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Synthesis, Characterization, Antibacterial properties and DNA Binding of a Th(IV) Complex

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Abstract

In this investigation, we have reportedthe synthesis of the complex $[Th(5,5´\text{-dmbpy})_3](NO_3)_4$**(1)**that 5,5´-dmbpy =5,5´-dimethyl-2,2´-bipyridine. This complex has been characterized using spectral methods (FT-IR, UV-Vis, ^{1}H-NMR and luminescence), elemental analysis and the Cyclic Voltammetry (CV) method. The FT-IR data shows that 5,5´-dimethyl-2,2´-bipyridine (5, 5´- dmbpy) ligand adduct to metal centers by nitrogen atoms. Electronic spectra of (1) shows ligand field transitions and charge transfer (CT) bands. Electrochemical data for the complex in the DMF solution show reduction and oxidationprocessesfor the Thorium ionandligand.The interactions of complex (**1**)withFS-DNAhave been investigated using UV–Vis and gel electrophoresis. The binding constant (K_b) was calculated using UV–Vis technique ($K_b=3.5\times10^5$). Also, DNA cleavage was studied using agarose gel electrophoresis. The antibacterial properties and fluorescence property of complex **(1)** have also been examined.The in vitro biological screening effects of the complex and ligand were tested against different types of bacterium and $[Th(5,5´\text{-dmbpy})_3](NO_3)_4$(1)shows antibacterial properties.

Keywords: Cyclic voltammetry (C.V), Electronic spectra, Thorium ion,gel electrophoresis, antibacterial.

1.Introduction

Compounds with bipyridinederivatives are the most common ligands [1]. The ligand 2,2′-bipyridine has a conjugation system depicted in figure 1. Most recently, great attention has been given to derivative of ligand 2,2'-bipyridine because of their influence in the area of organometallic and coordination chemistry [2, 3]. Thus, compounds which include bipyridine derivative ligands have found applications in various fields such as catalysis, luminescence, biological systems, organic light emitting diodes, and electrochemical studies [4-7].

Actinide ions usually have high coordination numbers and the type of obtainable polyhedron is influenced by the nature of the coordinating ligands [8, 9]. The metal thorium plays an important role in the Indian Nuclear Energy programs.A number of thorium nitrate complexes have been produced and investigated. The compound $[Th(NO_3)_4.(H_2O)_3]$ was one of the first 11-coordinate compounds to be recognized (Figure 2) [10]. we notified the synthesis of the compound with 5,5´-dimethylbipyridineunder formula $[Th(5,5´\text{-dmbpy})_3](NO_3)_4]$.

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Lanthanide and Actinide ions and their complex are used in bioinorganic chemistry due to their unique properties such as biological, pharmaceutical, magnetic, spectroscopic, luminescent, antibacterial and antitumor activities and DNA-binding affinity [11,12]. The interaction between metal complexes DNA is performed using covalent or non-covalent methods. Covalent interactions comprise the coordination of the nitrogenous base of DNA to the metal ion, whereas non-covalent interactions include three modes: groove binding, intercalation binding, and electrostatic interaction. [13,14].

In this paper, wehave reported the interaction of complex **1** with DNA *in vitro*. The DNA binding properties of this complex have been investigated through UV-Vis and gel electrophoresis. The *in vitro* biological screening effects of the synthesized complex(**1**) were tested against different microbial kinds.

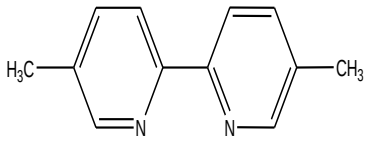

Fig.1. 5,5´-dimethyl-2,2·bipyridine

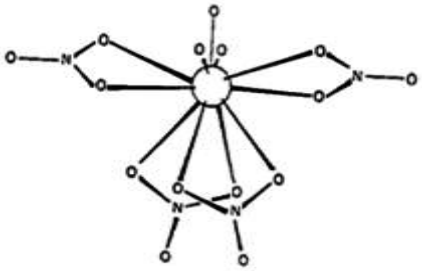

Fig.2. Structure of $Th(NO_3)_4(H_2O)_3$

2.Experimental

2-1. Materials and physical methods

All solvents and chemicals were purchased from AldrichandMerck.Infrared spectra (400-4000cm^{-1})were obtained as 1% dispersions in KBr pellets witha Shimadzu-470 Plusspectrometer.The ^{1}H-NMR spectrum was recorded at room temperature (25°C) with a Brucker 300 Ultrashield spectrometer in DMSO solution. Cyclicvoltammograms were obtained by use of a SAMA500 device. Elemental analysis was recorded with a Heraeus CHN Rapid analyzer. Melting point was acquired on an electrothermaldevice type 9100 melting point apparatus. Electronic absorption spectra were obtained on a Cary Bio 300 spectrometer at room temperature and ina DMF solution.

2-2.Synthesis of $[Th(5,5´\text{-dmbpy})_3](NO_3)_4$ (1)

A solution of 5,5´-dimethylbipyridine (0.04 g, 0.25mmol) in 10 ml methanol was addedto a solution of$Th(NO_3)_4$,$4H_2O$(0.138 g,0.25mmol) in 10 ml methanol. The resultingsolution was stirred and refluxedat60-65^{0}C for 24h.Brown colored deposits were seen on the walls of the balloon. The productwasdissolved in DMFsolution.After10 days, opalescent crystals were isolated.

3. Results and discussion

3.1.IR spectra$[Th(5,5´\text{dmbpy})_3](NO_3)_4$(1)

The Infrared spectrum of the free ligand 5,5´dmbpy contains a sharp band at 1615 cm^{-1}related to the stretching frequency of the C=N bond [15].This frequency shifted to a lower wavenumber in complex**(1)**.The IRspectrum of complex $[Th(5,5´\text{dmbpy})_3](NO_3)_4$ included two sharp bands at 1517-1300 cm^{-1} associatedwithν(C=N) and ν(C=C)vibrations [16]. This observation indicates the involvement of unsaturated nitrogen atoms of the C=N groups in bonding with the central metal ions[17].The vibration bands at 3100cm^{-1} and 2924 cm^{-1} in the complex are assigned to the stretching frequency of the ν(C-H) bond aromatics and aliphatic,respectively [18]. The bands observed in the range 833cm^{-1},639 cm^{-1} are attributed to ν(C=C=C) and ν(C=C=N) vibrations in the Pyridine rings [19-20].The band at 1620 cm^{-1}in the complex is associated with the stretching ν(N-O) in the complex[16]. The band at 512 cm^{-1} was related to Th–N stretching [21].

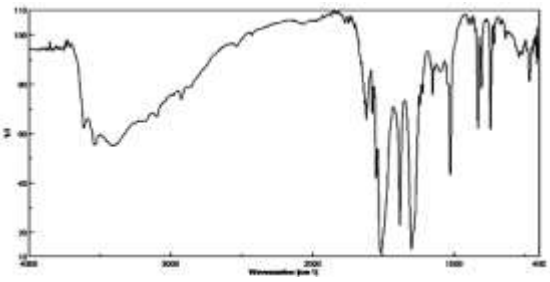

Fig.3. IR spectrum compound[Th(5,5′dmbpy)$_3$] $(NO_3)_4$using disk KBr.

3.2.Electronic excitation study

The UV–visible spectra of [Th(5,5´-dmbpy)$_3$] $(NO_3)_4$, was recorded in DMF solution(figure4).The electronic spectra of complex **(1)**inDMFsolution show several absorption bands in the UV regions. According toevidence affected by the intensity and position from comparison with the spectra of the free ligand 5,5′-dmbpy, the spectra show a very strong bandat the range 200-250 nm due to ligand-centered $\pi\rightarrow\pi^*$ transitions[22-24].The band observed at approximately313-330 nm is assigned to charge transfer transitions observed in similar complexes [25,26].Due to the poor solubility of the complex, it was not possible to conduct solvent dependence studies.

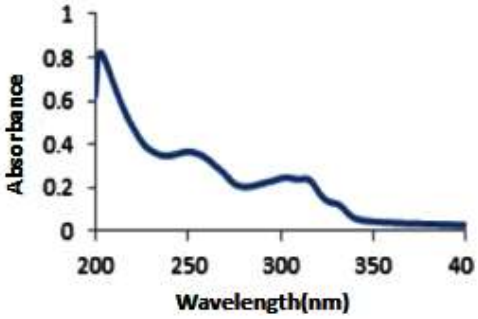

Fig.4. UV absorption spectra of [Th(5,5´dmbpy)$_3$] $(NO_3)_4$

3.3.Electrochemical Studies [Th(5,5´-dmbpy)$_3$]$(NO_3)_4$(1)

Cyclic voltammogram of the complex was recorded at −2.0 to 2.5 V vs. Ag/AgCl usingdifferent switching potentials at varying scan rates. The cyclic voltammogram of the complex was obtained at 25°C in DMF solution containing 0.1M TBAH as supporting electrolyte with scan speed of 500 mvs^{-1}(Figure.5). The voltammogramof the complex shows a quasi-reversible wave in the potential E_c=-1.98v related to the reduction ofthe ligand 5,5´dmbpyand the quasi-reversible wavesat potential E_c=-1.4v assigned to the reductionof thorium ion [27-29].

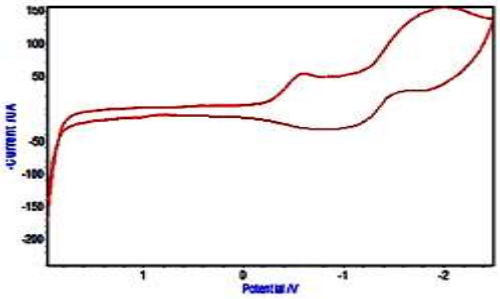

Fig.5. Cyclic voltammograms for compound [Th (5,5´-dmbpy)$_3$]$(NO_3)_4$in DMF at 25 °C.

3.4.^{1}H-NMRspectrumof Th[(5,5´-dmbpy)]$_3$ $(NO_3)_4$

The hydrogen atoms ofthe aromatic rings (H_c, H_d), (H_b)and methyl groups (H_a) were seen at approximately 7–9ppm, 3.34 ppm and 2.46 ppm respectively. Figure.6[30].

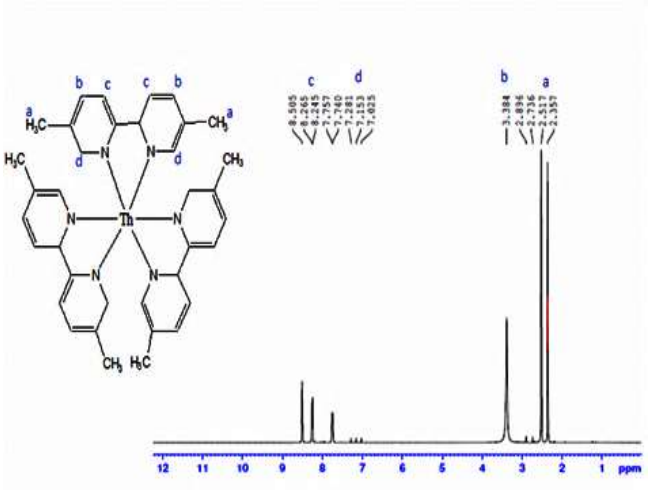

Fig.6. ^{1}H NMR spectrum of Th[(5,5´-dmbpy)]$_3$ $(NO_3)_4$in DMSO

3.5.Elemental analysis of compound

The proposed structures for the compounds were approved with elemental analysis. The results of the elemental analysis in the Table 1 are in good agreement withthose calculated for the proposed molecular formula.

Table1. Elementalanalysis (CHN)

Element	C		H		N	
Compound	Theory	Exp.	Calc.	Experimental	Theory	Experimental

1	47.3	47.2	4.16	4.12	13.8	13.7

3.6.Luminescent property

In recent years, luminescent metal compounds have been studied for importantapplications in the fields of biological probes and solar energy sensors and optoelectronic tools [31-33].The free 5,5'-dimethyl-2,2'-bipyridine ligand displays a maximum emission peak at 347 nm and two shoulders emission peaks at 307 and 425 nm which can be attributed to the $\pi \rightarrow \pi^*$ transitions of the ligand [34]. The thorium complex is emissive at room temperature.Figure7,shows an intra-ligand fluorescence related to the $\pi \rightarrow \pi^*$ transitions of the ligand 5,5'-dmbpy with maxima occurring at 364 nm[35]. Many aromatic ligands, such as 5, 5´-dimethyl-2,2'-bipyridine, possess some degree of fluorescence, which usually increases when coordinated to metal [36]. The thorium complex shows increased intensity of luminescence, compared with the free ligand 5,5'-dmbpy. Increased property and intensity of luminescence after complexation areof high interest due to the photochemical application of the corresponding compounds [37] (figure 7).

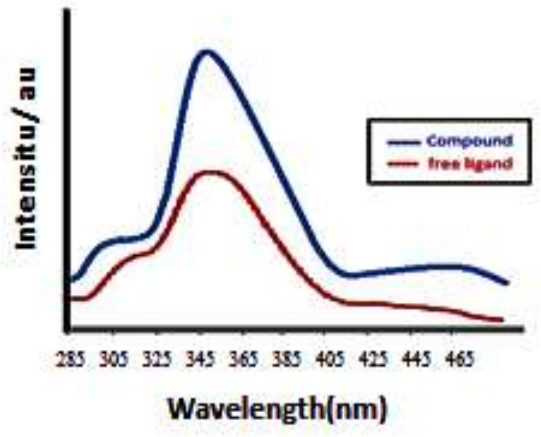

Fig.7. Fluorescence spectra of complex thorium and free ligand 5,5, dmbpyin the solvent methanol at room temperature

3.7.Electronic absorption spectra

UV-Vis spectroscopy was employed to determine the binding strength and binding modes of small molecules to DNA. The absorptionspectra ofthe fixed concentration of complex **1** (1.2×10^{-5}M) in the absence and presence of DNA (1.4×10^{-4} M, 0-20µl) can be seenin Figure 8. According to this figure, increased concentrations of FS-DNA led to decrease in the absorption band.We recorded the UV-Vis spectra between complex (**1**) and FS-DNA (Figure8). The experiment confirms that there is an interaction between complex(**1**) and FS-DNA.

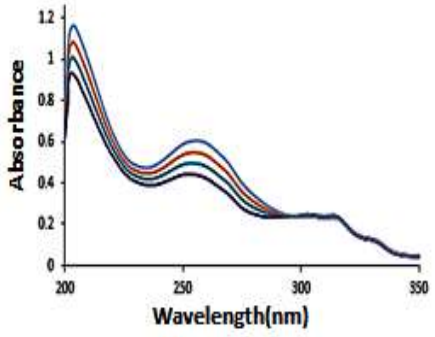

Fig.8. Electronic absorption spectra of complex(**1**) in the absence and presence of differentconcentrations of DNA.

The binding constant (K_b) can be determined using the curve of [DNA]/(εa-εf)$\times10^{12}$ versus [DNA] $\times$ 10^6. The binding constant is obtained from the ratio of the slope to the intercept (figure9). The value of K_b finally related to UV-Vis (3.5×10^5) is lower than that K_b related to a classical intercalator such as Ethidium Bromide (EB) (1.4×10^6) [42-44]. The EB is a classical intercalatorwith a completely flat structure. Ethidium Bromideeasily interacts with DNA and can change the DNA structure.Finally, it can be estimated that the binding mode of DNA-compound **1** was not intercalation.Also, there is hyper chromic shift which indicate that there is no interchalation interaction [38-41].As a result, binding mode between complex **1** with FS-DNA is groove binding, therefore the hydrogen binding have important role in the interction of DNA with complex**1**.

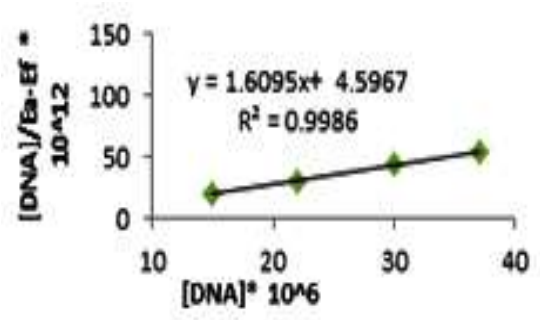

Fig.9. The curve of $[DNA]/(\varepsilon a-\varepsilon f)\times 10^{12}$ versus$[DNA]\times 10^{6}$

3.8.Agarose gel electrophoresis

Agarose gel electrophoresis method of FS-DNA display the interaction metal complex **1** with FS-DNA in tris buffer solution.The DNA cleavage by complex(**1**) was performed to test the ability of complex (**1**) to decrease the movement of FS-DNA in the agarose gel, using incubation of several samples containing anamount of DNA(1.4×10^{-3}M), and various concentrations of complex 1 in the Tris–buffer solution. All samples of different concentrations of complex(**1**) were mixed with 4 μL of loading buffer Methylene blue+ 5μl FS-DNA and shaken in order to mix. Next, the solution was loaded onto an agarose gel, and the samples were electrophoresedfor 15 min at a voltage of 100 v. After putting under the lights UV, the strips appear. Figure 10 proves the interaction complex **1**with the DNA. Agarose gel electrophoresis of Cleavage of DNA(1.4×10^{-3}M) with several concentrations of the Th(IV) compound at room temprature: lane (DNA): DNA control; lane 2: Th(IV) compund (1.2×10^{-5} M) + FS-DNA, lane 3: complex (2.9×10^{-5} M) + DNA, lane 4: complex (6.5×10^{-5} M) +FS-DNA, lane 5: complex (9.8×10^{-5} M) + FS-DNA.

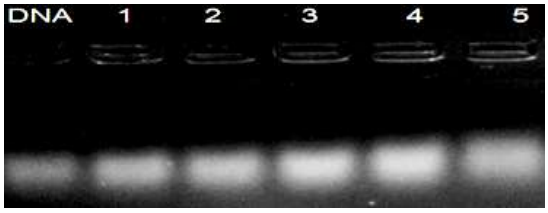

Fig.10. Gel electrophoresis of Cleavage of FS- DNA by several concentrations of complex(1) at 25 °C: one lane having: DNA control; lane 1-5: complex (1)+ DNA.

3.9.In vitroantibacterial activity

The antibacterial activities of the ligand and complex(**1**) were tested using the discdiffusion method against the species Staphylococcus aureus ATCC 25923 (gram positive bacteria) and Escherichia coli ATCC 25922 (gram negative bacteria). The MIC of complex(**1**) was tested against bacterial strains via a broth dilution method.

The minimum inhibitory concentrations (MIC) of the studied metal complex(**1**) and free ligand are summarized in Table 2. A comparative investigation of the ligand and the complex shows that complex(**1**) exhibits higher antibacterial activity than the free ligand. The increased activity of complex(**1**) can be explained on the basis of Tweedy's chelation theoryand Overtone's concept [45,46]. After chelation, there is a decrease in the polarity of the Th(IV) atom, because of the partial sharing of its positive charge with the donor groups and also due to π-electron delocalization on the whole chelate ring. Complex(**1**) prefers interactions with lipids which are important constituents of the cell wall. Also, the decreasing polarity led to increasing the lipophilic character of the chelates.An interaction between the lipid and the complex is successful, which may lead to further breakdown of the cell [47]. The results revealed that complex(**1**) is most effective against Staphylococcus aureus and Escherichia coli, while the free ligand has noactivity versus themsince the complex has less polarity related to the aromatic ring of free ligand. The increased power ofits lipophilic and final complex has more antibacterial activity than ligand.Complex(**1**) is more toxic towards the Gram-positive strain (Staph-ylococcus aureus) than the Gram-negative strain (Escherichia coli), Due to differences in the structure of the cell wall.

Table 2. The MIC and MBC and inhibition diameter zone values (mm), of the free ligand and its correspondingTh(IV) compound.

Compound	MIC(mg/ml)		MBC(mg/ml)		Inhibition zone(mm)	
	E-coli	S.aureus	E-coli	S.aureu	E-coli	S.aureus
Complex(1)	0.003-0.006		0.006-0.012		22-18	

5,5-dmbipy0.0125-0.0125 0.025-0.0256-6

4.Conclusions

In summary, in this article we reported the synthesis of the thorium (IV**)**complex with 5,5'-dmbpy as the ligand. This complex has been characterized using FT-IR, UV–Vis,^{1}H-NMR spectroscopies, elemental analysisand cyclic voltammetry (CV) techniques. The luminescence propertiesof5,5'-dmbpyligand and complex(**1**) were investigated. The intensity of luminescence properties increasedafter complexation. The interaction of complex (**1**) with FS-DNA was carried out using UV-Vis spectroscopy and agarose gel electrophoresis. The experimental results indicate that complex (**1**) interacts with DNA at quite low concentrations. The results indicate that the interaction mode of complex (**1**) and FS-DNA are groove binding. Agarose gel electrophoresis analysis shows that the destruction of DNA grows during the increasing process of the concentration of complex (**1**) added to DNA.This has been attributed to interactions between complex (**1**) and DNA. The biological activity ofcomplex(1) showed that the Th(IV) complex displays antibacterial activity.

10. Acknowledgements

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