Synthesis, Spectroscopy, Biological Activities and Thermodynamic Studies for New Complexes of Some Lanthanide Metals with Schiff's Bases derived from [2-acetylthiophene] with [2,5-dihydrazino-1,3,4-thiadiazole]

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Abstract

Reaction of 2-acetylthiophene and 2,5-dihydrazino-1,3,4-thiadiazole in refluxing ethanol gave 2,5 di(1-thiophen-2-yl-ethylidene)-hydrazine) 1,3,4-thiadiazole ligand (L), which was characterized by FTIR, UV-vis., ^{1}H-NMR and LC mass spectra and thermal analysis. The reaction of (L) with the metal ions [(M = [La(III), Nd(III), Gd(III) and Dy(III)] gave the corresponding complexes, characterized by FTIR, UV-Vis., magnetic susceptibility, conductivity measurements, thermal analysis and elemental analysis.

The parameters of thermodynamic, [ΔE^*, ΔH^*, ΔS^* and ΔG^*] were calculated using Coats-Redfern method by the TGA curve. The structures of the complexes were proposed from the spectral measurements. The preliminary results in vitro tests for antimicrobial activity showed that all new prepared complexes have a good activity to Escherishia coli, Staphylococcus aureus, Pseudononas aeroginosa and the yeast Candida albicans.

Keywords: Lanthanide complexes, Thermal analysis, Antimicrobial activity, Schiff's Bases Complexes, Spectral analysis.

Introduction

Interest in lanthanide chemistry has been recently increasing wing to use of lanthanide complexes as biological probes and in materials Schiff bases are very accomplished ligands in transition as well as inner-transition metal complexes with suitable properties for practical applications[1], a complexes derived from [2,5-dihydrazino-1,3,4-thiadiazole]. They are usually prepared as pentadentate Schiff base formed by the condensing of primary amines with active carbonyl compounds. The nitrogen donor organic compounds have a physiological importance[2] and play an active role by coordination of some metal ions to them[3]. Schiff bases possess chelation with sulfur and nitrogen donors[4].

Therefore, from pharmacology point view, Schiff base hydrazones are also interesting. Hydrazone derivatives have antimicrobial,[5] antitubercular,[6] anticonvulsant[7] and anti-inflammatory activities[8]. Condensation of primary amines with aldehydes forms Schiff bases-bimolecular that represents valuable intermediates in organic synthesis and, complexes with various applications[9]. Due to their structural chemistry and biological activities as antipyretics, analgesic and anti-inflammatory, thiadiazole and thiophene and their derivatives form a valuable class of organic complexes[10]. Some thiophene derivatives are widely used as painkiller medicines. Thiophene has potential to form different types of coordination complexes.

In addition, a variety of Schiff bases can be formed by thiophene and they are reported as reagents in clinical, biological and analytical applications[11-13]. In continuation of our work on the metal complexes of Schiff bases, we report here the study of some new [La(III), Nd(III), Gd(III) and Dy(III)], complexes of Schiff bases derived from 2-acetylthiophene with 2,5-dihydrazino-1,3,4-thiadiazole .

Material and Methods

All chemicals used in this work were of reagent grade supplied by Aldrich, Fluka and Sigma and used as supplied. The FTIR spectra in the range 4000-400 cm^{-1} were recorded as CeI disc on FTIR. The UV-Visible spectra were measured in ethanol using Shimadzu UV-Vis. 160 A-Ultra-violet Spectrophotometer in the range 200-1000 nm. Magnetic susceptibility for complexes was measured using Magnetic Susceptibility Balance Jhonson Mattey Catalytic Systems Division, at room temperature. The melting points of all new complexes were measured by using Gallencamp M.F.B600.010 F melting point apparatus. CHNOS Elemental Analyzer Model 5500 Carlo-Erba Instruments was used to measure elemental microanalysis.

Synthesis of [2,5-dimercapto-1,3,4-thiadiazole] [A]: Hydrazine hydrate (99%) (5 mL, 0.02 mol) was mixed with carbon disulfide (15 mL, 0.04 mol) and dry pyridine (50 mL), then refluxed for 5 hrs. Rotary evaporator was used to distill the excess solvent, the formed solid was separated out by adding 25 mL of water and 5 mL of hydrochloric acid. The mixture was then filtered off and the solid was re-crystallized with ethanol as solvent.

Synthesis of [2,5-dihydrazino-1,3,4-thiadiazole] [B]: 2,5-dimercapto-1,3,4-thiadiazole [A] (1.5 g, 0.01 mol) was dissolved in ethanol drop wise with stirring, hydrazine hydrate (5 mL, 0.02 mol) was added and the mixture then refluxed for 6 hrs, rotary evaporator was used to distill the excess solvent. The resulting solid was separated out on cooling, filtered off and re-crystallized from ethanol to give the desired product. m.p, yield, C.H.N.S analysis in table 1.

[2,5di (1-thiophen-2-yl-ethylidene)-hydrazine) 1,3,4-thiadiazole] [L]:

Method 1: A mixture of 2-acetylthiophene (1.90 g, 0.02 mol) in absolute ethanol (50 mL) with [B] (1.46 g, 0.01 mol) in absolute ethanol (50 mL) in 250 ml round bottom flask was taken and add 5 drops of glacial acetic acid, the mixture was refluxed on water bath at 80 ºC for 8 hours. The reaction mixture was then allowed to cool at room temperature and the precipitate was filtered off, dried and recrystallized from ethanol to give yellow powder.

Method 2: A mixture of [B] (1.46 g, 0.01 mol) with (1.90 g, 0.02 mol) 2-acetylthiophene was ground with a mortar, mixed, dried and subjected to microwave irradiation 280 W for 10 minutes, after completion the reaction mixture was cooled to room temperature; the solid obtained was re-crystallized twice from absolute ethanol, some of the physical data for these four complexes are listed in table 1.

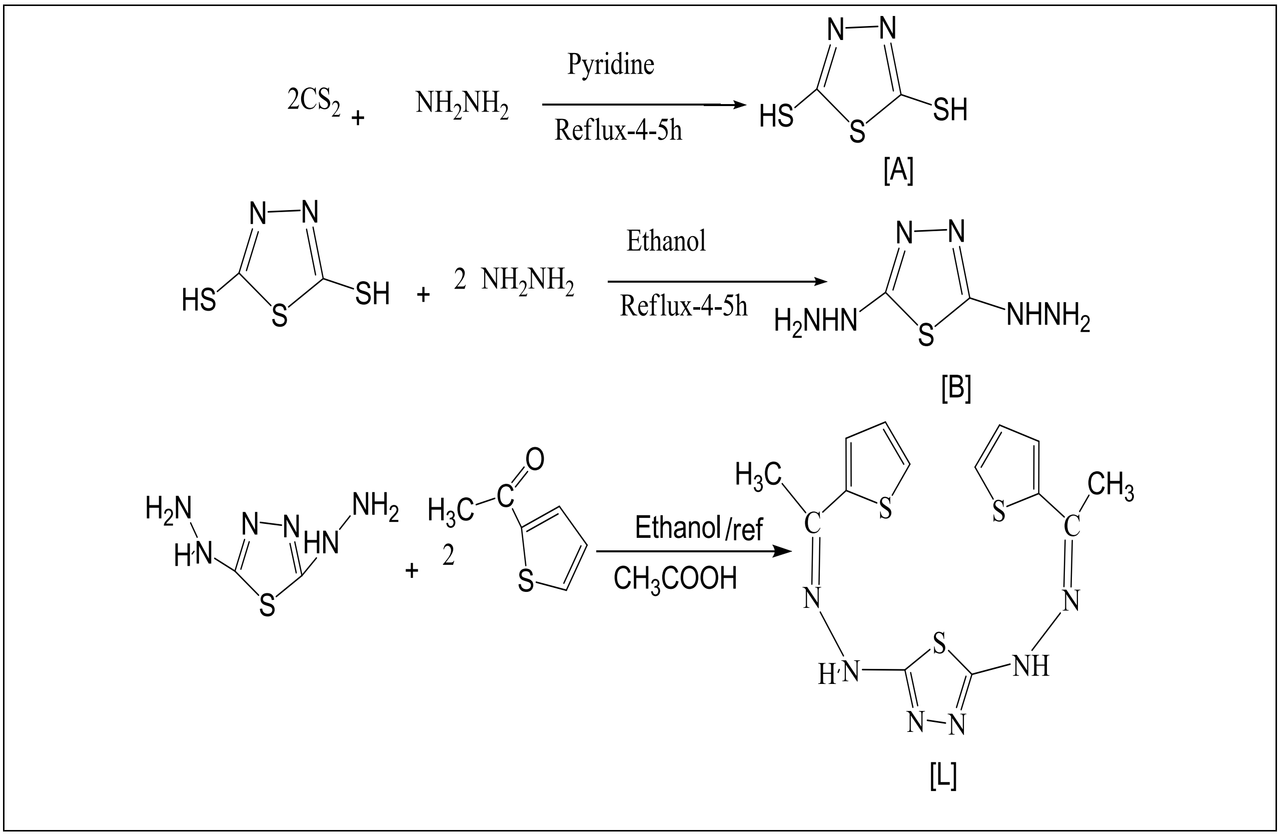
Preparation of complexes

Method 1: In 25 ml round bottom flask, add 10 ml ethanol of the metal salt of [La(III), Nd(III), Gd(III) and Dy(III)] added to (10 ml of an ethanolic) solution of the (L) in 1:1 (M(III) : L) molar ratio with stirring and refluxing for 3-4 hours on a water bath, the solution was concentrated to 5 ml and 10 ml of acetonitrile was added. The solid is filtered off, washed with mixture of ethanol and acetonitrile (1:2) volume ratio and dried in desiccator.

Method 2: 10 ml ethanolic solution of the metal salt of Ln(III), was added to10 ml an ethanolic solution of the (L) in 1:1 (metal : ligand) molar ratio in 25 ml round bottom flask and put in ultrasonic bath heating 80 ^{0}C. After 30 minutes, the solution was concentrated to 5 ml and add 10 ml of acetonitrile, the resulting solid was filtered off, washed with mixture of ethanol-acetonitrile (1:2) volume ratio and dried in desiccator.

Results and Discussion

The preparation of the ligand is presented in scheme (1). The reactions of the trivalent inner-transition metal ions [Ln(III)] with the ligand were monitored by the job and mole ratio methods and determine the shape of the complexes. The ratio of the [Ln(III)] to ligand (1:1) is shown in figures 3 and 4. The absorption bands due to the f-f transitions of the lanthanide ions could not be identified in the visible region of all these complexes. This may be probably attributed to the fact that the f-f transitions are very weak and the bands corresponding to these transitions are observed by the strong charge and transfer transition bands of the ligand (charge transfer from ligand to metal)[14]. Table 2 shows the same properties like magnetic moment, colors and electronic absorption bands for the ligand and the complexes.



Scheme 1: Synthesis of ligand

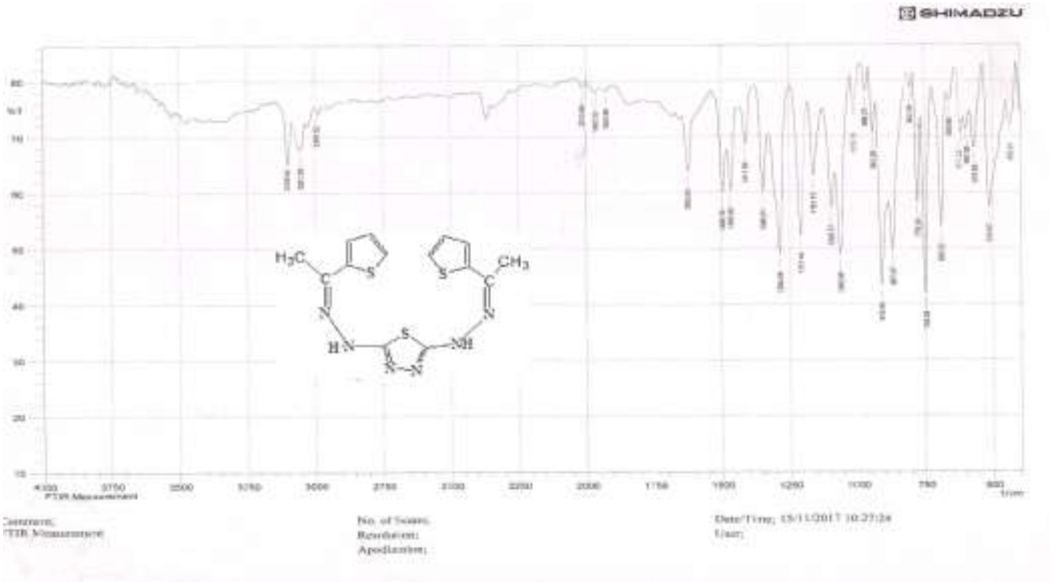


Fig. 1: IR- spectrum of ligand

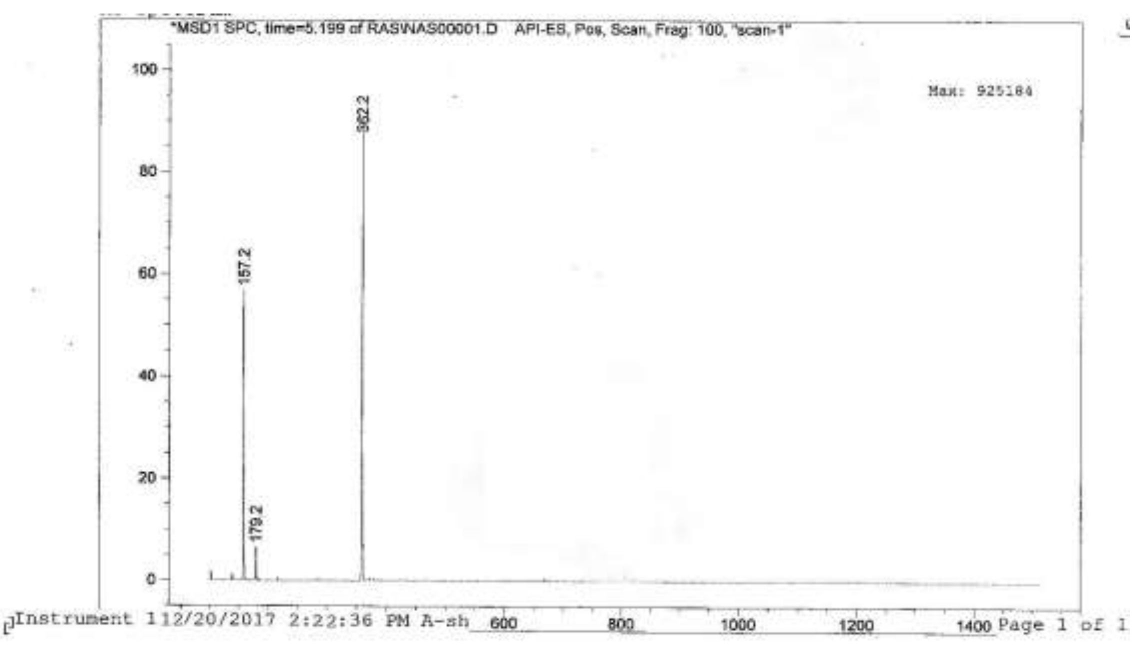
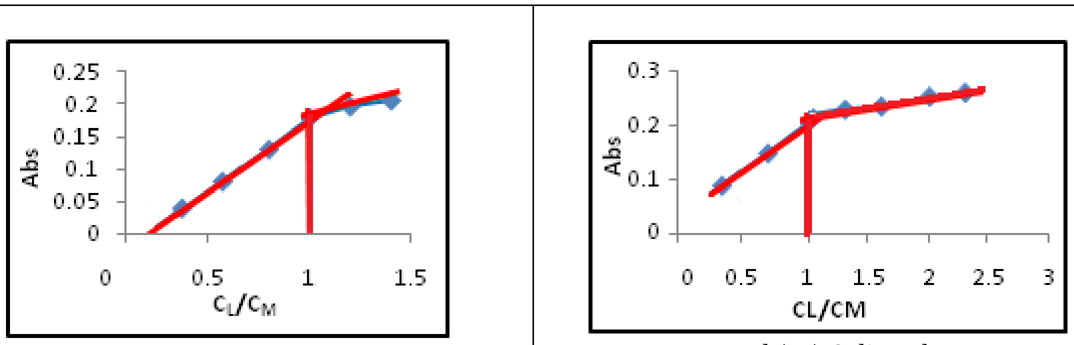


Fig. 2: LC-Mass spectrum of ligand

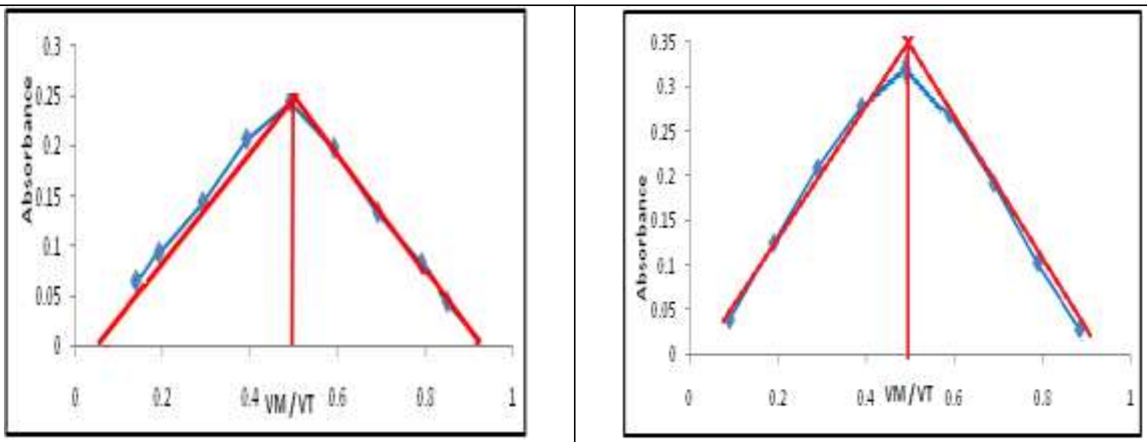
Table 1
The characterization data of the ligand and complexes

Complex Formula	Yield%	C	H	N	S	Cl	M
B $C_2H_6N_6S$	83	16.41 (16.43)	4.17 (4.14)	57.53 (57.49)	21.89 (21.94)	---	---
L $C_{14}H_{14}N_6S_3$	75	47.08 (46.39)	3.83 (3.89)	23.11 (23.18)	25.98 (26.54)	---	---
$[La (L) (H_2O)_2Cl]Cl_2$	59	29.96 (29.35)	2.94 (3.17)	15.40 (14.67)	15.91 (16.79)	5.99 (6.19)	24.60 (24.25)
$[Nd (L) (H_2O)_2Cl] Cl_2$	64	29.60 (29.08)	2.86 (3.14)	14.86 (14.53)	16.29 (16.64)	6.01 (6.13)	24.65 (24.95)
$[Gd (L) (H_2O)_2Cl] Cl_2$	78	28.99 (28.44)	2.78 (3.07)	14.62 (14.21)	16.01 (16.27)	6.27 (6.00)	26.14 (26.60)
$[Dy (L) (H_2O)_2Cl] Cl_2$	63	28.74 (28.19)	2.73 (3.04)	14.40 (14.09)	16.42 (16.13)	5.61 (5.94)	26.65 (27.24)



La (III) & ligand Nd (III) & ligand

Fig. 3: Mole Ratio Method



Gd (III) & ligand **Dy (III) & ligand**

Fig. 4: Continuous Variation

[2,5 di(2-thiophene methyl hydrazone) 1,3,4-thiadiazole] [L]: The FT-infrared spectra of the ligand showed the disappearance of the amine [NH_2] in the region (3402-3213) cm^{-1} and the appearance of new band is directional of the group amine at (1635 cm^{-1}) belonging to the group azomethine and the frequencies of the thaidiazole ring appeared at (1284-1346 cm^{-1})[15]. Table 3 contains the IR spectra values of the record.

Spectrum of ^1H-NMR ($CDCl_3$-400 MHz) showed several chemical shifts of the different proton of the recorded δ= 9.755 (s, 2 H, HN), 8.985 (s, 2H, CH=N), 6.531 -7.495 (m,6 H, tow thiophene ring), 2.4-3.4 (m, 6H, CH3), 1.744 (solvent+H_2O). The mass spectrum as shown in fig. 2 shows that the ligand mass corresponds to the theoretical calculation m/z=362.2 (M^{+1}).

Infrared spectral analysis of metal complexes: The FT-infrared spectra of the complexes show the azomethine band at 1635 cm^{-1} shift ($\Delta\upsilon$ = 30-36 cm^{-1}) in all the lanthanide complexes indicating the nitrogen coordination. In most of the complexes, a new band was introduced at the range 318-275 cm^{-1} which is due to the M-S vibrations which indicates that the metal in these complexes has a sulfur atom in the ligand. The broad bands at the range (3285-3378) cm^{-1} refer to [O-H] which may be of coordinated water[16]. The FT-infrared spectrum shows the M-N metal-nitrogen stretching of the prepared complexes in the confined area between (488-505) cm^{-1}, confirming the bonding of the metal with the Schiff bases by the nitrogen atom of the right group.[17]

Thermal analysis: The study of the thermal behavior is of great importance in the knowledge of many applications and the results of the study of thermodynamics studied ligands and complexes and the calculation of kinetic and thermodynamic factors. From the thermal TGA curves of the complexes, the first step in the thermal range (37-190 °C) for complexes represents the loss of water molecules while the second and third steps included a mass loss for part of the complex observed at the maximum temperature of the mass loss (T_{max}). At the end of the thermal plan, the remaining mass is equal to the mass of Ln_2O_3. Activation energy, (ΔS^*), (ΔH^*) and free energy ΔG^* (using the Coats and Redfern equation and all thermodynamic values, are given in table 4[18,19].

Biological Activity: New series containing 1,3,4- thiadizole and thiophene ring system was prepared with a view to explore the possibility of biological useful activity. The ager diffusion method was used to determine the antimicrobial activity of these complexes[20]. *Staphylococcus aureus*, *Pseudononas aeruginosa*, *Escherishia coli* and *Candida albicans* were used. A standard 5 mm diameter sterilized filter paper disc fattened with each new complex (1 mg per 1 ml of acetone) was placed on an agar plate cultivated with the test microorganism. Incubate the plates for 24 hrs at

37^{0}C. The inhibition zone formed was measured in mm and is represented by (+), (+ +) and (+ + +) depending upon the clarity and diameter as shown in table 5. The screening result shows that thiadizole and thiophene complexes have highest antibacterial activity against *Escherishia coli*.

Table 2
Magnetic moment and molar conductance and data electronic spectra

Ligand and Complexes	m.p. ^{0}C	conductivity (μS/cm) in DMSO	Magnetic moment (B.M)	Color	Absorption Bands (cm^{-1}) in ethanol	Bands Assignment
A	162-163	-	-	White-pink	43845	$\pi \rightarrow \pi^*$
					3099	$n \rightarrow \pi^*$
L $C_{14}H_{14}N_6S_3$	183-185	-	-	Yellow	40755	$\pi \rightarrow \pi^*$
					27200	$n \rightarrow \pi^*$
$[La(L)(H_2O)_2Cl]Cl_2$	300d	181	0	Pale yellow	43250	$\pi \rightarrow \pi^*$
					28674	$n \rightarrow \pi^*$
$[Nd (L) (H_2O)_2Cl] Cl_2$	300d	170	3,4	Pale orange	40300	$\pi \rightarrow \pi^*$
					27505	$n \rightarrow \pi^*$
$[Gd (L) (H_2O)_2Cl] Cl_2$	300d	189	7.7	yellow	42200	$\pi \rightarrow \pi^*$
					30040	$n \rightarrow \pi^*$
$[Dy (L) (H_2O)_2Cl] Cl_2$	300d	172	10.2	Pale yellow	40240	$\pi \rightarrow \pi^*$

Table 3
IR data of Ligand and its metal complexes (cm^{-1})

Symbol	ν(C=N)	ν(N-H)	ν(C-N=N-C)	ν(M-N)
L	1635(s)	3109	1284-1346	-
La(III)	1605(s)	3153 (s)	1258-1332m	498w
Nd(III)	1600(s)	3164(s)	1247-1345m	505w
Gd(III)	1601(s)	3147 (s)	1271-1316m	490w
Dy(III)	1599(s)	3169 (s)	1257-1311m	488w

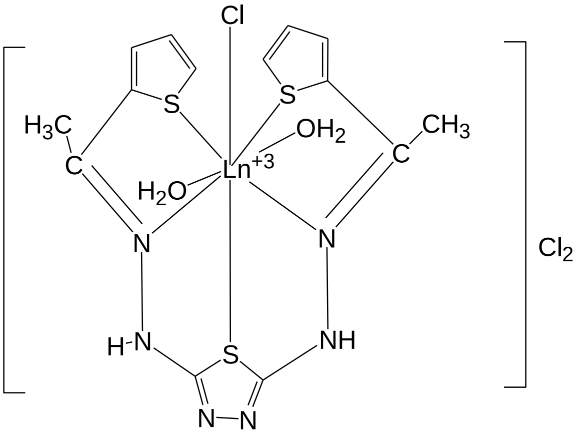
Table 4
The thermodynamic parameters of the L and lanthanide complexes

Sample (step)	T.range °C	N	R^2	T$_{max}$ °K	Ea K.J mol^{-1}	Δ H* KJ mol^{-1}	ZSec^{-1} x10^5	Δ S* J mol^{-1}K^{-1}	Δ G* KJ mol^{-1}
L$_1$(1)	37-300	1	0.99	512.79	170.4906	166.2344	1.7801	-34.0617	183.700
L$_1$(2)	300-700	0.9	0.99	780.77	7.87418	-14.3548	4.82	-354.698	262.5828
La(1)	37-180	0.9	0.99	423	125.9	46.49	7.68	-223.79	135.39
La (2)	180-395	0.9	0.99	554	54.214	121.04	0.5357	-100.31	169.81
La (3)	395-700	0.9	1	725.25	12.696	-5.734	4.91	-359.81	306.7
Nd(1)	37-170	0.9	0.99	348.5	6.79244	3.8784	970.1152	-93.3712	36.64
Nd (2)	170-360	0.9	0.99	538.11	8.6145	4.124	361.2055	-105.181	61.15
Nd (3)	37-170	0.9	0.99	348.5	6.79244	3.8784	970.1152	-93.3712	36.64
Gd(1)	37-190	0.8	0.99	480.8	23.71	19.72	1.6x10^{-4}	-321.9	174.52
Gd(2)	190-450	0.8	0.99	550	98.17	92.77	261.70	-205.2	226.16
Gd (3)	450-700	0.8	0.99	819	-10.14	-17.78	3.8x10^{-6}	-358.3	311.69
Dy(1)	37-170	0.8	0.99	415	133	49.24	2.9 x 10^{-6}	-232.5	229.53
Dy (2)	170-415	0.9	0.99	545	56	119.8	3.1 x 10^{-6}	-356.6	277.56
Dy (3)	415-700	0.8	0.97	720	16.2	-8.66	3.1 x 10^{-6}	-358.71	313.5

Table 5
Antibacterial activity of the prepared compounds

Symbol	Staphylococcus aureus	Escherishia coli	Pseudononas aeroginosa	Cndida albicans
L	++	+ + +	++	++
La(III)	++	++	+	+
Nd(III)	+	+++	++	++
Gd(III)	++	++	+++	++
Dy(III)	++	+ + +	++	++

Note (-) = no inhibition, (+) = (5-10) mm, (+ +)=(11-20) mm, (+ + +) = more than (20)mm



Proposed structure of [Ln (L) (H_2O)$_2$Cl] Cl_2
M = [La (III), Nd (III), Gd (III) and Dy (III)]

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