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## Review on Ln (III) Metal Complexes with N, S and 'O' Containing Heterocyclic Ligands

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### Abstract

The spectroscopic properties of the Ln (III) ions are unique due to shielding of the 4f orbitals by the filled 5s<sup>2</sup> and 5p<sup>6</sup> sub-shells. The electronic, in 4 f orbitals are Laporte forbidden. Most of the sharp lines like 4f↔4f transitions originating within the 4f-configuration of the lanthanide (III) ions are little affected by the environment of the lanthanide ions. Such transitions have been called hypersensitive transitions by Jorgensen and Judd. In lanthanides, transitions involve only a redistribution of electrons within the 4f-orbitals (f↔f transition). Which are orbitally forbidden by the selection rule. Crystal field effects in lanthanides are virtually insignificant due to 4f-electrons are well shielded from external charge by 5s<sup>2</sup> and 5p<sup>6</sup> sub-shells. Their absorption bands (f↔f transition) are very sharp. Their optical spectra are virtually independent of environment they show similar spectra in gas/solution/solid (sharp lines like typical gas atom spectra).

**Keywords:** Metal complexes, Judd Oflet parameters. Lanthanide ions

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### 1. Introduction

#### (i) Lanthanides:

Lanthanides are called first inner transition series and come immediately after lanthanum. They are classified as f block elements along with the actinides. They are commonly called the rare earths. They are characterized by the filling up of the 4f energy levels which are not usually involved in bonding. They have a generic symbol "Ln". The lanthanide exhibits a number of features in their chemistry that differentiate them from the d-block elements. Generally, lanthanides show +3 oxidation state with wide range of coordination number (CN. generally [1-12]). They form labile 'ionic' complexes that undergo facile exchange of ligand. The 4f orbitals in the Ln<sup>+3</sup> ion do not participate directly in bonding, being well shielded by the 5s<sup>2</sup> and 5p<sup>6</sup> orbitals. Their spectroscopic and magnetic properties are thus largely uninfluenced by the ligand. They prefer anionic ligands with donor atoms of rather high electronegativity (e.g. O, F) [13].

#### (ii) N, S and O containing ligands:

In coordination chemistry, a ligand is an ion or molecule (functional group) that binds to a central metal atom to form a coordination complex. Those ligands in which donor atom which attach to metal ion are N and S known as



N,S containing ligands. The various type N,S and O containing ligands recently used for synthesis of lanthanide chelates such as aminothaizoles, amino pyridines, tridentat Schiff base, thio semicarbazide, thiosemicarbazone, thiocyanate, thiourea, quinone, quinolone derivative benzothiazole derivatives [22-24,27-30] etc.

## 2. Metal Complexes

A metal complex consists of a central atom or ion, which is usually metallic and is called the coordination centre, and a surrounding array of bound molecules or ions, that are known as ligands or complexing agents. Many metal containing compounds, especially those of transition metals are coordination complexes. The complexes in which polydentate ligand present known as chelate complexes. The term Chelate derives from the Greek word for “Claw” and is applied to name ligands, which attach to a metal ion with two or more donor atoms through dative bonds. The central atom or ion, together with all ligands comprise the coordination sphere. Coordination refers to the “coordinate covalent bonds” (dipolar bonds) between the ligands and the central atom. The number of donor atoms attached to the central atom or ion is called the coordination number [14].

The lanthanide (Ln) elements in their stable oxidation state generally form trivalent cations whose chemistry is mainly determined by the ionic radii, which decrease from lanthanum to lutetium. The chemistry of lanthanides differs significantly from the chemistry of main group and transition metal elements because of the 4f orbitals that are spatially ‘buried’ inside the atom and are shielded from the ligand field [15]. Consequently, the chemistry of the lanthanide ions is largely determined by their sizes. Ln(III) forms coordination complexes with a wide variety of ligands [16].

Ln(III) ions are typically hard Lewis acids because of the high charge density and they prefer to bind to hard base atoms, viz. oxygen. Since the 4f electrons are spatially buried, the mixing of ligand and metal orbitals becomes insignificant and bonding between the ligands and the Ln(III) ions is largely electrostatic in nature. Observation of high coordination number (>6) is due to lack of any directional bonding character and large ionic size resulting poor stereochemical preferences and consequently.

The coordinating ligands in the complex occupy positions that minimize the steric repulsions between them. Therefore, the coordination environment around the Ln(III) centre often cannot be regarded as an idealized coordination polyhedron. The trivalent lanthanide ions barring La(III) and Lu(III) have unpaired f electrons and hence are paramagnetic. The magnetic moment values generally deviate from the spin-only values because of strong spin-orbit coupling. The Gd(III) ion has the maximum number (seven) of unpaired electrons with a magnetic moment of 7.94  $\mu_B$ , but the largest magnetic moments (10.4–10.7  $\mu_B$ ) are exhibited by Dy(III) and Ho(III) as a result of orbital contribution to the magnetic moment. In Gd(III), all the seven electrons have parallel spins and this high paramagnetism combined with a reasonably slow electronic relaxation rate makes Gd(III) complexes of macrocyclic organic ligands ideally suitable as contrast enhancement agents in clinical magnetic resonance imaging (MRI). Lanthanide ions differ from the d-block elements with small crystal field splitting [17-18].

The spectroscopic properties of the Ln(III) ions are unique due to shielding of the 4f orbitals by the filled 5s<sup>2</sup> and 5p<sup>6</sup> sub-shells. The electronic transitions within the 4f orbitals are Laporte forbidden. Besides, coupling with molecular vibrations is weak and the electronic spectra of lanthanide ions show very low molar extinction coefficients ( $\epsilon < 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ ) with narrow absorption bands. Therefore, the absorption spectra of lanthanide complexes are generally characteristics of ligand-centred absorption bands which are often very strong and most of the photophysical properties of the coordinating ligands are retained on complexation with a lanthanide ion. This is particularly true for La(III) (f<sup>0</sup>, diamagnetic) and Gd(III) (f<sup>7</sup>, paramagnetic) complexes since both the ions absorb in the UV region.

The study of the metal complexes of antipyrine in antineoplastic medication, molecular biology and bioengineering has become hotspots in recent years. A new Schiff base formed from pyridoxal, a vitamin and 4-aminoantipyrine is reported and the antibacterial activity of the newly synthesized Schiff base formed from 4-aminoantipyrine with vitamin B is explored. The Schiff base ligand forms very stable complexes with the lanthanide metals La, Ce, Pr, Nd, Sm, Gd, Tb, Dy and Er, their structural, spectroscopic, biological properties have been reported [19].



Lanthanide complexation chemistry has been studied intensively and progress has been stimulated by applications as bioactive probes for magnetic resonance, luminescence, in drug delivery and in cancer therapy. Trivalent lanthanide ions (III) form complexes with various organic molecules and supramolecular assemblies have been carried out in the solid and solution state which is of great importance scientifically, biologically and commercially. The design of organic ligands in the optimization of the specific properties (optical, luminescence, paramagnetic, biological) of the lanthanide complexes for biomedical applications received more attention in the last decades. Found on the physical and spectral properties, lanthanides have numerous applications, such as fluorescent probes in biological assays [20]. A novel potential tridentate Schiff base was prepared by condensing equimolar quantities of 2-hydroxyacetophenone and 2-aminopyrimidine in methanol. This ligand was versatile in forming a series of complexes with lanthanide ions such as La(III), Pr(III), Nd(III), Sm(III), Gd(III), Dy(III) and Yb(III). The ligand and the metal complexes were characterized through elemental analysis, molar conductance, UV-Visible, IR,  $^1\text{H}$  NMR, and mass spectral studies. The spectral studies indicated that the ligand was coordinated to the metal ion in neutral tridentate fashion through the azomethine nitrogen, one of the nitrogen atoms in the pyrimidine ring and the phenolic oxygen without deprotonation. The DNA cleavage studies of the ligand and the metal complexes were carried out and it was observed that the lanthanum (III) and neodymium (III) complexes cleaved the pUC19 DNA effectively. The ligand and the metal complexes were screened for their antibacterial activities. The metal complexes were found to be more potent bactericides than the ligand [21].

Lanthanide complexes of Eu(III), Gd(III), Nd(III), Sm(III), and Tb(III) with phenylthioacetic acid were synthesized and characterized by elemental analysis, mass, infrared radiation (IR), electronic spectra, molar conductance, thermogravimetric analysis (TGA), and powder X-ray diffraction (XRD). The lanthanide complexes were homodinuclear in nature. The two lanthanide ions were bridged by eight oxygen atoms from four carboxylate groups. Thermal decomposition profiles were consistent with the proposed formulations. Powder XRD studies showed that all the complexes were amorphous in nature. By antimicrobial studies these complexes exhibited more activity than the ligand itself. The DNA cleavage activity of the ligand and its complexes were assayed on CT DNA using gel electrophoresis in the presence of  $\text{H}_2\text{O}_2$ . The Eu(III) and Nd(III) complexes completely cleaved the DNA. The anticancer activities of the complexes were studied towards human cervical cancer cell line (HeLa) and colon cancer cells (HCT116) and it was found that the Eu(III) and Nd(III) complexes were more active than the corresponding Gd(III), Sm(III), Tb(III) complexes and the free ligand on both the cancer cells [22].

A novel microwave-assisted method was developed to synthesize a series of ruthenium-thiosemicarbazone complexes. The new thiosemicarbazone ligands are derived from benzo[*d*][1,3]dioxole-5-carbaldehyde (piperonal) and the complexes are formulated as [(diimine) $_2$ Ru(TSC)](PF $_6$ ) $_2$  (where the TSC is the bidentate thiosemicarbazone ligand). The diimine in the complexes is either 2,2'-bipyridine or 1,10-phenanthroline. The complexes have been characterized by spectroscopic means (NMR, IR and UV-vis) as well as by elemental analysis. Biophysical characteristics of the complexes by investigating their anti-oxidant ability as well as their ability to disrupt the function of the human topoisomerase II enzyme. The complexes are moderately strong binders of DNA with binding constants of  $10^4 \text{ M}^{-1}$ . They are also strong binders of human serum albumin having binding constants of the order of  $10^4 \text{ M}^{-1}$ . The complexes show good *in vitro* anticancer activity against human colon cancer cells, Caco-2 and HCT-116 and indeed show some cytotoxic selectivity for cancer cells. The IC $_{50}$  values range from 7 to 159  $\mu\text{M}$  (after 72 h drug incubation). They also have antibacterial activity against Gram-positive strains of pathogenic bacteria with IC $_{50}$  values as low as 10  $\mu\text{M}$ ; little activity was seen against Gram-negative strains. It has been established that all the compounds are catalytic inhibitors of human topoisomerase II [23]. [Cu(HL)Cl $_2$ ] complexes of chalcone-derived thiosemicarbazones were obtained with 3-phenyl-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone (HPyCTPh), complex (1), 3-(4-chlorophenyl)-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone (HPyCT4ClPh), complex (2), 3-(4-bromophenyl)-1-pyridin-2-ylprop-2-en-1-one thiosemicarbazone (HPyCT4BrPh), complex and 3-(4-nitrophenyl)-1-pyridin-2-ylprop-2-en-1-one thio semicarbazone (HPyCT4NO $_2$ Ph), complex showed interaction with bovine serum albumin (BSA) and deoxyribonucleic acid from calf thymus (CT-DNA) [24]. The cytotoxic activities of the thiosemicarbazones and complexes were tested against HL60 (wild type human promyelocytic leukemia), Jurkat (human immortalized line of T lymphocyte), MDA-MB 231 (human breast carcinoma) and HCT-116 (human colorectal carcinoma) tumor cell lineages. Upon coordination to copper (II) cytotoxicity significantly increased in



Jurkat, MDA-MB 231 and HCT-116 cells. Unlike the free thiosemicarbazones induced DNA fragmentation in solid tumor cells indicating their pro-apoptotic potential [25].

A family of 2-pyridineformamide-derived thiosemicarbazones and their gallium (III) complexes were tested against several isolates of pathogenic *Cryptococcus* strains. On complexation the antifungal activity significantly increases, suggesting coordination to gallium (III) to be an interesting strategy of antifungal dose reduction [26].

### 3. Importance of metal complexes

The coordinating chemistry of lanthanides, relevant to the biological, biochemical and medical aspects, makes a significant contribution to understanding the basis of application of lanthanide chelates, particularly in biological and medical systems. The design of organic ligands in the optimization of the specific properties [optical, luminescence, paramagnetic, biological (ant-viral, anti-tumor and anti-inflammatory)] of the lanthanide complexes for biomedical applications received more attention in the last decades. Found on the physical and spectral properties, lanthanides have numerous applications, such as fluorescent probes in biological assays.

Recently some Ln(III) ion {especially Gd(III)} widely used in Magnetic Resonance Imaging (MRI). It is the most important and prominent technique in diagnostic clinical medical and biomedical research (cancer diagnosis, photodynamic therapy, drug/gene delivery, biosensing and bioimaging). Praseodymium is a component of an alloy named misch metal which is used for manufacturing cigarette lighters. It is used as an alloying agent in other stronger metal alloys that are being specially used for manufacturing aircraft engines. In these alloys, it is mostly used along with magnesium. The oxides of all praseodymium have excellent refractory property. For this reason, along with other rare earth metals, it is a part of the core material of carbon arc lights which are popularly used in movie industry of the purpose of projection and studio lighting. Salts of praseodymium have a major role in glass and enamel industry. Here, it is used with a few other substances to add an intense yellow color to the manufactured glasses and enamels.

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