived from ligands N,N'-bis (salicylidene)cyclohexanediamine (L₁) and N,N'-bis (2-pyridinecarboxalidene) cyclohexanediamine (L₂) exhibited relatively poor activity under identical experimental conditions (Lu et al., 2006).

Six dioxomolybdenum(VI) complexes of Schiff-bases derivatives of trans 1,2-diaminocyclohexane and R-salicylaldehyde as well as 2-hydroxynaphthaldehyde have been synthesized and characterized. The catalytic activities of the complexes in the reaction of epoxidation of cyclohexene and 1-octene with *tert*-butyl hydroperoxide (TBHP) as oxidant have been studied. The synthesized dioxomolybdenum (VI) complexes are found to be very selective catalysts for the epoxidation of cyclohexene and 1-octene. High yield (90–100%) of epoxidation was found for the first of the reactions at 358 K; for the epoxidation of 1-octene the yield was in the range 15–74%. The best results were obtained for [trans-N,N'-bis-(4,6-dimethoxysalicylidene)-1,2-cyclohexanediaminato]-dioxomolybdenum(VI) and [trans-N,N'-bis-(2-hydroxynaphthylidene)-1,2-cyclohexanediaminato]-dioxomolybdenum. An increase in the reaction temperature may lead to an increase in the yield of the epoxide (Ambroziak et al., 2004).

Schiff-base derived from primary amine and 2-pyridinecarboxaldehyde formed complexes with methyltrioxorhenium. These complexes displayed high catalytic activity and selectivity in the epoxidation of cyclohexene with urea hydrogen peroxide adduct (UHP) as oxidant in methanol, but poor performances in the case of hydrogen peroxide (30%) as oxidant due to the decomposition of them (Qiu et al., 2009). Five tridentate Schiff base ligands, containing a mixed donor set of ONN and ONO were prepared by the reaction of benzhydrazide with the appropriate salicylaldehyde and pyridine-2-carbaldehyde and characterized. The complexes of these ligands were synthesized by treating an ethanolic solution of the appropriate ligand and one equivalent Et₃N with an equimolar amount of MnCl₂·4H₂O. These Mn(II) Schiff base

complexes are highly selective catalysts for oxidation of cyclohexene by PhIO under mild conditions. The only product of the reaction was cyclohexene oxide in the presence of imidazole. Adding nitrogenous donor imidazole made catalytic activity increase. These kinds of complexes are potentially important catalysts in quantitative cyclohexene oxidation or similar oxidation processes of hydrocarbons (Pouralimardan et al., 2007).

Nickel(II) Schiff base complexes of N,N'-bis(2-Hydroxyphenyl) ethylenediimine and N,N'-(2-hydroxyphenyl) acetylalidine N-(2-hydroxyphenyl) acetamide were used for epoxidation of olefins viz., cyclohexene, 1-hexene, cis- and trans-stilbenes, indene with sodium hypochloride (Kureshy et al., 2002).

Vanadium(IV) reacted with Schiff base ligand N-salicylidene-2-bromoethylimine (L) to form vanadium(IV) complex, which tested as catalyst for epoxidation of alkenes.

Various alkenes can be converted efficiently and selectively to their corresponding epoxides in the presence of catalytic amount of vanadyl Schiff base complex (Grivani et al., 2012).

A new heterogeneous catalyst by bridging an oxomolybdenum Schiff base on a polyhedral oligomeric silsesquioxane (POSS) has been generated via covalent attachment (Leng et al., 2014). The resulting POSS-bridged oxo-molybdenum Schiff base complex catalyst was fully characterized by ¹H NMR, XRD, FT-IR, SEM, TGA, and contact angle analysis, and its catalytic potential was studied for the epoxidation of alkenes using aqueous *tert*-butyl hydroperoxide (TBHP) as the oxidant. The catalyst was found to be highly efficient and showed higher catalytic reactivity than the corresponding homogeneous analogues with added benefits of facile recovery and recycling of the heterogeneous catalyst. The POSS-bridged oxo-molybdenum Schiff base complex was successfully reused for four runs without significant loss in activity. The unique three dimensional network catalyst structure and the hydrophobic properties of the POSS units in the catalyst are revealed to be responsible for the catalyst's excellent performance in epoxidation reactions (Fig. 8).

A series of tridentate Schiff base dioxomolybdenum(VI) complexes were tested as catalyst. The prepared heterogeneous catalyst is found to be highly reactive in the epoxidation of unfunctionalized olefins. Moreover, these catalysts are of higher stability and re-usability in the oxidation reactions and can be reused ten times without noticeable loss of activity. Excellent enantiomeric excess was obtained for the epoxidation of α -methylstyrene in this oxidant system, which do not involved any costly chiral ligand or additives, while the catalysts only effectively promote the process of catalytic reactions (Baojiao et al., 2015) (Fig. 9).

4.8. For hydrosilylation of ketones

Zinc Schiff base complexes derived from α -amino acids and 3,5-di-*tert*-butylsalicylaldehyde were tested for the catalytic asymmetric hydrosilylation of ketones, and the results showed that excellent yield values were obtained, which are the prominent examples of catalytic asymmetric hydrosilylation of ketones catalyzed with zinc complexes in the

presence of readily available and inexpensive α -amino acids based Schiff base ligands (Liu et al., 2012).

4.9. For synthesis of bis(indolyl) methanes

In recent years, a large trend towards synthesis of bis (indolyl) methanes and their derivatives has attracted much attention due to their synthetic as well as biological applications (Sadaphal et al., 2010; Yang et al., 2011). Cu(II) Schiff base complex is found to be an effective catalyst for the condensation reaction of indole with aldehydes using ethanol as the solvent. An aldehyde was activated by the catalyst and then carried out an electrophilic substitution at C-3 of an indole. After ring-opening reaction, the intermediate was served as an electrophile to attack a second molecule of indole, the target products were formed after loss of water. The products were obtained in high yields (up to 98%). The solution diluted with saturated sodium chloride solution and extracted with ethyl acetate, dried by magnesium sulphate, solvent was removed under reduced pressure to give a crude product which was purified by column chromatography on silica gel (ethyl acetate/petroleum ether 1:15). This method offers several advantages such as high yield of product, short reaction time, simple work up procedures and environmental friendly. Further work is in progress to extrapolate the catalytic activity of Schiff base complex to other organic transformation (Yang et al., 2011).

5. For removal of uranium (VI) from aqueous solutions

Magnetic Schiff base (ferroferric oxide/Schiff base composite) was prepared and could efficiently remove uranium(VI) ions from aqueous solutions. In this study, the effect of adsorption parameters such as pH value, adsorbent dose, shaking time, and temperature have been investigated and optimized. It is found that the maximum adsorption capacity of the magnetic composite toward uranium(VI) is 94.30 mg g⁻¹ obtained at pH = 6.0, adsorbent dose = 0.02 g, contact time = 6 h and temperature = 25 °C. The adsorbed uranium(VI) can be desorbed effectively (about 98.57%) by 0.1 M NaOH and the adsorption capacity is not significantly reduced after three cycles. It's suggested that this magnetic Schiff base can be used as a potential adsorbent for sorption uranium(VI) and also provides a simple, fast separation method for removal of uranium(VI) ions from aqueous solution (Zhang et al., 2012).

6. Urease inhibitory activities of Schiff base metal complexes

Transition metal Schiff base complexes derived from metal acetate (M = Mn(II) or Ni(II) or Co(II) or Cd(II)) and N,N'-bis (salicylidene)-1, 3-propanediamine (SALPD) or N,N'-bis (2-hydroxynaphthylmethenylimino)-1,3-propanediamine (NAPTPD) were synthesized and crystallographically characterized. Their urease inhibitory activities were evaluated. Three of them showed potent inhibitions against *jack bean* urease. Mn(II) complex possessed the best *jbU* inhibitory

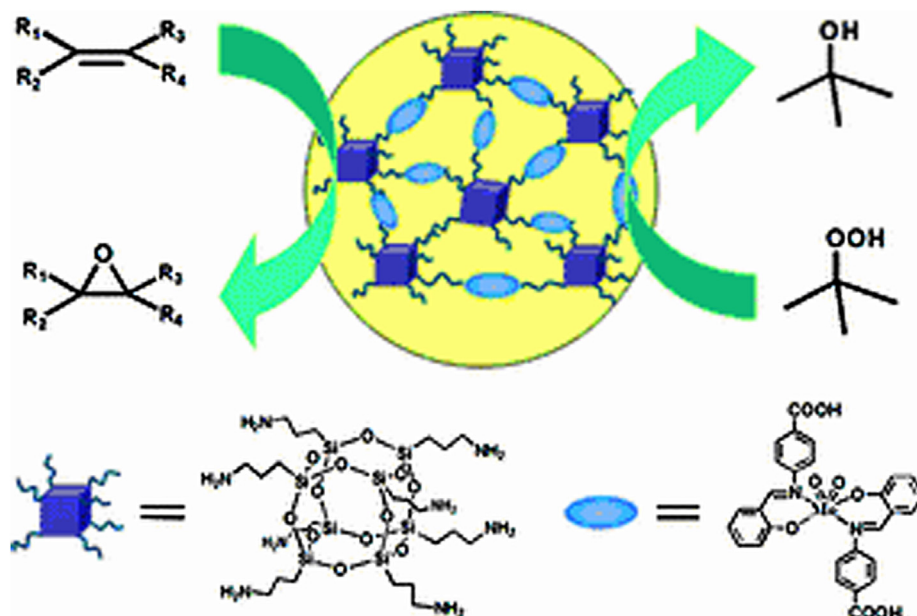


Fig. 8 – Mechanism of the catalytic reaction using investigated Mo complex.

activity with IC₅₀ of $8.30 \pm 0.93 \mu\text{M}$, which was much better than those of the corresponding ligand and control ion. The investigation on the stability constants and the structure activity relationships of the complexes indicated that the complexes interacted with the enzyme in the whole complex forms rather than the free ions (Shi et al., 2007).

Five mononuclear copper(II) and nickel(II) Schiff base complexes derived from 4-hydroxyphenethylamine and 2-phenylethylamine were synthesized and determined by single crystal X-ray analysis. The inhibitory activity of all the obtained complexes was tested *in vitro* against *jack bean* urease. It was found that copper(II) Schiff base complexes,

showed strong inhibitory activity against *jack bean* urease (IC₅₀ = 1.45–3.59 μM), while nickel(II) Schiff base complex, exhibited weak inhibitory activity (IC₅₀ > 50 μM). The results indicate that inhibitory activities of Schiff base metal complexes as the urease inhibitor depend on not only the organic ligands but also the central ions (Shi et al., 2007).

The Schiff base 2-[(E)-(quinolin-3-ylimino)methyl]phenol (H-QMP) was crystallized in Pc space group and complexed with Ni(II) and Co(II) in [M(QMP)₂] and Cu(II) and Zn(II) in [M(QMP)(CH₃COO)]H₂O compositions. Elemental analyses, mass spectrometry, IR, UV–vis spectroscopy, conductance study and magnetic susceptibilities were used to characterize

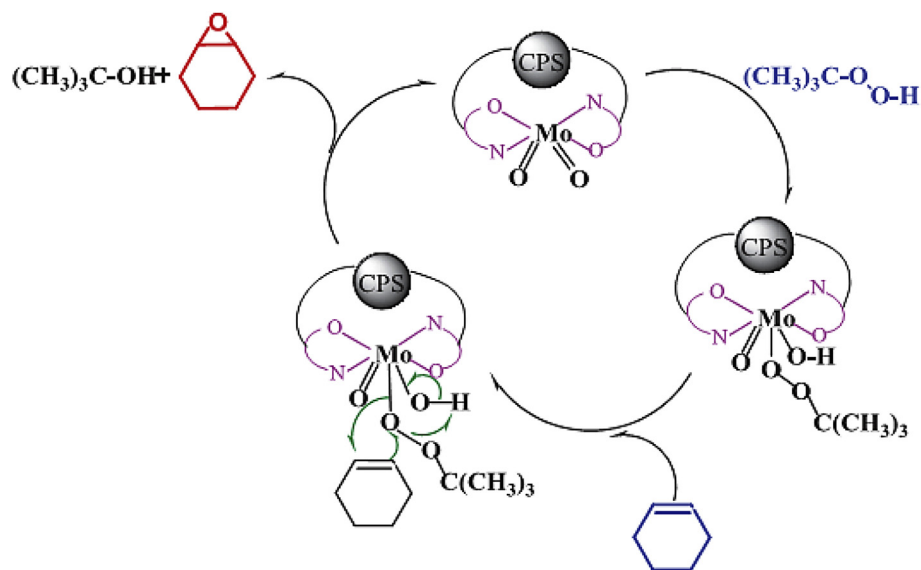


Fig. 9 – Catalytic mechanism of catalyst CPS-[MoO₂(ALGL)₂] in epoxidation of cyclohexene to cyclohexene oxide by TBHP.

the complexes. The thermograms obtained in the range of 30–1000 °C were used for kinetic and thermodynamic calculations. The activation energies and order of pyrolysis were calculated using Horowitz–Metzger method. The calculated activation energies were subsequently used for the calculations of thermodynamic parameters including ΔS° , ΔH° and ΔG° . It was found that the thermal stability and activation energy follow the order Cu(II) > Ni(II) > Co(II) > Zn(II). All the compounds were also studied for their urease and α -chymotrypsin inhibition, showing medium to moderate activities for both the enzymes except nickel complex. Nickel complex shows $IC_{50} = 9.9 \pm 0.124 \mu M \pm SEM$, and the activity was rationalized by carrying out molecular modelling studies (Ikrama et al., 2013).

6.1. In dyes

Chromium azomethine complexes, cobalt complex Schiff base (Befta, 1985), unsymmetrical complex 1:2 chromium (Mennicke and Westphal, 1984) dyes give fast colours to leathers, food packages, wools etc. Azo groups containing metal complexes (Dehnert and Juchemann, 1985) are used for dyeing cellulose polyester textiles. Some metal complexes are used to mass dye polyfibers (Kaul, 1985). Cobalt complex of a Schiff base (salicylaldehyde with diamine) has excellent light resistance and storage ability and does not degrade even in acidic gases (CO₂). Novel tetradentate Schiff base acts as a chromogenic reagent for determination of Ni in some natural food samples (Fakhari et al., 2005).

Four new azo dyes L1, L2, L3 and L4, were prepared by linking benzaldehyde p-aminobenzoylhydrazone (3), p-hydroxybenzaldehyde p-amino-benzoylhydrazone (4), naphthaldehyde p-aminobenzoylhydrazone (5) and p-methoxybenzaldehyde p-aminobenzoylhydrazone (6) to resorcinol and through diazo-coupling reactions. Mixed-ligand dinuclear complexes with general stoichiometry [Cu₂L(amino antipy.)₂]Cl₂ (11, 12, 13 and 14) was synthesized from azo ligands and bidentate ligand (4-aminoantipyrine) with copper. The structures of both azo dyes and their complexes were identified by elemental analyses (C.H.N), FTIR, H NMR, UV–Vis, atomic absorption and magnetic susceptibility (Jber et al., 2011).

Two low-dimensional oxime-containing Schiff base copper (I/II) complexes with iodine–copper cluster [Cu₂I₄]^{2–} bridges, namely {[Cu^I₄I₃(pop)₄]₂(Cu^I₂I₄)}·(CH₃CN)₂·H₂O (2) and [Cu^{II}₄I₂(pop)₄(Cu^I₂I₄)·(CH₃CN)]_n (3) (Hpop = 2-(hydro-xyimino)-N'-[1-(2-ylridyl)ethylidene]propane-ydrazone), have been synthesized from the reaction of [2 × 2] grid-like compound {[Cu^{II}I(pop)]₄·4H₂O (1) with equivalent Cu^I₂I₂ (iodine–copper clusters) under solvothermal condition and characterized by elemental analysis (EA), infra-red spectrum (IR), thermogravimetric analysis (TGA), and X-ray single-crystal/powder diffraction. The results show that 2 is 0-D discrete structure from assembly of one [Cu₂I₄]^{2–} unit and two [2 × 2] molecular grids 1 via μ_3 -I atom coordinating to Cu^I/Cu^{II} atoms. However, compound 3 presents 1-D wave-like chain, which is constructed by coordination of μ_2 -I atoms from [Cu^I₂I₄]^{2–} units with Cu^{II} atoms in [2 × 2] molecular grids (1). Moreover, catalytic experiments demonstrated that compounds 2 and 3 have promising visible-light-driven catalytic activity in degrading various organic dyes (Hong et al., 2014).

7. Conclusion

Schiff bases are considered as a 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 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.

List of abbreviations

IR	infrared
Bs	bromosalicylaldehyde
ala	alanine
phala	phenylalanine
aspa	aspartic acid
his	histidine
arg	arginine
X	halide
NMR	nuclear magnetic resonance
MS	mass spectroscopy
ROS	reactive oxygen species
CMCTS	carboxymethyl chitosan
BSA	bovine serum albumin
OPF	o-(1-ferrocenylethylideneamino)phenol
MFP	m-(1-ferrocenylethylideneamino)phenol
PFP	p-(1-ferrocenylethylideneamino)phenol
AAPH	2,2'-azobis(2-amidinopropane hydrochloride)
GSH	glutathione
DPPH	2,2'-diphenyl-1-picrylhydrazyl
ABTS	3-ethylbenzothiazolone-6-sulfonate
CIPO	carrageenan-induced paw oedema
HIPO	histamine induced paw oedema
FIPL	formalin-induced paw licking
AIW	acetic acid-induced writhing
PIST	phenobarbitone-induced sleeping time
MHV	mouse hepatitis virus
FIPV	feline corona virus
salen	salicylaldehydeethylendiamine
DHBP	2,2'-dihydroxybiphenyl
PDHBP	poly-2,2'-dihydroxybiphenyl
NMO	N-methylmorpholine-N-oxide
THF	tetrahydrofuran
DMF	dimethylformamide
UHP	urea hydrogen peroxide
POSS	polyhedral oligomeric silsesquioxane
TBHP	tert-butyl hydroperoxide

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