ejbps, 2020, Volume 7, Issue 11, 115-118. **Review Article** **SJIF Impact Factor 6.044**

EUROPEAN JOURNAL OF BIOMEDICAL
AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 11
115-118
Year: 2020

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDY OF NOVEL LN^{III}-15C5/B15C5 COMPLEXES

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Article Received on 16/09/2020 **Article Revised on 06/10/2020** **Article Accepted on 26/10/2020**

ABSTRACT

Crown ethers have many applications in catalysis, organic synthesis, biochemistry, microbiology, and material science. Their applications in biology include the ability to regulate enzyme activity, interaction with DNA, and as antimicrobial agents. Simple crown compounds have the ability to interact with enzymes. The crown ethers are excellent hosts for accommodating metal ions via ion-dipole interaction. Crown ethers have a lower coordination power towards lanthanides but they have selectivity to the best-fit metal ions. The present paper describes preparation, characterization and antimicrobial study of some novel lanthanide-crown ether complexes with 1,4,7,10,13-pentaoxacyclopentadecane(15C5) and benzo-1,4,7,10,13-1,4,7,10,13-pentaoxacyclopentadecane (b15C5) having general formula of $[Ln.L.(Pic)_3].3H_2O$, where $Ln^{3+} = Pr^{3+}/Nd^{3+}$, L = 15C5/b15C5 and $Pic^- =$ Picrate anion.

KEYWORDS: Simple crown compounds have the ability to interact with enzymes.

INTRODUCTION

Macrocyclic ligands form stable complexes with lanthanides and hence they serve as a platform to explore the coordination chemistry of these metal ions. Macrocyclic complexes of lanthanides are currently attracting much attention in radioimmunotherapy[1-4], radioimmunoscintigraphy (γ-scintigraphy)[5,6], positron emission tomography[7], as contrast-enhancing agents in MRI as NMR shift reagent[8-10], as NMR shift and relaxation agents for proteins and biological cations[11-12], and as fluorescent probes in fluoroimmunoassay.[13] Lanthanide luminescent probes are presently extensively used for studying metal ion sites in macrocyclic complexes and in biological systems.[14,15] One of the most interesting applications of lanthanide (III) macrocyclic complexes is the transesterification of RNA.[16-18] Dinuclear lanthanide (III) complexes are also important as reconfigurable photonic devices with potential applications in biomedical diagnostics and fluorescence imaging.[19-21] Dinuclear lanthanide complexes are also important in studying the molecular recognition processes.[22-26] A large number of lanthanide complexes with macrocyclic ligands have been successfully prepared and characterized and shows an increased interest in these types of complexes.[27-37] Crown ethers have a lower coordination power towards lanthanides but they have selectivity to the best-fit metal ions.[38-41]

MATERIALS AND METHODS

The ligands (15C5/b15C5), lanthanide oxides, picric acid and the solvents were obtained from Sigma Aldrich/Merck and were used without further purification. FTIR spectra were recorded by Perkin Elmer spectrometer RX1(4000-450 cm^{-1}). UV-visible spectral data were recorded through Systronic double beam spectrophotometer-2203(600-200 nm). The ^1H−NMR spectra of ligand and crown ether complexes were recorded in $CDCl_3$ by Bruker DRX-300.

Preparation of lanthanide picrate

1 mmole of lanthanide oxide was placed in a round bottomed flask, followed by the addition of 40 ml of (0.05 M) picric acid solution and refluxed at 78-80^{0}C until all the oxide was dissolved, the process took 10-12 hours. The clear yellow solution was filtered while hot and then concentrated on a watch glass at 40-50^{0}C to half of its volume. After that the solution was left over night to be air concentrated. After concentration and evaporation of the solution yellow crystals were formed. A solution of 1 mmole of 15C5/b15C5 in 25 ml of absolute ethanol was added to a solution of 1 mmole of lanthanide picrate in 25 ml of absolute ethanol and refluxed at 60^{0}C for one hour. Then the solution was left overnight. The gel type precipitate was treated with petroleum ether for several times till fine crystals precipitate. The developed crystals were collected and stored in a desiccator.

Table 1: Prominent IR bands of synthesized complexes (in cm^{-1})

Compound	ν_{as} (C–O–C)	ν_1 (–NO_2), ν_3 (–NO_2)	ν_s(C–H)$_{bending,}$ ν_{as}(–CH_2–)$_{bending}$	ν(N=O)$_{str}$ in C–NO_2	ν(M–O) / ν(M–O_{crown})
[Pr.15C5.(Pic)$_3$].3H_2O	1085	1623, 870	1436, 1328	1220	482, 525
[Pr.B15C5.(Pic)$_3$].3H_2O	1062	1614, 874	1440, 1324	1232	523, 542
[Nd.15C5.(Pic)$_3$].3H_2O	1076	1602, 860	1448, 1326	1222	528
[Nd.B15C5.(Pic)$_3$].3H_2O	1064	1628, 840	1450, 1322	1229	524, 580

FTIR study

The crown ethers display ν(–CH_2–) stretching vibrations at 2920±10 cm^{-1} and these are little affected on bonding with lanthanide ions. The most important band in the spectra of the complexes is that of the (C-O-C) stretching vibration. The crown ethers in uncoordinated state display ν(C–O–C) stretching vibration band near 1115±10 cm^{-1}. This ν(C–O–C) vibration band shifted to lower frequency by 15-75 cm^{-1} in almost all complexes suggesting involvement of crown ether oxygen in bond formation with lanthanide ions.[42] Some new bands appear in the spectra of the complexes which are absent in the spectra of the free ligand/lanthanide picrates at around 1537–1560 and 1320–1337 cm^{-1}. Significant shifts are observed in the complexes when compared to the spectra of the corresponding lanthanide picrates indicating that crown ethers are coordinated to the metal ion. Some complexes are hygroscopic in nature and thus their IR spectrum displays a broad band for water molecules around 3345–3420 cm^{-1}, with maxima near 3405±10 cm^{-1}. In the far-IR region new bands are found in the 425-580 cm^{-1} region, which may be assigned to the ν(Ln–O_{crown}) stretching frequency.[43-46]

^{1}H-NMR Study

Significant changes were observed in the chemical shift of 1-H in 15C5 and, 1-H as well as 2-H, in b15C5. After formation of the [Ln.L.(Pic)$_3$].nH_2O complex. The proton chemical shift δ(–CH_2CH_2O–) shows significant downfield shifts [Δδ(–CH_2CH_2O–) = 0.08-0.18 ppm], indicating metal-ligand bond formation. The degree of downfield shift shows the relative strength of the complexes.[47] The ^{1}H-NMR spectrum of b15C5 shows peaks at, δ_1=3.9–4.2 ppm, (16H, 4 –CH_2CH_2O–), δ_2=6.8–7.0 ppm, (4H, aryl –CH–) in $CDCl_3$. Reasons for this downfield shifts are the conformational change in the macrocyclic skeleton during complexation.[48] The shift of –CH_2– signals in complexes from free crown ether suggests the coordination of crown ethers with lanthanide ion.

Antibacterial and antifungal activities of prepared complexes

Antimicrobial test was performed using Kirby Bauer disc diffusion method.[49,50] Five bacterial isolates, Escherichia coli (gram negative), Staphylococcus aureus (gram positive), Enterococcus faecalis (gram positive), Bacillus subtilis (gram positive), Lactobacillus (gram positive) and one fungal isolate of Candida albicans were used in this work. The isolates were planted on the surface of an agar on petriplates incubated at 37°C for 24 hrs and stored at 4°C for the later use. Sterile filter paper dishes are placed in 4-5 places on the petriplates. The test compound was then added at the centre of each paper. The plates are inverted and then incubated for 16 hrs. After incubation depending on the strain and chemical complex inhibition zones were developed around each test sample. The diameter of the zone of inhibition around each disc was measured to the nearest millimeter.[51,52] Controlled experiments were performed and only equivalent volume of solvents were added and applied on the paper discs. The antimicrobial activities were expressed as minimum inhibitory concentration (MICS) values[53,54] corresponding to the lowest concentration of the compound that produces a measureable zone of inhibition. All the used ligands showed low activity against the tested bacteria and fungi while all the prepared complexes showed very good results. Table-2 shows the activities based on inhibition zones of the prepared complexes. All the prepared complexes gave good inhibition zones. Results of antimicrobial tests of synthesized complexes are listed below.

Table 2: Antimicrobial activities of synthesized complexes.

Compound	Antibacterial activity										Antifungal activity	
	Gram Positive								Gram Negative			
	S.aureus		E.faecalis		B.substillis		Lactobacillus		E.coli		C.albicans	
	1 mg	2mg	1 mg	2mg	1 mg	2 mg	1 mg	2 mg	1 mg	2 mg	1 mg	2mg
[Pr.15C5.(Pic)$_3$].3H_2O	--	--	--	--	-	-	-	--	-	-	-	-
[Pr.B15C5.(Pic)$_3$].3H_2O	-	--	--	--	-	-	-	--	-	-	-	--
[Nd.15C5.(Pic)$_3$].3H_2O	+	+	-	-	+	-	+	+	-	-	+	+
[Nd.B15C5.(Pic)$_3$].3H_2O	-	-	-	-	-	-	+	+	-	-	+	+

--Very active – Moderately active + Not active

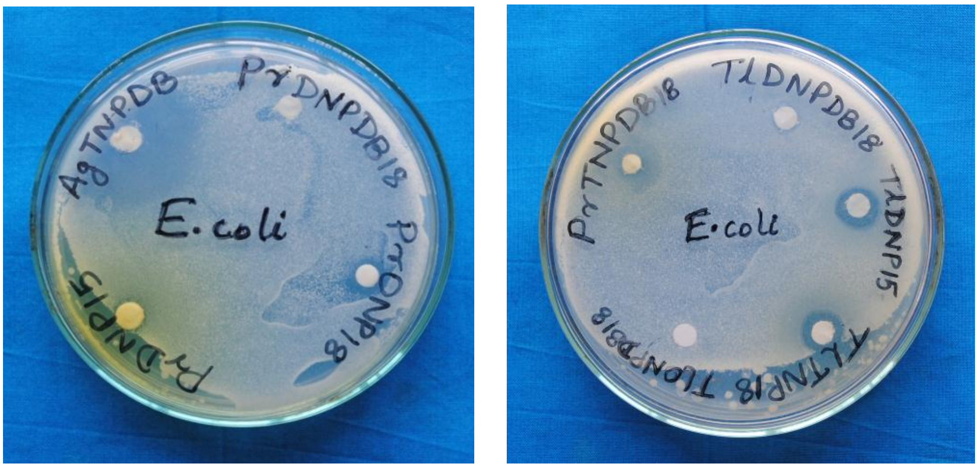

Fig. 1.1. Microbial study against E. coli.

Acknowledgement

We are thankful to the Head, SAIF, CDRI, Lukhnow, for providing FTIR-spectra, ^{1}H-NMR spectra and necessary facilities.

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