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RESEARCH ARTICLE

Synthesis, Characterization and Microbiological Studies of Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2} Chelates of Schiffs Base Derived from Vanillin and 2-Nitro Benzoic Acid

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ABSTRACT

In the present study an intermolecular reductive Schiff base formation from nitro derivative and benzaldehydes is carried out in the presence of iron powder and dilute acid. Schiff base has been synthesized from vanilline and 2-nitro benzoic acid. Metal complexes of the Schiff base were also prepared from salts of Ni (II), Co (II), Mn (II), Cu (II) and Zn (II) in an alcoholic medium. The chemical structures of the Schiff-base ligand and its metal complexes were confirmed by various spectroscopic studies. Molar conductivity measured revealed the non-electrolytic for Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2}. On the basis of the studies, the coordination sites were proven to come through the nitrogen atom of azomethine and the hydroxyl group of the carboxyl group of 2 nitro benzoic acid. The free Schiff base and its complexes have been tested for their antibacterial as well as antifungal activity by using disc diffusion method and the results discussed. The experimental results suggest that Schiff base derivatives are more potent in antibacterial and antifungal activities.

KEYWORDS

Schiff base, Vanillin, 2-Nitro Benzoic Acid, Metal Complexes, Antibacterial Activity, Antifungal Activity

INTRODUCTION

The formation of carbon–nitrogen double bond plays important role in organic synthesis. This can be achieved by the reaction of aldehydes and amines in acidic medium which leads to synthesis of Schiff bases (imines). Schiff base nucleus containing compounds created their own identity importance in pharmaceutical, medicinal, biochemical, industrial and agricultural sciences. They showed ranges of biological activities such as herbicidal, anti-bacterial, anti-viral, anti-fungal, anti-inflammatory and antioxidant activities.[1-6]

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In addition Schiff bases are also used in the synthesis of compounds with bioactivity such as β-lactams.[7] Metal complexes of Schiff bases are known to possess anti-fungal, anti-malarial, anti-neoplastic, anti-bacterial and anti-cancerous effects.[8] Cytotoxic and anti-proliferative effects of some Schiff bases on A549 (human small lung cancer) and (human cervix cancer) cell lines have also been reported.[9] Nitro and halo derivatives of Schiff bases have anti-microbial and anti-tumor activities.[10]

Furthermore, Schiff bases possess a variety of interesting results including inhibition of anti-mosquito larvae, herpes simplex (HSV-1) virus type 1, adenovirus and anti-mouse hepatitis virus.[11]

Among the organic reagents actually used, Schiff bases possess excellent characteristics, structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties.[12-13] Studies of new chemotherapeutic Schiff bases attract much attention in the field of pharmacology.[14-15]

Nowadays, the research field dealing with Schiff base coordination chemistry has expanded enormously. The importance of Schiff base complexes for bioinorganic chemistry, biomedical applications, supra-molecular chemistry, catalysis and material sciences, separation and encapsulation processes, and formation of compounds with unusual properties and structures has been well recognized and reviewed.

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.

We developed the new route for this synthesis, in which we maintain the green chemistry parameter. At the same time yield of product is also increased by maintaining purity of products.

Herein we wish to report our findings of a tandem iron reduction of nitroarenes and subsequent condensation of arylaldehydes under mild reaction conditions. The present aim of the work is to synthesize a Schiff base derived from vanillin and o-nitro benzoic acid and to prepare its transition metal complexes, characterize them and study their antibacterial and antifungal activities.

EXPERIMENTAL

Materials

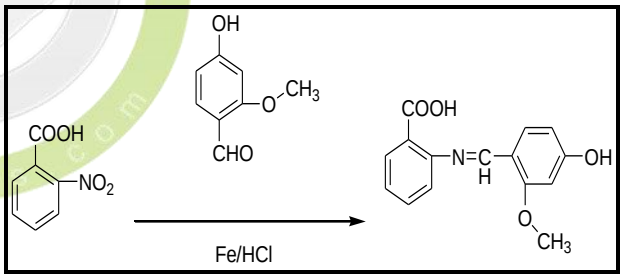
All the chemicals and solvents were of AR grade. Metal salts were purchased from Merck and Loba chemie, Mumbai, India. The elemental analyses were performed using vario EL elemental analyzer. IR spectroscopy analyses were recorded on Schimadzu FTIR 8400S spectrometer in 4000 - 200 cm^{-1} range using KBr pellet, while the UV-Visible spectra were recorded on a Schimadzu UV spectrometer in the wave length range of 200 – 800 nm.

The thermal analyses were recorded on a universal V4.3A TA instrument, while the ESR spectral analyses were recorded on a Bruker instrument at 300 and 77 K.

The molar conductance was measured on ELICO-CM180 using DMSO as the solvent at room temperature, whereas the antibacterial activity was determined with the disc diffusion method. Subsequently, stock solutions were prepared by dissolving the compounds, while DMSO and serial dilutions of the compounds were prepared in sterile distilled water to determine the minimum inhibition concentration (MIC). The diameter of the inhibition zones was measured in millimeters

Synthesis of Schiff Base

The intermolecular reductive Schiff base formation of vanillin and 2-nitro benzoic acid in ethanol/water yields a single product according to following reaction:



Hydrochloric Acid (0.13 mL, 4.5 mmol) was added to a mixture of 2 nitro benzoic acid (1.20 gr, 0.72 mmol) , vanillin (1.10 gr, 0.72 mmol), and iron powder (0.409 g, 7.32 mmol) in 24 mL of EtOH–H_2O (2:1 v/v) solution. The reaction was heated to 65°C for 1.5 h before being filtered while hot. The filtrate was extracted using CH_2Cl_2 (2 × 25 mL) after which the organic layers were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo to yield 1.60g (70%). Its melting point is 232°C

Preparation of the Metal Complexes

A mixture of the schiff base under investigation (0.01 mol) in 25 ml ethanol and the same amount of the same solvent of metal salt (0.01

mol) (MX_2, where M= Ni (II), Co (II), Cu (II) and Zn(II); X=Cl/NO_3/acetates) were refluxed for two hours at 70-80°C on water bath. On cooling, colored solid product was collected by filtration and then washed several times with hot ethanol until the washing becomes colorless. The product was dried in air and stored in a desiccator over anhydrous $CaCl_2$ under vacuum. All the metal complexes are colored and stable to air and moisture.

RESULTS

Electronic Spectral Analyses

Mn^{+2} and Co^{+2} complexes have octahedral geometry. Nickel (II) has a (d8) and its absorption is found at 648 (15432 cm^{-1}), 349 (28653 cm^{-1}) and 338 nm (29585 cm^{-1}) respectively for the nickel complex. This confirms the presence of an octahedral geometry for the nickel complex.

Copper (II) has a (d9) configuration having the following absorption found at 757.5 nm (13200 cm^{-1}) and 415 nm (24096 cm^{-1}) respectively.

Table 1: Analytical data and physical properties of the Schiff base metal complexes

Compound Empirical Formula	Elemental Analysis Found (calculated) %				Color	^(Ohm cm^2mol^{-1}
	C	H	N	M		
$[Mn^{+2}(L)_2(H_2))_2]$ $C_{30}H_{28}N_2O_4Mn^{+2}$	55.55 54.29	4.62 4.59	4.09 4.16	7.80 7.81	cream	1.42
$[Co^{+2}(L)_2(H_2))_2]$ $C_{30}H_{28}N_2O_4Co^{+2}$	55.90 56.07	4.68 4.72	4.39 4.40	8.82 8.70	pink	1.43
$[Ni^{+2}(L)_2(H_2))_2]$ $C_{30}H_{28}N_2O_4Ni^{+2}$	60.10 59.79	4.70 4.71	4.40 4.37	8.82 8.65	Green	1.91
$[Cu^{+2}(L)_2(H_2))_2]$ $C_{30}H_{28}N_2O_4Cu^{+2}$	55.30 56.01	4.65 4.68	4.34 4.39	9.40 9.67	green	1.85

Infrared spectra

Table 2: Infrared spectral data of Schiff base and Schiff base metal complexes cm^{-1}

Compound	ν(C=N)	ν(C-O)	ν(C=O)	ν(M-O)	νH_2O/OH
Schiff base	1589	1670	1690	--	---
CoL_2	1585	1597	1675	870	3273
NiL_2	1594	1650	1655	865	3275
CuL_2	1549	1655	1640	855	3246
ZnL_2	1543	1675	1635	849	3279
MnL_2	1550	1654	1650	840	3247

for the copper complex. This confirms the presence of octahedral geometry in the copper complex.

Zinc (II) shows absorption at 360 nm (27777 cm^{-1}) for the ligand metal charge transfer transition and this confirms the presence of an octahedral geometry in the zinc complex.

ESR Analyses

The ESR spectra of copper complex provide important information in studying the metal ion, while the ESR spectra of the Cu (II) complex are recorded at liquid nitrogen temperature (77 K) and room temperature (300 K). The spectrum of copper complex has a single intense absorption band in the high field region and its molecule is isotropic due to the tumbling motion of the molecule. When the complex is frozen to liquid nitrogen temperature, four well resolved peaks with low field region are obtained. This shows the presence of an octahedral geometry for the copper complex.

Antibacterial Activity

The antibacterial activity was determined with the disc diffusion. Stock solutions were prepared by dissolving the compounds, while DMSO and serial dilutions of the compounds were prepared in sterile distilled water to determine the minimum inhibition concentration (MIC). The nutrient agar medium was poured into Petri plates. A suspension of the tested microorganism (0.5 ml) was spread over the solid nutrient agar plates with the help of a spreader. Subsequently, fifty microlitres of the stock solutions were applied on the 10 mm diameter sterile disc. After evaporating the solvent, the discs were placed on the inoculated plates. The Petri plates were placed at low temperature for two hours to allow the diffusion of the chemical and then incubated at a suitable optimum temperature (29+/- 2ºC) for 30 - 36 h.

The diameter of the inhibition zones was measured in millimeters. The synthesized ligand and complexes were tested for their antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. Zn^{+2} and Cd^{+2} complexes show good antibacterial activity against the strain of bacteria taken under study.

DISCUSSION

Infrared Spectra

It is noted that the (OH) water is absent in the spectrum of the ligand but is present in the complexes. This shows the presence of hydration water in the complexes. This is supported by the presence of the M-O peaks noticed in the complexes and absent in the ligand.

The phenolic OH stretching does not undergo any change in the spectrum; hence, the phenolic OH group does not participate in the bond formation with metals. The frequency corresponding to the carboxylate hydrogen COOH stretching is found to be broad on the region (2586 cm^{-1}) in the ligand. This broad band is absent in all the complexes, showing the participation of carboxylate anion group in chelation.

The frequency corresponding to the (C=O) stretching in the region (1668 cm^{-1}) that is in the ligand is shifted to a lower frequency in the complexes. The frequency corresponding to (C = N) at 1585 cm^{-1} also shifts to lower frequency in the complexes and the frequency of (COO) present in the ligand 1481cm^{-1} is respectively shifted to the lower wave number.

Thus, it is concluded from the IR spectrum that the metals are participating in the bond formation through the azomethine C = N group and the carboxylate COO- anion of the acid group

UV Spectroscopy

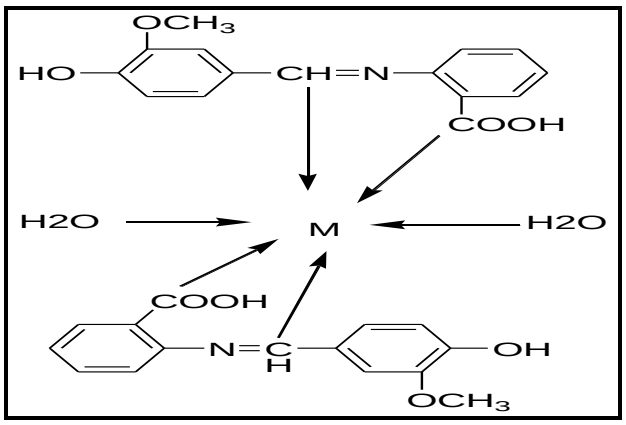
Based on the UV-visible spectroscopy, it is found that metals form complexes with the prepared schiffs base ligand with octahedral geometry

Thermal Analyses

The TGA analyses show the presence of octahedral geometry for the complexes. Two molecules of water are present in the coordination sphere that is lost in stage I. In

stage II, the complex decomposes and in stage III, the residue is formed. However, the calculated and observed values are almost the same.

Proposed Structure of Metal Complexes



M: Co, Ni, Cu, Zn and Mn

Antibacterial Activity

The antibacterial property of the ligands was compared to the complexes and as a result, the Zn^{+2} and Cd^{+2} complexes show good antibacterial activity against the strain of bacteria taken under study when compared to the ligand and other metal complexes taken for the study.

CONCLUSION

Schiff base have been prepared by a simple and environmentally friendly reductive imination procedure. This process tolerates various functional groups and often proceeds quantitatively with no need for purification. This methodology uses only Fe powder in acidic $EtOH/H_2O$ 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 vanillin and 2-nitro benzoic acid with metals such as Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2}. Both the structures of the complexes were confirmed by elemental analyses, IR, molar conductance, UV-Visible spectroscopy, thermo gravimetric analyses and ESR spectroscopic analyses.

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