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Biologically active 22-membered N_4 tetraaza macrocyclic triazoles: Template synthesis and spectroscopic approach

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Abstract

A series of La(III) and Th(IV) complexes have been synthesized by template condensation of *ortho*-phthalaldehyde, *bis*-(4-amino-5-mercapto-1,2,4-triazole-3-yl)alkanes and $La(NO_3)_3 .6H_2O$ /$Th(NO_3)_4$. $5H_2O$ in ethanol. These complexes were characterized by elemental analyses, magnetic susceptibility, molar conductance, spectral (IR, UV-Vis, ^{1}H NMR FAB-mass), and thermal studies. Elemental analyses suggest 1:1 stoichiometry. Spectroscopic study indicates that the coordination occurs through nitrogen of azomethine group and bridging bidentate nitrates. All the Schiff bases and their La (III) and Th (IV) complexes have been screened for their antibacterial (*Escherichia coli, Staphylococus aureus, Salmonella typhi, Pseudomonas aeruginosa)* and antifungal activities (*Aspergillus niger, Aspergillus flavus and Cladosporium)* by the minimum inhibitory concentration method. The DNA cleavage study was done by Agarose gel electrophoresis.

Key words: Synthesis, Complex, Macrocyclic, Bistriazole, Ortho-phthalaldehyde

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Introduction

Much research on macrocyclic complexes has been focused on species containing a first-row transition metal ion and a tetradentate ligand [1]. The interest in the study of macrocyclic complexes continues to expand because of their catalytic properties which have led to industrial applications in addition to their involvement in many important biological processes such as photosynthesis and dioxygen transport [2-3]. The macrocyclic Schiff bases have been widely studied due to their selective chelation to certain metal ions depending on the number, type and position of their donor atoms, the ionic radius of metal ion and coordinating properties of counterions [4-6].The formation of macrocyclic complexes depends significantly on the

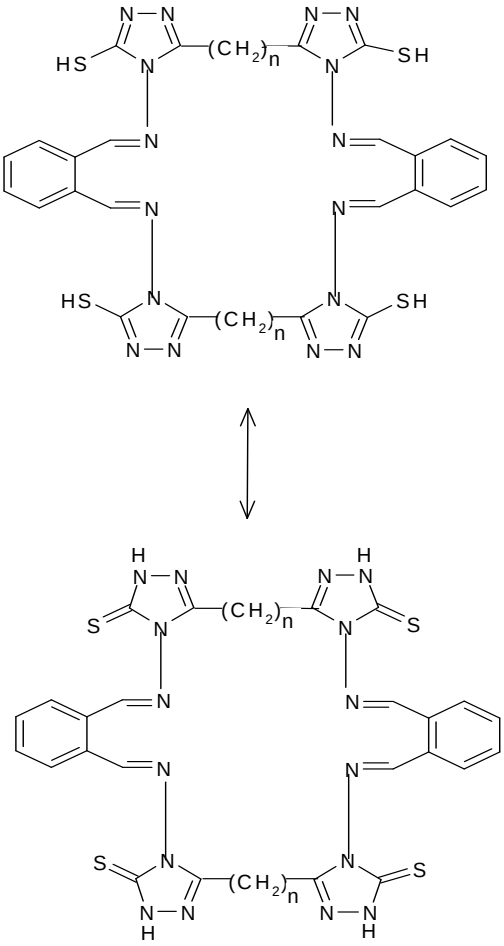
dimension of the internal cavity, on the rigidity of the macrocycle, on the nature of its donor atoms and on the complexing properties of the anion involved in the coordination [7-8]. These ligands are also of theoretical interest since they are capable of furnishing an environment of controlled geometry and ligand field strength [9-10]. The importance of macrocyclic ligands and their complexes is obvious when seen in relationship to natural products such as metalloprotein, vitamin B_{12} and chlorophyll [11]. A number of nitrogen donor macrocyclic derivatives have long been used in analytical, industrial and medical applications [12]. Macrocyclic metal complexes are of great importance due to their resemblances to many natural systems such as porphyrins and cobalamines. Macrocyclic nickel complexes find use in DNA recognition and oxidation while the macrocyclic copper complexes find use in DNA binding and cleavage [13-14]. Several macrocyclic complexes with tetraaza macrocyclic ligand, such as cyclen, cyclam or bicyclam were reported to exhibit antitumour activity [15]. The chemistry of macrocyclic complexes is also important due to their use as dyes and pigments as well as NMR shift reagents [16].Macrocyclic ligands with lanthanides have applications as contrast agents for magnetic resonance imaging [17], catalyst for specific cleavage of RNA [18], stains for fluorescence imaging [19] and cancer radiotherapy [20]. Thus, there has been continued interest in design of new macrocyclic ligands having various industrial applications [21-22].The complexes of macrocyles with lanthanide(III) ions have attracted attention as efficient catalysts for the cleavage of the phosphate ester bond [23]. Herein, we report the synthesis, characterization, *in vitro* antimicrobial studies of La (III) and Th(IV) complexes with 22-memberd N_4 tetraaza macrocyclic Schiff bases shown in Figure1.

Results and Discussion

All the La(III) and Th(IV) complexes are colored, non-hygroscopic solids and stable in air. The complexes are soluble in DMF and DMSO. Elemental analyses show 1:1 stoichiometry, The low conductivity values confirm the non-electrolytic nature of all the complexes. In order to establish whether water molecules present in the complexes coordinate to the metal, weighed complexes were dried over P_2O_5 in vacuum for 1h and then weighed again with no loss in weight, suggesting the water molecules are coordinated to the metal. All the complexes are diamagnetic.

Infrared spectra

Important IR frequencies of the Schiff bases and their La(III) and Th(IV) complexes are presented in Table 3 and Table 4. The Schiff bases have thiol and thione forms. A medium band at 3155 cm^{-1} due to ν (NH) indicates the thione form, while weak band centered at 2400 cm^{-1} due to ν (SH) is suggestive of thiol form. These observation confirm the thiol-thione tautomerism. A medium to high intensity band around 1630 cm^{-1} was assigned to ν(C=N) confirming the presence of *ortho*-phthalaldehyde. The NCSH and NHCS groups have thiamide-II vibrations, thiamide-III vibrations at 1045-1032 cm^{-1} and thiamide -IV vibrations (mainly from ν(C=S)) located at 750 cm^{-1}. In addition to above IR absorptions, medium intensity band in the 1600-1575 cm^{-1} region are regarded as a combination of C=N of triazole ring and aromatic C=C stretching vibrations.



$L^{I:}$ n=1, $L^{II:}$ n=2, $L^{III:}$ n=3, $L^{IV:}$ n=4.

Figure 1. Structure of Schiff bases (L^{I}-L^{IV}) in thiol-thione tautomeric forms

In the complexes we observed the following changes: (1) The characteristic band due to ν (C=N) appears around 1610-1600 cm^{-1} suggesting that the C=N group is coordinated to the metal through the nitrogen. The bands due to C=N of the heterocyclic ring for the complexes appears almost in the same region as observed in the ligands [27]. **(**2) A broad band of medium intensity at 3400-3300 cm^{-1} is due to symmetric and antisymmetric O-H stretching vibrations of lattice water [28]. Those at 3255 and 850 cm^{-1} are characteristic of coordinated water and band at 550 cm^{-1} is due ν (M-N) [29].**(**3) The infrared spectra of the nitrato complexes contain bands characteristic of both coordinated and ionic nitrates. The bands at 1470 cm^{-1} and around 1340 cm^{-1} are due to the ν (N=O) ν_1 and ν_{assym} (NO_2)(ν_5), respectively, of coordinated nitrate. The ν_{symm} NO_2 vibration (ν_2) at 1030 cm^{-1} is characteristic of bidentate chelating nitrate. The separation (Δν) of the nitrate stretching fundamentals (ν_1- ν_5) has been used as a criterion to distinguish between mono and bidentate chelating nitrates [30]. The magnitude of this separation (Δν=130) indicates bidentate coordination. (4) All the La(III) and Th(IV) complexes exhibited broad medium intensity band around 3140 cm^{-1} and weak band around 2350 cm^{-1} are due to ν (NH) and ν (SH) vibrations.

Table 3. Important infrared frequencies (in cm^{-1}) of Schiff bases L^{I}- L^{IV}

Ligands	ν(NH)	ν(SH)	ν(C=N)	Thiamide I	Thiamide II	Thiamide III	Thiamide IV
L^{I}	3142	2399	1624	1604	1318	1038	742
L^{II}	3152	2401	1626	1609	1314	1045	751
L^{III}	3149	2388	1632	1593	1315	1035	740
L^{IV}	3148	2383	1630	1595	1 318	1032	748

Table 4. The important infrared frequencies (in cm^{-1}) of La(III) and Th(IV) complexes

Complex No.	ν(C=N)	ν (NH)	ν (SH)	ν (M-N)	(N=O) ν_1	$\nu_{asym}(NO_2)$ ν_5	$\nu_{sym}(NO_2)$ ν_4
1	1603	3143	2361	551	1450	1321	1024
2	1604	3145	2349	543	1459	1335	1027
3	1605	3141	2362	545	1460	1336	1030
4	1602	3143	2349	547	1465	1339	1026
5	1600	3142	2347	549	1455	1334	1031
6	1608	3149	2351	550	1462	1340	1029
7	1610	3145	2358	548	1469	1338	1024
8	1611	3155	2348	546	1470	1340	1031

^{1}H NMR spectral studies

The ^{1}H-NMR spectra of all the Schiff bases exhibited signals at 13.6 and 13.4 ppm due to –NH protons. The resonance due to SH of all the compounds appear at 3.5 ppm indicating thiol-thione tautomerism. The azomethine protons in all the compounds appear at 8.91 ppm. Multiplets at 7.4-7.7 ppm are due to aromatic protons. The following changes were observed in the ^{1}H-NMR spectra of La(III) and Th(IV) complexes: (1)The signal due to azomethine (8.91) showed a downfield shift to 9.24 ppm indicating coordination of azomethine to the metal. (2) The signal due to coordinated water protons in the complexes were appeared at 5.4 ppm. (3) The signals at 3.5 ppm due to SH proton were unaffected in the metal complexes, indicate non-involvement of SH group in the coordination. The signals due to NH proton around 13.60 ppm, the aromatic protons at 7.4-7.7 ppm were unaffected in the metal complexes.

Electronic absorption spectra

The electronic spectra of the complexes for freshly prepared solutions in DMSO at room temperature showed broad band around 31000 cm^{-1} assigned to L→M charge transfer transition.

FAB-mass spectral studies of Schiff base L^{I} and its La(III) (1) and Th(IV)(5) complexes

The FAB mass spectrum of L^{I} shows molecular ion peak at *m/z* 684 equivalent to its molecular weight. Fragmentation leads to $[C_{26}H_{20}N_{16}S_4]^{+}$. The FAB mass spectrum of La (III) (1) complex

contains the molecular ion peak M^+ at *m/z* 1036 equivalent to its molecular weight. This molecular ion undergoes fragmentation with lost of five water molecules, giving [La (L^I) $(NO_3)_2]^+$ at *m/z* 946. Further, it lost two nitrate molecules gave fragment ion at *m/z* 822. The FAB mass spectrum of Th(IV) (5) complex exhibited molecular ion peak M^+ at *m/z* 1130 equivalent to its molecular weight. Lost of five water molecules gives $[Th(L^I)(NO_3)_2]^+$ at *m/z* 1040; further lost of two nitrates gives $[Th(L^I)]^+$ at *m/z* 916. All these fragmentation patterns are well observed in the FAB mass spectra.

Thermogravimetric analyses

TG and DTG studies were carried out for La(III)(2) and Th(IV)(6) complexes. These complexes decomposes gradually with formation of respective metal oxide above 600 ^oC shown in Figure 2 and Figure 3. The thermograms of La (III)(2) and Th(IV)(6) complexes show that, the lattice and coordinated water molecules removed between 65 and 235 ^oC respectively. The coordinated nitrate decomposes at 255 ^oC. There was steep decrease in the weight loss from 270-300 ^oC due to loss of *bis*-triazole moieties. The La(III)(2) and Th(IV)(6) complexes decomposed significantly form 420-500 ^oC; This is due to loss of *ortho*-phthalaldehyde moieties. Final weight corresponded to that of the metal oxide.

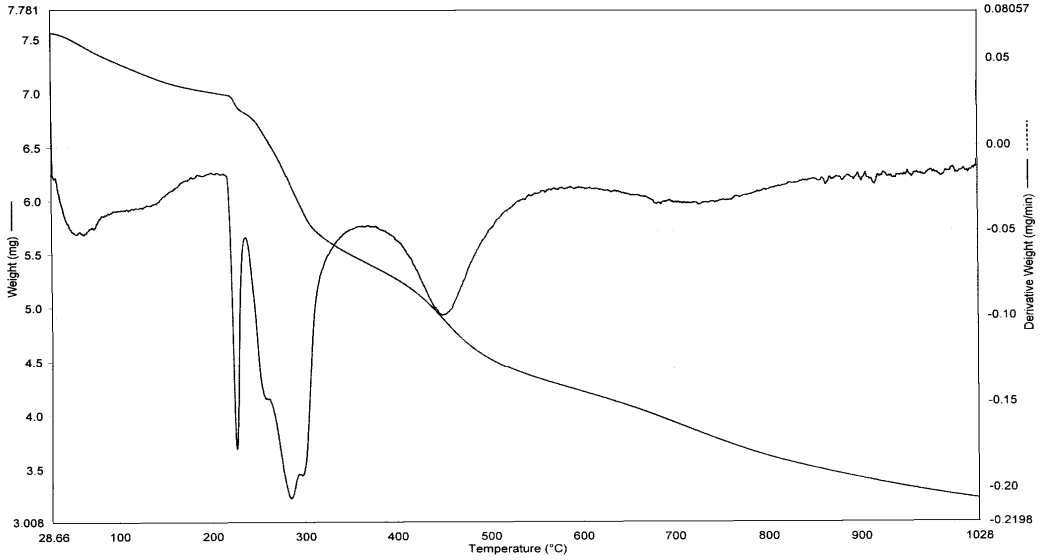


Figure 2. Thermogravimetric (TG/DTG) curves of La(III) (2) complex

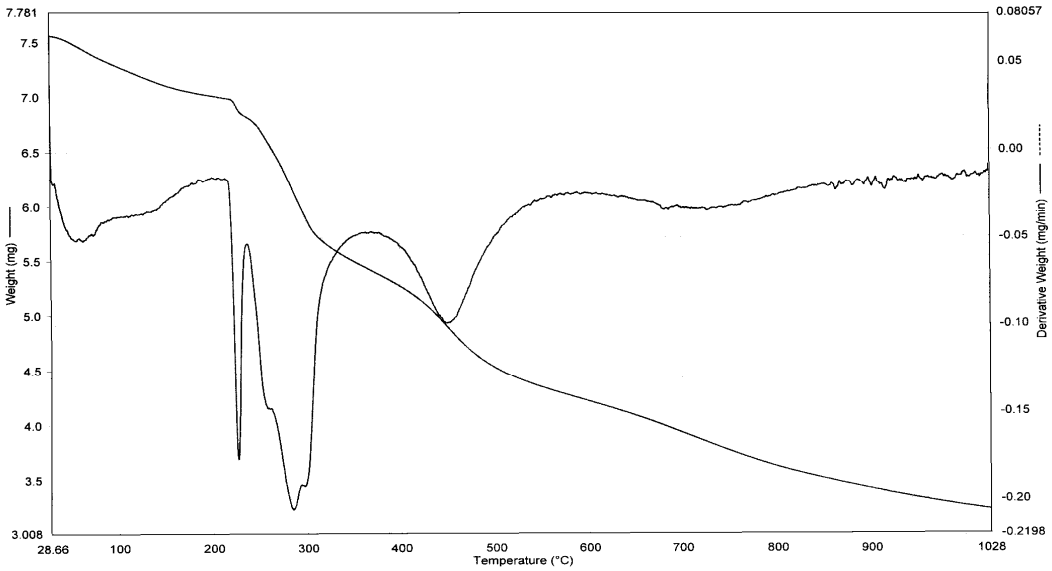


Figure 3. Thermogravimetric (TG/DTG) Curves of Th(IV) (6) Complex

Kinetic study

The Freeman and Carroll procedure was used to evaluate the kinetic parameters for decomposition from single experimental curve (Figure 4.) from the plot of $\Delta \log dw/dt / \Delta \log Wr$ versus $\Delta T^{-1} / \Delta \log Wr 10^3\ ^oK^{-1}$[31]. The order of the reaction and the energy of the activation are listed in Table 5.

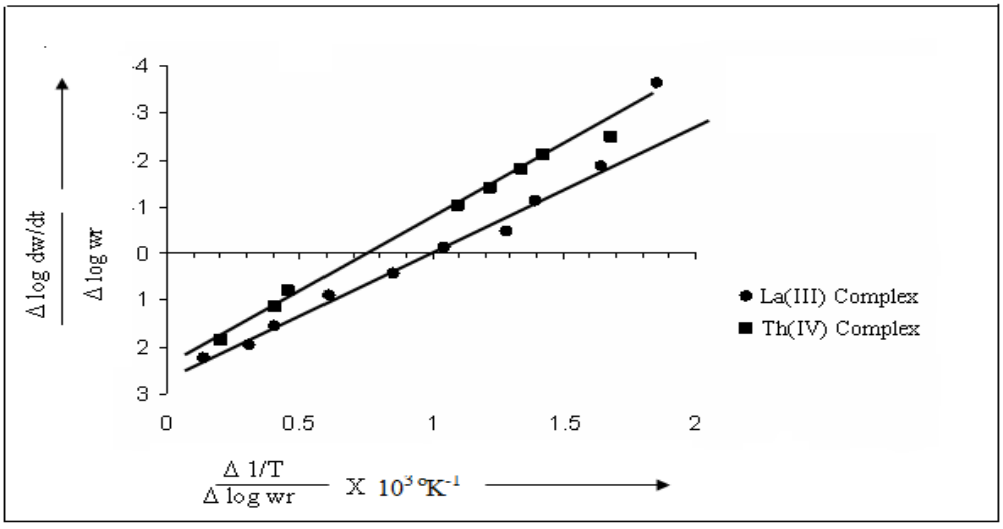


Figure 4. Kinetics of thermal decomposition study of La (III) (2) and Th (IV)(6) Complexes

Table 5. Thermogravimetric data of La (III) (2) and Th(IV)(6) complexes

Empirical formula	Decomposition temperature(^{o}C)	% weight loss Obsd.	Cacd	Inference	Order of reaction	Energy of activation
$[La(L^{II})(NO_3)_2(H_2O)_2].\ 3H_2O$	230-235	3.37	3.38	Loss of coordinate water molecules	0.88	12.98
	270-300	47.73	47.74	Loss of bis triazole moieties		
	420-500	19.16	19.17	Loss of aldehyde moieties		
$[Th(L^{II})(NO_3)_2(H_2O)_2].\ 3H_2O$	230-235	3.10	3.10	Loss of coordinate water molecules	0.69	18.37
	270-300	43.81	43.86	Loss of bis triazole moieties		
	420-500	17.59	17.61	Loss of aldehyde moieties		

Biological Activities

In vitro antibacterial and antifungal assay

Four Schiff bases and eight chemically synthesized complexes were screened for their biological activity by using four bacteria, namely *E. coli, S. aureus, S. typhi and P. aeruginosa* and three fungi namely *A.niger, A. flavus and Cladosporium* by the reported method [32-33]. The bacteria were subcultured in agar medium. The Petri dishes were incubated for 24h at 37 ^{o}C. The standard antibacterial drug (Gentamycine) was also screened under similar conditions for comparison. The fungi were subcultured in potato dextrose agar medium. Standard antifungal drug (Fluconazole) was used for comparison. The petri dishes were incubated for 48h at 37 ^{o}C. The wells were dug in the agar media using sterile metallic borer. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm). Growth inhibition was compared with standard drugs. In order to clarify any effect of DMF on the biological screening, separate studies were carried out with solvent DMF only it showed no activity against any microbial strains.

Minimum inhibitory concentration (MIC)

Some compounds showing promising antibacterial/antifungal activities were selected for minimum inhibitory concentration studies.

Antimicrobial results

The microbial results are systematized in Table 6 and Table 7 shown in Figure 5 and Figure 6. The antibacterial and antifungal studies suggested that, All Schiff bases show moderate activities against all the bacterial and fungal species. It was evident from the data that these activities significantly increased on coordination. This enhancement in the activities may be rationalized on the basis that the presence of C=N bond. It has been suggested that chelation/coordination reduces the polarity of the metal ion mainly because of partial sharing of its positive charge with a donor group within the whole chelate ring system [34-35]. This process of chelation thus increases the lipophilic nature of the central metal atom, which in turn, favors its permeation through the lipoid layer of the membrane thus causing the metal complex to cross the bacterial membrane more effectively so increasing the activity of the complexes. Besides this many other factors such as solubility, dipole moment, conductivity influenced by metal ion may be the possible reasons for the remarkable antibacterial activities of these complexes [36].

Table 6. Antibacterial and antifungal results of Schiff bases (L^{I}-L^{IV})

Ligands	Conc. (μgmL^{-1})	Anti bacterial activity (Zone of inhibition in %)				Antifungal activity (Zone of inhibition in %)		
		E. coli	*S. aureus*	*S.typhi*	*P.aeruginosa*	*A. flavus*	*Cladosporium*	*A. niger*
L^{I}	100	45	45	48	67	75	64	75
	50	50	-	-	58	74	66	61
	30	35	-	52	55	68	50	52
L^{II}	100	50	47	43	60	78	61	78
	50	58	36	38	52	71	67	40
	30	43	59	59	47	45	52	-
L^{III}	100	58	57	78	69	70	51	64
	50	61	46	77	57	94	78	71
	30	59	39	82	78	90	71	74
L^{IV}	100	47	60	46	63	74	72	79
	50	53	52	38	56	79	67	77
	30	61	46	-	48	77	54	71
DMF	100	6	6	6	6	6	6	6
	50	6	6	6	6	6	6	6
	30	6	6	6	6	6	6	6
Standard	100	99	99	99	99	98	98	100
	50	100	99	100	100	100	98	99
	30	98	99	100	99	99	99	100

Table 7. Anti bacterial and anti fungal results of La (III) and Th (IV) complexes (1-8) and standard

Complex No.	Conc. (μgmL^{-1})	Anti bacterial activity (Zone of inhibition in %)				Antifungal activity (Zone of inhibition in %)		
		E. coli	*S. Aureus*	*S.typhi*	*P.aeruginosa*	*A. flavus*	*Cladosporium*	*A. niger*
1	100	45	54	62	70	66	69	49
	50	-	46	54	64	61	68	-
	30	-	54	42	52	60	50	-
2	100	68	55	70	68	61	71	69
	50	54	48	59	61	60	63	60
	30	41	-	54	52	67	51	52
3	100	79	62	68	76	59	59	69
	50	67	60	59	74	58	61	68
	30	85	55	51	76	51	68	60
4	100	62	65	50	79	94	65	52
	50	55	68	60	67	84	67	53
	30	40	59	53	88	79	66	65
5	100	65	66	69	70	84	56	66
	50	58	60	61	64	77	62	60
	30	40	65	52	81	70	79	52
6	100	75	62	72	75	89	88	57
	50	58	74	68	70	81	82	69
	30	40	67	60	80	72	58	60
7	100	68	61	68	72	79	78	64
	50	62	64	57	66	71	67	70
	30	52	52	50	73	64	60	62
8	100	80	73	71	62	86	62	68
	50	81	62	51	66	83	54	54
	30	85	55	58	67	91	58	51
DMF	100	6	6	6	6	6	6	6
	50	6	6	6	6	6	6	6
	30	6	6	6	6	6	6	6
Standard	100	99	99	99	99	98	98	100
	50	100	99	100	100	100	98	99
	30	98	99	100	99	99	99	100

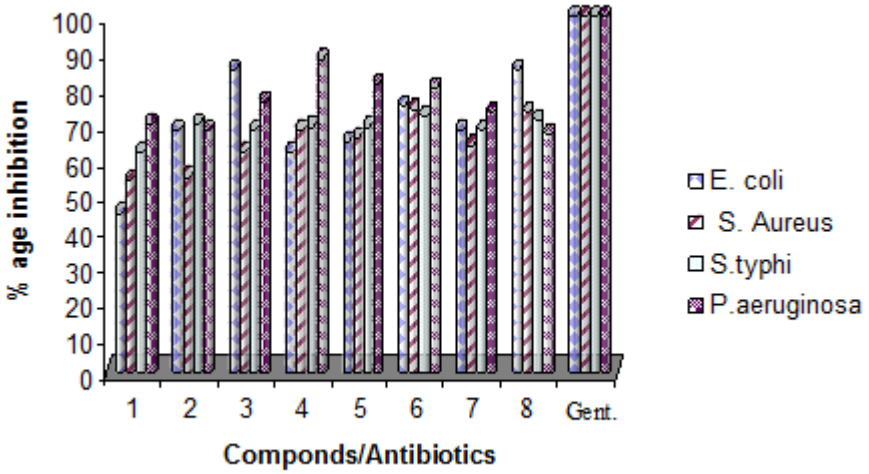


Figure 5. In vitro antibacterial spectrum of La (III) and Th (IV) complexes (1–8) and Gentamycin

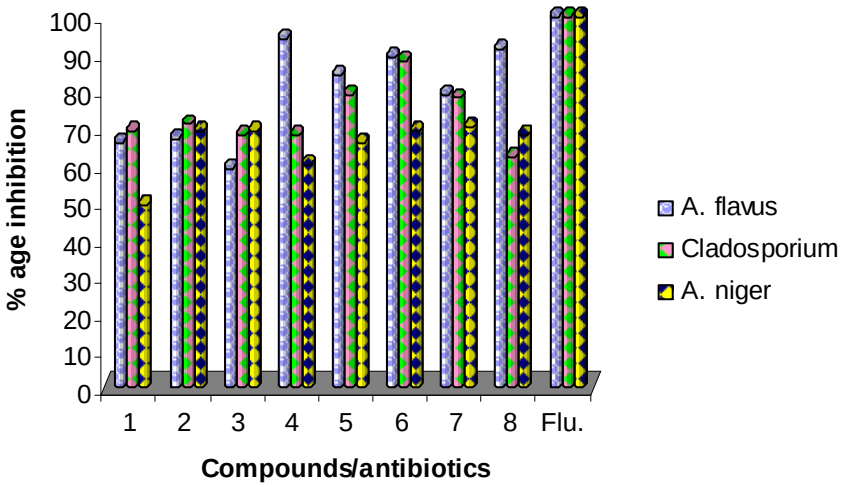


Figure 6. In vitro antifungal spectrum of La (III) and Th (IV) complexes (1–8) and Fluconazole

The MIC 10 μg/mL^{-1} was shown by compound L^{III} against *S. typhi, and A. flavus* and compound 4 against *A. flavus* and *P.aeruginosa* Compound 8 shown MIC 10 μg/mL^{-1} against *E coli and A. flavus*. In all other cases, the compounds exhibited MIC ranging from 10 μg/mL^{-1} - 100 μg/mL^{-1} against all the microbial strains some of them are given in Table 8.

Table 8. Minimum inhibitory concentration (μgmL^{-1}) results for some compounds

Compd.	Anti bacterial activity (Zone of inhibition in %)				Antifungal activity (Zone of inhibition in %)		
	E. coli	*S. Aureus*	*S.typhi*	*P.aeruginosa*	*A. flavus*	*Cladosporium*	*A. niger*
III	25	20	10	15	10	15	20
3	15	25	20	15	25	15	25
4	15	25	15	10	10	15	15
5	25	25	25	10	10	20	25
6	20	25	20	25	20	10	20
8	10	20	20	20	10	15	15

DNA cleavage experiment

Preparation of Culture media

Nutrient broth (peptone, 10; Yeast extract, 5; NaCl, 10 in (g/l)) was used for culturing of *E. coli*. The 50 ml media was prepared and autoclaved for 15 min at 121 ^{o}C under 15 lb pressure. The autoclaved media were inoculated with the seed culture and incubated at 37 ^{o}C for 24h.

Isolation of DNA

The fresh bacterial culture (1.5 ml) was centrifuged to obtain the pellet, which was then dissolved in 0.5 ml of lysis buffer (100 mM tris pH 8.0, 50 mM EDTA, 10% SDS). To this 0.5 ml of saturated phenol was added and incubated at 55 ^{o}C for 10 min. Then it was centrifuged at 10,000 rpm for 10 min. Then equal volume of chloroform : isoamyl alcohol (24:1) and 1/20th volume of 3M sodium acetate (pH 4.8) was added to this supernatant and centrifuged at 10,000rpm for 10 min. To this supernatant 3 volumes of chilled absolute alcohol was added. The precipitated DNA was Separated by centrifugation. Dry the pellet and dissolve in TE buffer (10 mM tris pH 8.0, 1 mM EDTA) and stored in cold condition.

Agarose gel electrophoresis

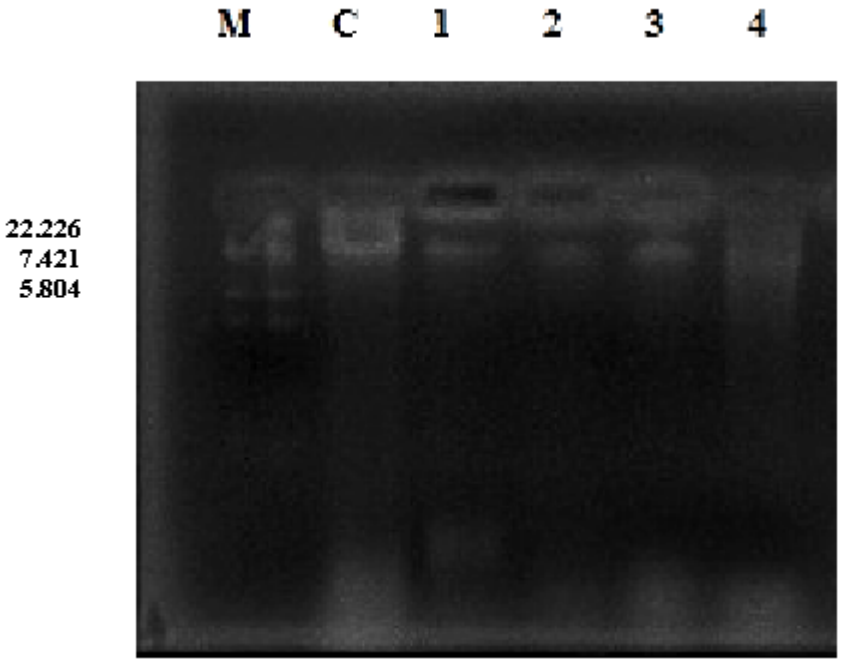
Cleavage products were analyzed by agarose gel electrophoresis method. Test samples (1 mg/ml) were prepared in DMF. The samples (100 μg) were added to the isolated DNA of *E. coli*. The samples were incubated for 2 hour at 37 ^{o}C and then 20 μl of DNA sample (mixed with bromophenol blue dye at 1:1 ratio) were loaded carefully into the electrophoresis chamber wells along with standard DNA marker containing TAE buffer (4.84 g Tris base, pH 8.0, 0.5 M EDTA/1 ltr) and finally loaded on agarose gel and pass the constant 50 V of electricity for around 30 min. Then removed the gel and stained with 10.0 μg/mL ethidium bromide for 10-15 min. the bands observed under UV transilluminator and photographed to determine the extent of DNA cleavage and the results are compared with standard DNA marker.

Electrophoretic analysis

Four La(III) (1-4) complexes were studied for their DNA cleavage activity by Agarose gel electrophoresis method (Figure 7). DNA cleavage reactions generally proceed via two major pathways (1) Oxidative cleavage of the sugar and / or nucleobase moiety and (2) hydrolytic pathway involving the phosphate group. Iron and copper complexes are known to be useful for oxidative cleavage of DNA involving nucleobase oxidation and / or degradation of sugar by abstraction of deoxyribose hydrogen atoms while complexes containing strong Lewis acids like

copper (II) and Zinc (II) are suitable for hydrolytic cleavage of DNA. Sigman *et al* have reported *bis*(phen)copper (I) complex as first "copper based chemical nuclease" that cleaves the DNA in presence of H_2O_2 and thiol [37]. Similarly, the anticancer antibiotic bleomycins containing iron cleave DNA in an oxidative manner [38].

The gel after the electrophoresis clearly revealed that, The gel shows that all complexes have the cleavage activity. Complex 1, 2 and 3 have acted on DNA as there was molecular weight difference between the control and the treated DNA samples. The difference was observed in the bands (Lane 1, 2 and 3) compared to the control DNA of *E. coli.* Whereas complex 4 shown such difference along with a streak, indicating unspecific cleavage too. This shows that, the control DNA alone does not show any apparent cleavage whereas La(III) complexes shown. However, the nature of reactive intermediates involved in the DNA cleavage by the complexes has not been clear. The results indicated the important role of metal in these isolated DNA cleavage reactions. As the compound was observed to cleave the DNA, it can be concluded that, the compounds inhibit the growth of the pathogenic organism by cleaving the genome.



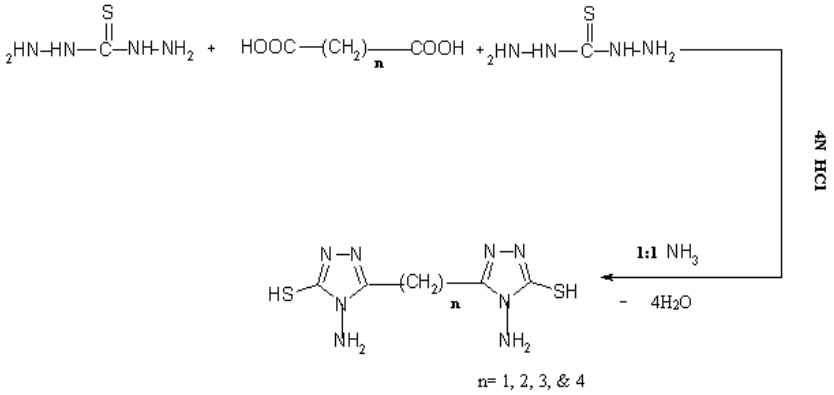
Materials and Methods

Experimental

All the chemicals used were of reagent grade. Solvents were distilled and dried before use according to the standard procedure [24]. The lanthanum of the complexes was analyzed by volumetric method using EDTA solution [25]. The thorium was determined by a gravimetrically as ThO_2 [25]. Carbon, hydrogen, nitrogen and sulphur were estimated by using C, H, N analyzer. The *bis*-(4-amino-5-mercapto-1,2,4-triazole-3-yl)alkanes prepared as reported[26]. *Ortho*-phthalaldehyde was obtained from Aldrich Chemical Company.

Synthesis of* bis-*(4-amino-5-mercapto-1, 2, 4-triazole-3-yl)alkanes

Thiocarbohydrazide (0.02 mol) was treated with 0.01 mol dicarboxylic acid (malonic, succinic, adipic and glutaric acid) in 4N HCl. The reaction mixture was refluxed for 6h and set aside overnight to cool. The *bis*-triazole was precipitated by the treatment of the reaction mixture with ammonia. The solid was filtered, washed with water and recrystallized from ethanol. Purity of the samples were verified by elemental analyses (Scheme 1).



Scheme 1. Synthesis of *bis*-(4-amino-5-mercapto-1,2,4-triazol-3-yl) alkanes

Synthesis of macrocyclic ligands (L^{I}-L^{IV})

Ortho-phthalaldehyde (2 mmol) in ethanol (25 ml) was added to an ethanolic solution of *bis*-(4-amino-5-mercapto-1, 2, 4-triazole-3-yl) alkanes (2 mmol, 25 ml) containing few drops of concentrated HCl. The reaction mixture was refluxed for 3h. The mixture was cooled to room temperature and the solvent removed under reduced pressure until solid formed that was washed with cold ethanol and dried under vacuum. M.P. 260-264 ^{o}C, yield (60-65 %), analytical data listed in Table 1.

Synthesis of La (III)(1-4) and Th (IV)(5-8) complexes

A hot super dry ethanolic solution (20 mL) of the metal nitrates (0.002 mol) was mixed with a hot ethanolic solution (25 mL) of bis-(4-amino-5-mercapto-1,2,4-triazole-3yl)alkanes (0.002 mol). The resulting solution was refluxed for a few minutes. Then a solution of *Ortho*-phthalaldehyde (2 mmol) in a minimum amount of super dry EtOH was added to it with constant stirring. Then, after refluxing the solution for about the separated complexes were collected by filtration, washed with hot ethanol and dried in vacuum desiccators over P_2O_5 (yield 55-60%), analytical data listed in Table 2.

Physical measurements Analysis

The IR spectra of the complexes were recorded on HITACHI-270 IR spectrometer in the 4000-350 cm^{-1} region in KBr disks. The electronic spectra of the complexes were recorded in DMF on VARIAN CARY 50-BIO UV-spectrophotometer in the region of 200-1100nm. The proton NMR spectra were recorded in DMSO-d_6 on a BRUKER 300 MHz spectrometer at room temperature using TMS as an internal reference. FAB-mass spectra were recorded on a JEOL SX 102/DA-600 mass spectrometer / data system using argon / xenon (6KV, 10 Am) as the FAB gas. The accelerating voltage was 10 KV and the spectra were recorded at room temperature *m*-nitro

Table1.Analytical data of Schiff bases L^{I}-L^{IV}

Ligand No.	Empirical Formula	C%		H%		N%		S%		Yield %	m.p. $^{o}_{C.}$
		Obsd.	Cacd.	Obsd.	Cacd.	Obsd.	Cacd.	Obsd.	Cacd.		
L^{I}	$(C_{26}H_{20}N_{16}S_4)$	45.17	45.61	2.14	2.92	32.14	32.74	18.09	18.71	62	260
L^{II}	$(C_{28}H_{24}N_{16}S_4)$	46.98	47.19	3.13	3.37	31.11	31.46	17.31	17.91	63	262
L^{III}	$(C_{30}H_{28}N_{16}S_4)$	47.91	48.44	3.41	3.78	29.97	30.27	17.21	17.29	65	261
L^{IV}	$(C_{32}H_{32}N_{16}S_4)$	49.54	50.00	3.98	4.16	28.94	29.16	16.43	16.66	60	264

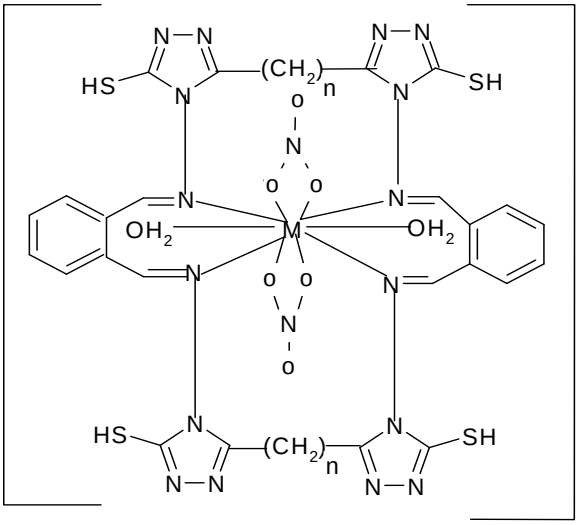
Table 2. Elemental analysis of La (III) Th(IV)complexes and their molar conductance data

Complex No.	Empirical formula	M%		C%		H%		N %		Molar conductance Ohm^{-1} cm^{2} $mole^{-1}$
		Obsd.	Cacd.	Obsd.	Cacd.	Obsd.	Cacd.	Obsd.	Cacd.	
1	$[La(L^{I})(NO_3)_2(H_2O)_2].\ 3H_2O$	13.12	13.39	30.18	30.08	2.48	2.89	21.48	21.60	20.14
2	$[La(L^{II})(NO_3)_2(H_2O)_2].\ 3H_2O$	12.78	13.04	31.12	31.55	2.88	2.81	20.94	21.03	21.51
3	$[La(L^{III})(NO_3)_2(H_2O)_2].\ 3H_2O$	12.14	12.70	32.16	32.93	2.29	2.74	20.11	20.49	23.92
4	$[La(L^{IV})(NO_3)_2(H_2O)_2].\ 3H_2O$	12.58	12.39	33.98	34.25	2.34	2.67	19.17	19.98	19.14
5	$[Th(L^{I})(NO_3)_2(H_2O)_2].\ 3H_2O$	11.87	12.29	27.14	27.61	2.36	2.65	19.28	19.82	18.63
6	$[Th(L^{II})(NO_3)_2(H_2O)_2].\ 3H_2O$	11.14	11.99	28.98	29.01	2.28	2.59	19.08	19.34	14.52
7	$[Th(L^{III})(NO_3)_2(H_2O)_2].\ 3H_2O$	11.21	11.71	30.18	30.55	2.39	2.52	18.27	18.88	19.60
8	$[Th(L^{IV})(NO_3)_2(H_2O)_2].\ 3H_2O$	10.98	11.41	31.08	31.63	2.21	2.47	18.01	18.45	18.61

benzyl alcohol was used as matrix. The mass spectrometer was operated in the positive ion mode. Thermogravimetric analyses were measured from room temperature to 1000 ^{o}C at heating rate of 10 ^{o}C / min. The data were obtained by using a PERKIN-ELMER DIAMOND TG/DTG instrument. Molar conductivity measurements were recorded on ELICO-CM-82 T Conductivity Bridge with cell having cell constant 0.51 and magnetic moment was carried out on Faraday balance.

Conclusion

The synthesized Schiff bases (L^{I}–L^{IV}) are tetradentate ligands through azomethine nitrogens. Bonding of ligands to metal was confirmed by analytical, IR, ^{1}H NMR, electronic, magnetic, FAB-mass, and thermal studies. In biological results it confirms that, all the Schiff bases are biologically active and their complexes have shown more promising activities than the Schiff bases. The interaction of La(III) complexes with DNA was investigated by gel electrophoresis technique. From the observation, it is found that all La(III) complexes cleave DNA more efficiently. The structure shown in (Figure 8) is proposed for complexes.



M= La (III) and Th (IV) n = 1, 2, 3, & 4

Figure 8. Proposed structure for La (III) and Th (IV) complexes

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Abbreviations used : BM-Bohr Magneton, FAB-Fast atom bombardment, TG/DTG-Thermogravimetric/Differential thermogravimetric analysis, DMF-N, N dimethylformamide, DMSO-Dimethylsulphoxide, IR-Infra red, MIC-Minimum Inhibitory Concentration, NMR-Nuclear Magnetic Resonance.