

Synthesis, Characterization and Antimicrobial Activity of Mixed Ligand Complexes of Dioxouranium(VI) with Isatin-3-phenyl Hydrazone.

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Complexes of dioxouranium(VI) with the Schiff base derived from a heterocyclic amide (isatin) and phenylhydrazine have been synthesized and their physico-chemical properties investigated using elemental analysis, molar conductance, molar mass determination, IR, UV-visible and ^1H NMR spectral data. Isatin-3-phenylhydrazone acts as a bidentate chelating agent coordinating through the oxygen and nitrogen atoms of $>\text{C}=\text{O}$ and $>\text{C}=\text{N}$ groups, respectively. Various anions such as acetate, lactate, nitrate, perchlorate, sulphate and thiocyanate act as secondary ligands by coordinating to the metal ion. Thermal stability and mechanism of decomposition of a few complexes were determined by TG and DTA techniques. X-ray diffraction study of the acetato complex suggests that it crystallizes in orthorhombic system. The ligand and some of its complexes were screened for their antibacterial and antifungal activities towards *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Cryptococcus neoformans* and *Candida albicans*.

Key Words: Isatin-3-phenylhydrazone, Dioxouranium(VI), Antibacterial, Antifungal.

INTRODUCTION

Schiff base complexes continue to attract many researchers because of its wide application in the field of agriculture as pesticides and in medicine as antibacterial, antifungal and anticoagulant agents. Metal complexes of Schiff bases have aroused considerable interest in view of their industrial and biological importance. The biological activity of Schiff bases is related to their affinity with metal ions. Several isatinoid compounds were reported to have antibacterial, antifungal and anti-inflammatory activities^{1,2}. Isatin or indole-2,3-dione is a unique molecule possessing both amide and ketocarbonyl groups. The C-3 carbonyl group of isatin is strongly electrophilic and it readily undergoes condensation and addition reactions. Isatin tautomerises and exists between the lactam (keto) and lactim (enol) structures. Schiff bases derived from isatin have shown different antimicrobial activity due to different nature of the carbonyl and amino components as well as its substituent³. In the present paper, the synthesis, characterization and antimicrobial activities of isatin-3-phenylhydrazone and its $\text{UO}_2(\text{VI})$ complexes are reported.

EXPERIMENTAL

Chemicals used for the synthesis of ligand and complexes were of AR grade. Isatin and phenyl hydrazine hydrochloride in 1:1 molar ratio were used for the synthesis of the ligand isatin-3-phenylhydrazone (IPH). Alcoholic solutions were mixed together and refluxed on a water bath for *ca.* 6 h. The resultant mixture was concentrated and cooled to get yellow crystals of isatin-3-phenylhydrazone. They were separated and recrystallised from alcohol.

Alcoholic solutions of uranyl acetate dihydrate and isatin-3-phenylhydrazone were mixed together in 1:2 molar ratio and refluxed for *ca.* 8 h. The liquid mixture was concentrated and cooled to get the solid complex. It is purified by repeated extraction with alcohol followed by petroleum ether (40-60 °C range) and dried in vacuo over phosphorus(V) oxide. Bright yellow solid was obtained with a melting point of 252 °C. Lactato, nitrate, perchlorate, sulphate and thiocyanate complexes were prepared by substitution method⁴. Alcoholic solutions of acetate complex was treated with appropriate amount of the corresponding lithium salt solutions and refluxed. The resultant mixture was concentrated and cooled to get crystals of the various solid complexes.

RESULTS AND DISCUSSION

All the complexes are yellow in colour and are found to be non-hygroscopic. They are moderately soluble in acetone, acetonitrile and methanol but almost insoluble in benzene and diethyl ether. Molar conductance data reveal the non-electrolytic nature of the complexes. CHN data and molar mass determination of the complexes are in agreement with the theoretical value calculated from the assigned formulae (Table-1). IR Spectra of the ligand and the complexes were recorded on an FTIR instrument in the range 4000-400 cm^{-1} . Electronic spectra were recorded on an UV-visible spectrophotometer in the range 200-600 nm. ¹H NMR spectra were recorded on a 300 MHz FT-NMR instrument using TMS as reference material and deuterated acetone as solvent. Thermal analysis was carried out on a thermal analyzer from ambient to 800 °C at a heating rate of 10 °C/min. X-ray powder diffraction was done on a Philips X-ray diffractometer.

IR spectra of the complexes show considerable shift in absorption frequencies of the coordinating groups of the ligands suggesting the coordination of those groups. IR spectra of isatin-3-phenylhydrazone exhibit a strong absorption band at 1720 cm^{-1} which is attributed to the $>\text{C}=\text{O}$ stretching vibration of isatin moiety. Lowering of $>\text{C}=\text{O}$ absorption frequency by 30-35 cm^{-1} in the complexes suggest the coordination of oxygen atom of $>\text{C}=\text{O}$ group. A sharp band of medium intensity observed at 1620 cm^{-1} is due to the stretching vibration of $>\text{C}=\text{N}$ group of the ligand while in the complexes this absorption band is lowered by 25-30 cm^{-1} suggesting the coordination of nitrogen atom of azomethine. An absorption band of medium intensity observed around 3156 cm^{-1} in the ligand is attributed to the N-H stretching vibration of the lactam-lactim equilibrium of isatin moiety. In the complexes this stretching frequency

TABLE-1
ANALYTICAL DATA OF SYNTHESIZED COMPLEXES

Complex	Elemental analysis (%):				Anion (%):		
	Found (Calculated)				Found (Calculated)		
	C	H	N	U	NO ₃ ⁻	SO ₄ ²⁻	NCS ⁻
[UO ₂ (IPH) ₂ (OAc) ₂]	44.27 (44.54)	3.36 (3.25)	9.58 (9.74)	27.54 (27.61)	–	–	–
[UO ₂ (IPH) ₂ (NO ₃) ₂]	38.59 (38.71)	2.43 (2.53)	12.66 (12.90)	27.58 (27.42)	13.86 (14.29)	–	–
[UO ₂ (IPH) ₂ (C ₃ H ₃ O ₃) ₂]	44.09 (44.25)	3.19 (3.49)	9.26 (9.11)	25.71 (25.82)	–	–	–
[UO ₂ (IPH) ₂ (NCS) ₂]	41.45 (41.86)	2.34 (2.55)	12.87 (13.02)	27.26 (27.68)	–	–	13.15 (13.49)
[UO ₂ (IPH) ₂ (ClO ₄) ₂]	35.51 (35.62)	2.29 (2.35)	8.67 (8.91)	25.43 (25.24)	–	–	–
[UO ₂ (IPH) ₂ SO ₄]	39.68 (40.00)	2.49 (2.62)	9.76 (10.01)	27.95 (28.34)	–	10.94 (11.43)	–
	Molar mass	Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)					
	Theor; (exp.)	PhNO ₂	CH ₃ OH	CH ₃ CN			
[UO ₂ (IPH) ₂ (OAc) ₂]	862.21 (857.08)	6.32	11.26	26.23			
[UO ₂ (IPH) ₂ (NO ₃) ₂]	868.04 (861.26)	1.14	6.87	5.10			
[UO ₂ (IPH) ₂ (C ₃ H ₃ O ₃) ₂]	922 (916.15)	4.01	18.30	14.88			
[UO ₂ (IPH) ₂ (NCS) ₂]	860.04 (855.39)	2.30	7.88	12.83			
[UO ₂ (IPH) ₂ (ClO ₄) ₂]	943.28 (937.69)	7.80	26.28	21.03			
[UO ₂ (IPH) ₂ SO ₄]	840.21 (836.54)	8.12	14.86	9.18			

is increased suggesting the existence of lactam (keto form). Another band observed around 3358 cm⁻¹ in the spectra of the ligand and the complexes shows that the –NH₂ group is not coordinated to the metal ion. Thus the IR spectra offer strong evidence for the neutral bidentate behaviour of isatin -3-phenyl hydrazone coordinating through carbonyl oxygen and azomethine nitrogen atoms. This is further substantiated by the presence of two new bands in the complexes at 530 and 420 cm⁻¹ which are assigned to U–O and U–N bond vibrations, respectively^{5,6}. IR spectra of acetato complex exhibit absorption bands at 1345 and 1595 cm⁻¹ which are assigned to the symmetric and asymmetric stretching vibrations of COO⁻ of acetate group suggesting monodenticity of coordinated acetate ion. Lactato complex exhibit a frequency separation of 250 cm⁻¹ between ν_{sym} and ν_{asy} suggesting monodentate coordination.

IR spectra of thiocyanato complex exhibited a sharp band at 2063 cm^{-1} indicating that the N atom of NCS^- is coordinated to the metal ion in a monodentate fashion. Nitrate and perchlorato complexes also exhibit monodentate coordination while sulphato group is coordinated through two of its oxygen atoms in a bidentate chelating manner. Mixed ligand complex with DMSO exhibited a sharp band at 1010 cm^{-1} which is attributed to the stretching vibration of $>\text{S}=\text{O}$ group of DMSO. A sharp band of medium intensity observed in the region $920\text{--}930\text{ cm}^{-1}$ is assigned to the asymmetric stretching vibration of uranyl ion. Since the symmetric stretching vibration at 840 cm^{-1} is not seen in the spectra it is confirmed that the oxygen atoms of uranyl ion are in the transpositions in all the dioxouranium(VI) complexes^{7,8}.

^1H NMR spectra of isatin-3-phenyl hydrazone shows a singlet at δ 10.7 ppm which is assigned to the proton of cyclic amido group. An intense signal observed at δ 12.8 ppm is due to the protons of $-\text{NH}-$ group of phenyl hydrazone. This proton is deshielded due to the resonance effect of phenyl group and hence the signal is obtained at low field (higher chemical shift). Multiplets observed at δ 6.8–7.3 ppm are assignable to the protons of heterocyclic ring. In addition to this the multiplets observed at δ 7.4–7.9 ppm in the spectra of the ligand are assigned to aromatic protons of benzene ring. In the NMR spectra of complexes, signals due to protons of cyclic amido group and $-\text{NH}$ of phenylhydrazone do not show any change in their δ value compared to the free ligand indicating that those N atoms are not coordinated to the metal ion.

UV-Visible spectra of the complexes exhibit a blue shift in the case of $n\rightarrow\pi^*$ transitions of both $>\text{C}=\text{O}$ and $>\text{C}=\text{N}$ groups suggesting the involvement of non-bonding electrons of oxygen and nitrogen atoms in coordination with the metal ion. A red shift was observed for $\pi\rightarrow\pi^*$ transitions in the complexes which further supports the coordination of lone pair electrons of oxygen and nitrogen atoms. Electronic absorption spectra of all the $\text{UO}_2(\text{VI})$ complexes exhibited an absorption band centered in the region 430–475 nm due to charge transfer transition from the apical oxygen to uranium coupled with some UO_2^{2+} vibrational frequency. The charge transfer is from a bonding orbital of UO_2^{2+} moiety to a non-bonding $5f$ atomic orbital of uranium. Another absorption band observed in the 400 nm region is due to the charge transfer transition from the p_π orbitals of the donor atoms of the ligand to $5f/6d$ orbitals of uranium. The bright colour of these complexes is due to such charge transfer transitions^{9,10}.

Thermal analysis of acetato complex of dioxouranium(VI) with IPH and its mixed ligand complex with DMSO were carried out in static air from ambient to $800\text{ }^\circ\text{C}$ at a heating rate of $10\text{ }^\circ\text{C}/\text{min}$ on a TG instrument. Acetato complex exhibited a two stage decomposition pattern. The complex is thermally stable upto $220\text{ }^\circ\text{C}$ beyond which it decomposes. From the mass loss data the final product of decomposition was found to be U_3O_8 (32.14 %) in acetato complex and 37.6 % in mixed ligand complex with DMSO. The final product of decomposition was found after 550 to $600\text{ }^\circ\text{C}$ in both complexes beyond which a plateau is observed in the TG curve.

X-Ray powder diffraction studies of the finely powdered sample of the compound $[\text{UO}_2(\text{IPH})_2(\text{OAc})_2]$ have been carried out in order to have an idea about the lattice dynamics of the compound. The data suggest an orthorhombic lattice to this derivative having unit cell dimensions; $a = 5.6781 \text{ \AA}$, $b = 4.7120 \text{ \AA}$, $c = 3.8752 \text{ \AA}$ and the Miller indices hkl along with relative intensity of peaks are recorded in Table-2.

TABLE-2
X-RAY POWDER DIFFRACTION DATA OF $[\text{UO}_2(\text{IPH})_2(\text{OAc})_2]$

2θ	$\text{Sin}^2 \theta$	d -spacing (\AA)	hkl	Rel. intensity %
13.9280	0.0147	6.3532	100	61.84
18.9224	0.02702	4.6861	010	35.75
20.9312	0.0329	4.2407	001	82.04
25.1663	0.0475	3.5358	110	70.36
25.6476	0.0493	3.4706	101	72.00
29.2935	0.0639	3.0464	011	39.26
34.0934	0.0859	2.6276	200	13.78

Antimicrobial activity of the ligand and its complex were done by disc diffusion method against *E. coli*, *S. aureus*, *P. aeruginosa*, *C. albicans* and *C. neoformans*. The results are given in Table-3. The complex showed moderate activity against *S. aureus* and *C. neoformans*. Ligand and the complex remained inactive towards *P. aeruginosa*. They exhibited mild activity towards *E. coli*.

TABLE-3
ANTIMICROBIAL ACTIVITY (DIAMETER OF INHIBITION ZONE IN mm)

	IPH	$[\text{UO}_2(\text{IPH})_2\text{Ac}_2]$
<i>E. coli</i>	7	7
<i>S. aureus</i>	6	17
<i>P. aeruginosa</i>	Nil	Nil
<i>C. albicans</i>	7	9
<i>C. neoformans</i>	12	15

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