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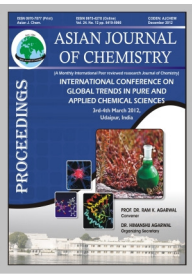

Synthesis, Spectral and Biological Studies on Novel Schiff Base Complexes of [Manganese(II), Copper(II), Nickel(II) and Cobalt(II)] Derived from 3-Chloro Benzohydrazide and Aldehyde Drivative†

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The novel Schiff base complexes of the type $[M'(L)_2]Cl_2/[M(L)_2Cl_2]$ {where M = Mn(II), Ni(II), Co(II) and M' = Cu(II), L = *N*'-(4-chlorobenzoyl)-3-hydroxy-5-methoxy benzaldehyde hydrazone} have been synthesized and characterized by various physico-chemical techniques (IR, NMR spectra, UV/visible spectra, EPR and CV studies). All the metals are coordinated in an octahedral geometry except copper(II) complex. Copper(II) complex is coordinated in square planar geometry. All the newly synthesized compounds were screened for their antimicrobial activity. Some of the compounds exhibited significant inhibition on bacterial and fungal growth as compared to standard drugs.

Key Words: Metal complexes, Physico-chemical techniques and Biological studies.

INTRODUCTION

Hydrazones are characterized by the presence of the triatomic grouping >C=N–N– groups. They can be considered as Schiff bases derived from hydrazine[1]. The nucleophilic reagents that can be used in these reactions are alkali hydroxides, alkoxides, azides, ammonia, amines and hydrazine. Thus, substitution reaction of halogen by amines is used to prepare amidrazones. Hydrazones exhibit a varied reactivity, taking part in reactions with nucleophiles, electrophiles and other chemical reagents[2]. Being ambident nucleophiles, hydrazones react with electrophilic reagents with participation of either the nitrogen atom (compounds), or the carbon atom of the azomethine group. Much attention has been paid to biologically active metal complexes in recent years. Oxygen and nitrogen donor ligands have been widely studied due to their high potential to coordinate with transition metals[3-5]. Compounds containing azomethine nitrogen and carbonyl oxygen groups have important position among organic reagents as potential donor ligands for the transition metal ions[6-11]. In this article, we have synthesized and characterized the spectral and biological studies on novel Schiff base and their transition metal complexes.

EXPERIMENTAL

All the chemicals used in the present investigations were of the analytical reagent grade (AR). 3-Chlorobenzohydrazide, 2-hydroxy-4-methoxybenzaldehyde (Sigma), metal salts and solvents were purchased from qualigens chemicals company. They were used as received.

Synthesis of ligand: 1 mmol of 3-chlorobenzohydrazide was dissolved in 30 mL methanol and 2 mL glacial acetic acid, warmed on a steam bath to a clear solution and 1 mmol methanolic solution of 2-hydroxy-4-methoxybenzaldehyde was added. The reaction mixture was stirred and refluxed on steam bath for 4 h. The solution was left over night, yellowish precipitate [**Scheme-I** (A)] was obtained. It was collected, washed and evaporate the solvent under reduced pressure to afford the product.

Synthesis of metal complexes: Ligand (0.02 mmol, 0.05 g) was added in methanolic solution of metal(II) chloride (manganese, cobalt/nickel) salts (0.01 mmol) and refluxed about 6 h. The resulting solution was kept 24 h at room temperature, coloured precipitates were obtained [**Scheme-I** (B)]. The precipitate was collected, washed with diethyl ether and evaporate the solvent under reduced pressure to afford the product.

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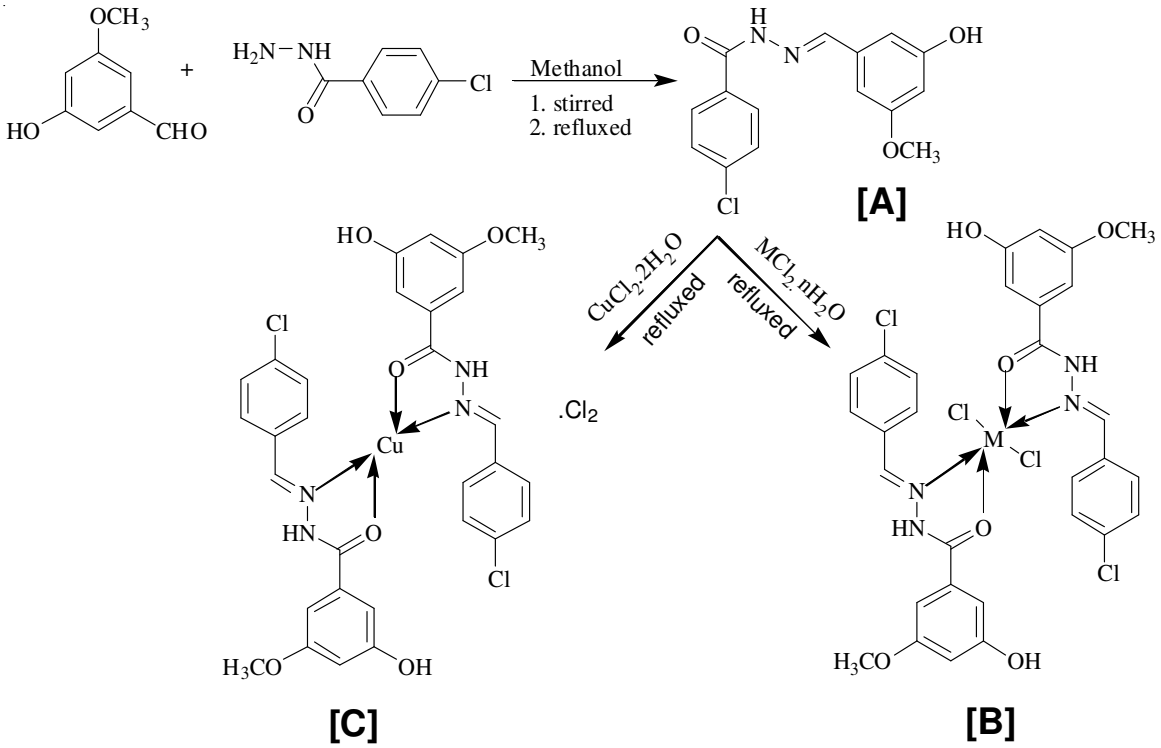

Scheme-I: Synthesis of hydrazone ligand and their metal complexes

Copper complex: In 10 mL (0.01 mmol) methanolic solution of copper(II) chloride was mixed (at pH-4.5) with 20 mL (0.02 mmol) solution of the ligand in acetone. The mixture was refluxed on water bath for 1 h, a light bluish colour was developed. This bluish solution was concentrated to a small volume to yield coloured precipitate [**Scheme-I** (C)], which was filtered, washed successively with ethanol, acetone and ether and dried for 2 h at 110 ºC.

Analytical data: Yield: 60 %; m.p. 240 ºC, m.w. 289.71, colour: yellowish; analytical data for $C_{15}H_{13}N_2O_3Cl$ found (calc.): C, 62.19 (62.11); H, 4.17 (5.10); N, 4.83 (16.77); Cl, 12.24 (12.15). IR (KBr, cm^{-1}): 1625 ν(C=N), 1690 ν(C=O), 3315 nOH, 1298 ν(C-NH). ESI-MS, *m/z* data found (calc.): 290 (289), ^{1}H NMR (DMSO-d_6) δ ppm: 8.17 (CH = N), 7.1 (HC-Ar), 7.83 (s, NH) 2.35 (CH_3). ^{13}C NMR (DMSO-d_6) δ ppm: 117.11 (CH-aromatic), 153.88 (C=O), 164.15 (CH=N), 17.6 (CH_3).

Copper complex: Yield: 28 %; m.p.: 285 ºC; m.w. 743.91; colour: dark bluish; analytical data for $[C_{30}H_{26}N_4O_6Cl_4Cu]$ found (calc.): C, 48.44 (48.15); H, 3.52 (3.35); N, 7.53 (7.20); IR (KBr cm^{-1}): 1610 ν(C=N), 1653 ν(C=O), 1298 ν(C-NH), 3393 ν(OH), 520 ν(M-O), 460 ν(M-N). ^{1}H NMR (DMSO-d_6) δ ppm: 8.17 (CH=N), 7.1 (HC-Ar), 7.83 (s, NH) 2.35 (CH_3). ^{13}C NMR (DMSO-d_6) δ ppm: 117.11 (CH-aromatic), 153.62 (C=O), 164.02 (CH=N), 17.6 (CH_3).

Nickel complex: Yield: 38 %; m.p.: 260 ºC; m.w. 739.06; colour: dark greenish; analytical data for $[C_{30}H_{26}N_4O_6Cl_4Ni]$ found (calc.): C, 48.75 (48.22), H, 3.55 (3.11), N, 7.58 (7.47). IR (KBr, cm^{-1}): 1601 ν(C=N), 1646 ν(C=O), 1298 ν(C-NH), 3350 ν(OH), 525 ν(M-O), 460 ν(M-N), 380 ν(M-Cl). ^{1}H NMR (DMSO-d_6) δ ppm: 8.17 (CH=N), 7.1 (HC-Ar), 7.83 (s, NH) 2.35 (CH_3). ^{13}C NMR (DMSO-d_6) δ ppm: 117.11 (CH-aromatic), 153.80 (C=O), 164.11 (CH=N), 17.6 (CH_3).

Cobalt complex: Yield: 35 %; m.p.: 260 ºC; m.w. 739.30; colour: dirty brownish; analytical data for $[C_{30}H_{26}N_4O_6Cl_4Co]$ found (calc.): C, 48.74 (48.15), H, 3.54 (3.35), N, 7.58 (7.50). IR (KBr, cm^{-1}): 1612 ν(C=N), 1663 ν(C=O), 1298 ν(C-NH), 3390 ν(OH), 525 ν(M-O), 465 ν(M-N), 385 ν(M-Cl). ^{1}H NMR (DMSO-d_6) δ ppm: 8.17 (CH=N), 7.1 (HC-Ar), 7.83 (s, NH) 2.35 (CH_3). ^{13}C NMR (DMSO-d_6) δ ppm: 117.11 (CH-aromatic), 153.50 (C=O), 164.10 (CH=N), 17.6 (CH_3).

Manganese complex: Yield: 35 %; m.p.: 260 ºC; m.w. 735.30; colour: dirty brownish; analytical data for $[C_{30}H_{26}N_4O_6Cl_4Mn]$ found (calc.): C, 49.00 (48.95), H, 3.56 (3.41), N, 7.62 (7.40). IR (KBr, cm^{-1}): 1606 ν(C=N), 1660 ν(C=O), 1298 ν(C-NH), 3368 ν(OH), 520 ν(M-O), 460 ν(M-N), 390 ν(M-Cl). ^{1}H NMR (DMSO-d_6) δ ppm: 8.17 (CH=N), 7.1 (HC-Ar), 7.83 (s, NH) 2.35 (CH_3). ^{13}C NMR (DMSO-d_6) δ ppm: 117.11 (CH-aromatic), 153.88 (C=O), 164.05 (CH=N), 17.6 (CH_3).

RESULTS AND DISCUSSION

The absorption bands in the region 3130-2940 cm^{-1} in the free ligand assigned to NH stretching frequencies agree with that found in ligand. This band does not go appreciable change in the complexes indicating non-involvement of amino nitrogen in coordination. Ligand chosen for the present studies show strong band at 1625 cm^{-1}, which assignment of (C=N) stretching frequency. In the spectra of the complexes ν(C=N) frequency shifted to lower *ca.* 15-20 cm^{-1} region[12]. This lowering in (C=N) frequency suggests that the unsaturated nitrogen of (C=N) group forming ligand is taking part in chelation. In the spectrum of ligand a band appeared in the range at 1690 cm^{-1} is due to carbonyl group which was shifting to the lower frequencies *ca.* 20-30 cm^{-1} region in the spectrum of all the metal complexes[13]. Further evidences of coordination of the ligand with metal

salts were established by FTIR spectrum in which some new bands appeared in the range 545-520, 465-455 and 385-360 cm^{-1} assigned to ν(M-O), ν(M-N) and ν(M-Cl), respectively. ^1H NMR spectra of the ligand, the signals of the -NH protons were observed as singlets at δ 11.83. These signals also appeared in the ^1H NMR spectra of the metal complexes indicating non coordinating the metal ions. The signals of the -CH=N proton which appears as singlets at δ 8.17 in the ligand show a shift to downfield in δ 0.03-0.08 after complexation. The shift indicates the coordination of the imines nitrogen to the metal center. The signals of the aromatic protons of the ligand appeared at δ 6.21-6.91 and the resonance lines found correspond to the calculated multiplicity. These signals do not suffer relevant changes in the chemical shifts for the metal complexes. The signals of the $-CH_3$ proton appears at δ 1.34-1.48 in the spectrum of ligand and complexes. The Mn(II), Ni(II) and Co(II) complexes are non-electrolytic and, Cu(II) complex electrolyte in nature by their molar conductivity (Λ_m) as measured in DMSO in the range 60-80 Ω^{-1} cm^2 mol^{-1} and 95 Ω^{-1} cm^2 mol^{-1}, respectively[15]. The EPR spectra of the Cu(II) complexes were recorded as polycrystalline sample at LNT since the rapid spin lattice relaxation of Cu(II) broaden the lines at higher temperature. The g(II) value for metal complexes is less than 2.3 suggesting a small amount of ionic character of the metal-ligand bond. The trend $g(II) > g_\perp > 2.0023$, suggests that the unpaired electron lie predominantly in the $d_{x^2-y^2}$ orbital characteristic of square planner Cu(II) complexes[15]. In the spectrums of UV/visible spectroscopy, the electronic spectra of Mn(II) complex shows three bands at 36500, 25423 and 19835 cm^{-1} assignable to $^6A_{1g} \rightarrow {}^4A_{1g}$ (4G), $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) and $^6A_{1g} \rightarrow {}^4T_{1g}$ (G) transitions respectively, which lie in the range as reported for octahedral geometries[16]. The magnetic moment of this compound 4.80 BM is an addition evidence for an octahedral structure. The electronic spectra of the present cobalt complex is very similar and consists of two main absorption bands at 9690 and 20340 cm^{-1} with two shoulders appearing between 16650 and 19380 cm^{-1}. The lowest and highest energy bands can be assigned to $^4T_{1g} \rightarrow {}^4T_{2g}$ (F) and $^4T_{1g} \rightarrow {}^4T_{1g}$ (P) (v_3), transitions, respectively and consistent with octahedral geometry[16]. The μ_{eff} value for present cobalt complex is 4.70 B.M. at room temperature within the range reported for the high spin octahedral cobalt(II) complex. The magnetic moment observed for the Ni(II) complex is 2.98 B.M. which is consistent with octahedral geometry. The electronic spectra of present nickel (II) complex recorded in ethanol consists of bands at 8520, 11640, 15325 and 25830 cm^{-1} are attributed to $^3Ag_{2g} \rightarrow {}^3T_{2g}$ and $^3A_{2g} \rightarrow {}^3T_{1g}$ transitions, respectively. The copper(II) complex exhibits magnetic moment 1.70 B.M. at room temperature for square planner geometry. The electronic spectra of the copper(II) complex display a broad band at 14320 cm^{-1} due to $^2B_{1g} \rightarrow {}^2E_g$ and two bands at 16395 and 27320 cm^{-1} assigned to *d-d* transitions[17] and a charge transfer band for a square planner environment.

Electrochemical behaviours: Voltammogram displays a reduction peak at E_{pc} = -1.4V with an associated oxidation peak at E_{pa} = -0.6 V at a scan rate of 50 mV/s. The peak separation of this couple (ΔE_p) is 0.8 V and increases with scan rate. The ΔE_p is 1.1 and 1.4 at scan rates 100 mV/s and 200 mV/s respectively. Thus, the analyses of cyclic voltametric responses at different scan rate give the evidence for quasi-reversible one electron reduction. The most significant feature of the Cu(II) complex is the Cu(II)/Cu(I) couple. The ratio of cathodic to anodic peak height was less than one. However, the peak current increases with the increase of the square root of the scan rates. This establishes the electrode process as diffusion controlled.

Microbiology assay: The antimicrobial activity was evaluated by using the cup-plate agar diffusion method[18] by measuring the zone of inhibition in mm. The antimicrobial activity was compared with standard drugs gentamycin and amphotericin B.

Antibacterial activity: The nutrient agar broth prepared by the usual method was dispensed in 50 mL quantities of different conical flasks. Then, the 0.5 mL culture of each bacterium (*S. aureus* ATCC 29253, *S. aureus* ATCC 3160) in nutrient agar broth was added and inoculated at 37 ºC for 24-48 h. The nutrient agar was melted at 100 ºC and after cooling to 56 ºC, was poured into petri plates of 13 cm diameter in quantities of 20 mL and left on a flat surface to solidify and the surface of the medium was dried at 37 ºC. Then, above subcultures of each bacterium were pipetted in to the nutrient agar plate. The cups (10 mm diameter) were formed with the help of borer in agar medium and filled with 0.04 mL (40 µg) solution of sample in DMSO. The plates were incubated at 37 ºC for 24-48 h and the control was also maintained with 0.04 mL of DMSO in a similar manner. After the completion of the incubation period, the zone inhibition growth in the form of diameter in mm was measured (Table-1).

Antifungal activity: *Cabdida albicans* (227) and *Staphylococcus cereviscae* (361) were taken for testing antifungal activity using cup-plate agar diffusion method. The culture was maintained on sabourauds agar slants, sterilized sabourauds agar medium was inoculated with 24-48 h old 0.5 mL suspension of fungal spores in a separate flask. The sabourauds agar was melted at 100 ºC and after cooling to 56 ºC, was poured into petri plates of 13 cm diameter in quantities of 20 mL and left on a flat surface to solidify and the surface of the medium was dried at 37 ºC. Then, above subculture of fungi was pipetted in to the sabourauds agar plate. The cups (10 mm diameter) were formed with the help of borer in agar medium and filled with 0.04 mL (40 µg) solution of sample in DMSO. The plates were incubated at 30 ºC for 48 h and the control was also maintained with 0.04 mL of DMSO in a similar manner.

After the completion of the incubation period, the zone inhibition growth in the form of diameter in mm was measured (Table-1). The zone inhibition tabulated reveal that the antibacterial activity of the compounds is specific to the microorganism examined. Analysis of the data showed that the general the fungi *C. albicans* (227) was more susceptible to the irreversible toxic effects of screened compounds than *S. cereviscae* (361).

Conclusion

In this article, we have described that the all the synthesized metal(II) complexes of hydrazone. The copper(II) complex has square planner geometry but rest complexes have octahedral geometry. The behaviours of antimicrobial activities showed that the complexes exhibit antimicrobial properties and it is

TABLE-1
ANTIMICROBIAL ACTIVITY OF NEWLY SYNTHESIZED LIGAND AND THEIR METAL COMPLEXES

Compounds	Time (h)	*S. aureus* MTCC 3160		*S. aureus* MTCC 25923		*C. albican* MTCC 227		*S. cereviscae* MTCC 36	
		Diameter of zone of inhibition (mm) 100 µg	50 µg	Diameter of zone of inhibition (mm) 100 µg	50 µg	Diameter of zone of inhibition (mm) 100 µg	50 µg	Diameter of zone of inhibition (mm) 100 µg	50 µg
Ligand	24	5	2	5	0	6	2	3	0
	48	6	2	7	1	7	3	5	2
Co(II) complex	24	10	12	13	6	9	7	9	8
	48	11	14	14	9	11	10	12	9
Ni(II) complex	24	9	8	10	8	10	7	11	8
	48	11	10	12	10	11	7	12	9
Cu(II) complex	24	13	9	12	10	13	10	12	10
	48	14	10	13	12	14	13	14	11
Mn(II) complexes	24	9	9	-	-	-	-	-	-
	48	12	10	9	9	8	-	-	-
Gentamycin	24	15	12	15	12	15	12	15	12
	48	15	12	15	12	15	12	15	12
Amphotericin –B	24	20	15	20	15	20	15	20	15
		20	15	20	15	20	15	20	15

important to note that they show enhanced inhibitory activity compared to parent ligand.

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