SYNTHESIS AND SPECTRAL STUDIES OF PLATINUM GROUP METAL COMPLEXES COMPRISING $\eta^5$- AND $\eta^6$-CYCLIC $\pi$-PERIMETER HYDROCARBONS WITH MULTIDENTATE NITROGEN DONOR LIGANDS

ABSTRACT

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY
IN
CHEMISTRY

BY
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The bond between metal and at least one carbon atom of an organic compound is defined as organometallic chemistry. There is some intense research in this field of chemistry with its innumerable applications. The realistic example of this type of compounds is vitamin B12. The first organometallic compound i.e., cacodyl was synthesized in 1760 containing arsenic as metal and the bond is σ bond. Later in 1827 W.C. Zeise synthesized another organometallic compound with metal to carbon π bond i.e., Zeise's salt of platinum metal. Synthesis of diethylzinc by E. Frankland in 1848 and discovery of nickel carbonyl by L. Mond in 1890 has brought immense attention towards metal carbon bonds. Serendipitous discovery of ferrocene by Pauson and Kealy and independently by E.O. Fischer and consequent characterization of its sandwich structure by R.B. Woodward and G. Wilkinson brought new dimensions in organometallic chemistry introducing sandwich compounds. Organometallic complexes found number of applications in catalysis and as reagents notably Grignard reagent using magnesium, Ziegler-Natta catalyst using aluminium, Heck reaction using organo palladium, Noyori catalyst and Grubbs catalyst using ruthenium. There are some potential achievements with this organometallic chemistry which are honoured by Nobel prizes in the 21st century viz., (1) W.S. Knowles, R. Noyori and Karl Barry Sharpless for asymmetric hydrogenation in 2001 (2) Y. Chauvin, R. Grubbs and R. Schrock on alkene metathesis in 2005 and (3) R. F. Heck, E. Negishi, A. Suzuki for palladium catalyzed cross coupling reactions in 2010 which emphasizes the importance of organometallic compounds. The utilization of organometallic complexes is not limited for chemical conversions but also found use in curing diseases. Among the noted examples are Paul Ehrlich’s arsenic based organometallic compound Salvarsan for the treatment of syphilis and titanocene dichloride (Cp2TiCl2), the first non-platinum organometallic complex to undergo clinical trials as a chemotherapy drug. Half-sandwich organometallic complexes possessing good amount of cytotoxicity with their different mechanism of action than the cisplatin in chemical biology.
Chapter 1

Introduction

Chapter 1 describes about the general introduction of the arene $d^6$ metal complexes and detailed description of arene $d^6$ metal complexes. Precisely the potential applications of arene $d^6$ metal complexes in the field of biology and catalysis has mentioned. Material and methods for the synthesis of compounds, techniques for characterization of the compounds are described. The biological and structural characterization methodologies for the biological activities and computational studies have described that generalizing for all the chapters 2-7.
Chapter-2

Arene ruthenium {1, 3, 5-tris(di-2-pyridylaminomethyl)benzene} complexes: Synthesis, structural and in vitro functional characterization

Mono-, di- and tri-nuclear half sandwich ruthenium complexes with 1,3,5-tris(di-2-pyridyl aminomethyl) benzene have been synthesized, characterized and their activity over four pathogenic bacteria and four cancer lines have been assessed. Antibacterial activity against four bacteria viz Staphylococcus aureus MTCC96; Escherichia coli MTCC739; Klebsiella pneumonia MTCC2653 and Pseudomonas aeruginosa MTCC2453. Antiproliferative activity against four cancer cell lines viz B16F10 (Mouse melanoma carcinoma), THP-1 (Human acute monocytic leukemia), PC3 (Human prostate carcinoma) and SK-OV-3 (Human ovarian carcinoma).
Chapter-3

The in vitro antitumor activity of oligo-nuclear polypyridyl rhodium and iridium complexes against cancer cells and human pathogens

Oligo nuclear polypyridyl half sandwich rhodium and iridium complexes have been synthesized and characterized. Their activity over four pathogenic bacteria and four cancer lines has been assessed. Antibacterial activity has been estimated against four bacteria viz. Staphylococcus aureus MTCC96; Escherichia coli MTCC739; Klebsiella pneumonia MTCC2653 and Pseuedomonas aeruginosa MTCC2453. Antiproliferative activity has been evaluated against four cancer cell lines viz. B16F10 (Mouse melanoma carcinoma), THP-1 (Human acute monocytic leukemia), PC3 (Human prostate carcinoma) and SK-OV-3 (Human ovarian carcinoma).
Chapter-4

Synthesis, structural, DFT studies and antibacterial evaluation of Cp* rhodium and Cp* iridium complexes using dipyridyl ketone based hydrazone ligands

Water soluble half sandwich 9th group mono- and di-nuclear complexes of dipyridyl ketone based hydrazone ligands (L1-L3) have been synthesized, characterized and their structural studies and antibacterial activity against four bacterial strains viz Staphylococcus aureus; Klebsiella pneumonia / B. thuringensis; Escherichia coli; Pseudomonas aeruginosa have been observed. The HOMO-LUMO gap for the complexes 1-4 has been rationalized by the DFT.
Abstract

Chapter-5
Synthesis, structural and biological studies of half-sandwich d\textsuperscript{6}-metal complexes with pyrimidine-based ligands

Reaction of 2-mercaptopyrimidine with rhodium and iridium dimers yielded four-membered metallacyclic complexes. These complexes exhibited considerable cytotoxicity and antibacterial activity. The selectivity index of these complexes is highest in the case of colorectal cell lines \textit{i.e.} HT-29 and BE. 2-amiono pyrimidine yielded binuclear complexes with rhodium and iridium but potent toxicity has not been found for these complexes. Computational and biophysical studies additionally supported the experimental results.
Chapter-6

Synthesis and biological studies of ruthenium, rhodium and iridium metal complexes with pyrazole-based ligands displaying unpredicted bonding modes

Mono, bis and bridged half-sandwich platinum group metal complexes with thienyl pyrazole and furyl pyrazole have been synthesized and their activity over four bacterial strains and interaction towards biomolecule (CT-DNA) have been assessed. Orbital occupancy and energy gaps between HOMO and LUMO on complexation have been rationalized by the density functional theory (DFT). *Staphylococcus aureus; Bacillus thuringiensis; Escherichia coli* and *Pseudomonas aeruginosa* have been considered for antibacterial activity. CT-DNA has been chosen as a biomolecule to elucidate the possible interaction between the new complexes and biomolecule.

Mono/bis substituted Complexes

Bridged Complexes
Chapter-7

Half-sandwich d^6 metal complexes with bis(pyridine carboxamide)benzene ligand: Synthesis and spectral analysis

Mono- and bi-nuclear half-sandwich d^6 metal complexes with bis(pyridine carboxamide)benzene ligand have been synthesized and characterized. Complexes 2-6 are additionally studied by single crystal x-ray analysis. Complexation occurred by the deprotonation of the amidato nitrogen of the ligand by using the base sodium methoxide (NaOMe). The effect of base has not influenced in the case of heavier congener.