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Antimicrobial Activities of a Mononuclear Manganese (II) Complex of Anthracenyl Terpyridine

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A B S T R A C T

A mononuclear manganese(II) complex $[Mn(atpy)_2](ClO_4)_2$ (1) where atpy is the tridentate ligand 4'-(anthracenyl-2,2':6',2''-terpyridine has been synthesized. Spectral techniques such as UV-Vis, FT-IR and ESI-MS were employed to characterize the compound. The compound showed a broad ligand to metal charge transfer transition in the 354 nm, according to the electronic spectra. The antimicrobial exercises of the ligand and its complex has additionally been done.

***Key words*:** Terpyridine, Complex, Manganese, Antimicrobial, UV-Vis

Due to their effectiveness and environmental acceptability, multi-component reactions (MCRs) have become more often used in recent years for the synthesis of a wide range of compounds. These procedures not only boost product yield but also minimize the number of laboratory procedures and the amount of solvents and chemicals required. Because of this, research in academia and business has emphasized more and more how effective and potent (MCR's) are as a tool in contemporary synthetic organic chemistry [1]. Proteins called enzymes and metallo-enzymes use metals to catalyze biological events. The active regions of a significant portion of newly discovered enzymes and proteins include metal ions. Metals are therefore becoming more and more recognized for their functions in biological processes [2]. Understanding a biological process' function, which is closely tied to geometric structure and the ultimate purpose of all biological activity, makes the expanding crystallographic database of protein structure increasingly significant. According to the ideas of similarity and inter-miscibility, bidentate or tridentate ligands with higher lipophilicity had stronger anti-microbial activity than monodentate ligands, and two different types of ligands in complexes had more anti-bacterial activity than a single ligand [3]. The capacity of 2,2′:6′,2″-terpyridines to chelate transition metals has generated a lot of interest in recent years. Numerous luminous metal compounds have been created as a result of the unique (photochemical) characteristics of their metal complexes. They have created a variety of luminous metal compounds [4] and photovoltaic device sensitizers thanks to the unique (photochemical) features of their metal complexes [5-6]. Electrochemical sensors have recently been created using ditopic terpyridyl units [7-8]. Due to the significance of terpyridine derivatives in photochemistry and biological reactions, we concentrated our efforts on the synthesis and research of terpyridine ligands that may be photoswitchable. Due to the wide range of chemical and physical characteristics of the complexes they form with various transition metal ions, functionalized 9-Anthracene 2,2':6',2'-terpyridines are becoming more and more important in scientific research. For synthetic chemists, it is especially difficult to integrate materials into polymeric structures and to modify various surfaces. Tridentate mono-terpyridine-complexes and hexadentate symmetric as well as asymmetric bis-terpyridine-complexes are the most prevalent coordination motifs in terms of their complexation chemistry. Asymmetric bis-complexation, in particular, with functionalized 2,2':6',2''-terpyridines of 9-Anthracene can produce useful chemical building blocks for well-defined structures. Additionally, anthracene functionalized terpyridines have been reported in which an anthracene unit served as a fluorescence sensor, spacer, or intercalator [9], among other functions [10-11]. In this article, we present the synthesis of a terpyridine complex with double anthracene functionalizations, and research on its antimicrobial activity.

MATERIALS AND METHODS

Anthracene-2-carboxaldehyde, manganese(II) perchlorate, and 2-acetyl pyridine were purchased from Sigma-Aldrich Chemicals and utilized exactly as supplied for the manufacture of terpyridine ligands. Common reagents such ammonium acetate, glacial acetic acid, hydrochloric acid, ammonia solution, and sodium hydroxide were supplied by SD Fine Chemicals in India. At the Centralized Instrument Facility Centre, CLRI, Chennai, a Euro Vector CHN analyzer was used to check the carbon, hydrogen, and nitrogen content of the recently synthesized ligand and manganese(II) complex. The FT-IR spectra of the ligand and complex as KBr pellets were

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captured using a Shimadzu FT-IR 8000 spectrophotometer in the 400–4000 cm^{-1} range. The characteristics of the ligand and complex were evaluated in the UV-visible spectrum using a Perkin-Elmer Lambda 35 spectrophotometer. The conductance values for the current metal (II) complex were measured at room temperature in 10^{-3} M DMF solutions using a dip-type conductivity cell and a digital conductivity bridge, the Systronics Direct Reading Conductivity Meter 304.

Preparation of ligands

Preparation of 4'-(1H-anthracen-2-yl)-2,2':6',2''-Terpyridine (Anthracene Terpyridine) (atpy) (L1)

Adapting a technique from the literature [12], 4'-(1H-anthracen-2-yl)-2,2':6',2''-terpyridine was synthesized. Using a mortar and pestle, 2-Acetylpyridine (10 mmol) and anthracene9-carboxaldehyde (5 mmol) were combined. The grinding was continued until an orange red powder formed (within 10 minutes). The powder was added to a suspension of ammonium acetate (2.5 g) in glacial acetic acid (10 mL) and heated to reflux for 2 hours. The crude product was precipitated out by the addition of water (5 mL). The product was filtered, washed with water and cold ethanol to get yellow powder, then column chromatographed using a 1:1 methanol-dichloromethane system. Yield: 1.48 g, 78%, Analysis Calculated for $C_{29}H_{19}N_3$: C, 85.08; H, 4.65; N, 10.27%; Found: C, 85.11; H, 4.59; N, 10.25%.

Synthesis of metal complex

Caution! During handling of the perchlorate salts of metal complexes with organic ligands, care should be taken because of the possibility of explosion.

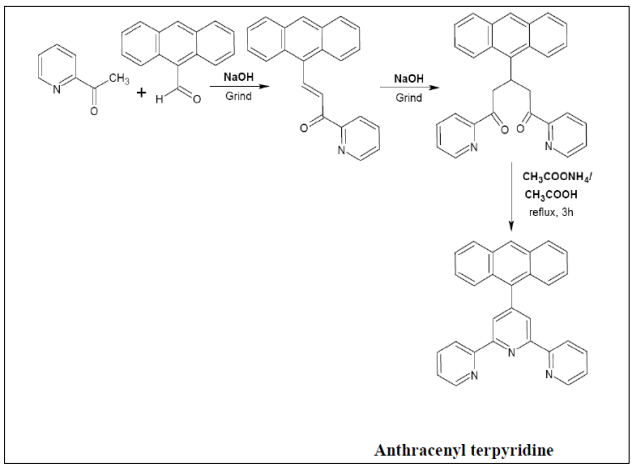

Fig 1 Synthetic scheme for anthracenyl terpyridine 1

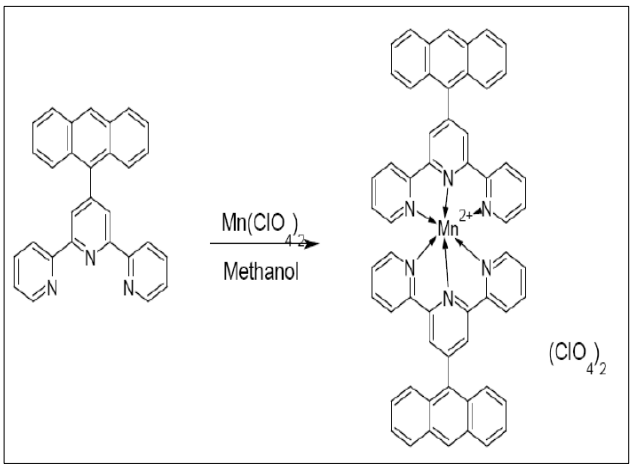

Fig 2 Synthetic scheme for complex 1

Synthesis of $[Mn(atpy)_2](ClO_4)_2$ (Cpx 1)

To a hot solution of $Mn(ClO_4)_2$. $6H_2O$ (2 mmol) in methanol, anthracenyl terpyridine (4 mmol) dissolved in methanol was added slowly and the reaction mixture was refluxed for 15 minutes. A white solid that separated out upon slow evaporation of the solvent, was filtered and washed with diethyl ether. Yield: 0.78 g (58%). Analysis Calculated for $C_{58}H_{38}MnN_6$: C, 78.63; H,5.69; N, 9.49; Mn, 6.20%. Found: C, 78.59; H,5.65; N, 9.46; Mn, 6.24%.

Antimicrobial assay

Two-gram positive (*Staphylococcus aureus* and *Bacillus subtilis*) and two-gram negative (*Escherichia* coli and *Pseudomonas aeruginosa*) bacteria, as well as two fungi (*Candida albicans* and *Aspergillus niger*), were obtained from KMCH, Coimbatore, and used for in vitro antimicrobial screening of test compounds. The Agar Well Diffusion assay was employed as the bioassay. For the study, Mueller Hinton Agar was produced. A sterile cotton swab was used to swab Mueller Hinton agar plates with a suspension of each bacterial species. The test chemicals were then thoroughly soaked on the sterilized filter paper discs. Each infected plate has impregnated dried discs placed on its surface. At 37 °C, the plates were incubated overnight. Each substance was tested three times against each organism. As a negative control, methanol was employed. Positive antibacterial controls included standard Gentamycin and Clotrimazole discs. The microorganisms' development was suppressed by the antimicrobial test materials, and a clear, unambiguous zone of inhibition was visible around the disc. The diameter of the zone of inhibition in mm was used to measure the antibacterial activity of the test drugs.

RESULTS AND DISCUSSION

Synthesis of ligand and metal(II) complex

The tridentate anthracenyl terpyridine ligand (atpy) was prepared according to a known procedure reported already and characterized. The metal(II) complex with formula $[Mn(atpy)_2](ClO_4)_2$ (1) where atpy is the tridentate ligand 4'-(anthracenyl-2,2':6',2''-terpyridine has been isolated from methanolic solution containing manganese(II) perchlorate as the starting material. Both ligand and complex were obtained in good yield and characterized by using electrical conductance, elemental analysis, UV-Vis and IR spectral techniques. The analytical data obtained for the new complexes given in (Table 1) agreed well with the proposed molecular formulae.

Table 1 Spectral and electrical conductance values of compounds

Compound	UV-Visible λ_{max}, cm^{-1}	IR cm^{-1}	Electrical conductance (Scm^2mol^{-1})
atpy (L1)	40486, 35336, 31949	3052, 1583,1240, 653	-
$[Mn(atpy)_2]$ $(ClO_4)_2$ (1)	40574, 35524, 31847	3054, 1599, 1247, 1087, 683	158

The synthetic scheme of the present complex is shown in (Fig 2). Based on electrical conductance measurement, manganese(II) complex is proposed to be 1:2 electrolyte as it measure molar conductance at 158 Scm^2mol^{-1} respectively in ~10^{-3} M DMF solution. The significant spectral data obtained for the present compounds are collected in (Table 1) and the corresponding UV-Visible spectra of metal complex is displayed in the (Fig 3).

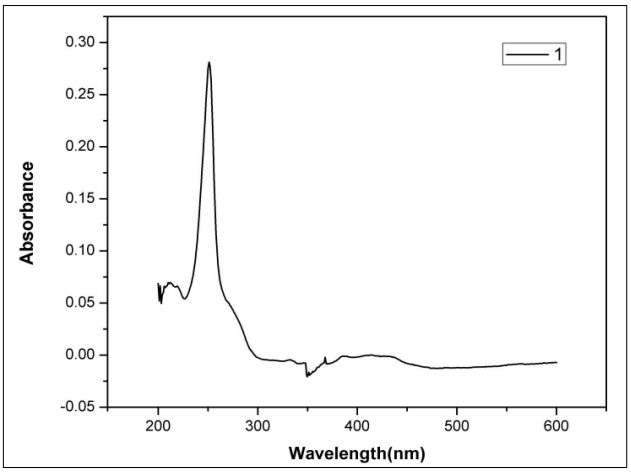

Fig 3 UV-Visible absorbance spectrum of manganese(II) complex

Electronic spectroscopy

UV-Visible spectra of both the ligand and the manganese to complex have been recorded at room temperature in acetonitrile solution. The anthracenyl terpyridine ligand (L1) shows UV absorption at 40486 cm^{-1} and 35336 cm^{-1} which are due to the aromatic π-π* transitions and another absorption observed at 31949 cm^{-1} is assigned to n-π* transition. Generally, compounds containing heteroatoms such as nitrogen, oxygen, Sulphur etc., have nonbonding electrons (n) in addition to σ and π electrons. Thus, the terpyridine derivative shows both π-π* and n-π* transitions in its UV spectrum. The manganese atom in the yellow coloured $[Mn(L1)_2](ClO_4)_2$ belongs to the $3d^5$ system and cannot exhibit d-d electronic transition, but its colour may be due to charge transfer transition measured at 31847 cm^{-1}.

IR Spectroscopy

The infrared spectrum of anthracenyl terpyridine containing manganese(II) complex recorded in KBr in the range 4000–400 cm^{-1} is shown in (Fig 4). The assignments of various absorption frequencies of L1 and the Manganese(II) complex are listed in Table 1. The CH stretching vibrations appear at 3052 cm^{-1}. The aromatic ring C=C and C=N stretching (skeletal) vibrations are observed at 1583–1440 cm^{-1}. The CH out-of-plane bending vibrations are seen at 785 and cm^{-1}. The in-plane ring deformation is observed at 653 cm^{-1}, while the out-of-plane ring deformation is found at 493 cm^{-1}. The ligand L1 has three possible potential coordination sites viz. three terpyridine N atoms. A comparison of the IR spectra of the manganese complex with that of the ligand L1 suggests the actual coordination sites of the ligand. Also, the mode of coordination of the perchlorate groups to the metal centre may be inferred from the IR spectrum of the present complexes. In the IR spectrum of the Manganese(II) complex, i.e. $[Mn(L1)_2](ClO_4)_2$, the skeletal vibrations of the aromatic heterocyclic rings are observed at 1599–1442 cm^{-1}, while in the ligand spectrum they are found at 1583–1440 cm^{-1}.

The position of these vibrational bands suggests the binding of the pyridyl nitrogen atoms to the metal ion [13-14]. The in-plane ring deformation vibration appears in the complex spectrum at 683 cm^{-1} whereas in the ligand spectrum it appears at a lower value of 653 cm^{-1}. The absorption of perchlorate ion in the spectrum is attributed to the appearance of a sharp peak at 1087 cm^{-1}.

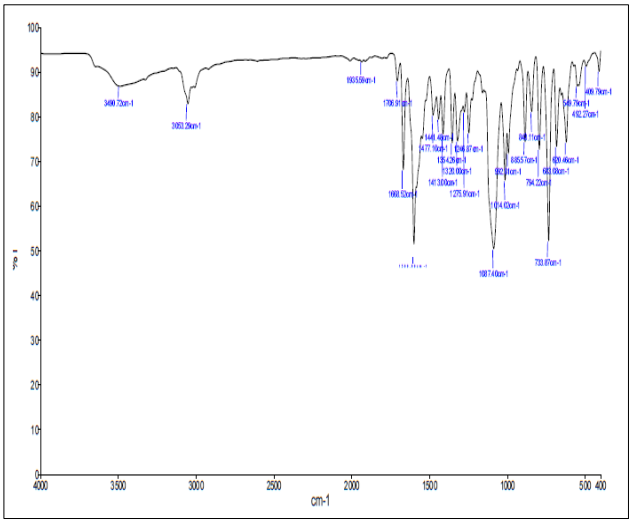

Fig 4 FT-IR spectrum of manganese(II) complex

Antimicrobial activity

The antimicrobial activities of both the ligand (L1) and its manganese(II) complex were studied by agar disc diffusion method and the results were shown in (Table 2-3). In vitro antimicrobial activity of a test drug is measured in terms of zone of inhibition produced. Higher the diameter of zone higher is the microbial growth inhibition. It is observed that the growth inhibition activities of the test compounds increase with increase of concentrations of test compounds. A comparison of the activities of the ligand and its complex against *S. aureus* shows the order: 1 > L1. It is to be noted that these compounds exhibit greater activity than the standard Gentamycin. Comparing the antibacterial activities of test drugs against *B. subtilis* shows the order : 1 > L1. In the case of *E. coli* the activities decrease in the order: 1 > L1. When the test drugs are assayed against *K. pneumoniae*, it is observed that compound 1 display greater activity. Thus, it is seen that the compounds tested are sensitive to the bacteria used, and all the compounds tested are much more active than the standard antibacterial drug namely gentamycin. The antifungal activity results furnished in (Table 3) indicate that the test drugs show enhanced activity against the test fungi (*Aspergillus niger niger* and *C. albicans*) when the concentrations of drugs are increased. Also, the test drugs are less sensitive against the fungi compared to the standard drug viz. clotrimazole. The activities of test drugs against *A. niger* decrease in the order : 1 > L1. The sensitivities of test drugs to *C. albicans* are found to decrease in the order : 1 > L1. The newly synthesized compounds showed zone of inhibition ranging from 9 to 29 mm. The comparative studies of the ligand and its zinc(II) complex signify that the complex showed significantly enhanced antimicrobial activity against microbial strains in comparison to the free ligands. The enhanced antimicrobial activity of the complexes can be explained by Tweedy's chelation theory and overtone's concept. According to the Overtone's concept of cell permeability, the lipid membrane surrounding the cell favors the passage of only lipid-soluble materials; therefore, liposolubility is an important factor which controls the antimicrobial activity. On chelation, polarity of the metal ion is reduced to a greater extent due the overlapping of the ligand orbital and partial sharing of the positive charge of the metal ion

with donor groups. Moreover, delocalization of the π-electrons over the whole chelate ring is increased, and lipophilicity of the complexes is enhanced. The increased lipophilicity enhances the penetration of the complexes into the lipid membranes and blocks the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism. In general, metal complexes are more active than ligands as they may serve as principal cytotoxic species.

Table 2 Antibacterial activity of ligand and its manganese(II) complex

Test drug	Zone of inhibition (mm)															
	S. aureus				*B. subtilis*				*E. coli*				*K. pneumoniae*			
	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL
atpy (L1)	10	12	14	16	18	20	22	25	20	24	27	30	10	13	14	18
$[Mn(atpy)_2](ClO_4)_2$ (1)	14	16	18	20	20	23	25	28	25	28	30	32	14	16	19	21
Gentamycin Standard	-	-	-	15	-	-	-	25	-	-	-	20	-	-	-	15

Note: Zone size less than 15 mm – Least active; 16 – 20 mm– moderately active; Above 20 mm – highly active

Table 3 Antifungal activity of ligand and its manganese(II) complex

Test drug	Zone of inhibition (mm)							
	A. niger				*C. albicans*			
	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL	25 µg/mL	50 µg/mL	75 µg/mL	100 µg/mL
atpy (L1)	10	14	18	20	14	17	19	22
$[Mn(atpy)_2]$ $(ClO_4)_2$ (1)	14	16	18	22	16	19	22	26
Gentamycin standard	-	-	-	22	-	-	-	28

Note: Zone size less than 15 mm – Least active; 16 – 20 mm– moderately active; Above 20 mm – highly active

The following is the order of antibacterial activity of test medicines against *Bacillus subtilis*: L2 > 3> L1 > 2 > 1. The activity of Klebsiella *pneumonia* diminishes in the following order: 2 > 1 > L1 > 3 > L2. When the test medications are tested against *P. aeruginosa*, compound 2 > 1 > 3 > L1 > L2 is found to have the most activity. As can be observed, the compounds examined are sensitive to the bacteria employed, and all of the compounds tested are significantly more active than gentamycin, the standard antibacterial treatment. The antifungal activity data in Table 3 show that increasing the concentrations of the test medications increases their effectiveness against the test fungus (*Aspergillus niger* and *Candida albicans*). In addition, when compared to standard drug viz. clotrimazole., the test medications are less sensitive to fungus. The activities of test drugs against *Aspergillus niger* decrease in the order : 2 > L2 > 1 ~ 3 > L1. The sensitivities of test drugs to *Candida albicans* are found to decrease in the order : 2 > 1 > 3 ~ L2 > L1. Zones of inhibition ranging from 10 to 25 mm were seen in the newly synthesized drugs. In comparison to the free ligands, the metal(II) complexes demonstrated dramatically improved antibacterial activity against microbial strains, according to comparative tests. Tweedy's chelation theory and the overtone notion can explain the complexes' increased antibacterial action.

CONCLUSION

Anthracenyl terpyridine ligand have been prepared and characterized In high yield, a mononuclear manganese(II) complex has been produced. Spectral techniques in the IR and UV-Visible range have been used to characterize the ligand and the complex. There is plenty of room for additional research. Some of the conclusions reached in this study are preliminary, and more research, including X-ray crystallographic and EPR spectral analyses, may be done to confirm the bonding modes and geometries of the synthesized metal complex. The ligand and complex both display improved antibacterial properties. The complex's chelating properties, however, have been demonstrated to increase its antibacterial activity.

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