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Economic Synthesis and Characterization of Schiff Base and Metal Complexes

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ABSTRACT

In the present study an intermolecular reductive Schiff base formation from nitroarene and benzaldehyde to yield diarylimine is carried out in the presence of iron powder and ammonium chloride. New Schiff base compound derived from 2 nitro pyridine with 2 hydroxy benzaldehyde and its transition metal complexes with Fe(II), Cu(II), Ru(III) and Rh(III) have been synthesized which were characterized. The ligand and metal complexes have been screened for their microbiological activity. The experimental results suggest that Schiff base and metal complex ligands are more potent in anti-bacterial activities.

Keywords: Tandem reaction, intermolecular reduction, metal complexes, green chemistry biological properties.

ARTICLE INFO

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1. Introduction

Tandem reactions have several advantages over a series of individual reactions. First, they allow construction of complex structures in as few steps as possible. However,

organic synthesis, i.e., chemistry by mankind, still uses often a simple step-by-step approach to convert a starting material **A** into a final product **C**, in which intermediate

products B is isolated and purified for next conversion step. Multistep synthesis of specialty chemicals normally requires stoichiometrically excess reagents, leading to high effluent loads. Hence, search is now on for clean, non-hazardous and 'green' chemical transformations, which will have negligible bi-products and high selectivity.

The chemistry of biological science has produced a number of compounds that are now employed as antibacterial agents. Such type of compounds revealed great promise in this area is the Schiff bases. Schiff bases are well known in the pharmaceutical industry and have been shown to possess a broad spectrum of biological activities. In light of these significances, a variety of synthetic strategies have been developed for the preparation of Schiff base, despite the progress, the synthesis of these compounds remains less than ideal. Thus, the development of environmentally friendly benign, high-yielding and clean approaches for the synthesis of Schiff base is still remains a highly desired goal in organic synthesis. [1]

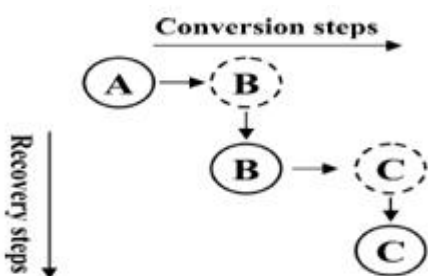


Figure 1

The reported Schiff bases exhibits antibacterial [2-5], antifungal [6] and antitumor activity [7]. This has led to concentrate deep research on this class of compounds [8]. Similarly, the presence of hetero-atoms in the Schiff bases

2. Materials and Methods

Experimental

All chemicals and solvents were of AR grade. The percentage compositions of the elements (CHNO) of the compounds were determined using an Elementar Vario Micro Superuser (CHNS) analyzer. The metal contents of the complexes were analyzed by ICPAES. The Infrared spectra were recorded as potassium bromide (KBr) discs using 8400S FTIR Perkin Elmer Spectrophotometer. The electronic Spectrum of complexes were recorded on ELICO SL -159 UV-Vis Spectrophotometer. The Electron spin resonance spectra (ESR) were recorded on Varian E - 112 ESR Spectrometer. Melting point of ligand and their metal complexes were recorded using Differential Scanning Calorimeter (DSC) instrument. The molar conductivity measurements were made on ELICO CM - 180 model using methanol as the solvent. Magnetic susceptibility of complexes was measured by Gouy's method.

Synthesis of ligand: 2-((pyridin-2-ylimino) methyl) phenol

enhances activity [9]. Current literature reveals that these pyridine compounds possess a variety of biological activities, such as vasodilator, bronchodilator, anti-atherosclerotic, anti-diabetic, anti-malarial, anti-inflammatory, anti-asthmatic, antibacterial, and tyrosine kinase inhibiting agents. During the past two decades, considerable attention has been paid to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donor atoms. Therefore, their synthesis has been the focus of much interest for organic and medicinal researchers. These promising results are encouraging further research in this field for future applications. Traditional formation of Schiff bases from nitroarene starting materials requires a two-step process in which the nitroarene is first reduced to the aniline, then isolated, and subsequently condensed with the desired carbonyl [10,11].

In view of these facts we can clear about that Schiff base are important not only in medical chemistry, but also in organic synthetic chemistry. Schiff base perhaps are synthesized in various method. Recently, catalytic Schiff base formation from nitroarenes and carbonyls has been reported [12,13]. Herein we wish to report our findings of a tandem iron reduction of nitroarenes and subsequent condensation of aldehydes under mild reaction conditions. In the present study an intermolecular reductive Schiff base formation from nitro pyridine and benzaldehyde is carried out in the presence of iron powder and ammonium chloride as weak dilute acid. In the present paper, metal complexes of Fe(II), Cu(II), Ru(III) and Rh(III) with Schiff base ligand derived from o-hydroxy benzaldehyde and 2- nitro pyridine have been synthesized and these complexes were characterized. The microbiological activities of the ligand and their metal complexes have also been studied.

15 gr Iron powder added to nitro compound (1 mole) ammonium chloride (4.5mole) heated to 85-95 °C and maintained to 90 to 120 minutes. Cool to 40°C 2 hydroxy benzaldehyde (1 mile) added and maintained at 65-75 °C for 6 hours. On cooling the reaction mixture, sharp yellow crystals separated out (yield 80%, m.p.70 -71°C)

Preparation of complexes with Schiff base ligand

The complexes of Fe and Cu were prepared by refluxing respective metal chloride in methanolic solution of ligand in molar ratio of 1: 2 at pH 5. The resulting mixture was refluxed on water bath for 3-5 hrs. After cooling at room temperature, brown colored solid were separated out which was filtered, washed with water and then with methanol. (yield 60 - 70%). For the preparation of Ru and Rh complexes, metal chloride were refluxed with ligand in molar ratio of 1:3 at pH 4 on water bath for 6 hrs. Brownish Black coloured product separate out on cooling which was collected by filtration, washed with water and then methanol. (Yield 40 - 50%).

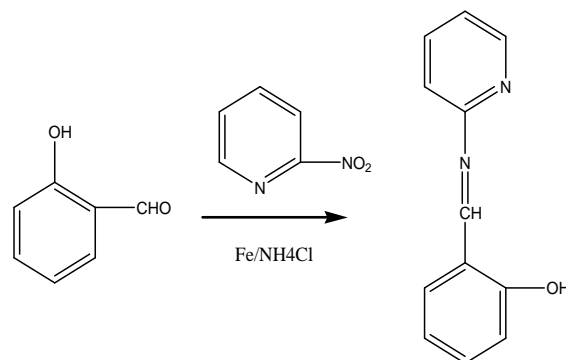


Figure 2

3. Results and Discussion

All the metal complexes are colored, solid, stable at room temperature and non-hygroscopic in nature. The Analytical and physical data of ligand and their metal complexes are

recorded in Table - 1. The metal complexes exhibit 1:2 and 1:3 (metal-ligand) stoichiometry.

Table 1

Compound/ color	Mol.Wt	M.Pt	Elemental analysis				$\mu_{\text{eff}}^{\text{BM}}$	Λ^{m} Ohm^{-1} $\text{cm}^2\text{mol}^{-1}$
			C	H	N	M		
SCB	198.00	71 °C	73.15	5.16	14.39	--	--	--
Fe SCB	450.00	>300 °C	64.04	3.92	12.39	12.45	5.12	37.98
CuSCB	457.00	178 °C	62.93	3.89	12.15	13.86	1.75	30.11
RuSCB	710.00	62 °C	60.82	3.70	11.76	14.21	1.83	24.00
RhSCB	712.40	>300 °C	60.92	3.68	11.70	14.35	1.90	28.00

Infrared Spectral Analysis

On the basis of Infrared spectra the presence of important functional groups in the compound can be identified. The Infrared spectrum of the ligand was compared with the spectra of Fe(II), Cu(II), Ru(III) and Rh(III) complexes.

The typical IR spectra were shown in Fig.1, 2, 3, 4 and 5 and data was summarized in Table-2 along their assignment.

Table 2: IR spectra data along their assignment.

compound	(-OH)	(C=N)	(C-N)	(C-O)	(M-N)	(M-O)
SCB	2796	1610	1491	1270	---	---
Fe SCB	---	1602	1532	1321	530	447
Cu SCB	---	1605	1532	1328	545	450
Ru SCB	3413	1607	1515	1319	560	470
Rh SCB	3426	1608	1518	1320	565	467

The IR spectrum of the ligand shows broad band at 1610 cm^{-1} , which was assigned to due C=N stretching of azomethine group [14]. In complexes this band was shifted to lower regions, 1602 cm^{-1} , 1605 cm^{-1} , 1607 cm^{-1} and 1608 cm^{-1} for Fe(II), Cu(II), Ru(III) and Rh(III) complexes respectively, suggesting the coordination of azomethine nitrogen to metal atom in complexation [15]. This was due to the donation of electron density from Nitrogen to metal. IR spectrum of the ligand shows a weak band around 2750 - 3000 cm^{-1} due to intramolecular hydrogen bonded -OH group [16]. This band is absent in the spectra of complexes indicating the dissociation of the phenolic proton on complexation and involvement of phenolic anionic oxygen in coordination [17]. Moreover, the strong band at 1280 - 1270 cm^{-1} due to C - O (phenolic) in the ligand has been

shifted to the 1330 - 1319 cm^{-1} in the spectra of complexes. The strong absorption band due to pyridine ring occurring at 1495 cm^{-1} (C-N-C) has shifted to higher region by 25 - 40 cm^{-1} in the complexes showing the participation of nitrogen atom of pyridine ring in the complexation [18]. The IR spectrum of Ru(III) and Rh(III) metal complexes exhibit a broad and strong absorption band in the region 3520 - 3170 cm^{-1} confirms the presence of (OH) absorption for lattice water [19]. New bands were observed between 800 - 500 cm^{-1} region in the complexes, which were absent in the spectrum of ligand. The bands between 500 - 565 cm^{-1} were assigned to stretching frequencies of (M-O) [20], the band between 471 - 450 cm^{-1} have been assigned to the stretching frequencies (M-N) respectively [21-22].

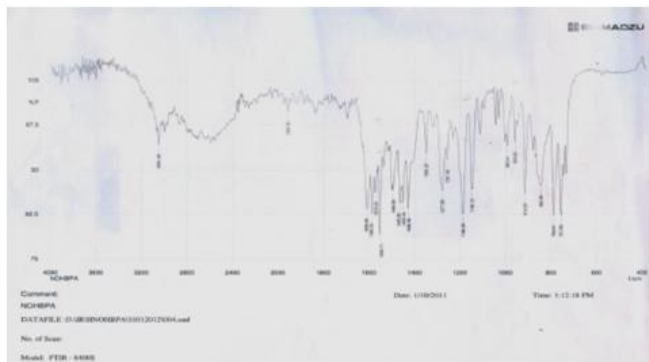


Figure 1: Schiff base 2-((pyridin-2-ylimino) methyl) phenol

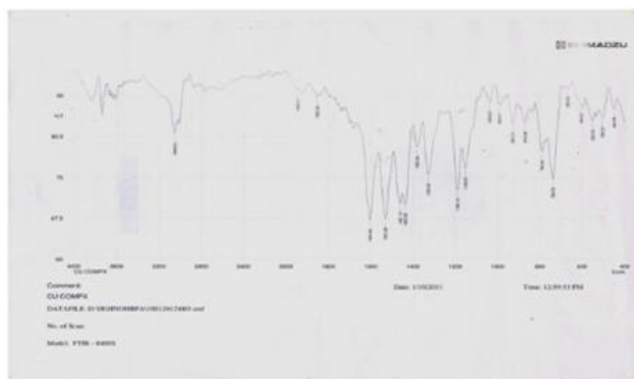


Figure 3: Copper complex

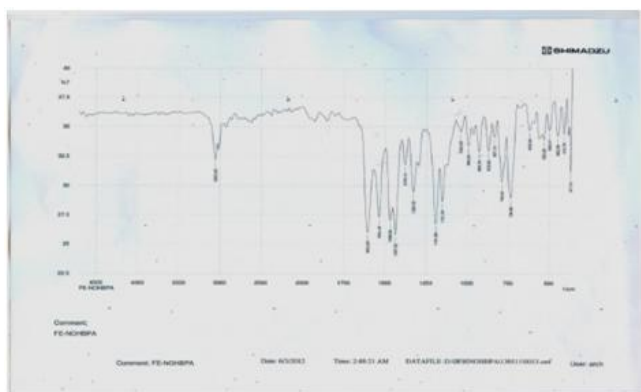


Figure 2: Fe complex

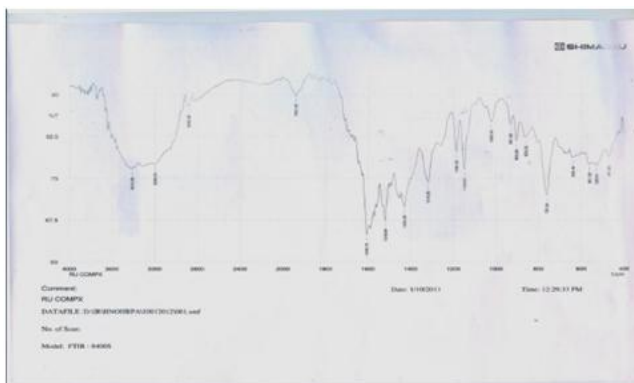


Figure 4: Ruthenium complex

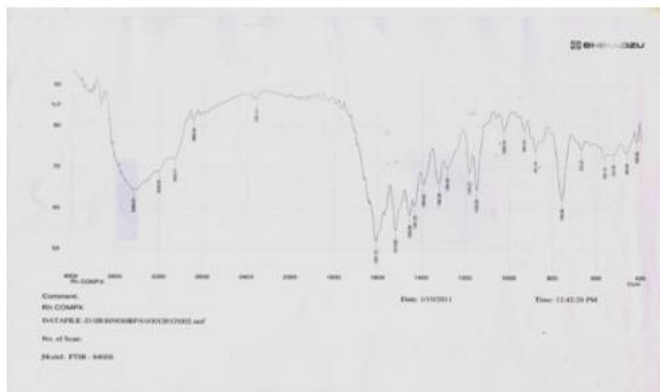


Figure 5: Rhodium complex

Molar Conductance

The molar conductance values of 1×10^{-3} M solution of metal complexes in methanol were measured at room temperature (Table-1) using an ELICO Conductivity meter (cell constant 1.0 cm^{-1}). These values were compared with known molar conductivities [22-23] which indicates the non-electrolytic nature [24] of the complexes.

Electronic spectra and Magnetic susceptibility measurements of complexes

In UV-Visible electromagnetic radiation, the transitions are associated with the electronic energy levels of the compound under investigation. The electronic spectra were recorded on ELICO SL 159 UV-Visible Spectrophotometer. The transition metal ions occur in a

variety of structural environments. Because of this, the electronic structures are extremely varied. The electronic structures have been identified with UV-Visible spectroscopy.

The nature of ligand field around the metal ion and the geometry of complexes have been deduced from the electronic spectra. The electronic absorption spectra of Fe(II) complex exhibit the band around $18,867.92 \text{ cm}^{-1}$ (530 nm) at room temperature which may be assigned to $5T_{2g} \rightarrow 5E_g$ transition [25-26] suggesting octahedral geometry and paramagnetic nature of complexes which is further supported by the magnetic moment value 5.15 B.M. . The Cu(II) complex exhibit the band at $18,518.52 \text{ cm}^{-1}$ (540 nm) which is assignable to $2E_g \rightarrow 2T_{2g}$ transition [26-27] suggesting octahedral geometry around Cu(II) ion.

The Cu(II) complex showed magnetic moment value lie in the range $1.76 - 1.78 \text{ B.M.}$ which is consistent with octahedral geometry. The Ru(III) and Rh(III) complexes display band at 18181.18 cm^{-1} (550 nm) and 19607.84 cm^{-1} (510 nm) which may be assigned to $2T_{2g} \rightarrow 4T_{2g}$ transition [28] suggesting octahedral geometry of complexes. The room temperature magnetic moment value of Ru(III) and Rh(III) complexes lie in the range of $1.73 - 1.90 \text{ B.M.}$ attributed to Octahedral structure. Electronic Spectra and Magnetic Moment of the Complexes are listed in Table-3.

Table 3: Electronic Spectra and Magnetic Moment of the Complexes.

compound	band max(nm)	μ_{eff} (B.M)
FESCB	528	5.14
CuSCB	540	1.79
RuSCB	550	1.82
RhSCB	510	1.87

Electronic Spin Resonance Spectra

ESR spectra of complexes provide information about the extent of the delocalization of unpaired electron. In the present study, the ESR spectra of complexes have been recorded on X - band at frequency 9.5 GHZ under the magnetic field strength 3400 gauss in DMF at room temperature(fig. 6 - 9) and their $g_x, g_y, g_z, g_{\text{avg}}$, and G values have been calculated. ESR spectra of the complexes revealed two g values (g_1 and g_2). the trend $g_1 > g_2$ shows that the unpaired electron is delocalized in $dx^2 - y^2$ orbital in the ground state of metal and spectra are characteristics of axial symmetry. The parameter g_{avg} was obtained by equation $[(g_{\text{avg}}) = 1/3 (g_1 + 2g_2)]$. Kvelson & Neiman [29] have reported that, $g > 2.3$ is the

characteristics of an ionic environment and $g < 2.3$ indicates a covalent character in metal ligand bonding. Applying this criterion, in the present compounds g indicate the prevalence of covalent character in metal - ligand bond[30]. The exchange coupling interaction has been explained by Hathaway expression $G = (g_1 - 2) / (g_2 - 2)$. According to Hathaway if the value of G is greater than four ($G > 4$), the exchange interaction is negligible whereas when the value of G is less than four ($G < 4$), a considerable exchange interaction is indicated in the complex. It is observed that G value for these complexes are less than four ($G < 4$), indicating considerable exchange interaction the complexes [31-32].

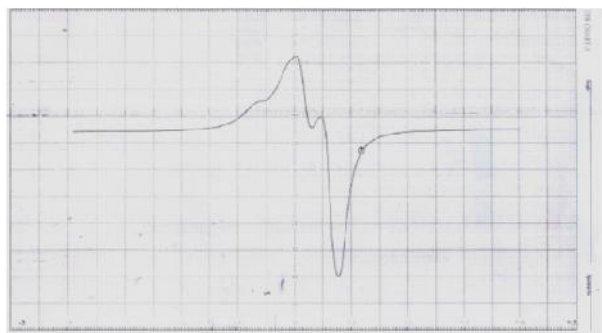


Figure 6: Fe complex

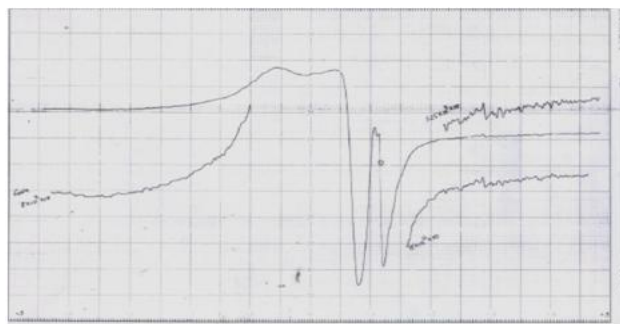


Figure 8: Ruthenium Complex

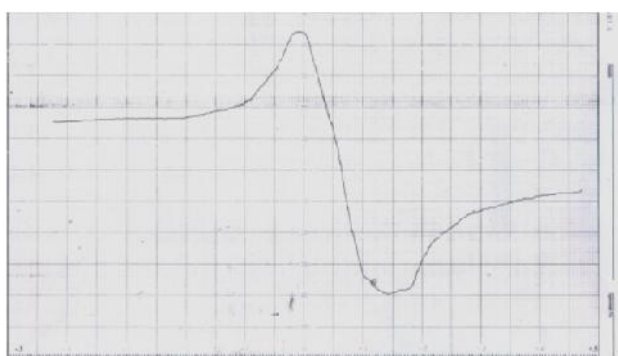


Figure 7: copper complex

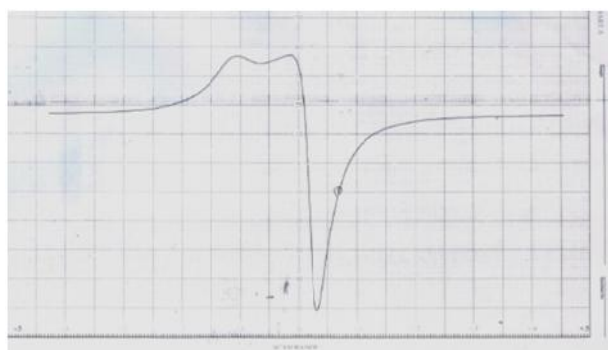


Figure 9: Rhodium Complex

Proposed Structure of Complexes:

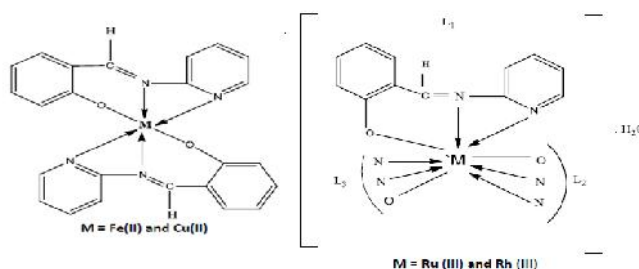


Figure 10

Biological Activity

Schiff base ligand and their metal complexes were screened for antibacterial activity against gram positive bacteria (staphylococcus aureus and Corynebacterium diphtheria), gram negative bacteria (Escherichia coli and Klebsiella pneumonia) and antifungal activity against (Candida albicans and Aspergillus species) by cup plate method [33-34]. The results of the biological activity of the metal complexes indicated the following facts. The increase in the biological activity of metal chelates was found due to the effect of metal ion on the metal chelates which could be explained on the basis of overtones concept and chelation

4. Conclusion

We developed the new route for Schiff bases in which we maintained the green chemistry parameter. At the same time yield of product is also increased by maintaining purity of products. This type reaction is economically attractive method for synthesis of Schiff base compounds and their derivatives. This methodology uses only Fe powder in acidic EtOH/H₂O as a reducing agent for nitro derivatives which upon reduction spontaneously condense with an aldehyde in situ. In this paper, we also reported the co-ordination chemistry of complexes derived from schiffs' base ligand obtained from the reaction of 2 hydroxy benzaldehyde and 2-nitro pyridine with metals such as

theory. On chelation the polarity of the metal ion reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charges of metal ion with donor groups. It was further noted that the delocalization of electrons over the whole chelate ring enhanced the lipophilicity of the complexes. This increased lipophilicity [35] enhanced the penetration of the complexes into lipid membrane and blocking the metal sites on enzymes of microorganism. The activity was compared with zone of inhibition was measured in millimeters.

Fe(II), Cu(II), Ru(III) and Rh(III). It can be concluded from the results of above study that Schiff base ligand acts as a very good tridentate complexing agent towards many transition metal ions during complexation. All the metal complexes showed enhanced microbiological activities as compared to ligand. Both the structures of the complexes were confirmed by spectral studies. The synthesized compounds therefore, present a new scaffold that can be used to yield potent antimicrobial compounds. It can be concluded that these compounds certainly holds great promise towards good active leads in medicinal chemistry.

5. Acknowledgements

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