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Synthesis, Characterisation And Antimicrobial Activity of Some Metal Chelates with Schiff base Derived from *o*-phenylenediamine and 1, 2-diacetylbenzene.

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ABSTRACT

Schiff base was synthesized by the condensation of *o*-phenylenediamine and 1,2-diacetylbenzene. The transition metal(II) complexes were formed by the reaction of Co(II), Ni(II) and Cu(II) bromide with the Schiff base ligands. The complexes were characterized by elemental analyses, molar conductance, infrared and electronic spectral data. The complexes exhibited various colours. They are also non-electrolytes in DMF, and are all airstable. The microanalysis results revealed that the Schiff base ligands coordinated to the metal ions in 1:2 (metal-ligand) molar ratio. The chemical structures of the Schiff-base ligand and its metal complexes were confirmed by various spectroscopic studies like IR, UV-VIS, elemental analysis, molar conductance, and magnetic susceptibility measurements. On the basis of elemental and spectral studies, 16-membered macrocycliccomplex $MLX_2$was assigned. (M=Co(II), Ni(II), Cu(II)), X=Cl^-, Br^-,NO_3^-, ClO_4^- and L is a Schiff base 16-membered macrocyclic ligands Metal ions belonging to transition metal family have unique capability to unite simple molecules with pairs of electron so as to develop assemblies for paying a catalytic roles in many biological processes such as oxygen in respiration and photosynthesis. Among the all donor atoms, nitrogen and oxygen have unparallel chemistry. Water having oxygen with two lone pairs and ammonia having nitrogen with one lone pair ligate with the metal ion to give complexes.The free Schiff base and its complexes have been tested for their antibacterial as well as antimicrobial activity by using disc diffusion method and the results discussed.

Keywords: Schiff base ligands, *o*-phenylenediamine and 1,2-diacetylbenzene infrared, Coordination complexes, characterization, antimicrobial activity

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INTRODUCTION

Schiff bases are compounds containing a carbon-nitrogen double bond (azomethine group), (C=N-) with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases are of the general formula R1R2C=N-R3, where R3 is an aryl or alkyl group that makes the Schiff base a stable imine. Schiff bases, named after Hugo Schiff, and their transition metal complexes continue to be of interest even after over a hundred years of study [1]. Schiff bases have a chelating structure and are in demand because they are easy to prepare and are moderate electron donors [2-3]. Schiff base metal complexes are still widely used in catalysis but increasingly with a slightly modified concept [4-6].

The chemistry of the carbon-nitrogen double bond plays a vital role in the progress of chemical sciences [7]. Schiff-base compounds have been used as fine chemicals and medical substrates. Muchattention has been devoted by bioinorganic as well as by medicinal chemists to the relationship between the metal ions and their complexes as antitumour and antibacterial agents [8]. Interaction of various metal ions with antibiotics may enhance or suppress their antimicrobial activity but usually in many cases the pharmacological activity of antibiotics after complexation with metals is enhanced as compared to that of free ligands [9]. Some novel transition metal [Co(II), Ni(II) and Zn(II)] complexes of substituted pyridine Schiff-bases have been prepared and characterized by physical, spectral and analytical data. The synthesized Schiff-bases act as deprotonated tridentate for the complexation reaction with Co(II), Ni(II) and Cu(II) ions [10]. Various transition and inner-transition metal complexes with bi-, tri- and tetra-dentate Schiff bases containing nitrogen and oxygen donor atoms, play an important role in biological systems [11].

There are certain metallo-elements without which the normal functioning of the living organism is inconceivable. Examples of such elements are, V, Cr, Mn, Fe, Co, Ni, and Cu. These elements are present in trace and ultra-trace quantities and play vital roles at the molecular level in a living system. These transition elements are known to form Schiff base complexes [12]. In this work, I report the results of studies on the synthesis, and characterization of series of complexes of the type MLX_2 (M=Co(II), Ni(II), Cu(II)), X= Br^- L is a 16-membered macrocyclic ligands (mac) Schiff base formed by the metal in catalyzed template Schiff base condensation between *o*-phenylenediamine and 1,2-diacetylbenzene.

EXPERIMENTAL

Materials and Methods

Most of the special chemicals used were of BDH, and AldrichAnalR grade and were used without further purification. They are: O-phenylenediamine and 1,2-diacetylbenzene and metal(II) bromide. Methanol was used as the medium in all preparations. The bacterial strains used are four Gram-negative bacterials : Escherichia coli. Pseudomonas aeruginosa, Salmonella typhi and Shigellaflexneri and two Gram-positive bacterials Bacillus subtilis and Staphylococcus aureus.Preparation of the Schiff base ligands, MLX_2:The ligands were prepared by modification of a literature procedure [8,13]. This was done by condensation of the O-phenylenediamine and 1,2-diacetylbenzene.

Some representative preparation of macrocyclic complexes are descriibed here. Analytical data for the complexes are given in Table-1.

Table -I: Elemental analysis data of the ligands and their Metal complexes

Compound	**% Found Calculated**			
	C	H	N	M
[Co(mac)Br_2]	64.32	4.75	9.38	9.89
[Ni(mac)B_2]	60.90	4.44	8.88	9.30
[Cu(mac)Br_2]	55.49	4.04	8.09	9.18

Preparation of 16 member macrocyclic coordination compound [3,4:11,12:7,8:15,16-tetrabenzo]- Dibromido-2,5,10,13-tetramethyl- 1,6,9,14 tetraazacyclohexadeca 1,5,9,13-tetraenatocohalt(II)represented by [Co (Mac)Br_2]

Cobalt (II) bromide hexahydrate (2.3g, 0.01 mol), 1, 2-diacetylbenzene (3.2g, 0.02 mol) and orthophenylenediamine (2.1, 0.02 mol) were refluxed together in the molar ratio 1:2:2 in ethanolic solution medium for 6 hours. A dark brown colored solid was obtained. It was filtered, washed, dried and analyzed.

Preparation of 16 member macrocyclic coordination compound [3,4:11,12:7,8:15,16-tetrabenzo]- Dibromo-2,5,10,13-tetramethyl- 1,6,9,14 tetraazacyclohexadeca 1,5,9,13-tetraenatocohalt(II) represented by[Ni(Mac^2)Br$_2$]

Nickel (II) bromide hexahydrate (2.3g, 0.01 mol), 1,2-diacetylbenzene (3.2g, 0.02 mol) and orthophenylenediamine (2.1g, 0.02 mol) were refluxed together in the molar ratio 1:2:2 in ethanolic solution medium for 6 hours. A dark brown colored solid was obtained. It was filtered, washed, dried and analyzed.

Preparation of 16 member macrocyclic coordination compound [3,4:11,12:7,8:15,16-tetrabenzo]-Dibromido-2,5,10,13-tetramethyl- 1,6,9,14 tetraazacyclohexadeca 1,5,9,13-tetraenatocopper(II) represented by[Cu(Mac)Br$_2$]

Copper (II) bromide hexahydrate (2.3g, 0.01 mol), 1,2-diacetylbenzene (3.2g, 0.02 mol) and orthophenylenediamine (2.1g, 0.02 mol) were refluxed together in the molar ratio 1:2:2 in ethanolic solution medium for 6 hours. A dark brown colored solid was obtained. It was filtered, washed with methanol [14], and dried over $CaCl_2$.

Physical Measurements

The Elemental analysis for C, H, and N were determined using a Perkin Elmer model 2400 series 11 CHNSO elemental analyzer. The percentage metal were determined by EDTA complexometric[15] titration. The molar conductivity measurements were done using a Conductivity Meter model 160 Orion with a cell constant of 0.82 at a concentration of dimethylformamide(DMF) 10^{-3} M at room temperature were measured using direct reading conductivity meter, Systronics conductivity bridge type 305. Infrared spectra were recorded on FTIR-84005 Model Spectrophotometer using Nujol mull techniques in the range 200-4000cm^{-1}. Spectra were recorded for both the ligands and the complexes. Electronic spectra of the ligands and complexes were recorded using UV/Vis 2500 Series Spectrophotometer in the range 200-1100 nm using chloroform and DMF as the solvent. Magnetic susceptibility data were recorded using Guoy method at room temperature using Hg [$Co(NCS)_4$] as Calibrate.

Antimicrobial activity of complexes

Antibacterial studies was made using the agar-well diffusion method [16]. The wells (6 mm in diameter) were dug in the media with the help of a sterile metallic borer with centers at least 24 mm apart (NCCLS, 1990). The recommended concentration of the test sample (1mg/ml in DMSO) was introduced in the respective wells. The plates were incubated immediately at 37°C for 24 hours. Activity was determined by measuring the diameter of the zones (mm) showing complete inhibition.

RESULTS AND DISCUSSION

The prepared ligands and their metal(II) complexes gave (%) yield ranging from 63 - 94. The complexes gave various shades of colours ranging from Faint brown to Blue. Magnetic Moment of Complexes 2.00-4.60 B.M. This indicates that the ligands or complexes are probably pure.(17,18) (Table II). The conductivity values(Table III) of the ligands and the complexes in DMF at the concentration 10^{-3} mol. dm^{-3} are in the range 14-22 S cm^2 mol^{-1}. This indicates that they are non electrolytes[19,20]. The microanalysis data of the ligands and the metal(II) complexes are presented in (Table I). In general, the complexes analyzed as [$M(Mac)Br_2$], where M = Co(II), Ni(II) or Cu(II). This shows that the complexes are anhydrous [21].

The IR spectra(Table IV) of the Schiff base ligand, showed bands resulting from The bands corresponding to (C=N), (M-N) and (M-X) stretchings were observed in the 1606-1613, 467-488 and 547-573 cm^{-1} regions respectively in both the ligands. The comparison of the IR spectra of the ligand and their metal(II) complexes indicated that the ligand is coordinated to the metal ions in different ways. The band appearing at(C=O) 1714-1725 cm-^{1}(N-H) 3430 due to 1,2-diacetyl benzene and dimethyl 0-phenylenediamine in the ligand is shifted to lower frequency by 2-10 cm^{-1} in the complexes, indicating the participation of the azomethine nitrogen in coordination [18] with the metal ion. Further evidence of the coordination of this Schiff-base ligand with the metal ions was shown by the appearance of weak frequency new bands at 453-478 and 508-577 cm^{-1}. These were assigned[17-24] to the metal-nitrogen (M-N) and metal-chlorine (M-Br) vibrations, respectively.

Table -II: Data of magnetic moment of the Co(II), Ni (II), Cu(II) complexes [M(Mac)X_2]

Complexes	Colour	μ_{eff} (B.M.)	Magnetic nature
[Co(Mac)Br_2]	Faint brown	4.60	Paramagnetic
[Ni(Mac)Br_2]	Pale green	3.20	Paramagnetic
[Cu(Mac)Br_2]	Blue	2.00	Paramagnetic

Table -III: Data of electrical conductance of theCo(II), Ni (II),Cu(II)) complexes [M(Mac)X_2]

Compounds	S cm^{2} mole^{-1}	solvent
[Co(Mac)Br_2]	18	DMF
[Ni(Mac)Br_2]	14	DMF
[Cu(Mac)Br_2]	22	DMF

Table IV: Infrared spectral bands (cm^{-1}) of Co (II), Ni(II) and Cu(II),Complexes, [M(Mac)X_2]

Complex	v(C=N)	v(M–N)	v(M–X)
[Co(Mac)Br_2]	1613	469	568
[Ni(Mac)Br_2]	1613	467	547
[Cu(Mac)Br_2]	1606	488	573

The electronic spectra of the ligands and the metal complexes were determined in DMF in the range 200–700 nm. On the basis of previous assignments of related complexes[13,25-28] band I, II and III represent transitions around 8880–17400, 15900 – 17400 and 21600 –24600 cm^{-1} respectively. The broad band at 26600–34600 cm-^{1} is assigned to d-d transition of the metal ions. The positions of these bands in the spectra of the metal complexes are consistent with the expected octahedral or tetrahedral geometry.(Table V)

Table V: Electronic transitions (cm^{-1}) of the Co(II), NIi(II), and Cu(II)complexes [M(Mac)X_2]

Compounds	U_1	U_2	U_3	C.T. Band
[Co(Mac)Br_2]	8880	17400	21600	34400
[Ni(Mac)Br_2]	9350	15900	24600	34600
[Cu(Mac)Br_2]	17400	-	-	26600

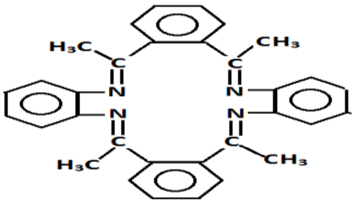
Antimicrobial activity of the Schiff base and its corresponding metal (II) complexes were determined against four Gram-negative (Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi and Shigellaflexneri) and two Gram-positive (Bacillus subtilis and Staphylococcus aureus) bacterial strains. The Schiff base compound exhibited varying degrees of inhibitory effects (low to moderate) on the growth of different tested strains (Table VI).

Table VI: Antimicrobial properties (primary screening) Metal(II) complexes

Inhibiiton zone diameter(mm)						
Gram-negative					Gram-positive	
Compound	Escherichia coli	Pseudomonas aeruginosa	Salmonella typhi	Shigella flexneri	Bacillus subtilis	Staphylococcus aureus
[Cu(Mac)Br_2	22	16	21	14	21	16
[Co(Mac)Br_2]	20	18	19	19	16	18
[Ni(Mac)Br_2]	21	20	22	21	19	18

The Schiff base, Ligand showed no inhibitory action against the Gram-negative species, Salmollellatyphi and Shigellaflexneri, and the Gram-positive species, Bacillus subtilis. In contrast, the growth of all the Gram-negative and Gram-positive species was inhibited by all the metal complexes under investigation. These results are similar to other reports in the literature[27,29],which stated that biologically inactive compounds become active and less biologically active compounds become more active upon coordination. In comparison, the uncomplexed ligand in present work, has been shown to be less active than the metal complexes.

The preliminary screening showed that the compounds Co(Mac)Br_2, Ni(Mac)Br_2 and Cu (Mac)Br_2, are the most active against both Gram-negative and Gram-positive organisms. The MIC of all the three active compounds varies from 10-100 µg/ml. The compound [M(Mac)X_2] proved to be the most active one. It inhibited the growth of Salmonella typhi, Shigellaflexneri and Bacillus subtilis at 10 µg/ml concentration. This study may serve as a basis for the chemical modifications directed towards the development of a new class of antibacterial agents. The complexes are multi-coloured, the ratio of metal to ligand are 1:2:2 in all the metal complexes as confirmed by their microanalysis. The complexes are non-electrolytes as confirmed from their conductivity measurements. The electronic spectral data suggest a plausible octahedral or tetrahedral geometry around the metal ions as shown in the proposed structures (Figure II). The Stereochemical environment of the metal ions in each case is octahedral . The 16-membered ligand bahaves in a tetradentate manner utilizing all of its nitrogen donor atoms. The anions are also coordinated to the metal ions in anunidentate manner. The broad nature of electronic spectral bands suggests tetragonal distortion in the complexes. The proposed structures of the ligand and metal (II) complexes(taking Coas representative metal) are shown in Figure-I and II. The in vitro antimicrobial screening of the complexes confirmed their potency against most of the microorganisms used in this study.



L1

Figure-I: Structure of Ligand(Mac)

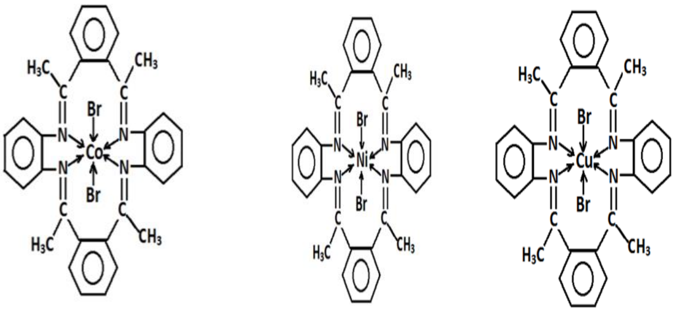


Figure II: Structure of the macrocyclic complex [Co(Mac)Br_2], Ni(Mac)Br_2 and Cu(Mac)Br_2

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