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ZR(IV) & TH(IV) COMPLEXES OF TETRADENTATE SCHIFFBASE LIGANDS: SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY

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Abstract-The tetradentate Schiff base ligand of di-α-formylmethoxybis (3-pentadecenyl phenyl) methane (DFMPM) and 2-aminothiophenol and complexes of Zr(IV) and Th(IV) were synthesized and characterized by elemental analysis, conductivity measurements, electronic, IR, ^{1}HNMR spectral measurements, Powder XRD and SEM. The conductance measurements indicate that all the complexes are non electrolytes. The Zr(IV) and Th(IV) complexes were screened for antimicrobial activity and DNA cleavage ability. SEM studies revealed the nano crystalline nature of the complexes.
Key words : DFMPM, 2-aminothiophenol , antimicrobial activity, DNA cleavage , SEM.

Introduction

Schiff base complexes play a major role in the development of coordination chemistry[1]. Because they have antimicrobial, anticancer, analgesic, anti-inflammatory, antifertility, and herbicidal applications[2,3]. Chelating ligands containing N, and S donor atoms show broad biological activity and are of special interest because of the ways in which they are bonded to the metal ions[4-7].In this present study, the tetradentate Schiff base ligand of di-α-formylmethoxybis (3-pentadecenylphenyl) methane (DFMPM) and 2-aminothiophenol and complexes of Zr(IV) and Th(IV) were synthesized and characterized by elemental analysis, conductivity measurements, electronic, IR, ^{1}HNMR spectral measurements, Powder XRD and SEM. The conductance measurements indicate that all the complexes are non electrolytes. The Zr(IV) and Th(IV) complexes were screened for antimicrobial activity and DNA cleavage ability. SEM studies revealed the nano crystalline nature of the complexes.

Materials and physical measurements

Cardanol was obtained from M/S Satya Cashew, Chennai, India. Formaldehyde (37% solution) hydrochloric acid, epichlorohydrin, 2-aminothiophenol, sodium hydroxide and other chemicals used were of AR grade quality obtained from Merk Chemicals. All the solvent used was purified by standard methods[16,17]. The micro analytical data (C, H, N) were collected using Perkin Elmer 2400 instrument. The metal ion intake were estimated by standard methods[16,17]. IR spectra were obtained using PE IR spectrum instrument model : system 2000. ^{1}HNMR spectra were obtained using AMX–300 MHz, FT NMR Spectrometer. Conductance measurements were obtained using systronics–305 conductivity meter. Electronic spectra of the ligands and its complexes was obtained using Perkins Elmer Lamda–25 UV-visible spectrometer in the range of 200-1100 nm. Surface morphological studies was obtained using JSM–5610 scanning electron microscope.HT-29(colon cancer) cell line was initially procured from National Centre for cell sciences, Pune.

Synthesis

Synthesis of bis(3-pentadecenyl)phenylmethane (BPPM), diglycidylether of bis (3-pentadecenylphenyl)methane (DEBPPM), di-αformylmethoxybis(3-pentadecenyl)methane (DFMPM) were prepared as per the earlier methods[16-19]

Synthesis of Schiff base ligands with DFMPM and 2-aminothiophenol

The synthesis of Schiff base ligand was carried out by reported methods[16]. Ethanolic solution of DFMPM and 2-aminothiophenol were taken in RB flask in 1:2 molar ratios and refluxed for an hour. The reaction mixture was poured in ice, an yellow compound of Schiff base ligands was obtained[16] (Scheme 1). The precipitated yellow compound was filtered, washed with water and dried over anhydrous calcium chloride. The crude sample was recrystalised from 50% absolute alcohol. Yield = 60% Melting point = 228°C.

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Scheme 1 : Structure of Schiff base ligand.

Synthesis of Schiff base metal complexes.

The metal complexes were prepared by adding aqueous solution of Zr(IV) nitrate and Th(IV) nitrate to the ligand in ethanol in 1:1 molar ratio and refluxed for about twelve hours at 80°C[17]. The precipitated solids were filtered, washed with ethanol, diethyl ether and hot water and finally dried under vacuum at 90°C. Yield = 57 – 61%.

Results and discussion

All the metal complexes are coloured solids, stable towards air and have high melting points (above 250°C). The complexes are insoluble in water and common organic solvents, but are soluble in DMF, $CDCl_3$ and DMSO.

Elemental Analysis

The analytical data suggest that all the complexes are mono nuclear with the ligands coordinated to the central metal atom. The metal to ligand ratio in all complexes was 1:1 (Table 1). Molar conductivities of (Table 2) showed that all the complexes are non - electrolytes because their conductivity values were low.

Table 1 : Physical characteristics and analytical data of the complexes

Ligand/ Complex	Yield %	Colour	Mol. formula	Mol.wt	Elemental Analysis		
					C	H	N
Ligand L $C_{59}H_{80}N_2O_2S_2$	59	Brown	$C_{59}H_{80}N_2O_2S_2$	912	77.68 (77.63)	8.66 (8.77)	3.05 (3.07)
$[ZrL(H_2O)_2(NO_3)_2]$	65	Brown	$ZrC_{59}H_{84}N_4O_{10}S_2$	1163.22	60.88 (60.86)	7.20 (7.22)	4.83 (4.81)
$[ThL(H_2O)_2(NO_3)_2]$	66	Brown	Th $C_{59}H_{84}N_4O_{10}S_2$	1304.04	54.30 (54.29)	4.30 (6.44)	3.44 (3.64)

Table 2 : Molar conductance data of the complexes

Ligand/Complex	Melting point ^{o}C	Molar conductance $ohm^{-1}cm^2 mol^{-1}$
Ligand L $C_{59}H_{80}N_2O_2S_2$	220	□
$[ZrL(H_2O)_2(NO_3)_2]$	> 250°C	9
$[ThL(H_2O)2(NO_3)_2]$	> 250°C	15

IR Sepctra

Selected IR spectral data for the ligand and its complexes are given in Table 3. The IR spectrum of the free ligand (Fig.1) is characterized mainly by the strong bands at 3008 cm^{-1} 2856 cm^{-1}, 2600 cm^{-1}, 1690 cm^{-1}, 1257 cm^{-1}, and 696 cm^{-1} which are attributed to the stretching frequencies of C – H, O – C, S – H, C = N, C – O – C and C–S respectively. The characterization absorption bands 3393 cm^{-1} and 3424 cm^{-1} range were attributed to – OH group of the lattice water or the coordinated water. In the IR spectrum of the complexes(Fig.2,3) the absorption bands in the range 2924 cm^{-1} and 2925 cm^{-1}, were assigned to C – H stretching frequencies. The absorption bands in the range 2854 $cm^{-1}$and 2855cm^{-1}were assigned to O – C stretching frequencies. The absorption bands in the range 2550 cm^{-1} and 2550 cm^{-1}were assigned to S – H stretching frequencies. The absorption bands in the range 1689 cm^{-1} and 1613 cm^{-1}were assigned to C = N stretching frequencies. The imine peak in the metal complexes showed change in shifts compared to the ligand indicating coordination of the imine nitrogen atom to the metal ion. The absorption bands in the range 1263 $cm^{-1}$and 1250cm^{-1} were assigned to C –O – C stretching frequencies. The

absorption bands in the range 690 cm-1and 690cm^{-1} were assigned to C –S stretching frequencies. Another absorption bands at 755 cm^{-1} and 740 cm^{-1} were assigned to M- N bonds and 426 cm^{-1} and 420 cm^{-1} were assigned to M – O bonds[8-13]

Table 3: Selected UV and FTIR frequencies (cm^{-1}) of the ligand and complexes

Ligand/ Complex	ν_{O-H}	ν_{C-H}	ν_{O-C}	$\nu_{S=H}$	$\nu_{C=N}$	ν_{C-O-C}	ν_{C-S}	M-N	M-O	$\lambda_{max\ (nm)}$		
$C_{59}H_{80}N_2O_2S_2$	–	3008	2856	2600	1690	1257	696	–	–	234	826	1183
$ZrL(H_2O)_2(NO_3)_2]$	3393	2924	2854	2550	1689	1263	690	755	426	236	240	365
$[ThL(H_2O)_2(NO_3)_2]$	3424	2925	2855	2550	1613	1250	690	740	420	241	348	1190

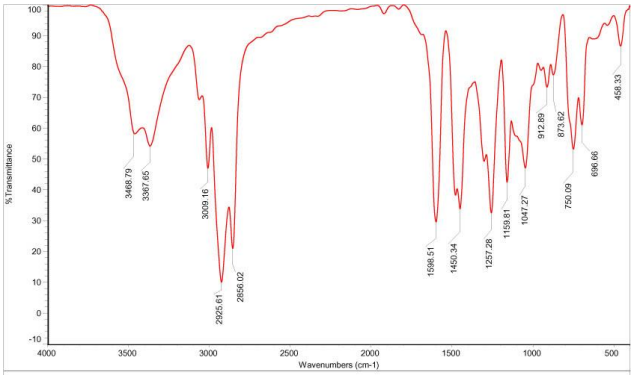

Figure 1 : FTIR Spectrum of Schiff base ligand

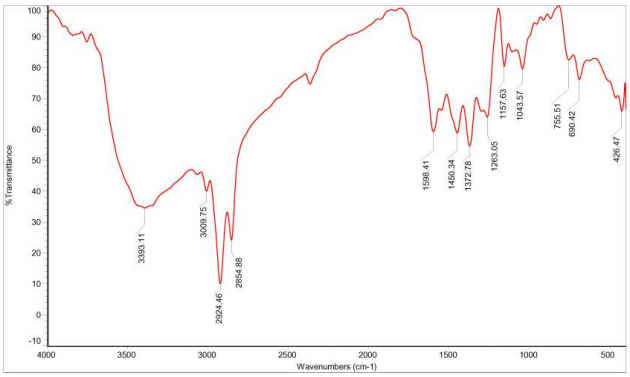

Figure 2 :FTIR Spectrum of Zr (IV) complex

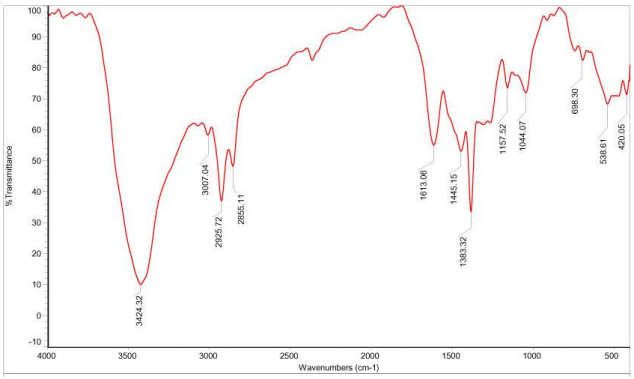

Figure 3: FTIR Spectrum of Th(IV) complex

^{1}H NMR Spectra

The ^1H NMR spectrum of the ligand (Fig.4) gave the signals for aromatic protons (δ = 7.001 – 7.14 ppm), O – CH_2 protons (δ = 3.696 – 3.797ppm), olefinic protons of the side chain (δ = 6.426 – 6.982 ppm), S-H protons (δ = 3.969 ppm) and H – C = N proton (δ = 7.2 ppm)[8-13].

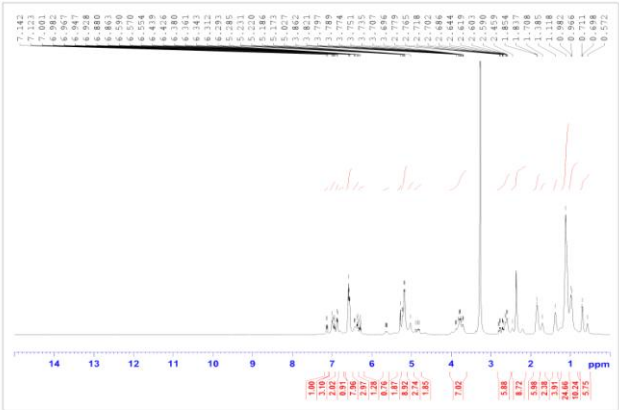

Figure 4 : ^{1}HNMR Spectrum of Ligand

The ^{1}HNMR spectrum of the Th(IV) complex (Fig.5) gave the signals for aromatic protons (δ = 7.096 – 7.163 ppm), O – CH_2 protons (δ = 3.698 – 3.993ppm), olefinic protons of the side chain (δ = 6.710– 6.758 ppm), S-H protons (δ = 2.8 ppm) and H – C = N proton (δ = 8.3ppm)

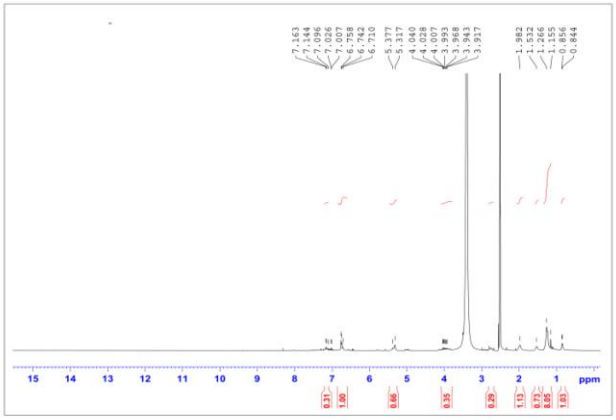

Figure 5 : ^{1}H NMR Spectrum of Th(IV) Complex

UV - visible spectra

The UV - visible spectra, are often very helpful in the evaluation of results furnished by other methods of structural investigation. The ligands showed a broad band at 244 nm which is assigned to $\pi \rightarrow \pi^*$ transition of the C = N chromophore[17]. On complexation this band was shifted to the lower wavelength suggesting the coordination of imine nitrogen with central metal ion. The UV absorption spectra of the Zr(IV) and Th(IV) exhibit only one extra highly intensive band in the region on 236 nm & 241 nm which may be due to charge transfer band besides ligand bands. Earlier researchers indicated that Zr(IV) has the coordination number of 4, 6, 7 and 8 and the coordination number of Th(IV) is also 6, 8 or 10. The Zr(IV) and Th(IV) formed 1 : 2 complexes. Hence the complexes of Zr(IV) and Th (IV) are believed to have the coordination number of 8. The – NO_3 group is present in the coordination sphere because conductance data showed that the complexes are non – electrolytes. On the basis of forgoing observation the probable structure of ligand and Zr(IV) and Th(IV) complexes may be presented as follows(Scheme.2) .This was also in accordance with earlier researchers[17 - 20].

Scheme 2 : Structure of Schiff base complexe of Zr(IV) or Th(IV)

SEM Analysis

Surface morphology of the Zr (IV) & Th(IV) complexes were shown in (Fig.6,7). The particle sizes of the Zr (IV) & Th(IV) complex were in the diameter range of few microns. Careful examination of the single crystal, clearly indicated the nano scale size of the single crystal of the complexes[17].

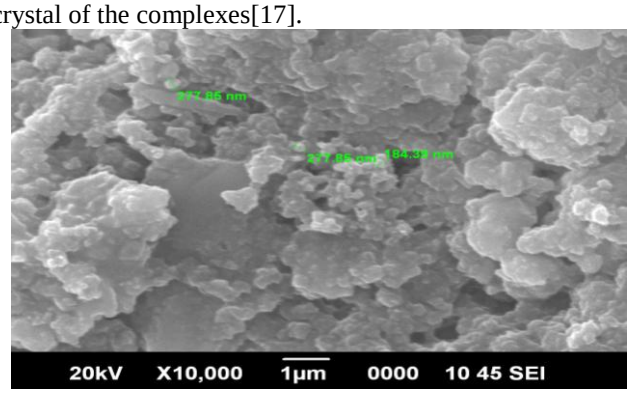

Figure 6: SEM image of Schiff base complex of Zr(IV)

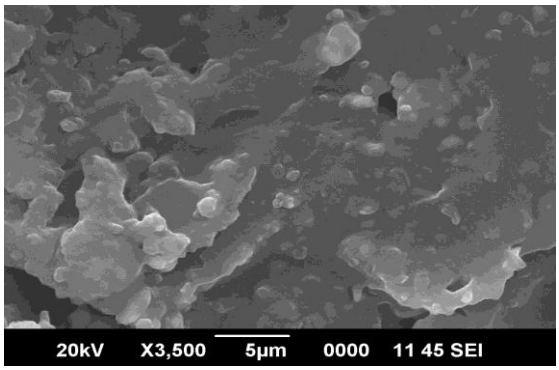

Figure 7: SEM image of Schiff base complex of Th(IV)

Powder XRD

Powder XRD patterns of Zr(IV) & Th(IV) complexes recorded in the range ($2\theta = 0 – 180^o$) were shown in (Fig 8,9). XRD patterns of the metal complexes show the sharp crystalline peaks indicating their crystallite phase. The average crystalline size (d_{XRD}) of the complexes were calculated using Scherrer's formula[20]. The Zr (IV)& Th(IV) complex have an average crystallite size of 14.5nm & 3.6nm respectively, showed the nano crystalline nature of the complexes.

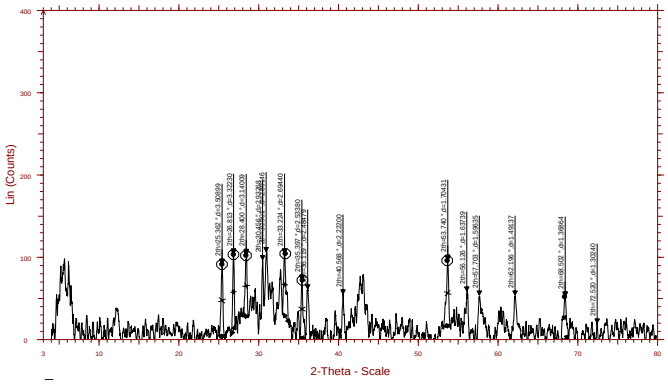

Figure 8: XRD Spectrum of Zr(IV)

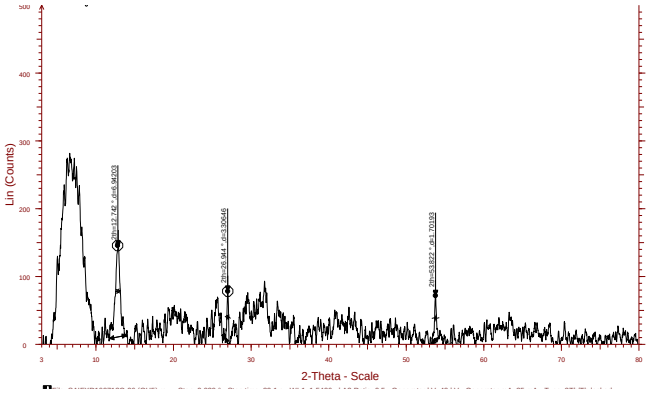

Figure 9: XRD Spectrum of Th (IV) Complex

Antimicrobial Activity

The biological activity of the ligands and their complexes` with Zr(IV) and Th (IV), have been screened for antimicrobial activity against bacteria (Klebsiella sps, E.coli, P.aeruginosa and S. aureus) and fungi (Candida sps and Aspergillus sps) by disc diffusion method. The concentration for these samples was maintained as 1mg/mL in DMSO. The results thus obtained were explained on the basis of Overtone's concept and Chelation theory[12-15]. The mode of action of the compounds may involve formation of a hydrogen bond through the azomethine group with the active centers of cell constituents, resulting in a interference with the normal cell process[12-15].

The variation in the activity of different complexes against different organisms depends either on impermeability of the cells of the microbes or difference in ribosome of microbial cell. A composition of the biological activity of the synthesized compounds with some known antibiotics (Chloramphenicol and Nystatin is presented in Table.4 & 5 It is observed that the Schiff base metal complex of Th(IV) exhibit better activity than the corresponding ligand and Zr(IV) complexes .

Table 4: Antimicrobial activity for Bacteria.

S.No	Samples	Media	Zone of Inhibition (mm)			
			Klebsiella	E.coli	aeruginosa	S.aureus
1	Ligand	Muller Hinton Agar	6.0	6.0	6.0	6.0
2	$[ZrL(NO_3)_2 (H_2O)_2]$		6.0	6.0	10.0	6.0
3	$[ThL(NO_3)_2 (H_2O)_2]$		14.0	12.0	6.0	14.0
4	PC (Chloramphenicol)		25.0	26.0	24.0	25.0
5	NC		6.0	6.0	6.0	6.0

Table 5: Antimicrobial Activity for fungi

S.No	Samples	Media	Zone of Inhibition (mm)	
			Candida sps	Aspergillus sps
1	Ligand	Muller Hinton Agar	6.0	6.0
2	$[ZrL(NO_3)_2 (H_2O)_2]$		6.0	8.0
3	$[ThL(NO_3)_2 (H_2O)_2]$		10.0	6.0
4	PC (Nystatin)		25.0	26.0
5	NC		6.0	6.0

DNA Cleavage Studies

The DNA cleavage activities of Schiff base ligand and its metal complexes at a 1μM concentration were studied using pUC18 DNA (2μg) in H_2O_2 (10 μL) in 30 mM Tris Buffer (pH 7.4) and upon irradiation with UV light. The reaction is modulated by metallo complexes bound hydroxyl radical or a peroxo species generated from the co-reactant H_2O_2.

It is evident from Fig .10, that the Th(IV) complex cleave DNA more efficiently in the presence of an oxidant than the ligand and Zr(IV) complex. This may be hydroxyl free radicals, which can be produced by metal ions reacting with H_2O_2 to produce the diffusible hydroxyl radical or molecular oxygen, which may damage DNA through Fenton type Chemistry.

This hydroxyl radical participates in the oxidation of the deoxyribose moiety, followed by hydrolytic cleavage of sugar - phosphate back bone[20,21]. Further, the presence of a smear in the gel diagram indicated the presence of radical cleavage.

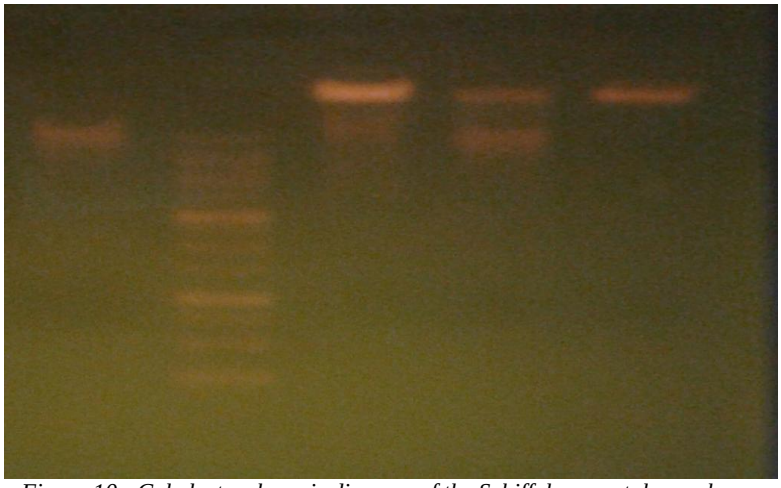

Figure 10 : Gel electrophoresis diagram of the Schiff base metal complexes.

Lane 1: Control DNA
Lane 2: Marker
Lane 3: DNA + L + H_2O_2
Lane 4: DNA +$[ZrL(NO_3)_2(H_2O)_2]$ + H_2O_2
Lane 5: DNA +$[ThL(NO_3)_2(H_2O)_2]$ + H_2O_2

Conclusion

Schiff base complexes of Zr(IV) and Th(IV) were synthesized from DFMPM using 2-aminothiophenol were clearly described and characterized on the basis of analytical and spectral data. The SEM , XRD analysis indicate that the crystals of Schiff base metal complexes are nano crystalline in nature. Anti microbial study showed that the complex of Th(IV) have higher anti microbial activity than Zr(IV). The DNA cleavage studies show that the Zr(IV) and Th(IV) complexes cleave DNA more efficiently.

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