Research Article

Synthesis and Biological Properties of Tb(III) Complex with 1-(2-hydroxy-4,6-dimethoxy phenyl)ethanone and Heterocyclic Ancillary Ligand

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ABSTRACT

The ternary Tb (III) ion complex, $Tb(HDMPE)_3$.nphen was synthesized by adopting solution precipitation method. The synthesized complex was identified on the basis of various techniques like elemental analysis, ^{1}H-NMR and FT-IR, We studied the antimicrobial and antioxidant properties of the ligand and complex Tb $(HDMPE)_3$. nphen. The *in vitro* antibacterial activities were studied by using Gram-positive bacteria: *B.subtilis, S.aureus* and gram-negative bacterium: *Escherichia coli.* The antifungal activities were studied by using fungi *C. albicans* and *A.niger.* The antibacterial activities of ligand is poor but better of Tb (III) ion complex $Tb(HDMPE)_3$.nphen than standard drugs ciprofloxacin and fluconazole. The antioxidant activities of the synthesized complex were determined by using DPPH method. The Tb (III) ion complexes Tb (HDMPE)3.nphen have poor antioxidant activities.

Keywords: Tb (III) complex, elemental analysis, ^{1}H-NMR, FT-IR, biological activities.

INTRODUCTION

The treatment of bacterial contaminations is progressively confounded by the capacity of microscopic organisms to create imperviousness to antimicrobial operators. Antimicrobial operators are regularly classified by their central component of activity. The topic of World Health Day, 2011, was "antimicrobial resistance: no activity today and no cure tomorrow". The destruction of antibacterial medication revelation brings the ghost of untreatable diseases. New approach towards antibiotic drug discovery and development would provide a platform for these initiatives [1-4].

Free radicals are particles containing unpaired electrons. The unpaired electron is a profoundly receptive "hot potato" that either "consumes" a particle (causes oxidative harm) or is passed from atom to atom bringing on transforming the beneficiary into a free radical and killing the contributor. A more exact analogy, notwithstanding, is to depict an unpaired electron as an atomic "shark" that grabs an electron from another particle, leaving the "casualty" particle with an unpaired electron. (The "hot potato" is truly the nonappearance of an electron accomplice for an unpaired electron.) Most frequently the unpaired electron ("shark") will grab a hydrogen particle (which is as great or superior to an electron, seeing that hydrogen iotas don't hold electrons firmly) from another atom. An illustration would be the situation of the hydroxyl radical (.OH) grabbing a hydrogen iota from a decreased glutathione (GSH) particle, bringing about a water atom and a glutathione radical [5-7].

In our earlier papers Eu(III), Tb(III) and Sm(III) complexes with β-Hydroxy ketones proved excellent antimicrobial agent[8-12]. Keeping this observation in mind and in continuation of our study on exploring the biological profile of complex compounds, I hereby report the synthesis, characterization, antimicrobial and antioxidant estimation of ternary Tb(III) ion complex "$Tb(HDMPE)_3$.nphen" by using 1-(2-hydroxy-4,6-dimethoxyphenyl) ethanone (HDMPE) as main ligand and 5-Nitro-1, 10-phenanthroline (nphen) as ancillary ligand.

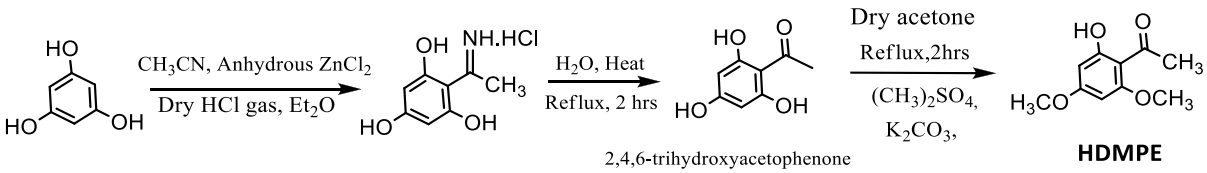
MATERIALS AND METHODS

benzene-1,3-5-triol,dimethyl sulphate, potassium carbonate, 5-Nitro-1, 10-phenanthroline,$Tb(NO_3)_3 5.H_2O$, xylenol orange and 1,1-Diphenyl-2-picrylhydrazylradical (DPPH) were purchased from Sigma-Aldrich and used as received. The microorganisms used in antimicrobial profile were purchased from Institute of Microbial Technology, Sector39-A, Chandigarh, India. Nutrient broth medium, nutrient agar medium, subouraud dextrose agar medium and subouraud dextrose broth medium were purchased from Hi-Media Pvt Ltd. The synthesized ligand HDMPE was recrystallized three times with methanol before synthesis of complex. The elemental analysis was accomplished by using thermo scientific flash 2000 elemental analyzer. The percentage of Tb(III) was estimated by complexometric titration with EDTA. The ^{1}H-NMR spectra were recorded on Bruker Avance II 400 spectrometer using tetramethyl silane (TMS) as an internal reference (chemical shift in δ ppm). Infrared spectra were recorded (Perkin Elmer spectrum 400) from 4000–400 cm^{-1}inKBr pellets. Antimicrobial and Antioxidant profile were determined by tube dilution method and DPPH method respectively. All measurements were made at room temperature unless otherwise stated.

Synthesis

Synthesis of ligand HDMPE

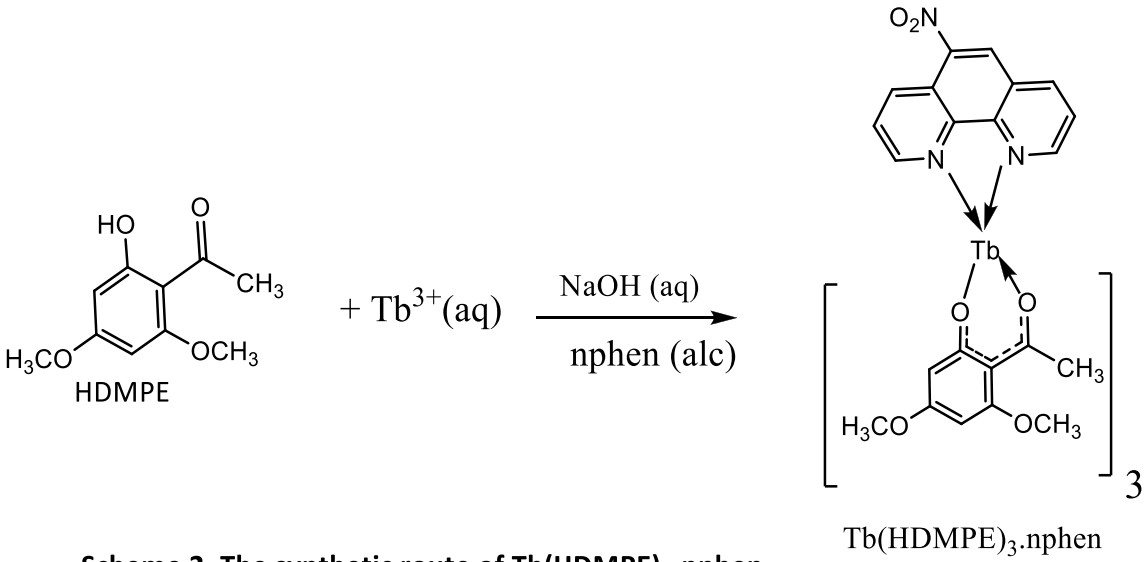
The ligand HDMPE was synthesized by adopting conventional method as per literature[13] and is given in Scheme 1 as follow:



Scheme 1. The synthetic route of ligand HDMPE.

Synthesis of complex Tb (HDMPE)$_3$. nphen

The complex was synthesized by mixing ethanolic solution of 3 mmol HDMPE ligand, and 1 mmol nphen with aqueous solution of 1 mmol $Tb(NO_3)_3.5H_2O$. Afterwards the pH of mixture was adjusted to 6.5 - 7, using aqueous NaOH (0.05 M) solution with constant stirring which give rise to into formation of white precipitates (Scheme 2). These precipitates were stirred for 3 h at about 40°C and then allowed to digest for 1 h. Finally, a suction filter was used to filter precipitates, washed with doubly distilled water and then with ethanol, dried in vacuum oven at 50 °C. The obtained complex was white powder with 79% yield. The powdered the complex was kept in sample tube in vacuum desiccator.



Scheme 2. The synthetic route of Tb(HDMPE)$_3$.nphen

Biological profile

Antimicrobial profile

Antimicrobial profile of synthesized ligand HDMPE and their corresponding Tb(III) ion complex 'Tb(HDMPE)$_3$.nphen' was estimated using tube dilution method[14]. The following bacteria were used for *in vitro* antibacterial profile, Gram-positive bacteria: *B.subtilis, S.aureus* and gram-negative bacterium: *Escherichia coli.* The following fungi were used for antifungal profile *C.albicans* and *A.niger.* The standard drugs ciprofloxacin and fluconazole[15] have also tested for their antibacterial and antifungal profile at the same concentration under the same condition as that of the tested HDMPE and Tb (HDMPE)$_3$.nphen. The dilutions of synthesized complex as well as standard drugs have been prepared in double strength nutrient broth I.P and sabouraud dextrose broth I.P media for bacteria and fungi respectively[16]. The standard, ligand and complex were dissolved in DMSO to give concentration of 100µg/mL. The incubation period for HDMPE and Tb(HDMPE)$_3$.nphen were 24 h at 37 °C for bacteria, 48 h at 37°C for *C.albicans* and 7 days at 25 °C for *A.niger* respectively. The zone of inhibitions of the antimicrobial profile has been recorded in terms of minimum inhibitory concentration (MIC).

Antioxidant profile

Antioxidant profile of synthesized ligand HDMPE and complex Tb (HDMPE)$_3$.nphen were determined by using DPPH method[17]. When DPPH reacts with antioxidant HDMPE and complex 'Tb (HDMPE)$_3$.nphen, it shows a significant absorption decrease at 517 nm. Methanol was used as a solvent for preparation of various concentrations (25, 50, 75, and 100) µg/ml of the materials. After a 30 minutes incubation period at room temperature, the absorbance was read against a blank at 517 nm. Tests were carried out in triplicate and ascorbic acid was used as a standard antioxidant. The DPPH

scavenging profile is expressed as IC_{50}, whose concentration is sufficient to obtain 50% of maximum scavenging profile. Standard curve is plotted for different concentration of ascorbic acid, ligand and complex. Scavenging of DPPH free radical was calculated as:

DPPH scavenging profile (%) = [(Ac-At) / Ac] ×100

Where, Ac is the absorbance of the control reaction and At is the absorbance of the test sample.

RESULTS AND DISCUSSION

Solubility

The complex $Tb(HDMPE)_3$.nphen was stable under atmospheric condition. The complex Tb $(HDMPE)_3$.nphen was found to be soluble in dimethyl sulfoxide, dimethyl formamide, chloroform and acetone, sparingly soluble in methanol and ethanol but insoluble in benzene and hexane.

Elemental analysis, ^{1}H-NMR and IR Spectra

The elemental analysis data for HDMPE ($C_{10}H_{12}O_4$) were found (calculated) % C, 60.87 (61.22); H, 6.14 (6.16); O, 32.19 (32.61) IR (KBr) cm^{-1} 3430 (b), 3099 (m), 3005 (w), 2943 (w), 2847 (w), 1640 (s), 1538 (s), 1457 (m), 1366 (s), 1324 (m), 1270(s), 1221 (s), 1207 (s), 1112 (m), 1079 (m), 1045 (w), 896 (m), 835 (m), 658 (m), 594 (s). ^{1}HNMR (400 MHz, DMSO): d 2.52 (s, 3H, CH3), 3.83 (s, 6H, OCH3), 6.02 (s, 2H, Ar-H), 13.84 (s, 1H, OH).

The elemental analysis data for $Tb(HDMPE)_3$.nphen ($C_{42}H_{40}O_{14}N_3Tb$) was found (calculated) % C, 51.96 (52.05); H, 4.12 (4.16); N, 4.25 (4.34); O, 22.98 (23.11); Tb, 16.03 (16.34). IR(KBr):cm^{-1} 2928 (m), 2456 (m), 2324 (w), 1612 (m), 1585 (s), 1558 (s), 1483 (s), 1371 (s), 1322 (m), 1234 (s), 1209 (m), 1144 (m), 1123 (s), 1053 (m), 902 (m), 868 (s), 839 (m), 820 (s), 781 (m), 762 (s), 686 (s), 624 (m), 542 (m), 428 (m).^{1}HNMR (400 MHz, DMSO): d 2.48 (bs, 9H, CH3), 3.45 (bs, 18H, OCH3), 6.20 (bs, 6H, Ar-H),7.65 (d, H, nphen), 7.94 (d, H, nphen), 8.42 (d, H, nphen), 8.62 (s, H, nphen), 8.86 (d, H, nphen), 9.04 (d, H, nphen), 9.15 (d, H, nphen).

Elemental analytical data indicate the stoichiometry of the ternary complex $Tb(HDMPE)_3$.nphen to be 3:1:1 (HDMPE: Tb: nphen). The ^{1}H-NMR spectrum of the ligand HDMPE showed singlet at δ 13.84 due to phenolic proton which disappeared in the complex Tb $(HDMPE)_3$.nphen was indicating that ligand is coordinated with Tb(III) ion through the oxygen atom of phenolic OH group of the ligand HDMPE. The FT-IR spectra of free ligand HDMPE exhibits abroad absorption band at 3430 cm^{-1} assigned to ν(O-H) stretching vibration which disappeared in the IR spectra of complex the $Tb(HDMPE)_3$.nphen. The free ligand also displays the intense C=O stretching vibration band at 1640 cm^{-1}, which was red shifted 28 cm^{-1} in complex the $Tb(HDMPE)_3$.nphen, indicating that phenolic and carbonyl group of HDMPE participated in coordination with Tb(III) ion[9,10,18]. The strong absorption band at 1585 cm^{-1} in complex the $Tb(HDMPE)_3$.nphen assigned to C=N stretching vibration, provided good evidence that the nitrogen atoms of nphen were coordinating with the Tb(III) ion[10,12,19]. The strong absorption band at 1558 cm^{-1} in complex the $Tb(HDMPE)_3$.nphen assigned to N=O stretching vibration. The peak for Ph-O vibration of free ligand HDMPE present at 1270 cm^{-1} showed a red shift of 36 cm^{-1} in the complex $Tb(HDMPE)_3$.nphen, indicating that the phenolic group is involved in coordination with the Tb(III) ion. The appearance of absorption bands at 542 cm^{-1} and at 428 cm^{-1} in the complex Tb $(HDMPE)_3$.nphen was assigned to ν(Tb-N) and ν(Tb-O)[10,18] respectively, which affirms that the nitrogen atoms of the nphen and oxygen atoms of the ligand HDMPE participated in coordination with the Tb(III) ion. Finally, it can be concluded from the FT-IR and ^{1}H-NMR spectra of the ligand HDMPE and complex Tb $(HDMPE)_3$.nphen, that the coordination of Tb(III) was through the oxygen atoms of phenolic and carbonyl group of ligand HDMPE and nitrogen atoms of the nphen.

Antimicrobial profile

The synthesized ligand HDMPE and $Tb(HDMPE)_3$.nphen were evaluated for their *in vitro* antimicrobial profile as tabulated in Table 1 and presented as bar diagram Figure 1. The antimicrobial profile has been investigated by taking ciprofloxacin and fluconazole[15] as standard drugs for antibacterial and antifungal profile respectively. The results revealed that the ligand HDMPE was having insignificant antimicrobial profile against bacterial and fungal strains, while Tb $(HDMPE)_3$.nphen showed moderate to good profile compared to the standard antibiotics and showed excellent profile against *S.aurius.* Moreover, it was interesting to note that Tb $(HDMPE)_3$.nphen proved to be better than the standard ciprofloxacin against *S. aurius*. Further it was noticed that complex was excellently active in case of *C.albicans,* while moderately active in case of *A.niger.* Moreover, it was interesting to note that Tb $(HDMPE)_3$.nphen proved to be better than the standard fluconazole against *C. albicans.* The increase in antimicrobial profile of the complex may be due to the presence of Tb (III) ion coordinated with the donor atom of the ligand which leads to the π- electron delocalization over the chelate rings[20].

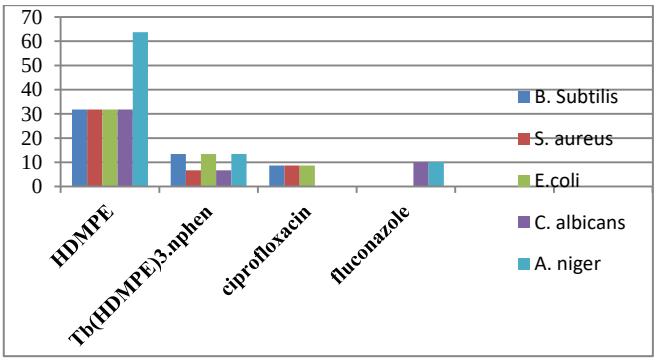


Figure 1: Bar diagram showing the antimicrobial activities of HDMPE and $Tb(HDMPE)_3$.nphen with respect to standard drugs.

Table 2: Minimum inhibitory concentration of HDMPE and Tb $(HDMPE)_3$.nphen

Compound	Minimum Inhibitory Concentration (µM/mL)				
	B. subtillis	*S.aureus*	*E.coli*	*C.albicans*	*A.niger*
HDMPE	31.8	31.8	31.8	31.8	63.7
$Tb(HDMPE)_3$.nphen	13.41	**6.70**	13.41	**6.70**	13.41
Standard.	8.71[a]	8.71[a]	8.71[a]	10.09[b]	10.09[b]

[a]Ciprofloxacin[b] Fluconazole

Antioxidant profile

In DPPH free radical scavenging profile, antioxidant reacting with stable free radical 2,2-diphenyl-2-picrylhydrazyl (DPPH) produced colorless 2,2-diphenyl-2-picrylhydrazyl. The absorbance decreased, after receiving hydrogen radical. The DPPH scavenging profile is expressed as IC_{50}. The IC_{50} value of ligand and $Tb(HDMPE)_3$.nphen were calculated from the graph plotted as inhibition percentage against concentration of HDMPE and $Tb(HDMPE)_3$.nphen as shown in Table 2 and Figure 2. The results show that ligand HDMPE and complex showed poor antioxidant profile as compared to standard ascorbic acid (IC_{50}= 43.78µg/ml).

Table 3: Percentage inhibition and IC_{50} values of DPPH radical scavenging profile of synthesized HDMPE and Tb $(HDMPE)_3$.nphen.

Compound	Concentration (µg/mL)				
	25	50	75	100	IC_{50}
HDMPE	23.12	43.02	60.08	80.83	60.42
$Tb(HDMPE)_3$.nphen	22.87	45.36	65.18	83.52	56.87
Ascorbic acid	34.02	56.22	76.12	92.01	43.78

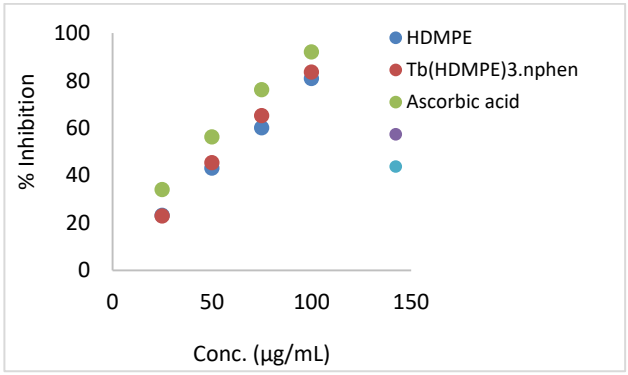


Figure 2: Percentage inhibition of HDMPE and Tb $(HDMPE)_3$.nphen with respect to standard ascorbic acid.

CONCLUSION

In this work, ternary Tb(III) complex, $Tb(HDMPE)_3$.nphen have been synthesized and characterized through various techniques like elemental analysis, FT-IR, ^{1}H-NMR spectroscopy. Variation in FT-IR and NMR spectra of free ligand (HDMPE) and complex have indicated that oxygen atoms of both phenolic as well as carbonyl group of ligand(HDMPE) and nitrogen atoms of ancillary ligand (nphen) were effectively coordinated to Tb(III)ion. This evolved complex has exhibits excellent *in vitro* antimicrobial profile against *S.aureus* and *C.albicans* but poor antioxidant profile as compared to standard ascorbic acid (IC_{50}= 43.78µg/ml).

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