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SYNTHESIS, CHARACTERIZATION, THERMAL AND KINETIC STUDIES OF LANTHANUM (III), THORIUM (IV) AND DIOXOURANIUM (VI) CHELATES WITH MULTIDENTATE LIGAND AND ITS *IN VITRO* ANTIBACTERIAL ANALYSIS

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ABSTRACT: Metal Complexes of lanthanum (III), Thorium (IV) and dioxouranium (VI) with Schiff base ligand ethyl 2-[[*(2E, 3Z)*-4-hydroxypent-3-en-2-ylidene] amino}-4, 5, 6, 7-tetrahydro-1-benzothiophene-3-carboxylate were prepared. All synthesized complexes were identified and confirmed by elemental analysis, molar conductance measurements and spectral analysis (UV-visible, IR and ¹H NMR). The conductance measurement suggested the non-electrolyte nature of the complexes and they were isolated in 1:2 (M: L) ratio. The thermal behavior (TGA/DTA) of the complexes was studied and kinetic parameter was determined by Coats-Redfern method. The data from thermo gravimetric analysis clearly indicates that decomposition of the complexes proceeds in two or three steps. The decomposition of all the complexes ended with the metal oxide. These metal complexes also showed its potential as an antibacterial agent against pathogenic strains causing urinary tract infections.

INTRODUCTION: Co-ordination chemistry of lanthanides and actinides is one of the active research fields in inorganic chemistry ¹⁻⁴. Lanthanides and actinides ion generally present a high coordination number and the type of polyhedron obtained influences the nature of the coordinating ligands. Lanthanum (III), Thorium (IV) and Uranium (VI) with small atomic radii and a high positive charge fulfills the optimum conditions for formation of complexes with high coordination number ⁵⁻⁷. Although metal complexes of heterocyclic Schiff base with d-block elements have been extensively studied, those of lanthanides and actinides have received less interest so far.

Schiff base ligand with thiophene moiety deserve special important because of the bioisosteric relationship of thiophene to benzene that has led to several biological studies. Both Lanthanide and actinide complexes are known to have antimicrobial properties ^{8, 9}. Generally metal complexes show better antibacterial activity as compared to the metal itself due to various factors like chelation, stability and presence of more than one active site ¹⁰.

With the evolution of super bugs like Extended Spectrum β -lactamase (ESBL) and Metallo- β -lactamase (MBL) producers which secrete enzymes that hydrolyse 3rd generation cephalosporins and Carbapenem antibiotics respectively, there is currently a need for alternate therapeutic agents ¹¹.

In this investigation, substituted 2-amino thiophene namely ethyl 2-amino-4, 5, 6, 7 tetrahydrobenzo (b) thiophene 3-carboxylate has been condensed with (*3Z*)-4-hydroxypent-3-en-2-one to form a

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potentially tridentate ligand viz ethyl 2-[[*(2E,3Z)*-4-hydroxypent-3-en-2-ylidene]amino]-4, 5, 6, 7-tetrahydro-1-benzothiophene-3-carboxylate have been synthesized and characterized by their elemental analysis, UV, IR and NMR studies. This ligand was used to synthesize Ln(III), Th(IV) and UO₂(VI) complexes. The complexes were characterized by elemental analysis, Molar conductance, along with electronic, infrared and NMR spectral analysis and further screened for its antimicrobial activity against gram negative ESBL and MBL producing uropathogens.

MATERIALS AND METHODS: All chemical used in the project work were of AR grade and was recrystallised while the solvent were purified and double distilled before use. Metal content was determined by the standard methods¹². Lanthanum, thorium and uranium were estimated by decomposing the complexes with boiling concentrated nitric acid and precipitating the metal hydroxide. The precipitate was filtered on Whatman filter paper and washed with distilled water. It was finally ignited and weighed as La₂O₃, ThO₂ and U₃O₈ respectively.

Molar conductance was measured in DMF (10⁻³ M solution) on an ELICO Digital Conductivity meter Model CM-180. The electronic spectra of the complex in DMF were recorded on UV-Systronic spectrophotometer. The IR spectra of these complexes were recorded in KBr disc on a Perkin Elmer Model 1600 FTIR Spectrophotometer. The ¹H-NMR Spectra was recorded in DMSO on a VXR-300S Varian Supercon NMR Spectrometer using TMS as the internal reference. Thermo gravimetric studies of the complex were done on Netzch-429 Thermoanalyser recording at a rate of 10°C min⁻¹.

Preparation of ligand: Ethyl 2-amino-4, 5, 6, 7 tetrahydrobenzo(b)thiophene 3-carboxylate is prepared according to a reported method¹³. To a solution of this thiophene derivative (0.01mol)

prepared in ethanol (20ml), a solution of (*3Z*)-4-hydroxypent-3-en-2-one (0.01mol) in ethanol (10ml) was added in small portion with constant stirring. The resulting solution was refluxed on a water bath for about four hours. On cooling the solution, the Schiff base crystallized. It was then filtered, washed and vacuum dried.

Further purification was done by crystallization from ethanol (MP 142°C).

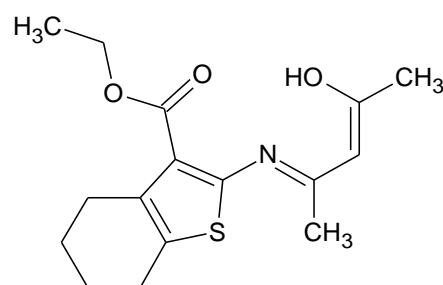


FIGURE 1: ETHYL 2-[[*(2E, 3Z)*-4-HYDROXYPENT-3-EN-2-YLIDENE]AMINO]-4,5,6,7-TETRAHYDRO-1-BENZOTHIOPHENE-3-CARBOXYLATE

Preparation of metal complexes: The metal complexes were prepared by the following general procedure. To a magnetically stirred and warmed ethanolic solution (20ml) of the ligand (0.02mol) was added an ethanolic solution of metal salts (0.01) dissolved in ethanol (10ml) in small volumes. After complete additions of the metal salt solution, the pH was adjusted to 7.5 by adding ethanolic ammonia. It was then refluxed for six hours in a water bath and the resulting solution was reduced to half the initial volume and allowed to stand overnight. The complex formed was filtered, washed successively with aqueous ethanol and ether. Finally the complex was dried in vacuum over P₄O₁₀.

Test organisms used in the study: 19 MDR (Multi-Drug Resistant) gram negative uropathogens were used in the study including 6 ESBL (Extended spectrum β-lactamase) and 7 MBL (Metallo-β-lactamase) producers (Table 1).

TABLE 1: TEST ORGANISMS USED IN THE STUDY

ESBL Producing uropathogens	MBL Producing uropathogens	Non- ESBL and MBL Producing MDR uropathogens
<i>E. coli</i> strain 1	<i>E. coli</i> strain 1	<i>Proteus vulgaris</i>
<i>Citrobacter diversus</i> strain 1	<i>E. coli</i> strain 2	<i>Proteus mirabilis</i>
<i>E. coli</i> strain 2	<i>Pseudomonas aeruginosa</i>	<i>E. coli</i>
<i>Pseudomonas aeruginosa</i>	<i>E. coli</i> strain 3	<i>Morganella morganii</i>
<i>Citrobacter diversus</i> strain 2	<i>Klebsiella pneumonia</i> strain 1	<i>C. diversus</i>
<i>Proteusvulgaris</i>	<i>Klebsiella pneumonia</i> strain 2	<i>Pseudomonas aeruginosa</i>
	<i>C. diversus</i>	

Antimicrobial susceptibility of uropathogens:

Antibiotic sensitivity test of the pathogens was carried out using Kirby Bauer method so as to obtain Antibiogram pattern¹¹.

Antibacterial activity: Antibacterial activity of the metal complexes was determined by Agar cup method. The metal complexes were dissolved in HPLC grade ethanol to obtain final concentration of 200 µg/µl. A loopful of the test isolates were inoculated in 10 ml of Brain Heart infusion (BHI) broth and incubated at 37°C for 24 hours in order to obtain actively growing log phase isolates. Sterile 20 ml of Luria Bertani agar was melted cooled to around 40°C and 0.4 ml test strain (0.1 O.D. at 530nm) was seeded and poured into a 9cm diameter aneubra Petri plates.

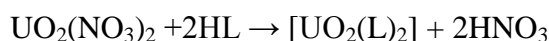
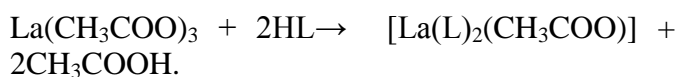
Using a sterile cork borer (8 mm in diameter), wells was punched in each plate after solidification of the medium. 50 µl of the test sample (metal complex) was then added to the wells and incubated at 37°C for 24 hours to observe the zones of inhibition against each metal complex. Control wells were also set up using 50 µl of ethanol (solvent) for each isolate. The mean value obtained for three individual replicates was used to calculate the zone of inhibition for each isolate^{14, 15}.

TABLE 2: PHYSICO-CHEMICAL CHARACTERISTICS OF SCHIFF BASE LIGAND AND ITS METAL COMPLEXES

Compound	Color	F. Wt	Elemental analysis (%) Found (calcd)				Molar Cond. (Ω ⁻¹ cm ² mol ⁻¹)
			C	N	S	M	
HL	Yellow	307.41	62.51 (63.02)	4.56 (3.86)	10.43 (9.56)	-	-----
[La(L) ₂ (CH ₃ COO)]	Off white	811.75	49.43 (50.31)	2.83 (3.45)	8.18 (7.90)	15.85 (17.11)	20.53
[Th(L) ₂ (NO ₃) ₂]	Royal crown	968.85	37.92 (39.67)	4.97 (5.78)	6.55 (6.62)	22.90 (23.95)	15.68
[UO ₂ (L) ₂]	Mercedes red	882.83	42.65 (43.54)	2.98 (3.17)	6.60 (7.26)	25.74 (26.96)	17.86

Infrared spectra: The important infrared frequency along with their assignments of ligands and their complexes are systematically given in **Table 3**. In the metal complexes, the ν(C=N) is displaced to lower wave number by about 20-30 cm⁻¹ on bond stabilization of the azomethine moiety upon coordination. The bond corresponding to the ester ν(C=O) has been shifted to lower frequency by about 30-35cm⁻¹ in the metal complexes indicating coordination by ester function¹⁷. A broad band at 3200cm⁻¹ which is assigned to the enolic OH group of the (3Z)-4-

RESULTS AND DISCUSSION: Analytical data indicated that ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate condensed with (3Z)-4-hydroxypent-3-en-2-one in 1:1 molar ratio and the product formed well defined complexes with the metal salts. Formation of the complexes can be symbolized as follows:



HL= ethyl 2-[[[(2E,3Z)-4-hydroxypent-3-en-2-ylidene]amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate

Formulation of the complexes has been based on their elemental analytical data, molar conductance values and thermogravimetric data. All complexes are brightly colored, stable and non-hygroscopic in nature. The complexes are insoluble in common organic solvent but soluble in DMF and DMSO and decomposed above 180°C. The molar conductance values support the non-electrolyte nature of the metal complexes¹⁶ as shown in **Table 2**.

hydroxypent-3-en-2-one moiety, this band disappears in the complexes indicates deprotonation of enolic group, which lead to a six-membered ring structure around metal ions. A strong band around 2930 cm⁻¹ due to ν(C-H) of cyclohexane did not show any appreciable change in metal complexes. The IR spectra of lanthanum complex display frequency band at 1425cm⁻¹ and 1234cm⁻¹ attributed to ν_a and ν_s respectively of acetate ion. This indicative of the coordination of the carboxylates ion whose free ν_a and ν_s display at around 1414 and 1100cm⁻¹ respectively.

The position of these bands in the complexes reveals the mode of coordination. The difference in the ν_a and ν_s in the complex which is 191cm^{-1} indicates a bridging coordination mode¹⁸. The nitrate complex of thorium show six NO stretching frequency bands, this is expected for its C_{2v} symmetry. A comparison of six infrared bands in Th^{+4} complex which occurs at $1520 (\nu_4)$, $1280 (\nu_1)$, $1038 (\nu_2)$, $800 (\nu_6)$, $736 (\nu_3)$ and $680 (\nu_5)$ with the known band of $\text{Th} (\text{NO}_3)_4 \cdot 5\text{H}_2\text{O}$ ¹⁹ in which bidentate character of the nitrate group has been established by X-ray diffraction²⁰ and Neutron diffraction studies²¹.

The magnitude of $\nu_4-\nu_1$ (240cm^{-1}) and $\nu_3-\nu_5$ (56cm^{-1}) further indicates the coordination of nitrate group

TABLE 3: IMPORTANT IR SPECTRAL BANDS OF SCHIFF BASE AND ITS METAL COMPLEXES

Compound	$\nu(\text{O-H})$	$\nu(\text{C=O})$	$\nu(\text{C=N})$	$\nu(\text{C=S})$	$\nu(\text{M-O})$	$\nu(\text{M}\leftarrow\text{O})$	$\nu(\text{M}\leftarrow\text{N})$	$\nu(\text{O=U=O})$
HL	3200br	1700s	1658s	608s	-----	-----	-----	
$[\text{La}(\text{L})_2(\text{CH}_3\text{COO})]$	-----	1670s	1635s	608s	548m	514m	478m	
$[\text{Th}(\text{L})_2(\text{NO}_3)_2]$	-----	1668s	1628s	610s	552m	519m	487m	
$[\text{UO}_2(\text{L})_2]$	-----	1675s	1643s	609s	570m	510m	467m	950s, 840m

HL= ethyl 2-[(2E, 3Z)-4-hydroxypent-3-en-2-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate

Proton NMR spectral data of the ligand supported the conclusion drawn on the basis of UV and IR spectral data. The absence of NH_2 proton signal in the NMR spectrum of ligand in DMSO-d_6 indicates successful Schiff base formation by replacement of the C=O group of (3Z)-4-hydroxypent-3-en-2-one. A signal at 13.2δ indicates the enolic proton and therefore the weakest shielded proton in the molecule. The disappearance of the signal at 13.2δ was confirmed to the fact that the ligand underwent deprotonation of the enolic OH group during complexation with the metal ions. The signal at 1.50δ (d) and 4.30δ (m) can be assigned for methyl and methylene proton respectively of the ester group. Two multiplets centered at $2.6-2.7 \delta$ and doublet at 1.2δ in the ligand and metal complexes are due to different hydrogen atom of the tetrahydrobenzothiophene ring. A signal at 5.8δ and 2.0δ is due to methine and two methyl group proton respectively.

The electronic absorption spectrum of the ligand in alcohol shows an intense band at 285nm may be assigned to intraligand $\pi \rightarrow \pi^*$ transition which is nearly unchanged on complexation, a broad band at 340 and 360nm may be assigned to the $n \rightarrow \pi^*$ and charge transfer transition of the azomethine and ester C=O group^{23, 24}.

in bidentate fashion. The presence of nitrate ion on the coordination sphere in Th (IV) complexes has also been supported by non-electrolyte nature of complex in DMF. The uranyl complex exhibit a strong band at 950cm^{-1} and the medium intensity band at 840cm^{-1} assignable to $\nu_{as}(\text{O=U=O})$ and $\nu_s(\text{O=U=O})$ mode respectively²². Infra spectra of the complexes also showed non-ligand band in the region $430-460\text{cm}^{-1}$ and $510-520\text{cm}^{-1}$, which could be assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ modes respectively¹⁸. Absence of $\nu(\text{M-S})$ band in the far infrared spectra of the metal complexes gives direct evidence to non-involvement of ring sulphur in bond formation (**Table 3**).

It is found that these bands were shifted to lower energy on complexation, indicating participation of these groups in coordination with the metal ions. In addition, the spectra of the complexes showed new bands observed in the $420-440\text{nm}$ range which may be attributed to the charge transfer transitions.

The electronic spectra of $\text{UO}_2(\text{IV})$ complexes display mainly one weak band at 420nm and a highly intense band at 320nm , which may be due to $^1\Sigma_g^+ \rightarrow ^3\pi_u$ transition and charge transfer transition respectively²⁵.

The first one of the transition is typical of the $\text{O} = \text{U} = \text{O}$ symmetric stretching frequency of the first excited state. It may be noted that the band occurring at 350nm due to uranyl moiety because of apical $\rightarrow f^0(u)$ transition²⁶ is being merged with the ligand band due to $n - \pi^*$ transition as evident from broadness and intensity.

The electronic spectra of La(III) and Th(IV) complex exhibit only highly intensive additional band in the region $410 - 410 \text{nm}$, which may be due to charge transfer besides the ligand bands. However, the electronic spectra could not provide structural details of these complexes.

Thermal decomposition of the complexes was studied by TG technique in nitrogen atmosphere. There is no weight loss up to 450K and this ruled out the presence of any water molecule in the complexes. The thermogram of La (III) complex indicated that it was stable up to 453K. Thermal decomposition took place in the temperature range of 453-883K. First TG loss was observed in 453-593K with the loss of CH_3COO , $2\text{C}_2\text{H}_5$, $2\text{C}_4\text{H}_5$ and $2(\text{O})$ (theo.31.57%.exp.,32.44%) followed by an exotherm at 523K.

Second TG loss was in the temperature range of 593-723K with a loss of tetrahydrobenzothiophene ring $2\text{C}_7\text{H}_{10}\text{OS}$ (theo.35.04%.exp., 34.78%) followed by an exotherm at 663K. Third TG loss for La(III) complex occurred in the temperature range of 723-883K with a loss of remaining ligand moiety $2\text{C}_3\text{N}$ and (O) (theo.13.32%.exp.,13.96%) followed by an exotherm 793K, the residue left was of weight correspond to $1/2 \text{La}_2\text{O}_3$ (theo.20.07%.exp., 18.82%).

The thermogram of Th(IV) complex indicated that it was stable upto 463K Thermal decomposition took place in the temperature range of 463-923K. First TG loss was observed in 463-573K with the loss of $2\text{C}_4\text{H}_{12}\text{O}$ (theo.15.71%.exp. 15.62%) followed by an exotherm at 533K. Second TG loss was in the temperature range of 573-683K with a loss of NO_3 and $2\text{C}_3\text{O}$ moiety (theo.23.54%.exp., 21.96%) followed by an exotherm at 663K. Third TG loss for Th (IV) complex occurred in the temperature range of 683-793K with a loss of $2\text{C}_6\text{H}_8\text{S}$ (tetrahydrobenzothiophene ring) (theo.23.16%.exp., 22.48%) followed by an exotherm at 713K.

Fourth TG loss for Th(IV) complex occurred in the temperature range of 793-923K with a loss of $2\text{C}_3\text{N}$ (theo.10.34%.exp.10.94%) followed by an exotherm at 813K. The residue left was of weight correspond to ThO_2 (theo.27.25%.exp. 28.00%). The thermogram of U(VI) complex indicated that it was stable upto 468K. Thermal decomposition took place in the temperature range of 468-883K. First TG loss was observed in 468-573K (Figure 1) with the loss of 2CH_3 , $2\text{C}_2\text{H}_5$ and 2O (theo.17.24%.exp., 17.62%) followed by an exotherm at 523K.

Second TG loss was in the temperature range of 573-718K (Figure 2) with a loss of $2\text{C}_6\text{H}_8\text{S}$ (tetrahydrobenzothiophene ring) (theo.25.41%.exp., 26.26%) followed by an exotherm at 663K. Third TG loss for U(VI) complex occurred in the temperature range of 718-883K with a loss of $2\text{C}_6\text{N}$ and $3(\text{O})$ of the ligand moiety (theo.25.55%.exp., 25.24%) followed by an exotherm at 753K. The residue left was of weight correspond $1/3 \text{U}_3\text{O}_8$ (theo.31.78%.exp., 30.88%). The TGA/DTA data of complexes are given in **Table 4**.

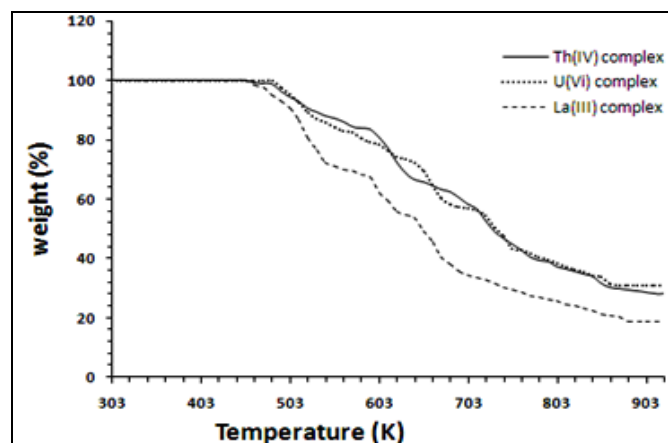


FIGURE 2: TG DIAGRAM OF COMPLEXES

TABLE 4: THERMOGRAVIMETRIC AND DIFFERENTIAL THERMAL ANALYSIS (TGA/DTA) OF COMPLEXES

Complexes	Temperature Range (K)	Weight loss (%) Exp. (Theo)	Decomposition Product	DTA peak ($^{\circ}\text{C}$)
[La(L) ₂ (CH ₃ COO)] C ₃₄ H ₄₄ N ₂ O ₈ S ₂ La	453-593	32.44(31.57)	C ₁₄ H ₂₄ O ₄	523(exo)
	593-723	34.78(35.04)	C ₁₄ H ₂₀ O ₂ S ₂	663(exo)
	723-883	13.96(13.32)	C ₆ N ₂ O _{1/2}	793(exo)
	>883(Residue)	18.82 (20.07)	1/2La ₂ O ₃	
[Th(L) ₂ (NO ₃) ₂] C ₃₂ H ₄₀ N ₄ O ₁₂ S ₂ Th	463-573	15.62(15.71)	C ₈ H ₂₄ O ₂	533(exo)
	573-683	21.96(23.54)	C ₆ N ₂ O ₈	663(exo)
	683-793	23.48(23.16)	C ₁₂ H ₁₆ S ₂	713(exo)
	793-923	10.94(10.34)	C ₆ N ₂	813(exo)
> 923(Residue)	28.00(27.25)	ThO ₂		
[UO ₂ (L) ₂] C ₃₂ H ₄₀ N ₂ O ₈ S ₂ U	468-573	17.62(17.24)	C ₈ H ₂₄ O ₂	523(exo)
	573-718	26.26(25.41)	C ₁₂ H ₁₆ S ₂	663(exo)
	718-883	25.24 (25.55)	C ₁₂ N ₂ O _{3.33}	753(exo)
>883 (Residue)	30.88 (31.79)	1/3U ₃ O ₈		

The kinetic parameters such as activation energies (E^*), enthalpy (ΔH^*), entropy (ΔS^*) and free energy change of decomposition (ΔG^*) were evaluated graphically by employing the Coats-Redfern relation ²¹:

$$\text{Log} \left[\frac{\log \{W_f / (W_f - W)\}}{T^2} \right] = \log \left[\frac{AR}{\theta E^*} \left(\frac{1 - 2RT}{E^*} \right) \right] - \frac{E^*}{2.303RT} \quad (1)$$

Where W_f is the mass loss at the completion of the reaction, W is the mass loss up to the temperature T , R is the gas constant, E^* is the activation energy in kJmol^{-1} , θ is the heating rate and $(1 - (2RT/E^*)) \approx 1$. A plot of the left-hand side of Eq. (1) against $1/T$ gives a slope from which E^* was calculated and A

(Arrhenius constant) was determined from the intercept. The entropy of activation (ΔS^*), enthalpy of activation (ΔH^*) and the free energy of activation (ΔG^*) were calculated using the following equation:

$$\Delta S^* = 2.303 R \log (A h / k T) \quad (2)$$

$$\Delta H^* = E^* - RT \quad (3)$$

$$\Delta G^* = \Delta H^* - T\Delta S^* \quad (4)$$

Where, k and h are the Boltzmann and Plank constants respectively. The calculated values E^* , A , ΔS^* , ΔH^* and ΔG^* for the decomposition steps are given in **Table 5**.

TABLE 5: KINETIC DATA ON COMPLEXES

Complexes	Temp Range(K)	E^* (kJmol^{-1})	$A(\text{s}^{-1})$	ΔS^* ($\text{JK}^{-1}\text{mol}^{-1}$)	ΔH^* (kJmol^{-1})	ΔG^* (kJmol^{-1})	R
[La(L) ₂ (CH ₃ COO)]	453-593	104.45	1.23×10^{10}	-56.54	100.09	133.97	0.849
	593-723	94.49	3.89×10^6	-125.41	88.98	172.13	0.988
	723-803	100.81	2.10×10^5	-151.19	94.22	1214.11	0.974
[Th(L) ₂ (NO ₃) ₂]	463-573	70.91	8.53×10^5	-136.23	66.47	139.08	0.914
	573-683	185.73	3.97×10^{14}	28.34	180.46	162.54	0.964
	683-823	208.36	2.56×10^{14}	23.66	202.43	185.56	0.977
	823-923	204.43	2.57×10^{12}	-15.69	197.67	210.43	0.976
[UO ₂ (L) ₂]	468-573	138.32	1.44×10^{13}	2.31	133.97	132.76	0.967
	573-718	119.57	4.92×10^8	-84.66	114.06	170.19	0.975
	718-883	95.75	1.63×10^5	-152.88	89.49	204.61	0.890

In the present studies, the numerical values of activation energy, frequency factor and entropy of activation indicates about smoothness of the feasibility and reaction rate of the initial reactants and intermolecular stage compounds. The calculated values of the activation energy of the complexes are relatively low indicating autocatalytic effect of the metal ions on the thermal decomposition of the complexes ²⁸.

The correlation coefficient of the Arrhenius plots of the thermal decomposition steps were found to lie in the range 0.849-0.988, showing a good fit with the linear function. The negative values for entropy of activated complexes (except second and third decomposition step of Th(IV) complex and first decomposition step of UO₂(VI) complex) have more ordered or more rigid structure than the reactants or intermediate and the reaction are slower than normal ²⁹. The order of stability of complexes on the basis of activation energy is [UO₂(L)₂] > [La(L)₂(CH₃COO)] > [Th(L)₂(NO₃)₂] (on

the basis of first decomposition stage) and [Th(L)₂(NO₃)₂] > [UO₂(L)₂] > [La(L)₂(CH₃COO)] (on the basis of second decomposition stage).

Antimicrobial susceptibility testing using Kirby Bauer method of gram negative uropathogens was carried out and it was found that these uropathogens were resistant to most of the antibiotics as shown in **Table 6**. All isolates were found to be Multiple Drug Resistant (Resistant to more than 3 antibiotics) including 3rd generation Cephalosporins (Ceftazidime, Cefotaxime and Ceftriaxone).

The effect of metal complexes on these test isolates are shown in **table 7** below. Ethanol (solvent) did not show any zone of inhibition against the test organisms. However metal complexes showed considerable zones of inhibition in its complex form as compared to ligand. The activity of metal complexes is enhanced due to chelation. The chelation reduces considerably the polarity of the

metal ions in the complexes, which in turn increases the hydrophobic character of the chelate and thus enables its permeation through the lipid layer of microorganisms³¹. As the positive charges of the metal are partially shared with the donor atoms present in the ligands and there is possible

electron delocalization over the metal complex formed, the lipophilic character of the metal chelate increases and favors its permeation more efficiently through the lipid layer of the microorganism, thus destroying them more forcefully³¹.

TABLE 6: ANTIBIOTIC RESISTANCE PROFILE OF THE UROPATHOGENS

Isolates	Antibiotic resistance profile		
ESBL Producing uropathogens			
	Sensitive	Intermediate	Resistant
<i>E.coli</i> strain 1	AS, AK, GF		BA, CF, PC, CH, RC, CI, TE, ZN, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Citrobacter diversus</i> strain 1	AS, BA, CH		CF, PC, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 2	AS, CH, AK, GF	ZN	BA, CF, PC, RC, CI, TE, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Pseudomonas aeruginosa</i>	CH, AK, GF		AS, BA, CF, PC, RC, CI, TE, ZN, GM, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Citrobacter diversus</i> strain 2	ZN, AK, GF	NX, CU, CP, PB, AS, CF, RC, GM	BA, PC, CH, CI, TE, TT, OX, RP, ZX, CB, NA, AG, FG
<i>Proteus vulgaris</i>	NX, AS, GM, AK	TT, RP, PC, RC, GF	BA, CF, CH, CI, TE, ZN, OX, ZX, CB, NA, AG, CU, CP, FG, PB
Non- ESBL and MBL Producing uropathogens			
<i>Proteus vulgaris</i>	AK, LOM, SPX, NET, CAZ, CIP, CPX, GEN, A/S, CZX, OF, PF, NX, CTR, CPZ, CTR, CFM, CPO, CPM		NA
<i>Proteus mirabilis</i>	CI, CF, BA, PB, CU, NA, NX, OX	TT, AG, CP, TE, AK	GF, GM, ZN, RC, CH, PC, AS, FG, CB, ZX, RP
<i>E.coli</i>	AG, CU, PB, PC	CB, CI	GF, AK, GM, ZN, TE, RC, CH, CF, BA, AS, FG, CP, CU, NX, NA, ZX, RP, OX, TT
<i>Morganellamorganii</i>	RC, CI, TE, PC, PB, AG, CU, OX	AK, GM, CH, CP	TT, RP, ZX, CB, NA, NX, FG, AS, BA, CF, ZN, GF
<i>C. diversus</i>	AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB		
<i>Pseudomonas aeruginosa</i>	TT, RP, AG, CU, FG, AS, CF, CH, CI, TE,	OX, CB, PB, ZN, PC	BA, RC, GM, AK, GF, ZX, NA, NX, CP
MBL Producing uropathogens			
<i>E.coli</i> strain 1	CH	PC	AS, BA, CF, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 2	CH	AK	AS, BA, CF, PC, RC, CI, TE, ZN, GM, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Pseudomonas aeruginosa</i>			AS, BA, CF, PC, CH, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>E.coli</i> strain 3	RC		AS, BA, CF, PC, CH, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB

<i>Klebsiella pneumonia</i> strain 1			AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>Klebsiella pneumonia</i> strain 2	CH	AK	AS, BA, CF, PC, CH, RC, CI, TE, ZN, GM, AK, GF, TT, OX, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB
<i>C. diversus</i>	OX, BA, CH, GM	TE, AK, GF	AS, CF, PC, CH, RC, CI, ZN, GM, TT, RP, ZX, CB, NA, NX, AG, CU, CP, FG, PB

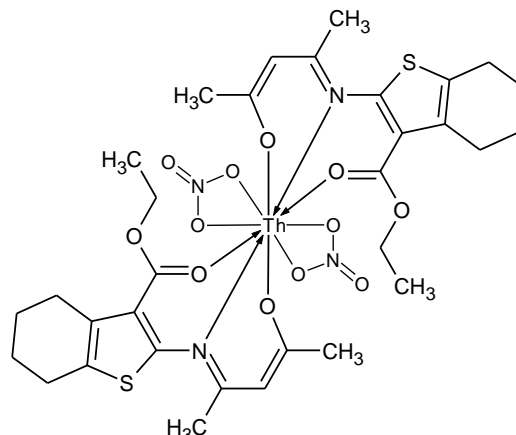
Key:

TT - Ticarcillin/clavulanic acid, OX - Oxytetracycline, RP - Ceftriaxone, ZX - Cefepime, CB - Cefuroxime, NA - Naladixic acid, NX - Norfloxacin, AG - Amoxicillin/clavulanic acid, CU - Cefadroxil, CP - Cefoperazone, FG - Ceftazidime, PB - Polymixin B, AS - Ampicillin, BA - Co-trimoxazole, CF - Cefotaxime, PC - Piperacillin, CH - Chloramphenicol, RC - Ciprofloxacin, CI - Ceftizoxime, TE - Tetracycline, ZN - Ofloxacin, GM - Gentamicin, AK - Amikacin, GF - Gatifoxacin

TABLE 7: ANTIBACTERIAL ACTIVITY OF SCHIFF BASE METAL COMPLEXES AGAINST DRUG RESISTANT UROPATHOGENS

Isolates	Metal complexes (200µg/µl)		
	[La(L) ₂ (CH ₃ COO)]	[Th(L) ₂ (NO ₃) ₂]	[UO ₂ (L) ₂]
ESBL Producing uropathogens showing zones of inhibition in mm			
<i>E. coli</i> strain 1	13	13	-
<i>Citrobacter diversus</i> strain 1	14	-	-
<i>E. coli</i> strain 2	-	-	-
<i>Pseudomonas aeruginosa</i>	-	-	-
<i>Citrobacter diversus</i> strain 2	-	14	11
<i>Proteus vulgaris</i>	-	16	13
Non- ESBL Producing uropathogens showing zones of inhibition in mm			
<i>Proteus vulgaris</i>	12	16	19
<i>Proteus mirabilis</i>	18	-	20
<i>E. coli</i>	-	-	-
<i>Morganella morganii</i>	-	17	-
<i>C. diversus</i>	12	14	15
<i>Pseudomonas aeruginosa</i>	17	16	20
MBL Producing uropathogens showing zones of inhibition in mm			
<i>E. coli</i> strain 1	-	-	12
<i>E. coli</i> strain 2	-	15	14
<i>Pseudomonas aeruginosa</i>	12	-	13
<i>E. coli</i> strain 3	15	12	-
<i>Klebsiella pneumonia</i> strain 1	13	13	13
<i>Klebsiella pneumonia</i> strain 2	13	16	-
<i>C. diversus</i>	-	-	-

CONCLUSIONS: From the present investigation it has been observed that a ligand ethyl 2-[[[(1E, 2E)-2-(hydroxyimino)-1-phenyl ethylidene] amino]-4, 5, 6, 7 tetrahydro-1-benzothiophene-3-carboxylate form a complex in 2:1 (ligand: metal) ratio. The data explain 10-coordinate complex of Th(IV), 8-coordinate complex of UO₂(VI) and La(III). The proposed structures of metal complexes are presented in **Figure 3-5**. The complexes also exhibited antimicrobial activity against MDR uropathogens producing ESBL and MBL enzymes.

**FIGURE 3: PROPOSED STRUCTURE OF Th (IV) COMPLEX**

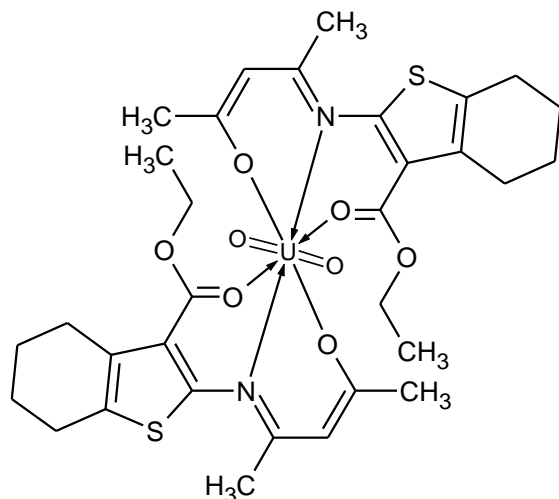


FIGURE 4: PROPOSED STRUCTURE OF UO (VI) COMPLEX

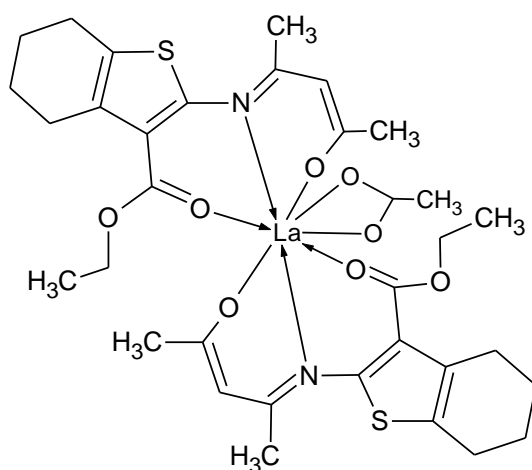


FIGURE 5: PROPOSED STRUCTURE OF La (III) COMPLEX

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