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Complexation Studies of some Inner Transition Metal Ions with Benzylpenicillin.

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Abstract

Chelated Lanthanide (III) complexes of type $[ML_2(OH_2)_2]Cl$ (Where "M" =La(III), Pr(III), Nd(III), Sm(III) & Dy(III), "L" = Benzylpenicillin) have been synthesized & characterized by their elemental analysis, molar conductance values, magnetic susceptibilities, UV, IR, NMR, & Electronic Spectral studies. In all the complexes, "Benzylpenicillin" acts as a tridentate ligand with coordination involving the carboxylate-O of Thiazolidine nucleus, 'O' of Amide and endocyclic N of β-Lactam ring. A coordination number of eight is assigned to the metal ion in all the complexes.

Keywords: Lanthanide(III) Metal Complexes, Benzylpenicillin, UV, IR, NMR, Electronic.

Introduction

Benzylpenicillin '[(2S,5R,6R)-3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo [3,2,0] heptane-2-carboxylic acid]' **[FIGURE-1]** is widely applicable against gram (+)-ive organisms & some gram (-)ive organisms such as *Neisseria gonorrhoea* and *Neisseria meningitids*. Specific indications for Benzylpenicillins include Cellulitis, Ineffective endocarditis, Gonorrhoea, Meningitis, Aspiration Pneumoniae, Lung Abscess, Community acquired pneumoniae, Syphilis, Septicemia in Children, Septic Arthritis, Gangrene diphtheria.....etc[1]. Benzylpenicillin is white crystalline powder that is soluble in water , sparingly soluble in alcohol[2].Most living systems contain metal ions for their proper functioning[3-6]. Many drugs possess modified toxicological and pharmacological properties when they are complexed with metal ions[7-17]. This work involves the synthesis and characterization of some inner transition metal complexes of Benzylpenicillin.

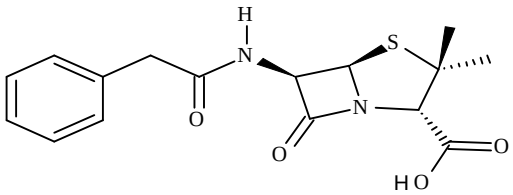

FIGURE-1: *Benzylpenicillin*

Materials and Methods

All the Chemicals and solvents used were of analytical grade. Metal salts (of 99.97% purity) i.e, $LaCl_3$, $PrCl_3$, $NdCl_3$, $SmCl_3$, $DyCl_3$ were purchased from Indian Rare Earth Udyog Mandal, Kerala, India and ligand i.e, Benzylpenicillin was purchased from CDH. All chemicals and solvents were used without further purification. Its molar conductance was measured by *Systronics Conductivity meter model-304* in $1x10^{-3}$DMF Solution.

The magnetic moment of the complexes were measured by Gouys method in Bohr Magneton unit at room temperature using $Hg[Co(NCS)_4]$ as the calibrant, in *Inorganic Research Laboratory, PG Department of Chemistry, L.N.M.U Darbhanga*. Elemental analysis of the complexes were carried out at CDRI-Lucknow. IR Spectra of the ligand and metal complexes were recorded on a *Perkin Elmer FTIR Spectrophotometer* using KBr disc method. The ^1H NMR Spectra of complexes was recorded in DMSO-d_6. All chemical shift values are expressed in δ–Scale downfield. Molecular weight of the complexes were determined by Camphor-Rast Method. Electronic Spectra of the complexes were recorded by the courtesy of CDRI & Dept. of Chemistry, IIT Delhi.

Preparation of Metal(III)-Complex :

Ln(III) complexes of Benzylpenicillin were prepared by taking different molar ratio of "Metal:Ligand" as 1:2. The complexes were prepared by adding a solution of corresponding metal(III) chloride (2.5 mmol) in ethanol (25 ml) to a solution of Benzylpenicillin (1.674g, 5 mmol) in a mixture of water : ethanol (25 ml, 1:1 v/v) with constant stirring. The p^H was adjusted between 7-8. The mixture was refluxed for 1h on a water bath and concentrated to half volume. Then on cooling to room temperature, the colored complex got precipitated slowly, which was filtered under suction, washed with distilled water & ethanol repeatedly. Now the complexes were dried over anhydrous Calcium Chloride in dessicator. (Yield: 55-68%)

Results and Discussion

Analytical data, Magnetic Moment, Molar conductance, % yield & Decomposition temperature are reported in Table-1. From the elemental analyses complexes may be formulated as $[LnL_2(OH_2)_2]Cl$, where, 'Ln= La(III), Pr(III), Nd(III), Sm(III) & Dy(III)' & 'L'=Benzylpenicillin. All these complexes are non-hygroscopic. At room temperature, Magnetic Moment of the complexes are in good agreement with the theoretical values calculated by Van-Vleck[16]. All the Ln(III)-Complexes were obtained in powder form with characteristic color. They are insoluble in common organic solvents and only soluble in DMF & DMSO. All the metal complexes decomposed below 400^0C.

Except La(III), all the Ln(III)-Complexes are paramagnetic in nature due to presence of unpaired 4f-electrons which are effectively shielded by $5s^2$ and $5p^6$ electrons. Complex of Sm(III) shows a very little deviation from Van-Vleck values[18], indicating a little participation of 4f-electrons in bonding. The relatively high value obtained in the case of Sm(III) complexes may be due to small **J-J** separation, which leads to the thermal population of the higher energy levels and show susceptibilities due to *First Order Zeemann Effect*[19].

IR Spectra of Benzylpenicillin and their Ln(III)-Complexes are reported in Table-2. The IR Spectra of all Benzylpenicillin complexes shows band at 3440-3400 cm^{-1} characteristic of coordinated water molecules[20]. In the IR Spectra of ligand endocyclic N stretching frequency of β-Lactam appeared at 1197 cm^{-1} which was shifted to lower frequencies .The band at 1750 cm^{-1} & at 1718cm^{-1} appeared due to C-O stretching of carboxylic acid of Thiazolidine nucleus & C-O stretching of Amide respectively which was shifted at a lower frequency upon complexation with Ln(III)-ions in the range of 1620-1590 cm^{-1} & 1700-1650 cm^{-1}. Shifting of these bands in all the complexes indicate that there is a coordinate covalent bonding through endocyclic N of β-Lactam, Oxygen of Amide group & carboxylic acid of thiazolidine nucleus of Benzylpenicillin with Lanthanide(III) central metal ion[21,22]. The presence of chloride ion in the structural configuration of these complexes suggests that Benzylpenicillin acts as a tridentate monoanionic molecule during complexation with metal ions. All of the above mentioned IR Spectral data suggests coordination number eight for all the synthesized 'Ln(III)-Benzylpenicillin' complexes **(Figure-2).**

^1H NMR spectra of ligand and their metal complexes were taken in DMSO-d_6. All the protons were found in their expected region[23]. A multiplet signals in the region of δ7.66-8.00 ppm due to aromatic ring protons[24]. A downfield shift in the region of δ2.0-2.1 appeared due to –COOH group proton, which disappeared in the spectra of complexes indicating the involvement of that proton during complexation. These results provide evidence in support of mode of bonding as discussed from the IR Spectra of complex.

Electronic spectral data for the solutions of Ln(III)-Benzylpenicillin complexes investigated in CH_3CN are reported in Table-3. For comparison, the spectral data for the corresponding aqueous salt solution are also given in the same table. Lanthanum(III) complexes have no significant absorption in the uv-region. Electronic spectra of Pr^{3+}, Nd^{3+}, Sm^{3+} & Dy^{3+} complexes show bands at lower energies than those of their aqua metal ions[25]. The absorption bands of Pr^{3+}, Nd^{3+}, Sm^{3+} & Dy^{3+} have been attributed to the transitions from ground levels i.e, $^3H_4$, $^4I_{9/2}$, $^6H_{5/2}$ & $^6H_{15/2}$ respectively to the excited j-levels of $4f^n$-configuration[26] of Ln(III) central metal ion. The various spectral parameters like, Nephlauxetic Ratio (β), Covalence factor ($b^{1/2}$), metal-ligand covalency % i.e, Sinhas Parameter (δ%) and covalency angular overlap parameter (η) have been calculated. The values of (1-β) and δ% comes out to be positive throughout which supports the evidence of strong coordinate covalent bonding in all the synthesized "Ln(III)-Benzylpenicillin" complexes.

Table-1 : Analytical, Magnetic Susceptibilty, Molar Conductance data of "Ln(III)-Benzylpenicillin" Complex.

				% (Obs./Cal.)				
S.No	**Complex**	**M. Formulae**	**M. Wt (Obs./Cal.)**	**C**	**H**	**N**	**Cl**	**Ln**
1.	$[LaL_2(H_2O)_2]Cl$	$C_{32}H_{38}LaO_{10}N_4S_2Cl$	876.24/876	43.87/43.83	4.37/4.33	6.42/6.39	4.02/3.99	15.89/15.86
2.	$[PrL_2(H_2O)_2]Cl$	$C_{32}H_{38}PrO_{10}N_4S_2Cl$	878.81/878	43.78/43.73	4.39/4.32	6.40/6.37	3.99/3.98	16.09/16.05
3.	$[NdL_2(H_2O)_2]Cl$	$C_{32}H_{38}NdO_{10}N_4S_2Cl$	881.23/881	43.62/43.58	4.38/ 4.31	6.39/ 6.35	3.99/ 3.97	16.39/ 16.34
4.	$[SmL_2(H_2O)_2]Cl$	$C_{32}H_{38}SmO_{10}N_4S_2Cl$	887.18/887	43.34/ 43.29	4.35/ 4.28	6.35/ 6.31	3.96/ 3.94	16.99/ 16.91
5.	$[DyL_2(H_2O)_2]Cl$	$C_{32}H_{38}DyO_{10}N_4S_2Cl$	899.50/ 899	42.75/ 42.71	4.26/ 4.22	6.28/ 6.22	3.95/ 3.89	18.09/ 18.02

S.No	**Complex**	**% Yield**	**Color**	**Decomposition Temp(^{0}C)**	**i_m (Ohm^{-1}cm^{2}mol^{-1})**	**«$_{eff.}$ (in B.M.)**
1.	$[LaL_2(H_2O)_2]Cl$	58	Light Yellow	332	10.6	Dia
2.	$[PrL_2(H_2O)_2]Cl$	56	Yellow	367	13.9	5.69
3.	$[NdL_2(H_2O)_2]Cl$	62	Yellowish White.	359	12.7	3.62
4.	$[SmL_2(H_2O)_2]Cl$	59	Pale Yellow.	362	10.1	1.59
5.	$[DyL_2(H_2O)_2]Cl$	65	Light Yellow	347	7.2	11.3

Where 'L'=Ligand

Table-2: IR Spectral data (in cm^{-1}) of ligand and complexes :

Functional Group	**Ligand Benzylpenicillin**	**Complexes**				
		La(III)	**Pr(III)**	**Nd(III)**	**Sm(III)**	**Dy(III)**
>N—	1197	1189	1187	1075	1335	1324
—C(=O)—OH	1750	1608	1614	1612	1601	1617
>C=O$_{Amide}$	1718	1605	1613	1672	1665	1667

Table-3: Electronic spectral data along with band-assignment (in cm^{-1}) and related bonding parameters of "Ln (III)- Benzylpenicillin" Complex.

Complex	Band Assignments	Bands of Ln^{3+}-aqua ions (in cm^{-1})	Bands of Complex (in cm^{-1})	Calculated Bonding Parameter				
				(1-β)	β	$b^{1/2}$	¢(%)	¦=
$[PrL_2(H_2O)_2]Cl$	$^3H_4 \rightarrow {}^3P_2$	22300	21500	0.0359	0.9641	0.0947	3.7236	0.0185
	$\rightarrow {}^3P_1$	21900	21000	0.0411	0.9589	0.1013	4.2861	0.0212
	$\rightarrow {}^3P_0$	20200	19700	0.0248	0.9752	0.0787	2.5430	0.0126
	$\rightarrow {}^1D_2$	16800	15900	0.0536	0.9464	0.1157	5.6635	0.0279
$[NdL_2(H_2O)_2]Cl$	$^4I_{9/2} \rightarrow {}^4G_{9/2}$	19330	19154	0.0092	0.9908	0.0479	0.9285	0.0047
	$\rightarrow {}^4G_{5/2}, {}^2G_{7/2}$	17485	17367	0.0068	0.9932	0.0412	0.6846	0.0035
	$\rightarrow {}^4F_{9/2}$	14730	14527	0.0138	0.9862	0.0587	1.3993	0.0070
	$\rightarrow {}^2S_{3/2}, {}^4F_{7/2}$	13688	13283	0.0296	0.9704	0.0860	3.0502	0.0152
	$\rightarrow {}^4F_{5/2}, {}^4H_{9/2}$	12790	12650	0.0110	0.9890	0.0524	1.1122	0.0056
$[SmL_2(H_2O)_2]Cl$	$^6H_{5/2} \rightarrow {}^7F_{5/2}$	33767	33520	0.0074	0.9926	0.0430	0.7455	0.0038
	$\rightarrow {}^4H_{7/2}$	28854	28367	0.0169	0.9831	0.0650	1.7190	0.0085
	$\rightarrow {}^4I_{7/2}$	26763	26240	0.0196	0.9804	0.0700	1.9991	0.0099
	$\rightarrow {}^4I_{15/2}$	22580	22315	0.0118	0.9882	0.0543	1.1940	0.0060
$[DyL_2(H_2O)_2]Cl$	$^6H_{15/2} \rightarrow {}^6F_{5/2}$	12135	11970	0.0136	0.9864	0.0583	1.3787	0.0069
	$\rightarrow {}^4I_{15/2}$	22630	22253	0.0167	0.9833	0.0646	1.6983	0.0084
	$\rightarrow {}^4G_{11/2}$	23710	23472	0.0100	0.9899	0.0502	1.0203	0.0051

Conclusion

Coordination number eight for all the synthesized metal complexes have been suggested on the basis of above discussion. Thus the probable structure for all these "Ln(III)-Benzylpenicillin" complexes may tentatively assigned as:

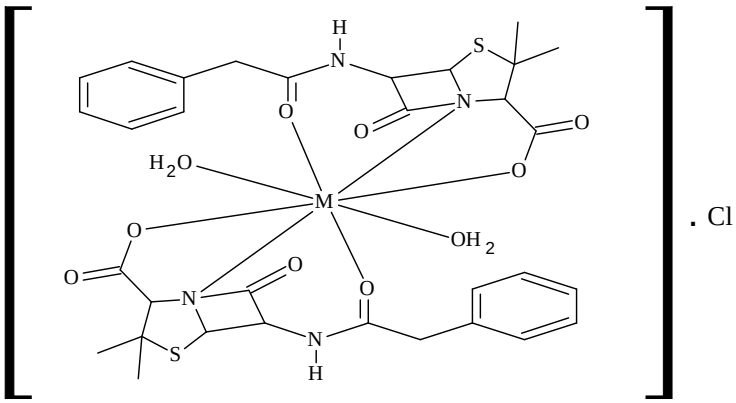

FIGURE-2: Proposed structure of "M(III)-Benzylpenicillin" Complex.

Where, M(III) =La(III), Pr(III),Nd(III), Sm(III) & Dy(III)

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References

1. S. Rossi : *Australian Medicines Handbook, Adelaide:* ISBN 0-9757919-2-3 (**2006**)
2. D.C. Plumb : *B-263* ,*Veterinary drug handbook, 4th Ed^{n}.:* ISBN: 0-8138-2442-7(**2002**)
3. B. Norden, P Lincoln, B Akerman, In E. Tuitec: A Sigel, S Sigel, Editors :*Metal ions in biological systems, New York: Marcel Dekker:* 1996*, vol* **33**
4. DR Williams: *The metals of life, London: Van Nostrand* (1971)
5. H Sigel, DB Mc Cormick : *On the discriminating behavior of metal ions and ligands with regard to their biological significance. Acct Chem Res :* 1970**,3(6),** 201-207
6. DR. Williams : *Metals, ligands & Cancer: Chem Rev,* 1972**,72(3),** 203-213
7. A Albert. *The variety of effects of chelating agents on organisms. Aust J Sci :* 1967**,30(1),** 1-7
8. S Kirschner, Y K Wei, D Francis, JG Bergman : *Anticancer and potential antiviral activity of complex Inorganic Compounds : J Med Chem:* 1966**, 9,** 369-372
9. Li-June Ming : *Structure and function of Metalloantibiotics*. *Med Res Rev,* 2003, **Vol. 23, No. 6,** 697-762
10. JK Barton: *Metal Nucleic Acid Interactions, Bio-Inorganic Chemistry, London University Science Books,* (1994)
11. J Hinton, RE Koeppe: *Complexing properties of Gramicidins. Metal Ion Biol Syst,* 1985**, 19,** 173
12. CA Claussen, EC Long: *Nucleic acid recognition by metal complexes of bleomycin. Chem Rev* 1999**,2797[32],** 99
13. Wu Guangguo, Wang Guoping, Fu Xuchun and Zhu Longguan : *Molecules* 2003, **8**, 287
14. Gao Fei, Yang Pin, Xie Jun and Wang Hongfei : *Jornal of Inorganic Biochemistry,* 1995, **60(1),** 61
15. H. Beraldo, D. Gambinob: *Mini reviews in medicinal chemistry,* 2004, **4(1)**, 31-39
16. Rajesh Kumar Mishra & B.G.Thakur: *Asian Journal of Chemistry,* 2015,**27(3)**, 860-864
17. Rajesh Kumar Mishra & B.G.Thakur: *American International Journal of Research in Formal, Applied and Natural Sciences*(AIJRFANS-IASIR, USA), 2014, **6(2),** 130-135.
18. J.H.Van Vleck and N.Frank : *Phys. Rev.,* 1929**, 34,** 1494
19. J.P.Phillips and L.L.Merritt: *J. Am. Chem. Soc.,* 1949 ,**71,** 3984
20. K. Nakamoto: *Infrared Spectra of Inorganic and Coordination Compounds. 2nd Ed^{n}, New York, Wiley Interscience* (1970)
21. J.R.Ferraro: *Low frequency vibrations of Inorganic and Coordination Compounds. Plenum Press, New York* (1970)
22. L.J.Bellamy : *The Infrared spectra of complex molecules. Methuen, London* (1964)
23. WW. Simmons: *The Sadtler handbook of Proton NMR Spectra. Sadtler Research Laboratories, Inc:* (1978)
24. N.K.Singh and Namita Rani Agrawal: *Indian J. Chem.,* 2001**, 13,** 1549
25. G.P.Choplin, D.E.Henrie and K.Buijs : *Inorg. Chem.,* 1966**, 5,** 193
26. R.K.Agarwal and Himanshu Agarwal: *Synth. React. Inorg. Met.-Org. Chem.* 2001 **,31,** 263

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