

NOVEL SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL STUDIES OF SCHIFF BASE METAL COMPLEXES OF NICKEL AND MANGANESE DERIVED FROM 2-NITRO BENZOIC ACID

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ABSTRACT

In the present study an intermolecular reductive Schiff base formation from nitro derivative and derivative of benzaldehyde are carried out in the presence of iron powder and dilute acid. Schiff base synthesis is usually acid-catalyzed and usually requires refluxing the mixture of aldehydes (or ketone) and amine in polar organic medium. The Schiff base complexes of Mn (II) and Ni (II) are characterized and screened for anti-bacterial studies.

INTRODUCTION

Schiff bases are important intermediates for the synthesis of various bioactive compounds. Furthermore, they are reported to show a variety of biological activities including antibacterial, antifungal, anti-cancer and herbicidal activities [1-5]. Schiff base (azomethine) derivatives, the C=N linkage is essential for biological activity, several azomethines were reported to possess remarkable antibacterial, antifungal, anticancer and diuretic activities [6-9]

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.

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. Recently, catalytic Schiff base formation from nitroarenes and carbonyls has been reported [10,11].

Since the first preparation of imines was reported by Schiff more than a century ago [13], a variety of methods/systems for the synthesis of imines have been described, such as ZnCl₂ [14], TiCl₄ [15], MgSO₄-PPTS [16], alumina [17], Ti(OR)₄ [18], Er(OTf)₃ [19], MgSO₄ [20], MgClO₄ [21], P₂O₅/Al₂O₃ [22], CuSO₄ [23], and NaHCO₃ in which metal species act as Lewis acids to activate the carbonyl group as well as facilitating the removal of water.

Recent years have witnessed a major drive to increase the efficiency of organic transformations while lowering the amount of waste materials.

All the facts discussed above plus the increased interest in environmental protection issues inspired us to

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develop an efficient, mild and practical one pot synthesis of imines from aromatic nitro compounds.

Tandem nitroarene reduction and intramolecular Schiff base condensation to give heteroarenes has been reported using iron in aqueous media. [24-26] surprisingly, the breadth of this methodology in an intermolecular application has not been previously reported.

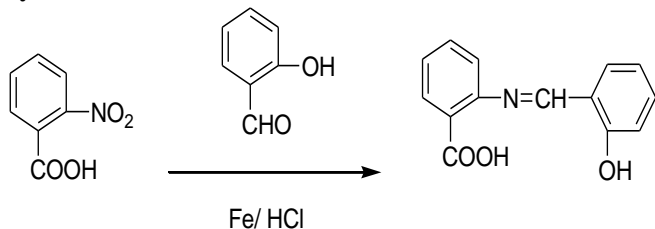
Korich developed a facile; an intermolecular reductive Schiff base formation from nitroarenes and benzaldehydes to yield diarylimines is carried out in the presence of iron powder and dilute acid. [27]

In the present study the synthesis of Schiff bases from nitro derivatives and derivatives of benzaldehydes are carried out in the presence of iron powder and dilute acid are reported.

MATERIALS AND METHODS

In preparation of reagents, chemicals of analytical grade purity were used. All weighings were observed on electrical metler balance model AB 54. Melting point on Gallenkamp melting point apparatus. Infra-Red spectra were recorded as KBr pellets on a Shimadzu FT-IR 157 Spectrophotometer. ¹H NMR Spectra were obtained using a Bruker 400 MHz spectrometer in d₆-dimethylsulfoxide (DMSO) solution with tetramethylsilane (TMS) as internal standard. Micro analytical data were determined using a CE-440 Elemental analyser, EAI Exeter Analytical Inc.

Synthesis of Schiff base



Hydrochloric Acid (4.5 mmol) was added to a mixture of 2 nitro benzoic acid (0.72 mmol), salicylaldehyde (0.72 mmol), and iron powder (7.32 mmol) in 26 mL of EtOH–H₂O (2:1 v/v) solution. The reaction was heated to 65°C for 4.5 h before being filtered while hot. The filtrate was extracted using CH₂Cl₂ (3 × 25 mL) after which the organic layers were combined, dried over MgSO₄, filtered, and concentrated in vacuo to yield Yellow-orange crystals dried in dessicator over phosphorous pentaoxide yield 63%; mp 198°C.

¹H NMR (δ DMSO-d₆): 13.06 (s, 1H, OHC=O), 8.95 (s, 1H, HC=N) 7.97 (d, 1H); 7.78 (d, 1H); 7.74 (t, 1H); 7.09 (t, 1H); 7.07 (d, 1H); 7.05 (d, 1H).

Anal. Calcd. for C₁₄H₁₁NO₃: C, 69.70; H, 4.56; N, 5.80. Found: C, 69.23; H, 4.53; N, 5.77.

Preparation of Schiff base metal complexes

The metal complexes were prepared by adding 25cm³ of ethanolic solution of metal chloride (0.01 mole) with ethanolic solutions of the prepared Schiff base (0.01 mole) followed by drop wise addition of aqueous ammonia. The resulting mixture was refluxed for two hours and the metal complex compounds that precipitated out were filtered and then washed repeatedly with hot ethanol until the washing was colourless. The product was air dried over phosphorus pentaoxide.

RESULTS AND DISCUSSION

The ligand prepared is crystalline orange; it is soluble in common organic solvents but insoluble in water. The proton NMR of all the Schiff bases showed a singlet at 8.95 - 9.00 ppm thus confirming the presence of the azomethine proton. The manganese (II) and nickel (II) Schiff base complexes prepared are crystalline brown and have decomposition temperatures 206°C and 245°C, respectively. These high decomposition temperatures, revealed the stability of the complex compounds in table 1

The solubility tests carried out on the ligand and its nickel (II) complex revealed that they are soluble in most common organic solvents but insoluble in water. However, the manganese (II) Schiff base complex is insoluble in such solvents except dimethyl sulphoxide in table 2

The IR spectral data of the ligand showed a band at 1619cm⁻¹, which is assigned to ν(C=N) stretching vibration, a feature found in Schiff bases. This band is also observable in the complex compounds, suggesting that the ligand has coordinated to the respective metal ions, resulting in the formation of the two complexes. The bands in the regions 511-556cm⁻¹ and 450-485cm⁻¹ are attributed to ν(M-O) and ν(M-N) stretching vibrations respectively, confirming the coordination of the Schiff base to the respective metal ions. The broad band in the region 3350-3560cm⁻¹ is accorded to ν(O—H) stretching vibrations, a feature indicating the presence of water shown in table 3

Biological Activity

The synthesized compounds SCB, SCBMn and SCBNi were screened for antibacterial activity against Gram positive bacteria strains (*Enterococcus faecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 25923) and Gram negative bacteria strains (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* by agar dilution method [28].

The compounds were dissolved in DMF and dioxane respectively with the sol- vents used as control. Series of agar plates containing different concentrations of antimicrobial agents (25, 12.5, 6.25, 3.125 and 1.56 mg/ml) were used to determine the susceptibility of the organisms. The different concentrations were added to the agar plates before solidifying. After the plates are set they were dried at



37°C with their lids tipped for 20 to 30 minutes in an incubator. The test plates were then inoculated with 1 ml of the test inoculum. The inoculum was diluted to contain 105 organisms per ml. The plates were inverted and incubated for 24 h at 37°C. The control and tests plates were examined for growth and minimum inhibitory concentration (MIC) value was then established.

Schiff bases SCB, SCBMn and SCBNi were screened for their in vitro antimicrobial activity against bacteria pathogens *S.aureus*, *E.coli*, *E.feacalis* and *P.aeruginosa* using agar dilution technique in DMF and dioxane. The results and MIC values are reported in Table 4.

Antimicrobial activity depends on the nature of bacterial strain, the solvent and chelating ability of the Schiff base. It is believed that Schiff bases act by forming a chelate with the bacterial strain. This may involve hydrogen bonding through the azomethine group with the active centres of cell constituents thus resulting in an interference with normal cell process [29]. Hence, the better the hydrogen bonding ability, the more active the compound.

The morphology of the cell wall is a key factor that influences the activity of antibacterial agents.

E.feacalis and *S.aureus* has the highest MIC values of 25 mg/ml and 12.5 mg/ml respectively in all the compounds tested. For these strains, the activity is independent on position of substituent, interference of compounds with bacterial cell wall and solvent used. In this study, Gram positive bacteria gave higher MIC values compared to gram negative bacteria tested. This may be due to the nature of the bacteria cell wall composed of peptidoglycan which is thicker in gram positive bacteria and this usually poses a barrier to the degree of diffusion of antibacterial agents into the enzyme.

The thinner cell wall of the gram negative bacteria leads to easier penetration/diffusion of the compound across the cell wall thereby giving better screening effect. Gram negative strains were more sensitive to solvent.

The lowest MIC values were reported in dioxane against *P.aeruginosa* for SCB and SCBMn and *E. coli* for SCBNi. The effect of solvent on inhibitory activity is pronounced in SCBNi with MIC values of 12.5 mg/ml in DMF and 3.125 mg/ml in dioxane when screened against *E. coli*. Thus, use of non-polar dioxane medium showed better inhibition with widely varying effects.

Table 1. The percentage yield, colour, decomposition temperature of the compounds

Compound	Color	% of Yield	Decomposition temperature
Schiff base ligand	Yellow-orange crystals	63	198
[MnLH20]H2O	Pale brown	60	205
[NiLH20]H2O	Pale brown	75	213

Table 2. Solubility studies

Compound	Water	Methanol	Ethanol	Acetone	DmsO	Ether	Acetonitrile	Nitrobenzene	MDC
SBLigand	IS	S	S	IS	S	IS	IS	IS	IS
SBCMn	IS	S	S	S	S	IS	IS	S	IS
SBCNi	IS	IS	IS	IS	S	IS	IS	IS	IS

IS: insoluble S: soluble

Table 3. The IR spectra of the Schiff base and complexes

Compound	$\sqrt{(C=N)} (cm^{-1})$	$\sqrt{(O-H)} (cm^{-1})$	$\sqrt{(M-O)} (cm^{-1})$	$\sqrt{(M-N)} (cm^{-1})$
Schiff base	1622	3345-3565	---	---
SBCMn	1620	3360-3570	510-555	450-490
SBC Ni	1619	3360-3560	520-560	440-470

Table 4: MIC values

Compound	<i>E.Coli</i>		<i>P.aeruginosa</i>		<i>E.feacalis</i>		<i>S.aureus</i>	
	Minimum Inhibitory Concentration (mg/ml)							
	DMF	DIOXANE	DMF	DIOXANE	DMF	DIOXANE	DMF	DIOXANE
1	6.0	6.25	6.25	1.75	25	25	12.5	6.25
2	6.0	10.0	6.25	1.50	25	25	12.0	6.00
3	12.5	3.50	6.25	6.00	25	25	6.25	6.00

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/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 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 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.

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