

Synthesis, Characterization and Antimicrobial Activity of Dioxouranium(VI) Complexes with Schiff Base Ligand Containing Indole Ring

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Complexes of dioxouranium(VI) with the Schiff base derived from indole-2,3-dione (isatin) and hydrazine have been synthesized and their physico-chemical properties investigated using elemental analysis, molar conductance and spectral analysis (IR, UV-Visible and ¹H NMR). Various anions such as acetate, lactate, nitrate, perchlorate, sulphate and thiocyanate act as secondary ligands by coordinating to the metal ion. Mixed ligand complexes of UO₂(VI) with dimethyl sulfoxide or diphenyl thiourea and isatin-3-hydrazone have been synthesized and characterized. The ligand and some of the complexes were screened for their antibacterial and antifungal activities towards *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Cryptococcus neoformans* and *Candida albicans*

Key Words: Indole-2,3-dione, Hydrazine hydrochloride, dimethyl sulfoxide, Diphenyl thiourea, Isatin-3-hydrazone, Antibacterial, Antifungal activity.

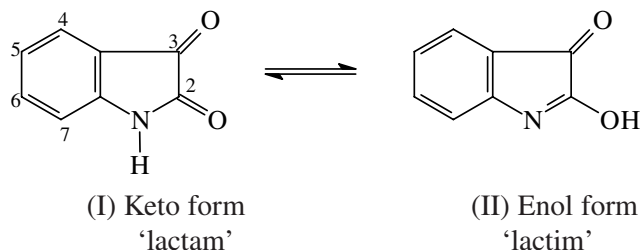
INTRODUCTION

Schiff bases and their metal complexes have been found to possess significant biological activities. Schiff base complexes continue to attract many researchers because of its wide application in the field of agriculture as pesticides and in medicine with their highly effective antibacterial and anticoagulant activities¹⁻⁵. Azomethine acts as herbicides, insecticides, nematocides, rodenticides and plant growth regulators. Although much attention has been directed to study the metal complexes of Schiff base ligands derived from isatin⁶, no investigation have appeared in literature to describe the metal complexation of isatin hydrazones with actinides.

Isatin or indole-2,3-dione is a unique molecule possessing both amide and ketocarbonyl groups. It has an active hydrogen atom attached to nitrogen (or oxygen) and an aromatic ring, which should substitute at 5 and 7 positions. It exists in tautomeric form and these functional characteristics

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play an important role in governing the various reactions of the molecule⁷. The C-3 carbonyl group of isatin is strongly electrophilic. As a result, isatin is readily involved in condensation and addition reactions. Isatin tautomerizes and exists between the lactam and lactim structures. X-ray diffraction by the crystal suggests that the lactam structure is dominant⁸.



In present paper, the synthesis, characterization and antimicrobial activities of dioxouranium(VI) complexes with isatin-3-hydrazone (INH) along with mixed ligand complexes of dimethyl sulfoxide (DMSO) or diphenyl thiourea (DPT) are reported.

EXPERIMENTAL

All chemicals used in the synthesis of ligand and complexes were of AR grade. Isatin-3-hydrazone was prepared by refluxing 1:1 molar alcoholic solutions of isatin and hydrazinedihydrochloride with an equimolar amount of sodium acetate trihydrate for about 8 h. The resultant liquid was concentrated and cooled to get reddish brown crystals of hydrazone. They were separated and recrystallized from alcohol (yield -70 %, m.p.-210 °C).

Acetato complex of uranium was prepared by refluxing alcoholic solutions of uranylacetatedihydrate and isatin-3-hydrazone in 1:2 molar ratio, 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 and dried *in vacuo* over phosphorous(V) oxide. Reddish brown crystalline solid was obtained with an yield *ca.* 75 %.

Nitrato, lactato, perchlorato, sulphato and thiocyanato complexes of uranium(VI) with isatin-3-hydrazone were synthesized from the acetato complex by substitution method⁹. Uranium(VI) acetato complex was dissolved in alcohol and treated with the respective anionic salt solutions *viz.*, LiNO₃, C₃H₅O₃Li, LiClO₄·3H₂O, Li₂SO₄·H₂O and NaNCS in appropriate molar ratios. They were mixed separately and refluxed on a water bath for about 6 h. The liquid mixture in each case was concentrated by evaporation and cooled to get crystals of the desired complex.

Mixed ligand complexes of uranium with isatin-3-hydrazone and DMSO or DPT were synthesized by refluxing alcoholic solutions of uranyl acetatedihydrate, isatin-3-hydrazone and DMSO or DPT in 1:2:2 molar ratio.

RESULTS AND DISCUSSION

All the complexes are found to be non-hygroscopic reddish brown crystalline solids. They are moderately soluble in methanol, nitrobenzene, acetonitrile and DMSO. Analytical data, molar mass and molar conductance data are given in Table-1. Molar conductance data reveal that the complexes behave as non-electrolytes indicating that the anions are coordinated to the metal ion. Metal content of the complexes were determined by oxalate-oxide method. IR spectra of the ligand and the complexes were recorded in the range 4000-400 cm⁻¹ employing KBr disc technique. UV-Visible spectra were recorded on a UV-Visible spectrophotometer in the range 200-600 nm. ¹H NMR spectra of the ligand and some of the complexes were recorded on a 300 MHz FTNMR spectrometer using deuterated acetone as solvent and TMS as reference material.

The ligand and the complexes were characterized on the basis of their IR spectra. IR spectra of complexes exhibit characteristic absorptions of all the functional groups of the ligand but with a downward shift in the case of coordinated groups. IR spectra of the complexes reveal the bidentate nature of the primary ligand by coordinating through carbonyl oxygen and azomethine nitrogen atoms. A strong absorption band observed at 1733 cm⁻¹ in the spectrum of the ligand is due to the >C=O stretching vibration of cyclic amido group, which shows a downward shift towards 1695 cm⁻¹ in the complexes, suggesting the coordination of carbonyl oxygen. An absorption band of medium intensity observed at 1614 cm⁻¹ in the spectrum of INH shifted to a lower wavenumber of 1590-1581 cm⁻¹ region in the complexes is attributed to >C=N group. Since the frequency is lowered by 25-30 cm⁻¹, the N atom of azomethine is coordinated to the metal ion. Therefore, it is inferred that the ligand INH acts as a bidentate chelating agent coordinating through the 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.

A strong band observed around 1007 cm⁻¹ in the spectra of mixed ligand complexes with DMSO reveals that the oxygen atom (>S=O) of DMSO is coordinated to the metal ion in a monodentate fashion. Mixed ligand complexes with DPT exhibited a sharp band at 1140 cm⁻¹, assignable to >C=S stretching frequency of diphenyl thiourea which is coordinated through S atom of >C=S group. Mixed ligand complexes with DPT show an additional band at 490 cm⁻¹ suggesting the presence of (U-S) bond.

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 OCO⁻ of monodentately coordinated acetate group. Similarly, the lactate group exhibits monodentate coordination through the oxygen

TABLE-1
ANALYTICAL DATA OF COMPLEXES

Complex	Elemental analysis %: Found (Calcd.)				Molar conductance ($\text{ohm}^{-1} \text{mol}^{-1} \text{cm}^2$)			Molar mass; found (calcd.)
	C	H	N	U	Methanol	Nitrobenzene	Acetonitrile	
$[\text{UO}_2(\text{INH})_2(\text{OAc})_2]$	33.35 (33.79)	2.17 (2.82)	11.39 (11.83)	33.69 (33.52)	13.26	8.25	14.10	705.38 (710.15)
$[\text{UO}_2(\text{INH})_2(\text{NO}_3)_2]$	26.49 (26.81)	1.64 (1.96)	15.19 (15.64)	33.59 (33.24)	5.63	4.20	17.23	712.54 (716.13)
$[\text{UO}_2(\text{INH})_2(\text{Lc})_2]$	34.14 (34.28)	3.02 (3.12)	10.49 (10.91)	31.14 (30.91)	8.64	2.58	15.73	764.63 (770.03)
$[\text{UO}_2(\text{INH})_2(\text{NCS})_2]$	30.24 (30.51)	1.65 (1.98)	15.29 (15.81)	33.54 (33.61)	3.63	10.75	9.78	705.25 (708.03)
$[\text{UO}_2(\text{INH})_2(\text{ClO}_4)_2]$	24.13 (24.27)	1.65 (1.77)	10.46 (10.62)	30.28 (30.09)	22.38	20.21	25.43	788.36 (791.03)
$[\text{UO}_2(\text{INH})_2\text{SO}_4]$	27.78 27.91	2.15 (2.04)	12.14 (12.21)	34.42 (34.59)	6.31	9.78	16.30	680.97 (688.03)
$[\text{UO}_2(\text{INH})_2(\text{DMSO})_2(\text{OAc})_2]$	33.01 (33.24)	3.14 (3.73)	9.20 (9.69)	27.63 (27.47)	15.73	2.58	8.64	816.28 (866.41)
$[\text{UO}_2(\text{INH})_2(\text{DPT})_2(\text{OAc})_2]$	46.94 (47.31)	3.24 (3.80)	11.46 (11.99)	20.58 (20.40)	12.20	8.31	6.36	1159.86 (1166.75)

atom of OCO⁻. Absorption bands observed at 1460, 1350 and 1000 cm⁻¹ in the spectra of nitrate complex are assigned to ν_4 , ν_1 and ν_2 vibrational modes, respectively of coordinated nitrate. Since the frequency separation between ν_4 and ν_1 is of the order 100-150 cm⁻¹, it is inferred that the nitrate ion is coordinated in a monodentate fashion. Perchlorato complexes show strong absorption bands at 1130 and 1042 cm⁻¹, which are the split components of ν_3 , revealing monodentate coordination of ClO₄⁻. Thiocyanato complex exhibits a sharp band at 2063 cm⁻¹ due to the C-N stretching vibration of thiocyanate. Another band of medium intensity observed at 780 cm⁻¹ is attributed to the >C=S stretching frequency of coordinated NCS⁻. Since the >C=S absorption frequency is more than 720 cm⁻¹ and the C-N stretching frequency is less than 2100 cm⁻¹, it is inferred that the thiocyanate ion is coordinated to the metal ion through N atom. IR spectra of sulphato complex displayed three bands around 1240, 1167 and 1076 cm⁻¹ which arises due to the splitting of the ν_3 vibrational mode of coordinated sulphate ion, revealing the bidentate chelating nature of sulphate¹⁰.

A sharp intense band observed in the region 920-930 cm⁻¹ is assigned to the asymmetric stretching vibration of uranyl ion (O=U=O). Since the symmetric stretching vibration at 840 cm⁻¹ is not seen in the spectra it is confirmed that the oxygen atoms of the uranyl ion are in *trans*-positions in all these complexes.

Electronic spectra of the ligand INH show absorption bands at 258 nm and 360 nm which are assigned to the $n \rightarrow \pi^*$ transitions of >C=O and >C=N groups, respectively. But the spectra of the complexes exhibited blue shift for the $n \rightarrow \pi^*$ transitions of both >C=O and >C=N groups suggesting the involvement of non-bonding electrons of oxygen and nitrogen atoms in coordination with the metal ion. Electronic spectra of all the complexes exhibited red shift for $\pi \rightarrow \pi^*$ transitions of >C=O and >C=N groups, suggesting the coordination of lone pair electrons of oxygen and nitrogen atoms to the metal ion.

¹H NMR spectra of INH and some of the complexes were recorded in an FT NMR instrument. NMR spectra of INH shows a singlet at δ 10.7 ppm due to the proton of cyclic amido group while the protons of -NH₂ group gives a singlet at δ 11.3 ppm. Appearance of these signals at the same chemical shift positions in the complexes too indicate that these N atoms are not involved in coordination. Multiplets observed at δ 6.8-7.3 ppm are assigned to the protons of heterocyclic ring. The appearance of a signal due to the -NH- proton of cyclic amido group at the same δ value is an additional evidence for the existence of lactam-lactim equilibrium in the keto form indicating the involvement of the oxygen atom of position 2 of isatin moiety as actual keto group. As evident from the IR spectra, NMR spectral data further confirms that the ligand INH is coordinated to the

metal ion through the oxygen and nitrogen atoms of $>C=O$ and $>C=N$ groups, respectively, but not through the N atom of amino group. Therefore, it is inferred that INH acts as a neutral bidentate chelating agent.

On the basis of these spectral and analytical investigations the following molecular formulae were suggested for the complexes: $[UO_2(INH)_2X_2]$, $[UO_2(INH)_2Y]$, $[UO_2(INH)_2(DMSO)_2(OAc)_2]$ and $[UO_2(INH)_2(DPT)_2(OAc)_2]$ where 'X' represents monovalent anions such as CH_3COO^- , NO_3^- , NCS^- , $C_3H_5O_3^-$, ClO_4^- and 'Y' represents bivalent SO_4^{2-} ion. Uranium exhibits a coordination number 8 in its complexes with INH while in the mixed ligand complexes with DMSO or DPT the coordination number was found to be 10.

Antimicrobial activity: The ligand INH and some of its complexes were screened for their antibacterial and antifungal activities against *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* and *C. neoformans* by agar diffusion method. Complexes such as $[UO_2(INH)_2(OAc)_2]$ and $[UO_2(INH)_2(DPT)_2(OAc)_2]$ are found to be moderately active against *S. aureus* and *Cryptococcus neoformans* but weakly active against *C. albicans*. Mixed ligand complex with DMSO was found to be highly active against *S. aureus* and *C. albicans* but it exhibited only moderate activity against *C. neoformans*. The ligand and the complexes were found to be inactive towards *E. coli* and *P. aeruginosa* except the mixed ligand complex with diphenyl thiourea, which exhibited mild activity against *E. coli*. Anyhow, the complexes are found to be more active than the free ligand, which is consistent with the reports that antibacterial properties of organic compounds are considerably enhanced by complexation with metal ions because metal complexes may serve as a vehicle for activation of ligand as the principal cytotoxic species.

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