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Synthesis, Structure Characterization and Antimicrobial Activity of Manganese (II) and Copper (II) Complexes of Isatinphenylhydrazone

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Abstract:
Mn(II) and Cu(II) complexes of isatinphenylhydrazone, a Schiff base derived from condensation of phenylhydrazine and isatin, (IPH) prepared in a 1:2 molar ratio (metal : ligand). These compounds have been characterized, using elemental analysis, Infrared, electronic absorption spectra and molar conductance measurement. The Infrared spectrum data revealed that the ligand, IPH behaves as a bidentate ligand coordinating to the metal ion using azomethine nitrogen of the hydrazine moiety and carbonyl oxygen of isatinchromophore. From the results of electronic spectra data, tetrahedral geometry was assigned to Mn(II) complex while Cu(II) complex adopt square planar geometry. The antimicrobial activities of the ligand and complexes were done against some bacterial and fungal strains in broth culture. The compounds exhibit moderate inhibitory effect on the microbes.

Keywords: *Isatinphenylhydrazone, Mn(II) and Cu(II) complexes, Infrared and Electronic spectra.*

1. Introduction

Hydrazones are versatile class of organic compounds that have been widely studied. The interest in their design, synthesis and characterization has come from applications in various fields. They have wide applications in biology, medicine, optics, catalysis and analytical chemistry.[1-5] They have been found to exhibit variety of pharmaceutical activities and often provide outstanding pharmacological potentials.[6, 7]Isatinphenylhdrazone has also been found to demonstrate a diversity of biological activities including antimalarial, antibacterial, antifungal, anticonvolusant, antitubercular, anti-inflammation, anticancer, enzymatic inhibition and these tend to be enhanced on complexation with biologically active metals[8-16] The biological activities of this compound arise from incorporation of phenylhyrazine ring with pharmacologically active indole ring into cells. Secondly, the efficacy of the inhibitory actions on the cell growth can be explained based on chelation theory. This research describes the synthesis, structure and antimicrobial activities of manganese (II) and copper(II) complexes of isatinphenylhydrazone (IPH).

2. Experimental

2.1. Materials and Methods

All chemicals used were of analytical grade. The molar conductance obtained from deuterated DMSO was done using a systronic direct reading Jenway 4510 conductance bridge with a conventional dip-type black electrode. Perkin Elmer PE 240 elemental analyzer, FT-IR Perkin Elmer 1600 spectrophotometer XB model with KBr disk and UV-Vis double beam PC scanning spectrophotometer, UVD-2690, 3.3 software version were used to obtain the elemental, infrared and electronic absorption spectral data. The melting point was recorded from Gallen Kemp melting point apparatus.

2.1.1. Synthesis of Ligand

Methanolic solution of Isatin (0.736g, 0.005mol) was added to phenylhydrazine (0.541g, 0.005 mole). Few drops of glacial acetic acid were also added. The mixture was stirred under refluxed at room temperature for 2 hours, after which it was allowed to stand overnight. On cooling, the yellow coloured precipitate was obtained after filtration. The precipitate was washed with ethanol and dried in a dessicator. The yield was 67%.

2.1.2. Synthesis of Mixed Ligand Complexes

Methanolic solutions of the ligand, isatinphenylhydrazone (0.949g, 0.004mol) and that of the respective metal salts (0.002mol) were mixed then stirring. This mixture was boiled under refluxed for 1 hour at room temperature and after, left to stand overnight. On cooling, the precipitate formed was filtered, washed with ethanol and dried in a dessicator.

3. Results and Discussion

The complexes were prepared by mixing the metal ions and the ligand in a 2:1 ratio in methanol. The ligand displaying bidentate mode; coordinated through azomethine nitrogen and carbonyl oxygen. The elemental analysis and % yield results of the synthesized complexes are presented in table 1. All the complexes are soluble in common coordinating solvents viz: DMF, DMSO and acetone, sparingly soluble in ethanol, methanol and insoluble in hexane and water. They are stable in air and show a range of colours such as yellow, green and brown, melting points are high, indicating strong bonding network and electrical conductance of these complexes are low (1.15ohm^{-1}cm^{-1}) showing their non-electrolytic nature.

Compound	Molecular Formula	% Yield	M.p. (^{o}C)		Observed (Calculated) %				Molar conductance (Ω^{-1}cm^2 mol^1)
					C	H	N	M	
IPH (Yellow)	$C_{14}H_{11}N_3O$ 237.27	67	215.7		70.81 (70.39)	4.64 (4.66)	17.70 (17.58)	-	-
$Mn(IPH)_2]Cl_2$ (brown)	$MnC_{28}H_{22}N_6O_2Cl_2$ 600.8	59	230.0		55.97 (55.64)	3.67 (3.62)	13.19 (13.72)	9.15 (9.01)	1.15
$Cu(IPH)_2]SO_4$ (dirty green)	$CuC_{28}H_{22}N_6O_6S$ 634.08	52	217.8		52.99 (52.80)	3.47 (3.21)	13.25 (13.30)	10.02 (10.7)	1.15

Table 1: Physical Properties of the ligand and its metal complexes

Compound	υ (C=O)	υ(C=N)	υ (N-N)	υ (M-O)	υ (M-N)
IPH	1681s	1610s	1168s	-	-
$[Mn(IPH)_2]Cl_2$	1687s	1607m	1174s	792w	692w
$[Cu(IPH)_2]SO_4$	1684m	1604w	1176m	498w	376w

Table 2: Important infrared spectral bands (cm^{-1}) and their assignments where s=strong; m=medium; b=broad; w=weak.

3.1. Infrared Spectra

The infrared results of the ligand with its metal complexes were recorded from 3900-375cm^{-1} region. The most important complexes and the proposed assignment are presented in table 2. These bands provide an insight into the coordinating sites of the ligand. The ligand can exhibit Lactam-lactimtautomerism owing to the presence of carboamide-NH-C=O functionality on isatin moiety.

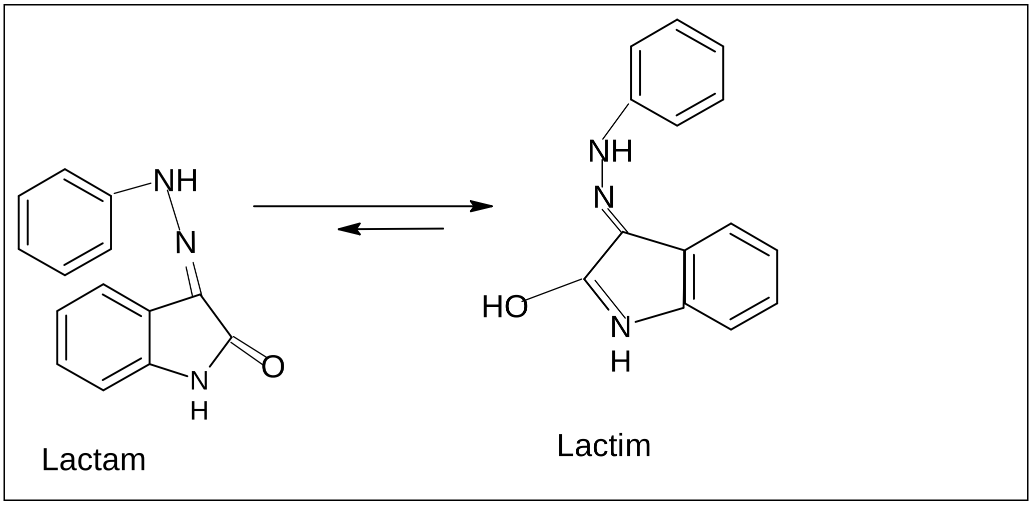

Figure 1: Tautermeric structure of Isatinphenylhydrazone

The presence of C=O band at 1681cm^{-1} on the infrared spectrum of the ligand suggest that this ligand remain in the lactam form.
The bands appearing at 1681 and 1610cm^{-1} on the spectra of ligands are from r C=O and r C=N$_{azomethine}$ mode respectively.
The vibration frequency generated by C=O bond, appearing in the IR spectrum of the ligand at 1681cm^{-1}, is shifted to higher values in the spectra of complexes, indicating the coordination of carbonyl to the metallic ion.[17]

The band at 1610cm^{-1} on the spectrum of ligand is from r C=N$_{azomethin}$. After coordination of azomethine nitrogen to the metal complexes, it shifted of to lower frequencies (1607cm^{-1}&1604cm^{-1}) this was supported by occurrence of rN-N band to higher frequencies (1174cm^{-1} & 1176cm^{-1}) in the spectra of complexes compared to the free ligand.[18,19] The far IR spectra of the complexes gave new bands within 792-495cm^{-1} which were attributed to r M-O and r M-N respectively.[20] In each complex, Isatinphenylhydrazone ligand coordinated to the central metal ion through azomethine nitrogen atom and carbonyl Oxygen atom. In conclusion, isatinphrnhydrazone ligand acted as a bidentate chelating agent.

Compounds	Band (cm^{-1})	ε(Lmol^{-1}cm^{-1})	Assignment	Geometry
IPH	31,250 25,974	135,600 149,200	π-π* n-π*	-
$[Mn(IPH)_2]Cl_2$	30,303 25,974 20,833 17,391	14,790 15,780 230 91	π-π* n-π* $^6A_1 \rightarrow ^4T_2$ $^6A_1 \rightarrow ^4E$ (^4G)	Tetrahedral
$[Cu(IPH)_2]SO_4$	28,571 20,202 15,385	13,850 215 90.4	n-π* $^2B_{1g} \rightarrow ^2E_g$ $^2B_{1g} \rightarrow ^2A_{1g}$	Square planar

Table 3: Electronic spectra bands (cm^{-1}) of the ligand and its metal complexes

3.2. Electronic Spectra

The electronic spectra data of the ligand and the metal complexes shown in table 3, support some conclusions about the stereochemistry of the complexes. In IPH, two bands at 31,250 and 25,974cm^{-1} observed in the UV region were assigned n-π* and π-π* transitions. These bands have been attributed to intraligand transitions, due to the presence of lone-pairs of electrons on the heteroatom (oxygen) and double bonds in the structure of IPH. From the spectra of the complexes these bands underwent a bathochromic shift. The bathochromic shift provided evidence for coordination of the metal ions to IPH. Apart from the intraligand transitions, the metal complexes also exhibited some d-d transition in the visible region of their spectra. In the visible region of the spectrum of $[Mn(IPH)_2]Cl_2$, several bands due to forbidden transition were observed. The band at 20,833 and 17,392cm^{-1}, assigned to $^6A_1 \rightarrow ^4T_2$ and$^6A_1 \rightarrow$ $^4E(^4G)$ respectively and are typical of tetrahedral manganese (II) complexes, since the molar absorptivity (ε) were in the range 100-300 Lmol^{-1}cm^{-1} due to accentric nature of tetrahedral complexes which leads to intensification of the absorption bands.[21] In $[Cu(IPH)_2]SO_4$, two bands at 20,202 and 15,385cm^{-1} have been attributed to $^2B_1g \rightarrow ^2Eg$ and $^2B_1g \rightarrow ^2A_1g$ transition respectively. The observed bands are typical of square plannar copper(II) complexes[22], being above 10,000cm^{-1} wave number and having molar absorptivity (ε) greater than 100Lmol^{-1}cm^{-1}.[23]

Antimicrobial Studies

The metal complexes and the ligand were screened against three bacterial strains; *S. aureus*, *E. coli*, *S. typhi* and fungal cultures viz. A. niger, and C. albican. The method used is Paper disk diffusion test . Nutrient agar was used to culture bacteria while Sabouraud dextrose agar was for fungi. The bacteria were transferred to the nutrient agar plate while same was done with fungi on Sabouraud dextrose agar plates. The compounds were dissolved in DMF to make a concentration of 1000μg/ml and the paper disk (0.7mm diameter size) were soaked in these test compounds, drained and spaciously placed onto the plates using sterilized forceps. The incubator was then set to 37^{0}C for normal growth of the strains. These inoculated plates were then allowed to stay in the incubator to allow the microbial growth. The period for bacteria growth was 36 hours while that of fungi was 72 hours. After the incubation period, the inhibition zones across the disks were then recorded in mm. The results are displayed in Table3. The evaluation of the obtained results as shown in Table 3 shows that these synthesized compounds gave fair zones of inhibition on the growth and proliferation of the microbes. Cu(II) chelate appears to be most sensitive compound against a broad spectrum of bacteria: *vizSalmonellatyphi, Staphylococcus aureus, Escherichia coli*. They have comparatively larger diameter of inhibition zones. For example, Cu(II) $(IPH)SO_4$ consistently show larger zones of inhibition ranging from 14.3-24.5mm for both bacteria and fungi. These greater antimicrobial effect is more from chelates than from the free ligand. Even Mn(II) complex follows the same trend. Explanation for this behavior is still based on chelation theory earlier reported where the polarity of the metal is reduced. This is because the chelation facilitates the movement of these complexes across the membranes. This increased movement is due to the fact that the chelation tends to reduce the metals polarity. This reduced polarity, then increases the lipophilic properties of the metals. When this is done, then it favours the penetration of the complexes across the membrane. This, then blocks the active sites which the microbes are supposed to act. This blocking tends to go along with the stopping of the entire respiration in the microbes.(24)(25).

Compound	*S. aureus*	*S. typhi*	*E. coli*	*C. albican*	*A.niger*
IPH	12.7	14.8	18.2	10.4	09.8
$Cu(IPH)_2SO_4$	15.7	24.5	19.3	15.5	14.3
Mn $(IPH)_2Cl_2$	14.9	17.7	16.6	15.4	18.5
Tetracycline/Flucanazole	15.5	18.2	18.2	20.3	16.8

Table 3: Diameter of Inhibition Zones (mm)

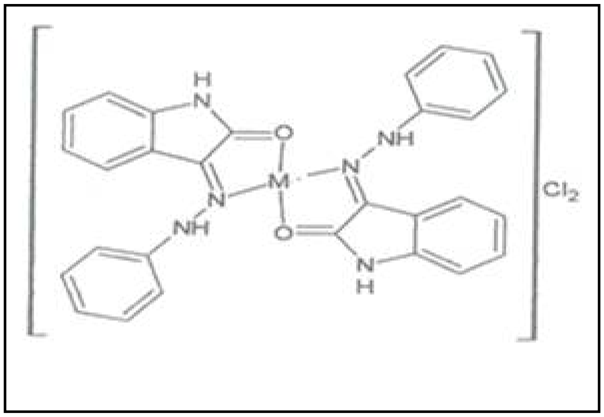

Figure 2: Proposed tetrahedral geometry of Mn (II) isatinphenylhydrazone

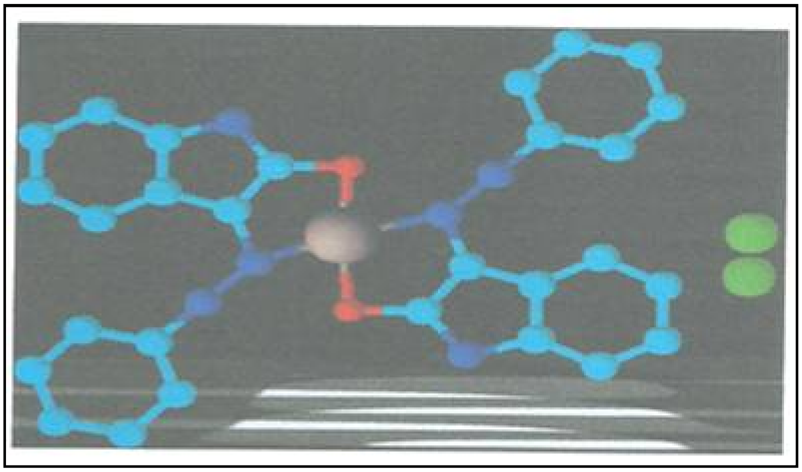

Figure 3: Three dimensional view for the proposed tetrahedral geometry of Mn (II) isatinphenylhydrazone

4. Conclusion

The complexes are all stable in air. Elemental analysis data have revealed the stoichiometric compositions for the complexes as 1:2 molar ratio (metal : ligand). Infrared spectra have shown that IPH coordinated as bidentate ligand. Electronic spectra data revealled that Mn(II) and Cu(II) complexes are four coordinate and adopt tetrahedral and square planar geometries respectively. The chelates were found to exhibit good antimicrobial activities.

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