

# Chelating Behaviour of Dihydrothieno[3,4, d] Pyridazine Derivatives with Some Lanthanide and Actinide Metals

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**Abstract:** Coordination compound formed by the interaction of Dihydrothieno[3,4-d]pyridazine with La(III), Ce(III), Sm(III), Th(IV) and UO<sub>2</sub>(II) are prepared and characterized by elemental analysis, IR, <sup>1</sup>H NMR Mass spectra and thermal analysis. The analysis data indicate that the ligand acts as bidentate on chelation, thermogravimetric analysis confirm the presence of coordinates water. The IR spectra indicate that coordination takes place through the nitrogen of amino group and C=O group of pyridazine ring. Antimicrobial activity of selected compounds against some bacterial strains was tested and confirm the antimicrobial activities of the ligand increase on coordination with the metal ion.

**Keywords:** Dihydrothieno Pyridazine, Complexes, IR, <sup>1</sup>H NMR, Mass Spectra, Thermal analysis, Antimicrobial activity

## Introduction

Recently pyridazine and thienopyridazine compounds have been reported to possess varied biological activities such as antimicrobial<sup>1</sup>, antihypertensive<sup>2,3</sup>, anti-inflammatory<sup>4</sup>, antifungal activities<sup>5</sup>, antimalarials<sup>6-14</sup>. Pyridazinone nucleus has been extensively studied in the search for new and selective medicinal agents as drugs acting on the cardiovascular system<sup>15</sup>. Furthermore, a number of thienopyridazines have been claimed to possess interesting biological and pharmacological activities such as, anticancer<sup>16</sup>, useful as oxidase inhibitor<sup>17-18</sup>. Complexation of thienopyridazine with transition and rare earth metals have been studied<sup>19-36</sup>.

## Experimental

All the chemicals used were of AR or BDH grade. Stock solutions ( $1.0 \times 10^{-3}$  mol dm<sup>-3</sup>) of the azo compounds and metal salts LaCl<sub>3</sub>.7H<sub>2</sub>O, Ce(NO<sub>3</sub>)<sub>3</sub>.6H<sub>2</sub>O, Sm(NO<sub>3</sub>)<sub>3</sub>.6H<sub>2</sub>O Th(NO<sub>3</sub>)<sub>4</sub>.5H<sub>2</sub>O and UO<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O are prepared by dissolving the accurate weight of the crystallized product in pure absolute ethanol. The thienopyridazines compound was

prepared according to references described earlier<sup>28</sup>. The ligands were prepared by condensation of ethyl cyanoacetate with ethylarylhydrazone -3-oxo-butyrates (**1a-c**) in presence of ammonium acetate. These compounds (**2a-c**) reacted with elemental sulphur in refluxing and acatalytic amount of triethylamino were added. The reaction mixture was heated at reflux for 30 minute, the solid product (**3a-c**) formed was collected by filtration and crystallized from ethanol yield (89%) yellow crystals.

The ligands used are ethyl 5-amino-3-(o-aminotoluene)-4-oxo-3,4-dihydrothieno[3,4-d]pyridazine-1-carboxylate (L<sub>1</sub>) and ethyl 5-amino-3-(4-nitrophenyl)-4-oxo-3,4-dihydrothieno[3,4-d]pyridazine-1-carboxylate (L<sub>2</sub>). In the preparation metal complexes (**4a-c**), the metal and the ligand were combined in 1:1metal:ligand ratio in the case of La(III), Ce(III), Sm(III), Th(IV) and UO<sub>2</sub>(II) using required quantities of ethanol so as effect the solubility of the metal salts and ligand. The contents were refluxed on a hot water bath for 1 h and the solid that separated was filtered and dried over silica gel (Scheme 1). The chelates were analysed for their carbon, hydrogen and nitrogen contents. The results of analysis are given in Table 1. Conductance measurements on the complexes were made in DMF at  $1 \times 10^{-3}$  mol dm<sup>-3</sup>.

**Table 1.** Physical properties, analytical data, formula weight (F.W.) and molar conductance ( $\Lambda$  ohm<sup>-1</sup> cm<sup>-1</sup> mol<sup>-1</sup>) of the prepared complexes

Compound	Molecular Formula	Found (Calcd.) %			F.W. Found	$\Lambda_M$
		C	H	N		
L1 ligand	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S	55.39(55.81)	5.04(4.65)	15.97(16.28)	344	-
L1-La complex	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S(Cl <sub>3</sub> )La.7H <sub>2</sub> O	25.99(26.84)	4.6(4.19)	7.49(7.83)	715.40	6.42
L1-Ce complex	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S(NO <sub>3</sub> ) <sub>3</sub> Ce.6H <sub>2</sub> O	24.42(24.67)	4.19(3.60)	11.51(12.59)	778.12	6.18
L1-Sm complex	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S(NO <sub>3</sub> ) <sub>3</sub> Sm.6H <sub>2</sub> O	24.50(24.35)	4.55(3.55)	11.60(12.43)	788.40	19.06
L1- UO <sub>2</sub> complex	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S (NO <sub>3</sub> ) <sub>2</sub> UO <sub>2</sub> .6H <sub>2</sub> O	22.85(22.69)	4.90(3.31)	9.77(9.93)	846.03	7.66
L1-Th complex	C <sub>16</sub> H <sub>16</sub> N <sub>4</sub> O <sub>3</sub> S(NO <sub>3</sub> ) <sub>4</sub> Th.5H <sub>2</sub> O	20.63(21.01)	2.67(2.84)	12.35(12.25)	914.04	7.02
L2 ligand	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S	49.96(50.00)	3.01(3.33)	15.40(15.55)	360	-
L2- La complex	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S LaCl <sub>3</sub>	30.52(29.73)	1.96(1.98)	10.20(9.25)	605.41	12.10
L2- Ce complex	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S(NO <sub>3</sub> ) <sub>3</sub> Ce. 3H <sub>2</sub> O	25.23(24.32)	3.31(2.43)	14.01(13.24)	740.12	12.99
L2- Sm complex	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S(NO <sub>3</sub> ) <sub>2</sub> Sm.6H <sub>2</sub> O	24.61(24.25)	2.92(3.23)	10.98(11.31)	742.40	8.68
L2- UO <sub>2</sub> complex	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S(NO <sub>3</sub> ) <sub>2</sub> UO <sub>2</sub> .3H <sub>2</sub> O	21.83(22.28)	2.76(2.23)	12.52(10.40)	808.03	6.72
L2- Th complex	C <sub>15</sub> H <sub>12</sub> N <sub>4</sub> O <sub>5</sub> S(NO <sub>3</sub> ) <sub>4</sub> Th. H <sub>2</sub> O	19.65(20.98)	2.30(1.83)	13.88(13.05)	858.03	9.19

### Instrumentation

The elemental analysis (C.H.N) were carried out by the Microanalytical Center, Cairo University. The IR (KBr) spectra were determined with Perkin-Elmer Infrared 127B spectrophotometer.

<sup>1</sup>H NMR spectra were recorded with a Bruker AMX-250 spectrometer. Mass spectra were recorded on a HPMS 6988 spectrometer. The thermographs of TGA of chelates were carried out by Cairo University; the data obtained were recorded using a Shimadzu TGA - 50H apparatus. The mass spectra were analysed by the EI technique at 80 eV, threshold output = 0.8 V and peak detection = 0.02 V. Molar conductance are performed using WPA CM35 Conductivity Meter cell fitted with platinized platinum electrodes.

### Antimicrobial studies

#### *Biological activity (Sensitivity tests) by Kirby-Bauer method*

Antimicrobial activity of the tested samples was determined using a modified Kirby-Bauer disc diffusion method<sup>37</sup>. Briefly, 100 µL of the test bacteria/fungi were grown in 10 mL of fresh media until they reached a count of approximately 10<sup>8</sup> cells/mL for bacteria or 10<sup>5</sup> cells/mL for fung<sup>38</sup>, 100 µL of microbial suspension was spread onto agar plates corresponding to the broth in which they were maintained.

Isolated colonies of each organism that might be playing a pathogenic role should be selected from primary agar plates and tested for susceptibility by disc diffusion method<sup>39</sup>, results in good batch-to-batch reproducibility. Disc diffusion method for filamentous fungi tested by using approved standard method (M38-A) developed by, evaluating the susceptibilities of filamentous fungi to antifungal agents<sup>40</sup>. Disc diffusion method for yeasts developed by using approved standard method (M44-P)<sup>41</sup>.

Plates inoculated with filamentous fungi as *Aspergillus flavus* at 25°C for 48 hours; gram(+) bacteria as *Staphylococcus aureus*. *Bacillus subtilis*: gram(-) bacteria as *Escherichia coli*, *Pseudomonas aeruginosa* they were incubated at 35-37 °C for 24-48 h and yeast as *Candida albicans* incubated at 30 °C for 24-48 h and, then the diameters of the inhibition zones were measured in millimeters<sup>37</sup>.

Standard discs of Ampicillin (Antibacterial agent). Amphotericin B (Antifungal agent) served as positive controls for antimicrobial activity but filter discs impregnated with 10 µl of solvent (distilled water, chloroform, DMSO) were used as a negative control. The agar used is Mueller-Hinton agar that is rigorously tested for composition and pH. Further, the depth of the agar in the plate is a factor to be considered in the disc diffusion method. This method is well documented and standard zones of inhibition have been determined for susceptible and resistant values.

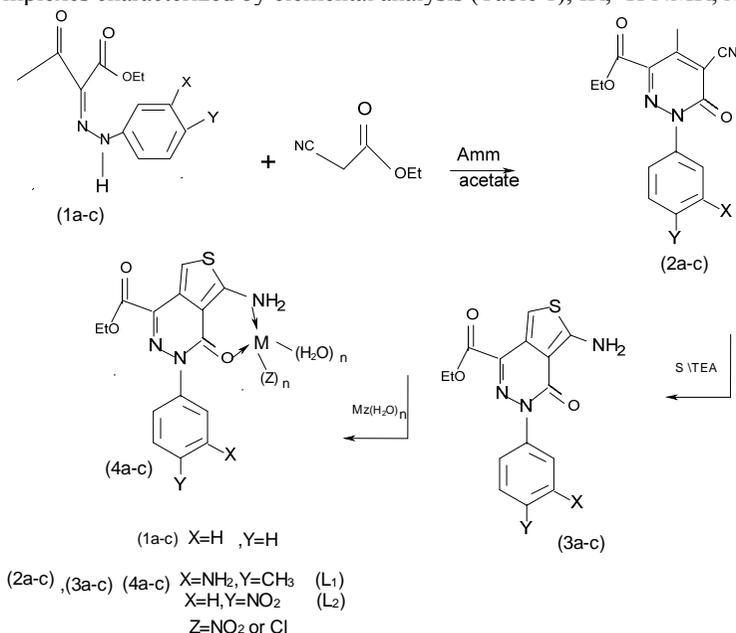
Blank paper disks (Schleicher & Schuell, Spain) with a diameter of 8.0 mm were impregnated 10 µ of tested concentration of the stock solutions. When, a filter paper disc impregnated with a tested chemical is placed on agar the chemical will diffuse from the disc into the agar. This diffusion will place the chemical in the agar only around the disc. The solubility of the chemical and its molecular size will determine the size of the area of chemical infiltration around the disc if an organism is placed on the agar it will not grow in the area around the disc if it is susceptible to the chemical. This area of no growth around the disc is known as a "Zone of inhibition" or "Clear zone". For the disc diffusion, the zone diameters were measured with slipping calipers of the National Committee for Clinical Laboratory standard<sup>42</sup>. Agar-based methods such as Etest and disk diffusion can be good alternatives because they are simpler and faster than broth-based methods<sup>43,44</sup>.

The tested compounds (a,1a,2a,3a,4a,5a, equal to L<sub>1</sub>, L<sub>1</sub>-Ce(III), L<sub>1</sub>-La(III), L<sub>1</sub>-Sm(III), L<sub>1</sub>-UO<sub>2</sub>(II) and L<sub>1</sub>-Th(IV) and b,1b,2b,3b,4b,5b, equal to L<sub>2</sub>, L<sub>2</sub>-Ce(III), L<sub>2</sub>-La(III), L<sub>2</sub>-Sm(III), L<sub>2</sub>-UO<sub>2</sub>(II) and L<sub>2</sub>-Th(IV), respectively) were dissolved in DMSO to give a final

concentration (1 mg/mL). Susceptible sterile discs were impregnated by the tested substance (50  $\mu\text{g}/\text{disc}$ ) via a means of micropipette. The biological activity for each substance was tested on surface-seeded nutrient agar medium with the prepared susceptible discs.

## Results and Discussion

Thienopyridazine ligands containing coordinate sites such as ethyl 5-amino-3-(*o*-aminotoluene)-4-oxo-3,4-dihydrothieno[3,4-*d*]pyridazine-1-carboxylate ( $L_1$ ) and ethyl 5-amino-3-(4-nitrophenyl)-4-oxo-3,4-dihydrothieno[3,4-*d*]pyridazine-1-carboxylate ( $L_2$ ) are good for chelation with La(III), Ce(III), Sm(III), Th(IV) and  $\text{UO}_2(\text{II})$  metals (Scheme 1). Treatment of metals with ligands  $L_1$  and  $L_2$  in ethanol gave stable six membered ring structure complexes characterized by elemental analysis (Table 1), IR,  $^1\text{H}$  NMR, Mass spectra.



Scheme 1

### IR spectra

The infrared spectral data provide some significant results which support the proposed formula of each complex (Table 2-3) isolated in the present study. The ligand exhibits a broad band at  $3431.7\text{ cm}^{-1}$  and  $3377.9\text{ cm}^{-1}$  for  $L_1$  and  $L_2$  due to  $\nu\text{NH}_2$  which appears lower shifted in the spectra of its complexes. This indicates that the nitrogen of this group is coordinated to the metal. The band that appears around  $1631.5\text{ cm}^{-1}$  and  $1628.6\text{ cm}^{-1}$  in the spectrum of the free ligands  $L_1$  and  $L_2$  respectively, probably attributed to  $\nu\text{C}=\text{O}$  ring vibration. The shift in frequency of this band on chelation is probably due to the involvement of C=O group in metal chelates ring. A new band appear at  $3906$ ,  $3848$ ,  $3751$  and  $3676\text{ cm}^{-1}$  due to presence water molecules in complexes prepared. Since it was known<sup>37</sup> that the free water absorb at  $3520\text{ cm}^{-1}$ . One can suggest that water molecules are loosely coordinated or exist as molecules of crystallization. Bands observed at  $840$ ,  $850$ ,  $876\text{ cm}^{-1}$  confirm the presence of coordinated lattice water molecules<sup>45</sup>. The high affinity of  $\text{H}_2\text{O}$  molecules for heavy metals with its small size and high coordination number of latter<sup>46</sup>, frequently leads to inclusion of  $\text{H}_2\text{O}$  molecules in coordination sphere of the metal ion.

**Table 2.** Fundamental Infrared Bands ( $\text{cm}^{-1}$ ) of  $L_1$  and its (1:1) Chelates

Ligand	Complexes Assignments					
	Ce(III)	La(III)	Sm(III)	UO <sub>2</sub> (II)	Th(IV)	
3431.7	3432.7	3392.2	3426.9	3425.7	3408.6	v(NH <sub>2</sub> ) stretching
2921.6	2923.6	2972.7	2973.7	2923.6	2920.6	v(H-aromatic)
2360.4	2367.2	2366.2	2364.3	2343.1	2340.2	v(CH <sub>3</sub> ),
1631.5	1633.4	1629.6	1635.3	1634.4	1634.3	v(C=O) stretching
-	875.5	876.9	876.5	834.1	809.9	v(OH)
-	555.4, 527.4	597.8	563.1	567.1	609.3	v(MN) stretching
-	450.3, 461.9, 475.4	457.1	438.7	420.4	425.1	v(MO)

**Table 3.** Fundamental Infrared Bands ( $\text{cm}^{-1}$ ) of  $L_2$  and its (1:1) Chelates

Ligand	Complexes Assignments					
	Ce(III)	La(III)	Sm(III)	UO <sub>2</sub> (II)	Th(IV)	
3477.9	3415.3	3425.9	3426.9	3431.7	3429.8	v(NH <sub>2</sub> ) stretching
2928.4	2923.6	2922.6	2920.7	2930.3	2926.5	v(H-aromatic)
1628.6	1652.7	1649.8	1656.6	1651.7	1637.3	v(C=O) stretching
-	850.4	852.4	850.5	852.4	841.8	v(OH)
-	580.5	528.4	692.3	580.4	533.2	v(MN) stretching
-	490.1	448.4, 433.9	430.9	422.3	441.6	v(MO)

Further, the ligand does not show up a band at  $748 \text{ cm}^{-1}$  due to  $\nu\text{C-S}^{47,48}$ , which undergoes does not shifted in complexes indicating that sulphur does not involved in complexation<sup>49</sup>. In the IR spectra of the chelate, an additional band is observed which are not found in the spectra of the free ligands. Of these, the bands around  $1030, 1031, 1032 \text{ cm}^{-1}$  observed in the spectra of UO<sub>2</sub>(II), Th(IV), Sm(III) complexes respectively, which are assigned to the coordinated NO<sub>3</sub> group to metal ion<sup>50,51</sup>. The bands at  $1272 \text{ cm}^{-1}$  in the case of La(III) complexes are due to (M-Cl). The UO<sub>2</sub>(II) complexes show strong bands at around  $928$  and  $815 \text{ cm}^{-1}$  assignable to  $\nu_{\text{as}}$  and  $\nu_{\text{sy}}(\text{O}=\text{U}=\text{O})$  modes respectively<sup>52</sup>, this indicates linearity of O=U=O is retained in complexes. Moreover, the two new bands observed in all complexes under study at  $530\text{-}580 \text{ cm}^{-1}$  and  $422\text{-}490 \text{ cm}^{-1}$  assigned to  $\nu\text{M-N}$  and  $\nu\text{M-O}$  stretching mode respectively<sup>53,54</sup>.

### <sup>1</sup>H NMR Spectra

The <sup>1</sup>H NMR Spectra of the free ligand signal  $L_1$  and  $L_2$  are appearing at  $\delta$  6.86 and  $\delta$  7.67 ppm respectively which is attributed to the peak of NH<sub>2</sub> protons of pyridazine ring, show little shift downfield in the spectra of the chelates  $\delta$  6.927-7.005 ppm for  $L_1$  and  $\delta$  7.69-7.95 ppm for  $L_2$  indicating some sort of deshielding as a result of complexation and confirming that this proton is replaced by metal ion. The hydrated nature of the free ligands and the isolated solid complexes is confirmed by the appearance of signal at  $\delta$  3.31-3.85 ppm region in the <sup>1</sup>H NMR spectra of all complexes. The downfield signal demonstrates clearly the

presence of latic water molecules, since the uncomplexed H<sub>2</sub>O proton occurs at  $\delta$  4.33 ppm<sup>55</sup>. On the other hand, the proton signal of the coordinated H<sub>2</sub>O molecules must exhibit at  $\delta$  2.88-3.29 ppm. The presence of water molecule is in agreement with the suggested formula based on the elemental analysis and is supported by thermal analysis data. The <sup>1</sup>H NMR spectra of the complexes show little downfield shifts in the signal of ring protons due to the deshielding effect of the metal ion<sup>56</sup>. The obtained data are listed in Table 4.

**Table 4.** Proton <sup>1</sup>H NMR spectral of ligands and complexes in DMSO

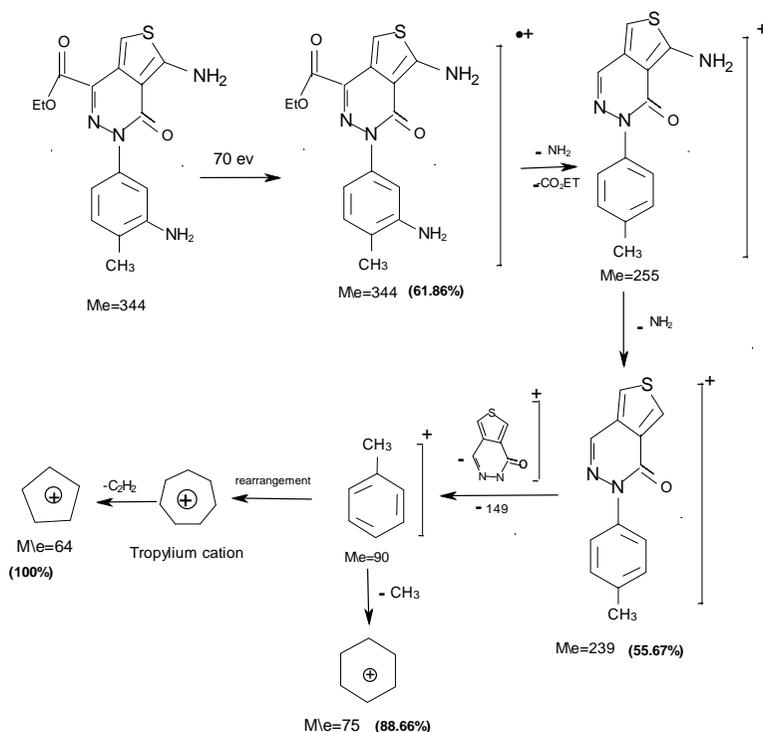
Compounds	$\delta$ H <sub>2</sub> O		$\delta$ NH <sub>2</sub>	$\delta$ (ring protons)
	Latic water	Coordinated water		
L <sub>1</sub>	-	-	6.862	7.64–7.670
L <sub>1</sub> -(La) <sup>3+</sup>	3.387	3.083	6.930	7.641–7.679
L <sub>1</sub> -Ce <sup>3+</sup>	3.394	3.253	6.927	7.65–7.680
L <sub>1</sub> -Sm <sup>3+</sup>	3.383	3.146	6.930	7.650-7.678
L <sub>1</sub> -(Th) <sup>4+</sup>	3.848	3.278	6.978	7.647-7.785
L <sub>1</sub> -(UO <sub>2</sub> ) <sup>2+</sup>	3.344	3.136	7.005	7.642-7.671
L <sub>2</sub>	-	-	7.67	7.90–8.330
L <sub>2</sub> -(La) <sup>3+</sup>	3.887	3.297	7.948	8.295–8.354
L <sub>2</sub> -Ce <sup>3+</sup>	3.316	2.884	7.950	8.295–8.303
L <sub>2</sub> -Sm <sup>3+</sup>	3.874	3.299	7.948	8.325-8.352
L <sub>2</sub> -(Th) <sup>4+</sup>	3.320	3.122	7.919	8.020-8.350
L <sub>2</sub> -(UO <sub>2</sub> ) <sup>2+</sup>	3.310	2.986	7.948	8.285-8.315

#### *Molar conductance*

The ionic nature of the complexes under investigation can be further confirmed by measurement of the molar conductance values of  $1 \times 10^{-3}$  mol dm<sup>-3</sup> solutions of the isolated complexes in DMF at 30°C. The obtained molar conductance values are listed in table 1. It is evident from the results that the molar conductance values of mononuclear [1:1]L<sub>1</sub> complexes is in the 6.18-19.06 S. mol<sup>-1</sup> cm<sup>2</sup> and [1:1]L<sub>2</sub> complexes is in the range 6.72-16.15 S. mol<sup>-1</sup> cm<sup>2</sup>, which are commensurate with values characteristic for neutral complexes<sup>57</sup>. This reveals a non-electrolytic nature of the synthesized complexes. These results support the suggested formula of the solid chelates on the bases of elemental analysis. Thus, the ligand acts towards the metals studied as a neutral, bidentate one coordinating through the nitrogen of NH<sub>2</sub> group and C=O group of pyridazine ring.

#### *Mass spectrum of the ligands*

The mass spectrum of the ligand L<sub>1</sub> gives a molecular ion of M/e = 344 of abundance 61.86%. The mass spectrum pattern gives a molecular ion of M/e = 255 which related to the mass of the reminder part of the ligand radical after losing of amino and EtO<sub>2</sub>C groups. This followed by losing NH<sub>2</sub> group forming a molecular ion of M/e = 239 of abundance 55.67%. This followed by losing C<sub>6</sub>HN<sub>2</sub>OS group forms a molecular ion C<sub>7</sub>H<sub>6</sub><sup>+</sup> positive radical M/e = 90. The remaining residual fragment of toluene (methyl benzene) positive radical C<sub>7</sub>H<sub>6</sub><sup>+</sup> Forming aresonance stabilized benzylic carbocation, which rearranges to tropylium cation, and this strong peak at m/e = 90 is a hallmark of compounds containing a benzyl unit. The minor peak C<sub>5</sub>H<sub>4</sub><sup>+</sup> M/e = 64 of abundance 100% represents loss of neutral acetylene from the tropylium ion. On the other hand, the mass spectrum pattern appears fragment of C<sub>7</sub>H<sub>6</sub><sup>+</sup> may be loss CH<sub>3</sub> group and giving phenyl group positive radical M/e = 75 of abundance 88.66%, this will appear clearly (Scheme 2) as followed.



**Scheme 2.** Mass spectra fragmentation of L<sub>1</sub>

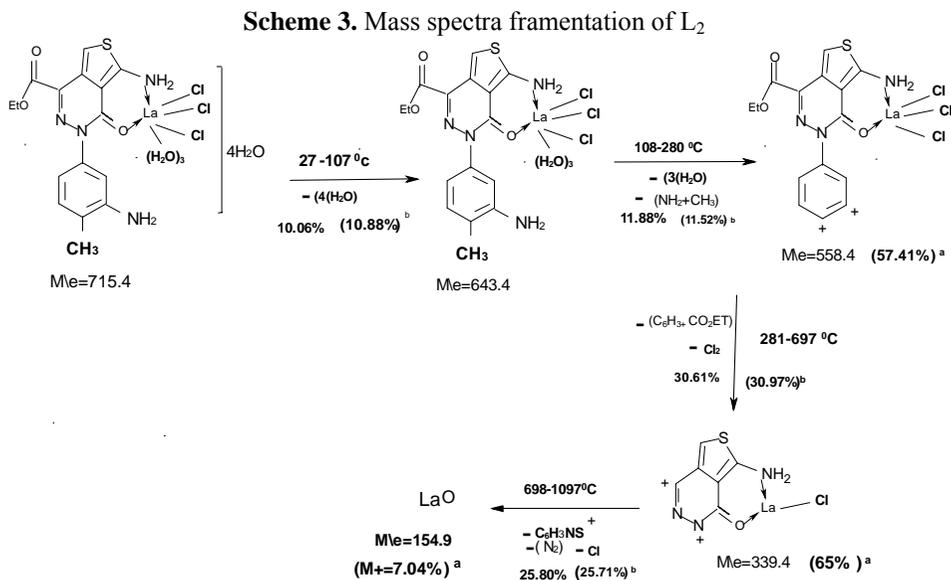
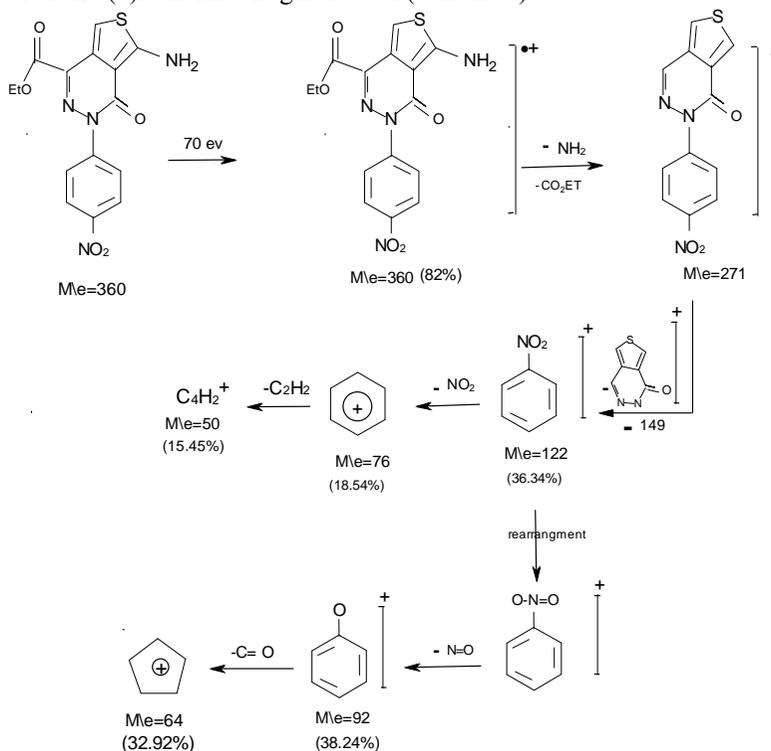
The mass spectrum of the ligand L<sub>2</sub> gives a molecular ion of M/e = 360 of abundance 82%. The molecular ion of M/e = 271 which related to the mass of the remainder part of the ligand radical after losing of amino and EtO<sub>2</sub>C groups. This followed by losing C<sub>6</sub>H<sub>2</sub>OS group forming a molecular ion of M/e = 122 of abundance 36.34%. The losing of mass of NO<sub>2</sub> is followed by forming phenyl radical M/e = 76 of abundance 18.54% and followed by losing C<sub>2</sub>H<sub>2</sub> group gave C<sub>4</sub>H<sub>2</sub><sup>+</sup> a molecular ion of M/e = 50 of abundance 15.45%.

On the other hand, mass spectrum of the molecular ion of M/e = 122 may be rearrangement and losing NO radical during fragmentation aryloxy is indicated by appearing of peak of M/e = 92 of abundance 38.24%. The losing of mass of C≡O group is followed by forming aromatic ring as positive radical C<sub>5</sub>H<sub>4</sub><sup>+</sup> a molecular ion of M/e = 64 of abundance 32.92%. The following (Scheme 3) show the above discussion.

#### Thermal analysis and mass spectra of the complexes

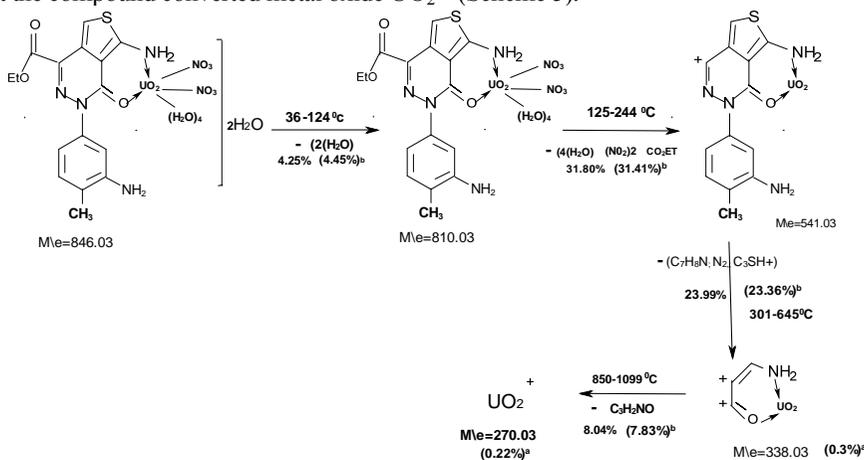
The TG thermogram of the (1:1) La<sup>3+</sup>-L<sub>1</sub> complex shows four thermal degradation stages changes at temperature ranges 27-107, 108-280, 281-697, -698-1097 °C. In the first stage, occurring at 27-107 °C the process is accompanied by a weight loss of 10.88% corresponding to evolution of four molecules of water of crystallization. In the second step at temperature range 108-280 °C three molecules of water coordination amine and methyl groups gives mass loss of 11.52% of abundance 57.41%, forming a molecular ion M/e 558.4. The third steps occurs at temperature ranges 281-697 °C, they may be regarded as a result of breaking two chloride ion, C<sub>6</sub>H<sub>3</sub><sup>+</sup> and EtO<sub>2</sub>C groups by weight loss of 30.97% forming molecular ion M/e= 339.4 of abundance 65%. The final step at temperature ranges 698-1097 °C represents

mass loss 25.71% of  $N_2$  gas, chloride ion and  $C_6H_3NS^+$ , so the compound convert into metal oxide (LaO)  $M/e$  154.9 of abundance  $M^+=7.04\%$ , where (a) is mass spectra fragmentation and (b) is thermal fragmentation (Scheme 4).



**Scheme 4. Thermal and mass spectra fragmentation of  $L_1+La(III)$  chelate**

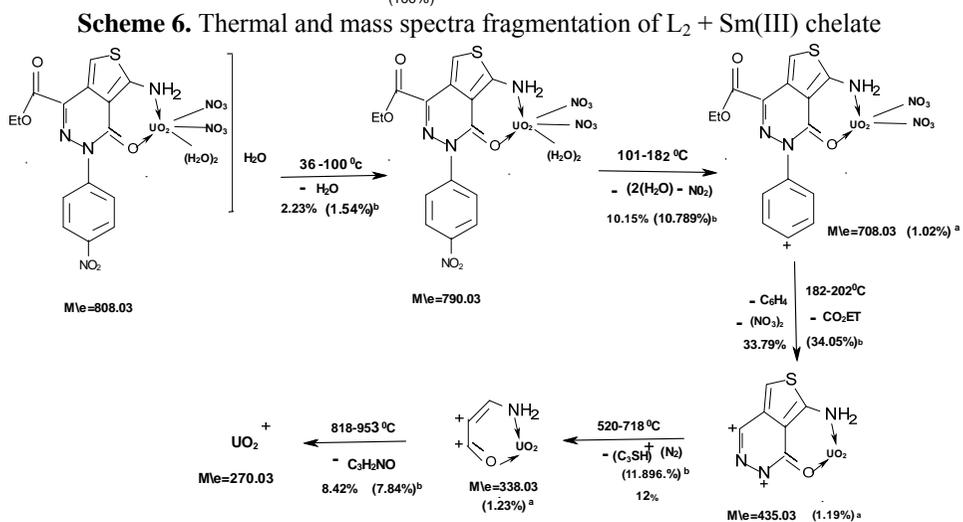
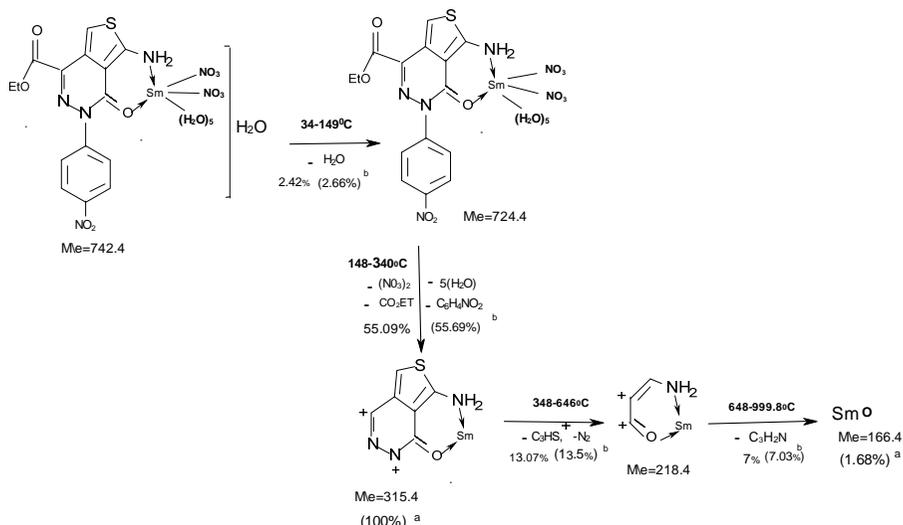
The TG thermogram of the (1:1)UO<sub>2</sub><sup>+2</sup>-L<sub>1</sub> complex shows four thermal degradation stages changes at temperature ranges 36-124, 125-244, 301-645, 850-1099 °C. In the first stage lies at 36-124 °C and correspond to loss two molecules of water of crystallization 4.45%. In the second inflection at temperature range 125-244 °C gives mass loss of 31.41% corresponds to the breaking of four molecules of water coordination, (NO<sub>3</sub>)<sub>2</sub> and EtO<sub>2</sub>C molecules ion M/e = 541.03. The third step in TG curve the complex loss 23.36% form its mass due to the elimination of N<sub>2</sub> gas ,C<sub>3</sub>HS<sup>+</sup> ,C<sub>7</sub>H<sub>8</sub>N group with in temperature at 301-645 °C ,forming molecules ion M/e =338.03(0.3%). The final step at temperature ranges 850-1099 °C represent , the loss of residual organic part ion 7.83% so that the compound converted metal oxide UO<sub>2</sub><sup>+2</sup> (Scheme 5).



**Scheme 5.** Thermal and mass spectra fragmentation of L1 + UO<sub>2</sub>(II) chelate

The TG thermogram of the (1:1) Sm<sup>3+</sup>-L<sub>2</sub> complex defines four thermal changes. The first stage at temperature range 34-149 °C is accompanied by a weight loss of one molecules of water of crystallization 2.66%. In the second step at temperature range 148-340°C, this peak represents the start of ligand degradation. The 55.69% mass loss corresponds to loss five molecules of water of coordination, (NO<sub>3</sub>)<sub>2</sub>, EtO<sub>2</sub>C and *p*-nitro benzene ,forming molecules ion M/e =315.4 of abundance 100%. The third inflection at temperature rang 348-646 °C gives a mass loss of 13.5 % corresponds to the breaking of N<sub>2</sub> gas and C<sub>3</sub>H<sub>5</sub><sup>+</sup> group forming molecules ion 218.4. The four stage at temperature range 648 – 999.8°C represents , the loss of residual organic part ion 7.03% so that the compound converted metal oxide SmO molecules ion M/e = 166.4 of abundance 1.68% (Scheme 6).

The pyrolysis of (1:1) UO<sub>2</sub><sup>+2</sup> - L<sub>2</sub> complexes shows five inflections in the TG curve. The first stage lies at 36-100 °C and corresponds to a loss of one molecule of water of crystallization (1.54%). The second inflection at temperature rang 101-182 °C gives a mass loss of 10.789 % corresponds to the breaking of two molecules of water coordination and loss of NO<sub>2</sub> group forming molecules ion 708.03 of abundance 1.02%. The third inflection at temperature range 182-202 °C, gave mass loss of 33.04% which corresponds to the breaking of (NO<sub>3</sub>)<sub>2</sub>, EtO<sub>2</sub>C and C<sub>6</sub>H<sub>4</sub><sup>+</sup> groups, forming molecules ion M/e= 435.03 of abundance 1.19%. The weight loss of 11.896% corresponds to the loss of N<sub>2</sub> gas and C<sub>3</sub>HS<sup>+</sup> group occurs at temperature range 520-718 °C in TG curve, forming a molecular ion M/e 338.03 of abundance 1.23%. In the final process at temperature range 818-953 °C, which due to loss of the remain part of C<sub>3</sub> H<sub>2</sub>NO with a mass of 7.84% then the complex converted metal oxide UO<sub>2</sub><sup>+2</sup> as an end product (Scheme 7).



### Antimicrobial activity

Structure-antimicrobial (biological) activity relation-ship for some selected newly synthesized dihydrothieno[3,4,D]pyridazine compounds a,1a,2a,3a,4a,5a, equal to L<sub>1</sub>, L<sub>1</sub>-Ce(III), L<sub>1</sub>-La(III), L<sub>1</sub>-Sm(III), L<sub>1</sub>-UO<sub>2</sub>(II) and L<sub>1</sub>-Th(IV) and b,1b,2b,3b,4b,5b, equal to L<sub>2</sub>, L<sub>2</sub>-Ce(III), L<sub>2</sub>-La(III), L<sub>2</sub>-Sm(III), L<sub>2</sub>-UO<sub>2</sub>(II) and L<sub>2</sub>-Th(IV), respectively were studied and determined against some bacterial *Escherichia Coli* (Gram-negative bacteria), *Staphylococcus Aureus* (Gram-positive bacteria), and fungi strains *Candida*, Ampicillim was used as the standard antibacterial agent and Amphotericin was used as the standard Antifungal agent. The antibacterial activity showed that all compounds were active against microorganisms. All compounds were less active in comparison to Ampicillim, which was taken as a standard drug. Further, investigation on the biological activity of these compounds will be considered in the progress. Inactive fungi strains (inhibition zone <9.3 mm).

The data obtained are expressed as size (mm) of inhibition zone. Diameter of the inhibition zones were high (22-18 mm), moderate (17-12 mm), slight (11-1 mm), no response (-). It is clear from the microbiocidal screening data that the metal complexes are more toxic in comparison to their parent ligand itself. Hence complexation increase the antimicrobial activity<sup>58</sup>, such increased activity of the metal complexes can also be explained on the basis of chelation theory<sup>59,60</sup>. Bacterial and fungus strains and the biological effect are shown in Table 5.

**Table 5.** Biological activity of some new synthesized complexes

Sample	Inhibition Zone diameter (mm/mg sample)			
	<i>Escherichia Coli</i> (G <sup>-</sup> )	<i>Staphylococcus Aureus</i> (G <sup>+</sup> )	<i>Candida Albicans</i> (Fungus)	<i>Aspergillus Flavus</i> (Fungus)
Control: DMSO	0	0	0	0
Ampicillin	22	18		
<i>Antibacterial Agent</i>				
<i>Amphotericin B</i>	-	-	19	16
<i>Antifungal Agent</i>				
a	10	10	12R	0
1a	11	10	9	0
2a	13	12	9	0
3a	12	11	0	0
4a	20	18	9	0
5a	11	16R	0	0
b	0	0	0	0
1b	11	11	0	0
2b	10	10	9	0
3b	9	0	9	0
4b	16R	16R	10	0
5b	11	11	10	0

The final conclusion from this work is that these novel compounds showed significant antibacterial activity according to the following factors:

- (1) Diameter of the inhibition zones were high in actinide complexes than lanthanide complexes
- (2) The presence of either electron donating and/or accepting group.

## Conclusion

Coordination compound formed by the interaction of dihydrothieno[3,4-d]pyridazine with La(III), Ce(III), Sm(III), Th(IV) and UO<sub>2</sub>(II) are prepared and characterized by elemental analysis, IR, <sup>1</sup>HNMR Mass spectra and thermal analysis. The analysis data indicate that the ligand acts as bidentate on chelation, thermogravimetric analysis confirm the presence of coordinated water. The IR spectra indicate that coordination takes place through the nitrogen of amino group and C=O group of pyridazine ring. Antimicrobial activity of selected compounds against some bacterial strains was tested and confirm the antimicrobial activities of the ligand increase on coordination with the metal ion.

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