



Synthesis, Characterization and Biological Activity of Dioxouranium(VI) Complex of Thiosemicarbazone

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ABSTRACT

The reaction of uranyl acetate with (E)-2-(2-(2-carbamothioylhydrazono)-2-phenylethylthio)acetic acid (H₂L) tridentate ligand in ethanol yields the [UO₂(L).H₂O] complex. Characterization of ligand and its dioxouranium complex has been carried out by elemental analysis, IR, Uv-Visible, ¹H NMR and mass spectra. Also, thermal analyses (TG and DTG) and molar conductivity measurements were conducted. The thermal behavior of the complex showed the lost of water molecule initially followed by decomposition of the remaining complex molecule in the subsequent steps. Antimicrobial screening of the free ligand and its complex showed that, the free ligand and metal complex possess significant antimicrobial activity towards two types of bacteria and two types of fungi.

Key words: Thiosemicarbazone, Dioxouranium(VI), Thermal analysis, Antimicrobial activity.

INTRODUCTION

Thiosemicarbazones are interesting ligands¹⁻³ with potential sulfur and nitrogen donors and have gained special attention not only because of the structural chemistry of their multifunctional coordination modes, but also because of their importance in analytical chemistry as well as biological activity. These compounds are good chelating ligands and have been used widely for extraction and spectrophotometric determination of several metal ions including uranium(VI)⁴⁻⁹. The strong impetus towards developing the coordination

chemistry of thiosemicarbazones stemmed from their remarkable biological activities which have been observed due to their metal complexing ability^{10,11}. Biological activities of the metal complexes differ from those of either the ligand or the metal ion itself, and increased and/or decreased biological activities are reported for various metal complexes. Uranium ions have attracted considerable interest because of their reactivity, coordination behavior, bonding interactions between the metal center and ligand and their possible applications, in recent years^{12,13}. Uranium chemistry is dominated by the uranyl ion, UO₂²⁺, because of its own peculiar

structure and its coordination chemistry¹⁴⁻¹⁶. Dioxouranium complexes have been studied extensively, because of the theoretical interest in the linear O=U=O group present in them^{17,18}. The metal–oxygen linear bonds of the uranyl ion are incredibly strong, unreactive, highly soluble and mobile in water. Because of these factors it is difficult to clean up water contaminated with uranyl ion and the problem becomes aggravated if uranium ion is radioactive. Hence, U(VI) quantification in environmental and biological samples is essential in order to assess the level of this ion in these matrices from the point of view of safety and economy. The ability of uranium to form complexes has been utilized for cleaning up uranium contamination in soils and in the nuclear industry where chelating agents are common constituents of fluids used to clean reactors.

By considering the emerging interest of dioxouranium(VI) in the medicinal chemistry, coordination chemistry and nuclear industry, we have synthesized a new ligand phenacyl thioacetic acid thiosemicarbazone (H_2L) and studied its coordination to dioxouranium(VI). The synthesized ligand and complex were characterized by elemental, spectral and thermal studies, and studied the antimicrobial activities of the free ligand and its complex.

EXPERIMENTAL

All reagents and solvents (Sigma-Aldrich), were of analytical grade and used without further purification. All reactions were carried out in carefully dried, freshly distilled solvents. Thermo-Nicolet FT-IR, Nicolet IR-200, USA spectrophotometer was used to record the IR spectra ($4000-400\text{ cm}^{-1}$) of the free ligand and its complex as KBr pellets. Elemental analyses were carried out using a Perkin Elmer 2400 and ^1H NMR spectra were recorded on Bruker AMX-300 MHz spectrometer operating at 300 MHz. Thermogravimetric experiments were carried out using NETZSCH STA409 simultaneous thermal analyzer with the heating rate of $10\text{ }^\circ\text{C}/\text{min}$.

Synthesis of ligand H_2L

Phenacyl thioacetic acid¹⁹ was prepared following the literature procedure and thiosemicarbazide was purchased. A solution of

0.091 g (1 mmol) of thiosemicarbazide in 1,4-dioxane (30 mL) was added drop wise to a solution of 0.210 g (1 mmol) of phenacyl thioacetic acid in 1,4-dioxane (10 mL). The mixture was refluxed for one hour, then concentrated to 20 mL and cooled to room temperature. A yellow solid obtained was collected by filtration, washed with cold ethanol and dried in vacuum. Yield: 0.22 g (92%). M.p.: $140\text{ }^\circ\text{C}$. Elemental analyses, Found (Calcd.) for $C_{11}H_{13}N_3S_2O_2$: C, 46.32 (46.62); H, 4.61 (4.62); N, 14.78 (14.83); S, 22.76 (22.63) %. Mass spectrum [m/z (%): 283 (100) [M^+]. IR data (KBr, cm^{-1}): 3443 $\nu(\text{NH}_2)$; 3287, 3165 $\nu(\text{NH})$; 1694.3 $\nu(\text{COOH})$; 1588.0 $\nu(\text{C}=\text{N})$; 834 $\nu(\text{C}=\text{S})$. ^1H NMR ($\text{DMSO}-d_6$): δ 3.63 (2H, s, CH_2S) δ 4.01 (2H, s, $\text{S}-\text{CH}_2-\text{C}=\text{O}$), δ 7.37-8.02 (5H, m, Ar-H), δ 8.41 (2H, bs, NH_2); δ 10.38 (s1H, bs, NH); δ 12.77 (1H, s, COOH).

Synthesis of complex

10 mL of hot ethanolic solution of H_2L (0.284 g, 1 mmol) and $[\text{UO}_2(\text{O}_2\text{CMe})_2] \cdot 2\text{H}_2\text{O}$ (0.424 g, 1 mmol) were mixed with constant stirring till a clear dark yellow solution was formed. The solution was refluxed for 3 h and the mixture was cooled to room temperature. The yellow solid obtained was filtered and washed with 50% ethanol and dried under vacuum over P_4O_{10} . Yield: 0.14 g (76%). M.p.: $406\text{ }^\circ\text{C}$. Elemental analyses, Found (Calcd.) for $C_{11}H_{13}N_3S_2O_5U$: C, 23.81 (23.20); H, 2.33 (2.30); N, 7.34 (7.38); S, 11.21 (11.26) %. Mass spectrum [m/z (%): 569.40 (100) [M^+]. IR data (KBr, cm^{-1}): 3265 $\nu(\text{NH}_2)$; 1590. $\nu(\text{COOH})$; 1521.0m $\nu(\text{C}=\text{N})$; 822 $\nu(\text{C}=\text{S})$; 423.0 $\nu(\text{M}-\text{N})$.

Antimicrobial activity

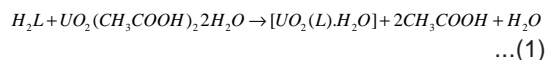
The antibacterial activities of both H_2L and complex were evaluated against the growth of *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) at different concentrations by disc diffusion technique adopting the experimental method of Benson²⁰. Twenty-five milliliters of sterilized nutrient agar media (NA) was purged in each Petri plates. After solidification, 0.1 mL of test bacteria was spread over the medium using a spreader. The test compounds in measured quantities were dissolved in DMF to get concentrations of 100, 50, 25 $\mu\text{g mL}^{-1}$. A control test was performed with test medium supplemented with DMF following the same procedures. The disc of Whatmann No. 1 filter paper having the diameter

5.00 mm each containing (1.5 mg cm⁻¹) of test compound was placed at four equidistant places at a distance of 2 cm from the center in the inoculated Petri plates. Penicillin was used as a standard. Petri plates were kept in refrigerator for 24 h for pre-diffusion and then incubated at 37° C for 24 h. All tests were carried out in triplicate.

The preliminary fungitoxicity screening of the compounds at different concentrations were performed against the test fungi, *Aspergillus niger* and *Helminthosporium oryzae* along with the standard fungicide Griseofulvin. Potato-dextrose agar (PDA) was used to evaluate the effect of the selected compounds under investigation on the mycelial linear growth of two tested fungi²¹. A zero(0) concentration treatment was prepared for each fungus, which contains equivalent volume of solvent only, and used as control. The fungal (48 h) cultures from slants were diluted with sterile water and mixed thoroughly to prepare a clear homogeneous suspension. The suspensions were uniformly spread over potato Dextrose broth and incubated at room temperature for 3 days at 420 rpm. The bacterial and fungal lawns were prepared by spread plate method.

RESULTS AND DISCUSSION

The ligand is derived from the condensation of phenacylthioacetic acid with thiosemicarbazide and is abbreviated H₂L (Fig. 1). Dioxouranium(VI) complex has been synthesized by the reaction between the ligand and metal-acetate in ethanol. The elemental analyses (Table 1) and EI mass spectrum of the ligand confirms the molecular formula as by showing the M⁺ peak at m/z 283 which is agreed with calculated mass m/z of 283.7. The other peaks are observed at m/z 44, 54, and 65 corresponds to various fragments of the ligand. In the free ligand the signal at δ 10.3 has been assigned to the hydrazine proton (NH) proves the thione form of the ligand, where as the missing signal for the hydrazinic proton in synthesized complex proves the ligand being in the tautomeric form. The two tautomeric forms of synthesized ligand H₂L in equilibrium are shown in Fig. 2. The metal chelate in the present investigation was prepared according to the Eq:



The complex being non-hygroscopic and stable in air, but insoluble in common organic solvents. The molar conductivity of the complex in DMF is very low, which suggests the nonelectrolytic nature²².

Infrared Spectroscopy

The characteristic IR bands of the complex (Fig. 3) differ from free ligand providing significant indications about the coordination and bonding sites of the ligand. The characteristic IR bands at 3443 cm⁻¹ can be assigned to the asymmetric ν(N-H) vibration of the terminal NH₂ group of ligand. The absence of large systematic shifts of ν_{as}(NH₂) and ν_{sym}(NH₂) modes at lower frequencies indicates no interaction between the terminal amino nitrogen of ligand and the metal ion on complexation. The other bands at 3287 and 3165 cm⁻¹ may be due to the symmetric ν(N-H) vibrations of the amino and imino groups. The appearance of a strong imine absorption at 1588 cm⁻¹ is due to ν(C=N). The coordination of the azomethine nitrogen to the metal center was confirmed in the IR spectra of complex by a shift of the ν(C=N) band to lower frequencies²³, along with the occurrence of a ν(N-N) band at higher frequency, relative to that of the free ligand. Additional evidence for coordination of the azomethine nitrogen is the presence of ν(M-N) bands in 425-455 cm⁻¹ range²⁴. The IR spectrum of the ligand shows a band at 1694 cm⁻¹, due to stretching frequency of (C=O) carboxylic group. In the IR spectra of complex, the band observed at 1590 cm⁻¹ corresponding to the coordinated carboxyl group²⁵. This indicates the coordination of metal ion to carboxylic group on deprotonation. The band at 834 cm⁻¹ which ascribed to the ν(C=S) stretching and bending vibration of thioamide group of the free ligand, are shifted to lower values (822 cm⁻¹), indicating coordination via thiolate sulfur in the complex²⁶. The complex exhibit strong bands in the region ~930-920 cm⁻¹ and the medium intensity band at ~840-820 cm⁻¹ which are assigned to ν_{as}(O=U=O) and ν_s(O=U=O) mode respectively²⁷. This indicates the presence of *trans*-UO₂ group in the complex²⁸. Besides these bands, a broad band at 3500 cm⁻¹ due to ν(O-H) of coordinated water

molecule is observed in the spectrum of complex and was also confirmed by elemental analyses and thermogravimetric analyses.

Electronic spectra and molar conductivity

The electronic spectra of the ligand and dioxouranium(VI) complex were recorded in DMF solution at room temperature. as a solvent. Solution of the free ligand, recorded in the 200-800 nm exhibited bands in the range 250-280 and 300-340 nm assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions associated with the azomethine linkage. These bands suffer marginal shifts on complexation. The

electronic spectrum of the yellow dioxouranium(VI) complex arise from the electronic transition of metal^{VI}ligand charge transfer. This is an allowed transition and produces broad, intense absorption at 600 nm tailing into the visible region which produce the intense yellow color. The magnetic measurement of the dioxouranium(VI) complexes are independent of field strength and temperature and the ground states of dioxouranium(VI) compounds contain no unpaired electrons the compounds are therefore weakly diamagnetic as expected²⁹. Molar conductivity of dioxouranium(VI) complex was $4.5 \text{ Ohm}^{-1}\text{Cm}^2\text{mol}^{-1}$, indicating a non-electrolyte.

Table 1: Analytical and physical data of H₂L and its complex

Compound	Colour	M.p Yield (%)	Elemental analysis found (Calculated) (%)			
			C	H	N	S
Ligand	Yellow (98)	143	46.32 (46.62)	4.61 (4.62)	14.78 (14.83)	22.76 (22.63)
Complex	Brown (76)	>400	24.65 (24.89)	3.34 (3.4)	6.63 (6.34)	10.12 (10.110)

$n \rightarrow \pi$

Table 2: Antibacterial activities of ligand and complexes

Compound	Zone of Inhibition in (mm)					
	Bacteria					
	<i>Staphylococcus aureus</i>			<i>Escherichia coli</i>		
	100 ppm	50 ppm	25 ppm	100 ppm	50 ppm	25 ppm
H ₂ L	8	5	3	9	5	3
Complex	12	7	4	11	6	5
Penicillin	12	8	-	10	7	-

Table 3: Antifungal activities of ligand and complexes

Compound	Zone of Inhibition in (mm)					
	Fungi					
	<i>Aspergillus niger</i>			<i>Helminthosporium oryzae</i>		
	100 ppm	50 ppm	25 ppm	100 ppm	50 ppm	25 ppm
H ₂ L	10	6	3	7	5	4
Complex	12	9	5	11	8	5
Griseofulvin	12	8	-	10	7	-

¹H NMR Spectra

The ¹H NMR spectra of the complex showed subtle difference in comparison to the free ligand. The ¹H NMR spectra of the ligand (H₂L) showed sharp singlets at δ 3.6 and δ 4.01 corresponding to CH₂S and S-CH₂-C=O. In the free ligand the single broad peak at δ 10.3 is assigned to the hydrazinic proton (NH). Absence of NH signal in the ¹H NMR spectrum of the complex indicates the thione form of the ligand in the solution indicating

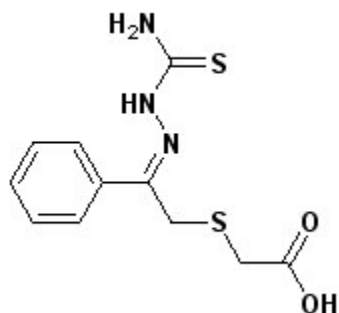


Fig. 1: Thiosemicarbazone ligand (H₂L)

the thioenolization³⁰. A broad singlet at δ12.77 is assigned to the carboxylic OH proton which was confirmed by deuterium exchange. The absence of proton signal at δ12.77 for carboxylic proton in the complex confirms the coordination of carboxylic oxygen after deprotonation in the complex.

Thermal study

The TG and DTG study of the complex recorded in the nitrogen atmosphere at constant heating rate of 10 °C/min is shown in Fig. 4. The TG of the complex indicates four steps in the decomposition process in the temperature range of 10-800 °C. In the first step of decomposition, there was a weight loss of 3.5 %, as against the calculated weight loss of 2.7% indicating loss of water molecule. The DTG of the uranyl complexes displayed an endothermic peak in the range, 160-240 °C, which confirms the presence of coordinated water molecule. The complex showed the second step decomposition between 188.3 °C and 343.5 °C due to removal of coordinated anions and half of the ligand. Finally the complex undergoes

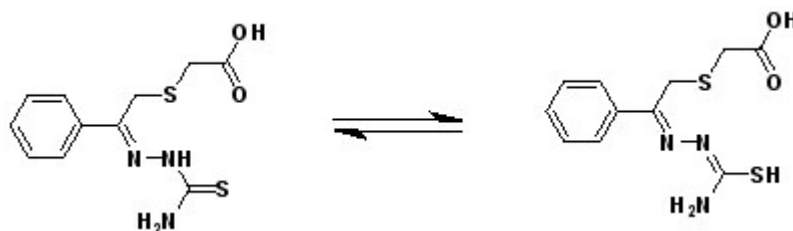


Fig. 2: Tautomeric forms of thiosemicarbazone

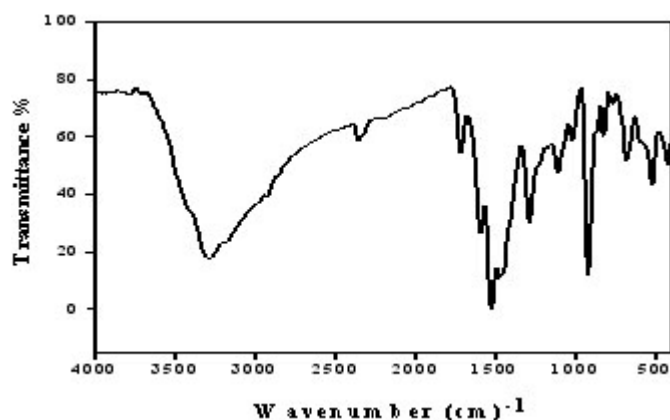


Fig. 3: IR spectrum of the dioxouranium complex

decomposition between 354-500 °C due to complete loss of remaining ligand. The residue at 800 °C confirms the formation of UO_3 which was further reduced to U_3O_8 as reported³¹.

Antimicrobial activity

The biological activity of new thiosemicarbazone, H_2L and its complexes were evaluated against *Staphylococcus aureus* and *Escherichia coli* bacteria and *Aspergillus niger*, *Helminthosporium oryzae* fungi using Penicillin and Griseofulvin as the reference. The obtained results

for antimicrobial studies have been reported in Table 2. Antifungal activity of the ligand and complex has been reported in Table 3. It is evident from the results that the ligand and the complex have good inhibitory action against the all microorganisms tested. Significantly higher inhibitory activity was displayed by the dioxouranium complex than that of the free ligand H_2L . It has also been observed that concentration played an important role in increasing the degree of inhibition; as the concentration increased, the activity also increased³².

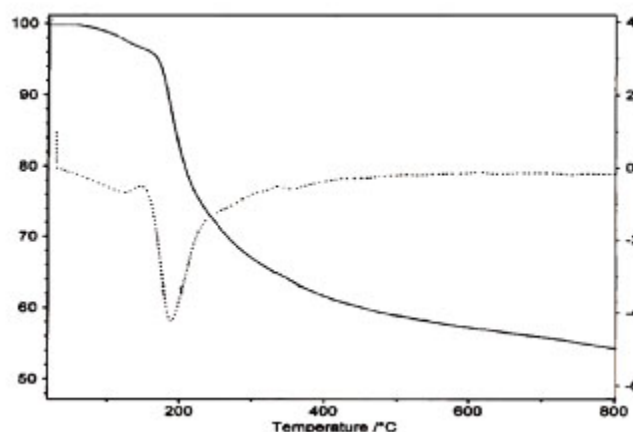


Fig. 4: TG-DTG curve of the complex

CONCLUSION

A new ligand, phenacyl thioacetic acid thiosemicarbazone (H_2L) was synthesized and its dioxouranium complex was prepared. Both compounds were characterized by physicochemical and spectroscopic methods. As per the spectral and thermal studies the ligand coordinated to dioxouranium ion through azomethine nitrogen, carboxylic and thiolate functional groups. The results of antimicrobial activity indicated that dioxouranium complex has a better inhibition than the free ligand against bacteria and fungi.

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