LITERATURE REVIEW ON SCHIFF BASES

Abstract

Schiff bases, derived from condensation reactions between primary amines and carbonyl compounds, have garnered substantial attention in the literature. This comprehensive review explores the diverse applications and synthetic methodologies of Schiff bases, emphasizing their significant role in medicinal chemistry, catalysis, and material science. The study delves into the structural aspects, elucidating the impact of substituents on the properties and reactivity of Schiff bases.

Noteworthy advancements in Schiff base research include the development of novel synthetic strategies, such as green and sustainable methodologies, enhancing their eco-friendly profile. The review scrutinizes the biological activities exhibited by Schiff bases, ranging from antimicrobial to anticancer properties, underscoring their potential in drug discovery. Additionally, the integration of Schiff bases into metal complexes is explored for its catalytic applications.

The literature also highlights recent breakthroughs in the design and synthesis of Schiff base-based materials with unique electronic and optical properties. Furthermore, insights into the mechanistic aspects of Schiff base reactions and their underlying kinetics contribute to a deeper understanding of their behavior.

Keywords: Schiff bases, condensation reactions, medicinal chemistry, catalysis, material science, synthetic methodologies, green chemistry, biological activities, metal complexes, catalytic application.

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"What is there in the name?",it's a common satirical idiom, but the Co-ordination chemistry is the name which is enough to tell its importance in various scientific fields. Co-ordination chemistry concerned with the formation of compounds by interaction of ligands with the various metal ions. The condensation products of amino compounds and carbonyl compounds named 'Schiff bases" have been attracted the attention of all organic ,inorganic and analytical chemist in the recent years. The reason behind this is that the Schiff bases are referred as so called "fortunate ligand' for many transition and inner-transition metal ions, and such coordination compounds have been extensively proven useful in various research fields. The fascinating feature of this class of ligand is the presence of azomethine linkage, because of which it has many biomedical applications such as ,anticancer, diuretic, anti-tumour, anti-HIV agents[1-4] .

The symbiotic synergy between Aromatic Schiff bases and their intricate metal companions orchestrates a harmonious ballet of catalytic transformations encompassing oxygenation, hydrolysis, electro reduction, and decomposition, as documented in references [5-7]. Noteworthy are the transition metal ion complexes ,where Schiff base adorned polymers emerge as catalytic virtuosos, choreographing the delicate pas de deux of hydrogen peroxides decomposition and ascorbic's acid oxidation. An additional intrigue unfolds with the revelation of the multifaceted catalytic prowess of cyanohydrins cobaltite, a discovery of paramount significance[8].

Series of transition metal complexes have been synthesized from '4-(1-4-(hydroxyl-3-methoxy-bezylidine –amino)phenyl)ethtylidene-amino)-1-pyrazole-3-one'.The study of these metal complexes have been shown that the co-ordination sites were Oxygen of the carbonyl group and Nitrogen of the Azomethine group. On complete study of all transition metal complexes Octahedral geometry have been recommended[9].

A ground-breaking series of novel transition meatal complexes has been successfully synthesized ,showcasing the versatility and potential of complexes of Cu(II), Co(II), Mn(II), Fe(II), Ni(II) and V(II) as key players in the realm of coordination chemistry. These remarkable complexes were meticulously crafted by employing a Schiff base derived from artful fusion of 5-Bromo-2-hydroxy Benzaldehyde and Aniline in alcohol medium. This Synthetic endeavour not only illustrates the ingenuity of molecular design but also underscores the precision of modern chemical synthesis techniques .All the prepared metal complexes were then analysed from the analytical data obtained from the NMR,IR. The prepared complexes were then subjected to the biological activity like ant-bacterial activity and these complexes exhibited good anti-bacterial properties[10].The proposed structure of metal complex of Schiff base is (Figure 1):

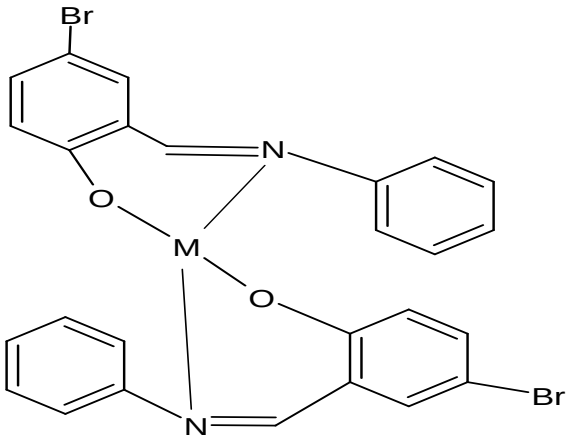

Figure 1: The Proposed Structure of Metal Complex of Schiff Base

A research paper entitled "Synthesis, Characterisation and biological properties of newly prepared Sc(III),Y(III),La(III), and Ce(III) complexes with the two ferrocenyl ligands of 1,1'-bis(2-thienylmethylidene)hydrazono-1-ethylferrocene and 1,1'-bis(2,3-dihydro-2-methyl benzothiazol-2-yl)ferrocene" mentioned that these organometallic compounds are potential ligands for lanthanide metals. All prepared complexes shows remarkable antibiotic activity. Scandium compounds have been found effective towards Salmonella Spp. and also found to have inhibition activity against *B.Subtillis* more than the standard drugs[11].'

' Li-Hua Wang, Lei Liang, Peng-Fe Li' have been synthesized a novel Eu(III) complex .This complex has been characterised on the basis of analytical data obtained from the NMR, IR , X-ray crystal diffraction methods and has good luminescence properties[12].

Schiff bases obtained from the Salphamethoxazole and Salicylaldehyde and Thiophene -2-Aldehyde complexed with many inner-transition metal ions such as La(III), Ce(III), Pr(III), Nd(III), Gd(III), Dy(III), Ho(III) and Er(III) have been synthesized and characterised on the basis of IR,NMR,UV-Visible Spectroscopy and Molecular weight determinations. It has been found that the Schiff bases acts as Monobasic bidentate ligands and rendered the metal eight- coordinated .These complexes have also shown greater efficacy than the Schiff bases against insects such as Cockroaches[13]

Emerging as a promising frontier, macro cyclic Schiff bases stands as a novel class of compounds, Showcasing their prowess as superior mediators for trans-metalation alongside select transition elements. A pioneering study by 'KhaliL K Abid &David E.Fenton' has unveiled the captivating realm of lanthanide complexes intertwined with these macro cyclic Schiff bases ,unveiling their remarkable kinetic lability that paves the way for trans-metalation interactions, particularly with Cu(II). This innovative research heralds a breakthrough, offering a glimpse into the dynamic dance of metal ions within these intricate molecular landscapes. The ingeniously illustrated structure, elegantly portrayed in Figure 2, encapsulates the essence of this transformative chemistry, bridging the realm of imagination and scientific exploration.

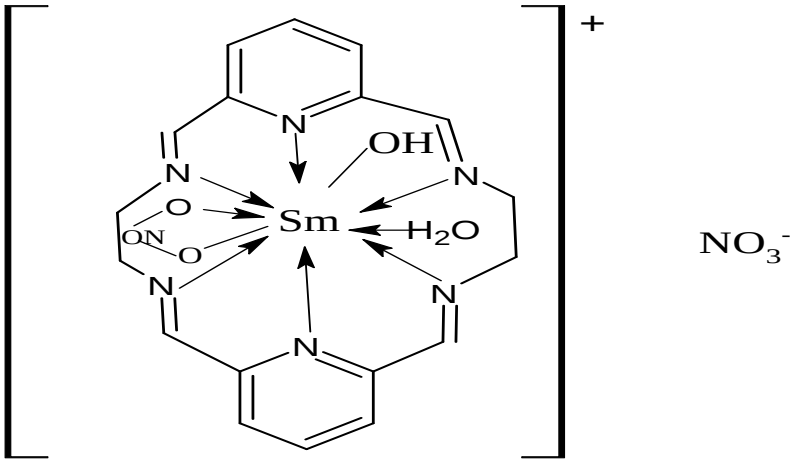

Figure 2: Schematic Representation of Macrocyclic Schiff bases and Metal Complex

Luminous and captivating, lanthanide complexes have long dazzled the scientific community, gracing countless pages of literature. In an ingenious endeavour,. 'Lada Puntus' and colleagues have orchestrated the synthesis of Schiff base-derived lanthanide complexes ,unveiling their mesmerizing dance in both 1:1 and 1:2 (Metal: Ligand) stoichiometric ratios. This symphonic creation emerged through the artful condensation of pyridoxal with Aspartic acid and L-Histidine .The spotlight shines on the lanthanoid Eu(III), casting its radiance upon the stage of optical spectroscopy and X-ray crystal diffraction. These observations reveal a breath-taking spectacles-an intricately distorted square anti-prism environment ,woven from the phenolic oxygen of pyridoxal, the nitrogen atom of carbon-nitrogen double bond ,the carboxylate groups of His and Asp, and the delicate tendrils of water molecules. A tetrahedral geometry emerges, birthing these complexes as luminescent marvels that enchant and inspires [15].

Two new Schiff bases containing olefin linkages were prepared from condensation of o-substituted aromatic amines with dicinnamoylmethane under special conditions .The existence of Schiff base ligands predominantly in the intramolecular hydrogen bonding with keto-enamine group [16].

In the research article by 'Sadeem M.Al-Barody & Hasina Ahmad' , the novel Schiff base N,N'-di-(4'-pentyloxy benzoate –salicylidene -)1',3'-diamino propane and their lanthanide complexes have been prepared. Investigation study shown the existence of two forms of ligands one is bidentate through the deprotonated phenolic oxygen and azomethine nitrogen competed seven co-ordinated which revealed that stoichiometry of the compounds depend on the number and different lengths of the terminal chains.[17].

'Kavitha Andiappan , Amandhavelu Sanmugam , Dhanasekaran Vikraman', prepared novel Schiff base ligand "N^2,N^3-bis (Anthracene-9-ylmethylene) pyridine-2,3 –diamine through the condensation of 2,6-diaminopyridine & Anthracene-9-Carbaldehyde" in 1:2 ratio. The analytical data obtained from FT-IR spectroscopy shown that the ligand was neutral bidentate ligand and bounded to the metal ions via two azomethine Nitrogens. Their lanthanide complexes with Pr, Er revealed that these compounds possess excellent anti-cancer activity against Vero, MCF7, and Hela cancer cells. Therefore these complexes can be a novel anti-tumour agents for humans[18].

Lanthanide complexes of Eu(III), Gd(III), Nd(III), Sm(III), and Tb(III) with the Schiff base derived from glcylglycine and 4-nitrobenzaldehyde were synthesized and characterized by various physico-spectral techniques. These complexes were then screened for anti-bacterial activity and anticancer activity. IR data shown that Schiff base ligand acts as tri-dentate monobasic ligand co-ordinated through azomethine nitrogen ,Peptide nitrogen, carboxylato Oxygen atoms. The Nd(III) complex has shown better efficacy against the gram negative bacteria such as *E.coli* as compared to the other complexes and free ligand. DNA cleavage study of the complexes has shown that the Eu(III) and Nd(III) complexes completely cleaved the DNA. Instead they did not have greater efficiency as compared to the well-known anti-cancer agents such as Cis-platin but can be acts as a potent anticancer agents on the cancerous cells[19].

Fluorescence study of Lanthanide complexes with the novel Schiff base have been reported. It was observed that under the excitation the Nd and Er complexes shows characteristic fluorescence[20].

In a pioneering endeavour 'Hitesh Patel, S .Bhutadiya, Jabli. J. Vora , Toral H.Yadav' embarked on a quest to synthesize inner-transition metal complexes featuring La(III), Ce(III), Pr(III) harmoniously entwined with a Schiff base born from the union of Anthranillic acid and Salicyaldehyde .The resulting intricacies were meticulously explored through an analytical symphony encompassing IR, UV-Visible ,NMR ,Magnetic moments and Thermal conductivity. The TGA Study unveiled a world of higher activation energies, hinting at catalytic prowess harboured by these complexes. Their multifaceted capabilities extended even further,as antibacterial trials showcased an elevated antimicrobial prowess compared to the standard a Schiff base drug Ciprofloxacin. The orchestration of these remarkable findings in encapsulated in the envisioned structures of the diverse lanthanide Schiff base complexes, elegantly portrayed in figure 3 and figure 4 ,laying bare a visual testament to their transformative potential[21]

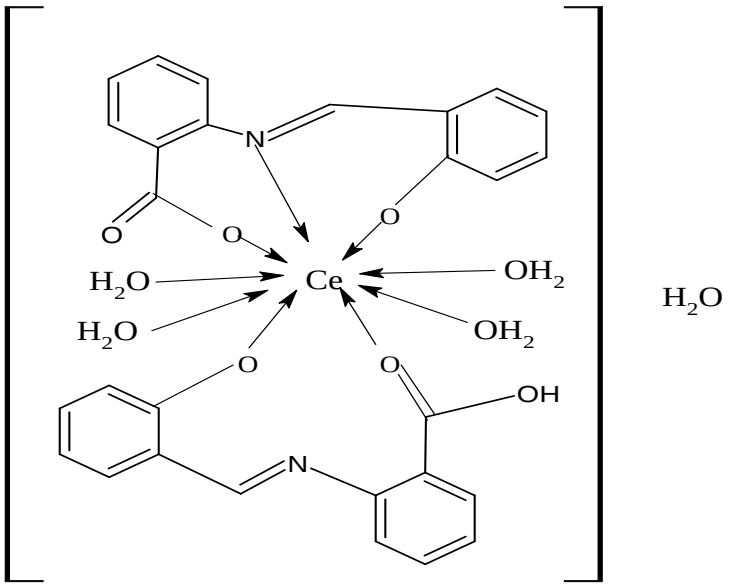

Figure 3: Cerium Complex of Schiff Base

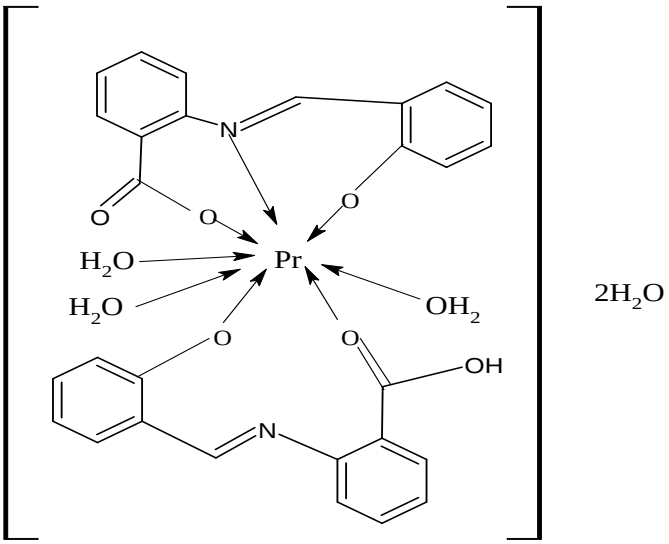

Figure 4: Praesodynium Complex of Schiff Base

Napthalene Schiff based compounds were synthesized by a condensation reaction of 1,5-Diamino naphthalene and 2-Hydroxy -3-Methoxy benzaldehyde. The inner-transition metals such as La(III) and Er(III) were chosen for complexing with the prepared Schiff base .The outcome from the data suggested that the complexes have tricapped trigonal prismatic geometry . The ligation through the Oxygen atom of –OH and azomethine nitrogen and five water molecules were out of the co-ordination sphere. The coordination number assigned was 9.These complexes were also screened for the antimicrobial activities and these complexes has shown excellent bactericidal potency and can be used as potent bactericidal agent [22].

In a comprehensive exploration, Alessia Cataleno' and collaborators delved into the intricate landscape of metal complexes bearing Schiff bases, unveiling their emergence as formidable anti-proliferative agents. The study illuminated how these Schiff base ligands, in harmonious union with diverse metal ions, wield a potent pharmacological arsenal, enhancing the efficacy of existing drugs. With a rich history as privileged ligands in organic synthesis, Schiff bases have now stepped into the limelight as pivotal tools for drug modification. Notably, the study shed light on the compelling potential of lanthanides and actinides as novel anticancer and anti-tumour agents, presenting a promising vista for medical advancements. Most strikingly ,these complexes have taken centre stage as prominent, contenders in the realm of liver cancer treatment , showcasing remarkable anti-proliferative activity against hepatocellular carcinoma-a beacon of hope in the fight against this formidable disease.[23]

'Sathiyanarayanan et al.' reported a series of Lanthanide(III) complexes with Schiff base particularly Pr, Sm, & Yb . In Vitro activity studies by MTT assay have been shown that compounds were active against Hela tumour cells. These compounds being the most active with an IC_{50} values equal to 34 microgram/millilitre[24].

Lanthanide complexes with Schiff bases have been extensively studied for their thermal and electrochemical properties. Cyclic voltammetry have been employed for the study of electrochemical properties. The influence of p^H on cyclic voltamograms indicated that there is increase in the nucleophilicity of organic compounds and anti-oxidant properties

is thermodynamically favoured with the increase in p^H . These complexes also shown promising results for the antibacterial and antifungal activities[25].

'Jing Xie et al' have isolated two novel complexes of lanthanides (La,Ce) with hydrazone Schiff base. The results obtained indicates that the two complex exerts considerable cytotoxic activity against three cancer cell lines i.e. Human lung cancer cell line A549, and human gastric cancer cell lines BGC823 and SGC7901. Therefore these complexes may be a useful tools for biomedical applications such as human cancer therapeutic fields[26].

The review paper by 'Wali A.Z'., focused the biological activities of Schiff base and their complexes. This paper enlighten the use of Schiff bases in the synthesis of many organic compounds. This review paper also includes various antimicrobial activities such as anti-fungal, anti-malarial, anti-inflammatory, anti-viral and anti-pyretic properties[27] .

The intricate dance of complex formation finds a pivotal partner in stability constants, orchestrating a delicate equilibrium that extends its influence to biological activities. A compelling symphony of scientific inquiry led by 'S.G.Shankarwar and associates' has unfurled an illuminating exploration into the stability constant of lanthanide complexes interwoven with Schiff bases.These Schiff bases derived from the condensation of Salicyalhydrazid with 4-Methoxy benzaldehyde,3,4,5 trimethoxybenzaldehyde and furfuraldehyde,became the protagonists of this study. Though meticulous potentiometric analyses conducted in a 40%THF-Water mixture and 0.1 M sodium perchlorate, the stability constants of these lanthanides were unveiled. A captivating revelation emerged as lanthanides gracefully choreographed 1:1 and 1:2 complexes with all the Schiff bases marked by a dramatic shift in log k at the enigmatic point of Gadollinium. This intricate narrative offers insight into the binding predilections of rare earth metal ion, as they harmoniously embrace oxygen atoms and tenderly caress nitrogen moieties within the Schiff bases- an enthralling revelation that augments our understanding of complexation dynamics.[28].

'S.Vidya Sagar Babu , K.S.V Krishnarao ,Yong Ill Lee', studied the luminescence and DNA binding properties of Ln(III)-Schiff base family. They synthesized penta-dentate Schiff base ligand containing N_3O_2 donor set. The Schiff base complexed with rare earth metals such as Pr, Nd, Sm and Eu. The analytical data obtained suggests that the ligand binds through two naptholic oxygen atoms, two azomethine nitrogen atoms, and one primary amine. IR study revealed that the nitrate groups present as ionic and co-ordinating ligands. Two water molecules are also incorporated in the co-ordination sphere. The complex are found to have good chelating ability and acts as a chromophore and can be used to absorb and transfer energy to lanthanide ions. These complexes also proved better binding capacity with DNA ,therefore regarded as efficient intercalators of DNA[29].

'Ahmed A. El-Sherif, Taha M.A.Eldebss', have been synthesized a novel Schiff base ligand and complexed with transition metal ions such as Cu(II), Ni(II), Mn(II), Co(II) and Zn(II). They have been concluded that the metal ions are co-ordinated through azomethine Nitrogen and phenolic oxygen atoms via deprotonation forming stable six membered heterocyclic ring. This study also revealed that the formation of complexes was spontaneous , exothermic and entropically favourable. Molar conductance studies suggested that complexes were of non-electrolytic in nature. The synthesized complexes have been subjected for the antimicrobial properties and results shown that these exhibits better

inhibition activity as compared to the parent ligand[30].The suggested structure of Schiff base ligand and its metal complexes where M=Cu(II), Ni(II), and Zn(II) (Figure 5)

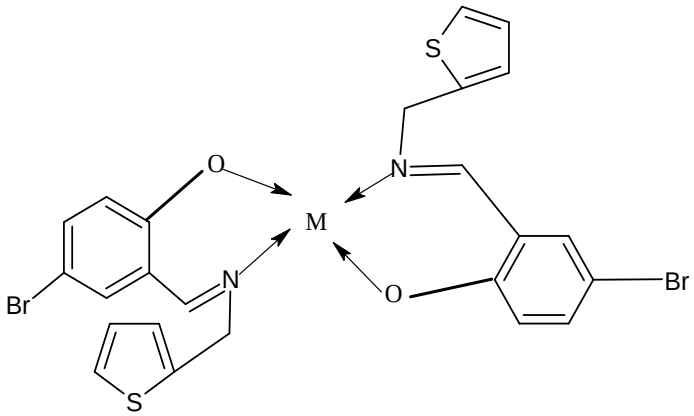

Figure 5: The Suggested Structure of Schiff base Ligand and its Metal Complexes where M=Cu(II), Ni(II), and Zn(II)

Embarking on an innovative path, a duo of novel Schiff bases enriched with a benzothiazole derivative emerged from the crucible of synthesis. These meticulously crafted Schiff bases then embarked on a transformative journey, forging intricate bonds with the inner-transitions elements ,Ce(III), Nd(III) and Pr(III). A fascinating orchestration was uncovered ,wherein the central metal ion orchestrated an elegant octet dance, embraced by the symphony of two ligand units, each in a harmonious tetra-dentate fashion. Casting a keen eye on the broader canvas of biological interactions, these complexes underwent probing examinations in the realm of cytotoxicity. Their positive charge reverberated in a captivating interaction with bacterial cells, unravelling a promising narrative of anti-bacterial activity primed to combat skin infections and food poisoning. As the curtain rises on microbial encounters, the ligands and complexes take centre stage, exhibiting their mettle against the backdrop of both gram-positive and gram-negative microbial culture, painting an inspiring tableau of potent results against pathogenic adversaries [31]. The intricate molecular tapestry of select metal complexes is unveiled, inviting our gaze to figures 6, 7 and 8 where their transformative architecture comes to life.

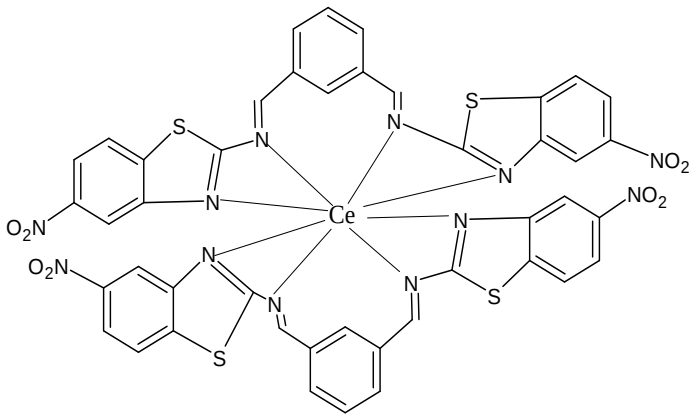

Figure 6: Ce Metal Complex

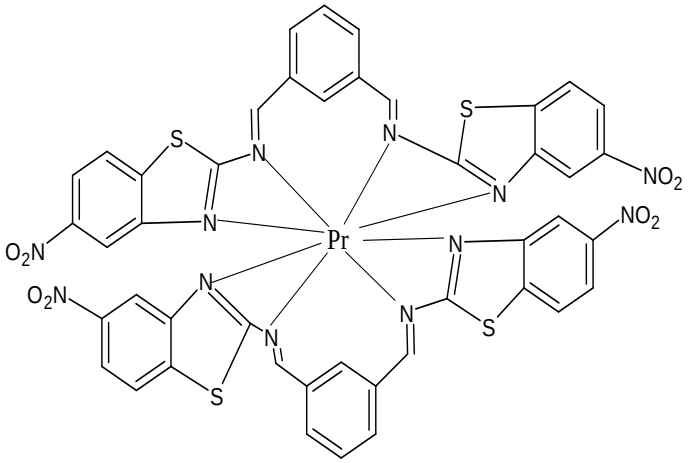

Figure 7: Pr Metal Complex

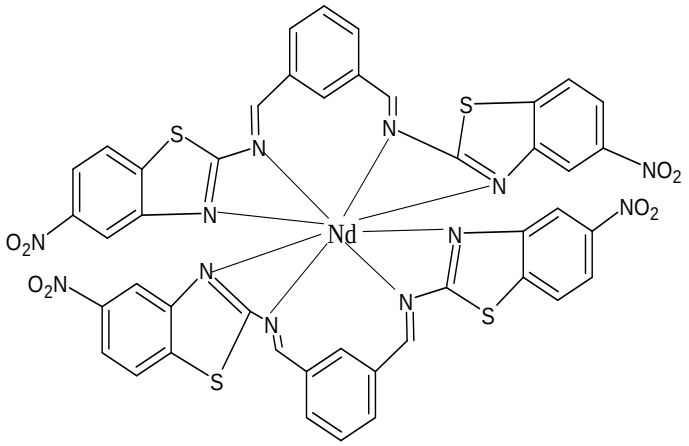

Figure 8: Nd Metal Complex

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